

**A RANDOMISED CONTROLLED TRIAL FOR
PRISM SPECTACLES FOR AGE-RELATED
MACULAR DEGENERATION: PRESCRIBING
STRATEGIES AND PREDICTIVE FACTORS FOR
SUCCESS**

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DECLARATION

No portion of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other university, or other institution of learning.

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Dedicated to my mum, for being
the brightest star guiding me
along the way.



*Fragancia única que dejo, fragancia sin
olor pero que perdura para siempre.*

*Lo que enseñó, lo transmitió con mucha
paciencia e ilusión.*

*Olvidarla imposible, bastaba mirarla a
los ojos para conocer su corazón,*

*Recuerdo es una palabra para grabar su
nombre, ya que siempre vivirá en nuestro
corazón.*

De sus alumnos

TABLE OF CONTENTS

ABSTRACT	6
CHAPTER 1	8
Age-related Macular Degeneration	
1.1 Introduction	8
1.1.1 Definition and classification	8
1.1.2 Epidemiology	12
1.1.3 Risk factors	14
1.1.3.1 Personal characteristics	14
1.1.3.2 Cardiovascular diseases	15
1.1.3.3 Environmental factors	16
1.1.3.4 Genetic factors	17
1.2 Medical and surgical treatment options	17
1.2.1 Elimination of neovascularisation	18
1.2.1.1 Laser photocoagulation therapy of extrafoveal or juxtafoveal CNVM.	18
1.2.1.2 Extraction of CNVM with and without transplantation of RPE	18
1.2.1.3 Macular translocation	19
1.2.2 Novel methods to treat neovascularisation	19
1.2.2.1 Photodynamic therapy (PDT)	19
1.2.2.2 Photochemical and thermal methods (Transpupillary thermotherapy)	20
1.2.2.3 Radiotherapy	21
1.2.2.4 Chemotherapeutic agents (Pharmacological Treatment)	21
1.2.3 Prevention of the neovascular response	22
1.2.3.1 Prophylactic laser to drusen	22
1.2.3.2 Diet and other risk factors	22
1.2.4 Future treatments	23
1.3 Impact of AMD	23
1.3.1 Visual impairment in AMD	23
1.3.2 Psychological impact	27
1.3.3 Factors affecting adjustment to low vision	27
1.3.4 Emotional reactions to loss of vision	29
1.4 Low vision in AMD	29
1.4.1 Low vision aids	30
1.4.2 Eccentric viewing and PRL	33

1.4.3	Determining the PRL	35
1.4.4	Steady eye strategy	36
1.4.5	Prism relocation	37
CHAPTER 2		43
Study design and non-clinical measures		
2.1	Aims of the study	43
2.2	Controlled randomised trial	45
2.3	Randomisation and masking	47
2.4	Sample size	47
2.5	Inclusion/exclusion criteria	48
2.6	Mini-Mental State Examination: MMblind	48
2.7	Patient recruitment	49
2.8	Reporting of the trial	51
2.9	Trial structure	51
2.10	Non-clinical measures	55
2.10.1	Quality of life	57
2.10.2	National Eye Institute Visual Functioning Questionnaire (NEI-VFQ)	59
2.10.3	Adaptation to Age-related Vision Loss Scale (AVL)	59
2.10.4	Melbourne Low Vision ADL index (weighted version)	60
2.10.5	Creating an interval scale: the Rasch model	61
2.10.6	Manchester Low Vision Questionnaire (MLVQ)	62
2.10.7	Diary	62
CHAPTER 3		64
Clinical measures		
3.1	Personal and background data	64
3.2	Visual functions	64
3.2.1	Visual acuity scoring for long distance	64
3.2.2	Bailey-Lovie reading chart	66
3.2.3	Single, crowded and repeated letter VAs	67
3.2.4	Perimetry (Bjerrum screen)	71
3.2.4.1	The area of scotoma	72
3.2.4.2	Evaluation of the NNPF position	73
3.2.5	Contrast sensitivity (Pelli-Robson)	73
3.3	Refraction	74

3.3.1	Subjective refraction	74
3.3.2	Prism prescription	75
3.3.3	Perceived disabilities and goals (MLVAI)	78
3.3.4	Low vision assessment	78
3.4	Dilation	79
3.4.1	Fundus photographs	79
3.4.1.1	Classification of AMD	80
3.4.1.2	Quantification of AMD	80
3.4.1.3	Evaluation of subfoveal damage	81
3.4.1.4	Evaluation of central fixation	81
3.4.2	Classification of cataracts (LOCS III)	81
3.5	Identifying fixation characteristics	82
3.5.1	Determining the static fixation position	83
3.5.1.1	Determining the position of the fovea	83
3.5.1.2	Determining the fundus magnification	86
3.5.1.3	Analysing the photographs	90
3.5.2	Dynamic Fixation	92
3.5.3	Eye-movement response to binocular prescribed prism	93
3.6	Frame and diary	95

CHAPTER 4 **97**

A description of the study population

4.1	Data management and quality	98
4.2	Demographics, patients' background information and cognitive status	99
4.3	Visual function data	101
4.3.1	Distance visual acuity	101
4.3.2	Near visual acuity	103
4.3.3	Single, crowded and repeated VAs data	104
4.3.4	Perimetry	106
4.3.4.1	Scotoma areas	106
4.3.4.2	NNPF positions	106
4.3.5	Contrast sensitivity	108
4.4	Refraction data	108
4.4.1	Conventional prescription results	108
4.4.2	Prism prescription results	111
4.4.3	Type of lenses prescribed	111

4.4.4	Reported disabilities	113
4.4.5	Low vision aids prescribed	114
4.5	Ocular pathology data	118
4.5.1	Classification of AMD	118
4.5.2	Quantification of AMD	118
4.5.3	Evaluation of subfoveal damage	120
4.5.4	Secondary ocular conditions	120
4.5.5	Classification of cataract	121
4.6	Central fixation data	122
4.7	Fixation stability, consistency and rod pursuit	123
4.8	Eye-movement response to prescribed prism	124

CHAPTER 5 **126**

Associations between visual variables

5.1	Characteristics of the three study groups	127
5.2	Magnifying power and visual acuity	127
5.3	Relationships between single, crowded and repeated letter	129
5.3.1	Crowded letter and conventional acuities	130
5.3.2	Crowded and single letter acuities	130
5.3.3	Repeated letter and prism acuities	131
5.3.4	Crowded and repeated letter acuities	133
5.4	AMD lesion size and scotoma area	134
5.5	NNPF and PRL	135
5.5.1	NNPF and PRL angular differences	135
5.5.2	NNPF and PRL distances from fovea	136
5.6	Cataracts and contrast sensitivity	137
5.7	Location of the fovea	138
5.8	PRL distance as a predictor of VA and Fixation quality	140

CHAPTER 6 **141**

Predicting the prescribed prism and the visual acuity improvement

6.1	Predicting the relocating prism	144
6.1.1	Predicting the prism power	146
6.1.2	Predicting the prism base direction	147
6.2	Predicting effectiveness of the treatment	148

CHAPTER 7

Discussion

156

7.1	Summary of the trial profile	156
7.2	AMD study population characteristics	156
7.3	Associations of visual variables in AMD	165
7.4	Predicting the prism	170
7.4.1	Determination of clinical characteristics of patients who would benefit from prism spectacles	171
7.4.2	Determination of the power and base direction of the optimal prism	172
7.5	The lack of prism effectiveness	174
7.6	Conclusions	175
7.7	Future research	177

APPENDICES

178

Appendix 1	Mmblind scoring sheet	178
Appendix 2	Patient contact letter with information sheet	179
Appendix 3	Patient consent form	184
Appendix 4	Patient last visit letter	186
Appendix 5	The orientation of the gap on Landolt-C optotypes	187
Appendix 6	Field test (Pilot testing)	191
Appendix 7	Prism prescription (Pilot testing)	202
Appendix 8	Elschnig ring	204
Appendix 9	Overlaying sheets to calculate location of fovea	206
Appendix 10	Effect of PRL distance on the angular difference between NNPF and prism base directions	207
Appendix 11	Calculation of angular differences	209
Appendix 12	Residuals vs Fitted plots and P-P plots for single regressions	212
Appendix 13	Prismatic effect of bifocals	216
Appendix 14	Supporting publications of the trial	220

REFERENCES

221

ABSTRACT

Purpose: To investigate the degree to which the optimal relocating prism can be predicted from clinical vision measures and to define the clinical characteristics of patients with age-related macular degeneration (AMD) who benefit from prism spectacles as part of a randomised controlled clinical trial to investigate the effectiveness of prism glasses in reducing disability.

Participants: Two hundred and forty three patients with AMD, 157 females and 86 males between 56 and 97 years of age and with binocular visual acuity (VA) between 0.42 and 1.68 logMAR were recruited at the Manchester Royal Eye Hospital.

Methods: A subjective refraction, including prescription of relocating prism, was carried out. Visual functions included distance and near VA, contrast sensitivity and kinetic perimetry (Bjerrum screen). A low vision assessment identified the patient's goals, and distance and near low vision aids (LVAs) were prescribed. The lesion characteristics were identified, along with the degree of lens opacification. Static fixation characteristics were analysed from fundus photographs whilst the dynamic eye-movement response to prism was filmed on video.

Patients were randomised into 3 treatment groups (with prescribed, standard or placebo prism spectacles) and given the corresponding study spectacles to wear for 3 months. The primary outcome measure was an improvement in VA defined as the difference between VA wearing the study spectacles after the 3 months and VA with conventional spectacles at the time of collection.

Results: The subjectively chosen optimal relocating prism had a median value of 7.8Δ (range $2-23\Delta$) and the four cardinal positions were preferred by most patients for the prism base directions, with the up and left positions being mostly selected (44% and 15% respectively). Visual functions and the static position of fixation were investigated as prism predictors, and multiple regression analysis indicated that, distance VA and Bjerrum screen perimetry were found to be strong predictors of prism power ($\beta = 4.04$ and 0.19 , $p < 0.001$ and $= 0.009$ respectively, $r^2 = 0.22$). Similarly, Bjerrum screen perimetry was able to predict the prism base direction to an accuracy of 30° for 40% of the patients. Thirty four percent of eyes with a horizontal prism and only 10% with a vertical prism made a recovery eye movement, which would nullify the effect of the prescribed prism. Ten percent of patients had a VA improvement of at least 0.1 logMAR after the three months. Visual functions, lesion, fixation and prescription characteristics, duration of condition and patient's living independence were investigated as predictors of VA improvement. Associations were weak, although, distance VA and type of AMD were found to be the best predictors ($\beta = -0.08$ and 0.04 , $p = 0.02$ and

0.08 respectively, $r^2 = 0.05$). Finally, the preferred retinal positions used for eccentric viewing were the lower and left hemi-fields with respect to the position of the scotoma.

Conclusions: Only a small variance of the prism seems to be predictable from the visual variables and clinical characteristics measured in the study. It was also only possible to make minimal prediction of the visual acuity improvement that patients would obtain from the study spectacles after the 3-months wear. The fact that the most frequently chosen positions to relocate the image with prism were those already used by patients when eccentrically viewing suggests that they have successfully learnt how to find an optimal retinal location, therefore limiting the chances of success of the prism relocation technique.

CHAPTER 1

Age Related Macular Degeneration

A good understanding of Age-Related Macular Degeneration (AMD) is necessary to appreciate the need for the present trial and the expectations of the participants. This chapter discusses some relevant aspects about AMD and its current medical and surgical treatments. The psychological impact of the condition in patients and the low vision facilities available are also described.

1.1 Introduction

This first section defines the condition and reviews the different types of AMD. It also provides a summary of the epidemiology and risk factors of the condition.

1.1.1 Definition and classification

Age related Macular Degeneration (AMD) is the leading cause of blindness and severe vision loss among older people in the United States (Klein et al., 1992a), the United Kingdom (Gafour et al., 1983) and other western nations (Mitchell et al., 1995), affecting 25 to 30 million people (WHO, 1998). It is a degenerative disorder of the central area of the retina and is diagnosed by a certain degree of visual loss with the presence of drusen and retinal pigment epithelium (RPE) atrophy or changes associated with subretinal neovascularization in people over 50 years of age (Klein et al., 1992a). The disease is usually bilateral, although it is common to find different degrees of atrophy in the two eyes.

In 1985 Haab defined this condition as Senile Macular Degeneration (SMD) but this term is not used any more. Instead, Age-Related Maculopathy (ARM) or AMD are the preferred

terms. According to The International Age-Related Maculopathy Epidemiological Study Group (1995) ARM describes the early stages of the condition, whilst AMD would apply for later stages of the disease.

There is no universally accepted definition of AMD and the generic term of macular degeneration refers to a large number of fundus appearances. When the diagnosis of ARM is based on objective findings alone, there is little agreement about issues such as how many drusen constitute normal aging rather than an abnormality for a given age. The diagnosis of ARM or AMD implies the presence of a visual acuity deficit or a threat to visual acuity and, according to The International Age-Related Maculopathy Epidemiological Study Group (1995), ARM is defined as “a disorder of the macular area of the retina, most often clinically apparent after 50 years of age, characterised by morphological changes in the macula seen in colour fundus transparencies without indication that they are secondary to another disorder”.

The potentially devastating, precipitous loss of central vision caused by haemorrhage that is often associated with neovascular AMD can be preceded by a number of subjective vision complaints. Blurred central vision with distortion is the most common early symptom. However AMD patients may also experience distortion without blurring (metamorphopsia), image shrinkage (micropsia), flashing lights (photopsia), or a blind spot (scotoma). Many patients do not notice any symptoms because the better eye compensates for these symptoms in the affected eye (Schwartz, 2000).

The disease can be classified into the early and the late stages:

The early stage is characterized by the presence of drusen and pigmentary abnormalities of the RPE (hyperpigmentation and hypopigmentation). Drusen are one of the earliest signs of AMD and confluent drusen present a significant risk factor for progression to the late stages of the disease (Bressler et al., 1990; Klein et al., 1997). With age, the conductivity of Bruch's membrane diminishes with the accumulation of lipid debris within it. These sub-RPE deposits or drusen interrupt the interrelationship of the RPE and the choriocapillaris and thus the degenerative spiral gathers momentum. They are typically mucopolysaccharides and lipids that probably develop early in adulthood but are rarely visible until later in life. Early in their development, these drusen may be undetectable ophthalmoscopically because of their small size and relatively normal overlying RPE (Schwartz, 2000). As deposits enlarge and overlying RPE thins, drusen assume a yellow or grey colour and are easily detected. Drusen can be hard, which appear as small punctate deposits, or larger soft dome-shaped elevations. At this stage most individuals have excellent visual acuity and are relatively asymptomatic despite decreased ability to read in poor light and mild metamorphopsia or distortion (Eisner et al., 1987). Commonly, there is loss of contrast sensitivity out of proportion to the loss of visual

acuity. The early loss of contrast sensitivity is thought to be a predictor of severe visual loss and the magnitude of the visual loss is related to the severity of the disorder (Kleiner et al., 1988). Drusen are also associated with significant degenerative changes in adjacent photoreceptor cells, thus compromising their function and leading to a more severe stage of the disease (Johnson et al., 2003).

Later stages: As the pathology progresses we can find choroidal neovascularization, RPE detachment (blister) and scar tissue deposits (disciform scars)(Albert & Jakobiek, 1994). AMD can be classified as atrophic (geographic) AMD or neovascular AMD. Atrophic AMD and neovascular AMD may be either different manifestations of the same disorder or different disorders. These conditions may have different causes. Separating them is useful, especially when examining risk factors. Occasionally, neovascular AMD develops in an area adjacent to or within an area of geographic atrophy. Thus, it is worth emphasizing that these definitions do not imply a single etiological entity (Schwartz, 2000).

Atrophic AMD is also known as geographic atrophy, non-exudative AMD or dry AMD. Geographic atrophy is defined as one or more circumscribed areas of RPE loss with visible choroidal vessels. There are three kinds of geographic atrophy (Schwartz, 2000):

-Drusen-unrelated geographic atrophy is usually associated with hyperpigmentation and begins around the perimeter of the fovea, expanding around the foveal centre, but sometimes sparing the fovea (Figure 1.1).



Figure 1.1: *Example of drusen-unrelated geographic atrophy.*

-Drusen-related geographic atrophy is the most common type of atrophy. In this case, the degeneration of the RPE is always more advanced overlying drusen and the pattern of atrophy initially reflects the pattern of drusen. This type of geographic atrophy also tends to spare the foveal centre until late in the course of the disease (Figure 1.2).



Figure 1.2: *Example of drusen-related geographic atrophy.*

-Geographic atrophy that follows the collapse of an avascular RPE detachment or tear. Visual acuity can remain quite good during the RPE detachment but when the RPE fails, the detachment settles as the RPE fluid pump declines. Once this occurs geographic atrophy appears rapidly (Figure 1.3).

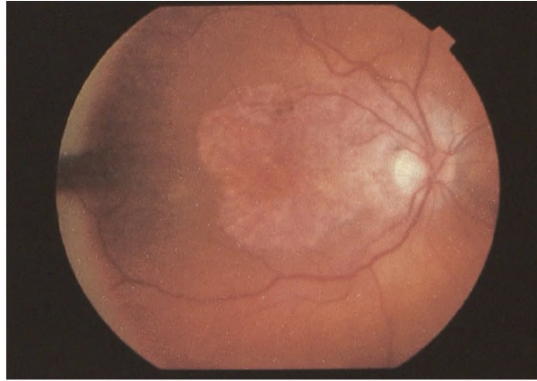


Figure 1.3: *Example of geographic atrophy following collapse of RPE detachment or tear.*

In all types of geographic atrophy, a slow reduction of visual acuity occurs, down to the 6/36 to 6/60 level. Atrophic AMD accounts for nearly 90% cases of AMD (Richer, 1999).

Neovascular AMD, also known as Exudative AMD and Wet AMD is identified by serous and haemorrhagic detachments of the RPE and retina caused by choroidal neovascularization (CNV). CNV is identified as the growth of abnormal new blood vessels from the choriocapillaris into the sub-RPE space, the subretinal space or both. This appears as a dome shaped elevation. This pathological angiogenesis is the basis of the disciform process, which results in cicatrization and loss of macular function: disciform scar (Bressler et al., 1988).

The Framingham Eye Study (Leibowitz et al., 1980) found that neovascular AMD only explained a minority (8%) of the AMD cases as compared to the atrophic type, which accounted for 80% of the cases and a 12% of unclassified cases. Although neovascular AMD is less common than geographic AMD, it accounts for approximately 85% of all patients suffering from severe visual loss (Edwards and Llewellyn, 1988). Thus, although most patients with AMD may not progress beyond the nonexudative stage, the small minority that do progress to the exudative stage are at greater risk to develop severe visual loss from this disease (Bressler et al, 1988). Also, this loss of vision is usually more rapid and generally occurs at an earlier age (Edwards and Llewellyn, 1988).

The atrophic type of AMD can occur in one eye with the neovascular type in the other eye (Klaver et al., 2001).

1.1.2 Epidemiology

Epidemiology is the study of the distribution and determinants of a disease, in our case AMD, and is usually studied by means of prevalence and incidence rates (Hatch, 1998).

Prevalence is defined as the proportion of cases in a population at one point in time, and is thus a static measure. Mathematically, $\text{prevalence} = \text{total number of cases} / \text{total population}$. For AMD, the number of affected cases increases with age but there is not an accepted age cut-off for studying prevalence in this disease. Comparisons between different studies are very difficult; since they have grouped patients into different age groups, different grading systems have been used and different degrees of pathology are considered to be the cut-off for AMD. Some of these studies include the Framingham Eye Study (Leibowitz et al., 1980), the National Health and Nutrition Eye Study (Golberg et al., 1988), the Copenhagen Study (Vinding, 1989) and the Chesapeake Bay Study (Bressler et al., 1990).

In 1991, Klein et al. developed the Wisconsin Age-Related Maculopathy Grading System (WARMGS), based on evaluation of stereoscopic 30° colour fundus photographs. Since its development, this grading system has become the gold standard for evaluation of AMD epidemiology. Later epidemiological studies have used this instrument, making some data comparison possible. The largest studies using this grading system include the Beaver Dam Eye Study (Klein et al., 1992a), The Rotterdam Study (Vingerling et al., 1995), The Blue Mountains Eye Study (Mitchell et al., 1995) and The Barbados Eye Study (Schachat et al., 1995). Table 1.1 shows the prevalence of AMD for different ages in these 4 large studies. They consistently show an increasing prevalence of AMD with age, increasing from 0-0.4 % for patients aged 40-50 to 11.0-18.5 % for those over 80 years of age.

Incidence is defined as the number of new cases for a given time period. Mathematically, $\text{incidence} = \text{new cases} / \text{population at risk (over 50 years of age)} \text{ per time period}$. Cohort studies are designed to consider the measurement of risk factor and disease by an alternative approach. In these type of studies, the risk factors of interest are determined before disease acquisition and the researcher then monitors the cohort over time to see how many individuals develop the disease (Hatch, 1998) and in that way, find the incidence rate. All the above-mentioned prevalence studies also followed the same cohort group of patients to investigate the incidence of new cases over the next several years.

Study	Number of patients	Age range (years)					Gender (75+)	
		43 - 54	55 - 64	65 - 74	75+	85+	Female	Male
The Beaver Dam Eye Study (Klein et al., 1992a)	4926	0.1	0.6	1.4	7.1	-	7.8	5.6
The Rotterdam Study (Vingerling et al., 1995)	6251	-	0.2	0.8	3.7 (75 - 84)	11.0	3.8	3.5
The Blue Mountains Eye Study (Mitchell et al., 1995)	3654	0	0.2	0.7	5.4	18.5	16.1 (ARM)	14.6 (ARM)
The Barbados Eye Study (Schachat et al., 1995)	3444	0.4 (40 - 49)	0.7 (50 - 59)	0.4 (60 - 69)	1.0 (70 - 79)	-	1.3	0.6

Table 1.1: AMD prevalence in different age groups (%) from recent epidemiological studies.

Study	Follow-up period	Number of patients	Age range (years)				
			43 - 54	55 - 64	65 - 74	75+	85+
The Beaver Dam Eye Study (Klein et al., 1997)	5 yrs	3583	0.0	0.3	1.3	5.4	-
The Beaver Dam Eye Study (Klein et al., 2002)	10 yrs	2764	0.1	1.0	4.4	9.5	-
The Rotterdam Study (Klaver et al., 2001)	2 yrs	4953	-	0	0.75	3.1 (75 – 84)	8.8
The Blue Mountains Eye Study (Mitchell et al., 2002)	5 yrs	2335	0	0.2	0.7	5.4	18.5
The Barbados Eye Study (Leske et al., 2004)	4 yrs	3193	0 (40 – 49)	0.6 (50 – 59)	2.4 (60 – 69)	5.4 (70 – 79)	-

Table 1.2: AMD incidence in different age groups (%) from recent epidemiological studies.

The difficulty when comparing data between these studies is that each followed their cohort group for a different period of time. In this way, the Rotterdam Study (Klaver et al., 2001) only followed patients for 2 years, whilst most studies followed them for 4-5 years (Klein et al., 1997; Mitchell et al., 1995; Schachat et al., 1995) or even 10 years (Klein et al., 2002). Table 1.2 shows the results for the incidence in these studies. As expected, the incidence increases with the follow-up time, e.g. for the age range 75+, incidence is only 3.1% for the 2 year follow-up study (Klaver et al., 2001) but increases to 5.4 % for a 5 year follow-up study (Mitchell et al., 1995) and to 9.5 % for the 10 year follow-up study (Klein et al., 2002). It can also be inferred from Table 1.2 that increasing age is a risk factor for AMD.

According to Klein et al. (1997) there is a higher risk of developing ARM in the fellow eye once the first eye has been affected. From those presenting with uniocular late stage ARM at baseline 22% developed late ARM in the fellow eye within 5 years. Similarly, Mitchell et al. (2002) also found that incidence for the development of late ARM in the second eye of participants with late ARM in one eye at baseline, was 26 times greater than the incidence of first eye involvement.

1.1.3 Risk factors

Although AMD is one of the leading causes of blindness in the developed countries (Ryan et al., 1999) and the incidence is expected to increase with the increasing life expectancy (Evans & Wormald, 1996), and to double in 35 years (Rosenthal & Kelly, 2001) there is little effective treatment for it. It is for this reason that there has been a large amount of research over the last decade aiming to find the risk factors for development of the disease. Avoiding risk factors would be a good way towards AMD prevention.

Risk factors have been studied to look for any possible association with AMD. Age seems to be the strongest factor and others include genetic factors, gender, cardiovascular disease, environmental factors, race and iris colour (Eye Disease Case Control Study Group, 1992).

1.1.3.1 Personal characteristics

Age

The condition is rarely seen before the age of 50. After the age of 50 the risk, and thus the incidence, increase steadily (see section 1.1.2). Nonetheless, ARM and AMD are not universal and although age is a strong risk factor, ARM and vision loss do not inevitably occur with advancing age.

Gender

Quite a few studies have implicated female gender as a risk factor AMD. As an example, in the Framingham Eye Study (Leibowitz et al., 1980) there was nearly twice the amount of women affected compared to men. Similarly, more recent studies (Klein et al., 1992a; Vingerling et al., 1995; Schachar et al., 1995) have shown a higher prevalence of AMD in women than men. In this way, for the +75 age range, AMD prevalence in women ranged between 1.3 and 7.8 %, and between 0.6 and 5.6 % for men (see Table 1.1).

Race

The Barbados Eye Study (Schachar et al., 1995), where 95% of the participants were blacks, had consistently lower rates of AMD prevalence when compared to other studies with a predominantly white population (Klein et al., 1992a; Vingerling et al., 1995; Mitchell et al., 1995) (see Table 1.1) therefore suggesting a higher prevalence of AMD in whites than in blacks. In contrast, another study from Klein et al. (1995) on racial/ethnic differences in AMD involving a large number of African Americans as well as white Americans found the prevalence higher for the black population when compared to whites only before the age of 60 and thereafter, the effect reversed.

Iris colour

Iris colour has been proposed as a risk factor for AMD (Sandberg et al., 1994) who found that AMD was more likely in light irides. On the other hand, there is no experimental evidence suggesting that more harmful light passes through a light coloured iris than a dark iris, since the epithelial pigment on the posterior iris absorbs the light and the Eye Disease Case Control Study Group (EDCCS)(1992) did not find such an association. However, Holz et al. (1994a) did report decreasing stromal iris pigmentation as a risk factor for AMD.

Refraction

Hyperopia was proposed as a risk factor in the Framingham Study (Leibowitz et al., 1980) but was not supported by the Watermen Study (Bressler et al., 1990).

1.1.3.2 Cardiovascular diseases

Different aspects of cardiovascular disease and its risk factors have been shown to be important factors for AMD and ARM. Important risk factors for cardiovascular disease are systemic hypertension, diabetes, high cholesterol and smoking (smoking is discussed under environmental factors).

The EDCCS reported that a high level of serum cholesterol (equal to or greater than 6.749 mmol/L) was associated with an increased risk of neovascular AMD. And the Macular Photocoagulation Study Group (MPSG) suggested that hypertension in patients with CNV

may be associated with higher rates of failed laser therapy (MPSG, 1993). Hyperglycaemia has also been reported to affect the normal structure and functioning of the RPE, Bruch's membrane, and the choroidal circulation. However, epidemiological studies have been inconsistent in proving any relationship between ARM and diabetes (Klein et al., 1992b and Klein et al., 1997). Furthermore, a recent cohort study (Klein et al., 2003) has shown a lack of association between hypertension, blood pressure, common carotid artery plaque, or any systemic inflammatory factors and ARM.

1.1.3.3 Environmental factors

Environmental factors seem to be linked to several age-related diseases such as cataracts (Javitt et al., 1996) and AMD. They are thought to produce oxidative stress (cellular damage caused by reactive oxygen intermediates), which decreases the macular pigment density and thus makes the retina more susceptible to degeneration (Beatty et al., 2001).

Smoking

Smoking has been widely demonstrated to be associated with AMD. Several large studies (Hyman et al., 1983; EDCCS 1992; Christen et al., 1996; Mitchell, P. et al., 2000) have reported a relationship between smoking and both early and late ARM. According to the MPSG (1986) smoking also increases the recurrence of CNV after treatment. Most studies place smokers at the three to four times higher risk than non-smokers for developing ARM and for progressing to the late, visually devastating forms of disease (AMD). On the other hand, a minority of smaller studies show no association between smoking and ARM (Maltzman et al., 1979; Hirvela et al., 1996), or even a decreased risk (West et al., 1989).

Alcohol

There are some studies reporting a possible relationship between alcohol and the risk of developing AMD. The Beaver Dam Eye Study (Ritter et al., 1995) reported an association between consumption of beer and ARM, but not for wine or spirits, or for overall alcohol consumption against AMD (Obisesan et al., 1998).

Light exposure

There is hardly any evidence that indirect exposure of the eyes to sunlight is in any way related to ARM or progression to AMD. One proposal suggests that the combination of blue light and lipid debris (lipofuscin) in the RPE space may act as a source of oxidative end products that could damage the RPE (Schwartz, 2000). The theory that cumulative damage from light toxicity may exceed the eye's ability to maintain normal function has not been supported by either the Chesapeake Bay Waterman Study (Bressler et al., 1990), the Eye Disease Case Control Study (1992), Hirvela et al. (1996) or Mitchell et al. (1995).

1.1.3.4 Genetic factors

Genetic predisposition is likely to be the strongest risk factor apart from advanced age. Seddon et al. (1997) proved a higher ARM rate among subjects with relatives suffering from ARM (24%) than those without a family history (11%).

Some genetic studies have tried to identify if there is any gene responsible for AMD. Neither TIMP3, nor ABCR have been shown to be related to AMD (Stone et al., 1998), although its mutations are responsible for Sorby's fundus dystrophy and Stargardt's disease respectively.

Another study (Schwartz, 2000) compared sibling pairs with spouses and demonstrated the concordance of macular drusen between siblings but not between spouses.

In conclusion, although a number of factors seem promising, only age and cigarette smoking are confirmed for increasing AMD risk (Hyman & Neborsky, 2002).

1.2 Medical and surgical treatment options

AMD may lead to loss of vision by atrophy of the retinal pigment epithelium or by development of choroidal neovascular membranes (CNVM) under the macula, which leak serous fluid and blood and ultimately cause a blinding disciform scar (as discussed in section 1.1.1). There is more research concentrated on this wet form of AMD than on the atrophic form.

This section concentrates on reviewing the treatment options currently being investigated and classifies the treatments according to the approach followed. There are three main approaches: elimination of the CNVM from the subfoveal area (by laser or surgery), modification of the CNVM (by laser radiotherapy or chemotherapeutic agents), or prevention of the formation of CNVM: prophylaxis (by laser, diet or gene targeting).

Another way to classify AMD treatment, not selected for this theses lies on the method used to treat the condition. Laser treatments include photocoagulation and photodynamic laser therapy (PDT). Surgery includes submacular and macular translocation surgery, whilst radiation includes external beam/teletherapy or episcleral plaque/branchytherapy. Chemotherapeutic agents include thalidomide, interferon, integrins and vascular endothelial growth factor inhibitors, which are all angiogenesis inhibitors. Finally, other treatments include gene therapy and transplantation of retinal pigment epithelium and photoreceptors.

1.2.1 Elimination of neovascularisation

1.2.1.1 Laser photocoagulation therapy of extrafoveal or juxtafoveal CNVM.

The Macular Photocoagulation Study demonstrated that laser photocoagulation could be effective in the long term in preventing or delaying severe visual loss. They ran long-term randomized clinical trials of laser photocoagulation of CNVMs associated with AMD. However, only less than 10% of patients presenting with AMD have CNVM of the appropriate type to be suitable for this treatment. Also, the recurrence rate of those who are suitable for treatment is very high (over 50% at 2 years) (Macular Photocoagulation Group, 1991). Some of the complications from laser treatment are Bruch's membrane rupture, haemorrhage and retinal pigment epithelium tears and inadvertent photocoagulation of the fovea, leading to unexpected visual loss. Ablation of the central photoreceptors results in an immediate decrease of about three lines of visual acuity. According to the Macular Photocoagulation Study Group (1994), the type of patients with subfoveal lesions that would obtain a visual acuity benefit after laser photocoagulation treatment were those with small or medium lesion size and a moderate to poor VA. Therefore, focal laser offers the possibility of prevention of a deep visual loss associated with end-stage disciform scarring at the cost of producing a central scotoma and thus making the treatment only worth it for a minority of cases. This explains why many clinicians prefer not to treat subfoveal CNVM.

The use of a foveal sparing argon laser photocoagulation technique has been proposed by Orth et al. (1994), which should in theory retain some cone function. This small study showed that in some cases visual acuity can be retained and stabilized. However, there is a need for a large, randomized, controlled clinical trial before any scientific conclusions could be made.

1.2.1.2 Extraction of CNVM with and without transplantation of RPE

Some small studies have attempted to remove the neovascular net with and without transplantation of the RPE but unfortunately, the results are disappointing, with few patients experiencing an improvement in visual acuity (Ciulla et al., 1998; Thomas et al., 1994). The removal of RPE cells in submacular surgery appears to limit the final visual outcome (Scheider et al., 1999), making this type of surgery ineffective for subfoveal CNVM in AMD. Human fetal RPE transplantation may offer a solution but after several attempts (Algvere et al., 1994; Humayun et al., 2000) it has still not been demonstrated to produce a definite positive effect on visual function. On the other hand, good tolerance of the graft seems to favour the future study of this technique (Humayun et al., 2000).

1.2.1.3 Macular translocation

Macular translocation or translocation surgery is another surgical approach investigated. It consists on moving the fovea to an area of healthy RPE. Once the fovea has been moved from the area of subfoveal CNVM, this membrane can then be treated with laser. Technically it's a more difficult procedure and may fail if there is insufficient translocation, recurrence of CNVM or the development of cystoid macular oedema. This technique also requires additional extraocular muscle surgery to correct the torsional complications acquired from such intervention (Benson, 2002).

Pieramici et al., 2000 have described a limited macular translocation technique with quite a lot of success on visual acuity, this improving by 6 lines 6 months after treatment. According to Fujii et al. (2000), complications from limited macular translocation include retinal detachment, retinal breaks, macular holes, macular fold and intraocular haemorrhage. In their study at least one of these complications occurred in 34% of the treated patients. Also, these complications appeared to be more likely if PDT had been previously applied (Stanaga et al., 2003). Macular translocation seems to be an exciting new technique that could prove to be beneficial with an improvement in surgical techniques and better selection of cases (Wong & Lois, 2000).

1.2.2 Novel methods to treat neovascularisation

1.2.2.1 Photodynamic therapy (PDT)

The rationale behind PDT is that photosensitized tissue can be selectively destroyed by a photochemical reaction (Chong & Bird, 1998). A light-activated drug is administered by intravenous injection. This drug attaches to lipoproteins, which are in high concentration on the proliferative vessels. Then, the dye will be irradiated with a precalculated dose of light at a particular wavelength corresponding to its absorption peak. This will create free radicals that will induce cell death. This is potentially a minimally invasive treatment that could reduce the damage to surrounding tissues occurring with laser photocoagulation. PDT has been proposed to treat CNVMs by destruction and therefore preventing leakage from the blood vessels (Chong & Bird, 1998; Ciulla et al., 1998; Wu & Murphy, 1999).

Several drugs are now under investigation. Most data are now available with visudyne (or verteporfine) and there is now evidence that PDT can reduce the risk of visual loss in eyes with subfoveal CNVM from AMD. The Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study Group, (2001) have reported some beneficial outcomes with respect to visual acuity and contrast sensitivity. Fifty-nine percent of verteporfin-treated patients, compared with 31% of placebo-treated patients, lost fewer than 15 letters over a

period of 2 years. The average of treatments was 3.4 and both the visual acuity and contrast sensitivity levels obtained 12 months after treatment were sustained through the 24-month examination. More recent studies keep on showing positive results. The Treatment of AMD With Photodynamic Therapy Study Group (2003) and Palmowski et al. (2002) showed how Verteporfin therapy can safely reduce the risk of moderate and severe vision loss in patients with subfoveal lesions and agreed on the treatment being more effective for small classic lesions. Similarly, the Treatment of AMD With Photodynamic Therapy and Verteporfin in Photodynamic Therapy Study Groups (2003) proposed that treating patients with smaller rather than larger neovascular lesions will likely result in a better level of visual acuity.

PDT has been approved by the NICE, who published the final guidance in 2003 (NICE, 2004). However, only patients with pure classic lesion are suitable for treatment automatically and thus, only helping a minority of the population with AMD.

1.2.2.2 Photochemical and thermal methods (Transpupillary thermotherapy)

Transpupillary thermotherapy (TTT) is a technique where heat is delivered to the RPE through the pupil using a modified diode laser. The aim of this technique is to occlude the neovascular vessels. In theory, the decreased heat levels delivered by TTT, in comparison to conventional laser photocoagulation, may result in less collateral damage to the adjacent normal retina. This technique has yet to be subjected to a randomized controlled trial and the optimal treatment parameters have not been established yet (Mainster & Reichel, 2000).

Reichel et al. (1999) treated 16 eyes for a minimum follow up of six months. Although they reported a decreased exudation on most of the treated eyes they did not use a consistent method to evaluate exudation, thus making this result difficult to interpret.

Algvere et al. (2003) followed 113 patients with wet AMD for 12 months after TTT treatment and concluded that TTT generally prevents moderate and severe visual loss at 12 months follow-up in occult CNV¹ with no classic CNV and for classic lesions, smaller than 3 mm in diameter. However, classic lesions larger than 3 mm in diameter responded poorly to the treatment.

¹ **Classic CNV** is characterized by welldemarcated boundaries of hyperfluorescence that can be discerned in the early phase of a fluorescein angiogram with progressive dye leakage pooling in the overlying subsensory retinal space. **Occult CNV** on the other hand encompasses a variety of fluorescein angiographic appearances that do not conform with the classic description. This second form of CNV may be caused by fibrovascular pigment epithelial detachments or a late leakage of undetermined source (Albert & Jakobiec, 1994).

1.2.2.3 Radiotherapy

External beam (teletherapy) and episcleral plaque therapy (brachytherapy) are still being investigated as modalities for the treatment of neovascularisation in AMD. Radiotherapy inhibits vascular endothelial cell proliferation in vitro and prevents angiogenesis in vivo (Reinhold & Buisman, 1973; Arlett & Harcourt, 1980), hence growing blood vessels may become non-perfused, whilst mature vessels remain unaffected. Radiotherapy also reduces inflammation and scarring (Verheij et al., 1994).

Chakravarthy et al. (1997) carried out a study on 19 AMD patients with CNVM and reported quite successful results in terms of the visual performance. Pre-treatment visual acuity was at least maintained for 78% of the patients at six months and 63% at the one year follow up, compared to the untreated control group, of whom only 14% maintained visual acuity at one year. More recent studies (Finger et al., 2003; Marcus et al., 2004) seem to offer promising results but there is a need for a RCT to prove the effectiveness of this treatment.

1.2.2.4 Chemotherapeutic agents (Pharmacological Treatment)

There is increasing interest in angiogenesis inhibitors such as interferon, thalidomide, integrins and anti-vascular endothelial growth factor (anti-VEGF) inhibitors for their potential in the treatment of neovascular AMD. In theory, they could be administered systemically or locally, into the vitreous or under the retina.

- Interferon has an inhibitory effect on the migration and proliferation of vascular endothelial tissue. Early studies (Gillies et al., 1993; Kirkpatrick et al., 1993) did not find an appreciable improvement in visual acuity or regression of membrane size after the treatment. Also, this treatment is potentially toxic and may carry some serious cardio-vascular complications. Indeed, in the only large multicentre, double-masked randomised controlled trial reported, patients treated with three injections per week for 52 weeks were more likely to have lost at least 3 lines of Snellen visual acuity than those treated with placebo (Pharmacological Therapy for Macular Degeneration Study Group, 1997).
- Thalidomide, which is a powerful teratogen, is angiogenic and thought to decrease blood vessel growth by decreasing the expression of the factors needed to stimulate angiogenesis. In theory, this could be useful in the treatment of CNVM (Kaven et al., 2001).
- Anti-VEGF inhibitors recently involved in trials are AMD Fab, protein Kinase-C beta and Steroid compounds (Ciulla, 2003). There is some recent evidence (The Eyetech Study Group, 2003) of promising results but no RCT has yet proved their benefits or safety.

1.2.3 Prevention of the neovascular response

1.2.3.1 Prophylactic laser to drusen

Around 12.4% of patients in the USA with bilateral soft drusen develop unilateral or bilateral CNV within 10 years (Lanchoney et al., 1998). There is clinical and epidemiological evidence that the presence of soft drusen is a risk factor for the development of CNV (Smiddy & Fine, 1984; Bressler et al., 1990; Holz et al., 1994b). It would thus sound reasonable to attempt to reduce the risk of neovascular membrane formation by reducing the number of drusen. Treatment for atrophic AMD is very rare at present and concentrates on trying to prevent this atrophic form of AMD to progress onto the neovascular form of AMD. The choroidal Neovascular Prevention Trial Research Group, a multicentre, randomised clinical trial of laser versus observation has proposed visual function improvements at one year and two years (Olk et al., 1999). Laser-induced drusen reduction in eyes with non-exudative ARMD was associated with improved visual acuity and contrast sensitivity at one year. CNV formation was, however, similar in treated and untreated eyes through the 2-year study.

1.2.3.2 Diet and other risk factors

Nutrition and antioxidant status have received increasing attention in explaining the development of ARM and AMD. Most nutritional theories presuppose a protective role of vitamins and minerals with antioxidant potential. The outer segments of the photoreceptors are rich in proteins and polyunsaturated fatty acids, which may be very vulnerable to oxidative damage. The combination of metabolism and light exposure can trigger formation of free radicals, which leads to the degradation of cellular proteins. Cellular mechanisms that have evolved to combat the destructive effects of free radicals may be particularly lacking in AMD patients, thus leading to the accumulation of peroxidation products.

Antioxidants, such as Vitamin C, E, carotenoids (lutein and zeaxanthin) and zinc have been suggested to provide possible protection against AMD (The Eye Disease Case Control Study (EDCCS), 1992; Richer et al., 2002). They may prevent cellular damage in the retina by reacting with free radicals produced in the process of light absorption (Ham, W., 1983).

Data from the AREDS suggests that higher than normal levels of carotenoids are associated with a decreased risk of neovascular AMD. Snellen et al. (2002) found in their case-control study that the prevalence rate of AMD in patients with low antioxidant intake and low lutein intake was about twice as high as that in patients with high intake. However, Flood et al. (2002), on their 5 year patient incidence follow-up, and Falsini et al. (2003), on their short-term antioxidant supplementation, found no evidence that antioxidant intake would decrease ARM incidence or stop it progressing.

Zinc has been found to have a positive treatment effect in AMD but quite toxic side effects when administered orally (Newsome and Swartz, 1988). According to Bressler et al. (1995a), vitamin E seems to be the only antioxidant to give a statistical significance on plasma levels of AMD patients. These data must be viewed in the light of The Eye Disease Case-Control Study (EDCCS) Group's (1992) finding that plasma levels of vitamin C and E and dietary intake of vitamin E were not associated with the presence or absence of AMD.

To date, the information obtained from epidemiological and clinical studies is conflicting, inconsistent and unproven. There is no conclusive evidence that dietary supplementation with vitamins, minerals, or trace elements leads to a decrease in visual loss secondary to AMD (EDCCS Group, 1992; Evans, 2001).

1.2.4 Future treatments

Suppression and modification of the neovascular response with novel anti-angiogenic factors and gene therapy are thought to be the future treatments of CNVM in AMD. Restoration of the normal anatomical relationships between photoreceptor, Bruch's membrane and RPE is the goal.

Both current and potential future treatments for AMD need to be further investigated and techniques need to be significantly improved before they can offer any reasonable benefit to the patient. Nowadays, there is not a curative treatment and benefits in terms of slowed progression are often small and the treatments available are only for the wet type of AMD. There is thus a major need for better therapies.

1.3 Impact of AMD

The irreversible visual impairment is an obvious consequence of AMD, but the psychological impact of the condition is also significant. The factors affecting the adjustment to the vision loss and the emotional reaction are reviewed in this section.

1.3.1 Visual impairment in AMD

Low vision is defined as a reduced visual acuity which even with the best optical correction provided by regular lenses still results in a visual performance in a standardised clinical test (such as Snellen letter chart) which is less than that expected for a patient of that age (Dickinson, 1998) and which causes restriction in a person's everyday life (Low Vision Services Consensus Group, 1999).

The International Classification of Impairments, Disabilities and Handicaps (ICIDH) (first mooted by the World Health Organisation in 1980) classified the terms disorder, impairment, disability and handicap to attempt to standardise the description of the functional consequences of disease at various levels.

The ICIDH was widely used and by 1994 it had been translated into 13 languages. However, some criticism was levelled at the ICIDH, in particular from people with disabilities and many professionals who were critical of the inadequate recognition given to the role of the environment in the creation of disability. As a result 7 years of revision and testing ensued and in 2001 the World Health Organization (WHO) endorsed by a new international classification of functioning and disability. ICF, also labelled as ICIDH-2 although it uses a different terminology, has moved away from being a “consequences of disease” classification (1980 version) to become a “components of health” classification. “Components of health” identifies the constituents of health, whereas “consequences” focuses on the impacts of diseases or other health conditions that may follow as a result. Thus, ICF takes a neutral stand with regard to aetiology so that researchers can draw causal inferences using appropriate scientific methods.

The ICF has been developed for use in describing functioning and disability, complementing the ICD, which focuses on diseases and health conditions. A person’s functioning or disability is conceived as a dynamic interaction between health conditions and environmental and personal factors. Functioning and disability are both multidimensional concepts and disability is the umbrella term for any or all of: an impairment of body structure or function, a limitation in activities, or a restriction in participation. These are the three components of the classification as defined in the context of a health condition.

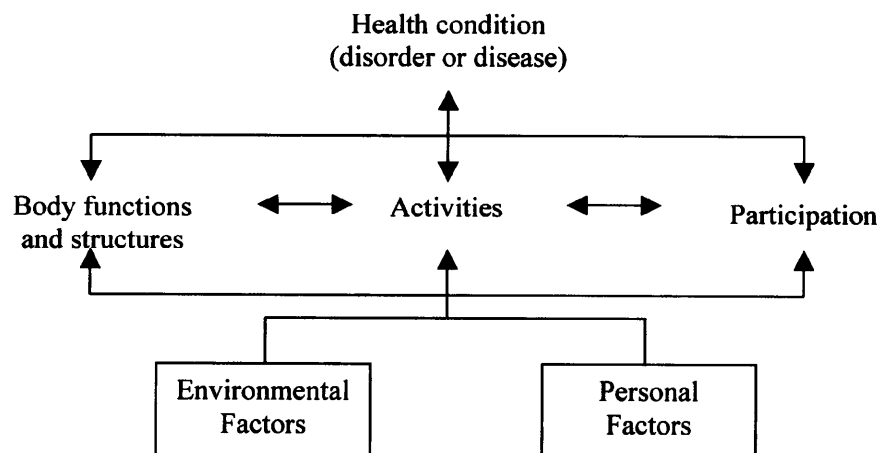


Figure 1.4: *Interactions between the components of ICF (adapted version).*

Because of the efforts taken to involve a wide range of disciplines and people in the redevelopment and testing, the ICF should be able to be used for an even wider range of purposes than its predecessor the ICIDH. Figure 1.4 shows the interactions between all the components of the ICF.

The definitions for the ICF components are:

Body functions are the physiological functions of body systems (including psychological functions).

Body structures are anatomical parts of the body such as organs, limbs and their components.

Impairments are problems in body function or structure such as a significant deviation or loss.

Activity is the execution of a task or action by an individual.

Participation is involvement in a life situation.

Activity limitations are difficulties an individual may have in executing activities.

Participation restrictions are problems an individual may experience in involvement in life situations.

Environmental factors make up the physical, social and attitudinal environment in which people live and conduct their lives.

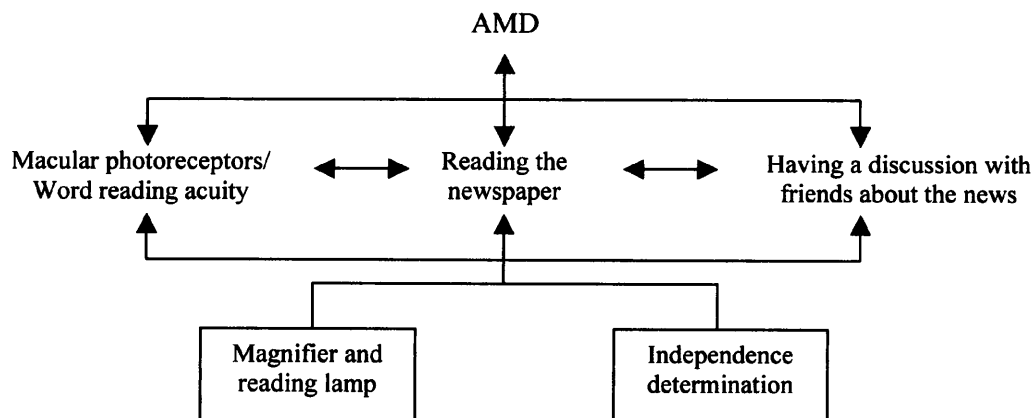


Figure 1.5: Example of interactions between components of ICF for a particular AMD case (adapted version).

In the case of an AMD patient, the following interaction shows an example of all the different components for a possible patient. That is: An elderly lady finds that reading is now very difficult due to ARM. She is very determined to read the newspaper for pleasure because she lives alone and obtains a magnifier from the hospital Low Vision Clinic. She is registered partially sighted and the local Social Services Department provide her with a reading lamp (see figure 1.5).

The ICF takes into account all the above-mentioned factors and classifies the human functioning and disability by means of complicated structural features represented by an alphanumeric system of codes for the different components, domains, categories, qualifiers and capacities that need to be considered for the classification.

In the United Kingdom, eligibility for welfare facilities is based on two functional definitions:

- **Blind:** 'So blind as to be unable to perform any work for which eyesight is essential' (as defined by the Blind Persons Act in 1920).
- **Partial sight:** 'Substantially and permanently handicapped by defective vision caused by congenital defect, illness or injury' (as defined by the National Assistance Act in 1948).

These categories imply different grades of vision (see Table 1.3) and have recently been renamed (<http://nwww.doh.nhsweb.nhs.uk/nhs/cvi2003.htm>) as Severely Sight Impaired (Blind) and Sight Impaired (Partially Sighted), although they keep the same original guidelines on acuity (see Table 1.3). Patients meeting these visual criteria and willing to get registered need to have the appropriate form, now known as **CVI 2003** in England and Wales, filled in by an ophthalmologist. The ophthalmologist keeps a copy of this form in the hospital notes and copies are then sent to the Local Authority (Social Services), to the OPCS (for epidemiological survey), to the GP and to the patient. This form has recently replaced the BD8 form and it is still to be reviewed in March 2004. Once this form has been completed Social Services should contact the patient within 2 weeks to carry out an assessment of their needs, give information on services and benefits (this is a statutory duty, even if patient decides not to be registered) and arrange for registration (with their consent). Two additional mechanisms for referral for assessment of needs have been introduced which had not been available previously:

- **RVI 2003:** Hospital eye service referral of vision impaired for social needs assessment, to be completed by Eye Clinic Staff.
- **LVI 2003:** Optometrist identification of a person with significant sight problems in the form of a letter concerning vision impairment needs which the patient can use to self-refer for assessment of needs.

These changes took place in November 2003 and thus after the recruitment period for the study (see section 2.7). Therefore the patients were registered using the BD8 form and the relevant sections of this thesis refer to the old terminology rather than the new one.

Severley Sight Impaired/Blind	Sight Impaired/ Partial sighted
<ul style="list-style-type: none"> • 3/60 or worse, if also worse than 1/18 • 3/60 – 6/60 with very contracted field (No long-standing conditions without marked field loss) • 6/60 or worse with markedly restricted fields, specially in the lower part (No hemianopia if 6/18 or better) 	<ul style="list-style-type: none"> • 3/60 – 6/60 with full fields • 6/24 or worse with moderate field constriction • 6/18 or better with gross field defect (Hemianopia or marked contraction such as due to RP or glaucoma)

Table 1.3: Grades of vision for the severe and moderate vision losses.

1.3.2 Psychological impact

Loss of vision is one of the most emotionally devastating physical problems. According to a survey conducted by Gallup in 1988 (cited by Augusto & McGraw, 1990), blindness was the most feared disability for 42% of the adults polled.

The impact of visual impairment extends beyond functional vision problems to a myriad of psychological issues ranging from grieving the loss of sight to the impact of loss on the family and significant others. It is virtually impossible to provide low vision care without being aware of the psychosocial impact of the loss of sight (Brilliant, 1999).

The loss of central macular vision results in some degree of image impairment in the direct line of vision, that is distortion in the early form of the disease, and scotomas in the more advanced stages of the disease due to scarring and loss of macular cones (Faye, 2000). It can be explained to patients suffering from AMD that only the central area of vision would be affected, leaving the peripheral vision still functional and thus there will always be some vision left “on the sides”. Patients can be reassured that they will not go completely blind solely from this condition.

Vision loss in later life may be regarded by families and professionals as less traumatic than the same degree of loss at a younger age (Defini, 2000). For an old adult with vision impairment there is usually some degree of usable vision left and some diminution of sensory acuity is accepted as a normal consequence of age (Horowitz & Silverstone, 1991), although there is always a fear of loss of independent living.

1.3.3 Factors affecting adjustment to low vision

Research suggests that the degree of vision impairment does not predict the way in which a person will adjust. Other variables contribute greatly to both rehabilitation outcome and psychosocial adjustment. No relationship has being found between the degree of vision loss

and the level of depression (Teitelbaum et al., 1994). Radloff (1977) and Turner and Noh (1988) found that older adults with disabilities were less likely than younger people to experience major depression, although they had an equivalent number of depressive symptoms.

Strongly related, AMD often occurs at a time of life when resources and social support are dwindling and physical health may already be compromised. Health problems and social isolation are associated with anxiety and depression in the older adult who is visually impaired. Even controlling for co-morbidity, vision impairment has been found to be an independent significant predictor of functional disability (Horowitz, 1998).

It is advisable to explore how much the patient knows about his/her problem since many patients with AMD are fearful that they will lose all their sight. Others, who have been told that they are legally blind, often do not understand the meaning and implications of this label. For many, hearing the word blind often confirms their fear of losing all their sight in spite of a stable prognosis.

It is also necessary to take into account the recency of onset. An individual who has recently been diagnosed with macular degeneration and comes in for a low vision evaluation may still be hopeful that conventional lenses may correct the problem.

Reinhardt (1996) found that community residents who had both a close friend and a close family member had higher life satisfaction, fewer depressive symptoms, and better adaptation to visual loss (except when poor health status and functional disability intervened) than those without friends or family. According to Freedman (1981), "If there is a single universal, it can be assumed that it is the entire family unit that is experiencing a vision loss and not just the individual sustaining blindness". The impact of visual impairment may be particularly significant for the older person living alone, forcing many older adults to question their ability to live independently.

Horowitz and Reinhardt (1998) also cited low educational status as a significant risk factor for poor adaptation to visual loss. This could be because people with lower educational status might find it more difficult to access services (Horowitz & Reinhardt, 1992).

Turner & Wood (1985) found that low income was a common part of the experience of living with a disability and thus, rather than predictors, income and career limitations were more likely to be consequences.

An individual's personality is another consideration. Someone who has history of anxiety and depression may react more intensely to the loss of sight and perhaps require psychosocial intervention to assist the adjustment process. Someone who has always been independent may

be more motivated to do whatever it may take to help get back the desired level of self-sufficiency than another person who has been more dependent on others (Brilliant, 1999).

1.3.4 Emotional reactions to loss of vision

The emotions an individual with an acquired vision loss might experience are similar to the process of going through the loss of a close friend or relative. This framework was first proposed by Kubler-Ross in 1969. She suggested five different stages of emotions regarding loss. It is important to note that not all individuals go through all of these grieving stages, nor do they experience them in the same order.

The first of these stages is *shock and denial*. This happens when the individual either realises that they have a problem with vision that is not correctable or is given the diagnosis. Shock is a normal response to an emotionally painful situation.

The second stage of grieving is *anger*. At this stage, the individual is beginning to feel the emotional impact of the loss. The person often asks, “Why is this happening to me?” and may feel resentful of others who have not experienced this loss.

The next stage of grieving is *depression*. At this point, the person may be feeling a deep sense of sadness about the loss and sense of hopelessness about the situation. *Bargaining* is the next stage and is usually the briefest in duration. At this point, the person is seeking to gain control by making deals or pacts to negotiate a change in the situation.

The last of the grieving stages described by Kubler-Ross is that of *acceptance*. Many visually impaired individuals have taken exception to referring to this last stage by the term acceptance because it has a connotation of willingly embracing the vision loss. A more accurate and acceptable term for this stage is *acknowledgement*, or making peace with the permanence of the visual impairment to move on with one’s life (Brilliant, 1999).

1.4 Low vision in AMD

A low vision service is 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 (Low Vision Services Consensus Group, 1999). The services should include:

- Planning the rehabilitative process, setting goals and support in understanding the limitations involved
- Addressing psychological and emotional needs

- Providing information and advice
- Assessing the person's visual function and providing aids and training
- Facilitating modification to the home, school and work environments

1.4.1 Low vision aids

The goal of low vision aids is to make the retinal image easier to see, and this often involves magnifying the retinal image of an object. By enlarging the size of the image that is projected onto the retinal surface, it is more likely that the image will be seen by the remaining healthy tissue surrounding compromised areas. Magnification is given by a direct increase of the linear size of a feature measured on the display screen, compared to that of the original object. There are four types of magnification used to achieve enlargement of retinal images (Dickinson, 1998):

1-Relative size magnification. The object is made larger. Examples of this include large-print books, enlarged numbers on telephone dials or buttons, large-print bank statements, music books, playing cards, knitting patterns and large-numeral clocks, watches and calculators. Computer displays can also offer increased letter size using image magnification software up to (typically) 16 X magnification.

Enlarging the size of the object is a simple method that does not require any instructions or eye examination, does not give the patient any optical restrictions (these include aberrations and reduced field of view), and can be used binocularly at a normal reading distance. By doubling the size of the actual object, the retinal image size will also be doubled, and thus, there is a direct relationship between increased object size and increased retinal image size.

Limitations of this method include the physical size of papers and books, the limited range of books available, and that magnification for text goes only up to approximately 2.5X.

2-Relative distance magnification. As objects are brought closer to the eye, the retinal image size is again enlarged proportionally. A closer object takes up a larger portion of the visual field and the image is larger on the retina. As the distance changes, the retinal image also changes, or is magnified, relative to that change of distance: a halving of the distance doubles the image size. This method of magnification is the most popular among people with visual impairment.

A plus lens can be used as a magnifying aid to allow the patient to obtain an increased retinal image size by holding an object close to the eye without requiring the accommodative effort that would usually be necessary to view at this distance. To obtain this magnification the object would need to be placed at the anterior focal point of the positive convex lens so that

the parallel light would leave the lens, the virtual image is at infinity, and the patient's accommodation can be relaxed. Depending on the visual tasks required by the patient, this lens can be close to the eye, or remote from it; that is spectacle-mounted, handheld or on a stand.

Mathematically, the magnification power is given by the old object distance divided by the new object distance (Dickinson, 1998). If plus lenses are used, then the object distance is the focal length of the lens, and the value is standardised by comparison with the 25cm object distance (focal length) of a +4.00DS lens. The limit of magnification with this system is approximately 20X.

3-Angular magnification (Telescopic magnification). Angular magnification is produced by a system of lenses such as in a telescope. Light rays leaving the system making a greater angle with the optical axis can cause images to appear at a closer distance than the actual location of the object. The image seen is virtual and actually at infinity, but objects appear smaller as they get further away, so when distant objects appear larger, they are interpreted as being closer. These are afocal systems, where parallel rays of light enter the telescope from an infinitely distant object, and parallel rays leaving the telescope form a final image at infinity.

In most cases however they can be modified to focus objects closer than infinity and can also be modified to correct for the wearer's spherical refractive error. Telescopic devices can sometimes be difficult to use and adapt to, due to their limited field of view and depth of field.

4-Real image magnification (Projection magnification). Print or images can be enlarged by optical projection devices, although nowadays this is more commonly done by electronic magnification, using a CCTV or a television reader. These devices are more expensive than optical LVAs, require more practice from the patient and are bulky to carry. Advantages include a rapid change of magnification without altering focus; normal working distance; longer duration of use than optical aids; and higher and reversible contrast (Goodrich, 1978).

All the LVAs are task specific and there is not a perfect LVA optimal for all tasks. They all have advantages and disadvantages and a low vision specialist should be able to provide the patient with the best aid that meets the patient's needs for the specific tasks required.

There are other visual means besides magnifiers and optical aids to assist partially-sighted individuals in their daily tasks by helping them to make the best use of their residual vision. These are illumination, contrast and tints.

Illumination is the primary and most crucial strategy. Illuminance is the quantity of light per unit area hitting the working surface or task. It is measured in lumens per square meter, also called lux, and is inversely proportional to the distance² between the light source and the

object. A normally sighted person, 65 years of age or older wanting to carry out a detailed visual task such as sustained reading or sewing would, according to the CIBS code (CIBS, 1984), need a recommended illumination of 450-600 lux. Sloan et al. (1993) found that some patients with macular disease benefit disproportionately from greatly increased levels of illumination: of the order of 2 log units above the optimum level for normally-sighted individuals. Jay (1980) and Lindner et al. (1989) recommended 500-1000 lux as a useful starting point illumination for the majority of low vision patients wanting to carry on a detailed close-work task. However, Eldred (1992) reported that low vision patients preferred much higher levels of illumination ranging between 5920 and 7534 lux.

The best source of light for low vision reading comes from a fluorescent task lamp. The high efficacy means that there is little energy lost in the form of heat and the lamp does not get as hot as an incandescent bulb does. This allows the patient to get very close to the lamp without getting burned. The close distance from lamp to task makes use of the 'inverse square' relationship to achieve high levels of illuminance on the task.

