A new algorithm for the relationship between vision and ametropia

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Thesis Summary

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Refraction simulators used for undergraduate training at Aston University did not realistically reflect variations in the relationship between vision and ametropia. This was because they used an algorithm, taken from the research literature, that strictly only applied to myopes or older hyperopes and did not factor in age and pupil diameter. The aim of this study was to generate new algorithms that overcame these limitations.

Clinical data were collected from the healthy right eyes of 873 white subjects aged between 20 and 70 years. Vision and refractive error were recorded along with age and pupil diameter. Re-examination of 34 subjects enabled the calculation of coefficients of repeatability. The study population was slightly biased towards females and included many contact lens wearers. Sex and contact lens wear were, therefore, recorded in order to determine whether these might influence the findings. In addition, iris colour and cylinder axis orientation were recorded as these might also be influential.

A novel Blur Sensitivity Ratio (BSR) was derived by dividing vision (expressed as minimum angle of resolution) by refractive error (expressed as a scalar vector, U). Alteration of the scalar vector, to account for additional vision reduction due to oblique cylinder axes, was not found to be useful.

Decision tree analysis showed that sex, contact lens wear, iris colour and cylinder axis orientation did not influence the BSR. The following algorithms arose from two stepwise multiple linear regressions:

BSR (myopes) = 1.13 + (0.24 x pupil diameter) + (0.14 x U)
BSR (hyperopes) = (0.11 x pupil diameter) + (0.03 x age) - 0.22

These algorithms together accounted for 84% of the observed variance. They showed that pupil diameter influenced vision in both forms of ametropia. They also showed the age-related decline in the ability to accommodate in order to overcome reduced vision in hyperopia.

Key words: Blur Sensitivity Ratio; astigmatism; optometric vector

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Glossary

Accommodation

The ability of the eye to change focus from far to near by increasing the power of the crystalline lens (Millodot, 2008). Accommodation naturally reduces with age.

Ametropia

The refractive state of an eye where, with accommodation relaxed, the image is not focused clearly upon the retina. It is the departure from emmetropia and is typically classified into myopia, hyperopia and astigmatism.

Axis

The meridian along which a cylindrical lens has zero power; or used to denote the principal optical meridia of an optical system. The axis can be represented as a continuum from 0 to 180 degrees, with 0 and 180 being synonymous and representing the horizontal meridian with 90 representing the vertical meridian. Figure G1 represents the standard axis notation. By convention the '°' degree symbol is not used so as to avoid confusion with '0'. This format is used for both right and left eyes and is not reversed.

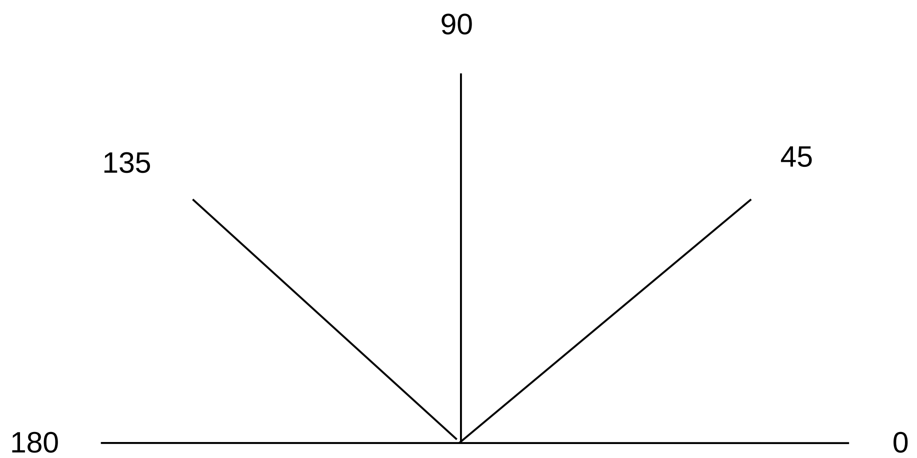

Figure G1: Axis of astigmatism notation. The same notation is used for right and left eyes.

Cycloplegia

Temporary paralysis or relaxation of the ciliary muscle and therefore crystalline lens to prevent accommodation. Cycloplegia is usually induced with eye drops such as cyclopentolate and is used to enable more accurate refraction.

Cylinder

A lens which has two principal powers along perpendicular axes, one of which is zero-powered. The cylinder power of a spectacle lens may be followed by the letters 'DC' (Dioptres Cylinder).

Cross-cylinder or Jackson cross-cylinder (JCC)

A lens which has a convex cylinder on one face and a concave cylinder on the opposite face with axes 90 degrees apart. These lenses have a mean spherical equivalent of zero as the cylinders have equal but opposite power.

Crossed cylinder

Two cylindrical lenses of any power with their axes crossed at any angle.

Dioptre

A lens with a focal length in air of 1 metre has a power of 1 dioptre (1D). Plus (+) lenses are convex and converge light. They are used to correct hyperopia. Minus (-) lenses are concave, diverge light and are used to correct myopia.

Emmetropia

Considered the perfect refractive state where light focuses upon the retina in a non-accommodating eye.

Mesopic vision

Conditions under which both rod and cone photoreceptors are active, within the range 10^{-3} to 3 cdm^{-2} (Charman, 1996).

Minimum Angle of Resolution (MAR)

Measured in minutes of arc (') this is the measurement of the smallest space within optotypes, or letters on the chart, that an eye can see. For example, if a subject can read a letter 'E' on the 6/6 line on the chart, the spaces between the limbs of the letter are calibrated to measure 1' at 6 metres. A similar letter on the 6/60 line is calibrated to have a limb separation of 10' at 6 metres. To convert a Snellen fraction into MAR, the denominator of the expression is divided by the numerator.

Photopic vision

Conditions under which only cone photoreceptors are active, over approximately 3 cdm^{-2}.

Presbyopia

The natural reduction in accommodation with age so hyperopia can no longer be overcome or near objects can no longer be focused when distance vision is corrected.

Scotopic vision

Conditions under which only rod photoreceptors are active 10^{-6} to 10^{-3} cdm^{-2} (Charman, 1996).

Sphere

A lens or optical system in which light is focused by the same amount in all meridia. The spherical power of a spectacle lens may be followed by the letters ‘DS’ (Dioptres Sphere).

Spherocylindrical lens

A lens with different powers along perpendicular axes. It may be formed by adding together a spherical lens and a cylindrical lens.

1. Purpose

1.1 Introduction

This chapter outlines the aims and objectives of the study presented in this thesis together with a list of objectives that were achieved as described in each of the following chapters.

1.2 The Problem

During their training optometry students are taught to initially estimate a subject's spherical and cylindrical error from their unaided vision. They are often given rules of thumb for estimating refractive error such as 'every 0.25D of spherical error or 0.50D of cylindrical error reduces Snellen acuity by one line' and 'larger pupils result in more blurred vision,' but such rules are vague and do not appear to apply to everybody. Aston University's optometry department supplements first year clinical refraction training with simulators that allow the student to learn how to carry out objective (streak retinoscopy) and subjective refraction (fan and block and Jackson cross-cylinder) on virtual patients. These refraction simulators use a regression formula that relates unaided vision to refractive error. This formula however does not account for the effects on aided vision of factors such as the type of ametropia (myopia, hyperopia or astigmatism), astigmatic axis or pupil size.

Aston University's optometry department also run 'Vision and Ametropia' practical classes for its first year undergraduate students. These classes demonstrate how the relationship between unaided vision and ametropia alters when myopia, hyperopia or astigmatism are present and how this relationship is influenced by pupil size. Students occasionally comment on departures in what they have observed in real eyes compared to the output of refraction simulators in virtual eyes (Dunne, pers. comm., unreferenced).

There is surprisingly little data available, especially from large, population-based studies which can be applied to making the refraction simulators more realistic. The purpose of the research presented in this thesis was therefore to collect this missing data with a view to improving Aston's refraction simulators.

1.3 How refractive error affects unaided vision

1.3.1 Emmetropia

Figure 1.1 shows an emmetropic eye which has no refractive error, within which light from infinity is focused to a point upon the retina (Logan, 2009). In reality this is a small circle of blur caused by aberrations within the optical system. Emmetropia is considered to be the perfect refractive state.

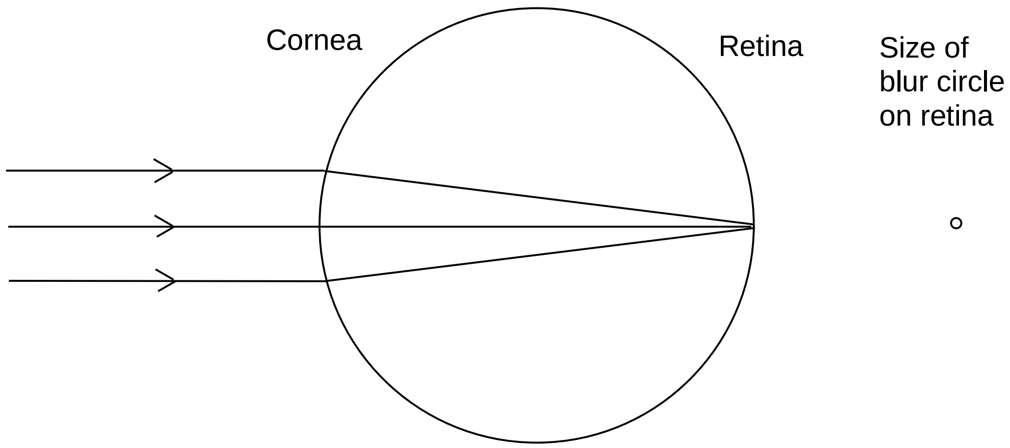

Figure 1.1: Light focused within an emmetropic eye. Light is focused upon the retina and the resultant blur circle is very small.

1.3.1.1 Aberrations

An aberration is defined as an optical defect where light rays do not form a perfect point focus after passing through the optical system (Millodot, 2008). Chromatic aberration is caused by different wavelengths of light being refracted differently within the optical system (Campbell & Gubisch, 1967). Short wavelength blue light is refracted more strongly than long wavelength red light, so in an emmetropic eye, blue light may be focused in front of the retina, green upon it and red behind the retina. If the subject is looking at a black letter on a white background, chromatic aberration is seen as a coloured fringe around the letter.

Monochromatic (or achromatic) aberrations occur even when only one wavelength of light is present in the system. They are caused when the wavefront from the theoretical focus of the optical system is not perfectly spherical. One of the commonest ways to represent monochromatic aberrations is by a series of Zernike polynomials, which break down the complex wavefront into a series of simpler waveforms. The first order Zernike polynomial is tilt, wherein the wavefront is tilted and is equivalent to prism. This does not affect vision. The second order polynomials represent aberrations the same as that expected from Jackson cross-cylinders as well as defocus, and these combine to give the spherocylindrical refractive error. Higher order aberrations cannot be corrected with conventional lenses. Third order polynomials include coma and trefoil, fourth order polynomials give rise to quadrafoil, fourth order astigmatism and spherical aberration (Voke, 2010). Higher order aberrations do not typically have as much effect on vision as refractive error, but they can significantly affect visual quality, especially in eyes with large pupils, resulting in blurring, ghosting, doubling of an image, glare and haloes.

1.3.2 Myopia

In a short-sighted or myopic eye such as that shown in Figure 1.2, light rays are focused in front of the retina, resulting in a blur circle upon the retina. Myopia may be caused by a steep cornea, too-powerful crystalline lens or greater than necessary axial length (Logan, 2009; Millodot, 2008; Rabbetts, 2007). It causes far vision to be blurred whereas near vision will be better focused.

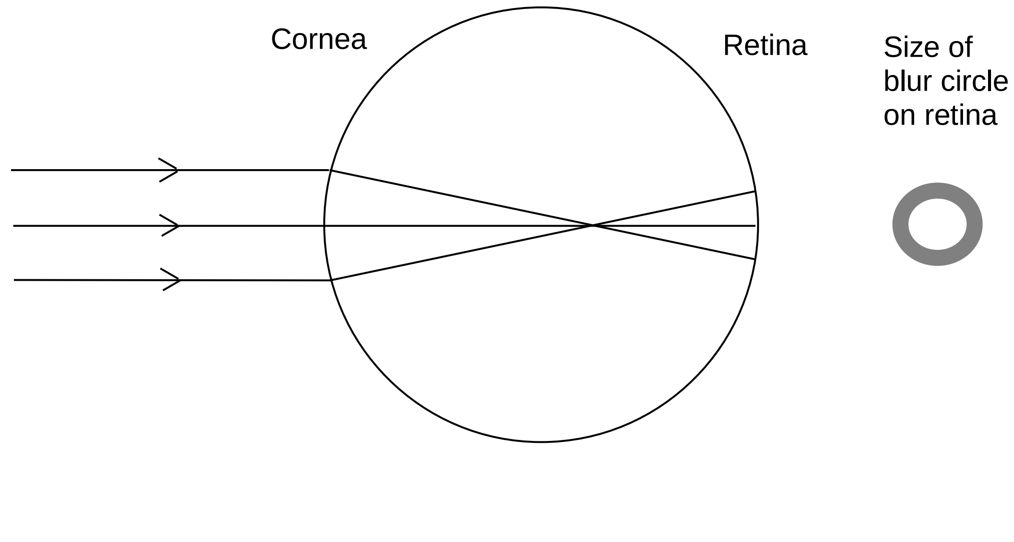

Figure 1.2: Light focused within a myopic eye. Light is focused in front of the retina, leaving a blur circle upon the retina (adapted from Millodot, 2008).

1.3.3 Hyperopia

A long-sighted or hyperopic eye may have a flat cornea, too-weak crystalline lens or short axial length, so light rays are focused behind the retina as shown in Figure 1.3. This means there will be a blur circle on the retina in an eye with no accommodation, but in an eye with adequate accommodation the effective power of the crystalline lens may be increased to move the pencil of light forward to focus nearer to the retina. The ability of younger eyes to accommodate and therefore bring the focal point onto the retina is a potential source of variability and inconsistency for both the optometrist during refraction and for studies investigating the effects of refractive error on vision, as hyperopes may effectively mask their refractive error through adequate accommodation. A young hyperope may have good vision at all distances, but the nearer an object is focused and the greater the refractive error, the greater the strain on the visual system and the greater the potential for blur.

1.3.4 Astigmatism

An eye with astigmatism has different refractive power in different meridia. In regular astigmatism these meridia will be perpendicular to one another with one meridian focusing light more powerfully than the other. This results in two lines of focus which could be on, in front of or behind the retina in any combination and dioptrically half way between these two lines of focus lies the ‘circle of least confusion’. This can make prediction of vision in astigmatism difficult especially in a hyperopic subject with adequate accommodation to bring either line of focus or the circle of least confusion onto the retina.

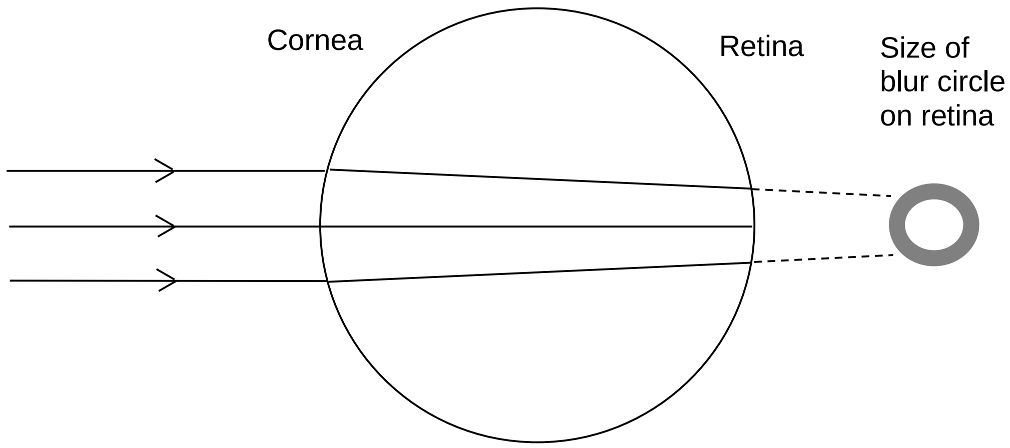

Figure 1.3: Light focused behind a hyperopic eye with relaxed accommodation. The resultant blur circle is shown on the retina as light is focused behind it, but in an eye with adequate accommodation, the focus can be moved forward, reducing the size of the blur circle and improving vision (adapted from Millodot, 2008).

Astigmatism can be classified in several ways. Orthogonal astigmatism has its axes near the 90 (vertical) and 180 (horizontal) degree meridia whereas in oblique astigmatism, cylinder axes are near the 45 and 135 degree meridia. An eye with with-the-rule astigmatism is steepest along the vertical meridian and is corrected with a minus-powered cylindrical lens with axis along the horizontal axis, whereas an eye with against-the-rule astigmatism has its steepest curvature horizontally, requiring a minus cylinder lens to be aligned along the vertical axis to correct the vision.

Tunnacliffe (1993) and Rabbetts (2007) classified astigmatism in the following way:

- Compound myopic astigmatism (CMA) has both lines of focus in front of the retina
- Compound hyperopic astigmatism (CHA) has both lines of focus behind the retina
- Simple myopic astigmatism (SMA) has one focus in front of the retina with the other focus on the retina
- Simple hyperopic astigmatism (SHA) has one focus on the retina and one behind it
- Mixed astigmatism (MA) has one line of focus in front of the retina and the other behind it.

Figure 1.4 shows light from infinity entering an eye with mixed astigmatism, where the first focal line is in front of the retina and the second focal line is behind it. In this particular instance the circle of least confusion lies upon the retina but this is not always the case even in mixed astigmatism.

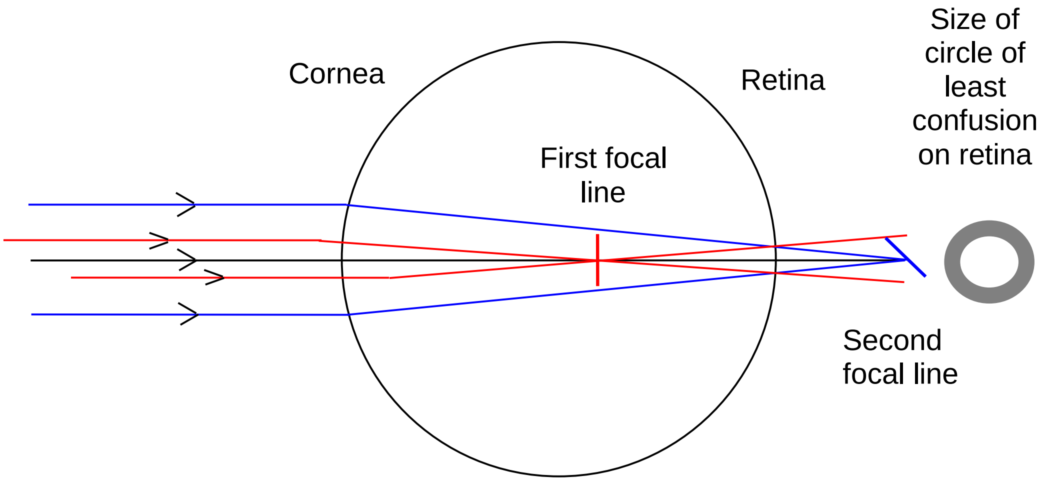

Figure 1.4: Light focused in an eye with mixed astigmatism. One line of focus is shown in front of the retina and the other behind it. The circle of least confusion is falling upon the retina in this example.

1.3.5 Relating vision to refractive error

It may initially seem obvious that the higher an eye's refractive error the less clearly it will see in an unaided state. While this is generally true for myopes, the same cannot be said for young hyperopes who may have approximately 9-10 dioptres of accommodation at 20 years of age (Jackson, 1907; Duane, 1908), and who for a short task such as measurement of vision could accommodate through 7 or more dioptres of hyperopia. As accommodation reduces with age, hyperopes' vision will reduce with time as they can no longer overcome the hyperopia and it will become a manifest refractive error, causing blur.

A common 'rule of thumb' given to students states that for every 0.25 dioptres of spherical error or 0.50 dioptres of cylindrical error the subject's unaided vision will reduce by approximately one line of Snellen acuity (Elliott, 2007). This is only an approximation, and with experience it becomes clear that not all eyes follow such a simple rule.

Similarly, many optometrists will be familiar with the +1.00D blur test, which is usually used to check that the patient's accommodation is fully relaxed and balanced at the end of a refraction. When refraction has been completed, a +1.00DS lens is introduced, blurring vision. It is often taught that vision will be blurred back to approximately 6/12 but there are patients who will only blur to 6/9 on this test while others will only see 6/18. Elliott (2004) suggested that vision should be reduced by approximately four lines of acuity when a +1.00D fogging lens is introduced but as different charts use different increments between lines this can be a confusing rule to follow.

Astigmatism is another source of confusion: an eye with a prescription of +1.50DS/-3.00DCx180 will have a circle of least confusion on the retina, with a mean spherical equivalent of zero, but it will not have clear unaided vision. Furthermore, would a different astigmatic axis of say 45, 60 or 90 affect the vision differently? Elliott (2007) suggested using best vision sphere, or mean spherical equivalent (half the power of the cylinder plus the power of the sphere) to estimate unaided vision. This is because uncorrected astigmatism is considered to have approximately half the effect on vision as uncorrected spherical ametropia. In this manner -0.50DC will have a similar effect on unaided vision to -0.25DS, but Elliott also noted that oblique cylinders were more detrimental to unaided vision than orthogonal cylinders.

Major Pincus (1946) was concerned by the possibility of malingerers being incorrectly classified upon recruitment to the U.S. Army. He reviewed the physical examination of 45 206 men and women and a further 7 482 refraction records. He performed half of the examinations himself and the other half were performed by a trained associate. Subjects were not permitted to squint or tilt or turn their head. If the subject could not read 20/400 they were walked closer to the chart until they could read the 20/400 line, where the distance from the chart in feet was recorded as the numerator of the Snellen fraction. By moving subjects closer to the chart, Pincus increased the precision of vision measurement by allowing measurements of, say, 10/400 or 5/400 rather than recording vision as being 'less than 20/400'. All of those under the age of 40 years had a cycloplegic refraction whereas those individuals aged 40 or over had their manifest refractive error recorded. He noted that the unaided vision of people with the same refractive errors could be different and the reasons he suggested this could be were age, fatigue, areas of infection, malnutrition and accommodative power. There is no information on the study population profile in Pincus's paper but only healthy eyes were included in his study.

Although he does not appear to have performed any statistical tests on the data he collected, Pincus made several observations about his data. He saw that as refractive error increased, unaided vision decreased and that as average age increased in hyperopes, unaided vision appeared to decrease, as would be expected by the reduction in accommodation with age. Age did not appear to influence unaided vision in myopes or those with mixed astigmatism. Oblique astigmatic axes not only occurred less frequently than vertical or horizontal astigmatism but also yielded lower levels of unaided vision. Another interesting observation that Pincus made was that when he attempted to simulate refractive errors on himself he felt he was recognising figures or numbers which a person with the corresponding 'natural' refractive error would not have been able to see. This however contrasts with observations made by Ohlendorf et al. (2011) who found the visual system to be more tolerant of real refractive errors than simulated errors. This has implications for studies that simulate refractive error with lenses so a large study with vision measurements taken with natural refractive states was needed. Pincus used a very large collection of records from which to draw conclusions and gave an anecdotal reason for not using simulated refractive error. He did not however take pupil size into account.

For demonstrating the relationship between vision and ametropia the Aston University refraction simulators use an algorithm based upon a paper by Raasch (1995) who used the data from the paper by Pincus to compare three different methods of modelling the influence on unaided vision of spherocylindrical refractive errors and to explore the relative influences on unaided vision of spherical defocus versus spherocylindrical defocus. Raasch described the change in power with meridian as a sinusoidal graph demonstrating the 'excess power' induced by the cylindrical component of a spherocylindrical refraction. This is shown in Figure 1.5.

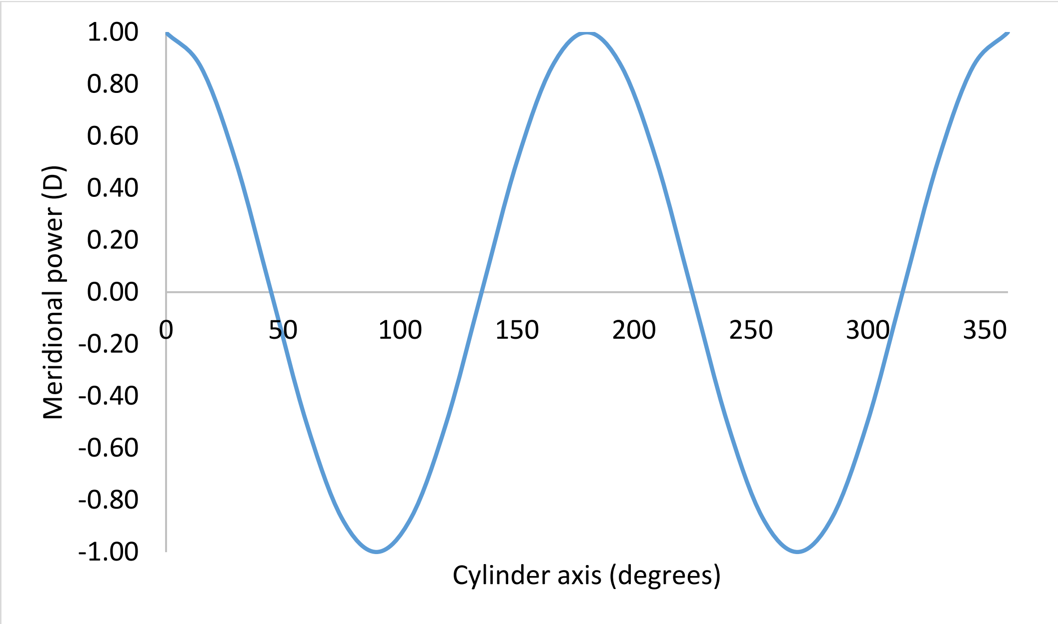

Figure 1.5: Power distribution of a lens with power +1.00DS/-2.00DC x 180.

In a purely spherical refractive error, the power distribution of the lens system does not change with meridian, i.e. the power is exactly the same whether it is measured vertically, horizontally or along an oblique axis (Raasch, 1995). A spherocylindrical refraction, which is a combination of both a spherical lens and a cylindrical lens, will vary in power according to the meridian. Figure 1.5 shows the power distribution of a spherocylindrical lens with the prescription +1.00DS/-2.00DC x 180. The greatest positive power of this lens is across the horizontal 0-180-360 degree meridian (along the minus cylinder axis) and the greatest negative power is across the vertical 90-270 degree meridian (perpendicular to the minus cylinder axis). The power follows a sinusoidal distribution with two periods through a 360 degree cycle with mean spherical equivalent (M) being represented by the power half way between the peaks and troughs, in this case (of mixed astigmatism) 0.00D. Changes to the spherical component alone will alter the vertical position of the curve but not its shape. Changes to the cylinder power will alter the amplitude of the peaks and troughs, whereas changes to the axis of astigmatism will shift the line along the x-axis. For an optometrist working in minus cylinder notation, the spherical power of the spectacle lens will be the highest point on the graph (+1.00D) and the cylinder will be the distance between this point and the trough (-2.00D). The minus cylinder axis is coincident with the highest peak (180). The total defocus can be thought of as the area between the curve and the baseline. The three methods of calculating total defocus were defined as ‘Root Mean Square,’ ‘Area’ and ‘Vector’ methods.

The Root Mean Square (RMS) method essentially squares the distance between each point on the curve and the baseline, finds the average of the squared distances, and then finds the square root of that average, and is shown by the equation

Equation 1.1 RMS = $\sqrt{\int_0^{2\pi} \frac{[S+C\,.\cos(2\theta)]^2}{2\pi}\, d\theta} = \sqrt{S^2 + \frac{C^2}{2}}$

Where S is the spherical component and C the cylindrical component of the refraction. The integration of the first expression makes direct calculation difficult, so when the integration can be performed to give the second expression. For spherical errors this is equivalent to measuring the distance between the curve (which for spherical errors is a straight line) and the baseline.

The area method calculates the area between the curve and the baseline and is shown in equation 1.2.

Equation 1.2 Area = $\int_0^{2\pi} \frac{S + C\,.\cos(2\theta)}{2\pi}\, d\theta$

The vector method was proposed by Thibos (1994) and it took into account the length of the vectors in a spherocylindrical refraction, and was given by the equation

Equation 1.3 Vector Length = $\sqrt{S^2 + C^2}$

None of these three methods of representing blur takes into account the axis of astigmatism.

Raasch used the data set from Pincus to determine which of the three methods of comparing spherocylindrical and spherical defocus made the best predictions with regard to empirical vision measurements because it was the largest existing set of data relating unaided vision to refractive error. He did not analyse data from hyperopic subjects as he considered accommodation to be too poorly controlled. This is despite the fact that Pincus carried out cycloplegic refractions in everybody under 40 years of age. Raasch could not control for pupil size as the military records lacked this data, but remarked that the data set represented the overall performance of eyes with their naturally-occurring pupil sizes.

He concluded that although it may be reasonable to use any of the three methods to determine total defocus in order to predict vision from refractive error, as correlation was high for all methods, the vector length was the best predictor of vision as it explained 92% of the variance compared to 85% for the RMS method and 84% for the blur area. The variance is the percentage change in a dependent variable that is explained by another, independent variable. In this instance, vision was the dependent variable and vector length, RMS and blur area were the independent variables. The three methods differed mainly in the weighting given to the cylindrical component. The greatest difference between the methods occurred when the cylinder was large in comparison to the sphere, as in mixed astigmatism and most notably if the mean spherical equivalent was zero. There was least difference between the methods in cases where the cylindrical component was small compared to the spherical component. The main advantage of the Raasch study was the large sample size of 7 000 recruits used to perform the analyses. He pointed out that this was an old data set and that methods of visual acuity measurement have changed but that the Pincus data set gave fine increments of visual acuity because the subjects were moved closer to the chart to extend the range of acuities measurable if they could not see the chart at the standard distance of 20 feet.

Raasch concluded that the vector addition model gave the highest correlation coefficient and was most consistent with the analysis of blur discs. The vector addition model gave the regression equation:

Equation 1.4 $$\mathrm{LogMAR} = 0.48 + 1.07\mathrm{Log}(U) + 0.46[\mathrm{Log}(U)]^2$$

Where U was the scalar vector and LogMAR is the logarithm base 10 of the minimum angle of resolution.

This paper has been quoted by many others (Raasch, 1997; Thibos et al., 1997; Raasch et al., 2001; Muñoz-Escrivá & Furlan, 2001; Reich & Ekabutr, 2002; Remón et al., 2006; Harris, 2007a; Atchison et al., 2009; Atchison & Mathur, 2011; Kobashi et al., 2012) and was the largest and most useful analysis of how unaided refractive error affects vision. It was this equation which was used in the Aston

University refraction simulators. However a broader contemporary study of subjects of all ages including eyes with different types of spherical and cylindrical refractive error together with known pupil sizes was needed in order to better represent what students and practitioners will see in practice.

Smith (1991) looked at previous studies to research the relationship between visual acuity and spherical refractive error in order to formulate a mathematical model to link acuity, refractive error and pupil size. The methods used in these studies varied, so many did not include pupil sizes, so where necessary Smith assumed a pupil diameter of 4mm. He pointed out that there are a number of factors affecting an individual's visual acuity such as target type, pupil size and subject's personality, but eventually arrived at the equations:

Equation 1.5 $MAR = kDE$ for high levels of ametropia

Equation 1.6 $MAR = \sqrt{[1 + (kDE)^2]}$ for low levels of ametropia

where D is the pupil diameter expressed in millimetres, E is the spherical refractive error and k is a constant which can be 'estimated from theory but should be determined from clinical studies'. The mean value of k was reported by Smith as 0.83 ranging from 0.55 to 1.33. What constitutes a 'high' or 'low' level of ametropia was not explained.

Tucker and Charman (1975) used constant chart luminance and a series of artificial pupils on two subjects (aged 26 and 36 years) under cycloplegia to investigate the effect of depth-of-focus on Snellen acuity. They used trial lenses to simulate refractive error. They found that for a given pupil diameter, the rate of recognition of a letter decreased as the angular subtense of the letter limb decreased, meaning that a letter was less likely to be accurately identified the smaller it became. They also found that positive lenses (simulated myopia) had a greater detriment to vision that the equivalent negative lens (simulated hyperopia) despite the use of cycloplegia. This was thought to be due to an increased in depth of focus when negative-powered trial lenses were used and a decreased depth of focus with positive powered lenses. This study used both cycloplegia and artificial pupils along with trial lenses to simulate a refractive error and only used two relatively young subjects who were thought to have acquired some skill in differentiating defocused letters through practice sessions which preceded the main study.

Although the point of this study was to investigate depth of focus, it gave useful information regarding vision and refractive error and acts as a reminder that unaided vision is influenced by depth of focus as well as spherocylindrical refractive error. Only two young subjects were used and this together with artificial pupils, cycloplegia and refractive errors simulated with lenses may raise questions about the applicability of these findings to real patients with real refractive errors. These issues are similar to those raised by Pincus.

All of the studies above demonstrated a need for the collection and analysis of a new large set of data across a range of subjects of different ages. Real pupil diameters needed to be taken into account as did unaided vision and refraction without cycloplegia. The Aston University refraction simulators have previously been based upon data for myopic eyes only so the relationship between hyperopia and unaided vision needed to be established to improve the realism of the simulators.

1.4 Objectives

The aim of the research presented in this thesis was to improve optometry teaching, especially with respect to refraction simulators by improving the formula used to relate vision to ametropia. To do this, a large sample of healthy individuals of both sexes with a large age range was used. The factors investigated include:

- Age
- Pupil diameter
- Magnitude and type of refractive error
- Magnitude and type of astigmatism

This study was designed to be relevant to training optometrists and possibly those already in practice so cycloplegia and artificial pupils were not used as the majority of refractions are performed under natural conditions without pupil dilation or cycloplegia. The results were used to produce a new algorithm for the refraction simulators to improve their relevance to the real world.

1.5 Summary

The largest compilation of data including unaided vision and refractive error was nearly 70 years old at the time of writing this thesis and did not take into account variables such as pupil diameter. The myopic data from this database was used by Raasch (1995) to create a formula for predicting vision based on refractive error and it is this formula which was subsequently used in the Aston University refraction simulators. Students reported that these simulators did not accurately reflect the relationship between vision and ametropia observed in real eyes. The study described in this thesis aimed to collect a new, large data set without artificial pupils or cycloplegia, which took into account factors such as the type of ametropia, age and pupil diameter to create a new algorithm for the refraction simulators. As far as the author is aware, no such data collection and analysis has been reported before and therefore, the work presented in this thesis represents an original contribution to knowledge.

2. Data Collection and Characteristics

2.1 Introduction

This chapter covers the logistics of data collection. This involved (1) ethical clearance and subject consent, (2) the monitoring of ambient and chart lighting conditions, (3) recording of age, sex and whether or not contact lenses were worn, and (4) retests in a subsample of subjects for the purposes of establishing the repeatability of each measurement made. In addition, this chapter discusses inclusion and exclusion criteria and presents the profile of the subjects in this study.

2.2 Research Ethics

This study received ethical approval from the Research Ethics Committee at Aston University (appendices 1 and 2) and all methods and processes used adhered to the Data Protection Act (1998) and the Declaration of Helsinki. Subjects were asked to read and sign a consent form (appendix 3) outlining the process they would follow and what would happen to the data collected. They were not penalised for not taking part nor were they rewarded for participating. A six-digit reference number generated by the practice's computer system was used to replace the identity of each subject. This meant that subject names, dates of birth and contact details were never stored in the database used for research purposes but if a question arose over a particular item of data it could be referred back to by accessing the practice computer system. Only three people had access to the research database (Rebecca Rushton, Mark Dunne [supervisor] and Richard Armstrong [statistical advisor]). None of the researchers had any financial or proprietary interest in any of the products used in this study.

2.3 Practice Setting

The practice was a medium-sized multiple (Specsavers) in Salisbury, England. All data were collected by the author, a fully qualified and experienced optometrist and the same examination room, equipment and chart set up were used throughout data collection.

2.4 Lighting

Luminance is a photometric term describing the way a surface emits or reflects light in a given direction and is measured in candelas per square metre (cdm^{-2}). This represents the visible light which the test chart emitted. Illuminance, also called illumination, is the quotient of luminous flux incident on a surface per unit area. It is measured in lux, which is defined as the illuminance produced by a luminous flux of one lumen uniformly distributed over one square metre (Millodot, 2008; Lighting Research Center, 2000). Illuminance represents the visible light incident at the eye. As refraction should be performed under conditions that reflect the subject's normal viewing conditions (Elliott, 2007), and most people do most viewing in light conditions, refraction was performed under photopic conditions, with luminance levels greater than 3.0 cdm^{-2} (Lighting Research Center, 2000).

The examination room lighting was kept at a constant photopic level during each eye examination by keeping the same lights on at all times. The illuminance incident at the subject's eye was measured using a digital Standard ST-1308 Light Meter (TENMA) by placing the light detector in front of the subject's right eye to ensure the light levels reaching the eyes were consistent throughout the day and throughout the study. This was measured thirty times over the first 4 days and was checked periodically throughout the study. Readings ranged from 87-117 lux (mean 106 lux, S.D. = 7 lux). Chart luminance was measured thirty times over 4 days at the beginning of the study using a Spectra Mini-spot Silicon Cell SpotMeter (Photo Research, Division of Kollmorgen Corporation, Burbank, California, USA) to confirm that it remained constant throughout the day.

2.5 Test Procedures

A standard eye examination was performed for each subject. This typically followed the sequence:

- Autorefraction
- History and symptoms interview
- Measurement of unaided vision
- Measurement of pupil diameter
- Binocular subjective refraction including Jackson cross-cylinder
- Slit lamp biomicroscopy

- Iris colour grading
- Binocular indirect ophthalmoscopy with Volk SuperField NC® (or Super VitreoFundus® for smaller pupil diameters)

A typical eye examination lasted 20-25 minutes.

2.6 Sample Profile

As most people in Salisbury were white (Office for National Statistics, 2004) the decision was taken to exclude other racial groups. The concern was that race could influence the outcomes of the study (Pan et al., 2013; Vitale et al., 2008; Semes et al., 2006; Logan et al., 2005; Kleinstein et al., 2003). Other ethnic groups could have been included but their numbers would have been too small to allow meaningful analysis of their impact on the study outcomes. Many subjects attending for eye examinations were also contact lens wearers. For the purposes of this study a subject was classed as a contact lens wearer if they had worn a contact lens at any point within 6 months prior to data collection. Exclusion of these subjects would have substantially reduced the size of the sample. In this case, numbers of subjects wearing or not wearing contact lenses were substantial enough to allow investigation of the effects of contact lens wear on the study outcomes (see Chapter 8).

Data were initially collected from 948 white subjects (560 females, 388 males) aged from 20 to 70 years (mean = 44.5, S.D. = 14.1 years) attending for routine eye examinations. This represented 29.7% of the 3 190 patients of all ages seen by the author for eye examinations in the 18 month data collection period (between October 2009 and March 2011). This age range was chosen as data was to be collected in 5 year strata, subjects aged under 18 years needed parental/guardian consent, and those over 70 were deemed more likely to have pathology such as cataract. Data were collected from the right eye only as inclusion of data from both eyes would have complicated statistical analysis (Armstrong, 2013).

In addition to excluding all racial groups except white people, other exclusion criteria were:

- Corrected visual acuity less than 6/7.5. Anything less than this could be indicative of pathology or amblyopia. This is the same criteria used by Elliott and Cox (2004) and Winn et al. (1994). Millodot (2008) defines amblyopia as 6/9 or worse in one eye but the letter chart used had lines for

6/7.5 or 6/10. A stricter criterion of 6/7.5 was used in the present study as subjects with vision of 6/10 are more likely to have pathology or amblyopia than those who can read 6/7.5.

- Unaided vision of less than 1/60. This was because (1) the patient chair prevented nearer testing distances and (2) non-chart based methods such as counting fingers and hand movements would have to be used at lower levels of vision, making meaningful analysis difficult. This approach was also taken by Patel et al. (2008);
- Use of taking medication which could affect a subject's judgement, for example sedatives;
- Use of medication which could affect their vision, pupil size, iris colour or any of the factors measured. This included medications such as anti-malarials or tamoxifen (both can affect vision), co-codamol (affecting pupil size), prostaglandin analogues (affecting iris colour) (Twa et al., 2004);
- Previous surgery on their right eye or that which may affect the right eye;
- Presence of ocular or systemic conditions likely to affect any of the factors measured, including pregnancy, diabetes, cataract, glaucoma etc. (Sheedy et al., 2004);
- If the optometrist suspected the subject of malingering, giving false or misleading results or having poor subjective responses;
- Refusal to participate in the study
- Incomplete data collection
- Unexpectedly good vision at a reduced testing distance (see Section 3.5)

After all exclusions there remained 873 data sets (515 female) with a mean age of 44.4 years (S.D. = 14 years). Data were collected in 5 year cohorts (20 to 24, 25 to 29, …, 65 to 70) and it was intended that at least 60 subjects would fall into each cohort, 30 from each sex. The dashed lines in Figure 2.1 show that each age cohort had at least 60 subjects although not every category had 30 males. Every group had over 30 females.

