Amblyopia and Strabismus in young Singaporean Children

Chia Wei-Lin Audrey

FRANZCO

This thesis is submitted to fulfill the requirements for the degree of

Doctor of Philosophy at the National University of Singapore

Saw Swee Hock School of Public Health

National University of Singapore

2013

DECLARATION

I hereby declare that the thesis is my original work and it has been written by me in its entirety.

I have duly acknowledged all the sources of information which have been used in the thesis.

This thesis has also not been submitted for any degree in any university previously.

Chia Wei Lin Audrey

30th January 2013

Acknowledgement

I would like to thank my supervisor, Professor Saw Seang Mei, for first getting me involved in the Strabismus, Amblyopia and Refractive Error in Singapore Preschool Children (STARS) study from its initiation in 2004-5, for allowing me to use the data collected in this study for material for this PhD thesis, and for the invaluable support and advice that she provided me throughout the way.

I would also like to thank the other members of my thesis advisory committee; Professor Wong Tien Yen and Dr Yvonne Ling for their help and support.

I would like to acknowledge the dedicated work and efforts of the entire STARS study team including Dr Mohamed Dirani, Mr Prabakaran Selvaraj, and Dr Arlie Jaurigue. I thank the various biostatisticians that have assisted me in providing help with statistical analysis and advice throughout the last 4 years including Dr Chan Yiong Huak, Miss Xiao Yu, Assistant Professor Ben Harlaand, Dr Peggy Chiang and Associate Professor Tai Bee Choo.

Finally, I would like to thank my various co-authors involved in the publication which have arisen from the PhD project.

Table of Contents

Summary

The aim of this thesis was to determine the prevalence of amblyopia and strabismus amongst Singaporean Chinese pre-schoolers. Other aims were to explore risk associations, to assess the efficacy of stereoacuity and refractive error as screening tools of amblyopia and strabismus, and to assess the effect of amblyopia and strabismus on quality-of-life.

3009 children (response rate 72.3%) were recruited into the population-based Strabismus, Amblyopia and Refractive Error study in Singaporean preschoolers study (STARS). The prevalence of amblyopia in children aged 30-72 months was 1.19% (95% CI 0.73-1.83), with most amblyopia being refractive (85%) rather than strabismic (15%). Amblyopia was found to be associated with myopia $\leq$-3.0D (OR 27.6, 95%CI 5.2-147.2), hyperopia $\geq$3.0D (OR 13.8, 95%CI 2.7-70.6), astigmatism $\geq$1.0D (OR 8.9, 95%CI 2.8-28.4), anisometropia $\geq$1.0D (OR 9.4, 95%CI 1.7-50.5) and strabismus (OR 14.5, 95% CI 2.2-96.8), after adjusting for age, gender, prematurity and socioeconomic status.

The prevalence of strabismus in children aged 6-72 months was 0.80% (95%CI 0.51-1.19) with an exotropia:esotropia ratio of 7:1. Strabismus was associated with lower paternal education (with ORs in father with higher education ranging from 0.07-0.23), astigmatism$\geq$1.0D (OR 3.5, 95%CI 1.0-12.0), concurrent amblyopia (OR 15.9, 95%CI 2.7-92.8), a parental history of strabismus (OR 17.9,

95%CI 1.1-278.3) and a sibling history of strabismus (OR 38.3, 95%CI 8.7-168.5).

Stereoacuity was assessed using the Randot Preschool Stereoacuity Test (RPST) in children aged 30-72 months. Stereoacuity was poorer (≥200sec) in children with amblyopia (38.4%) and strabismus (69.2%). However, good stereoacuity (40-60sec) was also recorded in 23.1% in each group. ROC analysis suggests that the RPST was more effective in detecting anisometropia >2.0D (auc 0.84, 95%CI 0.72-0.55), strabismus (auc 0.82, 95%CI 0.66-0.99), and amblyopia (auc 0.77, 95%CI 0.63-0.92) than high ametropia and astigmatism. However, our findings suggest that RPST lacks sensitivity:specificity balance to act as a sole screening test for amblyopia and strabismus.

Refractive error was assessed using cycloplegic autorefraction with a table-mounted auto-refractor when possible, and a hand-held autorefractor or retinoscopy when not. Since refractive error was used in the classification of amblyopia in this study, many autorefraction parameters were 'effective' in the detection of amblyopia (eg. astigmatism (auc 0.88), anisometropia astigmatism (auc 0.82), myopia (auc 0.78) and anisometropia (auc 0.72)). Autorefractive parameters, however, were poor predictors of strabismus (auc 0.51-0.69).

Health-related quality of life (HRQOL) was measured using the generic Pediatric Quality of Life inventory (PedsQL4). We found no difference in the PedsQL4

scores in children with and without amblyopia and strabismus. However, in a Childhood Development Survey, children with strabismus were found to have more speech (OR 4.71, 95% CI 1.52-14.59, p=0.007) and comprehension (OR 5.61, 95% CI 1.37-28.7, p=0.02) problems. Rasch analysis found misfit; reliability and validity issues with marked ceiling effect, suggesting that the PedsQL4 was a suboptimal scale with regards assessment of HRQOL in young Singaporean Chinese children with amblyopia and strabismus.

The findings from this study provided new information and insights about amblyopia and strabismus in the young Singaporean Chinese children, and will be useful in the planning and development of public health and medical services.

List of Tables (1/5)

List of Tables (2/5)

List of Tables (3/5)

List of Tables (4/5)

List of Tables (5/5)

List of Figures (1/3)

List of Figures (2/3)

List of Figures (3/3)

Glossary

'A' level	Advanced level
AAPOS	American Association of Pediatric Ophthalmology and Strabismus
ADVS	Activities of Daily Vision Scale
ALSPAC	Avon Longitudinal Study of Parents and Children
ANOVA	Analysis of variance
AS20	Adult Strabismus questionnaire
A&SQ	Amblyopia and Strabismus Questionnaire
AUC	Area under the curve
BMI	Body mass index
BPEDS	Baltimore Pediatric Eye Disease
BL	Body length
BW	Birth weight
B-VAT	Binocular vision testing system
CI	Confidence interval
CPP	Collaborative Prenatal Project of the National Institute of Neurological Disorders and Stroke
CVAQC	Cardiff Visual Ability Questionnaire for Children
DNBC	Danish National Birth Cohort
EQ	EuroQol (Quality of life)
ET	Esotropia
ETDRS	Early treatment diabetic retinopathy study
ETROP	Early Treatment for Retinopathy of Prematurity
GA	Gestational Age
HC	Head circumference
HDB	Housing Development Board
HUI	Health Utility Index
HRQOL	Health related Quality of Life
HSS	Health summary score

IXTQ	Intermittent Exotropia Questionnaire
IVI	Impact of Visual Impairment
logMar	Logarithm of the Minimum Angle of Resolution
LR	Likelihood ration
LVP-FVQ	LV Prasad Functional Vision Questionnaire
MCS	Millennium Cohort Study
MEPEDS	Multi-ethnic Pediatric Eye Disease study
'N' level	Normal level
NEI VF	National Eye Institute Visual Function Questionnaire
NICU	Neonatal intensive care
NPP	Negative Predictive Value
'O'-level	Ordinary level
OR	Odds ratio
PD	Prism Diopters
PedsQL4	Pediatric Quality of Life Inventory version 4
PPV	Positive predictive value
QOL	Quality of life
ROC	Receiver Operator Characteristic Curves
RPST	Randot Preschool Stereoacuity test
RR	Relative Risk
SE	Spherical equivalent
SF	Short Form
SPEDS	Sydney Eye Pediatric Disease study
SMS	Sydney Myopia Study
VA	Visual acuity
VIP	Vision in Preschool Study Group
USA	United States of America
XT	Exotropia

Chapter 1: Introduction

1.1 Amblyopia and Strabismus

Amblyopia and strabismus are two common pediatric eye conditions with functional and cosmetic consequences. Both should ideally be detected and treated early in childhood to maximize functional outcome. Amblyopia is a suboptimal vision in one or both eyes despite best spectacle correction and in the absence of any other ocular and neural abnormality (1,2). It occurs when there is a defect in visual development in the early years of life. Studies suggests that response to treatment is better in children younger than 7 years, but improvement can still occur in children up to the teenage years (2,2a). Strabismus is the misalignment of the eyes so that when one eye is fixating on a target, the other is fixated elsewhere (eg. inward, outwards, up or down). If left untreated, this condition may result in loss of binocularity (ie. the ability of the eyes to work together) and depth perception (2).

The medical significance and management of these 2 conditions are well described (3,4,5). The challenge remains to detect these conditions early enough for treatment to be successful.However, with an increasing need to justify cost-effectiveness in health screening and service provision, it was noted that there was a dearth of fresh information regarding the size of the problem (prevalence) and factors associated with these conditions.

Historical data may no longer be as relevant as social demographics, environmental and medical service structures have changed within many countries. There are questions regarding whetherthe frequency of various refractive errors, amblyopia and strabismus has changed, whether differences exist within different population groups, and how changes in health care, perinatal services and life-style mayhave altered both the incidence and types of ocular pathology, particularly in young, preschool children in whom the effect of these conditions are most significant.

In the early 2000s, several large population-based cohort studies were set up to study paediatric eye disease in young preschool children across the world. These included the MillenniumCohort Study (MCS) in the United Kingdom, the Multi-ethnic Pediatric Eye Disease study (MEPEDS) and Baltimore Pediatric Eye Disease study (BPEDS) in the United States, and the Sydney Eye Pediatric Disease study (SPEDS) in Australia (6,7,8). The Strabismus, amblyopia and refractive error in Singaporean preschooler study (STARS), which has a similar study design to the MEPEDS, BPEDS and SPEDS, commenced in 2006 and data collection was completed in 2009. Data from this study form the basis of results presented in this thesis.

1.2. Amblyopia

The term ‘amblyopia’ comes from the Greek word ‘amblu$\bar{o}$pos’ which means ‘*dim-sighted*’ (9).

Amblyopia occurs when there is suboptimal visionin one or both eyes despite best-corrected spectacle correction, and when there areno other anatomical ocular or cerebral visual pathway abnormalities to explain this visual impairment (1). It occurs as a result of disrupted or incomplete visual development during early childhood (10,11).

Normal visual development commence at childbirth when the child opens his/her eyes for the first time. It improves very rapidly in the first 6 months of life and then more gradually, reaching adult levels when the child is aged 4-6 years (12). This is accompanied by differential development of the retina foveal region, increased synaptic density within the primary visual cortex, and pruning of extraneous neuronal receptive fields; all of which result in improved spatial resolution and contrast sensitivity (ie. vision). This process is a competitive one, with neurons from each eye competing for space within the cortex (13-16).

Subsequently, if quality of visual stimuli from one eye is diminished (eg. because of high refractive error, an obstruction of visual axis, or an ocular misalignment) then visual development in the other eye may be quicker, leading to suboptimal

vision in the disadvantaged eye. Well-known ocular risk factors to amblyopia include high hyperopia (>4.00D), high myopia (<-8.00D), astigmatism (>2.00D), lid ptosis, childhood cataract and strabismus (1,2).

Treatment of amblyopia involves optimizing visual quality (eg. providing child with spectacles or removing any obstruction to the visual axis), and visual penalization of the better eye (eg. with occlusion patching or atropine) (3-4,17-20). There is a sensitive or critical period within the first 2 decades of life during which visual development must occur (2a,3). If treatment is not initiated prior to this time, adult levels of vision may never be achieved. Visual prognosis is poorer in children in whom deprivation occurred earlier in life, and in whom treatment is started too late (12-16).

1.2.1 Assessment of Amblyopia

Detection of amblyopia starts with assessment of visual acuity. In adults and children aged 6 years and above, this often involves testing how well the subjects are able to read letters on a distance chart with each eye. In illiterate or young subjects, test orthotypes may be changed so that subjects are asked to identify pictures, shapes or direction of which letters are pointing ('E' chart) (21-24). Orthotypes can be presented singly or at closer distances depending on level of

co-operation.In very young children who are unable to communicate verbally, matching tests or force-preferential tests may be used (21-23).

Testing vision in very young children can be challenging. Testability of visual acuity is generally poorer in younger children (25-29). Results from force-preferential tests (such as the Teller Acuity test) can be useful but may be subjective, observer dependent and depends on child's state of mind when tested (30-32). Tests commonly used in younger children (eg. Teller visual acuity, KayPic, single matching HOVT test) often underestimate visual acuity deficits. Children may perform less well because they do not understand what they are required to do, are not as confident with their letters, are particularly shy, poor communicators or have short attention span. Repeated visual acuity testing may be necessary to confirm presence or absence of visual impairment.

Testability of visual acuity in the MPEDS, BPEDS and SPEDS were very similar, 39-47% in children aged 30.0-35.9months, 79-86% in those aged 36.0-47.9months, 94-98% in aged 48.0-59.9months and 99-100% in those aged 60.0-72.0months (25,27,29).

Once suboptimal vision is established, then a thorough ocular examination is necessary to ensure that there are no other structural or correctable refractive causes of poor vision. Diagnosis of amblyopia is often easier when amblyogenic risk factors (such as an abnormal refractive error, visual obstruction or

strabismus) are also present. In younger children, in whom visual assessment may not be so reliable, finding co-existing amblyopic risk factors may be necessary to minimize the number of false positives detected.

1.2.2. Prevalence of Amblyopia

In a review of population-based and school-cohort studies, the global estimates of the prevalence of amblyopia range from 0.20-6.2% (Table 1.1) (6-8,33-58). Differences in study design, disease classification and response rates could account for some of the variability and disparity noted. Unfortunately, these differences also make direct comparison between studies difficult.

The similarity of design between the MEPEDS, BPEDS and SPEDS studies, however, make it easier to compare between these series of studies, although differences in response rate, assessment process and testabilitydo exist (6-8). In these studies, visual acuity was tested and re-tested by trained researchers under very controlled circumstances. All children were subsequently had their refractive error and eyes examined to exclude visual loss from refractive error or other anatomical cause.

In other population, school or army cohort studies involving older subjects, the diagnosis of amblyopia often depends heavily on structured visual acuity

assessment by trained study personnel (33-57). However, in some population-based studies, children are referred only if they failed visual screening during pre-existing health screening programs (52), self-assessment tests by parents (40) or by teachers at school (45). These latter studies depend on parents and care-givers to do the tests or to bring the children in for testing, and as such, the accuracyand response rates may vary. In other studies, determination of diagnosis may depend on parental response to questionnaires which can be subject to reporting or recall biases. (53-54).

In 2008, the Multiethnic Pediatric Eye Disease Study (MEPEDS) study group reported an amblyopia prevalence of 2.6% and 1.5% in 3007 Hispanic/Latino and African American children aged between 30-72months respectively (6). In 2009, Friedman et al, utilizing data from 2546 children enrolled in theBaltimore Pediatric Eye Disease study (BEPDS), noted amblyopia prevalence of 1.8% and 0.8% in Caucasian and African American children respectively (7). More recently, in the Sydney Paediatric Eye Disease (SPEDS) study, Pai et al (2012) found an amblyopia prevalence of 1.9% in 1422 predominantly white children (8).

There are also a few studies which look at amblyopia rates in East Asian children (Table 1.1). Matsuo et al (2007), in a questionnaire-based study of Japanese children aged between 1.5 and 12 years, reported prevalence rate for amblyopia ranging between 0-0.2% (53,54). Lim et al (2004) used a home screening unit to

identify at risk children amongst 26973 Korean childrenaged 3-5 years. Children who failed test presented themselves to healthcare centers and if children failed their visual acuity tests again, they were referred to an ophthalmologist. In total, amblyopia, mostly refractive, was detected in 0.4% of the 43% who responded (40). In Taiwan, Lai et al (2009) reviewed visual screening records of 625 preschool children and identified amblyopia, using various definitions, in about 5% (55). He et al (2004), primarily assessing visual impairment in 4,368 children aged 5-15 years in Guangzhou, China, reported amblyopia in 1.9% of their subjects (39), and Pi et al (2012) in a survey of 3469 children aged 6-16 years in ChongQing, China, noted amblyopia in 1.88% (56).

1.2.3. Types of amblyopia

Amblyopia can be classified as either being unilateral or bilateral. Unilateral amblyopia occurs when the visual image in one eye is compromised or blurred so that that eye is selectively disadvantaged. In contrast, bilateral amblyopia can occur when there are similar levels of obstruction/blur in both eyes. This is often the result of high uncorrected refractive error (eg. hyperopia, myopia or astigmatism) or equal obstruction in both eyes. Laterality of amblyopia was not always recorded in all studies, but where documented, unilateral amblyopia was often more common than bilateral amblyopia with unilateral:bilateral ratios

ranging from 1.7-16.0 (6-8,36,44,46,50-2,57) except in Ohlsson et al (2003)'s study of Mexican school-children where the ratio was close to 1 (38) (Table 1.1).

Amblyopia can also be classified according to etiology (ie. refractive, strabismic or deprivational) (1,58) (Table 1.2).In general, refractive amblyopia was more common than strabismic amblyopia in non-white populations (Table 1.2). Within predominantly white populations, refractive error accounted for 40-58% of amblyopia, and strabismus accounted for 33-56% (7,8,35,36,44,46,52,59). In East Asia, Middle East and amongst African Americans and Hispanic-Latinos in the US, however, refractive error and strabismus accounted for 54-86% and 3-33% of amblyopia respectively (6,34,39-42,50,53,56,60,61).

In terms of classifying the various types of refractive amblyopia, there was no universal convention (Table 1.1). Different studies often used different cut-off values. Anisometropia (ie. the difference in refraction between eyes) could be classified, in 0.25D increments, as a difference of 0.50 to 2.50D. Similarly, hyperopia could be defined as spherical equivalents greater than +0.50 to +4.00D, while myopia can be defined as being less than -0.50 to -3.00D. Astigmatism (ie. the cylindrical power of the eye) could be defined as being more than 0.50 to 2.50D. In general, however, anisometropia appeared to be the most common association with amblyopia followed by hyperopia in white children, while astigmatism was more common in East Asian children (Table 1.2).

Strabismus (or ocular misalignment) was also commonly associated with amblyopia, but occasionally it was uncertain whether strabismus wasthe primary or secondary event (ie. whether child became amblyopic because of strabismus, or whether child became strabismic because of amblyopia).

1.2.4. Factors associations with Amblyopia

The ocular associations of amblyopia are well-known with refractive errors (i.e. anisometropia, astigmatism and high ametropia), strabismus or any occlusion of the visual axis being cited as common risk factors (1,2,11,20). In 2003, the American Association of Pediatric Ophthalmology and Strabismus (AAPOS) visual screening committee posted guidelines, indicating that presence of anisometropia (spherical or cylindrical > 1.50D, hyperopia or myopia > 3.00D, astigmatism of >1.50D within 10^{o} of the 90^{o} or 180^{o} meridian or >1.00D in the oblique meridians, manifest strabismus, ptosis with margin reflex distance <1mm, or lens opacity > 1mm were potential amblyogenic factors (62).

Clinically, amblyopia has been strongly associated with refractive error(Table 1.3). In population-based studies, associations between anisometropia >1.00D and amblyopia were found in the Sydney Myopia Study (SMS) (OR 156, 95%CI 64-382) and in the Sydney Paediatric Eye Disease (SPEDS) study (OR 27.8, 95%CI 11.2-69.3) (8,44). Astigmatism >1.00D was associated amblyopia with an OR of

11.0 (95%CI 5.7-21.1) in the SMS and 5.7 (95%CI 2.5-12.7) in the SPEDS studies. Amblyopia was also strongly associated with strabismus in the SMS (OR 65, 95%CI 30-144) and in the SPEDS (OR 13.1, 95%CI 4.2-40.3) studies (8,44).

Another interesting question was whether birth, maternal or socio-economic factors were associated with amblyopia. It has been quite well demonstrated, for example, that strabismus, anisometropia, high myopia and therefore amblyopia were more common in premature children (44,63-66). In Australian children with modest prematurity (ie. birth weight 1500-2499g), Robaei et al (2006) found that the risk of amblyopia was increased by 4.5x (95%CI 1.9-10.6),compared to children of birth weights >2499g (44). In a separate study, Robaei et al (2008) also found that a past admission to NICU was associated with amblyopia (OR 5.0, 95% CI 21.-12.0) (46).Similarly, Schaliji et al (2000) in a parental questionnaire study of premature infants in the Netherlands, found that treatment for amblyopia was more commonly recorded in very premature children (gestational age, GA< 28weeks) (32%) compared tomoderately premature children (GA 28-32 weeks) (22%) and less premature children (GA 32-37 weeks) (10%) (67).

Maternal smoking was associated with amblyopia in the Avon Longitudinal Study of Parents and Children (ALSPAC) study (OR 1.4, 95%CI 1.0-1.9) and SMS (OR 2.2, 95%CI 1.0-5.0) studies (44,47). William et al (2008), in the ALSPAC study where 7825 children born between 1991-1992 were screened at aged 7 years, also found association with amblyopia in families with lower social economic

status(ie. those living in public rather than private housing) (OR 1.5, 95%CI 1.0-2.2), and also with a family history of amblyopia (OR 2.7, 95% CI 2.0-3.6) (47).

1.3 Strabismus

Strabismus comes from the greek word, strabismos which is the condition of squinting; and is derived from the word strabizein or strephein which is 'to twist'. (68).Strabismus occurs when there is a misalignment between eyes. There are several forms of strabismus (Table 1.4) (69). In the most common childhood comitant strabismus, the angle of deviation misalignment is similar in all position of gaze. There are also a set of incomitant strabismus, often associated with neurological or orbital problems, where the angle may vary with position of gaze. Deviations can be inward (esotropic) or outward (exotropic) or vertical (hypotropia/hypertropia). However, there are situations where individuals can overcome their eye deviations resulting latent or intermittent strabismus.

It is uncertain why some people develop strabismus. Eyes in young infants are often initially poorly co-ordinated and misaligned. Eye movement and vergence control improve at 10-15 weeks of age promoting ocular fusion so that eyes are usually well-aligned by 4 months (70-74). It is believed that the sensitive period for binocularity begins at 10-16 weeks of age and peaks at 1-3 years (75,76). Any disruption of ocular fusion and binocularity may perpetuate ocular misalignment and strabismus. Early correction of the misalignment (eg. with glasses or surgery) may help in the recovery of some binocular fusion.

1.3.1. Assessment of Strabismus

Strabismus is best evaluated using the cover-uncover or alternate cover test, in subjects with good vision in both eyes, by a trained orthoptist, optometrist or ophthalmologist (77).

In the cover test, subjects are tested to see if they have a manifest strabismus. The subject is seated using their best glasses correction and instructed to view a distant target. Each eye is covered in turn, and both eyes are observed for any movement. If the uncovered eye moves to take up fixation, then it is assumed that it had initially been mis-aligned. Often then, the covered eye would move horizontally or vertically to its resting position. The test can then be repeated for the other eye, and also for a near target, and with or without glasses. In the alternate cover test, subjects are tested to see if they have a latent strabismus. The occluder is moved from eye to eye without allowing the subject to acquire binocular fusion. Any latent strabismus may then become apparent. The test can then be repeated for a near target, and with or without glasses.

Should subjects be unable to maintain fixation on a target (eg. if theyhave poor vision in one or both eyes, are too young, or have decreased levels of consciousness), then misalignment of the eyes can be measured more grossly using the Hirschberg light reflex or Bruckner's test. In the Hirschberg pupillary light reflex test, the pupillary light reflex should be positioned centrally in the

cornea of both eyes as the child looks at the light. Displacement of the light reflex to one or other side may indicate presence of an ocular misalignment. In the Bruckner's test, if a child's pupillary reflex is viewed from a distance, it should appear symmetrical in both eyes. However, if reflex is duller or eccentric in one eye, this may indicate presence of strabismus or refractive error in that eye (77). These tests are not valid for small angle strabismus (microstrabismus).

The size of the misalignment can be measured using prisms. In the prism cover-uncover and alternate cover test, prisms are positioned in front of the eyes and are increased until there is no residual movement. In less co-operative subjects, prisms could also be placed in front of the eyes and increased/decreaseduntil the light reflex appears symmetrical in both eyes (Krimsky test).

Occasionally, when there is microstrabismus (eg. strabismus less than 10PD), eye movements and light reflex changes may not be obvious. In co-operative subjects, presence of microstrabismus can be measured using a 4 to 10PD prism test. With subjects focused on a distant target, a 4 to 10PD base-in prism is moved in front of one eye. If the eye moves to maintain fixation, then it is assumed that subject was using this eye. If it does not, then the subject is assumed not to be previously using the eye, and that a micro-strabismus may be present. The test can then be repeated in the opposite eye.

Full assessment is not complete until eye movements are assessed, and strabismus type and size can be measured in different positions of gaze to determine if there is comitance or incomitance. In comitant strabismus, the angle of deviation is similar in all positions of gaze, while in incomitant strabismus, angle of deviation may change in different positions of gaze.

Final determination of strabismus type is based on clinical history (age of onset, duration of strabismus, presence of double-vision and other symptoms, and changes over time), nature of strabismus (assessment findings of behavior during testing and over time, intermittency, variability, associated eye movement abnormalities, and response to full glasses correction), and other ocular assessments (visual acuity, glasses prescription, ocular and neurological examinations).

1.3.2. Prevalence of Strabismus

Overall, global estimates of strabismus in children and teenagers ranged from 0.13 to 4.7% (Table 1.5). Prevalence of strabismus in population with predominantly white ethnicity (2.3 to 4.2%) were generally higher than in those of East Asian descent (0.01 to 1.8%) (7,35,37,43,45,47,49,52-54,78-82). Children from Mexico, Iran, and African-American and Latino-Hispanic children in the USA had strabismus rates ranging from 2.0-2.5% (6,7,38,48,51,81).

Differences in how strabismus was identified in different studies might account for some of the differences in estimates. In the large population-based MEPEDS, BPEDS,SPEDS, STARS, ALSPAC,and Blue Mountain Study, subjects were sampled from the general population, and strabismus was assessed by trained observers.Strabismus was identified in this manner in many of the preschool or school cohort studies (35,37,38,45,48,49,51,56,79,80,82,83).

In other studies, visual problems were detected by pre-existing screening programs or home screening programs, after which it was left to parents to take their children to be examined by an ophthalmological service (40,52). In some studies, presence/absence was determined by a parental questionnaire (53,54,84). Identification of strabismus through these indirect means could result in reporting biases in prevalence estimates.

1.3.3. Types of Strabismus

The most common forms of childhood strabismus included the comitant esotropia and exotropia (Table 1.4). Other forms of strabismus were much less common, and often not described in detail in even in large population and school cohort based studies.

From the review of literature, the frequency of esotropia and exotropia might vary depending on ethnicity. In East Asian, Iranian and Native American children, the frequency of exotropia could exceed esotropia by 2.2 to 17.0 times (45,48,49,51, 53,79,82,83). In contrast, esotropia often exceeded exotropia by 1.1 to 9.0 times in white children (7,35,37,43,47,52,78,80), while in African-American, Hispanic-Latino-American and Mexican children, the ratio lay closer to 1.0 (6,7,38).

In these studies, there was often little detail regarding which types of esotropia or exotropia the children had, partly because it was difficult to classify strabismus typebased on a single visit. Often, differentiation between the commoner infantile, fully and partially accommodative and acquired-non-accommodative esotropia required a detailed history anda follow-up assessment when refractive errors were fully corrected with glasses.

In the Rochester Epidemiology Project, however, Greenberg et al (2007) were able to determine, through review of case-files, that in the 385 children with esotropia, 8.1% were congenital, 36.4% fully and 10.1% partially accommodative and 16.6% were acquired non-accommodative esotropia (85). Amongst the 205 children with exotropia, 51.7% had intermittent, 19.5% had convergence insufficiency and 0.5% had congenital exotropia (86). 14.6% had an exotropia associated with an abnormal central nervous system and 8.2% had a sensory exotropia.In a study done of 682 Singaporean children aged $\leq$ 16 years presenting to an eye clinic with commitant strabismus, 28% of children were found to be

esotropia; of whom 23% had infantile, 30% fully accommodative, 23% partially accommodative and 17% acquired non-accommodative esotropia (87). Of the 72% who were exotropic, 92% had intermittent exotropia; 59.5% of whom had the divergence-excess form, 29.0% had the basic form, and 11.5% had the convergence insufficiency form.

These studies suggest that amongst children with esotropia, the accommodative esotropias were more common; whilst amongst the exotropia group, intermittent exotropia dominate (6,81,85-87).

1.3.4. Factors associated with Strabismus(Table 1.6)

Studies on prematurity often demonstrate that the risk of strabismus increase with prematurity (65-67). Amongst the 342 children, reviewed at age 6 years, in the Early Treatment for Retinopathy of Prematurity (ETROP) trial, strabismus was noted in at least 30% of children with favorable visual and structural outcome, and up to 80% of those with ocular or cerebral abnormalities (88). Lindqvist et al, in a Norwegian study comparing very low birth weight babies (<1500g), small for term babies and normal term babies, found rates of strabismus of 32%, 19% and 11% in each group respectively at 14 years of age (64). They also found that very low birth weight babies had poorer stereopsis and convergence, and a higher risk

of nystagmus; but no difference in accommodative amplitudes, saccades and smooth pursuit (63).

In Australian children with modest prematurity (ie. birth weight 1500-2499g), compared to children with birth weights >2499g, Robaei et al (2006) found that the risk of strabismus was increased by 2.6x (95%CI 1.1-6.0) (80,81). Similarly, Schaliji et al (2000) in a parental questionnaire study of premature infants in the Netherlands, found that strabismus was more commonly recorded in the very premature children (GA < 28weeks) (39%) compared to the moderately premature children (GA 28-32 weeks) (33%) and less premature children (GA 32-37 weeks) (5%) (67).

Prematurity, which is often defined as GA <33-37 weeks, and BW < 1.5-2.5kg, was associated with strabismus in general in the MCS and SMS studies(OR of 2.9-3.5); specifically with esotropia in the ALSPAC (OR 2.5, 95%CI 1.6-3.9), MPEDS/BPEDS (OR 4.4, 95%CI 2.1-9.2) and DNBC (RR: 2.2, 95%CI 1.6-2.0); specificallywith exotropia in the MPEDS/BPEDS study (OR 2.5, 95%CI 1.2-5.3), and in both esotropia (OR 1.38, 95% CI 1.17-1.63 in BW 2000-2500g, and 3.26, 95%CI 2.50-4.25 in those BW< 1500g) and exotropia (OR 1.48, 95%CI 1.12-1.88 in BW 2000-2500g, and 4.01, 95%CI 2.77-5.80 in those BW< 1500g) in the CPP study (47,78,80,84,89,90,91).

Strabismus was also shown to be more strongly associated with white children compared to South Asian (RR 0.5, 95%CI 0.3-1.0) and black children (RR 0.2, 95%CI 0.1-0.6) in the MCS study; in white compared to black esotropic children in the CPP study (OR 0.55, 95%CI 0.45-0.66), and in white compared to non-white esotropic children in SMS study (OR 0.3, 95%CI 0.1-0.8) (78,80,84,89).