Contrast- Many low-vision patients have very poor sensitivity to low-contrast targets and as a result, small reductions in letter contrast significantly affect their reading performance (Rubin & Legge, 1989). However, low contrast sensitivity alone cannot be considered a visual impediment to reading as long as print contrast can be increased to compensate. The relevant visual factor, therefore, is print contrast relative to contrast threshold i.e. contrast reserve. Contrast reserve can be expressed as a ratio: $R_C = C_L/C_T$, where C_L is letter contrast and C_T contrast threshold of the patient (Legge et al., 1987). To achieve a fluent reading, a contrast reserve of 10:1 is required (Whittaker & Lovie-Kitchin, 1993).

Luminance describes the intensity of light emitted or reflected in a particular direction by an area that is either self-luminous, or is reflecting incident light and it is measured in candelas per square meter, also called nit. Luminance contrast is given by $L_{max}-L_{min} / L_{max}+L_{min}$, where L_{max} is the luminance of the brighter and L_{min} the luminance of the dimmer areas within the image. To maximise luminance contrast, a bright object and a dark background, or vice versa, is required. This contrast enhancement can be obtained with simple devices such as felt-tip pens, which increase the contrast of the original object, and typoscopes, which increase the retinal image contrast.

High levels of task lighting, with care to avoid glare can also improve the contrast. Glare is a sense of excessive brightness within the visual field, which can create discomfort (discomfort glare) or impair visual performance (disability glare) (Waiss & Cohen, 1992). Disability glare is distinguished by the change in retinal image contrast, and thus reduction in acuity.

Reversing the letter-background contrast on CCTVs can decrease glare and improve reading performance (Dickinson, 1998).

Tints- Short wavelengths are theoretically scattered more by the ocular media than yellow and red light and are consequently responsible for much of the disability glare (Bither and Hurt, 1988), which can decrease contrast sensitivity and VA. Patients suffering from albinism, retinitis pigmentosa, macular degeneration and glaucoma may experience similar symptoms, but the mechanisms are not well understood. Nonetheless, lenses absorbing the short wavelengths is recommended for a wide range of patients with disability glare. It has been widely reported that low vision patients may show strong subjective preference for particular tints (Hoelf & Hughes, 1981; Maino & McMahon, 1986; Provines et al., 1997) but there is no consistent objective benefit from using tinted lenses or filters (Eperjesi et al, 2002).

Some patients prefer light tints for indoor and darker tints for outdoors, although the majority only use the later. Tints have limited use in reducing disability glare and visors or hats with wide brims can be more effective in preventing light from a glare source from entering the eye.

If vision cannot be enhanced to allow the task to be performed it is possible that **sensory substitution** will be more appropriate with tactile or auditory displays being used on household appliances. Examples of these include talking watches, calculators and cooking appliances, and a liquid level indicator for filling cups. Reading is also possible using auditory (talking books) or tactile (Braille or Moon) methods.

1.4.2 Eccentric viewing and PRL

Patients with AMD have a central scotoma, which impairs the straight-ahead vision (Frenesson et al., 1995). These patients may deliberately view to the side of the object of interest. This technique is called eccentric viewing (EV) and the new area of the retina where the patient fixates is called preferred retinal location (PRL) or pseudofovea (Timberlake et al., 1986). Eccentric fixation differs from EV in that patients have the sensation of looking directly at the visual object during fixation with the eccentric PRL; i.e. the PRL has also replaced the fovea as the reference point for the ocularmotor system.

The obvious disadvantage of using an eccentric area of the retina is that resolution decreases as you move from the fovea (Whittaker et al., 1988), thus requiring magnification to compensate for this poor resolution. Difficulty experienced by this peripheral retina in decoding information (Rubin & Turano, 1994) when reading could explain why some patients with an acquired visual impairment do not choose to read with a PRL (Guez et al., 1993).

Another reason for people with central scotomas to not use EV could be that fixation control is not as precise with an extrafoveal point as it is with the fovea (Sunnness et al., 1996). For this reason, even patients with consistent optimal PRL for resolving letters might not be able to read since this involves a precise sequence of eye movements for the eye to move across the page from left to right with appropriate saccades and fixation pauses.

The most obvious hypothesis would be that the pseudofovea would be situated in the region of highest remaining acuity, at the edge of it that is closest to the fovea. It is known that subjects with normal macular function, when recognising letters in strings, or when reading words, have better recognition accuracy and reaction time on the right of the fixation point than on the left (Bouma, 1973; Bouma & Legin, 1977; Nazir, O'Regan & Jacobs, 1992; Mondor & Bryden, 1992; Fletcher & Schuchard, 1997). The visual span in reading is also asymmetric, more information being extracted from the region on the right of fixation than on the left (McConkie & Rayner, 1976; Rayner, Well & Pollatsek, 1980; Rayner et al., 1982; Underwood & McConkie, 1985). Also, when fixating a word, it is known that the optimal position to fixate is generally slightly left of the middle of the word, again suggesting that the right part of the field is more important than the left (O'Regan & Jacobs, 1992; Fletcher & Schuchard, 1997). Fine and Rubin (1999) found that patients with simulated scotomas performed better when fixating to the right than to the left due to the number of saccades required to successfully read the stimuli. Despite all these theories supporting the right hemi-field for EV, there are also studies advocating the left hemi-field for providing information about the beginning of a line while reading (Sunnness et al., 1996) and the need for left-to-right readers to monitor where their eyes have landed relative to the word previously fixated on the left (Guez et al., 1993). Trauzettel et al. (1994) and Fletcher et al. (1997) also found that the left hemi-field is preferred by patients with central scotomas for reading on the scanning laser ophthalmoscope. It can therefore be concluded that due to fixation characteristics the right hemi-field is expected to give better reading performance than the left hemi-field but findings show how the left hemi-field is actually selected by patients.

In contrast to the horizontal PRLs, there seems to be far more consistency for vertical EV. Petre et al. (2000) concluded that for reading tasks not involving eye movements, there is an advantage in eccentrically fixating if the text falls in the inferior rather than left visual hemi-field. This preference for the inferior visual field has been found in a large amount of studies (Timberlake et al., 1986; Whittaker et al., 1988; White & Bedell, 1990; McMahon et al., 1991; Guez et al., 1993) but there is no evidence supporting the upper field of view for EV. Furthermore, Nilsson et al. (2000) propose that relocating the PRL from an unfavourable (right or left) location to a more favourable location (above or below fixation) improves

reading speed dramatically. Therefore, the lower and left hemi-fields seems to be the preferred retinal area when replacing fixation as compared to the upper one.

Fixation stability decreases as the scotoma increases in size and the PRL becomes more eccentric, being acceptable for scotomas of less than 20 degrees in diameter (Zeevi et al., 1979; Whittaker et al., 1988). White and Bedell (1990) observed that when the lesion was stable, an extrafoveal PRL had become the new reference for oculomotor behaviour for 87% of their patients suffering from binocular central vision loss when assessed on a fundus camera. Also, Cummings et al. (1985) found that 72% of their patients with central scotoma in their preferred viewing eye had adapted a single strongly preferred viewing location and that control was, in other respects identical to that for normal patients. Patients with large scotomas (bigger than 20 degrees in diameter) tend to have several PRLs (Whittaker et al., 1988). This is probably due to different parts of the retina being better for different functions. Several studies (Duret et al., 1999; Deruaz et al. 2002) found that patients use several PRL in combination to read single words and the number and location of the PRL may change from one task to another, at least when the visual abilities required to perform the task are different.

Also, it must be noted that the monocular characteristics of a PRL cannot always be extrapolated to binocular viewing tasks (Schuchard & Fletcher, 1994; Labianca & Peli, 1996). Furthermore, Lei & Schuchard (1997) found that patients with central scotoma could have different PRLs depending on the illumination, so that for high illumination the location used to be within the area of the relative scotoma, usually at the fovea or just outside the dense central scotoma. On the other hand, for low illumination the PRL appeared to be located within an area of relatively healthy retina, immediately outside the relative scotomatous area. It can therefore be concluded that the location of the PRL is quite a complex procedure and that there is not a systematic location among AMD patients. However, there seems to be a preference for the inferior and left hemi-fields.

1.4.3 Determining the PRL

Due to the anatomy of the eye (decrease of photoreceptors from the fovea), there is a decline of VA towards the periphery of the retina. For training in the use of PRL it would be useful to know which part of the retina would be in the best condition to replace the fovea and become the PRL. Freeman & Jose (1997) propose a simple method to find the off-centre viewing spot. They show three lines of decreasing thickness above each letter or word, and three lines of increasing thickness below each letter or word. Patients need to try to centre their vision to the end of each line in turn to find the one that gives the clearest view of the letter in their peripheral visual field (see Figure 1.6).



Figure 1.6: Target used by Freeman and Jose to identify the PRL.

Frennesson et al. (1995) used a movable fixation bar to be placed above or below the letters to be read on the computer screen. The position nearest to the centre, which gave good acuity and allowed at least 8-10 letters to be seen simultaneously was selected for training.

Mackeben & Colebrander (1994) assessed the patient's ability to recognise letters at 32 locations within the central field trying to identify regions of intact retina that are most suitable for reading using "eccentric viewing". They attempt to find a large enough area to provide an acceptable level of fluency, that is, to fit 4 to 6 letters at a time (Legge et al., 1985a; Whittaker & Lovie-Kitchin, 1993). Fletcher et al. (1994) used a scanning laser ophthalmoscope to project targets directly onto the retina.

Another simple method is to use the Amsler grid with an added fixation cross. A sequence of questions can be carried out to establish the size of the central scotoma and which area of the visual field experiences the clearest vision (Dickinson, 1998). However, this grid only assesses the central 20° of vision, being therefore of limited use for cases of large longstanding central damage.

Due to the difficulty in achieving effective EV, training in the use of residual vision, such as training of eccentric viewing, is far more effective than mere instruction in restoring visual performance in practical situations, at least regarding the elderly AMD population (Nilsson, 1990). This training needs the service from a vision therapist and is time consuming.

1.4.4 Steady eye strategy

Frennesson et al. (1995) and Nilson et al. (2000) have attempted to train small groups of AMD patients to use a PRL, showing an increase in reading speed. Nevertheless, this training can be very difficult and tiring and the patient might need a LVA to supplement the reading.

Whilst normal subjects hold the text still and move their eyes along the lines when reading, patients with a macular scotoma tend to read best by moving the text from right to left whilst

being instructed to hold their eyes still and simultaneously adopting eccentric viewing. This technique is called Steady Eye Strategy (SES) (Collins, 1987) allowing each succeeding letter to be imaged in turn at the PRL and the words to be read accurately letter by letter. This method is difficult to learn and requires patients to practice daily to improve the technique and speed.

1.4.5 Prism relocation

Prism lenses should, in theory, be able to move the image away from the damaged macula to another part of the retina adjacent to the scotoma but with improved function to offer vision rehabilitation (the PRL).

As EV training is difficult and time-consuming, the idea of moving the image away from the scotoma to the PRL using a prism sounds appealing. Moving the image with a prism does not require an active change in fixation on the part of the patient. This method is called Prism Relocation Therapy, Prismatic Therapy or Prism Scanning (see figure 1.8). If a prism is introduced in front of a fixating eye the image will be moved towards the base of the prism by an amount proportional to the power of the prism (Woo, et al., 1996). By appropriate choice of prism base direction and power, the retinal image can be moved to the PRL with no active involvement of the patient. Bailey (1983), on the other hand, suggested that the theoretical basis of fitting prismatic lenses was flawed, since the normal eye would make a movement to resume its previous fixation pattern in response to the prism. There are 4 studies that have previously attempted to relocate the image with prisms: Romayananda et al. (1982), Rosenberg et al. (1989), Verezen et al. (1996) and Bertrand et al. (1997) (See Table 1.4).

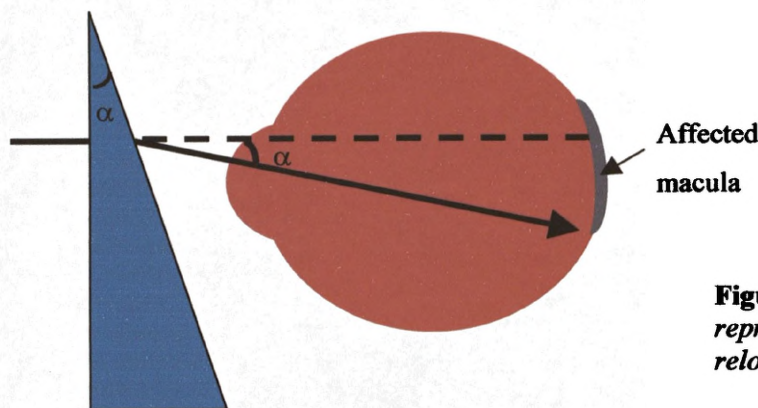


Figure 1.8: *Schematic representation of prism relocation.*

Romayananda et al., 1982

This research group from Philadelphia was the first to attempt to relocate the image from the fovea with prism glasses. They treated 59 patients of unknown ages and different types of macular lesion with prism glasses. They all had a reduced central vision and went through the

following tests: VA with best correction at near vision and distance vision, Amsler grid test, visual fields with Goldman perimeter, Fundus photography with and without fixation pointer and fluorescein angiography.

An appropriate size text (relative to the patient's near vision) was given to the patient and also an addition with the right power to compensate for the reading distance of each patient. While one eye was occluded, a 4 Δ prism is inserted with the axis that corresponded to the eccentric fixation point (found on a fundus photograph with a fixation pointer) in the trial frame and the patient rotated the prism to the position where the reading material was clearest. Stronger prisms of 5 to 10 Δ were added until best near vision was achieved. The prescription was then confirmed by adding ± 0.50 DS lenses until the patient saw the print as clearly as possible. The final prescription was monocular (best eye) or binocular (optimal prescription for each eye) dependant upon whether diplopia occurred.

Looking at their results most patients needed a 6 to 8 Δ prism and the larger the macular lesion, the higher the prism required. Ninety-five percent of patients chose a prism base in the superior 180 degrees.

Although they claimed 100% success (all patients became more independent and achieved an improved life), their study is subject to criticism. Subjects were only given reading glasses and thus performance was never tested on distance vision. Also, they did not have a placebo group or follow patients to check their progression with the prisms. Although this study establishes a simple method for prescribing prism to relocate the image, the assessment of results needs improvement.

Rosenberg et al., 1989

This second study group intended to improve Romayananda et al.'s work by carrying out a controlled clinical trial and evaluating the prisms on distance, near and intermediate (if requested) tasks.

Subjects were tested for distance vision and VAs for both eyes were measured with a LogMAR chart. The better-seeing eye was tested first on the near distance while looking at a multiple-dot chart. Since they do not mention about occluding the second eye it is presumed that they test the better eye while seeing the chart with both eyes. The subject was then asked to turn the head in the direction of best vision when viewing a target at the tested distance. Then, an arbitrary 8 Δ prism was placed with the base in the direction of head-turn and apex in the direction of the eye turn. If there was no response to head or eye turn (if subject moves the head to one side the eye would move to the opposite direction to compensate this movement), the patient rotated the axis to find the position of better vision. The optimum prism power was

then determined by using a bracketing technique. The correction was refined binocularly by having the subject rotate the prism axis on the poorer-seeing eye to the position of maximum binocular comfort with single vision. The procedure was then repeated for near vision and intermediate vision (if requested by patient).

Visual acuity and subjective impression were recorded and patients were then randomly assigned to control (placebo) or treatment group and dispensed the glasses. They attended a second visit to collect glasses and record distance, near vision, (both uncorrected, corrected and with prisms) and their impressions. On this second visit two other tests were performed: Visual fields with a Goldmann Hemispheric Perimeter to estimate the size of the scotoma created by the retinal pathology and fundus photography with fixation target to determine what area of the retina was used when using eccentric fixation.

Patients attended a third (6 weeks later) and fourth visit (3 months later) to repeat visual acuities and impressions. Treatment patients finished the study on the fourth visit whilst control patients were prescribed prism glasses then and entered in the treatment group.

A Chi-squared test was used to analyse data. Results compared the total number of patients who experienced an improvement in visual acuity, function and both together but failed to specify what determined any of these improvements. Comparisons between improvements in function or visual acuity alone did not show a statistically significant improvement but there was a weak statistically significant improvement in both visual acuity and function for the prism spectacle group of 91% compared to 62% for the control group. The improvement in VA in the control group could be explained by a placebo or learning effect.

There was no report of results obtained from the fundus photography or field test and how this compared to the prescribed prism. There was also no information of the amount of patients that made a head/eye movement when viewing VAs and subjective impressions were not reported either. Also, the authors did not clarify the prism powers and axes chosen by patients.

The authors suggested that, since the procedure involves minimal risk, it should be tried in patients where other approaches are ineffective and further studies are necessary. Although this study was more detailed than Romayananda et al.'s the authors did not report the exact amount of patients seen in the study. Also there could be selection bias when at the beginning of the study they discount those patients who did not show an immediate improvement with the prism.

Verezen et al., 1996

This study group seems to be the first one to evaluate prism relocation glasses specifically on AMD patients with a large central scotoma since in the previous studies patients tested other macular disorders besides AMD. They approached the technique in a different way by prescribing higher power prisms than the previous studies. Fifteen Δ or higher prisms were tested for distance viewing on 48 patients and patients who made a prism-induced repositioning eye movement on the presentation of the eccentric viewing prism were excluded.

The eye that showed the best combination of visual acuity, visual field and field acuity was used to prescribe the prism and the spectacles were dispensed with an identical power for the second eye to avoid diplopia and help towards cosmetic appearance and weight balance.

Results showed that 13 to 16 Δ were fitted in patients with 6/60 to 6/90 visual acuity and 17 to 20 Δ in patients with 6/90 to 6/300 visual acuity. Visual acuities with prism were not recorded in this study. Results were based on subjective answers to questionnaires regarding the usefulness of the spectacles. 38 out of the 49 patients answered the questionnaires. From those, the authors report a 61% success rate on wearing the glasses full-time.

Due to the high power of prescribed prisms there were several reasons for discontinuing the use of the spectacles, such as dizziness, headaches, distortion and the weight of the spectacles. A smaller prism might be sufficient to improve visual performance and thus avoiding the secondary effects from high power prisms. They only tested the eye with better visual acuity for prism when it could be that the eye with originally worse visual acuity could improve to be the better one once the prism was prescribed. Also, prism glasses were only prescribed for distance vision when results could be more successful on near vision. Finally, this study lacks a control group for before-and-after comparison and the recruitment selectiveness could have biased the results.

Bertrand et al., 1997

Although this is the latest of the four prism studies, it is quite interesting the fact that they did not make any reference to any of the three previous studies. They carried the study out on the smallest number of patients so far (14), these all being bilateral AMD sufferers. Patients were selectively chosen to have had a stable condition for a minimum of 3 months and being highly motivated to be re-educated to a new fixation technique.

Study		Romayananda et al. 1982	Rosenberg et al. 1989	Verezen et al. 1996	Bertrand et al. 1997
Subjects	Number	• 59	• No information given	• 48	• 14
	Ages	• No information given	• Over the age of 22 years	• 70 to 88 years	• Mean age 81 years
Diagnoses	• Macular lesions	• Macular lesions	• Macular disorder	• Bilateral end-stage AMD	• Bilateral macular degeneration
	V/A range	• 4M to 10M	• No information given	• 20/1000 to 20/150	• 1/20 to 3/10
Inclusion/Exclusion criteria	• Referred to the Low Vision Service of Temple Univ. Hosp. Dep. of Ophthalm.	• Referred to the Low Vision Service of Temple Univ. Hosp. Dep. of Ophthalm.	• Referred to the Low Vision Service at the New York Association for the Blind	• Pxs who made a prism-induced repositioning eye movement were excluded	• Motivated for re-education
Study design	• Treatment trial	• Treatment trial	• Control randomised clinical trial	• Treatment trial	• Treatment trial
Method to determine EV/PRL	• PRL assessed by examining fundus photos with a fixation pointer	• PRL assessed by examining fundus photos with a fixation pointer	• First, central fixation assessed with a standard black tangent screen with a large white X	• PRL position was identified from assessment of the corneal reflex while Px fixated the ophthalmoscope light at 50 cm distance	• Determination of PRL with visuscope
Method to determine prism	• Snellen Charts used.	• Snellen Charts used.	• Better seeing eye tested first	• The better eye was used for testing the EV prism. The other eye was occluded	• The prism base was prescribed to the same direction as that of the PRL
	• At very near vision (about 20cm) with an add of +6.00 DS	• At very near vision (about 20cm) with an add of +6.00 DS	• Px asked to turn head in the direction of best vision by fixating a target	• A prism of the tentative power with base in the EV direction was inserted in trial frame.	• Vertical component (up) of the eccentric viewing position was not prescribed
41	• Each eye tested monocularly and prism for both eyes determined by better eye	• Each eye tested monocularly and prism for both eyes determined by better eye	• An arbitrary 8 ^Δ placed with base in direction of head-turn and apex in the direction of the eye-turn. If there was no response to head or eye turn the Px rotated the axis to find the position of better vision	• If Px noticed improvement the prism power was increased in increments of 2 ^Δ .	• The technique used to prescribe prism power was not explained
	• 4 ^Δ prism inserted with corresponding axis to EV and rotated by Px until able to read clearly	• 4 ^Δ prism inserted with corresponding axis to EV and rotated by Px until able to read clearly	• Optimum prism power found by using a bracketing technique	• The effect of prism rotation was evaluated while fixating at a multi-dot chart.	
	• If reading does not become clear increase prism from 5 to 10 ^Δ until clearest	• If reading does not become clear increase prism from 5 to 10 ^Δ until clearest	• Eye refracted through prism	• The final prism was prescribed binocularly	
	• Check sphere by ±0.50 changes	• Check sphere by ±0.50 changes	• Prism prescribed and refined binocularly		
Repeat procedure for other eye	• Repeat procedure for other eye	• Repeat procedure for other eye			
	• Most Px needed a prism of 6-8 ^Δ	• Most Px needed a prism of 6-8 ^Δ	• No report of prescribed prism powers or base directions	• 13 ^Δ to 16 ^Δ fitted to Px with 6/60 to 6/90 VA	• Mean prism power 4 ^Δ to 5 ^Δ range
Characteristics of prism prescription	• For higher macular lesions higher prism required	• For higher macular lesions higher prism required	• 91% of the treated group improved	• 17 ^Δ to 20 ^Δ fitted to Px with 6/90 to 6/300 VA	• Base always horizontal
Effects of intervention	• 95% Px benefited from a base in the superior 180°.	• 95% Px benefited from a base in the superior 180°.	• Prism base directions not reported		
	• 100% success: near vision improving to a level that satisfied their functional needs. All patients achieved a reading ability of J14 (1.5M to 2M)	• 100% success: near vision improving to a level that satisfied their functional needs. All patients achieved a reading ability of J14 (1.5M to 2M)	• 60% of the control group did improve in VA, general performance or both	• 61% of those fitted with prisms showed a subjective VA imp.	• Mean DVA imp of 1.36 lines
Methodological limitations	• Only NV glasses	• Only NV glasses	• Assoc. between visual functions and prisms not investigated	• No VA imp. with prism relocation spectacles in comparison to EV VA.	• Mean NVA imp of 5 paragraphs and from P14 to P4
	• Patients not followed-up	• Patients not followed-up	• Prescribed prism details not specified	• None of the Pxs were able to read without the additional help of LVAs.	• Mean CS imp of 3.28 frequencies
	• Technique to determine success not specified	• Technique to determine success not specified	• The researchers were not masked	• Patients were selectively chosen	• Mean decrease of performing time for colour test of 50%
			• Patients were selectively chosen	• Patients were selectively chosen	• Patients were selectively chosen
			• No prism VAs reported	• Patients were not followed up	• Patients were not followed up
			• Glasses only prescribed for DV	• No placebo group	• No placebo group
				• No specification of DV and NV charts used	• No specification of DV and NV charts used

Table 1.4: Summary from previous studies on prism relocation

Their assessment consisted of a functional examination, where the following measurements were taken: distance and near VAs, Goldman perimetry, Farnsworth D15 colour test (controlling for performance time) and determination of the PRL with visuscope, before and after the prism prescription on the same visit, followed by an anatomic exam that included a bio microscopic assessment of the ocular fundus and a fluorescein angiogram.

The prism base was prescribed to the same direction as that of the PRL found with a visuscope, but they did not specify if the binocular prism was prescribed monocularly and then applied binocularly, or if it was prescribed binocularly. Also, the technique used to obtain the optimal prism power was not explained. The mean prism power range was quite low (4 to 5Δ) and the prism base was always horizontal (7 at 360° and 7 at 180°). They found that patients frequently had a vertical component (up) onto the eccentric viewing position but did not prescribe vertical prism bases because they were not thought to provide any extra benefit when tried on patients. They reported a mean distance VA improvement of 1.36 lines and of 5 paragraphs for near VA but they did not specify the type of charts used to measure both types of visions. They also found a mean improvement of contrast sensitivity of 3.28 frequencies (they did not clarify what exactly this improvement is) and a mean decrease on colour vision performance time of 50%.

Again, this study had a small and selected amount of patients, lacked from a clear prescribing protocol, a placebo group and patient follow-up.

Although, results from these previous studies are limited, they are sufficient to show that the concept of prism relocation for patients with central scotomas caused by AMD could improve vision and thus quality of life on these patients. However, there is a clear need for a randomised controlled trial to verify the effectiveness of prism relocation for AMD patients.

CHAPTER 2

Study design and non-clinical measures

2.1 Aims of the study

AMD affects people over the age of 50 (see section 1.1.1). As longevity is increasing, the elderly population grows as well, with the consequence of higher incidence of AMD (Rosenthal & Kelly, 2001). Current treatments available for AMD are very limited or still await large clinical trials before they can be considered effective and safe procedures.

Low vision devices, such as magnifiers can be useful for AMD patients but are very difficult to use due to the need to maintain a specific lens position, the reduction in the field of view and the difficulties navigating through text. Most low vision devices are specifically for reading but often the patient can only read for short periods of time before getting tired and frustrated (Watson et al., 1997). Other devices such as CCTV can be used for longer periods but are expensive and bulky to carry (Goodrich, 1978).

Eccentric viewing could help the patient but is difficult to learn/teach. Prism lenses suggest an alternative way to move images to parafoveal location and have been tried in previous studies (Romayananda et al., 1982; Rosenberg et al., 1989; Venezen et al., 1996 and Bertrand et al., 1997), all describing simple ways of prescribing prism lenses and reporting promising results although they all had different prescribing strategies. Unfortunately, these studies suffer from poor experimental design, lack of control groups and statistical analysis, and non-specific outcome measures, making their conclusions suspect.

The study reported in this thesis is a 3 arm randomised trial involving a total of 225 patients with the goal of trying to find out whether prism relocation therapy is able to reduce the disability experienced by patients with AMD in everyday tasks such as reading, watching TV and cooking. This study also aims to find a simple way to prescribe prism spectacles to

patients so that a simple protocol could be evolved for optometrists to use in their practice and with conventional instrumentation.

This study also evaluates how some factors, such as visual functions and fixation characteristics may predict the efficacy of prism relocation in unselected patients with AMD.

The primary and secondary aims of this study are:

Primary aim:

- i) To determine the effectiveness of prism spectacles as a method of relocating the retinal image in cases of AMD. Outcomes will be assessed in terms of traditional clinical vision measures, practical task performance, vision-related quality-of-life and the usage patterns of the various aids.

Secondary aims:

- ii) To determine the clinical characteristics of the patients who would benefit from prism spectacles.
- iii) To investigate the degree to which the optimal relocating prism can be predicted from clinical vision measures.
- iv) To explore the extent to which prism spectacles may obviate the need for conventional LVAs

Two researchers, those being one optometrist and one psychologist, carried out the study. The optometrist performed the clinical measurements on the patients whilst the psychologist conducted the non-clinical measurements (see section 2.9). The data presented in this thesis are those collected by the optometrist and covers aims ii) and iii) of the study whereas data for aims i) and iv) have been collected and presented in the second researcher's (the psychologist) thesis (Smith, 2004).

The large amount of data collected for this study provides an opportunity to investigate a large sample of the AMD population who were largely unselected (i.e., there were few exclusion criteria for the study). An additional aim for this thesis, in addition to the remit of the clinical trial, was therefore to describe the clinical population recruited for the study with respect to visual functions, low vision aids, features of the pathology and fixation characteristics.

The main outcome measure to evaluate the effectiveness of the prism spectacles was visual acuity improvement after three months wear compared to visual acuity on entry of the study. Other outcome measures included the non-clinical measures discussed in section 2.10.

2.2 Controlled randomised trial

The primary aim of this study was to evaluate the effectiveness of prism spectacles in AMD patients. Evidence had to be collected in a way that made the interpretation of the data unequivocal. For this reason, a controlled experiment was required to uncover the relative effects of having or not having the prism spectacles. A **control** group had to be included, where patients were wearing lenses without prism but matched in weight and thickness to prism lenses (placebo). So that the participants were unaware of the difference they also had to be randomly assigned to the “treatment” or “control” groups. In order to ensure that patients allocated to either the treatment or control group were not being biased, the treatment for each patient had to be decided by chance in a **random allocation**. Random allocation not only avoided personal biases, but also tended to balance the treatment group in respect of the effects of extraneous factors that may influence the outcome of treatment (such as sex, age and severity of AMD). Randomisation could not guarantee that the groups were exactly the same in the trial but it did ensure that, on average, there was comparability (comparability was later checked and reported in section 5.1). Furthermore, it enabled valid confidence intervals for treatment effects (differences) to be determined, taking into account chance fluctuations one would expect to result from the random allocation procedure.

This kind of experiment is called a **controlled randomised clinical trial**. This type of trial facilitates comparison between control and treatment groups taking into consideration the placebo effect. Thus, it was possible to conclude confidently that any differences observed between the two groups had arisen solely because of the differences between the spectacles worn (i.e., the effect of the treatment).

To ensure comparability of the different arms of the study it was vital that patients within each arm were treated in the same way all through the study. Besides the single aspect of their treatment, all groups had to receive the same attention to make them comparable. To avoid bias that may arise from the knowledge about the treatment group for each patient it was necessary to mask the optometrist prescribing the prism spectacles, the research psychologist measuring the outcomes as well as the patient him/herself. This study is thus a **double-masked randomised controlled trial**.

Previous studies (Romayananda et al., 1982; Roosenberg et al., 1989) used prescribing protocols to determine the required prism. A similar approach was adopted in this study (“custom” prism). It could be argued however, that (especially if there are multiple PRLs) any prism which moves the image out of the scotoma could be equally beneficial, thus suggesting that there ought to be a “random” prism group in which prism spectacles with a prism of

randomly-selected power and base direction were dispensed. In clinical practice, however, it is most unlikely that this would form a rational prescribing strategy. It would in fact be more useful to test a prism of fixed power and direction. It would be practically beneficial if this “standard” prism were shown to be effective, since it could be dispensed by a rehabilitation worker or other professional with no optometric expertise and/or given as a standard clip-on for patients to try before prescription lenses were made up.

In selecting this standard power, previous literature (Romayananda et al., 1982; Rosenberg et al., 1989) suggested that the most effective prisms for AMD patients were between 4-10 Δ , although Verezen et al. (1996) suggested that more powerful prisms (13-20 Δ) benefited patients with AMD by removing the need for eccentric viewing. Romayananda et al. (1982) found a correlation between the lesion size and the prism power, so that the larger the macular lesion, the larger would be the prism power prescribed for that patient. Verezen et al. (1996) also gave lower prisms (13-16 Δ) to patients with better VA (6/60 to 6/90) and higher prisms (17-20 Δ) to those with poorer VA (6/90 to 6/300). Based on these studies, two different standard prism powers were selected, depending on the baseline VA of the patient: these are 6 Δ if the VA ranges between 0.50 and 1.00 logMAR and 10 Δ if the VA in the better eye is between 1.02 and 1.68.

The standard prism base direction was also decided from previous literature findings. Romayanda et al. (1982) found that 95% of patients benefited from a base in the superior 180 degrees of field. It had also been suggested that on central vision loss, the PRL is usually located in the inferior part of the visual field (McMahon et al., 1991). Petre et al. (2000) also concluded that there is an advantage in eccentrically fixating such that text falls in inferior rather than left visual field. All these studies advocate the superior part of the retina for better functional results and therefore we have selected 90° to be the base direction for the standard prisms of both 6 and 10 Δ .

There were therefore two different treatment groups (custom and standard prism) and a no treatment group (placebo), making this study a 3-arm Randomised Control Trial (RCT), where the 3 arms were:

Arm 1 – Treatment: customised prism (prescribed)

Arm 2 – Treatment: standard prism (following the above-mentioned criteria)

Arm 3 – Placebo: control (no prism given but lenses matched for weight and thickness)

2.3 Randomisation and masking

Recruited patients were randomised to the three treatment arms, using sealed envelopes to conceal the “treatment” allocation (arm number) prior to recruitment and determination of eligibility. An academic colleague who was not involved in the conduct of the trial generated the random allocation sequence and the sealed envelopes. Each patient was therefore allocated to a specific arm of the study on completion of the first of the three study visits, this being with the optometrist at the MREH. During this first visit patients had their visual function tests and were tested to determine both a customised and a standard prism. Both prescriptions were then copied by the optometrist onto a separate prescription sheet and passed onto the principal optometrist at the MREH. He then opened the sealed envelope for the corresponding study number of the patient and ordered the appropriate spectacles to the allocated study arm. The optometrist did not see the patients again and thus remained masked during the whole patient follow-up.

Study spectacles were collected by patients on their second visit, which took place at the Department of Optometry and Neuroscience at UMIST, when they were also seen by the second researcher in addition to the patient. Placebo spectacles were matched on weight and thickness to the prism ones with the aim of masking the second researcher. Also, the lack of an optical background of the second researcher helped to assure the concealment of the allocations.

The Central Manchester Local Research Ethics Committee gave ethical clearance for the study (Reference number: CEN/00/150) and The Health Foundation supported the study (Grant: 1071/530).

2.4 Sample size

A sample size of at least 75 patients per arm of the trial allowed the study to detect a standardised difference in outcomes between two groups of 0.46, with 80% power at 5% (2-tailed) significance level. Because outcomes had to be adjusted for baseline measures, this difference in effect size was small, implying that the study was unlikely to miss any important differences between the groups.

It was aimed to recruit a minimum of 225 (75 per study arm) patients at the Manchester Royal Eye Hospital (MREH) in a period of 20 months.

2.5 Inclusion/exclusion criteria

The hospital notes of all patients attending the low vision clinic were assessed according to the following inclusion criteria:

- Primary diagnosis of bilateral AMD
- VA worse or equal to 0.50 logMAR (6/18 Snellen) in the better eye but better or equal to 1.68 logMAR (1/48) in at least one eye.

and exclusion criteria:

- Non-English speaker (poor communication in English will impair accurate recording of data such as VA and reading speed)
- Patients diagnosed with dementia/mental illness, since instructions regarding use of spectacles and recording of their use might not be remembered. Patients also had to score 16 or more on the MMblind when attending their first visit to the study (see section 2.6). This test provided the opportunity to screen patients who although not having a diagnosis of dementia/mental illness, would not have sufficiently good memory to supply the required feedback for the study
- Patients in a wheel chair or residents in a hospital or a nursing home (both of which might be expected to limit the range of daily activities undertaken)

All patients meeting the inclusion/exclusion criteria were approached and given the opportunity to take part in the study.

2.6 Mini-Mental State Examination: MMblind

The Mini-Mental State Examination (MMSE) was developed by Folstein et al. (1975) as a bedside test that could be used to detect cognitive impairment. The MMSE has been widely used as a method of screening for dementia. It is quick (about 10 minutes) and easy to administer.

The goal of using this MMSE is to identify and exclude any participants whose cognitive functioning may be an overriding factor in their ability to perform the outcome measures, for example, because of dementia. We are not expecting many (if any) participants to have dementia since they are most likely to have been screened out at the stage when the hospital files were assessed for the inclusion/exclusion criteria (section 2.5), i.e. prior to contacting the patient.

It has now been widely proved that age plays a big role in patient memory and this affects the cut-off figure. The MMSE score dropped as the age increased. Bleecker et al. (1988) showed

that the MMSE total score was significantly associated with age, but not with vocabulary (which increases with age), depression, or gender. The parts of the MMSE that were found highly associated with age were the recall of three items, the spelling of the word "world" backwards and the repetition of the phrase "no ifs, ands or buts".

Crum et al. (1993) also found a steady and consistent decline in the MMSE score as the age got higher. The scores also showed a greater variability as age increased. They also concluded that the MMSE scores varied with educational level and race (blacks were found to have higher prevalence of severe impairment as compared with either whites or Hispanics) but not with gender.

Visual impairment leads to missing values on some test items for visually impaired people, which prevents an accurate interpretation of the test result. For this reason, the items requiring vision could be excluded from the MMSE: this version of the MMSE was called MMblind (Reischies & Geiselman, 1997). The excluded items are naming (two items), reading, comprehension, copying, writing and instructions to handle the sheet of paper (three items), resulting in a maximum score of 22 points (compared to 27 on the original MMSE).

Reischies & Geiselman (1997) found that neither sensitivity², nor specificity³ of the shorter MMblind version was reduced in comparison to the MMSE. For the younger group, sensitivity and specificity for detecting dementia of 84.9 and 82.1 were found at a cut-off value of 18-19. For the older group, sensitivity and specificity were 73.4 and 78.1 at a cut-off value of 17-16. As this study involves patients selected with no upper age limit, a cut-off value of 16 (patients scoring 15 or less were not recruited in the study) was chosen.

The MMblind test was used in this study for patients on their first visit and prior to confirming their recruitment (see Appendix 1).

2.7 Patient recruitment

All patients meeting the inclusion/exclusion criteria (see section 2.5) were informed of the study and invited to participate by letter in the first instance. This letter (bold Arial with font size 18 point was used for any contact letter sent to the patients) and explained to patients the purpose of the study and what would happen if they decide to take part. There are two versions of this letter, one for new patients to the LVC and another for patients that have

² **Sensitivity** measures the proportion of diseased individuals that are correctly identified as diseased by the test (true positives as a proportion of the true positives plus the false negatives: $TP/(TP+FN) \cdot 100$)

³ **Specificity** measures how good the test is at correctly recognising normal patients and calling them normals (true negatives as a proportion of true negatives plus false positives: $TN/(TN+FP) \cdot 100$)

attended the LVC at least once (Appendix 2 shows a sample of the letter sent to patients that had already been to the LVC). The letter explained that the optometrist would contact them after a period of 1-2 weeks to see if they had any questions and to determine if they were able to take part in the study.

On their first visit, the patient signed a consent form (Appendix 3) prior to beginning the study. The consent form explained that there were no risks to their health by taking part and that they had the right to withdraw from the study at any time. This form was read to patients to ensure that all patients understood the conditions before signing.

Reasons for not participating	Number of cases
Reasons for unsuitability (did not meet the inclusion criteria when contacted)	54
Poor memory	18
Wheelchair	8
Profoundly deaf	7
Poor proficiency in English	4
Living in nursing home	4
Diagnosed with another eye condition that would interfere with the study	3
Deceased	3
In another study	2
Already wearing prisms for other condition	2
Illiterate	2
Having PDT treatment	1
Reasons for unsuitability (did not meet the inclusion criteria on first visit)	25
VA too good (0.46 logMAR or better)	21
MMSE not passed (score of 15 or less)	4
Reasons for refusing	93
Health problems	42
Not interested	39
Too far to travel	8
Unknown	2
Going away	1
Husband ill	1
Did not attend first visit	7
Unable to contact	20

Table 2.1: Reasons and numbers of patients invited to take part in the study but didn't participate.

Between July 2001 and March 2003, 442 patients were approached with the contact letter and invited to participate in the study (see Figure 2.1). Of these, 275 (62%) agreed to take part and were given an appointment for the first visit, 20 (5%) were unable to be contacted, 93 (21%) refused to take part and 54 (12%) were not suitable. 243 (88%) patients were randomised into the 3-arms of the study and the missing 12% out of the 275 that agreed to participate were not randomised due to poor memory (MMSE not passed), not attending the appointment or visual acuities outside the inclusion criteria. Table 2.1 gives the reasons and numbers of patients invited to take part in the study but who did not participate.

2.8 Reporting of the trial

An attempt has been made to follow all the guidelines set out in the revised recommendations made by the CONSORT (Consolidated Standards of Reporting Trials) group (Moher et al., 2001) for reporting of the trial. The CONSORT checklist was developed by a group of scientists and editors and offers a standard way for researchers to report trials. It includes 22 items (see table 2.2), based on evidence, that need to be addressed in the report; the flow diagram provides readers with a clear picture of the progress of all participants in the trial, from the time they are randomised until the end of their involvement. The intent is to make the experimental process more clear, flawed or not, so that users of the data can more appropriately evaluate its validity for their purposes. The proposed 22 items have been included in the RCT.

2.9 Trial structure

All patients meeting the inclusion/exclusion criteria were contacted by the optometrist and, if they agreed to take part in the study, an appointment was made for the first visit.

Patients were required to attend 3 visits in total (see flow chart in Figure 2.2). The first visit was at the MREH and the second and third visits at UMIST. The optometrist saw patients in the MREH at their first visit and the consent form was then signed by the patient. This visit took about 3-4 hours and included the following tests:

- MMblind (see section 2.6)
- Personal and background information (see section 3.1)
- Visual functions (see section 3.2):
 - Conventional and prism distance visual acuity scoring (ETDRS chart)
 - Conventional and prism near reading acuity (Bailey-Lovie reading chart)
 - Single, crowded and repeated letter VAs
 - Perimetry (Bjerrum screen)
 - Contrast sensitivity (Pelli-Robson)
- Refraction (see section 3.3):
 - Prism trial and prescription
 - Perceived disabilities and goals (MLVAI)
 - Low vision assessment

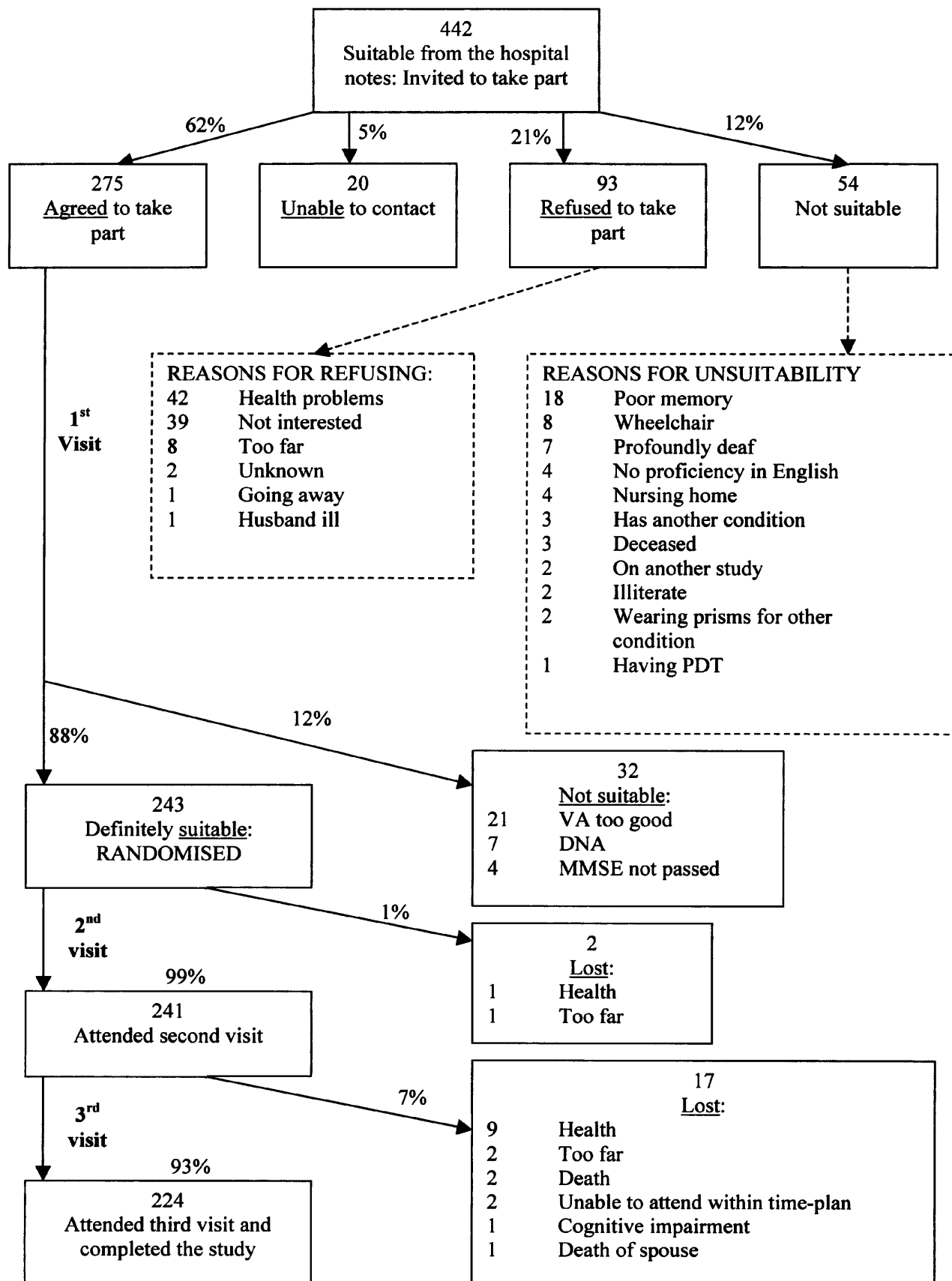


Figure 2.1: Flow diagram of Patient recruitment

Paper section and topic	Item num.	Descriptor	Reported on section/ chapter
Title and abstract	1	How participants were allocated to interventions.	2.3
Introduction			
Background	2	Scientific background and explanation of rationale.	1.3.4, 1.4.5
Methods			
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	2.5
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	2.9
Objectives	5	Specific objectives and hypothesis.	2.1
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements.	2.1
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	2.4
Randomisation, sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction.	2.3
Allocation concealment	9	Method used to implement the random allocation sequence, clarifying whether the sequence was concealed until interventions were assigned.	2.3, 2.9
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups	2.3, 2.9
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated	2.3
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); methods for additional analyses, such as subgroup analyses and adjusted analyses.	*
Results			
Participant flow	13	Flow of participants through each stage (a diagram strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analysed for the primary outcome.	2.7, 2.9
Recruitment	14	Dates defining the periods of recruitment and follow-up	2.4
Baseline data	15	Baseline demographic and clinical characteristics of each group.	Chapter 4
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention to treat." State the results in absolute numbers when feasible.	*
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group and the estimated effect size and its precision.	*, Chapter 6
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those prescribed and those exploratory.	Chapter 5
Adverse effects	19	All important adverse events or side effects in each intervention group.	N/A
Discussion			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes.	*
External validity	21	External validity of the trial findings.	*
Overall evidence	22	General interpretation of the results in the context of current evidence.	Chapter 7

Table 2.2: CONSORT checklist of items included for reporting a randomised controlled trial.

* These items have been discussed on the second researcher's thesis (Smith, 2004)

N/A These items were not applicable to this study

- Ocular pathology (see section 3.4):
 - Classification of cataracts (LOCS III)
 - Fundus photographs (classification of AMD and determination of the static fixation position)
- Dynamic fixation (see section 3.5.2)
- Assessment of eye movement response to binocular prescribed prism (see section 3.5.3)
- Frame selection for study spectacles and explanation of diary (see section 2.10.7)

Patients were recruited into the study for 4 months. During the first month patients adapted to the conventional LVAs acquired/updated at the first visit and also, to the new conventional prescription, if provided. They also completed the first four weeks of the diary commenting about the conventional aids prescribed.

To make sure the optometrist was masked all prescriptions were passed on to the principal optometrist of the MREH, who was involved in the study but not involved in patient assessment. He randomly allocated each patient to one of the 3 arms and ordered the appropriate spectacles from the optometrist's prescription. If conventional spectacles needed updating they were also ordered. Conventional spectacles were either posted to the patient or collected as soon as they were ready.

As soon as the study spectacles were ready, the second researcher telephoned the patient to administer 2 pre-intervention questionnaires: NEI-VFQ-25 (see section 2.10.2) and AVL (see section 2.10.3) and to make an appointment for the second visit.

During the second visit, patients collected the study spectacles (these were one of either custom, standard or the placebo spectacles, depending on the allocated arm for the particular patient) and the second researcher saw them. The following pre-intervention tests were then performed:

- Binocular DV and NV VA with conventional spectacles, LVAs and study spectacles
- Reading speed with conventional and study spectacles using the MNREAD acuity chart (Mansfield et al., 1993)
- The Melbourne Low-Vision Activities Index (weighted version) questionnaire (MLVAI(w)) with conventional spectacles and LVAs, if used to assess patient's performance on activities of daily life (Haymes et al., 2001b) (see section 2.10.4).
- The Manchester Low Vision Questionnaire (MLVQ) for LVAs to gather information on the success of low vision rehabilitation for patients with AMD (Harper et al., 1998) (see section 2.10.6).

Patients used the study spectacles for three months. During those three months they continued to complete a diary, this time including the study spectacles in it. Near the end of the 3 months trial with the study spectacles the second researcher contacted the patient to administer the NEI-VFQ-25 questionnaire again, this time as a post-intervention measure, and to make an appointment for the last (third) visit.

At the last visit, patients handed in the diary and the following post-intervention measures were carried out by the second researcher:

- Binocular DV and NV VA with conventional distance spectacles, LVAs, and study spectacles.
- Reading speed with conventional and study spectacles.
- MLVAI(w) with study spectacles and LVAs, if used.
- MLVQ- for study spectacles.

Patients were given a thank you letter (Appendix 4) on their last visit, thanking them for their co-operation and saying that from then on if they need any further appointments for the low vision clinic (LVC) they could ring the number for the Hospital LVC provided on the letter. Participants who had still been wearing their study spectacles at least occasionally at the time of the last visit were also contacted 9 months after recruitment time by the second researcher to check if they were still using the study spectacles. Finally, patients received a letter from the second researcher once the study was finished to inform patients of the findings from the study.

2.10 Non-clinical measures

Clinical tests of visual function have traditionally been used to assess visual performance but for the last few years there has been an increase in the use of patient-focused outcome measures. Massof & Rubin (2001) state that the National Institutes of Health, including the National Eye Institute, now requires measures of health-related benefits as outcome variables in studies they support. That is because clinical measures can be a poor guide to the benefits of interventions to reduce disability. This was proved by Leat et al.'s (1994) study where they evaluated a low vision clinic and found that logMAR visual acuity and reading rate were not

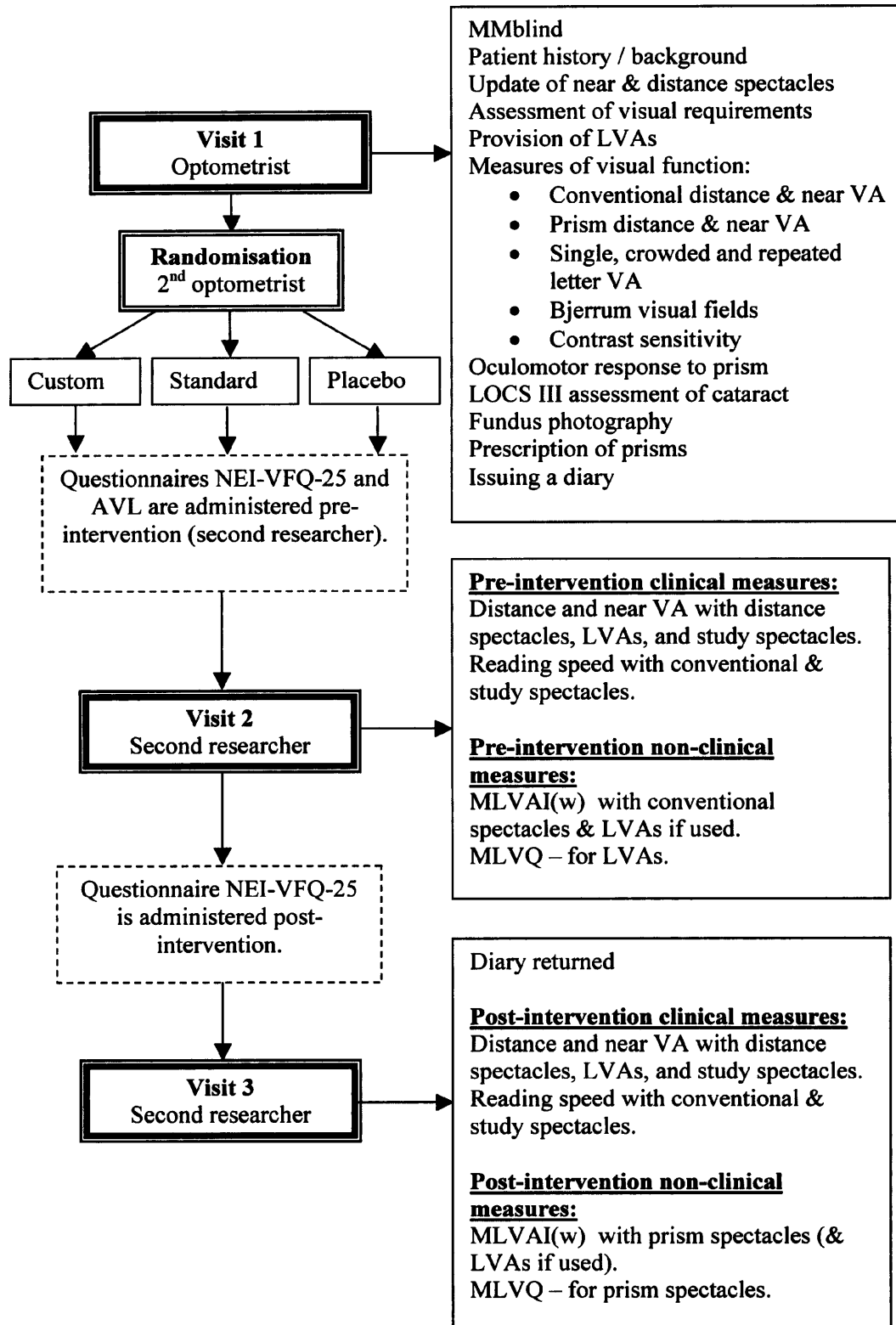


Figure 2.2 Participant's pathway through the study

associated with perceived success but, on the other hand, found a discrepancy between the ability to read 1M print in the clinic (75% of patients) and the reported ability to read regular-sized print at home (35%).

Non-clinical measures (also known as patient-focused outcome measures) are important in evaluation of the effectiveness of interventions that assess the quality of health care, improving clinical decisions and understanding the causes and consequences of differences in health-related quality of life (HRQOL). The main aim for this study requires an assessment of the impact of the prism spectacles on the patient. There is therefore a need to include appropriate non-clinical tests that can show any benefit that prism spectacles might give to AMD patients besides the visual functions and fixation characteristics evaluated in the study. This section will review the non-clinical measures that will be used in the study for this purpose by the second researcher.

2.10.1 Quality of life

Quality of life (QoL) has many definitions to many people. Arnold (1991) states that there are a variety of definitions in the literature that reflect the professional orientations of the authors. This makes QoL a complex phenomenon as individuals seem to have their own idea of what it means, but struggle to define it when trying to measure it. Clinically oriented researchers define QoL in terms of health status or functional capability, while others include life satisfaction, relations with others or material comforts. HRQOL can be said to measure functioning and well-being in physical, mental and social health realms of life and reflects the influence of a broad range of health conditions simultaneously (Mangione et al., 2001).

HRQOL is usually measured by means of questionnaires that should include enough items to cover a wide range of activities reflecting disability in activities that matter to the individual. An instrument or questionnaire is the set of questions used to assess daily functioning, or other aspects of health-related quality of life and the individual questions are called items (Seddon & Fong, 2001). All items are usually given equal values and thus tasks are given equal weight, regardless of the visual difficulty of the task. However, this scoring system may cause problems and interval scales have been developed to solve this problem (see section 2.10.5). A HRQOL questionnaire needs to have a high reliability and validity. An instrument is reliable when it gives reproducible and consistent results. Reliability can be measured as test-retest reliability, where the scores of the same test administered to the same group of people on two occasions within a short space of time should correlate with each other. Reliability can also be measured by its internal consistency, where the scores obtained by a group of individuals on each item should correlate with their total scores. Finally, inter-rater

reliability should be checked, where the ratings of two test administrators testing the same group of respondents should correlate. Validity, on the other hand, tests that an instrument measures what it intends to measure and sensitivity is one aspect of validity where a small but clinically important change in the study population following intervention should show in the analysis of the questionnaire (Seddon & Fong, 2001).

QoL measures may be generic or disease specific. Generic measures are those that can be used over a wide range of patients suffering from different diseases and with different characteristics. They can be used to compare different populations using the same criteria, which is necessary for policy analysts involved in health services evaluation and resource allocation. Examples of these include the Short Form 36 (SF-36) and the Sickness Impact Profile (SIP) (Bergner et al., 1986). Generic QoL measurements will not be used on this study, as they do not measure activities of every day life that are particularly affected by vision impairment. As examples, Scott et al. (1999) found that the SF-36 lacked sensitivity when used to evaluate outcomes following vision rehabilitation and similarly, Mangione et al. (1999) did not find it to be sensitive for discrimination of severity of AMD. Also, not including generic QoL measurements prevents patients from suffering respondent burden.

Disease-specific measures are, on the other hand, designed to focus on the complaints attributable to a specific diagnosis or patient population. These tend to be more sensitive than generic measures to clinically important changes (Patrick & Deyo, 1989). This sensitivity is quite important when evaluating clinical trials and since this study is carried out on low vision patients a test of vision-related QoL is required. Quality of vision is an integral part of QoL and is disease-specific. Reductions in visual acuity, central visual field, contrast sensitivity, colour discrimination and problems with glare recovery are initial impairments that cause the everyday problems for those with low vision, all of which impact on QoL. These questionnaires capture aspects of visual functioning not reflected in visual acuity and general health status measures.

The following sections in this chapter cover the instruments chosen for the study to measure QoL. The Adaptation to Vision Loss questionnaire (section 2.10.3) was only administered once in the second visit (baseline visit) to provide baseline information that could affect the outcome of the trial. The National Eye Institute Visual Functioning Questionnaire (section 2.10.2), the Melbourne Low Vision ADL Index (section 2.10.4) and the Manchester Low Vision questionnaires (section 2.10.6) were, on the other, administered in both the second and third (follow-up) visits to be used as outcome measures. Finally, the diary (section 2.10.7) was provided and explained in the first visit and returned on the third visit, as shown on flow-chart in Figure 2.2, and was also used to obtain outcome measures.

2.10.2 National Eye Institute Visual Functioning Questionnaire (NEI-VFQ)

The NEI-VFQ is one of the most widely used non-clinical instruments and was created when the National Eye Institute (NEI) saw the need for a visual functioning questionnaire that would measure not only a patient's symptoms and difficulty with specific tasks, but also how patients cope with the emotional and psychological affects of vision loss. Whereas most of the visual functioning questionnaires concentrated on particular diseases, such as cataracts, the NEI-VFQ was aimed to assess patients with a broad spectrum of diseases and vision impairments.

The original NEI-VFQ is composed of 51 items and has been proved successful in detecting disability across many different conditions (cataract, glaucoma, diabetic retinopathy and AMD) as the score was found to correlate with the visual acuity in the better eye of patients and also has a quite high content validity and internal consistency (Mangione et al., 1998). It has also proved to have a high test-retest reliability and thus been an appropriate tool to measure change in vision targeted HRQOL over time (Mangione et al., 1998). Over all, these positive qualities have made the NEI-VFQ the current "gold standard" of vision-related QoL.

Due to response burden, participation rates, data quality and cost a shorter version of the NEI-VFQ was later developed (Mangione et al., 2001). This shorter version has 25 items and can be administered in about 10 min. It keeps the same domains except for vision expectations, as some of these questions were upsetting to some participants and already correlated highly with the mental health domain in the original 51-item version.

The NEI-VFQ-25 was used in this study as one of the outcome measures for assessing the effectiveness of prism spectacles in patients suffering from AMD and so, the difference in the score was assessed pre- and post-intervention. It was administered by the psychologist over the phone prior to attending the second visit and again prior to the third visit. A telephone interview made the visit shorter and more confidential than what it might have been in the visit, when the patient might have come accompanied by a family member. This questionnaire has been previously validated for this delivery in patients with AMD (Miskala et al., 2003).

2.10.3 Adaptation to Age-related Vision Loss Scale (AVL)

Horowitz & Reinhardt (1998) developed the AVL to assess psychological adaptation to age-related vision loss by measuring three different domains: acceptance of the vision loss, attitudes towards rehabilitative training, and attitudes concerning relationships with family members and friends. The questionnaire was quite specific in that it was designed for older

participants with acquired visual loss: much previous research had focused on young and middle aged populations (Needham & Ehmer, 1980; Dodds et al, 1994).

In this study, participants' responses to the prism spectacles may be affected by some of the psychosocial factors that the questionnaire reveals. For example, participants with a realistic approach to both limitations and remaining capabilities could be sensitive to any subtle improvements in vision due to prism spectacles. On the other hand, participants who have difficulty overcoming the visual problem may have unrealistic expectations and may only experience disappointment if the prism spectacles do not make a dramatic visual improvement. Miller & Rollnick (1991) found that the participant's attitude to visual loss affects the placebo effect. They found that those participants willing to follow instructions or to take part in a study were associated with successful outcomes even when the treatment applied was a placebo. The use of the AVL questionnaire in this study should thus provide a baseline data for comparing psychological factors between groups that can be used to test if such factors are randomly distributed across all three arms of the study.

This questionnaire was administered over the phone to cut the length of the first visit down and also to make the interview more confidential, as patients may be influenced by the presence of the family member/friend that might be accompanying them when answering certain questions about family/friends relationships, such as "I feel comfortable asking my family and friends to help with things I can no longer do because of my vision loss".