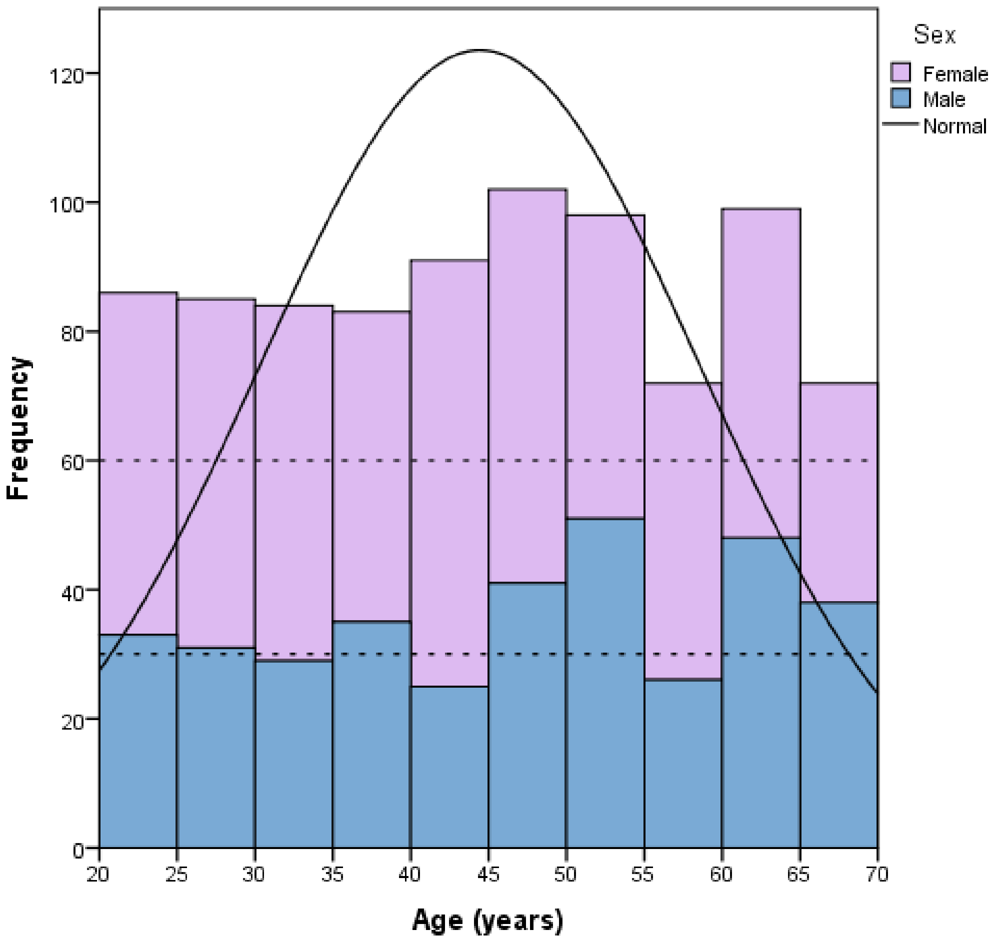

Figure 2.1: Frequency distribution of subjects' ages in 873 right eyes with proportion of each sex and overlaid normal distribution curve. The dashed lines represent intervals of 30 which is the number of subjects of each sex that the study aimed to examine.

As expected by the method of data collection and as shown in Figure 2.1, age was not normally distributed. In the 2011 census (Office for National Statistics, 2012), both the Wiltshire and England populations were greatest in the mid-forties with a smaller peak at age 64. Because of the much smaller population in this study the distribution was not so clear but the greatest frequency occurred at age 49 years. The 55-59 year age group showed the least number of subjects in this study (n = 72) whereas the census statistics for Wiltshire show the lowest number to appear in the 30-34 age category. This may be explained by the large number of contact lens wearers in this group, who tend to be younger.

According to the 2011 Census (Office for National Statistics, 2012) 52.9% of the population of the Salisbury area (all races) were female. In the current study 59.0% of subjects were female. This comparatively high proportion of female attendees is slightly higher than but still comparable to that found by other authors: Pointer

(2007) found 56% of his study group was female (of 1288 subjects); Montés-Micó & Ferrer-Blasco (2000) had a 52% female proportion (of 7621 subjects). In Machan et al.'s 2011 study looking into how representative the Waterloo Eye Study was of the general population, 54.1% of the 6397 subjects attending over a 1 year period were female and this was compared to a statistic that 51% of Canadians aged 15-64 were female (Machan et al., 2011; Statistics Canada, 2007).

It is possible that the higher than expected proportion of female subjects was due to female patients' tendency to prefer consultations with female health professionals and conversely male patients' preference for male health professionals (Menees et al., 2005; Bryson & Warner-Smith, 1998; Kerssens et al., 1997).

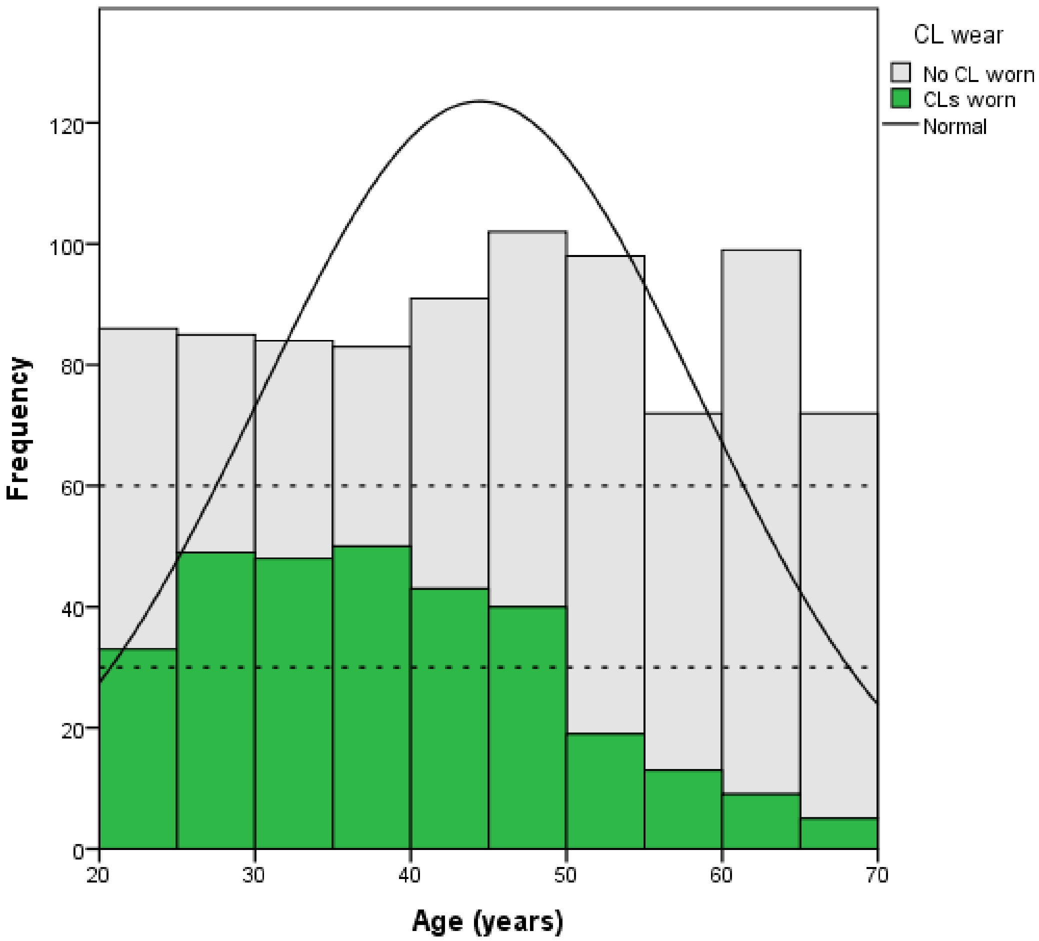

Figure 2.2: Frequency distribution of subjects' ages in 873 right eyes with proportion of contact lens wearers and overlaid normal distribution curve. The dashed lines represent intervals of 30 which is the number of subjects of each sex that the study aimed to examine.

Contact lens wearers made up 35.4% (n = 309) of the population of this study although this was not evenly distributed through the age groups as shown in Figure 2.2. Morgan (2009) estimated the national proportion of contact lens wearers to be 7.2%. The reason for this very large bias towards contact lens wearers was that the author was running a contact lens clinic on three out of the five days each week where patients could attend for a contact lens aftercare as well as an eye examination and many subjects from this study were examined on these days.

2.6.1 Repeatability

After the initial consultation subjects were invited back for a second appointment which was structured as described in Section 2.5 to measure from the right eye vision, refraction, pupil size and iris colour, to check repeatability of each measurement. The aim was to collect data from at least 50 randomly selected subjects, 5 of each sex within each age cohort.

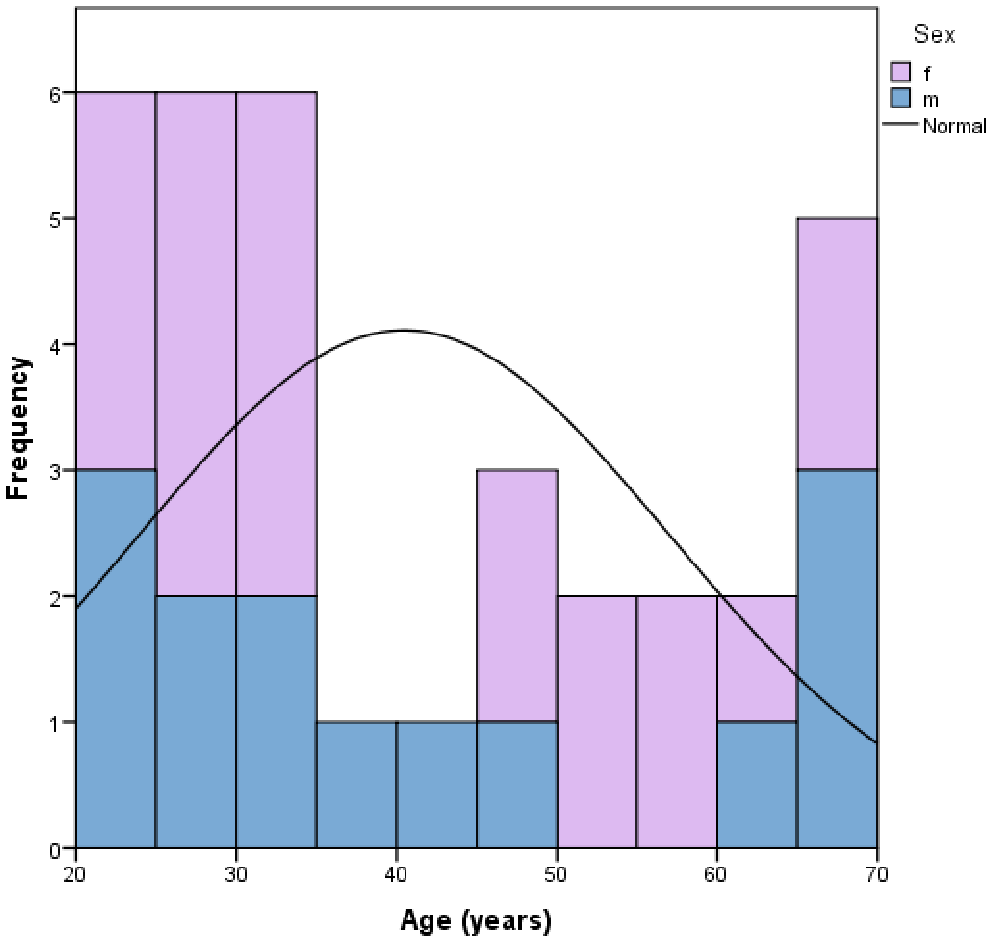

Figure 2.3: Frequency distribution of subjects' ages in 34 right eyes with proportion of each sex and overlaid normal distribution curve.

These second visits took place between 2 and 98 days (mean 19.8, S.D. = 18.5 days) following the initial consultation. The original notes were not referred to until analysis to avoid bias. A total of 34 subjects were included in the repeatability group ranging in age from 20 to 69 years (mean 40.5, S.D. = 16.5) as shown in Figures 2.3 and 2.4. Of these subjects, 58.8% were female (n = 20), as shown in Figure 2.3, and 44.1% (n = 15) were contact lens wearers as can be seen in Figure 2.4.

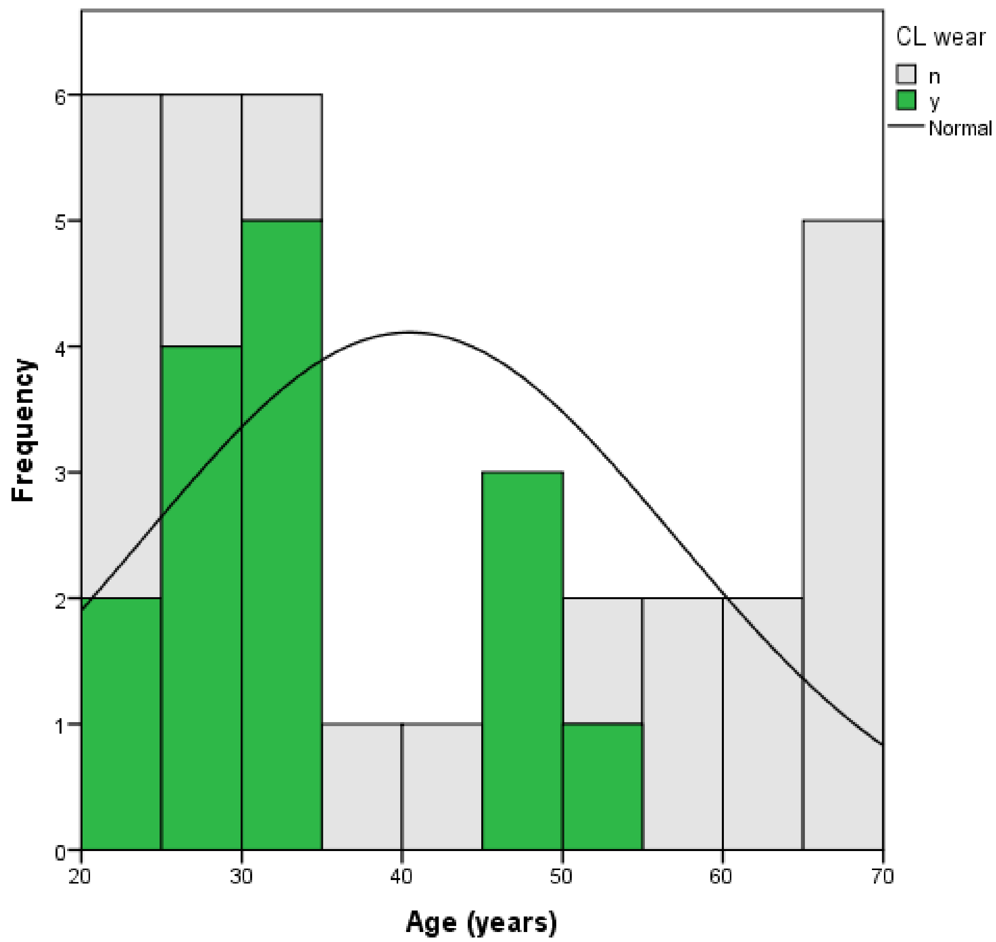

Figure 2.4: Frequency distribution of subjects' ages in 34 right eyes with proportion of contact lens wearers and overlaid normal distribution curve.

As the subjects had not come into the practice for their initial eye examination knowing that they would be taking part in the study, many were short on time and some were moving away from the area, so the repeatability was biased towards contact lens wearers (who often had to return for a check on new lenses) or subjects over 65 years of age who were retired and had more freedom to return to the practice for repeat measurements, hence the original aim of repeating measurements on 50 subjects was not achieved.

2.7 Summary

The location, type of practice and the sex of the optometrist may have led to an unusually high proportion of females and contact lens wearers amongst subjects of this study. The possible influence of sex and contact lens wear on the relationship between vision and ametropia is explored in Chapter 8. Recruitment targets meant that age was not normally distributed and the impact of this on multiple regression analysis, which requires normally distributed data, is explored in Chapter 9. Before discussing these aspects, more information on the measurement methods, frequency distribution and repeatability of unaided vision (Chapter 3), refractive error (Chapter 4), pupil size and iris colour (Chapter 5) are covered.

3. Measurement of unaided vision

3.1 Introduction

This chapter starts with a literature review detailing previously published methods of recording unaided vision including an overview of test chart design. The methods adopted in this thesis are then described and followed by presentation of the repeatability of the chosen method of recording unaided vision.

3.2 Literature review

The measurement of high contrast vision is one of the mainstays of the eye examination. It can provide the optometrist with a lot of information and is usually a simple task for the subject to carry out. There are many charts available for the measurement of vision but it is vital that whichever method is used it demonstrates a high degree of repeatability and reproducibility. In the UK, British Standard BS 4274-1:2003 (British Standards Institution, 2003) specifies the minimum requirements for test chart types in the determination of distance unaided vision and visual acuity.

There are different classifications of visual acuity but only resolution and recognition acuity will be covered in this thesis. Resolution acuity is the smallest detail the eye can resolve, for example being able to tell where the break in a Landolt C occurs. Recognition acuity is the smallest detail the eye can recognise, for example to be able to recognising the difference between Y and V. Other types of acuity include detection acuity which is the ability of the eye to see a tiny object or detail (for example a speck of dust or grain of sand), and hyperacuity, which is the ability of the visual system to determine differences between two stimuli, such as the misalignment of two lines (Millodot, 2008; Saunders, 2004).

3.2.1 Recording vision

Vision can be recorded as a Snellen fraction, Snellen decimal, minimum angle of resolution (MAR) or logarithm of the minimum angle of resolution (LogMAR). To record vision as a Snellen fraction, the distance from the chart at which the test is conducted is recorded as the numerator, at the top of the fraction. This distance may be measured in feet (common in the USA) or metres (common in Europe).

The standard testing distance is usually 20ft or 6m but other testing distances may be used. The line on the chart correctly read by the subject is recorded as the denominator on the bottom of the fraction. Each line on the Snellen chart is represented by a number which determines the distance at which the gaps between the limbs of the letters subtend 1 minute of arc ('). This means that if a subject can read all of the letters on the 6/6 line from 6m, their MAR is 1'. If the chart is calibrated in feet their vision will be recorded as 20/20. If this same subject is brought to 3m from the chart they should be able to read the 3/3 line. To convert a Snellen fraction to a Snellen decimal, the numerator is divided by the denominator. For example 6/6 = 1.0, 6/12 = 0.5, and so on. To convert a Snellen fraction to MAR, the denominator is divided by the numerator (i.e. the fraction is inverted). A vision of 6/12 equates to an MAR of 12/6 = 2'. The LogMAR score is the logarithm to the base 10 of this value. So 6/6 is equivalent to 20/20 and both have a minimum angle of resolution of 1' which gives a LogMAR score of 0.

Where a subject does not read the whole line correctly, it is usual to record the number of errors made. When recording vision as a fraction the number of incorrect letters is preceded by a minus symbol. If a subject made 2 errors when reading the 6/6 line, this is recorded as 6/6-2. If some extra letters can be read on the line below, the number of extra letters is recorded following a plus symbol. For example, if a subject correctly read the 6/6 line and correctly identified one letter on the following line, this would be recorded as 6/6+1.

With standard LogMAR charts each line represents 0.1 LogMAR and as each line contains 5 letters, each letter has a LogMAR value of 0.02. If one error was made when reading the 0.0 line, 0.02 is added to the line value of 0.0 so the vision would be recorded as 0.02. If the 0.3 line was correctly read and two letters beneath it were read, 2 x 0.02 is subtracted from the line value, giving a score of 0.26. Vision better than 0.0 LogMAR (6/6) has a negative value.

3.2.2 Chart design

There are many charts available for the measurement of vision and visual acuity, many of which were described by Bennett (1965). The Snellen chart introduced in 1862 (Snellen, 1862) is perhaps the most recognisable of these vision charts but has its limitations. It typically comprises of a series of black letters on a white background with one large letter at the top and an increasing number of letters of smaller sizes on subsequent lower lines. Over the years the Snellen chart has taken many forms and the term ‘Snellen chart’ no longer refers to a specific chart design (Bailey & Lovie-Kitchin, 2013; Williams et al., 2008; Bennett, 1965). Optotypes are standardised symbols used for the measurement of vision. They are usually letters though they can be numbers or pictographs and they may be serifed (E) or non-serifed (E). The original chart designs were serifed but modern charts tend to be non-serifed (British Standards Institution, 2003; Sloan, 1952). Each optotype is designed around a grid of typically 4 units wide x 5 units high, as in the British Standards letter set, or 5 units wide x 5 units high, as in the Sloan letter set, although Snellen’s original design used a framework that was 5 units high x 6 units wide. Limb widths of the optotypes are usually one unit. Raasch et al. (1998) compared the chances of correctly identifying British and Sloan letters against Landolt rings. They found visual acuity measurements to be slightly better but clinically insignificant (-0.005 LogMAR, less than 1 letter) when measured with the British Standard letters and better still (-0.038 LogMAR, nearly 2 letters) when measured using the Sloan letter set compared to Landolt rings. Hazel & Elliott (2002) found statistically better vision with Sloan letters than British Standard letters, and remarked that this could be due to the smaller 5 x 4 construction in the latter, however they found the difference in recorded vision to be clinically negligible. Little et al. (2012) compared paediatric vision charts and found differences in their ability to detect astigmatism, especially with-the-rule astigmatism. This may be due to the construction of the optotypes used, for example, Kay pictures which have few vertical lines prove resistant to the detection of astigmatism. The chart may be backlit or illuminated from in front although modern charts are usually projected, backlit or presented on a computerised screen (Cubbidge, 2009).

Popular alternative optotype designs include:

- Landolt C / Landolt broken ring

  This chart presents a series of ‘C’ optotypes in different orientations and the subject identifies where the gap in the ring occurs
- Tumbling E / Illiterate E

  This chart presents a series of ‘E’ optotypes in different orientations and the subject is to identify in which direction the limbs of the letter are pointing
- Lea symbols

Introduced in 1980 (Hyvärinen et al., 1980) this chart presents four symbols (circle, square, house, apple) which look very similar to one another when the limits of recognition visual acuity are reached.

Bailey and Lovie (1976) and Sloan (1980) highlighted several reasons why the Snellen chart is inappropriate for lower levels of vision but noted that the limitations in measurement of lower levels of vision with the Snellen chart were probably due to the chart construction – Snellen charts tend to be tall and narrow meaning many small letters can appear on the lower lines but only one large letter may appear at the top. On a classic Snellen chart the top line is one letter of size 6/60, the spaces between the limbs of the letter subtending 10', and beneath that two letters of 6/36, the spaces between the limbs of the letters subtending 6'. At the bottom of the chart, the 6/6 line equates to 1' and the 6/5 line 0.83'. The lower lines allow very fine differences in vision to be measured whereas the higher lines do not. Precision varies even more across Snellen charts because each letter can be given weight on the lower lines, with acuities such as 6/5-3 or 6/6+2 being recorded but with the higher lines having fewer letters there is less scope to precisely record exactly what the subject sees. Another drawback to the traditional Snellen design is that each line does not represent equal task difficulty to the subject by equalising the crowding phenomenon and there is little consistency in the space between letters or the space between rows.

The crowding phenomenon is the impairment of discrimination of objects when they are presented near other objects (Millodot, 2008). This means that if a single letter is presented on its own on a blank field, there is a much greater chance of that optotype being correctly identified than if it was presented with other letters or lines (Scialfa et al., 2013; Millodot, 2008; Rabbetts, 2007; Bouma, 1970). On a classic Snellen chart, the letters nearer the top of the chart are not crowded by as many other letters, meaning lower lines present a relatively more difficult task for the subject.

Another difficulty across charts is that not all letters are equally legible (McMonnies & Ho, 2000). Sloan et al. (1952) recommended the use of a set of 10 non-serifed letters (C, D, H, K, N, O, R, S, V, Z) within a square outline with a stroke width one-fifth the height of the letter. The British Standard BS 4274-1:2003 (British Standards Institution, 2003) specifies non-serifed letters of square construction with stroke width one-fifth the height of the letters and adopts a specific letter set

(C, D, E, F, H, K, N, P, R, U, V, Z). Reich and Ekabutr (2002) compared vision with simulated refractive errors for the Landolt C and Tumbling-E charts, finding that the two tests were comparable for all conditions except simulated against-the-rule astigmatism, with the Landolt C yielding worse vision than the Tumbling-E. Different axes of astigmatism may affect vision measurements (Kobashi et al., 2012; Mitchell & Wilkinson, 1974) and this is discussed further in Chapters 4, 6 and 7.

One way to equalise the task across the chart whilst improving the precision of vision measurement is to increase the number of letters on the higher lines. The chart designed by Bailey and Lovie (1976) aimed to present an equal task for each line by:

- Using standardised non-serif letters of near-equal legibility
- Presenting the same number of letters on every line
- Keeping between-letter spacing on each line equal to the width of the letters on that line
- Using between-row spacing equal to the height of the letters in the smaller row
- Using a geometric progression of letter size whose ratio or multiplier is equal to 0.1 log unit

This chart design ensures that there is increased sensitivity if a non-standard testing distance is used so if the subject cannot see the top line at 6 metres the testing distance can be reduced to 4, 2 or 1m (Sloan, 1980) with a temporary addition of +0.25D, +0.50D or +1.00D used to bring the chart into clear focus where necessary. The Bailey-Lovie design principles now form the 'gold standard' for visual acuity research (Bailey & Lovie-Kitchin, 2013; Hazel & Elliott, 2002).

There are several charts available which follow LogMAR scoring principles (Hazel & Elliott, 2002) but the best known is the Early Treatment of Diabetic Retinopathy Study (ETDRS) chart, which follows the principles of Bailey and Lovie (Bailey & Lovie-Kitchin, 2013; Ferris et al., 1982; Kassoff et al., 1979). Originally designed for use in a multi-centre study on the efficacy of treatment for diabetic retinopathy, this chart used 5 Sloan letters of 5x5 design on each row and was calibrated for use at 4m. In clinical practice it is better to use a testing distance of 6m as this equates more closely to optical infinity, with light from 6m having a divergence of -

0.17D which is less than the 0.25D increments used in spectacle refraction (Cubbidge, 2009).

Although many types of chart are available for the testing of vision, LogMAR style charts are the accepted gold standard and it was this type of chart which was used in the present study.

3.3 Methods

3.3.1 Unaided vision

3.3.1.1 Nidek SC-2000 test chart

Unaided vision of the right eye was measured using a computerized LCD chart (SC-2000 [UK Type], Nidek, Japan) with a mirror to take the viewing distance to 6 metres. The chart displays 8 lines of 5 high contrast non-serif black letters on a white background giving a range of acuities when viewed from 6m of 6/20 to 6/3 in a similar manner to the ETDRS chart, scored as 6m Snellen fractions. The ten 5 x 5 construction 'Sloan' letters (C, D, H, K, N, O, R, S, V, and Z) (Committee on vision, 1980; Sloan, 1952) are used in this chart.

3.3.1.2 Calculation of line and letter LogMAR values

The Nidek chart used was presented in a similar manner to an ETDRS chart but measurements were calibrated as a 6m Snellen fraction. A standard ETDRS chart has constant line values of 0.1 and constant letter values of 0.02. However, the non-LogMAR scoring format of the Nidek chart meant that LogMAR values had to be assigned for each line and letter in order to be comparable to previous studies.

1) The LogMAR value for each line was calculated using the equation:

Equation 3.1 LogMAR line value = $\log_{10}$ (Snellen denominator value / testing distance).

If the Snellen denominator value assigned to the last line read was 15 and the testing distance was 1m then the LogMAR value of that line was $\log_{10}$ (15/1) = 1.176.

2) The line interval was calculated by subtracting the value of the line in question from that of the line above it. In this case, the LogMAR value of the 1/15 line is 1.176. The line above it is 1/20, which has a LogMAR value of 1.301. The difference between the two line scores gives the line interval which is 1.301 - 1.176 = 0.125 LogMAR. For the top line, the line interval was taken to be the average of all of the other line intervals (always 0.103 LogMAR).

3) The letter value to be applied was taken as the line interval divided by the number of letters on the line (5). A letter on the 1/15 line therefore had a letter interval score of 0.125 / 5 = 0.025 LogMAR.

4) A LogMAR value adjusted for incorrect letters used the equation:

Equation 3.2 Adjusted LogMAR = LogMAR line value + (incorrect number of letters x the letter value for that line).

For example, if 3 letters were missed on the line then the adjusted LogMAR value became 1.176 + (3 x 0.025) = 1.251.

5) The adjusted LogMAR value was then converted to MAR. The equation used was:

Equation 3.3 $\text{MAR} = 10^{\text{Adjusted LogMAR value}}$

For example, the adjusted LogMAR score of 1.251 becomes $10^{1.251} = 17.8'$.

Appendix 4 shows a table displaying line and letter values. Each letter was given a value following cautions that visual acuity should be recorded with respect to the distance at which the measurements were taken (Cubbidge, 2009). The average line interval was 0.103 LogMAR and the average letter value was 0.021 LogMAR. This gave a theoretical precision of unaided vision measurement of ±0.021 LogMAR using this chart, compared to ±0.02 with a standard ETDRS chart.

3.3.1.3 Method of recording unaided vision

Vision of the right eye was recorded on a letter-by-letter basis to give the most precise results possible (Vanden Bosch & Wall, 1997). The right eye was chosen to be measured as a combination of right and left eyes in a sample requires more complex statistical analysis. An alternative would be to have chosen the dominant eye, but selection of ocular dominance is time-consuming in a commercial environment and is more difficult and prone to error than choosing either right or left eyes. If letters were read incorrectly on more than one line, the lowest line where the subject could read at least two letters was considered the lowest line read. This method was used as it is similar to that used by others (Lovie-Kitchin & Brown, 2000; Nichols et al., 2000; Haegerstrom-Portnoy et al., 1999; Raasch et al., 1998; Brown & Lovie-Kitchin, 1993) as astigmatic subjects frequently guess multiple letters incorrectly on several lines, sometimes wrongly guessing five letters on one line whilst still being able to read a few letters on the line beneath. Rosser et al. (2004) and Carkeet et al. (2001) required a full line of errors to be made before testing was ended, whereas Carkeet (2001) recommended stopping once four mistakes had been made on one line. Arditi and Cagenello (1993) required that their subjects guess at every letter on the chart. In the present study, subjects were simply asked to read to the lowest line they could, and when they could not read further, the test was terminated. The most precise method would be that which forced the subject to guess at every letter on the chart, but this would be time-consuming and is not feasible in a commercial environment. A method which requires a full line of letters to be read would give the least precise measure of vision, so a method which had been used by others which was between the two was selected as that used in the present study. An alternative approach would be to use a ‘staircase method’ (Cornsweet, 1962), which may more accurately pinpoint vision, but this method was deemed too time-consuming for commercial practice and was found by Hazel & Elliott (2002) to offer no significant benefit over the quicker method of letter-by-letter scoring.

Confusion between similar letters such as C and O were counted as a correct response (Bailey & Lovie-Kitchin, 2013; Atchison & Mathur, 2001; Lovie-Kitchin & Brown, 2000). A frosted occluder was used to cover the left eye when any measurements of vision were taken. This meant that the subject could not read any letters on the chart with the left eye but light could still enter it, minimising consensual pupil dilation. If the subject could not read the chart at 6m they were taken to 3m, then 2m then 1m. This allowed poor unaided vision to be measured in finer increments than 6/36, 6/60 or 6/120 if the top line could not be read. The subject was asked to guess at lower lines so best possible vision was recorded, as in other studies (Pointer, 2014) in order to reduce variability (Carkeet, 2001). On the SC-2000 chart the optometrist could choose between two charts identical apart from the letter selection (ETDRS 1 and ETDRS 2). Either chart was used and if it was considered at any time the subject was memorising letters the other chart was displayed to check acuity was being measured accurately.

Each subject's unaided vision was initially recorded in terms of

- The viewing distance
- The Snellen denominator value of the lowest line read
- The number of incorrect letter calls on that line

This information was used to convert Snellen vision into LogMAR vision by the process outlined in Section 3.3.1.2.

3.3.2 Lighting

As one of the factors under investigation was pupil diameter it was important to keep lighting levels as consistent as possible when measuring pupil diameter and unaided vision. This was achieved by keeping all lights on in the consultation room at all times, and by keeping the high contrast acuity chart and computer workstation screen on and slit lamp off as pupil measurements were taken. In addition to this, the room door and window blackout blind were kept closed throughout.

Chart luminance values found with the Spectra Mini-spot Silicon Cell SpotMeter (Photo Research, Division of Kollmorgen Corporation, Burbank, California, USA) were between 176 and 208 cdm^{-2} (mean 195 cdm^{-2}, S.D. = 8.9 cdm^{-2}) which was consistent with the British Standard BS 4274-1:2003, which requires chart luminance to be not less than 120 cdm^{-2} (British Standards Institution, 2003), and within the acceptable range of 80-320 cdm^{-2} quoted by Elliott (2007). Illuminance at the plane of the pupil was found to range between 87 and 117 lux (mean 105.8, S.D. = 5.82 lux) over the course of the study, with no diurnal or seasonal pattern apparent in changes in illuminance. Section 2.4 details the methods used to collect this data.

3.4 Repeatability of LogMAR scores

As detailed in Section 2.6.1, 34 subjects had measurements repeated for their right eyes. A Kolmogorov-Smirnov test demonstrated that LogMAR vision showed a significant departure from a normal distribution.

Here it should be noted that there is a difference between repeatability and reproducibility. Repeatability is the similarity of results when the same conditions are used. When investigating the repeatability of measurements of unaided vision this means measuring the similarity of the results obtained when the subject, optometrist, room, testing equipment and testing procedures are the same. Reproducibility measures the similarity of results gained when a different practitioner uses the same methods in a different setting. For example, Zadnik et al. (1992) investigated the *repeatability* of the measurement of refractive error and ocular components separated by 1-14 days, although this study used different examiners, the same equipment and procedures were used each time. Shah et al. (2009) investigated *reproducibility* by sending three subjects to have eye examinations performed by different practitioners in different locations using different equipment and techniques.

The 95% limits of agreement give the results within which 95% of readings will lie (Shah et al., 2009), in other words repeated measurements are not expected to lie outside of this range more than one in twenty times. It is calculated by multiplying the mean standard deviation of the differences between measurements by 1.96 (Shah et al., 2009; MacKenzie, 2008; Sheedy et al., 2004; Rosenfield & Chiu, 1995; Arditi & Cagenello, 1993). The 95% limits of agreement are also referred to as the coefficient of repeatability or COR (Bullimore et al., 1998).

Westheimer (1979) recommended the use of LogMAR as opposed to other scales of acuity when representing vision graphically and most other studies have done this (Mercer et al., 2013; Kamiya et al., 2012; Wolffsohn et al., 2011; Radhakrishnan et al., 2004; George & Rosenfield, 2004). Although MAR is used in analyses described in later chapters, the repeatability of LogMAR scores is shown in this section to allow comparison with other studies.

Elliott and Sheridan (1988) found a COR of ±0.21 LogMAR (10 letters) in their experiment with healthy eyes. They measured the subject's dominant eye with a

LogMAR chart at 4m. Their COR for visual acuity (best corrected vision) was much better at ±0.07 LogMAR (3.5 letters), suggesting that variability may be greater in eyes with poorer vision, this being similar to the findings by Carkeet et al. (2001) that variability was greater in unaided vision rather than aided visual acuity, and Rosser et al. (2004) that variability increased as optical defocus increased. They used a comparatively small number of subjects (n = 20) and refractive errors included were limited to less than ±6.00DS.

Siderov and Tiu (1999) found a COR of about ±1.5 LogMAR (8 letters) when investigating the variability of measurements of visual acuity (VA). Reeves et al. (1993) found that a 'significant change' which would be observed in only 5% of the population would constitute 2 lines of LogMAR vision (10 letters).

Leinonen et al. (2005) found a standard deviation of measurement error of ±0.04 LogMAR (2 letters) when investigating random error in measurement of visual acuity, which gave a COR of ±0.08 LogMAR (4 letters).

Ehrmann et al. (2009) found a COR of visual acuity testing of ±0.07 LogMAR (3.5 letters) when using a high contrast Bailey-Lovie (LogMAR) chart on a computer monitor. They found slightly better repeatability of ±0.06 LogMAR compared to ±0.07 LogMAR when using paper-based rather than monitor based charts, and that high contrast visual acuity was more repeatable than low contrast visual acuity. The subjects on average saw 1 letter more with the computerised chart than the paper chart, and it was thought that this may be due to more uniform illumination of the computer screen compared to the paper.

Figure 3.1 is a difference versus the mean plot, as described by Bland and Altman (1986), and was used to calculate the coefficient of repeatability (COR). It shows that repeated measurements varied between -0.2 and 0.5 LogMAR units which is up to 5 lines of acuity difference in the repeated measures. The mean difference was 0.05 LogMAR S.D. = 0.16 LogMAR units. The COR was calculated by multiplying the standard deviation of the mean difference by 1.96, giving a COR of ±0.31 LogMAR units (16 average letters).

Linear regression revealed a statistically significant relationship ($p = 0.002$) between the difference and mean of LogMAR scores (see Figure 3.1). This could show that repeatability got worse as vision got worse. Patel et al. (2008) found a similar effect when studying repeatability of visual acuity measurements in eyes with age-related macular degeneration, and Elliott and Sheridan (1988) found a higher COR for unaided vision compared to visual acuity.

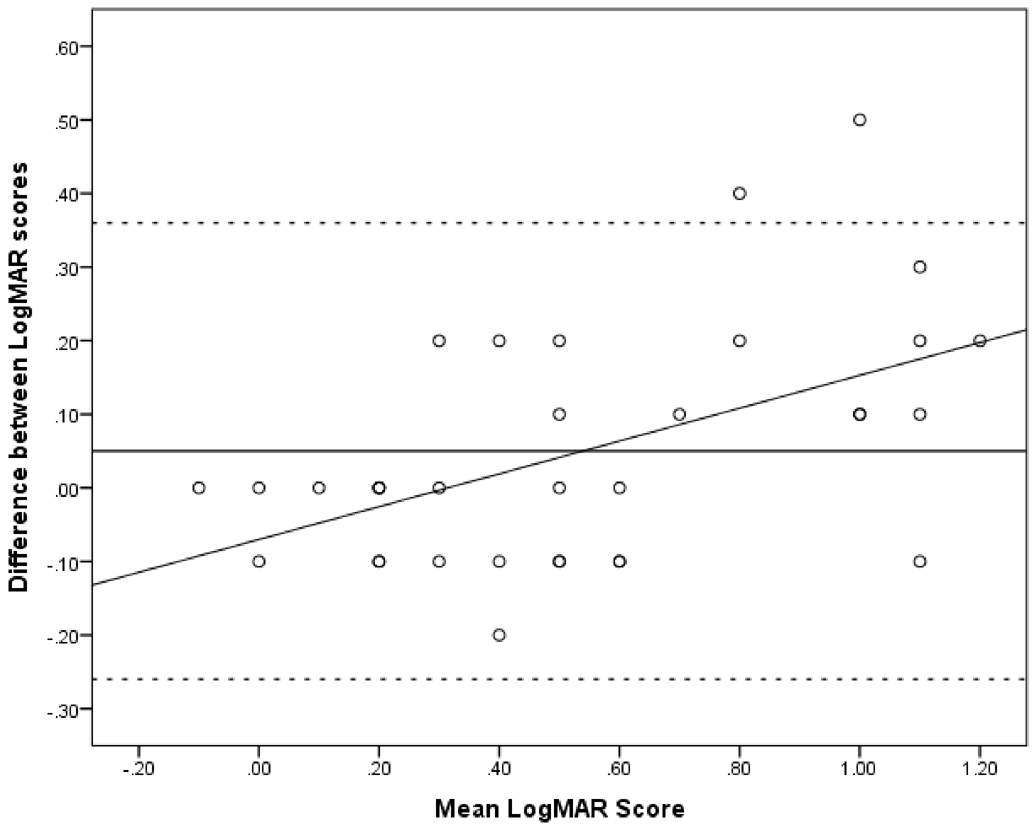

Figure 3.1: Difference versus the mean plot of LogMAR readings. The solid horizontal line shows the mean difference between LogMAR scores while the dashed lines show the 95% confidence interval. Linear regression gave a line with the equation y = (0.223 x mean LogMAR score) - 0.07. There is superimposition of 6 datum points as 34 eyes were used to plot this graph but only 28 points are visible.

3.5 The myopic far point problem

Although moving subjects closer to the chart enabled measurement of poor unaided vision, as a myope moves closer to the chart, the chart comes closer to their far point (Cubbidge, 2009; Sloan, 1951) although Dong et al. (2002) found vision to get worse at shorter testing distances. This means that a -1.00D myope whose far point lies at 1 metre may only read 6/12 at 6 metres, but at 1 metre they would be able to clearly see 1/3 and smaller lines if they existed. An example of this in the current study was a subject whose refractive error was -4.75/-0.25x115 who could not read anything on the chart at 2 metres but read 1/6. Theoretically this subject should have been able to see 2/12.

