THE PREVALENCE AND PROGRESSION OF ASTIGMATISM AND MYOPIA IN CHILDREN

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Thesis summary

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Optometrists are commonly asked how to manage and reduce progression of refractive errors. Epidemiological studies on refractive error are not representative of optometric practices. Therefore this study aimed to provide knowledge on prevalence and progression of astigmatism and myopia in children, allowing optometrists to use information collected routinely to advise on potential for refractive change, and to more accurately determine when the next examination should be. It also investigated the possible influence of astigmatism and myopia on one another. It was the first to investigate birth season and refractive progression, and in the UK to assess the influence of birth season on astigmatism and myopia in children.

This retrospective study analysed 900 subjective refractions of children under 19 years of age (mean 11.1 years) from two optometric practices in Liverpool. A subset of 242 of these children, tested longitudinally for a mean 5.97 years, was assessed for progression of astigmatism and myopia, using Decision Tree statistical Analysis to determine a possible association between astigmatism and myopia progression.

Cross-sectional data showed that boys were more likely to have astigmatism than girls ($p=0.004$). Age affected astigmatic axis, with against-the-rule and oblique astigmatism more prevalent in the older children, and with-the-rule prevalence reducing with age ($p=0.004$). Myopia increased with age ($p=<0.0001$).
Astigmatism increased by 0.04D/year (SD 0.087), and myopia by -0.15D/year (SD 0.23D). The presence of astigmatism was related to faster astigmatic progression ($p=<0.0001$). Being myopic was the sole risk factor for faster myopic progression ($p=<0.0001$). Birth season was unrelated to prevalence or progression of refractive error.

Advice on how sex, age and birth season may influence refraction can be discussed with patients and their families. Progression of astigmatism and myopia were not linked, suggesting that whilst they may share some risk factors, they appear to be independent of one another.

Key words:
Astigmatism; myopia; progression; birth season; sex

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This study is dedicated to the children of Liverpool. Thank you for inspiring me with your unique charm. Dream big, and you can achieve anything.

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Glossary
(Words in brackets represent the variables used in the study)

Accommodation – the mechanism by which the eye focuses on an object depending on its distance due to an adjustment in lens power

Age (younger, older) – in this study, age in years is median split for statistical analyses

Ametropia – a refractive state of the eye that is not perfect. Ametropia may be divided into myopia, hyperopia and/or astigmatism. See also refractive error

Astigmatism (absent, present) – refractive condition where two differently curved surfaces perpendicular to each other focus light at different positions

Astigmatic axis (none, WTR, ATR, oblique) – the angle at which one of the principal meridia of the astigmatism power lies. It varies from 1 to 180, with 180 being horizontal, and 90 vertical. In this study (and commonly in optometric practice in the UK), this is the axis of the most negative astigmatic power

Astigmatic Progression (lower, higher) – change in the state of astigmatism. In this study, it was represented as change in Dioptres per year (D/year) before median splitting for statistical analyses

ATR astigmatism – against the rule – negative astigmatic axes around the vertical. In this study, ATR astigmatism represents negative astigmatic axes of 90±20

Autorefraction – automated process to assess a patient's refraction by objective means

Autumn – season containing the months of September, October and November

Axial length – the distance of the length of the eye, from the cornea to the retina

Axis – see astigmatic axis

Birth season (Winter, Spring, Summer, Autumn) – the season in which an individual is born, split for the purposes of this study

Cycloplegia – reduced ciliary muscle function resulting in loss of accommodative function. Used temporarily by means of eye drops such as cyclopentolate in children where accurate refraction results are not possible by other means

Cycloplegic – referring to cycloplegia

Decision Tree Analysis – DTA – a form of multivariate statistical analyses usually assessing links between categorical data

Dioptre, D – unit of measurement of the power of a lens to refract light

Emmetropization – the process whereby the refraction of the eye uses a feedback mechanism through childhood to progress to (ideally) become emmetropic

Emmetropia – the ideal refractive state of the eye where there is no refractive error. In this study, emmetropia represents an SER of >-0.50 to <+0.50D

Hyperopia – a type of refractive error where the image is focused behind the retina. In this study, hyperopia represents an SER of ≥+0.50D

Median splitting – a method in statistical analyses to group and simplify continuous data into two categorical data groups, of one group lower and one higher than the median value

Myopia – a type of refractive error where the image is focused in front of the retina. In this study, myopia represents an SER of ≤-0.50D

Myopic Progression (lower, higher) – change in the state of refractive error. In this study, it was represented as change in SER in Dioptres per year (D/year) before median splitting for statistical analyses

Objective refraction – the process of refining a patient's refraction without their input, such as autorefraction, or retinoscopy

Oblique astigmatism – negative astigmatic axes around the oblique angles of 45 and 135 degrees. In this study, oblique astigmatism represents axes of 21-69 and 111-159

Optometrist – a medical professional who has passed professional qualifications to assess the health and refractive status of a patient. In the UK all optometrists must pass exams conducted by The College of Optometrists, and then be registered with the General Optical Council (GOC)

Refraction – the process of assessing a patient's refractive error

Refractive error (emmetrope, hyperope, myope) – ametropic condition of the eye. In this study, it refers to SER groups used in analyses

Retinoscopy – an objective method of measuring a patient's refractive error, by shining a light at the eye and observing the movements of the reflection

SER – spherical equivalent refraction, calculated as spherical power + astigmatic power/2

Spring – season containing the months of March, April and May

Subjective refraction – process of refining a patient's refractive error based on responses to specific questions

Summer – season containing the months of June, July and August

Visual Acuity – VA – a standardized measure of the ability to see high-contrast detailed objects

Winter – season containing the months of December, January and February

WTR astigmatism – with the rule – negative astigmatic axes around the horizontal. In this study, WTR astigmatism represents negative astigmatic axes of 180±20

Chapter 1: Introduction and objectives

1.1 Objectives

The reasons behind this study, a summary of its objectives and how this is developed are presented in this chapter.

1.2 The problem

Prevalence of myopia is increasing across the world (Holden et al., 2016), including Europe (Williams et al., 2015), North America (Vitale et al., 2008, Hrynchak et al., 2013) and Asia (Rudnicka et al., 2016). In addition to requiring increased optometric care, this leads to increasing associated health and economic issues (Baird et al., 2010; Flitcroft, 2012; Holden et al., 2016). Any research that finds associations or risk factors for refractive error may play a part in reducing the effect on the patient's wellbeing, (including vision and ocular health, and financially), and the wider economy is increasingly important.

As awareness of refractive error becomes more common, it is imperative that optometrists are able to answer any parental concerns regarding their child's vision and the potential outcome later in life, and provide information on risk factors (whether amendable or not). The small amount of research on the prevalence and progression of refractive error children attending community practice does not provide optometrists with sufficient information on risk factors, leaving them to rely on anecdotal evidence from their own experience, or to use information from epidemiological studies gathering data in different ways from their usual practice.

1.3 Study objectives

There were two sections to this study. The first involved cross-sectional analyses investigating associations from a large group of patients tested over a finite period from one of two practices in Liverpool, one in a city centre location, and the other, a suburb known as Old Swan (Figure 3.1). The second examined a smaller subsection of the cross-sectional group who had been seen at the practices for a

minimum period of five tests, or five years, so that factors associated with refractive progression could be studied.

Multivariate statistical analysis was used in the form of decision tree analysis (DTA) to assess the following objectives to enable further knowledge of refractive error in children attending community optometry practices, and to investigate associations that can be used by optometrists to explain risk factors in development to patients and their parents: -

- To investigate whether age has an influence on refraction (astigmatism and myopia) and its progression in children.
- To investigate whether sex has an influence on refraction (astigmatism and myopia) and its progression in children.
- To investigate whether birth season has an influence on refraction (astigmatism and myopia) and its progression in children.
- To investigate what the association between astigmatism and myopia progression in childhood might be, if any.

In analyzing this data, information was gathered on characteristics of those attending practice, and the prevalence and progression of refractive error. In addition to the above research, this provided normative data of those attending community practice in Liverpool, UK.

1.4 Overview of chapters

The analysis from data collected as part of this study form the following chapters: -

Chapter 2: Literature review
Discusses the previous prevalence research findings for astigmatism and myopia.
Chapter 3: Methodology
Describes the methods used in collecting and analyzing both cross-sectional and longitudinal data, and why certain criteria and analyses were chosen.
Chapter 4: Preliminary analyses of cross-sectional data.
Summarizes the demographic factors of the cross-sectional population of the study.
Chapter 5: Risk factors and associations of astigmatism and myopia.
Decision tree analyses (DTA) using cross-sectional data to examine whether age, sex and birth season affect refractive error, astigmatism, and astigmatic axis.

Chapter 6: Preliminary analyses of longitudinal data.
Summarizes the demographic factors of the longitudinal population of the study.
Chapter 7: Risk factors and associations of astigmatic and myopic progression.
Decision tree analyses of initial (risk) factors affecting progression of refractive error and astigmatism, including age, sex and birth season, and initial refraction.

1.5 Summary

There is little practice-based research providing information on risk factors affecting refractive error and its progression. Therefore, this study can be used to update optometrists with both normative data and potential risk factors for refractive error, and in the case of astigmatism, be broken down into its power and axis. It also included research on whether astigmatism and myopia may be linked. These results allow optometrists to use data to compare to their practice to guide patients and their parents on likely outcomes based on information that is easily collected from their own practice systems.

Chapter 2: Literature Review

2.1 Objectives

This chapter summarizes the previous prevalence research findings for astigmatism and myopia, and provides further detail on the variables investigated in this study.

2.2 Approach to literature search

Aston University Library Smart Search, which includes studies from a wide selection of databases (such as PubMed, Science Direct, and Wiley), along with Google Scholar, and the Cochrane Institute were used for a search of articles in peer-reviewed journals. Initially broad terms childhood astigmatism, and childhood myopia were used, and then the databases were searched with those terms for prevalence, progression and risk factors. Abstracts were then read to determine whether the research was pertinent to this study, and copies of those that were relevant were downloaded. The references of those articles also suggested new articles, which were used to find new information and enhance understanding. Further specific searches were conducted to find more detailed information (such as information on vitamin D as a risk factor for myopia). See appendix 3 for full details on the terms searched.

2.3 Astigmatism

Astigmatism is a type of refractive error where two differently curved surfaces perpendicular to each other focus light at different positions. Structurally, this can arise from the cornea, lens or both. In refraction notation, the difference in the power of the meridians represents the amount of astigmatism in dioptres (D). It may be classed as with-the-rule (where the negative cylinder axis is placed at or around the horizontal meridian), against-the-rule (where the negative cylinder axis is placed at or around the vertical meridian), or oblique (where a negative cylinder is placed at some point near the angles of 45 and 135 degrees). Most individuals will show some degree of astigmatism (Bennett and Rabbetts, pp.95, 1989), and a review by Read et al. (2014) found that it was feasible that the presence of even small

amounts astigmatism could have a significant effect on visual development and comfort. Astigmatism has been found to be higher in amblyopia (Harvey et al., 2004; Robaei et al., 2006). Guo and Atchison (2010) found astigmatism of 0.28D was enough to affect clarity of a line of 0.1 logMAR letters, and 1.00D induced astigmatism was sufficient to cause eyestrain and dry eye symptoms after a short period of concentrated computer work (Rosenfield et al., 2012).

Astigmatism changes throughout life, and there have been many studies charting its alterations from high astigmatism in infancy (Gwiazda, et al., 1984; Friling, et al., 2004), reducing in childhood due to possible links with emmetropization, and then an increase in the elderly (Katz et al., 1997). The axis of astigmatism has also been noted to change with age, with a decrease in with-the-rule (WTR) and increase in against-the-rule (ATR) astigmatism when measured both in longitudinal (Katz et al., 1997) and cross-sectional studies (Farbrother et al., 2004; Rezvan, et al., 2011). The mechanism that causes these changes is still largely unknown, although there are several (probably interacting) theories and risk factors, which will be discussed in section 2.3.2.

2.3.1 Prevalence

Table 2.1 shows a summary of the prevalence of childhood astigmatism assessed by different research groups across the world.

There appear to be large differences in prevalence of astigmatism between different ethnic groups - of particular note are the children from the Tohono O'odham tribe in the USA, who have a very high prevalence of astigmatism (Dobson et al., 2003), and Nepalese children having a low prevalence of only 2.2%.

However, there are different criteria for the definition of astigmatism, age group studied, and the method of measurement for many studies, making it difficult to compare results directly. The RESC studies were designed to use common protocol in different locations around the world to compare refractive error prevalence (Maul et al., 2000; Pokharel et al., 2000; Zhao et al., 2000). They found large variations in the different ethnic populations (see table 2.1). When astigmatism prevalence has been assessed based on ethnicity in studies in the USA, it has been found to show higher prevalence in Hispanic and Asian children (Kleinstein et al., 2003; McKean-Cowdin et al., 2011) compared with children of White European descent.

Author(s)	Location	N	Age	Definition	Refraction method	Prevalence
Lam et al. (1999)	Hong Kong	142	6-17 years	≥0.25D	Subjective refraction	32.4%
Zhao et al. (2000)	China (RESC)	5884	5-15 years	≥0.75D	Cycloplegic retinoscopy	15.0%
Pokharel et al. (2000)	Nepal (RESC)	5067	5-15 years	≥0.75D	Cycloplegic retinoscopy	2.2%
Maul et al. (2000)	Chile (RESC)	5303	5-15 years	≥0.75D	Cycloplegic retinoscopy	19.5%
Kleinstein et al. (2003)	USA (CLEERE)	2523	5-17 years	≥1.00D	Cycloplegic autorefraction	28.4%
Dobson et al. (2003)	USA (Tohono O'odham)	600	3-5 years	≥1.50D	Cycloplegic autorefraction & retinoscopy	31.7%
Shih et al. (2004)	Taiwan	22053	7-18 years	≥0.50D	Cycloplegic autorefraction	51.0%
				≥3.00D		1.8%
Tong et al. (2004)	Singapore (SCORM)	1019	7-9 years	≥1.00D	Cycloplegic autorefraction	19.3%
Huynh et al. (2006)	Australia (SMS)	1739	5.5-8.4 years	≥0.50D	Cycloplegic autorefraction	22.6%
				≥1.00D		4.8%
O'Donoghue et al. (2011)	UK (NICER)	1053	7-8 years	≥1.00D	Cycloplegic autorefraction	24.0%
			12-13 years			20.0%
Huang et al. (2014)	USA	4040	3-5 years	≥1.50D	Cycloplegic retinoscopy	17.0%
Jang et al. (2015)	South Korea	1079	8-13 years	>0.75D	Subjective refraction	9.4%
Chebil et al. (2015)	Tunisia	6192	6-14 years	≥0.75D	Cycloplegic autorefraction	6.67%
Larsson et al. (2015)	Sweden	217	10 years	≥0.50D	Cycloplegic retinoscopy	4.1%
Orlansky et al. (2015)	USA	122	3-5 years	≥0.50D	Retinoscopy	43.4%

Table 2.1: Prevalence of astigmatism in children from previous studies.

2.3.2 Risk factors for astigmatism

Table 2.2 shows the risk factors for astigmatism. There appears to be conflicting information on many factors, particularly regarding sex and prevalence, power and axis of astigmatism.

Risk factor	Theory	Supporting studies	Opposing studies
Ethnicity	Different races show varying prevalence of astigmatism	Kleinstein et al., 2003; Huynh et al., 2006; McKean-Cowdin et al., 2011	
Genetics	Family members may show genetic patterns of astigmatism	Twin studies: Hammond et al., 2001; Pärssinen et al., 2013. Gene loci studies: Lopes et al., 2013; Li et al., 2015.	Valluri et al., 1999; Lee et al., 2001
Sex	Prevalence of astigmatism varies with sex	Shekar and Srinivas, 2008	Kleinstein et al., 2003; Huynh et al., 2006; Lai et al., 2010; Rudnicka et al., 2010; Sanfillippo et al., 2015; Chebil et al., 2015
	Girls show higher power of astigmatism than boys	Huynh et al., 2006; Lai et al., 2010; Abbasi et al., 2013; Huang et al., 2014	Kleinstein et al., 2003; Fan et al., 2004; Rudnicka et al., 2010; Chebil et al., 2015
	Astigmatism type varies with sex	Farbrother et al., 2004; Huynh et al., 2006; Mandel et al., 2010; Fotouhi et al., 2011; Chebil et al., 2015	Rezvan et al., 2011
Palpebral fissure	Palpebral fissure slant affects astigmatic power and axis.	Garcia et al., 2003; Read et al., 2007	
Eyelid muscle tension	Eyelid muscle tension increases corneal astigmatism when narrowing inter-palpebral aperture	Read et al., 2007; Shaw et al., 2008; Rezvan et al., 2011	
Reading	Downward gaze affects corneal topography inducing astigmatism	Tong et al., 2004; Collins et al., 2005; Shaw et al., 2008	
Accommodation	Accommodation affects astigmatic power and axis	Byankuno et al., 1993; Tsukamoto et al., 2000	
Smoking	Mothers who smoke during pregnancy are more likely to have a child with higher astigmatic power	McKean-Cowdin et al., 2011	
Education	Astigmatism prevalence increases with increasing years in education	Wu et al., 2001	Katz et al., 1997
Family socio-economic class	Those in lower income classes show a higher prevalence of astigmatism	McKean-Cowdin et al., 2011	

Table 2.2: Summary of risk factors for astigmatism

2.3.3 How these risk factors may affect this population

Public Health England issues information annually in Health Profiles, giving figures for various health information compared to the English average. They are designed to help local authorities improve services to the local population. Figures from the Health Profiles (Public Health England, 2015), along with Census data (Liverpool City Council, 2013) and Local Authority data (Liverpool City Council, 2014 and 2015) suggest how the results gained from this study may be influenced by the profile of children in Liverpool compared with other English studies, such as the Aston Eye Study in Birmingham (Logan et al., 2011; Birmingham City Council, 2013).

Ethnicity

Ethnicity shows one of the greatest variables. McKean-Cowdin, et al (2011) found that Hispanic and African-American children aged 6 months to 6 years were more likely to have astigmatism ≥1.50DC than White European children (Odds ratios of 2.38 and 1.47 respectively). Kleinstein, et al. (2003) showed that Hispanic and Asian children aged 5-17yrs shared a similar prevalence of astigmatism ≥1.00DC (36.9% and 33.6% respectively), followed by White children (26.4%) and African-American children (20.0%). This information also suggests that there is a possible genetic link. Huynh et al. (2006) compared astigmatism in 6 year old children as part of the Sydney Myopia Study. They found that East and South Asians had a significantly higher prevalence of astigmatism compared with White European children ≥0.50D.

Census data for Liverpool from 2011 shows that 88.9% of the population was White (Liverpool City Council, 2013). The population consisted of 4.2% Asian, 2.6% Black, and 1.2% Arab. This is a lower than average Asian and Black population, and higher than average White and Arabian population, when compared to the overall England and Wales statistics. This may influence the results from the study towards those seen in other White European based studies. As the general population of England and Wales is 86% White European, the results from this study should be able to be directly transferred to other areas of the U.K.

Smoking

Research has shown that children whose mothers smoke during pregnancy show an increase in the prevalence of astigmatism (McKean-Cowdin et al., 2011).

Health Profile data reveal that smoking rates in adults for 2013 were significantly higher in Liverpool than in other parts of England, as were the percentage of

mothers who are smoking at the time of their child's birth (Public Health England, 2015). The current study may therefore show higher astigmatism amounts than in other UK studies; for example, the Health Profile for Birmingham (location of the Aston Eye Study) for the same year shows that mothers smoking at the time of birth were significantly lower than the English average, and the percentage of adults smoking were not significantly different from the national average (Public Health England, 2015).

Education

Astigmatism may vary with the number of years spent in education – Katz et al. (1997) found that astigmatism declined slightly with increasing years of education in African-American adults, although there was no association with White subjects, whilst Wu et al. (2001) found an increase in astigmatism prevalence with tertiary education in a Singapore-based study. It has also been noted that children aged 3-5 years score lower on measures of language and literacy, personal, social and physical development, communication and fine motor skills if they have astigmatism (Orlansky et al., 2015). Census data for Liverpool (Liverpool City Council, 2013) found that people living in Liverpool (particularly Old Swan) have a lower level of qualifications compared with England and Wales overall, and figures from the Health Profile for Liverpool in 2015 show that there were significantly fewer people with 5 GCSEs grades A*-C than the England average (Public Health England, 2015). Given all this data from the 2011 Census and 2015 Health Profile, it may be expected that a lower level of astigmatism will be found compared to other studies. Comparable figures for Birmingham show that the level of percentage of people with 5 GCSEs achieved at grades A*-C were similar to the England average (Birmingham City Council, 2013).

Socioeconomic status

The higher prevalence of astigmatism in the lower income classes compared to higher classes has also been found (McKean-Cowdin et al., 2011). Figures from the Liverpool Local Authority suggest that more children in Liverpool tend to be in the lower income families compared to the average for England (Liverpool City Council, 2014), and in fact, ranked 8th in the Income Deprivation Affecting Children Index (IDACI) (Liverpool City Council, 2015). This may suggest that a higher prevalence of astigmatism might be found in this population compared with other studies in the UK, although, Birmingham has a similar number of children living in lower income families (Liverpool City Council, 2014).

2.3.4 Progression of astigmatism

Table 2.3 shows former research on progression of astigmatism. These studies show very small changes, with astigmatism both improving and deteriorating, and no clear pattern with ethnicity. There are limited number of studies exploring this in comparison to other types of refractive error, covering a short timeframe of assessment. Only one study in the UK has investigated how astigmatic power changes over time, and this was not practice-based (O'Donoghue et al., 2015). Therefore, further knowledge of this subject would be valuable, using a wider age range of subjects, over a longer period, and for astigmatic axis change, such as will be examined by this study.

Author(s)	Location	N	Initial Age	Length of study	Progression
Zhao et al. (2002)	China	4662	5-13 years	28 months	-0.002D/year
Fan et al. (2004)	Hong Kong	108	27-77 months	5 years	+0.024D/year
Tong et al. (2004)	Singapore	842	7-9 years	4 years	-0.03D/year
Chia et al. (2009)	Singapore	400	6-12 years	2 years	-0.12D/year
Harvey et al. (2015)	USA	1594	3-10 years	3 years	-0.02D/year
		648	12-13 years		+0.06D/year
Pärssinen et al. (2015)	Finland	240 myopic children	8-13 years	23 years	-0.02D/year
O'Donoghue et al. (2015)	Northern Ireland	295	6-7 years	3 years	0.00D/year
		429	12-13 years		0.00D/year

Table 2.3: Longitudinal studies showing progression of astigmatic power

2.3.5 Sex and astigmatism

Kleinstein, et al. (2003), Fan et al. (2004), Huynh et al. (2006), Lai et al. (2010), Sanfilippo et al. (2015) and Chebil et al. (2015) found no significant differences in prevalence of astigmatism and sex. One study that has shown a statistically higher prevalence of astigmatism in boys was by Shekar and Srinivas (2008), who examined the association with sex and refractive error using Decision Tree Analysis (DTA). They found boys aged 5-8 years to show a higher prevalence of astigmatism compared with girls. However, older age groups up to 16 years did not show any difference between the sexes.

Greater differences have been found when determining the power and axis of astigmatism. Huynh et al. (2006) and Lai et al. (2010) did find a significantly higher power of astigmatism in girls compared to boys (but no difference in overall prevalence of astigmatism). There are several previous studies showing either no

statistical difference in astigmatism type (Rezvan et al., 2011), a higher amount of ATR astigmatism in boys (Farbrother et al., 2004; Fotouhi et al., 2011; Chebil et al., 2015), a possible association between being female and WTR astigmatism (Mandel et al., 2010; Fotouhi et al., 2011), or a higher prevalence of WTR astigmats in boys (Huynh et al., 2006). Whilst the Sydney myopia study (Huynh et al., 2006) also found a significantly higher number of oblique astigmats compared to the current study, (overall 39.1%), they also found no significant difference between the 2 sexes. This resulted in girls showing a higher proportion of ATR astigmatism.

Astigmatism progression is less frequently studied in terms of sex. Zhao et al. (2002) found that girls show larger astigmatic power increases than boys, and Tong et al. (2004) found that J_0 (WTR astigmatism) progressed faster in girls, but there was no difference in J_{45} (oblique astigmatism) progression. However, Pärssinen et al. (2015) found no association with sex and astigmatic progression.

This study will analyse astigmatic details of power, axis and progression and determine any association with sex to add knowledge to this current debate.

2.3.6 Birth season and astigmatism

The year in which the earth rotates is split into 4 seasons. These seasons bring variations in temperature, the amount of daylight, and other weather features. The season in which a given individual is born can affect their physical development and risk factors for many diseases, including cardio-vascular, respiratory and neurological conditions (Boland et al., 2015), and therefore may affect ocular refraction status. The weather changes occurring during the year also affect different parts of the world, making direct comparison of a season's effect on development difficult.

Animal studies have found that variations in light do not generally influence the prevalence of astigmatism in chicks (Stone et al., 1995) or monkeys (Kee et al., 2005). However, a study investigating lighting used at night in children under the age of 2 years found that those sleeping with fluorescent lighting were more likely to become astigmatic, suggesting that a disruption of the light-dark cycle could be an associated factor (Czepita et al., 2004), although incandescent lighting was not shown to be an influence.

Only one study was found examining astigmatism in 276,911 Israeli conscripts aged 16-22, and the time of birth, by Mandel et al. (2010). Astigmatism power was not influenced by the amount of daylight in the 30 days after birth. It did, however find

that WTR astigmatism was more commonly associated in those born in months with longer photoperiods, and ATR more common in those born in months with shorter photoperiods. They offered that this effect of birth month might not be causal, but linked with other environmental factors at the time of birth, such as breastfeeding, or ambient temperature. It is possible that in children, birth season may have more of an influence on prevalence or axis of astigmatism, and this is what this study will investigate. In addition, analyses will also be performed to see if birth season has an effect on astigmatic progression.

2.4 Myopia

Myopia is a condition whereby the power of the lens is too strong, or the axial length of the eye is too long, meaning that light entering the eye is focused before the retina (figure 2.1). Correction of myopia uses negative (concave lenses) to refocus the image at the retina allowing a patient to see distance vision clearly.

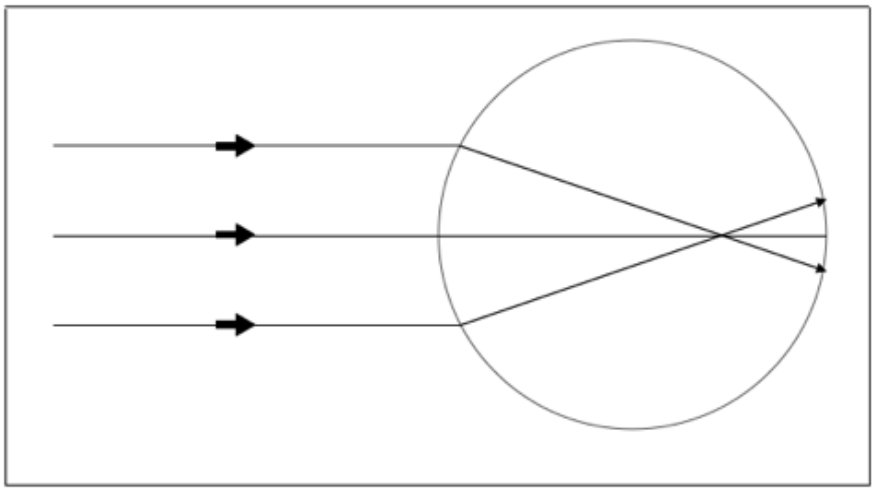


Figure 2.1: Image showing how myopia brings the focus of a distant object in front of the retina.