2.10.4 Melbourne Low Vision ADL index (weighted version)

The Melbourne Low-Vision Activities Index (MLVAI) has proven to be a highly valid and reliable standardised test of activities of daily living (ADL) performance for the general low-vision population. It may be used to assess patients with low vision and has the potential to be used as a measure of low vision rehabilitation outcomes. It was originally developed (Haymes et al., 2001a) to test activities of daily living (ADLs) appropriate for the low-vision population. The weighted version (MLVAIw) (Haymes et al., 2001b) only differs from the original in that each item is weighted by a subjective importance rating scale and thus measures disability impact. Therefore, a task that the participant would consider absolutely unimportant will get a score of 0 even if the participant can't perform the task. A zero score means there is no personal disability impact for the item.

The MLVAIw is composed of two parts: Part A measures performance of 16 complex instrumental ADL tasks by experimenter observation and part B the subjective assessment of performance of nine self-care ADLs. The items for the MLVAI were selected, from ADL

instruments used to assess the aged, as those that were more frequently used and showed consistency with research on the daily living problems reported by people with vision impairment. The items were selected based on the following selection criteria: importance in daily living, relevance in low-vision rehabilitation, and ability to distinguish between people with different amounts of vision impairment (Haymes et al., 2001a).

The MLVAIw has good reliability and validity (Haymes et al., 2001b) but suffers from some limitations such as being heavily biased to reading and not including some tasks that many patients find very important, e.g. watching TV. Another restraint is that it is carried out under an artificial controlled environment quite different from the everyday life conditions that patients will be exposed to while using the prism spectacles. However, it has the advantage of rating the ability of participants to perform typical vision-related ADLs in a manner that generally avoids reliance on participants' own subjective judgements of their performance. Overall, the MLVAIw was a useful test to be administered to patients as one of the outcome measures for this study and thus, on baseline and follow-up.

2.10.5 Creating an interval scale: the Rasch model

The classic test theory has been used to develop and validate most visual function instruments (Streiner & Norman, 1995). This theory assumes that each item contributes equally to the measure of the construct and that each item is measured on the same interval scale. This approach would thus be appropriate if all data obey these two assumptions. However, when the data has been collected by means of questionnaires, such as those discussed previously in this chapter, every question counted as an item and item responses were generally at the ordinal, or even nominal, level, and a linear combination of ordinal ratings produces meaningless numbers (Turano et al., 1999).

An alternative to this approach is the item-response theory (IRT), where the rating units that form an ordinal scale can be used to estimate values on an interval scale. A general item-response model was first developed by Birnbaum (1968) and then simplified by Rasch (1980). Rasch's model is the simplest model of IRT and is based on a probabilistic relation between any item's difficulty and any person's ability. That is, he argued that the difference between these two measures should govern the probability of any person being successful on any particular item: all persons should have a higher probability of correctly answering easier items and a lower probability of correctly answering more difficult items. Similarly, a difficult item has more chance of being performed by someone with good ability than someone with poor ability.

The Rasch model uses rating units of psychometric instruments to estimate values on an interval scale and allows the validity of any psychometric instrument to be tested with an objective set of criteria. This model also identifies redundant items, those that do not fit the presumed hierarchy, and gaps in the scale. Moreover, this model has already been used to re-evaluate some existing questionnaires such as the ADVS (Activities of daily vision scale) (Pesudovs et al., 2003) and VF-14 (Veloze et al., 2000). The Rasch model was thus chosen to evaluate MLVAI(w) results to assess the effectiveness of prism glasses in reducing disability in this study.

2.10.6 Manchester Low Vision Questionnaire (MLVQ)

The MLVQ was designed (Harper et al., 1998) to gather information on the success of low vision rehabilitation for patients with AMD. It measures different characteristics of LVA use. These include which common tasks are carried out with a LVA, patient satisfaction with the low vision clinic, patient knowledge of AMD and attitudes to low vision. It also asks participants to estimate the length of time they use each aid and to rate how useful the aids are to them. The level of difficulty using aids is rated and any difficulties with the aids are recorded.

For this study the MLVQ had to be adapted and the questions about the patient's satisfaction with the clinic and knowledge were excluded, as these were not relevant to the study. The patients were therefore only asked the questions on LVA extended to use of prism spectacles. Also, a few extra questions had been added with the intention of finding out where patients kept their LVAs and prism spectacles and who does each of the common tasks listed (if themselves alone, themselves with help, their partners or no-one).

The MLVQ was administered on both the second and third visits. Participants would have had the low vision aids for at least one month (this is the time-gap between the first visit, when they had the low vision assessment and second visit, when they collected the study glasses). The questionnaire was thus administered in the second visit for low vision aids and in the third visit for study spectacles.

2.10.7 Diary

Diaries are a type of self-completion questionnaire. Self-completion questionnaires have a number of advantages. They avoid the constraints of a structured interview with pre-defined questions and enable participants to comment on their experiences as they come across them and therefore avoid any bias that may affect a questionnaire that prompts selective recall of

past events. Also, they give an insight into the participants' everyday lives. Diaries, in particular also give participants the opportunity to mention information that they may have forgotten to mention or may not have had a chance to mention while being interviewed. Patients were asked to report once per week the length of time they have been using every low vision aid, the activity/es they were used for and any comments they might have about its usefulness, difficulties to use and any impressions they might want to comment.

One of the main goals from the use of a diary was to find out the frequency that patients used their study spectacles. A participant that found the spectacles useful would, in theory, have worn them more than another participant that did not find them beneficial. If the frequency of use was scored weekly there were less chances to miss information that may have been forgotten by the time participants got questioned with the MLVQ. This information could then be arranged into categories to be analysed for possible differences between the three arms of the study. The same analysis could be applied to find out if LVAs were been used less frequently after the study spectacles had been provided.

CHAPTER 3

Clinical measures

This Chapter describes the clinical measures performed by the optometrist during the first of the three study visits. This first visit took place at the MREH, where the following clinical measures were performed. These tests were done on both eyes once the patient had scored the minimal passing mark for the MMblid.

3.1 Personal and background data

Besides the clinical measures, some basic personal and background data were also collected from patients to provide demographic information about the population sample taking part in the study. The patient's title, name, surname, address and telephone number were recorded. This information was used later by the psychologist to contact them and arrange the appointment for second and third visits.

The age, gender and ethnic background were also recorded with the aim of providing some demographic data of the patients taking part on the study. Finally, the patient's living independence (living alone; with partner; with family or in sheltered accommodation), registration status (blind; partially-sighted; none), other ocular diagnoses and duration of impairment (self-reported) were noted.

3.2 Visual functions

3.2.1 Visual acuity scoring for long distance

Conventional Snellen charts, introduced in 1862 and reviewed by Bennett in 1965 are widely used in practice but are far from ideal for research and particularly for low vision research as

the amount of letters shown on the chart decreases for the rows. Also, for every level of VA the test chart does not present an essentially equivalent task. LogMAR charts have become more popular over the last few years to overcome these problems, where the VA ratings are given as the logarithm of the minimum angle of resolution, which is the logarithm to the base 10 of the angular subtense of the stroke widths of the letters at 6 m. One of the earliest logMAR charts is the Bailey-Lovie VA chart (Bailey & Lovie, 1976), which has all the following features:

- Similar legibility letters (Sloan et al., 1952).
- Equal geometric progression of letter size whose ratio or multiplier is $10^{\sqrt[5]{10}}$ (0.1 logMAR units or 1.2589).
- The same number of letters per acuity row: five letters. This gives the score for each letter of 0.02 log units, leading to the more accurate scoring by the exact number of letters read correctly.
- Uniform between-letter and between-row spacing: The between letter spacing is equal to one letter-width and the between-row spacing is equal to one letter-height of the underlying row. This warrants equivalent contour interaction at each acuity level.

The ETDRS chart was originally designed for the Early Treatment Diabetic Retinopathy Study (1980) and it is based on the Bailey-Lovie chart but incorporates recommendations of the Committee on Vision of the National Academy of Sciences-National Research Council (NAS-NRC) (NAS-NRC Committee of vision, 1980). These include a testing distance of 4, rather than 6 meters, the use of Sloan letters as the optotypes, several charts to avoid patients memorising letters and a minimum contrast of optotypes against background of 0.85. The use of different ETDRS charts for measuring VA on each eye has been proven to show a clinical unimportant (less than 0.5 letter) improvement in VA score after repeated use of the charts (Ferris et al., 1982). It is for this reason that different charts were used on each eye to avoid patient memorising letters.

The lighthouse ETDRS charts were used (Precision vision. La Salle, IL, USA). The chart was in an illuminated cabinet and had a luminance of 282.9 cd/m² (the Minolta Chroma meter CS-100 photometer was used). With the chart at a viewing distance of 4m patients were asked to read down the chart from left to right looking carefully at each letter in turn. The patient was encouraged to “guess” near the limit of their VA, in order to get more consistent responses. To assign the VA, the logMAR value for the lowest line on which any letters were read was recorded. Then, the letters read incorrectly should each be assigned a value of 0.02 logMAR units to be added to the logMAR value for the lowest line on which any letters were read.

If the patient was unable to see any letters at 4m-distance the chart was moved to 2m or 1m distance from the patient. The logMAR score was determined as above but +0.3 logMAR was added for the 2m-test distance and +0.6 logMAR for 1m-test distance.

3.2.2 Bailey-Lovie reading chart

Due to the central scotoma, the reading speed is much worse for patients with AMD compared to that of patients with equivalent acuity and an intact central field (Legge et al., 1985b) and thus, on patients with AMD, word reading acuity is substantially worse than Snellen letter acuity. The importance of the presence of context is commonly demonstrated in macular degeneration, where reading of isolated words is substantially worse than reading in sentences (Sloan & Brown, 1963). The Bailey-Lovie reading chart (Bailey & Lovie, 1980) has advantages for use in AMD in that it was designed using unrelated words (to avoid contextual clues) and thus testing near vision under more reliable conditions. Successive lines are also arranged in a logarithmic progression of size. The test is standardised by controlling typeface (Times Roman), spacing, and making each group of words of approximately equal difficulty. Also, there are several charts with different sets of words so that memorisation effects can be avoided. The Bailey-Lovie charts were thus selected for testing near vision in this study.

Near vision VAs were measured 3 times on each eye for every patient; that is before refraction to assess for the need of a near prescription change, after refraction and after prism prescription. To avoid patient memorising words the charts were changed for each eye. The charts were illuminated with a fluorescent lamp at a distance of about 40 cm, creating an illuminance on the chart of about 1100 lux.

Most of the low vision patients were accustomed to reading with a +4.00 add at 25 cm. It is thus appropriate to test near vision at the same distance and with the same standard add in all patients. The Bailey-Lovie near vision charts allow data to be collected in the two most popular notations used for near vision: the M system and the Point notation and is calibrated in logMAR as well. The M system is an angular measurement (although it wasn't used at one meter), where the 1M letter subtends 5 min arc at 1m and is the standard notation used in the US. The Point notation is, on the other hand, a linear measurement of the detail size of a letter and is the most commonly used notation for recording near vision print size in the UK. Although both notations can be converted into logMAR acuities (this is useful for later comparison with distance VA), having an angular notation makes the calculations simpler. Near vision was therefore recorded at 25 cm by the M value of the smallest line where the patient was able to read at least one word correctly.

3.2.3 Single, crowded and repeated letter VAs

Harris et al. (1985) described an acuity test for patients with a central scotoma that was intended to determine the optimum potential level of acuity. They had noticed that patients with central scotomas often had much worse vision than would be expected from the size of their field defect. They suggested this was because the patient did not spontaneously fixate with the best retinal locus, and in fact may have persisted with central fixation. The acuity test they used was described as a “full-field E” in which a printed card filled by identical letters was presented to the patient. As the patient looks towards the centre of the card, the repeated letter target is able to simultaneously test several foveal and parafoveal locations. If an area of healthy retina remains anywhere within the posterior pole, then the acuity should be representative of that optimal area. Testing with this target compared to a single letter target showed that mean improvement of acuity was 2.3x, although some patients showed improvements over 4x.

The test used targets of size 20/20 to 20/200, corresponding to a total letter size of 5 min arc to 50 min arc at a viewing distance of 35cm. Appropriate reading adds were used for the viewing distance. The E had the benefit that turning the printed card round gave random stimulus changes, and the threshold was taken as 75% correct. The cards were 24cm x 24cm in size: for the largest size letters (where card was filled) the area of stimulus subtended 38°, and the smallest angular stimulus was 24° square. The letter arrangement is as shown on figure 3.1: 0.5-letter-space between adjacent lines and a 2-letter-space between individual letters.

Regan et al. 1992 also designed a series of “repeated letter” charts, although this time intended to measure acuity in patients with amblyopia who showed inaccurate fixation. The letters were presented on cards 15cm x 15cm and viewed from 3m. Letters were chosen from a set of ten known to have approximately equal legibility (C D H K N O R S V Z) (Sloan et al., 1952). They were presented in a regular rectangular array, with 1-letter width separation.

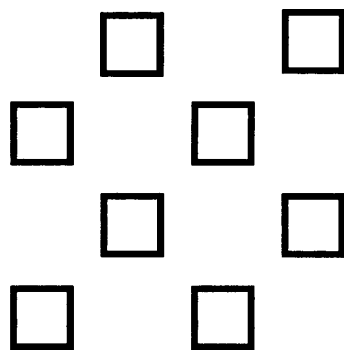


Figure 3.1: Letter spacing used by Harris et al. (1985) on their “full field E” charts.

It is well known that the ability to read correctly a target letter or judge the orientation of a target E is reduced when contours (such as straight lines or letters) are placed close to the target shape. This is called the 'crowding effect' (Flom et al., 1963) and is thought to be due to lateral inhibition between adjacent contours. Although this phenomenon has been well investigated in amblyopes it has also been demonstrated to have a bigger effect on visually impaired patients than in normals (Pardhan, 1997).

In Regan et al.'s (1992) repeated letter chart, the same letter was originally repeated over the whole area of the chart, but it was realised that the letters at the edge of the display may be easier to read because of the lack of surrounding contours (less lateral inhibition). This disadvantage would also have applied to the Harris et al. (1985) "full field" chart. The design was therefore modified so that only the central section of the display was filled by the repeated letters (subtending 46 min x 46 min), and this was surrounded by random letters continuing with the same size and spacing. Therefore, although this chart is designed to give optimal acuity measurement in the presence of a "gaze selection defect" this inaccuracy of fixation is presumably only a few minutes of arc in extent, rather than the (possible) several degrees of discrepancy in ARM between the fovea and the parafoveal location, which gives optimum acuity. It would also not be certain that the correct stimulus letter had been picked up from the central target array, rather than just chance identification from the surrounding random letters. Despite these reservations, this repeated letter chart appears to be the one used by Pardhan (1997) in her study of visually impaired patients. All five of her patients with macular degeneration showed better acuity with the repeated letter chart compared to a chart with lines of letters. She interpreted this as demonstrating a gaze selection defect, probably due to seeking the optimal eccentric viewing point.

According to Harris et al. (1985), the full field test could be a simple and quick method for testing all parafoveal areas simultaneously to determine the best resolution possible of any remaining areas in the retina. When used as a screening tool it may predict the VA improvement to expect with prism glasses. On the other hand, crowding the visual stimulus of interest could decrease VA due to a higher lateral inhibition (Flom et al., 1963). This crowding effect is known to be greater in the peripheral retina (Bouna, 1970; Jacobs, 1979; Levi et al., 1985; Flom, 1991; Latham, and Wittaker, 1996), which would of course be used by a subject viewing eccentrically.

In this study a comparison was made of the "single letter" (SL) acuity, the "crowded letter" (CL) acuity and the "repeated letter" (RL) acuity for AMD patients. Thus, three different test charts were designed for this study to display on a computer screen.

When using letters as targets in a RL array, an obvious “pattern” is perceived which appears to be detected quite independently of the letter discrimination. The Landolt C was therefore chosen as being least likely to show this pattern.

1- **SL target:** A single letter in the centre of the screen. The letter C can be thought of as drawn in a 5x5 box, then the width of the limb is 1, and the “gap” is 1. It can be presented in one of four different orientations - gap up, down, left, right - selected randomly by the computer program. (See figures 3.2 and 3.3.a).

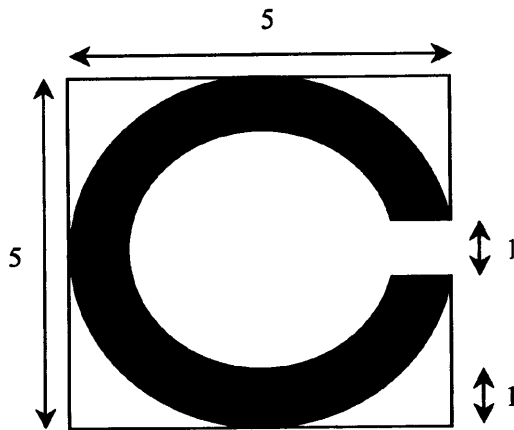


Figure 3.2: *Dimensions of letter C*

2- **CL array:** This consists of the target letter C with four Os of equal size placed above, below, right and left, at 1-letter width away from target (illustrated schematically below). The latter was created using the same target arrangement as in the Cambridge Crowding Cards (Clement Clarke International Ltd., London: Atkinson & Braddick, 1983): the Landolt C (of variable orientation) is displayed with an O above, below, right and left, separated in each case by 1-letter width (the separation is less in the Cambridge cards) (See Figure 3.3.b). This crowded letter visual acuity would be expected to show evidence of the contour interaction effect, with the difference between CL and SL acuities giving a quantifiable measure of this effect.

3- **RL array:** This is a rectangular grid of letter Cs of identical orientation (up, down, left or right), with a spacing of 1-letter width, to cover an area of 20x20cm on screen. Then, a final row of letter Os of equivalent size all around the grid beyond that to create a stimulus at the edge of the array which suffers from equal crowding to the targets in other locations. The outer “square” of Os was placed at a 1-letter width separation from the outermost Landolt C. Therefore the repeated letter array is a regular rectangular grid of Cs all of the same orientation and the separation of the letters is 1-letter width (to match the ETDRS chart) both horizontally and vertically (See Figure 3.3.c). This repeated letter visual acuity would be

expected to measure optimal visual acuity, and would therefore be expected to predict the best acuity achievable with any form of rehabilitation, which aimed to utilise the optimal PRL.

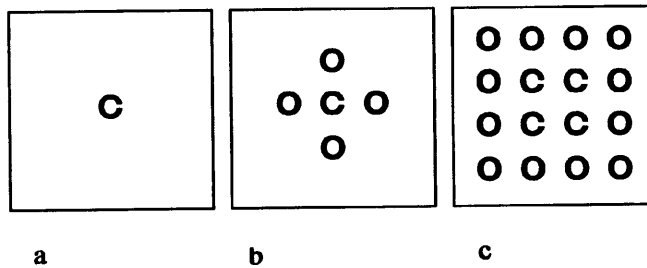


Figure 3.3: *Single letter (a), crowded letter (b) and repeated letter (c) displays.*

The letter arrays were displayed on a 19" monitor to assess single, crowded and repeated letter acuity on the AMD patients recruited for this study. Patients were seated at different distances from the screen depending on the VA of each separate eye (see Table 3.1):

114 cm (15x15 degrees ²)	57 cm (30x30 degrees ²)	28.5 cm (60x60 degrees ²)
0.18	0.48	0.78
0.48	0.78	1.08
0.65	0.95	1.26
0.78	1.08	1.38
0.88	1.18	1.48
0.95	1.26	1.56
1.02	1.32	1.62
1.08	1.38	1.68
1.13	1.43	1.73
1.18	1.48	1.78

Table 3.1: Sizes of Landolt-C stimuli for the three viewing distances and angular areas of display in logMAR.

Because the VA steps are smaller at further distances, it was advisable to seat the patient as far away from the screen as possible so that the collected data was as accurate as possible, this is at 114cm better than at 57cm and at 57cm better than at 28.5cm. For this reason, patients with VA between 0.50 and 1.18 (this VA range is common to both 114cm and 57cm distances) were tested at 114cm rather than at 57 cm. Similarly, patients with VAs between 0.78 and 1.48 were tested at 57 cm rather than 28.5cm. The size of the display was 30x30 cm, which at a testing distance of 57 cm subtends an angular area of 30x30 degrees². This angular area changed when the testing distance was altered (see Table 3.1).

VA range	Testing distance
$0.50 \leq VA \leq 1.18$	114cm
$1.18 < VA \leq 1.48$	57cm
$1.48 < VA \leq 1.68$	28.5cm

Table 3.2: Seating distances from monitor for different VA ranges.

Testing was monocular with the appropriate refractive correction for the testing distance. For each of the 3 experiments: single letter (SL), crowded letter (CL) and repeated letter (RL) two sizes bigger than the Landolt-C size corresponding to that eye's VA were presented initially. The patient distinguished the position of the gap by answering up, down right or left correctly. Five randomised positions of the Landolt-C were presented for each size. Size of the Landolt-C was decreased until 3 out of the 5 presentations were read incorrectly. That size was then recorded as the acuity threshold for each test.

All correct positions given by the patient were ticked in the answer sheet and the first experiment out of the three to be carried out was the SL, secondly the CL and finally the RL. This gave the patient a chance to become accustomed to the test before the screen appeared full of letters, which could have been a bit confusing to the patient. Nonetheless, many patients found the RL test confusing at first, and needed practice to obtain optimal results.

Schrauf & Stern (2001) found that the percentage of correct answers was significantly lowest when the gap of the Landolt-C was at 6 o'clock (they called this effect the 'gap-down' effect) on ocular disease-free normal sighted subjects. However, they did not find a statistically significant difference between left vs. right or orthogonal vs. diagonal gap detection. With the aim of checking if this effect happened in this study for the Landolt-C letters when displayed on the monitor a small study on some ocular disease-free normal sighted subjects was carried out (Appendix 5). Findings showed that when the vertical positions were compared to the horizontal positions the horizontal letters were easier to discriminate than the vertical ones. However, this finding was not likely to affect this trial's data as this effect would be expected to persist over the three types of stimuli and thus should not affect the difference between two types of VA (SL-CL and RL-CL), our main outcome. It may however affect the comparison between conventional VA and CL, and that between prism VA and RL.

3.2.4 Perimetry (Bjerrum screen)

After some pilot testing with Bjerrum screen and automated perimetry (Appendix 6), the Bjerrum screen was selected as the field test that most successfully plots the macular scotoma in patients suffering from AMD.

In this study, a modified Bjerrum screen was used, which instead of having a white fixation point attached at the centre for fixation had two white tape strips crossing perpendicularly to each other in the centre of the cloth and at an angle of 45 degrees from the horizontal line (see Figure 3.4). Patients were instructed to fixate at the point where the two white lines should cross while looking straight at it and not to try and move the eye to another position where

image might come clearer (thus use PRL). This eye movement was controlled by the tester checking the patient's fixation on the centre of the chart by direct observation during the testing and also by making sure that the scotoma recorded keeps a consistent shape through the test.

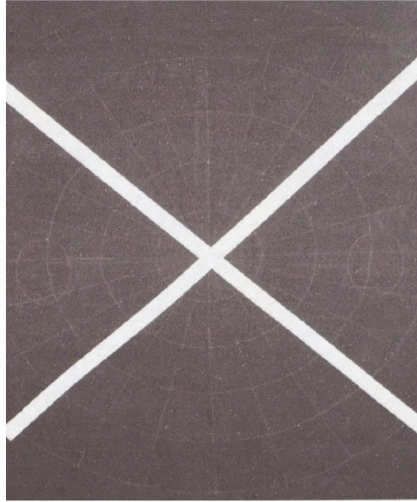


Figure 3.4: *Modified Bjerrum screen.*

A 4mm white target was attached to the end of the wand. After pilot testing this was found to be the most appropriate size. Smaller targets were difficult to discriminate and larger ones misplaced isopters, which mislead the size of the scotoma by making it look smaller than it really was. The target was moved from the periphery (non-seeing) until seen by the patient and the macular scotoma determined by continuing to move the target in towards the centre where the two white lines cross and asking the patient to report when the target disappeared. Black pins were inserted into the cloth at the positions where the target disappeared. At the end of the test these positions were transferred to a field chart.

The Bjerrum screen plot was used to calculate the area of the scotoma and the position of the nearest non-scotomatous point to fovea (NNPF).

3.2.4.1 The area of scotoma

The area of the scotoma was quantified by overlying a grid on top of the Bjerrum plots obtained from perimetry. All the squares of this grid had a standard length of 1° for both height and width. As the Bjerrum screen covers the central 60° of the field of vision, the grid would therefore have a radius of 30 squares. Counting the amount of full squares inside the perimeter line of the scotoma would give a quantified size of the scotoma area in grid units (i.e. degrees²) (see Figure 3.5 for example).

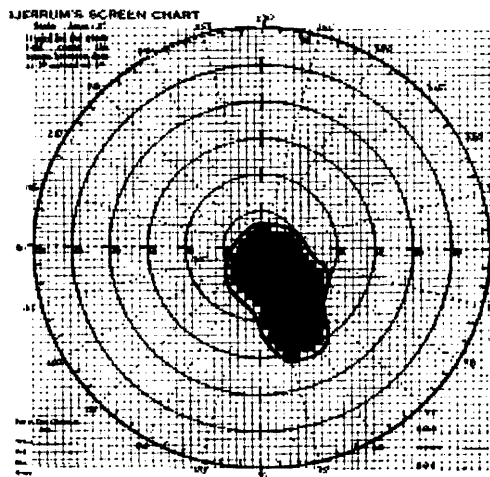


Figure 3.5: *Quantification of scotoma*

3.2.4.2 Evaluation of the NNPF position

The Bjerrum screen plot was also used to obtain information of the position of the nearest non-scotomatous point to fovea (NNPF). This position was assessed by observing the plot and deciding the closest area of retina to fovea outside the scotoma (see Figure 3.6 for example). If there were more than one area of retina outside the scotoma at the same distance from the fovea the largest one was selected as the NNPF.

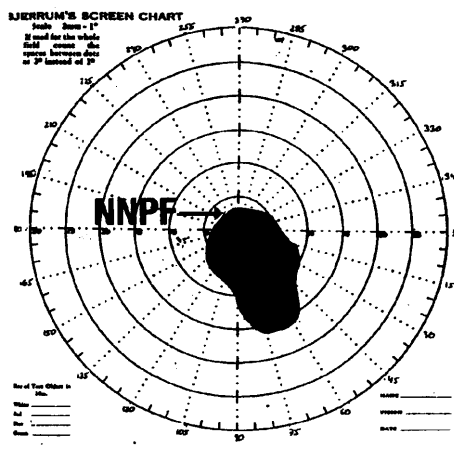


Figure 3.6: *Example of NNPF location at a distance from fovea of 3 degrees and an angular location of 225°.*

3.2.5 Contrast sensitivity (Pelli-Robson)

It has been suggested that it should be possible to determine if a subject's vision is abnormal by making only two measurements (Pelli et al., 1988). One measurement is required to reveal the existence of reduced acuity at high contrast and a second to reveal a contrast sensitivity loss at intermediate spatial frequencies. It should be possible to provide the first of these measurements using a standard high-contrast acuity chart (for example the ETDRS chart) and the second using a variable-contrast letter chart with letters of appropriate size. Central scotomas decrease the VA and thus, the high spatial frequencies are abnormal on AMD

patients. It would therefore be of interest to measure the contrast sensitivity for low-medium spatial frequencies. The Pelli-Robson chart (Pelli et al., 1988) has been designed to test the peak spatial frequency CS, being ≈ 2.5 c/degree the most important spatial frequency of these letters and it's therefore a good complement to the ETDRS chart for this study.

A reduction in contrast sensitivity (CS) has been demonstrated to significantly decrease a wide range of functional abilities of the patient. In this way, patients with low CS are very sensitive to reductions in letter contrast, which would cause an important effect in their reading performance (Rubin & Legge, 1989). Similarly, a reduction of CS has been shown to decrease patients' mobility (Brown et al., 1986).

Pelli-Robson contrast sensitivity charts (Clement Clarke International Ltd., UK) were used to evaluate the patient's CS. These charts make reliable measurements of CS are cheap and use letter targets, which are familiar to both patient and practitioner (Elliott & Whittaker, 1992). The illuminance of these charts was 100 cd/m^2 , which falls between the acceptable range of $60\text{-}120 \text{ cd/m}^2$ recommended by the authors.

Patients were seated in front of the chart at a distance of 1 meter from it. They were wearing the distance prescription with a +0.75 addition to compensate for the 1-meter distance and different charts were used for each eye to avoid the patient memorising the letters.

After trying this technique in pilot study patients, it was noticed that they tend to miss a lot of letters on one of the sides (depending on where the patient places the scotoma for using EV). For this reason, patients were encouraged to read further down on the same side of the chart, where they could see letters. According to Elliot and Whittaker (1992), any miscalling of letter C as an O should be accepted as correct to balance the legibility of the different letters in the chart. Log Contrast Sensitivity was then recorded as that of the last triplet where any letters had been seen minus 0.05 per letter missed in the same triplet. Conventionally, the score would be adjusted for letters missed in previous triplets, as well, but this was not done in this study because this was thought to be due to the scotoma characteristics rather than a reflection of the CS.

3.3 Refraction

3.3.1 Subjective refraction

All patients were refracted and those whose conventional prescription gave a minimal noticeable improvement (which according to our protocol was one and a half lines on the

chart, i.e. 0.14 logMAR) after having a subjective refraction had their conventional spectacles updated. It is in the interests of the study that patients should be wearing the prescription that gives them the optimal VA so that prism spectacles could be ordered to the same prescription with only the prism correction differing between the two pairs. Similarly, patients that were unsatisfied with the type of lenses they are wearing (single vision or bifocals) were given new conventional lenses. Patients not wearing an appropriate type of lenses for their need might result in not wearing the spectacles as much as they should. Making sure that the patient was happy with the spectacles was necessary to facilitate a proper comparison between conventional and prism spectacles.

3.3.2 Prism prescription

Prism prescribing strategies used on previous prism literature (Romayanda, 1982; Roosenberg et al., 1989; Verezen et al., 1996; Bertrand et al., 1997) were used to create a tentative prescribing method that was then refined by pilot testing (Appendix 7) and the following final technique was applied to first obtain the two monocular prism prescriptions and then assess which of these two would be the most appropriate for the binocular prism. Figure 3.7 shows a schematic representation of an example.

Monocular prisms were prescribed according to the following technique:

1. Occlude eye with better VA and perform the following steps on worst VA eye (only if VA of this eye is within inclusion criteria for the study and thus not >1.68 logMAR, otherwise go directly to the eye with better VA. By selecting worst VA eye first patient will not have the chance to memorize all details on the picture before the second eye is tested.
2. Give image of “real scene” (see picture A7.1 on appendix 7) to patient to hold at 25 cm with +4.00 add and instruct patient to concentrate on the face of the lady on the center of the photograph.
3. Place a 6Δ (if VA ranges from 0.48 to 1.00 logMAR) or 10Δ (if VA ranges from 1.02 to 1.68 logMAR) base UP prism in front of the worst vision eye (see example in figure 3.7).
4. Turn the prism base all around the 360° and instruct patient to report any subjective visual improvement or deterioration while fixating at the face in the photograph. The Bjerrum screen plot can be useful at this point for predicting the direction of the prism base chosen by the patient.

5. Record any preferred positions where vision improves to the nearest 10° step⁴.
6. For the preferred positions selected, group into those within a 90° quadrant. Within each group, get patient to select the best of them using a “position 1 or position 2” choice.
7. Compare the preferred prism base from each group by using a “number 1/number 2” choice to decide the final preferred prism base.

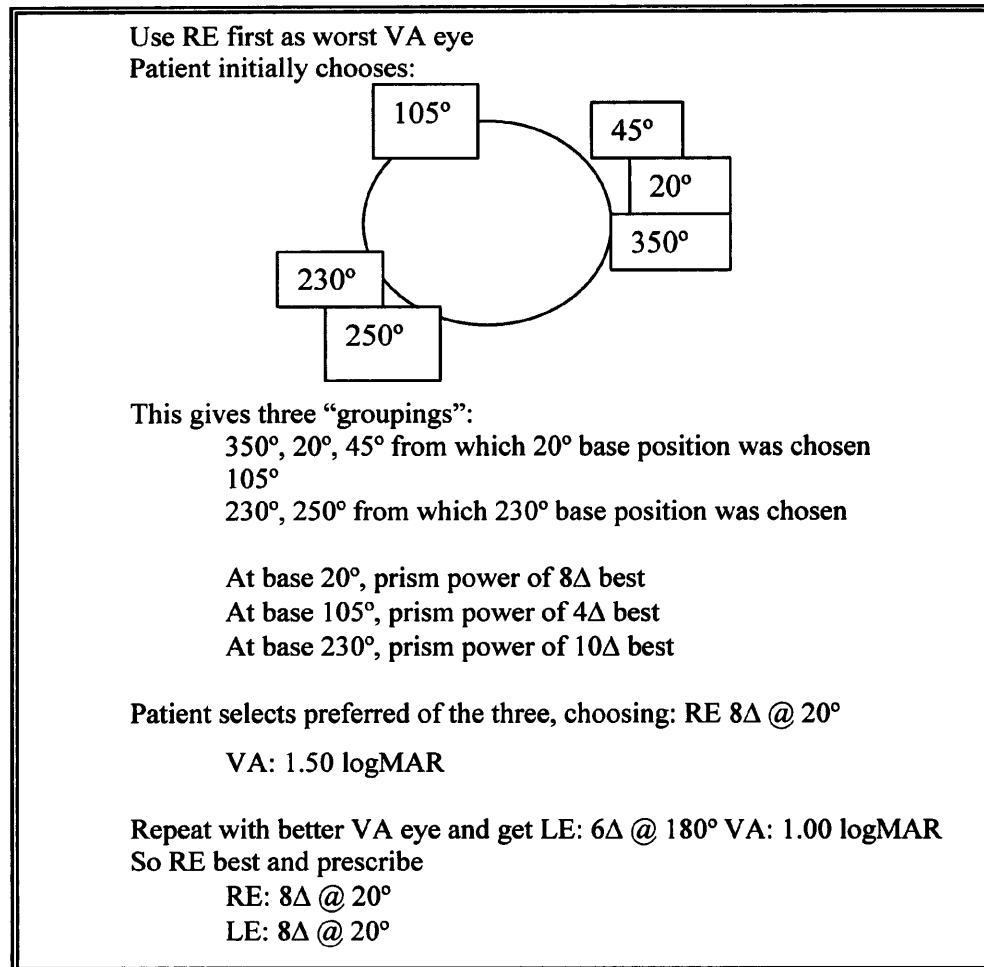


Figure 3.7: Schematic example representing the method used to obtain the binocular prism.

9. Not changing base direction, now try to change power of prism. Try 2Δ increase/decrease of power. If preferred, then put in and try a further change until the optimal and thus final prism power is found.
10. Measure the monocular near and distance (by removing the +4.00 add) prism VA.
11. Repeat steps 2 to 9 for better VA eye if applicable.

⁴ If patient doesn't find any subjective visual improvement on any base direction after rotating the base all around the 360° then a second forced-choice technique was used to make patient choose between prism base at 90°, 180°, 270° or 360°.

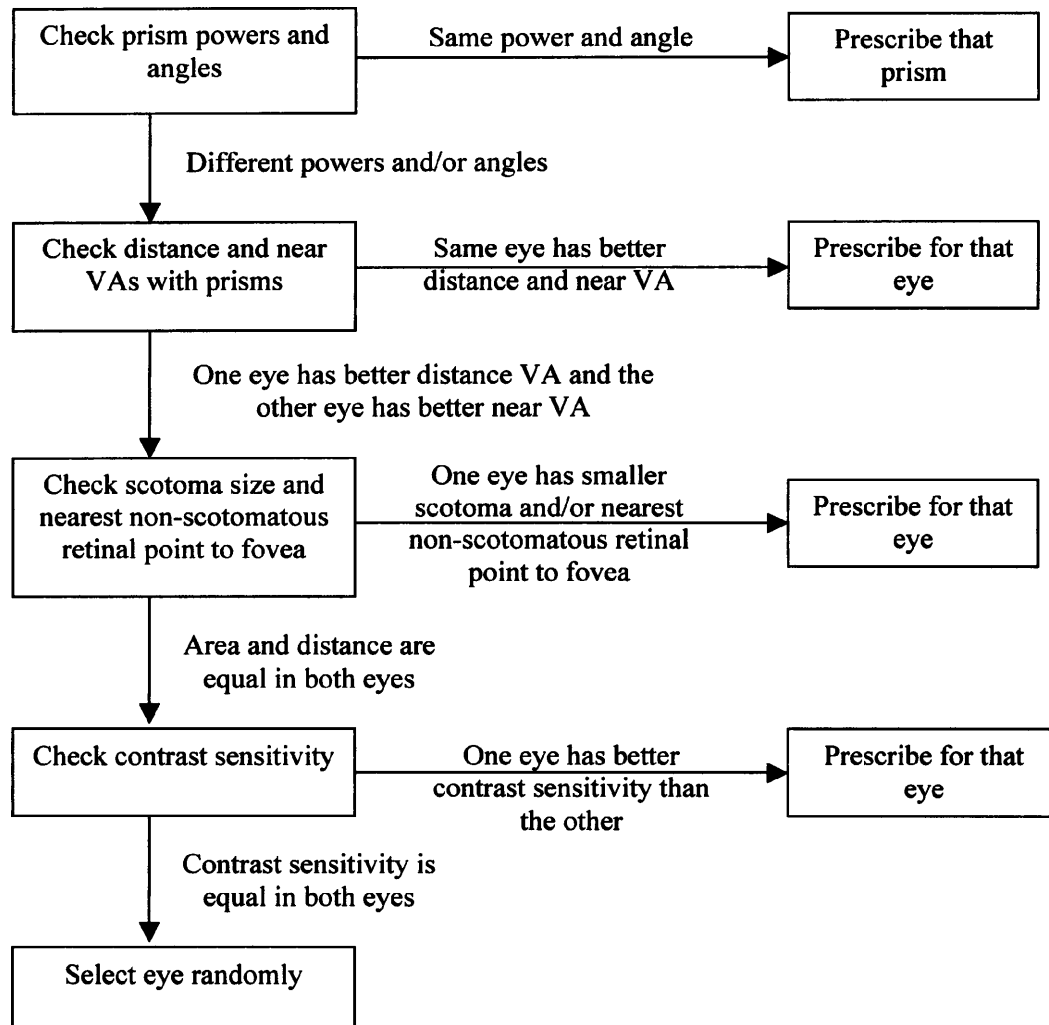


Figure 3.8: *Flow of binocular prism prescription strategy*

After obtaining the monocular prisms, the **binocular prism** power and base was selected as follows (see flow chart on Figure 3.8).

Exception: If the VA improvement after prism in the better eye is ≤ 0.02 logMAR and the prism power $\geq 6\Delta$ than the weaker eye's prism then prescribe for the weaker eye. Arguably, the small VA improvement may not be advantageous against the secondary effects of a large prism (e.g. dizziness, aberrations, weight).

As discussed in section 1.4.5, only a few small studies have previously attempted to use a prism-relocation technique. These studies lacked of a clear prism prescription protocol and thus, the above-mentioned technique used on this study had to be generated from an original pilot study (Appendix 7) and improved with prescribing experience.

3.3.3 Perceived disabilities and goals (MLVAI)

The Melbourne Low-Vision Activities Index (MLVAI) has already been discussed in section 2.10.4, where the weighted version was used by the second researcher as a measure of low vision rehabilitation outcomes. However, the activities composing the questionnaire were also used by the optometrist during the first visit, prior to the low vision assessment to define the perceived disabilities for every patient.

The original MLVAI (Haymes et al., 2001) was designed as a desk-based clinical assessment, comprising 18 observed items and 9 questions on broad self-care. The 18 observed items from the MLVAI were used to find out if the patient had any perceived disability in basic everyday activities. For this purpose, 2 of the 18 original items that were adding little discriminative value to the test had been eliminated. Those are the naming colours and buttoning shirt activities. Also, three extra items have been added: watching TV and two“other”. These were to give the patient a chance to mention any activities that might be a struggle and which are not included in MLVAI. The final version had therefore a total of 19 activities.

Although the items used were activities in the MLVAI they were treated as questions and the patient had to say if he/she could perform the named activity by answering yes/no. This information was used later to assist selecting LVAs for the patient.

3.3.4 Low vision assessment

All patients were given a low vision assessment (LVA) after refraction and prism prescription. The patient's goals reported on the MLVAI were used as a guide on the assessment. If they already had some low vision aids, these were tested to confirm that they were satisfactory to achieve the patient's goals. Aids were replaced if more appropriate alternatives were found. Those patients coming for their first LVA were equally tested for the most suitable aid/s that would assist them to achieve their goals. Also, advice on how to use the aids for a best performance was given.

For some of the MLVAI items, such as threading needles and using the telephone book, magnifiers may not be very useful and gadgets to thread needles and identify coins were demonstrated to patients as well as techniques for getting telephone numbers without having to read them. Magnification was therefore not exclusively used as a treatment strategy on the low vision assessment.

Finally, advice to improve lighting and contrast conditions at home were given as well as information leaflets about their condition and the Macular Disease Society. At this point

patients were also checked for registration. If their VA entitled them to a state of registration for which they were not registered this was then offered and the ophthalmologist informed.

3.4 Dilation

Patient's pupils were dilated at the end of the first visit to a minimum pupil diameter of 6 mm with 1-2 drops of 1% Tropicamide depending on amount of pigment in patient's irides. For some cases that may not dilate sufficiently (mainly diabetics) with Tropicamide 1%, 2.5% Phenylephrine was applied as well (providing patients did not suffer from a cardiovascular or respiratory condition). This pupil diameter allowed classification of the lens opacities and the use a digital fundus camera to take a photograph of the fundus and assess the patient's fixation. Prior to instillation of drops all patients were asked if they ever had a adverse reaction to drops since they all would have had their pupils dilated at least once to be diagnosed by the ophthalmologist. If there was a negative answer to this question and because they were in the hospital environment atmosphere, patients were considered safe to be dilated. However, they were all explained the symptoms of acute closed angle glaucoma and advised to return to hospital should any of those arise.

3.4.1 Fundus photographs

50 degrees digital fundus photographs were taken for every patient. This size provided enough magnification to classify the AMD and assess the eccentric fixation whilst still visualising the optic disc, which was required in order to determine the foveal position. Four photographs were taken for each patient, i.e. right and left eyes for both colour and red free. For the colour photographs, the patient was instructed to look straight ahead at a fixation light that was placed in front of each eye at the time. The red-free photographs helped visualise the blood vessels, which were useful for localising the fovea.

For the red-free photographs a fixation rod was presented to the patient to look at in the camera. This fixation target was internal to the camera and thus appeared on the photograph of the fundus. The patient was instructed to look at the tip of the rod. The position of this rod was assessed to evaluate the location of the possible PRL of the patient for that eye (see section 3.5.1).

Patients recruited in this study had a significant VA impairment of 0.50 logMAR or worse (see section 2.5) and thus they were expected to suffer the more advanced condition of AMD rather than the earlier ARM stage. This diagnosis was confirmed by an ophthalmologist when assessing both the colour and red-free photographs. He also classified the condition into dry,

wet or mixed AMD, quantified the damaged retina and assessed whether the damage was sub-foveal or not. Finally, he estimated from the red-free photographs if the patient was using central fixation.

3.4.1.1 Classification of AMD

During the last couple decades there has been quite a lot of interest on AMD epidemiology and a few different grading systems have been used in different studies. The Wisconsin Age-related Maculopathy Grading system (Klein et al., 1991) is the most comprehensive and more used grading system for ARM population-based studies up to date using colour stereoscopic photographs. This grading system has been used in many prevalence and incidence studies (see section 1.1.2). It looks at three lesion types: drusen (these are classified by size, type, area and confluence), other characteristics of AMD (such as RPE degeneration, increased pigment, RPE detachment, hard exudates, haemorrhages, geographic atrophy, retinal and oedema) and other lesions not considered characteristics of ARM (such as branch and central retinal venous or arterial occlusions, asteroid hyalosis, etc). However, this classification system, as well as the more simple ones used in previous studies (the National Health and Nutrition Eye Study (Golberg et al., 1988), the Copenhagen Study (Vinding, 1989) and the Chesapeake Bay Study (Bressler et al., 1990) have all been designed for epidemiological purposes and thus concentrate on the detection of early ARM signs whilst for the more advanced condition of AMD, which involves the classification of sub-retinal haemorrhages, geographic atrophy retinal pigmented epithelium detachment and fibrous tissue, the classification is quite coarse and is just based on grid sub-fields or disc sizes. They have also been used to assess interventions, which were expected to change lesion characteristics, where they needed accurate and sensitive assessments. However, this study is not expecting a change in lesion size as a result of the therapy and does not aim to include any epidemiological research. Therefore, because the only intention of classifying AMD is for supplying some statistical demographics, a thorough grading system such as the Wisconsin's would not be appropriate. A basic classification of AMD into the dry and wet forms made by the ophthalmologist covered the needs of the study.

3.4.1.2 Quantification of AMD

For the quantification of the AMD size, we were not interested in all the different damage components of the AMD (haemorrhages, oedema, exudates, etc) but on the overall size of the retinal damage, so that possible investigations between AMD retinal damage size and other data (such as scotoma size and visual acuity improvement after the 3-month period of prism wear) could be made. Drawing a perimeter line that involved all the damaged areas of the retina with the Topcon measurement utility provided an area size of the damaged retina.

However, it must be taken into account that the visible lesion might not have shown the whole non-functional area. The same procedure was then applied to obtain an optic disc size. Dividing the damaged area by the disc size gave a ratio size of the damaged area. This simple method satisfied the needs of the study and was therefore used by the ophthalmologist to quantify the size of the lesion.

3.4.1.3 Evaluation of subfoveal damage

Next, the ophthalmologist assessed the photographs and decided if the damaged area was subfoveal or not. As the condition was quite advanced for all patients taking part in the study, we would expect most patients to have the macula area affected and thus to have central scotomas in both eyes. However, it was interesting to check if that was the case and if there was a difference on success outcomes between the sub-foveal and non-subfoveal patients. It could be that patients with non-subfoveal damage could have a remaining area of healthy fovea that would not guarantee prism relocation success.

3.4.1.4 Evaluation of central fixation

The last evaluation made by the ophthalmologist involved a determination of whether the patient was fixating centrally or not. This was assessed by comparing the location of the end of the fixation stick that showed on the red-free fundus photograph with the avascular foveal area, and deciding if the two coincided. Having two methods to assess central fixation (an objective method is described on section 3.5.1) reassured that those patients found to be fixating on fovea when assessed with both this and the objective methods were less likely to suffer from analyses errors than those found to fixate on fovea by just one of the discussed methods.

3.4.2 Classification of cataracts (LOCS III)

The Lens Opacities Classification System III (LOCS III) (Chylack et al., 1993) is a simple system for classifying age-related humans lens opacities at the slit lamp or in retro-illuminated and slit lamp photographs. The LOCS III is a revised classification system that has good reproducibility and validity (Maraini et al., 1988) and has thus been selected for use in this study for lens opacities.

Once the pupil was fully dilated examination was made with the slit lamp set so that an angle between illumination and observation systems was 45 degrees for nuclear assessment and 0 degrees angle for cortical and subcapsular assessment. With the slit beam at 45 degrees angle, the slit height and width was adjusted so that the overall brightness of the corneal image and anterior subcapsular zone approximate those of nuclear colour/opalescence standard (NI). At

0 degrees, the brightness enabled to see all the opacities but not cause discomfort for the patient. The slit lamp beam was 0.2 mm wide and the optimal brightness was subjective.

Standards: The LOCS III photographic standards are boundaries of scaling intervals. When grading nuclear opacification (NO) or nuclear color (NC), the top 6 colour Zeiss slit photographs were used. When grading cortical and posterior sub-capsular (P) cataracts, the Neitz CTR colour retro-illumination photographs in the middle and lower rows of standards respectively were used as examples of various grades of cortical or posterior sub-capsular cataract.

Grading: The severity of the opacity must be more than that in the lower standard and less than or equal to that in the next higher standard. The interval was visualized as containing ten, 0.1 unit steps with an increasing grade signifying increasing cataract severity. The scales extend from 0.1 (clear or colourless) to 5.9 (very opaque) for cortical and posterior sub-capsular cataract, or to 6.9 (very opaque or brunescent) for nuclear change. A decimal grade was then assigned, using 0.1 unit steps, to the opacity. The decimal grade reflected the position of the unknown in the standard interval. One limitation of the grading in this study was the unavailability of photographs to repeat the grading and check for variability.

3.5 Identifying fixation characteristics

When a patient is suffering from AMD, they inevitably suffer a decrease in central visual acuity. As the fovea is normally the retinal area with the highest resolution, it has been used by the patient habitually throughout their life, and is the oculomotor reference, the patient may still preferentially use it, especially in the early stages of the condition. The oculomotor reference is the point on the retina to which an eye movement directs the image of the fixation target. It can be assumed that as foveal function is compromised, the patient would achieve a better visual performance by using an alternative retinal area (PRL). This might be expected to be the nearest non-scotomatous position to the fovea (to have the best resolution) but should also be large enough to analyse the particular fixation target being used.

Section 1.4.3 of the thesis stated how unpredictable the PRL could be as not all the patients with central scotomas adapt a PRL and, even for those who use a PRL, this might not be stable but change depending on factors such as the size of the scotoma, the task performed, and the illumination. Also, as concluded on section 1.4.3, there is disagreement in the literature on which part of the retina seems to be preferably chosen for a PRL.

The first investigation carried out was an assessment of the static fixation position, and whether this was foveal or parafoveal. By means of measuring the static position of fixation it was possible to assess if the patient had already chosen a PRL. This was performed by two different methods (one of which was the subjective assessment by the ophthalmologist, described above), but each involved analysis of fundus photographs, and thus only represented a sampling of fixation.

The angular position and direction of fixation, relative to the fovea, was also measured from the red-free photographs. It would be expected that when prescribing the prism for the patient, the power and base direction of the prism found from the patient's subjective response would be such that the image of the target would be displaced to the optimum PRL (if the optimum one had been selected).

3.5.1 Determining the static fixation position

Red-free photographs were taken while the patient was asked to look at the edge of a fixation rod. The angular displacement and direction of the fixation target from the fovea could then be calculated.

3.5.1.1 Determining the position of the fovea

With the aim of finding out whether the patient was fixating with the fovea or eccentrically and thus using a PRL, we first needed to find the position of the fovea. This is easily identified in young normal eyes by a bright reflex created by the contour of retina at that point (Ducrey et al., 1979). It is also possible using monochromatic photographs at wavelength 470 nm to see the darker region around the fovea corresponding to the macular pigment (Delori et al., 1977). The other distinguishing feature of fovea is that it is the centre of the so-called avascular zone, although this is not always present (Sander et al., 1994). The use of the red-free filter helps to visualise the blood vessels and thus the avascular zone of the fovea can be more easily identified. Patients with AMD are expected to have a central scar covering the fovea, which would make it difficult to locate when analysing the red-free photographs. Therefore, it was necessary to find an alternative method to locate the fovea.

The fovea is displaced slightly down from the horizontal line through the centre of the disc. The horizontal line between the nerve head and the foveal centre A and the distance line the centre of the nerve head and fovea C form an angle α of 6.1° (see Figure 3.9) (Williams & Wilkinson, 1992 and Barr et al., 1999).

There is also a horizontal displacement of the fovea from the optic disc. The ratio of the disc-to-macula-distance to the disc-diameter (DM:DD ratio) has been advocated as a method of

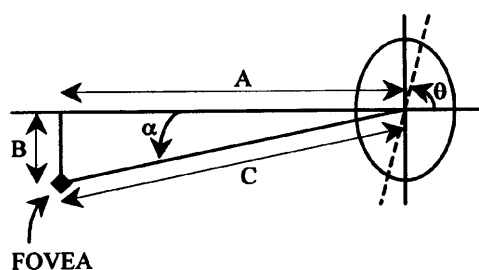


Figure 3.9: Diagram of the location of the fovea according to Williams & Wilkinson (1992), where:

$$DM:DD \text{ ratio} = c/DD.$$

supporting the diagnosis of optic nerve hypoplasia (Zeki et al., 1991; Barr et al., 1999) and microdiscs (Mok & Lee 2002). These previously mentioned studies assumed that DM is constant and thus the ratio would depend on DD. They compared the ratio for normal eyes with that for eyes with disc hypoplasia/microdiscs and provided a cut-off ratio value for normal eyes. A standard ratio for an average normal eye could therefore be obtained from these studies. Once the DD for a particular patient had been measured, and the appropriate ratio chosen, these could be used to calculate the DM distance for that same patient. Once the position in which the fovea lies was known, the relative position of the fixation target to the fovea could be determined.

Table 3.3 shows a comparison between results of normal adult optic nerve head dimensions and DM:DD ratios for some previous studies using fundus photographs measured on horizontal disc diameters and/or minor axis of a fitted ellipse:

Year	Px num	Authors	Horiz/vert disc. Diam. (mm)	Minor/major axis (mm)	DM/DD ratio
2002	88	Mok & Lee	$1.88 \pm 0.10/-$	-----/----	2.54 ± 0.13 using H/V
1999	125	Barr et al.	$86.6^5 \pm 0.6/-$	-----/----	2.82 ± 0.40 using ellipse
1992	66	Williams &	$1.78 \pm 0.21/-$	$1.75 \pm 0.2/-$	2.85 ± 0.35 using ellipse
		Wilkinson	1.90 ± 0.22	1.95 ± 0.2	2.59 ± 0.28 using H/V

Table 3.3: Mean values for nerve head diameters, axis and DM/DD ratios from previous literature findings.

Williams & Wilkinson (1992) used two different approaches to measure the DM:DD ratio. The first approach used an ellipse-fitting program, which yielded the major and minor axes of the fitted ellipse of the optic nerve, as well as the orientation of the ellipse. Figure 3.9 represents the posterior fundus of a right eye, and shows the trigonometric values A, B, C, and α , which were calculated to give the quantitative value of the position of the foveal centre relative to the nerve head. This approach took into account the possible tilt of the optic nerve as they also indicated the orientation of the major axis of the ellipse fitted to the nerve head relative to the horizontal with the angle θ . This angle was found to have a mean value of 82.7°

⁵ Barr et al. give a value of 86.6 mm for the horizontal disc diameter. This value should be a typing error as the eyeball is only about 27mm in diameter and anatomically it would be impossible to have an optic disc diameter of that size. They probably intended to write a disc diameter of 1.86 mm.

$\pm 27.5^\circ$, implying that the major axis of the nerve head tends to be oriented with the top of the major axis tilted roughly 10° inward toward the midline of the head. They found a mean C value of 4.90 mm and α of $6.1^\circ \pm 3.32^\circ$. Their mean DM:DD ratio was 2.85 ± 0.35 . Their second method was by means of using the horizontal disc diameter and this time the DM:DD they found was 2.59 ± 0.28 .

Barr et al. (1999) also took into account the optic disc tilt by calculating the DM:DD ratio from: $2 \cdot c1 / (a1 + a2)$ (see fig 4.10), where $a1$ and $a2$ were the major and minor elliptical axis respectively and $c1$ the distance between vertical meridians through the fovea and the disc centre. They found a mean disc diameter of 86.6 mm with an accuracy of $\pm 0.6\%$ and a DM:DD ratio of 2.82 ± 0.40 , which compares favourably with that found by Williams & Wilkinson.

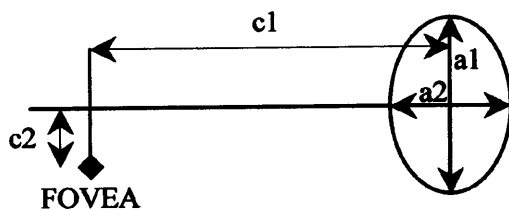


Figure 3.10: *Diagram of the location of the fovea according to Barr et al. (1992), where:*

$$DM:DD \text{ ratio} = 2 \cdot c1 / (a1 + a2).$$

Mok & Lee (2002) did not take the disc tilt into consideration and the DM:DD ratio was calculated from: $(a + b)/2a$, where $(a + b)$ was the disc-macula distance and $2a$ the horizontal disc diameter (see fig 4.11). They found a DM:DD ratio of 2.54 ± 0.13 in normal patients, which relates to the value that Williams and Wilkinson found using the same method of the horizontal disc diameter.

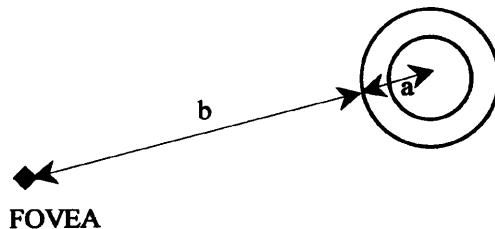


Figure 3.11: *Diagram of the location of the fovea according to Mok and Lee (1992), where:*

$$DM:DD \text{ ratio} = (a+b)/2a.$$

Looking at the results from the three previous studies we could conclude that the method used to calculate the DM:DD ratio does affect the result. That is, methods using an ellipse-fitting program tend to give quite high ratios (2.85 from Williams & Wilkinson and 2.82 from Barr et al.) compared with methods using the horizontal disc diameter (2.59 from Williams & Wilkinson and 2.54 from Mok & Lee).

All these studies involved a similar number of patients and therefore it is not obvious that one technique has greater credibility. The method of using the horizontal disc diameter is simpler and therefore more convenient to use in the current study to locate the fovea in AMD patients.

Having chosen the horizontal disc diameter as a means to work out the DM:DD ratio there was still a choice to insert this value into either Williams and Wilkinson's (W&W's) formula or Mok et al.'s. There was a clear advantage on using W&W's formula, this relating to the C value. To apply W&W's formula we only needed the horizontal disc diameter and the DM:DD ratio to obtain the C value (real distance between fovea and disc centre). Once we had this value we could simply locate the fovea by drawing a line from the disc centre at an angle of 6.1° below the horizontal line from the disc as long as C and the end of that line gave us the location of the fovea. On the other hand, Mok's formula did not take the exact horizontal value of the DD but instead measured the disc radius at the angle where it would cross the fovea (this is called a) and multiplied it by 2. Since we don't know the exact position of the fovea it was not possible to calculate the value of a accurately and thus W&W's formula was more appropriate to use in this study.

To calculate the c value we first needed to isolate the value C from W&W's formula:

$$C = DD \cdot DM:DD \text{ ratio}$$

If we now substituted the DM:DD ratio by 2.59 as found by W&W, where DD would be the horizontal disc diameter across the centre of the disc:

$$C = DD \cdot 2.59 \quad (4.1)$$

Once the location of the fovea was found we could then calculate the linear displacement of the fixation stick from it. In order to determine this linear displacement we needed to be aware of the magnification affecting the photograph. It has been widely reported that the size of a fundus photograph's feature needs to take into account the magnifications produced by both the camera and the eye (Littmann, 1982). Littmann addresses these two basic problems in calculating the real dimension of a retinal object using a fundus camera by firstly relating the height of the image on the camera film to the external angular difference (magnification produced by the camera) and secondly, once this relationship has been established, is to relate the external angular difference to the chord diameter of the retinal object (ocular magnification).

3.5.1.2 Determining the fundus magnification

Littmann (1982) devised a technique for determining the true size of a given fundus feature for the Zeiss Oberkochen telecentric camera. His formula is:

$$t = 1.37 \, q \, s$$

Where t is the true size of the retinal feature, s the measured size of the image on the fundus camera film and 1.37 is a constant and specific coefficient to the Zeiss Oberkochen instrument used by Littmann. Other imaging systems will have a different constant, and this has been determined using a model eye (Rudnicka et al., 1998). As the fundus photographs in this study were taken with a different camera (Topcon megalopus CCD with TL-209 fundus camera) the constant 1.37 will need to be replaced for the appropriate value of the camera used. This way we get:

$$t = p q s$$

This formula can be used to calculate the real distance between the fovea and the tip of the fixation rod for the AMD patient, where t is the real distance, p is the camera⁶ correction factor, which for telecentric instruments is a constant value over a wide range of ametropia. (for nontelecentric systems, the value for the correction factor p will not be a single constant value as with the telecentric systems but will vary according to the patient's ocular refraction). Factor q is the variable dependent on the optical dimensions of the eye (ocular magnification). This is unique to the human eye being imaged and is not affected by the fundus imaging system. Factor s is the size of the retinal distance measured on the fundus camera film.

Calculating the ocular factor q

The ocular magnification factor q can be obtained by various methods, with varying degrees of accuracy. The simplest is to assume a fixed value based on the Gullstrand schematic eye, but real eyes can vary as much as $\pm 16\%$ relative to this schematic eye (Barr, 1995). The assumption is that the more the standard parameters of this eye are replaced by "real" values measured from the actual eye, then the more accurate the value of magnification will become, and the more precisely the retinal dimension can be determined.

There is evidence that quantitative measurements that take into account total ocular magnification are considered to be more accurate than those that only take the magnification due to the instrumentation (Caprioli et al., 1986). Garway-Heath et al. (1998) compared methods available to correct the magnification of images that result from the optics of the eye. They concluded that the methods using axial length are most accurate. If the axial length is not known they recommend HRT (Heidelberg retina tomograph) and methods using keratometry and ametropia as methods that give results closest to the axial length methods. Bennett et al. (1994) give the following equation for calculating factor q from axial length:

⁶ A telecentric system is that in which the anterior principal focus F_c of the condensing lens is intended to coincide with P , the eye's first principal point. For a telecentric optical system the final image is at infinity, and so the ratio of the image size on the camera film plane (s) to the distance y (PcE) is a constant over a wide range of ametropia.

$$q = 0.01306 (x-1.82)$$

where x = the axial length for a particular eye

Other methods to calculate the q variable are keratometry, ametropia, anterior chamber depth and lens thickness. According to Garway-Heath et al. (1998), this methods require more detailed calculations and are not as accurate on it's own as axial depth.