Maternal smoking was associated with strabismus in the CPP (OR 1.83, 95%CI 1.51-2.22 for >2 packs/day in esotropic children, and OR 2.32, 95%CI 1.72-3.13 in exotropic children), ALSPAC (OR 2.5, 95%CI 1.3-4.8), and in the MEPEDS/BPEDS studies (OR 2.0, 95%CI 1.2-3.5 for esotropic children and OR 2.9 95%CI 1.8-4.6 for exotropic children) (25,47,78,89). Hakim et al (1992), in a USA cohort, found that smoking during pregnancy was associated with esotropia (OR 1.8, 95%CI 1.1-2.8) but not exotropia (92). Similarly, Torp-Pederson et al (2010), in the DNBC study, found an association between those children with congenital esotropia (RR 1.66, 95%CI 1.00-2.75) and accommodative esotropia (RR 1.52, 95% CI 1.07-2.18) and those children whose mothers who had smoked 5-10 cigarettes per day, and an association between exotropia (RR 1.60, 95%CI 1.45-2.68) and children whose mothers had smoked > 10 cigarettes per day (92). Smoking < 5 cigarettes per day was less likely to be associated with strabismus (93). Maternal smoking, however, was not associated with strabismus in the MCS or SMS studies (80,81,84).

The role of refractive errorin strabismus was examined in the MPEDS/BPEDS and SMS studies. In the MPEDS/BPEDS study, strabismus was associated with hyperopia >2.00D (OR > 6.4), anisometropia ≥ 1.00D (OR 2.0, 95%CI 1.1-3.7 for ET), and astigmatism 1.50-2.50D compared to < 1.50D (OR 2.5, 95% CI 1.3-4.8 for XT) (91). In the SMS, amblyopia, hyperopia ≥3.00D, astigmatism ≥1.00D and anisometropia ≥1.00D were all more common in strabismic children ($p<0.001$) (80).

There was also evidence that family history of strabismus or amblyopia wasassociated with strabismus (47,78,94-98). Children with strabismus were more likely to have a sibling with strabismus in the CPP (OR 2.0, 95%CI 1.2-3.2 for ET) and ALSPAC studies (OR 2.4, 95%CI 1.7-3.2) (47,78). In a review of 96 strabismic children, Ziakas et al (2002) found that 67% of those with accommodative esotropia (33/49), 42% with infantile esotropia (11/26), 33% with anisometropic esotropia (5/15) and 17% with exotropia (1/6) had at least one first degree relative with strabismus (95). Likewise, in a longitudinal study, Aurel & Norrsell (1990) found that strabismus developed in 6 of 34 (17%) of children with a parent or older sibling with strabismus (94). Matsuo et al (2002) also found a higher familial concordance with accommodative esotropia and intermittent exotropia (96). The chances of subsequent children developing strabismus is also increased if there is an older sibling with strabismus (89).

There has also been an association with increased paternal age (OR 4.9, 95%CI 1.6-15.0) in the SMS, and increased maternal age 30-34years compared to 20-24years (OR 1.4, 95%CI 1.1-1.7) in the CPP study (79,80). However, no association between paternal age and strabismus was noted in the MEPEDS/BPEDS (91).

Other isolated associations include a risk-association with female gender (OR 1.6, 95%CI 1.1-2.4 for exotropia) in the MPEDS/BPEDS study (91), and an association with intrauterine growth retardation (OR 4.5, 95%CI 1.8-10.8 for exotropia) in the ALSPAC study (47), with admission to NICU (OR 4.2, 95%CI 1.6-11.1) in the SMS study (44), with caesarean section (RR 1.6, 95%CI 1.1-2.3 for exotropia) in the DNBC study, and with having a professional parent (RR 6.8, 95%CI 1.7-28.0) (90) or an unemployed parent (RR 6.8, 95%CI 1.2-27.0) rather than technical-trained one in the MCS study(84).

1.4. Amblyopia and Strabismus and their effect on Stereoacuity

Stereoacuity is the ability of the brain to utilize images received from both eyes to perceive depth or 3-dimensional vision. It is not surprising, therefore, that it may be affected by conditions which degrades the image of one or both eyes or causes misalignment of eyes such as amblyopia and strabismus (99-106). Stereoacuity is measured in terms of seconds of arc (sec) with smaller values indicating better stereoacuity. Functionally, persons with better stereoacuity may perform better at motor tasks than those with poor stereoacuity (107).

Studies suggest that stereoacuity develops in the first 2 years of life and continues to improve over the next 6 to 10 years (108-116). There are many commercially available tests which can be used to test both near and distance stereoacuity in young children including the Stereo smile and Randot stereocards for preverbal children and the LangI/II, Frisby near and distance stereotest, Randot stereo-fly or butter-fly test (circles/animals), Random Dot E, Randot Preschool Stereoacuity Test, TNO test and mentor B-VAT for older children (8,112,114,115,117). These tests have different levels of difficulty and testability, and the range of stereoacuities measured can vary amongst different age groups; making direct comparison between tests difficult. (8,101,109,112,114,115,117-120). Another difficulty in assessing stereoacuity in very young child is ensuring that these children are able to perform test reliably, and that the stereoacuity obtained is a true estimate of the child's stereovision.

Birch et al (2005), on screening children aged 1 to 24months using the Randot Stereocards, found that the mean stereoacuity level in these children was approximately 600sec at 4months, 200sec at 6months, 100sec at 12 months and 70sec at 18months (112). Using the Randot Preschool Stereoacuity test, Birch et al (2008) found that mean normal stereoacuity in 3 year old children was 100sec, and 60sec and 40sec by 5 to 7 years of age (114). Similarly, Adams et al (2005), using the Distance Frisby test in children aged 3-6 years, found that the mean distance stereoacuity improved from 50sec in children aged <48months to 30sec in those aged $\geq$ 48months (117).

These studies suggested that stereovision developed as earlyas 3 months of age and continued to improve throughout the first decade of life so that the improvement seen in various studies might represent the natural development expected (108-116). There might, however, be a small proportion (10%) of normal individuals who never achieve their full stereo potential (115,120,121).

The Randot preschool stereoacuity test (RPST) was used to screen children aged 30-72 months in the MEPEDS, STARSand SPEDS studies. Testability in these studies in 30-36 month and 36-48months age groups was approximately 30% and 60-70% respectively, and but rose to >90% in children greater than 48 months of age (27,122,123). Testability was also slightly better in girls than boys (27,122,123). Testability and results from stereoacuity test, however, might

depend on dedication and perseverance of examiner with some studies achieving testability rates as high as 80% in children aged 3years (121,124). Fawcett & Birch (2000) were also able to demonstrate good test-retest correlation with the Randot preschool stereoacuity test in children aged 2-12 years (r =0.97) (125). However, Adler et al (2012) using the Randot circles test in children aged 4-12 years, found that stereoacuity improved by an average of 1 level when children were re-tested 8 days later with greater improvement seen in those with poorer initial stereoacuity values (116).

1.4.1. Relationship between Stereoacuityand Amblyopia, Strabismus and Other ocular diseases

Robaei et al (2007), in a study of 2342 Australian children aged 12 years, notedreduced stereoacuity (>120sec) with the TNO test in children with amblyopia (68.3%), strabismus (54.8%) and anisometropia (37.5%) compared to children without any of these conditions (1.4%) (102).

Artificially induced spherical and astigmatic anisometropia could degrade stereoacuity, dropping it into abnormal levels in otherwise normal individuals (126,127). Dobson et al in a study of 972 children (age 4-13 year old) found that small changes in hyperopia, myopia or astigmatism could cause significant changes in stereoacuity (104). Conversely, correction of pre-existing refractive

error improved stereoacuity in children who were otherwise visually impaired (102). Stereoacuity in children with amblyopia was reduced and often improved with treatment (101). However, some children with anisometropic amblyopia might still have lower stereoacuity compared to normal children even after successful treatment of their amblyopia (106).

Stereoacuity was also often poorer in the presence of strabismus (128). Stereoacuity in children with infantile esotropia, where the ocular misalignment was present within the first 6 months of life, was absent pre-operatively (129), and often remained poor even after very early strabismus surgery (130,131). Stereoacuity was also been found to be poorer in children with accommodative esotropia where ocular alignment might have been present earlier in life (129). This suggested that the critical periods for stereoacuity might occur as early as 3 months in infantile esotropia and 10 months in accommodative esotropia (132). In cases of intermittent strabismus, stereoacuity might fluctuate throughout the day depending on the level of binocular fusion, and it was uncertain whether poor stereoacuity preceded or resulted from strabismus (105,133-135).

1.4.2. Effectiveness of Stereoacuity as a screening test for Amblyopia and Strabismus

Overall, the studies suggest that stereoacuity levels were much less in children with amblyopia and strabismus. Distance stereopsis might also be more sensitive in the detection of ocular disorders than nearstereopsis (128).

The sensitivity and specificity of various stereoacuity tests depended on the age of the child, the 'difficulty' of the test, and the level at which the normal cut-off limit were set (Table 1.7). A low sensitivity level (ie. low true positive or high false negative rate) might occur when the test was too simple or the normal cut-off limit was set too low. Conversely, lower level of specificity (ie. low true negative or high false positive rate) might occur when the child tested was younger, the tests too difficult or normal cut-off limit was set too high.

It is doubtful whether stereoacuity can be used in isolation as a screening tool for ocular pathology. Prevalence of conditions such as amblyopia and strabismus are relatively low in paediatric populations (eg.<5%). As such, to minimize un-necessary referrals (false positives), the 'normal' stereoacuity cut-off needs to be set higher so as to achieve better specificity levels (eg. >90%). However, in such cases, test sensitivity (ie. the ability to detect true positives) is often sacrificed or compromised, which may potentially result in children with ocular disorders (but with milder stereoacuity defects) being missed (135,136). Thus to be a good

screening tool, sensitivity and specificity of tests should both ideally be high. From a review of the literature, there appears to be few stereoacuity tests that achieve this (Table 1.7).

1.5. Effectiveness of autorefractors refractive error estimates as a screening test for Amblyopia and Strabismus

As testability of visual acuity is low in young children, there has been great interest in the use of autorefractor readings as an alternative screening tool to identify children at risk (138). There are many types and brands of autorefractors, and individual differences in accuracy and reliability exist (139-147). There are also varying views about where different refractive cut-offs (eg. for hyperopia, myopia, anisometropia and astigmatism) should be set.

In recent years, there have been a series of studies examining the effectiveness of various screening methods by the Vision in Preschooler (VIP) Study Group, based in the United States involving 2588 children from 11 preschools (124,135,136,148). In these studies, there were strict definitions of how/when children were classified as being amblyopic, strabismic and having reduced visual acuity (Table 1.8). Refractive errors were deemed to be amblyogenic when cycloplegic refractions of astigmatism were>1.50D between principal meridians; hyperopia >3.25D in any meridian, myopia >2.00D in any meridian, or

anisometropia >1.00D difference in hyperopia, >3.00D in myopia, >1.50D in astigmatism (148).

Using these definitions, Ying et al (2011), in a study using ROC analysis to compare the effectiveness of non-cycloplegic retinoscopy, Retinomax autorefractor and SureSight Vision Screener as screening tools for amblyopia, strabismus, significant refractive error and reduced visual acuity, noted that thesetools had high area-under-the-curves (auc) ranging from 0.83-0.88 (148). With specificity held at 90-94%, the SureSight Vision screener and the Retinomax autorefractor had sensitivities of 63-64% (135,136). However, there was concern that the proportion of false negative (missed cases) wasstill too high.

As there is a tendency for most autorefractorsto underestimate hyperopia or overestimate myopia (141,142,145-147,149-151), there is debate whether cycloplegic refractions would provide more accurate results.Steel et al (2003), in a comparison of Retinomax Plus and Allyn SureSight vision, found that the 95%CI obtained was quite wide even in cyclopleged children suggesting that these devices were useful only for screening purposes (152). Using the VIP referral criteria for a specificity of 90%, Rowatt et al (2007), in a field study involving 2733 non-cycloplegic children using the Sure-Sight Vision Screener, noted a referral rate of 12.2% with a positive predictive value of 30% (153). With a specificity of 95%, the referral rate fell to 7.9%, but several cases of anisometropia were undetected.

To further improve sensitivity/specificity of the screening process, some investigators suggest combining autorefractor findings with other tests (eg. visual acuity assessment) to improve detection of amblyopia (154). Further analysis, however, would be necessary to determine whether these added benefits justify increase in screening costs (154). Adjustments of VIP criteria might also be explored to further improve the positive predictive value of this test (155).

In terms of screening for strabismus, autorefractor estimates appeared less useful and the use of either a cover-uncover test (in the hands of trained professional) or photoscreening or stereoacuity tests (in the hands of lay persons) might be more effective (137).

1.6. Effect of Amblyopia and Strabismus on Quality of Life

With pressure mounting on health care budgets, it is now not only necessary to justify costs of healthcare just on cure or survival rates but also to demonstrate a negative impact of disease and a positive treatment effect on a person's quality of life.

Instruments to measure health-related quality of life (HRQOL) could be generic (general) or specific to a disease, symptom or group of individuals. Popular generic quality-of-life questionnaires include the Medical Outcome Study Short Forms (SF-6, SF-12 and SF-36), EuroQol (EQ-5D), Health Utility Index (HUI2, HUI3) and Pediatric Quality of Life Inventory (PedsQL) (156,157). Instruments more specific to visual function include the National Eye Institute Visual Function Visual Function Questionnaire (NEI VF-25, VF-51), the Visual Function Index (VF-14), the Impact of Vision Impairment (IVI) and the Activities of Daily Vision Scale (ADVS) (158,159). Instruments specific to children include the Impact of Vision Impairment in Children (IVI-C), Cardiff Visual Ability Questionnaire for Children (CVAQC), and the LV Prasad-Functional Vision Questionnaire (LVP-FVQ) (160-163). Questionnaire specific for amblyopia and strabismus include the Amblyopia and Strabismus Questionnaire (A&SQ), the Adult Strabismus questionnaire (AS20) and the Intermittent Exotropia Questionnaire (IXTQ) (164-166).

1.6.1. Amblyopia and Quality of Life

Much of the focus of amblyopia on HRQOL has been directed more at the impact of its treatment rather than on the disease itself (167-175). Treatment of a child with amblyopia might involve spectacle wear, eye occlusion (eg. patching), drug penalization of the better eye (eg. with atropine eye drops) and frequent visits to the orthoptist or ophthalmologist. This could be time-consuming and stressful for both parents and child (167,171,173,175). Being amblyopic and requiring treatment might also identify the child as being different from their peers, and this might result in problems with peer interaction, sense of isolation, inferiority, frustration or embarrassment and interfere with their general education (168,172). Horwood et al (2006), in a study involving 6536 children in the ALSPAC study, found that children who were wearing glasses or had a history of patching were 35% more likely to have been bullied (170). Spectacle wear could also negatively affect the manner in which parent treat or interact with their children (175). Parents reported that the most common problems encountered with patching included having to overcome their child's resistance to treatment, fear that their children could not see well when they are patched, and worry how other children might stare and that their child might be treated differently (167). Atropine penalization appeared to be better tolerated but parents still reported problems having children comply with and accepting treatment (167). However, Choong et al (2004), in a clinic based study of 65 subjects, found only a transient initial

negative effect to glasses. They also found that the adverse effect of patching might be over-rated as they noted no difference in stress levels and psychological well-being between those who were and were not patched (168). Hrisos et al (2004), in a prospective review of 117 amblyopic children, noted that while children did resist and dislike treatment, there was no adverse effect on the child's general well-being and behavior (169).

Amblyopia itself could also have functional, emotional and social consequences. Functionally, children with amblyopia might have difficulties with associated mono-vision, poor stereopsis or altered visual field (eg. poorer hand-eye co-ordination, difficulty concentrating, becoming tired easily, or having problems with depth perception) (176-178). Webber et al (2008) found that children with amblyopia had more problems with fine motor skills such as drawing lines/symbols and with certain tasks (eg. sorting cards, stringing beads, displacing pegs) (176). Grant & Moseley (2011) noted key differencesin movement speed and accuracy invarious motor tasks in amblyopic persons compared to non-amblyopic persons (177).

Emotionally, amblyopic children and adults were more likely tobe worried about their eyes, of losing their better eye, being self-conscious (particularly if the amblyopia is associated with strabismus or glasses wear), or feeling inferior because of their condition (172,174). Socially, the amblyopic person might feel

different, isolated and have difficulties (secondary to these and other reasons) in interacting with their families and their peers (172,174).

Using a visual specific questionnaire, the VF-14, Sabri et al (2006) were able to detect difference between teenage amblyopic children and controls (78.9 vs 95.5) with greater psychological impact seen in those with noticeable strabismus (179). Using a more amblyopia/strabismus specific questionnaire, the A&SQ, Van de Graaf et al (2004, 2007, 2010) and Felius et al (2007), demonstrated lower HRQOL scores in their amblyopic/strabismus subjects compared to controls; with greater impact in the 5 domains of fear of losing better eye, distance estimation, visual disorientation, diplopia, and social contact/cosmetic problems (174,180-183).

The effect of amblyopia on quality of life and life-style in the longer term, however, might not be as substantial as feared. Rahi et al (2006) found that in the 1958 British birth cohort, there was no difference between people who did and did not have amblyopia in terms of their education, behavior, participation in social activities, employment, general and mental health, unintended injury or mortality (184). Similarly, Wilson & Welch (2012) in a prospective 1972-3 birth cohort (n 1037) found no difference between persons with amblyopia, recovered amblyopia and no amblyopia in terms of childhood motor development, teenage self-esteem and adult socio-economic status (186). Chua et al (2004), in the Blue Mountains Eye Study, noted that there was no difference in employment but that amblyopic

individuals were less likely to have completed tertiary education (2.5% vs 7.2%, p=0.05), and had an increased 5 year incidence risk of uncorrectable visual impairment > 6/12 in the better seeing eye (11.1% vs 1.7%) (185).

1.6.2. Strabismus and Quality of Life

Strabismus is the misalignment of the eyes which is often first noted by parents in the early childhood years, and is often quite obvious to bystanders. For this reason, the impact of strabismus on the psychological and social effects of HRQOL mightbe more prevalent than with amblyopia.

Studies show that strabismus had a negative impact on a person's self-image, interpersonal relationships, emotional and psychological state (179,187-201). If left untreated, it could not only result in loss of binocularity, depth perception and visual acuity (amblyopia), but might also have long-term consequences on the patient's personality, and a person's emotional, psychological and social functioning. This psychosocial impact affected all age groups (children, adolescence and adult life); more notably in the adolescent or young adults when self-consciousness and self-image might be of greater significance (194,199). Some studies suggest that prejudice against children with strabismus by their peers could occur from as early as 5 to 6 years of age (189,191,197). Parents of strabismic patients might also be affected emotionally and could develop a

strained, less supportive relationship with their affected children (195,202). Successful strabismus surgery improved the HRQOL, socially and emotionally, in both children and adults (192,203-206). Surgery was also found to be useful in the adults >65 years of age with psychological, social and even functional benefits (207).

The effectiveness of HRQOL questionnaires could be quite different in differentiating between persons with and without strabismus. For example, Hatt et al (2010), in a comparison of the visual specific VFQ-25 and the amblyopia / strabismus specific AS-20, found that more subjects had below-normal scores with the AS-20 compared to the VFQ-25 (90% vs 29%) (208). In a separate study, Hatt et al (2010) demonstrated more sub-normal scores in children with intermittent exotropia using the strabismus specific IXTQ compared to the more generic PedsQL4 (55% vs 18%) (209). In the MEPEDS study, Wen et al (2011) noted that parental-proxy PedsQL4 total scores, in African-American and Hispanic children aged 24-72 months, were significantly lower than in children with no strabismus (88.0 vs 91.8) after adjustment for age, gender, race and family income (210). This suggested that one needed to be careful when selecting the most appropriate questionnaire for assessing the impact of strabismus on HRQOL.

Chapter 2: Aims of the Study

The primary aims of this study were to determine the prevalence of amblyopia and strabismus, and to explore the risk-associations (demographic, maternal, birth, ocular and socioeconomic) of amblyopia and strabismus in young Singaporean children aged 6-72 months in the Strabismus, Amblyopia and Refractive error in Singaporean preschoolers (STARS) study, which was a population based cohort study involving 3009 Chinese children recruited from the South-Eastern region of Singapore.

The secondary aims were to assess the relationship between amblyopia and strabismus and other visual parameters (such as stereopsis and refractive error), and to evaluate the effectiveness of stereoacuity and autorefraction measures as screening tools to identify children with amblyopia and strabismus, and to determine the effect of amblyopia and strabismus on the child's quality of life and development.

It is hoped that this knowledge would lead to a better understanding of the magnitude, causes and effect of these two common paediatric conditions and aid in the planning and management of these conditionsin young Singaporean children.

Chapter 3: Research Design and Methods

3.1. Study Design

The Strabismus, Amblyopia and Refractive Error in Singapore Preschooler (STARS) study was a population-based cohort study designed for the study of peadiatric eye diseases in young Singaporean Chinese children aged 6-72 months. Children of the ages 6-72 months were chosen as study subjects as there was no epidemiological data about the ocular health of Singaporean pre-school children (as opposed to good data regarding older school age children from the School Cohort of Risk factors for myopia, SCORM, study). Amblyopia and strabismus were also two conditions best identified and treated at a young age, and a study of the magnitude, associations and effects in this age-group was deemed appropriate.

The study design of the STARS study was based on that of the Multi-ethnic Pediatric Eye Disease Study (MEPEDS) (211). This was so that a useful comparison could be made between STARS and other studies with similar design.

The MEPEDS was specifically designed to estimate age–specific prevalence of strabismus, amblyopia and refractive error, to determine the association between risk factors and these ocular conditions, and to evaluate the effect of these ocular conditions on health-related functional status (211).The MEPEDS study recruited 2994 African American and 3030 Hispanic children between 2005-8 (response

rate: 77%) (6). Recruitment of Asian-American and non-Hispanic white children is on-going.

There were also two other studies with similar designs including the Baltimore Pediatric Eye Disease Study (BPEDS) and the Sydney Paediatric Eye Disease Study (SPEDS). The BPEDS was designed to recruit 3000 children, aged 6-72 months, from the Non-Hispanic white and African-American ethnic groups (7,212). Recruitment and data collection occurred between 2003-2007 during which 2546 out of 4132 eligible children (participation rate: 59.5%) were examined. In SPEDS, a further 2461 children, aged 6-72 months, of mixed ethnicity (participation rate: 73.8%) were recruited between 2007 and 2009 (8,123).

3.2 Sample size calculations

In a sample size analysis based on estimates of amblyopia rates of 0.9-5.7%, and strabismus rates of 1.2-5.6%, the MEPEDS study team estimated that a sample size of 3000 would be required to determine prevalence of these amblyopia and strabismusin each ethnic group (211). Children aged 6-72 months in four ethnic groups (African American, Asian American, Hispanic/Latino and non-Hispanic White) would be sampled. To determine risk-factor associations, it was assumed that with a pooled sample size of 12,000 children, they would then be able to

detect odds of 1.8-2.2 with power of 80% when the prevalence of risk-factors was 0.20 or greater.

3.3 Recruitment

Singapore is a small tropical island nation (land area: 740km2) with a population of 3.27 million; of whom 2.51 million are of ethnic Chinese origin (213). Due to an active public housing program which started in the 1970s, the majority of population (84%) live in publicly built Housing Development Board (HDB) townships.

Chinese children, aged 6 to 72 months, from HDB townships of Bukit Batok, Clementi, Jurong East, Jurong West and South Central area of Queenstown and Bukit Merah in the South-Western region of Singapore were included in the study (Figure 3.1). To enumerate children eligible for the study, all HBD blocks within the area were first identified. With the assistance of the Ministry of Home Affairs, a list of Chinese households with young children was created, and the STARS study team then undertook a door-to-door exercise to verify and collate the number of eligible children within each household. Disproportionate stratified sampling by 6-month age groups was performed to achieve almost equal number of children in each 6 month age group. In this process, all eligible children were separated into 6 month age strata, and a fixed proportion of children were randomly selected from each strata so as to achieve the target of 4000 children (ie.

to achieve a sample size of 3000 taking into account a potential 30% non-participant rate). Parents of selected children were invited to bring their children to one of two visual screening sites; the Jurong Medical Center located in Jurong West, and the Singapore National Eye Center located in Bukit Merah. A total of 4162 Chinese children were eligible to participate in the study, with 3009 examined (response rate 72.3%).

3.4 Patient Consent

The aim of the study, the steps involved and the roles and responsibilities of parents were explained to parents prior to child's inclusion into the study. Informed written consent was obtained from parents and guardians.

3.5 Inclusion criteria / Exclusion criteria

After registration, the child's ethnicity was confirmed. Both the child's biological mother and father were required to be of Chinese descent. Children from non-Chinese ethnic groups were excluded from the study.

3.6 Data collection and measurement (Figure 3.2)

All study members were thoroughly briefed on study protocol prior to their involvement in the study to maintain consistency. A single study co-ordinator,

orthoptist and optometrist were employed throughout the three-year study period. Assessment of stereopsis, ocular alignment and motility was done by a fully qualified orthoptist. Cycloplegic refractions and retinoscopy was performed by a fully qualified optometrist. External eye, anterior examination and dilated fundal examinations were initially done by a team of 5 peadiatric ophthalmologists on a rotating basis in the first year, and then by an ex-paediatric ophthalmology fellow over the last two years of the study. Patient interviews were conducted by a team of trained researcher assistants led by the study co-ordinator.

3.6.1. Test of glasses

If children were already wearing glasses, the power of the glasses were determined using an automated lensometer, and the spherical, cylindrical and cylindrical axis in each lenses were noted.

3.6.2. Stereopsis (children aged 30 months or older)

Stereoacuity was assessed by a trained orthoptist or optometrist using the Randot Preschool Stereoacuity Test (StereoOptical Co, Inc, Chicago, Ill). Children were first tested with a non-stereo pre-test picture to ensure that they had figure recognition abilities. If so, they were seated comfortably and asked to wear glasses provided with the set. The first test plate, consisting of tests for 200 and 100sec of stereoacuity, was presented at 40cm, and children were asked to match

the 3 shapes within the 4 boxes, at the 200 sec level, to those on an accompanying matching chart. Children were considered to have passed each level if they were able to identify at least 2 of the shapes at that level. If children passed both the 200 and 100 sec tests on the first test plate, they were presented with the 60 and 40 sec test plate. If children failed the 200 and 100 sec tests, they were presented with the 400 and 800sec test plate.

3.6.3. Ocular alignment and motility

Ocular alignment was assessed using the Hirschberg light reflex, cover test and prism cover-uncover tests. Cover tests were performed by trained optometrist or orthoptist using fixation targets at both distance (6m) and near (30cm). The presence of strabismus, its characteristics (constant or intermittent), type (exotropia, esotropia, hyper/hypotropia or dissociated vertical deviation) and size (prism diopters) were also recorded.

Ocular motility was assessed using a moving target in horizontal and vertical positions of gaze. Any overaction or underaction of the superior, inferior, medial, lateral, superior oblique and inferior oblique muscles was identified. Presence and absence of nystagmus (rhythmic jerky eye movements) was documented.

3.6.4. Fixation preference

Fixation preference was tested by placing a 12PD base-down prism in front of the right and then left eye. If the child was fixing with the tested eye, then a downward movement of the tested eye would be noted. Ability of the child to alternate or hold fixation, and any eye preference was noted.

3.6.5. Visual acuity (children aged 30 months or older)

Distant logarithm of the minimum angle of resolution (logMAR) visual acuity was tested in each eye with and without glasses using a 4-meter ETDRS (Early-treatment diabetic retinopathy study) chart, where 5 equally spaced optotypes were presented on each line. Children were instructed to read the first letter of each line. When an error was made, they were instructed to read all the letters in the line above. If the child was able to read 3 or more optotypes correctly, then that line was taken as the baseline visual acuity with 0.02 added for each optotype missed.

In children in whom vision could not be tested by the above means, visual acuity assessment was repeated using the single letter uncrowded 4 meter Sheridan-Gardner test. The test was explained to parents and child. Children were asked to match the optotypes presented to them to a matching card. Smaller optotypes were presented until mistakes were made on 2 attempts at the same level. The

next larger optotype was presented and if the child was able to read this correctly, this was taken as the child's visual acuity. If not, the process was repeated and if the child failed again, progressively larger optotypes were presented until the child was able to identify 2 optotypes correctly at a similar level. Vision was measured in terms of Snellen visual acuity and converted to LogMar equivalents (Table 3.1).

Visual acuity was re-tested to verify visual acuity level in two circumstances. Firstly, children were re-tested, if they had VA 20/30 (logMar 0.18) or worse in one eye, or $\geq$ 2line difference between the two eye, and if there were identifiable unilateral or bilateral amblyogenic factor (Table 3.3). Secondly, children were also re-tested if VA was 20/60 (logMar 0.48) or worse in one or both eyes in children < 4years, or 20/50 (logMar 0.40) or worse in one or both eyes in children $\geq$ 4 years. When possible, a same-day cycloplegic manifest refraction was performed by the study optometrist. Alternatively, children were provided with Sheridan-Gardner optotypes to learn and a re-test date was organized.

3.6.6. External eye and anterior segment assessment

External eye, pupillary response and anterior segment assessment was performed by orthoptist and ophthalmologist. The pupillary response to light, and presence or absence of an afferent pupil defect was noted using a hand-held torch or direct

ophthalmoscope. The presence of ptosis, epiblepharon, cataract, and any other abnormality affecting lids, corneal, sclera or iris were noted.

3.6.7. Cycloplegia

Children were cyclopleged using 0.5% proparacaine, 1.0% cyclopentolate (Cyclogyl, Alcon-Couvreur) or 0.5% (if child was < 1year of age), and phenylephrine 2.5%, and then 2 further drops of 1.0% cyclopentolate or 0.5% (if child was < 1year of age) at 5 minute intervals. Children were then given 30 minutes to achieve full cycloplegia.

3.6.8. Biometry (children aged 30 months or older)

Axial length measures were performed using the IOL Master (Carl Zeiss Meditec, Dublin, CA). Other measurements also determined included anterior chamber and vitreous chamber depth.

3.6.9. Assessment of refractive error

Autorefraction was measured using the table-mounted autorefractor (Canon Inc Ltd, Tochigiken, Japan) for children aged 24 months or older, and the hand-held Retinomax autorefractor (Nikon corporation, Tokyo, Japan) for younger children or those unable to co-operate with the table-mounted autorefractor.Five

consecutive autorefractor readings were obtained from each subject, all of which had to be within 0.25D of each other.

In children in whom autorefraction was not possible, and or in whom cycloplegia was not done, retionoscopy was performed by a trained optometrist.

Spherical equivalent (SE) was then calculated as the sum of the spherical plus half the cylindrical error.

3.6.10. Fundus examination

Fundal examination was performed by the ophthalmologist using indirect ophthalmoloscopy. Any macular, disc, media, posterior pole or peripheral retina abnormalities were noted. Fundal photographs were also obtained from children aged 47 months or older.