The genetics in myopia (GEM) study describes myopia as 'a complex disease where both genetic and environmental factors and their likely interplay influence phenotype' (Baird et al., 2010). The paper also describes how the risk of retinal detachment, staphylomas, age-related macular degeneration, glaucoma and cataract is increased in myopes, especially in high myopia (≤-6.00D). There is much research on myopia development, as it is no longer seen as just a type of prescription requiring spectacle correction, but is known to lead to increased risks of disease, such as glaucoma, maculopathy and retinal detachment (Flitcroft, 2012).

In Western populations, high myopia (usually classed as greater than -6.00D) is seen in approximately 3% of the population, but in Asian populations, this rises to 10% (Wu et al., 2001; French et al., 2013; Holden et al. supplementary material, 2016). Therefore, risk of sight-threatening disease associated with high myopia could certainly be similar to other disease prevalence. The GEM study group (Baird et al., 2010) also conducted a lifestyle questionnaire and found that myopic patients wearing spectacles or contact lenses had significantly increased odds of concerns about injuring themselves, difficulties in coping with demands in life, difficulties fulfilling roles and less confidence joining in everyday activities compared with emmetropes, and myopes who had undergone refractive surgery. These results put the impact of myopia on patients' lives into perspective.

2.4.1 Prevalence

Table 2.4 shows a summary of the prevalence of childhood myopia assessed by different groups across the world. There are different criteria for the definition of myopia, age group studied, and the method of measurement, making it difficult to compare results directly. There are, however, clear differences between ethnic groups, with those in Eastern Asia showing a significantly higher prevalence of myopia (Zhao et al., 2000; Jang and Park, 2015; Guo et al., 2015) compared with White Europeans (Huynh et al., 2006; Larsson et al., 2015).

In terms of epidemiological studies on the UK population, there are few directly comparable studies to the current one. Pointer et al. (2001) assessed children attending an optometry practice for subjective refraction. However, it focused on longitudinal changes for the small group of 41 children. Other epidemiological studies in the UK have used either cycloplegic autorefraction or non-cycloplegic autorefraction (Williams et al., 2008; Rudnicka et al., 2010; O'Donoghue et al., 2010; Logan et al., 2011). Whilst this is useful to the practicing optometrist as a guide, subjective refraction is used in the majority of cases as the basis for whether or not to prescribe spectacles. They also examine a narrow age range, which is limiting in guidance for those outside that group.

There are several studies, which suggest that myopia prevalence is increasing (Vitale et al., 2008; Hrynchak et al., 2013; Williams et al., 2015; Rudnicka et al., 2016), with Holden et al. (2016) suggesting that by 2050, nearly half the worlds' population will be myopic. Therefore, any research that can add to the knowledge base of myopia and to help reduce its effects is valuable.

Author(s)	Location	N	Age	Definition	Refraction method	Prevalence
Robinson (1999)	Canada	10616	6 years	<-0.25D	Retinoscopy	6.0%
				≤-1.00D		1.8%
Zhao et al. (2000)	China (RESC)	5884	5-15 years	≤-0.50D	Cycloplegic autorefraction	14.9%
Pokharel et al. (2000)	Nepal (RESC)	5067	5-15 years	≤-0.50D	Cycloplegic autorefraction	1.2%
Maul et al. (2000)	Chile (RESC)	5303	5-15 years	≤-0.50D	Cycloplegic autorefraction	5.8%
Pointer (2001)	UK	41	7 years	≤-0.50D	Subjective refraction	5.0%
Zadnik et al. (2003)	USA	2583	Mean 10 years	≤-0.75D	Cycloplegic autorefraction	10.1%
Kleinstein et al. (2003)	USA (CLEERE)	2523	5-17 years	≤-0.75D	Cycloplegic autorefraction	9.2%
Huynh et al. (2006)	Australia (SMS)	1739	5.5-8.4 years	≤-1.00D	Cycloplegic autorefraction	1.4%
Cheng et al. (2007)	Canada	1468	6 years	≤-0.50D	Subjective refraction	22.4%
			12 years			64.1%
Williams et al. (2008)	UK (ALSPAC)	7825	7 years	≤-1.50D	Autorefraction	1.5%
Rudnicka et al. (2010)	UK (CHASE)	1179	10-11 years	≤-0.50D	Autorefraction	11.9%
O'Donoghue et al. (2010)	UK (NICER)	392	6-7 years	≤-0.50D	Cycloplegic autorefraction	2.8%
		661	12-13 years			17.7%
Logan et al. (2011)	UK (AES)	655	6-7 years	≤-0.50D	Cycloplegic autorefraction	9.4%
			12-13 years			29.4%
French et al. (2013)	Australia (SAVE)	2072	6-7 years	≤-0.50D	Cycloplegic autorefraction	14.4%
			12-13 years			29.4%
Jang and Park (2015)	South Korea	1079	8-13 years	≤-0.50D	Subjective refraction	46.5%
Guo et al. (2015)	China	1565	6-21 years	≤-0.50D	Cycloplegic autorefraction	60.0%
				≤-1.00D		48.0%
Larsson et al. (2015)	Sweden	217	10 years	≤-0.50D	Cycloplegic retinoscopy	7.8%

Table 2.4: Prevalence of myopia from previous studies on children.

2.4.2 Risk factors for myopia

The RESC group of studies used the same criteria to assess children from across the world, so were able to identify a more accurate variation due to ethnicity than other studies using different definitions of myopia, and different methods of assessing refraction (Zhao et al., 2000; Maul et al., 2000; Pokharel et al., 2000). Myopia shows more of a variation due to ethnicity than astigmatism. The CHASE study, based on 1179 10-11 year old children in the UK, found the prevalence of myopia to be 3.4%, 10.0% and 25.2%, for white European, African Caribbean and South Asian children respectively. They noted the reason for this was due to axial length differences (Rudnicka et al., 2010).

Other risk factors are described below, and split into modifiable (table 2.5) and non-modifiable (table 2.6) risk factors.

Risk factor	Theory	Supporting studies	Opposing studies
Reading/ near work	Longer time spent reading increases myopia prevalence	Jones et al., 2007; Ciuffreda et al., 2008; Williams et al., 2008; Cheng et al., 2012; Huang et al., 2015	O'Donoghue et al., 2015
Smoking	Parents who smoke during pregnancy are less likely to have a myopic child	Saw et al., 2004; Stone et al., 2006; Williams et al., 2008; Borchert et al., 2011;	Iyer et al., 2012; Guo et al. 2013
Education	Myopia prevalence increases with increasing years in education	Wu et al., 2001; Konstantopoulos et al., 2008; Mandel et al., 2008; Mirshahi et al., 2014; Williams et al., 2015	
Outdoor activity/Light exposure	Children who spend more time outdoors are less likely to be myopic, and show less myopic progression	Jones et al., 2007; Rose et al., 2008; Sherwin et al., 2012; Guggenheim et al., 2012; Norton and Siegwart Jr., 2013; Jin et al., 2015; Saxena et al., 2015	Cheng et al., 2012; Hsu et al., 2017
Seasons	Myopic progression slower through longer summer months	Donovan et al., 2012; Cui et al., 2013; Gwiazda et al., 2014	Fujiwara et al., 2012
Birth month/ season	Children born in months of the year with shorter daylight hours more likely to be myopic	Deng and Gwiazda, 2011; Matsuda et al., 2012; Ma et al., 2014	Mandel et al., 2008; McMahon et al., 2009; Boland et al., 2015
Sport	Children who spend more time doing physical activities are less likely to be myopic, and show slower myopic progression	Jones et al., 2007; Rose et al., 2008; Guggenheim et al., 2012; Pärssinen et al., 2014	
Nutrition	Nutrition may play a role in myopia development	Mutti and Marks, 2011; Yazar et al., 2014 (vitamin D)	Edwards et al., 1996; Lim et al., 2010

Table 2.5: Summary of modifiable risk factors for myopia

Risk factor	Theory	Supporting studies	Opposing studies
Ethnicity	East Asian children more likely to be myopic	Saw et al., 2003; Rose et al., 2008; Rudnicka et al., 2010 Borchert et al., 2011; Wen et al., 2013	
Genetics	Family history of parental and sibling myopia increases the risk of myopia	Lee et al., 2001; Jones et al., 2007; Konstantopoulos et al., 2008; Pärssinen et al., 2014; O'Donoghue et al., 2015	
Age	Myopia prevalence and mean SER increases with age	Logan et al., 2011; Guo et al., 2013; Li et al., 2015	
Sex	Myopia is more prevalent in girls	Zhao et al., 2000; Kleinstein et al., 2003; Plainis et al., 2009; Guo et al., 2013; Saxena et al., 2015; Rudnicka et al., 2016	Robinson, 1999; Maul et al., 2000; Rudnicka et al., 2010; Carter et al., 2013; O'Donoghue et al., 2015; Jang and Park, 2015
	Girls show a higher mean SER	Lin et al., 1999; Cheng et al., 2007	Zadnik et al., 2003; Cheng et al., 2012
Family socioeconomic class	Children from less deprived economic classes are more likely to be myopic	Morgan and Rose, 2005; O'Donoghue et al., 2015; Saxena et al., 2015	Williams et al., 2008
Seasons	Myopic progression slower through longer summer months	Donovan et al., 2012; Cui et al., 2013; Gwiazda et al., 2014	Fujiwara et al., 2012
Birth month/ season	Children born in months of the year with shorter daylight hours more likely to be myopic	Deng and Gwiazda, 2011; Matsuda et al., 2012; Ma et al., 2014	Mandel et al., 2008; McMahon et al., 2009; Boland et al., 2015

Table 2.6 Summary of non-modifiable risk factors for myopia

There is noted to be a large increase in the prevalence of school myopia in urban areas of East Asia, which, it is believed, has changed too quickly to account for genetic or evolutionary changes, which suggest more of an environmental aspect as the cause for the growing numbers of myopes (Morgan and Rose, 2005). This can also be seen in Alaskan Inuit, where the prevalence of myopia increased from 1.5% to 60% in one generation (Logan, 2009), through changes towards a more westernised lifestyle, including diet and the amount of near work performed.

2.4.3 How these risk factors may affect this population

Ethnicity

Although race could not be determined for a retrospective study such as this, 2011 census data for Liverpool shows 88.6% of the population to be White, 4.2% to be Asian, 2.6% to be Black, 1.2% to be Arab, 2.5% to be mixed, and 0.6% to be of

other ethnic origin (Liverpool, City Council, 2013). Old Swan demographics show a higher proportion of White people, with 92.5% of the population, and only 3.2% being from Asian origin, and 1.2% to be Black. This shows a cultural variation that is between the White European population of the NICER study (O'Donoghue et al. (2011), and the multi-ethnic population of the Aston Eye Study (Logan et al., 2011), the only other two large recent population studies on the prevalence of astigmatism in the UK.

Smoking

It has been shown that smoking when pregnant has been linked with a more hyperopic refraction in the child (Saw et al., 2004; Williams et al., 2008). Both maternal and paternal smoking has also been considered to provide a protective effect for myopia in the child (Stone et al., 2006). Health Profile data for Liverpool (Public Health England, 2015) show that there is a larger percentage of the population smoking in general, and when pregnant, compared with the rest of England. This could contribute to a lower prevalence of myopia compared with studies conducted where smoking rates are lower.

Education

Census data from 2011 shows that people living in Liverpool (particularly Old Swan) have a lower level of qualifications compared with England and Wales overall (Liverpool City Council, 2013), and figures from the Health Profile for Liverpool in 2015 show that there were significantly fewer people with 5 GCSEs grades A*-C than the England average (Public Health England, 2015). Given all this data from the 2011 Census and 2015 Health Profile, it may be expected that this could reduce the levels of myopia found compared to other studies (Wu et al., 2001; Mandel et al., 2008; Konstantopoulos et al., 2008).

Socioeconomic class

Children from more deprived economic backgrounds have been found to show a higher risk of myopia (O'Donoghue et al., 2015; Saxena et al., 2015). However, lower socioeconomic class has also been associated with a higher prevalence of hyperopia (Williams et al., 2008). Liverpool is an area with significantly higher levels of deprivation (Liverpool City Council, 2015), and children living in poverty compared to other areas of England recorded (Liverpool City Council, 2014; Health Profile 2015), which suggests that this may skew the myopia prevalence found in this study, and reduce the emmetropic prevalence.

2.4.4 Progression of myopia

Table 2.6 shows the results of previous studies on myopia progression. There are more studies investigating this type of refraction change than astigmatic progression. Location and ethnicity affects myopic progression in the same way they affect prevalence, with those in East Asia showing the fastest progression (Lam et al., 1999; Tan et al., 2000). Myopes are also seen to progress more quickly than other refraction types, regardless of region or whether assessments were made using subjective refraction or cycloplegic autorefraction (Lam et al., 1999; Tan et al., 2000; Pointer, 2001; Cheng et al., 2007, McCullough et al., 2016).

Author(s)	Location	N	Age	Length of study	Progression
Watanabe et al. (1999)	Japan	350	6 years	5 years	-0.15D/year
Lam et al. (1999)	Hong Kong	142	6-17 years	2 years	-0.32D/year
Tan et al. (2000)	Singapore	168	7,9 and 12 years	10 months	-0.87D/year
Saw et al. (2000)	Singapore	153 myopic children	6-12 years	2 years	-0.59D/year
Pointer (2001)	UK	41	7-13 years	6 years	-0.09D/year
Zhao et al. (2002)	China	4662	5-13 years	28 months	-0.18D/year
Cheng et al. (2007)	Canada	1468	6-12	6 years	-0.52D/year
French et al. (2013)	Australia	870	12 years	5-6 years	-0.16D/year
		1202	17 years		-0.15D/year
Pärssinen et al. (2014)	Finland	240 myopic children	9-13 years	23 years	-0.16D/year
McCullough et al. (2016)	Northern Ireland	212	12-13 years	6 years	-0.23D/year
		226	18-20 years		-0.10D/year

Table 2.7: Longitudinal studies showing progression of myopia

2.4.5 Sex and myopia

Sex has repeatedly been shown to be a factor in the development of myopia. Kleinstein, et al. (2003) found the prevalence of myopia ≥0.75D in school age children of 5-17 years of varying ethnic background to be 11.5% in girls and 7.1% in boys. Plainis et al. (2009) also found that there were higher levels of myopia in secondary school girls compared to boys. However, in the UK, there were no statistically significant differences in the prevalence of myopia in boys and girls (Rudnicka et al., 2010; O'Donoghue et al., 2015), and this has also been noted elsewhere (Fan et al., 2004; Wen et al., 2013). In adults, myopia tends to show higher prevalence in females compared to males (Dayan et al., 2005; Saw et al., 2008;), although this is not always statistically significant (Jobke et al., 2008;), and

some studies show no significant differences (Katz et al., 1997; Liang et al., 2009; Varma et al., 2013). It is therefore expected that the current study will show similar results, showing either greater prevalence for myopia in girls or having no statistically significant differences, and being unlikely that myopia would show higher prevalence in boys.

Rudnicka et al. (2016) performed a systematic review of myopia in children, and found that differences in sex varied with ethnicity. East Asian and White European girls and boys began to differ at the age of 9 years, and by the age of 18, girls were approximately twice as likely to be myopic than boys were. However, there were no significant differences in Hispanic or South Asian children.

The progression of refractive error has been shown to be higher in girls than boys (Pärssinen and Lyyra, 1993; Zhao et al., 2002; Hyman et al., 2005), which also contributes to them showing a higher mean spherical equivalent refraction (SER) (Guo et al., 2015). However, other studies have found no difference (Lam et al., 1999; French et al., 2013; McCullough et al., 2016).

As well as ethnicity variations, these more myopic tendencies in girls could also be associated with gender-biased hobbies, with more boys spending more time outdoors than girls (Rose et al., 2008; Collins et al., 2012). Differences in attitudes towards boys such as allowing them to spend more time alone outdoors (Mackett et al., 2007b) may also contribute to the environmental aspect of myopia.

This study will compare the subjective refractions to see if there are any differences in myopia prevalence, SER and progression between the sexes in children attending for sight tests in Liverpool to add to this current information.

2.4.6 Birth season and myopia

It has been reported that birth season may increase the risk of myopia or hyperopia (Boland et al., 2015). SER in infancy and early childhood has been found to be more myopic in those born in the winter months (Deng and Gwiazda, 2011; Ma et al., 2014). In another study of Japanese 3 and a half year old children (Matsuda et al., 2013), those born in September and October had a more hyperopic Rx compared with those born in the winter months (Mean SER +0.133D in autumn, and -0.143D in winter births).

The apparent protective effect of sunlight on myopia could be either due to the amount of daylight present in the months after birth, or the type of light, with a difference in wavelength between daylight and artificial lighting (Prepas, 2008). It

could also include indirect chemical interactions associated with light, such as vitamin D (Mutti, 2014), or dopamine moderation (Feldkaemper and Schaeffel, 2013; Norton and Siegwart Jr., 2013). From their analysis of both human and animal studies, Norton and Siegwart Jr. suggested that as light triggers dopamine production and release from retinal amacrine cells, it might then prevent the axial elongation that causes myopia to develop. In investigations into psychiatric disorders, dopamine metabolites were found in higher concentrations in the CSF in those born in winter months compared with those born in the summer both in infants (Chotati et al., 2006) and adults (Chotai and Adolfsson, 2002) – this affected likelihood of personality traits, leading to links with different suicide methods. Rada and Wiechmann (2006) found another neurotransmitter, melatonin, to show a diurnal variation in activity in ocular tissues. On further testing, they found that different types of melatonin were active in the day compared with at night. On systemic administration of melatonin, form-deprived chicks showed reduced anterior chamber growth and thinner retinal and choroidal tissues, demonstrating the effects on several ocular tissues important in eye development. In a study on adolescents in Israel, Mandel et al. (2008) made adjustments for education and average hours of daylight (photoperiod) in the 30 days following birth (rather than season of birth). They found that moderate and high myopia was more likely to occur in adolescents born in June and July. The odds ratio for high myopia ≤-6.00D was a significant 1.24 between the shortest when compared to the longest photoperiod. They suggested a chemical balance disruption between melatonin and dopamine might be the most likely reason, after variations had been noted in previous studies on these neurotransmitter levels after birth and into adulthood. In their review on the potential for a light-dark switch in the retina, Morgan and Boelen (1996) found greater activity of dopamine producing cells in light conditions and melatonin producing cells more active in darker conditions, linked by a reciprocal inhibitory relationship, and they also suggested that this interaction may be significant in eye growth and development.

Theory suggests that the amount of daylight at the time after birth may be the reason that more myopic refractions occur in those born in the months with fewer daylight hours (Deng and Gwiazda, 2011). This has been supported by animal studies which suggest that light intensity may have a controlling factor in emmetropization, with chicks receiving a lower light intensity more likely to become myopic (Cohen et al., 2011). Twelker et al. (2013) also suggested that pupil size in brighter light negates the effect of retinal blur from uncorrected prescriptions or from aberrations, reducing the stimulus to develop myopia.

An increased amount of daylight has been shown to have a continued protective effect on myopia development into childhood, with those who spend more time outdoors showing a lower risk of myopia (Jones et al., 2007; Rose et al., 2008; Sherwin et al., 2012), and slower myopic progression (Jin et al., 2015) than children spending more time indoors.

It has also been noted that both hyperopia and myopia have an increased prevalence in children born in October, and that children have the lowest risk for developing ametropia if they are born in April (Supplementary notes, Boland et al., 2015).

Children born between October and December have been found to have a larger corneal radius, confirming that season of birth does affect ocular growth (Matsuda et al., 2013), although no association between axial length and season of birth was found in the same study. Other studies have associated larger corneal radii with more hyperopic refractions (Hashemi et al., 2015; Zhang et al., 2015), and smaller radii with more myopic refractions (Blanco et al., 2008). The combined results indicate that hyperopia may also be more commonly found in children born in October (Supplementary notes, Boland et al., 2015).

These findings suggest that there is almost certainly a link between light and refractive development, although this is only part of the multifactorial effect on myopia. As the amount of daylight varies throughout the season in the UK, due to its latitude, it is a good location to examine the variance associated with the seasonal effect on refraction. Based on these previous findings, if any significant results are obtained for season of birth and myopia, it might be expected that those born in the autumn and/or winter months might be more likely to be myopic, as they would spend less time in daylight in the immediate post-natal period. It may, however, be that because this possible risk factor occurs so early in life, it may show too small an impact on myopia development and progression. Risk factors for myopia progression such as season of the year (Donovan et al., 2012; Gwiazda et al., 2014) and interventions that are designed to slow myopic progression such as multifocal prescribing or atropine treatment (Gwiazda et al., 2003; Walline et al., 2011; Pineles et al., 2017) tend to show immediate effects within a few months, so whilst birth season might show an impact in infants, the effect may be surpassed by modifiable/environmental (nurture) effects such as near work and time spent outdoors – see table 2.5, which may have a more additive and progressive effect

towards the emergence of clinical myopia between the ages of 6 and 7 years (Pointer, 2001).

2.5 Astigmatism and myopia

Spherical refractive error has been shown to affect the prevalence of astigmatism, with children with a spherical myopic prescription more likely to have astigmatism (odds ratio 4.6), children with hypermetropic (odds ratio 1.6) compared to emmetropic spherical refractions (McKean-Cowdin et al., 2011). The same study also found a slightly higher odds ratio for ATR compared with WTR astigmatism and myopia, confirming previous results by Gwiazda et al. (1984). The higher myopic and hypermetropic refractions in the study by McKean-Cowdin et al. (2011) show a greater level of astigmatism prevalence compared with a lower spherical prescription, a finding also noted into adulthood (Rezvan et al., 2011), particularly with WTR astigmatism (Farbrother et al., 2004). However, research methods differ, giving variable results. Fan et al. (2004) found no link between astigmatism and myopia and the initial examination of a longitudinal study. After 5 years, results showed that children presenting with higher astigmatism initially were more likely to show a more myopic spherical equivalent refraction (SER). The axis of the astigmatism was, unlike the studies above, not associated with myopia or myopic progression. Tong et al. (2004) also found that astigmats were also likely to progress to becoming myopes. McKean-Cowdin et al. (2011) meanwhile, found myopes showed a higher progression of astigmatism. However, some research has found no link between astigmatism and myopia progression (Goss and Shewey, 1990; Pärssinen et al., 2015). It is possible that other risk factors and associations such as ethnicity and family history are more dominant in the relationship, making specific details more difficult to find.

2.5.1 Aetiology of astigmatism and myopia

Emmetropization is the process whereby the refraction of the eye progresses to become emmetropic, creating a balance between the power of the cornea and/or lens and the axial length of the eye to allow perfect vision without the need for corrective lenses. The development of refractive error therefore represents a failure of the emmetropization process (Flitcroft, 2013). Although genetics plays a large part in the development of refractive error, there are also environmental influences, which can disrupt this process of normal development (see sections 2.3.2 and

2.4.2). In myopes, this has been shown to be due to increased vitreous chamber depth without the compensation by anterior eye changes (Gwiazda et al., 2000; Jones et al., 2005). There are many studies discussing how this may trigger myopia, with accommodation and near work being a considerable factor (Williams et al., 2008; Ciuffreda and Vasudevan, 2008; Huang et al., 2015). Sustained accommodation in near work causes near-induced transient myopia (Ciuffreda and Vasudevan, 2008), and the globe to become more prolate in shape, which, after ceasing near work, remains changed for longer in myopes (Walker and Mutti, 2002; Ciuffreda and Vasudevan, 2008). This increased time of scleral stretching results in permanent changes to the scleral fibroblasts, which could lead to a sustained increase in axial length (Cui et al., 2004). Another reason adding to an accommodative theory is that anti-muscarinic drugs such as atropine, have been found to reduce myopia progression (Chua et al., 2006; Chia et al., 2012; Clark and Clark, 2015), with Walline et al. (2011) and Lagrèze (2017) finding it was the most effective (although with considerable side effects) in their reviews of the literature.

Myopes have also been shown to show increased lag of accommodation, leading to an inaccuracy in focussing for near work (Schaeffel et al., 2003; Mutti et al., 2006). This puts the image behind the retina, and may therefore simulate scleral growth to cause further myopic progression (Schaeffel et al., 2003; Gwiazda and Weber, 2004). Bernsten et al. (2012) and Koomson et al. (2016) both assessed accommodative lag in myopic children, but could find no association between the relative hyperopic foveal blur and myopic progression. The different study designs may have affected these conflicting results (Day and Duffy, 2011), leaving the question still open of whether or not variable accommodative lag plays a factor in myopia development. Mutti et al. (2006) found no prior differences in accommodative lag between children who became myopic and those who remained emmetropic. They suggested that this difference in accommodative lag once myopic could possibly be due to the myopia, and not a cause of it.

Studies on examining the shape of the eye using MRI (Singh et al., 2006), retinal contouring (Logan et al. 2004) and peripheral refraction of the eye (Mutti et al., 2000; Calver et al., 2007; Smith et al., 2009) have been used to detail how the growth of the eyes may influence myopia development. Comparative hyperopic peripheral refraction, due to the eye being a more prolate shape, has been shown to be higher in progressing myopes (Mutti et al., 2006; Sng et al., 2011; Bernsten et al., 2011). This has led to increased interest in research into the management of

myopia using multifocal contact lenses (Queiros et al., 2016; Lagrèze et al., 2017). Peripheral defocus may be managed using contact lenses corrected centrally for distance refraction, and with a more hyperopic peripheral correction. These were found to reduce myopic progression in children (Sankaridurg et al., 2011), although it was not as significant with novel spectacle lenses designed to reduce peripheral defocus (Sankaridurg et al., 2010). Specialist contact lenses continue to be researched in children and adults, with positive results for myopic progression using centre distance multifocals (Walline et al., 2013; Turnbull et al., 2016) and for specialist lens designs providing some retinal defocus (Lam et al., 2014).

Animal studies in chicks and monkeys use induced or imposed spherical or cylindrical lenses to create artificial ametropia. They appear to show that the control for spherical defocus by plus and minus lenses can be accurate, and produces specific compensation to the different lens types in an attempt to emmetropize the imposed blur (Schmid and Wildsoet, 1997). Imposed cylindrical lenses produce incomplete compensation (Irving et al., 1991; Irving et al., 1995), spherical error, usually to the more myopic meridian (Schmid and Wildsoet, 1997; Kee et al., 2004), and with various adjustment for axis (Irving et al., 1995; Kee et al., 2003; Kee and Deng, 2008).