Littmann's (Littmann, 1982) method seems to have been widely used to correct for magnification due to the optical components of the patient's eye. It entitles obtaining a retinal photograph using a fundus camera set up in accordance with the principle of the telecentric ray pathway, estimating the patient's ametropia, radius of curvature of the anterior corneal surface and/or axial length of the eye. According to Barr's appraisal (Barr, 1995), this assessment estimates that 95% of measurements of the real dimension of a retinal object will be at least 93.29% accurate for 98% of the population.

This method has been calculated for the Gullstrand eye, where any ray directed towards the centre of the entrance pupil will be refracted through the centre of the real pupil and emerges directed from the centre of the exit pupil. It therefore follows that, by reversal of light, the ray from an extra-foveal point object which is refracted through the centre of the real pupil will be directed initially at the centre of the exit pupil and emerge at the anterior corneal surface detected from the centre of the entrance pupil. The angle that is subtended at the centre of the exit pupil is the internal angle and that subtended at the centre of the entrance pupil the external angle.

The factor q is the ratio between the chord diameter and the external angle. Knowledge of the external angle and the quotient q , therefore allows calculation of the chord diameter. The Littmann nomogram (Barr, 1995) shows the variation of the value q for a Gullstrand eye depending on the curvature of the cornea within a range of ametropia $-15D$ to $+15D$. For a medium corneal curvature value of 8mm the quotient q varies from 0.28 mm/ $^{\circ}$ for a $+5D$ ametropia to 0.31 mm/ $^{\circ}$ for an emetropic eye and to 0.34mm/ $^{\circ}$ for a $-5D$ ametropia. This would mean that for a $\pm 5D$ ametropia the image size would have ± 0.03 mm/ $^{\circ}$ change of size (10% size change). This error would add up to the fact that the system is not telecentric and thus a significant error might affect the magnification for eyes with a medium to high prescription. This will need to be considered on later analyses.

Overall magnification using the Topcon camera

A Topcon TL-209 fundus camera was used to take 50 $^{\circ}$ field pictures of the patient's fundus while looking at a fixation rod. This system is not telecentric on the image size, implying that the image height may not be directly proportional to the external angle when defocused as

would vary depending on the ametropia. Rather than 35mm film, this camera records images on a roper megaloplus 1.4i camera with a CCD area of 7.04 x 8.98mm. According to the manufacturers the relay-lens for the Kodak Megaplug has a magnification of 0.34x. This means that if the image mask on 35mm outlet on the TRC-50IX is 22 x 26 mm the image is projected as a real size of $0.34 \times (22 \times 26\text{mm}) = 7.48$ (beyond limit of CCD) x 8.84 mm. Besides this magnification factor we need to take into account the one from the field lens, which obviously varies depending on the field degree size of the photograph, and the manufacturer also assumes a Gullstrand schematic eye. Overall, the manufacturer therefore provides a guide to overall magnification stating that 1 mm on the CCD converts to 1.6 mm on the retina and thus (p x q) has a value of 1.6.

This magnification factor is already taken into account when measuring distance with the “measuring features” program facility from Topcon. This means that the figure obtained from measurements with the program already corresponds to the real size of that feature in the eye and thus has already been multiplied by factors p and q. The calculations are nevertheless prone to have some errors considering that the system is not telecentric.

A simple way to find out how accurate the measurement facility from Topcon was to compare a measurement such as the distance from fovea to temporal disc margin and compare it with the value for the same distance of the Gullstrand schematic eye, which is 3.42mm (Emsley, 1976). If the calculations made by Topcon are correct the two values should be quite close. The difference between these two values was investigated on 10 eyes of 10 different young patients with small prescription values (mean equivalent sphere ≤ 3.00 diopters) with a clear position of the fovea on the photograph and the mean value was 0.05mm. It was thus concluded that the difference between the two values was not significant and that the values obtained with the facility from Topcon have successfully taken into account the magnification produced by the system.

Calculating the position of fixation

When the fovea has been located (as described above), the linear displacement of the fixation stick from the fovea can be measured on the screen by means of tracing a line that would connect the fovea to the edge of the fixation rod. This value would then be the retinal distance FP (measured along the curve of the retina) in mm.

The angle subtended by this fixation rod (P) relative to the fovea (F) at the nodal point (N) is β (see Figure 3.12).

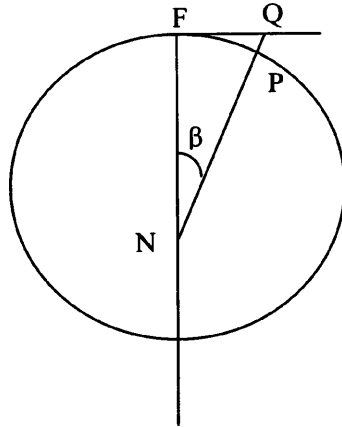


Figure 3.12: *The Gullstrand schematic eye.*

For the Gullstrand Schematic Eye the distance from the fovea to the nodal point (FN) is 16.68mm.

$$\tan \beta = FQ/FN$$

$$\beta \text{ in radians} = FP/FN$$

$$2\pi \text{ radians} = 360 \text{ deg, so } 1 \text{ radian} = 180/\pi \text{ deg}$$

$$\text{so } \beta \text{ in degrees} = \frac{FP \cdot 180}{FN \cdot \pi} = \frac{FP \cdot 180}{16.68 \cdot 3.142} = FP \cdot 3.43$$

$$\beta = FP \cdot 3.43 \text{ degrees}$$

(4.2)

3.5.1.3 Analysing the photographs

Each photograph was viewed on a computer screen connected to the hospital arcade, where the photographs had been stored. The horizontal disc diameter was measured and this value was introduced in formula (4.1) to work out the c value. Both the horizontal and vertical disc diameters were marked with straight blue lines on the disc between the two outer borders of the Elschnig ring (Appendix 8) as illustrated on sample on Figure 3.13. The point where the two lines cross was the centre of the disc. From the centre of the disc, a pink horizontal line was drawn towards the temporal side of the eye and across the picture by means of an acetate-overlying sheet (Figure A9.1 in appendix 9). A new red line could then be traced on the screen, starting at the centre of the disc and at an angle of 6.1° from the horizontal pink line. The length of this red line was the calculated value from formula 4.1 and the end of the line showed the position of the fovea.

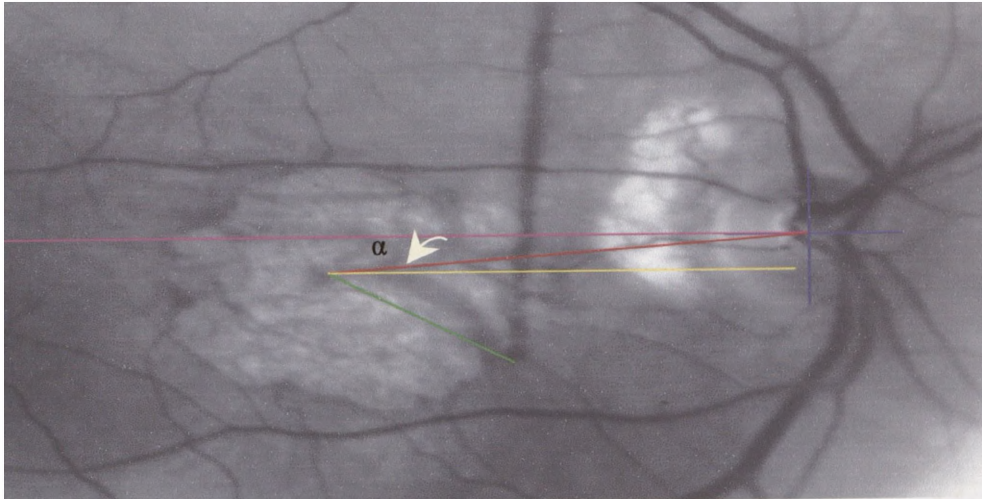


Figure 3.13: *Illustrated example of calculus of fovea, where different colour lines represent the following:*

- Horizontal and vertical OD diameters.
- Horizontal line going across the OD centre.
- Disc to fovea distance.
- Horizontal line going across fovea.
- Fovea to fixation distance

Once the position of the fovea had been found it was then possible to calculate the linear distance and angle separating the fovea from the tip of the fixation rod. A fifth green line was then traced to connect the fovea with the tip of the fixation rod. The program gave the length in millimetres between this two fundus features. This figure should be the distance between the fovea and the chosen PRL chosen by the patient while photographed concentrating at the tip of the fixation rod.

Finally, we needed to find the angle α at which the PRL was located with respect to the fovea. A second acetate sheet was then overlaid on the picture (Figure A9.2 in appendix 9). This acetate sheet had a drawing of a double protractor with the entire axis around the 360° degrees marked in groups of 10° (this is to match the accuracy to which the prism bases are prescribed). It was then possible to obtain the value of this angle by simply overlaying this double protractor on the fovea and deciding to which 10° angle group the line drawn connecting the fovea and the PRL was closer to. To make sure the double protractor was lying straight on the screen a sixth yellow line was marked on the screen. This was a horizontal line going horizontally from the fovea. The 0-180° line of the protractor had to be overlying this line on the screen. Also, the point where the 90-270° and the 0-180° lines of the protractor cross had to be overlaying the fovea to make sure the fovea was on the centre of the double protractor.

If the position of the PRL were to predict the prism base direction, an association between these two angles would be expected.

3.5.2 Dynamic Fixation

The patient's quality of fixation was also assessed to a dynamic target (patient fixating the same target but this time moving). With a progressive loss of central vision, there appear to be several possible fixation patterns that might be seen:

1. Foveal fixation maintained, and when target displaced, eye movements return image to fovea.
2. A single PRL selected and used consistently, and eye movements return image to this PRL.
3. Several different PRLs used, and/or fixation with the PRL not held. Eye movements do not consistently return images to, or maintain images at, this location. Although there is evidence that the PRL can vary in a systematic way as the requirements of the task to be performed change, the PRL would be unlikely to be required to change significantly during the course of a single, simple task. In this study it will be assumed therefore that such a performance represents poor dynamic fixation.

Cases 1 and 2 would show "good" scores for dynamic fixation, but they would each have a different static fixation position.

Three tests were carried out on each eye on the fundus camera:

Fixation stability: Patients were asked to fixate at the centre of a fixation rod for approximately 30 sec. A subjective evaluation of stability was made by a subjective quantification of the eye movement into 3 stability categories:

GOOD: Patients' eye did not move or moved less 1 time in 5 sec

MEDIUM: Patients' eye moved 2 or 3 times in 5 sec

POOR: Patients' eye moved 4 or more times in 5 sec

Fixation consistency: The fixation rod was moved to 5 different positions. A subjective evaluation of whether the fixation location is the same or different to the original fixation was made. Depending on the amount of different fixations to the original one it was classified in the 3 following categories:

GOOD: Patient fixated all 5 positions in same area of retina

MEDIUM: Patient fixated 3-4 positions in same area of retina

POOR: Patient only fixated 2 or fewer positions in the same area of retina

Rod pursuit: Patients were asked to follow the fixation rod. This rod was moved at a reasonable speed to be followed without having to move the eye with big saccadic movements but not as slow as to not appreciate a movement. A subjective evaluation of the ability to follow the rod was made and the eye was classified in one of the 3 categories below:

GOOD: Patients followed rod easily

MEDIUM: Patient followed rod but loses it sometimes

POOR: Patient lost rod constantly and/or did not follow it

3.5.3 Eye-movement response to binocular prescribed prism

The theoretical basis of prism relocation therapy is that the prism moves the target image onto the PRL, and “replaces” the need for the patient to make an eye movement to achieve this. This basic argument has been questioned by Bailey (1983), who suggested that after fitting a prismatic lens, the eye will make a re-fixation movement to resume the previous image location on the retina (whether central or eccentric). If this happens, the eyes should make a movement towards the prism apex when the prism is placed over the eyes, and move towards the prism base when the prism is removed. This recovery eye movement was however, not observed by Woo et al., 1996 on their normal subjects. The eye movements in response to introduction of a binocular prism were recorded with a video camera as a way to later assess the eye movement response to the prescribed prism.

When prescribing the prism for the patient we would expect the patient to get the foveal image displaced to the optimum PRL found from his/her subjective answers. However, according to Bailey (1983), after fitting a prismatic lens a normal eye will make a re-fixation movement to resume the previous image location on the retina. In order to determine if this movement takes place on AMD patients, the eye movements in response to introduction of a prism, were recorded with a video camera.

The movement response to the prescribed prism was subjectively assessed for both the magnitude and direction of movement. As the power of the prescribed prism increases, a bigger movement would be expected to take place when the prism is positioned (resuming fixation movement) and then removed from vision (recovery movement). A subjective impression of whether the magnitude and direction of either the resuming fixation or recovery movement corresponded to the power and base direction of the prescribed prism was made. This informed us if the patient’s eye movements were as expected from this power or over/under responding to the expectations. Larger or shorter eye movements than expected would mean an unanticipated reaction to the prism.

The direction of the resuming fixation/recovery eye movement was assessed and 3 possible responses were expected:

1. The eye might not response at all with an eye movement.
2. The eye movement would cancel the effect of the prism. That is, the eyes move towards the apex of the prism on putting the prism over, and towards the base on removing it.
3. The eye movement would “replace” eccentric viewing and move towards the base on putting the prism and towards the apex on removing it. However, this response could also be random as the patient wouldn’t necessarily move the eyes immediately and depending on whether the patient is using the ideal PRL or not this might not coincide with the chosen prism base.

Potentially, both the first and third type of responses would be a sign of possible benefit to the patient from the prisms. On the other hand, the second type of response could be associated with a no-benefit of the prisms to the patient and thus this is the type of response that will be looked for while performing this assessment.

The original target used was a black cross drawn on a piece of paper with the arms at 45° from the horizontal and vertical axis and with a side length of 5cm (a miniature of the Bjerrum screen’s fixation target). After testing it on a few patients it was experienced that, instead of the target being placed on the centre of the objective lens, because it would cover the view through it, it had to be to one side of the lens. Because the test needed to be done at a reasonably close distance from the patient to appreciate the movements of the eyes, the patient’s deviation of fixation from the objective was quite obvious, making the assessment of the eye movement more difficult. This is why the fixation target was removed. Instead, the patient was instructed to look at the camera’s objective lens and not to move the eyes from there. Although it could be argued that patients with a central scotoma would find it difficult to look at a small circle of about 3cm in diameter (this is the actual size of the objective lens), because the lens was in the centre of the camera, patients could use the surrounding camera as a reference.

The prism used to evaluate the eye movement response had the same power and base direction that the prescribed custom prism for the same patient. Originally, the prism was intended to be placed only in front of the eye to which the prism was prescribed for. However, after trying this technique on a few patients, and noticing no recovering eye movements at all, the approach was changed to the same prism being placed binocularly. A binocular prism gave a better reaction of the eyes. The prism was placed in front of both eyes by means of a clip-on frame, where two prism lenses with the same power and base were hooked. Only the movement of the prescribed eye was recorded. The second eye was only expected to have the

same movement direction and quantity as the recorded eye and thus not provide any extra information. Also, by only recording the one eye, the camera could be brought closer to the eye, giving a better view of the eye movements for latter evaluation.

The video camera was placed at a distance of about 40-50 cm from the eye and the patients were thus wearing the near vision spectacles. The night-shoot facility was only used on a few patients wearing a quite dense tint as this gives a better view of the pupil and therefore helping to assess the eye movements.

The prescribed prism was placed binocularly on top of the spectacles three times. Having the movements recorded three times for each patient made the assessment easier when viewing the video. The recovery movement was easier to assess than the initial movement. This is because when assessing the recovery movement there were no lens reflections as the lens has then been removed. This compared to the assessment of the initial eye movement, which had to be done when the lens was placed and thus with inevitable light reflections. The recovery movement was thus assessed in a similar way to performing a cover test: assessing the eye movement on removing the lens.

Two different Optometrists assessed the information obtained from this video. They independently assessed whether the patient made a recovery movement or not when the prism was placed, and/or a re-fixation in the opposite direction when it was removed. Only those patients whose eye movement was identified by both optometrists independently were definitely classified as making a re-fixation movement. Those that were only acknowledged by one of the assessors were not classified as such, but as a no movement made. Selecting only those patients that were considered to make a re-fixation movement by both optometrists gave reassurance on which are the patients that change fixation when using prism spectacles. This outcome could then be analysed as a possible prognostic factor for successful or unsuccessful use of prism spectacles.

3.6 Frame and diary

A range of both plastic and metal frames from the Norville Allyn range was shown to the patient to choose for the study spectacles. The patient was given the same lens type they were using if they were happy with them (that is single vision or bifocals) or changed if they preferred a different type of lenses, in which case the conventional spectacles were changed as well. If the patient did not wear any distance spectacles (small prescription and thus no VA improvement) the study lenses were made with a plano prescription. On the whole, we wanted the patient to be happy with their conventional spectacles to be able to properly compare with the same prescription study spectacles. If the vision could be improved at least one and a half

lines on the logMAR scale or if the change of prescription was of at least 1diopter of sphere or cylinder, new conventional spectacles/lenses were provided as well as the study ones.

Finally, a diary to fill in on a weekly basis was provided. All the low vision aids were numbered and patients were asked to keep record of all the activities they used them for, time used and any comments they may have wanted to make. This diary was completed for the conventional LVAs during the first month and until they attended the second visit to collect the study spectacles. Once they have the study spectacles these counted as another LVA to comment in the diary. Any possible changes on the patients' activities and performance, before and after getting the study spectacles, was evaluated by the second researcher.

CHAPTER 4

A Description of the Study Population

A total of 243 AMD patients were recruited to the study. This number was necessary to give the study sufficient power, but it also represented an opportunity to investigate a large sample of the AMD population selected with few exclusion criteria. The data collected in this study are therefore significant in understanding the effects of AMD in the population. This chapter presents the descriptive statistics for all data collected by the optometrist in the first visit.

Data was collected for both eyes for all 243 patients⁷. To facilitate the analyses carried out on the following chapters data has been organised and kept separated for better (BE) and worse (WE) VA eyes. For easier reference, figures for the two eyes are always adjacent, and organised so that the BE data appears on the left-hand side and the WE data on the right-hand side. Also, the X and Y-axes were modified when necessary to show equal range of values to facilitate comparison of data between eyes.

Because a large amount of the variables collected for the study did not have a normal distribution, and also for consistency reasons, the chosen parameters to describe the measures of central tendency and dispersion were the median, the interquartil range (IQR) and the maximum and minimum values (as suggested by Bland, 1995) rather than the median, standard deviation and ranges that are only adequate for normally distributed data. The median is the value that divides the bottom 50% of the data from the top 50% of the data and the IQR is a measure of

⁷ The area of the scotomas for the WE was the only exception of data not reported. The quantification of the area of scotoma proved to be a too time-consuming job due to the lack of a computerised program that would perform this task. The measurement had to be made manually by overlying an acetate grid (see figure 4.4) over the scotoma and manually counting the amount of degrees² inside the scotoma. This data was not needed for further purposes than for a poor description of the population and thus was not worth analysing it.

dispersion of the data set, showing the spread of the middle 50% of the data and is not affected by the extreme values (Stephens, 1998).

When reporting PRL positions, previous literature uses different interpretations of the visual system and therefore sometimes refers to the visual fields and others to the position of fixation. This could cause confusion as a subject fixating to the left is actually using the right hemi-field of vision. Furthermore, some studies report positions of fixation on retina where a superior position of fixation in the retina implies an inferior hemi-field selection. To avoid confusion, all data containing angular information has been presented and, later on discussed, with reference to the corresponding visual field.

A standard statistical software package (SPSS, version 11) (SPSSinc, Chicago, USA) has been used for all data analysis reported on chapters 4 and 5. However, a different statistical program: STATA (StataCorpLP, Texas, USA) was used to obtain the multiple regression models reported on chapter 6.

4.1 Data management and quality

Data were collected into data collection sheets as the tests were performed. Data that was relevant to the second researcher was entered into a patient database created using Microsoft Access 2000. This database was sent periodically to the second researcher as a mean to pass on the patients' contact details and other information that was considered useful to have for the second visit. Data were later on copied onto an SPSS spreadsheet for analysis.

Missing data: Some patients failed to perform certain tests. The most common tests they failed were those performed after dilation (fundus photography, assessment of fixation quality and LOCSIII) due to patients having difficulty accessing the instrument (fundus camera and/or slit lamp) to perform the test. A precise breakdown of the reasons for missing data has been provided in the corresponding sections below. The missing data were left as blank in the database so that the SPSS program could recognise them as "missing data".

With the aim of reducing the amount of typing errors and assessing the quality of the data the following actions were taken:

1. The data was entered into the program for 62 variables and 243 cases twice to reduce typing errors.
2. The quality of the data entered was tested by re-entering the data for a random 10% of the cases and working out a percentage typing error. This re-entering of the 10% of data was done both before and after the whole data was entered for the second time. Re-

entering the data provided an opportunity to observe the percentage reduction of typing errors after the second entrance relative to the first one. The original percentage error after the first entrance of data was 8% but after the second entrance this error was reduced to a 1%. After this significant reduction of errors the data could be treated as “clear from typing error data”.

4.2 Demographics, patients' background information and cognitive status

Gender: The number of females recruited in this study (157; 65%) was almost double the number of males (86; 35%). Considering that all patients that were attending the low vision clinic and met the inclusion criteria were invited to take part regardless of the gender this suggests a higher prevalence of females attending the low vision clinic.

Ages: The minimum and maximum ages of the 243 patients recruited for the study were 56 and 97 years respectively (median 81.1) (Figure 4.1).

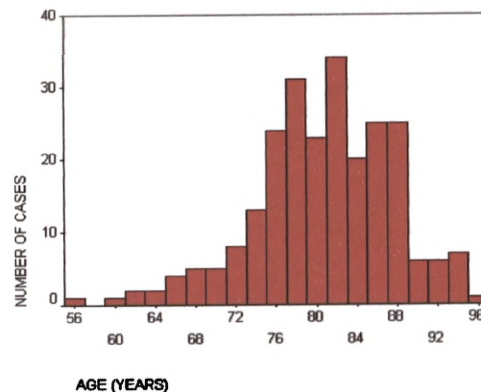


Figure 4.1: *Distribution of patients' ages.*

Race: Nearly all patients recruited for this study were Caucasian and only 2 patients had a different ethnic origin, which was Indian.

Living independence: More than half of the patients recruited for the study (130; i.e. 53%) lived on their own. 85 lived with their partner (35%), 16 lived with a family member (7%) and 10 lived in sheltered accommodation (5%). This shows that about half of the patients recruited were quite independent and therefore required to be self-sufficient with activities of daily living.

Registration status: A total of 81 (33%) patients were registered as partially sighted and 88 (36%) were registered as blind, leaving 74 (31%) that were not registered when they came for their first visit. Out of the 74 patients that were not originally registered 13 were suitable for partial sight registration and, after explaining the benefits and purposes of registration, 9 of them agreed to get registered. Similarly, 8 of the 81 patients that were registered as partially sighted were eligible for blind registration and 4 of them agreed to this change in registration category. For these cases, the BD8 form was filled in and signed by the patient, ready to be passed on to the ophthalmologist for his signature and further processing.

Duration of impairment: The median duration of the condition for the better eyes was 3.0 years, with minimum and maximum values of 0.3 and 40 years respectively (IQR 3.5). The median for the worse eye was 4.0 years with a minimum and maximum value of 0.1 and 40 years respectively (IQR 5.0) (Figures 4.2 and 4.3).

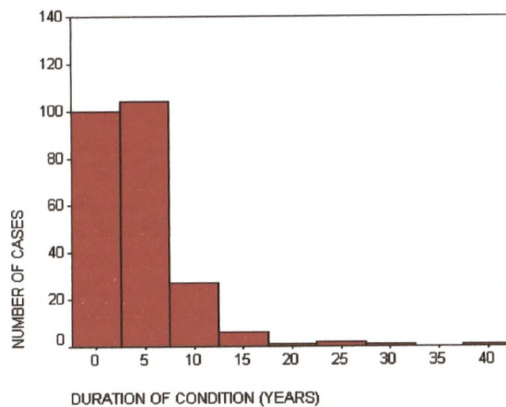


Figure 4.2: *Distribution of duration of condition for better VA eyes.*

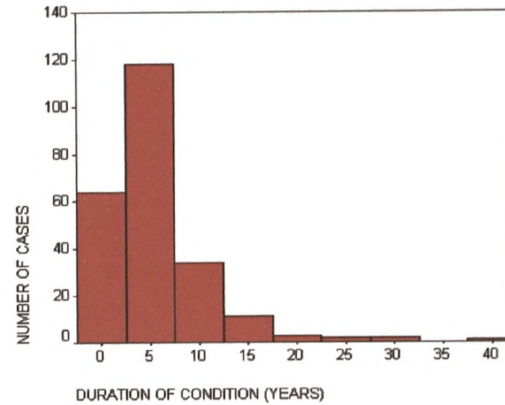


Figure 4.3: *Distribution of duration of condition for worse VA eyes.*

Cognitive state: Two hundred and fifteen of the recruited patients (88%) passed the MMSE quite easily with at least 20 correct answers out of the 22. The other 28 (22%) found it a bit more difficult and passed it with scores between 16 and 19 (see Table 4.1 for distributions of MMSE scores). The median score was 21.

MMSE scores	Number of cases
16	3
17	1
18	7
19	17
20	34
21	63
22	118

Table 4.1: MMSE scores.

4.3 Visual function data

4.3.1 Distance visual acuity

Out of the 486 eyes of the 243 patients recruited, 25 WE were not included because of having very poor VA (1.68 logMAR or worse). The distribution of the corrected distance visual acuity at the first visit of the remaining 461 eyes tested in the study had been plotted on Figures 4.4 and 4.5 for better and worse eyes respectively. The distributions of the prism distance visual acuities for BE and WE, also at first visit, were plotted on Figures 4.6 and 4.7 respectively.

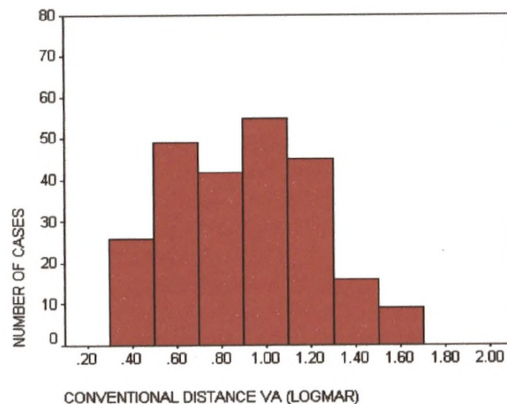


Figure 4.4: Distribution of conventional distance VA for better VA eyes.

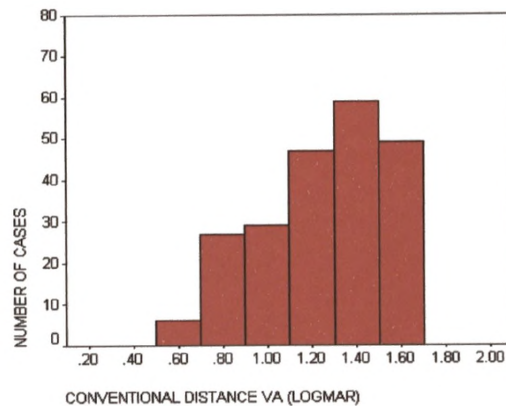


Figure 4.5: Distribution of conventional distance VA for worse VA eyes.

Patients were tested for prisms on a 'real scene' photograph and VA was then measured on the ETDRS chart. The medians, minimum and maximum values and IQR for conventional (conv), prism distance (dist) VAs and differences between prism and conventional VAs for both better and worse VA eyes are shown on Table 4.2. Ranges show that prisms seem to improve VA for some cases but cause it to deteriorate for other cases since the poorest acuity has deteriorated from 1.68 to 2.00 logMAR for the worse VA eyes. The median VA improvement for prism over the conventional VAs was -0.02 logMAR for both the better and worse VA eyes.

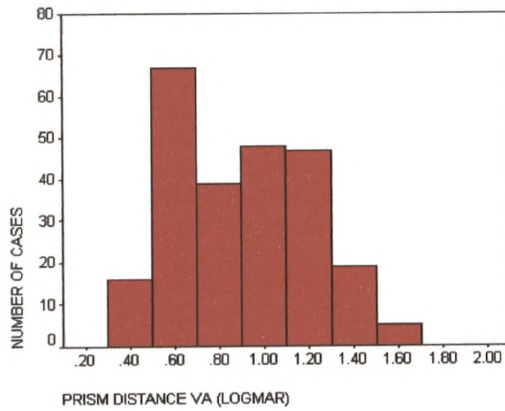


Figure 4.6: Distribution of prism distance VA for better VA eyes.

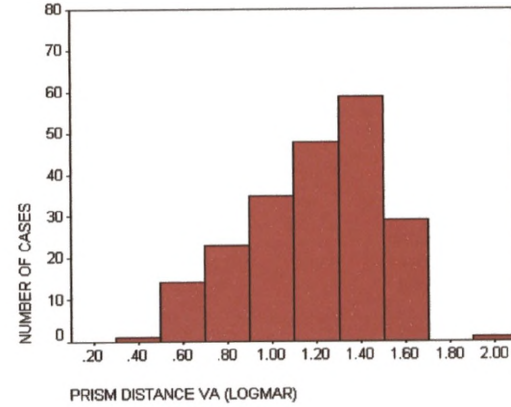


Figure 4.7: Distribution of prism distance VA for worse VA eyes.

Type of VA	Median	Minimum	Maximum	IQR
Conv dist VA for BE	0.93	0.42	1.60	0.48
Conv dist VA for WE	1.26	0.60	1.68	0.36
Prism dist VA for BE	0.90	0.30	1.62	0.52
Prism dist VA for WE	1.21	0.34	2.00	0.38
Prism-Conv dist VA for BE	-0.02	-0.60	0.54	0.12
Prism-Conv dist VA for WE	-0.02	-1.06	0.74	0.12

Table 4.2: Descriptive statistics for conventional and prism distance VAs for better and worse VA eyes in logMAR.

Figure 4.8 shows a scatter plot of conventional VA against prism VA. Prism VA for the BE was slightly better than conventional VA by a median value of -0.02 LogMAR (minimum and maximum values -0.60 and 0.54 respectively, IQR 0.12). The distribution of this difference is shown in Figure 4.9.

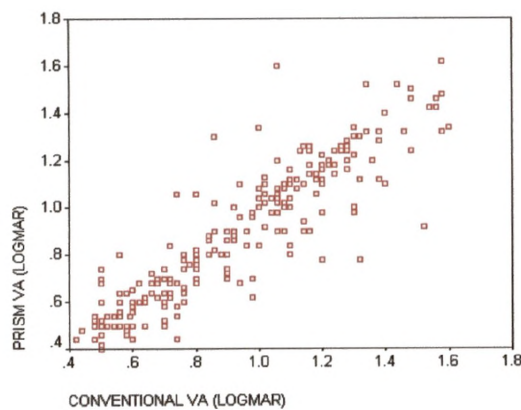


Figure 4.8: Scatter plot of conventional against prism distance VA for better VA eyes.

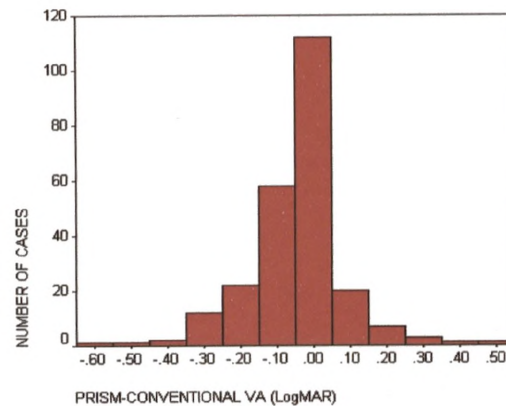


Figure 4.9: Distribution of the difference between conventional and prism distance VA for better VA eyes.

4.3.2 Near visual acuity

Near VA was originally recorded in the M system at a viewing distance of 25 cm (see section 3.2.2). However, to facilitate comparison between distance and near VAs data has been transformed onto LogMAR scale. To transform the size of the letters from the M system notation onto LogMAR VA formula (4.1) was applied:

$$\text{LogMAR near VA} = \text{Log}_{10}(\text{Msize}) + \text{Log}(1/X) \quad (4.1)$$

Where X = viewing distance in metres. Four BE and 57 WE were not able to read any words on the chart. These eyes were also measured with prism and 1 BE and 22 WE improved VA to a level that allowed them to be able to read some words on the chart. The distribution of the corrected near visual acuity for all eyes at the first visit in the study has been plotted in Figures 4.10 and 4.11 for BE and WE respectively. The distributions of the prism near visual acuities for BE and WE, also at first visit, were plotted in Figures 4.12 and 4.13 respectively.

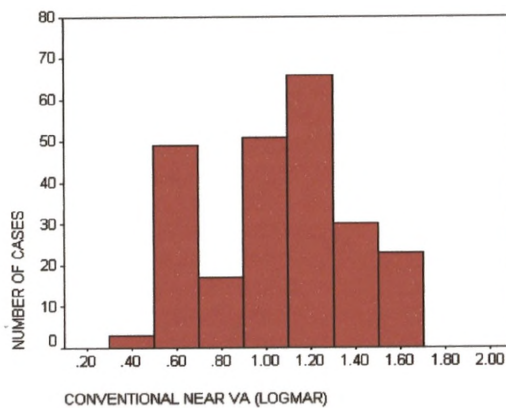


Figure 4.10: Distribution of conventional near VA for better VA eyes.

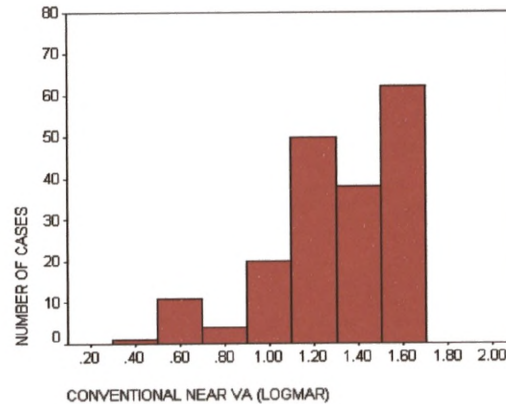


Figure 4.11: Distribution of conventional near VA for worse VA eyes.

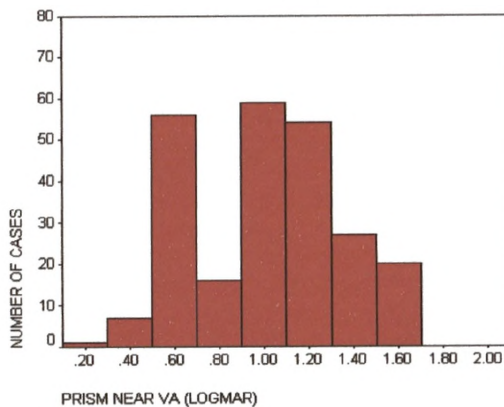


Figure 4.12: Distribution of prism near VA for better VA eyes.

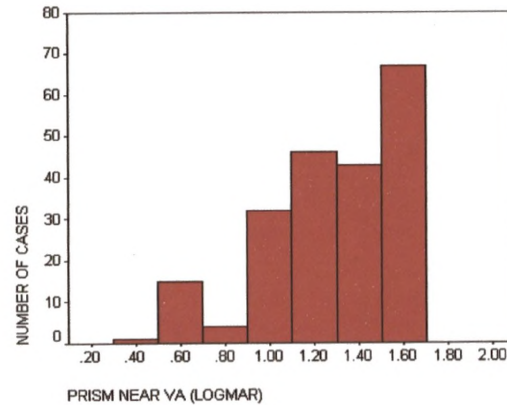


Figure 4.13: Distribution of prism near VA for worse VA eyes.

The medians, minimum and maximum values and the IQR for conventional (conv) and prism near VAs for both better and worse VA eyes are shown in Table 4.3.

Type of VA	Median	Minimum	Maximum	IQR
Conv near VA for better VA eyes	1.00	0.38	1.60	0.40
Conv near VA for worse VA eyes	1.30	0.30	1.60	0.40
Prism near VA for better VA eyes	0.90	0.11	1.64	0.52
Prism near VA for worse VA eyes	1.20	0.30	1.64	0.43

Table 4.3: Descriptive statistics for conventional and prism near VAs for better and worse VA eyes in logMAR.

There was no difference between conventional and prism near VAs for better VA eyes (median value 0.00 LogMAR, minimum and maximum values –1.00 and 0.82 respectively, IQR 0.10).

4.3.3 Single, crowded and repeated VAs data

Single letter (SL), crowded letter (CL) and repeated letter (RL) visual acuities were scored as Snellen fractions and then transformed onto the logMAR scale by using formula (4.2). This transformation allows future comparisons with both conventional and prism distance visual acuities as these were both recorded on the logMAR scale.

$$\text{LogMAR VA} = \text{Log}_{10}(\text{Snellen VA}^{-1}) \quad (4.2)$$

Table 4.4 shows the medians, minimum and maximum values and IQR for all three measures of letter VAs for both better and worse VA eyes and the distribution of these values can be seen in Figures 4.14 to 4.19.

Type of VA	Median	Minimum	Maximum	IQR
SL for better VA eyes	0.90	0.43	1.73	0.40
CL for better VA eyes	1.03	0.43	1.73	0.49
RL for better VA eyes	0.90	0.12	1.73	0.47
SL for worse VA eyes	1.12	0.43	1.78	0.48
CL for worse VA eyes	1.33	0.43	1.78	0.44
RL for worse VA eyes	1.12	0.43	1.73	0.43

Table 4.4: Descriptive statistics for SL, CL and RL VAs for better and worse VA eyes in logMAR.

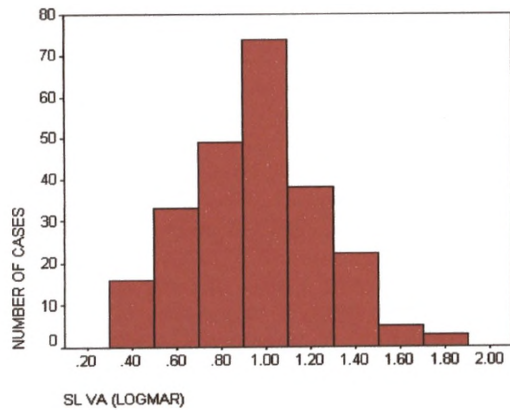


Figure 4.14: *Distribution of single letter VA for better VA eyes.*

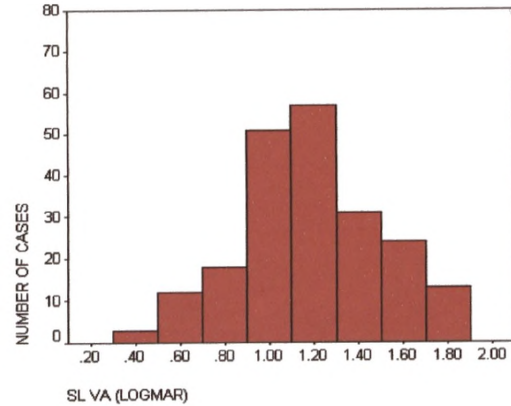


Figure 4.15: *Distribution of single letter VA for worse VA eyes.*

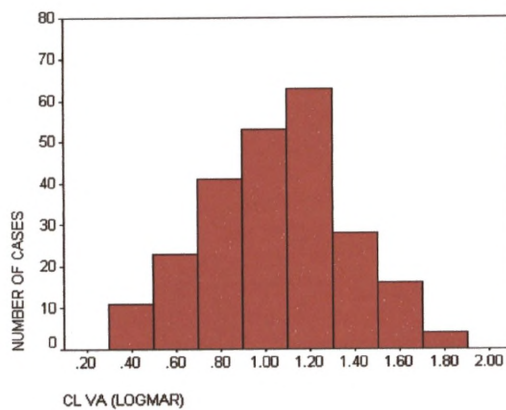


Figure 4.16: *Distribution of crowded letter VA for better VA eyes.*

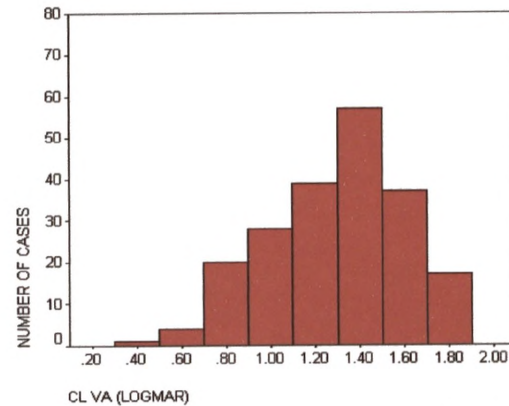


Figure 4.17: *Distribution of crowded letter VA for worse VA eyes.*

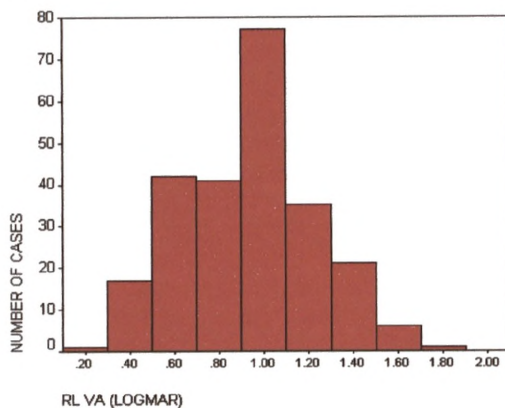


Figure 4.18: *Distribution of repeated letter VA for better VA eyes.*

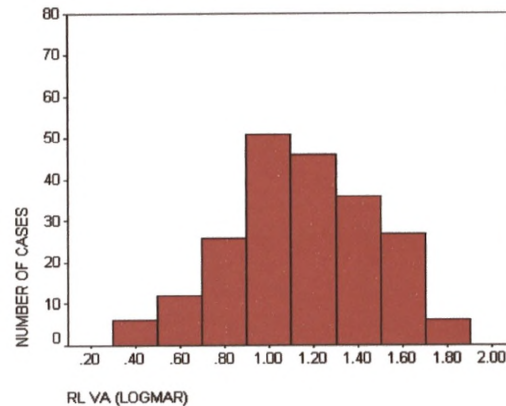


Figure 4.19: *Distribution of repeated letter VA for worse VA eyes.*

For the BE, the measures of the three different types of VA were highly correlated with each other: r ranging from 0.79 to 0.89 (see Table 4.5). This high correlations indicate that these three types of VA studied can not be treated as independent from each other in future analyses.

	CL	RL
SL	0.89	0.79
RL	0.86	

Table 4.5: Correlation matrix for SL, CL and RL VAs of BE.

4.3.4 Perimetry

The Bjerrum screen was used to plot the size, shape and position of the central scotoma following the strategy explained in section 3.2.4. Once the drawing of the scotoma was made, the area of this scotoma and the position of the NNPF were calculated.

4.3.4.1 Scotoma areas

The distribution of the area of the scotoma for 243 BE can be seen in Figure 4.20. The median area was 64 degrees² (minimum and maximum values 0 and 1529 respectively and IQR 187) and for 59% of eyes the area is 100 degrees² or smaller. The scotoma couldn't be traced on 39 (15% of the patients) BE. Because fixation was controlled while the Bjerrum test was being performed, these 39 cases were expected to be relative scotomas.

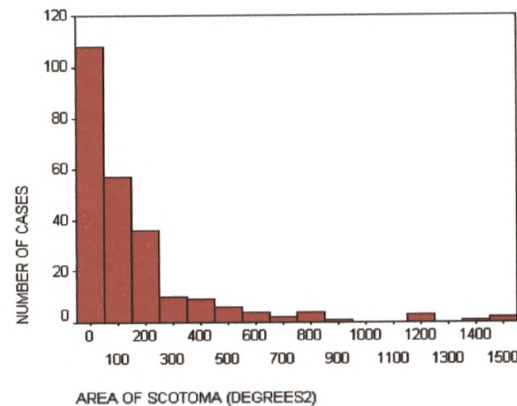


Figure 4.20: Distribution of areas of scotoma for better VA eyes.

4.3.4.2 NNPF positions

The distance and angle of the NNPF with respect to the fovea for the two eyes were measured from the Bjerrum plots. It wasn't possible to locate the position of the NNPF for 39 BE and for 38 WE for which it was not possible to plot a scotoma. The median NNPF distance value for BE was 2.0 degrees (minimum and maximum values 0 and 15 respectively, IQR 3) and for WE the median was 4.0 degrees (minimum and maximum values 0 and 22, IQR 5) (Figures 4.21 and 4.22). The prism powers required to make a displacement of the image from fixation to the NNPFs are 3.5Δ and 7.0Δ for BE and WE respectively.

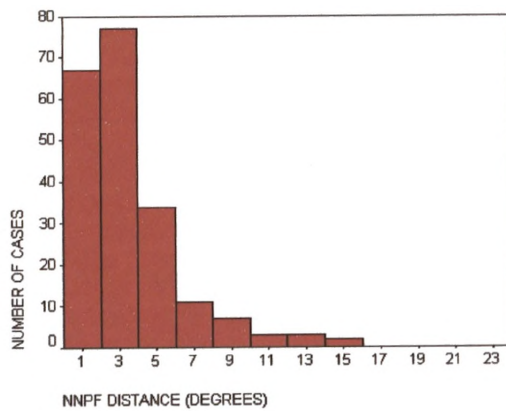


Figure 4.21: *Distribution of nearest non-scotomatous point to fixation (NNPF) distances for better VA eyes.*

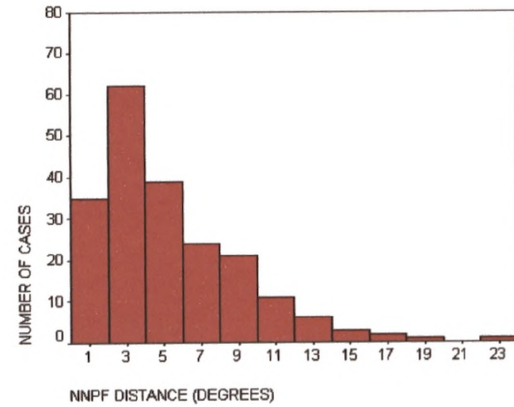


Figure 4.22: *Distribution of nearest non-scotomatous point (NNPF) to fixation distances for worse VA eyes.*

The distributions of the position angles of the NNPF BE and WE are shown on Figures 4.23 and 4.24. Cases where the scotoma plot did not show a clear NNPF (there was more than one position that could be chosen for the NNPF for being equally close to the centre of chart) are not included. In total, a NNPF direction was determined for 196 BE and 103 WE. It can be seen (Figures 4.23 and 4.24) that the angular positions of the NNPF with highest prevalence were down, left, up and right (270°, 180°, 90° and 360°, or the cardinal positions) had very high prevalence for the BE. However, this effect was not as obvious for the WE. Also, the inferior and left hemi-fields do seem to promise a better general success for relocation than the superior or right ones.

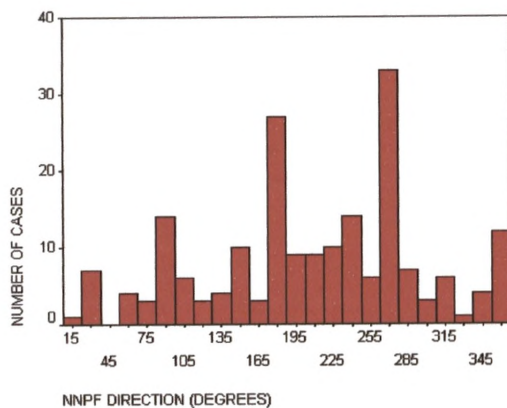


Figure 4.23: *Distribution of nearest non-scotomatous point to fixation directions for better VA eyes.*

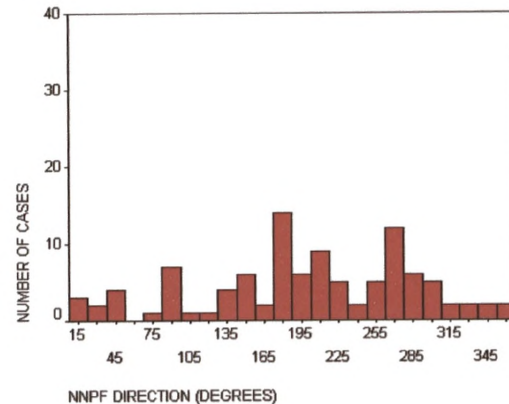


Figure 4.24: *Distribution of nearest non-scotomatous point to fixation directions for worse VA eyes.*

4.3.5 Contrast sensitivity

Contrast sensitivity was successfully measured on all 243 BE and 220 WE. The distribution for BE and WE can be seen in Figures 4.25 and 4.26. The median value for the log contrast sensitivity of the BE was 1.05 (minimum and maximum values 0.05 and 1.65, IQR 0.45). For WE, the median value was 0.70 (minimum and maximum values 0.00 and 1.50 respectively, IQR 0.65).

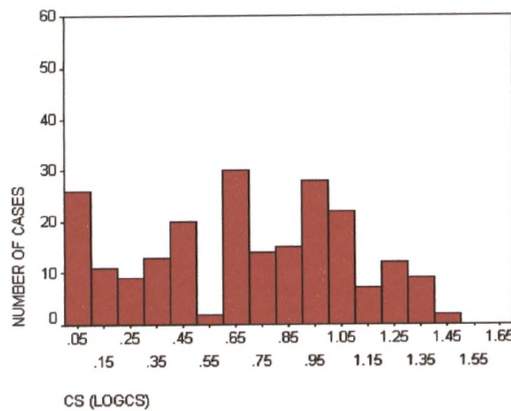


Figure 4.25: *Distribution of contrast sensitivities for better VA eyes.*

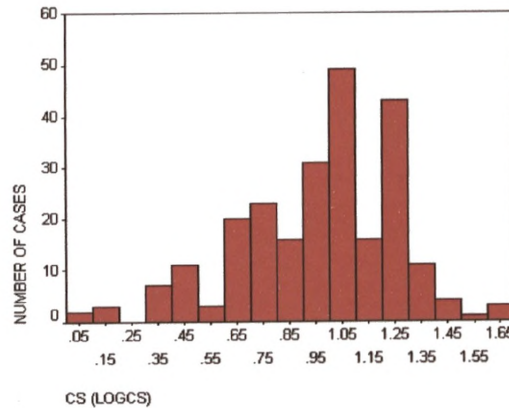


Figure 4.26: *Distribution of contrast sensitivities for worse VA eyes.*

4.4 Refraction data

4.4.1 Conventional prescription results

Prior to the low vision assessment patients had a full refraction to determine if their current prescription was optimal. Conventional spectacles were only updated for those patients whose visual acuity improved a minimum of one and a half lines on the logMAR scale or if the change of prescription was of at least 1 diopter of sphere or cylinder (as described in section 3.6).

Table 4.6 describes the median values, maximum and minimum values and the IQR of prescriptions among the 243 patients in the study showing that the ranges and medians were quite similar for BE and WE. Figures 4.27 to 4.30 show the distribution of the mean equivalent sphere and astigmatism powers for BE and WE. One hundred and seventy BE had some degree of astigmatism and a few less worse eyes (139) were also found to have some astigmatism. Figures 4.31 and 4.32 show the distribution of cylinder powers for BE and WE. Mean equivalent sphere (MES) values ranged from -16.75 to +13.25, median +0.82 dioptres for the BE and -13.00 to +13.75, median +0.81 dioptres for the WE. The distribution of the MES showed much higher prevalence of longsighted (62%) as compared to shortsighted (26%) and

emmetropic (12%) patients. All distributions were normal. For 84% of patients the MES power ranged between -2.00 and +4.00 dioptres.

Prescriptions	Median	Minimum	Maximum	IQR
BE sphere power	1.00	-14.50	12.50	3.00
BE cylinder power	1.00	0.25	6.50	1.50
BE MES	0.82	-16.75	13.25	2.38
WE sphere power	0.25	-13.50	13.00	2.50
WE cylinder power	1.00	0.00	4.00	1.00
WE MES	0.81	-13.00	13.75	2.00

Table 4.6: Descriptive statistics of patients' prescriptions in dioptres. NB-All prescriptions have been transposed to positive cylinders.

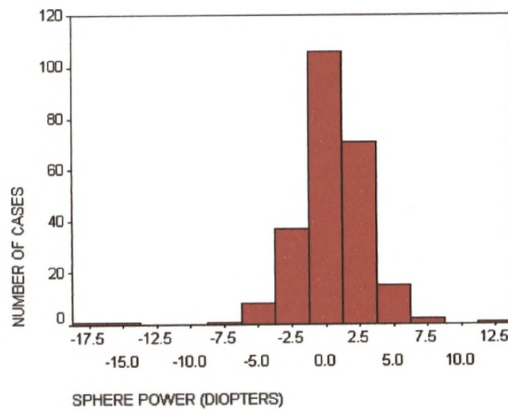


Figure 4.27: Distribution of mean equivalent sphere powers for better VA eyes.

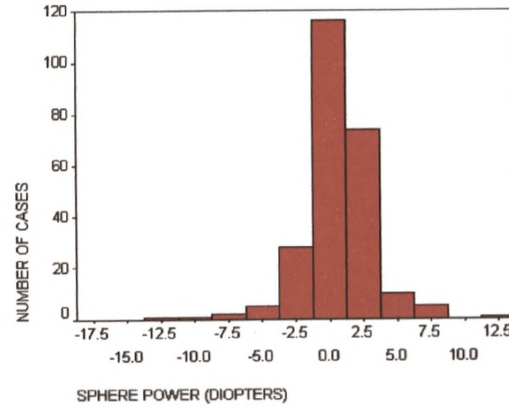


Figure 4.28: Distribution of mean equivalent sphere powers for worse VA eyes.

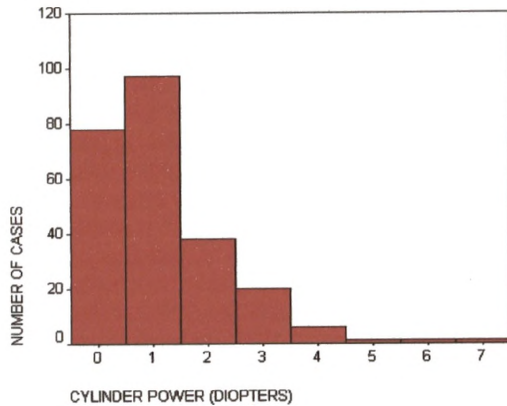


Figure 4.29: Distribution of cylinder powers for better VA eyes.

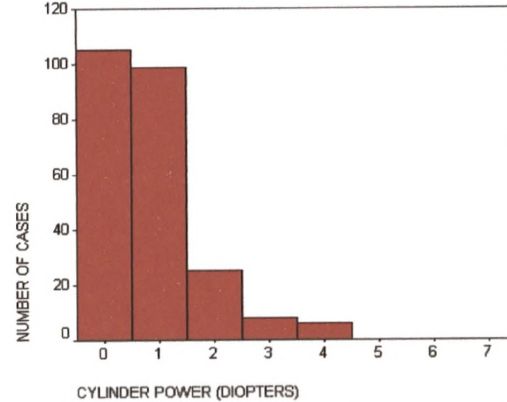


Figure 4.30: Distribution of cylinder powers for worse VA eyes.

The positions of the cylinder axis were distributed all across the 180° different degrees (see Figures 4.31 and 4.32), with 180° being the most popular position on both BE (32%) and WE (27%) when the prescription is on the positive cylinder power notation. This high prevalence of positive cylinder axis at 180° shows a dominance of astigmatism against the rule as compared to with the rule or oblique astigmatism.

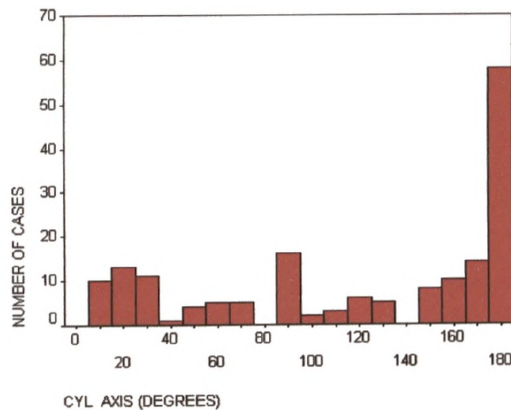


Figure 4.31: *Distribution of cylinder axis for better VA eyes.*

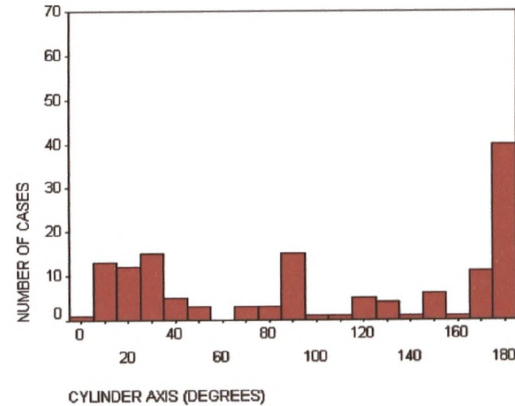


Figure 4.32: *Distribution of cylinder axis for worse VA eyes.*

Out of the 243 patients recruited 237 had near vision prescription (either single vision or bifocal lenses) and the remaining 6 patients didn't use a near prescription. These patients had no intention to use near vision spectacles and thus they were only prescribed distance ones. The three reasons for not having near vision prescription found were:

1. Two patients preferred to use hand magnifiers for reading without the near prescription.
2. Three myopic patients had a near prescription close to plano power and therefore did not find reading spectacles any advantage over not wearing them.
3. One patient did not perform any reading or near vision tasks.

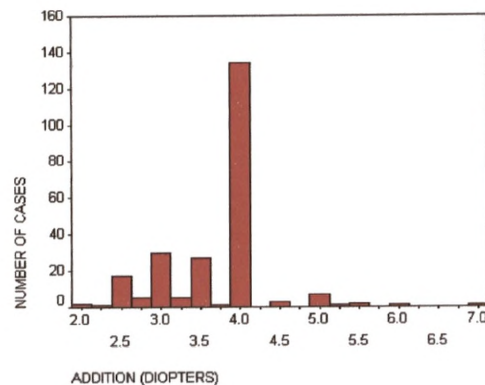


Figure 4.33: *Distribution of addition powers prescribed to patients.*

Out of the 237 patients using a near prescription, 6 of them had two different addition powers. These were cases where the patient needed both an intermediate and a reading prescription and thus two separate pairs of near vision spectacles were prescribed. The minimum and maximum values of addition powers prescribed for near vision are +2.00 and +7.00 dioptries respectively with a median of +4.00 dioptries (IQR 0.75). There was a preponderance of +4.00 prescribed additions due to the fact that larger additions would restrict vision to a very close working

distance, not appropriate for most activities, and weaker additions would not give an optimal near vision. The minimum and maximum values of addition powers prescribed for intermediate vision were +2.50 and +3.00 dioptres respectively with a median value of 2.50 dioptres (IQR 0.31).

4.4.2 Prism prescription results

Binocular prisms were prescribed to all 243 patients. These were worn during three months with the objective of investigating the main aim of the study: trying to find out whether prism relocation therapy can reduce the disability experienced by patients with AMD.

The minimum and maximum values of prescribed prism powers were 2 and 23 Δ , with a median of 8.0 Δ and IQR 4.0. The distribution of prism powers can be seen in Figure 4.34. The preferred prism power in 44% of patients was 6 Δ , followed by 10 Δ in 19% and 8 Δ in 16%.

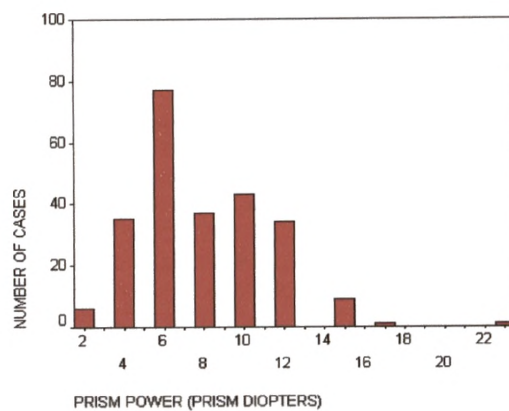


Figure 4.34: Distribution of prescribed prism powers.

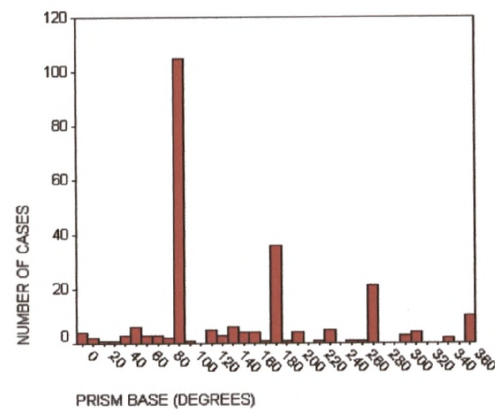


Figure 4.35: Distribution of prescribed prism bases.

The distribution of the chosen prism base directions shows a clear preference for the four cardinal positions (see Figure 4.35): the 90° position was chosen by 53% of patients (up position). 15% of patients chose the base at 180° (left), 9% at 270° (down), 6% at 0° (right) and only 10% chose other oblique positions.

4.4.3 Type of lenses prescribed

A total of 31 patients were given new conventional bifocals and 41 were given single vision lenses. The available bifocal segments were downcurve (R segment), flat-top (D segment) or curved-top (C segment). The segment size is expressed as the segment diameter in mm. The distribution of the different bifocal segments and the kind of single vision lenses given to

patients can be seen in Table 4.7. The other 171 patients didn't need a change of prescription and thus were not given new conventional spectacles.

Bifocal segments	Amount	Single vision lenses	Amount
D25	2	DV	8
D28	8	IV	1
D35	3	NV	30
D40	1	DV & NV	9
R22	1	DV, IV & NV	1
R24	3		
R25	6		
R28	6		
R38	1		
Total	31	Total	41

Table 4.7: Distribution of conventional bifocal and single vision lenses prescribed.

For the prism spectacles, 107 patients were prescribed bifocal lenses and 126 patients were given single vision lenses. The 10 remaining patients were given both a pair of bifocals and a pair of single vision lenses (see Table 4.8 for the distribution of lenses). Patients were only given both bifocals and single vision spectacles if a benefit from having different additions on bifocals from that on either near vision or intermediate vision spectacles was found. For all cases, the type of lenses prescribed in the prism spectacles was matched to that in the conventional spectacles to allow a fair comparison between them.