3.6.11. Family history

Family information collected included information regarding the father's and mother's dialect group (i.e. Hokkien, Teochew, Cantonese, Harrk, Hainanese, HokChew or Other). The parent interviewed was asked to estimate the total combined monthly household income (i.e. <$1000, $1000-2999, $3000-4999, >$5000). Father's and mother's highest educational level (i.e. none, primary,

secondary, ‘O’/’N’ level, ‘A’level/polytechnic/certificate/diploma or tertiary) was ascertained. Parents were asked about their smoking history (i.e. if they ever smoked, if they quit, at what age they started smoking, and number of cigarettes smoked per day. Parents were asked if they or their other children had any ocular history (i.e. if they wore glasses, contact lenses or have had refractive surgery, and if they had a history of amblyopia or strabismus).

3.6.12. Clinic Questionnaire

The clinic questionnaire included questions regarding the child’s country and place of birth. Details regarding the maternal prenatal and perinatal history were obtained including maternal age when the child was born (in years), any maternal illness during pregnancy (eg. anemia, hypertension, diabetes) (yes/no, and if yes, the type of illness), any use of prescribed or traditional medicines during pregnancy (yes/no, and if yes, the name of medicines), maternal smoking during pregnancy (including months and number of cigarettes smoked) and intake of alcohol during pregnancy (including months and average number of drinks per week or day).

Details of child’s medical history included child’s birth weight (in grams), gestational age (in weeks), length (in cm) and head circumference (in cm) at birth (as documented in child’s health booklet),any admission of child to the neonatal intensive care unit (yes/no), presence of asthma (yes/no), allergies (yes/no),

mental retardation (yes/no), developmental delay(yes/no), febrile fits (yes/no), diabetes (yes/no), co-ordination/motor problems (yes/no), heart problems (yes/no), speech/hearing problems (yes/no), attention deficit/learning difficulties (yes/no) or other problems (yes/no/specify). Parents were also asked if their child had been breast fed, and if so, details were collected regarding the age (in months), length (in months), type (ie. exclusively, mostly or partly breast fed), and method of breast-feeding (ie. direct from the breast, expressed or partly by each).

In children >24 months, the child's ocular history was also ascertained. Parents were asked, whether in the last 12 months, if their children had difficulty drawing/coloring, closed or covered an eye in sunlight or when concentrating on a task (yes/no). They were asked how often their child's eye was checked (never, 6 monthly, once a year or once in 2, 3, 4, 5 or more years), whether they were ever told their child needed glasses or contact lenses (yes/no) and if so, they were asked whether they child wore glasses (yes/no), and the number of hours their child wore glasses each day. Parents were also asked if the doctor had ever told them that their child had amblyopia (ie. poor vision that cannot be corrected with glasses or contact lenses and the eye looks normal) (yes/no), and if so, when they were first diagnosed, if their child had received treatment, and what sort of treatment their child received (ie. glasses or contact lenses, patching, eye drops, vision therapy or if other, to specify that), the duration of treatment (in years), whether or not the treatment had been stopped or was still on-going. Parents were

then asked if the doctor had ever told them that their child had strabismus (eyes that are not properly lined up; when one eye looks straight ahead, the other crosses or wanders out) (yes/no) and if so, when it was first diagnosed (month and year), age of the child when he/she was first diagnosed (years), whether their child had received treatment for strabismus (yes/no), and what kind of treatment the child received. Finally, parents were asked whether child has ever been diagnosed as having cataracts, glaucoma, retinopathy of prematurity, eye tumor or retinoblastoma, optic nerve hypoplasia, cortical visual impairment or any other eye problem (yes/no).

In the survey about outdoor, indoor and pre-school activities, parents were asked, on a normal day, for how many hours their child spent sleeping, indoors and outdoors; and for outdoor activities, parents were asked to state the type of activities the child did, and the number of hours per week spent on each activity. Parents were asked to estimate the number of hours per day spent (during the weekday and on weekends) on reading/writing, colouring/drawing, watching tv, playing tv games, hand-held video games, playing outdoors and on outdoor leisure activities.

3.6.13. Quality of Life Questionnaire (children aged 24-72 months)

Health related quality of life was assessed using trained interviewers using the PedsQL4 using parental proxies. The PedsQL4 instrument comprised of 4

sections with physical, emotional, social and school functioning. In each section, parents were asked if their child had problems with various skills which are rated as ‘never a problem’, ‘almost never a problem’, ‘sometimes a problem’, ‘often a problem’ and ‘almost always a problem’.

For children aged 25-48 months, physical function included questions as to whether the child had problems with walking, running, participating in active play or exercise, lifting something heavy, bathing, helping to pick up toys, having pains or aches, and low energy levels. Emotion function included problems with feeling afraid/scared, sad/blue, angry, not sleeping or worrying. Social function included problems playing with other children, other children not wanting to play with him/her, being teased by others, not being able to do things that other children their age could do, or not able keep up when playing with other children. School function (applicable only if child was attending school or daycare) included problems doing the same school activities as their peers, missing school/daycare because they were not feeling well or because they needed to go to see a doctor or visit the hospital.

In children aged 49-72 months, physical function included problems walking more than 1 block, running, participating in sports or exercise, lifting something heavy, taking a bath/shower by themselves, doing chores like picking up their toys, having pains/aches and low energy levels. Emotional function included problems feeling afraid/scared, sad/blue, angry, not sleeping and worrying about

what will happen to them. Social function included problems getting along with other children, other children not wanting to be their friend, being teased by other children, not being able to do the things that other children their age can do and not keeping up when playing with other children. School function included problems paying attention in class, forgetting things, not keeping up with school activities, missing school because of not feeling well, and missing school to go to the doctor or hospital.

Together the physical function made up the physical health summary score (HSS) and the emotional, social and school function made up the psychological HSS. Scores from all domains were combined to form a total score.

3.6.14. Child Development Questionnaire

In assessing childhood development, parents were asked if they were concerned (yes, a little, no) about their child's learning, development and behavior (developmental delay), talking or speech (speech), understanding what is said (comprehension), use of his fingers or hands (fine motor skills), use of his arms or legs (gross motor skills), child's behavior (behavior), child's ability to get along with others (social functioning), child's ability to learn to do things for himself (learning) and child's ability to learn preschool or school skills (preschool skills) (Table 3.2).

3.7. Definitions (Table 3.3)

Strabismus

Children were classified to have strabismus if any tropia was present at distance or near, with or without spectacles (211).

Refractive error

Anisometropia, the presence of significant refractive error differences between the two eyes, was defined as spherical when there was a difference in spherical equivalent, or astigmatic when there was a difference in cylinder power. Isometropia occurred when less significant refractive differences were present between the two eyes. Levels of amblyogenic anisometropia and isometropia varied for both ametropia (myopia or hyperopia) and astigmatism, depending on whether the children had unilateral or bilateral amblyopia.

Amblyopia

Unilateral amblyopia was defined, as in the MEPEDS, as a $\geq$ 2-line difference in best VA, when < 20/30 (logMAR 0.18) in the worse eye, and with amblyogenic factors such as past or present strabismus, anisometropia ($\geq$1.00D difference in hyperopia, $\geq$3.00D difference in myopia, or $\geq$1.50D difference in astigmatism), and past or present obstruction of the visual axis (211).

Bilateral amblyopia was defined as best VA in both eyes < 20/40 (logMAR 0.3) in children aged 48 to 72 months, or < 20/50 (logMAR 0.4) in children aged < 48 months, in the presence of amblyogenic factors such as hyperopia ≥ 4D, myopia ≤ -6.00D or astigmatism ≥2.50D, or past or present obstruction of the visual axis (211).

3.8. Data management and analysis

Data was entered into database separately by 2 persons, and the entries were then compared for differences so as to minimize data entry errors.

Analysis of prevalence of amblyopia and strabismus:

Age and gender-specific prevalence rates for strabismus and amblyopia were calculated. Poisson distribution was used to construct 95% confidence intervals for all prevalence estimates. Data were weighted to the Singapore Population Census 2000, taking into account disproportionate age sampling and familial clustering (213). All statistics were performed using commercially available software, Stata 10 (StataCorp, Texas, USA).

Analysis of risk-factor associations of amblyopia and strabismus:

Potential risk factors were first analyzed by comparing children with and without strabismus, amblyopia and amblyopia (including past history of amblyopia) in bivariate models using either the t test, non-parametric Wilcoxon rank or the chi-

square test. If significant differences ($p<0.20$) were shown in the univariate models, these risk factors were included together with all known risk factors based on prior evidence in multiple logistic regression models with either strabismus or amblyopia as dependent variables.Care was taken not to include highly correlated factors such as birth weight and gestational age, paternal and maternal education levels, and parental education levels and household income in the same model. Manual backward stepwise elimination procedures were performed to choose the most parsimonious model. Two-tailed P-values less than 0.05 were considered statistically significant. Odds ratios (OR) and 95% confidence intervals (95% CI) of OR were presented. Statistical analyses were performed in SPSS (Statistical Package for Social Science, SPSS V18.0, SPSS Inc., Chicago, IL).

Analysis of stereoacuity and its association with amblyopia and strabismus:

Associations between stereoacuity (good, fair and poor) and various demographic, birth, maternal factors and ocular factors were assessed using the t-test, ANOVA or the chi-square test. Ordinal logistic regression was used to identify potential associations using a manual backward stepwise elimination to obtain a parsimonious model. Care was taken not to include highly correlated factors such as birth weight, gestational age and NICU admission; or parental education and household income in the same model. Odds ratios (OR) and 95% confidence intervals (95% CI) were presented. Statistical analyses were performed in STATA 11.0 (StataCorp, College Station, Texas, USA). Two-tailed P-values

≤0.05 were considered statistically significant. Sensitivity (true positive/true positive+false negative) and specificity (true negative/true negative+false positive) across stereoacuity cut-offs in detecting anisometropia, astigmatism, high ametropia, presence of amblyopia and strabismus were assessed. Receiver Operating Characteristic (ROC) curves of sensitivity versus 1-specificity were created to evaluate efficacy of the RPST as a diagnostic tool; and area under the curve values (with 95%CI) was assessed. Positive and negative likelihood ratios (LR+ and LR-) were calculated. Optimal cut-offs for screening, assuming specificity of at least 90% were calculated for the detection of amblyopia, strabismus and refractive errors, and positive predictive values for these parameters were assessed.

Analysis of refractive error and its association with amblyopia, strabismus and impaired visual acuity (VA < log Mar 0.3 and 0.4)

To determine effectiveness of cycloplegic refractive errors in detecting amblyopia and strabismus, sensitivity and specificity of different refractive components (anisometropia, ansisometropic astigmatism, hyperopia, myopia and astigmatism) was assessed. Since, definition of amblyopia in this study was heavily dependent on refractive criteria, the evaluation of refractive error as a screening tool of amblyopia may be artificially elevated. The role of refractive error in detecting visual impairment (VA <logMAR 0.3 and 0.4) without amblyogenic refractive requirements were also assessed.

Receiver Operating Characteristic (ROC) curves of sensitivity versus 1-specificity were created to evaluate efficacy of the refractive parameters as a diagnostic tool; and area under the curve values (with 95%CI) was assessed. Positive and negative likelihood ratios (LR+ and LR-) were calculated. Optimal cut-offs for screening, assuming specificity of at least 90% were calculated for the detection of visual impairment, amblyopia and strabismus, and positive predictive values for these parameters were determined.

Analysis of quality-of-life and development parameters in children with and without amblyopia and strabismus

Linear regression of PedsQL4 scores was performed, adjusting each score by age, gender and socioeconomic group; and differences between scores in children with and without strabismus and amblyopia were assessed using post-hoc estimation test using STATA (Ver 11.2, StataCorp, Texas, USA). Differences between children with and without strabismus and amblyopia in the Child Developmental Survey using chi-squared test, and logistic regression adjusting for age, gender and socioeconomic statuswere also performed.

Rasch analysis was performed to determine the reliability, validity and measurement characteristics of the PedsQL4. Raw ordinal scores were converted into an intervalscale (expressed in log of odds units, or logits), and item difficulty (item measure) were calculated in relation to person ability (person measure) by placing both on the same linear continuum.

The PedsQL4 scale was assessed for item fit, uni-dimensionality, content validity (person-item targeting), and internal reliability (person separation index) (Table 3.4).

Item fit was a measure of how well items discriminated between respondents, how well item difficulty targeted person ability, and the appropriateness of the response scale (214). In the ideal circumstance, item fit would be 1.0. If item fit is poor, then responses could be explored to see if items should be removed to achieve a better fit within the category. The behavior of the response categories was evaluated to determine if higher categories (better scores) did in fact represent better functioning. An assessment of person-item targeting (a measure of content validity) determined if there was a good match between item and person means (ie. ideally 0-1). Higher levels indicated presence of floor or ceiling effects. The person separation index (PSI) determined if the test was able to discriminate between high and low performers (ie. was a measure of internal reliability). The person separation index (PSI) should ideally be > 2.0. Finally, the instrument was assessed for uni-dimensionality, measured in terms of the principal components (PCA) in raw variance and in eigenvalue (%). The PCA should ideally be low (≤50) and the eigenvalues <2. Higher levels would suggest that there might be excessive noise which interfering with dimensionality of the instrument, or the instrument might not be measuring the one underlying trait (HRQOL) which investigators are targeting.

Winsteps (Ver. 3.74 J.M Linacre, Chicago, Illinois, USA) was used to perform Rasch analysis on the PedsQL4 data with the Andrich rating scale model(215). Rasch analysis was carried in five domains of the PedsQL4 for both amblyopia and strabismus: physical functioning, emotional functioning, social functioning, school functioning, and the psychosocial health. The school functioning and psychosocial health summary scores were separated into younger (25-48 months) and older (49-72 months) children for both amblyopia and strabismus because of difference in item numbers.

Rasch-adjusted scores (a.k.a. person measures) were then created for each of the PedsQL4 domains by calibrating person measures (expressed in logits) along a hierarchical scale, resulting in a linear response measure.Linear regression of scores was then performed, adjusting each score by age, gender and socioeconomic group; and differences between Rasch scores in children with and without strabismus and amblyopia were assessed using post-hoc estimation test using STATA (Ver 11.2, StataCorp, Texas, USA).

Chapter 4: Results

4.1 Study population

3009Chinese children aged 6-72 months (response rate 72.3%) were recruited into the study. As per study design, there were approximately equal number and equal proportion of male and female children in each 6 month age range (Table 4.1).

4.1.1 Comparison of Study and general Singapore populations

The study area included a large part of the South-Western region of Singapore including the townships of Bukit Batok, Clementi, Jurong East, Jurong West and South Central area of Queenstown and Bukit Merah (Figure 3.1).The majority (84%) of the Singapore population live in these townships. Based on Population Census 2000 data, no distinctive demographic differences were noted between this region of Singapore and the rest of the island (Table 4.2) (213,216-218). However, parents of children recruited for this study were generally better educated with higher incomes than other young Singaporean adults aged between the ages of 20-40 years, suggesting some under-representation of the poorer, less educated, and lower income groups within the population.

4.1.2. Differences between Responders and Non-responders

Parents were invited to bring their children to one of two visual screening sites. A total of 4162 Chinese children were eligible to participate in the study, with 3009 examined (response rate 72.3%). There were no significant gender (p=0.65) or age (p=0.18) differences between participants and non-participants (216,217). Response rates in different age groups were similar, and ranged between 71 and 74%. There were, however, significant area differences (p <0.001) with participation rates of districts closer to examination sites (located in Jurong West and the Southern Central township of Bukit Merah) being greater than those located further away (Table 4.3)

4.2 Identification of subjects with Amblyopia

Identification of children aged 30.0-72.0 months with amblyopia involved a 2 step process. Children had to first undergo a visual acuity (VA) test either with the EDTRS logMar VA test or the Sheridan Gardner test. Children were deemed to have failed this test if best VA in both eyes < 20/50 (logMAR 0.4) in children aged 30.0-47.9 months, or < 20/40 (logMAR 0.3) in children aged 48.0-72.0 months, or if there was ≥ 2-line difference in best VA with VA in the worse eye being < 20/30 (logMAR 0.18) (Table 3.3).

Children were then diagnosed with amblyopia if there was past or present strabismus, or obstruction of the visual axis, or amblyogenic levels of refractive error which differed for unilateral and bilateral amblyopia. In unilateral amblyopia, children were required to have anisometropia ($\geq$1.00D difference in hyperopia, $\geq$3.00D difference in myopia, or $\geq$1.50D difference in astigmatism), and in bilateral amblyopia, children had to have hyperopia $\geq$ 4.00D, myopia $\leq$ -6.00D or astigmatism $\geq$2.50D in both eyes (Table 3.3).

An attempt was made to perform VA in all 2015 children aged 30.0-72.0 months. Three hundred and thirty-three children (16.5%) were excluded because of an inability to complete VA testing. Of these, 67.1%, 23.0%, 4.0%, 1.2% of children were aged 30.0-35.9, 36.0-47.9, 48.0-59.9 and 60.0-72.0 months respectively (Table 4.4). Most of the children were able to perform EDTRS logMar visual testing but approximately 30% were tested using the single-optotype uncrowded Sherdian-Gardiner matching test (27,216). Children able to complete VA tests were more likely to be older ($p<0.001$), female ($p=0.03$), have parents with higher education levels ($p=0.02$) and were less likely to be myopic (<-3.00D) ($p=0.01$) (27,218).

Cycloplegic refraction was available in 1796 (89.1%) of the 2015 children aged 30 to 72 months, and in 1521 (90.5%) of the 1682 children in whom VA could be tested. Non-cycloplegic autorefraction and manifest refraction were available for

the remaining children. The mean spherical equivalent (SE) in those who were able and unable to complete VA test was 0.69+/-1.12D and 0.41+/-1.24 respectively ($p<0.0001$). However, there was no significant difference between children who were or were not able to complete the VA testing, in terms of the proportion with either hyperopia $\geq$3.00D (1.6% vs 1.2%, p=0.58), myopia $\leq$-6.00D (0.3% vs 0.4%, p=0.76) or astigmatism $\geq$2.50D (1.9% vs 2.4 %, p=0.60). Overall, significant amblyogenic refractive risk factors were identified in 15 (4.5%) of the 333 children unable to complete the VA screening testing, and in 86 (5.1%) in whom VA could be assessed (p=0.86) (Table 4.5).

4.3 Prevalence of Amblyopia

Of the 1682 children in whom VA assessment was possible, 48 (2.9%) met the VA criteria for amblyopia, but of these, 28 (58%) were not considered amblyopic because insufficient amblyogenic risk-factors were identified. In these 28 subjects, 19 (67%) had minimal refractive error, with no past or present strabismus or visual obstruction. Nine children, however, missed refractive cutoff levels by smaller margins; 4 children with potential unilateral amblyopia had astigmatism between 1.50 and 4.00D, but with anisometropic astigmatism <1.50D; while 5 children with potential bilateral amblyopia had astigmatism between 1.25 and 2.50D.

Twenty children satisfied all amblyopic requirements, so that the overall amblyopia prevalence in this study amongst children aged 30 to 72 months was 1.19% (95%CI 0.73-1.83) (Table 4.6). There was no significant difference in amblyopia prevalence between boys and girls (p=0.22), and no age trend was evident (p=0.37).

Amblyopia was attributed to refractive error in 17 children (85%) and to strabismus in 3 (15%) (Table 4.7). Among children with unilateral amblyopia, the most frequent refractive error was anisometopic astigmatism $\geq$ 1.50D (n=7), followed by anisometropic myopia $\geq$ 3.00D (n=2) and anisometropic hyperopia $\geq$ 1.00D (n=2). In the bilateral amblyopia group, refractive errors recorded included astigmatism $\geq$ 2.50D (n=2), combined astigmatism and myopia $\leq$ -6.00D (n=2), combined astigmatism and hyperopia $\geq$ 4.00D (n=1) and myopia $\leq$ -6.00D (n=1). There were also 70 children (3.9%) with amblyogenic refractive error risk factors who were not amblyopic (ie. did not meet the amblyopia visual acuity criteria) (Table 4.5). Of the 3 children whose amblyopia was attributed to strabismus, two had intermittent exotropia while one had a constant esotropia. There were no cases of deprivational amblyopia.

Based on questionnaire information, parents of 15 children, aged 30 to 72 months, reported that their child had previously been diagnosed and treated for amblyopia. One child was unable to co-operate with the VA testing and 2 were found to be still amblyopic at our examination.The remaining 12 children (with presumably

successfully treated amblyopia) were aged 63.5 +/- 9.7 months (range 53.2 – 72.0 months), 6 had high astigmatism ≥1.50D, 2 had anisometropia ≥1.00D, 1 had strabismus, and no cause was identified for 3 subjects.

Only 2 of the 20 children identified as being amblyopic in the STARS study were reported to have a past history of amblyopia.

4.4. Identification of children with Strabismus

A total of 3009 children aged 6 to 72 months were assessed for strabismus and assessment was possible in 2992 (99.4%) children. Seventeen children (0.5%) were excluded because of an inability to perform a reliable cover-uncover or alternate cover test. These included 1 child (0.5%) aged 6.0-11.9 months, 3 children (0.5%) aged 12.0-23.9 months, 2 (0.4%) aged 24.0-35.9 months, 5 (0.8%) aged 36.0-47.9 months, 3 (0.5%) aged 48.0-59.9 months and 3 (0.5%) aged 60.0-72.0 months.Those unable to co-operate were not significantly different from those who were able to co-operate with tests in terms of age, birth-weight, gestational-age, maternal peri-natal factors, socioeconomic class, and refractive error.

4.5. Prevalence of Strabismus

The overall prevalence of strabismus in children aged 6 to 72 months was 0.80% (95%CI 0.51-1.19) with exotropia exceeding esotropia by a ratio of 7:1 (Table 4.8). There was no significant difference in strabismus prevalence between boys and girls (p=0.52), and there were no age trends (p=0.08).

The most frequent strabismus type was intermittent exotropia (58%), followed by constant exotropia (25%) and constant esotropia (12%). One subject, a 71 month old boy, had an isolated dissociated vertical deviation (DVD) (Table 4.9). Three children (12%) with strabismus were also amblyopic. There were no sib-pairs (ie. none of the children identified with strabismus in this study were siblings).

Eleven parents stated that their child had been diagnosed with strabismus in the past and in 8 cases, strabismus was detected on cover-uncover test. In the 3 cases in whom strabismus was not detected, 2 were reported as having had no treatment for strabismus, while 1 had undergone surgery.

4.6. Risk factors associated with Amblyopia

Univariate analysis of child, maternal, birth, socio-demographic, ocular and family factors suggested that some birth factors (ie. admission to neonatal

intensive care), ocular factors (ie. strabismus and refractive error) and family factors (ie. family history of amblyopia or strabismus) may be important risk associations with amblyopia (Table 4.10-15).

Additional analysis was also performed for amblyopia including the 13 children whose parents reported that their child had a past history of amblyopia (ie. amblyopia including past history of amblyopia).

4.6.1. Child factors

There was no gender associations related with amblyopia (OR 1.5, 95%CI 0.6-3.6, p=0.39) or amblyopia (including past history of amblyopia) (OR 1.4, 95%CI 0.7-2.8, p=0.33) (Table 4.10.1-2).

Body mass index (i.e. weight in kilograms divided by square of height in meters) (BMI) was calculated for each child, and there was also no association noted between BMI and amblyopia (p=0.43-0.72) (Table 4.10.1-2).

4.6.2. Birth factors

Birth parameters available for analysis were birth weight (BW), gestational age (GA), birth length (BL) and head circumference (HC). BW was correlated with GA (R2=0.27), BL (R2 =0.55) and HC (R2=0.42) (Figure 4.1.1, 4.1.2 and 4.1.3).

The mean BW was 3098.7g (95%CI 3078.4-3118.9g) and the mean GA was 38.4weeks (95%CI 38.3-38.4weeks). The mean BL was 49.2cm (95%CI 49.0-49.3cm) and HC was 33.5cm (95%CI 33.4-33.6cm).

The majority of children (who were able to be tested for amblyopia) had a BW of > 2500g (n 1496, 88.9%). Only 5 children (0.2%) had BW <1500g. Similarly, the majority of children had GA > 37 weeks (n1254, 74.6%). Only 7 children (0.4%) had a GA of ≤32 weeks.

No child with amblyopia (including past history of amblyopia) was born with BW <1500g or GA ≤32weeks. A total of 91 children (5.4%) had an admission to the neonatal intensive care unit (NICU). This included 3 children with amblyopia, and 3 who had a past history of amblyopia.

Univariate analysis found no association between amblyopia and BW or GA. Odds ratio (OR) of amblyopia in children with BW > 2500g was 0.5 (95%CI 0.1-1.7, p=0.22) compared to children of BW <2500g; OR in children with GA >37 weeks was 0.9 (95%CI 0.3-2.9, p=0.93); and OR in children with past admission to NICU was 3.1 (95%CI 0.9-10.8, p=0.09).

However, in children with amblyopia (including past history of amblyopia), the mean HC was slightly smaller (32.9 vs 33.6cm, p= 0.03) and these children were

more likely to have had a previous admission to the NICU (18.2% vs 5.3%, p=0.01) (Table 4.11.2).

4.6.3. Maternal/Prenatal factors

Maternal factors available for analysis included maternal age, presence of illness, medication, smoking and alcohol use during pregnancy and breast feeding in the post-partum period.

The mean maternal age was 30.4 years (95%CI 30.2-30.6years). There were 9 mothers (0.5%) who were aged <18 years, and 198 mothers (11.9%) who were aged > 35 years.

Very few parents reported that they smoked (30, 1.8%) or drank alcohol (15, 0.9%) during their pregnancy. No child who had amblyopia (including past history of amblyopia) had a mother who had smoked or drank alcohol during their pregnancy. Many parents breast-fed their child for at least 1 month after the birth of their child (75.7%).

Univariate analysis suggested that there was poor association between these maternal factors in children with amblyopia or amblyopia (including past history of amblyopia) (Table 4.12.1 and 4.12.2). The mean maternal age of mothers with children with amblyopia was 32.3 years (95%CI 30.4-33.9) compared to those

with no amblyopia (30.4 years, 95%CI 30.2-30.6, p=0.09). Children with amblyopia were no more likely to have mothers with maternal illness such as anemia, high blood pressure and diabetes (p=0.16-0.96). The OR of breast-feeding and amblyopia was 1.2 (95%CI 0.4-3.7, p=0.71); and the OR of breast feeding and amblyopia (including past history of amblyopia) was 0.7 (95%CI 0.4-1.6, p=0.42).

4.6.4. Socioeconomic factors

Socioeconomic factors available included maternal and paternal educational levels and the monthly household income.

Most mothers completed 'A'/polytechnic or tertiary education (n 926, 55.9%) while 609 mothers (37.2%) achieved secondary/ 'O' level education. Fathers were also more likely to have attained tertiary education (n 984, 59.4%), with 30.9% (n512) achieving secondary/ 'O'/ 'A'/ polytechnic education. There were, however, a small number of mothers (119, 7.2%) and fathers (158, 9.6%) who had no or primary level education (Table 4.13).

Parents were more likely to have similar education levels, and parents with higher education levels were more likely to have higher monthly household incomes (Table 4.13).

Univariate analysis suggested that there was no association between maternal and paternal education levels or household income with amblyopia or amblyopia (including past history of amblyopia) (Table 4.14.1, Table 4.14.2).

The OR of amblyopia in children whose mother had secondary /'O' level education and 'A'/polytechnic/tertiary education was 2.0 (95%CI 0.3-15.7) and 1.2 (95%CI 0.2-9.2) respectively compared to mothers with no/primary education (p=0.43). OR of amblyopia in children whose fathers had secondary /'O' level education and 'A'/polytechnic/tertiary education was 1.3 (95%CI 0.3-5.9) and 0.8 (95%CI 0.2-3.7) respectively compared to fathers with no/primary education (p=0.61). OR of amblyopia in households with monthly income of S$3000-4999 was 1.0 (95%CI 0.3-5.9) and with incomes of $\geq$ S$5000was 1.4 (95%CI 0.5-4.4) compared to those with incomes of <$S3000 (p=0.72) (Table 4.14.1).

The OR of amblyopia (including past history of amblyopia) in children whose mother had secondary /'O' level education and 'A'/polytechnic/tertiary education was 1.0 (95%CI 0.3-3.5) and 0.6 (95%CI 0.2-2.1) respectively compared to mothers with no/primary education (p=0.35). OR of amblyopia in children whose fathers had secondary /'O' level education and 'A'/polytechnic/tertiary education was 0.5 (95%CI 0.2-1.5) and 0.4 (95%CI 0.2-1.1) respectively compared to fathers with no/primary education (p=0.19). OR of amblyopia in households with monthly income of S$3000-4999 was 0.6 (95%CI 0.2-1.6) and with incomes of

≥S$5000was 0.9 (95%CI 0.4-2.1) compared to those with incomes of <$S3000 (p=0.55) (Table 4.14.2).

4.6.5. Ocular factors

Ocular factors available for analysis include spherical equivalent (SE), astigmatic or cylinder power, anisometropia (the difference in SE between eyes) and the presence/absence of strabismus.

Spherical equivalent (SE) and cylindrical power between the right and left eye were highly correlated (R2 =0.87 and R2=0.66 respectively) (Figure 4.2.1 & 4 2.2). The SE and cylindrical power of both eyes were averaged to attain a mean SE and cylindrical score for each subject.

Univariate analysis suggested amblyopiawas associated with high hyperopia≥3.0D (OR 52.9, 95%CI 13.5-297.7, p=<0.001) and myopia ≤ -3.0D (OR16.7, 95%CI 4.2-66.6, p<0.001) compared to emmetropia (SE -1.00 to +1.00D) (Table 4.15.1). Similarily, amblyopia was highly associated with astigmatism ≥ 1.0D (OR 3.8, 95%CI 1.1-13.7, p=0.03) and astigmatism > 2.0D (OR 30.5, 95%CI 10.8-86.1, p<0.001) compared to astigmatism < 1.0D; and anisometropia 1.0-2.0D (OR 13.6, 95%CI 2.9-64.6, p=0.001) and anisometropia > 2.0D (OR 20.5, 95%CI 4.2-100.9, p<0.001) compared to anisometropia < 1.0D

(Table 4.15.1). Children with amblyopia were also more likely to have concurrent strabismus (OR 28.1, 95%CI 7.2-110.3, p<0.001) (Table 4.15.1).

Amblyopia (including past history of amblyopia) was associated with hyperopia≥3.0D (OR 27.8, 95%CI 7.6-101.1, p=<0.001) and myopia ≤ -3.0D (OR 8.8, 95%CI 2.4-32.4, p<0.001) compared to emmetropia (SE -1.0 to +1.0D) (Table 4.15.2). Amblyopia was also associated with astigmatism > 2.0D (OR 24.4, 95%CI 11.0-54.1, p<0.001) compared to astigmatism < 1.0D; and anisometropia 1.0-2.0D (OR 8.2, 95%CI 1.8-38.4, p=0.006) and anisometropia > 2.0D (OR 31.3, 95%CI 8.9-110.4, p<0.001) compared to anisometropia < 1.0D (Table 4.15.2). Children with amblyopia were also more likely to have concurrent strabismus (OR 34.9, 95%CI 10.9-111.5, p<0.001) (Table 4.15.2).