Studies assessing the link in growth and ocular development are yet to suggest a definitive answer linking astigmatism and myopia. There are two main theories; both suggest that myopia is (at least in part) triggered by astigmatism. The first relates to the fact that astigmatic blur disturbs accommodation, and the second, that ocular growth affects tension on the ciliary muscle and lens, creating a pseudo-cycloplegia, both of which then trigger axial length growth and myopia development (Gwiazda et al., 2000). Increased ciliary body thickness has been associated with greater axial length and myopia. This could be due to restriction of equatorial growth, causing axial length increase (Jeon et al., 2012). Whilst Gwiazda et al. (2000) suggested that there was some interdependency between astigmatism and spherical ametropia, they acknowledged that there were formed in separate growth areas, with astigmatism coming primarily from the anterior eye, and myopia shift coming from vitreous chamber growth. Chu and Kee (2015), however, found that imposed cylindrical lenses caused both anterior and posterior segment changes, suggesting there may be some posterior response to astigmatism development. Animal studies using induced astigmatism suggest that it does not necessarily cause myopia. In experiments on peripheral refraction, Sng et al. (2011) found that peripheral

astigmatism did not affect myopia development or progression. In addition, Kee and Deng (2008) found that high levels of spherical defocus could cause significant ATR astigmatism. Perhaps in some patients the emmetropization fails in terms of axial adjustment for anterior and posterior growth changes, leading to both astigmatic and spherical error development (Kee et al., 2004; Kee and Deng, 2008; Irving et al., 2015).

This study was designed to assess progression of both astigmatism and myopia, to determine whether one type of refraction influences the progression of the other, which may support theories of links between them. In addition, it was aimed to increase knowledge of refractive error for any future development in treatment, and to allow practitioners to give the best advice possible to their patients.

2.6 Summary

Previous studies show that not only are there various methods of achieving refraction results, with or without cycloplegia, but also different ways of assessing refraction using various autorefractors, retinoscopy or subjective refraction, with different definitions for refractive error. Despite the fact that these studies suggest they are assessing refraction by a gold standard, it may be suggested that because they do not use exactly the same criteria, they are open to variation in the results in the same way that subjective results may be. Some studies also consider subjective refraction to be the gold standard, using that as a basis to find comparisons for other tests. Therefore, for the purposes of this study, the most valid method to get results which are able to provide solid information to community optometrists, is to use the method most commonly undertaken and understood by them – subjective refraction. The statistical analysis used to access the data and find associations can also vary between studies. This makes it more difficult to compare the conclusions gained from other authors. This study attempts to gain enough data to be representative of many community optometric practices, using the methods used commonly by optometrists, analysing data usually gained as part of a sight test, so that the information can be directly transferred back into clinical practice to allow thorough discussions on possible future outcomes for patients. Regional differences such as smoking and education levels may need to be taken into account to reflect these influences. The continuing varying debate of whether sex influences refraction, and

the novel investigation of season of birth affecting astigmatism development was investigated, and associations between astigmatism and myopia.

Chapter 3: Methodology

3.1 Objectives

This chapter describes the methods used in collecting and analyzing both cross-sectional data and longitudinal data, and discusses why certain criteria and analyses were chosen.

3.2 Research ethics

Application for ethical approval was made to the Health and Life Sciences Research Ethics Committee at Aston University. It was deemed to have low potential risk, and approval was granted in November 2014 to begin collecting data (appendix 2).

The data were collected anonymously from two Specsavers practices. A privacy statement on the Specsavers website (Specsavers, 2016) provides information to patients about what is done with their personal details. It advises them that any part of their personal information, including prescription results, may be collected and processed by those working for the Specsavers group. For this reason, and as there were no interventions or changes in the test methods, no informed consent was required for the patients or their parents.

All data was collected in practice from computerised records, using only the patient number as a reference into a single paper source. Therefore, once the information was out of the practice, there was no way to identify the patients, or connect them to the prescription, other than to use their patient number back in the practice if any details needed to be confirmed. This was therefore in line with the Data Protection Act (1998).

Once the data had been removed from the practices, only three researchers had access to it (Laura Knowles, Nicola Logan and Mark Dunne). None of the researchers had any financial or proprietary interest in any of the products described or used as part of the study.

3.3 Practice setting

3.3.1 Locations

The two practices used for the studies were both part of the joint venture group Specsavers Opticians. The smaller, suburban practice in the Old Swan area of Liverpool, opened in 2007, and the larger, central city Liverpool Lord Street practice opened in 1989. The author had worked in the Lord Street practice from 2001 until 2007. She was the director of the Old Swan practice from 2007 until 2016, and her business partner was the director of both practices. This provided standardisation of patient care and common treatment of patients, and equipment providers and maintenance. The Lord Street practice underwent relocation in 2010, and with it came an upgrade of equipment.

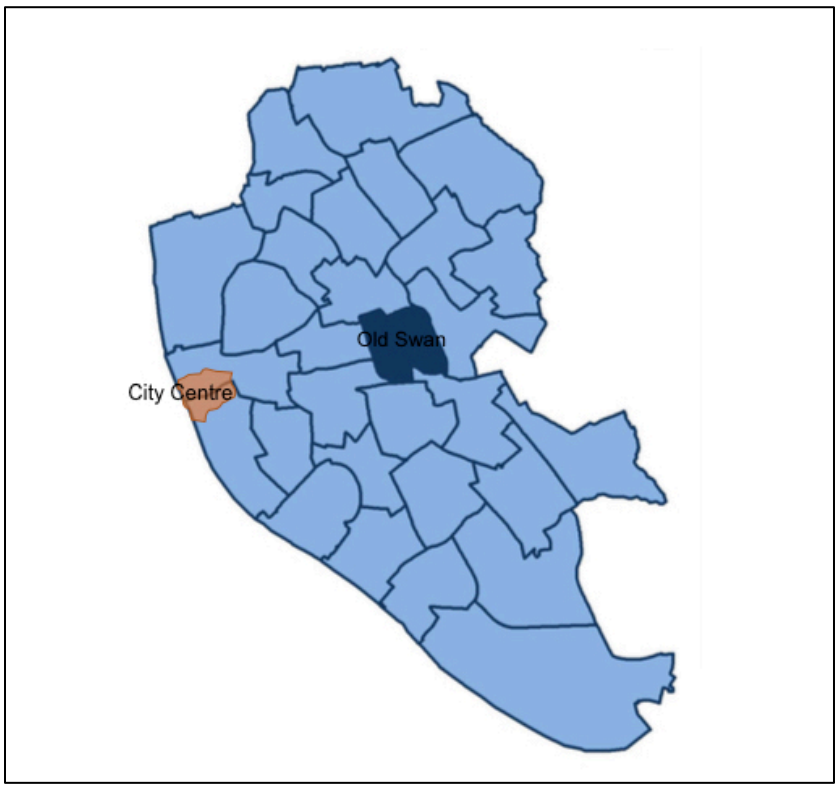


Figure 3.1: Map of Liverpool showing City Centre and Old Swan locations. Image taken from https://liverpool.gov.uk/media/9959/old-swan.pdf

The population of Old Swan was 16,212 in 2014, with 3152 children under 16 years of age (Liverpool City Council, 2016), and the practice in Old Swan had a relatively small catchment area. By comparison, the city centre had a higher population of 23,388, with only 1006 children under the age of 16 years (Liverpool City Council, 2016). However, the patients attending this practice tend to come from a wider

catchment area of the city as they come in for work and shopping.

The England Indices of Deprivation use information on demographics such as employment, income, health and crime to calculate a relative measure of deprivation for comparison, and is published for each local authority area. Liverpool overall has the highest level of deprivation compared to the rest of England, with nearly a quarter of England's most deprived area in the city (Liverpool City Council, 2015). The Old Swan practice is located in the lowest 10% of deprived areas in England. The city centre Lord Street practice is located in a much less deprived part of the city, just worse than average for England.

3.3.2 Test room equipment

Each testroom (the single location of the Old Swan practice, and both premises of the Lord Street practice) was designed by the Specsavers business development team, and built by Specsavers approved shop fitters. They were measured to be 3.2 metres in length as is the standard used by Specsavers, with a mirror used to create testing distance of 6m.

Autorefractors used were Nidek Tonoref II in Old Swan, and the Nidek ARK530A in Lord Street (both supplied, installed and regularly serviced by Birmingham Optical Group and their engineers).

Testroom charts currently in both practices are the Nidek SC-1700 or the SC-2000 (supplied, installed and checked by Birmingham Optical Group and their engineers in both practices). The LCD backlights were all set of 4, giving consistent contrast between the brightness of the screen and black letters, as the manufacturers' factory (and recommended) setting.

Both practices use the Nidek RT-2100 or RT-5100 phoroptor heads (supplied, installed, and checked by Birmingham Optical Group and their engineers). Where a phoroptor was unavailable, or it was difficult to achieve a reliable refraction (for example if a child struggled to maintain sitting still to look through the phoroptor apertures), an Oculus trial frame and reduced aperture trial lenses were used to complete the subjective refraction.

3.3.3 Lighting

All Specsavers practices underwent re-lamping in 2012 using the same manufacturer of lamps, and the same company for installation. This was to ensure

both consistency for sight test results, and that the practices looked bright, and allowed sufficient lighting for patients to choose spectacles.

3.3.4 Optometrists involved

Results from four optometrists were used in the cross-sectional part of the study, including the author. This included two from each practice. The optometrists involved were all trusted employees of Specsavers, two of them having been the author's pre-registration students. All were UK trained and examined, and were registered with both the General Optical Council (GOC) and Ophthalmic National Performers List.

Due to the nature of the practice logistics, and convenience for the patient, the same optometrists were not necessarily available to test patients on a repeat basis. Therefore, for the longitudinal data, all patients with the required timescale of data were included, regardless of who tested them. However, this is reflective of many, particularly larger high street practices, and the results can still be used to gather relevant information to guide optometrists in this similar environment.

3.3.5 Participants

The participants were patients aged 1-18 years (mean 11.1 years) at the time they were tested in 2013. Patients were excluded from the study if they had conditions likely to affect the prescription of VA, such as strabismus, amblyopia, ptosis, corneal opacity or disease, cataract or IOL. Of the 960 patients examined by the four optometrists, 60 patients were excluded in total: 57 with strabismus/amblyopia, 1 with keratoconus, 1 with IOLs, and 1 with unilateral lid scarring (with consequently higher astigmatism). This left 900 patients for data analysis. There were 545 girls (60.5%), and 355 boys (39.5%). This allowed analyses to find associations in the large amount of cross-sectional data. From this group of patients tested in 2013, further data were collected from patients who had previously visited either of the practices for a minimum of 5 tests, or over a period of 5 years or more. To expand this group numbers, the patients who had been tested 4 times, or over 4 years in 2013 were highlighted, and their records checked again in 2015 to see if they had returned for an additional sight test, allowing them to be incorporated into the study before statistical analysis began. This number of longitudinal patients totalled 242 patients, including 138 girls (57.0%) and 104 boys (43.0%), and allowed investigation into relationships around refractive progression as part of the longitudinal section of the study.

3.4 Test procedures and limitations

3.4.1 Test methods

All patients attending either store received an initial 'pre-test', which included (non-cycloplegic) autorefraction, before seeing an optometrist. Non-contact tonometry, visual fields and fundus photography were tested as deemed necessary by the testing optometrist (rarely in patients under 19 years of age).

The monocular subjective refraction method was used by all optometrists, obtaining the most plus prescription to gain maximum visual acuity (VA), along with the Jackson cross-cylinder method to assess astigmatism power and axis.

Cycloplegic refractions were undertaken if a reliable result was not obtained through subjective testing and/or there were symptoms to suggest further investigation was warranted. The College of Optometrist Management Guidelines (College of Optometrists, 2014) advise that cycloplegic refraction should be considered in children

> *"to give an accurate assessment of the refractive error, which is the major factor in amblyopia or squint."*

Scheiman and Wick (2008) also discuss that

> *"Static retinoscopy and dry subjective refraction are sufficient to determine the refractive error in most cases. When esophoria is present or latent hyperopia is suspected, a cycloplegic refraction may be helpful."*

This occurred in only 2 patients from the cross-sectional data. This may be considered low for optometric practice, although there is no current information on the number of cycloplegic refractions completed in general practice to the author's knowledge.

This may be because the number of patients in the younger age groups, for whom cycloplegic refraction may have had the most benefit, were of low volume in the study (there were 29 patients aged 1-5yrs).

It could be the case that some of the patients had previously had a cycloplegic refraction in the practice or elsewhere (possible as the children's' hospital Alder Hey is located near to the Old Swan practice). Other possibilities include a reliable level of VA and/or refraction was achievable without subjecting the patient to what were deemed unnecessary tests, or were deemed to be low risk for amblyopia or squint

from the other tests performed. Squint and amblyopia are usually related to hyperopic corrections or accommodative issues, and so are less relevant in this study, as it is the myopic and astigmatic powers of refraction that are being assessed.

3.4.2 Inter-test variability

It is well documented that some degree of variability is to be expected between tests completed at different times (Freeman et al., 1955; Zadnik et al., 1992; Rosenfield and Chiu, 1995; Elliott et al., 1997). Zadnik et al. (1992) assessed the power in the vertical meridian using several techniques, and found that non-cycloplegic subjective testing showed a repeatability of ±0.63D at the 95% limit of agreement, whilst for cycloplegic autorefraction the repeatability was ±0.32D. However, results for non-cycloplegic and cycloplegic retinoscopy were less reliable, at ±0.78D and ±0.95D respectively. Rosenfield and Chiu (1995) assessed SER, and found that there was a similar degree of repeatability with subjective refraction and auto-refraction at 95% limits of agreement of ±0.29D for subjective testing compared to ±0.27D in auto-refraction. These studies all suggest that a subjective refraction may be variable by between 0.27D to 0.63D for an individual patient (and therefore a change in prescription of 0.50D to 0.75D should be considered significant in any patient). It should be noted that these amounts are not directly comparable as some studies looked at horizontal or vertical meridians (or both), and some on SER or spherical results.

Of this group, only Rosenfield and Chiu (1995) studied astigmatism power repeatability, and found there was less variation for astigmatism power than for sphere or SER power (±0.16D, ±0.27D and ±0.29D, respectively for 95% limits of agreement), and that cylinder axis assessment would be within 17.1 degrees for 95% limits of agreement. Lam et al. (1999) found that there was an individual repeatability of 0.50D for astigmatic power, and so this higher level as taken as the significant amount of astigmatism to be deemed a change.

3.4.3 Inter-clinician variability

It is also understood that refraction results may vary with different clinicians. Most studies confirm that results will be within 0.50D of each other (Perrigin et al., 1982; Bullimore et al., 1998; MacKenzie et al., 2008; Shah et al., 2009; Reinstein et al., 2014). Leinonen et al. (2006) found slightly higher variability, with up to ±0.74D between clinicians.

Perrigin et al. (1982) and Shah et al. (2009) found similar results that (non-cycloplegic) subjective refraction would be within ±0.25D 93% and 90% of the time (respectively) for spherical results, and 93% for astigmatic results (the same value). The results for a refraction to be within ±0.50D were 99% and 98% respectively for spherical values, and 99% and 100% for astigmatic values.

Bullimore et al. (1998) found an average difference between 2 optometrists' subjective refraction for 86 patients to be -0.12D (with one optometrist consistently finding more myopic results), +0.01D difference in J_0 values, and 0.00 difference in J_{45} between the clinicians. Although the variations in prescription were wider when compared with autorefraction, the mean difference is still smaller than a single refraction step of 0.25D.

In this study, 4 clinicians (one of which was the author) were used to gain a large number of patient episodes allowing data with sufficient power to be obtained. They were all UK trained and registered, with 2 of them the author's pre-registration students, so likely to work their routine test procedure in a similar manner.

Although inter-clinician variability may add another level of error to any results, this is typical of community practices where a different optometrist may see a patient for different tests within the same practice, or coming from a different practice.

3.4.4 Cycloplegia vs. non-cycloplegia

Whilst cycloplegic auto-refraction may be taken as the gold standard for epidemiological refraction studies in children (Zhao et al., 2004; Fotedar et al., 2007), there is also some suggestion that it should also be the case in adults (Morgan et al., 2015). Cooper et al. (2011) however, states that there

> *"is no perfect gold standard for refraction, because many factors in addition to VA can be considered, including the patient's accommodative ability, blur interpretation, contrast sensitivity, cognitive ability, ambient and task lighting, and visual demands, among others."*

In addition, Bullimore et al. (1998) wrote that

> *"Traditionally, the clinician's refraction has been used as the gold standard against which other techniques, including automated refraction, have been judged."*

In studies that do use cycloplegia to determine a subject's refraction, the method and drugs used to obtain cycloplegia, and assessment of whether full cycloplegia has been attained varies. Tropicamide (Lin et al., 1999; Shih et al., 2004), cyclopentolate (Zhao et al., 2002; McKean-Cowdin et al., 2011), or combinations of both (Kleinstein et al., 2003; Pärssinen et al., 2014) have been used. Some also use sympathomimetics (Larsson et al., 2015), or various anaesthetic drops before cycloplegia installation (Egashira et al., 1993; Huynh et al., 2006; Giordano et al., 2009; Logan et al., 2011). Others use cycloplegia in younger children but not in older children (Edwards and Shing, 1999; Fotouhi et al., 2011), and they may use between 1 and 3 drops of cycloplegic agent.

They may also differ in the collection of results; with different time periods between drop installation, after cycloplegic installation, and with only some checking whether cycloplegia has been attained.

This means that direct comparison is not always possible, and as such, it could be considered that there may be no gold standard of data collection, just a best comparison. Indeed, the American Academy of Ophthalmology (2012) suggests that levels of cycloplegia will vary according to weight, iris colour and dilation history, and that

> *"Tropicamide and phenylephrine may not be strong enough to produce adequate cycloplegia".*

Some studies do not use cycloplegia at all (Pointer, 2001; Williams et al., 2008; Plainis et al., 2009; Rezvan et al., 2011). Funarunart et al., (2009) state their belief that non-cycloplegic retinoscopy and subjective refraction was clinically accurate enough to be used for refractive error screening in school children, after comparison with a cycloplegic refraction.

Non-cycloplegic refractions are likely to give a more negative refraction in children compared with cycloplegic assessment, due to residual accommodation (by between approximately 0.50D and 0.75D (Fotouhi et al., 2012; Hiraoka et al., 2014; Hu et al., 2015). All optometrists involved in this study were trained to give the maximum plus prescription to give optimum visual acuity to reduce this effect. In their review of cycloplegia, Eperjesi and Jones (2005) confirm cycloplegia can be of use in optometric practice for cases involving latent hyperopia, esotropia and non-organic visual loss. As subjective refraction is the standard test used in UK optometric practice to obtain spectacle prescriptions, and retrospective data was collected for this study, it was believed that the non-cycloplegic results would be

more relevant to the community optometrist interested in myopia and astigmatism, who does not cycloplege the majority of their younger patients routinely.
Prescribing full cycloplegic refractions is also uncommon, as there is a need to leave some accommodative lag, and as Cooper et al. (2011) report that

> *"Subjective refraction, verified by trial framing, still is the best method of achieving this clinical goal in most typical patients".*

In their comparison of two autorefractors, Elliott et al. (1997) and Isenberg et al. (2001) both compare results to their gold standard of subjective refraction, showing that this method clearly has a place for both epidemiological studies and community-based practice.

In terms of astigmatism, there appears to be less variation between cycloplegic and non-cycloplegic assessment than with spherical error. A mean astigmatic power difference of 0.02D was found on comparison of autorefraction with subjective refraction (Bullimore et al. 1998). Funarunart et al. (2009) found that non-cycloplegic autorefraction, retinoscopy and subjective refraction showed a clinically acceptable agreement in astigmatic power when compared to cycloplegic refraction. In terms of cylinder axis, only the autorefractor was outside their clinical acceptance level of 80% within 10 degrees – for subjective results 97.5% of the test results were within 10 degrees. Spherical subjective refraction also reached their clinically acceptable results, and so they concluded that subjective refraction, or retinoscopy without cycloplegia was adequate to screen children for spectacle requirements.

3.4.5. Method of assessment of refraction

Different studies also use different methods to assess refraction. Various auto-refractors may determine refraction (Kleinstein et al., 2003; O'Donoghue et al., 2011; McKean-Cowdin et al., 2011), or retinoscopy (Gwiazda et al., 2000), and thus giving varying prevalence data (Zhao et al., 2000; Maul et al., 2000).

Studies comparing different autorefraction machines and retinoscopy methods have found variations in results for both SER and astigmatism, even under cycloplegic conditions in children (Gwiazda and Weber, 2004; Isenberg et al., 2001; Choong et al., 2006; Prabakaran et al., 2009; Funarunart et al., 2009; Arici et al., 2012), and non-cycloplegic conditions (Cooper et al., 2011). Choong et al. (2006) compared cycloplegic autorefraction with non-cycloplegic subjective refraction in children as part of the RESC study, and found that, although the monocular subjective SER

was more myopic by 0.26D if cycloplegia was not used, the astigmatism power and axes remained similar, and were in fact, more variable when measured on 3 autorefractors, even under cycloplegia.

Adult studies also show some variation in both spherical/SER data (Elliott et al., 1997; Gwiazda and Weber, 2004; Cooper et al., 2011) and astigmatic data (Bullimore et al., 1998; Gwiazda and Weber, 2004; Cooper et al., 2011). Bullimore et al. (1998) found that the SER could be up to ±0.81D different between autorefraction and cycloplegia (which they noted was similar to the inter-clinician repeatability). Cooper et al. (2011) found that some autorefractors tended to over-estimate low astigmatism by as much as -0.87D, which could also be out by more than 10 degrees in the axis when compared to subjective refraction.

This shows that spherical and astigmatic results vary when measured under different conditions, and that consistency is important when comparing the results from any study.

3.5 Methodological modifications

Initially all children were going to be considered for the study. For Old Swan (the smaller practice), the two employed optometrists covered each other's holidays so no locums were used. However, when gathering data from Lord Street (the larger practice), it was noted that many locums were hired as well as the employed optometrists. It was therefore decided that using data from two optometrists from each practice would reduce the likely inter-clinician variability, whilst still giving enough data. The subsequent number of sight tests in 2013 still provided sufficient data for a small effect size to be recorded with an alpha level of 0.05 and 80% power.

In order to increase the numbers for the longitudinal study, those patients who had been tested 4 times, or over 4 years at their sight tests in 2013 were noted down and their records rechecked again in 2015. If there were further tests completed, these patients were added to the data to improve the statistical power.

3.6 Data collection

Data were collected initially using NHS submission forms, selecting those children who were tested by the specific optometrists from all NHS patients. Later, the newly formed NHS audit team was able to supply more specific information on children's' sight test data, which allowed more efficient collection of data.

Data were taken from refractions of the right eye, as previous studies have found high correlation between right and left eyes for both SER (Lin et al., 1999; Fan et al., 2004; Gwiazda and Weber, 2004; MacKenzie, 2008; Giordano et al., 2009; Fotouhi et al., 2011; Pärssinen et al., 2013) and astigmatism (Fan et al., 2004; Giordano et al., 2009; Pärssinen et al., 2013; Marasini, 2016). Many epidemiological studies therefore use information from the right eye only for their assessments so as not to duplicate work or influence results (Edwards and Shing, 1999; Goss, 1999; Fan et al., 2004; Harvey et al., 2014; Pärssinen et al., 2014).

It should, however, be noted that in some studies, the axes of astigmatism may not show a direct association between eyes, as determined by McKendrick and Brennan (1997), or may show mirror symmetry as found in a larger study by Guggenheim, et al. (2008). Solsona (1975) studied more than 51,000 patients' refractive error data, and when he looked at the axis of astigmatism, found that 67.5% of them showed mirror symmetry to within 10 degrees. If mirror symmetry is assumed to be the norm, the definitions used for WTR, ATR and oblique astigmatism should still give comparable results to previous studies of refraction using the right eye only for data (Zadnik et al., 2003), and will be sufficient for this study to give reliable results on prevalence and progression.

The refraction from all children tested in 2013 was recorded along with date of birth, patient number and date of test, with no information to allow identification of the patient externally, as the data was removed from the premises to be inputted into Microsoft Excel (Microsoft Office, 2011). There were two Excel spreadsheets designed to allow analysis of both the cross-sectional and longitudinal parts of the study.

3.7 Definitions

The same definitions for refractive error and astigmatism were used in all statistical analyses for both cross-sectional and longitudinal data, summarized in table 3.1.
The refractive data were calculated as spherical refractive equivalent (SER): -

$$SER = \text{spherical power} + \frac{\text{astigmatic power}}{2}$$

as used by Thibos et al. (1997), Funarunart et al. (2009), French et al. (2013).

Astigmatism was defined as being present if the patient showed a power difference between axes ≤-0.50DC, myopia as ≤ -0.50D, and hyperopia as ≥+0.50D, with emmetropia >-0.50 to <+0.50D. These levels were chosen as they represent a figure between three studies of inter-test repeatability (section 3.4.2) and of inter-clinician variability (section 3.4.3). As routine refraction is measured in 0.25D steps, these figures suggest that changes of around 0.50D are required before we can say that there has been a significant change in refraction. The American Optometric Association (AOA, 2006) suggest that changes as low as 0.25D may be discernable to some patients who are more sensitive to blur, and the College of Optometrists (2014) suggest that only some patients will benefit from prescription changes of 0.25D. Although Rosenfield and Chiu (1995) found a smaller repeatability for astigmatism of ±0.16D (and ±17.1 degrees for axis), Villegas et al. (2014) and the AOA (2006) suggest that the minimum astigmatic correction to show an improvement in VA is likely to be 0.50D.

The definition of with-the-rule (WTR) astigmatism was split as negative cylinder axes at 180±20, against the rule (ATR) as negative cylinder axes at 90±20, and oblique axes between 21 and 69, and 111 and 159. This is the same definition used in previous studies by Shih et al. (2004) and Rezvan et al. (2011).

Variable	Sub category	Definition
Astigmatism	Absent	<0.50D
	Present	≥0.50D
Astigmatic axis	None	-
	WTR	180±20
	ATR	90±20
	Oblique	21-69 and 111-159
Refractive error	Emmetrope	>-0.50 to <+0.50D
	Hyperope	≥+0.50D
	Myope	≤-0.50D

Table 3.1: Summary of refraction criteria and their definitions.

Seasons were divided using similar methods in previous studies (McMahon et al., 2009; Ma et al., 2014): -

- Winter – December, January, February
- Spring – March, April, May
- Summer – June, July, August
- Autumn – September, October, November

Because different studies use different definitions for astigmatism power and axis, direct comparison between studies is difficult. Thibos et al. (1997) described the power vectors J_0 and J_{45} in order to combat this, to combine the power and axis into a single resultant comparable figure: -

$$J_0 = -0.5(C \times \cos[2a])$$

$$J_{45} = -0.5(C \times \sin[2a])$$

J_0 represents the power in the vertical meridian (90°), and J_{45} the power at the oblique meridian of 45°. A positive J_0 represents WTR astigmatism, and a negative J_0 represents ATR astigmatism. A positive J_{45} represents a negative astigmatic axis at <90°, and a negative J_{45} at >90°.

Frequency graphs were drawn for the measures J_0 and J_{45} to allow for comparison between other studies and included in chapter 4. However, as J_0 and J_{45} are not used in practice, and astigmatic power and axis were chosen for analysis in chapters 5, 6 and 7, to allow direct comparison with clinical practice optometry.

3.8 Statistical analyses

Microsoft Excel (Microsoft Office 2011) spreadsheets were programmed to convert the sphero-cylinder sight test results into categorized data. There were two Excel spreadsheets designed to allow analysis of both the cross-sectional and longitudinal parts of the study. For longitudinal data, Excel was programmed to use the intervals between the initial and final sight tests, and, using the total change in refraction, the mean slopes of myopic and astigmatic progression were calculated. Excel spreadsheets for both cross-sectional and longitudinal data were then transferred to IBM SPSS (v.23) for analysis.