Sloan (1980) recommended compensating for these effects by adding positive lenses to correct for the effects of light vergence. For example a +0.50D temporary addition was recommended for 2m viewing and a +1.00D addition for viewing at 1m. This was not adhered to in the current study as this would have necessitated the introduction of a trial frame and lenses which could have affected pupil size (one of the other parameters of interest). In order to explore whether this might have adversely affected the measurements of unaided vision made in this study, a table (see Appendix 5) was used to identify lines of letters at each testing distance that should have been read at the previous (greater) testing distance. Any subject whose unaided vision, in terms of minimum angle of resolution, should have been measurable at a greater distance than it was (lines greyed out in Appendix 5) was excluded from further analysis. By this means, 31 sets of data (all myopes) were excluded. This represented only 6.6% of the 469 myopes originally included in the study.

3.6 Discussion

The coefficient of repeatability found in this study was greater than was reported in other studies. Elliott and Sheridan (1988) found a COR of ±0.21 LogMAR (±10.5 letters). Siderov and Tiu (1999) found the COR of visual acuity to be approximately ±1.5 lines (7 letters) whereas Arditi and Cagenello (1993) found it to be ±0.1 LogMAR units (5 letters). Sheedy et al. (2004) found repeatability of visual acuity (not unaided vision) measurements to be ±9 letters. The current study found a coefficient of repeatability of ±0.31 LogMAR (15.5 letters). The differences in repeatability between the studies could be explained because Elliott and Sheridan (1988) measured vision from the dominant eye at 4 metres and there was a much narrower age range (mean 64, S.D. = 6 years compared to 44.2 S.D. = 14 years) and fewer subjects (20 compared to 873). Siderov and Tiu (1999) specifically excluded subjects with unaided vision worse than 6/60. Arditi and Cagenello (1993) used 5 highly practiced subjects who when reading the chart were only allowed to guess letters by responding with a letter from the Sloan set which would increase the chances of them guessing correctly. Whether repeat readings were taken on the same day can also affect readings of repeatability. Differences in motivation, tear film quality and general health could increase the variability in readings taken on different days along whereas if repeated readings were taken on the same day there could be an element of learning which would decrease variability. It is also possible that the higher COR found in the present study is due to methodological differences in the calculation of LogMAR vision, whereas most of the other studies used vision charts with LogMAR scoring, the LogMAR values in the present study were derived from the Snellen fractions displayed on the Test Chart SC-2000.

3.7 Summary

The method of recording unaided vision adopted where possible best practice from the research literature. Notable departures were the lack of use of temporary additions when moving subjects closer to the chart for the purposes of recording poor vision. Nevertheless, problems caused by moving myopic subjects closer to the far point only affected 6.6% of the myopic eyes measured which were excluded from the analysis. Repeatability of 3 lines was found which was higher than previously reported. Repeatability deteriorated with poorer unaided vision, an observation made in previous literature.

4. Measurement of refractive error

4.1 Introduction

A literature review of the measurement, recording, distribution and repeatability of refractive error is provided in this chapter. This is followed by a description of the methodology and initial findings of the present study. Initial findings include the distribution and repeatability of refractive error measurements.

4.2 Literature review

4.2.1 Representation of refractive error

4.2.1.1 The standard notation

Optometrists write a subject's distance prescription with 3 components: spherical power, cylindrical power and cylinder axis. This 3 part definition of a refractive error is simple for clinical refraction but can be difficult to analyse statistically due its polar nature (Raasch et al., 2001; Thibos & Horner, 2001; Bullimore et al., 1998; Thibos et al., 1997).

4.2.1.2 Problems in analysing the standard notation

It is often necessary in research to perform statistical analyses on refractive error data, for example to comment upon the different types of refractive error, their distributions or changes over time (Thibos & Horner, 2001). The classical sphere / cylinder x axis (S / C x θ) notation is not amenable to statistical analysis (Viana & Lakhsminarayanan, 2014; Rubin & Harris 2001). Difficulties in analysing the conventional sphere, cylinder and axis notation arise in part due to the fact that the three properties are not independent of one another (Thibos, 1997; Raasch, 1995). A cylindrical lens has a spherical equivalent so plano-cylindrical lenses have a non-zero spherical equivalent, and rotating a high-powered cylinder will produce a larger effect on vision than rotation of a low-powered cylinder, showing that cylinder power has an effect on cylinder axis (Raasch et al., 2001). Thibos et al. (1997) explained that because a cylinder has a spherical component, in order to keep the circle of least confusion focused on the retina when one adds a cylindrical lens during refraction, one must compensate with a sphere of half the power and opposite sign.

Axis of astigmatism also presents a problem when using the standard notation. For example, the numerical mean of two prescriptions, one with axis 178 and the other with axis 2, is 90, which represents a vertical axis. To an optometrist, it is clear that the mean axis is in fact along the horizontal 180, the point half way between the two readings on the axis scale (Elliott et al., 1997).

4.2.1.3 Alternative methods of representing refractive error

To conduct statistical analyses it can be useful to represent the power distribution described in Figure 1.5 as a single figure but it is difficult to adequately represent all three components of the standard notation in this way. Reduction of the refractive error to the mean spherical equivalent (M) is familiar to most optometrists and is easily calculated by adding the spherical component to half the magnitude of the cylindrical component. In the example used in Figure 1.5 this is +1.00DS plus half of -2.00DC, equalling 0.00D. This single value does not adequately express cylinder power or orientation. In this example, the mean spherical equivalent of 0.00D clearly does not induce the same blur as a purely spherical lens of power 0.00D.

Gartner (1965) suggested that any astigmatic value could be described by an ‘optometric vector’ and as such, the sum of oblique cylinders can be calculated by summing their vectors.

In 1976 Humphrey created an automatic refractor based on a patent which he filed in 1973, using a spherical lens and two spherocylinders of fixed orientation but variable power (Alvarez, 1978; Humphrey, 1976; Humphrey, 1973; Alvarez, 1967). The so-called ‘Humphrey notation’ decomposed cylinder power (C) into two crossed cylinders at 0 and 45 degrees (C_0 and C_{45} respectively). This principle of astigmatic decomposition was used by Bennett (1984) and was first described by Stokes (1883) who showed that any two cylinders with their axes crossed obliquely will result in an equivalent spherocylinder. Conversely, this means that a spherocylindrical lens can be represented as two cylinders of given axes. With this method it was important to pay due attention to the spherical equivalent of the lens. According to Bennett and Rabbetts (1984), Humphrey’s parameters were:

Equation 4.1 $M = S + C/2$

Equation 4.2 $C_0 = C \cos(2\theta)$

Equation 4.3 $C_{45} = C \sin(2\theta)$

Where S is the sphere, θ is the axis of the cylinder. Deal and Toop (1993) pointed out that this system is similar to one which uses a combination of a spherical lens and two Jackson cross-cylinders (JCCs). Thibos et al. (1997) explained that if the axis of astigmatism needs to be incorporated into the analysis, scalar quantities such as M must be replaced by a method suitable for a three dimensional vector. As optical power varies sinusoidally with meridian, the power profile may be described by Fourier analysis with a series of three Fourier coefficients, the axes on the dioptric space of the vector representing three lenses which when added together equate to the spherocylindrical lens in question. These three lenses are equivalent to M and two JCCs, one with orthogonal power measured along the 180 axis, called J_0, the other with power measured along the oblique 45 axis, known as J_{45}. Thibos et al. (1997) continued by deriving a Fourier decomposition in polar form, which is defined by its axis, θ. This gave the equation

Equation 4.4 $P(\theta) = M + J\cos(2(\theta - \alpha))$

Where P is lens power, M is mean spherical equivalent and J is a Jackson cross-cylinder at axis α. By replacing astigmatic axis with two JCCs, a cosine JCC at 0 (J_0) and a sine JCC at 45 degrees (J_{45}) computation becomes easier. This method uses trigonometry to define the rectangular form of the Fourier decomposition. Thibos et al. (1997) defined this by

Equation 4.5 $P(\theta) = M + J_0\cos2\theta + J_{45}\cos2\theta$

Rabbetts (2007) defines J_0 and J_{45}:

Equation 4.6 $J_0 = -1/2C\cos2\theta$

Equation 4.7 $J_{45} = -1/2C\sin2\theta$

Where a cosine JCC (J_0) is negative, the maximum power of the lens is in the vertical meridian and can be used to correct against-the-rule astigmatism, whereas a positive J_0 would correct with-the-rule astigmatism. As cylindrical blur equates to half the same amount of spherical blur the factor of two is built into this equation so that equal amounts of M, J_0 and J_{45} give equal amounts of blur, improving upon Humphrey's notation. The Fourier parameters of Thibos et al. are related to Humphrey's notation by the following equations:

Equation 4.8 $C_0 = -2J_0$

Equation 4.9 $C_{45} = -2J_{45}$

Graphically, the power profile fits a curve with M representing a constant and the two JCCs representing two sinusoidal curves. Thibos et al. described how this representation was mathematically useful but a vector graph can be more useful for comparing different lenses, the addition of obliquely-crossed cylinders and other practical problems. Each of the terms M, J_0 and J_{45} can be represented on a three-dimensional graph and the power profile can be represented by a single point within this dioptric space, and each point within this three-dimensional space represents a unique spherocylindrical power (Raasch et al., 2001). Thibos and Horner (2001) pointed out that the main advantage of this 3-part vector decomposition system is that all three components are independent of one another. This means that a spherical lens cannot be produced by any combination of cross-cylinders and neither the J_0 nor J_{45} components can be produced by any combination of the remaining two components. This means that each combination of M, J_0 and J_{45} describes a unique lens, and changing any of these values changes the lens described.

Many authors have since used the M / J_0 / J_{45} notations for analysis (Best, 2013; Baskaran et al., 2011; Liu et al., 2011; Rozema et al., 2011; Mathur et al., 2009; Miller, 2009; Remón et al, 2009; MacKenzie, 2008; Remón et al., 2006; Jorge et al., 2005a; Haegerstrom-Portnoy et al., 2002; Thibos & Horner 2001; Bullimore, et al., 1998).

As previously stated, it can be useful to define refractive error as a single number. Undoubtedly some directional information will be lost by doing this (Naeser & Hjortdal, 2001), so representation of astigmatic axis may not be precise enough for certain calculations or analyses. Rabbetts (2007, 1996) used the M, J_0 and J_{45} quantities to define a scalar vector, U, which defines refractive error as a single number and describes the length of the vector when represented in 3D space. U is defined as:

Equation 4.10 $U = \sqrt{(M^2 + J_0^2 + J_{45}^2)}$

Being a root mean square, U always has a positive value.

In order to test whether oblique astigmatic axes give different vision to orthogonal astigmatism Rabbetts (1996) suggested weighting U towards oblique astigmatic axes by a factor of two, defined in Rabbetts (2007) as:

Equation 4.11 $U_w = \sqrt{(M^2 + J_0^2 + 2(J_{45}^2))}$

where U_w is U weighted towards J_{45}.

An alternative, related approach to the analysis of refractive error is that of dioptric power matrices, first proposed by Long (1976) for solving the problem of calculating prism in decentred lenses. The use of matrices has since been developed by Saunders (1984), Harris (1992, 1990a, 1990b), Keating (1997a, 1997b, 1980), Deal and Toop (1993) and Campbell (1997). These matrices consist of vertical, horizontal and torsional components, all of which are measured in dioptres (Elliott, 1997). These matrices can be resolved to form a vector represented in 3 or 4 dimensional space. Many studies have since used matrices to represent refractive error (Viana & Lakhsminarayanan, 2014; Joubert & Harris, 1997; Elliott et al., 1997; McKendrick & Brennan, 1996).

Harris (2007b) and Raasch (1997) agreed that vector and matrix representation of refractive power were similar to one another in thin lens systems, although for thick systems the matrix method more fully represents the full character of dioptric power. Ocular refraction is a thin lens system (Harris, 2000). However a number of authors (Koch, 2001; Naeser & Hjortdal, 2001) have admitted that Harris's methods using matrices are complex, and that in order to use them the operator must have a good understanding of matrices and their operations. As a relatively simple method of representing refractive error was required, it was decided that the scalar vector method would be used for analysing refractive error in the present study.

4.2.2 Repeatability of measurement of refractive error

There is no 'gold standard' for the measurement of refractive error, but it is generally accepted that subjective refraction gives the most accurate measurement due to the ability of the subject to refine their prescription through feedback to the optometrist through a series of questions and lens presentations (Shah et al, 2009; MacKenzie, 2008; Sheedy et al., 2004; Elliott et al., 1997).

Rosenfield and Chiu (1995) investigated the repeatability of subjective refraction under masked conditions and found a coefficient of repeatability (COR) of ±0.31D in the spherical component and ±0.27D in the spherical equivalent (M). Zadnik et al. (1992) found a COR of ±0.63D in non-cycloplegic subjective refraction, although they used power in the vertical meridian for their calculations. Sheedy et al. (2004) found the COR to be ±0.53D in the spherical equivalent of the right eye. Bullimore et al. (1998) found a COR of ±0.78D for M; ±0.38D for J_0 and ±0.31D for J_{45}.

Shah et al. (2009) found in their study of reproducibility of refractive error measurement that the spherical equivalent of refractions was within ±0.75D 95% of the time and within ±1.00D 100% of the time. MacKenzie (2008) found 95% reproducibility limits of agreement of ±0.78D for M, ±0.24D for J_0 and ±0.17D for J_{45}, similar to that found by Bullimore et al. (1998).

<u>4.3 Methods used in the present study</u>

4.3.1 Clinical measurement of refractive error

Objective refractive error was estimated by an average of either 3 or 5 readings by autorefraction (Tonoref II, Nidek, Japan). This method of objective refractive error measurement was chosen as in the commercial environment this was more time effective than retinoscopy. Retinoscopy has been shown to be more repeatable than autorefraction in non-cycloplegic conditions (Rotsos et al., 2009; Jorge et al., 2005b), but subjective refinement was performed in all cases in the present study to give the final refractive correction. After measurement of unaided vision (see Section 3.3.1.3) the objective findings were placed into a trial frame with trial lenses and the left eye occluded with a frosted occluder. The subject was shown a duochrome chart displaying black numbers on a split red and green background. The spherical correction was adjusted until the numbers on the green background were seen slightly more clearly than those on the red. This ensured the subject's accommodation was active and the circle of least confusion was behind the retina and could therefore be brought forward onto the retina by accommodating slightly (Elliott, 2007). A JCC was used to refine the axis and then the magnitude of astigmatism, and the same was repeated for the left eye. The left eye was then blurred back to approximately 6/12 with a +1.00D lens and spherical refinement was performed binocularly, the left fogged eye having relaxed accommodation to give the highest positive/least negative result so the resulting prescription involved as little accommodation as possible. This 'push the plus' methodology has been advocated by others (Pointer, 2014; McKendrick & Brennan, 1996; Rosenfield & Chiu, 1995). Although some subjects had a modified prescription given in their spectacles (Hrynchak et al., 2012), it was the full refractive correction which was recorded for this study. Best corrected distance visual acuity was measured. All refractions were recorded in minus cylinder form and although refraction was performed on both eyes, the present study used measurements from only the right eye.

4.3.2 Classification of refractive groups

As one of the aims of this study was to investigate and measure the extent to which astigmatism and astigmatic axis affected unaided vision, refractive error was decomposed into vectors, as used by Rabbetts (2007) and defined in Section 4.2.1.3. Mean spherical equivalent (M) was calculated for each eye by adding the sphere value to half of the cylindrical power value. Each refractive error was then weighted mathematically into 'orthogonal' and 'oblique' components, using J_0 and J_{45} respectively (see Section 4.2.1.3, Equations 4.6 and 4.7). Scalar vectors U and U_w as defined by Rabbetts (2007) (see Section 4.2.1.3, Equations 4.10 and 4.11) were calculated for each subject.

It is straightforward to classify simple myopia and hyperopia with no astigmatism but for those with mixed astigmatism, such as a refractive error of +0.50/-1.00x180 it can be difficult to decide whether they should be classified as myopes, hyperopes, emmetropes or something else due to one line of focus being in front of the retina and the other behind it. Refractive error was classified as described by Tunnacliffe (1993) (see Section 1.3.4):

Scalar vector U has no sign so a sign had to be added using a quantity called 'U sign'. Those subjects that had compound or simple hyperopic astigmatism were given a 'U sign' value of +1, and those with compound or simple myopic astigmatism were given a U sign value of -1. Those subjects with mixed astigmatism were assigned the U sign value of 0. The originally calculated U value was multiplied by the U sign value and the refractive groups of eyes assigned as follows:

- Myopic if U x U sign < -0.50D
- Hyperopic if U x U sign > +0.50D
- Other if U x U sign is greater than or equal to -0.50D and less than or equal to +0.50D

This is a complicated way of saying that myopes with a scalar vector, U, of greater than 0.50D were assigned a negative value of U. Similarly, hyperopes with a value with a U value greater than 0.50D were assigned a positive value of U.

Use of 0.50D was as a cut-off between groups was in keeping with previous studies (Logan et al., 2005), and was also justified by the observation that the COR of U in other studies was around ±0.50D (see Section 4.2.2). Subjects with mixed astigmatism were classed as being near-emmetropes if U was less than 0.50D, but astigmats if U was more than 0.50D. These astigmats were further classed into 'orthogonal' and 'oblique'. The 'orthogonal' astigmats were those whose absolute J_0 scores were greater than their J_{45} scores, while the 'oblique' astigmats were those whose absolute J_{45} scores exceeded their J_0 scores.

4.4 Results

Spherical refractive error in the right eyes (in minus cylinder notation) ranged from -6.75D to +10.00D. Cylindrical refractive error ranged from 0D to -5.00D. The highest powers recorded in any one meridian were -8.25D and +10.00D.

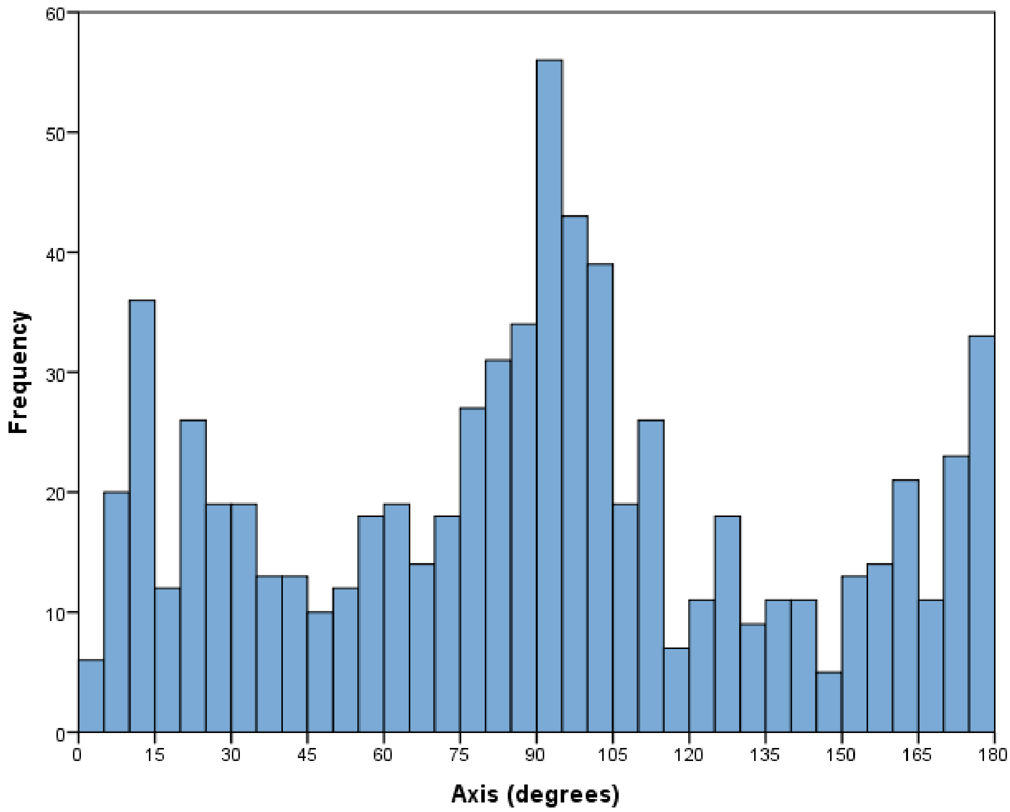

Figure 4.1: Frequency distribution of raw cylinder axis orientation of 746 right eyes, showing predominance of orthogonal axes around 90 and 180.

As can be seen in Figure 4.1, astigmatic axis follows neither an even nor a normal distribution, but reflected that found by others (Read et al., 2007; Farbrother et al., 2004; McKendrick & Brennan, 1997; Pincus, 1946) with most of the cylinder axes found around 90 and 180 axes with comparatively few in the oblique ranges. In the current study 391 out of 532 eyes (73.5%) with astigmatism were defined as having orthogonal astigmatism, and 141 had oblique astigmatic axes, shown in Figure 4.2. Of 873 eyes, 341 (39.1%) were classified as having no astigmatism.

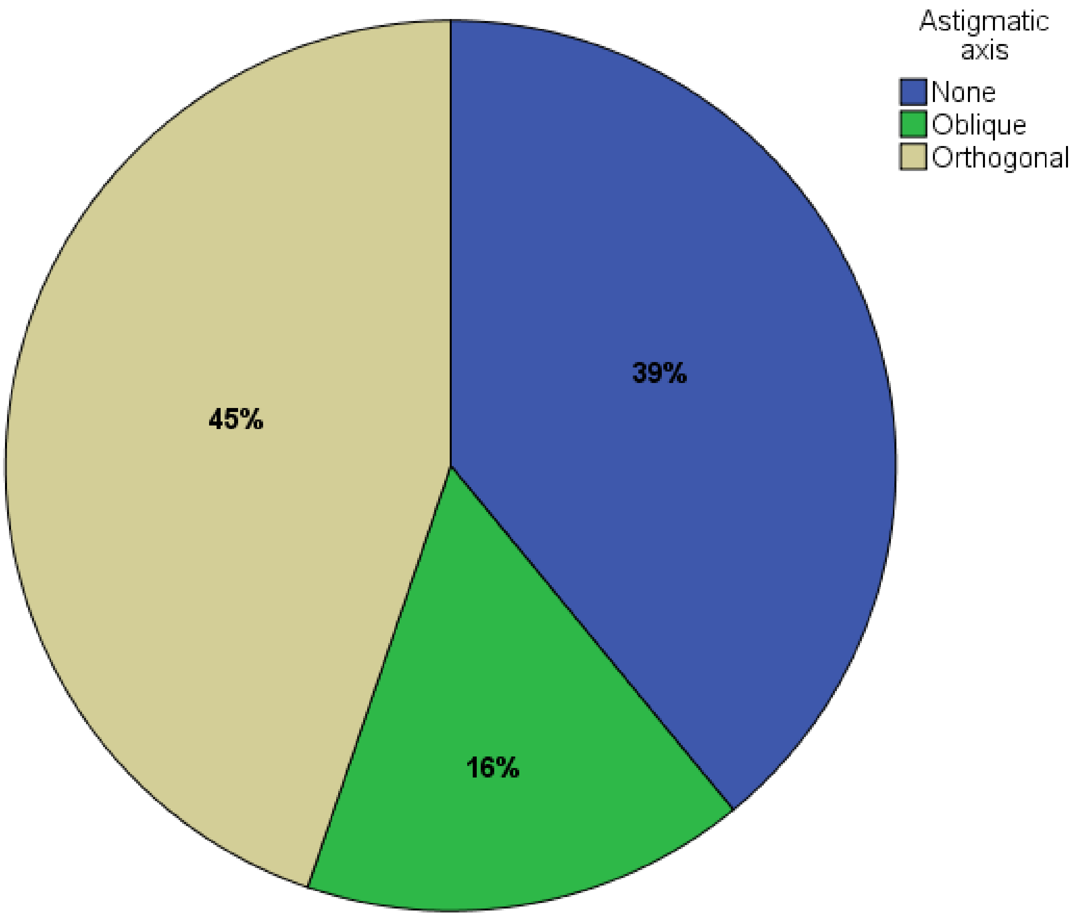

Figure 4.2: Distribution of different types of astigmatic axes in 873 right eyes. Eyes with no astigmatism represented 39% (n = 341) of the sample, 45% (n = 391) had orthogonal astigmatic axes whereas 16% (n = 141) had oblique axes of astigmatism. This more sophisticated manner of representing astigmatism utilised the J_0 and J_{45} vectors.

Mean spherical equivalent M, shown in Figure 4.3, ranged from -7.00D to +9.38D (mean -0.89D, S.D. = 2.30D). The component J_0, shown in Figure 4.4 ranged from -2.14D to +2.02D (mean -0.04D, S.D. = 0.40D) and J_{45}, shown in Figure 4.5 ranged from -0.91D to +2.02D (mean +0.02D S.D. = 0.22D). U and U_w, shown in Figures 4.6 and 4.7 respectively ranged from 0 to 9.40D with the mean U 1.94D (S.D. = 1.60D) and U_w 1.95D (S.D. = 1.60D). When signs were added to U and U_w to enable comparisons with M, mean U was -0.90D (S.D. = 2.34D) and mean U_w was -0.90D (S.D. = 2.36D).

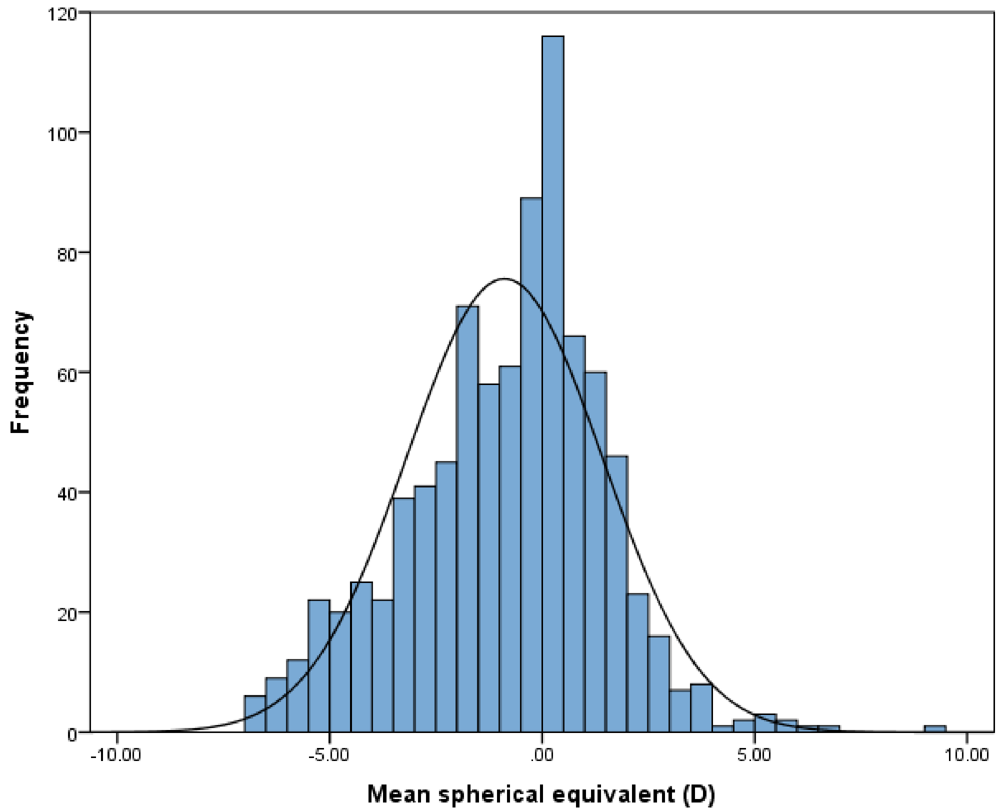

Figure 4.3: Frequency distribution of mean spherical equivalent (M) in 873 right eyes with overlaid normal distribution curve.

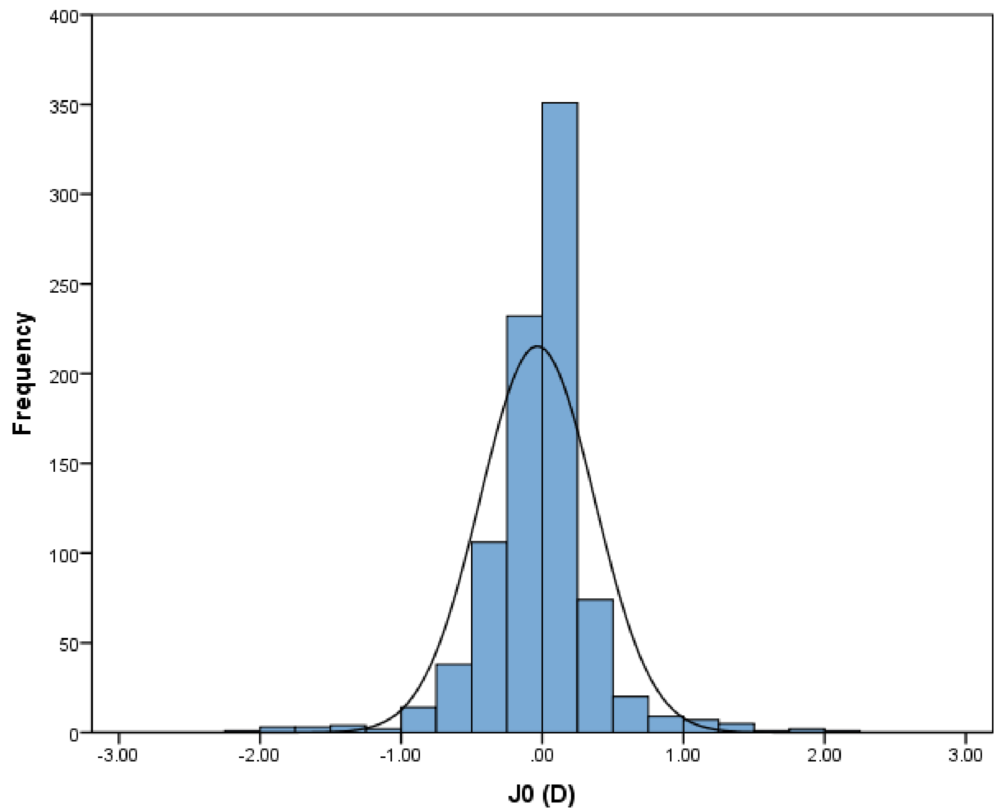

Figure 4.4: Frequency distribution of orthogonal component (J_0) in 873 right eyes with overlaid normal distribution curve.

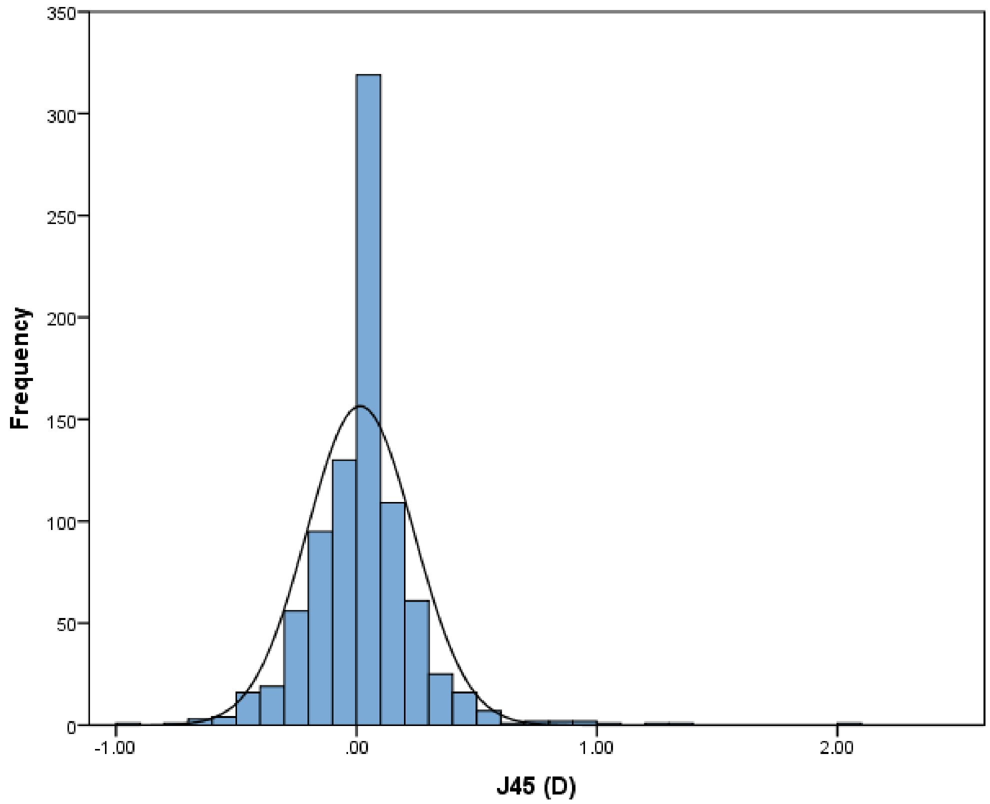

Figure 4.5: Frequency distribution of oblique component (J_{45}) in 873 right eyes with overlaid normal distribution curve.

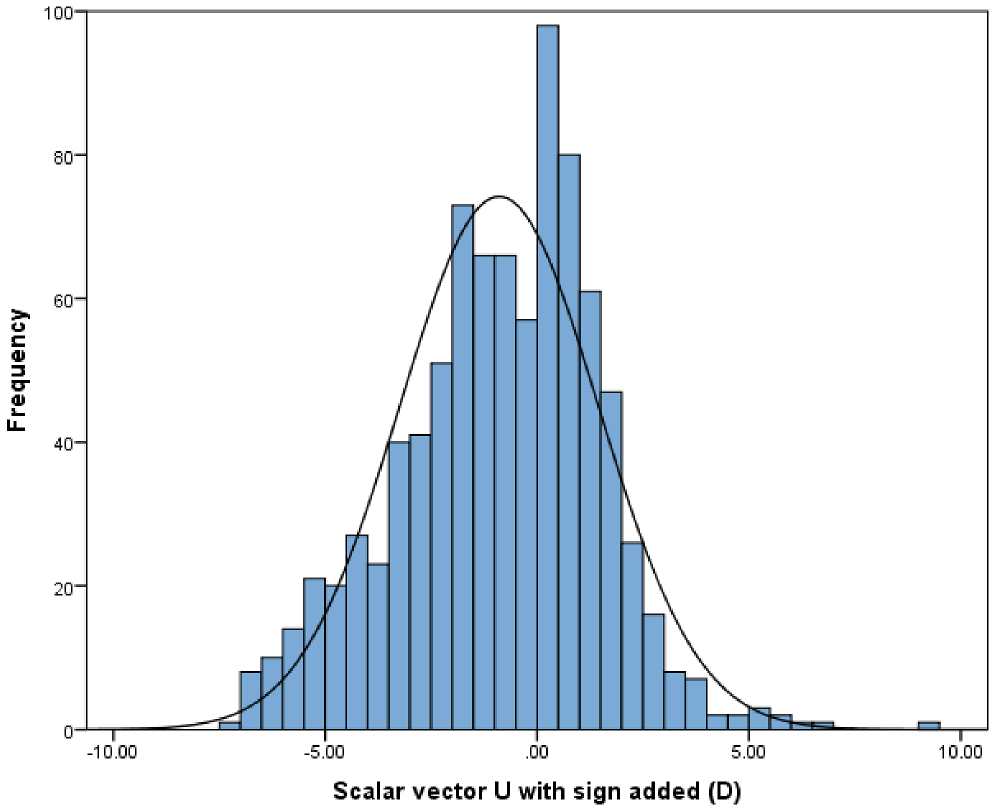

Figure 4.6: Frequency distribution of scalar vector (U) in 873 right eyes with overlaid normal distribution curve.

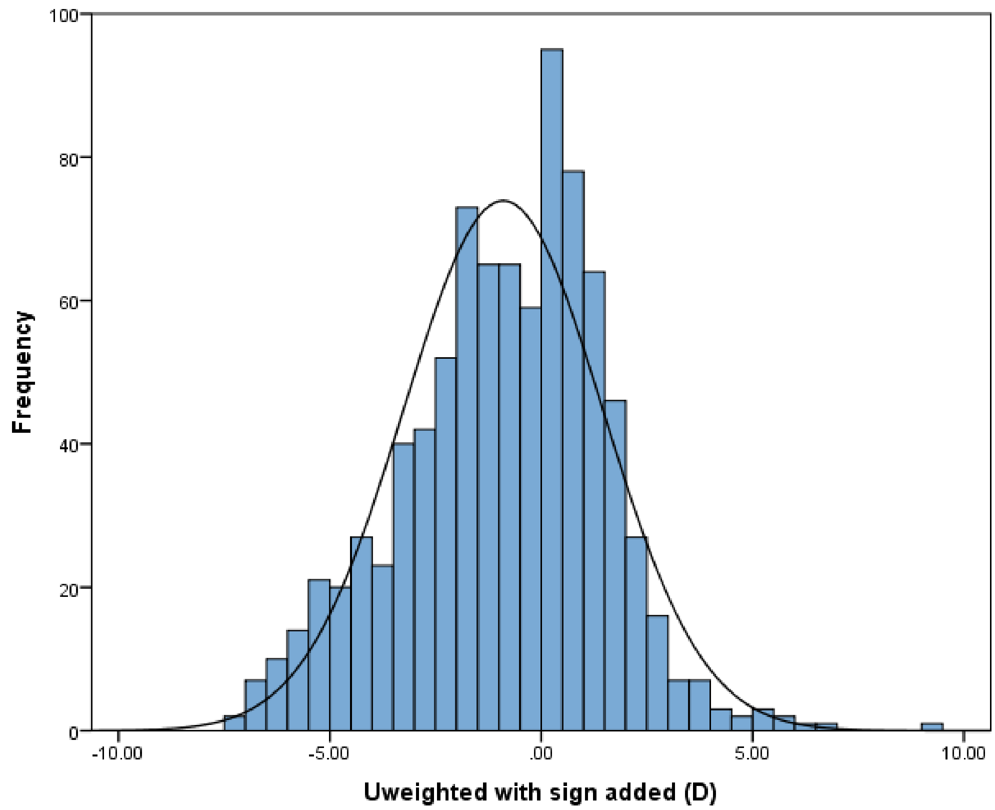

Figure 4.7: Frequency distribution of weighted scalar vector (U_w) in 873 right eyes with overlaid normal distribution curve.

As initially calculated scalar vectors U and U_w were always positive in value, the data represented in Figures 4.6, and 4.7 had signs added according to the sign for mean spherical error, M. All three methods of representing refractive error as a single number (M, U and U_w) had similar frequency distributions once signs were added. None were normal, all of them being leptokurtic and slightly skewed. Kurtosis describes the shape of the distribution in that positive kurtosis (leptokurtosis) shows a steeper, sharper peak than the normal distribution whereas negative kurtosis (platykurtosis) shows a flatter, lower peak than the normal distribution. Skewness describes the asymmetry of the distribution curve. A positive skew demonstrates a peak towards the negative end of the scale with a longer 'tail' towards positive values, whereas data with a negative skew will have a 'tail' pointing towards the negative side of the scale and a peak nearer the positive end. Table 4.1 summarises the frequency distributions of all parameters shown in Figures 4.1 to 4.7. All values had a positive kurtosis and most had a negative skew. In the case of cylinder powers this negative skew was high and expected, as cylinders were measured in minus powers.

	Mean	S.D.	Median	Skew	Kurtosis
M	-0.89	2.30	-0.50	-0.18	0.42
U with sign	-0.90	2.34	-0.73	-0.14	0.27
U_w with sign	-0.90	2.36	-0.73	-0.14	0.25
J_0	-0.04	0.40	0.00	-0.06	5.97
J_{45}	0.02	0.22	0.00	1.51	11.82
Sphere	-0.57	2.31	-0.25	-0.12	0.49
Cylinder	-0.65	0.66	-0.50	-2.47	8.73

Table 4.1: Distributions of M, U (with sign), U_w (with sign), J_0, J_{45}, sphere and cylinder in 873 right eyes.

None of the parameters shown in Table 4.1 were normally distributed. A Kolmogorov-Smirnov test revealed that all of the parameters shown in Table 4.1 showed a statistically significant departure from normality (the p-value was 0.01 or less in all cases) It was important to determine this information as multiple linear regression used in Chapter 9 assumed data to be normally distributed.