Bifocal segments	Amount	Single vision lenses	Amount	Bifocal and single vision	Amount
C28	3	DV only	11	R24 + IV	1
D25	10	NV only	1	R25 + IV	1
D28	31	NV/DV	111	D25 + NV	1
D35	10	NV/IV	1	D28 + NV	5
D40	1	NV/IV/DV	2	R22 + NV	1
R22	6			R24 + NV	1
R24	10				
R25	11				
R28	10				
R38	14				
R40	1				
Total	107	Total	126	Total	10

Table 4.8: Distribution of prism bifocal segments and single vision lenses prescribed.

Nine patients contacted us after they had finished their participation in the study requesting new spectacles. Two of them wanted to change from bifocal to single vision because they were not using the prism spectacles for reading and thus the segment was only interfering with the distance vision activities. One patient wanted a pair of tinted spectacles for the sun, and another wanted lenses to an alternative frame. Four patients wanted a spare pair of spectacles and one

patient had new spectacles made due to being part of the placebo arm but very successful with the prism on the first visit.

Three patients were originally wearing varifocal lenses and although the laboratory made an attempt to make prism-controlled varifocals they were unsuccessful due to lens blank substance not being thick enough to work the requested prism. These patients were therefore changed to single vision or bifocal lenses, as preferred, for the conventional pair/s and the matching type of lenses were ordered with the prism prescription. It was felt that the change of lens type could confound the results for such patients, and so wearing these lenses became an exclusion criterion for the study.

4.4.4 Reported disabilities

All 243 patients were given a low vision assessment on their first visit. During this low vision assessment patients had a chance to discuss the problems they had been experiencing while performing activities of daily living. To form a starting point for the low vision assessment, patients were asked a total of 17 questions derived from the MLVAI with the aim of determining their disabilities. Patients were also given the opportunity to state any other activities that they found difficult to perform. Providing low vision aids to help reduce these disabilities was the primary goal of the assessment.

Table 4.9 shows the number of patients that reported a disability on each of the fields. The left column contains the 17 activities from the MLVAI and the right contains all the other extra activities that patients reported. From the MLVAI, the most commonly reported (by at least 50% of patients) were: Recognising faces (80%), threading a needle (61%), reading the newspaper (58%), using the telephone book (58%) and identifying coins (53%). The most popular activities suggested spontaneously by patients were: shopping (14%), seeing bus numbers (7%) and knitting/sewing (4%).

The optometrist then assessed all the LVAs the patient currently used to see if they were adequate. If this was the case, patients were kept with the same LVAs but if performance was not satisfactory a revision of the adequate use of the instrument and magnification was made to improve the performance. In some cases, when the instrument wasn't the most appropriate one for the desired task to perform, this might be changed for another LVA.

MLVAI disabilities	Number cases	Other disabilities	Number cases
Recognising faces	195 (80%)	Shopping	33
Threading a sewing needle	148 (61%)	Seeing bus numbers	18
Using the telephone book	140 (58%)	Knitting/sewing	10
Reading newspaper print	142 (58%)	Crossing the road	7
Identifying coins	128 (53%)	Cooking	6
Reading a medicine label	119 (49%)	Gardening	4
Reading package label	120 (49%)	Drawing	4
Reading a letter	118 (49%)	Seeing the steps on stairs	4
Watching television	108 (44%)	Navigating	4
Writing a cheque	106 (44%)	Fitting key on lock	3
Reading an account	105 (43%)	Cutting nails	2
Reading digital display	90 (37%)	Distinguishing colours	2
Telling time: watch	77 (32%)	Playing tennis	1
Pouring	68 (28%)	Using the washing machine	1
Telling time: clock	64 (26%)	Using scissors	1
Using the telephone	53 (22%)	Playing bridge	1
		Doing crosswords	1
		Dressing up	1
		Collecting stamps	1
		Shaving	1
		Using microscopes	1
		Finding things in the house	1
		Eating	1
		Using the computer	1
		Cleaning	1

Table 4.9: Disabilities reported by patients.

4.4.5 Low vision aids prescribed

The final amount and types of LVAs that patients had after the low vision assessment was recorded together with the prescribed magnification for each instrument and came to a Figure of 660. These recorded LVAs included both the old aids that were found useful and the new ones prescribed on the day. These were used by patients during the next four months of the study and reported in their diary. The types and numbers of LVAs, together with the range of magnification that patients had during the study are shown in Table 4.10 Magnification ratings are those used by the manufacturers: if devices were not labelled, no measurements were taken.

Patients had a median value of 3.0 magnifiers (Figure 4.36) (minimum and maximum values 0 and 8, IQR 1).

The most popular LVAs used by patients in the study were the illuminated stand magnifiers (SMI) and the illuminated hand magnifiers (HMI), followed by the non-illuminated hand magnifiers (HM), the non-illuminated stand magnifiers (SM) and the pocket hand magnifiers (PHM). These 5 types of magnifiers are all relative distance magnification devices and together account for 79% of the LVAs used in the study. Many patients also benefited from relative

distance magnification when watching TV, they were advised to sit as close to TV as possible which, in many cases was more convenient and comfortable than wearing a distance LVA (telescopes).

Types of LVAs	Total amount	Type of magnification	Range of magnification
Non-illuminated hand magnifiers	89	Relative distance	1X – 10X
Illuminated hand magnifiers	147		2X – 12X
Non-illuminated stand magnifier	25		2.8X – 12.5X
Illuminated stand magnifier	218		2.5X – 15X
Clip-on magnifiers	2		?
Pocket hand magnifier	46		2X – 10X
Near vision cap (telemicroscopes)	3		1.2X
Hyperoculars	8		?
Base-In prism half-eye spectacles	9		1.5X – 2.5X
Variable focus stand	1		?
Chest magnifier	15		2X
Spectacle-mounted DV binoculars	33	Angular	2.5X – 8X
Spectacle-mounted DV monoculars	7		4X-8X
Hand-held DV binoculars	2		8X
Hand-held DV monoculars	19		2.7X-8X
Ring telescope	3		2.8X
Spectacle-mounted NV binoculars	2		2.5X
Spectacle-mounted NV monoculars	6		2.8X – 10X
CCTV	4	Real-image	N/A
TV reader	8		N/A
Portable CCTV	1		N/A
Bright fields and bar rulers	12		1.8X – 2.8X
Total amount of LVAs	660		

Table 4.10: Types and amounts of LVAs that patients had during the study. The range and type of magnification for each type of LVA is also shown.

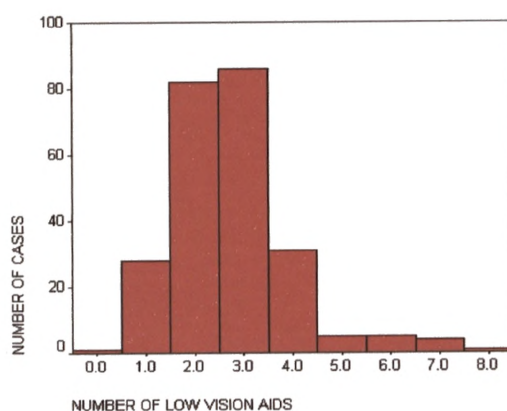


Figure 4.36: Distribution of the number of low vision aids per patient.

Distance telescopes (DVTs) were also frequently used by patients for distance vision. Spectacle-mounted telescopes (40 in total, 33 monoculars and 7 binoculars) were more common

that hand-held telescopes (21 in total, 2 binoculars and 19 monoculars). Ring telescopes were only used by three patients. These 5 types of telescopes provide angular magnification and accounted for 9% of the LVAs used in the study.

The remaining 12% of LVAs consisted of other less common instruments providing relative size magnification (telemicroscopes, hyperoculars, base-in prism half-eye spectacles, variable focus stands and chest magnifiers), angular magnification (spectacle-mounted near vision binoculars and monoculars) or real-image magnification (CCTVs, TVreaders, portable CCTVs, bright fields and bar rulers).

Relative size magnification was not provided directly from the low vision assessment, but samples of large print were shown to the patients and guidance onto how and where to get these facilities was provided.

For the 3 types of magnification that were physically provided in the low vision assessment, and as can be anticipated from the previous paragraphs, the most common was the relative distance magnification (85%), followed by the angular magnification (11%) and the real-image magnification (4%).

Figures 4.37 to 4.42 show the distribution of magnification powers for the six most popular LVAs in the study (SM, SMI, HM, HMI, PHM and DVTS). For those cases where patients had more than one magnifier of the same type (for different goals, such as different print sizes) the one with the highest power was selected for the analysis. Table 4.11 has the descriptive statistics for these LVAs..

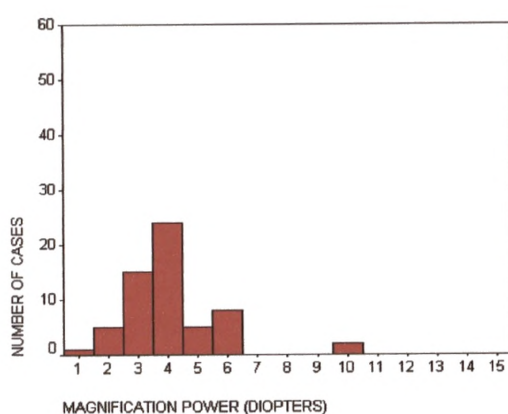


Figure 4.37: *Distribution of the highest prescribed power of hand magnifiers.*

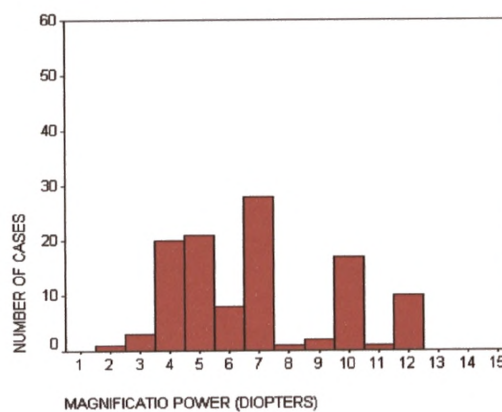


Figure 4.38: *Distribution of the highest prescribed power of illuminated hand magnifiers.*

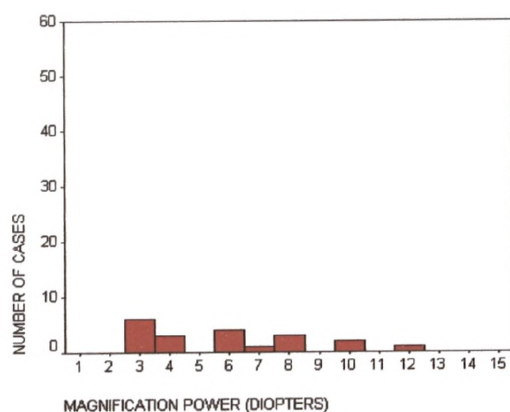


Figure 4.39: Distribution of the highest prescribed power of stand magnifiers.

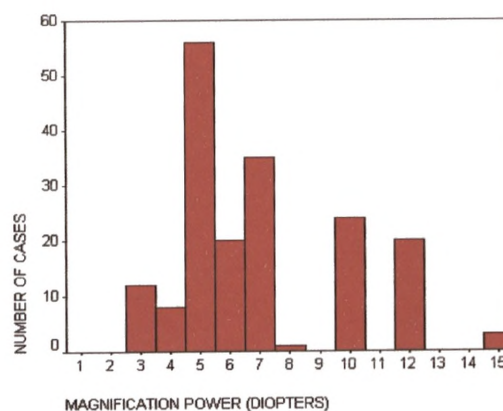


Figure 4.40: Distribution of the highest prescribed power of illuminated stand magnifiers.

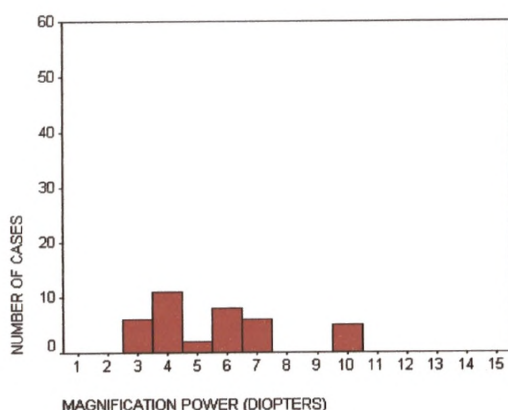


Figure 4.41: Distribution of the highest prescribed power of Pocket hand magnifiers.

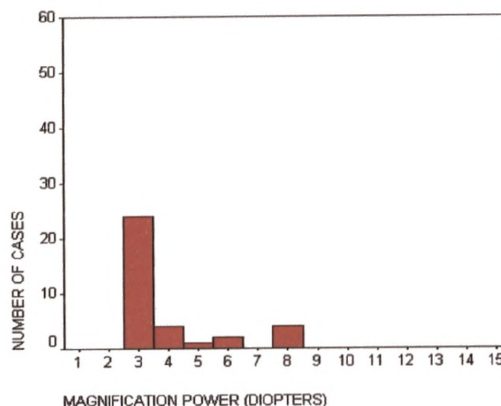


Figure 4.42: Distribution of the highest prescribed power of distance vision telescopes.

LVA	Median	Minimum	Maximum	IQR
SM	6.0	2.8	12.0	5.0
SMI	6.0	2.5	15.0	5.0
HM	3.5	1.0	10.0	1.4
HMI	7.0	2.0	12.0	4.8
PHM	5.5	2.5	10.0	3.5
DVTS	3.0	2.5	8.0	1.0

Table 4.11: Descriptive statistics of magnification powers for the most popular LVAs in the study.

4.5 Ocular pathology data

4.5.1 Classification of AMD

All fundus photographs were classified by an ophthalmologist into the dry, wet and mixed forms of AMD. For some cases, the ophthalmologist did not agree on the diagnosis of AMD when assessing the photographs and a new diagnosis was given for those cases. The AMD lesion was then classified into subfoveal and non-subfoveal, as well as quantified for size (see section 3.4.1).

Out of all the 486 eyes, 405 were classified as AMD cases, from which 288 (71%) were the wet form of AMD, 116 (29%) the dry form, and 1 was mixed. 43 eyes had missing data and 9 were impossible to classify due to quite advanced cataract that caused the quality of the pictures to be below a minimal level that would permit any assessment (see Table 4.12).

Classification of diagnoses	Number of cases
AMD cases	405
Wet	288
Dry	116
Mixed	1
Non-AMD diagnoses:	29
No AMD	9
ARM	9
Vitelliform macular dystrophy	2
Pattern dystrophy	2
Best disease	2
Chorioretinal atrophy	2
Miopic degeneration	2
Unknown	1
Missing data	43
Poor quality pictures	9

Table 4.12: Classification of conditions diagnosed from fundus photograph observation.

Interestingly, 29 eyes were not classified as AMD cases. Nine of these 29 eyes were not found to have any sign of AMD on either the colour or the red-free photographs. Nine more were cases of early ARM. One case was impossible to classify from the information in the photographs and the other diagnoses made were: vitelliform macular dystrophy, pattern dystrophy, Best's disease, choreoretinal atrophy and myopic degeneration (Table 4.12).

4.5.2 Quantification of AMD

The ophthalmologist also made an assessment of the relative size of the macular lesion in each case. The median value was found to be 4.8 disc diameters (minimum and maximum values 0.1

and 34.0 respectively, IQR 5.9) for BE and 6.2 disc diameters (minimum and maximum values 0.1 to 60.0 respectively, IQR 7.0) for WE. The distributions can be seen in Figures 4.39 and 4.40.

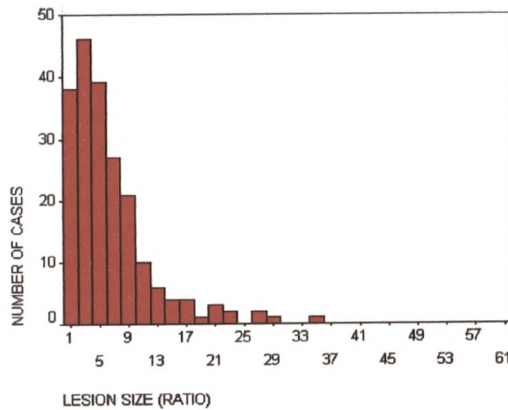


Figure 4.43: Distribution of the relative size of lesion for better VA eyes.

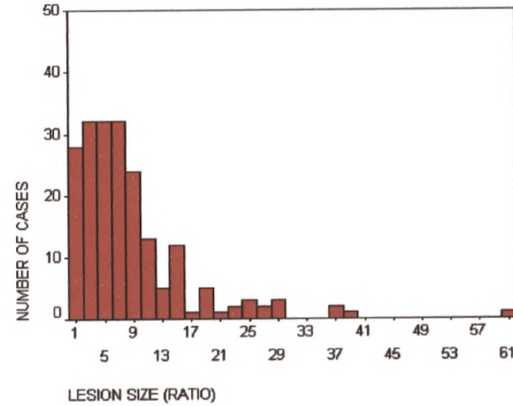


Figure 4.44: Distribution of the relative size of lesion for worse VA eyes.

The relative size of the lesion provided a quick estimation of the size of the damage but for comparison purposes it would be more practical to know the size of the lesion in degrees². The area of the lesion can be calculated from the area of the optic disc. Assuming the optic disc is an ellipse, the area can be calculated from the major and minor radii using formula (4.3):

$$\text{Area of ellipse} = \pi \cdot a \cdot b \quad (4.3)$$

where a and b are the major and minor radii of the ellipse respectively.

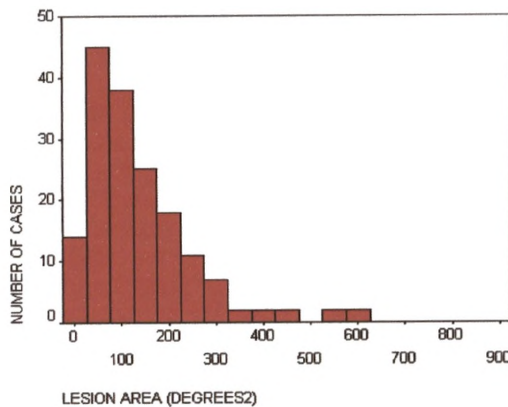


Figure 4.45: Distribution of the area of lesion in degrees² for better VA eyes.

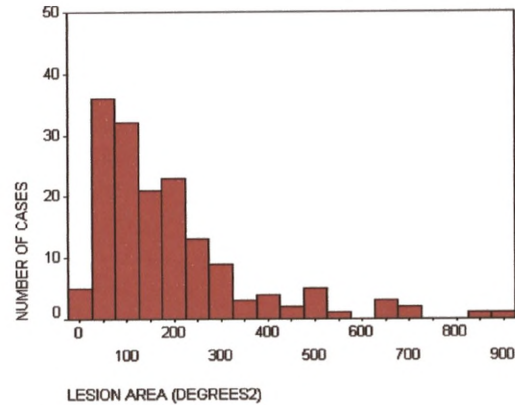


Figure 4.46: Distribution of the area of lesion in degrees² for worse VA eyes.

The diameters of the optic disc for every individual patient were measured from the fundus photographs (see section 3.5.1.3) and the radius of the ellipse obtained by dividing the diameter by 2. Radius in millimetres was converted to degrees (see formula 4.2). Knowing the area of the

optic disc in degrees² for each individual allows the relative size of the lesion (in disc diameters) to be converted to an absolute area (in degrees²).

The distribution of the absolute areas of the lesions can be seen in Figures 4.45 and 4.46. This time, the median value for the size of the lesion was found to be 121 degrees² (minimum and maximum values 2 to 693 respectively, IQR 126) for BE and 124 degrees² (minimum and maximum values 11 to 879 respectively, IQR 172) for WE.

4.5.3 Evaluation of subfoveal damage

Finally, the ophthalmologist made a subjective assessment of whether the damage was subfoveal or not on the BE. As discussed above, 34 (14%) BE couldn't be assessed due to photographs being missing or having too poor quality. Out of the 209 eyes that were assessed, as many as 204 (84%) were classified as subfoveal, and only 5 (2%) BE were considered as possible non-subfoveal cases, although the ophthalmologist couldn't be certain from the photographs. This finding is not very surprising as patients had a visual acuity of 0.50 logMAR or worse when recruited and thus were in the more advanced form of AMD, rather than the early ARM condition, and considering the significant visual loss that they have, by definition we would not expect these patients to have a non-affected fovea.

4.5.4 Secondary ocular conditions

From the 243 patients recruited, 71 reported at least one additional ocular condition. These conditions were not considered to be the main cause of visual loss (as the patient would not then have met the inclusion criteria for the study in section 2.5). Out of these 71 patients 19 had a

Secondary ocular diagnoses	Number of cases
Cataracts	30
Diabetes	26
Glaucoma	14
Amblyopia	7
Dry eyes	2
Entropion	2
Corneal graft	4
Blepharitis	1
Retinal detachment	2
Shingles	1
Uveitis	1
Strabismus	1
Corneal ulcer	2
Total	71

Table 4.13: Number of patients affected by secondary ocular conditions.

third ocular diagnoses and again 2 out of these had a fourth diagnoses, adding up to a total of 93 secondary diagnoses, which are listed in Table 4.13. 16 patients reported to be pseudophakic in one eye, and 26 in both eyes at recruitment time. At this point, 2 patients had had YAG laser in one eye for treatment of wet AMD and 3 had had it in both eyes.

4.5.5 Classification of cataract

Although only 27 (11%) patients reported having cataracts when asked for secondary ocular diagnoses, as mentioned above, when assessed on the slit-lamp, as many as 81% of eyes were classified as having some degree of cataract with the LOCSIII.

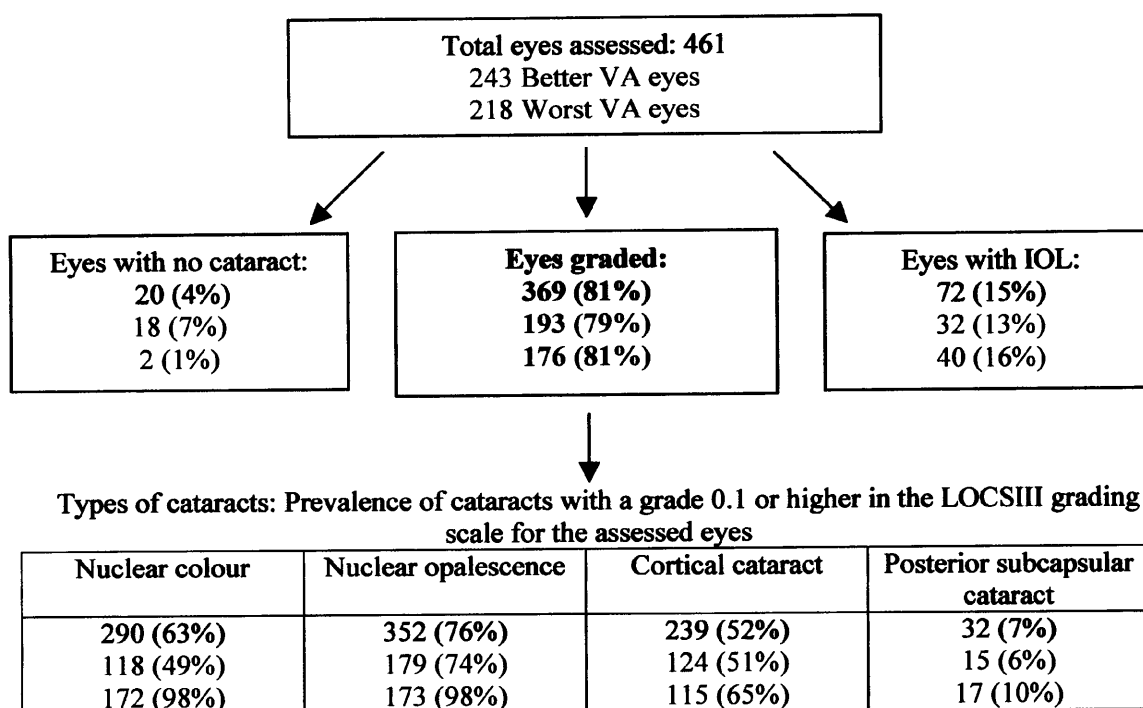


Figure 4.47: Prevalence of cataracts.

From the 243 patients recruited 243 BE and 218 WE were classified with LOCSIII (the remaining 25 WE had very poor VA and were thus not assessed), giving a total of 461 eyes to be assessed for cataracts (94% of the total 486 eyes). 72 (15%) out of these 461 eyes had had a cataract operation and had an intraocular lens (IOL). 20 (4%) had no cataracts and the remaining 369 (80%) eyes had some degree of cataract. The prevalence of the different kind of cataracts for the 369 eyes can be observed in Figure 4.47. The most prevalent type of cataract was the nuclear cataract (98% eyes had some degree of nuclear colour and 97% had some degree of nuclear opalescence) followed by the cortical cataract (67%) and finally, posterior subcapsular cataract was only present in 9% of the 461 eyes.

4.6 Central fixation data

In a young normal eye, the foveal reflex is a clear indication of the optimum fixation position. In an older eye, especially with scarring from AMD, the location of the fovea is difficult to determine, making quantification of fixation characteristics uncertain. In this study two different methods were used to assess central fixation.

Firstly, the subjective assessment of an ophthalmologist of whether the PRL was located in the foveal avascular zone was made on the better eyes and only 60 (24%) out of the 243 better eyes appeared to fulfil this condition. On 152 (63%) BE, the PRL fell outside the foveal avascular zone, and the remaining 31 (13%) eyes could not be assessed due to photographs being missing or having too poor quality.

A different method of measuring fixation from the same photographs was also used. Following the calculations from method described in section 3.5.1, the position of the fovea was determined, and the distance and angular position of the PRL with respect to the fovea was then obtained by drawing a line on the photograph that would connect the fovea and the PRL. When drawing this line with the Topcon program a measurement of its length in millimetres was given, and this could be converted to an angular separation distance of the PRL with respect to the fovea. The distribution of these distances for the BE of the 243 patients showed a median of 3.73 degrees (minimum and maximum values 0 to 22.87 respectively, IQR 4.2) (Figure 4.48). For WE, the median value was 4.90 degrees (minimum and maximum values 0 to 20.89 respectively, IQR 6.4) (Figure 4.49). The prism powers required to make a displacement of the image from fixation to the selected PRLs are 6.5 Δ and 8.6 Δ for BE and WE respectively.

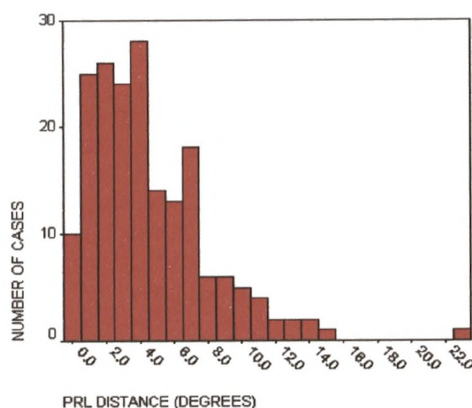


Figure 4.48: *Distribution of the preferred retinal locus distances for better VA eyes.*

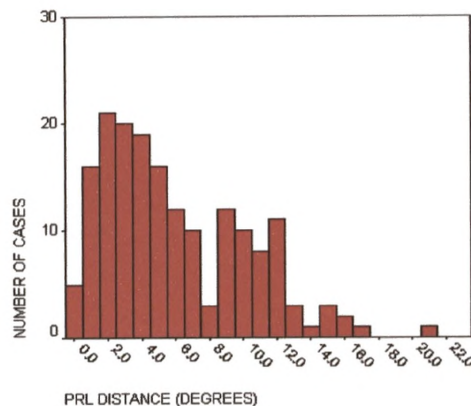


Figure 4.49: *Distribution of the preferred retinal locus distances for worse VA eyes.*

The angular location of the PRL position with respect to the fovea was also calculated by means of the method explained in section 3.5.1.3. The distribution of these angles can be seen in Figures 4.50 and 4.51 for BE and WE respectively. Both distributions show the highest peak between 170-270° (left and lower hemi-fields) and the lowest at 340-90° (right and upper hemi-fields), this difference being more obvious for the WE than for the BE. This means that the area between the left and lower hemi-fields was the preferred one for spontaneous EV.

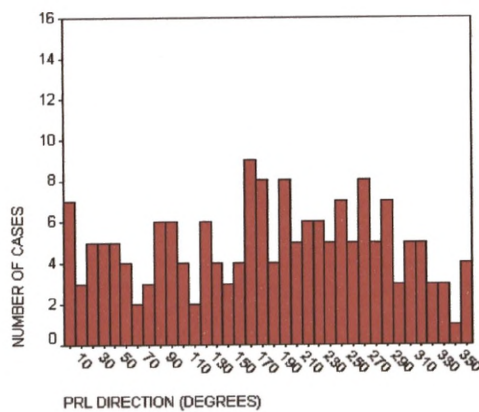


Figure 4.50: *Distribution of the preferred retinal locus directions for better VA eyes.*

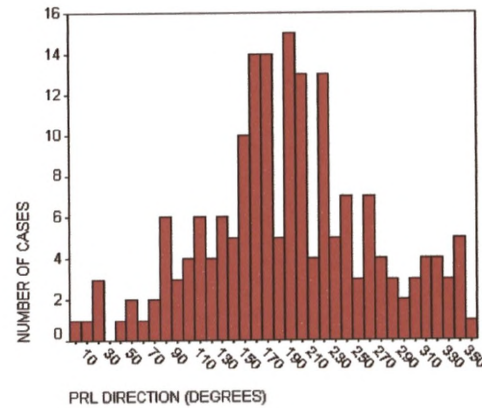


Figure 4.51: *Distribution of the preferred retinal locus directions for worse VA eyes.*

4.7 Fixation stability, consistency and rod pursuit

Dynamic fixation was assessed by asking the patient to look at a fixation rod in a fundus camera. Three different aspects of the dynamic fixation: fixation stability, fixation consistency and rod pursuit were subjectively assessed and quantified onto a good, medium or poor scale (see section 3.5.2).

The three above-mentioned aspects of the dynamic fixation were translated into a numerical scale of 0, 1 or 2. Adding up all these three values gave an overall dynamic fixation quality performance of a value between 0 and 6. A total of 232 BE were assessed for dynamic fixation and the distribution of values for fixation stability, fixation consistency, rod pursuit and dynamic fixation can be seen in Table 4.14. The majority of patients performed quite well on the test, obtaining a scale value of 2, which represented a good performance (as described on section 3.5.2). A lower prevalence of patients performing moderately or poorly, and thus scoring as 1 or 0 respectively was found. The missing 11 eyes were not possible to assess due to several reasons (4 patients could not have the test done because the fundus camera was out of order on the day, on 5 patients the media was too dense to allow for assessment and 2 patients couldn't reach the chin and/or forehead rest due to mobility problems).

Scale values	Fixation stability	Fixation consistency	Rod pursuit	Fixation quality
0	32	55	37	15
1	57	42	56	16
2	143	135	137	27
3				22
4				19
5				24
6				109

Table 4.14: The number of patients with fixation quality graded at each level.

Table 4.15 shows the correlation factors for the BE, where the different aspects of dynamic fixation: fixation stability (FS), fixation control (FC) and rod pursuit (RP), were quite highly correlated with each other: r ranging from 0.59 to 0.77. This high correlations indicated that the three aspects of dynamic fixation studied could not be treated as independent from each other in future analyses.

	RP	FC
FS	0.59	0.62
FC	0.77	

Table 4.15: Correlation matrix for FS, FC and RL RP.

4.8 Eye-movement response to prescribed prism

All 243 patients were assessed for a binocular eye-movement response when the prescribed prism was placed in front of the eyes (see section 3.5.3).

There were no replacement movements observed on any patient that would suggest that the prism was replacing the EV. Only 43 (18%) patients made an eye movement that would cancel the effect of the prism. That was, the eyes consistently move towards the apex of the prism on putting the prism over, and towards the base on removing it. The other 200 (82%) patients did not make an eye movement, or if they did it was a random movement (see Figure 4.53 for distribution of these eye responses).

The frequency of eye movements for prescribed horizontal prism bases (0° and 180°) was compared to that of eye movements for prescribed vertical prism bases (90° and 270°). Interestingly, the findings were that out of the 127 patients that were prescribed vertical prism bases, only 13 (10%) made a cancellation movement. On the other hand, from the fewer 50 patients that had been prescribed horizontal prism bases a total of 17 (34%) made a cancellation movement (see Figure 4.52).

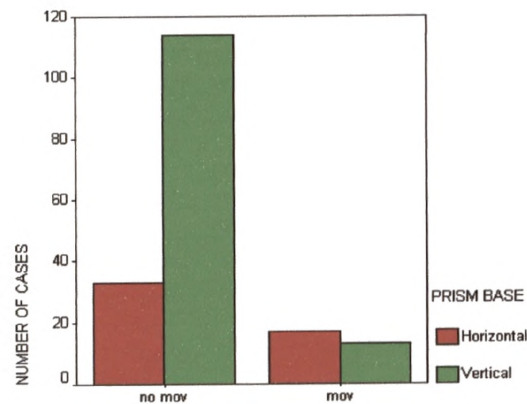


Figure 4.52: *Distribution of better VA eye-movement response to prism for vertical and horizontal prism bases.*

This chapter has described the study population with simple descriptive statistics. The investigation of associations between variables measured for the study has been explored in chapter 5, and chapter 6 investigates, by means of multiple regression analyses, the second and third aims of the study: to determine the clinical characteristics of the patients who would benefit from prism spectacles and to investigate the degree to which the optimal relocating prism can be predicted from clinical vision measures. Finally, the discussion of all these finding takes place in chapter 7.

CHAPTER 5

Associations between visual variables

Chapter 4 has provided a description of the AMD population by means of descriptive statistics. This chapter studies the data from a different statistical level and describes the population by means of investigating associations between variables measured for the study. Application of the theory of linear models (such as linear regression or multiple linear regression) rests on the assumption that the data being modelled comes from a Normal distribution and a linear relation, at least approximately, exists between the dependent variable (modelled) and the independent variables (regressors). Additionally, in order to allow statistical tests on the computed model parameters to be performed, the modelling errors (residuals) are assumed to be mutually independent and normally distributed with zero mean and constant variance. Many of the variables were not normally distributed even after logarithmic transformation. Therefore, the use of parametric statistics required justification and, for those cases where an association was found by regression analysis, statistical significance of such association had to be assessed. Two types of plots were particularly important in this study to analyse the residuals: P-P plots and Residuals vs Fitted plots, which have been put together in appendix 12 for reference. The P-P plots were used to check the assumption of residual normality. In this type of graph the ordered residuals were plotted against the corresponding cumulative “proportions” of the standard Normal distribution. If the residuals lay on a straight line it could be safely assumed that they were normally distributed. Residual vs Fitted plots, as its name implies, relate the fitted values obtained from the linear model and their corresponding residuals. When the residuals appeared to be randomly scattered, the assumption of constant variance could be accepted. The independence of the residuals could also be checked graphically, however, in this study, independence could be reasonably assumed as there were no relations among the different subjects.

5.1 Characteristics of the three study groups

It was important for the successful operation of the trial to assign patients randomly to the three arms. If this had been successfully accomplished, the characteristics of the three groups should be equivalent, and there should therefore be no bias of the results by this means.

Table 5.1 shows the frequencies and percentages of the categorical variables collected in the study for the three arms (custom, standard and placebo). Similarly, Table 5.2 shows the median values and interquartile ranges of the continuous variables for the three arms. Both tables show no significant difference of frequencies or median values between the three arms of the study. We can therefore conclude that the randomised strategy had been successful at distributing patients among the three arms and it is therefore not expected that analyses between arms would suffer from being biased.

Variables	Custom arm	Standard arm	Placebo arm
Num pxs	80 (33%)	81 (33%)	82 (34%)
Gender	28 (12%) Males 52 (21%) Females	27 (11%) Males 54 (22%) Females	31 (13%) Males 51 (21%) Females
Living Independence	45 (19%) Alone 4 (2%) Family 29 (12%) Partner 2 (1%) Sheltered	42 (17%) Alone 7 (3%) Family 25 (10%) Partner 7 (3%) Sheltered	43 (17%) Alone 5 (2%) Family 31 (13%) Partner 3 (1%) Sheltered
Reg. status	22 (9%) None 24 (10%) P. sighted 34 (14%) Blind	25 (10%) None 29 (13%) P. sighted 27 (11%) Blind	27 (11%) None 28 (12%) P. sighted 27 (12%) Blind
Type of AMD	24 (12%) Dry 43 (20%) Wet 0 (0%) Mixed	22 (11%) Dry 47 (23%) Wet 0 (0%) Mixed	19 (9%) Dry 52 (25%) Wet 1 (0%) Mixed
Num sub. damage	64 (31%)	68 (33%)	72 (36%)
Num central fix.	21 (35%)	24 (40%)	15 (25%)
Type lenses	34 (14%) Bif 46 (19%) SV	39 (16%) Bif 42 (17%) SV	44 (18%) Bif 38 (16%) SV

Table 5.1: Frequencies and percentages of the categorical variables for the three arms.

5.2 Magnifying power and visual acuity

As AMD progresses, visual acuity decreases and thus one would expect the patient to need higher magnification in order to obtain the same acuity (Doris et al., 2001). A direct relationship between visual acuity and the prescribed magnification would therefore be predicted.

The most popular low vision devices prescribed were: hand magnifiers, illuminated hand magnifiers, stand magnifiers, illuminated stand magnifiers, pocket magnifiers and distance vision telescopes. The degree to which VA can predict the prescribed magnification power was investigated by means of simple regressions. The dependent variable was thus the magnification

power of the low vision devices and the independent variable was near or distance visual acuity, depending on the distance that the LVA to be investigated was to be used for. Result values can be seen in Table 5.3.

Variables	Custom arm	Standard arm	Placebo arm
Age mean (yrs)	81 (IQR = 9)	80 (IQR = 8)	81 (IQR = 8)
Duration (yrs)	3.0 (IQR = 3.9)	3.5 (IQR = 5.5)	3.0 (IQR = 5.0)
MMSE (score)	21 (IQR = 1)	21 (IQR = 2)	22 (IQR = 1)
Dist VA (mean)	0.79 (IQR = 0.44)	1.08 (IQR = 0.53)	1.06 (IQR = 0.55)
Prism dist VA	0.73 (IQR = 0.40)	0.91 (IQR = 0.55)	1.04 (IQR = 0.59)
NearVA (mean)	2.9 (IQR = 2.4)	3.2 (IQR = 3.4)	3.2 (IQR = 2.2)
Prism near VA	2.0 (IQR = 2.8)	3.2 (IQR = 2.4)	2.5 (IQR = 2.4)
Scot area	56 (IQR = 178)	97 (IQR = 188)	99 (IQR = 193)
Contrast sensit	1.00 (IQR = 0.35)	1.00 (IQR = 0.35)	1.05 (IQR = 0.35)
Single letter va	0.90 (IQR = 0.40)	0.90 (IQR = 0.38)	0.90 (IQR = 0.40)
Crowded letter va	1.03 (IQR = 0.47)	1.12 (IQR = 0.45)	1.03 (IQR = 0.54)
Repeated letter va	0.90 (IQR = 0.36)	0.90 (IQR = 0.47)	0.90 (IQR = 0.42)
Rx best sphere	0.94 (IQR = 2.19)	1.13 (IQR = 2.53)	1.87 (IQR = 2.38)
Pres. prism power	6.0 (IQR = 3.5)	8.0 (IQR = 6.0)	8.0 (IQR = 6.0)
Num of LVA	3.0 (IQR = 1.0)	2.0 (IQR = 1.0)	3.0 (IQR = 1.0)
Cortical cat.	1.0 (IQR = 1.9)	1.1 (IQR = 1.9)	0.5 (IQR = 1.4)
Nuclear colour	4.0 (IQR = 2.0)	3.8 (IQR = 1.9)	3.5 (IQR = 1.5)
Nuclear opals.	4.0 (IQR = 1.8)	3.5 (IQR = 1.1)	3.5 (IQR = 1.0)
Post. subcapsular	0.1 (IQR = 0.0)	0.1 (IQR = 0.0)	0.1 (IQR = 0.0)
Lesion area (deg ²)	92 (IQR = 89)	107 (IQR = 111)	130 (IQR = 159)
PRL distance	3.8 (IQR = 3.8)	3.7 (IQR = 4.7)	4.6 (IQR = 4.5)
NRL distance	2.0 (IQR = 2.8)	2.0 (IQR = 3.3)	2.0 (IQR = 2.5)
Fixation stability	2.0 (IQR = 1.0)	2.0 (IQR = 1.0)	2.0 (IQR = 1.0)
Fixation consist	2.0 (IQR = 1.0)	2.0 (IQR = 1.0)	2.0 (IQR = 2.0)
Rod pursuit	2.0 (IQR = 1.0)	2.0 (IQR = 1.0)	2.0 (IQR = 1.0)
Fixation quality	6.0 (IQR = 2.8)	5.0 (IQR = 3.0)	5.0 (IQR = 4.0)

Table 5.2 Median values and interquartile ranges of the continuous variables for the three arms.

Quite a strong and statistically significant association was observed between visual acuity and magnification for all of the near vision devices (β ranged 2.03 to 6.08, $p < 0.001$ to 0.0001), meaning that for every ten lines on the logMAR scale (1.0 logMAR), the magnification power changed by between 2.03 and 6.08 times. However, the magnification power of the distance telescopes didn't show any association with distance visual acuity ($\beta = -0.16$) and the distribution of Residuals vs Fitted plots on appendix 12 shows no valid association.

Most of the patients had more than one low vision device (see section 4.4.5) with a mean of 3.0 devices per patient. The main reason for patients having more than one magnifier is to be able to perform different activities that require different extent of visual field/levels of visual acuities, or type of low vision devices (since different devices are more or less adapted to particular tasks or handling situations). For example, it might be expected that patients would be prescribed a weaker magnifier for use with large print and a stronger one required for normal size print (N8

usually). However, it is extremely unlikely that patients would have been prescribed a magnification stronger than required due to the disadvantages of higher magnification (primarily a reduction in the visual and depth of field). If prescribing of devices happened in this way, analysis of the highest magnification power prescribed for the patient should show a stronger association with visual acuity than if devices were investigated separately, since the confounding factor of 'task for which a device is best suited' was removed from consideration.

Magnifier type (magnification)	β	p	95% Confidence intervals	r^2	Num of cases
Hand held	2.03	<0.001	0.81 to 3.25	0.14	60
Illuminated hand held	5.56	<0.0001	7.11 to 4.01	0.31	112
Stand	6.08	=0.014	1.67 to 10.49	0.25	20
Illuminated stand	5.63	<0.0001	4.49 to 6.77	0.35	179
Pocket hand held	5.59	<0.0001	7.66 to 4.24	0.56	38
Distance vision telescope	-0.16	=0.90	-2.23 to 2.55	0.00	35
Highest magnification	6.41	<0.0001	5.47 to 7.35	0.44	229

Table 5.3: Simple regression results for near/distance VA as the predictor of low vision aids' devices magnification power.

The highest magnification power across all near vision devices was therefore created as a new dependent variable. This variable had the additional advantage that it could be analysed for all patients, rather than just the subsets of patients who had particular devices. The regression result for this new variable was also shown in Table 5.3. As predicted, the strength of the association was greater and had a better distribution of Residuals vs Fitted plots than for any of the devices separately. For every ten-logMAR lines, magnification power was estimated to increase by 6.41 times ($p < 0.0001$). However, this coefficient was not as high as would have been expected: Ten lines of VA improvement should theoretically require $10 \times 1.25 = 12.5$ times magnification (Bailey & Lovie, 1976). One possible explanation for this lower value found could lie on the disadvantages involving higher magnification (such as smaller field of view and depth of focus) for which patients might prefer to sacrifice the acuity reserve required for pleasure reading for a poorer visual acuity that would fulfil spot reading requirements.

5.3 Relationships between single, crowded and repeated letter

As described on appendix 6, single letter, crowded letter and repeated letter visual acuity measurements were performed while patients sat at 3 different distances from the screen where they were displayed (1.14, 0.57 or 0.285 metres). The choice of the distance depended on the visual acuity of the eye to be tested and patients were seated as far away from the monitor as possible. Closer distances increased the acuity steps of the letters to be tested and thus made the

measurements more discreet and less accurate. The step change of the letters displayed was doubled for 0.57 metres as compared to 1.14 metres and similarly, doubled for 0.285 metres as compared to 0.57 metres (thus, four times compared to 1.14 metres). This means that the measurements made for the poorest VAs would be expected to not be as accurate as measurements for better VA patients. Also, as discussed on appendix 7, it could be expected that patients performed better on the horizontal than vertical gap positions.

5.3.1 Crowded letter and conventional acuities

The CL VA should predict the original acuity when tested with the conventional prescription, when no rehabilitation strategy has been used and patients are not expected to be benefiting from the optimal acuity. It should therefore be expected a strong relationship between them. The CL VA reasonably matched the conventional VA (mean difference 0.10, sd 0.22) and 33% of results differed by less than 0.10. 72% had better conventional VA than predicted (Figures 5.1, where points are around the 1:1 ratio line, and 5.2).

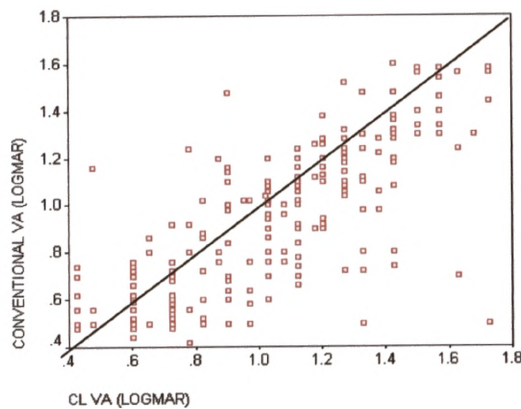


Figure 5.1: Scatter plot of crowded against conventional distance VA for better VA eyes

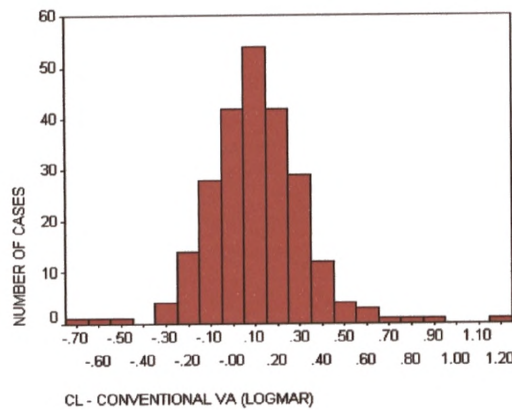


Figure 5.2: Distribution of the difference between crowded and conventional distance VA for better VA eyes

When introducing the CL VA as the independent variable and the conventional VA as the dependent variable into a single linear regression a high and statistically significant dependency was found ($\beta = 0.73$, $p < 0.0001$, $r^2 = 0.56$, 95% CI 0.67 to 0.83).

5.3.2 Crowded and single letter acuities

It has been previously discussed (section 3.2.3) that the ability to read correctly a target letter or judge the orientation of a target letter (such as Tumbling E or Landolt C) is reduced when contours (such as straight lines or letters) are placed close to the target shape. A reduction of crowded letter visual acuity when compared to single letter visual acuity would be expected.

Single letter (SL) VA was indeed found to be better than crowded letter (CL) VA in almost all subjects (mean difference 0.11logMAR, sd 0.13) when the single-crowded (SL-CL) letter difference was calculated (see Figure 5.4). The mean SL/CL ratio was 1.13 ± 0.17 (range 0.71 to 1.87). See scatterplot on Figure 5.3, showing most points above the 1:1 ratio line. This ratio was smaller than that found by Pardham (1997) on her 4 AMD patients, this ranging between 1.68 and 2.08.

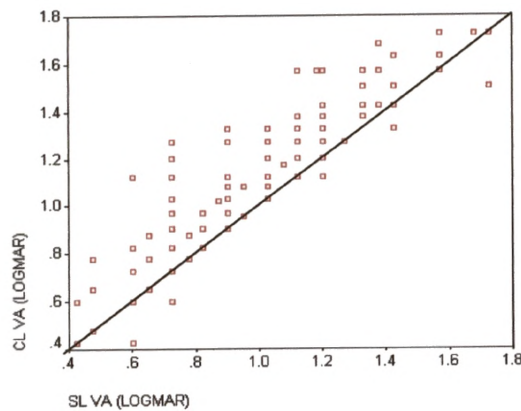


Figure 5.3: Scatter plot of single against crowded distance VA for better VA eyes

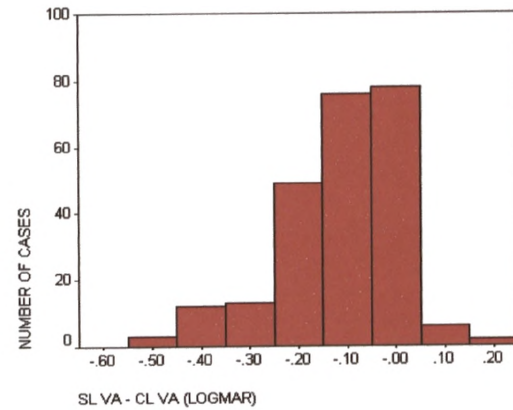


Figure 5.4: Distribution of the difference between single and crowded distance VA for better VA eyes

Contour interaction is thought to be greater for peripheral than for foveal vision (Leat et al., 1999), so this SL-CL acuity difference was expected to show an association to the NNPF and PRL distances. When the NNPF distance was analyzed as the independent variable the NNPF was found to be a very poor predictor of the SL-CL acuity difference ($\beta = -0.0079$, $p = 0.18$, $r^2 = 0.28$). The PRL distance from fovea is a more direct measure of the area of retina being used and was found to be a good predictor of the SL-CL acuity difference, although the coefficient is very small ($\beta = -0.01$, $p < 0.0001$, $r^2 = 0.09$).

Scotoma area and lesion size would for similar reasons be expected to be associated to SL-CL acuity difference. The lesion area was associated with the SL-CL acuity ($\beta = -0.01$) so that for every 100 degrees² change in lesion area there was a change of -0.01 on the SL-CL acuity difference. However, this change wasn't significant ($p = 0.35$, $r^2 = 0.03$). Similarly, for 100 degrees² change in scotoma area there is a change of $\beta = -0.005$ on the SL-CL acuity difference that again isn't significant ($p = 0.11$, $r^2 = 0.01$).

5.3.3 Repeated letter and prism acuities

The RL VA should also most accurately predict the final acuity, (Harris et al., 1985) which could be achieved by the patient using prism relocation (or any other rehabilitation strategy).

Therefore, there should be a strong relationship between prism VA and RL VA. The RL VA was well matched to the prism VA (mean difference 0.03, sd 0.22, range -0.78 to 0.91) and 37% of results differed by less than 0.1, but 58% of subjects still had better prism VA than predicted (Figure 5.5). Figure 5.6 shows the distribution of these differences (points are around the 1:1 ratio line).

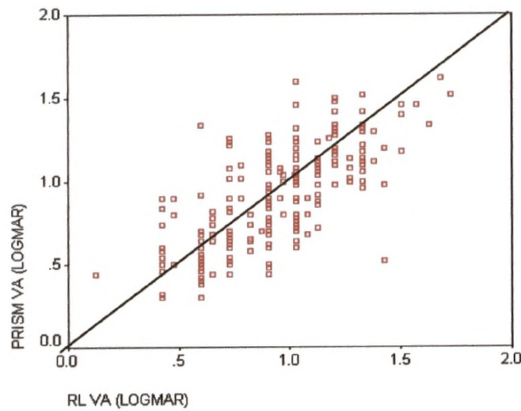


Figure 5.5: Scatter plot of repeated against prism distance VA for better VA eyes

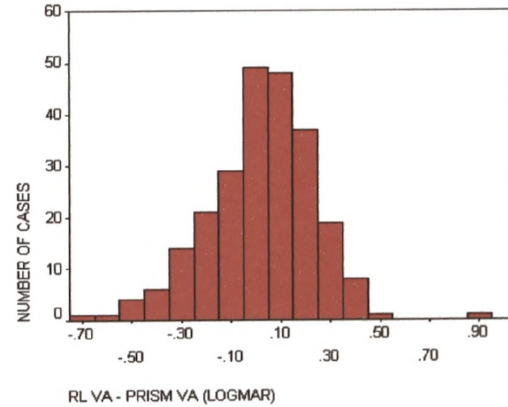


Figure 5.6: Distribution of the difference between repeated and prism distance VA for better VA eyes

When introducing the RL VA as the independent variable and the prism VA as the dependent variable into a single linear regression a high and statistically significant dependency was found ($\beta = 0.777$, $p < 0.0001$, $r^2 = 0.541$, 95% CI 0.68 to 0.88) and thus, for every line of logMAR RL VA the prism VA varies 0.777 times.

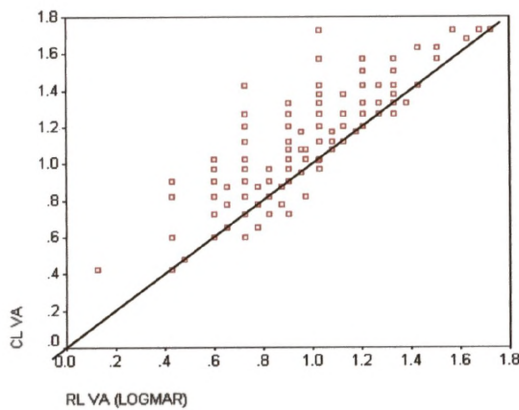


Figure 5.7: Scatter plot of repeated against crowded distance VA for better VA eyes.

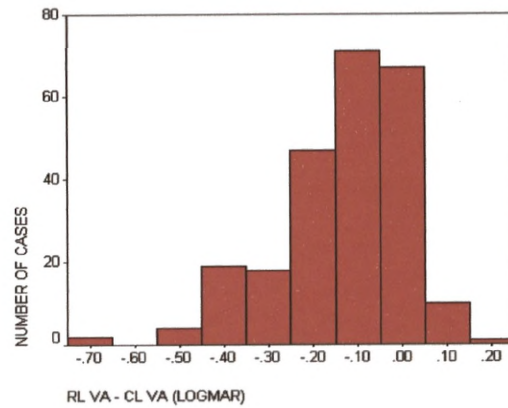


Figure 5.8: Distribution of the difference between repeated and crowded distance VA for better VA eyes.

5.3.4 Crowded and repeated letter acuities

Inaccurate or unstable gaze could result in a subject reporting a letter other than the letter he/she intended to fixate. This has previously been described as a gaze selection defect (Regan, 1992; Pardhan, 1997). RL VA uses a two-dimensional array of identical targets across the full central field to simultaneously present targets to both foveal and parafoveal retina, measuring the optimum VA without accurate fixation. Therefore, the difference between RL and CL VA would represent a gaze selection defect.

RL VA was indeed found to be better than CL VA (mean difference 0.13logMAR, sd 0.15) when the repeated-crowded (RL-CL) acuity difference was calculated (see Figure 5.8 for the distribution of these differences scatterplot on Figure 5.7, showing most points above the 1:1 ratio line). The mean RL/CL ratio was 1.17 ± 0.24 (range 0.81 to 3.41), again smaller than Pardhan's (1997) finding of 1.71 and that of Harris et al's (1985) of 2.00. It was also interesting to compare the RL-CL difference on patients with foveal fixation (PRL within 1 degree from fovea) and those with paracentral fixation (PRL further than 1 degree from fovea). In theory, patients with foveal fixation should have a bigger RL-CL difference because they are currently not fixating optimally, whilst those with paracentral fixation are presumably using an effective area of retina already and shouldn't get such a difference. However, there was no statistical difference between the mean RL-CL difference for the eyes fixating on the fovea (-0.14 ± 0.14) and for the eyes fixating on the parafovea (-0.14 ± 0.15).

The RL-CL acuity difference would be expected to be associated to the fixation quality. This is because a patient who might have found a successful area of retina (PRL) and is able to sustain it would be expected to already be benefiting from the optimum (in this case the RL) acuity. In this case, the RL-CL acuity difference should be small. On the other hand, someone who hasn't learnt to use an optimal PRL and isn't therefore benefiting from an optimum VA should have a visual acuity improvement when tested on RL as compared to CL and the RL-CL difference should be noticeable.

For the study eyes, the different measures of fixation quality: Fixation stability (FS), fixation consistency (FC) and rod pursuit (RP) were highly correlated with each other: r values ranged from 0.59 to 0.77 (see Table 4.15). These have thus been added together to give an overall quality of fixation (QF), which was then be used to predict the RL-CL difference.

However, when introducing the fixation quality as the independent variable and the RL-CL acuity difference as the dependent variable in a simple regression the results showed no association between them ($\beta = 0.0044$, $p = 0.355$, $r^2 = -0.001$). Similarly, the RL-CL acuity difference was expected to predict the VA improvement with the prism as compared to the

conventional prescription. Again, results showed no association, between the two variables ($\beta = 0.031$, $p = 0.536$, $r^2 = 0.02$).

5.4 AMD lesion size and scotoma area

The size of the lesion in the retina was quantified from fundus photographs to yield an area in degrees². The result of this lesion at the macula is a central scotoma, which was measured using the Bjerrum screen and its size recorded in degrees². It would be expected that these two measures would be strongly linked.

The distribution of the difference (area of scotoma – area of lesion) can be seen on Figure 5.9. The area of the scotomas were generally much larger than the size of the lesions and the median value of the difference between the area of the scotoma and the lesion size was 71 degrees² (range –29 to 1509, sd 252).

It has been previously reported that the size of the lesion influences visual function in eyes with AMD (Hogg et al., 2003 and Doris et al., 2001) and can have a role on the effectiveness of some treatments such as Verteporfin therapy (TAP Study Group, 2002 and 2003). A poor correlation between lesion size and VA of 0.09 on BE was found by Doris et al. (2001) and of 0.34 between lesion size and CS. Hogg et al. (2003) found that atrophy measured on colour photography was a good predictor of visual function, being near visual acuity the most marked one.

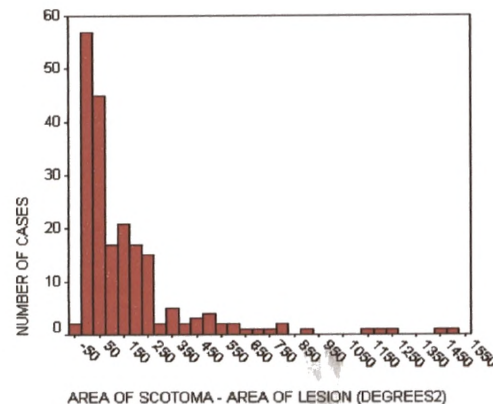


Figure 5.9: *Distribution of differences between areas of scotomas and areas of lesions.*

The association between the above-mentioned visual functions were thus investigated by means of Pearson's correlation coefficients. Findings showed an association between lesion size and distance VA, near VA and CS of $r = 0.20$, 0.21 and -0.16 respectively. We could therefore conclude that lesion size only plays a limited role on the visual functions of these AMD patients. However, when this association was investigated with a regression equation, and the area of scotoma or size of lesion were entered into the equation as an independent variable and

distance VA as the dependent variable (the size of the central damage would be expected to be a direct cause of the VA loss on AMD patients), the two independent variables showed some association, and the area of scotoma was far more significant ($p < 0.0001$) than size of lesion ($p = 0.011$) (see Table 5.4). For every 100 degrees² of scotoma size, VA changed by 0.4 logMAR, which is four lines on the ETDRS chart. Near vision was also tested as a dependent variable and the regression parameters, although not shown were found to be no different to the distance vision ones.

Independent variable	β	p	95% Confidence intervals	r^2
Scotoma area	0.0004	<0.0001	0.0004 to 0.0004	0.10
Size of lesion	0.0005	$=0.011$	0.0005 to 0.0005	0.04

Table 5.4: Simple regression results for scotoma area and size of lesion as the predictors of distance VA.

5.5 NNPF and PRL

The position of the NNPF was obtained from the Bjerrum screen plots that were plotted while controlling the patient's fixation (see section 3.2.4.2) while the patient was instructed to look at the centre of the fixation cross. If the NNPF was the closest healthy area of retina to the scotomatous area we would expect the patient to choose this area of retina when using eccentric viewing.

Similarly, the PRL position was obtained while the patient was instructed to look at the tip of a fundus camera fixation rod (see sec 4.5.1). However, this time the optometrist didn't have any control over the patient's fixation and although the patients were asked to look at the tip of the stick they could very easily use eccentric vision and thus use a subjectively chosen PRL. The position of the PRL would be expected to be at the closest area of healthy retina from fovea (resolution decreases as we move away from fovea) and thus should in theory be the same position as the NNPF. Also, it should be born in mind that for the PRL the accuracy of the location of the fovea could be better for some cases than for others (see appendix 17).

In this section, the relationship between the NNPF and PRL locations was investigated. That is, the distance and angular positions of NNPF and PRL from fovea will be compared (see appendix 18 for calculus of the angular differences).

5.5.1 NNPF and PRL angular differences

The distribution of the differences of angles between the PRL and NNPF directions from fovea can be seen in Figure 5.10 for a total of 149 better VA eyes that could be analysed. If there were

no association between the two angles, we would expect the angular differences to be distributed randomly. The observed distribution (grouped into six categories) of angular differences can be compared with the expected distribution, which (see Table 5.5) shows how more patients than expected had smaller angular differences. As many as 74% of patients had an angular difference of 60° or less between these two angles. It can therefore be concluded that the PRL and the NRL angles were not randomly distributed but reasonably close to each other.