Decision Tree Analysis (DTA) is a non-parametric multivariate statistical test, which can be used to explore the influence of independent variables on a dependent variable. The resulting tree diagram places the variables along different branches according to the strength of their influence on the dependent variable assessed, with

stronger variables closer to the top of the tree. The method has previously been used in ophthalmological research (Twa et al., 2005; Shekar and Srinivas, 2008; Yu et al., 2011; Rushton et al., 2016).

This study used The CHAID (CHi-squared Automatic Interaction Detection) algorithm as the growing method as used by Dunstone et al. (2013) and Rushton et al. (2016).

The number of independent variables that influence the dependent can also be specified. Although there are no guidelines to specify the node sizes in DTA (Collins et al. 2010, p291) advised that it should be guided by the sample size. SPSS uses default node sizes of 100 in the parent node, and 50 in each child node. Appendices 4 and 5 show the frequency tables for each category of data. As the frequencies were small in several groups, and as this study wanted to investigate all potential associations, the parent nodes were reduced to 10 and child nodes to 5. The number of branches was set to 10 (changed from the default of 3), to allow full tree growth and to explore all potential effects. Once analysed, this change from the default did not affect the results, suggesting their strong significance.

Decision tree analysis is designed to work with categorical data. As some of the variables used were continuous (age, astigmatic and myopic progression), the data was changed to categorical data. As arbitrary splits for age could not be decided upon, median splits were used to divide the data into two groups. For refractive error results, the decision was made to classify the split at the point of significant change in repeatability data as discussed in sections 3.4.2 and 3.4.3, i.e. 0.50D. Progression of myopia and astigmatism were categorized by median splitting, rather than the grouping of significant refractive change, as both measures of the mean annual progression were significantly smaller than the 0.50D changes seen in repeatability studies (Rosenfield and Chiu, 1995) or refraction guidelines (Villegas et al., 2014). These outcomes are summarized in table 3.2.

Variable	**Sub category**	**Cross-sectional**	**Longitudinal**
Age	Younger	<11.1 years	<8.8 years
	Older	≥11.1 years	≥8.8 years
Astigmatic Progression	Lower	-	<0.014D/year
	Higher	-	≥0.014D/year
Myopic Progression	Lower	-	>-0.10D/year
	Higher	-	≤-0.10D/year

Table 3.2: Summary of variables used and their definitions

Alongside each DTA illustration, model summary information was displayed to show the variables investigated, the growth method, the parent and child node information and a summary of the significant results.

G*Power3 software was chosen to calculate sample power (Faul et al., 2007). With the conventional alpha level of 0.05 and power of 80%, G*Power3 calculated that for the maximum degrees of freedom of 9 in this study (that is 1 minus 4 seasons multiplied by 1 minus 4 axis categories), the minimum sample size required to show a medium effect was 174. This was exceeded in both the cross-sectional (n=900) and longitudinal (n=242) studies. Iacobucci et al. (2015) suggested that categorizing continuous data reduced the power by 20%, particularly when using median splitting. A 20% reduction in participants for both the cross-sectional and longitudinal sections of the study maintained the minimum sample size set by G*Power (720 and 194 respectively).

3.9 Variables of cross-sectional study

The data collected as described above were divided into the following categorical groups to find results of the prevalence of different forms of refraction, and whether there may be links with certain independent variables: -

Dependent variables

- Astigmatism (absent, present)
- Astigmatic axis (none, WTR, ATR, oblique)
- Refractive error (myope, hyperope, emmetrope)

Independent variables

- Age (younger, older, divided by median splitting)
- Sex (female, male)
- Birth season (Spring, Summer, Autumn, Winter)

3.10 Variables of longitudinal study

The longitudinal section of the study was designed to analyse progression of astigmatism and myopia. As well as the independent variables used to analyse the cross-sectional data, measures of initial refraction details were used to assess

whether they may play a part in astigmatic or myopic progression. They were categorized: -

Dependent variables

- Astigmatic progression (lower, higher, divided by median splitting)
- Myopic progression (lower, higher, divided by median splitting)

Independent variables

- Initial age (younger, older, divided by median splitting)
- Sex (male, female)
- Birth season (Spring, Summer, Autumn, Winter)
- Initial astigmatism (absent, present)
- Initial axis (none, WTR, ATR, oblique)
- Initial refractive error (myope, hyperope, emmetrope)

3.11 Summary

There are many studies analysing refraction in full epidemiological studies, with many claiming to be based on gold standard protocols. However, these protocols may not be directly comparable to each other, nor the standardized testing used in optometric practice, meaning few can be used as a direct source of information and comparison by community optometrists. As well as providing normative data from a population of children attending community practice, this study was designed to enable optometrists to make judgments on the care of their patients based on comparative practice-based research, using information that will be readily available to clinicians as part of their daily practice.

Chapter 4: Cross-sectional analyses of astigmatism and myopia

4.1 Objective

This chapter includes the frequency distributions of the population studied using methods explained in chapter 3. Prevalence of astigmatism and myopia in children who attended two optometric practices for sight testing in 2013 are presented, as are Chi-square associations between the variables.

4.2 Results

4.2.1 Demographic Factors

The refractions of 900 children under 19 years (age range 1-18, mean 11.1yrs) were recorded from samples from the two practices (figure 4.1). 429 children were from Old Swan, and 471 were from the practice in central Liverpool. There were 545 girls (60.6%), and 355 boys (39.4%) (Figure 4.2). The higher numbers of girls attending for a sight test was significantly higher when measured using one-sample Chi-square testing ($p=<0.001$).

The patients were split across all four seasons in terms of their season of birth (figure 4.3), and differences were not significant on one-sample Chi-square testing ($p=0.951$).

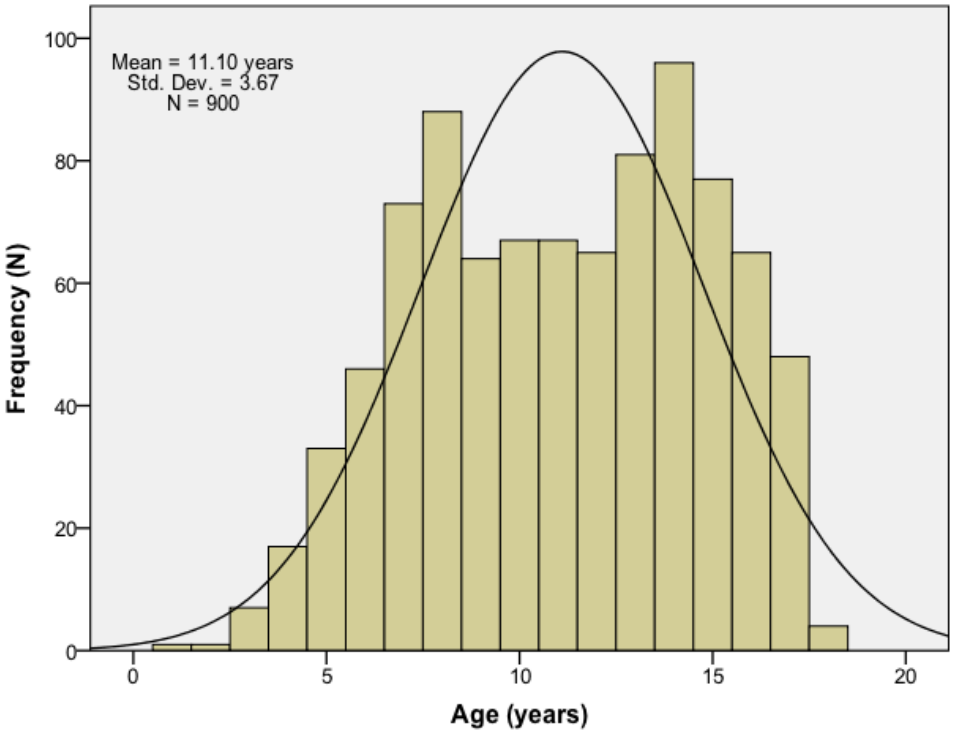


Figure 4.1: Frequency distribution graph showing age of subjects attending for a routine sight test at both practices. Normal curve shown for comparison.

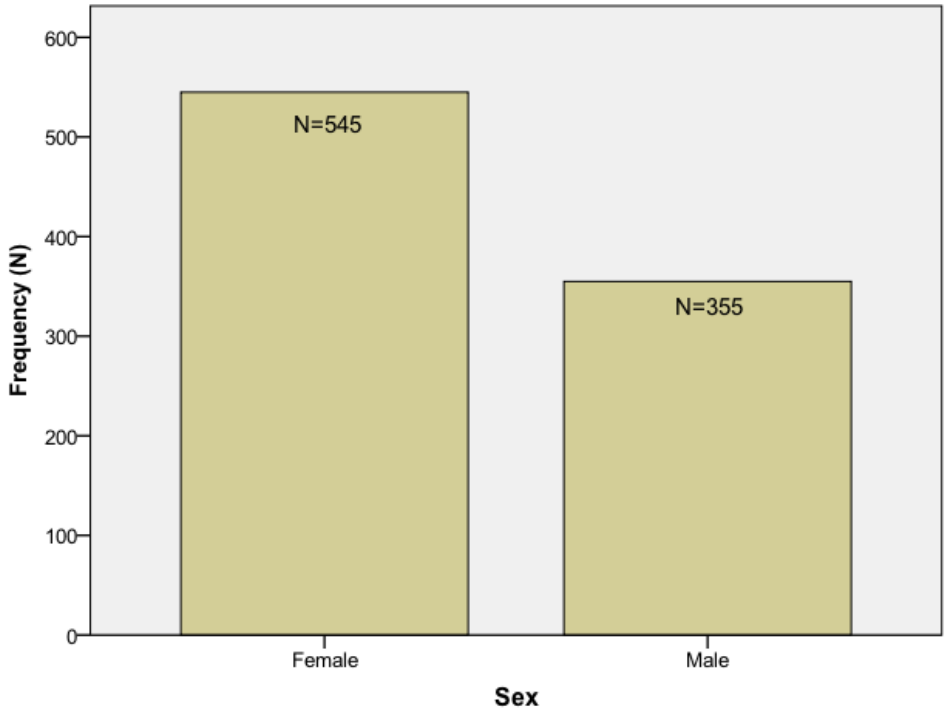


Figure 4.2: Sex of patients attending the two practices for a routine sight test.

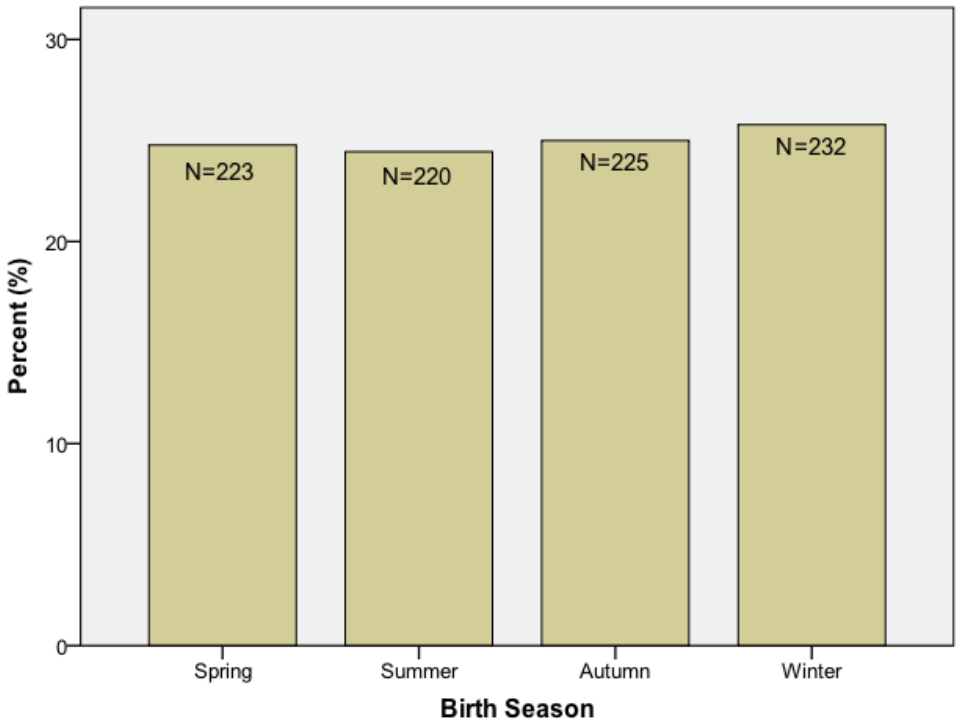


Figure 4.3: Distribution of patients according to birth season.

4.2.2 Astigmatism

403 children (44.8%) had astigmatism ≥0.50D (figure 4.5). If the power was increased to ≥1.00D, as has been used by Kleinstein et al. (2003), Tong et al. (2004) and O'Donoghue et al. (2015), the prevalence was 147 (16.3%). Some studies also discuss those with high astigmatism ≥3.00D (Gwiazda et al., 2000; Farbrother et al., 2004, Harvey et al., 2014), which include 21 of the sampled children (2.3%).

The overall prevalence of astigmatism was similar for myopes and hyperopes, with 55.4% of hyperopes, and 51.5% of myopes having astigmatism ≥ -0.50D.

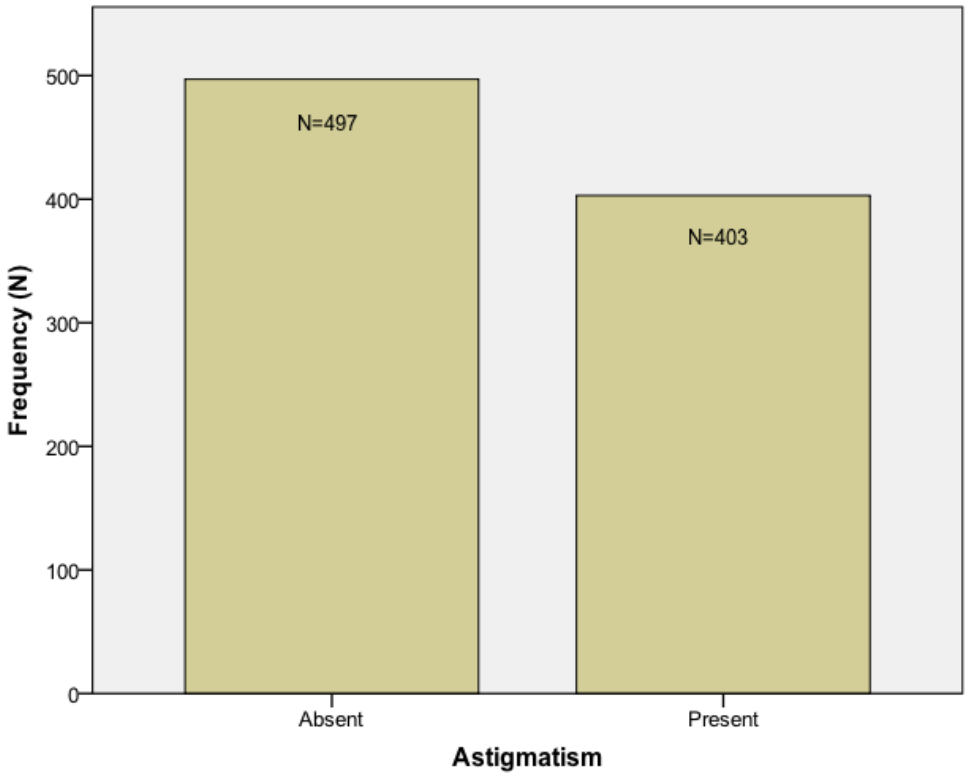


Figure 4.4: Patients with astigmatism ≥0.50D present and those with astigmatism <0.50D (classed as absent).

The maximum amount of astigmatism was 5.25D, and the population overall showed a mean astigmatic power of 0.54D (SD 0.73). Figures 4.5 and 4.6 show the distribution of the astigmatic powers J_0 and J_{45} for comparison with other studies using different criteria for axis. The large peaks around zero for both J_0 and J_{45} show that the majority of astigmatism was small or absent. The mean J_0 (0.979) represents higher amount of WTR astigmatism compared with ATR, as shown in Figure 4.7. The mean J_{45} (0.0196) represents a slight preference for oblique astigmatism at the axis of 135.

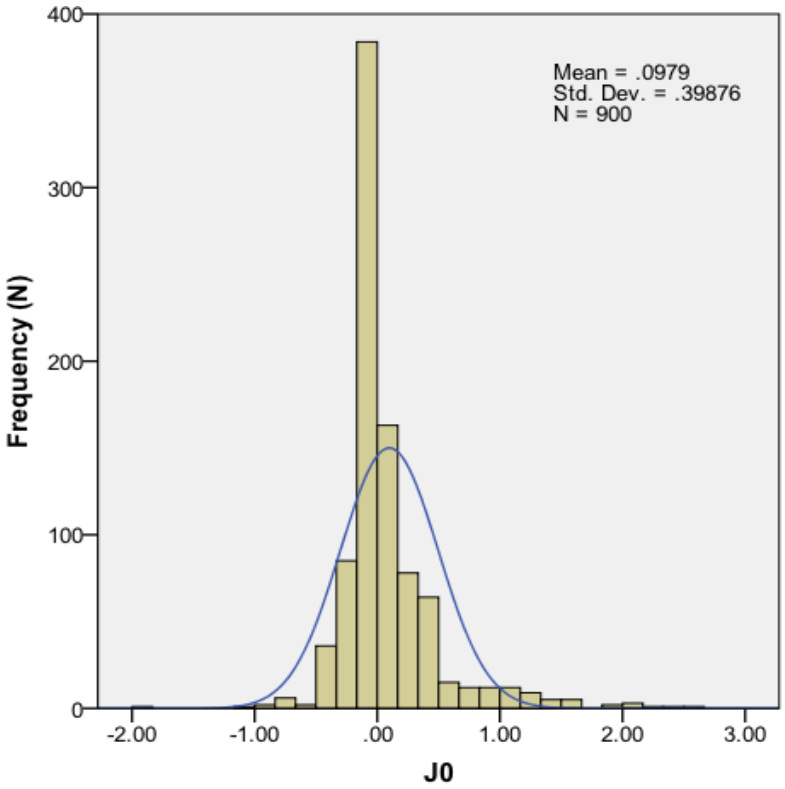


Figure 4.5: Frequency distribution of J_0 in the cross-sectional population. The normal curve is shown for comparison.

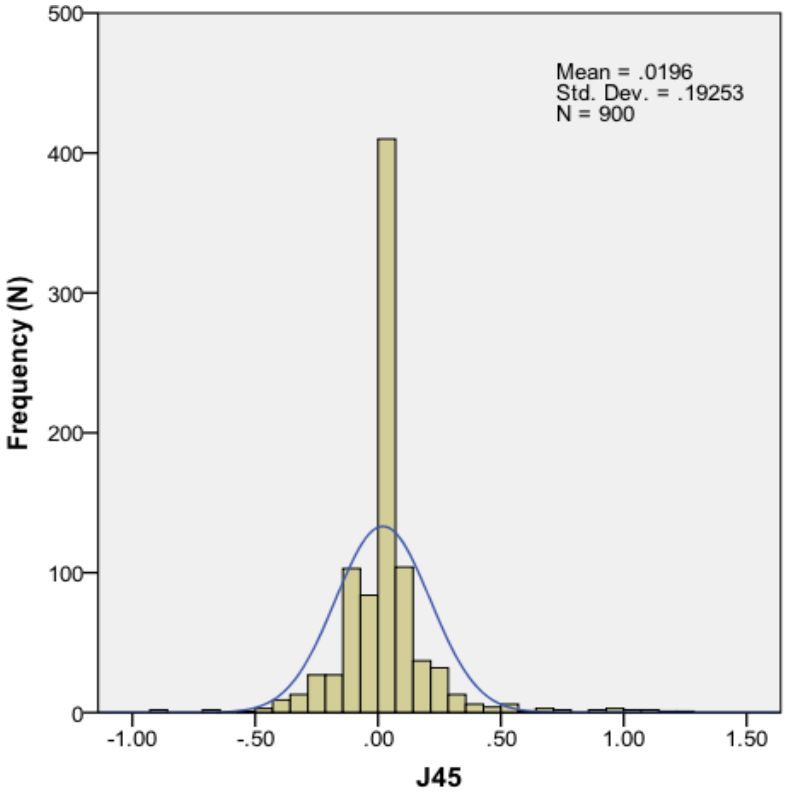


Figure 4.6: Frequency distribution of J_{45} in the cross-sectional population. The normal curve is shown for comparison.

Figure 4.7 shows the distribution of astigmatic axis groups in the population tested. Of those with astigmatism ≥-0.50D, WTR astigmatism accounted for the majority, with 199 (49.4%) children. 127 children had ATR astigmatism (31.5%), and 77 had oblique astigmatism (19.1%).

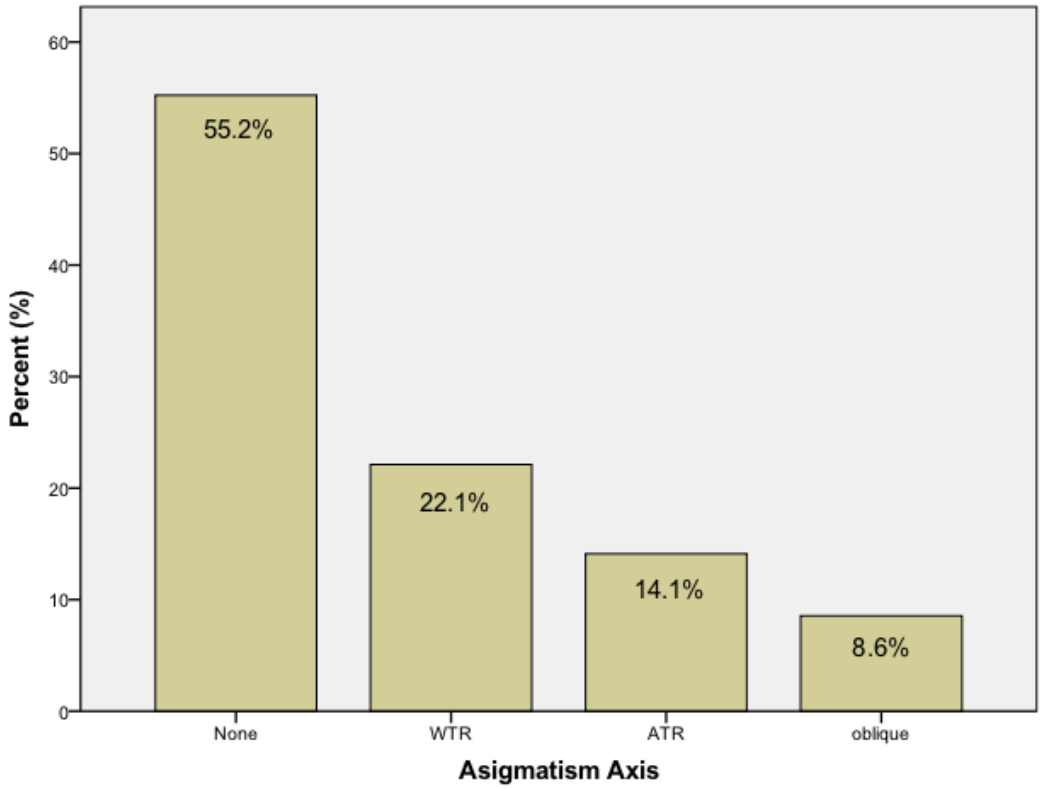


Figure 4.7: Distribution of patients within each cylindrical axis group.

4.2.3 Spherical refractive error

The distribution of refractive error is shown in Figure 4.8. The range of SER was +7.88 to -8.88D (mean +0.04D, SD 2.037). The distribution shows the highest peak around the low refractive errors as may be expected from previous studies (Pokharel et al., 2000; Zhao et al., 2000).

The prevalence of myopia was 29.3% (with 264 children having an SER of ≤-0.50D). There were 351 emmetropic children (a prevalence of 39.0%) and 285 hyperopes with a prevalence of 31.7% (Figure 4.9).

207 of the myopes had an SER of ≤-1.00D (23.0%), a definition also used in previous studies (Huynh et al., 2006; Logan et al., 2011; Guo et al., 2015), and 7 had SERs of high myopia ≤-6.00D (0.8%).

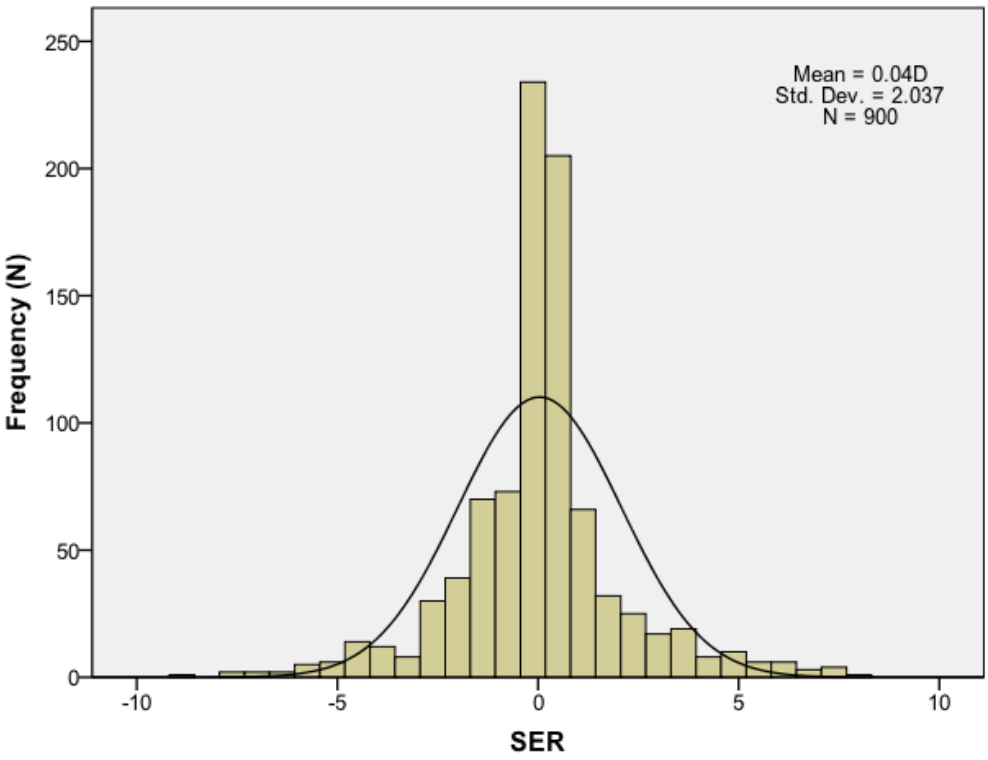


Figure 4.8: Frequency distribution of spherical equivalent refraction (SER) in patients attending a routine test in the two practices. The normal curve is shown for comparison.