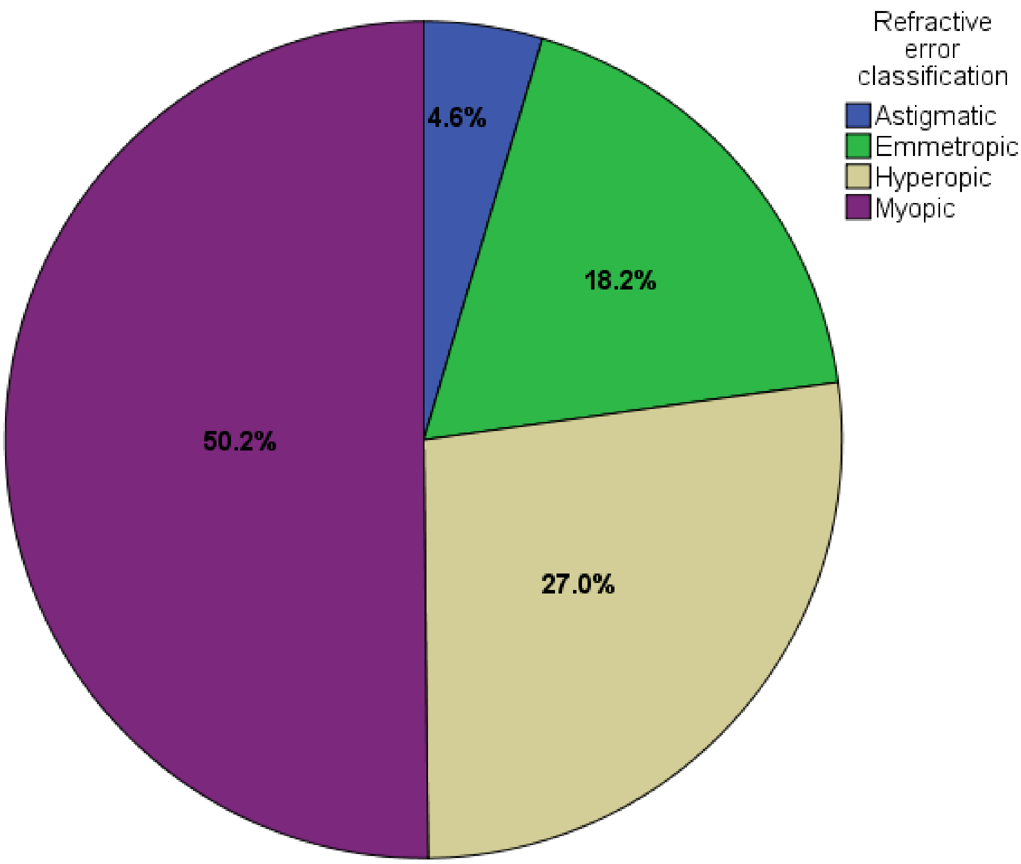

Figure 4.8: Proportion of eyes within each class of refractive error of 873 right eyes.

Figure 4.8 shows that myopic refractions predominated (438 eyes, 50.2% of sample). Hyperopic eyes made up 27.0% (n = 236), emmetropes 18.2% (n = 159) with near-emmetropic astigmats making up 4.6% (n = 40).

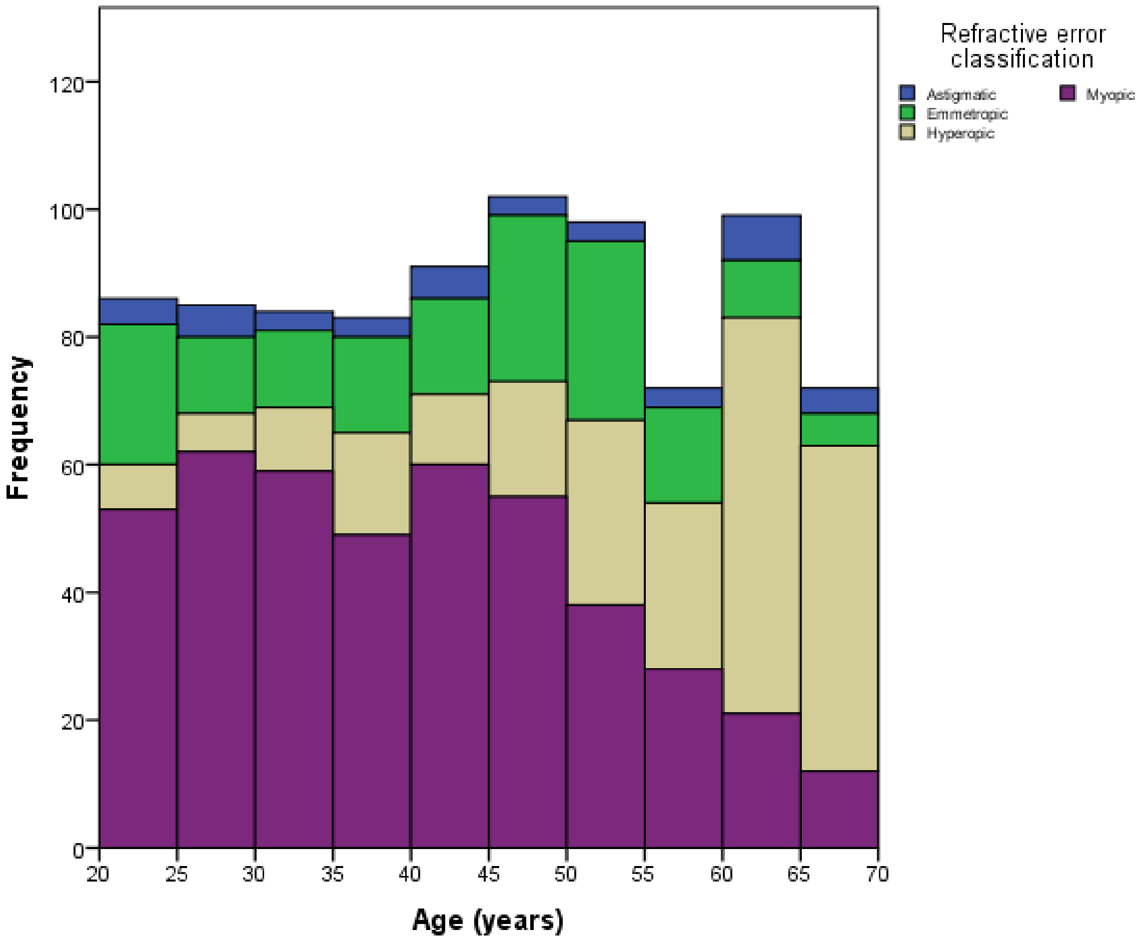

Figure 4.9: Distribution of refractive error by age in 873 right eyes.

Figure 4.9 shows similar information organised by age group. This chart clearly shows that the proportion of myopic refractive errors reduced with age whereas the proportion of hyperopic errors increased. In the younger age groups below age 55, myopic refractive errors dominated, but in the 60-70 age range hyperopic refractive errors showed the greatest frequency.

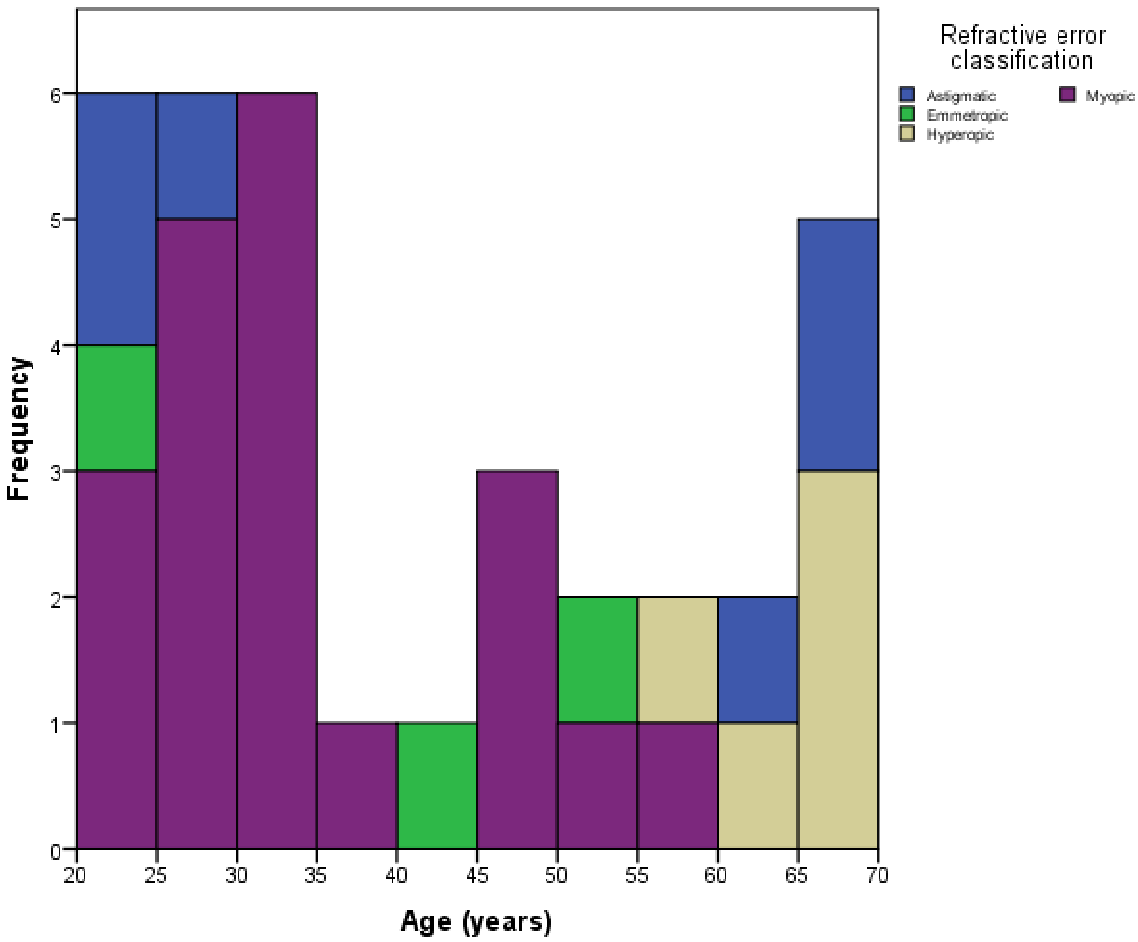

Figure 4.10: Distribution of refractive error by age in 34 right eyes.

The distribution of refractive error by age is shown in figure 4.10. It reflects the general trend of figure 4.9 that myopes predominate in the younger age categories and hyperopes in the older age groups.

	Mean difference	COR
M	0.06D	±0.34D
U	0.02D	±0.33D
U_w	0.03D	±0.33D
J_0	-0.00D	±0.16D
J_{45}	-0.01D	±0.25D

Table 4.2: Summary of difference versus the mean plots for M, U, U_w, J_0 and J_{45}.

As detailed in Section 2.6.1, 34 subjects had repeat measurements taken at a later date in order to establish the repeatability of refractive error measurements in this study. Difference versus the mean plots (Bland & Altman, 1986) were created in order to determine the coefficient of repeatability (COR) for unweighted scalar vector U, weighted scalar vector U_w, mean spherical equivalent M, orthogonal astigmatic vector component J_0, and oblique astigmatic vector component J_{45} (Figures 4.11-4.15). Table 4.2 summarises the mean difference between measurements, and the coefficient of repeatability for the 34 eyes in the repeat readings sample.

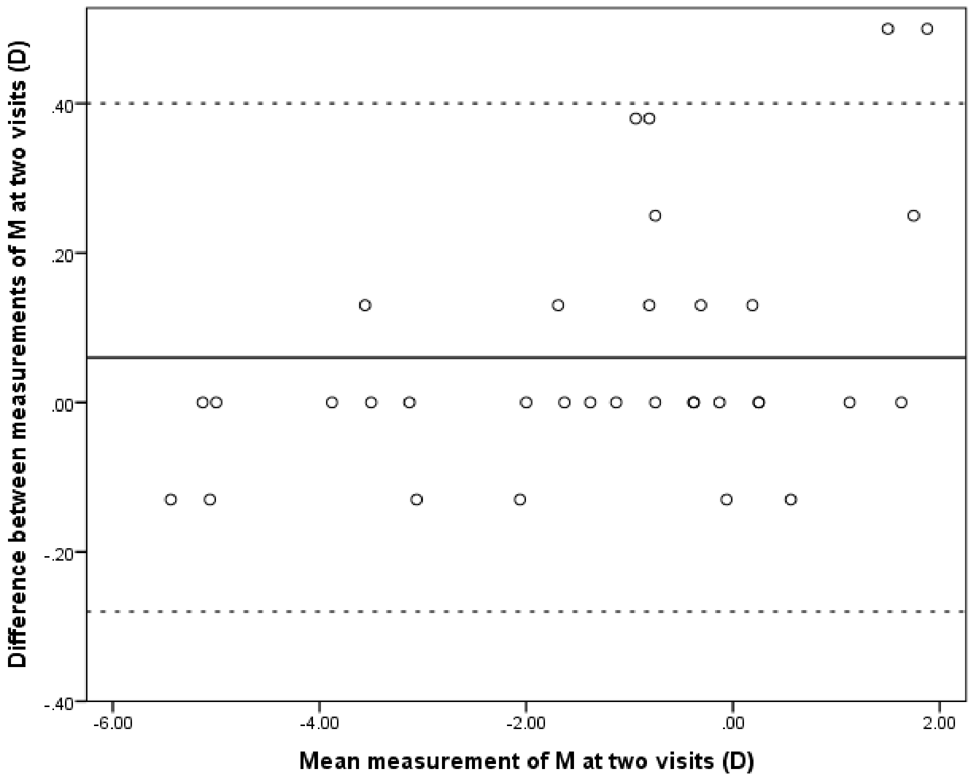

Figure 4.11: Difference versus the mean plot for mean spherical equivalent (M) in 34 right eyes. The mean difference between measurements was 0.06D as shown by the solid line, and COR was ±0.34D as shown by the dashed lines.

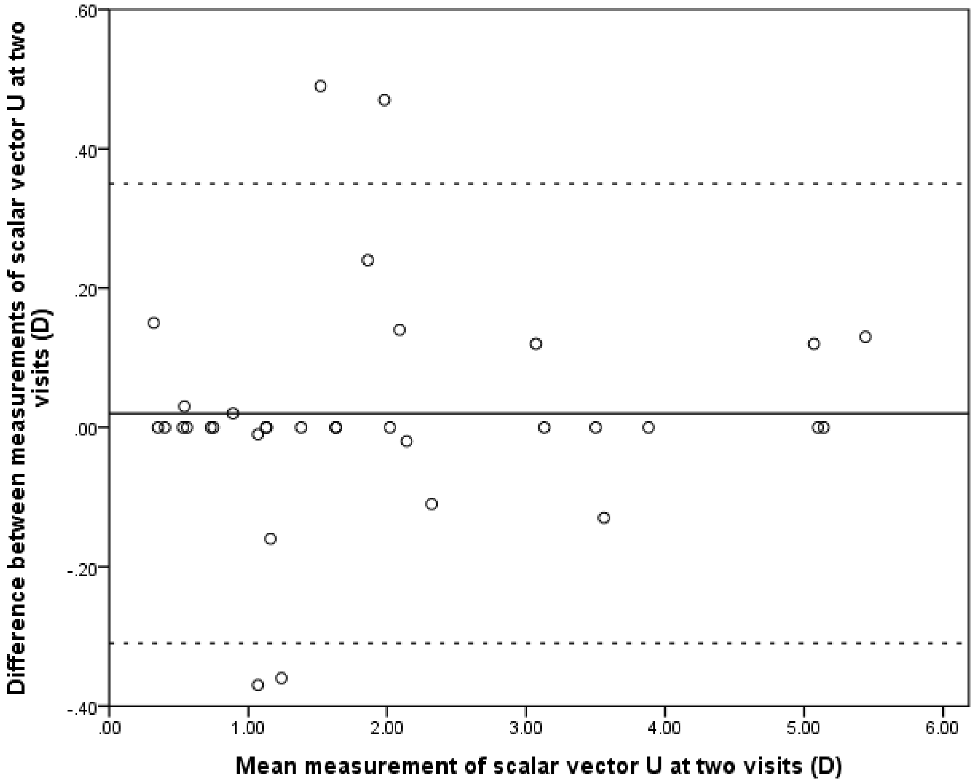

Figure 4.12: Difference versus the mean plot for scalar vector (U) in 34 right eyes. The mean difference between measurements was 0.02D as shown by the solid line, and COR was ±0.33D as shown by the dashed lines.

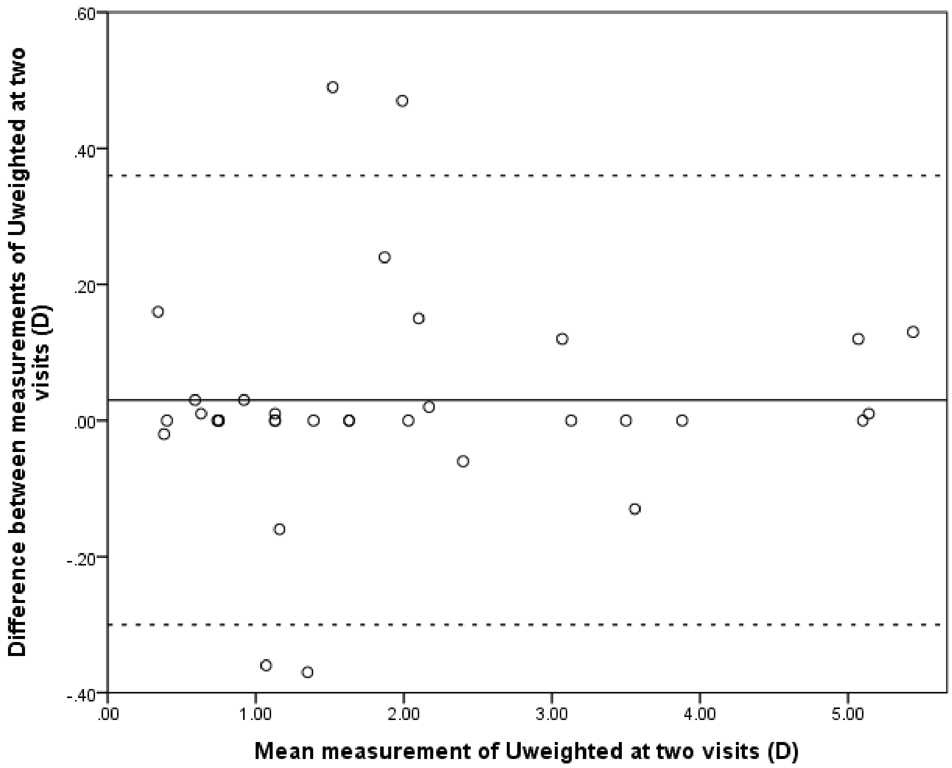

Figure 4.13: Difference versus the mean plot for the scalar vector weighted towards the oblique component (U_w) in 34 right eyes. The mean difference between measurements was 0.03D as shown by the solid line, and COR was ±0.33D as shown by the dashed lines.

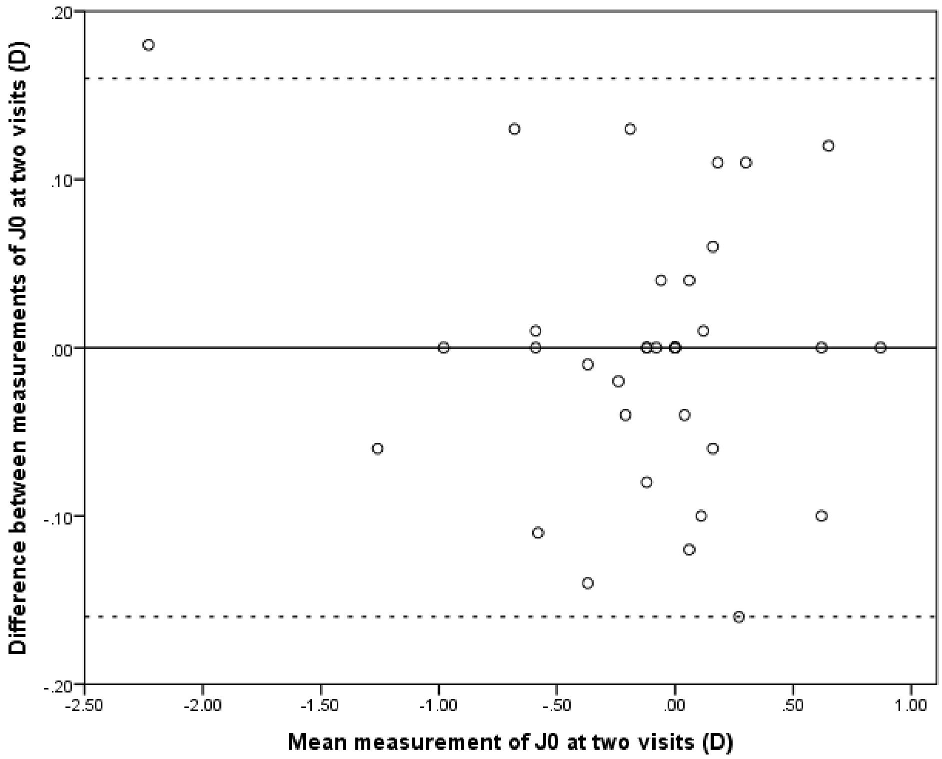

Figure 4.14: Difference versus the mean plot for the orthogonal component (J_0) in 34 right eyes. The mean difference between measurements was 0.0D as shown by the solid line, and the COR was ±0.16D as shown by the dashed lines.

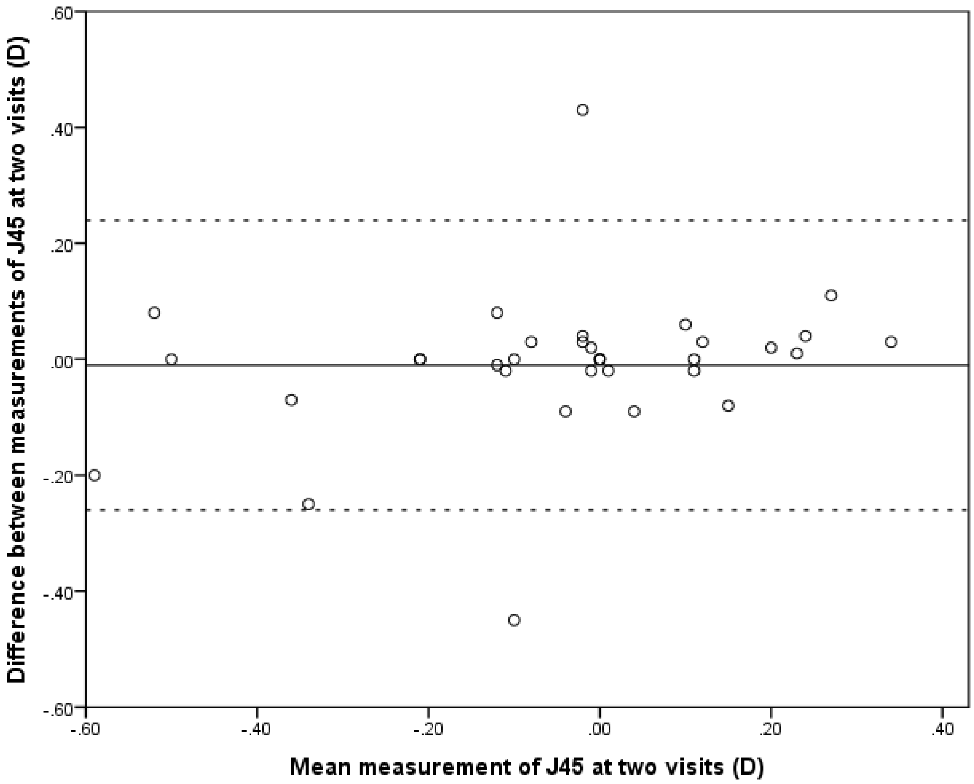

Figure 4.15: Difference versus the mean plot for the oblique component (J_{45}) in 34 right eyes. The mean difference between measurements was (-)0.01D as shown by the solid line, and the COR was ±0.25D as shown by the dashed lines.

4.5 Discussion

Pincus (1946) found that most of the refractive errors found in his study were between 0 and ±4DS. The present study found 95% of the data to lie between -5.25DS and +4.00DS (2 standard deviations either side of the mean). He also noted that myopic corrections predominated and in the present study, 50% of eyes were classified as myopic, as opposed to hyperopic or near-emmetropic. The data also agreed with previous studies (Read et al., 2007; Farbrother et al., 2004; McKendrick & Brennan, 1997; Pincus, 1946; Bannon & Walsh, 1945) in that orthogonal astigmatism predominated (73.5% of 532 astigmatic eyes).

A Kolmogorov-Smirnov test for normality showed that the parameters describing refractive error were not normally distributed, with positive kurtosis. This was in agreement with previous literature (Flitcroft, 2014; Zadnik & Mutti, 2006; Logan et al., 2005; Sorsby et al., 1960). Zadnik and Mutti (2006) noted that the distribution of refractive error can be affected by a number of factors including:

- Age – refractive errors tend to become more hyperopic between the ages of 20 and 70 years (Lee et al., 2002; Saunders, 1986; Saunders, 1981)
- Sex – some studies have found females to be more myopic than males (Xu et al., 2005)
- Ethnicity – subjects from the Far East typically have more myopic refractive errors, Hispanics having a lower incidence of myopia (Pan et al., 2013)
- Geography – subjects from urban areas generally have a greater prevalence of refractive errors than those from rural areas (Gao et al., 2012; Pokharel et al., 2010; Uzma et al., 2009; Czepita et al., 2008; Prema et al., 2008; Xu et al., 2005)
- Diet – some studies have shown that the modern diet may increase the risk of developing myopia (Cordain et al., 2002)
- Time – perhaps due to changes in diet, environment and urbanisation, some studies have found an increase in myopia over time (Morgan et al., 1975) although others have refuted this (Park & Congdon, 2004)
- Personality – some studies have found a relationship between personality types and refractive error, such as myopes tending to be more introverted (Beedle & Young, 1976; Lanyon & Giddings, 1974) although others have not found any connection between refractive error and personality (Bullimore et al., 1989)

- Systemic conditions – subjects with collagen disorders such as Marfan's syndrome are frequently highly myopic (Kanski, 2003); populations with Down syndrome show greater proportions of both myopic and hyperopic refractive errors, possibly due to a failure of the Emmetropisation process (Fong et al., 2013; Al-Bagdady et al., 2011)
- Ocular diseases – nuclear sclerotic cataracts tend to give a myopic shift, conditions which cause a raising of the macula, such as central serous retinopathy can cause a hyperopic shift, corneal diseases and trauma can cause a variety of refractive error changes

Sorsby et al. (1960) found a peak frequency of mean spherical equivalent between 0 and +1.00D in a sample of 1033 young male army recruits. This was also the case in the current study where the most frequently occurring value (mode) of M was +0.13D, although because of the non-normal distribution of M, both the mean and median values fell between 0.00 and -1.00D. Logan et al. (2005) found that 50% of white students in their UK-based study were myopic, 18.8% were hyperopic and 31.2% were emmetropic. This was similar to that found in the current study (50.2% myopic, 27.0% hyperopic, 18.2% emmetropic and 4.6% near-emmetropia astigmatic). However Sorsby et al. (1960) found the majority of refractions to be hyperopic.

Previous authors (MacKenzie, 2008; Sheedy et al., 2004; Bullimore et al., 1998; Rosenfield & Chiu, 1995) found COR for mean spherical equivalent (M) to be between ±0.27 and ±0.78D. The present study found the COR for M to be ±0.34D, towards the lower (more repeatable) end of this range. The present study found the COR of J_0 and J_{45} to be ±0.16D and ±0.25D respectively, similar to those values found by MacKenzie (2008) and Bullimore et al. (1998).

Differences between this and previous studies could be due to the ranges of ages and refractive errors included. MacKenzie (2008) accepted that this was a potential drawback of his study as reproducibility is a function of both age and refractive state, and presbyopes are less likely to tolerate a greater range of spherical refractions due to their reduced ability to accommodate through a lens which has too much minus power. The present study involved mainly myopes and older hyperopes. Had more young hyperopes been included in the sample it is possible that the greater accommodation these young hyperopes demonstrate could increase variability further. Other studies have found that perception of blur may vary depending on refractive error, with myopes experiencing less blur with defocus than emmetropes (Vasudevan et al., 2006; Radhakrishnan et al., 2004; Rosenfield & Abraham-Cohen, 1999). Different study populations may also give varying results. For example Zadnik et al. (1992) used mainly students and university staff; Bullimore et al. (1998) recruited subjects from a university eye centre; Leinonen et al. (2006) based their study on subjects who had been referred to hospital for cataract surgery; Sorsby et al. (1960) studied young, male army recruits. It should be remembered that the present study excluded subjects under the age of 20 and over the age of 70 years, only included white subjects, and there was a large proportion of contact lens wearers and females, so this may not perfectly reflect the general population of Salisbury with healthy eyes.

4.6 Summary

The subjective refractive error of 873 right eyes was measured using methods typically found in high street practice. Representation of refractive error by optometric vectors as used by previous studies was used to describe the distribution and repeatability of the data collected. None of the data were normally distributed, and the coefficient of repeatability of refractive error was found to be similar to that found in the literature.

5. Measurement of pupil size and iris colour

5.1 Introduction

This chapter begins with a literature review of the measurement of pupil size and iris colour and their possible influence on vision. The methods used in this study to measure pupil size and iris colour are then described before the distribution and repeatability of each is discussed.

5.2 Literature Review

5.2.1 Pupil Size

The purpose of the pupil is to regulate light passing into the eye because the retina is more efficient at greater levels of illumination (Rabbetts, 2007; Winn et al., 1994; Campbell & Gregory, 1960). Its size is controlled by the synergistic actions of the radial dilator pupillae and sphincter pupillae muscles, which are controlled by the sympathetic and parasympathetic nervous systems respectively (Spalton et al., 2005; Kanski, 2003; Winn et al., 1994).

The 'blur disc' is the circular patch of light formed upon the retina when an image is not sharply focused (Tunnacliffe, 1993). The diameter of the blur disc is affected by refractive error and pupil size and in an emmetropic eye is theoretically zero. An increase in refractive error will increase the diameter of the blur disc, resulting in blurred vision. A smaller pupil reduces the size of the blur disc diameter, and there is an accompanying reduction in optical aberrations, thus improving vision. A small pupil can also increase the eye's depth of focus, which is the axial distance in front of and behind the retina over which (for a system with a set focus) an image remains clear. However, a smaller pupil will decrease retinal illumination which may adversely affect visual acuity and a very small pupil will further reduce vision due to diffraction effects (Rabbetts, 2007; Atchison et al., 1979). Rabbetts (2007) showed that peak visual acuity occurred with pupils around 3mm, but it is unclear at what luminance this occurred.

The pinhole test involves the placement of an opaque disc with a small pinhole in its centre in front of the eye, simulating the effect of a very small pupil. Peripheral aberrations are excluded, allowing through only the central 'chief rays' to focus within the visual system. In healthy eyes with refractive error there may be an improvement in vision compared to unaided vision, whereas no improvement or even a worsening will be seen in eyes with amblyopia, media opacities and other abnormalities.

5.2.1.1 Factors affecting pupil size

Pupil size is affected by a number of factors. Ocular trauma, iris lesions and abnormalities within the neural pathways controlling pupil reactions can cause miosis (reduction in pupil size) or mydriasis (increase in pupil size) or a distortion of the normal pupil shape on either a temporary or permanent basis (Spalton et al., 2005; Kanski, 2003). Pupil diameter is known to increase with emotional excitement or arousal (Partala & Surakka, 2003), and under the effects of topical or systemic drugs (Larson, 2008; Merzouki et al., 2008). Miosis occurs naturally along with accommodation and convergence as part of the ‘near focusing triad’ so one would expect unaided myopes to have larger pupils than unaided hyperopes. Pupil size has been shown to decrease with age (Cakmak et al., 2010; Twa et al., 2004; Wyatt, 1995; Winn et al., 1994; Said & Sawires, 1972; Birren et al., 1950).

Winn et al. (1994) investigated the effect of age, gender, refractive error and iris colour on light-adapted pupil diameter at five different lighting levels (9, 44, 220, 1 100 and 4 400 cdm^{-2}). They used a Hamamatsu perceptoscope connected to a Canon R1 infrared optometer and an oscilloscope to measure pupil diameter. They noted the presence of hippus – a vermiform movement of the pupillary border – at all light levels apart from when the pupil was extremely constricted. They found that pupil diameter was independent of sex, refractive error and iris colour but found a linear decrease in pupil diameter with age of between 0.04 and 0.02 mm per year depending on illumination, with the effect being more evident at the lower levels of illumination. Their findings did not support the previously-held theory that females and myopes had larger pupils but did support the expectation that unaided myopes may have had larger pupils than unaided hyperopes. In their study, refractive error was corrected and convergence and accommodation were controlled.

Bergamin et al. (1998) also found no difference in pupil size according to iris colour (blue versus brown). They used a modified Octopus 1-2-3 automated perimeter to measure a number of pupillometric parameters.

Cakmak et al. (2010) performed a retrospective study using data from 412 prospective candidates for refractive surgery, equally split between males and females. Pupil diameter was measured using a COAS Ocular wavefront analyser under mesopic conditions (0.6 lux). Myopes were found to have the largest pupils, hyperopes the smallest, and those subjects with mixed astigmatism were in between. This supports the theory of pupil constriction with accommodation, as hyperopes have more active accommodation and would therefore be expected to have smaller pupils than myopes who should have maximally relaxed accommodation. Cakmak et al. however did not feel the differences in pupil size between the three groups was attributable to accommodation effects. The same study also compared the effect of different types of astigmatism (with-the-rule, against-the-rule and oblique axes) on pupil size. A statistically significant difference in mesopic pupil diameters was only found between with-the-rule and oblique astigmatic axes. There was no description in the paper about how the different types of astigmatism were defined. Spherical refractive error, age and astigmatic refractive error were found through multivariate correlation analysis to have moderate correlation with pupil diameter, though the coefficient of determination (R^2) was very low, so these three factors could only predict the expected pupil size in 20% of cases. No statistically significant correlation was found between pupil diameter and either sex or axis of astigmatism. They found a negative correlation of pupil size with age, with a 0.04 mm reduction in pupil size per year of age.

Jones (1990) investigated previous claims that women and myopes had larger pupils than men or emmetropes. Dynamic infrared pupillometry was used to measure pupil diameter and no difference was found between the sexes or between myopes and emmetropes. Jones stated that it was reasonable to assume that under different experimental conditions emmetropes may have smaller pupils at near than unaided myopes due to the comparative increase in accommodative demand and associated pupil constriction.

Pupils are not perfectly round and Wyatt (1995) found them to generally have a greater vertical diameter in the dark but in light conditions they were more round, with the major axis of the ellipse being near horizontal. However he noted that individual variations were high. Khanani et al. (2004) found that the dark-adapted vertical pupil diameter was larger than the horizontal diameter with a mean horizontal to vertical ratio of 0.97. A highly precise method of measuring pupil size could therefore be affected by not only the light conditions in which the measurements were taken, but also the axis along which the pupil diameter was measured.

Pupil size has been repeatedly found to decrease with increasing age whereas iris colour and sex do not appear to have an effect. Refractive error including type of astigmatism may affect pupil size.

5.2.1.2 Methods of measuring pupil size

Measurement of pupil diameter is very easily made with a rule. If pupil diameter significantly affects unaided vision, such simple measurements could be used at the beginning of an eye examination to help determine how much reduced vision could be attributed to pupil size as opposed to refractive error. However, there are many other more precise methods for measuring pupils. Most studies comparing techniques for pupil measurement involve taking readings under scotopic or mesopic light conditions. This is mainly because these studies have been concerned with determining the maximum natural pupil diameter before refractive surgery goes ahead. If the ablation zone (treatment zone on the cornea) is too small the patient can experience night vision problems due to increased peripheral aberrations (Yoon et al., 2007; Chaglasian et al., 2006).

Twa et al. (2004) compared the estimation of horizontal pupil diameter by measurements made with infrared video recording (the reference standard), the Colvard pupillometer, digital photography, semi-circular templates and a millimetre rule, under three different levels of illumination (dark, <0.63 lux [scotopic]; dim, 5 lux [mesopic]; bright, 1000 lux [photopic]) on 45 healthy right eyes. Accommodation was controlled by asking the subjects to fixate upon a target 4m away. Measurements under the dark condition were not possible with the semi-circular templates or rule due to the difficulty of seeing the scales in low light levels. It was found that the video recording provided the most repeatable results followed by digital photography. The pupillometer, rule and templates had similar 'moderately reliable' repeatability. Bright conditions yielded the greatest repeatability whereas dark conditions gave the poorest repeatability, as found by others (Chaglasian et al., 2006). Repeatability in bright conditions was ±0.38 mm for the infrared video device, ±0.41mm for digital photography, ±0.72mm for the semi-circular template and ±0.79mm for the millimetre rule. Despite finding statistically significant differences between the different measures of pupil size, Twa et al. conceded that the clinical relevance of these differences was debatable, with a maximum difference between techniques (comparing the video method with the measurement with a rule) being ±0.56 mm.

Schmitz et al. (2003) compared the Colvard pupillometer, Procyon P2000SA infrared dynamic pupillometer and the Asclepion WASCA (Wavefront Aberration Supported Cornea Ablation) Workstation which utilised a Hartmann-Shack aberrometer. The authors concluded that all three methods gave reliable results. The Colvard pupillometer was easiest to handle and economically the most attractive option but also demonstrated the greatest intra- and inter-individual variance of measured pupil diameters.

Chaglasian et al. (2006) compared the Colvard pupillometer with the Bernell printed pupil gauge used in conjunction with a penlight with cobalt blue filter in subjects prior to undergoing refractive surgery. This pupil gauge used a selection of semicircles from 3 to 8 mm at 1 mm intervals and was held temporal to the eye in the corneal plane. The Bernell card gave a larger pupil measurement than the pupillometer under both mesopic and scotopic conditions with greater variation under the lower light levels.

Brown and Bradley (2011) compared the Marco Nidek ARK530-A autorefractor pupillometer function, Keeler PupilScan II pupillometer and NeurOptics PLR-200 pupillometer and found that the autorefractor had an unpredictable bias towards underestimating pupil diameter when compared to the NeurOptics pupillometer. The Keeler instrument also tended to underestimate pupil size and required significant skill and knowledge to take an accurate measurement.

Scheffel et al. (2010) found no statistically significant differences when measuring the pupils of moderate to high myopes under mesopic (0.4 lux) conditions using the Colvard, PupilScan II and Procyon P2000SA pupillometers.

Mantry et al. (2005) measured pupil diameter with the Nidek AR700A autorefractor and the Colvard pupillometer and found comparable results under both mesopic and photopic conditions, though under photopic conditions the pupillometer gave a slightly lower average reading than the autorefractor.

Kohnen et al. (2004) compared a Procyon digital infrared pupillometer (as the reference standard) with the Colvard pupillometer, a Bausch and Lomb Zywave aberrometer, a WASCA aberrometer and the Orbscan II topography system with respect to their measurement of pupil size. They found that the Zywave wavefront sensor, with the fixation turned off, gave scotopic pupil measurements most similar to the reference standard, with the other instruments, including the Zywave with the fixation target switched off giving statistically significant different measurements.

Bradley et al. (2005) also found that the Colvard pupillometer was susceptible to user error while Yang et al. (2006) found that an infrared digital photographic system gave more repeatable results than the Colvard pupillometer.

There are many methods available to estimate pupil size. The most accurate and repeatable methods involve the use of photographic and videographic equipment and aberrometers, none of which are readily available to typical high street optometrists. Equipment such as the Colvard pupillometer is slightly less accurate or repeatable but is portable, relatively inexpensive and easy to use. The comparison methods using rules or semi-circular gauges may be the least repeatable methods available to estimate pupil size but they are inexpensive, portable and very readily available to optometrists. They are still reasonably accurate and repeatable (Twa et al., 2004) and were used in the present study due to their ease of use and availability.

5.2.1.3 Effect of pupil size on vision

Atchison et al. (1979) investigated aided and unaided myopia, pupil size and vision under two lighting conditions: that of constant chart luminance and that of constant retinal illuminance. The latter was achieved by varying the chart luminance with a continually variable rheostat in order to investigate the effect of varying retinal illuminance when pupil size changes. This study employed 22 natural myopes aged 19-36 years with dilated pupils and artificial pupils from 1-8 mm. No eye had astigmatism over 0.50D. For unaided myopes vision was best with 2.5 mm pupils for between 0.75D and 1.00D of myopia. Improvements in vision were continuing at 1 mm as pupil diameter was decreased in the higher myopes. In corrected myopes they found that the constant chart luminance gave a better acuity for large pupils whereas better acuity was achieved in small pupils under the constant retinal illuminance condition. Acuity was found to be best with a 2 mm pupil under constant retinal illuminance and with a 3 mm pupil under constant chart luminance. Acuity decreased rapidly below 2 mm. In unaided myopes the same study found the relationship between vision and pupil size to be very important, with a steady improvement in vision as pupil size decreased. For unaided myopes with a spectacle prescription of -3.00D or less a pupil size of 1 mm gave rise to vision close to that of corrected myopes with the same pupil size of 1 mm. The pupil dilation and cycloplegia adopted in that investigation meant that its results may not be exactly the same as seen in practice.

Kamiya et al. (2012) used cycloplegic refraction and five artificial pupils of 1-5 mm diameter along with simulated astigmatism of 1, 2 and 3 dioptres at 90 and 180 on 20 young subjects to explore the effects of pupil size on unaided vision in astigmatism. Smaller pupil diameters gave better unaided vision than the larger diameters. Optimum vision was found to be achieved with the 2 mm pupil for 1D of astigmatism but with 1mm for 2D and 3D of astigmatism. The authors assumed that the pupil-dependent effect of increasing depth of focus, and a decrease in higher order aberrations and light scatter, on unaided vision may be larger than the counteractive effect of diffraction and reduced luminance for a 1 mm pupil in eyes with high astigmatism. This study used artificial pupils and cycloplegic refraction for the sake of accuracy as it was intended to be used by refractive surgeons and not high street optometrists. The authors pointed out that one of the limitations of the study was the young age of subjects (mean 26.7 years, S.D. = 4.9 years) who tend to have with-the-rule astigmatism and larger pupils. For that reason, their study might not apply to every population.