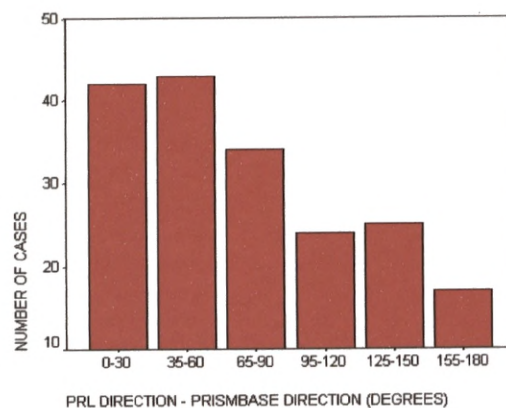


Figure 5.10: *Distribution of angular differences between preferred retinal locus and prism base directions for better VA eyes.*

Angular difference	Observed frequency	Expected frequency
0-30°	37 (25%)	24.8
35-60°	37 (25%)	24.8
65-90°	31 (21%)	24.8
95-120°	22 (15%)	24.8
125-150°	14 (9%)	24.8
155-180°	8 (5%)	24.8

Table 5.5: Observed and expected frequencies for angular differences between preferred retinal locus and nearest non-scotomatous point to fovea directions.

5.5.2 NNPF and PRL distances from fovea

If the patient had subjectively chosen a PRL location, the PRL distance from fovea should in theory predict the NNPF distance from fovea. It would thus follow to investigate the association between these two measurements.

When this association was investigated by means of single linear regression, and the PRL distance was introduced as the independent variable and the NNPF distance as the dependent variable, the result showed no association ($\beta = 0.076$, $p = 0.21$, $r^2 = 0.01$, 95% CI -0.04 to 0.20) between these two variables. This means that the NNPF distance was not effective in predicting the distance of the chosen PRL for patients when using eccentric fixation.

5.6 Cataracts and contrast sensitivity

It has been widely suggested (Koch, 1989; Adamsons et al., 1992; Rubin & Adamsons, 1996; Adamsons I et al., 1996) that VA provides an inadequate assessment of vision in cataract patients and other test of vision, such as contrast sensitivity (CS) should be measured in addition to VA. However, other studies (Chylack et al., 1993; Maraini et al., 1994; Chylack et al., 1995) have suggested that CS provides little useful information beyond VA about vision in cataracts. Furthermore, there is some controversy about which spatial frequency provides more information (Elliott & Situ, 1998). Elliott & Situ (1998) concluded that measuring low spatial frequency CS or large letter CS, such as measured with the Pelli-Robson chart, is of little value in very early cataract. Although the study didn't include any co-morbid eye disease, a previous study (Elliott and Whittaker, 1992) included 4 AMD patients and results on those suggested that VA tends to be a better screener for cataract and AMD than low spatial frequency CS and thus are consistent with Elliott & Situ's findings (1998).

Cataracts can have a serious impact on patient's VA and thus on quality of life (Monestam and Wachmeister, 2004) but the benefit of cataract removal on patients with advanced central visual loss has been debated. Several studies proved that cataract surgery may be a risk factor for progression of degenerative changes and could thus increase the risk of central visual loss (Goldberg et al., 1988; Klein et al., 1994). However, later studies (Armbrecht et al., 2000; El Mallah et al., 2001) suggest a visual function and quality of life improvement on advanced AMD patients after undergoing cataract extraction. Since there is evidence (El Mallah et al., 2001) that cataract removal could be of benefit for AMD patients, it would follow to investigate if CS ports any extra information of the visual problem on AMD patients.

Cortical and nuclear cataracts of LOCS grade 2.0 or less have been shown to have negligible effects on Pelli-Robson CS (Lasa et al., 1999) and therefore were not be analysed. Posterior subcapsular cataracts, on the other hand, have proved to have a dramatic effect on vision even on the early days (Elliott et al., 1989, Lasa et al., 1992 and Adamson et al., 1991) and thus shouldn't be included on the same analysis. The amount of eyes with pure PSC was quite small ($n = 24$) and so was the amount of pure cortical cataracts ($n = 13$). However, the majority of lenses contained pure nuclear opacity or predominantly nuclear cataract with cortical grade ≤ 2.0 ($n = 274$). This finding is quite similar to Elliott & Situ's (1998), who decided to only analyse the association between only pure nuclear opacities (pure and with cortical grade ≤ 2.0) and CS. The same strategy was thus followed to analyse the data in this study.

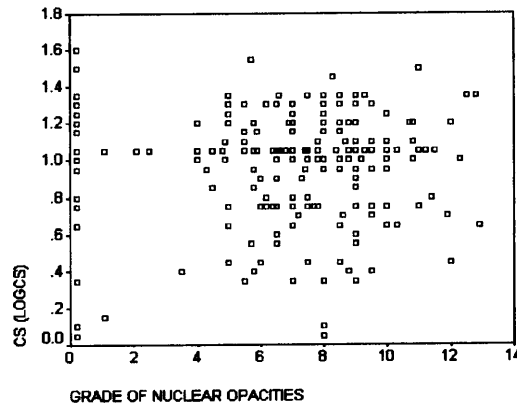


Figure 5.12: Scatter plot of nuclear opacities grade against contrast sensitivity for better VA eyes.

When the association between nuclear opacities (pure and with cortical grade ≤ 2.0) and CS was investigated on better VA eyes, the nuclear opacities didn't seem to be a good predictor of CS ($\beta = -0.002$, $p = 0.77$, $r^2 = -0.007$) (see Figure 5.12 for nuclear opacities plotted against CS). This results disagrees with Elliot and Situ's (1998), who found that low spatial frequency contrast sensitivity varied by a factor of $\beta = 0.12$ times with the nuclear opacity ($r^2 = 0.37$) on their free from other co-morbid eye disease patients. This discrepancy could be due to AMD having a marked effect on CS and masking the association, suggesting that AMD is a bigger influence on CS than cataract. If this is the case, it could be that patients with AMD might not benefit much from having their cataracts removed. It also suggests that the degree of cataract that patients had on this study shouldn't have biased the results of the prism spectacles wear.

5.7 Location of the fovea

Static fixation was measured by means of two different methods. The first method involved an objective calculation of the position of the fovea with respect to the optic disc (see section 3.5.1). The static fixation position, or subjectively chosen PRL, would then be calculated with respect to the calculated location of the fovea. However, due to the several approximations that had to be made to obtain this measurement (already discussed on section 3.5.1) this data is bound to have some errors.

The second method was a subjective assessment of the location of the avascular zone of the macula by an ophthalmologist (see section 3.4.1.4). He then decided if the chosen PRL fell on this avascular area or not. Since this method did not depend on any calculations it was expected to be more accurate than the first one.

Out of the 243 better eyes, only 138 eyes had been able to quantify with both methods. The other 105 eyes had missing data for one or both methods, due to poor quality of the photographs. Out of the 50 better VA eyes that were found to fixate on the avascular zone, only 18 (36%) had the PRL at a distance from the calculated foveal location of 1° or less and 32 (64%) had it further away (see Table 5.6). The consistency of results for the fixation outside the avascular zone and further than 1° from the fovea were quite strong as only one eye (1%) out of the 88 fixating outside the avascular zone was calculated to be within 1° from fovea.

	PRL within 1° from fovea	PRL beyond 1° from fovea
Fixation on avascular zone	18	32
Fixation outside avascular zone	1	87

Table 5.6: Prevalence of patients with central and eccentric fixation for the two methods used to assess central fixation in the study.

If both methods were accurate we would expect most eyes to be classified as foveal fixation and PRL within 1° from fovea or as non-foveal fixation and PRL beyond 1° from fovea. However, there seemed to be some discrepancy for those eyes that had the PRL beyond 1° from fovea but have been classified as fixating on the avascular zone. It was interesting to check how much farther than 1° were the 32 eyes that fall under this category. Figure 5.13 shows the distributions of the distances between PRL and calculated fovea for the 50 eyes classified as fixating on the avascular zone with a median value 1.55 ± 1.90 degrees. We can therefore conclude that the objective method used to calculate the PRL distance appears in agreement with the subjective method for 36% of the patients and that, with the exception of two cases (clearly seen on Figure 5.13), the results agree to a maximum eccentricity error of 4.70 degrees.

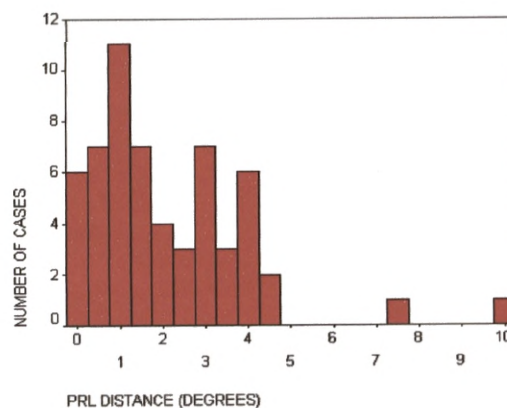


Figure 5.13: Distribution of PRL distances for better VA eyes classified as fixating on the avascular zone.

The large amount of patients fixating eccentrically by both methods (87 out of 138, that's 63%) suggests that patients have already learnt to use eccentric viewing and therefore limiting the chances of prism relocation success.

5.8 PRL distance as a predictor of VA and Fixation quality

Section 3.2.3 discussed how the resolution in the retina decreases towards periphery and thus VA would decrease as we move away from fovea. It is also well known that the position of the PRL is chosen to be right on the edge of the scotoma (Fletcher et al., 1994). Patients with a large scotoma would thus be expected to have a larger PRL distance for having to displace fixation to a more eccentric retinal location. We could therefore anticipate that patients with a large PRL distance would suffer from worse VA than patients with small PRLs. As expected, PRL distance showed a significant ($p < 0.001$) association with VA so that VA varied by 0.03 logMAR for every degree of PRL distance ($r^2 = 0.09$, 95% CI 0.02 to 0.04).

Similarly, as we move away from fovea it has been proved that the difficulty to maintain fixation would increase (Whittaker et al., 1988; Zeevi et al., 1979) and thus, as the PRL distance increases the fixation quality decreases. Single regression showed a significant association ($p < 0.001$) between the two variables on this study and fixation quality varied by 0.2 units for every degree of PRL distance ($r^2 = 0.08$). However, data deviated significantly from the normal distribution and thus regression was not appropriate. Pearson's correlation coefficient for these two variables was $r = 0.30$, therefore the association was only weak.

According to Nilsson (1990) the PRL distance can predict the degree of magnification required by the patient for near vision reading. However, the findings from this study show that the patient actually needs a mean of 2.4 times magnification more than that predicted by the PRL distance although linear regression showed a very significant association between these two variables ($p < 0.001$) so that for every degree of PRL distance, magnification changes by 0.4 times ($r^2 = 0.19$, 95% CI 0.28 to 0.52).

CHAPTER 6

Predicting the prescribed prism and the visual acuity improvement

The “custom” prism in this study was prescribed on the basis of the patients’ subjective assessment of the improvement in their discrimination of a photograph at a close viewing distance. It was often difficult for the patient to make a precise judgement and it required a tester experienced in techniques of subjective refraction to guide the patient. To save practitioner’s time and effort, it would be useful to be able to determine whether any of the clinical vision variables could be used to predict the power and base direction of the optimal prescribed prism.

The three arms of the study have been compared by means of ANCOVA analysis, and these data have been reported in detail elsewhere (Smith, 2004). It was found that there was no significant effect of randomisation group on distance VA, our primary outcome measure, when adjusted for baseline ($F(2, 220)=0.46$; $p=0.63$). No other significant effects of randomisation group were found on other outcome measures (maximum reading speed, reading VA, and visual functioning questionnaires: NEI-VFQ-25 and MLVAI Part-2). A total of 23 patients (10%) were however found to have a clinically significant visual acuity improvement, i.e. ≥ 0.16 logMAR⁸ (when wearing the study spectacles on the last visit as compared to the visual acuity with conventional spectacles on the second visit). The data were also analysed on an individual patient basis to determine whether any of the variables (for example, type of AMD or eye

⁸ The test-retest reliability of the ETDRS chart when determined for a young normally-sighted population was found to be ± 0.16 logMAR by Hazel & Elliott (2002) and ± 0.14 logMAR by Arditi & Cagenello (1993), i.e. one and a half lines on the chart. However, equivalent measures have not been obtained for an elderly group.

movement characteristics) could be used to predict the degree of improvement in acuity expected after three months of prism wear.

This chapter concentrates on investigating whether potential predictor variables were associated with prism power and degree of VA improvement. It therefore deals with the second and third aims of the study. In each case, the technique used to investigate the association involves single and multiple regression analyses. First, the potential predictor variables were determined on the basis of clinical judgement and face validity. These were then investigated by means of single regressions for associations between themselves, and also for the degree to which each of the independent variables predicted the dependent variable. All these findings were then used as a diagnostic of multiple regression, where the combination of all these variables was investigated for a possibly higher association than that obtained by single variable methods.

There are various multifactorial techniques that could have been used to analyse the associations between the predicting variables and the dependent variable (prism power or VA improvement). Factor analysis takes a large set of variables and looks for a way that the data may be 'reduced' or summarised using a smaller set of factors or components. It does this by looking for 'clumps' or groups among the inter-correlations of a set of variables (Pallant, 2001). However, the procedure for this technique is quite complicated as it involves a number of steps: assessment of the data, factor extraction and factor rotation. A more appealing technique for reducing variables is the stepwise regression. This approach can be used with both multiple linear and logistic regression and is a one-step procedure. Also, it is a very useful technique for selecting a small set of predictor variables for purposes of standardisation and prediction. However, this model is difficult to interpret because variables are chosen without considering how variables are interrelated and what aspects of the whole physiological system they represent. Stepwise regression has also been criticised because it can yield a biologically implausible model (Greenland, 1989) and can select irrelevant, or noise, variables (Flack & Chang, 1987; Griffiths & Pope, 1987). The ideal approach would be to assess the importance of each variable included on the model, so that the choice of variables to include is made with knowledge of exactly what those variables measure and their association with each other. The interactive model fits this requirement because the decision to include a variable may be made on the basis of the change in coefficient for another variable in the model rather than on the basis of statistical significance.

The interactive model was then used as the technique to predict prism power and VA improvement. The process of this model building is summarized on the following 8 steps (Hosmer & Lemeshow, 2001) that cover the regression diagnostics and the multiple regression modelling:

Regression diagnostics: Single regressions of all dependent variables with the independent variable were performed. The information obtained from these simple regressions was used to create the best fitting multiple regression model.

1. A correlation matrix showing the association between all the variables was produced. When the two variables to be checked for association were continuous, the correlation factor showed the degree of association. However, if one of the variables was categorical, a t-test or an analysis of variance (depending on whether the categorical variable was dichotomous or polychotomous) was performed. Finally, if both variables were categorical, the association was then investigated by means of contingency tables. Highly associated dependent variables provided the same information to the multiple regression and thus care was taken not to introduce both into the same regression.
2. Dependent variables were checked for normality. If it helped, data was transformed by taking the log of all values. If it did not, advice on how serious the problem was taken and univariable linear regression models showing the distribution of Residuals vs Fitted plots were assessed. Residuals are the difference between the values of the outcome predicted by the model and the values of the outcome observed in the sample. They represent the error present in the model and thus the validity of the model. Care was taken when interpreting the regression outcomes for those cases where the distribution of residuals for the univariable regression was not as expected.
3. If any of the variables selected for the model had a substantial amount of missing data a dummy variable was created in order to compare the means between the variable with the missing data and a new one where the missing values have been substituted by the mean value of the variable. Not finding a statistical difference between the two means gave some evidence that the missing data was not special in providing a best or worst outcome.

Multiple regression modelling:

4. Variables were selected for the multivariable analysis. Any variable whose univariable test had a p-value < 0.025 was a candidate for the multivariable model along with all variables of known clinical importance. Variables were tested on a significance order so that the second most significant one was tested with the first most significant variable, then the third with the first most significant and the least significant one was tested last with the first one.
5. The importance of each variable included in the model needed be verified by comparing each estimated coefficient with the coefficient from the model containing only that variable. Variables that did not contribute to the model based on these criteria were eliminated and a new model fitted. Also, the estimated coefficients for the remaining

variables were compared to those from the full model. In particular, we were concerned about variables whose coefficients had changed markedly in magnitude. This indicated that one or more of the excluded variables were important in the sense of providing a needed adjustment of the effect of the variable that remained in the model. This process of deleting, refitting, and verifying continued until it appeared that all the important variables were included in the model and those excluded were clinically and/or statistically unimportant.

6. At this point, it was advisable to add back into the model any variable not selected for the original multivariable model. This step was helpful in identifying variables that by themselves were not significantly related to the outcome, but made an important contribution in the presence of other variables.
7. Once the model containing the essential variables was obtained a better look at the variables in the model was recommended. The question of the appropriate categories for discrete variables should have been addressed at the univariable stage but for continuous variables, the assumption of linearity in the regression was checked.
8. Once the main effects model had been refined and it had been ascertained that each of the continuous variables was scaled correctly, the model was checked for interactions among the variables. Interactions between two predictor variables arise when one variable has a different effect on the outcome depending on the value of the other variable.

All analyses on this section were only performed with 'better VA eyes' data, as the binocular prism was prescribed to the BE in 95% of patients. The remaining 5% were cases for which the prism VA for both eyes was the same and thus the second and/or further steps of the binocular prism prescribing strategy covered on section 3.3.2 had to be applied.

6.1 Predicting the relocating prism

This section investigates how well the subjectively determined relocating prism can be predicted from measures of visual function among AMD patients or from PRL characteristics. Kinetic perimetry (area of scotoma and NNPF distance and direction), logMAR distance visual acuity, near word reading acuity, contrast sensitivity and PRL distance and direction were investigated as possible prism predictors:

- **Distance VA:** Previous literature suggests that VA is associated with the prism power required for prism relocation. Verezen et al. (1996) prescribed lower prism powers to patients with better VA and higher prisms to those with poorer VA.

- **Near VA:** Near VA would be expected to be strongly associated with distance VA and thus should provide the same information on the prism prediction. However, it should be tested as well as the distance VA so that the one with the bigger association can be selected for the analyses. It may have a greater correlation than distance VA since the prism was prescribed on the basis of a near task, and that task involved face recognition which has been shown to correlate with reading acuity (Bullimore et al., 1991).
- **Contrast sensitivity:** It could be that contrast sensitivity, for being a visual function would influence the amount of prism power required for prism relocation. Makela et al (2001) found that contrast sensitivity in the peripheral retina was not as efficiently processed as that in the central retina and that there was a need for increase of contrast (contrast scaling) as retinal eccentricity increased.
- **Area of scotoma:** The larger the scotoma, the more likely that the prism will need to be larger in order to move the image out of the scotoma. This would be expected to relate to NNPF but because scotomas are sometimes irregular in shape/size, the area of scotoma does not always represent the NNPF well and thus it was recommended to include this variable in the analysis.
- **NNPF location:** The NNPF was also obtained from kinetic perimetry and is a consequence of the shape and location of the scotoma. It is determined by the linear distance and the angular direction from fixation and it thus provides information to predict both prism power and base direction. Theoretically, the position of the NNPF should predict the amount and direction of relocation required to move the image out of the scotoma area. However, it could be that the NNPF is not wide enough and thus the patient might end up choosing a different area of retina for relocation.
- **PRL location:** Similarly to the NNPF, the PRL was determined by both a linear and an angular component. If the patient had found an adequate PRL, its distance and direction could have predicted the prism power and base direction for the corresponding prism to relocate image onto that selected PRL location. If the prism was doing exactly the same as the patient was already achieving for themselves then the VA may not improve and the gain may be in terms of (e.g.) comfort rather than VA. However, There are three possible reasons why such a relationship may not exist:
 1. The fixation position was determined photographically, and represents a sampling of fixation position, which may not be representative.
 2. The task for the patient when the fundus photograph was taken was static fixation of a simple pointer. When the prism was being prescribed the patient was performing a dynamic task looking at a picture and describing details from it.

3. If the patient had already optimised his or her eccentric viewing technique and thus was making optimum use of a suitable PRL, the use of a prism may disrupt his or her fixation pattern, and may bear no relation to the degree of image shift. This may be more likely with patients who have had a longer duration of the condition.

6.1.1 Predicting the prism power

The relationship between the prescribed prism power and the above-mentioned variables was investigated in this chapter section. Distance and near VAs, contrast sensitivity and NNPF and PRL eccentricity, were introduced as independent variables into single regressions, where prism power was the independent variable. Table 6.1 shows the results of these regressions, where all variables show strong associations. However, the regression for the PRL distance as an independent variable has a p value >0.025 and thus it is not significant.

Independent variables	β	p	Confidence intervals	Adjusted r^2
Distance VA	0.46	<0.0001	0.35 to 0.59	0.19
Near VA	0.44	<0.0001	0.28 to 0.60	0.10
Contrast sensitivity	-1.98	<0.005	-3.31 to -0.65	0.03
Area of scotoma	0.29	<0.0001	0.13 to 0.45	0.05
NNPF distance	0.32	<0.0001	0.16 to 0.48	0.08
PRL distance	0.12	0.07	-0.02 to 0.26	0.01

Table 6.1: Simple regression outcomes for prism power as the dependent variable.

Correlations between visual functions variables are shown in Table 6.2. Some of these are moderately strong, suggesting that the predictions for separate variable should not be regarded as independent. For these cases, only one of the variables, i.e. the one showing a stronger association in the single regressions was considered.

	NNPF distance	Contrast sensitivity	Near VA	Distance VA	Scotoma area
PRL distance	0.101	0.215	0.307	0.303	0.225
Scotoma area	0.430	0.225	0.351	0.321	
Distance VA	0.270	0.400	0.670		
Near VA	0.343	0.456			
Contrast sensitivity	0.364				

Table 6.2: Correlation matrix of independent variables for prism power regression.

Following the above-mentioned steps, the best model for prism power prediction was investigated and Table 6.3 contains the results for the model. The variables giving a best fit were distance VA and NNPF distance, explaining 22% of prism power prediction (adjusted $r^2 = 0.22$ with a significance of $p = 0.05$). Figures 6.1 and 6.2 show the P-P plot, showing a good fit to the normal line distribution of values, and the Residual vs Fitted plots for the final model,

these being quite well distributed. There were no important interactions between the variables included in the regression and the outlier that can be seen on the Residuals vs Fitted plots (Figure 6.1) did not affect the regression outcome when removed.

Independent variables	B	p	95% Confidence intervals
Distance VA	4.04	<0.001	2.77 to 5.31
NNPF distance	0.19	0.009	0.05 to 0.33

Table 6.3: Best fitting multivariable model for prism power prediction.

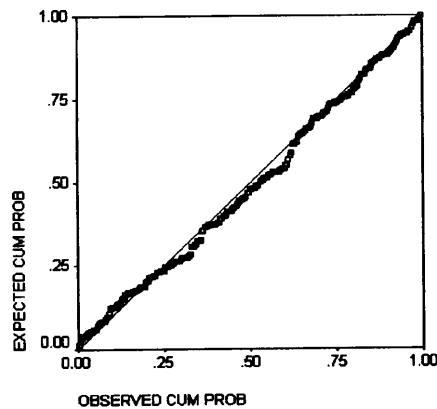


Figure 6.1: Normal P-P plot for of best fitting multiple regression model for prism power prediction.

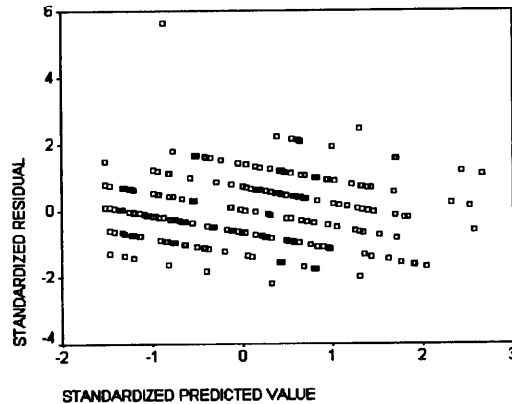


Figure 6.2: Residuals vs Fitted plots of best fitting multiple regression model for prism power prediction.

6.1.2 Predicting the prism base direction

Out of all the visual functions tested in this study, the Bjerrum screen is the only one that provides us with an angular value that could be compared to that of the prism base direction. The rest of the visual functions are based on other scales (logMAR or linear), which don't provide any angular information. In theory, the NNPF would be expected to be chosen as the area for prism relocation and thus the angular location of this point (obtained from kinetic perimetry) could be expected to be associated with the base direction of the subjectively prescribed relocating prism. Similarly, the subjectively chosen PRL location with respect to the fovea could be expected to show a close angular position to the subjectively chosen prism base direction.

After applying the above-mentioned calculations to the (PRL-base direction) and (NNPF-base direction) differences, the distributions for both of these differences are shown in the figures below (6.3 and 6.4). Similarly to section 5.5, where the relationship between NNPF and PRL angles was calculated, it can be argued that if there were no association between the two angles, the angular differences would be expected to have a random distribution. The observed

distribution (grouped into six categories) of angular differences could be compared with the expected distribution, which (see Table 6.4) showed how many more patients than expected had smaller angular differences. This effect was more obvious for the NNPF than for the PRL, suggesting that the NNPF is better predictor than the PRL for the prism base direction. For 40% of the cases, the difference of angle between the NNPF and the prism base was of 30° or less. This can be observed on Figures 6.3 and 6.4, where the difference of angles between the NNPF and the prism base direction has a much higher prevalence for small differences than for big angle differences.

Angular difference	Observed frequency for NNPF (% of total)	Expected frequency for NNPF (n = 180)	Observed frequency for PRL (% of total)	Expected frequency for PRL (n = 185)
0-30°	72 (40%)	30 (17%)	42 (23%)	30.833 (17%)
35-60°	38 (21%)	30 (17%)	43 (23%)	30.833 (17%)
65-90°	28 (15%)	30 (17%)	34 (18%)	30.833 (17%)
95-120°	20 (11%)	30 (17%)	24 (13%)	30.833 (17%)
125-150°	10 (6%)	30 (17%)	25 (14%)	30.833 (17%)
155-180°	12 (7%)	30 (17%)	17 (9%)	30.833 (17%)

Table 6.4: Observed and expected frequencies of angular differences between prism base direction and NNPF and PRL directions.

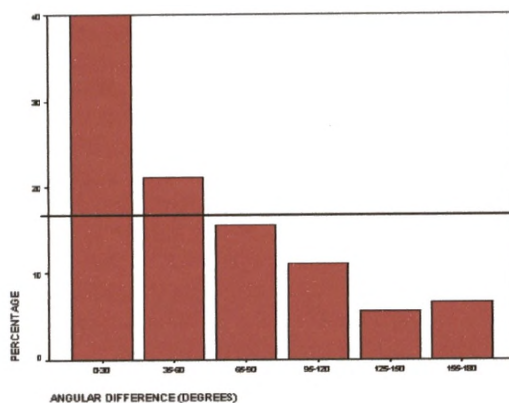


Figure 6.3: Distribution of angular differences between NNPF direction and prism base with line of expected frequency.

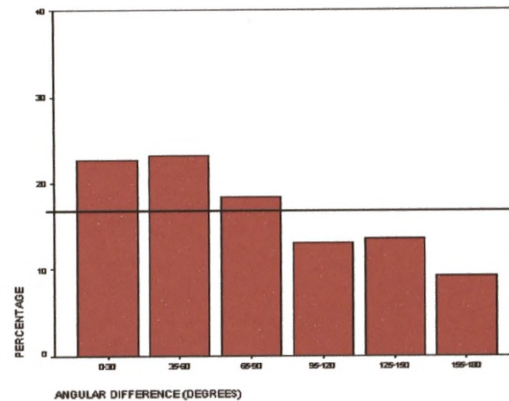


Figure 6.4: Distribution of angular differences between PRL direction and prism base with line of expected frequency.

6.2 Predicting effectiveness of the treatment

As discussed on section 5.1, there was no significant effect of randomisation group on distance VA, our primary outcome measure, when adjusted for baseline or on other outcome measures either. However, 23 patients (10%) were found to have a clinically significant visual acuity improvement, i.e. ≥ 0.16 logMAR (although there was no mean improvement: mean value 0.00

logMAR, range -0.42 to 0.46 logMAR) when wearing the prism spectacles on the last visit as compared to the visual acuity with conventional spectacles on the second visit. This section concentrates on investigating all variables that might potentially be associated with an improvement in visual acuity over time, and specifically whether the effects of these variables depended on patients wearing the prescribed prisms. If the effect of a potential predictor depends on whether or not a patient was wearing a prism, it becomes possible to characterise those patients that are likely to benefit from the prism spectacles. This section is going to concentrate on investigating all the variables that would be expected to have an association with improvement in VA from prism and therefore attempt to use these to predict those patients that are likely to benefit from the prism spectacles. Also, this investigation provided the opportunity to examine if any of the variables identified suggest that the patient characteristics from the previous prism relocation studies may explain the much higher rates of success that they found. Data was analysed for the 224 patients that completed the study. These analyses need to take into account the fact that patients in only one of the three study arms had the custom prism, and patients in another arm had no prism at all. Two different approaches could have been used to do this: (a) include only patients from the custom (or standard) group in the analyses, or (b) include all patients and then investigate interactions of predictor variables and 'arm'. The second approach was chosen because it directly compares the effect of a predictor variable in different arms and because it makes best use of the available data, thus maximising the statistical power of the analyses.

Before the multiple regression model can be applied, we need to define the dependent and independent variables to be considered into the equation:

Defining the dependent variable: The main outcome measure in this study is the distance VA improvement with prism spectacles as compared to conventional spectacles over the 3-month prism wear period. The two visual acuities to be compared for defining the dependent variable are thus the measured VA on the 3rd visit with prism/study spectacles (p3) and the measured VA on the 2nd visit with conventional spectacles (c2). These two VAs were measured under the same binocular conditions by the same experimenter and have a three-month time space between them that would allow for patient adaptation to new spectacles. The difference between these two VA (p3-c2) will be the dependent variable in the multiple regression equation and will be called p3-c2VA.

Defining the independent variables (predictors): Predictors are all those variables for which there is a possible hypothesis that they can predict visual acuity success. All predictors were considered as independent variables on the regression model. The variables that were

considered as predictors and the hypothesis for why they were considered as predictors are the followings:

- **Distance conventional VA (c1VA):** It could be that prisms only work for patients with a certain level of acuity and if acuity is too good/poor then they might not be so useful.
- **RL-CL VA:** this VA difference represents the potential improvement of VA with prism Rx as compared to conventional Rx (see section 3.2.3). A large value for this difference should predict prism success.
- **Area of scotoma:** It could be that prisms are only successful at relocating the image for a small size scotoma and wouldn't be successful for large scotomas, or the other way around.
- **NNPF distance:** the equivalent argument also applies here.
- **Type of AMD:** It could be that the dry type of AMD would be a better predictor of prism success since it is a more stable condition than the wet type. The wet type, on the other hand, is more likely to give absolute scotomas so prism spectacles could be of benefit to this type as well.
- **PRL distance:** Patients using a PRL are likely to have adapted better to the AMD and thus might not find prisms as useful as someone whose PRL distance would be 0.
- **Fixation quality (FQ):** It could be that patients that have adapted to use eccentric viewing and are already good at it might not find prism spectacles quite as good as patients who have not adapted properly.
- **Eye movement response to prism:** It could be that those patients whose eyes make a refixation movement when the binocular prism is added don't find the prisms as useful since the eye movement is cancelling out the effect of the prism.
- **Type of lenses on spectacles:** Bifocal lenses are less predictable in the sense that they induce unavoidable prismatic effect in the near zone which, depending on the prescription and type of segment, could be cancelling or enhancing the prescribed prismatic effect.
- **Mean equivalent sphere (MES):** Patients with high prescriptions are more prone to have fitting problems, as spectacles would be expected to slip down the nose due to weight. This would mean that patients will not be looking through the optical centre of the lens and would result on patient not having the correct prism.
- **Prescribed prism power:** It might be that there is a limit to which prism power would be beneficial and above that value unwanted secondary effects (such as weight, nausea, aberrations and dizziness) might interfere with the possible benefit they might provide.
- **Duration of condition on second affected eye:** Patients with longer standing AMD on the second affected eye might have adapted more to the condition and be more likely to have already developed useful eccentric viewing. According to White and Bedell (1990), patients with longer duration since onset showed oculomotor behaviours qualitatively more like

	NNPF distance	Distance VA	RL-CL VA	Area of scotoma	Type of AMD	PRL distance	FQ	Movement response	Type of Spectacles	MES	Prism power	Duration of condition
Independence	A	A	A	A	X ²	A	A	X ²	X ²	A	A	A
Duration of condition	0.10	0.12	-0.02	0.08	t	0.25	-0.11	t	t	-0.08	0.16	
Prism power	0.27	0.44	-0.22	0.24	t	0.13	0.29	t	t	-0.10		
MES	0.06	0.06	-0.05	0.01	t	0.02	-0.15	t	t			
Type of spectacles	t	t	t	t	X ²	t	t	X ²				
Movement response	t	t	t	t	X ²	t	t					
FQ	-0.23	-0.41	0.06	-0.21	t	-0.30						
PRL distance	0.10	0.27	0.21	0.23	t							
Type of AMD	t	t	t	t								
Area of scotoma	0.43	0.20	0.12									
RL-CL VA	0.03	-0.17										
Distance VA	0.27											

Table 6.5: Correlation matrix of independent variables for multiple regression.X² Refer to Table 6.6 for results of Chi squared analyses

t Refer to Table 6.7 for results of t-test analyses

A Refer to Table 6.8 for results of ANOVA analyses

those of normals. Similarly, Crossland et al. (2004) found that fixation stability improved in the majority of their subjects over the first twelve months after onset of scotoma in the second eye and that it was correlated with an increase in reading speed. These patients might therefore not find the prism spectacles much of an advantage.

- **Living independence:** Patients living with partners and/or family tend to not need to do as many tasks as patients who live on their own and thus have to manage to do tasks themselves. This could thus limit the patient's incentive to try the glasses and adapt to them.

Although some of the variables have been described as possible predictors on previous literature some others have been added to the list without this type of support. However, the hypothesis just described for them made it worth it testing. Also, the fact that patients were not selectively recruited with respect to any of these variables offered the possibility to investigate any additional variables that could be expected to influence p3-c2VA.

Variables	X^2	Critical value for $\alpha = 0.05$
Type AMD / Type spectacles	0.35	3.84
Type AMD / Independence	0.88	7.82
Type AMD / Movement response	0.34	3.84
Movement Response / Type spectacles	1.02	3.84
Type spectacles / Independence	2.57	7.82
Movement response / Independence	1.21	7.82

Table 6.6: Results of Chi squared analyses for two categorical variables.

Table 6.5 shows the association between all the above-mentioned independent variables to be assessed on the multiple regression. Some of the variables were continuous but others were categorical (either dichotomous or polychotomous) and thus investigating the associations between them involved a few different types of analyses (Chi squared, t-tests or ANOVA) besides correlations, which could only be applied to 2 continuous variables. For clarity reasons, only the correlation factors r for those variables that were both continuous have been included on the table. For other cases, where Chi squared (the two variables are categorical), t-test (one variable is dichotomous and the second was continuous) or ANOVA analyses were applied, an indication (X^2 , t or A , respectively) has been placed on the corresponding box to indicate the table that contains the relevant information for those variables: Table 6.6 for X^2 , Table 6.7 for t-test and Table 6.9 for ANOVA results. No interactions were found between the independent variables.

Table 6.9 shows the results of the simple regressions for all the independent variables when analysed with p3-c2VA as the dependent variable. Only 3 variables seem to show some degree of significance: Distance VA and Type of AMD.

Variables	t	p
Type spectacles / Area scotoma	1.09	0.278
Type spectacles / Conventional VA	0.53	0.598
Type spectacles / RL-CL VA	-1.36	0.175
Type spectacles / PRL distance	1.52	0.130
Type spectacles / Best sphere	-3.19	0.002
Type spectacles / Prism power	1.14	0.256
Type spectacles / Duration AMD	1.78	0.076
Type spectacles / Fixation quality	0.37	0.713
Type spectacles / NNPF distance	0.65	0.517
Type AMD / Area scotoma	0.48	0.632
Type AMD / Conventional VA	3.15	0.003
Type AMD / RL-CL VA	0.34	0.734
Type AMD / PRL distance	-1.46	0.153
Type AMD / Best sphere	1.88	0.066
Type AMD / Prism power	2.40	0.019
Type AMD / Duration AMD	2.23	0.032
Type AMD / Fixation quality	0.00	0.997
Type AMD / NNPF distance	-0.54	0.593
Movement response / Area scotoma	1.84	0.071
Movement response / Conventional VA	1.91	0.062
Movement response / RL-CL VA	0.45	0.658
Movement response / PRL distance	2.05	0.044
Movement response / Best sphere	0.37	0.715
Movement response / Prism power	-1.10	0.277
Movement response / Duration AMD	-0.36	0.720
Movement response / Fixation quality	-1.87	0.066
Movement response / NNPF distance	0.89	0.378

Table 6.7: Results of t-tests for one dichotomous and one continuous variable.

Variables	ANOVA results
Independence / Conventional VA	F = 0.19 (df = 3,24, p = 0.90)
Independence / RL-CL VA	F = 0.32 (df = 3,24, p = 0.81)
Independence / Area scotoma	F = 1.34 (df = 3,24, p = 0.26)
Independence / PRL distance	F = 1.36 (df = 3,18, p = 0.26)
Independence / Best sphere	F = 0.99 (df = 3,24, p = 0.40)
Independence / Prism power	F = 0.16 (df = 3,24, p = 0.92)
Independence / Duration AMD	F = 0.56 (df = 3,24, p = 0.64)
Independence / Fixation quality	F = 1.83 (df = 3,23, p = 0.14)
Independence / NNPF distance	F = 1.23 (df = 3,20, p = 0.28)

Table 6.8: Results of ANOVA analyses for one polychotomous and one continuous variable.

The best linear fitting model for prediction of p3-c2VA after applying the 8 previously-mentioned steps only managed to predict 5% (adjusted $r^2 = 0.05$ with a significance of $p = 0.01$) of the association between p3-c2VA and the only two variables that were found to show some degree of prediction were c1VA and Type of AMD (see Table 6.10 for multiple regression results). For every 10 lines of c1VA on the logMAR scale, p3-c2VA changed by -0.08 logMAR. p3-c2VA was also better for dry versus wet AMD by 0.04 logMAR (2 letters). Finally, p3-c2VA was worst for the cases that hadn't been classified due to poor quality of the photographs

when compared to the wet AMD type. The P-P plot and the Residuals vs Fitted plots can be seen in Figures 6.5 and 6.6, showing a reasonable fit. The slight S-shape of the P-P plot implies that the residuals are kurtosed.

Independent variables	β	p	95% CI	Adjusted r^2
Distance VA	-0.07	0.03	-0.13 to -0.0	0.02
RL-CL VA	0.05	0.45	-0.08 to 0.18	-0.00
Area of scotoma	0.00	0.98	-0.00 to 0.00	-0.00
NNPF distance	-0.01	0.02	-0.02 to -0.00	0.02
PRL distance	0.00	0.82	-0.01 to 0.01	-0.01
Fixation quality	0.00	0.54	-0.01 to 0.01	-0.00
Prism power	-0.01	0.06	-0.01 to 0.00	0.01
Duration AMD	-0.00	0.29	-0.01 to 0.00	0.00
Mov. response	-0.03	0.18	-0.08 to 0.02	0.00
Type AMD	0.05	0.03	0.00 to 0.09	0.03
1 st Independence condition	0.01	0.57	-0.03 to 0.05	0.00
2 nd Independence condition	-0.07	0.12	-0.15 to 0.02	0.02
3 rd Independence condition	-0.06	0.23	-0.15 to 0.04	0.00
Type spectacles	-0.01	0.79	-0.04 to 0.03	0.00
Best sphere	-0.00	0.99	-0.01 to 0.01	-0.00

Table 6.9: Single regression outcomes.

Independent variables	β	p	95% CI
Distance VA	-0.08	0.02	-0.14 to -0.01
Dry-Wet AMD	0.04	0.08	-0.00 to 0.08
Other-Wet AMD	-0.06	0.05	-0.12 to 0.00

Table 6.10: Best fitting multivariable model for multiple regression.

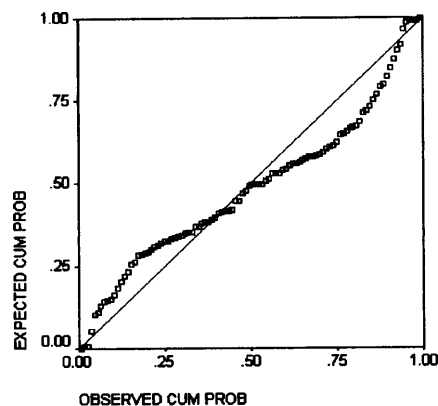


Figure 6.5: Normal P-P plot for of best fitting multiple regression model for treatment effectiveness.

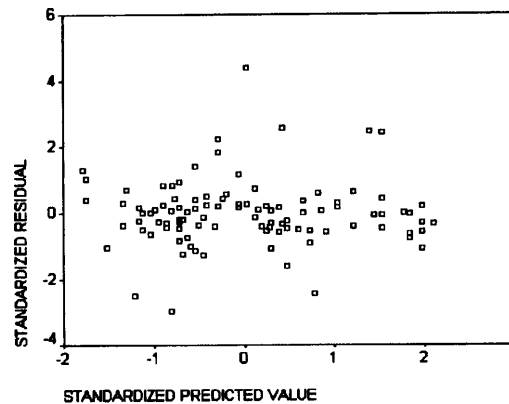


Figure 6.6: Residuals vs Fitted plots of best fitting multiple regression model for treatment effectiveness.

Interactions between the arms and the variables were then checked for all the studied variables. The rationale for examining interactions can be illustrated by describing an example: PRL distance might predict p3-c2VA for patients in the custom and standard groups, but not for

patients in the placebo group because patients fixating on fovea might not find the prism useful and this would only affect those who actually got the prism. Similarly, the eye movement response to prism would not be expected to have any effect on the results achieved by the placebo group. Finally, the prescription power and type of bifocal could affect the VA by inducing a prismatic effect that could cancel the relocating prism effect: this again might affect custom and standard arms, but not placebo (Appendix 14). Differences of this kind in the effect of a variable across the three arms represent interactions of the variable and arm. There were no strong hypotheses about interactions involving the rest of the variables. Surprisingly, the findings showed no effect of interaction between the expected functions and thus, the VA improvement is not associated with the prism, but to patient's other characteristics.

On the other hand, two unexpected interactions were observed. First, the effect of having unclassified AMD type was associated with a -0.15 logMAR ($p = 0.05$) smaller change in the custom group and a -0.12 ($p = 0.09$) logMAR smaller change in the standard group than in the placebo group. This interaction was not considered to be important because of its marginal significance level and because it involves a heterogeneous group of patients whose AMD could not be classified from the fundus photographs. Second, "having a partner" was associated with a -0.34 logMAR ($p = 0.001$) change in the custom group, but no significant change in the other two groups. This interaction was also considered unimportant since, for partners to have a differential effect for patients in different arms, they would need to have known what group patients were in. Since the trial was double-blinded (i.e. neither patient nor the researcher measuring outcome knew the allocation of patients to groups), partners could not have known this information.

Overall, only a small proportion (5%) of the variance in prism success seems to be predictable from the visual variables and clinical characteristics measured in the study. Similarly, it was also only possible to make minimal prediction (21% of the variance) of the visual acuity improvement that patients would obtain from the study spectacles after the 3-months wear.

CHAPTER 7

Discussion

7.1 Summary of the trial profile

This randomised controlled trial was carried out in response to the systematic evidence about the effectiveness of prism relocation in improving the performance of AMD patients in activities of daily life. Four small and limited studies had previously been carried out (see section 1.4.5). All showed positive results, but lacked a number of features of high quality evidence such as a sufficient number of patients, an appropriate placebo group and a clear prism prescription protocol.

In addition to this aim, and the other aims of the study (see section 2.1), this trial also provided the opportunity to monitor over time a wide range of clinical and psychophysical data in a large sample of subjects with AMD. The next following sections discuss, the characteristics of the study population, the association between visual variables and the findings concerning the effectiveness of prism spectacles.

7.2 AMD study population characteristics

Age and gender

The median age of 81 years for patients taking part in the study concurs well with the findings of epidemiological studies, that recognise age as a major determinant of AMD prevalence (Klein et al., 1991; Vingerlin et al., 1995; Mitchel et al., 1995). It is therefore not surprising that the patients in the study are elderly. Taking into account that patients contacted and offered the opportunity to take part in the study were not selected for gender, it's quite striking that the prevalence among females was nearly double that amongst men. However, it must be considered that the gender could have been biased at the stage where patients were contacted by phone to check if they wanted to take part as there could be a possibility that women were more

prepared to take part on the study that men. Still, when data of patients contacted but not taking part on the study was reviewed it was found that as many as 74% of them were women, reassuring a much higher prevalence of women compared to men in this study, which could be due to women living longer (Luy, 2002) and, arguably being more likely to seek healthcare.

Living independence and registration

It was found that more than half of the patients lived on their own, while most of the rest lived with their partners or family and only a small amount lived in sheltered accommodation. This high figure of patients living alone indicates the importance of independence for these people and the stimulus to find a rehabilitative treatment that would be effective in improving patients' performance in activities of daily life. Becoming registered as partially sighted or blind could be a way to provide a bit of help to these patients as they receive a visit from a social worker after registration in the house that assists them on some daily activities of life performance. As many as 33% of patients were registered as partially sighted and 31% as blind, giving a total percentage of 64% of patients being registered. This figure is quite high compared to Robinson et al. (1994) who found that only 48% of suitable patients from three hospitals were registered.

Secondary diagnoses

One of the main criticisms of the four previous studies (Romayananda et al., 1982; Rosenberg et al., 1989; Verezen et al., 1996; Bertrand et al., 1997) attempting to relocate the image on fovea is that patients were selectively chosen and thus did not necessarily represent the general population with AMD. Data from these studies may be strongly biased by the recruitment, which might be one factor explaining the positive outcomes they had. This RCT included patients with secondary eye diseases, providing that AMD was the main cause of visual loss. As expected from the patients' age range, there was a high prevalence (25%) of secondary ocular diagnoses, these being mainly cataracts, diabetes and glaucoma, accounting for 45%, 32% and 13% of the total amount of secondary diagnoses respectively. These figures are quite high when compared to Schuchard et al.'s (1999), gathered from the interview on the first visit to a rehabilitation service. Their most common secondary diagnostic was glaucoma (8%) followed by cataracts (4%) but the fact that their study was retrospective and based on patients that had been tested on a scanning laser ophthalmoscope (SLO) could explain this difference: The authors do not comment on the inclusion criteria followed to perform the SLO evaluation, where a clear media would be expected to have been an important factor. Also, it is quite likely that the system used in this study to classify cataract (LOCSIII) was far more sensitive to detecting very early signs of cataracts than the hospital diagnoses, more likely to only include the more severe cases.

Similarly to AMD, cataracts are a common bilateral condition affecting elderly people (Courtney, 1992) and there is overwhelming evidence that a significant proportion of older people have both conditions (Liu et al., 1989; Klein, 1992a). There is also some evidence that they have common risk factors (Wilson et al., 2001) and mechanisms of pathological action (Delcourt et al., 1999; Chiou, 2001). As therefore expected, this study has found a high prevalence of cataract in our AMD population. Only a minority of a 4% of the analysed eyes were free from cataracts and 16% were pseudophakic. Besides these eyes, the great majority (80%) had some degree of cataract. This figure compares to the smaller percentage of 11% reported by patients and thus shows how the LOCSIII grading system was very sensitive and detected not only those advanced and longstanding cases of cataracts but also the early ones. There was a marked difference of prevalence for the three different types of cataracts. Nuclear cataracts were by far the higher prevalence type of cataract (79% eyes had some degree of nuclear colour and 95% had some degree of nuclear opalescence) amongst the graded eyes. There was also a high prevalence of cortical cataracts (65% of eyes) and only a minority of 9% had posterior subcapsular cataracts. Although the percentage prevalences reported in this study include both eyes rather than the eye with more advanced cataract only, as prevalence studies do (e.g. McCarty et al, 2003; Tsai et al, 2003), it is interesting that the frequency values for the three types of cataracts do agree with those found in large epidemiological studies. This could be due to the fact that the prevalences found in the better and worse eyes were very similar for all types of cataract besides nuclear colour cataract, which was twice as prevalent in worse eyes than in better eyes and results are thus expected to be the same as if only the eye with more advanced cataract was considered. Tsai et al. (2003) also used the LOCSIII to study the prevalence of cataracts among a Chinese population with a mean age of 72.2 years and found nuclear cataracts to have the highest prevalence (39%) over cortical cataracts (22%) and a minority of Posterior subcapsular (9%). Also, McCarty et al. (2003) carried a study for incidence of cataract on a Melbourne population with a mean age of 62.5 years and found nuclear cataract to have the highest value (16%), followed by cortical (8%) and posterior subcapsular (7%). Although the relative prevalence of the three types is the same as in our study the absolute percentages are higher in this study. The first most obvious explanation would lie on the fact that our study population had a much higher mean age when compared to the other two studies' population. Also, our prevalence of cataract includes the very early sign that can be detected whilst the other studies only include those cases above a certain threshold values (2.0 or greater on the LOCSIII). However, it can be said that there is a big association between cataract and AMD on this study population. This finding agrees with Javitt et al. (1996) who proposed that both diseases are linked by the same environmental factors.

Visual acuity

Conventional visual acuities had a median value of 0.93 and 1.26 logMAR for better and worse VA eyes respectively in the present study. These improved marginally only to 0.90 and 1.21 logMAR when the VA was measured with the subjectively chosen prism. The median improvement of VA with prisms when compared to conventional VA was 0.04 logMAR for eyes with better VA, i.e. 2 letters on the ETDRS chart. This improvement is very small when compared with Bertrand et al.'s (1997) findings of a mean improvement of 1.36 lines, although they did not specify the type of chart used. The other three above-mentioned studies reported a visual function improvement when using the prism but did not state the amount of improvement. This high VA improvement on Bertrand's study was likely to be due to a strong placebo effect. This study aimed to test the effectiveness of prism relocation in the general population with AMD without any training, although a 3-month follow up to control for prism adaptation was employed. The median VA improvement of -0.02 logMAR between prism and conventional lenses found in this study is unlikely to offer a visual function improvement, especially when the test-retest reliability of the ETDRS chart has been estimated to be ± 0.16 logMAR, i.e. 1.5 lines for normally sighted subjects (Hazel & Elliott, 2002). No median near VA improvement was found. The range of VA improvement with prism compared to the conventional VA was large for both better and worse VA eyes (-0.60 to 0.54 and -1.06 to 0.74 respectively). These large ranges show that for some patients the prism improved VA whilst for others it caused VA to deteriorate. These large range of VA improvements could be due to an unreliability/variability of the measurement, since patients could be making different efforts to read when the two measurements were made. Also, it could be that the subjective improvement noticed by patients on the 'real scene' photograph might not represent a VA improvement.

VA distributions (distance, near, conventional and prism) showed a bimodal distribution, which seemed to be more prominent on the near vision distributions than on the distance ones and seemed to happen, although to a lesser extent, on the single, crowded and repeated letters as well. There is a clear fall in the number of subjects with VA in the 0.70-0.90 logMAR range. This effect cannot be explained by the technique used to measure VA as the ETDRS chart has a constant size ratio between adjacent lines, uses changes in viewing distance to provide additional sizes, and is scored letter-by-letter. There is no reason why this VA range would be more difficult for patients to read than the rest of the lines. However, when the data was compared to that collected for another RCT (Russell, 2003) two years earlier, with the same number of subjects from the same LVC and using the same test for recording VA, the distribution of distance VA also seemed to show the same effect at the same VA range, the data being collected by a different clinician than in this study.

Contrast sensitivity

As expected, contrast sensitivity was better in the better VA eyes (1.05 logCS) than in the worse VA eyes (0.70 logCS) with a difference between median values of 0.35 logCS. These values are comparable to the mean binocular CS found by Bellmann et al. (2003) on 250 patients with AMD of 0.95 logCS who had a mean VA of 0.46 logMAR. The one line difference of better CS found in this study could be due to the technique used to record CS, where only the letters not seen in the last triplet were discounted from the final score. Not surprisingly, these values are much lower than those found on a free from disease population with a similar age range: 1.90 log CS (Mantylarvi & Laitinen, 2001). The median value of 1.05 logCS found in the BE of the study patients gives them a contrast threshold of 7.8. This contrast threshold should be enough to provide a 10:1 reserve for most reading tasks, and thus enough contrast for fluent reading (Whittaker and Lovie-Kitchin, 1993).

Refractive power

The majority of patients (84%) had a mean equivalent sphere power between -2.00 and +4.00 diopters, with a median power of 0.82 diopters on better VA eyes. The most prominent ametropia was hyperopia (62%) and only 26% were miopic, leaving a minority of 12% of emmetropic patients. These figures concur well with the findings from the Blue Mountains Study (Attebo et al., 1999) where 90% of the population were on the same range of refractive errors, mean value +0.67 diopters and the prevalence of hyperopic, miopic and emmetropic patients was 57%, 15% and 28% respectively. Astigmatism against the rule was the most common type of astigmatism among the patients recruited for the study. This finding is not surprising since astigmatism against the rule has been reported to increase with age (Gudmundsdottir et al., 1999; Haegerstrom-Portnoy et al., 2002; Attebo et al., 1999). However, Haegerstrom-Portnoy et al. (2002) still found a prevalence of $\geq 1.00\text{D}$ astigmatism with the rule of 50% in their 'over 80 years of age' group. This finding shows that although astigmatism with the rule decreases with age it is still quite prevalent in elderly people. Also, it must be borne in mind the fact that 16% of the patients had had cataract surgery, which results in a refraction change of the eye (Storr-Paulsen et al., 1999) and would have therefore biased the prescription values. The median value of the additions was 4.00 diopters, which is not surprising, since this is the conventional strongest addition routinely prescribed for constant wear to give an optimal NV acuity without compromising other near vision tasks. Any higher addition is, by convention, a magnifier (Dickinson, 1998).

Type of lenses

A total of 31 conventional bifocals were issued, being downcurved (R) (17 cases) or flat-top segments (D) (14 cases), with the D28, R24 and R25 segment diameter being preferred. A total of 41 conventional spectacles were issued, with most of these being NV spectacles. The high

amount of NV spectacles prescribed is explained by those cases where patients were wearing a conventional NV add of +2.50 and found that a +4.00 add gave them a VA improvement, therefore, warranting a change of NV prescription. Conventional spectacles were only issued to those few subjects who showed a change in prescription, so the prism spectacles give a better indication of the type of lenses worn during the study since these were given to all patients. A total of 107 patients were wearing bifocals, of which the medium size segments were again the most chosen ones (D25, D28, D35, R24, R25, R28 and R38). Equal numbers of D and R segments (52) and only a minority of 3 C segments were prescribed. A total of 126 patients were issued with single vision lenses and the combination of distance and near vision spectacles was the most popular one. This finding is not surprising, as most patients tend to have vision goals at all distances and therefore required both prescriptions. There were 10 cases where patients had a combination of bifocal and single vision spectacles. These were the cases where patients needed an intermediate prescription besides the distance and near ones and rather than having 3 pairs of spectacles preferred to have distance and near/intermediate in the bifocals and the remaining prescription type in a single pair of spectacles. The most popular combination of bifocal and single vision lenses was the distance and intermediate bifocal with near single vision spectacles. If the near vision correction was used in conjunction with a magnifier, it was often difficult to adopt the correct gaze angle looking down through the bifocal segment whilst positioning the magnifier close enough to the eye to obtain an adequate field of view: In such cases, single vision reading lenses were arguably more appropriate.

Prescribed prisms

Patients preferred a prism power with a median value of 8Δ (equivalent to 4.6°) and for 93% of them it ranged between 4 and 12Δ (2.3 to 6.8°). These findings are quite similar to Romayananda's et al. (1982), for whom most of their patients chose prism powers between 6 and 8Δ (range between 4 and 10Δ). They used a similar bracketing technique to that used in this study and they also found that the prism base directions were mainly distributed in the upper hemifield. In the present study, the upper hemifield accounted for as many as 78% of the base directions, with 90° being the preferred position in 53% of patients. The other three cardinal positions were also frequently chosen by patients (15% of patients chose the base at 180° , 9% at 270° and 6% at 0°) compared to oblique positions, which only counted for 10% of the cases. Verezen et al (1996) fitted higher prism powers, ranging from 13 to 20Δ by using a different technique: they attempted to relocate the image to the PRL used by the patient with the tentative prism power and base direction but did not report the prism base directions outcomes. Similarly, Rosenberg et al. (1989) and Bertrand et al. (1997) did not report prism powers or base directions, and so no comparison could be made with their findings. The fact that most patients preferred the relocation of the image in the upper hemi-field suggests the superior retina for

improved function for rehabilitation purposes. Our finding of a preferred prism relocation in the upper hemi-field relate to Frennesson et al. (1995), who found that moving the fixation vertically improved patient's ability to read. They also found that a small amount (i.e. 6.2°) was the mean displacement needed to visualise the print shown to the patient, this value is smaller than our finding of 4.6° and this discrepancy could well be explained by the worse mean VA (1.48 logMAR) of their patients.

Patients' perceived disabilities

AMD results in a decrease in the patients' quality of life (Davis et al., 1995). The effect of low vision interventions on objective task-specific measures of functional abilities, such as reading speed, reading duration, and ability to read a certain print size has previously been reported as beneficial to the patient (Nillson, 1990). Patients' perceived disabilities and patients' goals were determined by means of the MLVAI (Haymes et al., 2001). By far the most frequently reported limitation was recognising faces. As many as 80% of the recruited patients stated inability perform this task. High prevalence of face recognition disability has been widely reported previously (Bullimore et al., 1991) among AMD patients, relating to the high amount of cases found. Other task difficulties with a high prevalence among the study patients were reading newspaper print (58%), reading package labels (49%), reading medicine labels (49%) and reading a letter (49%). It can therefore be concluded that, another disability affecting the vast majority of AMD patients, besides recognising faces, is reading. Again, reading has previously been reported as a main disability in AMD patients (Timberlake, 1987; Elliott et al., 1997). Other tasks that were also highly reported were threading a needle (61%), identifying coins (53%) and using the telephone book (58%), which is not surprising due to the high visual acuity required to perform these meticulous but essential activities of daily life.

Low vision aids

The low vision assessment given to patients on the first of their three study visits aimed at improving the patients' performance on the reported tasks. However, for some of the tasks (such as face recognition) the amount of help that could be offered to patients was quite limited and thus, the LVA selection was targeted towards reading tasks: this aim is usually achieved well in low vision clinics (Humphrey and Thompson, 1986). This explains why the majority of LVAs prescribed were for near vision tasks. The median number of aids per patient was 3 and the typical set of aids was a large illuminated stand magnifier to keep at home and a smaller hand-held magnifier offering portability. The third LVA was very often a weak and old magnifier they had bought when the condition was at an early stage and thus with a weaker magnification than required to accomplish their aims. Therefore, the most popular LVAs among patients were the illuminated stand magnifiers (218 cases) for providing good illumination and stability on page. As many as 147 patients used illuminated hand magnifiers, finding their size appropriate

to carry around without compromising the light, which they found crucial. Smaller numbers of non-illuminated magnifiers were used among patients (87 hand-held and 25 stand magnifiers). These figures emphasize the importance of lighting for patients with AMD, and general advice on illumination was usually welcomed by patients.

Pocket hand magnifiers were also quite popular as a secondary magnifier to carry around, these being usually required to complement the primary device. For distance vision, the most popular aids were spectacle mounted binoculars (33 cases) for television or watching theatre performances and hand held monoculars (19 cases) for spot viewing bus numbers or details in the street. Telescopes were not generally prescribed for TV purposes, since most patients preferred to get closer to the TV and therefore use relative distance magnification, compared to the inconveniences of using angular magnification (weight and narrow field of view).

As expected, the magnification power of the near vision aids was closely related to near VA. This is not surprising since the near vision goal for most of the patients was reading newspaper print and thus there was a standard print size goal (M1). However, there was no association between magnification power of the distance vision aids and distance VA. One reason for this lack of association is likely to be that aids were prescribed with the aim of improving visual performance on the distance but without a standard visual goal, therefore giving a high variability of required magnifications. Part of the reason for this is that the range of distance telescopes was very limited for the binocular telescopes that only had magnifications of 2 or 3X. An association between magnification of monocular distance telescopes and VA as these come in a wider range of magnification powers (2 to 8X), although the choice of telescope may also be influenced by the need to optimise field of view. The very small amount of patients that used this type of LVA did not provide enough data to investigate the association.

Assessment of the pathology

The prevalence of patients diagnosed with dry versus wet AMD has been typically reported as about 90% versus 10% in the general AMD population (Leibowitz et al., 1980; Richer, 1999). However, in low vision clinics, a much higher prevalence of the wet form is expected. This is due to the dramatic drop of macular visual function that takes place on the wet type versus the slow and gradual drop on the dry type (Sunness et al., 1995). Schuchard et al. (1999) found in a population of AMD patients referred to a vision rehabilitation service, that the prevalence of impairment caused by dry versus wet AMD was nearly 50-50%. The present study found that the prevalence of people referred to the LVC at the MREH with central visual function impairment caused by dry AMD is less than half (29%) of the population with wet AMD (71%).

When the fundus photographs of the recruited patients were assessed by the ophthalmologists to confirm the diagnosis of AMD, a total of nine eyes were classified as early ARM cases (i.e. only having some drusen), and a further 9 eyes did not show any pathological signs. Eight of these 18 eyes were better VA eyes and had reasonable VA (mean 0.63 logMAR, range 0.48 to 0.80) and six of those eight patients had no scotoma on the Bjerrum screen plot. A possible explanation for this discrepancy between diagnoses could lie on the lack of fluorescein angiograms. These might have shown a small defect not visible on fundus photographs, which does not give an absolute scotoma and thus, does not cause a drastic VA reduction. Furthermore, five patients were given completely different diagnoses, including Vitelliform macular dystrophy, Pattern dystrophy, Best's disease, Choreoretinal atrophy and Myopic degeneration. Intra-observer variability has been reported in age-related maculopathy and macular degeneration (Scholl et al., 2002). Sperduto et al. (1986) reported a disagreement of around 28% between clinical and reading centres when ophthalmologists were asked to assess all causes of visual impairment. The fact that the ophthalmologist had to make his judgement on only fundus photographs could have affected the diagnoses as compared to the original diagnoses made while the patient was assessed in vivo where a direct view of the fundus of the eye was available. These discrepancies are not likely to have affected the trial, as all these conditions are likely to cause central visual loss, and thus it could be expected that these patients might also benefit from the prism relocation treatment.