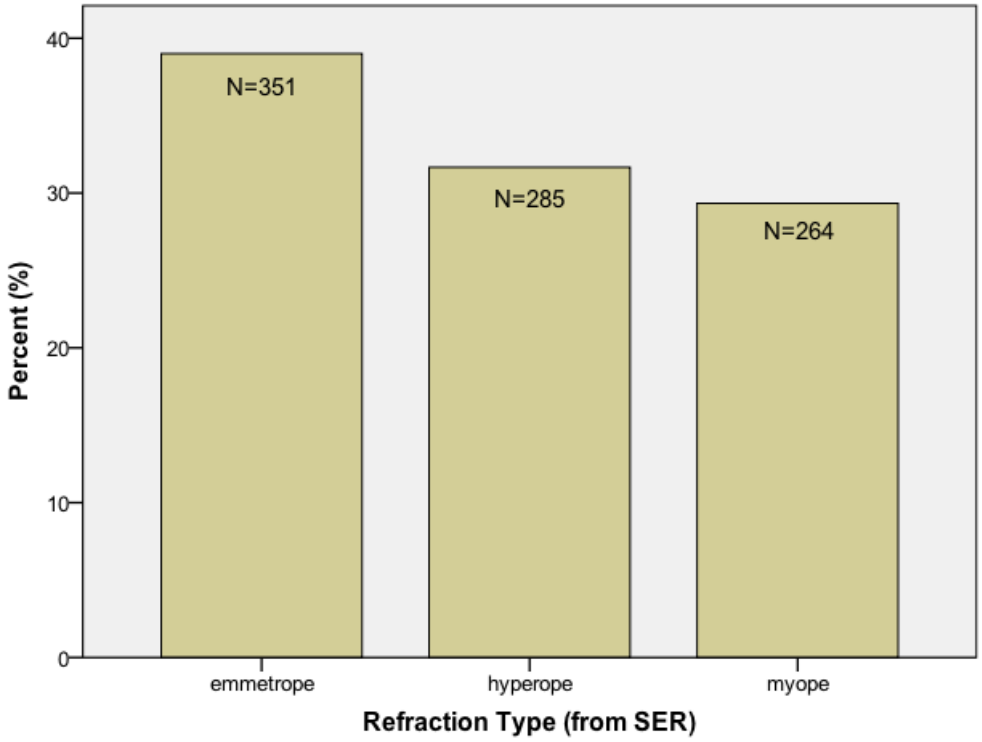


Figure 4.9: Distribution of refractive error groups. Myopia ≤-0.50D, emmetropia >-0.50D to <+0.50D, and hyperopia ≥+0.50D SER. N = 900.

4.2.4 Statistical analyses

None of the continuous data was normally distributed, similar to other studies (Cheng et al., 2007; Li et al., 2015). Any continuous data was converted to categorical data and median splitting was applied prior to DTA (chapter 5). Therefore, Chi-square testing for associations was performed, as shown in table 4.1.

Chi-square	Sex	Birth Season	Astigmatism	Axis	Refractive Group
Age	19.208****	1.560	0.716	13.253***	73.824****
Sex		2.624	7.936***	11.309**	4.216
Birth Season			2.577	10.117	4.639
Astigmatism				900.00****	44.68****
Axis					76.093****
Significance: *p=0.05, **p=0.02, ***p=0.01, ****p=0.001					

Table 4.1: Chi-square associations between the variables analysed from cross-sectional data.

Whilst it is understood that there should ideally be no significant inter-associations within this data for DTA, these violations are impossible to eliminate, with some potential meaningful but unlikely results, such as an association between age and the sex of the patients. Whilst they should be acknowledged, they can be overlooked for the purposes of the study as they may introduce confounding if analysed alone. DTA attempts to remove this confounding, to give more reliable statistically significant conclusions than using Chi-square analysis to assess inter-associations alone.

4.3 Discussion

4.3.1 Demographic factors

Overall, more girls (n=545, 60.6%) than boys (n=355, 39.4%) attended for an eye test. Pointer (1996, 2000) noted a significant pattern in female preponderance for attending for sight tests, and it has been reported that women are generally more likely to utilize eyecare services (Wang et al., 1999; Keefe et al., 2002; Harris and Sampson, 2005; Hoffelt et al., 2011; McAlinden et al., 2016). It could suggest that girls may be more aware of their visual requirements, or have higher expectations of their vision compared with boys. It may also suggest a higher prevalence of all types of refractive error, meaning a more frequent attendance to appointments. However,

of the patients attending who were emmetropic, there was no difference between the sexes.

The prevalence data is also likely to be skewed to show higher prevalence rates of all types of refraction compared with epidemiological studies assessing the ocular details of school classes, because those children with reduced visual acuity are more likely to attend a practice more frequently to have their eyes examined. Therefore, the prevalence data for all types of prescription are likely to be higher, and that of emmetropes lower, compared with studies that use broader methods of gathering data, for example, from school classes.

4.3.2 Astigmatism

Compared with the spherical part of a prescription, astigmatism is less affected by whether or not cycloplegic refraction is carried out, in terms of sphero-cylindrical power and axis, and J_0 and J_{45} measurements (Fotouhi et al., 2011; Arici et al., 2012). Bullimore et al. (1998) found little difference between cycloplegic autorefraction and subjective refraction results for both cylinder power and axis, and Funarunart et al. (2009) found subjective cylindrical power was only 0.02D more myopic without cycloplegia. However, comparisons between different autorefractors have found significant differences under cycloplegic conditions (Gwiazda and Weber, 2004; Choong et al., 2006) and non-cycloplegic conditions (Cooper et al., 2011). Funarunart et al. (2009) found that in determining cylinder axis, subjective refraction was more repeatable than autorefraction, meaning that subjective refraction by experienced clinicians in this study may be at least as good an estimate of prevalence, power and axis in optometric practice as cycloplegic autorefraction.

Assuming the ethnicity of the population studied is similar to that of Liverpool measured as part of the Census in 2011, most patients will have been of white British origin. White European children have been shown to have the lowest prevalence of astigmatism when compared to other ethnicities, notably East and South Asians (Kleinstein et al., 2003; Huynh et al., 2006; Wen et al., 2013; Huang et al., 2014). The majority of astigmatism was low or absent (Figure 4.4), with mean values for J_0 and J_{45} (Figures 4.5 and 4.6) similar to other studies assessing astigmatism in the predominantly White European population (Sanfilippo et al., 2015), with greater WTR than either ATR or oblique astigmatism types. The mean

astigmatic power (of 0.54D) was also similar to the median 0.50D power previously tested in White European children in the NICER study (O-Donoghue et al., 2011).

The difference in the prevalence of each type of cylinder axis may not be directly comparable to other studies, which may use different definitions for the axes. This study split the range of axes into three similar groupings: WTR 180±20, ATR 90±20, oblique 21-69 and 111-159 (Shih et al., 2004; Rezvan et al., 2011).

Eyelid pressure is likely to cause changes with the axis of astigmatism, and it has been suggested that WTR astigmatism becomes more predominant in childhood as the continually repeating blink reflex affects the corneal curvature in the vertical meridian (Read et al., 2007). Rezvan et al. (2011) also suggest that

> *"the higher prevalence of squinting among myopes, causes the eyelids to squeeze the corneal surface and lead to WTR astigmatism"*.

Chinese schoolchildren show a significantly higher proportion of WTR astigmatism compared with white European (Fan et al., 2004), and this supports the theory that structural features play a role.

4.3.3 Spherical refractive error

Figure 4.8 shows the distribution of all the SER results from all children. The large central peak represents the high number (and majority) of patients being with SERs around the zero measure. In the current study, they represent emmetropes, having refractive errors in the range of >-0.50 and <+0.50D. This is similar to the findings of French et al., (2013) using data from both Australian and Northern Ireland White European children.

Cycloplegic refraction has been suggested to be the gold standard for epidemiological studies, and not using it in subjective refraction may give a more myopic refraction in children by between 0.25 and 0.50D (Funarunart et al., 2009; Hiraoka et al., 2014). All optometrists in practice are trained to understand how certain prescriptions may affect unaided vision, and will push for the maximal plus prescription that gives the patient the best visual acuity to allow them to make an educated judgment on the final refraction given (Rosenfield and Chiu, 1997; Pointer, 2001; Cheng et al., 2007). Therefore, although the myopia prevalence of 29.3% in this study is higher than that of other epidemiological studies using cycloplegia in the UK, such as the NICER study (O'Donoghue et al., 2010) or the Aston Eye Study

(Logan et al., 2011), the data is intended for use by community optometrists who would not routinely use cycloplegia on their patients.
As ethnicity plays a large role in the prevalence of myopia, it could be assumed that the likely comparable myopia prevalence in Liverpool could be between the prevalence of the NICER study in predominantly white Europeans (17.7% in 12-13 year olds) and the Aston Eye Study (29.4% in 12-13 year olds). This assumption comes from the Census ethnicity data of Liverpool showing predominantly white Europeans population, but with a higher number of Asians than Northern Ireland, and fewer than in Birmingham.

Health Profile data records that Liverpool has a higher percentage of smokers in the population (Public Health England, 2015), and for pregnant women smoking at the time of delivery than the national average for England. These two factors have both been shown to have a protective effect for myopia of up to 1.10D in Asia (Saw et al., 2004; Iyer et al., 2012) and has been demonstrated, to be associated with a more hyperopic SER in children of smokers in the UK (Williams et al., 2008), and the USA (Stone et al., 2006). It is therefore likely that this factor may increase the hyperopic refractions in the sample to reduce myopia prevalence. Future research in this area in the UK could be used to ascertain whether we can further develop our skills, in order to gauge the correct sight test recall for a child and give relevant advice to parents concerned about their future. It is also straightforward to ask this in addition to the usual questioning performed at sight tests. Whilst it is not advisable to suggest smoking in order to protect children from myopia development, due to the multitude of significant health risks associated with smoking, further research could be used to find an associated chemical protector for myopia.

This study does show similar prevalence of myopia to a comparable study based in the UK, using similar methods to those used here. Pointer (2001) used subjective refraction on those attending his optometric practice, and found that at 11 years of age (the average age of children in this study), the prevalence of myopia was 25.0%. Although the study by Pointer was much smaller, using data from only 53 patients, it compares well with the results from our analysis, where the overall myopia prevalence for those with an average age of 11.1 years was 27.3%. Refining data from 11 year olds alone, the myopia prevalence found in Liverpool was 23.9%. The data from 7 year olds are also comparable between the studies, with a prevalence of 5.0% in Pointer's study, and this study's finding of 5.5% of the patients having myopia of -0.50D or more. The study by Pointer was a longitudinal

study following patients for 6 years, and will be discussed later within the longitudinal data results.

There are few comparable European studies available discussing the prevalence of myopia. Plainis et al. (2009) compared Greek and Bulgarian children age 10-15 years under non-cycloplegic autorefraction, and found that Greek children were more likely to be myopic and Bulgarian children less likely than the children tested in this study were.

A more recent Swedish study by Larsson et al. (2015) showed a lower prevalence of myopia in 10 year old children of 7.8% (≤-0.50D SER), although this may be expected as the methods used cycloplegic retinoscopy. Accounting for an expected -0.50D more myopic prescription if non-cycloplegic methods were used in assessment, the prevalence in this study for 10 year old children reduces to 10.4%. This smaller difference may be due both to genetic and environmental influence.

Studies testing predominantly children of European descent but based in various countries around the world can also be compared. Robinson (1999) used non-cycloplegic retinoscopy in Canadian 6 year olds, recording the prescription in the horizontal meridian (rather than SER). This gives a similar prevalence of 6% having a myopic refraction <-0.25D. The results from this study show that using an SER definition of ≤-0.50D, 6.5% of 6 year old children are myopic.

Zadnik et al. (2003) assessed children in the USA with a mean age of 10 years old, and found that 11.6% of children were myopic under cycloplegic autorefraction conditions, with an SER of ≤-0.50D. This is a lower figure than the 16.4% found in the current study, but may be attributable to the cycloplegic nature of the assessments, and the fact that a population attending a clinical setting will be different from a population study based in a school (as was the study by Zadnik et al., 2003). Kleinstein et al. (2003) covered a wide range of ages (5-17 years) in the CLEERE study on myopia in the USA, although fewer than half of the children assessed were white. They found an overall prevalence of myopia from cycloplegic autorefraction ≤-0.75D to be 9.2%, but only 4.4% in white children, which is significantly lower than in the current study.

Australian children show a lower prevalence of myopia than those from the UK (French et al., 2012). However, there are no studies using practice-based data for directly comparable results. Cycloplegic autorefraction results from the Sydney Adolescent Vascular and Eye Study (French et al., 2013) show the prevalence of myopia ≤-0.50D in 12 year olds to be 14.4%, and in 17 year olds to be 29.6%. When looking at those specific age groups in this study, the prevalence results were

32.3% and 47.9% respectively, and allowing an extra -0.50D SER for not completing a cycloplegic refraction (Hiraoka et al., 2014), the figures reduce to 24.6% and 41.7%. These differences are widely thought to be attributed to the large disparity in time spent outdoors, and volume of close work undertaken by children in the various countries (Rose et al., 2008; French et al., 2012).

When compared with studies in children of non-European ethnicity, the prevalence of myopia in this study sits well below previously reported figures, particularly for eastern Asia. For example, Jang and Park (2015), in their study using (non-cycloplegic) autorefraction and subjective refraction in South Korea, found 46.5% of children aged 8-13 years were myopic ≤-0.50D. Another practice-based study of subjective refraction on Chinese-Canadian children in Canada found a prevalence of 24.9% and 71.2% for 6 and 12 year olds (Cheng et al., 2007), showing that genetics, as well as environmental conditions affects myopia development. Guo et al. (2015) found a prevalence of 60% after cycloplegic autorefraction on children with a mean age of 11.9 years. Other countries may show a much lower prevalence of myopia, with Muma et al. (2009) completing cycloplegic retinoscopy on children in Kenya and noting 1.7% of children aged 12-15 years were myopic, and Carter et al. (2013) finding a very low 0.9% after cycloplegic autorefraction on children aged 5-16 years in Paraguay.

Whilst older studies may give comparable results in terms of methods of assessments (before autorefractors were considered to give reliable results), the accuracy of the results cannot always be relied upon, as it is widely thought that a child's environment and use of technology is changing the way myopia emerges and progresses (Vitale et al., 2008; Williams et al., 2015).

4.3.4 Statistical analyses

Data that does not follow a normal distribution has commonly been found in refractive error data (Lam et al., 1999; Cheng et al., 2007; Li et al., 2015), and the spread of cross-sectional data reflected this.

There were also associations found between the median split categorical variables using Chi-square testing (Table 4.1). Whilst this is not ideal for DTA to be carried out, it is impossible to get rid of all correlations in a refractive error study, particularly as some parameters cannot exist without the other (such as astigmatism and axis). It should therefore be acknowledged as a limitation, but can be overlooked as in previous DTA research by Rushton et al. (2016). Zhang (2005) reported that

dependence between variables may cancel each other out and that inter-dependence was not problematic, and Gurney (2016) investigated the accuracy of variables that were inter-correlated, and found for his research that Bayes analysis was around 95% accurate, despite some inter-correlation between the variables.

4.4 Summary

The population of this study represents a larger age range compared to other community practice based prevalence studies (Pointer, 2001; Cheng et al., 2007), and therefore gives a more representative view of children likely to be seen in optometric practice. The finding that more girls attend optometric practice was similar to other studies, which suggests that more encouragement for boys to attend for routine testing may be advisable.

Chapter 5: Risk factors and associations of astigmatism and myopia

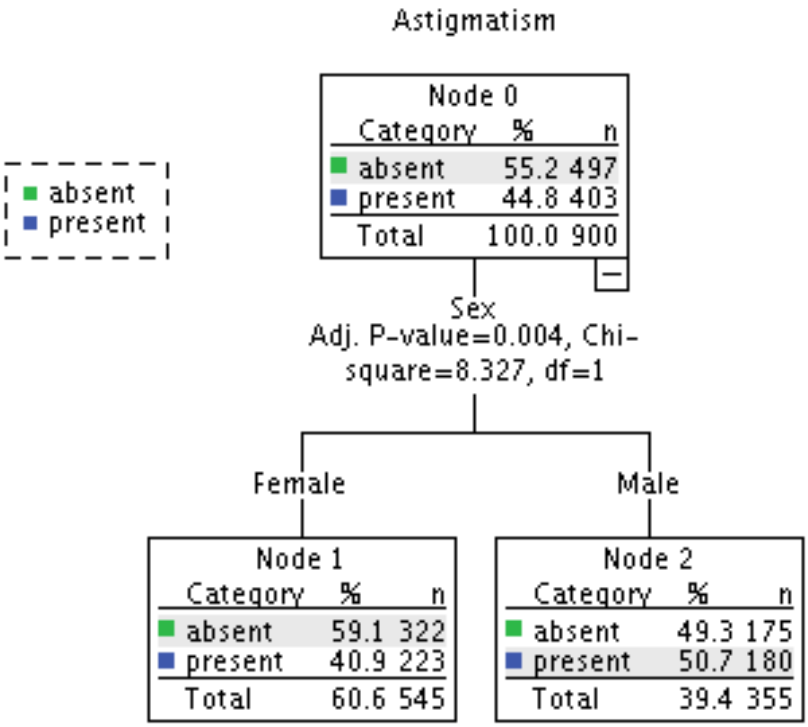
5.1 Objectives

Data presented in chapter 4 is examined in more detail in this chapter, to determine the dependence of astigmatism and refractive error on age, sex and season of birth using decision tree analysis (DTA).

5.2 Results

5.2.1 Astigmatism

Figure 5.1 shows the DTA examining the influences on astigmatism presence. It shows that sex is a determining factor in this population on the presence of astigmatism, with boys showing a significantly higher prevalence of astigmatism ≥0.50D ($p=0.004$). It shows that there was no influence of age or birth season on the presence or absence of astigmatism.

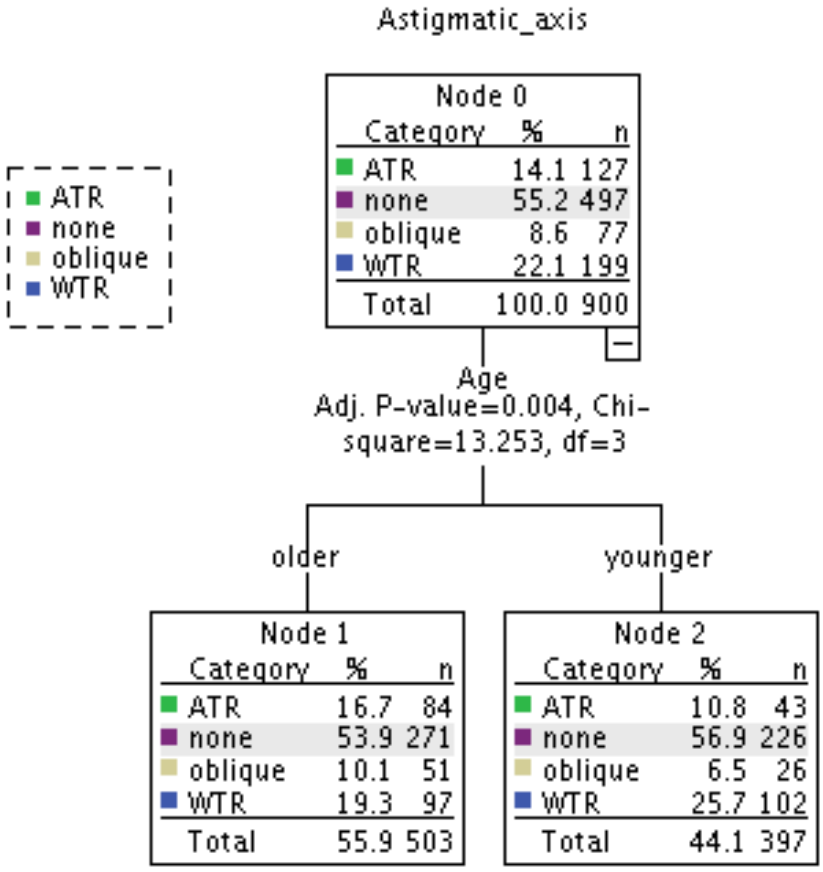


Model Summary

Specifications	Growing Method	CHAID
	Dependent Variable	Astigmatism
	Independent Variables	Age, Sex, Birth Season
	Validation	None
	Maximum Tree Depth	10
	Minimum Cases in Parent Node	10
	Minimum Cases in Child Node	5
Results	Independent Variables Included	Sex
	Number of Nodes	3
	Number of Terminal Nodes	2
	Depth	1

Figure 5.1: Decision Tree Analysis assessing independent variables age, sex and birth season on the presence of astigmatism.

5.2.2 Astigmatic axis



Model Summary

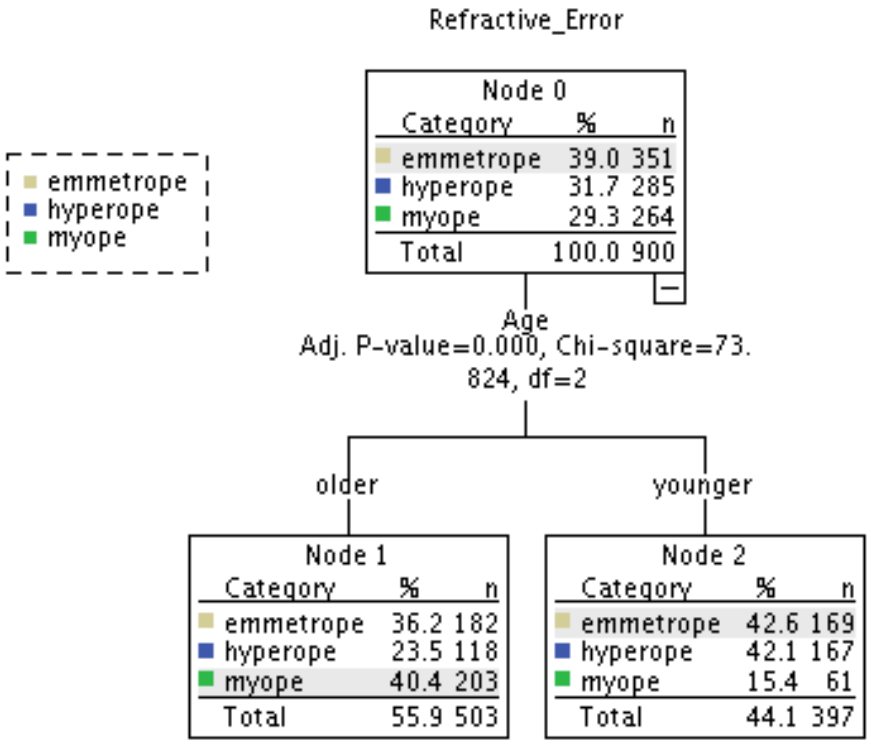
Specifications	Growing Method	CHAID
	Dependent Variable	Astigmatic axis
	Independent Variables	Age, Sex, Birth Season
	Validation	None
	Maximum Tree Depth	10
	Minimum Cases in Parent Node	10
	Minimum Cases in Child Node	5
Results	Independent Variables Included	Age
	Number of Nodes	3
	Number of Terminal Nodes	2
	Depth	1

Figure 5.2: Decision Tree Analysis showing the possible influencing factors of age, sex and birth season on astigmatic axis type.

The only significant influencing factor on astigmatic axis was age, with an apparent shift to reduced WTR astigmatism and increased ATR and oblique astigmatism after the median split age of 11.1 years (p=0.004).

5.2.3 Spherical refractive Error

The primary factor affecting each refractive error group (myopia, hyperopia or emmetropia) was age (figure 5.3). The prevalence of myopia under the median split age of 11.1 years was 15.4%, which increased to 40.4% above 11.1 years, with both emmetropic and hyperopic refractive error reducing.



Model Summary

Specifications	Growing Method	CHAID
	Dependent Variable	Refractive Error
	Independent Variables	Age, Sex, Birth Season
	Validation	None
	Maximum Tree Depth	10
	Minimum Cases in Parent Node	10
	Minimum Cases in Child Node	5
Results	Independent Variables Included	Age
	Number of Nodes	3
	Number of Terminal Nodes	2
	Depth	1

Figure 5.3: Decision Tree Analysis investigating age, sex and birth season as possible influencing factors on refractive error type.

5.3 Discussion

5.3.1 Astigmatism

Out of the three variables investigated, sex was the only one to impact on the presence of astigmatism, with a higher prevalence in boys (50.7%) than in girls (40.9%). This is in contrast to many studies, which suggest no statistical difference in prevalence between the sexes (Kleinstein et al., 2003; Fan et al., 2004; Huynh et al., 2006; Lai et al., 2010; Chebil et al., 2015; Sanfilippo et al., 2015). One study that has shown a statistically higher prevalence of astigmatism in boys was by Shekar and Srinivas (2008), who examined the association with sex and refractive error using DTA, who found boys aged 5-8 years to show a higher prevalence of astigmatism compared with girls. However, they found that older age groups up to 16 years did not show any difference between the sexes.

It could also be that as boys have been shown to have better visual acuity (Pointer, 2014), so they are less affected by symptoms and therefore less likely to present at practice with problems. However, epidemiological studies mentioned above assessing a more even split of the sexes have found similar results, suggesting this to be a true finding for this population. The difference in vision also suggests biological differences in the structure of the eye itself between girls and boys may be contributing to astigmatic differences. This could be due to orbital bone structure, or eyelid pressure affecting the presence of astigmatism such as found by Read et al. (2007), where the slant of boys' eyelids were different to girls.

Age did not affect the presence of astigmatism in this study. This has previously been shown in Northern Ireland by O'Donoghue et al. (2011), who found no significant difference in prevalence of astigmatism between a group of children aged 7-8 years and a group of 12-13 years of age. In a later study following the same group of children (O'Donoghue et al., 2015), no significant change in prevalence was found when retesting 3 years later. However, they did note that the children initially presenting with astigmatism were not necessarily the same children who had astigmatism after 3 years, suggesting there is a dynamic element to astigmatism through childhood.

Birth season did not affect the presence or absence of astigmatism in this group of children. This is in agreement with the only other study assessing time of birth (as a measure of photoperiod in the 30 days after birth) and astigmatism (Mandel et al., 2010). In addition, animal studies have also shown that variations in photoperiod

had little on astigmatism (Stone et al., 1995; Kee et al., 2005). Despite a possible theory that disruption of a light-dark cycle disruption might lead to astigmatism in children (Czepita et al., 2004) as discussed in section 2.3.6, there is no evidence from this study that it affects astigmatic development, and it may be that if there is any influence, it is too short-lived and then overcome by later stronger risk factors for development such as ethnicity (Kleinstein et al., 2003) or orbital and eyelid structure (Read et al. 2007).

It is, however, in contrast to some studies on spherical refractive error, where the theory that the amount of daylight hours around birth affects myopia development (McMahon et al., 2009; Ma et al., 2014). This may be because natural daylight exposure has not been shown to influence astigmatism development in risk factor studies in the same way that it can affect myopia development (Rose et al., 2008; Sherwin et al., 2012; Jin et al., 2015).

5.3.2 Astigmatic axis

Age was the only factor affecting the astigmatic axis, with those over the median split age of 11.1 years showing higher amounts of ATR and oblique astigmatism, and lower amounts of WTR (or no) astigmatism compared to the younger age group.