Donnelly and Roorda (2003) used a computer model combined with a Shack-Hartmann wavefront analyser on 16 young adults to ascertain optimum pupil size. They were looking for the optimum pupil diameter for both lateral resolution (i.e. a blur circle on the retina) and axial resolution (the spread of focus in the anterior-posterior direction) with respect to optimal images obtained when using a scanning laser ophthalmoscope. They found that the average ideal pupil size for axial resolution was larger (mean 4.30mm, S.D. = 1.19mm) than that for lateral resolution (mean 2.46mm, S.D. = 0.66mm). This they pointed out was similar to previous data from Campbell and Green (1965) who stated that for a pupil size of over approximately 2.4 mm the optics of the eye will contribute to the reduction in vision whereas, for example, with a 2 mm pupil, the reduction in vision due to the nervous system (density of photoreceptors, retinal ganglion cells etc.) was approximately twice that due to the eye's optics.

Laughlin (1992) used information theory to postulate optimum pupil sizes for maximum vision. Information theory provides an objective measure of image quality that depends upon both image sharpness and sensitivity. An optimum pupil diameter of approximately 2.5 mm in bright light conditions (10^4 cdm^{-2}) and 6.5 mm in dim light (0.01 cdm^{-2}) was found.

Tucker and Charman (1975) found when using cycloplegia, artificial pupils and simulated refractive error using a phoropter that for a given refractive error a larger pupil generally gave worse visual acuity. An optimal pupil diameter was found to be approximately 3 mm with their particular Snellen test chart and illuminance of approximately 500 lux. They cited diffraction as the likely limit on acuity in small pupil diameters, and retinal and other factors when the pupil diameter exceeds 3 mm. Depth of focus was found to be greatest with smaller pupils up to approximately 4 mm. They suggested this was partly due to optical factors such as spherical and chromatic aberration but may also be caused by the Stiles-Crawford effect which would limit the effective pupil size on depth of focus for large pupils. The Stiles-Crawford effect is the directional sensitivity of the fovea in photopic conditions, with maximum stimulation of the photoreceptors occurring from light from the centre of the pupil. Light from the edge of the pupil strikes the cone photoreceptors obliquely and results in a reduced response (Millodot, 2008; Rabbetts, 2007; Stiles & Crawford, 1933). Depth-of-focus was found to decrease with both increasing pupil size and acuity. This was consistent with later work from Atchison et al. (1997).

Optimum pupil diameter appears to be around 3 mm in photopic conditions. For smaller pupil diameters there is increased diffraction and reduced retinal illumination. For larger pupil diameters, aberrations, retinal and neural factors reduce the quality of the retinal image. Many previous studies have used cycloplegia, corrected refractive error or artificial pupils which do not necessarily accurately reflect the conditions seen in high street practice or university clinics.

5.2.2 Iris Colour

Iris colour was included as a parameter in the present study as it was hypothesised that an eye with a lighter-coloured iris could have more light scatter, and therefore worse vision. The iris is made of five layers. Anteriorly to posteriorly these are the anterior border layer, the stroma, the sphincter muscle, the dilator muscle and the posterior pigmented epithelium (Sturm & Larsson, 2009; Spalton et al., 2005; Imesch et al., 1997). It is considered that the anterior border layer and stroma are most influential in the perceived colour of an eye and that the perceived differences in iris colour between eyes is due mostly to the quantity of melanosomes within these cells (Sturm & Larsson, 2009; Eagle, 1988) and the ratio of the two types of melanin, eumelanin and pheomelanin (Imesch et al., 1997; Wilkerson, 1996). Classification of iris colour is made more difficult due to coloured patterns on the iris such as the peripapillary ring which is a differently and often more darkly pigmented annulus adjacent to the pupil margin in some eyes (Sturm & Larsson, 2009; Mackey et al., 2011).

Iris colour is generally fairly stable after the age of 6 years although it has been estimated that 10-15% of white people have changes in eye colour throughout adolescence and adulthood (Bito et al., 1997; Imesch et al., 1997). This may be due to genetic factors but other causes of iris colour change can include trauma, pathology and medication (Spalton, 2005, Imesch et al., 1997).

Systems for the grading or classification of iris colour fall broadly into three categories: subjective colour naming, subjective comparison with a grading scale, and objective with the use of electronic equipment.

Birren et al. (1950) found no relation between pupil size and iris colour (or skin colour) after splitting the research group into ‘light’ and ‘dark’ irides. Having a two-option grading scale may lack the precision to confirm whether iris colour has an effect of vision and there was no cut-off point for ‘mid-coloured’ irides.

Hammond et al. (1996), when investigating the relationship between iris colour and macular pigment optical density, asked subjects what colour their eyes were. Indeed some interviews were conducted over the telephone. Eyes were then put into one of three groups, with blue or grey eyes put into group I, green or hazel into group II and brown or black into group III. This simplistic approach may not be very scientific but is likely to work fairly well if one is looking for general trends, though not everybody knows the colour of their own eyes (without checking) and other people have heterochromia (different coloured irides) so may not be able to give a straightforward answer. Repeatability of iris colour grading was probably very poor due to people having different perceptions of their own eye colours but this limitation was not discussed.

Dain et al. (2004) used a three-point classification system where subjects were classified by both their iris colour and skin tone. Group 1 comprised of light blue or green irides and a fair complexion. Group 2 comprised of with brown irides and fair to olive complexions. Group 3 had brown eyes and an Asian skin tone. The point of the study was to use iris and skin pigment as an indicator of macular pigment so for the purposes of the study this would have worked fairly well. However, this might be inadequate for investigating the effects of iris colour on vision in the present study.

Nischler et al. (2013) investigated the effect of iris colour on intraocular straylight, contrast sensitivity and best corrected visual acuity. Eyes were classified into four groups: light blue, blue-grey, green-hazel and brown Caucasian. Non-Caucasian brown eyes were excluded from the study due to the sample size being too small. In order to grade iris colour, a penlight was shone into a non-dilated eye and the colour determined subjectively. The colour classification system was simple but there was no mention as to whether the examiner was trained in any way to accurately assess iris colour. This study found that light blue eyes had poorer contrast sensitivity and greater intraocular straylight than those eyes with more pigment (thought to be due to greater iris translucency) but there was no difference in visual acuity. The authors noted that there was no significant difference between blue-grey and darker irides, presumably due to the blue-grey iris having a highly pigmented epithelium and stroma when compared to light blue irides. This was a straightforward and user-friendly way of categorising iris colour but no repeatability data was available from this study.

Illustration removed for copyright restrictions

Figure 5.1: Standard A used by Seddon et al. (1990).

Illustration removed for copyright restrictions

Figure 5.2: Standard B used by Seddon et al. (1990).

Illustration removed for copyright restrictions

Figure 5.3: Standard C used by Seddon et al. (1990).

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Figure 5.4: Standard D used by Seddon et al. (1990).

Seddon et al. (1990) developed a system for grading iris colour using standard photographs (see Figures 5.1 to 5.4). The study used a set of standard photographs to be compared to test photographs of irides of various colours. An iris was considered to be grade 1 if it had brown or yellow pigment less than or equal to standard A (in terms of total visible iris area); grade 2 if it had less than or equal to the amount of pigment than standard B (but more than standard A); grade 3 if it had less than or equal to the amount of pigment than standard C (but more than standard B); grade 4 if it had less than or equal to the amount of pigment than standard D (but more than standard C); grade 5 if it had more pigment than standard D. Two examiners graded photographs and any discrepancies were arbitrated by an adjudicator who had no prior knowledge of the previous examiners' judgements. Out of 324 photographs, the graders only disagreed by more than one grade on two photographs. Eighty-four percent of the photographs were given the same grade by the different examiners. Out of 47 photographs shown twice the graders agreed with themselves 83% of the time. The conclusions reached by the study group were that repeatability and reproducibility of grades was high and that the system was reliable and simple to use. This system has been used successfully in many studies since (Fraser-Bell et al., 2010; Twelker et al., 2009; Bergamin et al., 1998; Mutti et al., 1994; Winn et al., 1994). Winn et al. noted that category 5 (dark brown) was not used during their study as all of the subjects were white.

German et al. (1998) used colour photographs of different coloured irides in combination with an objective computer-based system. The Seddon system described above was used as a comparison. Twenty subjects from each of the five Seddon categories were photographed along with four volunteers with albinism (graded as 0). These photographs were then scanned into a computer and the red (R), green (G) and blue (B) intensity values seen in Paint Shop Pro™ were recorded. The same was then done with all 85 Farnsworth-Munsell 100 hue test caps to allow for calibration taking into account differences in colour variations induced by scanning, printing and other processes. Pupil diameters were measured before and after topical instillation of 1% tropicamide to measure time to maximum dilation and recovery time as well as maximum percentage increase in pupil diameter. The results showed that the Seddon grading system correlated well with the objective system in that lighter coloured irides as graded by either system responded equally to tropicamide. The authors concluded that the calibration of the computer system was relatively straightforward and suggested it could be used to monitor changes in iris colour over time, for example in Horner's syndrome or Fuch's heterochromic iridocyclitis. The main disadvantage of this system for the purposes of the present study is that many practitioners do not have the time or instant access to a computer during clinic hours due to commercial pressures.

Mitchell et al. (2003) investigated the effect of iris colour on intraocular pressure by comparing eyes to three standard colour photographs which were used in the Beaver Dam Eye Study. The classifications and prevalence of these iris colours were blue (50%), hazel or green (28%), tan-brown (12%) and dark brown (10%).

Jonas et al. (2006) looked into whether iris colour had an effect on optic nerve head dimensions and glaucoma risk and, although they did not go into detail on their method for iris classification, they looked at irides under a slit lamp and under natural light and put them into groups of blue (n = 875), green (n = 321), brown (n = 574) and mixed colour (n = 203). The proportions of eyes in the first three categories are similar to those in the study of Mitchell et al. (2003) which used a different classification technique. The biggest limitation in this classification system was the inclusion of a 'mixed' category, which presumably could have held blue-green eyes and green-brown eyes, which are clearly different colours, with different amounts of pigment. This approach would not be useful for a study researching the effect of iris colour on some other parameter.

Melgosa et al. (2000) used a spectroradiometer to measure the colour of 72 artificial irides, 25 ocular prostheses from the same manufacturer and 40 right irides from recruits using two different methods. Eleven observers were also asked to match one of the 72 artificial irides to each of the 25 ocular prostheses. They found good correlation between iris colour perceived by observers and colour measured by the spectroradiometer but most of the time the prosthetic iris chosen as the closest match to the iris being classified was not in fact the same colour. They concluded that iris colour measurement using spectroradiometers was still in its infancy, but this type of quantitative characterisation could be used to establish the relationship between iris colour and other parameters in future research. This approach was not used in the present study due to its complexity.

Takamoto et al. (2001) took three photographs of subjects' irides at three different exposures with both a millimetre scale and colour test pattern within shot. One of these exposure levels was chosen as being most reproducible and this exposure level was used in two follow up visits months later. The authors said that further studies were required but it was possible that this method could be used for objectively monitoring changes in iris colour over time. The protocol employed involved determining different photographic exposures for each iris colour which means that the grading of iris colour would need to be done before the colour was measured. This would not be a useful technique for a busy practitioner even if they had the time and technology to hand as although it seems to have merit for longitudinal monitoring the different exposures used would not allow for a strict comparison between eyes.

Bradley et al. (2010) took a high-resolution digital slit lamp photograph of 262 eyes which were then subjectively classified into one of five groups. Although the paper shows five reference photographs it was not stated whether these were the photographs used by the two graders nor is it explained how irides were put into the groups (for example whether they used closest match or, like the Seddon system required the photographs to show the maximum pigment allowed to place an eye in that category). The same iris photographs were analysed objectively on-screen by a Minolta TV Color Analyzer which looked at a circle at 3 o'clock on the iris and measured hue, saturation and luminance. These objective measurements were plotted against subjective assessments. The authors concluded that the objective method was suitable for classification of blue and brown eyes but it did not uniquely classify hazel (green-brown) eyes. Hazel iris colour which is perhaps most difficult to classify subjectively due to the different quantities and patterns of brown pigment which can cause some observers to classify such eyes as brown, some green, and others hazel. Once again this technology is too complex for most high street optometrists.

Bailey et al. (1991) discussed the negative effects of having too-coarse a scale when using a grading system. However, for iris colour there are so many variables that determine what colour category an iris falls into, a four- or five-point grading scale seems to be most appropriate and is indeed what most studies seem to use. On the other hand, use of too many categories may give slightly less accurate readings with the possibility of eyes being too easily misclassified. A photographic scale goes some way to eliminating error when compared to a purely subjective ('blue,' 'grey,' 'hazel,' 'brown') system.

Of the three broad types of grading system the purely subjective type seems to be too open to bias, especially in 'borderline' cases such as blue-grey or green-brown irides. The grading systems which use a scale with which to compare the iris being graded to is straightforward to use and may be helpful in borderline cases. The electronic and objective methods of grading are likely to be as repeatable as, if not more so, than the grading-scale comparison type but the equipment is not readily available for most practitioners and would cause more interruption of a routine eye examination than the other two systems.

<u>*5.3 Methods*</u>

5.3.1 Pupil size measurement

Figure 5.5: Semi-circular template used to measure vertical pupil size (Matheson Optometrists, UK).

Vertical pupil diameter was measured using a template rule designed for measuring pupil diameters (Matheson Optometrists, UK) (see Figure 5.5). This was held by the temporal edge of the subject's pupil. Vertical pupil diameter was easier to measure than horizontal diameter as (a) the rule blocked less light than if it was held above the pupil and (b) the subject's nose did not obstruct free movement of the rule. The rule used had semi-circular templates along its edge from 1 mm to 9.5 mm in diameter in 0.5 mm intervals. This was similar to the method used by others (Elliott & Cox, 2004). Although there are a wide range of more precise automated pupil measuring devices available (Kohnen et al., 2004; Twa et al., 2004; Bradley et al., 2005; Yang et al., 2006), the purpose of this study was to take measurements in a manner that would be accessible to the high street optometrist. Other methods of pupil measurement were attempted, including the use of digital photography, a pupil measurement scale on the autorefractor and use of a subjective pupil gauge which required feedback from the subject. All of these methods were too lengthy in the clinical setting so were discarded in favour of the semi-circle template rule. Three measurements were taken from the right eye only and the results were averaged. The subject was asked to fixate a letter at the top of the test chart at 6m; that is, 6m when seen through a mirror set 3m from the subject. If vision was worse than 6/20, the subject was asked to fixate the top of the letter chart. In either case, the left eye remained uncovered throughout measurement to avoided unwanted consensual pupil dilatation. Spectacles and contact lenses were removed so measurement conditions were the same as those used to record unaided vision (see Section 3.3.1.3). A pilot study into the measurement of pupil size found that when three vertical measurements were taken with the semi-circular template, pupil diameter could be measured with a precision of ±0.4-0.7mm, and the coefficient of variation was 0-9%.

5.3.2 Iris colour classification

Iris colour was classified according to the Iris Colour Classification System developed by Seddon et al. (1990) (see Figures 5.1 to 5.4 and Section 5.2.2). A paper copy of the grading standards was visually compared to the view of each subject's right iris observed using a white light beam on a slit lamp in a fully illuminated consulting room.

5.4 Results

5.4.1 Pupil size

Average vertical pupil diameter ranged from 2.3-7.5 mm (mean 4.3mm, S.D. = 0.8 mm). Figure 5.6 shows that the data were not normally distributed and exhibited positive skew of 0.47 and kurtosis of 0.16 with a cluster around the 4mm mark (median 4.2 mm, mode 4 mm). A Kolmogorov-Smirnov test showed that pupil sizes were not normally distributed.

Figure 5.7 shows the measured reduction in pupil diameter with age. A straight line (Spearman's correlation coefficient) accounts for 20% of the observed variance and was statistically significant (p = <0.01) and shows that average pupil diameter decreases by 0.03 mm per year of age. The colours of the datum points reflects information shown in figure 4.9, that the proportion of myopic eyes reduced and the proportion of hyperopic eyes increased with age. There does not appear to be a noticeable difference between pupil diameters of the different refractive groups within each age range, but taking the data set as a whole the myopic eyes had larger pupils than the hyperopic because they tended to be younger.

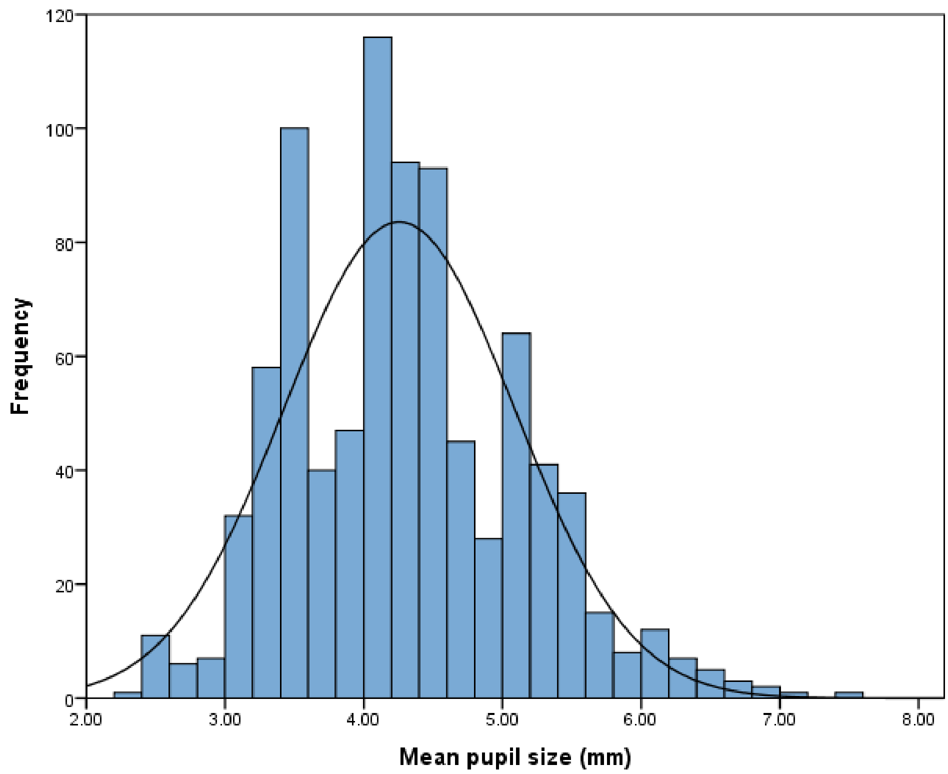

Figure 5.6: Frequency distribution of mean pupil size in 873 right eyes with overlaid normal distribution curve.

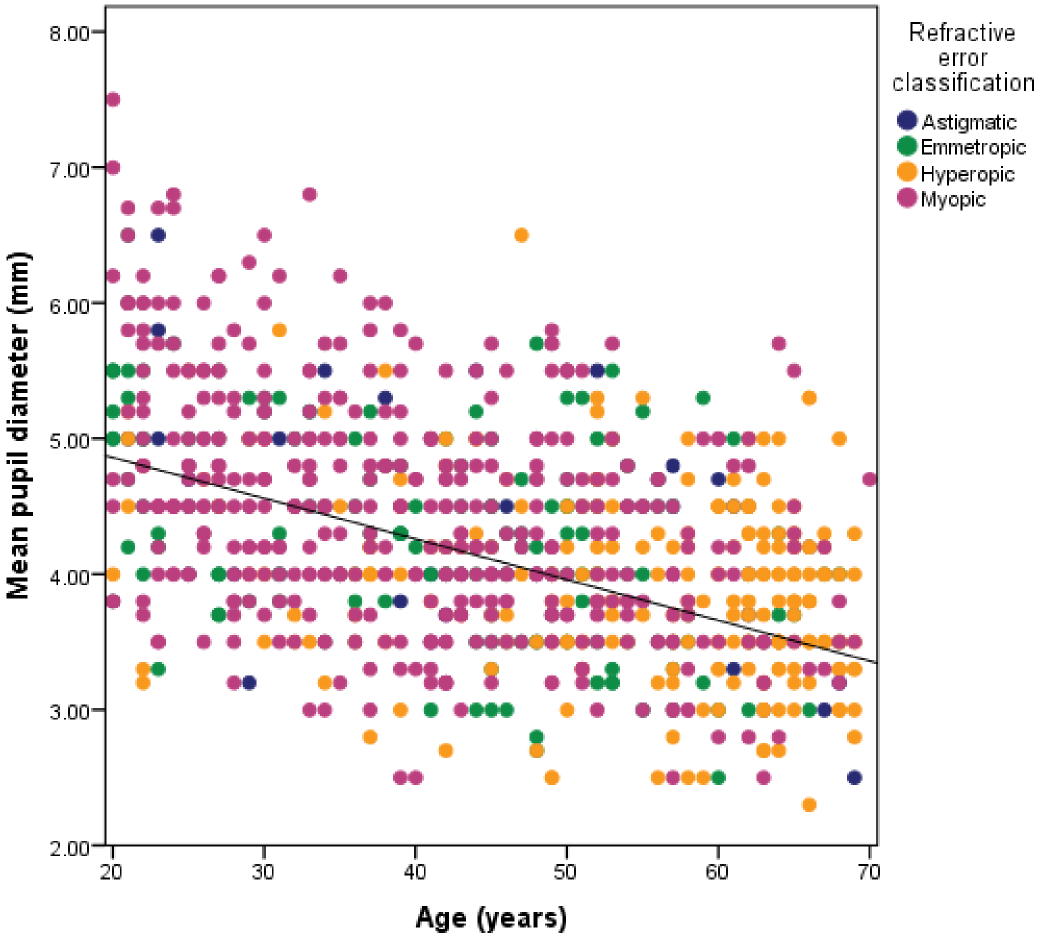

Figure 5.7: Change in mean vertical pupil size with age categorised by refractive error. Linear regression produced a best fit line with the equation: mean pupil diameter = (-0.03 x age) + 5.46. r^2 = 0.20 (Spearman's rank correlation coefficient). This graph shows data from 873 right eyes. Some of the datum points are superimposed.

Figure 5.8 shows a difference versus the mean plot (Bland & Altman, 1986) illustrating the differences between repeated measurements of the average vertical pupil size made in 34 right eyes over 18 months (see Section 2.6.1). Any datum point lying along zero on the y-axis had identical repeated mean values at each sitting. Any datum point above or below zero represented subjects that had larger average pupil diameters at the first or second visit respectively. The broken lines illustrate the coefficient of repeatability (COR) which was ±1.2 mm. Recall that pupil measurements were made to the nearest 0.5 mm so the COR represents just over 2 measurement intervals.

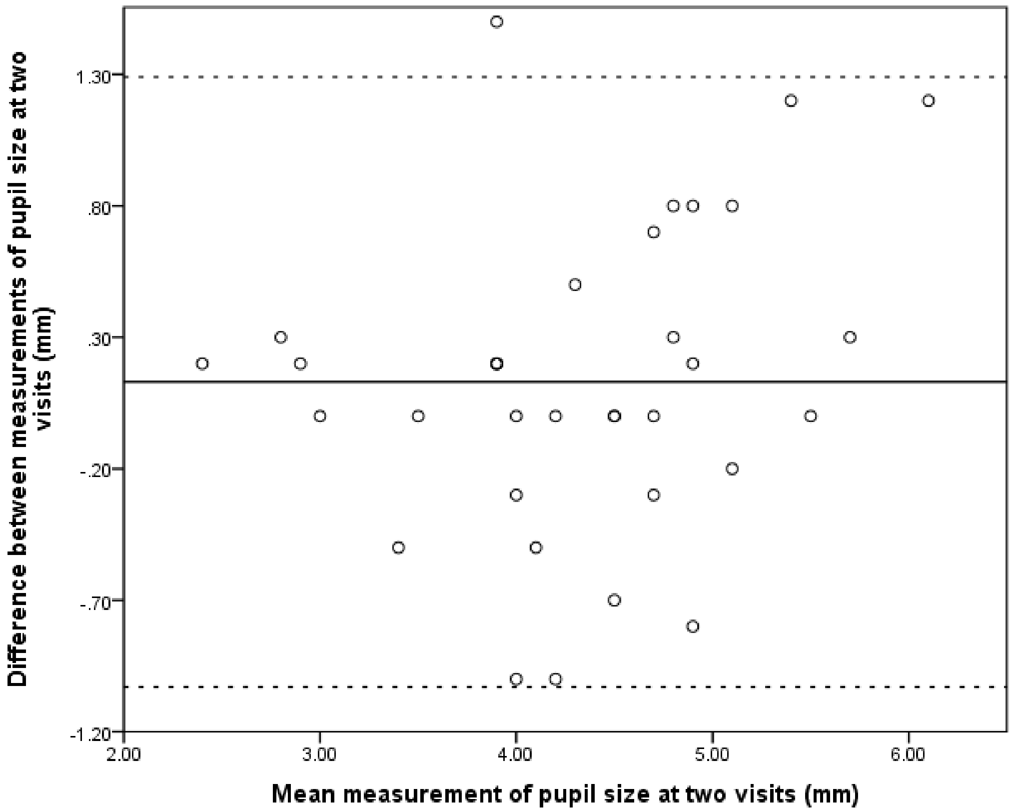

Figure 5.8: Difference versus the mean plot of average vertical pupil size for 34 right eyes. The mean difference is 0.13 mm between measurements as shown by the solid line, with a COR of ±1.16, shown by dashed lines. 31 points are visible with 3 points being superimposed.

5.4.2 Iris Colour

Iris colour distribution according to the Seddon scale was not evenly distributed, with 66.3% (n = 579) being grade 1 (light blue or green); 8.1% (n = 71) grade 2; 11.6% (n = 101) grade 3; and 14.0% (n = 122) grade 4 (dark brown). None had very dark brown (grade 5) irides. This information is shown in Figure 5.9.

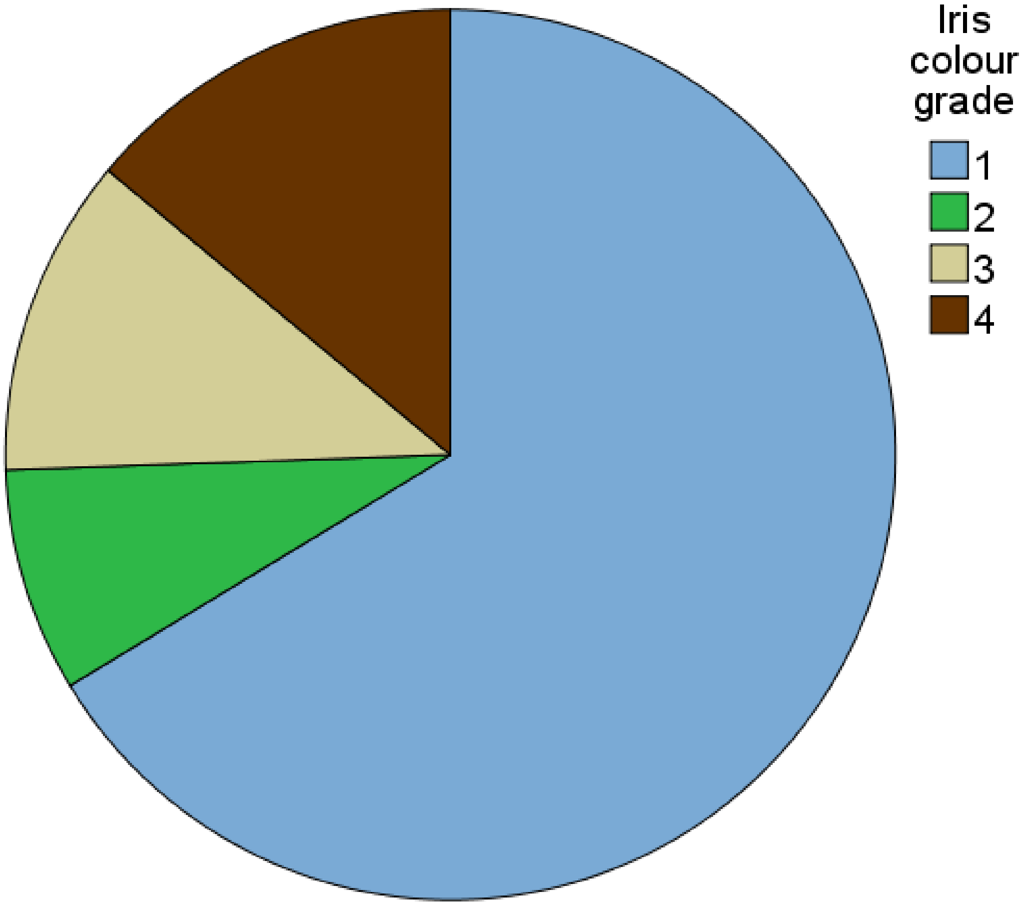

Figure 5.9: Pie chart showing proportions of iris colour grades in 873 right eyes. Grade 1 shows the highest proportion at 66.3% (n = 579), grade 2 the least at 8.1% (n = 71), grade 3 11.6% (n = 101) and grade 4 14.0% (n = 122).

On repeat testing, 3 of the 34 eyes (8.8%) were reclassified by iris colour. All were placed in a higher (darker) category on the second visit with two eyes originally categorised as a grade 3 being assessed as grade 4 on repeat testing and one eye originally graded as grade 2 being reclassified as grade 3.

5.5 Discussion

The change in pupil diameter with age was similar to that found in the previous literature. The linear equation for change in photopic pupil diameter (average 106 lux) with age was

Equation 5.1 Pupil diameter (mm) = (-0.03 x Age) + 5.46

Alfonso et al. (2010) formulated the equation:

Equation 5.2 Pupil diameter (mm) = (-0.02 x Age) + 5.51

The differences between the two studies could be due to different populations, differences in lighting levels or differences in measurement of pupil diameter (Alfonso et al. used an infrared pupillometer). Hashemi et al. (2009) found that linear regression predicted a 0.021 mm reduction in pupil diameter per year and that 24% of the change in pupil diameter could be predicted by age. Winn et al. (1994) also found that pupil diameter reduced by 0.04mm per year in mesopic conditions and 0.02 mm per year in bright light conditions. Given that COR is just over 1mm, the differences between these equations falls within the repeatability of the technique used in the present study.

Kobashi et al. (2012) found an average pupil diameter of around 3.8 mm in 20 subjects under 400 lux illuminance conditions using an infrared video pupillometer, and Hashemi et al. in The Tehran Eye Study (2009) found a mean photopic pupil diameter of 3.7 mm, both of which are slightly less than that found in the present study, but their measurements were taken under 480 lux luminance conditions compared to the 106 lux average in the current study. Hashemi et al. found a positive kurtosis of 0.06 compared to 0.16 in the present study.

Twa et al. (2004) found 95% limits of agreement between two examiners (rather than the COR of intra-examiner repeatability measured in the present study) of ±0.72 mm for semi-circular templates under 1000 lux conditions and ±1.41mm for the templates under 5 lux dim conditions. The COR in the present study lies between these two values at ±1.16 mm. This was most likely to be due to the illuminance conditions in the current study being somewhere between the two values, at 106 lux.

Measurement of pupil diameter using a semi-circular gauge with 0.5 mm increments and averaging 3 measurements was sensitive enough to detect subtle changes with age which agreed with previously published studies. A potential disadvantage to using a printed pupil gauge in practice is that pupil size measurement is very difficult in low light levels but its main advantage is its accessibility to high street optometrists and students.

Iris colour was not evenly distributed, with 66% of eyes in this study being grade 1. This large number of blue-eyed people could potentially bias the results. This is further investigated in Chapter 8. A similar high proportion of light or blue eyes has been reported in other studies on white populations (Nischler et al., 2013; Jonas et al., 2006; Mitchell et al., 2003; Winn et al., 1994).

There was agreement of 91% on repeated classification of iris colour in 34 eyes. This was slightly higher than the 83% intra-examiner agreement reported by Seddon et al. (1990).

Grading of iris colour using Seddon's Iris Colour Classification System gave similar results to previous studies in terms of distribution of iris colour and repeatability of grading.

5.6 Summary

The method of pupil measurement used for this study was less sophisticated than those used in other studies but was specifically chosen for its accessibility to optometrists in practice, yet it was still capable of showing subtle changes such as the decrease in pupil diameter with age.

Both pupil diameter and iris colour showed good repeatability and similar distributions to those found in similar studies. Raasch's equation relating vision to refractive error (see Equation 1.4, Section 1.3.5; Raasch, 1995) did not take into account pupil diameter or iris colour. The influence of both on refractive error will be considered in Chapter 8, which will show whether the large proportion of subjects with grade 1 (light) irides was a source of bias in the present study.

6. Should the scalar vector be weighted?

6.1 Introduction

This chapter contains a description of an investigation carried out to determine whether the scalar vector (U) should be weighted towards oblique astigmatic axes, as suggested by Rabbetts (see Equation 4.11, Section 4.2.1.3; Rabbetts, 1996).

6.2 Literature Review

There is a general belief amongst practitioners that oblique astigmatic axes (around 45 and 135) have a greater detriment to vision and visual acuity than orthogonal astigmatism (with axes around 180 and 90) (Elliott, 2007) and indeed, this was the effect observed by Pincus (1946).

Rabbetts (1996, 2007) suggested that oblique cylinder axes had a greater effect on the blurring of Snellen vision than orthogonal astigmatism due to the principal meridia of roman letters being vertical and horizontal, and should be given double-weighting in equations exploring the effects of astigmatic axis on vision when using the vector length method (see Section 4.2.1.3). Rabbetts suggested that the J_{45} component was multiplied by two in Equation 4.11, giving U_w.

Abrahamsson and Sjöstrand (2003) looked into the development of amblyopia with respect to astigmatic axis and found that refractive errors reduced or disappeared in children with orthogonal astigmatism but not in those with oblique astigmatic axes. The authors proposed that as astigmatic axes tend to be mirror symmetrical in nature (Guggenheim et al, 2008) the dissimilar images received by the visual cortex in oblique cylinder axes make processing difficult.

Remón et al. (2006) researched the effect of cylinder axis on vision. Simple myopic astigmatism was induced with cylinders from +0.25DC to +3.00DC at axes of 0, 30, 45, 60 and 90 in four subjects with natural pupils using a phoropter. They did not control for pupil size or accommodation as they wanted to investigate the eye in its natural state (although they artificially induced astigmatism with phoropter lenses). They found that the type of chart used to measure vision had a greater influence on the visual acuity than astigmatic axis. Variability in visual acuity was greater with the same magnitude and axis of astigmatism in different eyes than when different axes of the same magnitude of astigmatism were induced in the same eyes. This suggested that axis of astigmatism was less important than other variables. They concluded that visual acuity could be associated with a single refractive parameter, scalar vector U (without weighting), confirming the usefulness of the vector U for analysing simple myopic astigmatism.

Wolffsohn et al. (2011) found that visual acuity was reduced by approximately 0.15 LogMAR per dioptre of cylinder lens power when various JCCs were introduced, and that (minus) cylinders with a 90 degree axis gave the best overall visual performance, with axes of 45 degrees giving the worst reading performance. Little et al. (2012) found similar results in that the least degradation in vision was induced by positive cylinders at 180 (i.e. induced with-the-rule astigmatism).

Atchison and Mathur (2011) looked into the effect of small amounts of cross-cylinder blur on vision in 8 subjects aged 22-55 years. Room lighting was varied so pupils measured at least 4 mm in diameter when measured with a clinical rule and the left eye was occluded. A prescribed lens was placed at the back of a trial frame while a cross-cylinder lens was introduced at the front of the trial frame and testing was performed at a 9.5 m distance. Four different cross-cylinder powers (plano, +0.12DS/-0.25DC, +0.25DS/-0.50DC, +0.37/-0.75DC) were used on both high- and low-contrast charts at various axes (30-180 in 30^{o} increments for the lower powers and 15-180 in 15^{o} increments for the higher powers). As expected, the greater the power of the introduced lens, the greater the detriment to visual acuity and while visual acuity in some subjects varied a lot according to cylinder axis, in others there was very little difference, pointing to other interacting factors. For the group as a whole, maximum visual acuity was recorded with the negative axis at 165 with worst acuity at around 60. They concluded that the results were broadly in agreement with the previous study by Atchison et al. (2009) and proposed that these effects could be to do with neural adaptation in that certain subjects may be more attuned to their natural cylinder axes than others and may have comparatively better or worse acuity based on these axes. If this was the case then a much larger representation of subjects would be required to minimise bias from a small number of naturally-occurring astigmatic axes. When compared to spherical blur the comparable cross-cylinder blur actually degraded vision at twice the rate, which was not expected from geometric calculations or from Atchison et al. (2009) which found defocus and astigmatic blur limits to be similar.

Kobashi et al. (2012) used cycloplegia, 3 mm artificial pupils and simulated astigmatic error to investigate the effect of axis of astigmatism on visual performance. They investigated the effect of 1.00D, 2.00D and 3.00D positive cylinders placed at 90, 45 and 180 degrees in front of 38 right eyes using a luminance of 80 cdm^{-2}. They found that vision was better with less astigmatism and that oblique astigmatic axes had a greater effect on vision than orthogonal astigmatism. They also found that with-the-rule astigmatism gave slightly better vision than against-the-rule. It should be noted that Ohlendorf et al. (2011) found that the visual system appeared to be more tolerant of real refractive defocus than simulated defocus, especially in astigmatism.

Vinas et al. (2013) found that induced astigmatism had a lesser effect at the 90 axis than the 0 or 45 axes but noted that the impact of astigmatism on vision was dependent on previous astigmatic experience, with a strong bias toward the natural axis of the eye being tested.

In summary, the axis of astigmatism may have an influence on visual acuity, with oblique axes giving the worst vision. The research carried out to date has not been conclusive. Because of this Rabbetts (2007) suggested weighting oblique axes by a factor of two when examining the effect of axis upon vision when using the vector model. As many of the studies described above used induced astigmatism, and several have pointed to the fact that induced refractive errors may give different results to those found naturally, possibly due to adaptation to the eye's naturally-occurring astigmatism, the current study used data from a large number of real subjects with real refractive errors without cycloplegia or artificial pupils to investigate whether the scalar vector, U, should be weighted. This would also inform the approach to be taken for research presented in the following chapters. That is, should weighted or unweighted vectors be used to investigate the relationship between vision and ametropia?

6.3 Methods

The weighted vector, U_w, was calculated for each eye using the formula from Rabbetts (2007) (see Section 4.2.1.3 and Equation 4.11). Linear regression was performed comparing U and U_w to MAR. For these regressions only those eyes with simple or compound myopia (see Section 1.3.4) were included (n = 438) as vision in the myopes was less likely to be affected by age or accommodation than the hyperopic eyes. The linear regression analyses were used to compare results obtained for theoretical values of U and U_w to confirm whether there was any clinical difference between the two vectors.

6.4 Results

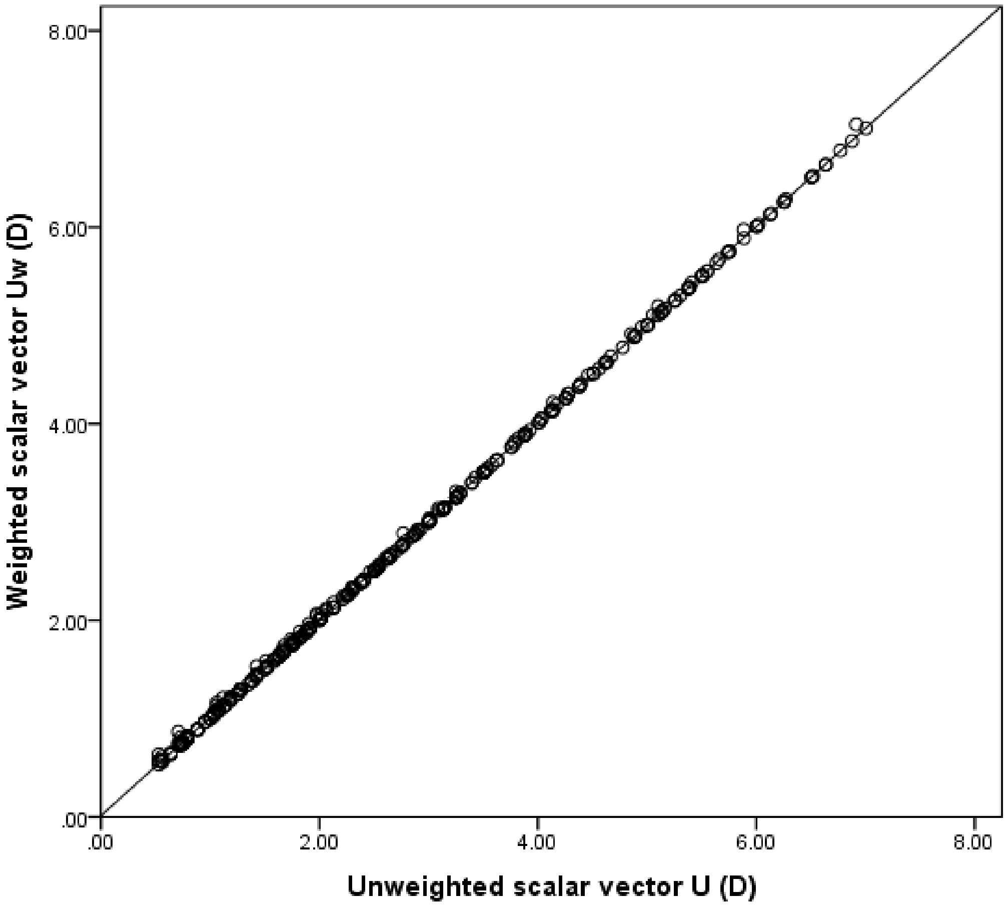

Figure 6.1: Correlation of U and U_w in 438 right eyes with simple or compound myopic astigmatism. Spearman's rank correlation coefficient (r) was 1.00. Linear regression gave a best fit line with the equation $U_w = U + 0.01$.