Care, however, needs to be taken in interpreting these results as refractive error and strabismus was used as part of the definition of amblyopia in this study, and this may artificially inflate the odd-ratios associated with these variables.

4.6.5. Family factors

Family history of amblyopia or strabismus in parents and siblings was available for analysis.

Univariate analysis suggested that children with amblyopia or amblyopia (including past history of amblyopia) were more likely to have a sibling with amblyopia or strabismus (Table 4.16.1 and 4.16.2).

Amblyopia risk was increased when children had a sibling with amblyopia (OR 4.7, 95%CI 1.0-20.8, p=0.03) and a sibling with strabismus (OR 8.9, 95%CI 1.9-41.1, p<0.001).

Amblyopia (including past history of amblyopia) was increased when children had a sibling with amblyopia (OR 40.5, 95%CI 21.4-101.1 p<0.001) and a sibling with strabismus (OR 8.1, 95%CI 2.3-29.0, p=0.01).

4.6.7. Multivariate analysis of amblyopia related risk associations

The variables of age, gender, factors which had a p-value <0.20 on exploratory univariate analysis (ie. maternal age, refractive error, strabismus, sibling with amblyopia or strabismus) and factors found to be relevant in literature review (ie. prematurity, maternal smoking and socioeconomic status) were included in the initial multivariate model for amblyopia and amblyopia (including children with past history of amblyopia). Maternal smoking was, however, subsequently omitted from the analysis as none of the children with amblyopia had mother who smoked during pregnancy (Table 4.17.1 and 4.18.1).

In the most parsimonious model, after backward elimination of variables, amblyopia was associated with myopia ≤-3.0D (OR 27.6, 95% CI 5.2-147.2, p<0.001), hyperopia ≥3.0D (OR 13.8, 95%CI 2.7-70.6, p=0.002), astigmatism ≥1.0D (OR 8.9, 95%CI 2.8-28.4, p=0.009), anisometropia ≥1.0D (OR 9.4, 95%CI 1.7-50.5, p<0.001) and strabismus (OR 14.5, 95% CI 2.2-96.8, p=0.006), after adjusting for age, gender, prematurity and socioeconomic status (Table 4.17.2).

In the most parsimonious model for amblyopia (including past history of amblyopia), associations were noted with myopia ≤-3.0D (OR 8.2, 95% CI 1.3-52.3, p=0.03), hyperopia ≥3.0D (OR 7.8, 95%CI 1.7-36.1, p=0.008), astigmatism ≥1.0D (OR 9.1, 95%CI 3.5-23.6, p<0.001), anisometropia ≥1.0D (OR 12.5, 95%CI 3.3-47.2, p<0.001), strabismus (OR 12.5, 95% CI 2.6-60.2, p=0.002) and a sibling with history of amblyopia (OR 56.4, 95%CI 19.4-164.0, p<0.001), after adjusting for age, gender, prematurity and socioeconomic status (Table 4.18.2).

4.7 Risk factors associated with Strabismus

As mostchildren had exotropia (83%), the comparison of children with and without strabismus was mainly a comparison of children with and without exotropia.

Only 3 children had esotropia; all were hyperopic between 1.00-2.00D, had low levels of anisometropia (0-0.50D) and astigmatism ≤1.00D. They came from slightly lower socio-economic group with parents achieving primary/ secondary education and with a monthly household income <S$3000. The child withDVD was also from the lower socio-economical group, had a SE of –9.00D and astigmatism of 4.10D in the worse eye and anisometropia of 2.10D.

Exploratory univariate analysis was performed to determine associations between strabismus and various child, birth, maternal/prenatal, socioeconomic, ocular and family factors.

4.7.1. Child factors

No association noted between age, gender, BMI and strabismus (Table 4.10.3).

OR of strabismus in male children was 1.3 (95%CI 0.6-2.9, p=0.54). There was also no association noted between BMI and strabismus (p=0.39).

4.7.2. Birth factors

There was no association with strabismus and birth weight, gestational age, birth length or head circumference (Table 4.11.3).

Odds ratio (OR) of strabismus in children with BW > 2500g was 2.2 (95%CI 0.7-6.5, p=0.14) compared to children of BW <2500g; OR in children with GA >37 weeks was 0.9 (95%CI 0.3-2.4, p=0.83).

Children with strabismus were, however, more likely to have a previous admission to the NICU (16.7% vs 5.5%, p=0.02) (Table 4.11.3).

4.7.3. Maternal/Prenatal factors

Univariate analysis suggested that there was poor association between maternal age, breast feeding and strabismus. No child with strabismus had a mother who smoked or drank alcohol during pregnancy (Table 4.12.3).

The mean maternal age of children with strabismus was 30.0 years (95%CI 27.9-32.1) compared to those with no strabismus (30.6 years, 95%CI 30.4-30.8, p=0.52). Children with strabismus were no more likely to have mothers with maternal illness such as anemia, high blood pressure and diabetes (p=0.77). The OR of breast-feeding and strabismus was 0.7 (95%CI 0.3-1.7, p=0.41).

4.7.4. Socioeconomic factors

Children with strabismus were more likely to have a mother with no/primary school education (35% vs 6.6%, p=0.001), a father with no/primary school

education (33.3% vs 9.8%, p<0.001), and to come from a household with a monthly income <S$3000 (58.3% vs 23.8%, p<0.001) (Table 4.14.3)

4.7.5. Ocular factors

Univariate analysis suggested that subjects with strabismus were more likely have astigmatism > 1.0D (45.8% vs 17.4%, p<0.001), anisometropia > 2.0D (8.3% vs 0.5%, p<0.001) and amblyopia (21.4% vs 1.0%, p<0.01) (Table 4.15.3).

OR of strabismus when astigmatism was 1.0-1.9D was 2.8 (95%CI 1.1-7.4, p=0.04) and OR when astigmatism was ≥ 2.0D was 8.6 (95%CI 3.0-24.4, p<0.001) compared to astigmatism < 1.0D. OR of strabismus when anisometropia was ≥ 2.0D was 18.4 (95%CI 3.9-85.8, p<0.001) compared to anisometropia < 1.0D. OR of strabismus when child was amblyopic was 28.1 (95%CI 7.1-110.3, p<0.001).

4.7.5. Family factors

Children with strabismus were more likely to have a sibling with a history of amblyopia (12.5% vs 1.9%, p=0.01) or a sibling with a history of strabismus (29.2% vs 0.8%, p<0.001). Although the difference did not reach statistical significance, they were also more likely to have a parent with a history of

amblyopia (12.5 vs 5.0, p=0.10) or strabismus (4.2% vs 0.7%, p=0.17) (Table 4.16.3)

OR of strabismus when there was a sibling with amblyopia was 7.4 (95%CI 2.2-25.6, p=0.08), and OR of strabismus when there was a sibling with strabismus was 54.1 (95%CI 20.4-143.2, p<0.001).

4.7.6. Multivariate analysis of strabismus related risk associations

The variables of age, gender, factors which had a p-value <0.20 on exploratory univariate analysis (ie. admission to NICU, refractive error, amblyopia, socioeconomic status, family history of strabismus and amblyopia) and factors found to be relevant in literature review (ie. prematurity, maternal smoking and maternal age) were included in the initial multivariate model for amblyopia and amblyopia (including children with past history of amblyopia) Maternal smoking was, however, subsequently omitted from this model as no child with a strabismus had a mother who smoked during her pregnancy (Table 4.19.1).

In the most parsimonious model, after backward elimination of variables and adjustment for age, gender and prematurity, strabismus was associated with lower paternal education level with children whose father had secondary/'O' or 'A'/polytechnic/tertiary level education having an OR 0.07 (95%CI 0.01-0.58, p=0.01) and OR 0.23 (95%CI 0.06-0.89, p=0.03) respectively compared to

children whose father had no/primary education. Children with strabismus were also more likely to have astigmatism ≥1.0D (OR 3.5, 95%CI 1.0-12.0, p=0.04), concurrent amblyopia (OR 15.9, 95%CI 2.7-92.8, p=0.002), a parent with history of strabismus (OR 17.9, 95%CI 1.1-278.3, p=0.04) and a sibling with history of strabismus (OR 38.3, 95%CI 8.7-168.5) (Table 4.19.2).

4.8. Stereoacuity and its association with Amblyopia and Strabismus

4.8.1. Assessment of Stereoacuity

Stereoacuity testing using the Randot Preschool Stereoacuity Test (RPST) was attempted in 2009 children (51% male) aged 30-72 months. Only 32% of children aged 30.0-35.9 months and 66% of children aged 36.0-41.9 months were able to perform the test. Testability improved to 84% in those aged 42.0-47.9 months and approached 98% after the age of 48.0 months (Figure 4.3.1).

Of the 481 subjects who were unable to co-operate with the test, 410 (85.2%) were aged <48months. Younger children (<48months) who were unable to perform tests had demographic, birth and ocular characteristics similar to those who recorded good-fair stereoacuity. However, older children unable to perform tests were more similar to those who recorded poor stereoacuity (Table 4.20).

Ordinal logistic regression suggested that in younger children (<48months) who were unable to perform the test, risk associations include younger age and male gender (OR1.3, 95%CI 0.9-1.9,p=0.013), birth weight <3000g (1.4, 95%CI 1.0-2.0, p=0.030), hyperopia ≥2.0D (OR 2.5, 95%CI 1.3-4.9, p=0.005) and having fathers with no/primary education (OR 3.5, 95%CI 1.8-5.9, p<0.001) (Table 4.21). However, in older children, anisometropia ≥2.0D (OR 8.7, 95%CI 2.0-38.2, p=0.004) and having mother with no/primary education (OR 5.2, 95%CI 2.0-38.2, p=0.004) were more important.

4.8.2 Factors that affect Stereoacuity levels obtained

In the 1528 children able to perform the test, younger children (<48 months)recorded lower levels of stereoacuity than older children (Figure 4.3.2) with only 22% of children aged 30.0-35.9 months able to report seeing the 40-60sec plates, compared to 48%, 68% and 84% of children aged 36.0-47.9, 48.0-59.9 and 60-72 months respectively.

Univariate analysis suggested that younger age, lower birth-weight/gestational-age, high ametropia, anisometropia, astigmatism, amblyopia, strabismus and past neonatal intensive care admission were all associated with poorer stereoacuity (Table 4.20).

After ordinal logistic regression, it was noted that younger age (OR 1.10 95%CI 1.07-1.10, p<0.001), anisometropia ≥1.0D (OR 2.9, 95%CI 1.1-7.8, p=0.33), astigmatism ≥1.0D (OR 1.9, 95%CI 1.4-2.3, p<0.001), hyperopia ≥2.0D (OR 1.7, 95%CI 1.1-2.6), amblyopia (OR 6.3, 95%CI 1.8-20.9), strabismus (OR 37.7, 95%CI 11.0-129.4, p<0.001) and having mothers with no/primary education (OR 1.76, 95%CI 1.1-2.8, p=0.015) were more likely to be associated with poorer stereoacuity (Table 4.22) with birth and other demographic factors being less relevant.

Overall, poorer stereoacuity (ranging from 200sec to none) was present in 38.4%, 69.2% and 38.1% in children with amblyopia, strabismus and anisometropia >1.0D respectively (Figure 4.4). However, 4.3% of normal children without amblyopia, strabismus or significant refractive error had abnormal stereoacuity levels. Also of note was that some children with amblyopia (23.1%) and strabismus (23.1%) were able to record good stereoacuity levels of 40-60sec, compared to 74.3% of children with no ocular abnormalities.

4.8.3. Potential role of Stereoacuity as a screening test for Amblyopia, Strabismus and other ocular disorders

Sensitivity and specificity of different cut-offs to detect presence of amblyopia, strabismus, as well as presence of refractive errors (such as hyperopia/myopia,

anisometropia and astigmatism) were calculated and Receiving Operating Characteristic (ROC) curves were plotted from these values (Figure 4.5.1 and 4.5.2).

The area-under-the-curve (auc) was greatest for anisometropia >2.0D (0.84, 95%CI 0.72-0.55), strabismus (0.82, 95% CI 0.66-0.99) and amblyopia (0.77, 95% CI 0.63-0.92) (Table 4.23). For detection of anisometropia >2.0D, an optimal cutoff was achieved using a 100s cutoff (sensitivity 0.87, specificity 0.68) (Figure 4.5.2). For the detection of strabismus, when a 200s cutoff was used, the sensitivity was 0.71 and specificity was 0.95; and for detection of amblyopia, the optimal cutoff was 100s (sensitivity 0.80, specificity 0.68) (Figure 4.5.1).

If, in order to increase specificity (or limit false negative rate), the specificity was set at >90%, then using cut-off of 200s, then sensitivity for strabismus was 71%, and sensitivity for amblyopia was 40%. If this cut-off was used in the STARS population, of the 1528 children screened, 30 would have failed the RPST (referral rate 1.2%), with a positive predictive value of 27% (43% false negative)for strabismus, and positive predictive value of 17% (67% false negative) for amblyopia (Table 4.25). This suggests that some children with amblyopia and strabismus would be mis-diagnosed as being ‘normal’ if the RPST was used as the sole screening tools for these conditions.

4.9. Refractive error and its association with Amblyopia and Strabismus

Cycloplegic autorefraction was available in 1796 (89.1%) of the 2015 children aged 30 to 72 months, and in 1521 (90.5%) of the 1682 children in whom VA could be tested. Non-cycloplegic autorefraction and manifest refraction were available for the remaining children.

In this study, the definition of amblyopia required child to fail a visual acuity test, and also have amblyogenic risk factors (Table 3.3). The refractive error criteria were quite strict. In unilateral amblyopia, there needed to be at least 1.00D of anisometropic hyperopia, 3.00D of anisometropic myopia and a >1.50 difference in astigmatism between eyes. For bilateral amblyopia, there needed to be hyperopia > 4.00D, myopia < -6.00D or astigmatism >2.50Din both eyes (211).

The American Association of Pediatric Ophthalmology and Strabismus (AAPOS) recommendations of amblyopic risk factors, however, are more lenient (ie. anisometropia >1.50D, hyperopia >3.50D, myopia <-3.00D, astigmatism >1.50D at the 90 or 180 degree meridian or >1.00D in the oblique meridian) (62). If these more liberal criteria were used in our study, the amblyopia prevalence would increase 2.7-fold to 3.27%, with rates of 2.41%, 4.26%, 2.75% and 3.15% in the 30 to 35 month, 36 to 47 month, 48 to 59 month and the 60 to 72 month age-groups, respectively.

To determine if refractive error measurements (ie. cycloplegic autorefraction) can be used to detect children who had impaired visual acuity (ie. visual acuity ≤ 20/40 (logMar 0.3) or ≤ 20/50 (logMar 0.4) in at least one eye), amblyopia and strabismus, sensitivity/specificity for various refractive cut-off points and their ROC were created (Figure 4.6.1-5).

Impaired visual acuity in this case was defined as a visual acuity ≤20/40 (logMar 0.3) or worse in at least one eye, which is a commonly used cut-off level for amblyopia in studies involving older children and adults. A separate category of visual acuity ≤ 20/50 (logMar 0.4) was also created, as the ≤ 20/40 criteria may be too stringent for the preschool age-group.

4.9.1. Potential role of refractive error, determined by cycloplegic refraction, as a screening test for visual impairment, Amblyopia and Strabismus

Autorefraction values appear to be poor predictors of impaired visual acuity ≤ 20/40 with astigmatism being the only parameter which achieved an area-under-the-curve (auc) more than 0.7 (auc 0.75) (Table 4.25). The best balance between sensitivity/specificity was using a cut-off of 1.50D of astigmatism (sensitivity 0.58, specificity 0.75).

For detection of impaired visual acuity ≤ 20/50 in at least one eye, astigmatism (auc 0.87) had the best predictive value with the best balance between sensitivity/specificity again at a cut-off of 1.50D (sensitivity 0.67, specificity 0.74) (Table 4.25). Anisometropic astigmatism (auc 0.82) with cut-off at 1.00D was a close second, followed by myopia (auc 0.77) with cut-off at -3.00D and anisometropia (auc 0.72) with cut-off at 1.50D (Table 4.25).

Not surprising, since refractive error was used as a factor in the classification of amblyopia in this study, the auc with many autorefraction parameters was high in the detection of amblyopia; astigmatism (auc 0.88), anisometropia astigmatism (auc 0.82), myopia (auc 0.78) and anisometropia (auc 0.72) (Table 4.25).

In contrast, the auc for the detection of strabismus was relatively poor (auc 0.51-0.69) (Table 4.25).

4.10 Health related Quality of Life (HRQOL) measures

The Pediatric Quality of Life Inventory (PedsQL4) was used to assess HRQOL in children aged between 24 and 72 months. Of the 2266 children who were eligible, 1936 (85.5%) and 1935 (85.4%) participated in the PedsQL4 questionnaire and Child Development Survey respectively.

Children with strabismus

All 1936 children were screened for strabismus, but status in 12 children (0.6%) could not be ascertained due to poor co-operation.Children unable to co-operate with strabismus screening had significantly lower school functioning and social functioning scores (Table 4.26). Of the remaining 1924 children, 22 children had strabismus (18 exotropia, 3 esotropia and 1 dissociated vertical deviation).

A comparison of children with and without strabismus showed that there was no difference in PedsQL4 total scores before and after adjustment for age, gender, and socioeconomic status (Table 4.26). There was a trend towards lower scores in the emotional subgroup with 5 of the 22 strabismic children (23%) recording a score of $\leq$ 80 (Figure 4.7), but the overall emotional subscore was not different between the groups (p=0.65). No significant difference was also noted for the physical, social and school scores, or the physical and psychological health summary scores (HSS).

In the 3 children with esotropia (1 male and 2 females, aged 2.4, 2,8 and 4.5 years), physical health HSS, psychological HSS and total scores were 97.8 (5.5), 95.1 (7.4) and 96.1 (6.2) respectively which is not significantly different from those children with exotropia.

In the Child Development Survey, parents with children with strabismus were more likely to report problems with speech (concerns about how children talked and made speech sounds) and comprehension (concerns about how child understood what parents say) but note less problems with social functioning (concerns about how their children got along with others) (Table 4.27). After adjusting for gender, age and past admission to a neonatal intensive care unit, children with strabismus were more likely to have speech (OR 4.71, 95%CI 1.52-14.59, p=0.007) and comprehension (OR 5.61 95%CI 1.37-28.7, p=0.012) problems.

There were no marked differences in development findings between esotropic and exotropic children except in the preschool skills category where 2 parents of the 3 children (67%) with esotropia reported problems compared to 3 parents of the 18 children (17%) with exotropia.

Children with amblyopia

Visual screening and thus amblyopia assessment was performed in children aged above 30 months (n 1741). Amblyopia assessment was not possible in 285 children (16.4%). Children unable to complete the test had, paradoxically, slightly higher school functioning scores (Table 4.26). There was no difference in all PedsQL4 subgroups, summary and total score between children with and without

amblyopia before and after adjustment for age, gender, and socioeconomic status (Table 4.26).

There was also no difference noted in Child Development Survey (Table 4.27). Children with amblyopia were no more likely to have developmental delay, speech, fine and gross motor skills or social functioning problems. In particular, no parent reported problems in pre-school skills or with learning.

Children with both amblyopia and strabismus

Only 3 children (2 male, 1 female; aged 4.5, 4.8 and 6.5 years) had both amblyopia and strabismus. The physical HSS, psychological HSS and total scores in these children were 98.0 (SD 3.5), 98.7 (SD 2.3) and 98.3 (SD 2.9) respectively, all of which were not significantly different from children without amblyopia or strabismus (p value: 0.99, 0.42 and 0.55 respectively). In terms of childhood development, 1 parent noted ‘a little’ problem in preschool, while another had ‘a little’ problem with their behavior.

4.10.1 Analysis of the effectiveness of the PedQL4 in measuring HRQOL in children with Amblyopia and Strabismus: Rasch analysis

Fourteen sets of Rasch analysis were conducted (Table 4.28 and 4.29). First, across all scales scores were reversed for Rasch analysis purposes giving participants with less perceived difficulty the higher score and vice versa. Second, the items were then fitted to the Rasch model. Examination of these items indicated for the majority of scales that category 2 (sometimes a problem) did not have a point along the ability continuum where it was the most likely response. Consequently these items were recoded by collapsing categories 2 (sometimes a problem) and 3 (often a problem).

There were signs of item misfit i.e. having infit residual values >1.3. Frequently recurring misfitting items were 12 ("Trouble sleeping?"), 20 ("Missing school/day care because of not feeling well?"), and 21 ("Missing school/day care to go to the doctor or hospital?"). These items were removed in their respective scales and the remaining items all subsequently showed values <1.3. The PSR (person separation reliability) was almost 0.0 for most scales, which means that this instrument was not able to clearly discriminate between at least three groups or strata of person ability. In other words the PedQOL4 was not sensitive enough to distinguish between high and low performers. More items may be needed. The PCA (principal component analysis) of the residuals of the raw variance explained were low (Table 4.2.8 and 4.2.9); though the unexplained variance by

the first contrast of the residuals were <2.0 eigenvalues units. This implies that the instrument was most likely not unidimensional i.e. not only measuring the one underlying trait (HRQOL).

Ideally, the mean and SD values are expected to approximate 0 and 1, respectively in order to suggest that this scale has substantial validity. The large difference in item and person mean suggests that overall participants had a higher level of ability than the average of the scale items meaning that most items of the questionnaire were too easy to perform for this population. These parameters indicate that the PedsQL4 is a suboptimal scale to assess parental perception of their children's health-related QoL with amblyopia and strabismus.

Differences in Rasch-adjusted scores in children with and without strabismus and amblyopia

Analysis of Rasch-adjusted score showed that the sub-scores and health summary scores were not significantly different in children with and without amblyopia and strabismus (Table 4.30), except for a slightly higher than expected school functioning score in older children with strabismus.

Chapter 5: Discussion

5.1. Aim of the study

The main purpose of this study was to determine, for the first time, what the prevalence of amblyopia and strabismus is in young preschool Singapore Chinese children and to determine whether there were any unique risk-factors associated with these conditions. A secondary aim was to determine if stereoacuity and refractive error measurements were useful screening tests for these 2 conditions in preschool children. This information will be useful in the planning of public visual screening programs, firstly to quantify the size of the problem, and secondarily to determine if there are populations at greater risk which may benefit more from screening.

There are several birth cohort and population-based cross-sectional studies which aim to achieve similar goals such as the Avon Longitudinal Study of Parents and Children (ALSPAC) and Millennium Cohort Study (MCS) based in the UK, the Collaborative Prenatal Project of the National Institute of Neurological Disorders and Stroke (CPP) study, Multi-ethnic Pediatric Eye Disease (MEPEDS) and Baltimore Pediatric Eye Disease Study (BPEDS) based in the USA, the Sydney Myopia Study (SMS) and Sydney Pediatric Eye Disease Study (SPEDS) based in Australia and the Danish National Birth Cohort (DNBC) Study based in Denmark (6-8,25,44,47,78,80,84,89,90,91). All these studies were based in Northern

America, Europe and Australia (i.e. in predominantly non-Asian populations), and results from these studies may not be directly applicable to an Asian population.

Three of the above studies, the MEPEDS, BPEDS and SPEDS share a similar study design to that of the Strabismus, Amblyopia and Refractive error in Singaporean preschooler study (STARS). In each study, investigators recruited 3000 children from each population/ethnic group. Subjects from each study underwent a similar range of visual assessments, utilized the same classification criteria for amblyopia and strabismus, used the same categorization of risk factors and employed the same tool to assess HRQOL (211). This was extremely useful as direct comparisons could be made between studies. Differences between ethnic groups could also be identified and assessed. A summary of the findings within the MEPEDS, BPEDS, SPEDS and STARS is provided in Table 5.1.

However, as each study was done by a different investigation team with slightly different priorities, interest and investigative processes, differences between the studies would exist. In the STARS study, for example, visual acuity was measured by LogMAR EDTRS chart when possible or Sheridan Gardner HOVT test if not. In the other studies, only the Sheridan Gardner HOVT test was used (216,218). This was because investigators in the STARS study felt that the average Singaporean preschooler at age 4 years was literate enough to co-operate with the LogMAR test, and that it would provide a more accurate reading. Since the LogMAR EDTRS test is ‘harder’, this might have made the visual criteria

more stringent in the STARS study. Similarly, stereoacuity was measured only by the Randot Preschool Stereoacuity Test in the STARS and MEPEDS study, but other tests (ie. Lang II and StreoSmile Test II) were also used in the SPEDS study (123). Subtle differences might exist in the manner in which children were assessed or data recorded and in perceptions regarding which steps were of greater importance; and this might lead to systemic differences between studies.

5.2. Achieving a representative sample

In cross-sectional cohort studies of this nature, it was important to ensure that the studied population was adequately representative of the study area, and also the general Singaporean population.

In this study, the regions selected were Housing Development Board (HDB) townships in South-West Singapore. These townships consisted of high-rise public apartments which the government started to build in the 1970s. The majority (84%) of the Singapore population lived in such townships which were quite evenly spread throughout the island state (Figure 3.1). Population 2000 census was used to provide a socio-economic profile of 20-40 year old Chinese men and women who would be within the same age-group as most parents in the STARS study (213). A comparison of the socio-economic variables (ie. parental education, employment and income) suggested that there were no marked

demographic differences between this region of Singapore and the rest of the island (Table 4.2). Parents of children recruited for this study were generally better educated with higher incomes than other young Singaporean adults aged between the ages of 20-40 years, suggesting some under-representation of the poorer, less educated, and lower income groups within the population (Table 4.2).Parents who lived closer to examination sites were also more likely to bring their children for assessment than those living further away (Table 4.3). Response rates in different age groups were similar, and ranged between 71 and 74%, with an overall response rate of 73% (Table 4.3). This response rate was very similar to that noted in the MEPEDS (77%), BPEDS (62%) and SPEDS (74%) studies (6-8).

Overall, children in this study appeared to berepresentative of the Singaporean Chinese preschool children in Singapore.As there was very little other demographic and clinical information available about non-responders, presence of selection bias in some variables cannot be excluded.

5.3. Detection and classification of Amblyopia and Strabismus

Identification of amblyopia in children in this study was more problematic than strabismus.

In studies involving older children and adults, most investigators often used a visual acuity cut-off of 6/12 (20/40) or worse, provided there were no other ocular/neurological to explain the poor vision (Table 1.1). Diagnosis was easier if there were amblyogenic risk factors of refractive error, strabismus or deprivation (eg. ptosis) but these latter factors were often not considered vital in diagnosis. The assumption here was that older children and adults could be depended upon to provide reliably and accurate visual acuity measurements.

In preschool children, classifying amblyopia based only on visual assessment might not be as reliable and accurate. Children might fail visual assessment for a multitude of reasons; they might not understand the test, not know their alphabet/numbers well, or become tired or bored while doing the test. For these reasons, the investigators in the MEPEDS group developed an amblyopia definition with both visual and amblyogenic restrictions (Table 3.3). Unilateral amblyopia was defined as a $\geq$ 2-line difference in best VA, when < 20/30 (logMAR 0.18) in the worse eye, and with amblyogenic factors such as past or present strabismus, anisometropia ($\geq$1.00D difference in hyperopia, $\geq$3.00D difference in myopia, or $\geq$1.50D difference in astigmatism), and past or present obstruction of the visual axis (211). Bilateral amblyopia was defined as best VA in both eyes < 20/40 (logMAR 0.3) in children aged 48 to 72 months, or < 20/50 (logMAR 0.4) in children aged < 48 months, in the presence of amblyogenic factors such as hyperopia $\geq$ 4D, myopia $\leq$ -6.00D or astigmatism $\geq$2.50D, or past or present obstruction of the visual axis (211).

Some would argue that the refractive criteria in this definition were too strict and would result in some 'amblyopic' children being defined as not amblyopic (219). In our study, visual acuity could not be tested in 333 (16.5%). Of those in whom visual acuity was possible, 48 (2.8%) subjects failed visual criteria, 28 (58%) of whom were not considered amblyopic because they did not have refractive errors that met the amblyopic definition. Some of these children could have clinically been amblyopic (218).

In contrast, the identification of strabismus was relatively straight forward, particularly when assessed by a team of trained orthoptists, optometrists and ophthalmologist. Testability was much higher, and only 17children (0.5%) could not be accurately assessed (218).

5.4. Prevalence of Amblyopia and Strabismus

5.4.1. Prevalence of Amblyopia

In this study of young Singaporean Chinese children aged 30-72 months, we reported a prevalence of amblyopia of 1.19% (95% CI 0.73-1.83) (218). Unilateral amblyopia was twice as frequent as bilateral amblyopia. Amblyopia

was associated with a refractive error in more than 90% of children, with astigmatism being the most frequent amblyogenic risk factor.

5.4.2. Comparison of prevalence of Amblyopia between ethnic groups

Compared to similarly aged children in the MEPEDS, BPEDS and SPEDS study, Chinese children in the STARS study had much lower prevalence of amblyopia than Hispanic/Latino children (2.5%, 95%CI 1.8-3.4) in the MEPEDS study, slightly lower prevalence than in predominantly white populations in the BPEDS (1.8%, 95%CI 0.9-3.1) and SPEDS (1.8%) studies, and roughly similar prevalence to African American children in the MEPEDS (1.5%, 95%CI 0.9-2.1) and BPEDS (0.8%, 95%CI 0.3-1.6) studies (Figure 5.1) (6-8).

Differences in study design and the lack of a consistent definition of amblyopia made comparison with other studies difficult (Table 1.1). Rates in other predominantly white populations range from 0.7-4.4% (33,35,36,37,43,44,46,47,52,57). In two previous studies involving Singaporean Army recruits, prevalence of amblyopia were found to be 0.73% in 1980s, and 0.34% in the early 2000s (34,42). Estimates from other Asian populations vary widely from Japan (0-0.2%), Korea (0.4%), China (0.9-2.8%), Tibet (1.0%), Malaysia (2.0%), Taiwan (2.2%) and Hong Kong (2.7-3.8%). (39-41,45,49,50,53,56,61).

Overall, these statistics suggest that although the rates of amblyopia differed between studies, there were no marked difference in prevalence between the various ethnic groups.

There were, however, differences in the types of amblyopia within different populations. Refractive amblyopia was more common in East Asia, African American and Hispanic/Latino children, whilst strabismic amblyopia was more common in white children (Table 1.2). In the STARS study, Singaporean preschool children were more likely to have refractive (85%) rather than strabismic (15%) amblyopia. This finding was also noted historically in Singaporean army recruits where refractive amblyopia accounted for 54-65%, while strabismic and combined strabismic-refractive amblyopia were at 4-19% and 16-13% respectively (34,42). Likewise, lower levels of strabismic and combined strabismic-refractive amblyopia have also been noted in preschool children in other East Asian countries such as China (3-31%), Malaysia (23%), Japan (20%), Korea (3%) and Taiwan (3%) (39,40,41,50,53,56,61). In contrast, a greater proportion of amblyopia in white children in the USA, UK and Australia was strabismic (26-34%) or combined strabismus-refractive amblyopia (0-27%), with refractive amblyopia at 40-63% (6-8,35,36,44,47,52).