Astigmatic axis has been shown to change with age in childhood in previous studies. Gwiazda et al. (1984) assessed children aged 0-6 years, and found a similar number of children under 3 years of age had ATR and WTR astigmatism. They reported a predominance of ATR astigmatism in children between 3 and 4½ years of age, and a change in predominance to WTR astigmatism after this time, similar to a study by Dobson et al. (1984). Fotouhi et al. (2011) found that after age 6, WTR tended to reduce in prevalence, and ATR astigmatism increased up to age 20, similar to results found by Rezvan et al. (2011), Mandel et al. (2010) and also in this study. However, Shih et al. (2004) found that WTR astigmatism increased in prevalence with age in a Singaporean population of 7-18 year olds. This shows a potential difference due to ethnicity, with those with narrower palpebral apertures, tighter eyelid musculature, and more myopic refractions causing WTR astigmatism (Read et al., 2007; Rezvan et al., 2011), thus compounding genetic effects. Li et al. (2015) also suggest that ATR and WTR astigmatism may have different genetic aetiologies, and therefore should be researched separately. A smaller proportion of children in all of these studies were found to have oblique astigmatism at all ages, and was also the smallest group in this study.

Sex showed no influence on astigmatic axis in this study, which is similar to previous results by Rezvan et al. (2011). Several previous studies show varying results, which may depend on definitions of astigmatism and genetic influences. Previous research has found a higher number of ATR astigmats in boys (Fotouhi et al., 2011; Chebil et al., 2015), a possible association between being female and WTR astigmatism (Mandel et al., 2010; Fotouhi et al., 2011), and a higher prevalence of WTR astigmats in boys (Huynh et al., 2006). Whilst the Sydney myopia study (Huynh et al., 2006) also found a significantly higher number of oblique astigmats compared to the current study, (overall 39.1%), they also found no significant difference between the 2 sexes for this type of astigmatism.

Birth season showed no influence on astigmatic axis, as with astigmatic power, in contrast to the only previous study found. The study by Mandel et al. (2010) on Israeli conscripts found that WTR astigmats were more likely to have been born in the months with longer photoperiods, and ATR astigmats in the months with shorter photoperiods. Those with oblique astigmatism were unaffected by photoperiod around birth. It is, however, not directly comparable to this study, as it was conducted on a different age group (16-22 year olds), and in a location at latitude closer to the equator (with an associated smaller variation in seasonal daylight hours). If the amount of daylight at birth was a significant factor, the findings may be expected to be more obvious in a location with wider variation in daylight hours such as the UK. However, this was not the case, and the results found by Mandel et al. could possibly be associated with other factors, such as ambient temperature.

5.3.3 Spherical refractive error

As research has previously shown, the prevalence of myopia increased with age (Saw, 2003; Morgan and Rose, 2005; Guo et al., 2013; Rudnicka, 2016), and this was statistically the only variable affecting refractive error group. Myopia was the primary refractive error type after the age of 11.1 years, and this is similar to the crossover point suggested by Gwiazda et al. (2000) of 12 years. However, it is older than that suggested by Pointer (2001) in his practice-based UK study, which extrapolated longitudinal data to find the crossover to myopia was at age 6-7 years. As median splits were used in this study, further investigation of the refractive error at each age could find the exact crossover point where myopia prevalence overtakes that of hyperopia and emmetropia.

Myopia was more prevalent in girls, with 31.6% of girls compared with 25.9% of boys (172 and 92 children, respectively). However, this did not show as a statistically significant difference between the sexes on DTA. This is consistent with other studies assessing sex and refractive error in developed countries studying subjects of European ethnicity (Robinson, 1999; Zadnik et al., 2003). Shekar and Srinivas (2008) also used DTA to analyse refractive errors in children, and found no statistical difference for the prevalence of spherical refractive error between girls and boys age 5-16 years. There are also studies covering children aged 5-21 years, which do find a statistically significantly higher prevalence of myopia in girls (Lin et al., 1999; Kleinstein et al., 2003; He et al., 2004; Cheng et al., 2007; Guo et al., 2015; Saxena et al., 2015). Many of these studies were in Asia, which is suggestive of an ethnic difference in refractive error development.

Birth season did not influence the presence of refractive error in this group of children. This is in contrast to some studies, which suggest a higher prevalence of myopia in those born through the winter months. This may be due to varying seasonal weather factors in the countries of the studies (including the USA, Japan, China, and Israel), which vary from the UK in terms of temperature, humidity, and other climatic features. In the only UK practice-based study on birth season, there was a significant risk factor for high myopia (OR 1.17) for those born in summer compared to winter, but not for low or moderate myopia (McMahon et al., 2009). They suggested that the reason could be due to the association with birth weight, temperature and other weather variations that change during the seasons, rather than specifically the photoperiod, and parents job roles may influence them to plan for starting a family. That was a very large study, on over 74,000 adults aged 18-100 years, so whilst the current study did not find any association between season of birth and refraction in childhood, the progression of myopia continuing from the teens may have an effect on ultimate adult refraction. It could be that season of birth affects progression of refractive status, and a later chapter on progression of refraction (Chapter 7) will examine whether birth season affects changes throughout childhood. The results show that, as discussed in more detail in section 2.4.6, whilst birth season may show a very small link with refractive error in the early months after birth, it appears that other environmental factors such as time spent outdoors, or near work may have more of an impact on visual stimulation and ocular development due to its subsequent and accumulative nature (Rose et al., 2008; Huang et al., 2015). Whilst it has been found that season affects progression of myopia, with less of a progression in the summer months associated with longer

daylight hours (Donovan et al., 2012; Gwiazda et al., 2014), there have been no reports of whether season of birth affects progression of ocular refraction, which will be assessed in chapter 7.

5.4 Summary

These results show that age has a significant effect on both astigmatic and spherical refractive error in children. Observation of children prior to the age of 11 years must be seen as an important time to assess for developing myopia, and additionally boys with regard to astigmatism. This is to ensure they have the optimum visual acuity, and to guide them and their parents as to the known risk factors to help them prevent future progression.

This study has shown the novel research finding that season of birth has little or no influencing factor on any part of astigmatism, or refractive error in children in Liverpool.

Chapter 6: Longitudinal analyses of astigmatism and myopia

6.1 Objectives

Preliminary data collected over time from a subset of children tested in the cross-sectional part of the study are presented in this chapter. Using methods detailed in chapter 3, graphs showing frequency distribution of factors are shown, including the progression of refractive error and astigmatism, and tests for Chi-square associations between the variables. This allows further assessment of data on progression of astigmatism and myopia and whether they may be related to each other and/or to additional risk factors in the following chapter.

6.2 Results

Data from 242 patients contributed to this longitudinal data analyses (data from 167 participants from the city centre practice and 75 participants from Old Swan practice). The discrepancy in number from each practice reflects the fact that the city centre practice had been operating for a longer period.

The initial sight tests were completed between 2006 and 2011, and the final tests between 2013 and 2015. The mean period from the initial sight test was 5.97 years (range 3.42-9.06 years, SD 1.09).

6.2.1 Demographic factors

The mean age at the initial visit was found to be 8.73 years (range 2.5-15.6 years, SD 2.60).

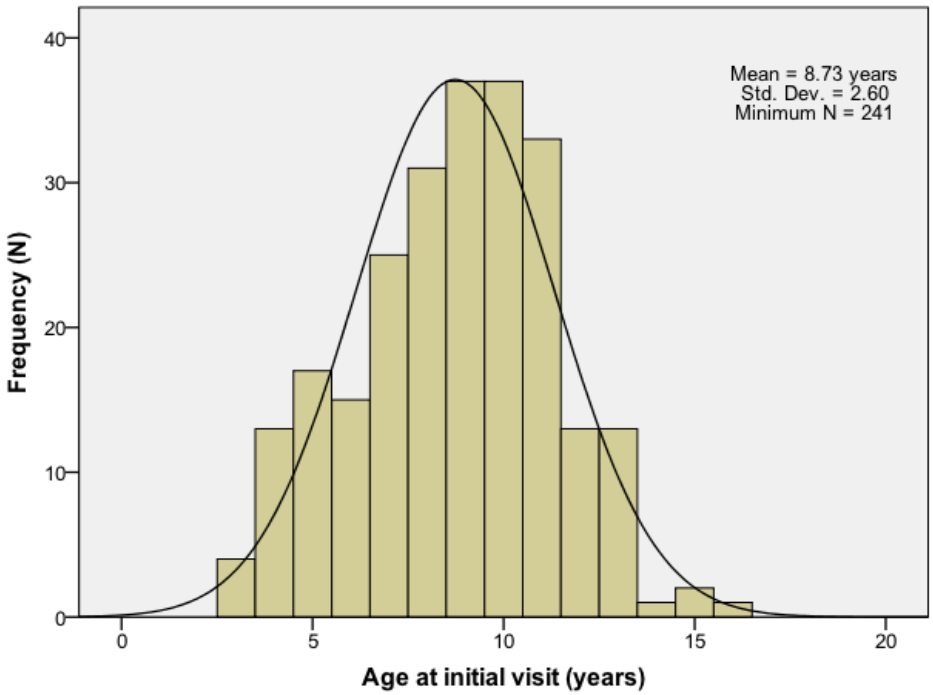


Figure 6.1: Frequency distribution graph showing age at initial visit for those patients attending for a minimum of five tests or five years.

There were more girls (57.0%) attending than boys (43.0%), similar to the cross-sectional group of patients (figure 6.2, see section 4.3.1). In this group of patients, there were significantly more girls than boys returning for repeated eye examinations (one-sample binomial test, p=0.034).

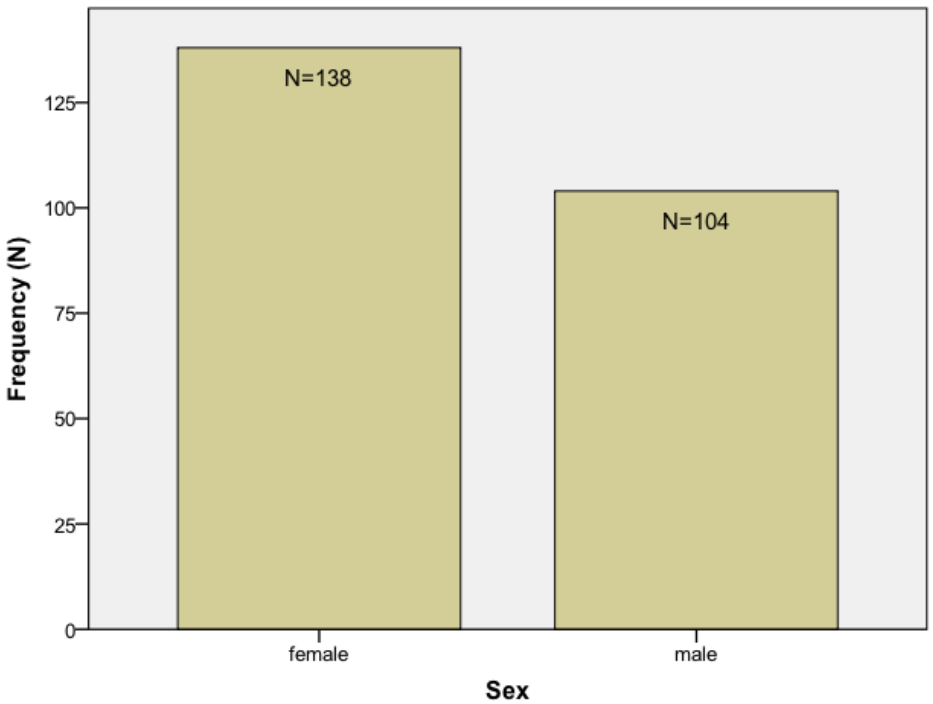


Figure 6.2: Sex distribution of patients in the progression study. Total N = 242.

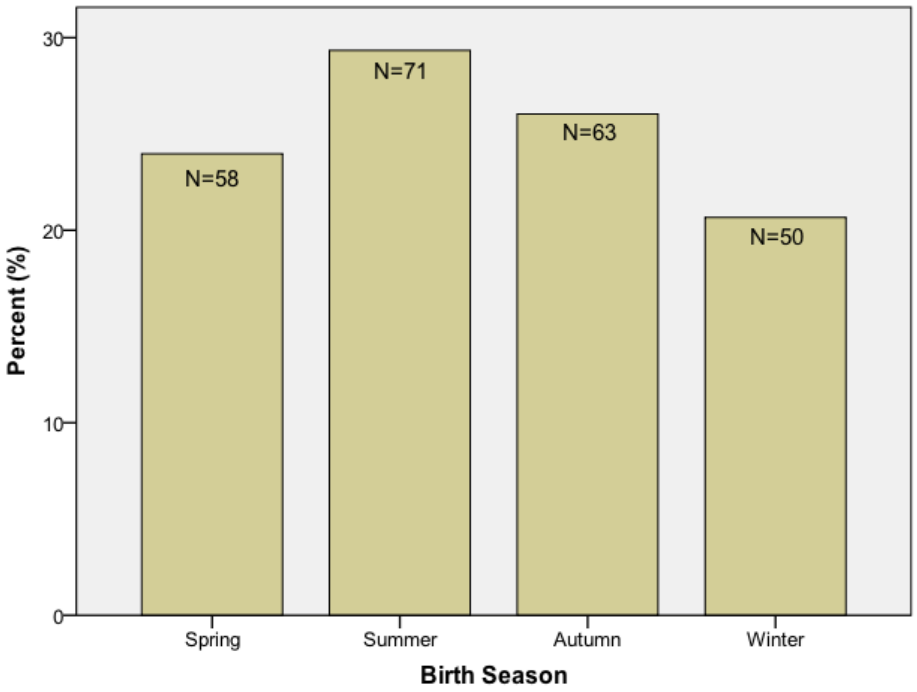


Figure 6.3: Distribution of patients according to their birth season. Spring = March, April, May, Summer = June, July, August, Autumn = September, October, November, Winter = December, January, February. Total N = 242.

Figure 6.3 shows the spread of patients by their season of birth. There appears to be fewer patients born in winter compared with summer, but this was not a significant difference on 1-sample Chi-square testing (p=0.278).

6.2.2 Astigmatism

Most patients had no astigmatism (<0.50D) at their initial visit. Over time, however, the numbers of patients with astigmatism increased, so most patients had astigmatism by their final visit (figure 6.4).

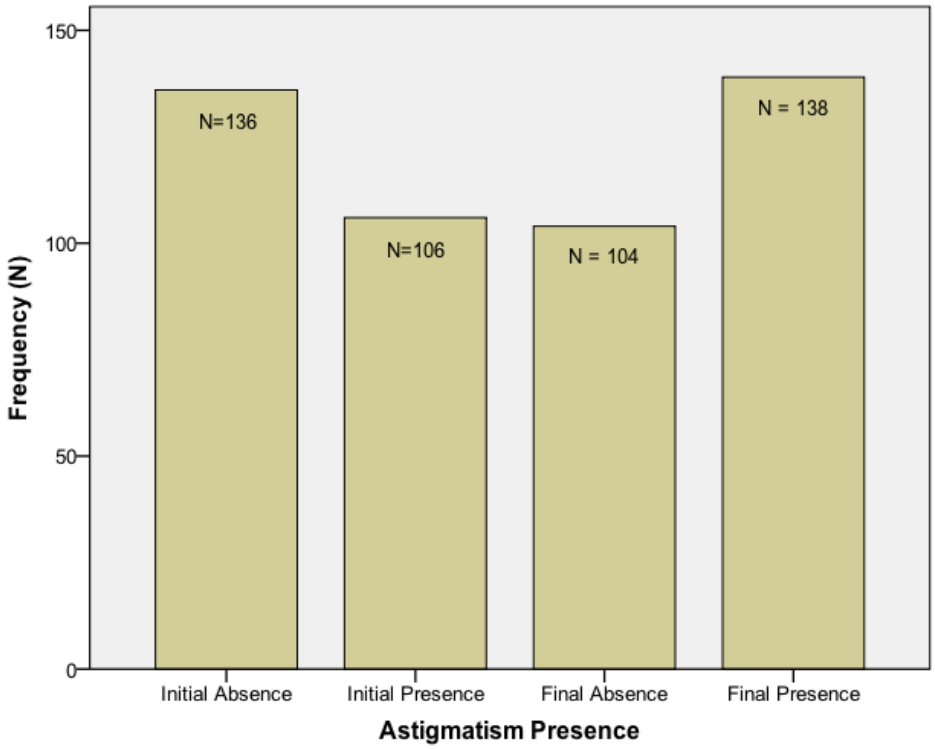


Figure 6.4: Graph comparing the absence and presence of astigmatism at the initial and final visit for the 242 patients. Presence of astigmatism was classed as ≥0.50D of astigmatism.

All types of astigmatism increased through the course of time (figure 6.5), but the biggest increase came from oblique astigmatism (94.3% increase, compared with 20.4% increase for WTR, and 13.3% increase for ATR astigmatism).

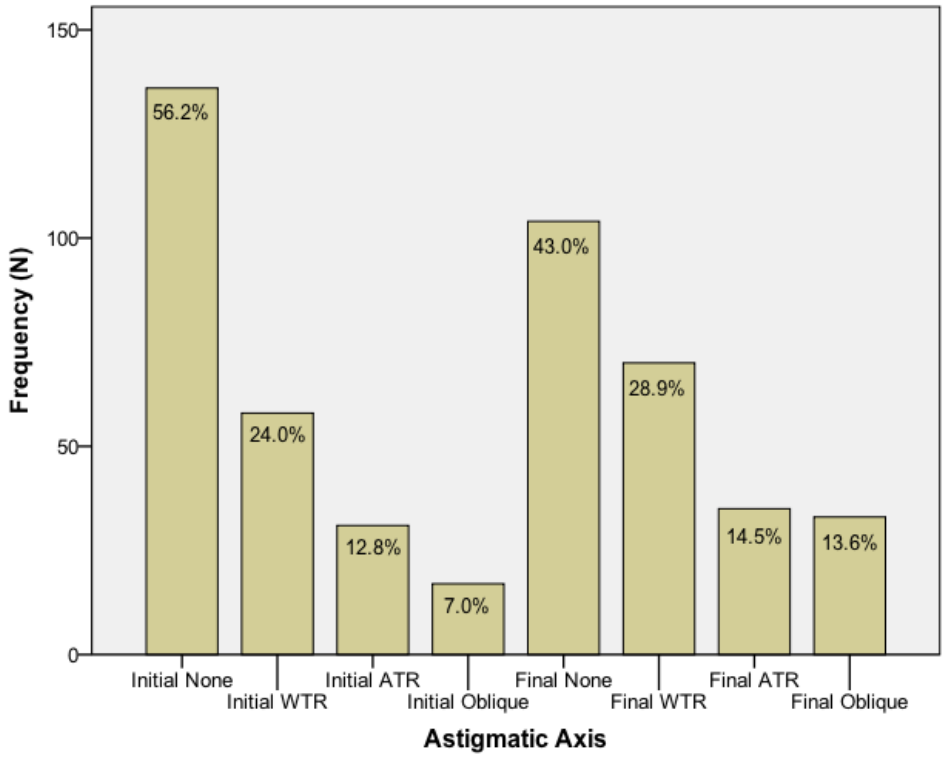


Figure 6.5: Astigmatic axis at initial and final visits. N = 242.

6.2.3 Astigmatic progression

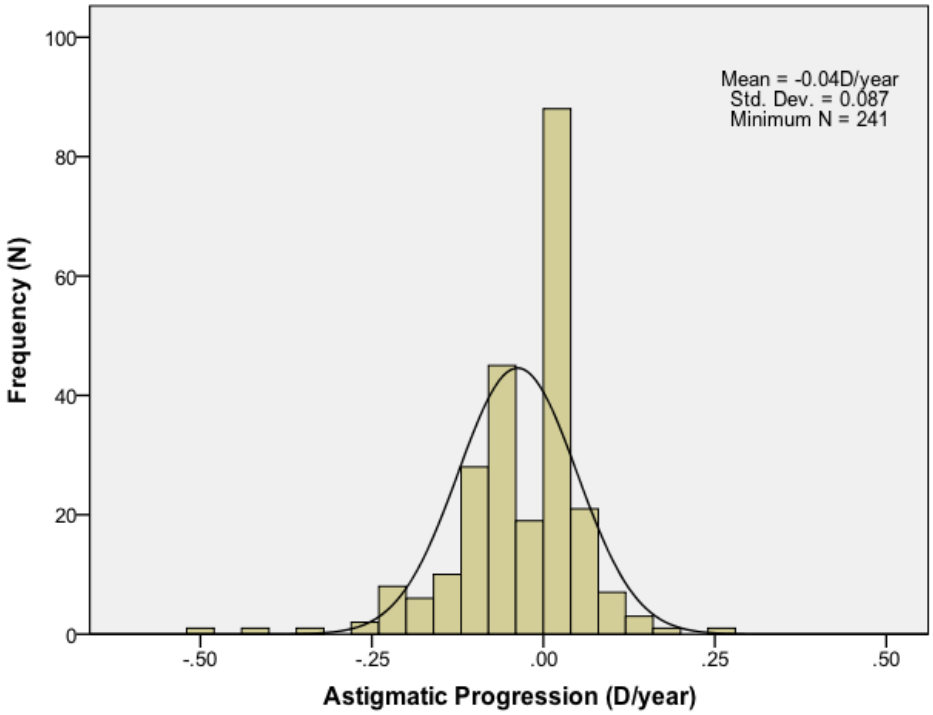


Figure 6.6: Progression in astigmatic power from the initial visit. A negative change represents an increase in astigmatic power, as negative astigmatic notation was used in the practices.

The progression of astigmatic power (calculated as the mean change over the individual patient's total follow up period) did not follow a normal distribution (figure 6.6), and centred on a near zero change, with a mean increase of 0.04D per year (range +0.25 to -0.48D per year, SD 0.087).

6.2.4 Spherical refractive error

The number of patients by refractive group is shown in figure 6.7, as defined in section 3.7. Most patients at baseline were hyperopic at the mean age of 8.73 years, and fewest were myopic. However, this dynamic changed after the mean period of 5.97 years, when most patients were myopic.

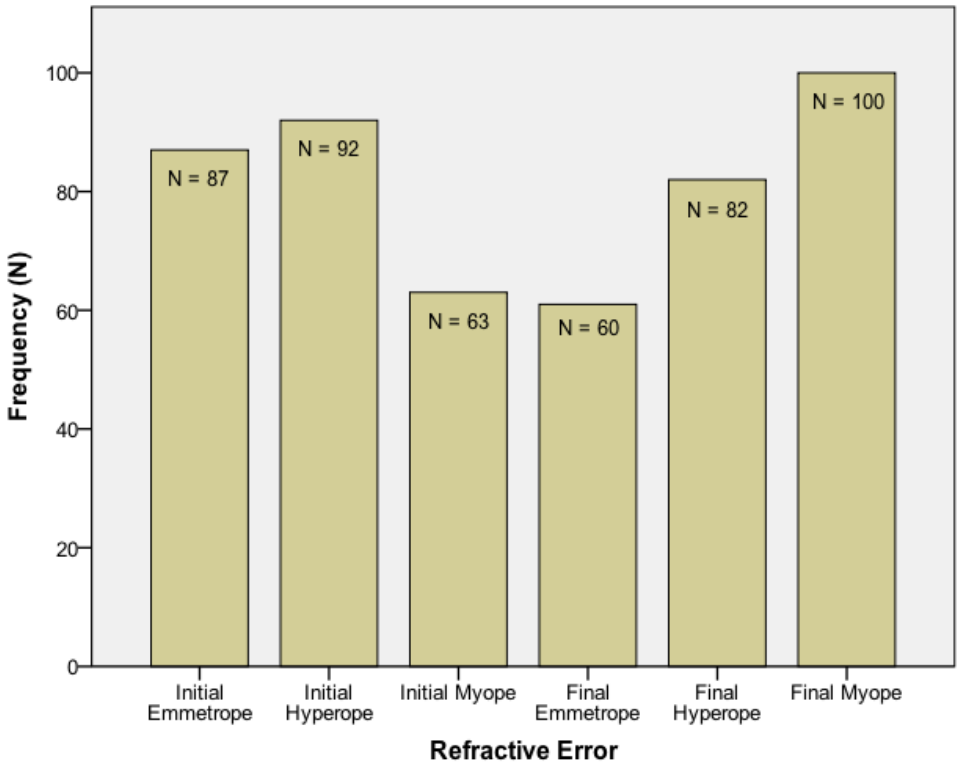


Figure 6.7: Distribution of refractive error at initial and final visits. Myopia ≤-0.50D, hyperopia ≥+0.50D, emmetropia >-0.50 to <+0.50D.

6.2.5 Myopic progression

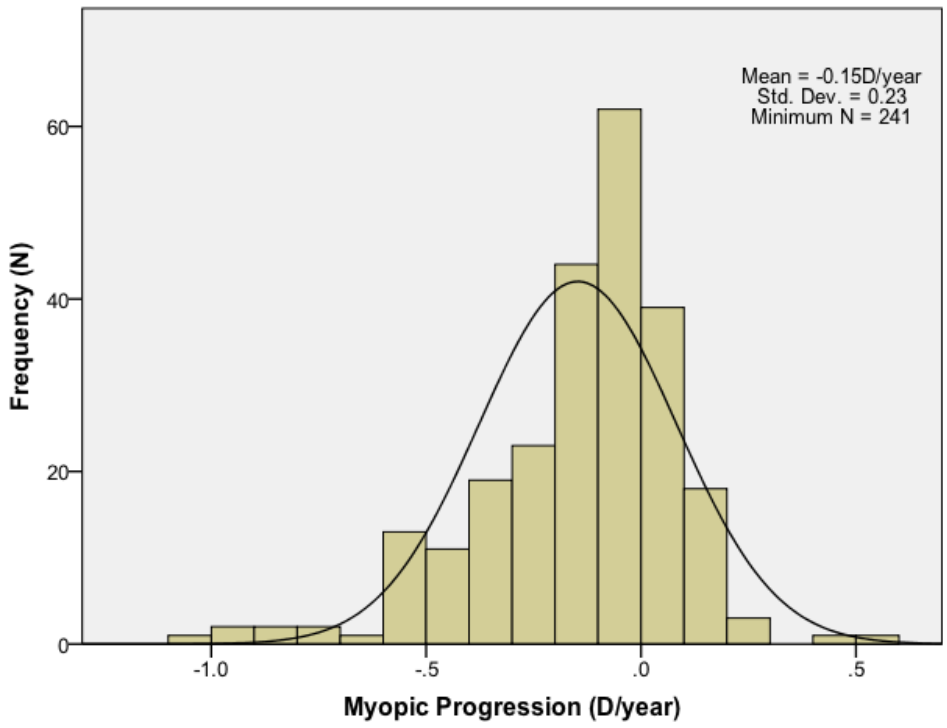


Figure 6.8: Mean progression of refractive error per year from the initial visit.

The change of predominant refraction type to myopia at the end of the study predicts a myopic shift over time (Figure 6.8). The mean change in SER (calculated as the mean change over the individual patient's total follow up period) for all patients was -0.15D per year (range +0.52 to -1.03D per year, SD 0.23). These results were further analysed by DTA in chapter 7 to obtain any statistically significant differences between initial refraction, sex, age, birth season and astigmatism that might affect progression of refractive error.