Figure 6.1 shows a plot of U versus U_w. There is hardly any variability between the two parameters and the Spearman's rank correlation coefficient, r, is 1.00, indicating a perfect positive correlation, and was highly statistically significant ($p = <0.01$). Correlation was expected to be very high as U and U_w measure the same thing, refractive error. It is likely to be lower with measurements of two different parameters, such as refractive error and unaided vision.

Because correlation between U and U_w was so high in the myopic group, the same analyses were performed on 236 hyperopes. This information is shown in

Figure 6.2. Spearman's rank correlation coefficient was again perfect at 1.00, and was highly statistically significant (p = <0.01).

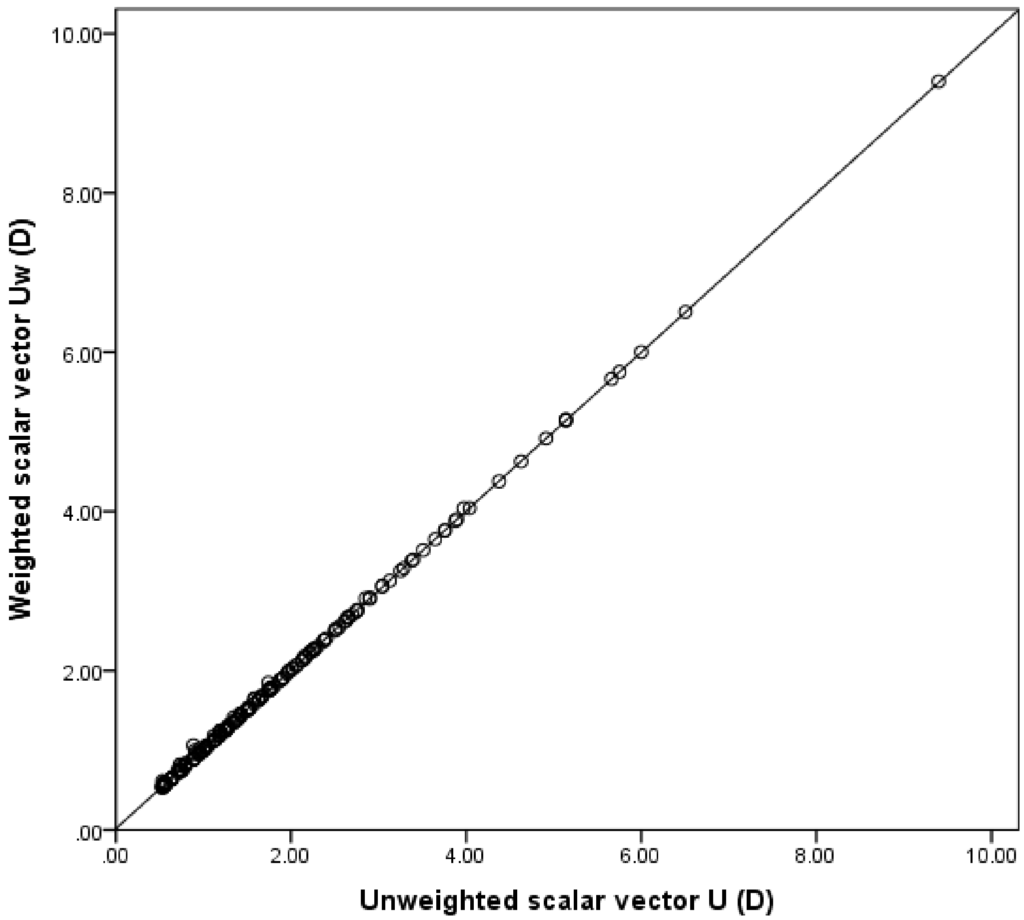

Figure 6.2: Correlation of U and U_w in 236 right eyes with simple or compound hyperopic astigmatism. Spearman's rank correlation coefficient (r) was 1.00. Linear regression gave a best fit line with the equation $U_w = U + 0.02$.

Figures 6.3 and 6.4 show the linear regression of the minimum angle of resolution, MAR, versus the unweighted and weighted scalar vectors, U and U_w respectively in 438 myopic eyes. The linear regression analyses gave the equations:

Equation 6.1 $MAR = 2.99U – 0.8$

Equation 6.2 $MAR = 2.99U_w – 0.84$

Spearman's rank correlation coefficients were 0.92 in both instances, and highly statistically significant (p = <0.01). The coefficient of determination (r^2) was 85%, meaning that 85% of the change in MAR could be accounted for by either U or U_w.

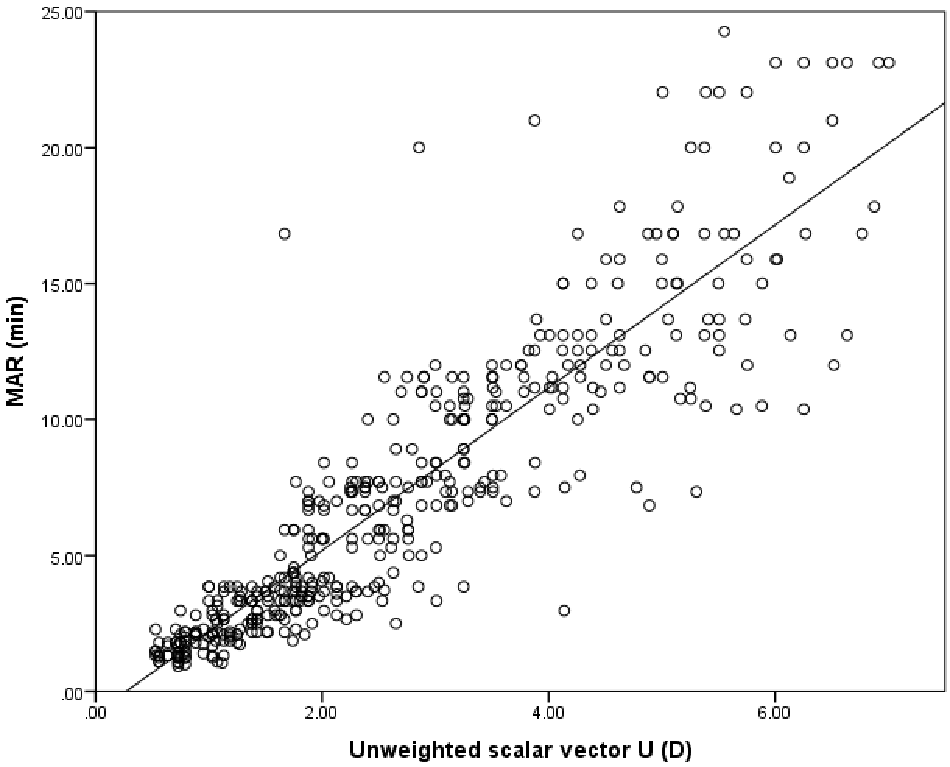

Figure 6.3: Correlation of scalar vector (U) with minimum angle of resolution (MAR) in 438 right eyes with simple and compound myopic astigmatism. The regression line is fitted to the equation MAR = 2.99U - 0.84. The coefficient of determination, r^2 was 85%.

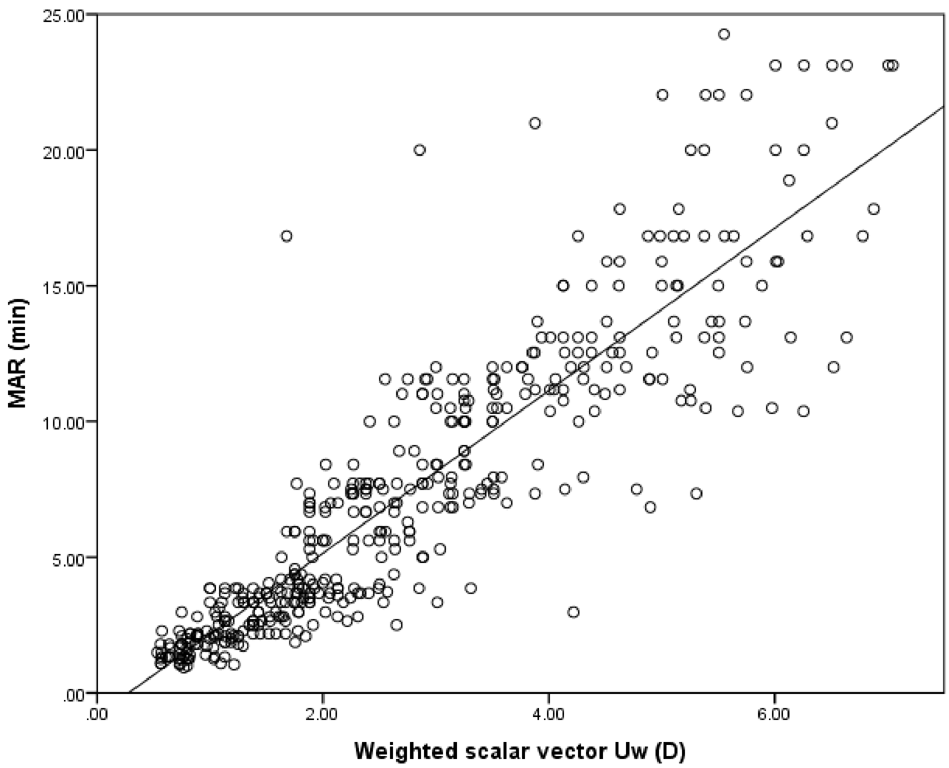

Figure 6.4: Correlation of weighted scalar vector (U_w) with minimum angle of resolution (MAR) in 438 right eyes with simple and compound myopic astigmatism. The regression line is fitted to the equation MAR = $2.99U_w$ - 0.8. The coefficient of determination, r^2, was 85%.

Table 6.1 below shows the differences in LogMAR vision when the linear regression formulae in Equations 6.1 and 6.2 were applied to different values of U and U_w. Theoretical values of U and U_w were entered into the regression equations to produce values for MAR, which were then converted to LogMAR for comparative purposes. The differences between the LogMAR values predicted by each equation are shown in the right-hand column and show that the maximum difference appeared in low refractive errors and were only as much as 0.02 LogMAR which is equal to one letter on the chart.

U (D)	MAR (‘)	LogMAR	U_w (D)	MAR (‘)	LogMAR	Difference
7.00	20.1	1.30	7.00	20.1	1.30	0.00
6.00	17.2	1.23	6.00	17.1	1.23	0.00
5.00	14.2	1.15	5.00	14.1	1.15	0.00
4.00	11.2	1.05	4.00	11.1	1.05	0.00
3.00	8.2	0.91	3.00	8.1	0.91	0.00
2.00	5.2	0.71	2.00	5.2	0.71	0.00
1.00	2.2	0.34	1.00	2.2	0.33	0.01
0.50	0.7	-0.16	0.50	0.7	-0.18	0.02

Table 6.1: Comparison of theoretical values for MAR calculated from 438 right eyes with simple and compound myopic astigmatism. The columns ‘U’ and ‘U_w’ show the theoretical values for each of these parameters. The columns headed ‘MAR’ and ‘LogMAR’ give the theoretical minimum angle of resolution (in minutes) and LogMAR values calculated using Equations 6.1 and 6.2. The difference between LogMAR values for U and U_w are displayed in the right-hand column.

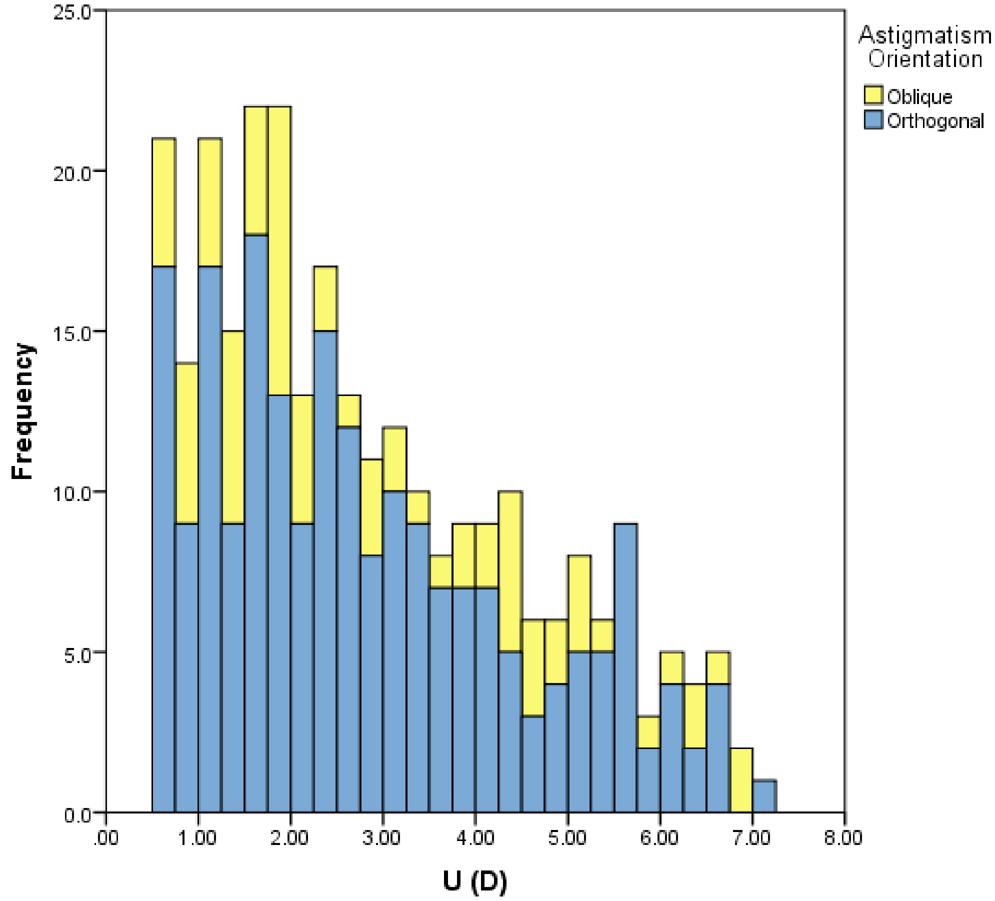

Figure 6.5: Frequency distribution of orthogonal versus oblique astigmatic axes in 438 myopic eyes. Orthogonal astigmatism accounted for 73% of eyes with astigmatism (n = 391).

Figure 6.5 shows that amongst the myopic eyes, orthogonal astigmatism, where J_0 was greater than J_{45}, predominated. It was possible that the large number of eyes with orthogonal astigmatism diluted the difference in MAR values arising from U and U_w. To investigate this further, the linear regression analyses were repeated using only those myopes with oblique astigmatic axes, where J_{45} was greater than J_0 (n = 71). Spearman's rank correlation coefficient was 0.95 for both U and U_w, meaning the coefficient of determination, r^2, was 90%. Within this sample of eyes, the regression equations obtained were:

Equation 6.3 $\quad$ MAR = 3.03U – 0.97

Equation 6.4 $\quad$ MAR = 3.04U_w – 1.09

This information is shown in Figures 6.6 and 6.7 respectively.

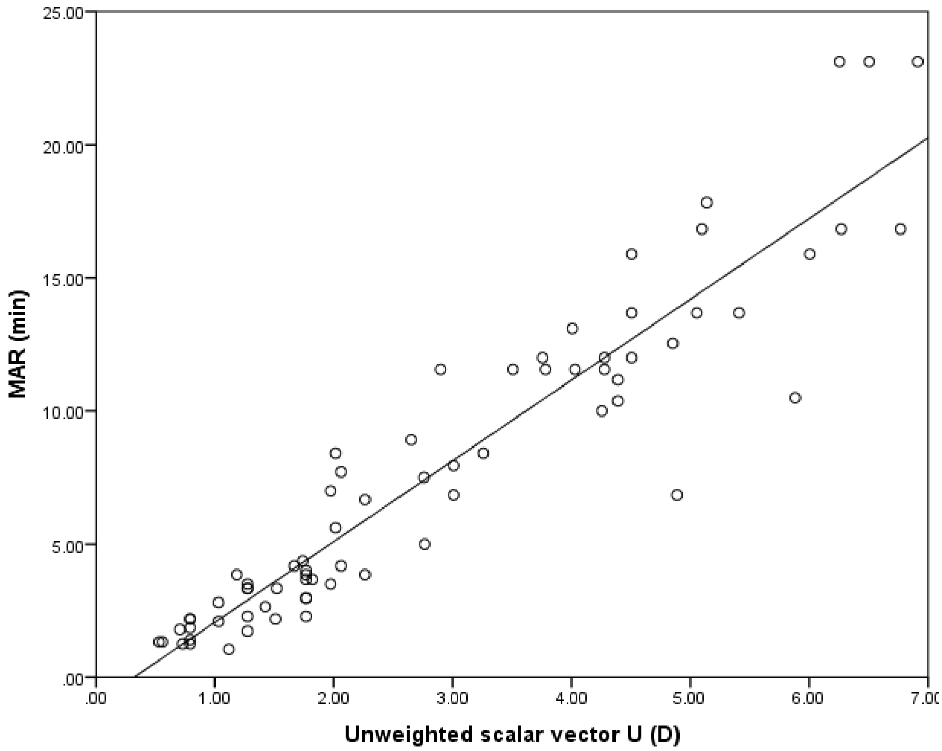

Figure 6.6: Correlation of unweighted scalar vector (U) with minimum angle of resolution (MAR) in 71 right eyes with simple and compound oblique myopic astigmatism. The regression line is fitted to the equation MAR = 3.03U - 0.97. The coefficient of determination, r^2, was 95%.

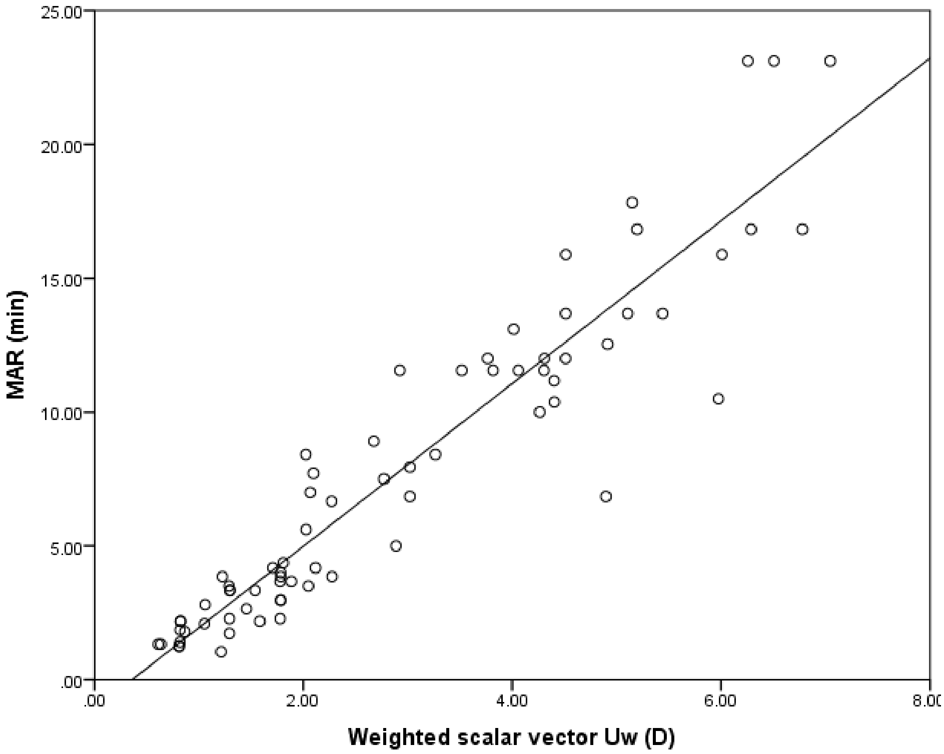

Figure 6.7: Correlation of weighted scalar vector (U_w) with minimum angle of resolution (MAR) in 71 right eyes with simple and compound myopic oblique astigmatism. The regression line is fitted to the equation MAR = $3.04U_w$ - 1.09. The coefficient of determination, r^2, was 95%.

Table 6.2 summarises the results when the MAR was calculated from theoretical values of U and U_w.

U (D)	MAR (‘)	LogMAR	U_w (D)	MAR (‘)	LogMAR	Difference
7.00	20.2	1.31	7.00	20.2	1.31	0.00
6.00	17.2	1.24	6.00	17.2	1.23	0.00
5.00	14.2	1.15	5.00	14.1	1.15	0.00
4.00	11.2	1.05	4.00	11.1	1.04	0.00
3.00	8.1	0.91	3.00	8.0	0.90	0.01
2.00	5.1	0.71	2.00	5.0	0.70	0.01
1.00	2.1	0.31	1.00	2.0	0.29	0.02
0.50	0.5	-0.26	0.50	0.4	-0.37	0.10

Table 6.2: Comparison of theoretical values for MAR calculated from 71 right eyes with simple and compound myopic oblique astigmatism. The columns ‘U’ and ‘U_w’ show the theoretical values for each of these parameters. The columns headed ‘MAR’ and ‘LogMAR’ give the theoretical minimum angle of resolution (in minutes) and LogMAR values calculated using Equations 6.3 and 6.4. The difference between LogMAR values for U and U_w are displayed in the right-hand column.

Table 6.2 shows that applying linear regression to only the myopes with oblique cylinder axes gave a greater difference in the predictive power of U and U_w, but the maximum difference was still in the lower values of U and only gave a maximum difference of 0.1 LogMAR, or one line of acuity. This is still lower than the COR of ±0.31 LogMAR found in Chapter 4.

6.5 Discussion

Figure 6.1 indicates that weighted and unweighted scalar vectors were very highly correlated. This was, however, expected because both U and U_w measured refractive error so an increase in refractive error will naturally result in an increase in both U and U_w. The graph comparing the two values shows only very minor variation between the two. Application of the regression formulae relating weighted and unweighted scalar vectors to the MAR, as shown in Table 6.1 shows that U and U_w gave almost identical results. Repetition using regression formulae obtained only from myopic astigmats with oblique cylinder axes showed a greater difference between U and U_w (Table 6.2). The maximum difference occurred with low values of U and could show a maximum difference of 1 LogMAR line which was not considered to be clinically significant as the repeatability for measuring unaided vision was ±0.31 LogMAR units, equivalent to about 3 lines of vision.

Further analysis in Chapters 7, 8 and 9 investigating blur and the factors affecting unaided vision, including the influence of cylinder axis orientation, used the more simply calculated U rather than U_w as both vector quantities represented refractive error in a similar way.

6.6 Summary

A literature review showed that some studies found an effect on vision of astigmatic axis orientation. Because of this, it had been suggested that the oblique component of refractive error (J_{45}) should be double-weighted when using scalar vectors. Weighted, U, and unweighted, U_w, scalar vectors were calculated for all myopic astigmats in the study population. A comparison of linear regression formulae describing the relationship between both forms of scalar vector and MAR revealed very little difference the two. This comparison was repeated for myopic astigmats with only oblique cylinder axes. This also showed little difference between the two types of scalar vector. This being the case, unweighted scalar vectors, being easier to calculate, were used for the remainder of this study.

7. Blur Sensitivity Ratio

7.1 Introduction

This chapter introduces the Blur Sensitivity Ratio (BSR). It represents the reduction in vision (expressed as the minimum angle of resolution, MAR) per dioptre of blur (expressed as scalar vector, U).

The BSR encapsulates the relationship between vision and ametropia in a single figure. The rationale here was to simplify statistical analyses, presented in Chapters 8 and 9, aimed at determining which variables (age, pupil diameter, sex, iris colour, contact lens wear and cylinder axis orientation) influenced the single dependent variable, BSR.

The purposes of this chapter are to:

- Establish that the BSR has not been described before in the literature
- Consider whether the denominator for BSR (scalar vector U) could be replaced by the more easily calculated mean spherical equivalent (M)
- Present the frequency distribution and repeatability of the BSR
- Make a comparison of the BSR with previously reported levels of visual reduction found when using the well-known +1.00D blur test.

7.2 Literature Review

A thorough literature search was conducted using online databases and a comprehensive list of search terms (see appendix 6). No reference to a quantity encapsulating refractive error and unaided vision could be found. This confirms as far as possible that the BSR is a novel aspect of this study.

7.3 Should the denominator of BSR be the scalar vector or mean spherical equivalent?

As BSR represents the reduction in vision per dioptre of ametropia, the calculation of BSR could proceed with either scalar vector U or mean spherical equivalent M as denominator. The mean spherical equivalent is a familiar concept to most optometrists and is simply calculated.

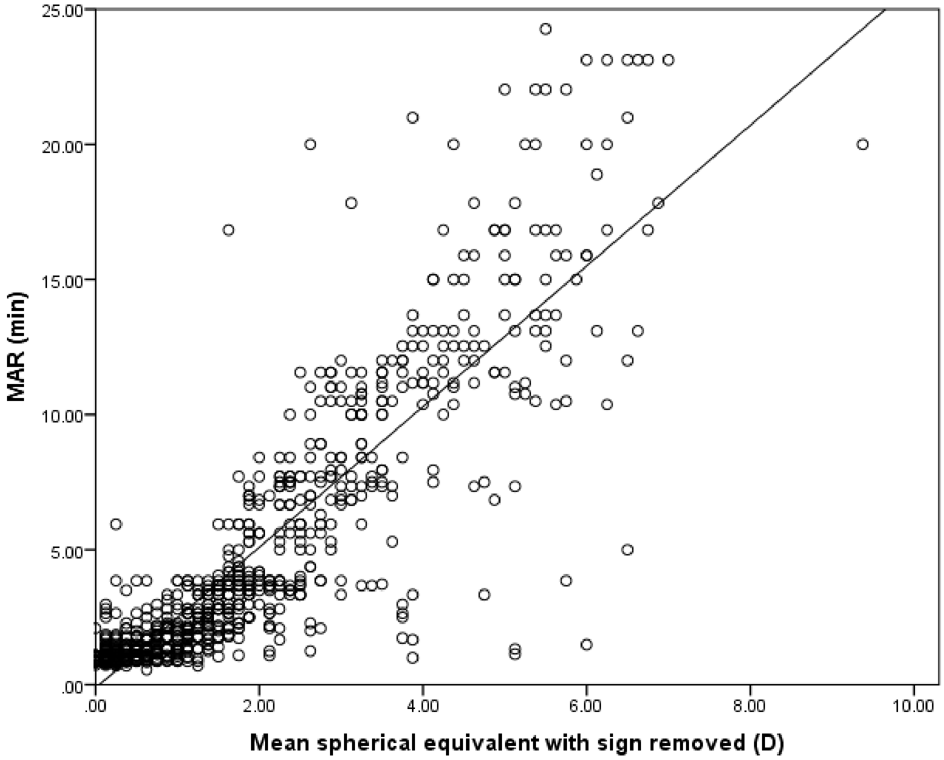

Figure 7.1: Minimum angle of resolution (MAR) plotted as a function of absolute mean spherical equivalent (M) for 873 right eyes. The regression line follows the equation MAR = 2.6M – 0.12, and has a coefficient of determination (r^2) of 78%.

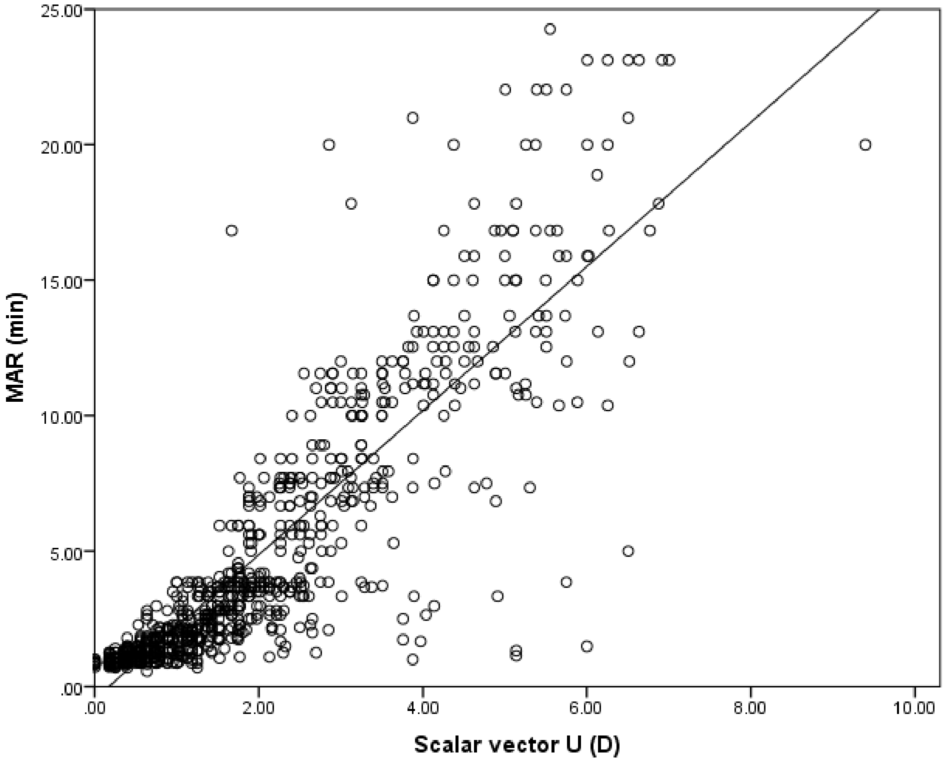

Figure 7.2: Minimum angle of resolution (MAR) plotted as a function of scalar vector (U) for 873 right eyes. The regression line follows the equation MAR = 2.66U – 0.45, and has a coefficient of determination (r^2) of 81%.

Figures 7.1 and 7.2 show that similar coefficients of determination arose for the linear regressions of the minimum angle of resolution plotted as a function of the absolute mean spherical equivalent (i.e. with the sign removed) and the scalar vector U (which has no sign). Scalar vector U however, accounted for a slightly higher proportion of variation in the minimum angle of resolution (r^2 = 81%) than mean spherical equivalent (r^2 = 78%). This supported the notion that scalar vector U should be used as the denominator in the calculation of BSR rather than mean spherical equivalent M.

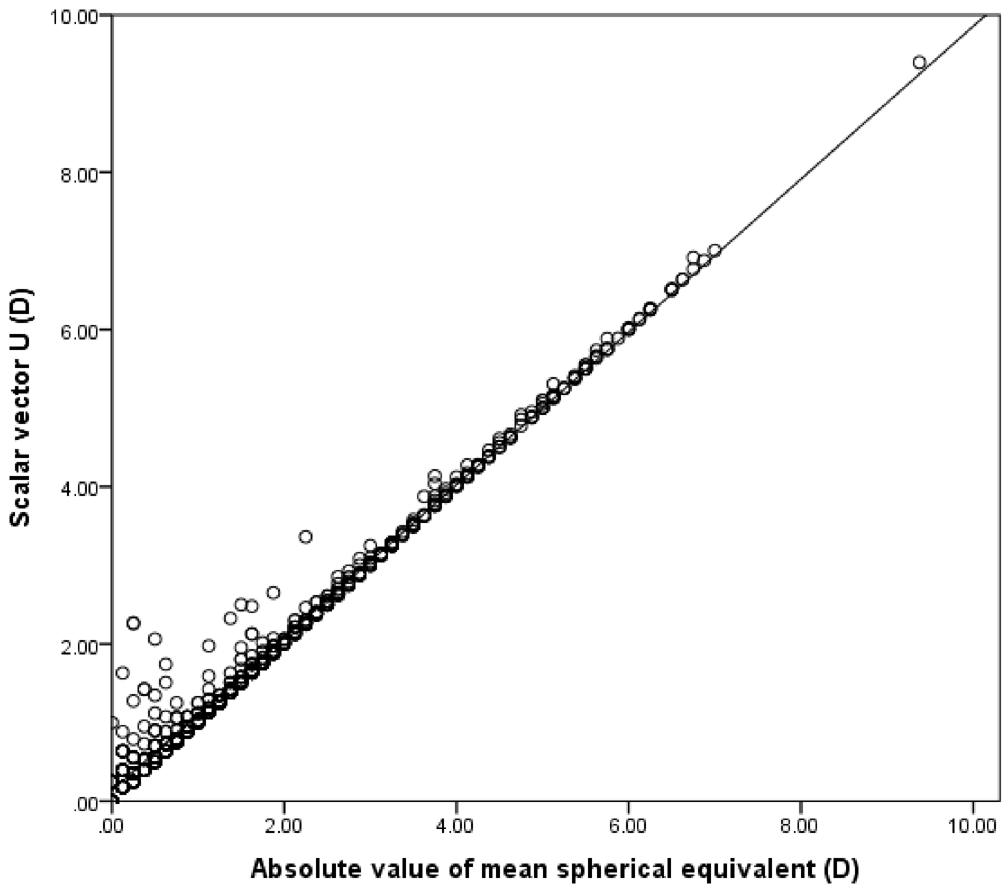

Figure 7.3: Scalar vector (U) plotted as a function of the absolute mean spherical equivalent (M) for 873 right eyes. Both variables are very highly correlated (Spearman's r = 0.99, $p < 0.001$). The regression line has a coefficient of determination (r^2) of 96%. The line is fitted to the equation $U = 0.97M + 0.14$. Note however the growing differences between both quantities as they approach zero.

Figure 7.3 shows that scalar vector U is was very highly correlated with the absolute mean spherical equivalent. This was to be expected as both quantities measure the same thing: refractive error. However, it also shows that the differences between both quantities increased as they approached zero. This was most likely due to mixed astigmatism giving low values of M but higher values of

U. That is, scalar vector expressed the optical blur in mixed astigmatism while the mean spherical equivalent effectively hid it. Raasch (1995) had previously shown that scalar vector was likely to give a truer picture. Therefore, despite the simplicity of calculating mean spherical equivalents, the scalar vector U became the preferred denominator for the BSR.

7.4 Frequency distribution of the BSR

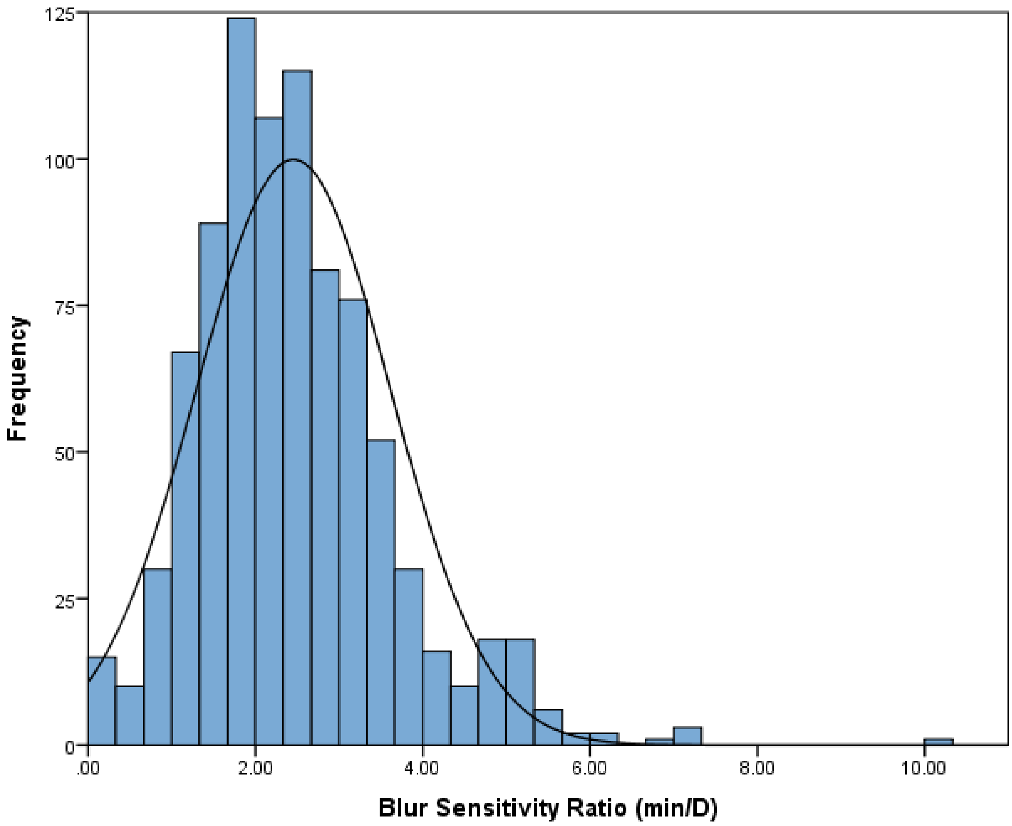

Figure 7.4: Frequency distribution of the Blur Sensitivity Ratio for 862 right eyes measured in minutes per dioptre (minD^{-1}) as calculated using scalar vector, U, with overlaid normal distribution curve. Data were excluded (11 eyes) if U had a value of zero, meaning that a BSR of infinity would have arisen. Mean BSR was 2.5 minD^{-1}, S.D. = 1.2 minD^{-1}.

Figure 7.4 shows that BSR was not normally distributed, and this was confirmed by a Kolmogorov-Smirnov test, which showed a statistically significant deviation from a normal distribution ($p = <0.01$). The mean BSR was 2.5 minD^{-1} (S.D. = 1.2minD^{-1}), the median 2.3 minD^{-1} (interquartile range 1.7-3.1 minD^{-1}) and there was a positive skew of 1.2 and positive kurtosis of 2.9. One outlier had a BSR of 10.1minD^{-1} and this was from an eye with a spectacle prescription of -1.25/-0.75x75 whose unaided vision was 1/15-2. Those eyes whose scalar vector was zero (n = 11) were excluded because this gave rise to a BSR of infinity.

These were emmetropic eyes so analysis of refractive error and its effect on vision became meaningless in these cases. Although the data were not normally distributed, the mean and median were similar to one another and further analyses could be performed as though the data followed a normal distribution.

7.5 Repeatability of the BSR

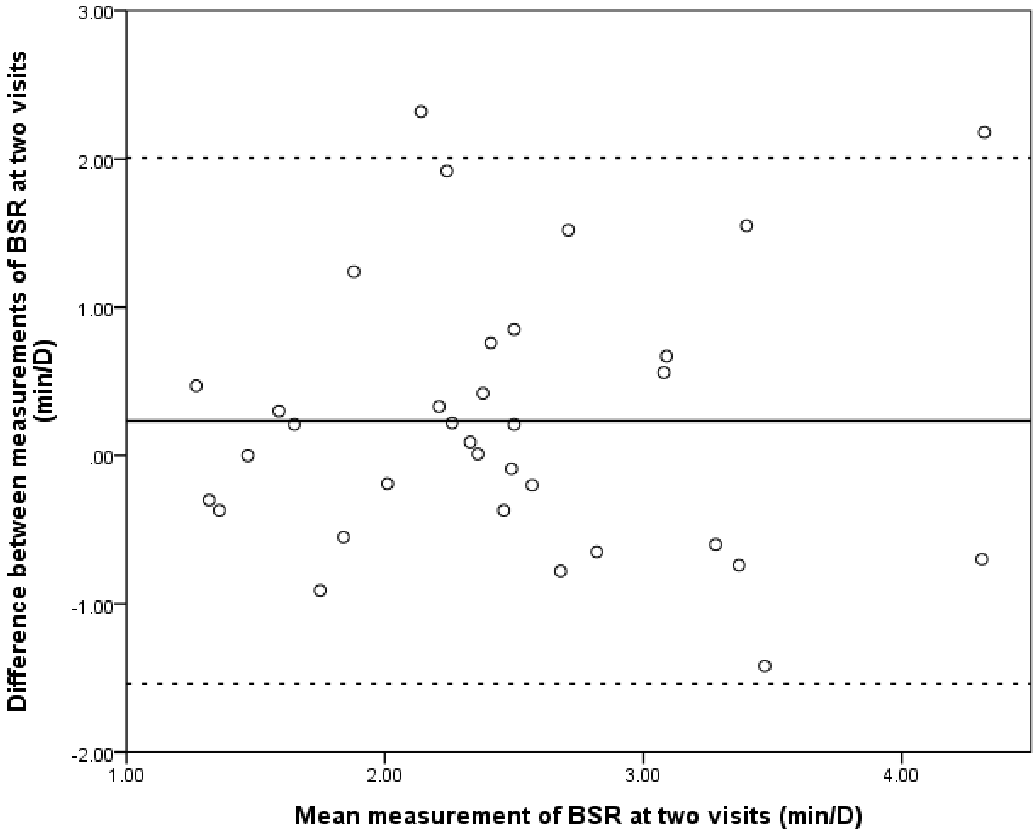

Figure 7.5: Difference versus the mean plot of the Blur Sensitivity Ratio for 34 right eyes. The mean difference is 0.23 minD^{-1} between measurements as shown by the solid line, with a COR of ±1.8 minD^{-1}, shown by dashed lines.

Section 7.4 showed that the departure from normality of the BSR could be reasonably ignored. Therefore it was acceptable to produce a difference versus the mean plot (Figure 7.5; Bland & Altman, 1986) in order to derive a Coefficient of Repeatability (COR) (Bland & Altman, 1986) for the BSR. Here the COR represented 1.96 multiplied by the standard deviation of the mean difference between repeated measurements (Bland & Altman, 1986). A Coefficient of repeatability of ±1.8 minD^{-1} was found.