The patients recruited to this study suffered from relatively advanced AMD that had caused significant visual acuity deterioration. It is thus expected that the lesion would have extended and affected the fovea (besides the above-mentioned cases where the diagnosis may have been different) and the lesions would be expected to be subfoveal, rather than the non-subfoveal type of lesion, which is more likely to happen among early ARM cases with better vision. As expected, the vast majority of the assessed better VA eyes (84%) had a subfoveal lesion, 14% were not classified and only 2% were considered as possible non-subfoveal cases. This rate of non-subfoveal cases is quite low when compared with Moisseiev et al. (1995), who found 8 out of 37 (22%) of their subjects being extrafoveal cases. However, they only reported those cases with classic active choroidal neovascularization (CNV) and this figure could well change if the occult and combined types of active CNV and the pigment epithelium detachment, hemorrhage and disciform cases were included.

7.3 Associations of visual variables in AMD

Repeated, crowded and single letter VAs

A crowding effect (or contour interaction) has been demonstrated on not only amblyopes but also in visually impaired patients, including AMD cases (Pardhan, 1997). The crowding effect is known to get worse towards the periphery of the retina (Latham and Whittaker, 1996). It is therefore expected that AMD patients, who use a PRL away from the fovea, might suffer from this effect. Pardhan (1997) found a mean ratio of 1.11 between single-letter acuity and letter-line acuity in normal subjects. This ratio increased to a value of 1.79 for patients with AMD. These values are similar to those found by Regan et al (1992) on amblyopic adults (1.75) and normal adults (1.1). The mean SL/CL ratio found in the present study was 1.13, indicating that patients do suffer from a crowding effect, although the effect seems to be much smaller than that found by Pardhan (1997). This difference could be because patients in their studies had a reasonably good VA, since worse VA suggests a PRL further from the fovea, with the potential for worse crowding (Latham and Whitaker, 1996). No association was found in the present study, however, between NNPF distance, PRL distance, scotoma size or area of lesion and contour interaction (SL/CL difference). This finding is quite surprising since contour interaction is thought to be greater for peripheral than for foveal vision and thus, on increasing size of AMD damage and the subsequent increase of NNPF and PRL distances would have been expected to be good predictors of contour interaction. An explanation for this lack of association could lie in the technique used in the study to measure SL, RL and CL, where patients were allowed as much time as required to perform the task, and thus had plenty of chances to resolve the task. This approach could have resulted in an attenuation of the SL/CL VA difference. It is possible that extra time improves fixation accuracy, thus helping CL VA more than SL VA.

Full-field VA test have previously been advocated for measuring the optimal VA in patients with central scotomas (Harris et al., 1985; Pardhan, 1997). These authors suggested that patients with central scotoma had much worse vision than expected from the size of their field defect, because they did not spontaneously fixate with the best retinal locus, but might be persisting with central fixation. It is argued that showing the patient a chart with repeated letters would give the patient the chance to find the optimal vision without using eccentric vision. It is for this reason that this test should, in theory, be a good predictor for the optimal vision to be expected after a rehabilitation strategy, in this case being prism relocation. As expected, there was a strong association between repeated letter VA and prism VA, (mean difference 0.03, sd 0.22, range -0.78 to 0.91 logMAR) and 37% of results differed by less than 0.1 logMAR, but 58% of subjects still had better prism VA than predicted. Pardhan (1997) also studied the RL/CL ratio on some patients with AMD looking for gaze selection defects (a RL/CL ratio bigger than one

proves the existence of a gaze selection defect). The mean RL/CL ratio found in this study was 1.17. This ratio is much lower than the mean ratio reported by Harris et al. (1985) of 2.00. A possible explanation for their higher VA improvement could be that they did not control for the more easily seen letters on the edge of the cards, as these would lack the crowding effect expected on the test designed for this study. Pardham, (1997) also reported a higher mean RL/CL ratio of 1.71. Although this author crowded the letters on the edge of the card, the quite good VA of the patients in this study (the worst VA patient had a VA of 0.60 logMAR) suggests a quite recent onset of the condition and that therefore they might not have learnt to find and sustain a PRL for eccentric viewing. This finding compares with our patients having a longstanding condition resulting in a probable better adaptation to using a PRL, and thus, a smaller gaze-selection defect; in this study. The majority (68 %) of patients seemed to already be using a PRL.

Lesion and scotoma sizes

The lesion is the objective sign that can be seen when looking at the AMD patients' fundus and the scotoma would be the subjective symptom that patients get as a result from the damage. It is therefore expected a close association between these two variables. The areas of the scotomas were generally much larger than the size of the lesions by a median difference value between them of 71 degrees². A possible explanation for this could be that the photographs are probably not showing the full size of the lesion and a fluorescein angiogram might be needed to properly quantify the full size of the damage. Kim et al. (2003) also found that the size of the lesion when measured with optical coherence tomography was always smaller than when measured by fluorescein angiography, corroborating how a fluorescein angiogram can find a larger region of damage than other non-invasive methods. Another explanation could lie in the patient and clinician's reaction time. Labianca & Peli (1996) concluded that central scotoma size is exaggerated by kinetic perimetry when the technique was performed by moving the target from the central scotoma to the periphery of retina. When using the same technique, Timberlake et al. (1986) found that the area of the scotoma, as measured on the Bjerrum screen, was consistently smaller than that obtained on the SLO thus suggesting an even bigger discrepancy, which they proposed might have been a result of differences in stimulus velocity in the two techniques. In our case, the Bjerrum screen technique relies on a patient's reaction time when moving the target into the central scotoma, rather than from the scotoma to periphery of retina, a strategy that could therefore account for the smaller scotoma areas as compared to the lesion size.

The size of the central damage might be expected to be a direct cause of the VA loss in patients with AMD and one might expect that scotoma area/lesion size and VA would show an association. Hogg et al. (2003) found that atrophy measured on colour photography was a good predictor of visual function, being near visual acuity the most marked one. Similarly, Schuchard

et al. (1999) concluded that, as disease progresses, visual function generally declines and scotomas get bigger. Our findings showed that there was an association between the two variables and that scotoma area was a more significant predictor of distance VA than the lesion size, so that for every 100 degrees² of scotoma size, VA changed by 0.4 logMAR, or four lines on the ETDRS chart.

Relationship between PRL, NNPF and prescribed prism distance and direction

The PRL or pseudofovea is the new area of the retina where the patient with central visual loss fixates (Timberlake et al., 1987). Although using EV to re-fixate on a healthier area of retina sounds like a straightforward strategy that should give the patient an immediate visual benefit it carries certain disadvantages, such as a decrease of resolution (Whittaker et al., 1988) and a reduction in decoding information and fixation control abilities (Guez et al., 1993), which explains why the position of the PRL is chosen to be right on the edge of the scotoma (Fletcher et al., 1994). As expected, the PRL distance from fixation was a good predictor of visual acuity and fixation quality. Although this finding does not agree with Timberlake et al. (1987), who concluded that residual visual acuity cannot be predicted from fixation eccentricity and that fixation stability did not systematically relate to fixation locus eccentricity. The reason for their lack of association could be that they only assessed 3 patients and thus did not have enough data for statistical evaluation.

The position of the PRL was obtained while the patient was instructed to look at the tip of a fundus camera fixation rod, and calculated by means of measuring the distance between fovea and the tip of the fixation stick. Because this method is subject to several assumptions, the accuracy for determining the central fixation cases was compared with a subjective assessment of fixation on the avascular zone. The two methods appeared to be quite consistent for as many as 36% of patients when fixating centrally and thus, not using EV. It could be argued that the method of asking patients to fixate at the end of a fixation rod created an artificial and dark visual environment for the eye and therefore, the fixation under those circumstances might not necessarily be the same as the chosen one while patients perform a more natural task such as reading with daylight. However, although there is plenty literature supporting how the PRL location could vary depending on the performed task (Lei & Schuchard, 1997; Duret et al., 1999), once the new PRL becomes the new reference for oculomotor behaviour, the patient will not voluntarily attempt to use central fixation (White and Bedell, 1990). We could thus conclude that those 36% of cases fixating on the fovea would belong to patients who have not learnt to use EV, and thus the ones that could find more benefit from prism relocation. However, the large majority of patients (63%) were found to already be using a PRL on fixation, which would reduce the prism relocation chances of success.

It could be that even for those 63% of patients using a PRL they might not be using the most appropriate area of retina and might still benefit from prism relocation onto a new and better PRL that was not originally chosen. The lower (Timberlake et al., 1987; White & Bedell, 1990; Whittaker et al., 1991; Guez et al., 1993; Petre et al. 2000) and left (Sunnness et al., 1996; Fine & Rubin 1999) hemi-fields have previously been advocated for preferred chosen PRL locations. Our findings show that the preferred hemi-fields by patients when attempting to view the fixation stick eccentrically were the left and lower ones. The superior and right hemi-fields were, on the other hand, chosen by far less patients. These findings agree with those from previous literature advocating the superior and left hemi-fields.

The NNPF was calculated from the Bjerrum screen plots. This position should, in theory, predict the location of fovea that the patient might find of most use for EV, as it locates the nearest non-scotomatous point to fixation and that the area of retina that should offer best resolution and decoding information, and fixation control abilities (Whittaker et al., 1988; Guez et al., 1993). Our findings show that the NNPF is most often in the inferior and left hemi-fields suggesting that these areas offer the best chance of good vision, and that PRLs should be selected to make use of them. When we compare these findings with those from the chosen PRL locations, it looks as if the patients have successfully chosen the PRL at the predicted area of retina from the NNPF and therefore the left and inferior hemi-fields. This means that perhaps most patients are already choosing the correct PRL when eccentrically viewing and therefore, there is only a slight opportunity that prism relocation could find a better location for eccentric viewing than the one they seem to already be using.

Findings show that as many as 74% of patients had an angular difference of 60° or less between the NNPF and PRL angles, thus reiterating how the NNPF direction can assist with the prediction of the subjectively chosen PRL. However, there was no association between the distances of these two positions. This lack of association agrees with Labianca and Peli's (1996) findings. They proposed that since PRLs are usually on the edge of a central scotoma (Timberlake et al., 1987; Fletcher et al., 1994), if the central scotomas had been centered around the fovea, then the PRL eccentricity should increase as central scotoma size increases (and therefore NNPF). If the PRL distances were consistently larger than the NNPF distances we could still expect an association between the two variables. The fact that there is no association could be due to some patients not fixating on fovea when instructed to, while the Bjerrum test was performed, with the consequence of the NNPF distance measuring the distance from healthy retina to fixation, rather than to fovea. However, the lack of fixation control is expected to vary in patients, as some patients find it easier to relocate images than others (Nilsson, 1990). Our findings therefore suggest that the variability of decentration of the central scotomas could be a reason for the lack of association between the two distances, but still gives a reasonable

agreement of the two angular positions. Another reason that could account for this lack of association could be the fact that the PRL might not be chosen on the closest area of healthy retina to the fovea, due to other interfering factors such as need for a larger visual field than the offered in the NNPF. The median prism power prescribed for the better VA eyes had a power 8Δ , which is very similar to the median prism power required to relocate the image onto the subjectively chosen PRL (6.5Δ), but much bigger than the required to relocate onto the NNPF (3.5Δ), again suggesting that the prism is relocating to the already chosen PRL.

The fact that many patients have already chosen their own PRL location that has more chances to offer an improved function for rehabilitation purposes does not mean that this position is the optimal one. There is always a possibility that the area of retina that promises a better function for rehabilitation (NNPF) might be beaten by another area, that although not as close to fovea, might offer other advantages, such as a wider field of view. The technique used to prescribe prism in this study gives patients the chance to experience relocation at all directions, and thus included areas of retina that might not have been tested previously. The fact that the preferred position for image relocation was the inferior hemi-field, followed by the left, then the upper and finally the right hemi-fields supports the original NNPF findings of the inferior and left hemi-fields promising the better chances of rehabilitation. It can therefore be concluded that patients do successfully correct EV to the most promising area of retina, although it cannot be proved that using the NNPF for EV will guarantee an improvement on visual function. The fact that most patients already choose the correct NNPF for the PRL, limits the role of prisms, which would thus be restricted to avoiding problems from unnatural/uncomfortable head postures or gaze positions.

There is also the possibility that even when the prism succeeded in relocating the image to the optimum area of retina, the eye would make a recovery movement that would cancel the prism effect. This effect was originally suggested by Bailey (1983) and also observed by Woo et al. (1996), based on the response of normal subjects, but to date has not been shown to happen in patients with central visual loss. The study findings show that only a minority (18%) of patients made an eye movement that would cancel the prism effect, and interestingly, this movement was more than three times more common in patients with horizontal prism bases than with vertical bases. However, the higher prevalence of horizontal movement could be an artefact due to eyes making more horizontal than vertical fixation movements. Nevertheless, if the movement is genuine, it does suggest poorer success of prism with horizontal bases, since it would mean that the recovery eye-movement is impairing the prism from succeeding on relocating the image. This higher stability for vertical bases could explain the largely preferred prism base of 90° , and thus the inferior hemi-field against the right or left ones. Also, if the same horizontal instability happens with spontaneous eye movements that take the target off

fovea, patients might not be able to maintain a horizontal PRL and have a better chance of maintaining a vertical one. Finally, previous literature have proposed the importance of the lower field of vision for navigating as the reason why patients choose this area of retina for eccentric viewing (Petre et al., 2000).

The majority of prism bases chosen by the patients to relocate the image were on the lower and left hemi-fields, positions that had already been chosen by the patient for a PRL. This finding shows how the relocation therapy has failed to find a new area of retina that would improve visual function and that patients have already managed to find the optimal PRL on their own, without the help from the prism. If this is the case, the prisms would be of no benefit to the patient, and the disadvantages of the use of these lenses (aberrations, weight, dizziness) would certainly outweigh the limited chances of improvement. Also, the fairly small median value of PRL displacement needed to obtain the optimal position of eccentric viewing that we found would not be expected to create problems from unnatural head postures, again cancelling the need to use prism spectacles.

7.4 Predicting the prism

The primary aim of this study was to determine the effectiveness of prism spectacles as a method of relocating the retinal image in cases of AMD and as reported previously (see section 5.1) there was no significant effect of randomisation group on distance VA, our primary outcome measure. This finding is discussed in the second researcher's thesis (Smith, 2004) together with the fourth aim (to explore the extent to which prism spectacles may obviate the need for conventional LVA). This section is therefore going to concentrate on the discussion of the second (determination of the clinical characteristics of the patients who would benefit from prism spectacles) and third (investigation of the degree to which the optimal relocating prism can be predicted from clinical vision measures) aims of the study. Determining the clinical characteristics of the patients that would benefit from prism spectacles could be very useful for selecting the correct type of patients out of the population with AMD that would benefit from the prism relocation technique. However, since prisms didn't offer any benefit to the present study patients (Smith, 2004), investigating the type of patients that had a VA improvement over the three months of prism wear would clarify if the previously reported success in literature from this relocation technique is due to the type of patients recruited or to a placebo effect. Similarly, being able to predict the optimal prism for patients would save the clinician from having to go through the complicated and time-consuming prescription protocol but the fact that there was no outcome difference between the two treatment arms of the study (custom and standard prism) suggests no need to pursue a custom prism. Nonetheless, this investigation was

followed for further understanding of the factors influencing the selection of the prism and because data had been collected mainly for this purposes.

7.4.1 Determination of clinical characteristics of patients who would benefit from prism spectacles

Previous studies have selectively chosen the type of patients to whom they wanted to apply their prism relocation technique. Rosenberg et al. (1989) only prescribed prisms to those patients that demonstrated an improvement on the acuity task or by clinical impression. Verezen et al. (1996) excluded patients that had unrealistic expectations about the treatment or other ocular diseases and those that made a prism-induced repositioning eye movement on the presentation of the eccentric viewing prism. Similarly, Bertrand et al. (1997) only selected patients that had a stable condition over the last three months. It can therefore be said that there is an expectation that the treatment might be more effective on a certain type of patient than on others.

It has therefore been attempted to investigate if patients with some particular characteristics would benefit from the treatment more than others. The prediction of VA success was studied by means of simple and multiple regression and was defined by the visual acuity difference between that measured with the prism spectacles after three month wear and with the conventional spectacles at baseline.

All measured variables collected in the study that were thought to be possible predictors of success were tested as independent variables into the multiple regression. These included, distance VA, RL-CL VA, area of scotoma, NNPF distance, fixation quality, prism power, duration of the condition, eye-movement response to prism, type of AMD, patient's independence, type of spectacles and prescription. Some of these variables were investigated following suggestions from previous studies (these include VA, duration of the condition, eye-movement response to prism and type of AMD). The remaining of the variables studied, although they had not been proposed in previous literature, have been included because there was some rationale for which they might influence the success of the treatment. The fact that patients had not been selected following any particular criteria offered the opportunity to investigate any variables that were thought to have a possible influence on the success rate. This analysis may identify the factors that produced the much higher success rates in earlier studies.

Both single and multiple regression results showed no association between predictor variables and prism-conventional VA over the three months of prism wear (p3-c2VA). The best fitting model included conventional distance VA measured on first visit (c1VA) and type of AMD. P3-c2VA was estimated to increase by 0.08 logMAR (four letters on the ETDRS chart) per

logMAR unit of c1VA (10 lines) and by 0.06 (six letters on the ETDRS chart) for the dry type of AMD patients whilst there was no VA improvement associated with the wet type of AMD. This finding is not very surprising, as it is well known that the dry type of AMD is more stable over time, progressing more slowly than the wet type (Sunness et al., 1995). It is thus quite likely that any possible VA improvement obtained from the prism spectacles would get concealed by a progression of the condition over the three months of patient follow up. However, the proportion of patients with eccentric fixation was equal for both groups (dry and wet) outnumbering that of patients fixating on fovea by 4 times. This suggests that the amount of patients with central and eccentric fixation was well distributed among the wet and dry types of AMD and thus, the type of AMD would not be expected to have biased data.

Nevertheless, these two variables only explain a small proportion (5%) of the variance in prism success. This finding could be explained by the lack of prism success. It could be that the changes in VA that were measured as a result of the study were unrelated to the prisms, but due to spontaneous changes in PRL or to some patients making greater efforts on later visits. Also, the lack of prediction suggests that besides VA and type of AMD, the rest of the factors that might have been present in other studies, such as making a prism-induced repositioning eye movement, did not prove to make a significant influence on VA success. Therefore, all these findings indicate a large placebo effect in the previous prism relocating studies (Romayananda et al., 1982, Rosenberg et al., 1989, Verezen et al., 1996 and Bertrand et al., 1997). Finally, the lack of interaction between the variables expected to be affected by the treatment arm (PRL distance from fixation, eye recovery movement, type of lenses worn and prescription power) demonstrates a lack of prism effect.

7.4.2 Determination of the power and base direction of the optimal prism

With the aim of saving clinician's time to prescribe an adequate relocating prism, the prediction of prism base and power has been investigated. Previous prism relocation literature findings suggest an association between prescribed prism power and VA (Romayananda et al., 1982 and Verezen et al., 1996). Romayananda et al. (1982) also found an association between macular lesion and prism power. Rosenberg et al. (1989), Verezen et al. (1996) and Bertrand et al. (1997) prescribed their prisms based on the direction of patient's eccentric viewing which suggests that the PRL and NNPF could assist with the prescription of the optimal prism. However, these studies had very simple prescribing protocols and lacked enough data to investigate if the combination of all these variables could give a better prediction of the optimal prism than just a single variable. The associations between visual function variables (these

including distance and near VAs, contrast sensitivity, area of scotoma and PRL and NNPF distances) and optimal relocating prisms both individually and in combination have been investigated by means of simple and multiple regressions.

As expected, simple regression analyses showed that both distance and near VAs are significant predictors of prism power, so that prism power was estimated to increase by 0.47Δ per logMAR line, by 0.44Δ per M scale unit on the Bailey near vision chart, by -1.98Δ per logCS units and by 0.29Δ per 100 grid units of scotoma area and by 0.32Δ per NNPF distance degree. Although prism power increased by 0.12Δ per PRL distance degree, it was not a significant predictor for prism power. This finding is quite surprising as one might expect that the larger the scotoma size the higher the distance that the eye would need to move fixation and this should have been expected to be associated to the prism power needed to perform such a movement. However, the NNPF gave a significant association with prism power, thus was a better predictor than PRL of the optimal prism. The fact that the NNPF is a better predictor of prism power than the PRL could be due to the fact that a large number of scotomas were not centred around the fixation point on the Bjerrum screen. This finding could mean that patients have already learnt to use eccentric fixation and find it difficult to fixate back on the fovea when requested to do on the Bjerrum screen. In this case, they might be happy to continue to make part of the full relocation eye movement and the prism might only need to take account of the remaining area of scotoma that obstructs their vision. While the NNPF distance would be able to predict this power, the PRL distance, being measured from the fovea, rather than the fixation point, would not supply this information. This would result on the NNPF distance being a better predictor of prism power than the PRL distance.

When checking the association between variables for prism power prediction, multiple regression analyses showed that the best fitting model included distance VA ($\beta = 4.04$) and NNPF distance ($\beta = 0.19$) as predictors of prism power. It can therefore be concluded that visual functions play a large role in predicting the optimal prism power. However, this model only predicts the prism power for 21% of the variance and therefore does not make it powerful enough to substitute the role of the optometrist using the prescribing strategy used in the study to obtain the precise prism power.

Prediction of prism direction was also investigated by means of the two variables that have an angular value, those being the PRL and NNPF positions. When comparing the distribution of the angular differences between the prescribed prism base and both the PRL and NNPF positions both variables showed an association with the prism base, but the NNPF was again a better predictor than the PRL for the prism base direction. As many as 40% of cases had an angular difference of 30° or less between NNPF directions and prism bases compared to only

23% between PRL directions and prism bases. This means that patients preferred to relocate the image onto the NNPF rather than onto the chosen PRL.

7.5 The lack of prism effectiveness

The lack of a significant effect of randomisation group on distance VA, our primary outcome measure, or on any of the other outcome measures used in the study, has demonstrated the lack of effectiveness of prism spectacles. On an individual basis, only 10% of patients in the custom prism group obtained a VA improvement of ≥ 0.16 logMAR. The range of change of VA improvement with prism ranged from -0.42 to 0.46 logMAR with a mean of 0.00 logMAR for this group. This finding compares to Bertrand's mean improvement of 1.36 lines (they do not specify the scale used to measure VA) and with the higher success rates of 100% for Romayananda (1982), 91% for Rosenberg (1989) and 61% for Verezen, who do not specify what VA difference they rate for success.

Findings from this study showed that most patients (63%) have already learnt to use eccentric fixation and are successfully using a PRL. The fact that patients are already benefiting from eccentric viewing limits the chances of patient's visual improvement from prism relocation to only those cases where the chosen PRL might be improved by a different retinal location that could be found from the prescribing prism technique. However, as discussed earlier in this chapter, our findings show that patients seem to have selected a PRL on the areas or retina that were previously advocated by previous eccentric viewing studies (although it cannot be proved that they are the optimal ones for image relocation). It can therefore be concluded that patients have already learnt to use eccentric viewing and that the PRL selected is already the optimal one, leaving little chance of success for the prism relocation technique. The prisms therefore offer no advantage as an alternative way of relocating the image compared to simply using eccentric viewing.

The fact that only a minority of 18% of patients made a recovery eye movement that would cancel the effect of the prism has demonstrated that prisms do apparently successfully relocate the image to a new area of retina, but this recovery eye movement was only assessed short-term and could be that those cases with no immediate eye movement have a gradual drift over a period of days/weeks. Also, if patients were already successfully using an appropriate PRL, this recovery movement would imply that patient preferred the original PRL to the newly relocated area of retina. This recovery movement was more likely for the horizontal prism bases than for the vertical ones but because the majority of patients preferred a vertical base for prism relocation, any effect on prism relocation success could only be expected for that minority of horizontal cases.

Finally, the type of spectacle prescription and lenses could have also played a role in the effectiveness of the prisms (see appendix 13). Patients with high prescriptions could have experienced cancellation of the prism effect if they were not looking through the centre of the lenses as the prescribed prism effect could be cancelled when the prism power induced by the appropriate head movement is the same power and opposite base direction to the prescribed prism. For example, a myope wearing lenses with power of -5.00 dioptres would suffer from a base down effect when moving eyes down 1cm (20°) to read: a downcurve bifocal segment would induce even greater base down prism. Considering the median prescribed prism power was 8Δ it would cancel at least two thirds of the originally prescribed prism power and therefore decrease the effect of the prism and the chances of success. If this effect was significant, the clinician could expect some patients with AMD to report better/worse vision when turning the head/eyes to look through the edge of the lens, but there is no report in the literature describing such an effect.

Similarly, the risk of possible cancellation of the prism would be greatest for near vision in bifocals, since the wearer cannot avoid looking away from the optical centre of the main lens: in single vision lenses, the patient can always adjust head position to view near to the optical centre of the lenses. As the size and power of the bifocal segment increases, it produces a base down effect that would cancel a prescribed base up prism although this is only expected to happen on the round segments as for the C and D segments the optical centre is located on the same position as on the near point of vision. It is also possible that the single vision lens wearer may experience the same effects depending on the zone of the lens they choose to use (i.e., whether they drop their head or their eyes when reading). If the prescribed prism had been neutralised by the prismatic effect of the spectacles, it might be expected that the type of lenses worn would have been significant in the regression equation used to predict success with prism spectacles. In fact, the type of lens did not seem to be a factor in predicting success, but this may be because the effect is dependent on the prescription as well as the type of lens. This way, small prescriptions will induce smaller prismatic effects, and the prism may be increased for some patients rather than decreased, e.g. if the patient in the example above was a +5.00 hyperope.

7.6 Conclusions

The typical participant in the study was 81 years old, lived alone (53%) and had been diagnosed of AMD three years ago. The main goal from the low vision assessment was to be able to read and the most popular low vision aids were illuminated hand and stand magnifiers. Cataracts were very common (81%) and CS was reduced to a mean value of 1.05 logCS (range 0.05-1.65)

on the better eyes, explaining why lighting advice was very important among this population. The median scotoma area was 64 degrees² (range 0 to 1529) and the preferred positions for eccentric viewing were the inferior and left hemi-fields of vision at a median distance from fixation of 3.73 degrees (range 0 to 22.87) and had good fixation quality. The median prism power selected by patients was 8.0Δ (range 2 to 23) and the preferred prism base direction was at 90°.

Data collected in this study has proved that there was no significant difference between the three arms of the study (Smith, 2004), and therefore that patients do not find the prism relocation technique of benefit. This finding could be due to a number of factors. First, the majority of patients (63%) were already using a PRL, and for a large proportion of them, the relocation was subjectively chosen to be the same area of retina that was already being used as a PRL (as discussed on section 7.5). The fact that the prisms did not relocate the image onto a new area reduced the usefulness of the lenses to their possible role in avoiding problems from abnormal postural positions, which did not seem to outweigh the disadvantages of these lenses (weight, aberrations, distortions, dizziness, etc). Secondly, although they did seem to relocate onto what promised to be the ideal area of retina, or NNPF, there could be a better PRL that prisms did not successfully locate. However, finding a better location for the PRL that could give a better visual functional result seems to be a far from easy target to achieve, since repeated letter visual acuity failed to obtain a significantly better VA than that obtained from the prism VA (mean difference 0.04, sd 0.22). Furthermore, even when patients might be using a consistent optimal PRL for resolving letters they might not be able to perform dynamic tasks, such as reading, since this involves a fixation control of eye movements for the eye to move across the page from left to right with appropriate saccades and fixation pauses. Moreover, the PRL selected by the prism relocation technique might not have a large enough field to perform such dynamic tasks.

Most patients did not make a short-term eye recovery-movement (only 18% did), and thus move the image from the PRL, although it could be that over a longer period of time the eyes might adapt to the prism and thus cancel the relocation effect to go back to the original PRL. Also, the high rate of patients with wet AMD found in the study (71%) could have resulted on a high risk of VA deterioration over the three months of prism wear that could account for the lack of VA improvement (mean 0.00 logMAR, range -0.42 to 0.46) when wearing the prism spectacles on the last visit as compared to the VA with conventional spectacles on the second visit.

Finally, only a small proportion of variance in the optimal prism power for relocation (23%) is explained from the visual functions and the clinical characteristics measured in the study, suggesting that optimum prism prescribing needs to be undertaken by an optometrist with

objective feedback from the patient. It was also possible to make only minimal prediction (5%) of the visual acuity improvement that patients would obtain from the study spectacles after the 3-month wear, perhaps because the variation is due to fluctuations in vision unrelated to prism wear.

7.7 Future research

Prism relocation did not succeed in finding a PRL that would decrease a patient's disability. Given the scale of low vision problems and the limitation of medical treatments other relocation techniques such as eccentric viewing or steady eye strategy for dynamic tasks such as reading need to be investigated. Previous studies on eccentric viewing are as poor as the prism ones and the need for a proper randomised controlled trial to determine the effectiveness of this treatment should be carried. Training patients to use eccentric viewing is a difficult and time consuming task, and a study proving its usefulness would prevent practitioners' disappointment before they embark into the time-consuming method.

The large placebo effect found in the trial (Smith, 2004) reiterates the importance of including a control group in future clinical trials looking for possible treatments for AMD as the patients in this study have demonstrated to have a larger incentive to seek improvements.

The Bjerrum screen, although a very useful test to assess central scotomas in patients with AMD, is time consuming and requires experience. Fixation control also plays a big role. There is a need for a quicker, better fixation controller and simple technique that would not need so much practice to successfully define the specifications of the central scotomas and identify the PRLs. Although perimetry has progressed very quickly over the last 2 decades, priority has always been given to glaucoma detection and field losses due to neurological anomalies but there is no successful automated program to detect and quantify central scotomas that controls for fixation successfully. Scanning laser ophthalmoscopes seem to be acceptable for research purposes but are expensive, difficult to use and time consuming, which makes them impossible to use in clinical practice. Due to the expected increase in the population with AMD over the coming years, there is a need for an efficient technique that would compete with the Bjerrum screen in clinical practice.

APPENDIX 1

Mmblind scoring sheet (Reischies & Geiselmann, 1997)

			Max. score
	ORIENTATION		
What is today's date?	Year?	Season?	5()
	Date?	Day?	
	Month?		
Where are you now	Country?	Hospital?	5()
	County?	Floor?	
	Town?		

REGISTRATION

Ask the patient if you may test his/her memory. Name three objects (apple, tree and penny), one second to say each. Ask patient to repeat. Repeat until all three are learnt, maximum six trials, then abandon. Score how many of the three words were repeated correctly.

3()

ATTENTION AND CALCULATION

Ask the patient to count back from 100 by sevens, stop after 5 subtractions. If cannot/will not perform this task, ask to spell 'world' backwards. Score number of letters in correct position.

5()

(Correct answers: 93 86 79 72 65)

RECALL

Ask for the three objects given previously (apple, tree and penny)

3()

LANGUAGE

Ask the patient to repeat the following sentence:

'No ifs, ands or buts'

1()

APPENDIX 2

Patient contact letter with information sheet

**Academic Department of Ophthalmology
Manchester Royal Eye Hospital
Oxford Road
Manchester
M13 9WH
Tel. 0161 276 5614**

Dear _____,

Your consultant contacted us recently to send you an appointment to attend the low vision clinic at the Eye Hospital. We believe you have attended for this appointment and may have been loaned some low vision devices, such as magnifiers.

The purpose of this letter is to ask you if you would consider taking part in a study about Prism Spectacles which is being carried out jointly by Manchester Royal Eye Hospital and the Department of Optometry and Neuroscience at UMIST. You are under no obligation to take part in the study and your clinical care at the Eye Hospital will not be affected in any way should you decide not to take part.

Please read the enclosed information carefully so that you can decide whether or not you would like to take part.

Yours sincerely

Isabel Cacho
Research Officer (Low Vision)

INFORMATION SHEET FOR PATIENT

Project: The Effectiveness of Prism Spectacles in Age-related Macular Degeneration

Supported by PPP Healthcare Trust.

Research Team:

Dr Harper, Mr Bishop and Isabel Cacho (Research officer):
Manchester Royal Eye Hospital, Oxford Road, Manchester,
M13 9WH

Dr Dickinson and Heather Smith (Research Officer):
Department of Optometry and Neuroscience, UMIST, PO
Box 88, Manchester, M60 1QD

You will already have attended the low vision clinic for an initial assessment of your vision by an optometrist. You may already have been loaned one or more aids, which we hope are useful. We are now asking if you would like to volunteer for a study on prism spectacles.

What is the purpose of the study?

The aim of the study is to find out whether patients who suffer from age-related macular degeneration would benefit from the use of Prism Spectacles, in addition to or instead of their conventional spectacles and/or magnifying devices. To do this we need to ask patients to use conventional magnifying devices and spectacles at home over a period of 1 month, keeping careful record of how much the devices are used, how useful they are, and whether they cause any difficulties. The patient would then be given Prism Spectacles in addition, and would be asked to use them as much as possible for the next 3 months, in order to compare them to the conventional devices.

What are Prism Spectacles?

In age-related macular degeneration, the central part of the vision is lost or distorted, but the peripheral vision is still good. The Prism Spectacles are designed to make use of this peripheral vision, and so improve performance for both long-distance and close-up vision. They appear similar to normal spectacles, but the lenses will be slightly thicker and heavier than usual. In order to find the best way to prescribe Prism Spectacles, we will give each patient spectacles which will include a different amount of prism. This means that some spectacles are likely to be more effective than others. If at the end of the study we find that your spectacles did not have the best amount of prism in them, we will make you a different pair of spectacles to try.

What will I have to do if I take part?

Your participation in the study will last for about 4 months and will involve 1 visit to the Manchester Royal Eye Hospital and 2 visits to the Department of Optometry and Neuroscience at UMIST.

Isabel Cacho, Optometrist and Research Officer, will see you at the Manchester Royal Eye Hospital. She will test your vision, update your glasses if necessary and prescribe the Prism Spectacles. She will also check that you have the right devices and are using them correctly. Any other devices that might be of benefit will be loaned to you.

After 1 month of using the conventional devices you will be asked to attend the Department of Optometry and Neuroscience at UMIST to have your Prism Spectacles fitted. During your visit to UMIST the Research Psychologist, Heather Smith will test your performance on some visual tasks, and ask you some questions. You will then take home your Prism Spectacles and use these in addition to your conventional devices for the next 3 months.

During your participation in the study you will be telephoned twice by Heather, who will check on your progress, answer any queries, and encourage you to keep a diary about your devices and Prism Spectacles. Heather will also telephone you two more times (towards the end of the first month and towards the end of the third month) to ask some questions relating to your vision.

At the end of 3 months you will return to the Department of Optometry and Neuroscience at UMIST to repeat the same tests and answer the same questions that you did in your previous visit to UMIST. Your spectacles and aids will also be updated as required. There will be no charge for the Prism Spectacles, and you will be able to keep them at the end of the study if you wish.

What risks are involved in taking part in the research study?

There are no risks to your health from taking part in the study.

What will happen to all the information about my eye health and vision?

Personal information will be kept confidential.

Am I entitled to any travel costs to attend for appointments?

Your normal visits to the MREH low vision clinic form part of the standard low vision care at this hospital and travel costs cannot be reimbursed for these, but we will pay your travel expenses for any additional visits to UMIST that are necessary for the study.

What will happen if I decide not to take part in the research study?

You do not have to take part in the study if you do not wish to. We will see you in the low vision clinic as planned and

your management at the Eye Hospital will continue in the normal way. Similarly, if you change your mind about taking part, you have the right to leave the study at any stage without this affecting your management at the Eye Hospital.

What should I do if I want to know more about the research study?

You are welcome to ask any questions you like about the study at any stage. You can contact us if you wish, by telephoning Isabel Cacho on 0161 276 5614.

What will happen next?

Isabel will contact you within 2 weeks. She can answer any questions and you can let her know if you are interested in taking part.

Whatever you decide, an appointment will then be arranged for you in the low vision clinic at MREH. You will be assessed for conventional devices, even if you decide you do not want to go on to have the Prism Spectacles.

Thank you very much for considering taking part in our research. Please discuss this information with your family, friends or GP if you wish.

APPENDIX 3

Patient consent form

Title of Study: The Effectiveness of Prism Spectacles in Age-related Macular Degeneration

Hospital/Institution:

Manchester Royal Eye Hospital, Oxford Road, Manchester, M13 9WH and

Department of Optometry and Neuroscience, UMIST, PO Box 88, Manchester, M60 1QD

Subject's surname:.....

Other names:.....

Date of Birth:.....

Sex: (please tick) Male Female

Age:.....

Name of Investigator: Isabel Cacho

Manchester Royal Eye Hospital Tel: 0161 276 5614

The study involves the objective assessment of the effectiveness of prism spectacles in improving the vision of patients with age-related macular degeneration. The prism spectacles are compared to conventional spectacles and low vision aids by a range of clinical and "real-life" visual performance measures.

I confirm that I have explained the clinical trial and supplied the subject with an information sheet, which in my judgement is suited to the understanding of the subject.

Signature:.....Date...../...../.....

PATIENT

(This part to be completed by the patient)

1. Please read this form very carefully.
2. If there is anything that you don't understand about the information sheet or you wish to ask any questions, please speak to the investigator named on this form.
3. Please check that all the information on the form is correct. If it is and you understand the explanation then sign the form below.

YES I have been given a verbal and written explanation of the study by the investigator named on this form. It includes my rights as a patient and what is to be done to me. I have been given the opportunity to ask questions.

YES I have had enough time to think about the study, talk to relatives and friends about it and to decide without pressure if I want to take part.

YES I understand the decision is up to me and that I can change my mind without it affecting how I am treated in the future.

YES I have been assured that all information collected in the study will be held in confidence.

YES I agree that the researcher may withdraw me from the study in the interests of my health or welfare.

YES I therefore agree that I will take part in this study.

Signed:.....Date:...../...../.....

APPENDIX 4
Patient last visit letter

UMIST Low Vision Clinic
Dept. of optometry and neuroscience
UMIST
PO Box 88
Manchester
M60 1QD

Manchester Royal
Eye Hospital
Oxford Road
Manchester
M13 9WH

Dear

Thank you very much for taking part in the prism relocation study. Your participation in this study is very important to us and we would like to thank you for your co-operation.

Today you have attended the last of your three visits and have completed the study. You are now welcome to keep your prisms glasses we have provided for you if you find them useful. Within the next 2 years we aim to find out the most useful lens out of those in our study. If we find that the prism lens you have been wearing is not the effective one overall, we'll be happy to supply you with new lenses at the end of the study, to ensure that you have this improvement.

From today onwards you can continue your visits to the hospital's low vision clinic as normal. If you would like to make an appointment, please, telephone this number: 0161 276 5535 as and when necessary.

Thank you once again for your valuable co-operation.

APPENDIX 5

The orientation of the gap on Landolt-C optotypes

Schrauf & Stern (2001) found that the percentage of correct answers was significantly lower when the gap of the Landolt-C was at 6 o'clock (they called this effect the 'gap-down' effect) on ocular disease-free normal sighted subjects. A pilot study was carried out with the aim to investigate if there is such effect in the Landolt-C test that was to be carried on the study patients.

Twelve disease-free normally sighted subjects were assessed on the single letter test monocularly to test if there is a 'gap-down' effect. The sizes of the letters were a minimum of 10 pixels height and width, rising in multiples of 10 to a size of 100 pixels. Altering the patient-screen's distance from 28, 57, 124, 228 or 456 cm as necessary also changed the size of the letters. The combination of these letter sizes and testing distances gave a large range of visual acuities between 6/2 (-0.48 logMAR) and 6/360 (1.78 logMAR).

This test was performed under 5 different conditions for every subject in both eyes and the lenses were calculated for every subject to reach the same VA levels:

1. Conventional Rx: Corrected with the optimal distance vision prescription (VA).
2. Blurring grade 1: Over the optimal distance prescription a blurring lens of +1.00, creating a mild VA impairment (BL).
3. Fogging grade 2: Over the optimal distance prescription a semi-translucent lens that would create a quite significant contrast sensitivity loss (about 0.75 logCS) (AM).
4. Fogging grade 1: Over the optimal distance prescription a semi-translucent lens that would decrease the contrast sensitivity to a level that would cause the same visual acuity impairment than that caused on blurring grade 1 (FO).
5. Blurring grade 2: Over the optimal distance prescription a positive lens with a power that would decrease VA to the same level as on fogging grade 2 (BR).

Vision and contrast sensitivity were thus as closely adjusted as possible for conditions 4 and 5 so that to match the VA of conditions 2 and 3 respectively. However, it could not be guaranteed that the two grades of conditions succeeded on producing the same VA impairment for fogging and blurring.

If there was a gap-down effect to be found by testing the 5 different conditions we would be able to find out if this effect increases with blurriness or contrast sensitivity because the patients taking part in this study would be expected to suffer from some degree of contrast sensitivity and acuity reduction.

Five Landolt-C letters for each of the 4 gap positions were shown to the subjects (up, down, right and left) and presented with random gap positions at an easily discriminated size, which was decreased to smaller sizes until the critical size was found. The critical Landolt-C discriminated would be the smallest size at which a minimum of 3 out of the five presentations were correct. This way, four different threshold Landolt-C sizes were obtained for every of the 5 conditions.

Results:

Results for the four gap positions were compared by means of calculating ‘adjusted’ standard errors and confidence intervals, taking account of the fact that the observations occur within subjects and thus might not be independent. Using linear regression models allows the effects for differences to be estimated more easily.

When an arbitrary position (up) was chosen as a baseline against which the other three positions (down, right and left) are compared to, the down position was not found to differ from the baseline ($p=0.513$) and the right and left positions differed significantly from the baseline. Also, both their coefficients were similar (-0.14 logMAR) (see table A5.1). This justified collapsing gap position into a binary variable, i.e. vertical or horizontal for the following analyses. The fact that the coefficient for the horizontal positions was negative indicates that these have a better resolution than the vertical positions.

Gap position compared	Coefficient	p	95% CI
Baseline (Up)	-0.25 (constant)	0.015	-0.44 to 0.06
Down	-0.04	0.513	-0.17 to 0.09
Right	-0.14	0.006	-0.23 to -0.05
Left	-0.14	0.005	-0.22 to -0.05

Table A5.1: Regression parameters for down, right and left positions when compared against up position as the baseline condition.

The effect of gap position under normal conditions was firstly analysed. There was no grade or type of lens variable, and R/L eye didn’t make any difference. The regression table A5.2 shows that gap position does not have any effect when vision was not blurred or fogged; this finding was the same irrespective of whether the data were pooled for up/down or right/left (coefficients for different positions were within about 1 logMAR letter of each other).

When the five different conditions were investigated by mean of the binary variable, as expected, there was a highly significant main effect of grade, so that the ‘severe’ grade made VA almost 5 lines logMAR worse (coefficient = 0.48) than the less severe grade. There was also a borderline main effect of type of lens ($p=0.059$), with fogging being worse than blurring (coefficient = 0.08) (Table A5.3).

Gap position compared	Coefficient	p	95% CI
Baseline (up)	-0.08 (constant)	0.009	-0.14 to -0.02
Down	-0.02	0.500	-0.09 to 0.04
Right	-0.03	0.279	-0.08 to 0.03
Left	-0.01	0.766	-0.09 to 0.07

Table A5.2: Regression results for down, right and left positions when compared against up position under normal conditions.

Condition	Coefficient	p	95% CI
Baseline (grade 1, blurring, vertical)	-0.27 (constant)	0.094	-0.48 to -0.06
Grade 2	0.48	0.000	0.36 to 0.59
Fogging	0.08	0.059	-0.00 to 0.15
Interaction: grade/type lens	-0.08	0.052	-0.16 to 0.00
Horizontal	-0.12	0.005	-0.19 to -0.04
Interaction: position/type lens	0.06	0.008	0.02 to 0.09

Table A5.3: Regression results when the baseline condition consists of grade1, blurring and vertical gap position.

However, both of these main effects needed to be interpreted also taking into account the borderline interaction between grade and type of lens ($p=0.052$); the coefficient for the interaction, which represented the less severe grade of fogging, implied that fogging was only worse for the less severe grade (by 0.08 logMAR, see table A5.3), and that the results for the two conditions converged for the more severe grade (i.e. +0.08, the main effect, -0.08, the coefficient for the interaction = 0.059).

Then, there was a main effect of vertical versus horizontal (combining up/down and right/left observations; coefficient = -0.12 for horizontal, i.e. horizontal is better than vertical by this amount). But there was also a gap position by type of lens interaction (coefficient = 0.06, $p=0.008$), which indicated that the difference between vertical and horizontal positions was -0.12 (Table A5.3) for blurred conditions but only about half this size (i.e. -0.12 + 0.06) for fogging lenses.

The two above-mentioned interactions can be observed on Figure 5.1. The graph could be considered as four pairs of adjacent bars, each pair made up of blurring and fogging lenses. If we consider the first and second pairs together, and the third and fourth pairs together, the differences between horizontal and vertical positions were smaller for the third and fourth pairs than for the first and second pairs. Therefore, the effect of vertical/horizontal position differed according to the grade, i.e. there was “an interaction of position and type of lens”. Similarly, if we now consider the first and third pairs, and the second and fourth pairs, and imagine the average of each pair of bars, there was a difference in the overall performance between blurring and fogging lenses in grade-1, but less so between blurred and fogging lenses in grade-2. So, the effect of type of lens was not consistent for the two grades and thus there was “an interaction of

type of lens and grade". However, because there was no guarantee that the difference between grade-1 to grade-2 blurring wasn't exactly the same as the difference between grade-1 and grade-2 fogging, this interaction was not very important.

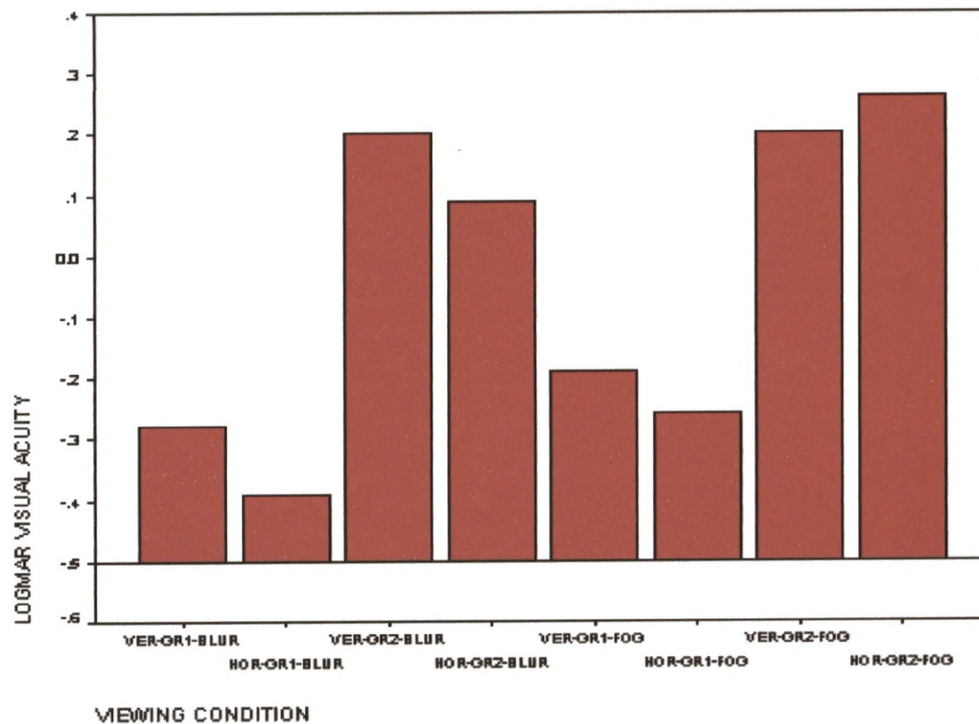


Figure A5.1: *Distribution of the mean VAs for the 8 viewing conditions.*

Conclusions:

Although Schrauf & Stern (2001) found that the percentage of correct answers was significantly lowest when the gap of the Landolt-C was at 6 o'clock, this small study has demonstrated that for normal subjects, when Landolt-Cs were displayed on a monitor with the gap randomly presented at the four cardinal positions there was no position effect when subjects were wearing the optimal refraction correction. However, when subjects were blurred with plus lenses or fogged with lenses that decreased the CS, the horizontal gap positions were seen better (3 letters of mean VA improvement) than the vertical ones, this effect being twice as strong for the blurred conditions than for the fogged ones.

As expected, when the same presentations were displayed, but this time with two different grades of blurriness/fogginess the severe grade made VA almost 5 lines logMAR worse than the less severe grade and fogging being worse than blurring. Interactions between grade and type of lens showed that fogging was only worse for the less severe grade and that the results for the two conditions converge for the more severe grade. However, this interaction was not very important because there was no guarantee that the difference between the two grades of blurring was not exactly the same as the difference between the two grades of fogging.

APPENDIX 6

Field test (Pilot testing)

The aim of this initial pilot study was to determine a method that could both quantify the area of the central scotoma for statistical analysis, and also identify the area of nearest non-scotomatous point to fixation (NNPF). It was felt that the latter might be closely associated to the relocating prism power and base direction prescribed, and perhaps give an appropriate initial estimate to provide a starting point for the prescribing of the relocating prism. A static perimeter (Humphrey Visual Field Analyser (HVFA) Model 670) and a kinetic method (Bjerrum screen at 1m) were compared in order to decide which of these methods was more appropriate for the above-mentioned aims. The disadvantage of the kinetic method is that it is difficult to quantify the results with a single value. HVA is, on the other hand, easier to quantify due to its static technique (easy to count missed stimuli) but patients find it difficult to fixate even with the special diamond provided for those with a central scotoma. Finding the blind spot prior to the test is also a quite difficult task in these patients, since the instrument assumes a position for it that may not be accurate if there is eccentric viewing. In the case of the Bjerrum screen, any shift in blind spot position is easily plotted as the examiner can adjust the target location as required. The two methods were compared on 2 normally sighted subjects with a simulated impairment of central vision and then on 18 AMD patients.

Testing low vision patients using the Bjerrum screen requires very few modifications to the standard technique. In order to make fixation easier for patients, a large fixation cross extending across the full screen was used.

The standard programs of the HVFA present stimuli well spaced in the central region, and thus insufficient points are sampled to be able to clearly define and quantify the scotoma. A customised program for the HVFA was therefore designed to test the central 10° of retina⁹ with much more detail than the region between 10° to 20° degrees away from fixation. This program had 99 stimulus presentations concentrating mainly on the central 20°, aiming to identify the closest non-scotomatous region to the fovea. Because this area is most relevant in testing the shape and size of the central scotoma, the program was designed so that the space between stimuli for the central 6° had a 2° separation, changing to 3° separations for the area between 6° and 9° away from fixation. Also, a further 16 stimuli were positioned at 16° from fixation. Also, 16 more stimuli were presented in areas between the fixation targets used, ie. 2 stimuli in between each spoke (see figures A6.2 and 6.3) at 22° and 28° from fixation. Finally, 6 more

⁹ For consistency, the areas of retina and scotomas referred to have always been specified as radial distances from fixation in degrees.

stimuli were presented in the area of the physiological blind spot to control fixation (Figure A6.1).

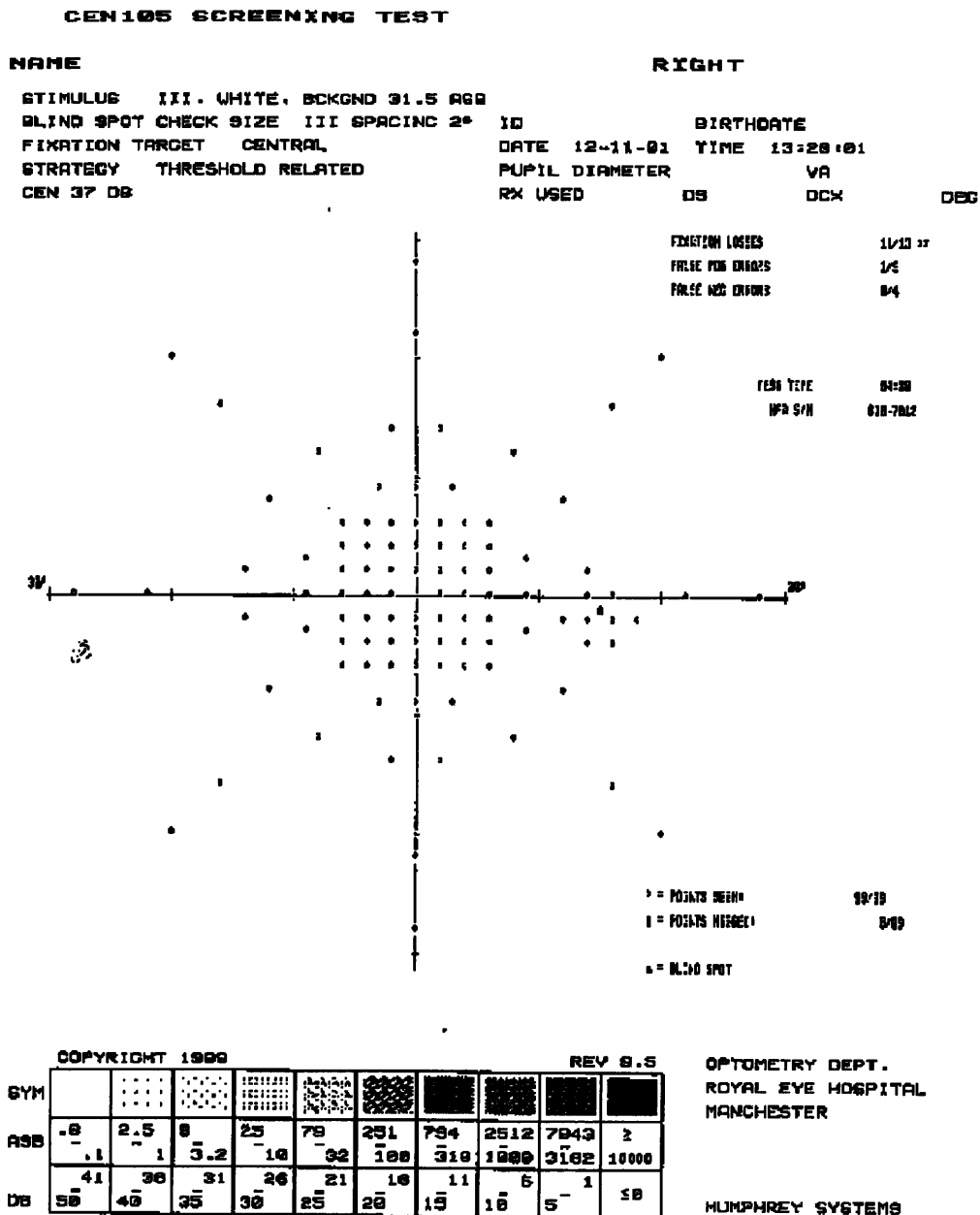


Figure A6.1: Location of the 99 stimuli of the customised program for the HVFA.

The static technique of the HVFA gave the option of threshold or suprathreshold programs. Determining the threshold at every point in the field obviously gives more complete information, but takes much longer. The suprathreshold program also requires a threshold measurement to be taken in the centre in order to set a suitable suprathreshold level for the remaining points. Due to the location where the threshold is tested (inside the central 9 degrees)

this area is not visible for most patients with a central scotoma. This difficulty was avoided for low-vision patients by using the normal age-matched values with the HVFA.

An attempt was also made to improve the patient's fixation by trying different fixation targets, i.e. a large cross, and radial spokes, as suggested by Mackeben & Colebrander (1994) on the HVFA screen. The colour of the radial spokes was black to maximise the contrast with the white background. Since the viewing distance of the HVFA is 30 cm, and the size of the test field is 30°, the equivalent size for the spokes to match the angular size and location of the spokes used by Mackeben & Colebrander (1994), was 12 cm in length, with a maximum width of 1.2 cm and with a triangular shape. A blank circle of diameter 5.3 cm (5°) was present in the centre (see Figure A6.2).

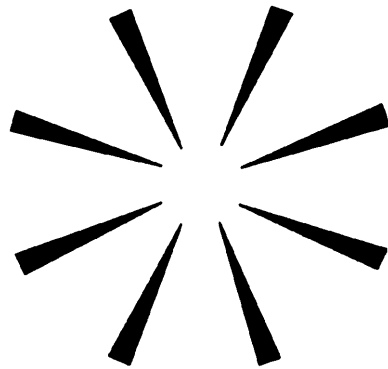


Figure A6.2: *Triangular spokes*

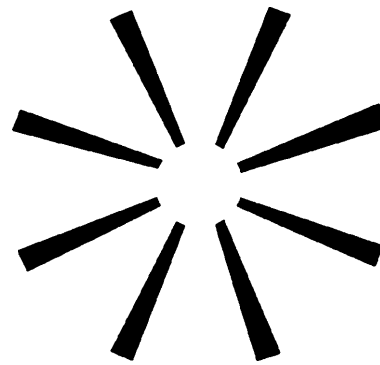


Figure A6.3: *Squared spokes*

Instead of leaving the blank circle in the middle, the spokes could also be extended to the centre of the screen and then cut at the 5.3 cm distance from the centre so that to have a squared, rather than triangular shape. These new spokes would have a maximum width of 10mm, narrowing to 3mm near the centre. This small modification to Mackeben and Colebrander's target gave the powerful illusion of a circle at 10° from fixation that could help the patient to fixate (see Figure A6.3), although this illusion might only happen for normally sighted patients. The two different types of spokes were tested in two normally sighted patients with central visual loss simulation and the effect of different number of spokes was also evaluated on threshold and suprathreshold programs. The most appropriate program, fixation target and amount of spokes for measurement of central scotoma was evaluated in 2 normals with simulated scotoma and then tested in 18 AMD patients.

METHODS IN NORMALS WITH SIMULATED SCOTOMA

On the HVFA, an absolute positive central scotoma was simulated using a cloth circle of various sizes. Two different sizes of black cloth circles were used to represent different sizes of central scotoma, these being 5° and 10° in diameter. 16 different combinations of fixation

targets, simulated scotomas, and suprathreshold or threshold programs were tried on 2 normal patients (see Table A6.1 for combination of circles and spokes):

1. Suprathreshold program with conventional fixation target (a small light straight ahead of the patient in the centre of the screen) to establish the correct sensitivity.
2. Full threshold program with conventional fixation target to establish normal sensitivity map for the patient.
3. Suprathreshold program with simulated scotoma of 10° and two radial spokes at an angle of 180° from each other and at an angle of 22.5° from the vertical axis.
4. Full threshold program with the same circle and spokes as in 3.
5. Suprathreshold program with simulated scotoma of 5° and same spokes as in 3.
6. Suprathreshold program with simulated scotoma of 10° and 2 squared spokes in the same position as in 3.
7. Suprathreshold program with simulated scotoma of 5° and same spokes as in 6.
8. Full threshold program with simulated scotoma of 5° and same spokes as in 6.
9. Suprathreshold program with simulated scotoma of 10° and four radial spokes all at 22.5° from the vertical axis.
10. Suprathreshold program with simulated scotoma of 5° and same spokes as in 9.
11. Suprathreshold program with simulated scotoma of 10° and four squared spokes in the same position as in 9.
12. Suprathreshold program with simulated scotoma of 5° and same spokes as in 11
13. Suprathreshold program with simulated scotoma of 10° and 8 radial spokes, all separated 45° from each other and at an angle of 22.5° from the vertical and horizontal axis.
14. Suprathreshold program with simulated scotoma of 5° and same spokes as in 13.
15. Suprathreshold program with simulated scotoma of 10° and 8 squared spokes in the same positions as in 13.
16. Suprathreshold program with simulated scotoma of 5° and same spokes as in 15.

In order to find the correct threshold for the normal patients in the presence of a simulated scotoma, the program was left to run the threshold part without the black circle. The program was then be paused and the first black circle placed on the centre of the screen. As the rest of the program ran, all the lights falling on the black circle were invisible to the patient and thus simulated an absolute scotoma.

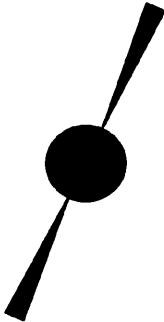
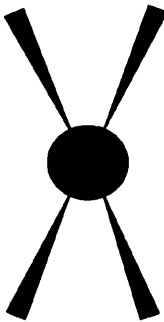
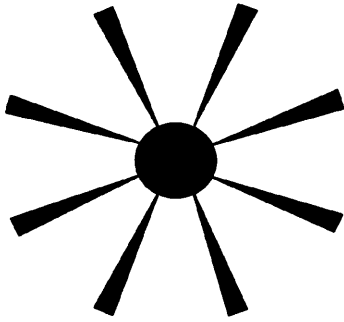
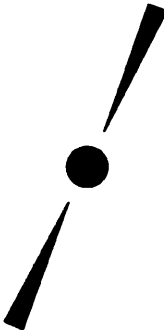
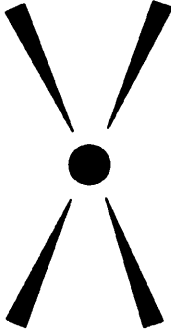
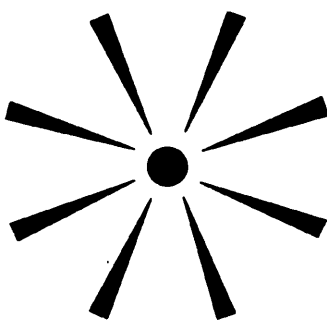
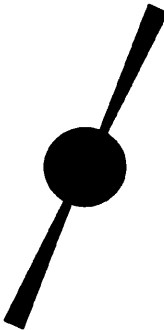
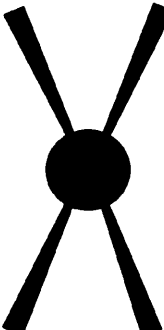
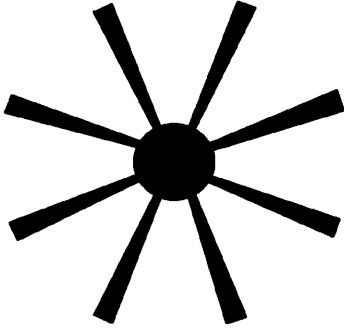
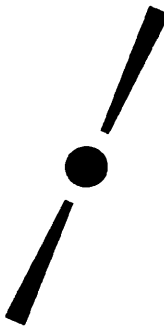
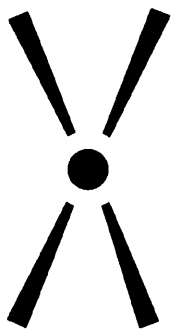
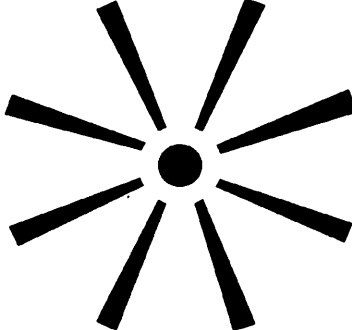
	2 Spokes	4 Spokes	8 Spokes
10° Circle Radial Spoke			
5° Circle Squared Spoke			
10° Circle Radial Spoke			
5° Circle Squared Spoke			

Table A6.1: All combinations of spokes and scotomas used in normals with simulated scotoma.