6.2.6 Statistical analyses

None of the continuous data was normally distributed, similar to other studies (Cheng et al., 2007; Li et al., 2015) and to the cross-sectional data from this current study (see Chapter 4). As categorical data was used in DTA (using median splitting to categorize any continuous data as detailed in section 3.8), Chi-square testing was used to check for associations between the variables (table 6.1). Ideally there would be no associations found for any multivariate statistical analyses, however, similar to the cross-sectional data (section 4.2.6), there were some inter-associations. DTA attempts to remove the confounding effect of Chi-square inter-association testing, allowing more meaningful conclusions to be drawn, but it should be acknowledged that the table below does show some associations between the variables, which may limit the validity of the results.

Chi-Square	Sex	Birth Season	Initial Astigmatism	Initial Axis	Initial Refractive Error	Astigmatic Progression	Myopic Progression
Initial Age	3.11	4.77	1.67	12.97***	27.04****	0.81	4.28*
Sex		1.01	2.42	15.83***	2.20	2.04	0.70
Birth Season			3.53	11.32	12.16	1.41	2.40
Initial Astigmatism				242.00****	19.06****	12.24****	0.002****
Initial Astigmatic Axis					23.69****	15.20***	0.32
Initial Refractive Error						1.13	35.36****
Astigmatic Progression							0.15

Significance: * p=0.05, ** p=0.02, *** p=0.01, **** p=0.001

Table 6.1: Chi-Square testing for associations between variables for longitudinal data.

6.3 Discussion

6.3.1 Demographic factors

As with the cross-sectional subjects, there were more girls attending regular sight tests than boys, and this has been the case for many refractive error studies (Pointer, 2001; O'Donoghue et al., 2015). The difference was significant in this group of patients, which finds that girls are more likely to attend regularly for ophthalmic services. Whilst there is little difference from cross-sectional results in the prevalence of spherical refractive error, it suggests that more encouragement is required for boys to attend for sight tests and monitoring of refraction to ensure the best development possible. Undercorrected refractive errors have been shown to give reduced child-development scores (Orlansky et al., 2015; Harvey et al., 2016), so optometrists play a crucial role in enabling children to develop to their maximum potential.

There was no significant difference in the number of children attending from any birth season, suggesting that any results found in chapter 7 using this variable will be significant.

6.3.2 Astigmatism

Astigmatic power was found to increase by 0.04D/year. This change is very small compared with the repeatability differences for astigmatism (Rosenfield and Chiu, 1995; Villegas et al., 2014), and so could be seen as a small enough change to be deemed clinically insignificant, as indeed, it is not measurable in a clinical setting.

6.3.3 Spherical refractive error

The mean myopic progression of -0.15D/year found in this study is higher than the comparable previous UK study of 60 children monitored from the age of 7 years by Pointer (2001), who found a progression of -0.09D/year in his practice-based study. This could be due to the larger population assessed, the older mean initial age in this study, or to the growing increase in myopia prevalence (Hrynchak et al., 2013; Williams et al., 2015). Those more recent studies assessing White Europeans as the predominant ethnic background show similar progression, with French et al. (2013) finding a progression of -0.16D/year following 12 year olds for 5-6years in Australia.

However, these figures based on those of White European origin are all lower than progression in other regions, with the likelihood of progression being higher in East Asian populations. Tan et al. (2000) for example, found a progression of -0.87D/year

in a population of 7-12 year old myopic and non-myopic children using cycloplegic autorefraction in Singapore, although this was over a short average period of 10 months. Using subjective refraction over 2 years, Lam et al. (1999) found a progression of -0.32D/year in 6-17 year old children from Hong Kong, and Cheng et al (2007) assessed 6-12 year old Chinese-Canadian children in a practice environment using subjective refraction over a retrospective 8 years and found a progression of -0.52D/year.

6.3.4 Statistical analyses

Data that does not follow a normal distribution has commonly been found in refractive error data (Lam et al., 1999; Cheng et al., 2007; Li et al., 2015), and the spread of longitudinal data reflected this.

There were also associations found between the variables using Chi-square testing (table 6.1). Whilst this is not ideal for decision tree analysis (DTA) to be carried out, it is impossible to get rid of all correlations in a study of this design, particularly with parameters that cannot exist without the other (such as astigmatism and axis). It should therefore be acknowledged as a limitation, but can be overlooked as in previous DTA by Rushton et al. (2016). Zhang (2005) reported that dependence between variables may cancel each other out, and Gurney (2016) investigated the accuracy of variables that were inter-correlated, and found for their research that Bayes analysis was around 95% accurate, despite some inter-correlation between the variables.

6.4 Summary

The results of this chapter display the demographics and types of refraction found in the practices where patients have been attending for several years. This allows refraction and other demographic data to be tracked to find potential associations and risk factors, particularly for those involving astigmatism and myopic refractions and how they may interact and influence each other. Of particular note is the fact that more girls attend for regular sight testing, which suggests more engagement with boys, their parents and/or guardians may be required to ensure good visual and cognitive development.

Chapter 7: Risk factors and associations of progression of astigmatism and myopia

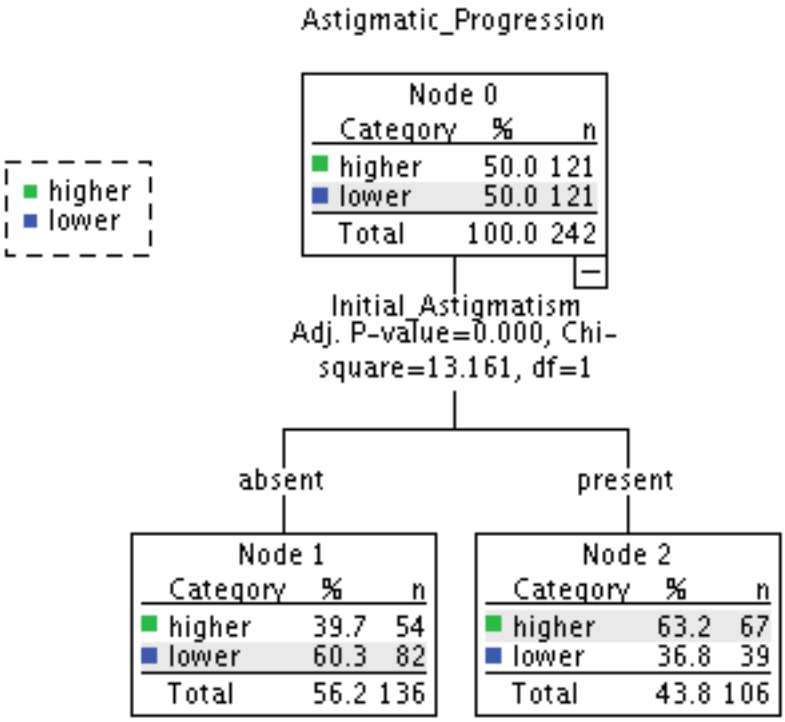
7.1 Objectives

Multivariate analyses of longitudinal data are detailed in this chapter, in order to determine relationships that may affect changes in refractive error. Age, sex, season of birth, initial astigmatism, astigmatic axis and refractive error is assessed using decision tree analysis (DTA) to examine any influence on the progression of both astigmatism and myopia.

7.2 Results

7.2.1 Astigmatism progression

Mean astigmatism power progression was -0.04D/year, representing a mild increase in astigmatism. Median splitting grouped the patients into those with lower progression (<0.014D/year) and those with higher progression (≥0.014D/year). The DTA diagram is shown in figure 7.1. The only influencing factor on astigmatic progression in this study was the presence or absence of astigmatism (p=<0.001). Those patients with astigmatism ≥0.50D at the initial visit progressed at a faster rate (mean -0.07D/year compared with those with astigmatism of <0.50D (-0.02D/year).

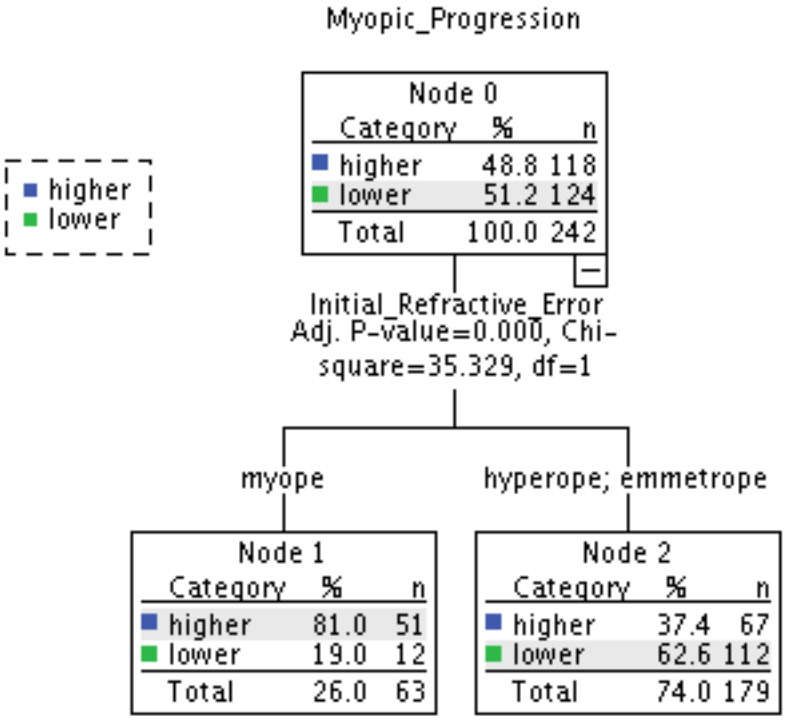


Model Summary

Specifications	Growing Method	CHAID
	Dependent Variable	Astigmatic Progression
	Independent Variables	Sex, Initial Age, Birth Season, Initial Astigmatism, Initial Axis, Initial Refractive Error
	Validation	None
	Maximum Tree Depth	10
	Minimum Cases in Parent Node	10
	Minimum Cases in Child Node	5
Results	Independent Variables Included	Initial Astigmatism
	Number of Nodes	3
	Number of Terminal Nodes	2
	Depth	1

Figure 7.1: DTA showing the influencing factors on astigmatic power progression. The negative change represents an increase in astigmatic power.

7.2.2 Myopia progression



Model Summary

Specifications	Growing Method	CHAID
	Dependent Variable	Myopic Progression
	Independent Variables	Sex, Initial Age, Birth Season, Initial Astigmatism, Initial Axis, Initial Refractive Error
	Validation	None
	Maximum Tree Depth	10
	Minimum Cases in Parent Node	10
	Minimum Cases in Child Node	5
Results	Independent Variables Included	Initial Refractive Group
	Number of Nodes	3
	Number of Terminal Nodes	2
	Depth	1

Figure 7.2: DTA showing factors affecting progression of myopia.

Median splitting was used to split the myopic progression into a lower myopic progression group with a change of >-0.10D/year, and those with higher myopic progression showing ≤-0.10D/year changes. The DTA presented in figure 7.2 shows that myopes progress at a significantly faster rate (-0.33D/year, SD 0.26, p =<0.001) compared with non-myopes (-0.08D/year, SD 0.18).

7.3 Discussion

7.3.1 Astigmatism progression

The mean change in astigmatism, whilst significant, was clinically small, as has been previously noted in chapter 6. The result found in the current study of -0.04D/year is similar to other studies (Tong et al., 2004; Pärssinen et al., 2015). Whilst it is also within the range found in reliability studies (Rosenfield and Chiu, 1995; Lam et al., 1999), this small but statistically significant progression was found due to the high statistical power of the study.

Overall, progression of astigmatic power tended to stay relatively stable with time, and was not linked with age in this study. Most patients stayed in the same group for astigmatic power and axis that they began. However, as with previous longitudinal studies (Tong et al., 2004; Pärssinen et al., 2015; O'Donoghue et al., 2015), astigmatism power was found to vary in each individual, with increasing and decreasing power, and changes within the cylinder axis groups. Figures 7.3 and 7.4 shows changes in the presence or absence of astigmatism, and changes in astigmatic axis groups from their initial to their final refraction.

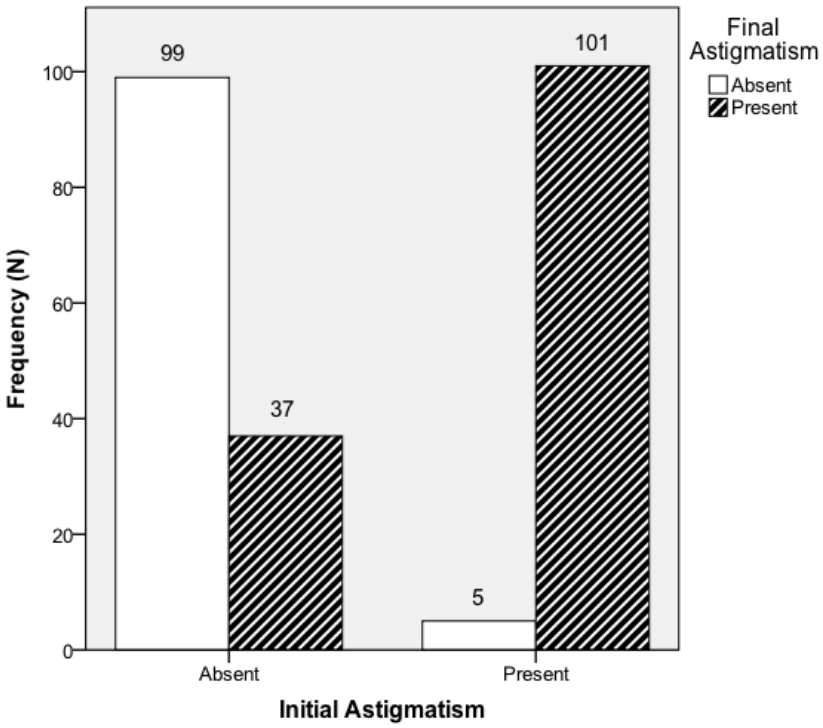


Figure 7.3: Changes in the astigmatism presence between initial and final refraction. Whilst most patients stay in the same group, some patents switch, with some becoming astigmatic, and some patients (albeit 5) reducing their power to become classed as having no astigmatism.

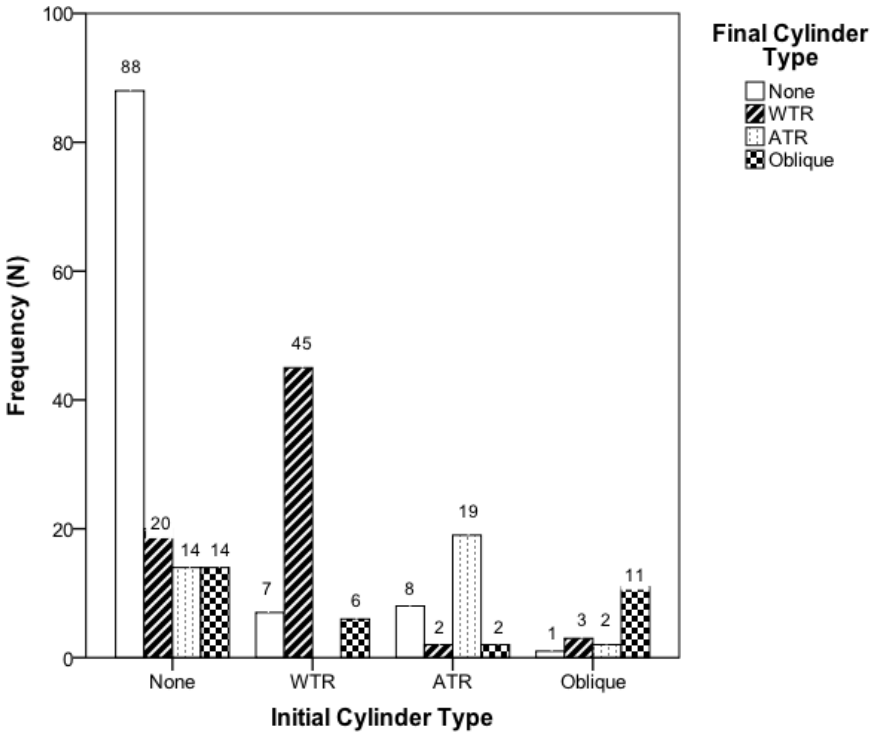


Figure 7.4: Graph showing the changes in the axis astigmatism between initial and final refraction. Whilst most patients remain in the same group in which they began, others vary without preference.

There was no influence of sex on astigmatic progression in this population. This is similar to Pärssinen et al. (2015) who found no significant difference in astigmatic children in Finland, but in contrast to Zhao et al. (2002) and Tong et al. (2004) who found astigmatism that was more progressive in girls in China and Singapore. However, this could be due to the different locations and possible genetic and morphological differences between European and Asian children (Garcia et al., 2003; Read et al., 2007).

In addition to birth season not affecting astigmatism prevalence or axis (Chapter 5), this study found no association between birth season and astigmatic progression.
This is the first study to the author's knowledge examining these variables. This is likely to follow on from cross-sectional results, and findings from Rose et al. (2008), Sherwin et al. (2012) and Jin et al. (2015), that time spent outdoors does not affect prevalence of astigmatism in the same way that it affects myopia, and from Mandel et al. (2010) who found that astigmatic power was not affected by the amount of daylight in the 30 days after birth.

7.3.2 Myopia progression

Patients who have a myopic refraction with an SER of -0.50D or more are likely to progress more quickly than emmetropes or hyperopes. The myopes in this study progressed at a mean rate of -0.33D/year, and non-myopes at -0.08D/year, with no statistically significant differences between hyperopes and emmetropes (Figure 7.5). This is similar to results found by McCullough et al., (2016) examining mainly White European children aged 6-7 years in Northern Ireland, who found progression of -0.23D/year in myopes and -0.09D/year in non-myopes, and Pointer (2001), who found myopes progressed at -0.22D/year in his practice-based UK study. These differences have also been found in other ethnic groups. Zhao et al. (2002) examined Chinese children of a similar age to the current study, and found myopes progressed at -0.36D/year and non-myopes at -0.15D/year (with the quicker progression due to ethnicity). Studies using subjective refraction have found similar results (Lam et al., 1999; Cheng et al., 2007). Initial refraction was the only influencing factor affecting the myopic progression in the current study, with more hyperopic initial refractions less likely to become myopic, and all myopes remaining so.

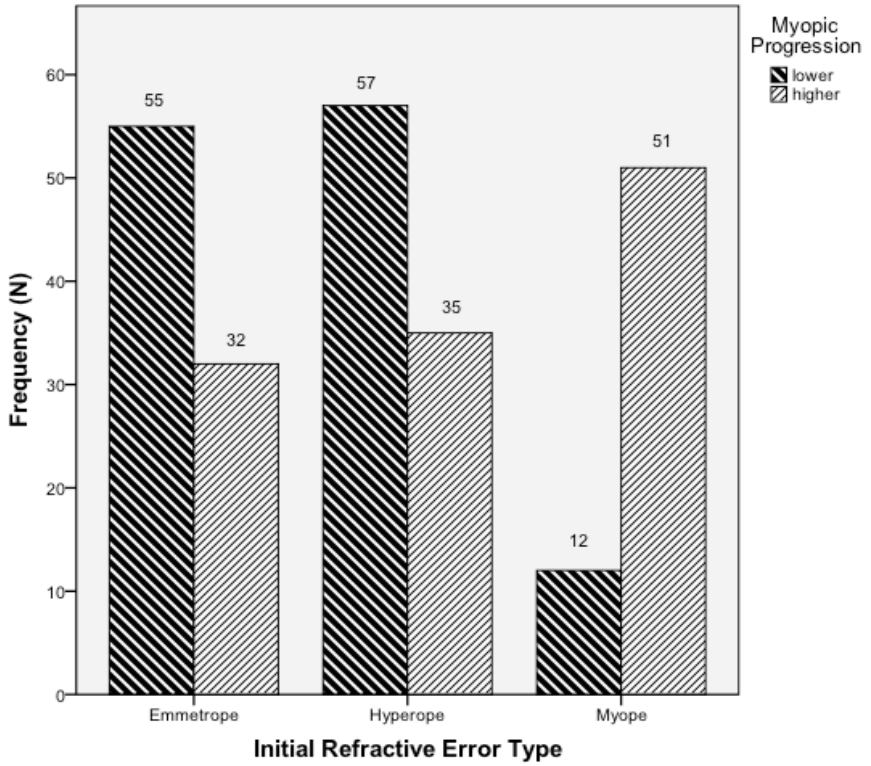


Figure 7.5. Graph showing myopic progression for patients with the different refractive error groups. Whilst emmetropes and hyperopes tend to show lower myopic shifts, myopes tend to progress at a faster rate.

Lam et al. (1999) and Saw et al. (2000) assessed Hong Kong and Singaporean children (respectively) and noted that myopic progression varied with age. They found those aged 6-10 years showed a faster rate of change than those over 10 years, and they suggested this was linked with emmetropization. Medina (2015) found that myopic progression using retrospective subjective refraction also varied with age in the USA, but the starting age range was wider (2-22 years), and only examined 13 patients. In the NICER study assessing White European children, McCullough et al. (2016) found younger children (aged 6-7 years, -0.23D/year) progressed more quickly than older children (aged 12-13 years, -0.10D/year). Whilst this can be used to compare myopic children, the data from hyperopic children were not used in the statistical analysis, so may not be directly compared to this study. In addition, the age range used was different to the current study. There were no changes with age affecting refraction progression in the current study, and this may be because the progression amounts are much smaller in this predominantly White European population than in East Asian populations. In a more comparable study to the current one (using practice-based subjective refraction and on patients with a more similar age range), following a group of 582 myopes in the USA, Goss (1987) found that myopia progression followed a linear path between the ages of 6 and 15 years, finding results in accordance with this study.

Sex did not affect progression of myopia in this population, challenging results from previous studies other studies where girls show faster progression (Pärssinen et al., 2014; Saw et al., 2005). Zhao et al. (2002) found that girls showed a -0.21D/year faster myopic progression compared to that seen in boys. Whilst the age range at baseline was similar to the current study, the follow up was over a shorter period of follow up (28 months). Hyman et al. (2005) also found faster progression in girls, although that study conducted in the USA found a smaller difference of -0.05D/year, and only examined myopes. However, other studies have found no significant difference in myopia progression (Lam et al., 1999, Saw et al. 2000). In studies examining a more similar ethnicity to the current study of mainly White Europeans, French et al. (2013) and McCullough et al. (2016) found the similar result that sex did not influence progression of myopia. In the most recent practice-based study in the UK (to the author's knowledge), sex was not examined (Pointer, 2001).

Birth season was not found to influence the progression of myopia, and this was the first study to investigate this variable. Despite the amount of natural daylight or time spent outdoors in childhood being linked with myopia progression soon after (Rose

et al., 2008; Sherwin et al., 2012; Jin et al., 2015), and some studies linking photoperiod at birth with myopia prevalence (Deng and Gwiazda, 2011; Matsuda et al., 2012; Ma et al., 2014), the amount of light present at birth was not linked with future myopic progression in this study. This could be because the short period of lighting conditions around the time of birth become overshadowed by other genetic and environmental factors through childhood.

7.3.3 Link between astigmatism and myopia progression

Myopia is considered a failure of emmetropization by Flitcroft (2013) and Medina (2015), but neither mention astigmatism and how this may play a role in myopia development. Indeed, that small study by Medina et al. (2015) of 13 new myopes were chosen because they had <0.75D of astigmatism.

Fan et al. (2004) found that patients with astigmatism at an initial examination predisposed them to greater myopic progression. Within that group, the SER progressed more as the astigmatic power increased. Fan et al. (2004) also demonstrated that initial cylinder axis did not affect the progression of refractive error. However, Gwiazda et al. (2000) suggested that between the ages of 6 and 12 years, there was some interdependency between the astigmatism and SER, as those with ATR astigmatism were more likely to become myopic. These results suggest that astigmatism disrupts the emmetropization process, and subjects the eye to unnecessary axial length growth as it tries to correct the astigmatism (Fulton et al., 1982, Gwiazda et al., 2000).

In this group in the current study, however, who were followed for the mean time of 5.97 years, neither astigmatism power nor axis affected myopic progression, supporting results from previous studies using both subjective and cycloplegic refraction (Goss and Shewey, 1990; Pärssinen et al. 2015).

7.3.4 Link between myopia and astigmatic progression

Some studies show that astigmatism is significantly more likely to progress in myopes compared with hyperopes (Fulton et al., 1982; Tong et al., 2004; McKean-Cowdin et al. 2011). In the current study, myopes showed faster astigmatic progression (0.06D/year) than non-myopes (0.03D/year), however it was not statistically significant using DTA.

The results from the current study have found no link between astigmatism and spherical refractive error, suggesting different aetiologies. Ehrlich et al. (1997) also found that SER and astigmatism progressed independently of one another in infants up to twenty months of age, and these results are in accordance with some treatment studies for myopia, which have shown no change in astigmatic characteristics. For example, atropine has been found to slow myopic progression (Chua et al., 2006, Walline et al., 2011; Chia et al., 2012), Chia et al. (2009) found that it had no effect on progression of astigmatism in children aged 6-12 years. They concluded that accommodation had no influence on astigmatism, as did Irving et al. (1991) and Schmid and Wildsoet (1997) in their experiments on chicks. Peripheral defocus research (Smith et al., 2009, Irving et al., 2015; Queiros et al., 2016; Lagrèze et al., 2017; Tarutta et al., 2017) also suggests that manipulation with certain contact lenses reduces relative hyperopic defocus in myopes, but does not change astigmatism. Ongoing research is needed to determine why some studies confirm a relationship between astigmatism and myopia, but others, like this current study, show no link between refractive error types on either prevalence or progression.

7.4 Summary

This study shows the novel finding that season of birth has no effect on long-term changes in myopia or astigmatism in this group of patients from Liverpool. The data and statistical analysis also show that age does not influence these variables, so progression of refractive error appears linear with time.

Spherical refractions of ≤-0.50D and the presence of astigmatism appear to suggest that a child is more likely to progress in myopia and astigmatism respectively than non-astigmats, emmetropes or hyperopes. Although myopes show slightly higher astigmatic progression, the results from this study suggest that whilst astigmatism and myopia may share some risk factors, they do not significantly influence one another's progression.

Chapter 8: Conclusions and future research

8.1 Objectives

Results found from both the cross-sectional and longitudinal groups are summarized in this chapter. Strengths and limitations of the study are discussed, and future related research ideas are also proposed based on the findings.

8.2 Key points and findings

The study findings of prevalence of refractive error are similar to those of other epidemiological studies in the UK on White European children, despite the different testing methods.

8.2.1 Refractive error and progression

Myopia progressed at a mean rate of -0.15D/year, and astigmatism at -0.04D/year (see section 6.2). This study found that children between the ages of 5 and 17 years show similar rates of progression, and was higher in the prior presence of astigmatism and myopia (before the median split initial age of 8.8 years).

Being astigmatic or not did not affect myopic refraction progression (-0.15D/year compared with -0.14D/year respectively). Being myopic or not did not affect astigmatic progression (0.06D/year and 0.03D/year respectively).

8.2.2 Age and refractive error

Of patients with astigmatism, WTR astigmatism was the most common type at all ages, but ATR and oblique astigmatism became more common after the age of 11 years (section 5.2.2). Age did not influence the presence of astigmatism (section 5.2.1), but did influence SER (section 5.2.3), with children under 11 years most commonly emmetropic (42.6%), and children older than 11 years most likely to be myopic (40.4%).

8.2.3 Sex and refractive error

Boys were more likely to have astigmatism than girls were (section 5.2.1), but sex did not influence the axis of astigmatism, the prevalence of myopia, or the

progression of either astigmatism or myopia (sections 5.2.2, 5.2.3, 7.2.1 and 7.2.2 respectively).