The mean BSR of 2.5 minD^{-1} gave a LogMAR equivalent of 0.4 LogMAR for 1 dioptre of blur. This is in agreement with previous literature on the +1.00D blur test

(Elliott, 2007; Rabbetts, 2007; Elliott & Cox, 2004; Fletcher & Still, 1991; O'Leary, 1988).

The refraction simulators could randomly generate a virtual patient with a particular U value and from this generate an appropriately realistic quantity of blur so the student could perform a virtual refraction with the data presented to them.

A given value of U can be multiplied by the expected BSR to give the expected MAR. MAR can be multiplied by 6 to give the Snellen denominator at 6 m or by 20 to give the Snellen denominator in feet or the log10 value would give the LogMAR reading. Equally, a subject's expected refractive error can be estimated from their unaided vision by dividing their MAR by the BSR. If their refractive error is significantly less than this expected figure it could be that the reduction in their vision is pathological, not refractive.

7.6 The +1.00D blur test

The validity of the BSR could be examined by comparing typical BSR values found in this study with previous reports of visual reduction expected when carrying out the well-known +1.00D blur test (Elliott, 2007; Rabbetts, 2007). This test is used during eye examinations to check the end-point of refraction to ensure that accommodation is fully relaxed with the refractive correction in place and that the eyes are balanced. Briefly, at the end of a subjective refraction, an additional +1.00DS blurring lens is introduced and the subject is asked which line can be read. A suitable drop in vision signals that accommodation is indeed relaxed, whereas an insufficient drop in vision indicates that the subject was accommodating. As the BSR represents the visual reduction per unit of dioptric blur then it becomes immediately apparent that typical results for the +1.00D blur test should equate to typical BSR values. The problem with the +1.00D blur test is that there is considerable variation in the reduction of vision that occurs. Most text books suggest that a reduction in vision to between 6/12 and 6/18 is expected (Rabbetts, 2007; Elliott, 2007; Fletcher & Still, 1991; O'Leary, 1988).

Elliott and Cox (2004) used a LogMAR chart and noted that the expected drop in vision of 4 lines on the LogMAR chart (0.4 LogMAR) was not necessarily equivalent to a drop of 4 lines on a standard Snellen chart due to the inconsistent change in letter size between lines on the latter. Best corrected visual acuity affects the amount by which vision blurs with the +1.00D blur test and it was recommended that the Snellen denominator be multiplied by 2.5 to give the expected level of blur with the +1.00DS lens in situ. For example an eye with best corrected visual acuity of 6/4 would blur back to 6/10. This equates very well to the average BSR of 2.5 $minD^{-1}$. They suggested that variables influencing differences in levels of blur using this test included pupil size and differences in ocular aberrations.

7.7 Summary

The Blur Sensitivity Ratio was introduced in this chapter. A literature review revealed that it had not been described before. It represents the reduction in unaided vision per dioptre of blur. Use of the mean spherical equivalent as a denominator, rather than the mathematically more complex scalar vector, was ruled out as this would lead to underestimation of blur in mixed astigmatism. The similarity in the mean and median of BSR values indicated that it was reasonable to ignore its departure from being normally distributed. This meant that a valid COR could be calculated and that the BSR could be used for multiple regression analysis (for which a normal distribution is a requirement). BSR values could be conveniently compared to previous reports of vision to be expected when using the +1.00D blur test during eye examinations. Observed BSR values were in good agreement with the findings of these reports. The BSR, developed to serve as a single dependent variable for statistical analyses, is put to use in the next chapter in which the influences upon vision and ametropia of sex, contact lens wear, iris colour and cylinder axis orientation are explored.

8. Decision Tree Analysis of factors influencing Blur Sensitivity Ratio

8.1 Introduction

This study aimed to investigate the effect on vision of different types of factors, both discrete and continuous. Multiple linear regression cannot handle discrete data whereas Decision Tree Analysis (DTA) can use any type of data so offers a convenient way of investigating to what extent factors such as sex, iris colour and contact lens wear affected unaided vision in a way which multiple linear regression cannot.

8.2 Literature review

Decision Tree Analysis is a non-parametric test which calculates which independent variable has the greatest effect upon the dependent variable and to what extent it exerts its effect. DTA essentially predicts an outcome for a second group given the outcome observed for the first group (Ritschard, 2013). Its uses include (Norušis, 2011):

- Prediction: creating rules to be used in the prediction of future events
- Data reduction and variable screening: selecting predictors from a large set of variables for use in a parametric model
- Interaction identification: identifying relationships which occur only in certain subgroups
- Category merging and discretizing continuous variables.

DTA can be presented graphically as a branching diagram. All of the data are presented in the top node (parent node). The effect upon the dependent variable of the independent variable which exerts the greatest influence is calculated and presented as the first branch in the diagrammatic tree. Each subsection within this lower branch is called a 'child node'. If no other independent variables influence the dependent variable there will be no more branching. When using SPSS statistical software, the minimum number of cases within each node can be specified. This means that if the minimum number of cases is set at 50, there will be at least 50 cases in each child node. The software will not consider variables to significantly influence the independent variable if the number of cases within a child node is less than 50 in this case. If further independent variables influence the dependent variable the tree will branch further until the effect is statistically insignificant.

DTA has previously been used by others in relation to optometry:

- Chandra Shekar and Sesha Srinivas (2008) used DTA to classify refractive error.
- Dunstone et al. (2013) used DTA in their investigation into the retinoscopy habits of UK optometrists.
- Frick et al. (2009) used DTA to compare the cost-effectiveness of two methods of screening for refractive error.
- Guillon and Maissa (2005) used DTA to elucidate the symptoms most predictive of dry eye.
- Twa et al. (2005) used DTA to classify corneal shape as normal or keratoconic.

The CHAID (Chi-Squared Automatic Interaction Detection) algorithm was proposed by Kass (1980) as an improvement to the pre-existing AID (Automatic Interaction Detection) algorithm. The CHAID algorithm utilises built-in statistical significance testing to use the most significant predictor and allows multi-way (not just binary) splits. It only accepts ordinal or nominal categorical data (continuous data are transformed into ordinal predictors by SPSS before analysis). CHAID was used in two of the previously mentioned studies (Guillon & Maissa, 2005; Dunstone et al., 2013).

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8.3 Methods

SPSS v.21 (IBM SPSS Statistics) was used to perform the Decision Tree Analyses. The CHAID growing method was used as it allowed multi-way splits, so where more than two classes of one variable existed (for example 4 classes of iris colour), each class could be quantified by its influence on BSR. The default settings of 3 levels maximum tree depth and minimum number of cases 100 for the parent node and 50 for the child node were used. Only eyes classified by refractive groups as being hyperopic or myopic were selected (n = 674) for this analysis as those classed as near emmetropes showed little variation in refractive error and vision, as expected. The dependent variable was BSR and independent variables were

- Sex

- CL wear
- Iris colour
- Refractive group (hyperopes, myopes)
- Cylinder axis orientation (orthogonal, oblique)

8.4 Results

Figure 8.1 shows the DTA results for factors affecting BSR. Node 0 (BSR) contained 674 data sets, with mean BSR 2.2 $minD^{-1}$ (S.D. = 0.9 $minD^{-1}$), representing 100% of the data in this analysis. The factor having the greatest influence on BSR was refractive group, shown in the first split. Mean BSR was 1.6 $minD^{-1}$ (S.D. = 0.7 $minD^{-1}$) for hyperopes and 2.6 $minD^{-1}$ (S.D. = 0.9 $minD^{-1}$) for myopes. Within the hyperopic group, no other factors were considered to influence BSR, so node 1, which represents 236 hyperopic eyes is a terminal node, with no subsequent child nodes. Within the myopic group (n = 438), cylinder axis orientation influenced BSR. Node 3 contained those myopic eyes considered to have no astigmatism (n = 156) whereas node 4 combined those with orthogonal and oblique astigmatism (n = 282). Interestingly, this shows that it is in fact not the orientation of the astigmatic axis, but merely the presence of astigmatism which influences BSR.

Sex, contact lens wear and iris colour did not influence Blur Sensitivity Ratio according to Decision Tree Analysis.

The tree had only 2 levels, and each node had over 100 cases, so the default settings of 3 levels and a minimum of 100 cases for parent nodes and 50 for child nodes did not artificially restrict the analysis, so even if more nodes were allowed by the settings used in the DTA analysis, no more variables would have been selected as significant.

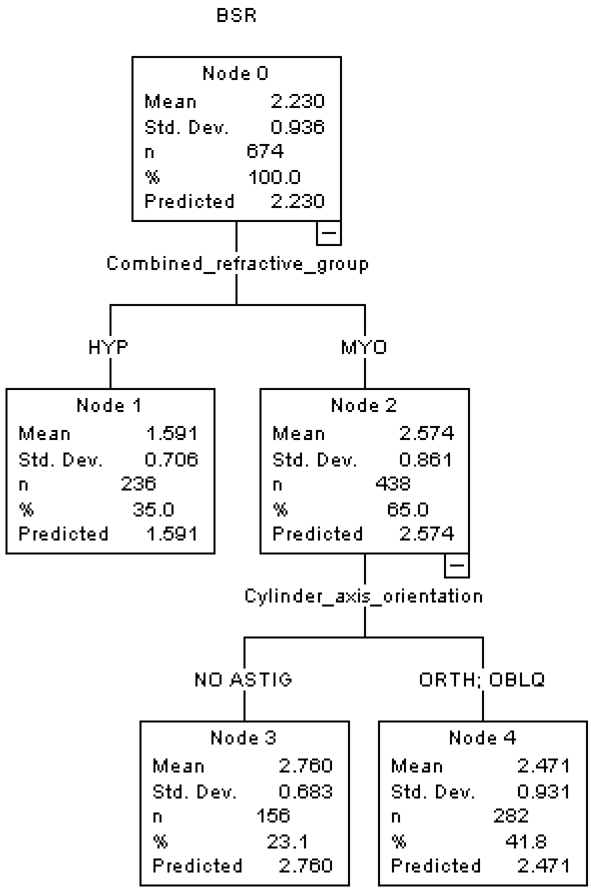

Figure 8.1: Decision Tree Analysis (CHAID growing method) showing the factors affecting BSR of 674 right eyes with myopia and hyperopia. Combined refractive group i.e. hyperopia ('HYP', n = 236) or myopia ('MYO', n = 438) had the greatest influence on BSR as shown by the fact it is the first branch in the diagram. Cylinder axis orientation appeared to influence BSR in the myopic group but node 2 was split between eyes with no astigmatism ('NO ASTIG', n = 156) and eyes with either oblique ('OBLQ') or orthogonal ('ORTH') cylinder axes (n = 282), meaning that in the myopic group, only the presence or absence of astigmatism affected BSR.

8.5 Discussion

That cylinder axis orientation had no significant effect was in agreement with Remón et al. (2006), but contrasted with other previous observations (Vinas et al., 2013; Kobashi et al., 2012; Little et al, 2012; Atchison & Mathur, 2011; Wolffsohn et al., 2011; Pincus, 1946) that oblique astigmatic axes gave rise to worse vision than orthogonal astigmatism. Of these studies, several noted that previous experience of astigmatism appeared to influence vision, so natural astigmatic errors appeared to have less of a deleterious effect on vision than induced astigmatism. The present study measured natural refractive error so was most similar in nature to that of Pincus (1946).

That hyperopes had a lower BSR than myopes was not surprising, as young hyperopes can use accommodation to overcome blur so as a group, unaided hyperopes are overall not affected by dioptric blur in the same way myopes are. This is similar to the effect observed by Tucker and Charman (1975) who noted that induced hyperopia had less of a detrimental effect on vision than induced myopia, despite the use of cycloplegia in their experiment.

The finding that iris colour does not have a significant effect on BSR was in agreement with Nischler et al. (2013). That sex and contact lens wear did not appear to have an effect on vision means contact lens wearers did not need to be excluded from further analysis or analysed separately from non-contact lens wearers, and males and females could be analysed together.

The DTA analysis showed agreement with Remón (2006) that astigmatic axis had little effect on unaided vision. It also supported the earlier finding in Chapter 6 that using unweighted scalar vector, U, rather than vector, U_w, weighted towards oblique cylinder axes, was sufficient as oblique cylinders did not result in worse unaided vision than orthogonally-orientated cylinders. These findings were however in contrast to those of Rabbetts (1996, 2007) who stated that Snellen acuity was better for orthogonal cylinder axis orientations due to the Roman alphabet used on a Snellen chart being dominated by vertical and horizontal lines.

DTA ruled out sex, contact lens wear, iris colour and axis of astigmatism as having a significant effect on unaided vision. Presence of astigmatism was found to affect BSR but this was already encapsulated within the scalar vector U, so no further analysis of this variable was deemed necessary. This meant that further analysis of these discrete variables was unnecessary and that only the remaining continuous variables (age, pupil diameter, and scalar vector) needed to be included in multiple linear regression. Regression analysis would be carried out separately for hyperopes and myopes as DTA showed that mean BSR was different for each of these two groups. It also showed that concerns about the current sample being biased towards females and contact lens wearers as well as having a large proportion of blue eyes was not an issue. The findings of this study could therefore be generalised to other white practice based populations.

8.6 Summary

Decision tree analysis showed that sex, iris colour and contact lens wear did not have a statistically significant effect on unaided vision. Cylinder axis orientation also had no effect on unaided vision. Multiple linear regression could therefore continue based purely on the remaining variables (age, pupil diameter, scalar vector).

9. Stepwise Multiple Linear Regression Analysis of Factors Influencing Blur Sensitivity Ratios

9.1 Introduction

This chapter presents the application of stepwise multiple linear regression which was carried out to determine the factors that influence variations in the Blur Sensitivity Ratio; that is age, pupil diameter and scalar vector U. A review of the literature shows that such an analysis has not been reported before now. This information is used to create a new set of equations relating vision to ametropia. These new equations are compared to that of Raasch (which is currently used in refraction simulators used at Aston University but does not account for pupil size and age) to determine which most closely models the observed relationship between vision and ametropia. Finally, a method is proposed to incorporate the new equations in refraction simulators for the purpose of making them more realistic.

9.2 Literature review

In a situation where a number of independent variables could influence a dependent variable, multiple linear regression can be used to select a subset of these variables to create a linear equation which best predicts the dependent variable (Armstrong et al., 2011).

Raasch (1995) used a second order polynomial to obtain the formula used in the Aston University refraction simulators (see Equation 1.4, Section 1.3.5). This formula allowed calculation of LogMAR vision from scalar vector U, but did not take into account other variables. Raasch himself conceded that pupil size would affect vision but the original data set (Pincus, 1946) did not include the measurement of pupil size, so his formula represented the aggregate performance in that group of eyes over a range of pupil sizes. Multiple linear regression was used in the present study to improve upon this formula by including other variables (such as pupil size and age).

Multiple linear regression has been used in many other studies concerned with eyes and vision (Ishii et al., 2013; Zhang et al., 2013; Ravikumar et al., 2012; Liu et al., 2011; Cakmak et al., 2010; Fotouhi et al., 2012; Hashemi et al., 2009; He et al., 2009; Oshika et al., 2006; Mitchell et al., 2003; Mikelberg et al., Hazel et al., 2000; 1989; Ehlers et al., 1975). It is a parametric test that is, strictly speaking, ideally suited to (Armstrong & Hilton, 2011):

- Dependent and independent variables which are normally distributed
- Independent variables which are relatively independent of one another (i.e. are not highly intercorrelated)

The two main types of multiple linear regression are the step forward (step up) and step backward (step down) methods. Simply put, in the step forward method, variables are entered into the equation and tested for statistical significance. When an introduced variable does not change the outcome significantly, it is excluded from the final equation. In the step backward method, the multiple regression of the dependent variable on all of the independent variables is first calculated. Then variables which do not contribute significantly are removed one at a time until removal of further variables has a statistically significant effect upon the resulting equation (Armstrong & Eperjesi, 2007). The two types of analysis can give different results.

The present study aimed to use step backward multiple linear regression to create an algorithm which could be used in refraction simulators to give undergraduate optometry students a more realistic experience. The step backward method was chosen as it may retain more variables than the step forward method and could generate a more accurate equation. The creation of an equation using multiple linear regression to relate unaided vision to ametropia while accounting for age and pupil size is another novel aspect of this study. A literature review (appendix 7) showed that such a study has not been reported before now.

9.3 Normality and inter-correlation between variables

Multiple linear regression assumes that data are normally distributed and that none of the independent variables are inter-correlated. None of the variables used in this analysis were normally distributed, as shown in Figures 2.1 (age, Section 2.6), 5.6 (pupil size, Section 5.4.1), 4.6 (scalar vector U, Section 4.4) and 7.4 (BSR, Section 7.4). This was also demonstrated with Kolmogorov-Smirnov tests carried out in Sections 3.4 (U), 5.4.1 (pupil size) and 7.4 (BSR). To investigate how non-normally distributed data might influence the findings of this study, parametric (Pearson's correlation coefficient) and non-parametric (Spearman's rank correlation coefficient) correlations were performed for each combination of variables (BSR, age, pupil size and scalar vector U). The thinking here was that unlike parametric correlation coefficients, non-parametric correlation coefficients should not be influenced by the distribution of the data. Should very similar correlation coefficients emerge from both types of test then this would indicate that the observed departures from perfect normal distributions could reasonably be expected to make little difference to the study outcomes. Tables 9.1 (Pearson's correlation coefficients) and 9.2 (Spearman's rank correlation coefficients) show that very similar correlation coefficients arose. Therefore, the observed departures from normally distribution were unlikely to affect multiple linear regression (Armstrong & Hilton, 2011).

	BSR	U	Pupil size	Age
BSR	1.00	-0.03	0.19*	-0.16*
U		1.00	0.03	-0.17*
Pupil size			1.00	-0.46*
Age				1.00

Table 9.1: Pearson's correlation coefficients for scalar vector U, BSR, pupil size and age for 873 right eyes. Asterisks (*) indicate statistically significant correlations at the 0.01 level.

	BSR	U	Pupil size	Age
BSR	1.00	-0.06	0.22*	-0.22*
U		1.00	0.02	-0.12*
Pupil size			1.00	-0.44*
Age				1.00

Table 9.2: Spearman's rank correlation coefficients for vector U, BSR, pupil size and age for 873 right eyes. Asterisks (*) indicate statistically significant correlations at the 0.01 level.

Tables 9.1 and 9.2 did however show that statistically significant inter-correlations existed between (1) scalar vector U and age and (2) pupil size and age. These inter-correlations could, potentially, have altered the relative influences of scalar vector U, pupil size and age on the BSR as shown in the findings of the present study.

9.4 Stepwise multiple linear regression

SPSS v.21 (IBM SPSS Statistics) was used to perform step backward multiple linear regression. The dependent variable was BSR while the independent variables were age, pupil size and scalar vector U.

Other variables (sex, contact lens wear, orientation of cylinder axis, iris colour) had already been excluded by DTA (Chapter 8) so were not included in this analysis. Presence of astigmatism, indicated by DTA as a variable affecting BSR, is encapsulated by U, so was not further analysed.

9.5 Results and discussion

Step backward multiple linear regression was performed separately on 438 myopes and 236 hyperopes (as classified in Section 4.3.2). This analysis revealed that only pupil size and scalar vector U influenced BSR in myopes (Equation 9.1) and only pupil size and age influenced BSR in hyperopes (Equation 9.2).

Equation 9.1 $BSR_m = 1.13 + (0.24 \times \text{pupil size}) + (0.14 \times U)$

Equation 9.2 $BSR_h = (0.11 \times \text{pupil size}) + (0.03 \times \text{age}) – 0.19$

ANOVAs carried out on each regression analysis showed that both were statistically significant (for myopes $F_{2,435} = 29.44$, $P < 0.001$; for hyperopes $F_{2,233} = 26.99$, $P < 0.001$) but only accounted for a small proportion of the variance in BSR (0.12 for myopes and 0.19 for hyperopes). The B values and standard errors are given for each analysis in table 9.3.

		B value	Standard Error
Myopes	(Constant)	1.13	0.22
	U	0.14	0.02
	Pupil Size	0.24	0.05
Hyperopes	(Constant)	-0.19	0.35
	Age	0.03	0.00
	Pupil Size	0.11	0.06

Table 9.3: B values and standard errors for multiple linear regression on 438 myopic and 236 hyperopic right eyes.

Multiplying the resulting BSR values arising from both equations by the scalar vector U recorded for each myope and hyperope gave predicted values of MAR. These predicted values of MAR were correlated against the originally observed MAR values to derive Pearson's correlation coefficients for myopes and hyperopes. These coefficients were squared to give coefficients of determination (r^2) of 0.82 for myopes and 0.51 for hyperopes.

This showed that while age, pupil size and U only accounted for relatively little of the variation in BSR, the actual agreement between observed and modelled MAR was much higher. A better model could have been developed using more variables, that remain unknown, but these unknown variables are not likely to impact much on the agreement between measured and modelled MAR values.

9.6 Comparison of predictions made using the new equations versus the Raasch equation

The refraction simulators developed at Aston University currently use Raasch's (1995) formula (Equation 9.3):

Equation 9.3 $$\text{LogMAR} = 0.48 + 1.07[\text{Log}(U)] + 0.46[\text{Log}(U)]^2$$

Raasch had excluded data from hyperopes to derive Equation 9.3 so it only strictly applies to myopes. Yet, the refraction simulators apply Equation 9.3 to both myopes and hyperopes.

For the purposes of this comparison, Raasch's equation (9.3) and the new Equations 9.1 and 9.2 were applied to 862 eyes from the present study. Eleven absolute emmetropes (with a spectacle prescription of 0.00DS) were removed as they would have given an impossibly large value of BSR. When using the new equations, Raasch's equation was applied to all 862 eyes. New Equation 9.1 (for myopes) was applied to all eyes with a mean sphere of less than zero while Equation 9.2 (for hyperopes) was applied to all eyes with a mean sphere of greater than zero. The mean sphere had to be used as scalar vector U has no sign.

Taking the antilog of the results of Raasch's equation gave rise to MAR values. For the new equations, BSR values were converted to MAR by multiplying BSR by scalar vector U. The MAR values resulting from all equations were converted to a Snellen denominator by multiplying MAR by 6.

Figure 9.1 compares the observed Snellen denominator values to those values generated using Raasch's equation (9.3) and the new equations (9.1 for myopes and 9.2 for hyperopes). In this figure, the Snellen denominator at 6m viewing distance is plotted on the vertical axis against scalar vector U on the horizontal axis. Visual inspection of the figure shows that the new equations more closely reflect the measured Snellen denominator values compared to Raasch's equations. Correlations between observed and predicted Snellen denominator values showed that predicted values arising from the new equations accounted for more of the observed variation in measured values (r^2 = 0.84) than did the predicted values based on Raasch's formula (r^2 = 0.72).

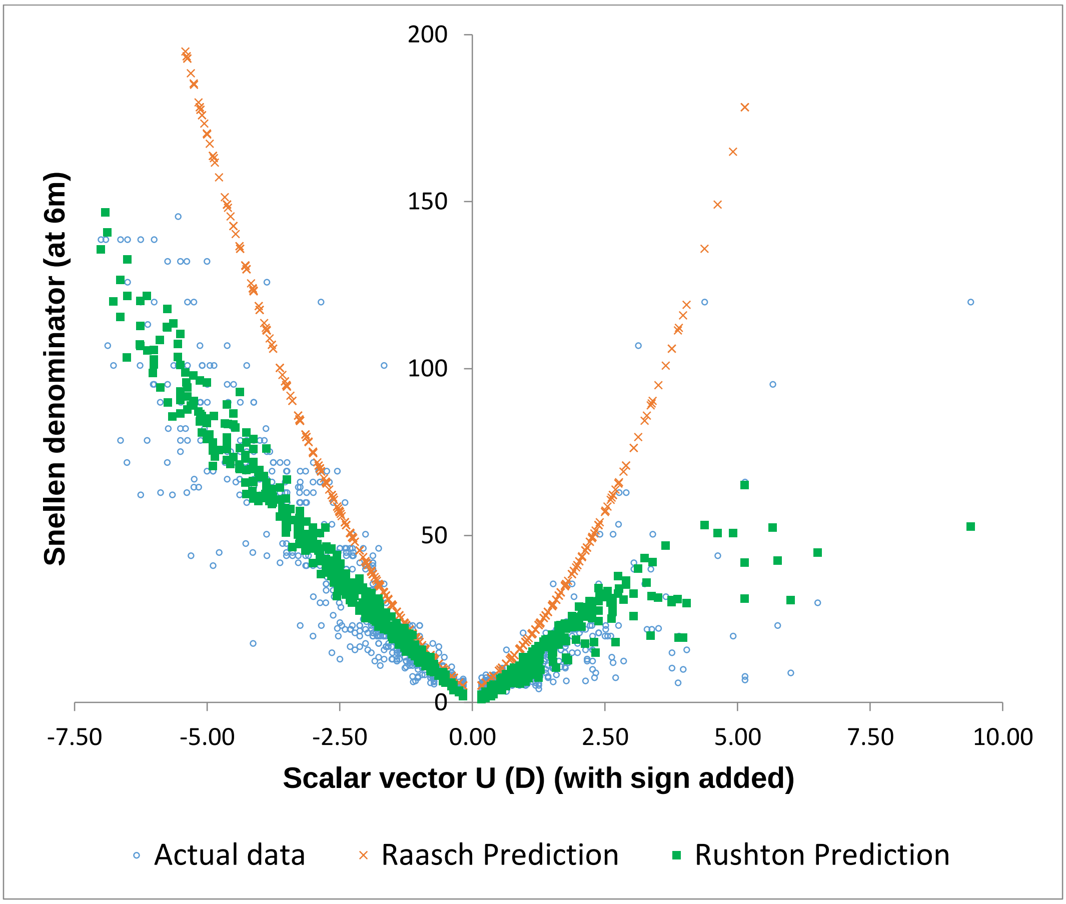

Figure 9.1: Snellen denominator for 6m viewing distance plotted as a function of scalar vector U for 862 right eyes (11 absolute emmetropes removed). The actual (observed) Snellen denominator values are shown (small blue open circles) together with those predicted using the new equations (green filled squares) derived for myopes (Equation 9.1) and hyperopes (Equation 9.2) and Raasch's equation (orange crosses).

9.7 Handling near-emmetropes

The intention was to use the new equations in the refraction simulators developed at Aston University. Raasch's equation (9.3) had the advantage that it could be used for predicting vision for any degree of near-emmetropia as, for example, a scalar vector U of 0.12D gave rise to a plausible predicted Snellen fraction of 6/4.6. On the other hand, for the same scalar vector U value, the new equations predicted implausible Snellen fractions of 6/1.5 for myopes and 6/1.0 for hyperopes. A simple remedy would be to set a lower limit for the predicted Snellen fraction of, say, 6/5. This, however, would not be realistic as, in real life, the Snellen fraction representing best vision varies from person to person.

In an attempt to arrive at a variable lower limit for use in the refraction simulators, an analysis was carried out on the best corrected visual acuity of 150 of the subjects of this study. The age range in this sample was 20 to 69 years (mean 46 years, S.D. = 14 years). Pupil diameters ranged from 2.5 to 6.7 mm (mean 4.1 mm, S.D. = 0.8mm). The best corrected Snellen fraction ranged from 6/7.6 to 6/3 (Snellen denominator mean 5.6, S.D. = 0.7). An ANOVA carried out on the linear multiple regression describing the dependence of best corrected MAR values on age and pupil size showed that no statistically significant relationship existed ($F_{2,147} = 0.45$, $P = 0.64$). As neither age or pupil diameter influenced MAR then it seemed reasonable to quote a cut-off value with upper and lower limits based on 2 standard deviations either side of the mean. These were, for MAR, 1.1 and 0.7 which correspond to Snellen fractions of 6/6.6 to 6/4.0.

The proposed remedy is described in Equation 9.4:

Equation 9.4 Minimum Snellen denominator at 6m = (S x 2.6) + 4

The value S is a value between 0 and 1 that is randomly generated. The value of 2.6 represents the difference in the Snellen denominator (for a 6 m testing distance) between its upper (6.6) and lower (4.0) limits (6.6 – 4.0 = 2.6) as found in the analysis just described. The value 4 represents the lowest possible Snellen denominator (taken from the lower limits found in the analysis just described).

By randomising S in Equation 9.4, best corrected Snellen fractions of between 6/4 and 6/6.6 could be generated for the refraction simulators. As near-emmetropia was approached, during a simulated refraction, the predicted Snellen fractions arising from new Equations 9.1 (for myopes) or 9.2 (for hyperopes) would be allowed to fall to the randomly generated lower limit. The variation in best corrected visual acuity that students would experience from one 'virtual patient episode' to another would now reflect, more realistically, what happens in real patients.

9.8 A proposed algorithm for the Aston University refraction simulators

One of the aims of this study was to produce a new algorithm for the Aston University refraction simulators so that undergraduate students would have a more realistic experience when refracting their 'virtual patients'. The algorithm could follow these steps:

Step 1: Randomly generate the virtual patient's age between 20 and 70 years.

Step 2: Randomly generate the pupil diameter from 2.3 – 7.5 mm.

Step 3: Randomly generate spherocylindrical refractive errors:

- Spheres from -6.75 to +10.00DS
- Cylinders up to -5.00DC
- Randomly generated cylinder axes.

Note: steps 1-3 limit virtual patient characteristics to those that fall within the range of the data found in the present study.

Step 4: Convert the spherocylinder into mean spherical equivalent (M) and scalar vector (U).

Step 5: The BSR formula used depends on the sign of M. If M is negative (myopia, Equation 9.1 above is applied whereas Equation 9.2 is applied if M is positive (hyperopia).

Step 6: The Snellen denominator at 6 m is calculated from the BSR by multiplying it by scalar vector U and 6.

Note: Snellen denominators which fall between typical chart values could be assigned appended letters.

Step 7: As emmetropia is approached, the Snellen denominator is allowed to fall to a randomised lower limit calculated using Equation 9.4 (described in Section 9.7).

9.9 Comparison of findings to previous work

The new equations show that vision in myopes was affected by pupil size and scalar vector, U. As pupil size increased, so did the BSR. This means that less reduction in vision per dioptre occurs in smaller pupils. This is consistent with previous studies (Kamiya et al., 2012; Kobashi et al., 2012; Hashemi et al., 2009; Donnelly & Roorda, 2003; Laughlin, 1992; Atchison et al., 1979; Tucker & Charman, 1975) that have shown the optimal photopic pupil diameter to be between 2 and 4 mm. This is most likely due to the reduction in peripheral aberrations with smaller pupils, as discussed in Section 5.2.1. The equation for myopes also shows that BSR increases as U increases. This means that a higher refractive error will produce more blur per dioptre than a lower refractive error. This is in contrast to the findings of Smith (1991) whose equation (see Equations 1.5 and 1.6, Section 1.3.5) described a linear relationship between vision and ametropia, but similar to the findings of Raasch (1995), whose equation (see Equation 1.4, Section 1.3.5) described an increasing quantity of blur per dioptre with increasing refractive error.

In hyperopes vision is affected by pupil size in a similar manner to myopes. Age was the second variable in the equation to affect BSR, showing that an increase in age increased blur per dioptre. This was expected as increasing age equates to a reduction in accommodative ability to overcome hyperopia. Scalar vector U did not feature as a significant variable in the hyperopic group. This may be because there were few hyperopes in the younger age categories so variability in vision between high and low levels of hyperopia within these age groups may not have been easily determined. However, the high number of hyperopes in the older age groups, who have limited accommodation should have been enough to elicit any significant differences in BSR with varying levels of U. There were, however, few eyes with high levels of hyperopia, compared to those with high levels of myopia, so it could be that a greater number of eyes in the hyperopic group with high U values would have elicited an effect on BSR from scalar vector U. In terms of BSR, defined as blur per dioptre of ametropia, age is a more significant factor in the blur than the level of ametropia itself due to the loss of accommodation with age. Once this is taken into account, scalar vector U has a much lesser effect on the level of blur per dioptre.

One of Pincus's (1946) observations was that vision decreased as age increased amongst the hyperopes but age did not affect myopes. He also remarked that vision decreased as refractive error increased. The current study agreed with him on the first point but only for myopic eyes on the second observation.

9.10 Summary

Backward stepwise multiple regression gave rise to new equations describing the relationship between the BSR and ametropia. One equation applies to myopes in which pupil size and the scalar vector influence BSR. The other equation applies to hyperopes in which pupil size and age influence BSR. That larger pupils brought about greater reduction of vision with increasing myopia or hyperopia is well known. That age influenced BSR in hyperopes was likely to be due to the reduction of accommodative amplitude with age. Both equations more realistically reflected the observed relationship between vision and ametropia than Raasch's equations previously used in Aston University's refraction simulators. As emmetropia was approached, both new equations predicted implausible levels of best corrected visual acuity. A remedy for this involved use of a limit for best corrected visual acuity that could be randomly varied to simulate inter-individual variations seen in real subjects. A scheme was proposed for the inclusion of both new equations in Aston University's refraction simulators for the purposes of making each virtual patient episode more realistic.

10. Summary

10.1 Introduction

This chapter begins with a summary of the previous chapters. A comparison is then made between the findings presented in this thesis and the previous work of Pincus (1946). This comparison is made because the output of algorithms arising from the present study which relate vision to ametropia were compared with the output of an algorithm generated by Raasch (1995) from the dataset of Pincus (1946). Some examples are also given which show how the algorithms arising from the present study could be used to help teach first year undergraduate optometrists in their vision and ametropia practical classes. This is followed by a critical evaluation of the limitations of the present study, recommendations for further work, and a summary of the conclusions.

10.2 Review of study findings

Chapter 1 set out the primary objective of the thesis: to develop a new algorithm for predicting unaided vision resulting from ametropia. The intention was to use this algorithm in the Aston University refraction simulators. Refraction simulators had previously used Raasch's algorithm (Raasch, 1995) which did not account for factors such as age and pupil size and was only based on data collected from myopes. In addition, Raasch's algorithm was based on unaided vision prior to the introduction of LogMAR charts. The novelty of the study presented in this thesis is therefore (a) the use of LogMAR charts; (b) the inclusion of both myopes and hyperopes and (c) inclusion of age and pupil size. A secondary objective was to examine the influence of the orientation of the correcting cylinder axis. This was of interest because Aston University runs practical training sessions aimed at exploring the relationship between vision and ametropia. In these sessions, students are taught that oblique cylinder axes may give rise to poorer unaided vision than orthogonal cylinder axes.

The logistics of data collection from the healthy right eyes of 873 white subjects recruited over an 18 month period were outlined in Chapter 2. Repeat measurements were made on 34 of these eyes in order to establish Coefficients of Repeatability (COR) for each measurement. It was apparent that the sample predominantly comprised female subjects (59%) and included many contact lens wearers (35%). Therefore, additional objectives of this thesis were to explore the influence of sex and contact lens wear on the relationship between vision and ametropia. Ages ranged from 20 to 70 years. An attempt was made to even out the distribution of age in the sample and this resulted in a non-normal distribution.

Chapter 3 presented a literature review on the measurement of unaided vision prior to describing how vision was recorded and showing the frequency distribution and repeatability of the data collected. Vision was measured using a LogMAR style test chart under monitored photopic light levels, although because vision was recorded in Snellen fractions and the furthest measurements were measured at 6.5m instead of 6m, a logarithmic progression was not followed in the recording of vision. Subjects were moved closer to the chart if vision was poor. Snellen acuity, with appended letters (effectively letter-by-letter), was initially recorded before being converted into Minimum Angle of Resolution (MAR). The MAR was recorded because it was likely to be linearly related to ametropia and was readily re-convertible to Snellen notation in feet (as used in the USA) and metres (as used in Europe). For comparison with previous studies, LogMAR values were calculated and were not found to be normally distributed. Unaided visions ranged from 6/3 to 6/146. The COR was ±0.31 LogMAR, a little higher than found in previous studies and this may have been due to differences in study populations and methods of data collection. Limitations of the measurement method were discussed, namely the effect of moving myopes with poor vision closer to the test chart and hence their far point, before explaining how these were overcome.

Chapter 4 presented a literature review on the measurement, representation and repeatability of refractive error. Spherocylindrical refractive error was measured using an autorefractor followed by subjective refinement under monitored photopic light levels. Raasch's (1995) approach to representing refractive error was adopted, using a scalar vector calculated from Fourier components. Spherical refractive error ranged from -6.75 to +10.00DS with up to 5.00DC of astigmatism. Cylinder axis was predominantly orthogonal (73.5%). The scalar vector was used to classify emmetropic (scalar vector U within ±0.5D, n = 199), myopic (U <-0.5D, n = 438) and hyperopic (scalar vector >+0.5D, n = 236) eyes. None of the parameters were normally distributed. The COR for mean spherical equivalent was ±0.34D and for both U and U_w it was ±0.33D.

Chapter 5 presented literature reviews on the measurement of pupil diameter and iris colour. The influence of iris colour on the relationship between vision and ametropia had never previously been investigated. Vertical pupil diameter was measured with a rule under monitored photopic lighting conditions and ranged from 2.5 to 7.5 mm. It was not normally distributed and had a COR of $\pm$1.2 mm. Iris colour was recorded using an established Iris Colour Classification System (Seddon et al., 1990). The majority of the sample (66%) had light blue/green irides. Identical iris colour classification arose in 91% of repeat readings.

Chapter 6 explored Rabbetts' (1996) recommendation to weight the scalar vector in order to account for the effects of oblique cylinder axes. A literature review was also carried out on the effect upon vision of oblique versus orthogonal astigmatism. Regression analyses showed that almost identical relationships arose between weighted or unweighted scalar vectors (U and U_w). Because orthogonal astigmatism predominated within the myopic group, a second set of linear regression analyses were performed using just those eyes with oblique astigmatic axes (n = 71). This showed a greater difference in levels of MAR predicted with U and U_w, but those differences still fell below the COR. The unweighted scalar vectors were therefore used in the remainder of the study.

Chapter 7 introduced the Blur Sensitivity Ratio (BSR). Initially, this ratio simplified determination of the influences of sex, contact lens wear, iris colour and cylinder axis orientation on the relationship between vision and ametropia. That is, a variable was required that simultaneously encapsulated the influence of ametropia on unaided vision. BSR does this as it expresses the drop in vision (i.e. MAR) with blur (i.e. scalar vector U). However, BSR was also found to be useful for multivariate analyses and has the potential to serve as a single figure expression of the relationship between vision and ametropia that could be used in refraction simulators and for training optometry undergraduates. A literature review confirmed that the BSR had not been described before. BSR was not normally distributed and had a COR of $\pm$1.8 minD^{-1}. Mean BSR was 2.5 minD^{-1} so that 1.00D of blur reduces MAR to 2.5 min, equating to a Snellen equivalent of 6/15, very close to the expected reduction for the +1.00D blur test, reinforcing the notion of using BSR for teaching undergraduates.

In Chapter 8, Decision Tree Analysis (DTA) was used to determine the factors influencing BSR. DTA has the advantage over multiple linear regression in that it can be applied to discrete data (i.e. sex, contact lens wear, iris colour classification, refractive group and cylinder axis orientation). The analysis showed that BSR was primarily influenced by refractive group; in particular, hyperopes showed lower BSR values than myopes. This was to be expected because hyperopic blur can be overcome with accommodation. Another important finding was that sex and contact lens wear did not affect BSR, so concerns in Chapter 2 about a bias towards females and contact lens wearers in the study population were unfounded. The finding that iris colour exerted no influence on BSR also removed any concerns about the bias towards light blue/green irides in the study population. Cylinder axis orientation had no statistically significant effect on BSR, reinforcing the findings of Chapter 6.

In Chapter 9, multiple linear regression was used to show that the BSR in hyperopes was influenced by pupil diameter and age while BSR in myopes was influenced by pupil diameter and scalar vector U (i.e. the degree of myopia). The regression equations formed the basis of a new algorithm to be incorporated in refraction simulators used at Aston University. Discrete variables (sex, CL wear, iris colour classification, refractive group and cylinder axis orientation) could not be included in multiple linear regression analysis but DTA had already shown that of these factors, only refractive group influenced BSR. That none of the continuous variables (BSR, age, pupil diameter and scalar vector) were normally distributed and many of them were interrelated raised issues about the validity of using multiple linear regression. Nevertheless, the new algorithm accounted for more (84%) of the observed variation in unaided vision than Raasch's (1995) algorithm (72%).

10.3 Comparison to Pincus's conclusions

The present study was based upon work by Raasch (1995) who used data collected by Pincus (1946). Pincus did not perform any statistical analyses upon his data set, but did make the following observations:

- The majority of refractive errors lay between 0 and 4DS and 0 and 3DC. In the present study, 90% (n = 789) of sphere values fell between ±4.00DS and 99% (n = 861) of cylinder values were less than or equal to 3.00DC.
- Myopic corrections predominated. In the present study, 50% (n = 438) were classified as being myopic.