5.4.3. Prevalence of Strabismus

The prevalence of strabismus in young Singaporean Chinese children aged 6 to 72 months was 0.80% (95%CI 0.51-1.19), with the prevalence of exotropia and esotropia being 0.70% (95%CI 0.41-1.03) and 0.10% (95%CI 0.002-0.29) respectively (218).

5.4.4. Comparison of prevalence ofStrabismus between ethnic groups

Findings from this study and a review of the literature, suggested that differences did exist between ethnic groups with prevalence of strabismus being lower and with exotropia being more common in East Asian populations (Table 1.5).

Strabismus estimates from Chinese children in the STARS study were lower than in the Hispanic/Latino (2.4%, 95%CI 1.9-3.0) and African American (2.5%, 95%CI 2.0-3.1) children who participated in the MEPEDS, and with white (3.3%, 95% CI 2.3-4.6) and African American (2.1%, 95%CI 1.3-3.0) children in the BPEDS (Figure 5.1) (6,7). It was also lower than in children aged between 4 and 13 years in the United States, United Kingdom, Sweden and Australia where the reported prevalence ranged between 2.3 to 4.2 % (Table1.5) (35,37,43,47,52, 78,84). In general, strabismus rates were lower in East Asian populations within Australia, and in Japan (0.01-0.35%), Hong Kong (1.7%), Korea (1.8%), Nepal

(1.3%), Tibet (2.5%) and China (0.3%) (45,49,53,56,79,80,82). The cause of this difference was uncertain, although genetic predisposition and lower hyperopia rates might be responsible for the lower rate of strabismus in East Asia populations.

Also of note was that the prevalence of both esotropia and exotropia were much lower in Chinese children in the STARS study than in the Hispanic/Latino, African American and white American children in the MEPEDS and BPEDS (Figure 5.1). The prevalence of exotropia in STARS was almost half, and the prevalence of esotropia was one-tenth of that reported in the MEPEDS, BPEDS and SPEDS studies.

There was a marked inverse ratio of esotropia: exotropia in East Asian populations (Table 1.5). The exotropia: esotropia ratio in most East Asian populations was often reported to be greater than 2:1 (Table 1.5) (45,49,53,56, 79,82,83,218,220). Furthermore, the exotropia: esotropia ratio appeared to be increasing in Hong Kong and Japan, presumably as their populations became less hyperopic (221,222). By contrast, esotropia was more common than exotropia in many non-Asian populations (35,37,42,47,52,78,84). However, a shift towards exotropia might also be occurring in the West as the exotropia: esotropia ratio in white children in the BPEDS study and 12-year-old children in Australia were recently reported to be 1.2:1 and 1.3:1, respectively (7,80).

5.4.5. Factors that alter Amblyopia and Strabismus prevalence rate

One factor which could affect the prevalence of amblyopia was the manner in which it was defined. The prevalence could be artificially inflated if visual acuity or amblyogenic criteria were lowered. For example, if the more liberal American Association of Pediatric Ophthalmology and Strabismus (AAPOS) refractive criteria was used in our study, the amblyopia prevalence in young Singaporean Chinese children would increase 2.7-fold to 3.27%, with rates of 2.41%, 4.26%, 2.75% and 3.15% in the 30 to 35 month, 36 to 47 month, 48 to 59 month and the 60 to 72 month age-groups, respectively.

The prevalence rate would also depend on whether or not children with the condition attended the study (ie. responded). As visual screening occured in all kindergartens in Singapore (ie. in children aged 4-5 years of age), some of these children might already be under medical care and parents might not have bothered to bring their children in for screening resulting in an under-estimation of prevalence. Conversely, in families where parents suspected an eye problem, or in whom there was a strong family history of eye disorders, parents may have been more motivated to participate.

Error might also occur in the classification of amblyopia, particularly when visual acuity assessment was difficult. Half of the children aged 30 to 48 months were

unable to co-operate with the optoype identification tests used, making any estimation of amblyopia prevalence in this group unreliable (27,216). Children who were unable to do the VA test were excluded from the study, but some of these children might have been amblyopic. Children who cooperated but failed the VA test were also required to have certain levels of amblyogenic risk factors to be considered amblyopic; some of these children might have had amblyogenic factors (eg. hyperopia or astigmatism) which had lessened over time, or milder combinations of amblyogenic risk factors; i.e. they might have been amblyopic but mis-diagnosed as not having amblyopia.

The prevalence of amblyopia might also be underestimated in populations where there was early visual screening and treatment. Eibscihitz-Tsimhoni et al (2000) noted thatprevalence of amblyopia in the 8-year-old population screened and not screened in infancy to be 1.0% and 2.6% respectively (p=0.010) (223). Similarly, a study that assessed 7843 children aged 7 years of age of the 1991-2 birth cohort in England, recorded a prevalence of past/present ambylopia of 3.6%; with most having had treatment, thus leaving only 0.6% with impaired vision (7). Amblyopia rates amongst 18-year-old army recruits Singapore fell from 0.73% to 0.35% between 1980s and 2000s, possibly due to improve visual screening and treatment of amblyopia over time (34,42). In Denmark, differences between prevalence of amblyopia in older people (prior to when screening and treatment programs were started) and young school children suggest that the rate of cure of amblyopia in the present Danish system was 60-70% (224).

In terms of strabismus, prevalence might be determined by ethnic composition within each country (Table 1.5). However, even in ethnically uniform societies, prevalence and type of strabismus could change over time (eg. with changes in refractive error, perinatal medical care and or social behavior). As noted, more recent prevalence data in the MEPEDS, BPEDS and SPEDS study now suggest tharthe esotropia: exotropia ratio has fallen (Table 1.5); and even amongst Asian societies, there was a trend to increased exotropia (221).

5.5 Risk associations of Amblyopia and Strabismus

5.5.1. Factors to consider in risk association analysis

Prevalence measures were based on whether amblyopia or strabismus was identified at the time of the study (ie. cross-sectional). However, in risk association analysis, it was necessary to take into account those children who might have had past, treated amblyopia or strabismus.

In the case of amblyopia, 13 parents reported that their child had been diagnosed as having past amblyopia. One was identified in our assessment, and 2 were amongst those in whom visual assessment was not possible. Three appeared to have completed treatment and were no longer amblyopic. In the remaining 8, full

details were not available, and it is uncertain if they ever did have amblyopia. A separate analysis was therefore done in which these subjects were included as having amblyopia (including past history of amblyopia) to determine if differences exist.

In terms of strabismus, 11 parents reported that their child had strabismus previously, and 9 were identified in our study. Orthoptic assessment was not possible in one child, and one child had previous strabismus surgery.As the additional numbers were small, a separate analysis including those with reported strabismus was not performed. Similarly, as there were very few esotropic cases, no attempt was made to separate the strabismus group further into those with esotropia and exotropia.

Unfortunately, the STARS study, with a sample size of 3000 subjects, was not powered to detect risk associations especially if the prevalence of risk factors was also small. In the original MEPEDS study, the plan was to merge data from all 4 ethnic groups studied (ie. 12,000 children) for this analysis (211). Based on historical data, the MEPEDS study group estimated that prevalence of amblyopia and strabismus would lie between 2-4%. With this sample size, they hoped to be able to detect odds ratio of greater than 1.8-2.2 for risk factors with prevalence >0.20 with adequate power (80%) (211). In the STARS study, with a sample size of 3000, and assuming a prevalence of 3%, we would only detect an odds ratio of >2.12for risk factors with a prevalence >0.20 (Table 5.2). As many of our risk

associations had prevalence much less than 0.20 (Table 5.2), and as our analysis was further handicapped by the lower than expected prevalence of amblyopia (1.19, 95%CI 0.72-1.83) and strabismus (0.80, 95%CI 0.51-1.19) in our population, a significant result would only have been detected when the OR were greater than 3.5 if risk exposure was 0.10 (or 10%) and when OR were greater than 4.4 if risk exposure was 0.05 (or 5%).

Much of the information collected regarding the child's risk profile (eg. birth, maternal and socioeconomic factors) and presence of past amblyopia and strabismus was collected from a clinical questionnaire, and thus depended on parental recall and responses (a potential source of bias).

There were also differences in risk factor exposure between different studies (Table 5.3). On extracting risk prevalence data from the various published manuscripts, it was noted that mothers of children in the STARS study had much lower rates of maternal smoking and alcohol intake during pregnancy. Whilst there were more babies born of gestational age <37 in the STARS study, the proportion of babies with birth weight <2500g was quite similar. There was insufficient information to determine if the proportion of very premature babies in the various studies were similar, and as risk of ocular disorders in more premature babies could be expected to be higher, this might result in greater risk associations in populations with greater proportions of more premature children. The

difference in risk factor exposure in various studies could explain why significant associations were identified one study but not another.

5.5.2. Factors associated with Amblyopia

In this study involving young Chinese children, we found that amblyopia was associated with strabismus (OR 18.0, 95%CI 3.3-97.8), anisometropia (OR 20.6, 95%CI 4.6-91.7) and astigmatism (OR 8.9, 95%CI 2.9-26.8) (Table 1.3). Prematurity, past admission to NICU, maternal age and maternal smoking, family history of amblyopia/strabismus, lower social economic status were not associated with amblyopia.

A review of the ALSPAC, SMS and SPEDS studies showed associations between amblyopia and prematurity, past admission to NICU, family history of strabismus or amblyopia, maternal smoking, concurrent strabismus, anisometropia, astigmatism, hyperopia and lower socioeconomic status (Table 1.3) (8,44,47).

The most common risk factors associated with amblyopia were ocular factors such as refractive error and strabismus (Table 1.3). This relationship was greatest with anisometropia >1.00D, followed by strabismus and astigmatism >1.00D (44,47). These findings were mirrored in the STARS data, although hyperopia was less relevant in STARS, probably because of the lower rate of this condition

in the Singaporean children. As a refractive criteria was used in the definition of amblyopia in the STARS study, care should be taken in interpreting this result as odd-ratios might be artificially elevated.

Prematurity (i.e. BW<2.5g or GA < 37weeks) and past admission to NICU were associated with amblyopia in the SMS study (OR 5.0) (Table 1.3) (8,44), but not in the SPEDS and STARS studies (8). There were several reasons why no association with prematurity was seen in STARS. Active ophthalmology follow-up of premature children (< 32weeks and 1500g) in Singapore meant that premature children with strabismus and amblyopia might already be under care, and thus did not present for study. Advances in neonatal care might also have altered risk.

Maternal smoking was associated with amblyopia in the ALSPAC (OR 1.4, 95% CI 1.0-1.9) and SMS (OR 2.2, 95%CI 1.0-5.0) (Table 1.3) (44,47). However, as none of the child with amblyopia in the STARS study had a mother who smoked during pregnancy, we were unable to assess risk involved in this variable in Singaporean children.

Finally, an increased amblyopia risk was noted with family history of amblyopia in the ALSPAC study (47). In our Singaporean subjects, children with amblyopia were more likely to have a sibling with amblyopia (10% vs 2.3%) and strabismus (10% vs 1.2%), but this association was not statistically significant.

5.5.3. Factors associated with Strabismus

Young Singaporean Chinese children with strabismus were more likely to have astigmatism ≥1.0D (OR 3.5, 95%CI 1.0-12.0, p=0.04), concurrent amblyopia (OR 15.9, 95%CI 2.7-92.8, p=0.002), a parent with history of strabismus (OR 17.9, 95%CI 1.1-278.3, p=0.04), and a sibling with history of strabismus (OR 38.3, 95%CI 8.7-168.5) (Table 4.19.2). Strabismus was also associated with lower paternal education level with children whose father had secondary/'O' or 'A'/polytechnic/tertiary level education having an OR 0.07 (95%CI 0.01-0.58, p=0.01) and OR 0.23 (95%CI 0.06-0.89, p=0.03) respectively compared to children whose father had no/primary education.

Findings from the ALSPAC, MCS, CPP, MEPEDS, BPEDS, SMS and DNBC studies showed associations between strabismus and white ethnicity, prematurity, admission to NICU, family history of strabismus or amblyopia, maternal smoking, increased maternal age, concurrent amblyopia and lower parental education status (Table 1.6) (47,78,80,81,84,89,90,91). Differences in age, ethnicity, disease definitions and data collection made direct comparisons between some studies difficult. Also, none of these studies were based in East Asia where the prevalence of exotropia and myopia were higher.

Prematurity was the factor most consistently associated with strabismus in many studies with a 2.5 to 4.4 times increase in strabismus was noted in premature

children in the SMS, CPP, DNBC and MEPEDS/BPEDS studies (Table 1.6) (47,78,80,81,84,89,90,91). No association was found between strabismus and prematurity in the STARS study. As with amblyopia, premature children with amblyopia might not have presented because they were already under care, or advances in neonatal care might have decreased risk. Alternatively, prematurity might be less associated with exotropia, which was more common in Asian populations.

Maternal smoking was another factor closely associated with strabismus with OR of 1.2-2.9 in the ALSPAC, CPP, MEPEDS/BPEDS and DNBC studies (47,78,89,91,93). As no child with strabismus had a mother who smoked, it was not possible to analyse the risk of maternal smoking on strabismus in the STARS study.

Childhood strabismus was associated with a family history of strabismus and amblyopia in the ALSPAC (OR 2.4, 95%CI 1.7-3.2) and a sibling with strabismus in the CPP (OR 2.0, 95%CI 1.2-3.2) (Table 1.6). In the STARS study, we found that children with strabismus were more likely to have a sibling with strabismus (OR 41.2, 95%CI 9.0-188.0) (Table 4.19). The tendency to higher familial concordance with strabismus was also been noted in other studies (47,78,94-98).

Children with strabismus in STARS and MCS were more likely to have parents with lower educational levels and household incomes (Table 1.6). In the STARS

study, children with a father with 'A'/polytechnic/tertiary education were less likely to have strabismus (OR 0.2, 95% 0.1-0.9), while in the MCS study, children with professional parents were less likely to have strabismus (OR 0.7, 95%CI 0.5-1.0) (Table 4.19). This suggested that there might be environmental and developmental factors which predispose a child to strabismus. Alternatively, there might be family groups who are trapped within a lower socioeconomic level by the social, psychological and cosmetic disadvantages associated with strabismus. Parental education and socioeconomic status were, however, not found to be a significantly associated with amblyopia or strabismus in the SMS, ALSPAC and MEPEDS/BPEDS studies (47,80,91).

Studies have also demonstrated possible associations between strabismus and parental age with Chew et al (1994) noting an increased maternal age with esotropia in the CPP study (OR 1.4, 95%CI 1.1-1.7 in mothers aged 30-34years compared to 20-24years), while Robei et al (2006) noted increased association with increasing paternal age in the SMS study (OR 4.9, 95%CI 1.6-15.9) (Table 2.1) (78,80). There was, however, no association between maternal age and strabismus in the MEPEDS/BPEDS and STARS studies (91).

5.5.4. Implications of risk factor associations in Amblyopia and Strabismus

There are several risk factors which could predispose a person to a disorder of disease. These include genetic, demographic (eg. age, gender, race), clinical (eg. pre-existing medical conditions), environmental (eg. climate, exposure to toxin), health-related behavior (eg. substance abuse) or cultural (eg. societal or religious beliefs) factors (299). In assessing and managing risk, one would need to take into account the magnitude of the association, and whether the risk was modifiable. In cross-sectional studies, it was also important to remember that associations identified might not be always causative. Understanding the risk associations wouldallow public health services to determine if prevention of the disease (eg. by reduction of risk exposure in the general population) or if targeted intervention (eg. in high-risk individuals or groups) was possible and acceptable.

A review of the literature suggested that there were factors, in particularly prematurity and maternal smoking, which were strongly associated with both amblyopia and strabismus. A causal relationship between both prematurity and maternal smoking,and amblyopia or strabismus, was plausible as both could have an effect on neural or brain development. In the immediate post-natal period, premature children were at greater risk of respiratory distress syndrome, bronchopulmonary dysplasia, hypoglycaemia, hyperbilirubinaemia, periventricular leukomalacia, intraventricular haemorrhage, cerebral palsy, epilepsy, global developmental delay, and retinopathy of prematurity (300-304).

In the longer-term, premature children were also more likely to have learning difficulties (eg. poor school performance, lower academic achievement, poor language and verbal fluency), cognitive impairment (eg. lower intelligent quota scores, greater special school admissions, lower educational qualifications), poorer neuro-motor skills, visual and hearing impairment, and behavior or psychiatric problems (eg. negative affect, hyper-activity, low attention span, lower self-esteem) (300-304).

Maternal smoking has been associated with maternal problems such as spontaneous abortions, placental abruption or previa, preterm birth, intrauterine growth retardation, still birth and sudden infant death syndrome (306-307). Children of mother who smoked during pregnancy were also more likely to have attention-deficit hyperactivity disorder (ADHA), learning difficulties and behavior problems, and to develop asthma, childhood brain tumour and leukemia/lymphoma. In the longer term, data from human and animal studies suggest that prenatal nicotine exposure could also increase the risk in of adult obesity, type 2 diabetes, hypertension, ischemic heart disease, and infertility. These effects of maternal smoking are believed to the result of exposure to toxic agents within the cigarette smoke and chronic hypoxia on neurological and systemic development of the fetus/child, and alterations in metabolic functions as a result to chronic nicotine exposure (306-7).

Prematurity and maternal smoking were not associated with amblyopia or strabismus in the STARS study but it given the strong evidence noted in other studies, it would be foolish to dismiss it. The factors that were associated with amblyopia (refractive error and concurrent strabismus) and strabismus (refractive error, concurrent amblyopia, a family history of strabismus and lower socioeconomic status) in the STARS study were not easily modifiable. However, understanding which factors were associated with greater risk was useful if only to help physicians better understand the conditions and to identify individual or groups at risk. An increased awareness of these factors amongst healthcare professionals and the general public might help in earlier detection and treatment of these conditions.

5.6. Screening for Amblyopia and Strabismus

Since amblyopia and strabismus are 2 conditions which occur early in life, and could result in visual impairment, many developed countries have screening programs in place to try and identify and treat these conditions early. Variability exist between countries with regards age of screening, types and range of tests used, persons assigned to perform tests and in their diagnostic and referral criteria (225-228).

In Singapore, health screening in schools was introduced by the then Public Health Department under British colonial rule in the 1920s. However, comprehensive visual screening of all children did not occur till school attendance rates rose in the 1950s. The School Health Services teams from the Ministry of Health, Health Promotion Board, have conducted visual acuity screening using a Snellen or EDTRS logMar visual chart in primary schools (ie. in children aged 6 years) for many decades, and this was extended to preschool children (ie. children aged 4-5years) from 2002. Children identified as being having sub-normal visual acuities were referred to local paediatric ophthalmology centers for more thorough assessments. Children were also screened for strabismus (with cover-uncover test), stereopsis (with near Frisby) and color defects (with the Isihara plates) at aged 6 years.

Visual screening programs vary between countries, and even within states and counties within countries (Table 5.4). In the United Kingdom, visual screening for amblyopia, refractive error and strabismus is offered by an orthoptist-lead service in children aged 4-5 years (227). Child Health services in many states in the United States also recommend visual screening at entry to kindergarten or school, and through the early school years (2,225,226).In Australia, it is recommended that children receive a general eye check atinfancy,and a vision screen at 4 years (225,230,311). In some European countries (eg.Sweden, Denmark), visual screening begins at infancy (2,311). In many European countries (eg. Germany, Eastern Europe) and much of Asia, Africa and South America, there are no

childhood visual screening guidelines. In these areas, visual screening may not occur, or be sporadic or patchy. Questions remain regarding the optimal age of screening, whether early detection and treatment lead to tangible longer-term benefits in visual function and the cost-effectiveness of visual screening programs (225-230).

5.6.1. Factors to consider when assessing effectiveness of screening tools

In order for a screening tool to be effective, it needs to be cheap, easily-available, simple to use, accurate, acceptable and repeatable (226). The sensitivity (ie. the ability of the test to pick up true positive cases) and specificity (ie. the ability of the test to detect true negative cases) are also important (Figure 5.2). If sensitivity was high, then a negative result would rule out disease; and if specificity was high, then a positive result would rule in disease (231). In conditions where prevalence was low (such as amblyopia and strabismus), then a specificity which was too low will lead to an unacceptable number of false negative referrals; which might in turn result in un-necessary clinic/hospital visits, stigma, anxiety, need for additional tests and even treatment in a young child. For this reason, some investigators preferred to maintain specificity high (eg. >90%). The disadvantage of this was that sensitivity was lower; and the positive predictive value (ie. the percentage of cases detected by a positive result) of the test might be decreased.

The positive predictive value (PPV) also depended on proportion of disease in sample and was lower when prevalence was low.

Receiving Operator Curves plots sensitivity against 1-specificity, and the area under the curve (auc) could be calculated to determine how effective a screening tool was. An auc closer to 1.0 suggested that the screening tool had both a high sensitivity and specificity, and that it was more effective in identifying presence of disease.

A diagnostic test could also be assessed by its positive or negative likelihood ratios (231). The likelihood ratio for a positive test (LR+) was calculated as sensitivity/ (1-specificity), while a likelihood ratio for a negative test (LR-) was (1-Sensitivity)/Specificity. A high LR+ (>10) or low LR- (<0.1) indicate a large conclusive change from a pre- to post- test probability of disease/no disease. LR+ of 5-10, or LR- of 0.1-0.2 suggest moderate shifts; LR+ of 2-5, or LR- of 0.2-0.5 suggest small but sometimes important shift in probability; while LR+ of 1-2, or LR- of 0.5-1 suggest small, rarely important change in probability.

Currently, most visual screening programs utilize visual acuity as a means to screen for visual impairment. However, visual acuity assessment is time-consuming and requires children to be willing and able to co-operate with tests. In preverbal children, non-verbal visual acuity tests available such as the force-preferential tests (eg. Teller or Cardiff cards), where children are judged

subjectively by their preference to look in the direction of an object (eg. stripped pattern rather than a unmarked surface) (231). However, sensitivity/specificity of these tests might be user-dependent. In some studies, the high levels of sensitivity and specificity were obtained (31,32). However, in others, these tests were found to underestimate or miss cases of visual impairment (30,233,234). Long term predictability of tests (ie. ability of test done at younger age to predict future visual impairment) could vary, particularly if initial test was abnormal (232,235,236).

In older children, visual acuity tests included pictures (eg. Kay Pic, Lea symbols) or optotype matching or identification (eg.Sheridan Gardner, Snellen, logMar visual acuity) (237). Visual acuity measured with different tests were not necessary equivalent (238). For example, the use of single or uncrowded optotypes would often under-estimate the level of visual impairment (239-241).

Testability of visual acuity was much lower in children under the age of 4 years (24-27). Unfortunately, children who were unable to be tested were also more likely to have pathology; Macquire et al (2007) in a review of children unable to perform visual acuity and stereoacuity tests in the Vision in Preschoolers (VIP) study, noted that these children were twice as likely to have the ocular condition for which they are being screened for than children able to perform tests (242). This suggests that in order to be useful, any screening tool should have a reasonable testability rate for the ages in which it is being utilized.

While a negative or 'normal' result often excluded amblyopia, the presence of a sizeable false positive rate (29-81%, ie. unnecessary referrals) (243-246) and false negative rates of as high as 20% (ie. cases missed) (2,247,248) noted in some optotype-based screening programs were unacceptable.

Besides visual acuity, other screening programs utilitzed other screening tools such as refractive error (either measured through retinoscopy, table mounted or hand-held auto-refractors), pupillary light reflex (via Bruchner's reflex or photoscreeners such as the MTI or plusoptix photoscreeners), cover/uncover tests and stereoacuity to screen for amblyopia and strabismus (Table 5.4) (135,136,248-266). A review of the literature found that no one test was entirely effective and combining tests might yield better results (263, 266). Kulp et al (2009) in an assessment of various screening tools suggested that a combination of visual acuity and refractive error might be useful for the detection of amblyopia; while the use of either a cover-uncover test (by a professional) or stereoacuity test (by a lay-person) might be most useful in the detection of strabismus (266). Further studies would be necessary to determine if the increased yield obtained from adding more tests to the community screening program was worthy of the additional cost.

5.6.2. The Randot Preschool Stereoacuity Test in the detection of Amblyopia and Strabismus

As demonstrated in other studies, in STARS, there was a gradual improvement of testability and stereoacuity measured in children aged from 30 to 72 months (8,27,114,122-125). Whether or not this reflected a true development change or just an improvement of a child's ability to perform better was debatable. Regardless, the clinician assessing very young children would need to take this potential 'improvement' and other limitations of the test into account.

Children with amblyopia and strabismus did have poorer stereoacuity (101,104-106). Depending on the degree of amblyopia and intermittency of strabismus, some amblyopic and strabismic children might have good stereoacuity. In STARS, children with amblyopia and strabismus recorded a poorer stereoacuity (200sec to none) in 38.4% and 69.2% respectively, but good stereoacuity (40 to 60sec) was also recorded in 23.1% in each group.

Unfortunately, the Randot Preschool Stereoacuity Test (RPST) demonstrated poor testability in younger children aged below 48 months (8,27,122). Testability of other stereoacuity tests (eg. LangII, StereoSmile Test, Random E) were higher; but further study would need to be done to determine which would be most effective in the screening of vision in this young age (8,29,119).

The RPST also appeared to be more effective in detection of strabismus (auc 0.82, 95%CI 0.66-0.99), than amblyopia (auc 0.77, 95%CI 0.63-0.92) (Table 4.23). If specificity was maintained over 90%, so as to limit the number of false negatives, then the optimal normal cut-off using the RPST in the STARS study was 200sec (Table 4.25). Using this cut-off, 30 of the 1528 children who were able to perform the RPST would have been deemed to have failed screening with a positive predictive values (PPV) for amblyopia and strabismus of 17% and 27% respectively. Likelihood ratios were better for strabismus (LR+ 14.4, LR- 0.3). The PRST missed 67% of children with amblyopia and 48% with strabismus (ie. an unacceptable number of children with pathology).

These findings suggested that the sensitivity and specificity of the PRST was poor and that it would not be useful as a sole test for identification of children with amblyopia and strabismus (267).

5.6.3. Effectiveness of the autorefractor refractive error estimates in detection of Amblyopia and Strabismus

Given that the testability of visual acuity was low in younger children, could autorefraction values at this age be more effective as a screening tool? Such equipment was easily available, increasingly economical, potentially portable,

relatively easy to use and could be applied to both verbal and non-verbal children (8,147,152).

Testability, validity and reliability of different equipment were variable. The ability to test refraction using table mounted autorefractors in young children less than 54 months of age was less than with hand-held devices (8,148). Table-mounted devices might be more accurate and reliable than hand held devices particularly in the assessment of hyperopia (146,147,250).

There has also been debate about the effectiveness of non-cycloplegic autorefraction, particularly in the detection of hyperopia which was a common cause of amblyopia and strabismus in non-Asian population (140-142,145,148-151). Hyperopia was often under-estimated under non-cycloplegic conditions and cases of high hyperopia could be missed. Administering cycloplegic drops to a large number of school-children in a screening exercise would be a daunting proposition as children often do not like eye drops. The eye drops might need to be administered 2-3 times, parental consent would be required, and there were potential side effects (eg. allergy, flushing, tachycardia, blurred vision and light sensitivity for 2-3 days) related to the drops. Very rarely, children might also develop a severe allergic reaction (rashes, anaphylactic shock) or behavior changes (hyperactivity, confusion, disorientation, hallucination and seizures) with cyclopentolate eye drops (268).

In the STARS study, it was difficult to accurately assess the role of refractive error in screening for amblyopia as refractive criteria was used in the classification of amblyopia which might artificially inflate the association between the two conditions. Indeed, the effectiveness of many autorefraction parameters in the detection of amblyopia was high; astigmatism (auc 0.88), anisometropia astigmatism (auc 0.82), myopia (auc 0.78) and anisometropia (auc 0.72) (Table 4.25).

An alternative way to determine if autorefraction was a useful screening tool, using STARS data, was to see if it was effective in detecting visual impairment (eg. visual acuity of <20/50 in one eye) (Table 4.25). If autorefraction was used only to detect impaired visual acuity alone, then astigmatism ≥1.5D was the best parameter (aus 0.87), followed by anisometropia astigmatism >1.0D, myopia <-2.00 and anisometropia >1.5D (Table 4.25). These findings suggest that autorefraction could identify some of the refractive risk factors associated with amblyopia. However, further studies would be necessary to determine if autorefraction by itself was as effective as the current visual acuity screening, and whether combining the tests would be cost-effective.

In terms of identifying strabismus, the auc for all refractive parameters was relatively poor (auc 0.51-0.69). This suggested that refractive error as measured with autorefractors would not be an effective screening tool for strabismus. This was not surprising as there were many types of strabismus, and their refractive

associations were very varied. Also, extremes of refractive error were not typical of intermittent exotropia, which is the most common strabismus in East Asian populations.

5.6.4. Implications for effectiveness of the current screening of Amblyopia and Strabismus in Singapore

Currently, the visual screening in Singapore children includes uncorrected and corrected visual acuity assessments at ages 4-16 years with a cover-uncover test, the Frisby near stereoacuity test and colour vision test at aged 6 years. This visual screening is closely integrated into the school health program which also includes general health checks (height and weight), dental screening, scolosis screening and childhood immunization programs.

Testability of visual acuity in children aged 48-56 months (ie when visual screening is commenced) was good (96%), while in children just 12 months younger (aged 36-48 months), testability was much lower (77%). This meant that visual acuity screening from age 48 months was quite appropriate. There was also no evidence that earlier visual screening was predictive of later visual function, or that treatment of amblyopia under the age of 4 years greatly improved final outcome (271-279).

In STARS, visual acuity testing alone identified 48 children with suboptimal vision, 28 (58%) of which was not classified as being amblyopic because of lack of amblyopic risk factors (ie. possible unnecessary referral). However, of greater concern was that 18 (90%) of 20 children who were found to be amblyopic had no past history of amblyopia suggesting that these cases might have been missed by the pre-existing School Health Service visual screening program. We have no information regarding how many of amblyopia the School Health Services did identify each year, and whether the overall yield made the cases missed more acceptable. Sensitivity of the visual acuity test in the VIP studies was estimated to be 60% when specificity was kept at 94%, suggesting that there might be cases missed with each screening episode (136).

The testability of the table mounted autorefraction in the STARS study was 63% and 82% at the age of 36-47 and 48-60 months respectively (27). Testability was better with the hand-held Retinomax in the MEPEDS study (98%), suggesting that selection of the right autorefraction tool was important (310). Using the table-mounted autorefractor, autorefraction was effective in detecting visual impairment <20/50 in terms of astigmatism $\geq$1.5D, anisometropia astigmatism and anisometropia >1.5D, refractive errors often associated with amblyopia (Table 4.25).