8.2.4 Birth season and refractive error

Birth season did not influence the prevalence or progression of astigmatism or myopia (sections 5.2 and 7.2), suggesting that conditions of light-dark cycle and weather effects such as sunshine hours or temperature at the time of birth do not impact the future refractive error of patients. This was a novel finding in children for astigmatism, and progression of both astigmatic and spherical equivalent refractive error.

8.3 Suggested guidelines and advice for clinicians and families

Although the power of astigmatism may not change with clinical significance, the axis of astigmatism may change over time. With the trend of myopic progression occurring at a steady pace through childhood, regular follow up appointments are advisable to ensure the correct spectacles (if required) are being used. The results from this study can be used to present advice for clinicians, patients and their families: -

- Spherical equivalent refractions of ≤-0.50D particularly prior to the age of 11 years (from median splitting) should be a trigger to monitor children more closely for signs of myopic progression, and have discussions regarding risk factors that can possibly manage or reduce progression, such as spending time outdoors and regular breaks from near work.
- Astigmatism of ≥0.50D particularly prior to the age of 11 years (from median splitting) should be a trigger to monitor children more closely for signs of astigmatic progression, and changes with astigmatic axis.
- It is advisable to bring all the family for regular eye examinations, even though there may be no symptoms (especially the case for boys, who showed lower attendance but higher astigmatic error).
- Season of birth did not affect refractive error or its progression in this population.

Recent analysis from the CLEERE study group in the USA (Zadnik et al., 2015) on predicting myopia development by the age of 13 years showed that the single best predictor of myopia onset out of 13 possible risk factors was the cycloplegic

spherical refractive error (SER) of less than +0.75D at age 6. They did note that some of the predictors measured, such as axial length or lens power, would not be possible to measure at a routine sight test, so acknowledged that SER would also be a feasible measure to use to guide parents. Whilst cycloplegic refraction in clinical practice on all children at age 6 could be considered, results using non-cycloplegic refraction might be more useful to community optometrists.

McCullough et al. (2016) also suggested advice on eye examination recall for children in the UK based on research findings from the NICER study, which collated data from 18-20 year olds and their prior cycloplegic refractions. They advised that children aged 6-7 years who are myopic or at risk of myopia should have a sight test every year. At the age of 12-13 years, sight tests could be every 2 years unless there are progressive changes, which may warrant earlier recall. This reflected the findings that older children, whilst more likely to be myopic, showed slower progression changes than younger children, in contrast to the current study. They also did not advise on other age groups.

The studies by Zadnik et al. (2015) or McCullough et al. (2016) gave no indication of prediction of astigmatism. Whilst the current study did not specifically analyse refraction at particular ages to find specific future chances of developing refraction, it does provide insight into astigmatism and myopia in clinical practice and how this changes with time in order to give advice to clinicians. Annual sight tests should be advised for patients under 11 years of age who are myopic or who have astigmatism. After the age of 11 years, eye tests every two years can be advised unless there are other risk factors such as family history, or if the refraction is changing rapidly.

8.4 Future research

- Why do more girls than boys attend for eye examinations, and what can we do as clinicians to promote ocular healthcare to boys as well as girls?
- What specific age is the risk factor of crossover into myopia? Further research from this current data spread could assess the mean sphere progression, and compare both the cross-sectional and longitudinal data.
- Does rate of myopia progression vary with age of onset? Whilst some studies have suggested that progression of myopia does vary with age, this

study found no such pattern. Further research could assess whether myopia progression varies with the age of initial refraction. This may need a longer study period, and more patients to achieve this.

- Can we predict the future outcome of refraction based on subjective refraction data? Some statistical analyses, such as Bayes (as used by Zadnik et al., 2015), use past data to predict future results. Testing a large number of patients until the age of 18, then retrospectively analyzing their data may help us to see whether specific future patterns appear. Further research may help to provide expected refraction results to guide patients and their parents more specifically. If this is combined with ethnicity data and other risk factors from other studies or meta-analyses, a more accurate model could be proposed.

8.5 Study limitations and strengths

8.5.1 Limitations

The figures for prevalence are not representative of the total population. Rather, they show those who present themselves at practice for regular checks, who are likely to be those who struggle with their vision, or are keen (or have keen parents) to monitor their ocular health. The lower socioeconomic class of Liverpool compared to other regions of the UK may also skew the data to show higher prevalence of certain refractive errors than epidemiological studies may show. However, this study was designed to find results to be used as a guide for the community optometrist, who may only have to make adjustments for the demographics of the area in which they practice.

Median splitting makes results very clear to see, however it also loses some of the power in any statistical analyses. For example, the exact age at which myopia becomes more prevalent is lost, as only younger or older status is compared.

DTA is a statistical test that relies on the fact that there are no inter-associations between the variables tested. As this is rarely the case (see sections 4.2.6 and 6.2.6) this can be seen as a recognized limitation of DTA. However, using Chi-square inter-association analysis to obtain significant results may be misleading due to the confounding effects. Although the statistically significant inter-associations between the variables revealed by Chi-square tests may distort the outcome of

DTA, this method of multivariate analysis is likely to be better than basing findings on individual Chi-square tests because it accounts for confounding between multiple variables.

There were no repeatability results for either the clinicians or the patients. Fewer optometrists were sampled where possible to limit these effects. However, this represents typical community practice, where an optometrist gives a judgment based on a single snapshot in time, based on the previous notes of different optometrists.

Whilst it is clear that ethnicity plays a large role in the prevalence of refractive error, this was not noted at the time of the sight test. Therefore, a generalization was required based on Census data for ethnicity. In the same way, family history of refractive error was not asked at all sight tests, and therefore no adjustments were possible for this risk factor.

Although keratometry readings may be useful in aiding statistical analysis of prescription to determine if the prescription is lenticular, corneal, or a combination of both, these are not routinely noted in either practice. In addition, it has been found that, whilst the corneal radius of infants may alter with time (Gwiazda, et al., 1984), it does not tend to alter with age in childhood (Zadnik et al., 2003).

8.5.2 Strengths

Whilst this study cannot directly compare to full epidemiological prevalence studies, it gives a large-scale representation to the children attending community practice, the last of which occurred in the UK more than 15 years ago (Pointer, 2001).

The power of the study was high, so the results gained can be used with confidence, and allowed for the loss of power from median splitting.

The length of progression of the study of near to 6 years allows a longer timescale than some other longitudinal studies assessing refractive progression. This would have been longer had the smaller Old Swan practice been open for longer period at the time of starting the study.

The variation in age at the start of the longitudinal allowed greater analysis of whether age had an influence of refractive progression, compared to other studies, which start refracting at a particular age (Pointer, 2001).

Whilst the absence of cycloplegic refraction could be seen as a limitation, the author considered it to be a strength, in that it highlights information that is useful for community optometrists.

8.6 Conclusions

This study reports normative data for children attending a typical community practice in Liverpool, which can be likened (with allowance for various regional demographic differences) to other optometric practices. Whilst sex has been shown to affect astigmatism power and spherical refraction, it only influenced astigmatic axis in this population. The study also showed that birth season did not appear to influence refractive error in children, a novel finding for astigmatism, and both astigmatic and myopic progression. Whilst the presence of astigmatism did not affect prevalence or progression of myopia, and vice versa in this population, previous research has shown that they can be linked, and are multifactorial (Irving et al., 2015). Therefore, research and debate should be continued from both epidemiological and aetiological perspectives to refine data to advise and possibly treat refractive error progression.

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Appendices

Appendix 1: Research Protocol

Clinical Research Protocol Laura Mills

Title
Astigmatism in Myopia Development

Summary

Purpose:

To survey the characteristics of astigmatism in refractive error, both cross-sectionally and longitudinally, with particular reference to myopia development and progression.

Research participants:

Children under aged 18 attending 2 practices in Liverpool, UK.

Duration:

Cross-sectional study recording data over the year 2013.
Longitudinal data covers changes recorded from at least 5 years or 5 visits prior to 2013

Methods:

The records of children aged 0 to 18 will be investigated from 2 practices in Liverpool and the prescriptions of the right eyes recorded, along with the visual acuity, and the age and sex of the patient.
Statistical analysis will be used to determine longitudinal changes in assessing cylinder progression, particularly with reference myopia, and to use cross-sectional data to determine whether there is an association between cylindrical refractions and sex, and whether they have an impact on visual acuity.

Introduction

Objectives, questions or hypotheses:

To determine if there is a link between the progression of astigmatism and myopic prescriptions from longitudinal retrospective data of patients under 18 years of age.
To determine from cross-sectional data if there is a link between sex and astigmatism.
To determine how the level of visual acuity might vary in astigmatism in childhood.

This will allow optometrists to understand what prescriptions and VA is within normal limits, and deliver advice to patients and their families on the risk factors associated with changes in prescriptions.

How the study meets clinical needs:

Advice is often sought by parents on how their child's prescription will vary with time, and if there are any external influences that may affect it, in order to minimize any progression and dependence on spectacles. Prescription changes may impact children in the future in terms of practicality, and their career choices. Astigmatism prevalence varies with ethnicity, and in early astigmatism the prescription may emmetropize, meaning there is a need to monitor the patient rather than to dispense glasses. However, as a child gets older, astigmatism and myopia may be associated, meaning a child may need more regular assessment. Therefore it is important for community optometrists to be aware of certain risk factors and patterns in progression of certain prescriptions to be able to communicate effectively with their patients, and to understand when to prescribe, and when to monitor a prescription.

Scientific debate:

There is evidence to show that astigmatism rates are higher in myopes, and also that females are more likely to be myopic. Other studies suggest, that there is no difference in the rates of astigmatism between the sexes. This study will investigate the progression of astigmatism in myopes, and also to determine whether there is a link with prevalence of astigmatism and sex.

Methods; What will be done and which research participants will be involved:

A retrospective analysis of patient records from 2 practices in Liverpool (one in the city centre, and one in a suburb), will be used to gain data on the refraction, sex and VA for the right eye for each included patient.
The data of patients who have visited the practice for 5 or more visits, or who have been a patient for more than 5 years will be used in a longitudinal study to assess progression of the astigmatism in relation to the spherical correction.
Cross-sectional data of patients who have visited the practice in 2013 will be used to find out if there is a correlation between the level and prevalence of astigmatism in the different sexes, and if there is a correlation between the level of astigmatism and VA.
The definition of with-the-rule (WTR) astigmatism will be negative cylinder axes at 180±20, against the rule (ATR) as negative cylinder axes at 90±20, and oblique axes between 21 and 69, and 111 and 159.
The power of astigmatism will be defined as ≥-0.50DC, myopia as ≥-0.50D, and hypermetropia as ≥+0.50D.
The data will include information from the right eye only.
The study will exclude those children with current disease likely to affect the prescription, such as cataract or IOL, corneal opacity, ptosis, strabismus and amblyopia. Cycloplegic refractions will be included where they have been deemed necessary by the optometrists to gain the full prescription.

Statistical analysis will be used, including correlation and ANOVA regression tests to assess the results. Matrix data will be considered rather than using spherical equivalent refractive error as found in some studies, as it is suggested that it may be more accurate in assessing cylindrical data (Kaye and Harris, 2002).

Literature review

Astigmatism is well known to change throughout life, and there have been many studies charting its changes from high astigmatism in infancy (Gwiazda, et al., (1984); Weinberger, et al., 2004), reducing in childhood due to possible links with emmetropization, and then an increase in the elderly (Katz, Tielsch and Sommer, 1997). The axis of astigmatism has also been noted to change with age, with a decrease in WTR and increase in ATR astigmatism when measured both in longitudinal (Katz, Tielsch and Sommer, 1997) and cross-sectional studies (Farbrother, Welsby and Guggenheim, 2004; Rezvan, et al., 2011). The mechanism that causes these changes is still largely unknown, although there are several (possibly interacting) theories and risk factors.

The prevalence of astigmatism has varied from study to study. The NICER study (O'Donoghue et al., 2011) found that refractive astigmatism of 1.00DC or more had a prevalence of 24% in 6-7year olds, and 20% in 12-13 year old children, based on a predominantly Caucasian population in Northern Ireland. Different studies, however, may involve different definitions used to categorise patients, which vary between 0.25DC (Pärssinen, et al., 1991) and 1.50DC (McKean-Cowdin, et al., 2011) for astigmatism, the statistical analysis methods used, and the age, race, and number of subjects. These, and other risk factors discussed below, make it difficult to analyse results and compare studies directly.

There are many potential risk factors for astigmatism that have been investigated as well as age. Race or ethnicity shows one of the greatest variables. McKean-Cowdin, et al (2011) found that Hispanic and African-American children aged 6mths to 6yrs were more likely to have astigmatism ≥1.50DC than white children (Odds ratios of 2.38 and 1.47 respectively). Kleinstein, et al. (2003) showed that Hispanic and Asian children aged 5-17yrs shared a similar prevalence of astigmatism ≥1.00DC (36.9% and 33.6% respectively), followed by white children (26.4%) and African-American children (20.0%). However, a study on those over 40 years of age found that the prevalence of astigmatism was higher in White participants compared to African-Americans (Katz, Tielsch and Sommer, 1997). This information also suggests that there is a possible genetic link. However, this has not been confirmed, with some twin studies finding significant differences between monozygotic and dizygotic twins (Hammond, et al., 2001), some only a proportion of the variation in astigmatism linked with genetics (Pärssinen, et al., 2013), and other studies finding little correlation between family members (Valluri, et al., 1999; Lee, et al., 2001).

There has also been suggestion that children whose mothers smoke during pregnancy, and those who come from lower income families show an increase in the amount of astigmatism (McKean-Cowdin, et al., 2011). It may also vary with the amount of years spent in education – Katz et al. (1997) also found that astigmatism declined slightly with increasing years of education in African-American adults, although there was no association with White subjects.

Spherical refractive error has also been shown to affect the prevalence of astigmatism, with children with a spherical myopic prescription more likely to have astigmatism than children with hypermetropic and emmetropic spherical refractions, with a slightly higher odds ratio for ATR compared with WTR astigmatism and myopia (McKean-Cowdin, et al., 2011). The higher myopic and hypermetropic refractions in this study show a greater level of astigmatism prevalence compared with a lower spherical prescription, a finding also noted into adulthood, particularly with WTR astigmatism (Farbrother, Welsby and Guggenheim, 2004). Gwiazda, et al.

(1984) also demonstrated this link with myopia, though this time with ATR astigmatism.
There are 2 main theories of how astigmatism may relate to myopia. The first relates to the fact that astigmatic blur causes reduced accommodation, and the second, that ocular growth affects tension on the ciliary muscle and lens, creating a pseudo-cycloplegia, both of which then trigger axial length growth and myopia development (Gwiazda, et al., 2000).
Animal studies on chicks and monkeys have found that spherical defocus by plus and minus lenses produces specific compensation to the different lens types in an attempt to emmetropize the imposed defocus (Schmidt and Wildsoet, 1997). Form deprivation, however, tends to produce significant amounts of myopia as axial length increases. When astigmatism is imposed (regardless of axis), the compensated changes tended to produce oblique cylinder axes in monkeys (Kee, et al., 2003), which suggests that the normal compensation or emmetropization process for astigmatism does not apply in the same way as the response to spherical ametropia.
In monkey studies, imposed astigmatism has not been found to induce myopia, but rather small amounts of hyperopia (Kee, et al., 2004). Kee and Deng (2008) later found that high levels of spherical defocus (with both plus and minus lenses) could cause significant (ATR) astigmatism. This suggests that astigmatism does not necessarily cause myopia, but perhaps, that in some patients the emmetropization fails in terms of axial adjustment for spherical errors as well as anterior changes, which affects astigmatism development.

Sex has repeatedly been shown to be a factor in the development of myopia – Kleinstein, et al. (2003) found the prevalence of myopia ≥0.75D in school age children of 5-17yrs of varying ethnic background to be 11.5% in girls and 7.1% in boys. Plainis, et al. (2009) also found that there were higher levels of myopia in secondary school girls compared to boys. If there was a link between myopia and girls, and increased astigmatism in myopes, it might be thought that there would also be higher prevalence of astigmatism in girls. However, Kleinstein, et al. (2003) found no significant differences in prevalence of astigmatism and sex, and Rezvan, et al. (2011) found that there was no significant differences in axes of astigmatism, when comparing WTR, ATR and oblique axes between the sexes. Farbrother, et al. (2004) saw that the odds of having ATR astigmatism were slightly increased in males, and Katz, Tielsch and Sommer (1997) found slightly more men had astigmatism than women, but this was not significant. These potential conflicting results raise questions, which will be investigated further in this study.

In further investigation of the axis of astigmatism, Gwiazda, et al. (2000) and Friling, et al. (2004) both found a predominance of ATR corneal astigmatism in newborns. Gwiazda went further to note that children who are born with ATR astigmatism usually remain so, whilst most of those with WTR astigmatism tend to change to ATR by school age. This appears to contradict a previous study by Gwiazda, et al. in 1984, which found a predominance of ATR corneal astigmatism before the age of 4½ years, and a higher prevalence of WTR astigmatism after 4½ years of age, with none of the children with WTR astigmatism developing ATR astigmatism with increasing age. It is also disputed by figures from a study by Varghese, et al. (2005), who found that 55.3% of the newborn babies examined had WTR astigmatism, 11.4% had ATR astigmatism, and 33.3% had no astigmatism (leaving no results for oblique astigmatism!). O'Donoghue et al. (2011) found that most refractive astigmatism was oblique. This suggests a wide variation of prescriptions in the very young, and how it may be difficult to assess or predict how the eyes will emmetropize. McKean-Cowdin, et al. (2011) reported that there was a higher incidence of WTR astigmatism in pre-school children, and found no significant

difference between children with ATR astigmatism and their ethnicity, although WTR astigmatism showed a higher odds ratio in Hispanic children (2.38) and African-American children (1.37), when compared with White children. Although most studies will define the oblique astigmatic axes, most do not discuss this in the results, only tending to compare WTR and ATR. This study will assess all axes of astigmatism.

It can be seen that there is some conflict between results from different studies as to the nature and associations of astigmatism. This study aims to find results from a genuine optometry practice setting, which can be directly compared and used by community optometrists with relevance to their patients.

Selection of research participants

The records of all children who became patients when they were under 18 years of age will be analysed for the cross-sectional part of the study to assess prevalence of astigmatism, and whether the degree of astigmatism has a bearing on visual acuity. Those with at least 5 visits or were patients over 5 years will be used for the longitudinal part of the study looking at the development and change of myopia with astigmatism.
G*power 3 software suggests that for the study proposed, with an alpha level of 0.05, a minimum sample size of 614 subjects would give enough information to show significant findings. It is expected that, due to the age of the practice(s), there will be more than this number, improving on accuracy of results.

Risks and benefits

There will be no risk to the patient as this will be a retrospective study, looking at past data, with no extra participation involved.
It is unlikely that there will be any immediate benefit to the subjects themselves by participating, as there are no interventions involved.

Recruitment of Research Participants

As this is a retrospective and anonymous study, there will be no recruitment requests or requirements.

Informed consent

There is no requirement to obtain consent from patients or their parents, as only prescriptions, VA and sex of the patient will be extracted – no personal identifying data will be removed from the practice.

Privacy and confidentiality

All records are currently kept in a secure location in practice, and will not be removed from the practice for the purpose of analysis. Therefore, there is little risk of data protection being broken as no names or contact information will be taken.

Ethics section/Limitations

The data that will be recorded will be information from 2 practices, one large city centre practice that has been open for 23 years, the other a smaller practice in one of the suburbs that has been open for 6 years. This will lessen the variations that may occur from assessing only those patients and families that will make the journey into the city for their eye examinations, although it is likely that because of its age and size, the majority of the records will be from the central practice. The data is also likely to be skewed to show higher prevalence of refractive error, as more patients will refer themselves or their children if they are struggling with their vision.

The city centre practice moved locations in 2010, and with it came a change in testrooms and equipment. There are also many optometrist results data to be analysed, testing in several rooms. Nidek phoroptor heads (both the RT2100 or RT5100) have been used in most of the testrooms since 2004, although sometimes it would have been necessary to use a testroom with trial frame and lenses. Whilst this may have an small effect on VA and prescription, as each patient may have been seen by a different optometrist each visit, with varying equipment, it is hoped that this effect will be too small to affect the results, as each room is measured and has been installed by experienced shop fitters and Nidek engineers.

Snellen acuities may be limited in their scope for certain patients, such as amblyopes, for whom crowding variability may vary according to the number of letters in a row, or on the screen. LogMAR would have been a preferred choice of VA measurement due to its consistency at all noted measurements of acuity. However because this is a retrospective study, for which amblyopes have been excluded, and with all measurements having been taken in the form of Snellen acuity, this is the unit of measurement used. Snellen acuities have been used in some previous retrospective refraction studies, however (Rosenfield and Chiu, 1995; Pointer, 2001). This may also be more useful for community optometrists to interpret the results of this study, and apply it to their patients.

Whilst cycloplegic auto-refraction may be taken as the 'gold standard' for refraction studies, different studies have used different drugs to obtain cycloplegia: tropicamide (Zadnik et al., 1992), cyclopentolate (McKean-Cowdin et al., 2011), or both (Kleinstein et al., 2003). Some studies do not use cycloplegia at all (Pointer, 2001; Plainis et al., 2009; Rezvan et al., 2011), and as this is a retrospective study, subjective responses will be used. Many refraction studies use cycloplegic auto-refraction to determine refraction (eg. McKean-Cowdin et al., 2011; Kleinstein et al., 2003) or retinoscopy (Gwiazda et al., 2000). Zadnik et al. (1992) found that non-cycloplegic subjective testing showed a repeatability of ±0.63D at the 95% limit of agreement, whist for cycloplegic autorefraction was ±0.32D. They suggested that only changes of 0.75D or more are outside the range of measurement error for non-cycloplegic subjective refraction. However, results for non-cycloplegic and cycloplegic refraction were worse, at ±0.78D and ±0.95D respectively. Rosenfield and Chiu (1995) found that there was a similar degree of repeatability with subjective refraction and auto-refraction at 95% limits of agreement of ±0.29D for subjective testing compared to pl/min 0.27D in auto-refraction. Whilst non-cylcoplegic refractions are likely to give a slightly more negative refraction in children due to residual accommodation, compared with cycloplegic assessment. We are trained to give the most plus prescription that will give optimum visual acuity, and as this is the standard test used in UK optometric practice, it is believed that the figures will be more relevant to community optometrists.

The data from the right eye only has been used. It has been demonstrated in previous studies that the mean spherical power and the amount of astigmatism is similar between eyes (Pärssinen, et al., 2013). It should, however, be noted that the axes may not show a direct association between eyes, as determined by McKendrick and Brennan (1997), or show mirror symmetry as found in a larger study by Guggenheim, et al. (2006). If mirror symmetry is assumed to be the norm, the definitions used for WTR, ATR and oblique will still give comparable results to previous studies of refraction using the right eye only for data (Zadnik, Manny and Yu, 2003).

Although keratometry readings may be useful in aiding statistical analysis of prescriptions, these are not routinely noted in either practice. Also, it has been found that, whilst the corneal radius of infants may alter with time (Gwiazda, et al., 1984), it does not tend to alter with age in childhood (Zadnik, Manny and Yu, 2003).

Results may be presented differently in different studies, with varying definitions of significant refractive data sets, and the statistical analysis used to assess the data and find patterns. This makes it harder to compare the conclusions gained from other authors. This study will try to gain enough data to be representative for most community optometrists, and be clear in its presentation so that they can understand it and be able to simply transfer it to their clinical practice.

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Appendix 3: Literature review search

Databases searched:

The Cochrane Library (www.thecochranelibrary.com)
Directory of Open Access Journals (www.doaj.org)
Google Scholar (scholar.google.co.uk)
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)
Web of Knowledge (apps.webofknowledge.com)
Wiley (www.wileyopenaccess.com)

Terms searched:

Astigmati* AND child*
Astigmati* AND “risk factors”
Astigmati* AND progression
Astigmati* axis AND child*

Myopi* AND child*
Myopi* AND “risk factors”
Myopi* AND progression

Myopi* AND astigmati* AND child*
Myopi* AND astigmati* AND development

Repeatability AND “subjective refraction”
Repeatability AND “cycloplegic refraction”

Appendix 4: Frequency tables for cross-sectional and longitudinal patients

Table A1: Cross-sectional summary table

		Sex		Birth Season				Astigmatism		Axis				Refractive Group		
		F	M	Win	Spr	Sum	Aut	Abs	Pre	None	WTR	ATR	Obl	Em	Hy	My
Age	Young	208	189	100	95	105	97	226	171	226	102	43	26	169	167	61
	Old	337	166	132	128	115	128	271	232	271	97	84	51	182	118	203
Sex	F			137	145	132	131	322	223	322	102	77	44	200	173	172
	M			95	78	88	94	175	180	175	97	50	33	151	112	92
Birth Season	Win							133	99	133	47	33	19	96	69	67
	Spr							119	104	119	52	28	24	95	64	64
	Sum							114	106	114	52	30	24	82	76	62
	Aut							131	94	131	48	36	10	78	76	71
Astigmatism	Abs									497	0	0	0	242	127	128
	Pre									0	199	127	77	109	158	136
Axis	None													242	127	128
	WTR													48	95	56
	ATR													45	29	53
	Obl													16	34	27

F: Female
M: Male

Win: Winter
Spr: Spring
Sum: Summer
Aut: Autumn

Abs: Absent
Pre: Present

WTR: with-the-rule
ATR: against-the-rule
Obl: Oblique

Em: Emmetrope
Hy: Hyperope
My: Myope

Young: Younger
Old: Older

Low: Lower
High: Higher

Table A2: Longitudinal summary table

Astigmatic Progression		Initial Refractive Group			Initial Axis				Initial Astigmatism		Birth Season				Sex		Age			
High	Low	My	Hy	Em	Obl	ATR	WTR	None	Pre	Abs	Aut	Sum	Spr	Win	M	F	Old	Young		
																	78	60	F	**Sex**
																	46	58	M	
															20	30	19	31	Win	**Birth Season**
															23	35	32	26	Spr	
															31	40	37	34	Sum	
															30	33	36	27	Aut	
											30	42	34	30	52	84	68	68	Abs	**Initial Astigmatism**
											33	29	24	20	52	54	56	50	Pre	
									0	136	30	42	34	30	52	84	68	68	None	**Initial Axis**
									58	0	22	16	9	11	36	22	22	36	WTR	
									31	0	8	9	7	7	7	24	20	11	ATR	
									17	0	3	4	8	2	9	8	14	3	Obl	
					5	7	10	65	22	65	16	33	20	18	35	52	45	42	Em	**Initial Refractive Group**
					6	12	33	41	51	41	31	26	17	18	45	47	31	61	Hy	
					6	12	15	30	33	30	16	12	21	14	24	39	48	15	My	
		30	50	41	5	9	25	82	39	82	31	32	32	26	46	75	58	63	Low	**Astigmatic Progression**
		33	42	46	12	22	33	54	67	54	32	39	26	24	58	63	66	55	High	
60	64	12	57	55	8	17	29	70	54	70	30	37	27	30	57	67	55	69	Low	**Myopic Progression**
61	57	51	35	32	9	14	29	66	52	66	33	34	31	20	47	71	69	49	High	