- Oblique cylinders gave worse unaided vision. As seen in Chapter 8, this was not shown in the present study.
- Vision decreased in hyperopes as age increased. This was shown to be the case as in Equation 9.2, BSR increased with subject age in hyperopes.
- Age did not influence vision in myopes. Equation 9.1 showed that age did not influence BSR in myopes in the present study.
- As refractive error increased, vision decreased. This appears to be logical but Equation 9.2 showed that refractive error did not significantly affect vision in hyperopes in the present study although it was true for myopes. It should be remembered that Pincus used cycloplegia in all subjects under the age of 40, meaning that accommodation could not be used in the younger subjects unlike in the present study. The present study included subjects between the ages of 20 and 70 years and it is logical to assume that there would be a difference in unaided vision between a sixty year old with a high degree of hyperopia compared to one with a low degree of hyperopia. Multiple linear regression however found that over the entire group of hyperopes, age was a more important predictor of BSR than refractive error.

The present study agreed in most aspects to the conclusions reached by Pincus. This shows that the data sets, despite being from different populations and measured under different conditions, demonstrated similar characteristics.

10.4 Application of algorithms in 'Vision and Ametropia' classes

Aston University optometry undergraduates participate in 'Vision in Ametropia' practical classes. During these classes they have a number of assignments to improve their understanding of the relationship between ametropia and its effect on vision. One of the assignments requires the student to add negative spherical lenses in front of their subject's eye, simulating hyperopia and another requires them to add positive lenses, simulating myopia. Students record the resulting visual acuity for each lens addition and plot their results on a graph. Pupil size is measured with both the most positive / least negative and the least positive / most negative lenses which give best visual acuity.

Equations 9.1 and 9.2 can be used by undergraduates to compare their findings to data collected, in the present study, on a large population sample. For example, in a 20-year old emmetropic student with a pupil size of 5mm, the expected reduction in vision for varying degrees of simulated myopia and hyperopia is shown in Figure 10.1.

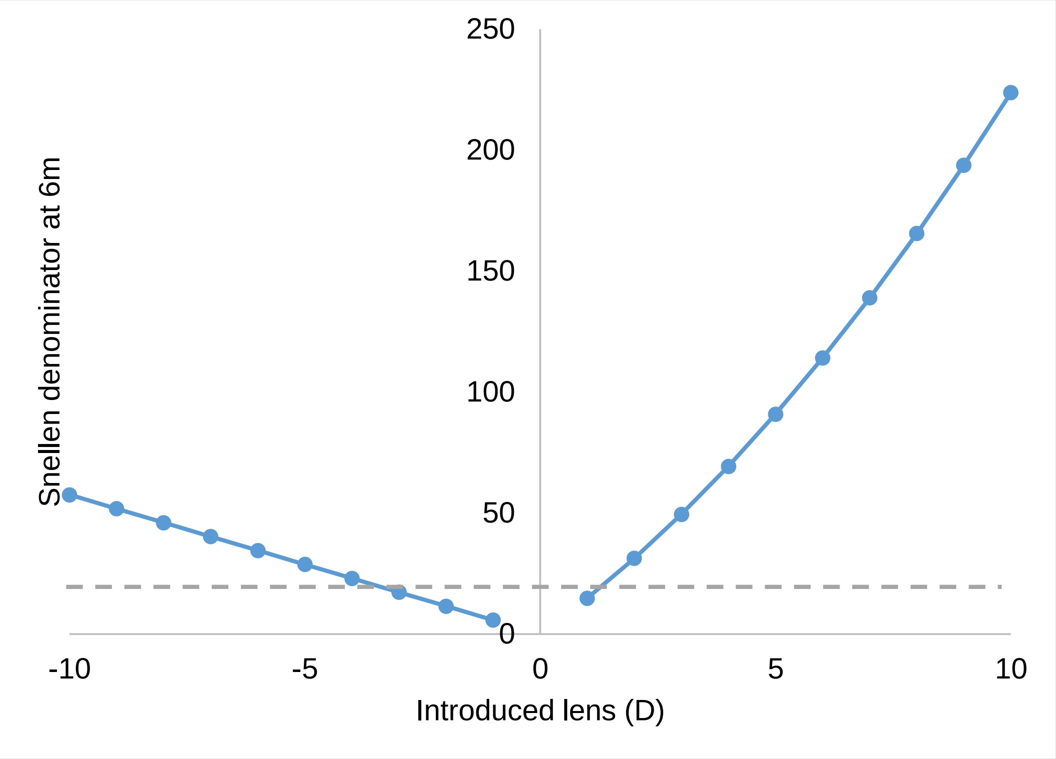

Figure 10.1: Expected vision for a 20 year old emmetropic subject with 5 mm pupils when positive and negative lenses are used to simulate myopia and hyperopia. The dashed line shows 6/18.

Students' recordings could vary slightly from this graph as the pupil size in Figure 10.1 was set at 5 mm for all calculations. However, pupil size would, in reality, be expected to reduce as more negative lenses were introduced in front of a naturally emmetropic eye, bringing about accommodation and pupil miosis. This would mean that the left side of the graph would be flatter as progressively smaller pupils would give better vision. The same information can be plotted using LogMAR scoring. The logarithmic scale gives a different appearance, as seen in figure 10.2.

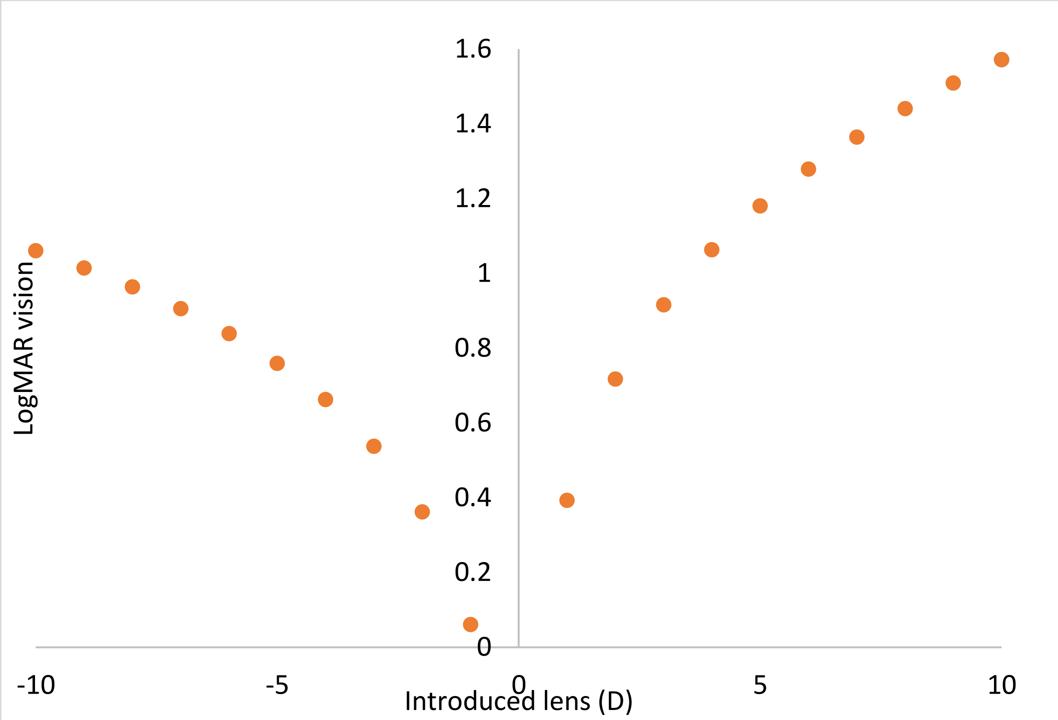

Figure 10.2: Expected vision for a 20 year old emmetropic subject with 5 mm pupils when positive and negative lenses are used to simulate myopia and hyperopia, plotted according to LogMAR vision.

In another practical experiment, students are asked to place in front of their subject's eye both the most positive and most negative lens that gave visual acuity of around 6/18 according to the experiment detailed above. For this 20 year old emmetropic student this would be lenses of approximately +1.25D and -3.75D according to Figure 10.1. With these lenses in position, a series of artificial pupils are introduced. With pupils of 2, 3, 4 and 5 mm the graph in Figure 10.3. would be produced.

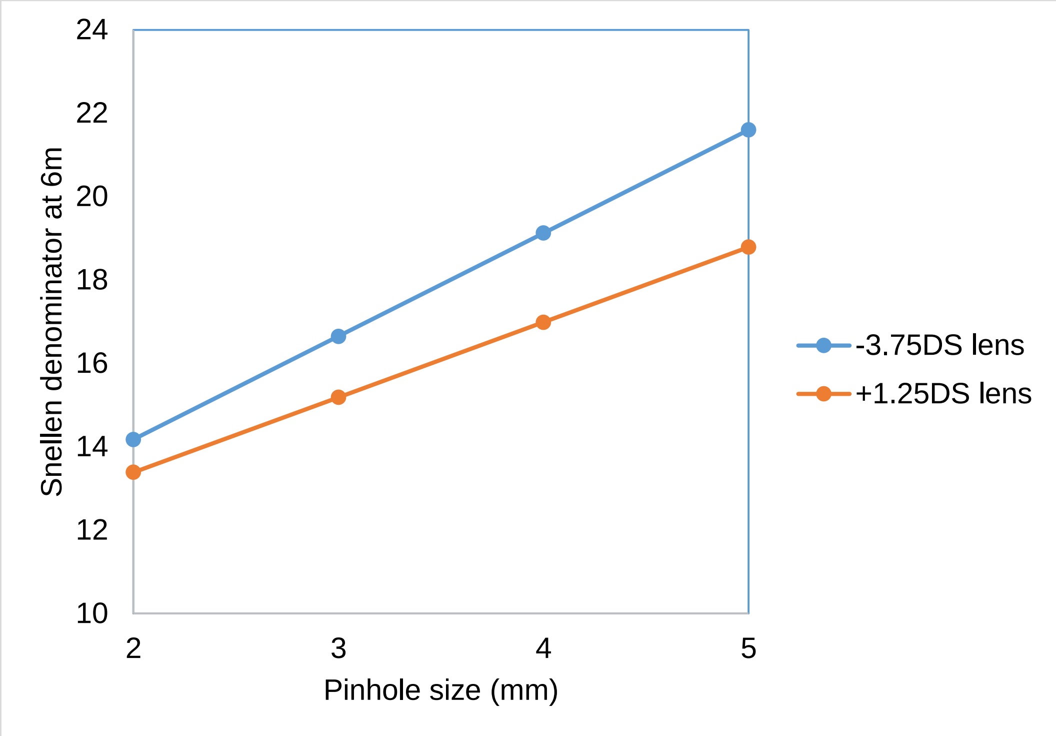

Figure 10.3: Expected vision in a 20 year old emmetropic subject with a +1.25DS lens and a -3.75DS lens in front of the eye and with artificial pupils from 2 to 5 mm.

10.5 Critical evaluation of the limitations of the present study

Although more sophisticated techniques were available for some measurements (e.g. infrared pupillometers for measuring pupil size or photographic equipment for measuring iris colour), these techniques were not adopted in the present study due to their inaccessibility to the high street optometrist. These limitations were discussed in Chapter 5. Nevertheless, the techniques used in the present study showed good repeatability. Figure 5.7 showed that measurement of pupil size with the semi-circular gauge was precise enough to clearly show a decrease in pupil size with age which matched with previous studies using more precise techniques.

The Test Chart 2000 is an ETDRS chart with a logarithmic progression of letter sizes but unfortunately the letter sizes are assigned Snellen fraction values rather than LogMAR values. This necessitated the conversion of vision measured from Snellen to LogMAR values which may not have been accurate. Ideally the use of a chart calibrated in LogMAR would have been used. A greater number of larger lines on the chart, for example lines going to 6/60 would have reduced the need to move subjects closer to the chart and reduced the impact of the myopic far point problem detailed in section 3.5.

The actual viewing distance of the chart by the subject was 6.5 metres which could have impacted the accuracy of calculations. Those six subjects who read 3/10 were excluded as they should have been able to read 6/20, but in reality they may not have been able to read 6.5/20 and should have been included in analyses (see Appendix 5), although this is likely to have had a negligible impact on a large data set. Because the testing distance in reality was greater than that assumed by the calculations made, vision would have been apparently worse than it should have been, meaning more blur per dioptre and an artificially high BSR. Mean BSR was recalculated after taking into account the increased testing distance of 6.5m and was shown to be 2.4minD^{-1}. This is considerably less than the coefficient of repeatability of 1.8minD^{-1} so would probably have had only a small impact on further analyses. Measurements taken at 1, 2 and 3m were accurate so DTA and multiple linear regression analysis were performed on a mixture of BSR values that were correct (1, 2 and 3m readings) and incorrect (6.5m readings that were assumed to be at 6m).

An alternative termination rule when measuring vision may have given different results, especially regarding repeatability. Rosser et al (2004) suggested that variability was reduced if testing stopped once a full line of errors was made, whereas Carkeet (2001) recommended stopping once four errors had been made on a line when using a LogMAR style chart.

The poor coefficient of repeatability of unaided vision compared to previous studies could be due in part to inaccuracies in the conversion between Snellen and LogMAR in this study which would be helped by using a chart with LogMAR scores. It may have also been influenced by the large range of refractive errors and the large number of naïve subjects included in the study. Most other studies have used a much smaller sample size, often with trained subjects and limited refractive errors.

Potential sources of bias in the data collection included:

- Subjects were attending for a routine eye examination. They were not randomly recruited from the general public
- Subjects had chosen to visit Specsavers opticians. This meant that the research could represent subjects with a particular set of personality types or socioeconomic backgrounds which could skew distributions of vision and refractive error (Goverdhan et al., 2011)

- The optometrist conducting the eye examinations was female. As detailed in Section 2.6, this may have been one of the reasons for the high proportion of females although this has been shown to have no effect on BSR. It is also possible that some subjects chose to have (or not to have) their eye examination with this optometrist due to personality or other factors
- The optometrist ran a contact lens clinic 3 days per week so as explained in Section 2.6 a lot of subjects were current, past or potential contact lens wearers. Many of these subjects were young and myopic and once again, could have been of certain personality types
- The examination room was upstairs so some subjects who would otherwise have been included in the research may not have been able to be examined in an upstairs room due to, for example, reduced mobility or having pushchairs with them, although as there was a good representation across all of the age groups this is likely to have had only a minimal effect.

One factor which could not reasonably be controlled was whether subjects habitually wore a visual correction. Several authors (Mankowska et al., 2012; Wang et al., 2006; George & Rosenfield, 2004; Radhakrishnan et al., 2004; Rosenfield & Abraham-Cohen, 1999) have written about 'blur adaptation', which is the phenomenon whereby a person adapts to the blur in their vision. This could potentially affect their unaided vision or their subjective refraction.

Only 34 subjects re-attended to enable measurements of repeatability to be made. This could have affected the repeatability, especially as these subjects were not evenly spread across age groups.

Figure 7.2 showed that MAR and U demonstrated a linear relationship. This was necessary in order to perform multiple linear regression, however, would an alternative line fit the data more accurately and help to solve the difficulties of calculating vision in those with near-emmetropia? A second order polynomial, such as that used by Raasch (1995) was found to give the same r^2 value as the linear equation, offering no benefit and making further analysis more complex. Another alternative would be to try to fit two lines, one for higher levels of ametropia and one for lower levels, similar to that suggested by Smith (1991). This could produce a better fit for lower levels of ametropia and could be investigated in future analyses.

There were limitations in the methods used to create the formulae. The most important of these was perhaps that the data were not normally distributed as multiple linear regression assumes. Section 9.3 detailed the steps taken to ensure that these incorrect assumptions would have minimal impact upon the final formulae.

Overall the methods used in the present study demonstrated good repeatability in line with previous studies. The collection of a large quantity of data with natural pupils and manifest refractive error (without cycloplegia) has resulted in the creation of an algorithm which is more representative of what a practicing optometrist is likely to find in general high street practice. The new formula and algorithm improve upon that which was used previously and take into account more individual factors (i.e. age and pupil size).

10.6 Suggested Further Work

As this study only included white subjects, ideally a similar study including individuals from different racial groups would be carried out to confirm whether race had a significant influence on unaided vision and whether the algorithms created in this study were applicable to different populations. By including darker-skinned individuals, grade 5 irides (very dark brown) could be included to increase any minute differences which may exist between light and dark irides.

10.7 Conclusions

A large quantity of data was collected from a white population in Salisbury, Wiltshire. This included refractive error, pupil size, age, iris colour and contact lens wear. Data were collected under photopic conditions with natural pupils, without cycloplegia and with natural unaided refractive error. Weighting the scalar vector used to represent refractive error towards oblique cylinder axes was not found to be beneficial. The novel concept of Blur Sensitivity Ratio (BSR) was introduced to encapsulate both blur and refractive error in one entity. The data were used to form two multiple linear regression equations which were used to create a new algorithm for refraction simulators with a view to improving the experience of undergraduate optometry students.

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Appendices

Appendix 1: Research protocol

RESEARCH PROTOCOL (Project 305)

Multiple regression analysis of the factors affecting unaided vision in healthy adult eyes

SUMMARY

Purpose
The purpose of this cross-sectional study is to use multiple regression analysis to model the influence upon unaided human vision (i.e. vision experienced without the use of spectacles or contact lenses) of (i) spherocylindrical refractive error (i.e. long-sightedness, short-sightedness and astigmatism), (ii) pupil diameter and (iii) age. It is intended that the modelled data will be incorporated into refraction simulators to improve the training of optometry undergraduates.

Research participants
All visitors to Specsavers Opticians in Salisbury between the ages of 20 and 70 will be invited to participate in the study. The invitation to participate will not be made on the basis of any private or NHS treatment that they have received or are receiving from Specsavers Opticians. Participants will simply represent a cross-section of healthy eyes.

Duration
It is anticipated that the research will take place over an 18 month period from June 2009 and until December 2010.

Methods, procedures and follow-up
Once informed consent has been obtained, a standard eye examination (lasting approximately half an hour) will be conducted to ensure that each participant meets the inclusion criteria (that they do not wear contact lenses, have not received any eye surgery in the past and have no eye abnormality or pathology). The standard eye examination includes the measurement of unaided vision (using LogMAR charts), sphero-cylindrical refractive error (using retinoscopy followed by cross-cylinder subjective refraction) and pupil diameter (using a frame ruler). It also includes screening for external and internal eye abnormalities and pathology (using slit lamp biomicroscopy and ophthalmoscopy). No new experimental procedures will be carried out on any participant. Participants that agree to a second visit will sit a second standard eye examination so that the test-retest reproducibility of each measurement can be assessed.

INTRODUCTION

Purpose and justification
The purpose of this cross-sectional study is to use multiple regression analysis to model the influence upon unaided human vision (i.e. vision experienced without the use of spectacles or contact lenses) of (i) spherocylindrical refractive error (i.e. long-sightedness, short-sightedness and astigmatism), (ii) pupil diameter and (iii) age. It is intended that the modelled data will be incorporated into refraction simulators that are currently used by our optometry undergraduates. It is well

known that unaided vision is influenced by the factors mentioned above. Yet, there are no formulae for calculating the dependence of vision on all of these factors. One particularly neglected area in this field relates to how astigmatism that is orthogonal or oblique in nature influences unaided vision. Orthogonal astigmatism leads to unequal clarity of horizontal and vertical lines. This influence of this type of astigmatism on our ability to see letters and objects is less than that of oblique astigmatism. This is because oblique astigmatism also causes horizontal and vertical structures to appear tilted. Again, there are no formulae that relate this aspect of astigmatism to unaided vision. This project is justified because it represents translational research in which data collected in practice will be used to improve undergraduate training. This, in turn, will improve refractive procedures carried out in practice.

How the study meets clinical needs
The optometric profession constantly strives to improve its services to the community. This study will contribute to these efforts by using data collected in practice to improve refraction simulators used for undergraduate training. Better trained graduates will inevitably offer better service to the community.

Scientific debate
All optometry undergraduates are taught to use unaided vision to make initial estimates of refractive error. Aston University has recently pioneered the evaluation of simulators designed to allow students unlimited experience of performing refraction on virtual patients. These simulators use a regression formula that describes the dependence of unaided vision on refractive error. Unfortunately, this regression formula does not account for the effects of age, pupil size or even the type of astigmatism (i.e. orthogonal or oblique). Our students, therefore, find that the refraction simulator does not always replicate the variations of unaided vision recorded in patients that they encounter in training clinics. Aberrations that normally occur in the human eye reduce vision at larger pupil diameters so it follows that the relationship between unaided vision and refractive error is dependent on pupil diameter. Pupil diameter also increases with age and varies widely between individuals. That unaided vision is dependent on the type of astigmatism is well known. Yet, a formula to express this dependency remains elusive. The regression formula currently used in our simulators makes use of Fourier decomposition that expresses astigmatism as orthogonal and oblique power vectors which are then combined into a scalar quantity. Yet, the scalar quantity does not differentiate orthogonal from oblique astigmatism. It has been suggested that weighting the oblique power vector by a factor of two could improve estimates of unaided vision that use the scalar quantity but this suggestion has not yet been tested. The use of matrices for describing astigmatism may also prove to be more valuable for our purposes.

How the study is appropriate
This research proposal has been written with a view to generating a regression formula that can predict the variation of unaided vision that occurs with varying degrees of oblique astigmatism and individual variations in pupil diameter that occur with advancing age. We believe that the incorporation of such a formula into our refraction simulators will generate more realistic variations in unaided vision in virtual patients.

What will be done and which research participants will be involved
All visitors to Specsavers Opticians in Salisbury between the ages of 20 and 70 will be invited to participate in the study. The invitation to participate will not be made on the basis of any private or NHS treatment that they have received or are

receiving from Specsavers Opticians. Participants will simply represent a cross-section of healthy eyes.
Once informed consent has been obtained, a standard eye examination (lasting approximately half an hour) will be conducted to ensure that each participant meets the inclusion criteria (that they do not wear contact lenses, have not received any eye surgery in the past and have no eye abnormality or pathology). The standard eye examination includes the measurement of unaided vision (using LogMAR charts), sphero-cylindrical refractive error (using retinoscopy followed by cross-cylinder subjective refraction) and pupil diameter (using a lens ruler). It also includes screening for external and internal eye abnormalities and pathology (using slit lamp biomicroscopy and ophthalmoscopy). No new experimental procedures will be carried out on any participant. Participants that agree to a second visit will sit a second standard eye examination so that the test-retest reproducibility of each measurement can be assessed. Anonymised data will be entered in an electronic database. A statistical package (SPSS) will be used to generate a regression formula that describes the dependence of unaided vision upon spherocylindrical refractive error, pupil diameter and age. The test-retest reproducibility of each measurement will be assessed by calculating the interval over which 95% of the numeric differences between repeated measurements fall.

LITERATURE REVIEW

All optometry undergraduates are taught to use unaided vision to make initial estimates of the spherical (i.e. the degree of long-sightedness or short sightedness) and cylindrical (i.e. the degree of astigmatism) components of refractive error. Aston University has recently pioneered the evaluation of simulators designed to allow students unlimited experience of performing refraction on virtual patients (Prajapati and Dunne, 2009). These simulators use a regression formula that describes the dependence of unaided vision on the spherical and cylindrical components of any given refractive error (Raasch, 1995). Unfortunately, this regression formula does not account for the effects of age, pupil size or even the type of astigmatism (i.e. orthogonal or oblique). Our students, therefore, find that the refraction simulator does not always replicate the variations of unaided vision recorded in patients that they encounter in training clinics.
Aberrations that are present in all human eyes reduce vision when pupil diameters are larger than about 1.5 mm (Rabbetts, 2007 pp 25). Note here that the pupil may vary from 1 to 8 mm in diameter (Forrester et al., 1996). It, therefore, follows that the relationship between unaided vision and refractive error is dependent on pupil diameter. Pupil diameter also increases with age, though there is a large variation between people in any age group (Winn et al., 1994; Rabbetts, 2007 pp 27).
That unaided vision is dependent on the type of astigmatism (i.e. orthogonal or oblique) is well known (Rabbetts, 2007, pp 92). Yet, how do we generate a formula to express this dependency? The mathematic analysis of astigmatism is complicated. Astigmatism is recorded by optometrists in terms of a cylindrical power along a specified cylinder axis. The cylinder axis may be oriented anywhere within a 180 degree scale. Orientations of 90 and 180 degrees represent orthogonal astigmatism. Orientations of 45 and 135 degrees represent oblique astigmatism. All other orientations have varying degrees of obliquity. Approximately 30% of people exhibit varying degrees of oblique astigmatism according to a study carried out in the mid 1960s (Bennett, 1965; Rabbetts, 2007 pp 424). Two people with identical cylindrical powers but at different cylinder axes will have unequal unaided visions. Calculating just how unequal the unaided vision of these two people would be still remains elusive. We do know that mathematical problems associated with astigmatic powers expressed along different axes are solved by the use of Fourier decomposition that expresses astigmatism as

orthogonal and oblique power vectors (Thibos et al., 1997). These power vectors can be combined into a scalar quantity (Rabbetts, 2007 pp 97) that currently gives us the best means of modelling the dependence of unaided vision in spherical and astigmatic refractive errors (Raasch, 1995). However, the scalar quantity still does not differentiate between oblique and orthogonal astigmatism. It has been suggested that weighting the oblique power vector by a factor of two could improve estimates of unaided vision that use the scalar quantity (Rabbetts, 1996, 2007) but this has not yet been put to the test. In addition, an alternative method of using matrices for describing astigmatism might prove to be more useful for our purposes (Long, 1976; Keating ,1981a,b; Harris, 1988, 1994; Harris and Malan, 1992).

OBJECTIVES

This research proposal has been written with the aim of generating a regression formula that can predict the variation of unaided vision that occurs with varying degrees of oblique astigmatism and individual variations in pupil diameter that occur with advancing age. This aim is to be achieved via the following objectives:

1. To carry out the necessary measurements in a large sample of healthy male and female participants aged between 20 and 70 years;
2. To measure unaided vision using a standard LogMAR chart;
3. To measure the spherocylindrical refractive error using retinoscopy and cross-cylinder subjective refraction methods;
4. To measure pupil diameter using a frame ruler;
5. To determine the test-retest reproducibility of all measurements by repeating tests on a proportion of the participants, evenly distributed across gender and age.
6. To determine the dependence of unaided vision on spherocylindrical refractive error, pupil diameter and age using multiple regression analysis.

RESEARCH PARTICIPANTS

It is anticipated that at least 60 participants (with equal numbers of males and females) will be recruited in each of 10 five-year age cohorts (20 to 24, 25 to 29, 30 to 34, 35 to 39, 40 to 44, 45 to 49, 50 to 54, 55 to 59, 60 to 64 and 65 to 70). This adds up to a minimum total sample size of 600.

This is well within what is achievable in a typical optometry practice over the 18 month research period.

At least 50 of the participants (5 from each age cohort) will be invited to attend a second visit so that the reproducibility of each measurement can be assessed.

Inclusion criteria: People between the ages of 20 and 70 years who are able to give informed consent.

Exclusion criteria: No contact lens wear, no previous eye surgery, no eye abnormalities or pathology. These exclusion criteria exist on the grounds that these factors are likely to confound the causes of reduced unaided vision being studied.

RISKS AND BENEFITS

Risks involve (1) the inconvenience of sitting for up to two 20 minute eye examinations and (2) compromising confidential information relating to unaided vision, refractive error, pupil diameter and age due to its storage in an electronic database. All measurements are those routinely carried out during a standard eye examination and both the collection of data and its storage in anonymised form will be carried out by a registered optometrist. So this project carries minimal risk to the wellbeing of the research participants.

Benefits to research participants are only likely to be indirect as this research will contribute to enhanced training of undergraduate optometrists that may improve optometric services to the community in the future.

RECRUITMENT

All visitors to Specsavers Opticians in Salisbury between the ages of 20 and 70 will be invited to participate in the study. There will be no use of external recruiters or recruitment advertisements. Vulnerable participants, deemed unable to give informed consent, will not be included in this study. Data collected from any participant will be stored electronically in anonymised form until the research has been completed and written up; it is anticipated that this will be no later than June 2010. At that point, the electronic database will be destroyed.

INFORMED CONSENT

Initial informed consent will be gained at the time of recruitment. Each potential participant will be given the opportunity to read the consent form and ask any questions before giving consent to participate. The consent form will make it clear that participation is voluntary and that no sanctions will be taken against any person who refuses to participate or withdraws from this project one recruited. As vulnerable participants will not be included in this study, there will be no need for surrogate permission. There is also no need for family consent as this study does not involve the collection of sensitive data relating to family history.

PRIVACY AND CONFIDENTIALITY

Only anonymised data will be recorded on an electronic database. These data will be analysed at either Specsavers Opticians in Salisbury and/or Aston University by Mark Dunne (supervisor), Richard Armstrong (co-supervisor) and Rebecca Rushton (postgraduate research student on the Ophthalmic Doctorate programme). Only these individuals will have access to the data. The results of this study are to be written up in the form of a postgraduate thesis and will be published in appropriate academic and professional journals. The identity of participants will not be revealed in the thesis or any publication.

ETHICS SECTION

The primary ethical issues raised by the scientific design of this protocol are (1) the inconvenience of sitting for up to two 20 minute eye examinations and (2) compromising confidential information relating to unaided vision, refractive error, pupil diameter and age due to its storage in an electronic data base. Although these aspects of the study mean that this protocol has some ethical issues, the scientific information to be gained is important because this research will contribute to enhanced training of undergraduate optometrists that may improve optometric services to the community in the future. The risks to research participants, apart from the inconvenience of participation, are that confidential data could be revealed to parties other than members of the research team. It would be impractical, however, to obtain this information without the use of an electronic database. Therefore, we believe that to manage appropriately the ethical complexities inherent in this study, it is necessary to put the following additional protections of the research participants in place. They are that (1) informed consent is required before any participant's data can be recorded or analysed and (2) only anonymised data will be recorded. By instituting these additional protections, the risks have been appropriately minimized, and a reasonable and ethically acceptable balance between risks and benefits has been established.

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Appendix 2: Ethics approval

Aston University

MEMORANDUM

REGISTRY & PLANNING SERVICES

DATE: 5 June 2009

TO: Dr Mark Dunne,
Life & Health Sciences

FROM: John Walter,
Academic Registrar

SUBJECT: **Project 305: Multiple regression analysis of the factors affecting unaided vision in healthy adult eyes**

I am writing to inform you that a Sub-Group of the University's Ethics Committee has, on behalf of the Ethics Committee, approved the above-mentioned project.

The details of the investigation will be placed on file. You should notify me of any difficulties experienced by the volunteer subjects, and any significant changes which may be planned for this project in the future.

Best wishes,

Secretary to the Ethics Committee

Appendix 3: Consent form

CONSENT FORM (Project 305)

RESEARCH WORKERS

Rebecca Rushton, Specsavers Opticians, Salisbury
Mark Dunne, Life & Health Sciences, Ophthalmic Research Group, Aston University
Richard Armstrong, Life & Health Sciences, Ophthalmic Research Group, Aston University

PROJECT TITLE

Multiple regression analysis of the factors affecting unaided vision in healthy adult eyes

INVITATION

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

WHAT IS THE PURPOSE OF THE STUDY?

The results of this research will aid training of student optometrists and enable qualified optometrists to make swifter and more accurate decisions in the way they prescribe spectacles and contact lenses. In order to do this, we want to see how your vision without spectacles or contact lenses is influenced by (1) how long or short sighted you are, (2) how much and what type of astigmatism you have, (3) the size of your pupil and (4) your age. This information will be used to develop a formula that will be used in computer simulators for training student optometrists how to prescribe. Personal benefits arising from your participation in this research are only likely to be indirect as this research is ultimately aimed at improving optometric services to the community in the future.

WHY HAVE I BEEN CHOSEN?

All visitors to Specsavers Opticians in Salisbury, between the ages of 20 and 70, will be invited to participate in this study. It is important for you to understand that your invitation to participate has not be made on the basis of any private or NHS treatment that you have received or are receiving from Specsavers Opticians.

WHAT WILL HAPPEN TO ME IF I TAKE PART?

The study will take place in this practice over the next 18 months. The information we need can be collected during your routine eye examination. This includes: (1) using a letter chart to measure your vision without glasses; (2) using standard techniques to measure the amount of long-sightedness, short-sightedness or astigmatism that you have; (3) using a standard pupil ruler to measure pupil size; (4) grading the colour of eyes; and (5) using standard techniques to check that your eyes are healthy. No new experimental procedures will be carried out and no eye drops will be used. One additional visit, lasting about half an hour, may be required to re-record this information but this will not be a full eye examination. Your measurements will be analyzed after being entered in an electronic database. As for any standard eye examination, your optometrist is qualified to treat, or refer for further treatment, any eye problems identified during the examination.

ARE THERE ANY POTENTIAL RISKS IN TAKING PART IN THE STUDY?

There is very little risk involved in this study. Sitting for up to two half-hour eye examinations will cause you some inconvenience. The eye examination itself uses standard techniques performed by a qualified optometrist trained to minimise any risks to your eyes.

DO I HAVE TO TAKE PART?

You do not have to take part in this study if you do not wish to. No sanctions will be taken against any person who does not wish to take part or who withdraws from the study at any time.

EXPENSES AND PAYMENTS

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

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

Your privacy and confidentiality will be vigorously protected to the maximum extent permissible by law. Your results will not be stored with any personal details, such as your name and address. This step has been taken to protect your anonymity in the unlikely event that your eye measurements, stored on a computer, are unintentionally revealed.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

Your results will be analyzed in this practice and at Aston University by Mark Dunne, Richard Armstrong and Rebecca Rushton. Only these individuals will have access to the data. The results of this study are to be written up in the form of a thesis and will be published in appropriate academic and professional journals. Your identity will not be revealed in the thesis or any publication. The database containing your results will be erased on completion of this research project. This is likely to be no later than 30 December 2010. Please contact Rebecca Rushton in this practice if you want a copy of the published research.

WHO IS ORGANIZING AND FUNDING THE RESEARCH?

Rebecca Rushton is carrying out this research project as part of her postgraduate research with the School of Life and Health Sciences at Aston University. There is no funding for this study.

WHO HAS REVIEWED THE STUDY?

The study has been submitted for review and approval by Aston University's Research Ethics Committee.

WHO DO I CONTACT IF SOMETHING GOES WRONG OR I NEED FURTHER INFORMATION?

Please feel free to contact Dr Mark Dunne (m.c.m.dunne@aston.ac.uk

WHO DO I CONTACT IF I WISH TO MAKE A COMPLAINT ABOUT THE WAY IN WHICH THE RESEARCH IS CONDUCTED?

If you have any concerns about the way in which this study has been conducted, then you should contact Secretary of Aston University's Research Ethics Committee (j.g.walter@aston.ac.uk, 0121 204 4869).

VOLUNTEER CONSENT FORM

PROJECT TITLE

Multiple regression analysis of the factors affecting unaided vision in healthy adult eyes

RESEARCH WORKERS

Rebecca Rushton, Specsavers Opticians, Salisbury
Mark Dunne, Life & Health Sciences, Ophthalmic Research Group, Aston University
Richard Armstrong, Life & Health Sciences, Ophthalmic Research Group, Aston University

1. I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I agree to take part in the above study.

____________________ ____________________ ____________________
Name of volunteer Date Signature

VOLUNTEER CONSENT FORM

PROJECT TITLE

Multiple regression analysis of the factors affecting unaided vision in healthy adult eyes

RESEARCH WORKERS

Rebecca Rushton, Specsavers Opticians, Salisbury
Mark Dunne, Life & Health Sciences, Ophthalmic Research Group, Aston University
Richard Armstrong, Life & Health Sciences, Ophthalmic Research Group, Aston University

1. I confirm that I have read and understood the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

3. I agree to take part in the above study.

____________________	____________________	____________________
Name of volunteer	Date	Signature

Appendix 4: Vision chart line and letter values

Testing distance (m)	Snellen denominator at 6m	LogMAR (line)	LogMAR (line interval)	LogMAR (letter interval)
1	20	1.301	0.103	0.021
1	15	1.176	0.125	0.025
1	12	1.079	0.097	0.019
1	10	1.000	0.079	0.016
1	7.5	0.875	0.125	0.025
1	6	0.778	0.097	0.019
1	5	0.699	0.079	0.016
1	4	0.602	0.097	0.019
1	3	0.477	0.125	0.025
2	20	1.000	0.103	0.021
2	15	0.875	0.125	0.025
2	12	0.778	0.097	0.019
2	10	0.699	0.079	0.016
2	7.5	0.574	0.125	0.025
2	6	0.477	0.097	0.019
2	5	0.398	0.079	0.016
2	4	0.301	0.097	0.019
2	3	0.176	0.125	0.025
3	20	0.824	0.103	0.021
3	15	0.699	0.125	0.025
3	12	0.602	0.097	0.019
3	10	0.523	0.079	0.016
3	7.5	0.398	0.125	0.025
3	6	0.301	0.097	0.019
3	5	0.222	0.079	0.016
3	4	0.125	0.097	0.019
3	3	0.000	0.125	0.025
6	20	0.523	0.103	0.021
6	15	0.398	0.125	0.025
6	12	0.301	0.097	0.019
6	10	0.222	0.079	0.016
6	7.5	0.097	0.125	0.025
6	6	0.000	0.097	0.019
6	5	-0.079	0.079	0.016
6	4	-0.176	0.097	0.019
6	3	-0.301	0.125	0.025
		Mean	***0.103***	***0.021***
		Max	***0.12***	***0.02***
		Min	***0.079***	***0.016***

Appendix 5: Expected vision at various testing distances

Testing distance	Snellen denominator	Adjusted Snellen denominator at 6m
1	20	120
1	15	90
1	12	72
1	10	60
1	7.5	45
1	6	36
1	5	30
1	4	24
1	3	18
2	20	60
2	15	45
2	12	36
2	10	30
2	7.5	23
2	6	18
2	5	15
2	4	12
2	3	9
3	20	40
3	15	30
3	12	24
3	10	20
3	7.5	15
3	6	12
3	5	10
3	4	8
3	3	6
6	20	20
6	15	15
6	12	12
6	10	10
6	7.5	8
6	6	6
6	5	5
6	4	4
6	3	3
6.5	20	18
6.5	15	14
6.5	12	11
6.5	10	9
6.5	7.5	7
6.5	6	6

6.5	5	5
6.5	4	4
6.5	3	3

This table shows the equivalent Snellen denominator if vision were tested at 6m. That is to say, were a subject was walked nearer to the chart, their minimum angle of resolution should be expected to remain constant. As detailed in Section 3.5, this was not always the case, as in myopes the chart was moved closer to their far point. The greyed-out text shows levels of vision which should theoretically have been recorded at a greater distance. As an example, if a subject could not read anything at 6m, they were moved to 3m from the chart. If at this point they read 3/6, they should have been able to read 6/12. Because of this apparent anomaly in their minimum angle of resolution, they were excluded from the data set.

As the chart was actually viewed at 6.5m, the bottom section of the table shows Snellen equivalents at 6m for this testing distance. This extended testing distance means that those subjects who read 3/10 would probably not have been able to read 6.5/20 and should have been included in the analysis.

Appendix 6: BSR literature search

The following online databases were searched with reference to Blur Sensitivity Ratio:

The Cochrane Library (www.thecochranelibrary.com)
Directory of Open Access Journals (www.doaj.org)
Google Scholar (scholar.google.co.uk)
HighWire (www.jstor.org/)
Ingentaconnect (www.ingentaconnect.com/)
JSTOR (www.jstor.org/)
Mendeley (www.mendeley.com/)
Microsoft Academic Search (academic.research.microsoft.com/)
Pubmed (www.ncbi.nlm.nih.gov/pubmed)
Scielo (www.scielo.org)
Science.gov (www.science.gov/)
Scirus (info.scirus.com/)
ScienceDirect (www.sciencedirect.com/)
Scopus (www.scopus.com)
Science Accelerator (www.scienceaccelerator.gov/)
Web of Knowledge (apps.webofknowledge.com)
Worldcat.org (www.worldcat.org/)
Worldwidescience.org (worldwidescience.org/)

All of these databases were searched with the following terms:

Vision AND ratio AND “dioptric blur”
Vision AND quotient AND “dioptric blur”
Vision divided by diopt*
Acuity divided by diopt*
LogMAR divided by diopt*
“angle of resolution” divided by diopt*
“angle of resolution” divided by refracti*
LogMAR divided by refracti*
Acuity divided by refracti*
Vision divided by refracti*
Blur tolerance
Blur sensitivity
“blur sensitivity ratio”
“angle of resolution” AND scalar vector
Snellen AND scalar vector
LogMAR AND scalar vector
Blur per diopt*

Appendix 7: Multiple linear regression literature search

The following databases were searched with reference to multiple linear regression:

The Cochrane Library (www.thecochranelibrary.com)
Directory of Open Access Journals (www.doaj.org)
Google Scholar (scholar.google.co.uk)
HighWire (www.jstor.org/)
Ingentaconnect (www.ingentaconnect.com/)
JSTOR (www.jstor.org/)
Mendeley (www.mendeley.com/)
Microsoft Academic Search (academic.research.microsoft.com/)
Pubmed (www.ncbi.nlm.nih.gov/pubmed)
Scielo (www.scielo.org)
Science.gov (www.science.gov/)
ScienceDirect (www.sciencedirect.com/)
Scopus (www.scopus.com)
Science Accelerator (www.scienceaccelerator.gov/)
Worldcat.org (www.worldcat.org/)
Worldwidescience.org (worldwidescience.org/)

All of these databases were searched with the following terms:

'multiple linear regression' AND refraction simulator vision
'multiple linear regression' AND human vision model
computer algorithm vision refractive error
computer model of factors influencing human vision