Both visual acuity and autorefraction tests were less effective in screening for strabismus (Table 1.9). The cover-uncover test (in the hands of professionals), and

stereoacuity or photoscreener tests (in the hands of the lay-person) appeared better (266). Children in Singapore were screened for strabismus (with cover-uncover test and Frisby stereoacuity) at aged 6 years. Testability of the cover test and Randot Preschool Stereoacuity test at this age was good (97% and 98% respectively) (27). However, the usefulness of strabismus screening (ie. its ability to detect new previously unidentified strabismus) at this age was uncertain. As strabismus was a more visible condition than amblyopia, many children might have already presented before the aged of 6 years to their healthcare professional. Some would also argue that treatment of childhood strabismus (eg. infantile or accommodation esotropia) wouldhave been more effective if it had occurred earlier (ie. at onset).

5.6.5. Factors to consider when developing a screening program for Amblyopia and Strabismus

In 1968, Wilson & Jungner developed World Health Organism guidelines to public health screening which are still applicable today (308). These state that in planning a screening program, several conditions need to be met: the condition should be an important health problem, there should be a treatment for the condition, facilities for diagnosis and treatment should be available, there should be a latent stage of the disease, there should be a test or examination for the condition, the test should be acceptable to the population, the natural history of

the disease should be adequately understood, there should be an agreed policy on who to treat, the total cost of finding a case should be economically balanced in relation to medical expenditure as a whole, and case-findings should be a continuous process, not just a 'once and for all' project.

Naturally when assessing the importance of a health problem, one needs to take into account the impact the condition will have on an individual or society's well-being in terms of morbidity and mortality. Neither amblyopia nor strabismus are life-threatening conditions. The main impact of these conditions lay in their effect on motor and visual function, psychosocial wellbeing and potential loss of visual function.

The natural history of both amblyopia and strabismus is well known. Amblyopia, a failure of visual development begins in infancy, and the more common childhood strabismus usually presents before the age of 4 years. Thetreatment of these conditions are well established. Amblyopia treatment if implemented early enough in childhood can be very successful (309). Treatment outcomes for strabismus are more variable, depending on type of strabismus and level of pre-existing visual acuity (eg. amblyopia) and binocular fusion capacity (eg. stereoacuity) (309). In general, provision of earlier treatment or intervention often offers children a better chance of a good outcome.

Visual screening has been practiced in Singapore for many years, and there is already an established infrastructure in place of screening, diagnosis and treatment. There are clear referral guidelines. Children found to have visual impairment or strabismus are referred to paediatric ophthalmology services around the island where appropriate treatment can be initiated.

School health screening is well accepted by children, parents and society in Singapore. It is an on-going program present in Singapore since the 1920s. Almost all the screening tests are non-invasive and occur during school hours so that neither parent nor child is greatly inconvenienced. Most parents and health-care professionals (eg. paediatricians and paediatric ophthalmologist) depend the services of the School Health Services to monitor and screen for a variety of medical conditions (including visual problems) in young children. It is difficult to think of an alternate way to provide such services. In fact, ending part or all of the School Health Services program, particularly in a cost-cutting exercise, would probably face community resistance.

Unfortunately, there has not been a thorough review of the school visual screening program, and there is currently no data about how effective the program is in identifying amblyopia and strabismus in Singapore, or whether there is a better, more cost-effective way to achieve similar or better results.

The challenges lies in identifying which the screening tool to use for greatest effectiveness (ie. testability, validity and reliability), in determining which age of the child to test (usually less or greater than 48months), in deciding whom should administer the test (e.g. trained or lay-person), defining what referral criteria to use and clarifying how best to test the effectiveness of the program (125,135,225-230, 237-9,277). From the findings in STARS and a review of the literature, what is apparent is that there was no single ideal test or normal cut-off point (Table 1.9, Table 4.25). However, there is also no global consensus on what best visual screening practice is. Recommendations by public health services vary widely between countries, and actual practices can differ even within the same country. In many countries, visual screening does not occur routinely.

Whether the total cost of funding a visual screening program is economically balanced in relation to medical expenditure as a whole depends on the healthcare priorities in individual countries, resources available, the political will and leadership, lobbying of interest groups, and whether intervention would be accepted by the population (309). Although visual screening was performed in many developed countries, a review of various screening programs suggest that it was still not possible to determine if visual screening was truly cost-effective (26,28,230,237,244-246,269-276).

5.6.6. Recommendations for screening of Amblyopia and Strabismus in Singapore

With regards visual screening in Singapore, one might question whether it was cost-effective to screen children for conditions which only affect a small proportion of the population (<1-3%). Since having good vision was deemed to be an important functional attribute, most authors advocated some form of community visual acuity screening in children. There is good evidence that visual screening can reduce visual loss secondary to amblyopia by 50-60% (7,34,42,223,224,309). Models of the cost-effective of screening and treatment of amblyopia suggested that there are real medical and cost benefits of interventions (237,278-9).

Before making recommendations to alter the current visual screening program in Singapore, it is useful to evaluate the role and effectiveness of the current screening program. This could be done by a thorough review of the number of referrals are created by the screening in the first year of screening when children are 4 years old, and in each subsequent years. An assessment then needs to be made as to how many true cases of amblyopia were identified in the first year (yield and false positive rate), and the number of cases identified in the subsequent 1-2 years when children are aged 5 and 6 years (ie. missed or new cases) to determine if annual testing was justified. A similar review of cover-uncover test and stereoacuity at aged 6 years would also needed to determine if

these tests were useful to identify new previously undiagnosed cases of amblyopia and strabismus. Cost effectiveness of the program could then be calculated.

A final recommendation on visual screening would depend on the outcome of the review of the current screening program. However, in terms of amblyopia, the author would suggest that the visual acuity screening by trained persons from the School Health Service starting at 4 years is quite feasible with a repeat visual acuity check at least once between 5-6 years so that any children missed on the first screening could be identified at the next visit. The yield of screening for amblyopia beyond age of 6 years is questionable as it would be progressively less likely for a screening program to identify new amblyopic children (225). In Singapore, however, screening of uncorrected visual acuity between 6 to 12 years has been useful in monitoring myopia prevalence in the general population, and continued screening could be justifiable for this reason.

It is questionable whether other tests (eg. non-cycloplegic refraction or photoscreening) should be added to visual acuity screening to increase yield, or whether they could be used to replace visual acuity with greater cost-effectiveness. This strategy could be tested in the field by running a parallel program (eg. one with and without additional test) and assessing outcome.

The role of a cover-uncover and stereoacuity test at age 6 years should also be critically reviewed to determine if it was useful in identifying new cases of

amblyopia or strabismus. Since most of the common childhood strabismus presents early in life and is quite visible, a public-health program to educate parents or healthcare professionals on how to identify the condition and the importance of early referral may be more cost-effective and useful.

5.7. HRQOLassessment of Strabismus and Amblyopia

The effect of disease on quality of life can be assessed by several health-related quality of life (HRQOL) instruments (158). In each case, a decision needs to be made in choosing which instrument to use. These instruments (or questionnaires) often address 3 domains (ie. physical/functional, psychological/emotional and social) through a series of questions. The impact on HRQOL is then expressed in sub and total scores. The developers of such HRQOL instruments need to refine and validate their questionnaires in their own communities. When using these instruments in different communities, cultures and nations, it is important also to determine if these instruments remain valid (i.e. measures what is supposed to measure), reliable (i.e. reproducible) and responsive (i.e. able to detect real changes in quality-of-life) (156,158,159).

Strabismus is a condition where there is misalignment of one eye. This often is quite visible to the casual observer and thus has the potential to identify the child or person as being different or abnormal. The common negative themes associated

with strabismus include impacts on one's self-esteem, social confidence, interpersonal relationship, depth perception, employment, finding a life partner and mental health (e.g. anxiety and depression) (187-203).Several studies have demonstrated improved psychosocial scores after successful strabismus surgery (192,199,204,280), suggesting that correction of the strabismus is beneficial and cost-effective (203,205).

In the STARS study, we found no difference in PedsQL4 scores in young Singaporean children with and without strabismus or amblyopia. In the child development survey, children with strabismus were found to have increased risk of speech (OR: 4.71, 95% CI 1.52-14.59, p=0.007) and comprehension (OR: 5.61, 95% CI 1.37-28.7, p=0.02) problems after adjustment for gender, age and past admission of neonatal intensive care unit.The PedsQL4 has not been validated in use in Singaporean Children with strabismus and amblyopia. Rasch analysis found misfit; reliability and validity issues with marked ceiling effect, suggest that the PedsQL4 was a suboptimal scale with regards assessment of HRQOL in young Singaporean Chinese children with strabismus and with amblyopia.

HRQOL and strabismus

With regards strabismus, the PedsQL4 findings in the STARS study were at odds with those noted in the Multiethnic Pediatric Eye Disease Study (MEPEDS) where similarly aged African-American and Hispanic children in North America with strabismus were found to have small but statistically significantly differences

in PedsQL4 physical HSS (90.2 vs 94.1, p<0.01), psychological HSS (86.7 vs 90.4, p<0.01) and total scores (88.0 vs 91.8, p<0.01) after adjusting for age, gender, race and family income (210).

It is interesting to speculate why no PedsQL4 differences were noted in our study. One possibility was that strabismus truly has no adverse effects of the quality of life in young Singaporean children aged < 72 months. Differences between studies might be related to type and severity of the strabismus present in the different populations. In the MEPEDS study, approximately 52% of children had esotropia (6) while in the STARS study, the majority of children (n18, 82%) were exotropic, most (n12, 71%) of which was intermittent (i.e. not present all the time). Furthermore, in Asian children, who have wide epicanthic folds, the presence of exotropia might not be so evident. Younger children might also be less self-conscious and troubled by their appearance (189,197). Hatt et al (2009) in a study of young children with intermittent exotropia found that only 20% of children aged between 5-7 years were aware of their strabismus compared to >60% of older children (281).

It could also be that Singaporean Chinese parents were simply less culturally inclined to perceive or report any negative effect of their children's overall quality of life. There were marked ceiling effect with>80% of parents affording their children a >90 score for each category (Figure 4.7). The overall physical HSS (98.0 vs 94.1), emotional function (93.8 vs 87.0), school function (94.4 vs 90.8), social function (98.2 vs 93.0), psychological HSS (95.6 vs 90.1) and total scores

(96.5 vs 91.8) were all higher than those reported in the MEPEDS African-American and Hispanic children from the United States (210).

Perhaps, the generic PedsQL4 might not be specific enough to identify those with quality of life issues in children with strabismus and a difference might have been noted if a more vision or disease specific HRQOL instruments was applied (206,208,209). Indeed, parents in the STARS study did note comprehension and speech problems in strabismus children in the Child Development Survey; and these items might have been more relevant to strabismus. It was difficult to know if children truly have problems in comprehension and speech or were they to have been perceived as having such problems secondary to their strabismus. Studies have shown that persons with strabismus were more likely to be mistakenly perceived as being less intelligent (19,188,205). As the eye deviates, the children might appear to be less focused and parents might feel that their child might not understand them. In intermittent exotropia, the eye was more likely to deviate as children become distracted or tired, and inattentiveness or disinterest might thus be more easily identified than in non-strabismus children.

HRQOL and amblyopia

With regards amblyopia, both the STARS and MEPEDS studies found no difference in HRQOL between children with and without amblyopia (210). Amblyopia is a condition in which the vision in one or both may be decreased. As in children with strabismus, amblyopic children might have difficulty with visual

function (e.g. poor stereopsis, depth perception and hand-eye co-ordination skills). Unless there was concurrent strabismus, amblyopia was not physically obvious and children were often identified only after school screening. The treatment of amblyopia, which often involved repeated visits to hospital, wearing glasses, patching one eye or administering eye drops, might have more effect on a child's HRQOL and relationships within the family than the condition itself (170,171,283). There was evidence that the greatest impact may be at treatment initiation, that acceptance of treatment improved over time and that there was often no long-term impact of children's overall psychosocial well-being (167-169,172).

Rahi et al (2006), looking results from when their subjects were aged 33 years from the 1958 British birth cohort, noted no difference in education outcomes, behavioral or social difficulties, accidental injuries, general or mental health, employment and mortality in the 429 people identified as being amblyopic (i.e. with unilateral poor vision at age 16 years) compared the 8432 people with normal vision (184). Chua et al (2004), however, using data from the Blue Mountain Study, found that the 118 (3.2%) who had amblyopia had no difference in employment status but were less likely to complete higher education, and had an increased risk of injury to the better eye compared to those who were not amblyopic (185).

Hence, like in strabismus, the PedsQL4 might not be specific to pick up HRQOL issues in amblyopic individuals. Felius et al (2004) and Van de Graaf et al (2009) using the Amblyopia & Strabismus Questionnaire (A&SQ) showed that persons with amblyopia have fears of losing the better eye, problems with distance estimation, visual disorientation, diplopia and social contact (181,182). Webber et al (2008) in an experiment where 82 amblyopes (mean age 8.2+/-1.7 years) were put to a series of tests assessing visual motor control and upper limb speed and dexterity, found that the amblyopes took longer or made more errors when asked to draw straight paths, copy some shapes, drawing vertical lines, making dots, putting pennies in boxes, sorting cards and displacing pegs (176). The questions in the PedsQL4 questionnaire regarding physical function (ie. walking, running, participation in active play or exercise, lifting a heavy object, bathing, doing chores, having pain and aches, low energy levels), and also in the Child Development Survey regarding fine and gross motor skills were quite general, and possibly did not go into sufficient depth to identify smaller targeted deficits in motor function. A performance based assessment might have been more revealing.

Other factors to consider in evaluating HRQOL findings

The assessment of the impact of strabismus and amblyopia on HRQOL was handicapped by the small number of strabismus and amblyopic cases in the STARS study. The use of parental proxy measures might also add bias. Several authors had demonstrated different scores in questionnaires completed by children

and parental proxies (156,284,285); while parents tended to overestimate the HRQOL of normal children and underestimated the HRQOL of children with a medical disorder (284,286), children tended to use more extreme values when rating themselves on a HRQOL scale (287). Care needed to be taken when assessing parental-proxy results as it might not truly reflect the manner and extent of disease on the children themselves.

5.8. Strengths of this study

The main strength of this study was the utilization of a large population based cross-sectional design consisting of a single ethnicity. Assessment of study population characteristics suggested that it is relatively representative of Chinese children and families across Singapore. The response rate to the study was high (74%), and similar to that of the MEPEDS, BPEDS and SPEDS studies; which were of similar design.

Collection of data was performed in a very systematic manner. In most cases, interviewers were blinded to the children's eye conditions as the team performing interviews were different from those who later examined the children for eye conditions.

5.9. Weaknesses of the study

One of the main limitations of the study was the low number of strabismus and amblyopia cases. This was partly because the sample size calculation was based on older, mainly Western data, which suggested that the prevalence of strabismus and amblyopia lay between 3-5%. As it turned out, prevalence of strabismus (0.8%, 95%CI 0.51-1.19) and amblyopia (1.2%, 95% CI 0.73-1.83)were much lower in the STARS study, possibly due to racial composition and also to pre-exiting screening programs and easy access to healthcare which allowed for early detection and treatment of both conditions.

The study also depended on parents bringing their child for assessment on a volunteer bases. Although the response rate was quite good (74%), there might still be differences between the non-responder and responder group. Children with strabismus and amblyopia who were already under care might not have presented for the study.

There was also a subset of children (10%) in whom cycloplegic refractions were not available. Refractive data in these children might not be as accurate, and this could also have led to an under-estimation of hyperopia in the population.

In terms of assessing risk associations, the plan was for data from MEPEDS, BPEDS, SPEDS and STARS to be pooled. The studies were therefore

inadequately powered to measure risk-factor association with strabismus or amblyopia in individual ethnicities.

As the study population was very young, the assessment of visual acuity (and hence amblyopia) was at times difficult, as children might fail vision tests for reasons other than amblyopia. Amblyopia was thus also defined using refractive and strabismus components. The use of refractive component to define amblyopia also meant any analysis of refractive components and its role in amblyopia might be biased.

Although an attempt was made to obtain as much data as possible in an objective manner (eg. use of child's health booklet with entered maternal and birth parameters), much of the information was obtained on site from parents. Parental response to some questions (eg. maternal illness, smoking or drug use, household income or family history of strabismus and amblyopia) might be subject to recall bias and error.

Finally, the HRQOL instrument used may be too generic, and the use of parental-proxy might add to bias as it was based on parental perceptions of how disease was affecting their child, rather than on the child's own perception of disease. Any conclusion on the effect of amblyopia and strabismus on HRQOL based on the PedsQL4 might be premature.

Chapter 6: Summary and Future Directions

6.1. Summary of Findings

The STARS study recruited 3009 Chinese children (response rate 72.3%) from South-West Singapore. The study population was quite representative of the general Singapore population, although responders were more likely to be better education with higher monthly household incomes, and to live closer to examination centers.

The prevalence of amblyopia in Singaporean Chinese children aged 30 to 72 months was 1.19% (95%CI 0.73-1.83), using amblyopia criteria from the STARS, MEPEDS, BPEDS and SPEDS studies.This prevalence was lower than that the Hispanic/Latino children (2.5%, 95%CI 1.8-3.4) in the MEPEDS study and predominantly white populations in the BPEDS (1.8%, 95%CI 0.9-3.1) and SPEDS (1.8%) studies; and similar to African American children in the MEPEDS (1.5%, 95%CI 0.9-2.1) and BPEDS (0.8%, 95%CI 0.3-1.6) studies. Prevalence of amblyopia, using the more liberal American Association of Pediatric Ophthalmology and Strabismus (AAPOS) refractive criteria, however, was 3.27%.

Amblyopia in Singaporean Chinese Children was more likely to be associated with refractive (85%) rather than strabismus (15%), whereas amblyopia in Caucasian children in the USA, UK and Australia was more likely to be associated with strabismus alone (26-34%) or combined strabismus and refractive error (0-27%), rather than refractive error alone (40-63%).

Amblyopia was associated with refractive error, strabismus, prematurity, maternal smoking, lower socio-economic status and a family history of amblyopia in other studies. In young Singaporean Chinese children, amblyopia was only found to be associated with myopia $\leq$-3.0D (OR 27.6, 95% CI 5.2-147.2, $p<0.001$), hyperopia $\geq$3.0D (OR 13.8, 95%CI 2.7-70.6, $p=0.002$), astigmatism $\geq$1.0D (OR 8.9, 95%CI 2.8-28.4, $p=0.009$), anisometropia $\geq$1.0D (OR 9.4, 95%CI 1.7-50.5, $p<0.001$) and strabismus (OR 14.5, 95% CI 2.2-96.8, $p=0.006$), after adjusting for age, gender, prematurity and socioeconomic status.

The prevalence of strabismus in young Singaporean Chinese children aged 6 to 72 months was 0.80% (95%CI 0.51-1.19), with an exotropia:esotropia ratio of 7:1. Prevalence of strabismus in Chinese children appears to be lower than that in Hispanic-Latin, African American and white children int eh MEPEDS, BEPEDS and SPEDS studies.

Strabismus was associated with prematurity, white ethnicity, maternal smoking, refractive error, family history of amblyopia/strabismus, paternal age, female

gender, interuterine growth retardation and admission to NICU in other studies. In young Singapore Chinese children, strabismus was only found to be associated with lower paternal education level with children whose father had secondary/'O' or 'A'/polytechnic/tertiary level education having an OR 0.07 (95%CI 0.01-0.58, p=0.01) and OR 0.23 (95%CI 0.06-0.89, p=0.03) respectively compared to children whose father had no/primary education, astigmatism ≥1.0D (OR 3.5, 95%CI 1.0-12.0, p=0.04), concurrent amblyopia (OR 15.9, 95%CI 2.7-92.8, p=0.002), a parent with history of strabismus (OR 17.9, 95%CI 1.1-278.3, p=0.04) and a sibling with history of strabismus (OR 38.3, 95%CI 8.7-168.5)

Steroeacuity was tested using the Randot Preschool Stereoacuity test (RPST) in children aged 30-72 months. Poor stereoacuity (200sec to none) was noted in 38.4% of children with amblyopia and 69.2% of children with strabismus. Good stereoacuity (40 to 60sec) was also recorded in 23.1% in each group.

ROC analysis suggested that the RPST was most effective in detection of anisometropia >2.0D (auc 0.84, 95%CI 0.72-0.55) and strabismus (auc 0.82, 95%CI 0.66-0.99), rather than amblyopia (auc 0.77, 95%CI 0.63-0.92). The PRST lacked the appropriate balance between sensitivity and specificity to act as a sole test for identification of children with amblyopia or strabismus.

Not surprising, since refractive error was used as a factor in the classification of amblyopia in this study, many autorefraction parameters were 'effective' in the

detection of amblyopia (eg. astigmatism (auc 0.88), anisometropia astigmatism (auc 0.82), myopia (auc 0.78) and anisometropia (auc 0.72). Autorefractive parameters were poor predictors of strabismus (auc 0.51-0.69).

There was no difference in PedsQL4 scores in young Singaporean children with and without amblyopia and strabismus in the STARS study. However, in the Childhood Development Survey, children with strabismus were found to have increased risk of speech (OR: 4.71, 95%CI 1.52-14.59, p=0.007) and comprehension (OR: 5.61, 95%CI 1.37-28.7, p=0.02) problems after adjustment for gender, age, socioeconomic statues and past admission of neonatal intensive care unit.Rasch analysis found misfit; reliability and validity issues with marked ceiling effect, suggesting that the PedsQL4 was a suboptimal scale with regards assessment of HRQOL in young Singaporean Chinese children with amblyopia and strabismus.

6.2. Future Directions

From the STARS study, the prevalence of amblyopia and strabismus in young Singaporean children was 1.19% (95%CI 0.73-1.83) and 0.80% (95%CI 0.51-1.19) respectively. In terms of burden of disease, this prevalence was low compared to the prevalence of conditions such as hypertension (≥140/90mmHg), diabetes, high cholesterol (≥6.2mmol/l), obesity (BMI ≥ 30kg/m2), and smoking

(≥ 1 cigarette per day) which affects 23.5%, 11.3%, 17.4%, 10.8% and 14.3% of Singaporeans aged 18-69 years (2010 data) (288).Given the current birth rate of 30-40,000 per year, our findings suggest that up to 300-400 babies born each year will develop amblyopia, strabismus or both. The challenge is to ensure that these ocular conditions maintain relevance in a general health screening program.

There are three important components of any health program; to screening if practical, treat when necessary and prevent when possible.

Currently the visual screening program in Singapore involves annual visual acuity assessment in children aged 4-16 years and cover-test, stereoacuity and colour vision tests at aged 6 years by trained personnel. This regime has proven effective in reducing prevalence of amblyopia in many populations. Given the potential effects of amblyopia on long-term vision, some form of screening is useful, especially if it also helps in the identification of uncorrected refractive error (eg. myopia). It may be important to know if the current program is indeed cost-effective, and if there are better, more effective screening models. Questions remain with regards what is the best practice; who to screen (which age-group), what screening tools to use (which is most sensitive and specific) and who should screen (a professional or lay-person). Other factors to consider is whether altering the current screening practices will improve yield, whether screening specifically for strabismus is needed, and whether there are adequate processes to ensure proper follow-up and treatment of children identified during screening. More

studies will be needed to better assess the pros and cons, and the cost-effectiveness of the current Singapore visual screening program.

Even if there is effective screening for amblyopia and strabismus in young children, there is still a question if screening and treatment does have a long-term effect on HRQOL with true physical, emotional and social benefits to the individual, their families and communities. Such HRQOL studies are very much in their infancy in Singapore. Results from the STARS study suggest that generic instruments such as the PedsQL4 are inadequate measures of HRQOL effects of amblyopia and strabismus in young Singaporean Chinese children. Further work needs to be done to determine which HRQOL instruments are more useful. These instruments need to be better validated and refined; or new, more precise and reliable instruments may even need to be developed to better quantify the HRQOL effects of amblyopia, strabismus and its treatment in the Singapore population.

Finally, detection and treatment aside, it is also important to consider if it was possible to prevent strabismus and amblyopia form occurring in the first place. Unfortunately, many of the risk associations of amblyopia and strabismus identified in this study (eg. refractive error and family history of amblyopia and strabismus) are not amendable to manipulation As STARS was not properly set up to identify risk associations, and as the number of cases of amblyopia and strabismus were small; a case-control study supplementing cases (from paediatric

ophthalmology clinics) may be a relatively cost-effective was to determine if more modifiable factors, such as prematurity and maternal smoking are or are not associated with amblyopia and strabismus in Chinese children.

Chapter 7: Reference:

1. Holmes JM, Clarke MP. Amblyopia. Lancet 2006; 367: 1343-51.

2. Carlton J, Karnon J, Czoski-Murray C, Smith KJ, Marr J. The clinical effective and cost-effectiveness of screening programs for amblyopia and strabismus in children up to the age of 4-5 years; a systemic review and economic evaluation. Health Technol Assess 2008; 12: 1-194.

2a. Holmes JM, Lazar EL, Melia BM, AStle WF, Dagi LR, Donahue SP, Frazeir MG, Hertle RW, Repka MX, Weise KK, PEDIG. Effect of age on response to amblyopia treatment in children. Arch Ophthalmol 2011; 129(11): 1451-7

3. Stewart CE, Moseley MJ, Fielder AR. Amblyopia therapy an update. Strabismus 2001; 19: 91-8.

4. Quinn GE, Beck RW, Holmes JM, Repka MX. Recent advances in the treatment of amblyopia. Pediatrics 2004; 113: 1800-1802

5. Holmes JM, Repka MX, Kraker RT, Clarke MP.The treatment of amblyopia.Strabismus.2006; 14: 37-42.

6. Multi-ethnic Pediatric Eye Disease Study Group. Prevalence of amblyopia and strabismus in African American and Hispanic children aged 6 to 72 months, Ophthalmology 2008; 115: 1229-1236.

7. Friedman DS, Repka MX, Katz J, Giordano L, Ibironke J, Hawse P, Tielsch JM. Prevalence of Amblyopia and Strabismus in White and African-American Children Aged 6 through 71 Months: The Baltimore Pediatric Eye Disease Study. Ophthalmology 2009; 116: 2128-34.

8. Pai AS, Rose KA, Leone JF, Sharbini S, Burlutsky G, Varma R, Wong TY, Mitchell P. Amblyopia prevalence and risk factors in Australian preschool children. Ophthalmology 2012; 119: 138-44.

9. http://www.merriam-webster.com/dictionary/amblyopia, 4 Oct 2012

10. Levi DM. Visual processing in amblyopia: human studies. Strabismus 2006; 14: 11-19.

11. Kanonidou E. Amblyopia: a mini review of the literature. Int Ophthalmol 2011; 31: 249-56.

12. Maurer D, Lewis TL. Visual and spatial contrast sensitivity: normal development and underlying mechanisms in *Sensory and sensorimotor systems*, 237-251.

13. Wiesel TN, Hubel DH. Effects of visual deprivation on morphology and physiology of cells in the cat's lateral geniculate body. J Neurophysiol 1963; 26: 978–993.

14. Hubel DH, Wiesel TN. Receptive fields of cells in striate cortex of very young, visually inexperienced kittens. J Neurophysiol 1963; 26: 994–1002.

15. Wiesel TN, Hubel DH.Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens.J Neurophysiol 1965; 28: 1029–1040.

16.Espinosa JS, Stryker MP. Development and plasticity of the primary visual cortex.Neuron.2012; 75: 230-49.

17. Moseley M, Fielder A, Stewart C. Compliance with amblyopia therapy. Arch Ophthalmol.2001; 119: 1226.

18. Quinn GE, Beck RW, Holmes JM, Repka MX; Pediatric Eye Disease Investigator Group. Recent advances in the treatment of amblyopia. Pediatrics.2004; 113: 1800-2.

19. Loudon WE, Simonsz HJ. The History of the Treatment of Amblyopia. Strabismus 2005; 13: 93-106.

20. Simons K. Amblyopia characterization, treatment, and prophylaxis. Surv Ophthalmol. 2005; 50: 123-66.

21. Atkinson J, Braddick O. Assessment of visual acuity in infancy and early childhood. Acta Ophthalmol 1983; 157: 18-26.

22: Thompson C, Drasdo N. Clinical experience with preferential looking acuity tests in infants and young children. Ophthalmic Physiol Opt 1988; 8: 309-21.

23 Mohn G, van Hof-van Duin J, Fetter WP, de Groot L, Hage M. Acuity assessment of non-verbal infants and children: clinical experience with the acuity card procedure. Dev Med Child Neurol 1988; 30: 232-44.

24. Vision in Preschoolers Study Group. Preschool visual acuity screening with HOTV and Lea symbols: testability and between-test agreement. Optom Vis Sci 2004; 81: 678-83.

25. Cotter SA, Tarczy-Hornoch K, Wang Y, Azen SP, Dilauro A, Borchert M, Varma R; Multi-Ethnic Pediatric Eye Disease Study Group. Visual acuity testability in African-American and Hispanic children: the multi-ethnic pediatric eye disease study. Am J Ophthalmol 2007; 144: 663-7.

26. Schmucker C, Grosselfinger R, Riemsma R, Antes G, Lange S, Lagrèze W, Kleijnen J. Diagnostic accuracy of vision screening tests for the detection of amblyopia and its risk factors: a systematic review. Graefes Arch Clin Exp Ophthalmol 2009; 247: 1441-54.

27. Trager MJ, Dirani M, Fan Q, Gazzard G, Selvaraj P, Chia A, Wong TY, Young TL, Varma R, Saw SM. Testability of vision and refraction in preschoolers: the strabismus, amblyopia, and refractive error study in singaporean children. Am J Ophthalmol 2009; 148: 235-241.

28. Chou R, Dana T, Bougatsos C. Screening for visual impairment in children ages 1-5 years: update for the USPSTF. Pediatrics 2011; 127: 442-79.

29. Leone JF, Gole GA, Mitchell P, Kifley A, Pai AS, Rose KA. Visual acuity testability and comparability in Australian preschool children: the Sydney Paediatric Eye Disease Study. Eye 2012; 26: 925-32.

30. Ellis GS Jr, Hartmann EE, Love A, May JG, Morgan KS. Teller acuity cards versus clinical judgment in the diagnosis of amblyopia with strabismus. Ophthalmology 1988; 95: 788-91.

31. Drover JR, Wyatt LM, Stager DR, Birch EE. The teller acuity cards are effective in detecting amblyopia. Optom Vis Sci 2009; 86: 755-9.

32. Drover JR, Morale SE, Wang YZ, Stager DR Sr, Birch EE. Vernier acuity cards: examination of development and screening validity. Optom Vis Sci 2010; 87: 806-12.

33. Hopkisson B, Clarke JR, Oelman BJ. Residual amblyopia in recruits to the British Army.Br Med J (Clin Res Ed).1982; 285: 940.

34. Quah BL, Tay MT, Chew SJ, Lee LK.A study of amblyopia in 18-19 year old males.Singapore Med J 1991; 32: 126-9.

35. Preslan NW, Novak AS. Baltimore visual screening Project.Ophthalmology 1996; 103:105-9.

36. Attebo K, Mitchell P, Cumming R, Smith W, Jolly N, Sparkes R. Prevalence and causes of amblyopia in an adult population. Ophthalmology 1998; 105: 154-9.

37. Ohlsson J, Villarreal G, Sjostrom A, Abrahamsson M, Sjostrand J. Visual acuity, residue amblyopia and ocular pathology in a screening population of 12-13-year-old children in Sweden. Acta Ophthalmol Scand 2001; 79: 589-85.