For the HVFA, the effectiveness of the different fixation targets was assessed on the 2 normal subjects with simulated central scotomas using “fixation losses”, “false positive” and “false negative” values supplied on the printout. The 2 subjects were 26 and 28 years old and were wearing their distance vision prescription. Approximately 15 targets were presented to determine each of the values by the following criteria:

1. In the blind spot area: any seen stimuli by the observer on this area were assumed to arise because fixation had changed and were therefore counted as fixation losses.
2. At an intensity below threshold, any seen stimuli were counted as false positives.
3. At supra-threshold intensity in areas in which targets had previously been identified, any stimuli not subsequently seen were counted as false negatives.

The time taken for each of the plots in the presence of a simulated central scotoma was also determined.

RESULTS AND CONCLUSIONS IN NORMALS WITH SIMULATED SCOTOMA

Testing time for threshold and suprathreshold programs were compared. The average time for a threshold program on the normal subjects with simulated scotoma was 20 min and only 6 min for the suprathreshold program. This implies that carrying a threshold test on a patient will take more than 3 times longer than a suprathreshold program. To save time and to avoid tiredness, suprathreshold programs were chosen for later examinations in the AMD patients.

Combination number	FP (%)	FN (%)	FL (%)	Testing time (min)	FP (%)	FN (%)	FL (%)	Testing Time (min)
Patient: JS					Patient: IC			
1	0	0	0	5	0	0	0	5
2	25	7	4	15	0	0	4	17
3	11	17	38	7	0	17	0	8
4	6	0	0	24	0	5	18	23
5	0	0	0	5	0	0	0	6
6	11	50	18	7	0	20	13	7
7	0	0	15	5	0	0	8	6
8	16	5	47	23	0	0	0	19
9	0	43	18	8	0	0	18	7
10	22	0	0	6	0	0	17	5
11	11	43	17	8	0	50	0	8
12	11	0	0	5	0	20	0	6
13	22	67	22	7	0	0	0	7
14	0	0	14	5	0	0	15	6
15	22	50	6	8	11	50	0	8
16	11	0	15	5	11	0	54	5

Table A6.1: False positive, false negative, fixation losses and testing times obtained for the 16 combinations of fixation targets, simulated scotomas, and suprathreshold or threshold programs.

There was no systematic difference in the amount of false positives (FP), false negatives (FN) and fixation losses (FL) on the outcomes of the two normally sighted patients when trying to fixate at the centre of the screen with all different combinations of spokes (see table A6.1). Taking combination “1” and “2” as gold standard, there were no systematic changes after adding the scotomas and fixation targets. This could imply that the normal subjects did not use the spokes to act as fixation targets but used the centre of the black “simulated scotoma” circle instead. It was therefore decided to use the target that had more information to assist patient’s fixation, i.e. the eight squared spokes.

METHODS IN AMD PATIENTS: STATIC AND KINETIC PERIMETRY

The HVFA and the Bjerrum screen were used to compare kinetic and static techniques of perimetry in 18 AMD patients.

Bjerrum screen: This test was carried out on 18 AMD patients. A white tape was used to mark two long lines across the screen. These two lines were perpendicular to each other and at an angle of 45° from the horizontal and vertical axis. This cross was used as a big fixation target. Patients were instructed to look straight-ahead at the centre of the cross, even if it looked distorted or appeared to be missing. Patients were also asked not to change fixation from that position.

The test was carried out by moving the target from the periphery towards the centre of the screen, starting at a position where the stimulus could be seen. As the target approached the area of the central scotoma it eventually disappeared. A black pin was then placed in the point where the target disappeared. By repeating this procedure for all the radial lines (24 with 15° angle between them), the shape of the scotoma could be determined.

The position of the physiological blind spot could be determined periodically in order to check that the patient keeps on fixating on the centre. Once the first few pins had been placed on the chart these were also used to control the patient’s fixation. If the patient moved fixation, the point where those pins originally disappeared changed. This was used to demonstrate to the patient that he/she was losing concentration and if explained properly it could help the patient understand better what he/she was doing.

Two different target sizes were tried: 4mm and 10mm. The 10mm target size could be misleading since it would make the size of the relative scotoma appear smaller than it really was. The smaller target gave a more accurate location of the isopters. Most patients were able to perform the test with the smaller target as well as with the large one, although some with very large scotomas could only detect the larger target. The smaller target was therefore selected as default and changed for the larger one if patients failed to see it.

Subject	FP (%)	FN (%)	FL (%)	Testing time (min)	FP (%)	FN (%)	FL (%)	Testing time (min)
Cross					Squared spokes			
HF	0	0	69	10	0	14	65	9
	0	20	29	6	11	0	13	7
PF	11	0	54	0	40	60	6	0
	11	25	8	0	0	19	6	0
AC	11	20	88	7	0	0	32	7
	0	33	1	10	0	17	93	8
DJ	0	0	0	7	0	0	5	8
	0	0	0	7	0	0	0	8
Mean values	4.1	9.6	31.1	7.4	1.4	8.9	35.9	7.4
MH	0	67	86	8				
	0	40	24	7				
BQ	0	0	0	7				
	0	0	13	7				
FB	0	25	17	9				
	0	17	36	8				
RR	0	33	13	6				
	0	0	27	7				
LN	0	0	75	5				
	0	33	36	6				
BM	0	0	21	6				
	0	0	79	7				
ML	0	1	0	7				
	0	67	22	7				
JS	0	17	88	6				
	11	20	80	7				
SL	11	40	21	6				
	0	0	93	7				
MT	0	20	0	7				
	0	33	35	9				
CS	0	40	93	8				
	0	0	79	8				
HW	0	0	93	9				
	0	20	67	10				
VT	0	0	1	7				
	0	20	1	8				
Total mean values	14	20	49	7				

Table A6.2: False positive, false negative, fixation losses and testing times obtained for the 16 AMD subjects with the fixation cross and for 4 AMD subjects with the squared spokes on right and left eyes (top and bottom figures for each subject respectively).

HVFA: Two fixation targets were first tested tested four of the AMD subjects to decide on an appropriate fixation target:

1. The 8 squared spokes from the pilot test on normally-sighted individuals with a simulated central scotoma (Figure A6.3). The customised program with 99 stimuli described above (Figure A6.1) was used with this fixation target.

2. A simple large cross with the two crossing lines perpendicular and at 45° to the horizontal line, which had been used previously in Bjerrum screen plotting for AMD patients. The width of the lines for the cross was 3mm, which was the width of the previously-tested spokes at their narrowest end (see Figure A6.4). A second customised program with the same stimulus density on the central 9 degrees, as on the 99 stimuli program, but with the target positions slightly changed to move out of the areas where the two lines comprising the large cross were positioned. The amount and eccentricity of the stimuli at 16°, 22°, and 28° were also slightly rotated, again to avoid the area where the black cross was positioned. The total number of stimuli for this second program was 88 (Figure A6.5).

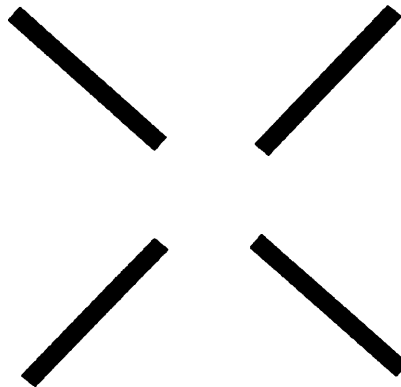


Figure A6.4: *Target cross.*

The subjective impression from the four AMD subjects was that the two targets were equally efficient to assist with fixation. The findings from the test (Table A6.2) show less fixation losses for the cross (mean value 31.1) than for the squared spokes (mean value 35.9). However, the cross seemed to give a higher amount of false positives and negatives (4.1 and 9.6 respectively) than the squared spokes (1.4 and 8.9 respectively). There was therefore no clear benefit from one particular stimulus. The cross stimulus was selected to perform the static perimetry on the remaining 12 AMD subjects, since it was a very similar stimulus to the cross used on the Bjerrum screen and thus give comparable fixation conditions for the two techniques.

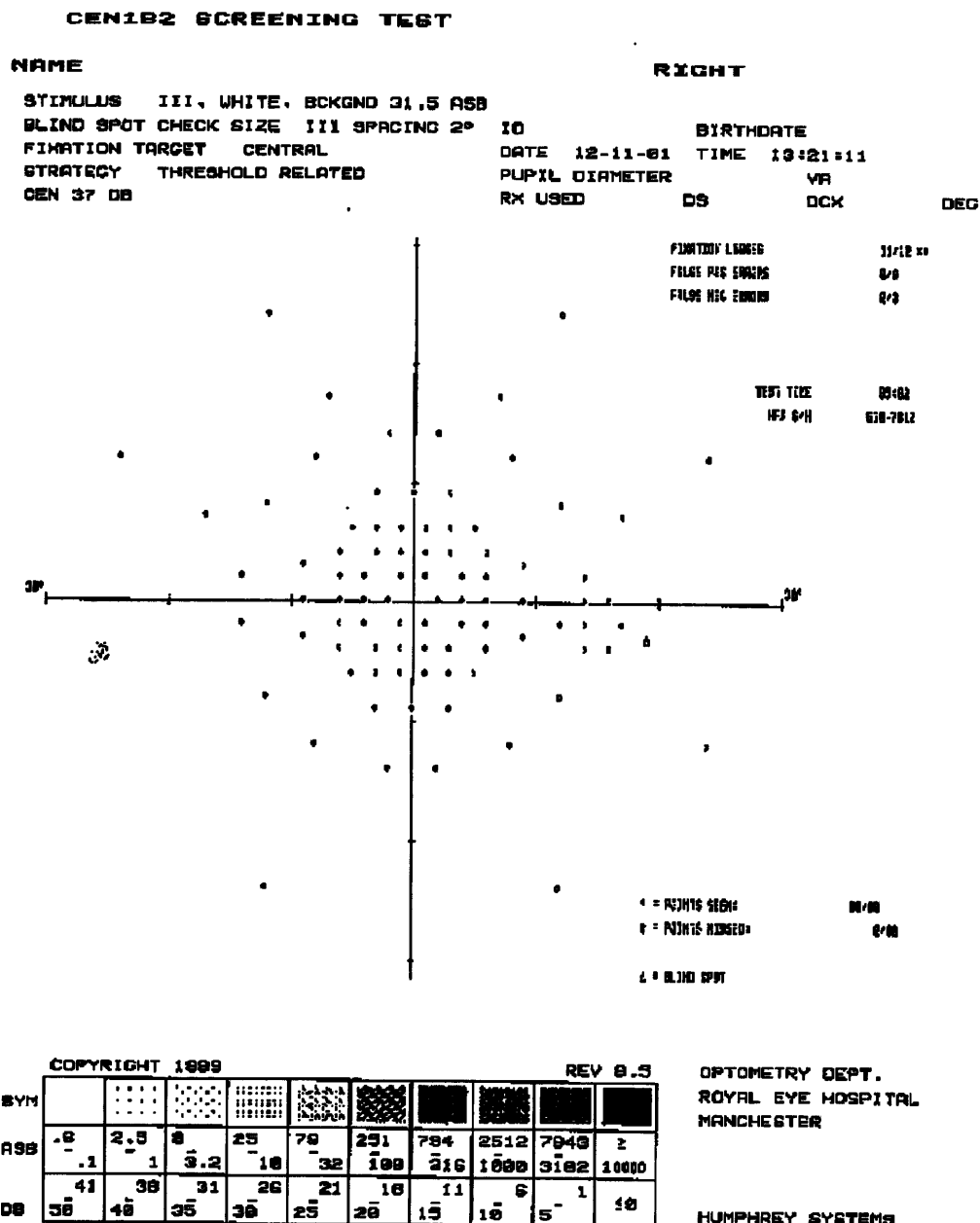


Figure A6.5: Customised program for the HVFA with 88 stimuli.

RESULTS IN AMD PATIENTS: STATIC AND KINETIC PERIMETRY

It was felt a much better control over the patients when testing them with the Bjerrum screen rather than with the HVFA, where larger amount of fixation losses gave unreliable results. This was because the Bjerrum screen gave the examiner the possibility to retest those locations that might have been affected by a change of fixation (as observed by the examiner). Also, when subject's fixation seemed to have changed, the test could be paused to re-instruct the patient to fixate centrally. The HVFA program, on the other hand, stopped several times (average of 3 times per patient) due to difficulty trying to locate the blind spot and even when the blind spot

had been located, patients found it very difficult to maintain fixation. The mean percentage of fixation losses was 49 (range 0 to 100, sd 0.36). For repeatability, the mean percentage of false positives and false negatives were 1 (range 0 to 11, sd 0.04) and 20 (range 0 to 100, sd 23) respectively. According to Ander son and Patella (1999), the maximum scores to make the reliability of the instrument acceptable are 20%, 10-15% and 33% for fixation losses, false positives and false negatives respectively. The extremely high rate of fixation losses on the AMD subjects (as many as 69% had a fixation loss score outside the proposed reliability criteria) and false negatives (31% of subjects outside the proposed reliability criteria) made the test very unreliable. This high rate was not surprising as they were all long standing cases of advanced AMD (VA range 0.82 to 1.66logMAR) and false negative errors have been reported to increase with increasing depth of visual field defect (Bengtsson & Hejil, 2000). The very low rate of false positives was likely to be due to the fact that patients found it very difficult to see any stimulus and thus would not recognise a stimulus unless it was very clear to them.

CONCLUSIONS IN AMD PATIENTS: STATIC AND KINETIC PERIMETRY

Patients generally found it more difficult to perform field tests on the HVFA than on the Bjerrum screen. The patients' subjective response to the HVFA was that they did not feel confident about seeing any stimuli and didn't understand what they were doing even after several sets of instructions were given. Because of the amount of fixation losses and times that the program had to stop, the HVFA results were not though to be reliable. Fixation was better controlled on the Bjerrum screen by constant checking of the position of the scotoma. The Bjerrum screen was therefore selected for the assessment of the central scotoma on the study patients.

APPENDIX 7

Prism prescription (pilot testing)

The techniques used in previous studies to prescribe prism relocation to AMD patients were described in Chapter 3. Because the prisms were to be used for “general purpose”, rather than simply for reading, it was decided to use a complex picture/photograph, rather than simple letters or words. The advantage of using a picture against letters is that a picture has more detail than plain letters. Also, if the patient concentrated on a letter chart he/she would end up memorising them, whereas attention could always be directed to a different part of the picture. Memory could also create a problem if visual acuity needed to be measured after prescribing the prism. Although this problem could have been solved by having plenty spare charts it did seem to make more sense to give the patient a completely different target to concentrate on.

Both pictures in the long distance (projected slides) and in the near vision (magazine pictures) were tried to see if the distance of the picture affected the prescription of the prism. Patients' subjective impressions were that it was easier to discriminate changes in acuity produced by different prism powers and base directions when tested on the near vision rather than on the distance vision. When using 35mm slides for the projection of pictures at distance the room lights needed to be off. This decrease in luminance could well have contributed to the difficulty in distinguishing different prism powers and base directions. Besides that, the quality of the slides and projector might have affected the contrast of the image. It was thus decided that for this study, prisms would be prescribed while the patient concentrates on a near vision picture while wearing the appropriate near vision add. A near vision photograph also had the advantage of being a method easy to be applied by an optometrist in practice.

Bullimore et al (1991) found a good correlation of face recognition as a function of letter chart acuity ($r=0.59$, $p<0.05$) and word reading acuity ($r=0.85$, $p<0.001$). The pictures selected for both the distance viewing slides and the near vision photographs were thus all having the face of at least one person and different colour objects to look at. From the tested near vision photographs, a preferred one by the 18 pilot AMD patients was selected for use in the trial patients. This picture had the face of a lady on the centre of the photograph, wearing a blue t-shirt with a baby in her arms (in a white blanket) in the foreground and a brown building in the background with a blue sky (Figure A7.1). This picture had some large and easy to recognise details and also some smaller and therefore more difficult details, so that to cover the needs for patients with a large range of VAs.



Figure A7.1: *“Real scene” photograph used to prescribe prisms on near vision.*

As prism was rotated from a starting position at 90° anticlockwise any positions giving a subjective visual improvement were recorded in degrees. If more than one position had been recorded, the optimal one was selected by using a 2-AFC. Once the degree for the base of the prism had been obtained, the optimal power was then found by showing the patient the next higher and lower prism power in steps of 2Δ and selected by means of a bracketing technique.

Rosenberg et al. (1989) prescribed different prism for distance, intermediate and near vision requirement. However, they didn't report any findings on the numbers of patients that actually had a different prism for the different distance tasks or any reasons for such a need. The other 3 previous prism relocation studies (Romayananda et al., 1982; Verezen et al., 1996; Bertrand et al., 1997) only prescribed prisms at near distance although they might then be worn for distance vision, as on Verezen et al. (1996) study. There is no evidence to prove that the optimal relocating prism would vary for the different viewing distances. In this study, the prism power and base direction found from the near vision test was prescribed for all distance prescriptions.

APPENDIX 8

Elschnig ring

When trying to mark the horizontal and vertical disc diameters of the optic nerve head a problem was encountered: a ring a bit lighter in colour than the neuroretinal ring surrounded the margin of the disc. This ring was found to be very prominent and consistent in all photographs (Figures A8.1 and A8.3) and quite distinguished from peripillary atrophy as this last one is visible apart from the bright ring on those patients that show this atrophy (Figure A8.2).



Figure A8.1: *Elsching ring on a red-free fundus photograph.*

Figure A8.2: *Peripapillary atrophy on a red-free fundus photograph.*

Figure A8.3: *Elsching ring on a colour fundus photograph.*

Also, this ring is as visible on the colour photographs. This ring is called the Elschnig ring and it consists of the connective tissue that extends between the choroids and optic nerve head (Shields, 1998) and seems to be used for defining the edge of the optic nerve on optic nerve head studies by using the inner circle (Burk et al, 1990). In order to calculate foveal position for this study, it was necessary to measure the disc diameter. Therefore to decide which of the two borders of the ring (the inner or the outer) should be used to define the edge of the optic disc, the fundus photographs of some young patients with a clear position of the fovea on the photograph were evaluated. Ten photographs from 10 different patients' eyes (right or left eye chosen arbitrarily) were taken with the red-free filter. Patients were hospital patients with a healthy fundus and an age range between 18 and 22 years and thus with fully developed eyes, which would be expected to have the same anatomical sizes as our elderly AMD population. The position of the fovea calculated from the DM/DD ratio was drawn on the photograph for both the DDs defined by the inner and outer borders of the Elschnig ring. The distance between these positions and the real location of the fovea (the error) was measured and the results are shown on table A8.1.

Px	Eye	DD outer ring	DD inner ring	Error using outer ring	Error using inner ring
GA	Right	4.4	3.9	-0.301	-0.676
AB	Left	4.4	3.6	-0.137	-0.601
SC	Right	4.5	4.4	-0.340	-0.399
SC	Left	4.9	4.7	-0.290	-0.312
GC	Left	4.4	3.9	-0.373	-0.651
AD	Right	4.3	3.9	-0.199	-0.413
ND	Right	5.3	4.8	+0.678	+0.376
RD	Right	4.2	3.4	-0.169	-0.648
JF	Left	4.1	3.8	-0.270	-0.455
AH	Left	4.9	4.3	+0.098	-0.310
Means				0.286	0.484

Table A8.1: DDs and distances in mm. between real and calculated position of the fovea for inner and outer Elschmig ring borders in millimetres. Minus error values means that the calculated distance of fovea from disc is shorter than the real one. Oppositely, a positive error value implies a longer calculated distance from fovea than the real one.

As seen on the table, the absolute value of the error is smaller for 9 out of the 10 eyes when the DD is defined by the outer border of the Elschmig ring compared to that obtained from the inner border. It was therefore decided to use the outer border of the ring to define the edge of the disc and thus the DD. Even for the DM values obtained by this method the fovea is still found at a bit shorter DM distance than the real one. This implies that the calculated DM distance would be expected to have an error of about 0.286 millimetres (≈ 1 degree) smaller for these subjects. As a result, we can conclude that using the outer border of the ring will provide the most accurate method to measure the DD.

APPENDIX 9

Overlaying sheets to calculate location of fovea

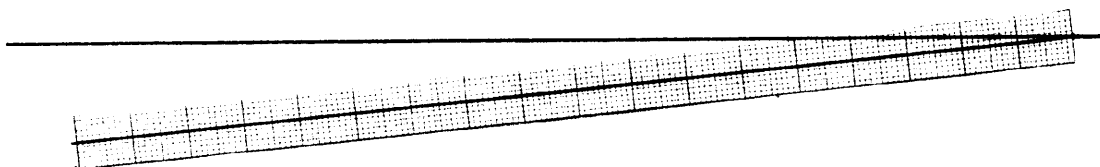


Figure A9.1: *Overlaid used to measure the length of the red line. The horizontal line was placed on top of the pink line, so that the point where that line and the ruler line converge should coincide with the centre of the optic nerve head (where the two blue lines cross).*

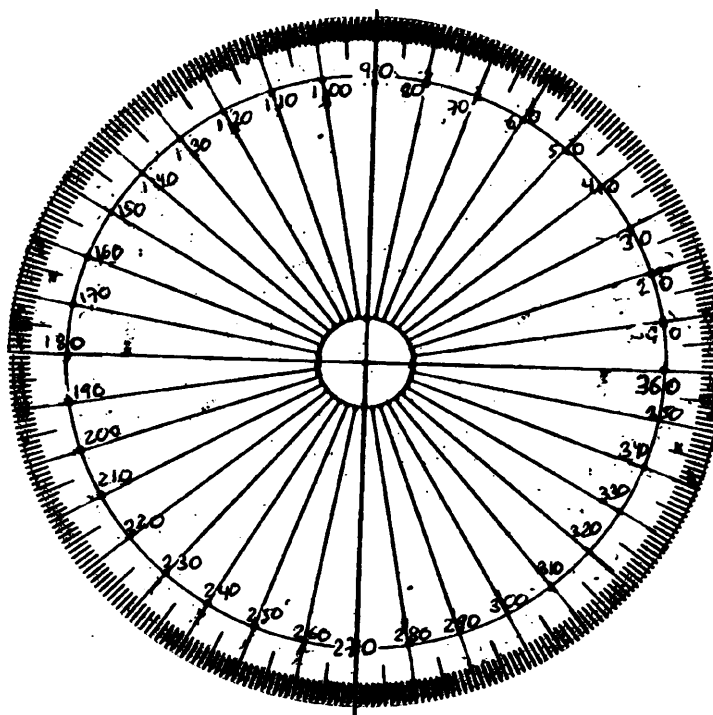


Figure A9.2: *Overlaid used to measure the angle between the green and yellow lines. The 180-360° line should coincide with the yellow line.*

APPENDIX 10

Effect of PRL distance on the angular difference between NNPF and prism base directions

Calculating the position of the fovea by means of the objective method discussed on chapter 4 has the limitation of using a single generalised DM/DD ratio for all patients it could thus be expected that for some patients the accuracy of the location of the fovea would be better than for others. A small error in determining the location of the fovea would have a bigger effect on the measured angle between the fovea and PRL when the distance value between them is small than when it is large. This effect can be seen in Figure A10.1, where two foveal locations have a small angular separation for a large PRL to fovea distance and a larger angular separation for a smaller PRL to fovea distance. It could therefore be expected that as the distance between the fovea and the PRL increases, the angle between them is bound to not be as accurate if there is any inaccuracy in determining foveal position. This error would be significant when comparing the PRL position to the prescribed prism base direction. The difference between these two angles would influence the usefulness of the PRL location in predicting the base direction of the subjectively chosen prism. The magnitude of this possible effect should be checked to test the extent to which it could influence the results.

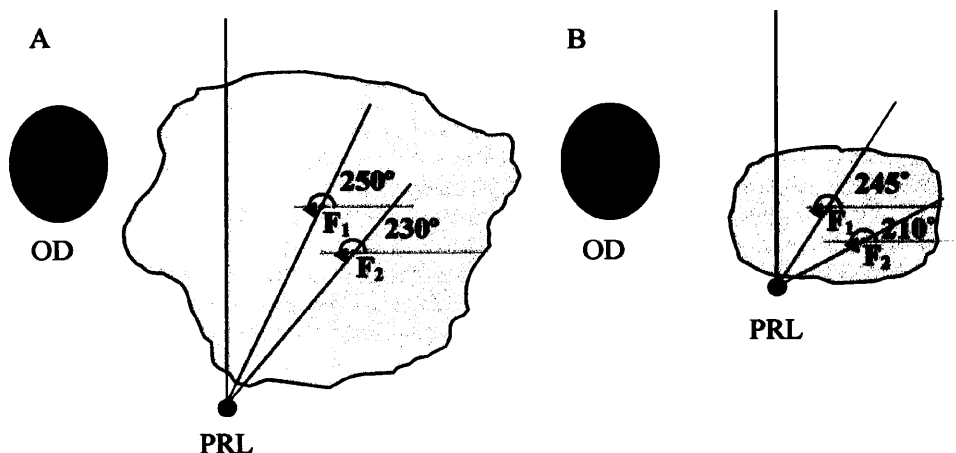


Figure A10.1, A: Two foveal locations have an angular separation of 20° (measured from the fovea) when the fovea to PRL distance is large. **B:** The same two foveal locations have now a much larger angular separation of 35° when the fovea to PRL distance is small.

To investigate the possible influence of this error, the relationship between the distance of PRL to fovea and the difference between prism base and PRL directions was investigated. Three possible distributions could be expected as the distance between fovea and PRL increases:

1. The angle difference between PRL location and prescribed prism base decreases/increases linearly, depending on whether the error angle falls between the

positions of the PRL and the prism base direction or away from the prism base direction position. This effect would be significant and should be considered in the regression analysis between PRL location and prism base direction. The distance between fovea and PRL would be a predictor of the difference between the angles.

2. The angle difference stays constant. This would prove no effect of accuracy of measurement, and would suggest that the distance between fovea and PRL would prove to be an equally good or poor predictor of the base direction for all PRL positions.
3. The angle difference between PRL location and prescribed prism base shows a more complex relationship. This case would simply make the prediction of prism base direction overall less accurate.

Graph A10.2 shows the scatter plot for the distance of PRL to fovea against the difference between prism base and PRL directions. The angle differences between PRL location and prescribed prism are equally widespread for large and small PRL to fovea distances. It can thus be concluded that this effect would not affect the results.

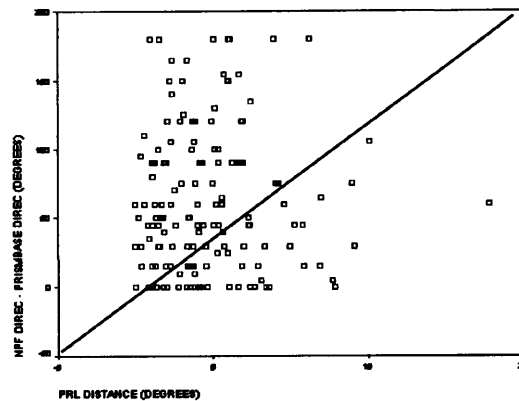


Figure A10.2: Scatter plot of preferred retinal locus distance against difference between nearest non-scotomatous point to fovea and prism base direction of better VA eyes.

APPENDIX 11

Calculation of angular differences

The most obvious way to find out the relationship between two angles would be subtracting one from the other and taking the absolute value of the difference. This subtraction should give the angular separation between them. However, both the PRL and NNPF angle values are interval scaled and due to the circular shape of the circle where they fall, relationship between these is not straightforward. That is because these values fall into a 360° circle and therefore values such as 20° and 300° are only 80° apart but any analytical program would consider them as having a difference of 280°. However, this analytical problem does not occur for all values. If we divide the 360° circle into four different areas and we call the A, B, C and D, where:

- **A** covers values from 0° to 85°
- **B** covers values from 90° to 175°
- **C** covers values from 180° to 265°
- **D** covers values from 270° to 355°

And compare two values falling on any of these different areas we have 6 possible combinations:

$$C_n^N = N! / (n!(N-n)!)$$

where N = the total number of cases, in this case 4 and n = the number of items selected. Then:

$$C_4^2 = 4! / (2!(4-2)!) = 4! / (2! \cdot 2!) = 24 / (2 \cdot 2) = 6$$

The 6 possible combinations are: **AB, AC, AD, BC, BD** and **CD**. We also have the possibility of both values falling on the same area and thus 4 more cases: **AA, BB, CC** and **DD**, adding to a total of 10 cases. The cases AB, BC and CD are easy to analyse since the values falling on area B are on the next higher interval scale than those in area A and thus the absolute value of taking A from B, or B from A will give us the correct difference in degrees. For example:

AB 120°-30° = 90°

60°-140 = 80°

BC 100°- 200° = 100°

250°-170° = 80°

CD 260°-350° = 90°

300°-265 = 35°

This will also apply to the cases AA, BB, CC and DD, where the values are quite close to each other. For example:

AA 90°- 30° = 60°

BB 100°-150° = 50°

CC $200^{\circ}-250^{\circ} = 50^{\circ}$

DD $355^{\circ}-355^{\circ} = 0^{\circ}$

Unfortunately this simple method of taking the absolute value of the subtraction does not always apply to those cases where one of the two values does not fall on the next higher interval area to the other one. This will thus not apply to cases AD, BD and AC. For example:

AD $30^{\circ}-300^{\circ} = 270^{\circ}$ (the real value is 90°)

$270^{\circ}-85^{\circ} = 185^{\circ}$ (the real value is 175°)

BD $120^{\circ}-315^{\circ} = 195^{\circ}$ the real value is 165°

$340^{\circ}-120^{\circ} = 220^{\circ}$ (the real value is 140°)

AC $85^{\circ}-265^{\circ} = 180^{\circ}$ (this time we get the real value)

$0^{\circ}-265^{\circ} = 265^{\circ}$ (the real value is 85°)

$30^{\circ}-260^{\circ} = 230^{\circ}$ (the real value is 130°)

Having a closer look at all the examples shown above we can conclude that after the subtraction and taking the absolute value the result is the real value only if this obtained figure lies between 0° and 180° . If this figure is 185° or higher then this value will not be the real one. We will call this figure obtained from the absolute value of the subtraction X.

It is for this reason important to find a way to transform these X values into the real values, which we will call Y. Depending on the value X we have two formulae to apply in order to find Y:

1. If $270 \Rightarrow X > 180$, then $Y = X - ((X-180) \times 2)$
1. If $X > 270$, then $Y = 360 - X$

With these formulae we can now obtain the real amount of degrees between the prism base direction and the NPF direction. This is all simplified into a diagram (see figure A11.1).

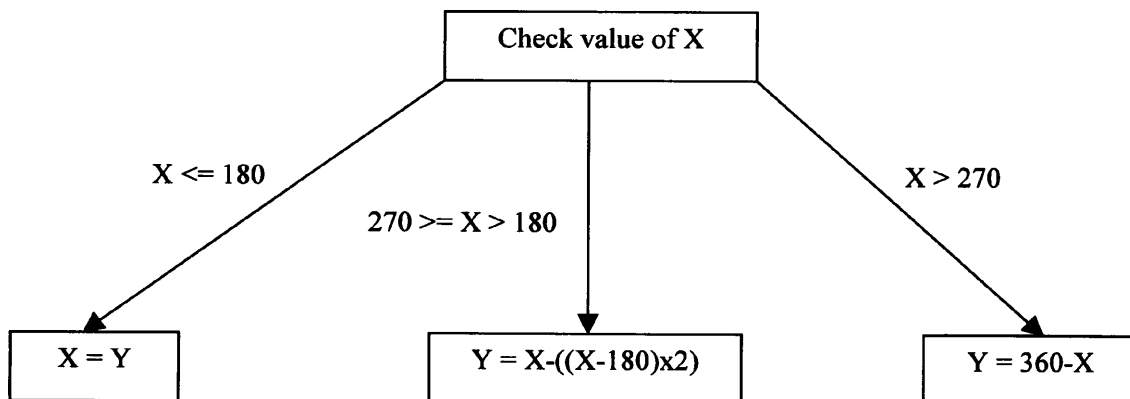


Figure A11.1: *Diagram to calculate the Y value.*

Some examples resolved:

$$\begin{array}{lll}
 270^\circ - 85^\circ = 185^\circ & X=185, 270^\circ \geq X > 180^\circ, & Y=185-((185-180) \times 2)=175^\circ \\
 260^\circ - 350^\circ = 90^\circ & X=90^\circ, X < 180 & Y=X=90^\circ \\
 30^\circ - 260^\circ = 230^\circ & X=230^\circ, 270^\circ \geq X > 180^\circ, & Y=230-((230-180) \times 2)=130^\circ \\
 10-300 = 290^\circ & X=290^\circ, X > 270^\circ & Y = 360-290=70^\circ
 \end{array}$$

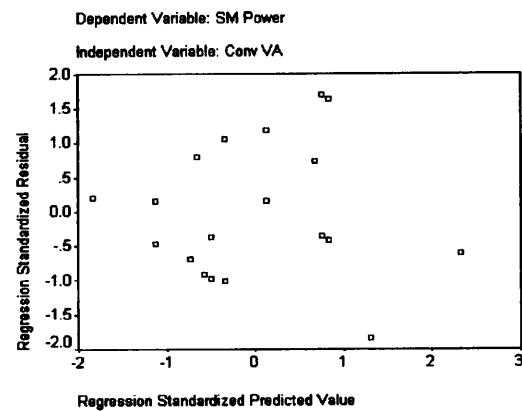
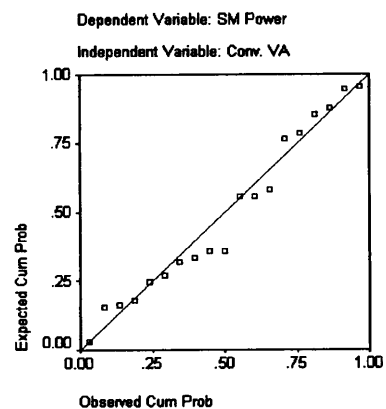
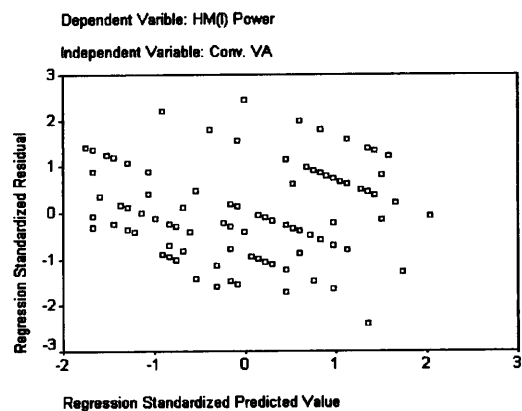
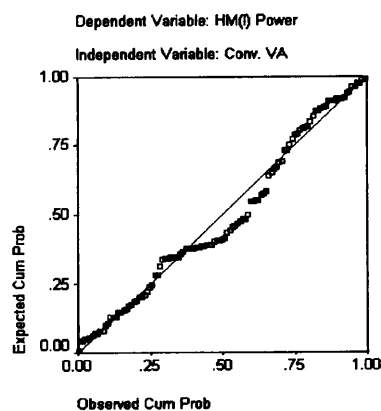
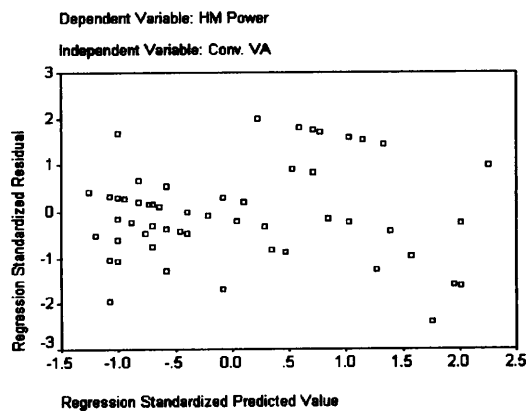
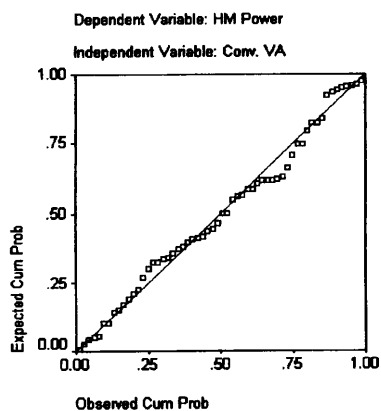
For quick reference of the Y values I have created a table showing all the Y values for all X values going from 0° to 355° on 5° steps:

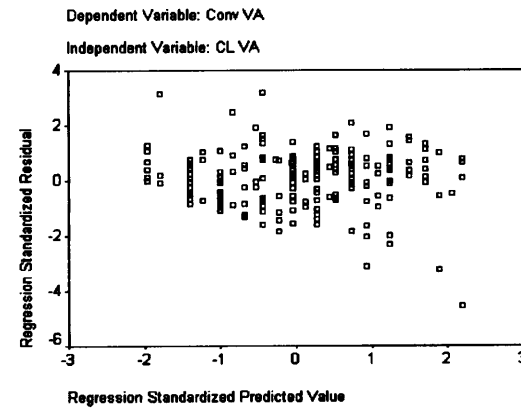
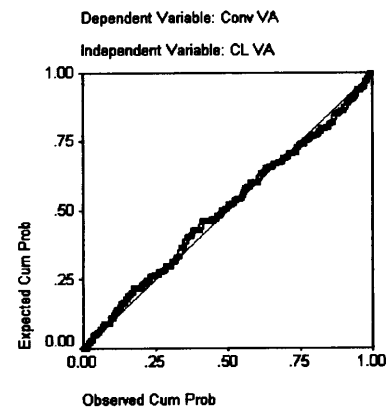
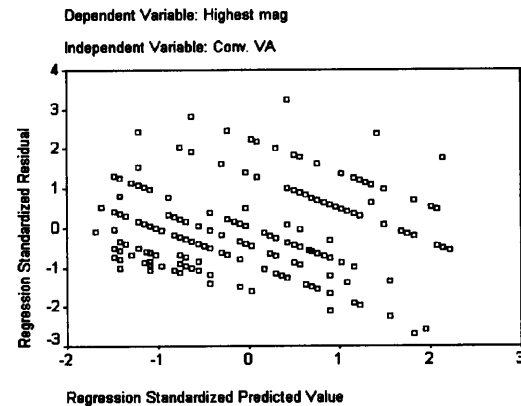
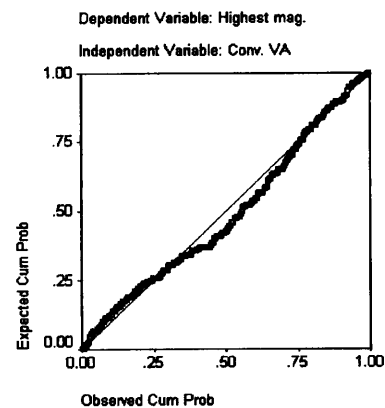
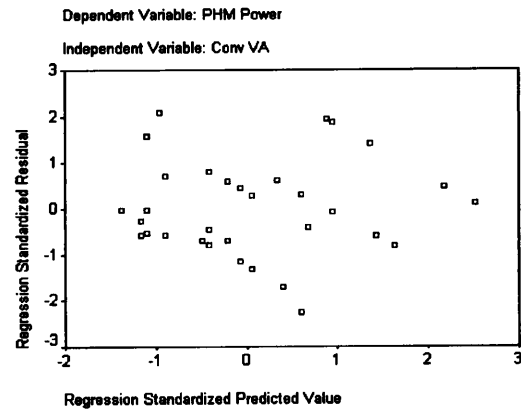
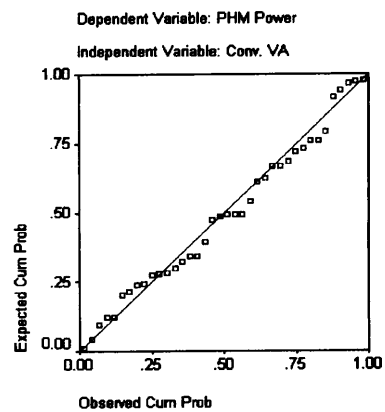
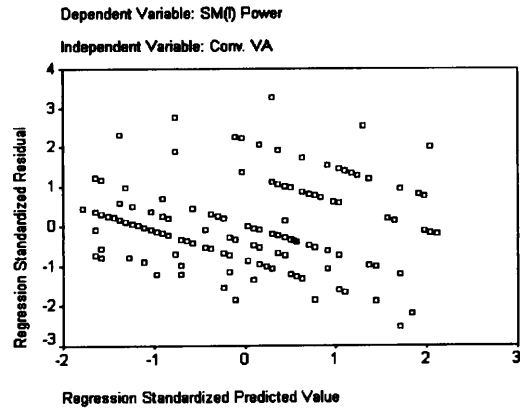
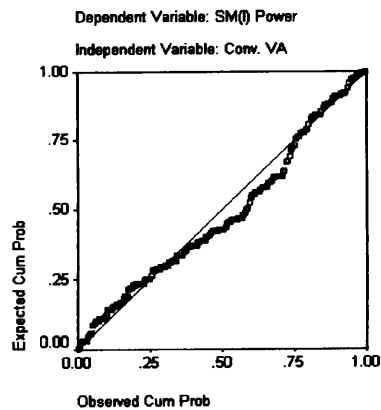
X	Y	X	Y	X	Y	X	Y
0	0	90	90	180	180	270	90
5	5	95	95	185	175	275	85
10	10	100	100	190	180	280	80
15	15	105	105	195	165	285	75
20	20	110	110	200	160	290	70
25	25	115	115	205	155	295	65
30	30	120	120	210	150	300	60
35	35	125	125	215	145	305	55
40	40	130	130	220	140	310	50
45	45	135	135	225	135	315	45
50	50	140	140	230	130	320	40
55	55	145	145	235	125	325	35
60	60	150	150	240	120	330	30
65	65	155	155	245	115	335	25
70	70	160	160	250	110	340	20
75	75	165	165	255	105	345	15
80	80	170	170	260	100	350	10
85	85	175	175	265	95	355	5

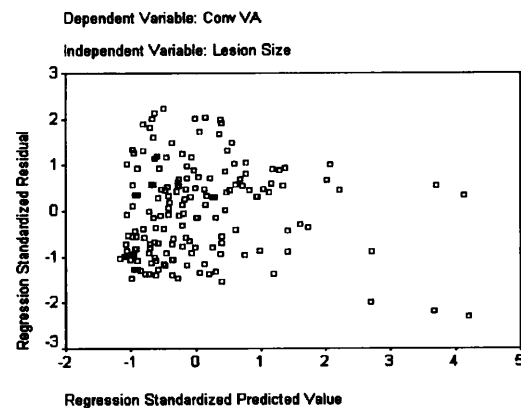
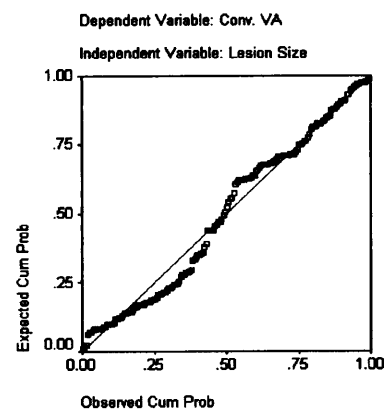
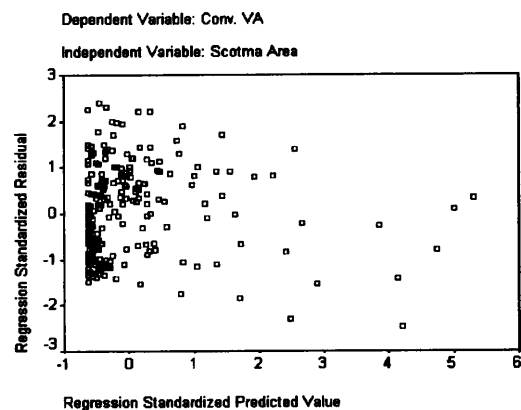
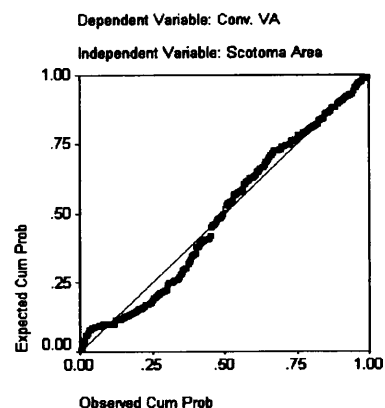
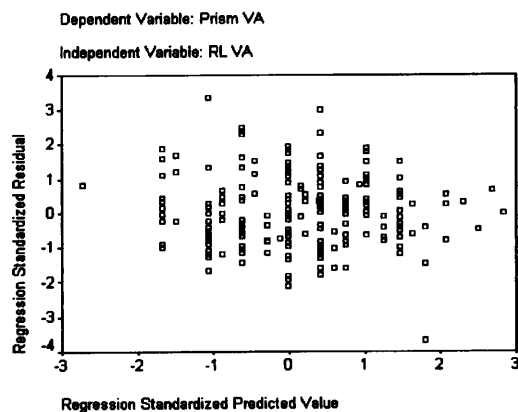
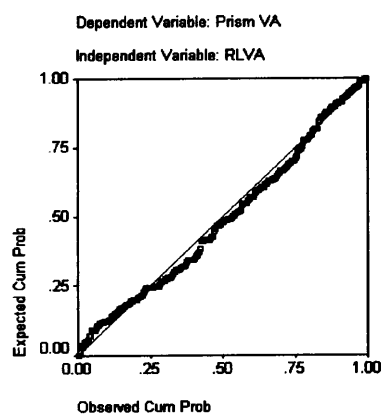
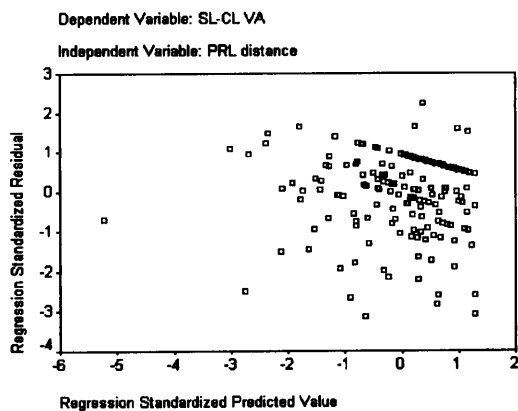
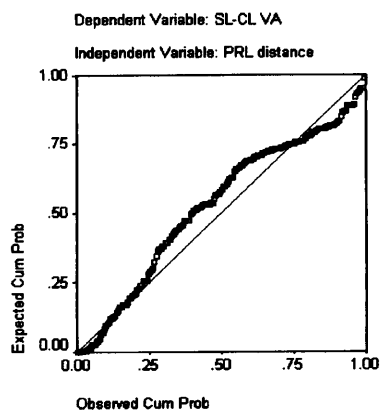
Figure A11.1: Y values for all corresponding X values.

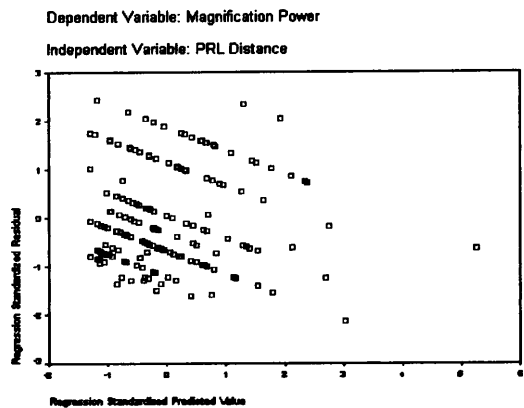
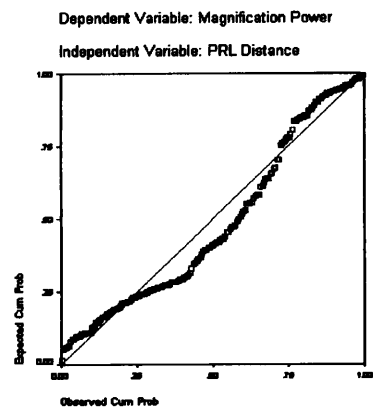
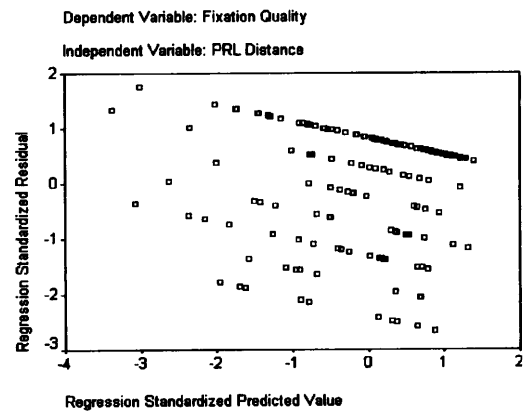
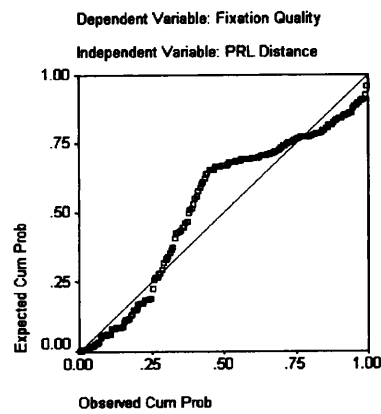
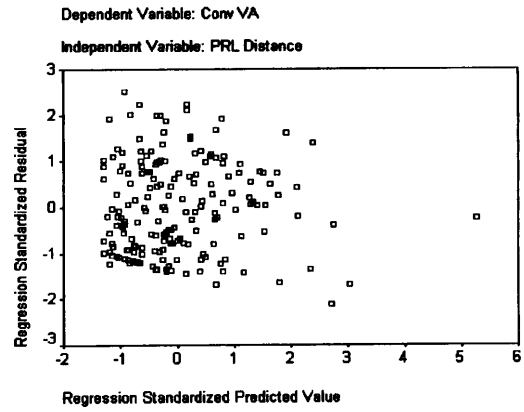
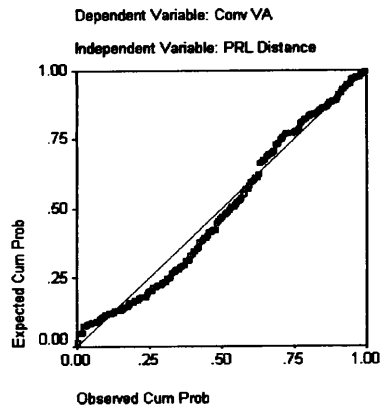
APPENDIX 12

Residuals vs Fitted plots and P-P plots for single regressions









APPENDIX 13

Prismatic effect of bifocals

In the context of this study, a relevant optical effect of spectacle lenses is the prismatic effect induced when the patient views away from the optical centre. In single vision lenses, the patient can always choose to view through this position by turning their head rather than their eyes in lateral gaze. In bifocal lenses, however, the patient must look down to use the near segment, and cannot avoid the prismatic effect occurring in the near visual zone of the lens. Optically, a bifocal lens can be thought of as being made from two separate components: a main lens, whose power is that of the distance prescription, added to which is a supplementary segment lens whose power is equal to the reading addition (Jalie, 1999). As the eye looks through the distance optical centre of the lens there is no prismatic effect but when the eyes move down to read, and thus use the segment part of the bifocal, a prismatic effect is induced.

There are two main groups of bifocals: the round (R segment), and the D or C segments (shaped segments). Both the D and C segments have the same prism qualities with the only difference of the D segment being flat at the top, while the C segment has a curved top. These two groups of bifocals induce different amounts of prism effect. It could be that the success of prism glasses for near vision tasks might be affected by this prism effect. Next, the amount of prism effect will be studied with the aim to work out the possible effect on the patients caused by different prescriptions and bifocal segments.

Naturally, the eyes move from the straight ahead position about 8mm down and converge 4mm to read. This will thus give as a 8mm vertical deviation and a 2mm horizontal deviation for each eye when looking through the Near Vision Point (NVP).

Prentice's rule for prismatic effect of a lens:

$$P = cF \quad (A13.1)$$

Where c is the descentration in cm and F is the power of the lens

Downcurve segment bifocals (R segments)

If we consider an average lens to have a power of +3.00, for a 8mm deviation from the centre, the prism power induced according to this formula would be $P = 0.8 \times 3.00 = 2.4 \Delta$ base up. This would be the amount of prism power due to the distance component of the prescription, which the subject would be exposed to every time the eyes are lowered to do near vision work. It is also necessary to consider the effect of the segment as well.

If the subject were prescribed a round segment for near purposes, for example, the segment would exert base-down prism at the near visual point, which would act to neutralise the base-up effect of the main lens.

Near addition	22mm round seg.	28mm round seg.	38mm round seg.	45mm round seg.
+1.00	0.6 Base Down	0.9 Base Down	1.4 Base Down	1.75 Base Down
+1.50	0.9 Base Down	1.35 Base Down	2.1 Base Down	2.62 Base Down
+2.00	1.2 Base Down	1.8 Base Down	2.8 Base Down	3.5 Base Down
+2.50	1.5 Base Down	2.25 Base Down	3.5 Base Down	4.37 Base Down
+3.00	1.8 Base Down	2.7 Base Down	4.2 Base Down	5.25 Base Down
+3.50	2.1 Base Down	3.15 Base Down	4.9 Base Down	6.12 Base Down
+4.00	2.4 Base Down	3.6 Base Down	5.6 Base Down	7.0 Base Down

Table A13.1: Prismatic effect at NVP due to the bifocal segment.

Sphere Power	Vertical Prismatic Effect	Horizontal Prismatic Effect
+0.25	0.2 Base Up	0.05 Base Out
+0.50	0.4 Base Up	0.1 Base Out
+0.75	0.6 Base Up	0.15 Base Out
+1.00	0.8 Base Up	0.2 Base Out
+1.50	1.2 Base Up	0.3 Base Out
+2.00	1.6 Base Up	0.4 Base Out
+2.50	2.0 Base Up	0.5 Base Out
+3.00	2.4 Base Up	0.6 Base Out
+3.50	2.8 Base Up	0.7 Base Out
+4.00	3.2 Base Up	0.8 Base Out
+4.50	3.6 Base Up	0.9 Base Out
+5.00	4.0 Base Up	1.0 Base Out
+5.50	4.4 Base Up	1.1 Base Out
+6.00	4.8 Base Up	1.2 Base Out
+6.50	5.2 Base Up	1.3 Base Out
+7.00	5.6 Base Up	1.4 Base Out
+7.50	6.0 Base Up	1.5 Base Out
+8.00	6.4 Base Up	1.6 Base Out
+8.50	6.8 Base Up	1.7 Base Out
+9.00	7.2 Base Up	1.8 Base Out
+9.50	7.6 Base Up	1.9 Base Out
+10.00	8.0 Base Up	2.0 Base Out
+10.50	8.4 Base Up	2.1 Base Out
+11.00	8.8 Base Up	2.2 Base Out

Table A13.2: Prismatic effect at the NVP due to plus spherical power.

N.B. for minus powers reverse the base direction. 0.25 intervals can be found by simple addition.

The prism due to the segment can be deduced as follows. Suppose the segment diameter is 38mm. The distance from the dividing line to the geometrical (and optical) centre of the segment is 38/2 or 19mm. We are going to consider the prismatic effect at the NVP 8mm below the distance optical centre and 5mm below the segment top for an add of +2.00. Since the NVP lies 5mm below the segment top, it must lie 14mm, or 1.4cm, above the segment centre. Hence,

the prism due to the segment is: $P = 1.4 \times 2.00 = 2.8\Delta$ base down. The total prismatic effect at the NVP is the sum of 2.4Δ base up and 2.8Δ base down, which is 0.4Δ base down.

Table A13.1 shows the amounts of base down prism produced by round segment bifocals at a NVP 5mm below the segment top for different segment sizes and addition powers. The prism power increases both as the addition and the segment size increase. Tables A13.2 and A13.3 show the prismatic effect produced by different spherical and cylindrical powers.

Axis direction		Prismatic effect in Δ	
R eye	L eye	Vertical	Horizontal
180	180	0.80 Base Up	0
5	175	0.81 Base Up	0.07 Base Out
10	170	0.81 Base Up	0.14 Base Out
15	165	0.80 Base Up	0.21 Base Out
20	160	0.77 Base Up	0.28 Base Out
25	155	0.73 Base Up	0.34 Base Out
30	150	0.69 Base Up	0.40 Base Out
35	145	0.63 Base Up	0.44 Base Out
40	140	0.57 Base Up	0.48 Base Out
45	135	0.50 Base Up	0.50 Base Out
50	130	0.43 Base Up	0.51 Base Out
55	125	0.36 Base Up	0.51 Base Out
60	120	0.29 Base Up	0.50 Base Out
65	115	0.22 Base Up	0.47 Base Out
70	110	0.16 Base Up	0.43 Base Out
75	105	0.10 Base Up	0.39 Base Out
80	100	0.06 Base Up	0.33 Base Out
85	95	0.02 Base Up	0.27 Base Out
90	90	0	0.20 Base Out
95	85	0	0.13 Base Out
100	80	0	0.06 Base Out
105	75	0	0.01 Base In
110	70	0.03 Base Up	0.08 Base In
115	65	0.07 Base Up	0.14 Base In
120	60	0.11 Base Up	0.20 Base In
125	55	0.17 Base Up	0.24 Base In
130	50	0.23 Base Up	0.28 Base In
135	45	0.30 Base Up	0.30 Base In
140	40	0.37 Base Up	0.31 Base In
145	35	0.44 Base Up	0.31 Base In
150	30	0.51 Base Up	0.30 Base In
155	25	0.58 Base Up	0.27 Base In
160	20	0.64 Base Up	0.23 Base In
165	15	0.70 Base Up	0.19 Base In
170	10	0.74 Base Up	0.13 Base In
175	5	0.78	0.07 Base In

Table A13.3: Prismatic effect at the NVP due to each +1.00D of cylinder power.
N.B. for MINUS cylinder powers reverse the base direction and for other cylinders, multiply the values given in this table by the new cylinder.

Negative lenses produce the opposite base direction and thus the amount of prismatic effect is the same as in the tables but reversing the base direction. As stated above, the total prismatic effect of the bifocal is the sum of the segment prismatic effect and of the distance lens prismatic effect. Since the round segment always produces a base down prism on the NVP, patients with a positive lens (giving a base up on the NVP) would experience less difference in the prismatic effect at the NVP in bifocals compared to single vision lenses, than patients with a negative lens.

D and C segments (shaped segments)

If we consider a segment size of 28x19 and the NVP is located in exactly the same position, 8mm below the distance optical centre (Od) and 5mm below the segment top, then it will be appreciated that the optical centre of the segment, Os, now coincides exactly with the NVP and the segment adds no prism at this point and the prismatic effect at the centre of the NVP would thus be the same as it would have been if the segment didn't exist.

It can therefore be expected that the type of bifocal segment and the prescription of the patient could, depending on the direction of the eye movement from the optical centre of the lens cancel or increase the prismatic effect.

Appendix 14

Supporting publications of the study

Poster presentations

Cacho, I., Dickinson, C.M., Smith, H.J. and Harper R.A. (2002) Prescribing strategies for prism relocation. In: *Proceedings of Vision 2002*. The 7th International Conference on Low Vision, Sweden, 2002, p. 111

Dickinson, C.M., Smith, H.J., Cacho, I. and Harper, R.A (2002) Reading performance in the presence of a central scotoma. In: *Proceedings of Vision 2002*. The 7th International Conference on Low Vision, Sweden, 2002, p. 108

Smith, H.J., Dickinson, C.M., Cacho, I., Reeves, B.C and Harper, R. (2002) Measuring impairment, disability and handicap in AMD. In: *Proceedings of Vision 2002*. The 7th International Conference on Low Vision, Sweden, 2002, p. 150

Cacho, I., Dickinson, C.M., Smith, H.J., Harper, R.A. Reeves, B.C. (2003) The use of visual function measures for predicting a relocating prism for patients with AMD. *Invest.Ophthalmol. Vis. Sci.*, **44**(Suppl): 3090

Dickinson, C.M., Cacho, I., Harper, R.A. and Smith, H.J. (2002) Using visual acuity to investigate contour interaction and gaze selection defects in age-related macular degeneration. *Invest.Ophthalmol. Vis. Sci.*, **44**(Suppl): 1816

Oral presentation

UK Multi-disciplinary Low Vision Rehabilitation and Research Conference. Vision Sciences, Aston University, December 2003. Talk: "Fixation characteristics and visual acuity in people with AMD

Paper

Smith, H.J., Dickinson, C.M., Cacho, I., Reeves, B.C. and Harper, R.A. (2004) A randomised controlled trial to determine the effectiveness of prism relocation spectacles for patients with age-related macular degeneration. *Invest.Ophthalmol. Vis. Sci.* Under review

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