38. Ohlsson J, Villarreal G, Sjostrom A, Cavazos H, Abrahamsson M, Sjostrand J 2003. Visual acuity, amblyopia, and other ocular pathology in 12- to 13- year old children in Northern Mexico. JAPPOS 2003; 7: 47-53.

39. He M, Zeng J, LiuY, Xu J, Pokbarel GP, Ellwein LB. Refractive error and visual impairment in urban children in Southern China. Invest Ophthalmol Vis Sci 2004; 45: 793-99.

40. Lim HT, Yu YS, Park SH, Ahn H, Kim S, Lee M, Jeong JY, Shin KH. Koo BS. The Seoul Metropolitan Preschool vision screening programs: result for South Korea. Br J Ophthamol 2004; 88: 929-33.

41. Goh PP, Abqariyah Y, Pokharel GP, Ellwin LB. Refractive error and visual impairment in school-aged children in Gombak District, Malaysia. Ophthalmology 2005; 112: 678-85.

42. Rosman M, Wong TY, Koh CLK, Tan DTH. Prevalence and causes of amblyopia in a population-based study of young adult men in Singapore. Am J Ophthalmol 2005; 140: 551-2

43. Donnelly UM, Stewart NM & Hollinger M. Prevalence and outcomes of childhood visual disorders, Ophthalmic Epidemiol 2005; 12: 243-50.

44. Robaei D, Rose KA, Ojaimi E, Kifley A. Martin FJ & Mitchell P. Causes and associations of amblyopia in a population-based sample of 6-year-old Australian children, Arch Ophthalmol 2006; 124: 878-84.

45. Lu P, Chen X, Zhang W, Chen S & Shu L. Prevalence of ocular disease in Tibetan primary school children, Can J Ophthalmol 2008; 43: 95-9.

46. Robaei D, Kifley A, Rose KA & Mitchell P. Impact of amblyopia on vision at age 12 years: findings from a population-based study, Eye 2008; 22: 496-502.

47. Williams C, Northstone K, Howard M, Harvey I, Harrad RA & Sparrow JM. Prevalence and risk factors for common visual problems in children: data from the ALSPAC study, Br J Ophthalmol 2008; 92: 959-64.

48. Yekta A, Fotouhi A, Hashemi H, Dehghani C, Ostadimoghaddam H, Heravian J, Derakhshan A, Yekta R, Rezvan F, Behnia M, Khabazkhoob M.The prevalence of anisometropia, amblyopia and strabismus in schoolchildren of Shiraz, Iran. Strabismus 2010; 18: 104-10.

49. Fan SP, Lai C, Lau HHW, Cheung EYY, Lam DSC. Change in vision disorders among Hong Kong preschoolers in 10 year. Clinical and Experimental Ophthalmol 2011; 39: 398-403.

50. Wang Y, Liang YB, Sun LP, Duan XR, Yuan RZ, Wong TY, Yi P, Friedman DS, Wang NL, Wang JJ. Prevalence and causes of amblyopia in a rural adult population of Chinese: the Handan Eye Study. Ophthalmology 2011; 118: 279-83.

51.Faghihi M, Ostadimoghaddam H, Yekta AA. Amblyopia and strabismus in Iranian schoolchildren, Mashhad. Strabismus 2011; 19: 147-52.

52. Zvarnstrom G, Jakobsson P, Lennerstrand G. Visual screening of Swedish children: an ophthalmological evaluation. Acta Ophthalmol Scand 2001; 79 :240-244.

53. Matsuo T, Matsuo C, Matsuoka H, Kio K. Detection of Strabismus and amblyopia in 1.5- and 3-year-old children by a preschool vision screening program in Japan. Acta Med Okayama 2007; 61: 9-16.

54. Matsuo T, Matsuo O. The prevalence of strabismus and amblyopia in Japanese elementary school children. Ophthalmic Epidemiol 2005; 12: 31-6.

55. Lai YH, Hsu HT, Wang HZ, Chang SJ, Wu WC. The visual status of children ages 3 to 6 years in the vision screening program in Taiwan. J AAPOS.2009; 13: 58-62.

56. Pi LH, Chen L, Liu Q, Ke N, Fang J, Zhang S, Xiao J, Ye WJ, Xiong Y, Shi H,Zhou XY, Yin ZQ. Prevalence of eye diseases and causes of visual impairment in school-aged children in Western China.J Epidemiol.2012; 22: 37-44.

57. Brown SA, Weih LM, Fu CL, Dimitrov P, Taylor HR, McCarty CA. Prevalence of amblyopia and associated refractive errors in an adult population in Victoria, Australia. Ophthalmic Epidemiol.2000; 7: 249-58.

58. Powell C, Hatt SR. Vision screening for amblyopia in childhood. Cochrane Database Syst Rev. 2009; 8: CD005020. doi: 10.1002/14651858.CD005020.pub3

59. Beck RW. Clinical research in pediatric ophthalmology: the Pediatric Eye Disease Investigator Group. Curr Opin Ophthalmol.2002; 13: 337-40.

60. Xiao X, Liu WM, Zhao WX, Wang Y, Zhang YJ. [Prevalence of astigmatism in 2023 children with amblyopia].Zhongguo Dang Dai Er Ke Za Zhi.2011; 13: 462-5.

61. Chang CH, Tsai RK, Sheu MM. Screening amblyopia of preschool children with uncorrected vision and stereopsis tests in Eastern Taiwan. Eye 2007; 21: 1482-88

62. Donahue SP, Arnold RW, Ruben JB. Preschool vision screening: What should we be detecting and how should we report it? Uniform guidelines for reporting of results of preschool vision screening studies. J AAPOS 2003; 7: 314-5.

63. Lindqvist S, Vik T, Indredavik MS, Skranes J, Brubakk AM. Eye movements and binocular function in low birthweight teenagers. Acta Ophthalmol 2008; 86: 265-74.

64. Lindqvist S, Vik T, Indredavik MS, Brubakk AM. Visual acuity, contrast sensitivity, peripheral vision and refraction in low birthweight teenagers. Acta Ophthalmol Scand 2007; 85: 157-64.

65. O'Connor AR, Stephenson TJ, Johnson A, Tobin MJ, Ratib S, Fielder AR. Strabismus in children of birth weight less than 1701g. Arch Ophthalmol 2002; 120: 767-73.

66. Repka MX. Ophthalmological problems of the premature infant.Ment Retard Dev Disabil Res Rev 2002; 8: 249-57.

67. Schalij-Delfos NE, de Graaf ME, Treffers WF, Engel J, Cats BP. Long term follow up of premature infants: detection of strabismus, amblyopia, and refractive errors. Br J Ophthalmol.2000; 84: 963-7.

68. http://www.merriam-webster.com/dictionary/strabismus, 4 Oct 2012

69. MacEwen C & Gregson R (2003). Manual of Strabismus surgery. Butterworth Hwinemann. Great Britain.

70. Sondhi N, Archer SM, Helveston EM. Development of normal ocular alignment.J Pediatr Ophthalmol Strabismus 1988; 25: 210-1.

71. Archer SM, Sondhi N, Helveston EM. Strabismus in infancy.Ophthalmology 1989; 96: 133-7.

72. Thorn F, Gwiazda J, Cruz AA, Bauer JA, Held R. The development of eye alignment, convergence, and sensory binocularity in young infants. Invest Ophthalmol Vis Sci 1994; 35: 544-53.

73. Braddick O. Binocularity in infancy. Eye (Lond) 1996; 10: 182-8.

74. Braddick OJ, Atkinson J. Some recent findings on the development of human binocularity: a review. Behav Brain Res 1983; 10: 141-50.

75. Banks MS, Aslin RN, Letson RD. Sensitive period for the development of human binocular vision. Science 1975; 190: 675-7.

76. Hohmann A, Creutzfeldt OD. Squint and the development of binocularity in humans.Nature 1975; 254: 613-4.

77. Day SH, Sami DA 2011, 'History, examination and further investigations' in Taylor D, Hoyt CS (eds), *Pediatric Ophthalmology and Strabismus*, 3rd Edition, Elsevier Saunders, China, p . 72-3.

78. Chew E, Remaley NA, Tamboli A, Zhao J, Podgor MJ, Klebanoff M. Risk factors for esotropia and exotropia. Arch Ophthalmol 1994; 112: 1349-1355.

79. Nepal BP, Koirala S, Adhikary S, Sharma AK. Ocular morbidity in schoolchildren in Kathmandu. Br J Ophthalmol 2003; 87: 531-4.

80. Robaei D, Rose KA, Kifley A, Cosstick M, Ip JM, Mitchell P. Factors associated with childhood strabismus: findings from a population-based study, Ophthalmology 2006; 113: 1146-53.

81. Robaei D, Kifley A & Mitchell. Factors associated with a previous diagnosis of strabismus in a population based sample of 12-year old Australian children, Am J Ophthalmol 2006; 142: 1085-8.

82. Yoon KC, Mun GH, Kim SD, Kim SH, Kim CY, Park KH, Park YJ, Baek SH, Song SJ, Shin JP, Yang SW, Yu SY, Lee JS, Lim KH, Park HJ, Pyo EY, Yang JE, Kim YT, Oh KW, Kang SW. Prevalence of eye diseases in South Korea: data from the Korea National Health and Nutrition Examination Survey 2008-2009. Korean J Ophthalmol 2011; 25: 421-33.

83. Garvey KA, Dobson V, Messer DH, Miller JM, Harvey EM. Prevalence of strabismus among preschool, kindergarten, and first-grade Tohono O'odham children. Optometry 2010; 81: 194-9.

84. Pathai S, Cumberland PM, Rahi JS. Prevalence of and early-life influences on childhood strabismus: findings from the Millennium Cohort Study. Arch Pediatr Adolesc Med 2010; 164: 250-7.

85. Greenberg AE, Mohney BG, Diehl NN, Burke JP. Incidence and types of childhood esotropia: a population-based study. Ophthalmology 2007; 114: 170-4.

86. Govindan M, Mohney BG, Diehl NN, Burke JP. Incidence and types of childhood exotropia: a population-based study. Ophthalmology 2005; 112: 104-8.

87. Chia A, Roy L & Seenyen L. Horizontal Comitant Strabismus in Singapore, British J Ophthal 2007; 91:1337-40.

88. VanderVeen DK, Bremer DL, Fellows RR, Hardy RJ, Neely DE, Palmer EA, Rogers DL, Tung B, Good WV; Early Treatment for Retinopathy of Prematurity

Cooperative Group. Prevalence and course of strabismus through age 6 years in participants of the Early Treatment for Retinopathy of Prematurity randomized trial. J AAPOS.2011; 15: 536-40.

89. Podgor MJ, Remaley NA, Chew E. Associations between siblings for esotropia and exotropia.Arch Ophthalmol 1996; 114: 739-44.

90. Torp-Pederson T, Boyd HA, Poulsen G, Haargaard B, Wohlfahrt J, Holmes JM, Melbye M. Perinatal risk factors for strabismus. Int J Epidemiology 2010; 39: 1229-39.

91. Cotter SA, Varma R, Tarczy-Hornoch K, McKean-Cowdin R, Lin J, Wen G, Wei J, Borchert M, Azen SP, Torres M, Tielsch JM, Friedman DS, Repka MX, Katz J, Ibironke J, Giordano L; Joint Writing Committee for the Multi-Ethnic Pediatric Eye Disease Study and the Baltimore Pediatric Eye Disease Study Groups. Risk factors associated with childhood strabismus: the multi-ethnic pediatric eye disease and Baltimore pediatric eye disease studies. Ophthalmology.2011; 118: 2251-61.

92. Hakim RB, Tielsch KM. Maternal cigarette smoking during pregnancy: a risk factor for childhood strabismus. Arch Ophthalmol 1992; 110: 1459-62.

93. Torp-Pederson T, Boyd HA, Poulsen G, Haargaard B, Wohlfarhrt J, Holmes JM, Melbye M. In-utero exposure to smoking, alcohol, coffee, and tea and risk of strabismus. Am J Epidemiology 2010; 171: 868-75.

94. Aurell E, Norrsell K. A longitudinal study of children with a family history of strabismus: factors determining the incidence of strabismus. Br J Ophthalmol 1990; 74: 589-594.

95. Ziakas NG, Woodruff G, Smith LK, Thompson JR. A study of heredity as a risk factor in strabismus. Eye 2002; 16: 519-21.

96. Matsuo T, Hayashi M, Fujiwara H, Yamane T, Ohtsuki H. Concordance of strabismic phenotypes in monozygotic versus multizygotic twins and other multiple births. Jpn J Ophthalmol 2002; 46: 59-64.

97. Michaelides M, Moore AT. The genetics of strabismus. J Med Genet 2004; 41: 641-646.

98. Wilner JB, Backus BT. Genetic and environmental contributions to strabismus and phorias: evidence from twins. Vision Research 2009; 49: 2485-2493.

99. Reinecke RD. Stereoacuity assessment in amblyopia. Trans Ophthalmol Soc U K 1979; 99: 398-400.

100. Manny RE, Martinez AT, Fern KD. Testing stereopsis in the preschool child: is it clinically useful? J Pediatr Ophthalmol Strabismus 1991; 28: 223-31.

101. Lee SY, Isenberg SJ. The relationship between stereopsis and visual acuity after occlusion therapy for amblyopia. Ophthalmology 2003; 110: 2088-92.

102. Richardson SR, Wright CM, Hrisos S, Buck D, Clarke MP. Stereoacuity in unilateral visual impairment detected at preschool screening: outcomes from a randomized controlled trial. Invest Ophthalmol Vis Sci 2005; 46: 150-4.

103. Robaei D, Huynh SC, Kifley A, Gole GA, Mitchell P. Stereoacuity and ocular associations at age 12 years: findings from a population-based study. J AAPOS 2007; 11: 356-61.

104. Dobson V, Miller JM, Clifford-Donaldson CE, Harvey EM. Associations between anisometropia, amblyopia, and reduced stereoacuity in a school-aged population with a high prevalence of astigmatism. Invest Ophthalmol Vis Sci 2008; 49: 4427-36.

105. Hatt SR, Mohney BG, Leske DA, Holmes JM. Variability of stereoacuity in intermittent exotropia. Am J Ophthalmol 2008; 145: 556-561.

106. Wallace DK, Pediatric Eye Disease Investigator Group. Stereoacuity in children with anisometropic amblyopia. JAAPOS 2011; 15: 455-61.

107. O'Connor AR, Birch EE, Anderson S, Draper H; FSOS Research Group. The functional significance of stereopsis. Invest Ophthalmol Vis Sci 2010; 51: 2019-23.

108. Romano PE, Romano JA, Puklin JE. Stereoacuity development in children with normal binocular single vision. Am J Ophthalmol 1975; 79: 966-71.

109. Fox R, Patterson R, Francis EL. Stereoacuity in young children. Invest Ophthalmol Vis Sci. 1986; 27: 598-600.

110. Ciner EB, Schanel-Klitsch E, Herzberg C. Stereoacuity development: 6 months to 5 years. A new tool for testing and screening.Optom Vis Sci. 1996; 73: 43-8.

111. Oduntan AO, Al-Ghamdi M, Al-Dosari H. Randot stereoacuity norms in a population of Saudi Arabian children. Clin Exp Optom 1998; 81: 193-197.

112. Birch EE, Morale SE, Jeffrey BG, O'Connor AR, Fawcett SL. Measurement of stereoacuity outcomes at ages 1 to 24 months: Randot Stereocards. J AAPOS 2005; 9: 31-6.

113. Fawcett SL, Wang YZ, Birch EE. The critical period for susceptibility of human stereopsis. Invest Ophthalmol Vis Sci 2005; 46: 521-5.

114. Birch E, Williams C, Drover J, Fu V, Cheng C, Northstone K, Courage M, Adams R. Randot Preschool Stereoacuity Test: normative data and validity. J AAPOS 2008; 12: 23-6.

115. Kulp MT, Mitchell GL. Randot stereoacuity testing in young children. J Pediatr Ophthalmol Strabismus 2005; 42: 360-4.

116. Adler P, Scally AJ, Barrett BT. Test--retest variability of Randot stereoacuity measures gathered in an unselected sample of UK primary school children. Br J Ophthalmol 2012; 96: 656-61.

117. Adams WE, Leske DA, Hatt SR, Holmes JM. Defining real change in measures of stereoacuity. Ophthalmology 2009; 116: 281-5.

118. Simons K. Stereoacuity norms in young children. Arch Ophthalmol.1981; 99: 439-45.

119. Simons K. A comparison of the Frisby, Random-Dot E, TNO, and Randot circles stereotests in screening and office use. Arch Ophthalmol 1981; 99: 446-52.

120. Lam SR, LaRoche GR, De Becker I, Macpherson H. The range and variability of ophthalmological parameters in normal children aged 4 1/2 to 5 1/2 years. J Pediatr Ophthalmol Strabismus 1996; 33: 251-6.

121. Birch E, Williams C, Hunter J, Lapa MC. Random dot stereoacuity of preschool children. ALSPAC "Children in Focus" Study Team.J Pediatr Ophthalmol Strabismus 1997; 34: 217-22.

122. Tarczy-Hornoch K, Lin J, Deneen J, Cotter SA, Azen SP, Borchert MS, Wang Y, Varma R; Multi-Ethnic Pediatric Eye Disease Study Group. Stereoacuity testability in African-American and Hispanic pre-school children.Optom Vis Sci. 2008; 85: 158-63.

123. Pai AS, Rose KA, Samarawickrama C, Fotedar R, Burlutsky G, Varma R, Mitchell P. Testability of refraction, stereopsis, and other ocular measures in preschool children: the Sydney Paediatric Eye Disease Study. J AAPOS.2012; 16: 185-92.

124. Schmidt PP, Maguire MG, Moore B, Cyert L; Vision in Preschoolers Study Group. Testability of preschoolers on stereotests used to screen vision disorders. Optom Vis Sci 2003; 80: 753-7.

125. Fawcett SL, Birch EE. Interobserver test-retest reliability of the Randot preschool stereoacuity test. J AAPOS 2000; 4: 354-8.

126. Schmidt PP. Sensitivity of random dot stereoacuity and Snellen acuity to optical blur. Optom Vis Sci 1994; 71: 466-71.

127. Oguz H, Oguz V. The effects of experimentally induced anisometropia on stereopsis. J Pediatr Ophthalmol Strabismus 2000; 37: 214-8.

128. Rutstein RP, Corliss DA. Distance stereopsis as a screening device. Optom Vis Sci 2000; 77: 135-9.

129. Birch EE, Wang J. Stereoacuity outcomes after treatment of infantile and accommodative esotropia. Optom Vis Sci. 2009; 86: 647-52.

130. Birch EE, Fawcett S, Stager DR. Why does early surgical alignment improve stereoacuity outcomes in infantile esotropia? J AAPOS.2000; 4: 10-4.

131. Birch EE, Stager DR Sr, Berry P, Leffler J. Stereopsis and long-term stability of alignment in esotropia. J AAPOS.2004; 8: 146-50.

132. Fawcett S, Leffler J, Birch EE. Factors influencing stereoacuity in accommodative esotropia.J AAPOS.2000; 4: 15-20.

133. Holmes JM, Birch EE, Leske DA, Fu VL, Mohney BG.New tests of distance stereoacuity and their role in evaluating intermittent exotropia.Ophthalmology.2007; 114: 1215-20.

134. Hatt SR, Haggerty H, Buck D, Adams W, Strong NP, Clarke MP. Distance stereoacuity in intermittent exotropia. Br J Ophthalmol.2007; 91: 219-21.

135. Schmidt P, Maguire M, Dobson V, Quinn G, Ciner E, Cyert L, Kulp MT, Moore B, Orel-Bixler D, Redford M, Ying GS, VIP study group. Comparison of preschool vision screening tests as administered by licensed eye care professionals in the Vision in Preschoolers Study. Ophthalmology 2004; 111: 637-50.

136. Ying GS, Kulp MT, Maguire M, Ciner E, Cyert L, Schmidt P, Vision in Preschooler Study Group. Sensitivity of screening tests for detecting vision in preschoolers-targeted vision disorders when specificity is 94%. Optom Vis Sci 2005; 82: 432-8.

137. VIP study group. Does assessing eye alignment along with refractive error or visual acuity increase sensitivity for detection of strabismus in preschool vision screening. Invest Ophthalmol Vis Sci 2007, 48: 3115-25.

138. Miller JM, Harvey EM, Dobson V. Visual acuity screening versus noncycloplegic autorefraction screening for astigmatism in Native American preschool children. JAAPOS 1999; 3: 160-9.

139. Kinge B, Midelfart A, Jacobsen G. Clinical evaluation of the Allergan Humphrey 500 autorefractor and the Nidek AR-1000 autorefractor. Br J Ophthalmol.1996; 80: 35-9.

140. Cordonnier M, Kallay O. Non-cycloplegic screening for refractive errors in children with the hand-held autorefractor Retinomax: final results and comparison with non-cycloplegic photoscreening. Strabismus.2001; 9: 59-70.

141. Liang CL, Hung KS, Park N, Chan P, Juo SH. Comparison of measurements of refractive errors between the hand-held Retinomax and on-table autorefractors in cyclopleged and noncyclopleged children. Am J Ophthalmol.2003; 136: 1120-8.

142. Iuorno JD, Grant WD, Noël LP. Clinical comparison of the Welch Allyn SureSight handheld autorefractor versus cycloplegic autorefraction and retinoscopic refraction.J AAPOS.2004; 8: 123-7.

143. Gwiazda J, Weber C. Comparison of spherical equivalent refraction and astigmatism measured with three different models of autorefractors. Optom Vis Sci. 2004; 81: 56-61.

144. Pesudovs K, Weisinger HS. A comparison of autorefractor performance.Optom Vis Sci. 2004; 81: 554-8.

145. Cordonnier M, De Maertelaer V. Comparison between two hand-held autorefractors: the Sure-Sight and the Retinomax. Strabismus.2004; 12: 261-74.

146. Farook M, Venkatramani J, Gazzard G, Cheng A, Tan D, Saw SM. Comparisons of the handheld autorefractor, table-mounted autorefractor, and subjective refraction in Singapore adults. Optom Vis Sci. 2005; 82: 1066-70.

147. Prabakaran S, Dirani M, Chia A, Gazzard G, Fan Q, Leo SW, Ling Y, Au Eong KG, Wong TY, Saw SM. Cycloplegic refraction in preschool children: comparisons between the hand-held autorefractor, table-mounted autorefractor and retinoscopy. Ophthalmic Physiol Opt. 2009; 29: 422-6.

148. Ying GS, Maguire M, Quinn G, Kulp MT, Cyert L, Vision in Preschoolers (VIP) Study Group. ROC analysis of the accuracy of nonscycloplegic retinoscopy, retinomax, autorefractor and SureSight Vision Screener for preschool vision screening. Invest Ophthalmol Vis Sci 2011; 52: 9658-64.

149. Paff T, Oudesluya-Murphy AM, Wolterbeck R, Swart-van den Berg M, de Nio JM, Tijssen E, Schalij-Delfos NE. Screening for refractive errors in children: the plusix S08 and the Retinomax K-plus2 performed by a lay screener compared to cycloplegic retinoscopy. JAAPOS 2010; 14: 478-83.

150. Zhao J, Mao J, Luo R, Li F, Pokharel GP, Ellwein LB. Accuracy of noncycloplegic autorefraction in school-age children in China. Optom Vis Sci.2004; 81: 49-55.

151. Choong YF, Chen AH, Goh PP.A comparison of autorefraction and subjective refraction with and without cycloplegia in primary school children.Am J Ophthalmol.2006; 142:68-74.

152. Steele G, Ireland D, Block S. Cycloplegic autorefarction results in pre-school using the Nikon Retinomax Plus and the Welch Allyn SureSight. Optom Vis Sci 2003; 80: 573-7.

153. Rowatt AJ, Donahue SP, Crosby C, Hudson AC, Simon S, Emmons K. Field evaluation of the Welch Allyn SureSight vision screener: incorporating the vision in preschoolers study recommendations. J AAPOS.2007; 11: 243-8.

154. Konig HH, Barry JC. Economic evaluation of different methods of screening for amblyopia in kindergarten. Pediatrics 2002l 109: e59.

155. Silverstein E, Lorenz S, Emmons K, Donanhue SP. Limits on improving the positive predictive value of the Welch Allyn SureSight for preschool vision screening. JAAPOS 2009, 13: 45-50.

156. Clarke SA, Eiser C. The measurement of health-related quality of life (QOL) in paediatric clinical trials: a systematic review. Health and Quality of life outcomes 2004; 2.66.

157. Tosh J, Brazier J, Evans P, Longworth L. A review of generic preference-based measures of health-related quality of life in visual disorders. http://dx.crossref.org/10.1016/j.jval.2011.08.002.

158. Massof RW, Rubin GS.Visual function assessment questionnaires. Surv Ophthalmol 2001; 45: 531-48.

159. Margolis MK, Coyne K, Kennedy-Martin T, Baker T, Schein O, Revicki DA. Vision-specific instruments for the assessment of health-related quality of life and visual functioning: a literature review. Pharmacoeconomics 2002; 20: 791-812.

160. Gothwal VK, Lovie-Kitchin JE, Nutbeti R. The development of the LV Prasad-Functional Vision Questionnaire: a measure of functional vision

performance in visually impaired children. Invest Ophthalmol Vis Sci 2003; 44: 4131-9.

161. Felius J, Stager DR, Berry PM, Fawcett SL, Stager DR Jr, Salomao SR, Berezovsky A, Birch E. Development of an instrument to assess vision-related quality of life in young children. Am J Ophthalmol 2004; 138: 362-72.

162. Khadka J, Ryan B, Margrain TH, Court H, Woodhouse JM. Development of the 25-item Cardiff Visual Ability Questionnaire for Children (CVAQC). Br J Ophthalmol 2010; 94: 730-5.

163. Cochrane GM, Marella M, Keeffe JE, Lamoureux EL. The Impact of vision impairment for children (IVI_C): validation of a vision-specific pediatric quality-of-life questionnaire using Rasch Analysis. Invest Ophthalmol Visc Sci 2011; 52: 1632-40.

164. Hatt SR, Leske DA, Bradley EA, Cole SR, Holmes JM. Development of a quality-of-life questionnaire for adults with strabismus.Ophthalmology.2009; 116: 139-144.

165. Hatt SR, Leske DA, Yamada T, Bradley EA, Cole SR, Holmes JM. Development and initial validation of quality of life questionnaires for intermittent exotropia. Ophthalmology 2010; 117: 163-8.

166. Carlton J, Kaltenthaler E. Health-related quality of life measures (HRQoL) in patients with amblyopia and strabismus: a systemic review. Br J Ophthalmol 2011; 95: 325-30.

167. Pediatric Eye Disease Investigator Group. Impact of patching and atropine treatment on the child and family in the amblyopia treatment study. Arch Ophthalmol 2003; 121: 1625-32.

168. Choong YF, Lukman H, Martin S, Laws DE. Childhood amblyopia treatment: psychosocial implications for patients and primary carers. Eye 2004; 18: 369-75.

169. Hrisos S, Clarke MP, Wright CM. The emotional impact of amblyopia treatment in preschool children. Ophthalmol 2004; 111: 1550-6.

170. Horwood J, Waylen A, Herrick D, Williams C, Wolke D, the Avon Longitudinal Study of Parents and Children Study Teams. Common visual defects and peer victimization in children. Invest Ophthalmol Vis Sci 2005; 46: 1177-1181.

171. Dixon-Woods M, Awan M, Gottlob I. Why is compliance with occlusive therapy for amblyopia so hard? A qualitative study. Arch Dis Childr 2006; 91: 491-4.

172. Koklanis K, Abel LA, Aroni R. Psychosocial impact of amblyopia and its treatment: a multidisciplinary study. Clin Experiment Ophthalmol 2006; 34: 74

173. Lazarczyk-Kirejczyk J, Szulc A, Bakunowicz-Łazarczyk A. [The psychological consequences of amblyopia]. Klin Oczna. 2010; 112: 82-4.

174. Carlton J, Kaltenthaler E. Amblyopia and quality of life: a systemic review. Eye 2011; 25: 403-13.

175. Yamada T, Hatt SR, Leske DA, Holmes JM. Spectacle wear in children reduces parental health-related quality of life. JAPPOS 2011; 15: 24-8.

176. Webber AL, Wood JM, Gole GA, Brown B. The effect of amblyopia on fine motor skills in children. Invest Ophthalmol Vis Sci. 2008; 49: 594-603.

177. Grant S, Moseley MJ. Amblyopia and real-world visuomotor tasks. Strabismus 2011 ;19: 119-28.

178. Suttle CM, Melmoth DR, Finlay AL, Sloper JJ, Grant S. Eye-hand coordination skills in children with and without amblyopia. Invest Ophthalmol Vis Sci 2011; 52: 1851-64.

179. Sabri K, Knapp CM, Thompson JR, Gottlob I. The VF-14 and psychological impact of amblyopia and strabismus. Invest Ophthalmol Vis Sci 2006; 47: 4386-92.

180. van de Graaf ES, van der Sterre GW, Polling JR, van Kempen H, Simonsz B, Simonsz HJ. Amblyopia & Strabismus Questionnaire: design and initial validation. Strabismus.2004; 12: 181-93.

181. Felius J, Beauchamp GR, Stager DR Sr, Van De Graaf ES, Simonsz HJ. The Amblyopia and Strabismus Questionnaire: English translation, validation, and subscales. Am J Ophthalmol.2007; 143: 305-310.

182. van de Graaf ES, van der Sterre GW, van Kempen-du Saar H, Simonsz B, Looman CW, Simonsz HJ. Amblyopia and Strabismus Questionnaire (A&SQ): clinical validation in a historic cohort. Graefes Arch Clin Exp Ophthalmol.2007; 245: 1589-95.

183. van de Graaf ES, van Kempen-du Saar H, Looman CW, Simonsz HJ.Utility analysis of disability caused by amblyopia and/or strabismus in a population-based, historic cohort.Graefes Arch Clin Exp Ophthalmol 2010; 248: 1803-7.

184. Rahi JS, Cumberland PM, Peckahm CS. Does amblyopia affect education, health and social outcomes? Findings from the 1958 British birth cohort.BMJ 2006, dol:10.1136/bmj.38751.597963.

185. Chua B, Mitchell P. Consequences of amblyopia on education, occupation and long term vision loss. Br J Ophthalmol 2004; 88: 1119-21.

186. Wilson GA, Welch D. Does amblyopia have a functional impact? Findings from the Dunedin Multidisciplinary Health and Development Study. Clin Experiment Ophthalmol 2012 Jun 19. doi: 10.1111/j.1442-9071.2012.02842.x.

187. Satterfield D, Keltner JL, Morrison TL. Psychosocial aspects of strabismus study. Arch Ophthalmol 1993; 111: 1100-5.

188. Olitsky SE, Sudesh S, Graziano A, Hamblen J, Brooks SE, Shaha SH. The negative psychosocial impact of strabismus in adults.J AAPO.1999; 3: 209-11.

189. Paysse EA, Steele EA, McCreery KM, Wilhelmus KR, Coats DK. Age of the emergence of negative attitudes toward strabismus. JAAPOS 2001; 5: 361-6.

190. Menon V, Saha J, Tandon R, Mehta M, Khokhar S. Study of the psychosocial aspects of strabismus. J Pediatr Ophthalmol Strabismus 2002; 39: 203-8.

191. Johns HA, Manny RE, Fern KD, Hu YS. The effect of strabismus on a young child's selection of a playmate. Ophthalmic Physiol Opt 2005; 25: 400-7.

192. Archer SM, Musch DC, Wren PA, Guire KE, del Monte MA. Social and emotional impact of strabismus surgery on quality of life in children. J APPOS 2005; 8: 148-51.

193. Hatt SR, Leske DA, Kirgis PA, Bradley EA, Holmes JM. The effects of strabismus on quality of life in adults. Am J Ophthalmol 2007; 144: 643-7.

194. Mckenzie JA, Capo JA, Nusz KJ, Dieh NN, Mohney BG. Prevalence and sex difference of psychiatric disorderes in young adults who had IXT as children. Arch Ophthalmol 2009: 127: 743-7.

195. Kothari M, Balankhe S, Gawade R, Toshnival S. Comparison of psychosocial and emotional consequences of childhood strabismus on the families from rural and urban India. Indian J Ophthalmol 2009; 57: 285–288.

196. Chua Y, Shao Y, Lin S, Xiong KY, Chen WS, Li YY, Yi JL, Zhang L, Tan G, Tang J. Vision-related quality of life and emotional impact in children with strabismus: a prospective study. J Int Med Res 2009; 37: 1108-14.

197. Lukman H, Kiat JE, Ganesan A, Chua WL, Khor KL, Choong YF. Strabismus-related prejudice in 5-6-year-old children. Br J Ophthalmol 2010; 94: 1348-51.

198. Durnian JM, Owen ME, Baddon AC, Noonan CP, Marsh IB. The psychosocial effects of strabismus: effect of patient demographics on the AS-20 score. J AAPOS 2010; 14: 469-71.

199. Durnian JM, Noonan CP, Marsh IB. The psychosocial effects of adult strabismus: a review. Br J Ophthalmol 2011; 95: 450-3.

200. Mojon-Azzi SM, Kunz A, Mojon DS. Strabismus and discrimination in children: are children with strabismus invited to fewer birthday parties? Br J Ophthalmol 2011; 95: 473-6.

201. Anderson HA, Manny RE, Fern KD. Prejudice to strabismus in young children. Br J Ophthalmol 2011; 95: 751.

202. Akay AP, Cakaloz B, Berk AT, Pasa E. Psychosocial aspects of mothers of children with strabismus. J AAPOS 2005; 9: 268-73.

203. Beauchamp CL, Beauchamp GR, Stager DR, Brown MM, Brown GC, Felius JF. The cost utility of strabismus surgery in adults. JAPPOS 2006; 10: 194-9.

204. Jackson S, Harrad RA, Morris M, Rumsey N. The psychosocial benefits of corrective surgery for adults with strabismus. Br J Ophthalmol 2006; 90: 883-8.

205. Nelson BA, Gunton KB, Judith NL, Nelson LB, Drohan LA. The psychological aspects of strabismus in teenagers and adults and the impact of surgical correction. JAPPOS 2008; 12: 72-6.

206. Chai Y, Shao Y, Lin S, Xiong KY, Chen WS, Li YY, Yi JL, Zhang L, Tan G, Tang J. Vision-related quality of life and emotional impact in children with strabismus: a prospective study. J Int Med Res. 2009; 37: 1108-14.

207. Merrill K, Satterfield D, O'Hara M. Strabismus surgery on the elderly and the effects on disability. J AAPOS.2010; 14: 196-8.

208. Hatt SR, Leske DA, Bradley EA, Cole SR, Holmes JM. Comparison of quality-of-life instruments in adults with strabismus.Am J Ophthalmol.2009; 148: 558-62.

209. Hatt SR, Leske DA, Holmes JM. Comparison of quality-of-life instruments in childhood intermittent exotropia.J AAPOS.2010; 14: 221-6.

210. Wen G, McKean-Cowdin R, Varma R, Tarczy-Hornoch K, Cotter SA, Borchert M, Azen S; Multi-ethnic Pediatric Eye Disease Study Group. General health-related quality of life in preschool children with strabismus or amblyopia. Ophthalmology 2011; 118: 574-80.

211. Varma R, Deneen J, Cotter S, Paz SH, Azen SP, Tracy-Hornoch K, Zhao P.The multiethnic pediatric eye disease study: design and methods. Ophthalmic Epidemiol 2006; 13: 253-62.

212. Friedman DS, Repka MX, Katz J, Giiordano L, Ibironke J, Hawes P, Burkom D, Tielsch JM. Prevalence of Decreased visual acuity among Preschool Aged children in an American Urban population: the Baltimore Pediatric Eye Disease Study, Methods and Results. Ophthalmology 2008; 115: 1786-95.

213. Leow BG. Singapore: Census of Population 2000. Department of Statistics, Singapore 2001.

214. Lamoureux E, Pesudovs K. Vision-specific quality-of-life research: a need to improve the quality. Am J Ophthalmol 2011; 151: 195-7.

215. Linacre JM. WINSTEPS Rasch measurement computer program. Chicago: Winsteps.com; 2008.

216. Dirani M, Zhou B, Hornbeak D, Chang BC, Gazzard G, Chia A, Ling Y, Selvaraj P, Young TL, Varma R, Wong TY, Saw SM. Prevalence and causes of decreased visual acuity in Singaporean Chinese preschoolers.Br J Ophthalmol 2010; 94: 1561-5.

217. Dirani M, Chan YH, Gazzard G, Hornbeak DM, Leo SW, Selvaraj P, Zhou B, Young TL, Mitchell P, Varma R, Wong TY, Saw SM. Prevalence of refractive error in Singaporean Chinese children: the strabismus, amblyopia, and refractive error in young Singaporean Children (STARS) study. Invest Ophthalmol Vis Sci 2010; 51: 1348-55.

218. Chia A, Dirani M, Chan YH, Gazzard G, Au Eong KG, Selvaraj P, Ling Y, Quah BL,Young TL, Mitchell P, Varma R, Wong TY, Saw SM. Prevalence of amblyopia and strabismus in young singaporean chinese children. Invest Ophthalmol Vis Sci 2010; 51: 3411-7.

219. Arnold RW 2009. Amblyopia and strabismus prevalence (letter). Ophthalmology 2009; 116: 365-6

220. Chia A, Seenyen L, Quah BL. A retrospective review of 287 consecutive children presenting with Intermittent Exotropia in Singapore. J APPOS 2005; 9: 257-63.

221. Yu CB, Fan DS, Wong VM, et al. Changing patterns of strabismus: a decade of experience in Hong Kong. Br J Ophthalmol 2002; 86: 854-6.

222. Matsuo T, Matsuo C. Comparison of prevalence rates of strabismus and amblyopiain Japanese elementary school children between the years 2003 and 2005. Acta Med Okayama.2007; 61: 329-34.

223. Eibschitz-Tsimhoni M, Friedman T, Naor J, Eibschitz N, Friedman Z. Early screening for amblyopic risk factors lowers the prevalence and severity of amblyopia. JAAPOS 2000; 4:194-9.

224. Vinding T, Gregersen E, Jensen A, Rindziunski E. Prevalence of amblyopia in old people without previous screening and treatment.An evaluation of the present prophylactic procedures among children in Denmark. Acta Ophthalmol (Copenh).1991; 69: 796-8.

225. Commonwealth of Australia. National Children Vision Screening project: discussion paper. Oct 2008; http://ww2.rch.org.au/emplibrary/ccch/DiscussPaper_ VisionScreeningProject.pdf

226. C Green Health Info. A review of the science underlying preschool vision screening with implications for BC (Nov 2005); http://www.health.gov.bc.ca/library/publications/year/2005/ Final-PreschoolVisionOct31.pdf viewed 31st Oct 2012

227. The UK NSC policy on Visual defect screening in children; http://www.screening.nhs.uk viewed 31st Oct 2012.

228. Substitute House Bill 1951. Visual Screening of Children in Pubic Schools – Final Report (December 2006), Washington State Department of Health; http://sboh.wa.gov/Rules/doc/SHB 1951-VisualScreeningReport-2005.pdf viewed 31st Oct 2012.

229. Committee on Practice and Ambulatory Medicine, Section on Ophthalmology. Eye examination and vision screening in infants, children, and young adults. Pediatrics 2006; 98: 153-7.

230. Institute for Quality and Efficiency in Health Care: Executive Summaries [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2005-. Available from http://www.ncbi.nlm.nih.gov/books/NBK84153/

231. JAMA evidence: User's guide to the medical literature. Second edition. Guyatt G, Rennie D, Meade MO, Cook DJ (ed). McGraw Hill Medical. 2002.

232. Mash C, Dobson V. Long-term reliability and predictive validity of the Teller Acuity Card procedure. Vision Res. 1998; 38: 619-26.

233. Kushner BJ, Lucchese NJ, Morton GV. Grating visual acuity with Teller cards compared with Snellen visual acuity in literate patients. Arch Ophthalmol.1995; 113: 485-93.

234. Sharma P, Bairagi D, Sachdeva MM, Kaur K, Khokhar S, Saxena R. Comparative evaluation of Teller and Cardiff acuity tests in normals and unilateral amblyopes in under-two-year-olds. Indian J Ophthalmol.2003; 51: 341-5.

235. Spierer A, Royzman Z, Chetrit A, Novikov I, Barkay A. Vision screening of preverbal children with Teller acuity cards. Ophthalmology.1999; 106: 849-54.

236. Dobson V, Quinn GE, Siatkowski RM, Baker JD, Hardy RJ, Reynolds JD, Trese MT, Tung B. Agreement between grating acuity at age 1 year and Snellen acuity at age 5.5 years in the preterm child. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Invest Ophthalmol Vis Sci. 1999; 40: 496-503.

237. Schmucker C, Grosselfinger R, Riemsma R, Antes G, Lange S, Lagrèze W, Kleijnen J. Effectiveness of screening preschool children for amblyopia: a systematic review. BMC Ophthalmol.2009; 16; 9: 3.

238. Cyert L, Schmidt P, Maguire M, Moore B, Dobson V, Quinn G; Vision in Preschoolers (VIP) Study Group. Threshold visual acuity testing of preschool children using the crowded HOTV and Lea Symbols acuity tests.J AAPOS.2003; 7: 396-9.

239. Lagrèze WA. Vision screening in preschool children: do the data support universal screening? Dtsch Arztebl Int. 2010; 107: 495-9.

240. Schlenker MB, Christakis TJ, Braga-Mele RM. Comparing a traditional single optotype visual acuity test with a computer-based visual acuity test for childhood amblyopia vision screening: a pilot study. Can J Ophthalmol. 2010; 45: 368-74.

241. Omar R, Hussin DA, Knight VF. Comparison of Lea Symbols chart and Sheridan Gardiner chart in assessing vision screening among pre-school children: a Malaysia perspective. J Med Assoc Thai.2012; 95: 412-7.

242. Maguire MG; Vision in Preschoolers Study Group. Children unable to perform screening tests in vision in preschoolers study: proportion with ocular conditions and impact on measures of test accuracy. Invest Ophthalmol Vis Sci. 2007; 48: 83-7.

243. Vision in Preschoolers (VIP) Study Group. Effect of age using Lea Symbols or HOTV for preschool vision screening. Optom Vis Sci. 2010; 87: 87-95

244. Tjiam AM, Groenewoud JH, Passchier J, Loudon SE, De Graaf M, Hoogeveen WC, Lantau VK, Juttmann RE, De Koning HJ, Simonsz HJ. Determinants and outcome of unsuccessful referral after positive screening in a large birth-cohort study of population-based vision screening. J AAPOS.2011; 15: 256-62.

245. Anstice N, Spink J, Abdul-Rahman A. Review of preschool vision screening referrals in South Auckland, New Zealand. Clin Exp Optom. 2012; 95: 442-8.

246. Mema SC, McIntyre L, Musto R. Childhood vision screening in Canada: public health evidence and practice. Can J Public Health. 2012; 103: 40-5.

247. Newman DK, Hitchcock A, McCarthy H, Keast-Butler J, Moore AT. Preschool vision screening: outcome of children referred to the hospital eye service. Br J Ophthalmol 1996; 80: 1077-1082.

248. Newman DK, East MM. Preschool vision screening: a negative predictive value for amblyopia. Dr J Ophthalmol 1999; 83: 676-9.

249. Kennedy RA, Sheps SB. A comparison of photoscreening techniques for amblyogenic factors in children. Can J Ophthalmol. 1989; 24: 259-64.

250. Harvey EM, Miller JM, Wagner LK, Dobson V. Reproducibility and accuracy of measurements with a hand held autorefractor in children. Br J Ophthalmol.1997; 81: 941-8.

251. Hatch S, Tibbles CD, Mestito IR, Read R, Traveis L, Richman J. Validity and reliability of the MTI photoscreener. Optom Vis Sci. 1997; 74: 859-64.

252. Weinand F, Gräf M, Demming K. Sensitivity of the MTI photoscreener for amblyogenic factors in infancy and early childhood. Graefes Arch Clin Exp Ophthalmol.1998 ; 236: 801-5.

253. Cordonnier M, Dramaix M. Screening for refractive errors in children: accuracy of the hand held refractor Retinomax to screen for astigmatism. Br J Ophthalmol.1999; 83: 157-61.

254. Simons BD, Siatkowski RM, Schiffman JC, Berry BE, Flynn JT. Pediatric photoscreening for strabismus and refractive errors in a high-risk population. Ophthalmology.1999; 106: 1073-80.

255. Tong PY, Bassin RE, Enke-Miyazaki E, Macke JP, Tielsch JM, Stager DR Sr, Beauchamp GR, Parks MM. Screening for amblyopia in preverbal children with photoscreening photographs: II. Sensitivity and specificity of the MTI photoscreener.Ophthalmology.2000; 107: 1623-9.

256. Donahue SP, Johnson TM, Leonard-Martin TC. Screening for amblyogenic factors using a volunteer lay network and the MTI photoscreener. Initial results from 15,000 preschool children in a statewide effort.Ophthalmology.2000; 107: 1637-44.

257. Berry BE, Simons BD, Siatkowski RM, Schiffman JC, Flynn JT, Duthie MJ. Preschool vision screening using the MTI-Photoscreener. Pediatr Nurs. 2001; 27: 27-34.

258. Paysse EA, Williams GC, Coats DK, Williams EA. Detection of red reflex asymmetry by pediatric residents using the Brückner reflex versus the MTI photoscreener.Pediatrics. 2001; 108: E74.

259. Enzenauer RW. The efficacy of photoscreening for amblyopiagenic factors in a high risk population. Binocul Vis Strabismus Q. 2003; 18: 233-40.

260. Kemper AR, Keating LM, Jackson JL, Levin EM. Comparison of monocular autorefraction to comprehensive eye examination in preschool –aged and younger children. Arch Pediatr Adolesc Med 2005; 19: 435-9.

261. Kim AH, Chen J, Ottar-Pfeifer W, Lengauer B, Holgado S, Stager DR Sr, Parks MM, Beauchamp GR, Scott W, Marsh MJ, Tong PY. Screening for amblyopia in preverbal children with photoscreening photographs: IV. Interobserver variability in photograph grading: origin and method of reduction. Binocul Vis Strabismus Q 2005; 20: 71-80.

262. Salcido AA, Bradley J, Donahue SP. Predictive value of photoscreening and traditional screening of preschool children. J AAPOS.2005; 9: 114-20.

263. Vision in Preschoolers Study Group. Does assessing eye alignment along with refractive error or visual acuity increase sensitivity for detection of strabismus in preschool vision screening? Invest Ophthalmol Vis Sci. 2007; 48: 3115-25.

264. Rogers DL, Neely DE, Chapman JB, Plager DA, Sprunger DT, Sondhi N, Roberts GJ, Ofner S. Comparison of the MTI Photoscreener and the Welch-Allyn SureSight autorefractor in a tertiary care center. J AAPOS.2008; 12: 77-82.

265. Matta NS, Singman EL, Silbert DI. Performance of the Plusoptix vision screener for the detection of amblyopia risk factors in children.J AAPOS.2008; 12: 490-2.

266. Kulp MT; Vision in Preschoolers Study Group. Findings from the Vision in Preschoolers (VIP) Study. Optom Vis Sci. 2009; 86: 619-23.

267. von Noorden GK. Stereoacuity testing does not replace visual acuity testing. Arch Ophthalmol 1986; 104: 1112-3.

268. Side effects of cyclopentolate. http://www.medicinenet.com/ cyclopentoloate_hydrochloride-eye_drop/article.htm, viewed November 2012

269. Williamson TH, Andrews R, Dutton GN, Murray G, Graham N. Assessment of an inner city visual screening program for preschool children. Br J Ophthalmol 1995; 79: 1068-73.

270. Tananuvat N, Manassakorn A, Worapong A, Kupat J, Chuwuttayakorn J & Wattananikorn S. Vision screening in schoolchildren: two years result. J Med Assoc Thai 2004; 87: 679-84.

271. Cools G, Houtman AC, Spileers W, Van Kerschaver E, Casteels I. Literature review on preschool vision screening. Bull Soc Belge Ophtalmol. 2009; 313: 49-63.

272. Groenewoud JH, Tjiam AM, Lantau VK, Hoogeveen WC, de Faber JT, Juttmann RE, de Koning HJ, Simonsz HJ. Rotterdam Amblyopia screening effectiveness study: detection and causes of amblyopia in a large birth cohort. Invest Ophthalmol Vis Sci. 2010; 51: 3476-84.

273. Mathers M, Keyes M, Wright M. A review of the evidence on the effectiveness of children's vision screening.Child Care Health Dev. 2010; 36: 756-80.

274. Chou R, Dana T, Bougatsos C. Screening for Visual Impairment in Children Ages 1-5 Years: Systematic Review to Update the 2004 U.S. Preventive Services Task Force Recommendation [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2011 Feb. Available from http://www.ncbi.nlm.nih. gov/books/NBK52708/

275. Hu VH, Starling A, Baynham SN, Wager H, Shun-Shin GA. Accuracy of referrals from an orthoptic vision screening program for 3- to 4-year-old preschool children. J AAPOS.2012; 16: 49-52.

276. Rein DB, Wittenborn JS, Zhang X, Song M, Saaddine JB; the Vision Cost-effectiveness Study Group. The Potential Cost-Effectiveness of Amblyopia Screening Programs.J Pediatr Ophthalmol Strabismus.2012; 49: 146-155.

277. Simmers AJ, Gray LS, Spowart K. Screening for amblyopia: a comparison of paediatric letter tests. Br J Ophthalol 1997; 81: 465-69.

278. Membreno JH, Brown MM, Brown GC, Sharma S, Beauchamp GR. A cost-utility analysis of therapy for amblyopia. Ophthalmolgo 2002; 109: 2265-71.

279. Konig HH, Barry JC. Cost effectiveness of treatment for amblyopia: an analysis based on a probabilistic Markov model. Br J Ophthalmol 2004; 88: 606-12.

280. Fujiike K, Mizuno Y, Hiratsuka Y, Yamada M; the strabismus surgery study group. Quality of life and cost-utility assessment after strabismus surgery in adults. Jpn J Ophthalmol 2011; 55: 268-76.

281. Hatt SR, Leske DA, Holmes JM. Awareness of exodeviation in children with intermittent exotropia.Strabismus.2009; 17: 101-6.

282. Hatt SR, Leske DA, Holmes JM. Responsiveness of health-related quality-of-life questionnaires in adults undergoing Strabismus surgery.Ophthalmology.2010; 117: 2322-2328.

283. Carlton J. Clinician's perspectives of health related quality of life (HRQoL) implications of amblyopia: a qualitative study. Br Ir Orthopt J 2011; 8: 18-23.

284. Jozefiak T, Larsson B, Wichstrøm L, Mattejat F, Ravens-Sieberer U. Quality of Life as reported by school children and their parents: a cross-sectional survey. Health Qual Life Outcomes. 2008 May 19;6:34. doi: 10.1186/1477-7525-6-34.

285. Cremeens J, Eiser C, Blades M. Factors influencing agreement between child self-report and parent proxy-reports on the Pediatric Quality of Life Inventory 4.0 (PedsQL) generic core scales. Health Qual Life Outcomes. 2006; 4: 58

286. Upton P, Lawford J, Eiser C. Parent-child agreement across child health-related quality of life instruments: a review of the literature. Qual Life Res 2008; 17: 895-913.

287. Davis E, Shelly A, Waters E, Davern M. Measuring the quality of life of children with cerebral palsy: comparing the conceptual differences and psychometric properties of three instruments. Dev Med Child Neurol. 2010; 52: 174-80.

288. Ministry of Health, Singapore. Disease burden (2010) at http://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_ Singapore/Disease_Burden.html, viewed November 2012.

289. Yassur Y, Yassur S, Zifrani S, Sachs U, Ben-Sira I. Amblyopia among African pupils in Rwanda. Brit J Ophthal 1972; 56: 368-70.

290. Hopkisson B, Clarke JR, Oelman BJ. Residual amblyopia in recruits to the British Army.Br Med J (Clin Res Ed). 1982 Oct 2;285(6346):940.

291: Schmidt PP. Vision screening with the RDE stereotest in pediatric populations. Optom Vis Sci.1991; 71: 273-81.

292: Ruttum MS, Nelson DB. Stereopsis testing to reduce overreferral in preschool vision screening.J Pediatr Ophthalmol Strabismus.1991; 28: 131-3.

293. Hope C, Maslin K. Random dot stereogram E in vision screening of children. Aust N Z J Ophthalmol.1990; 18: 319-24.

294. Moll AM, Rao RC, Rotberg LB, Roarty JD, Bohra LI, Baker JD. The role of the random dot Stereo Butterfly test as an adjunct test for the detection of constant strabismus in vision screening. J AAPOS.2009; 13: 354-6.

295. Chang CH, Tsai RK, Sheu MM. Screening amblyopia of preschool children with uncorrected vision and stereopsis tests in Eastern Taiwan. Eye (Lond). 2007 ; 21: 1482-8.

296. Huynh SC, Ojaimi E, Robaei D, Rose K, Mitchell P. Accuracy of the Lang II stereotest in screening for binocular disorders in 6-year-old children. Am J Ophthalmol.2005; 140: 1130-2.

297.Ohlsson J, Villarreal G, Sjöström A, Abrahamsson M, Sjöstrand J. Screening for amblyopia and strabismus with the Lang II stereo card. Acta Ophthalmol Scand.2002; 80: 163-6.

298. Williams F, Beneish R, Little JM. TNO random-dot stereogram and visual acuity.Am Orthopt J. 1978; 28: 110-2.

299. Pencheon D, Guest C, Melzer D, Muir Gray JA (editors) 2006, 2nd edition. Oxford handbook of public health practice. Oxford University Press, Italy.

300. Pitcher JB, Schneider LA, Drysdale JL, Ridding MC, Owens JA. Motor system development of the preterm and low birthweight infant. Clin Perinatol. 2011 Dec;38(4):605-25.

301. Xiong T, Gonzalez F, Mu DZ. An overview of risk factors for poor neurodevelopmental outcome associated with prematurity. World J Pediatr. 2012;8(4):293-300

302. Kelly MM. Comparison of functional status of 8- to 12-year-old children born prematurely: an integrative review of literature. J Pediatr Nurs. 2012;27(4):299-309.

304. van Noort-van der Spek IL, Franken MC, Weisglas-Kuperus N. Language functions in preterm-born children: a systematic review and meta-analysis. Pediatrics. 2012;129(4):745-54.

305. Harijan P, Boyle EM. Health outcomes in infancy and childhood of moderate and late preterm infants. Semin Fetal Neonatal Med. 2012;17(3):159-62.

306.Bruin JE, Gerstein HC, Holloway AC. Long-term consequences of fetal and neonatal nicotine exposure: a critical review. Toxocological Sciences 2010; 116(2): 364-74.

307. Bublitz MH, Stroud LR. Maternal smoking during pregnancy and offspring brain structure and function: review and agenda for future research. Nicotine& tabacco research 2012; 14(4): 388-97.

308. Wilson JMG, Jungner G. Principles and practice of screening for disease, public health papers no 34. WHO 1968.Genva. Printed in France

309.de Koning HJ, Groenewoud JH, Lantau VK, Tjiam AM, Hoogeveen WC, de Faber JT,Juttmann RE, Simonsz HJ. Effectiveness of screening for amblyopia and other eye disorders in a prospective birth cohort study. J Med Screen. 2013;20(2):66-72.

310. Borchert M, Wang Y, Tarczy-Hornoch K, Cotter S, Deneen J, Azen S, Varma R; MEPEDS Study Group. Testability of the Retinomax autorefractor and IOLMaster in preschool children: the Multi-ethnic Pediatric Eye Disease Study. Ophthalmology. 2008 Aug;115(8):1422-5

311. Morcos A, Wright M. National Children's Vision Screening project: final report (May 2009). http://www.rch.org.au/uploadedFiles/Main/Content /ccch/Vision_Screening_Final_Report_May_2009.pdf

Chapter 8: 8.1. Tables and Figures

Table 1.1: Prevalence of amblyopia: Cohort studies ranked according to age (1/5)

Study	Country (Year)	Study population	Type	Definition of amblyopia used	Prevalence	Unilat: Bilat
STARS	Singapore (2010)	30 to 72 month old (n 1682)	Pop	Unilateral: VA <20/30 in the worse eye, 2 line difference and amblyogenic factors. Bilateral: VA both eyes <20/40 (age 48-72months) or <20/50 (age <48months), and amblyogenic risk factors	1.19%	2.3: 1
MEPED study group (6)	USA (2008)	30 to 72 month old (n 3207) - Hispanic/Latino - African American	Pop		2.6% 1.5%	4.8: 1 3.6: 1
BPEDS, Friedman et al (7)	USA (2009)	30 to 72 months oldchildren (n 1546) - White - African American	Pop		1.8% 0.8%	12 : 0 6 : 1
SPED, Pai et al (8)	Australia (2011)	30 to 72 month old children (n 1422)	Pop		1.9%	1.7:1
Matsuo et al (53)	Japan (2007)	1.5 & 3 year old (n 6900)	Pop (self-screen)	As determined by ophthalmologist	0%-0.18%	-
Chang et al (61)	Taiwan (2007)	3 to 6 year old (n 5232)	Pop	VA <20/20 with amblyogenic risk factors	2.2%	-

Table 1.1: Prevalence of amblyopia: Cohort studies ranked according to age (2/5) (continue)

Study	Country (year)	Study population	Type	Definition of amblyopia used	Prevalence	Unilat: Bilat
Lim et al (40)	Korean (2004)	3 to 5 year old kindergarten children (n 36973) response 42%	School (self-screen)	VA <20/40 (age≤ 3years), <20/32 (age >3years) or 2 line difference	0.42%	-
Preslan & Novak (35)	USA (1996)	4 to 7 year old preschool/ school children (n 680)	School	VA <20/30 with amblyogenic risk factors	3.9%	-
Fan et al (49)	Hong Kong (2011)	4 to 6 year old preschool children (n 1424)	School	VA ≤20/40 with amblyogenic risk factors, or 2 line difference	3.8% (1996-7) 2.7% (2006-7)	-
Kvarnstrom et al (52)	Sweden (2001)	4 to 10 year old children (n 3126)	Pop	VA ≤ 20/30	2.9%	5.2 : 1
Robaei et al (44)	Australia (2006)	6 year old school children (n 1739)	School	VA <20/40 or 2 line difference	0.7%- 1.8%	16: 1
Williams et al (47)	UK (2008)	7 year old (n 7825)	Pop	VA <20/40, 2 line difference or past history	3.6%	-
He et al (39)	China (2004)	5 to 15 year old (n 4364)	Pop	VA ≤20/32 and other factors	0.87%	-

Table 1.1: Prevalence of amblyopia: Cohort studies ranked according to age (3/5) (continue)

Study	Country (year)	Study population	Type	Definition of amblyopia used	Prevalence	Unilat: Bilat
Matsuo& Matsuo (54)	Japan (2007)	6 to 13 year old (n 113763)	Pop	As determined by ophthalmologist	0.14% - 0.20%	-
Lu et al (45)	Tibet (2008)	6 to 14 year old school children (n 1084)	School	VA ≤20/30 with no organic cause	1.02% (0.42-1.61)	-
Pi et al (56)	China (2012)	6-16 year old school children (n 3469)	School	VA <20/25	1.88%	
Faghihi et al (51)	Iran (2011)	6 to 21 year old school children (n 2510)	School	VA <20/30 or 2 line difference with no organic cause	1.9% (0.94-2.90)	1.9 : 1
Goh et al (41)	Malaysia (2005)	7 to15 year old (n 4634)	Pop	VA ≤20/32 and other factors	2.0%	-
Yekta et al (48)	Iran (2010)	7-17 year old school children (n 2638)	School	VA <20/30 or 2 line difference with no organic cause	2.31% (1.45-3.16)	-
Donelly et al (43)	Ireland, UK (2005)	8-9 year old children	Pop	VA < 20/60	1.13%	-
Robei et al (46)	Australia (2006,2008)	12 year old school children (n2353)	School	VA <20/40 or 2 line difference	0.4%	11.5 :1

Table 1.1: Prevalence of amblyopia: Cohort studies ranked according to age (4/5) (continue)

Study	Country (year)	Study population	Type	Definition of Amblyopia used	Prevalence	Unilat: Bilat
Ohlsson et al (38)	Mexico (2003)	12 to13 year old school children (n1035)	School	VA ≤20/40 or 2 line difference and amblyogenic factors	2.5%	1.1 : 1
Ohlsson et al (37)	Sweden (2005)	12 to13 year old school children (n1046)	School	VA ≤20/40, 2 line difference with no organic cause	1.1%	-
Yassur et al (289)	Rwanda (1972)	10 to18 year old school children (n 1550)	School	VA ≤20/40	1.2%	-
Quah et al (34)	Singapore (1991)	18 year old army recruits (n 6556)	Army	VA≤20/40 with no organic cause	0.73%	-
Rosman et al (42)	Singapore (2005)	18 year old army recruits (n 122596)	Army	VA ≤20/40 with no organic cause	0.34%	-
Hopkisson & Clark (290)	UK (1982)	18-30 year old army recruits (n 8570)	Army	VA≤20/30 with no organic cause	4.4%	-
Wang et al (50)	China (2011)	30-80 years old (n 6830)	Pop	VA ≤20/32 with no organic cause	2.8% (2.61-3.42)	1.5 : 1

Table 1.1: Prevalence of amblyopia: Cohort studies ranked according to age (5/5) (continue)

Study	**Country (year)**	**Study population**	**Type**	**Definition of Amblyopia used**	**Prevalence**	**Unilat: Bilat**
Attebo et al (36)	Australia (1998)	49 years and older (n 3654)	Pop	VA $\leq$ 20/30 with no organic cause VA $\leq$ 20/40 with no organic cause	3.2% 2.9%	117: 1
Brown e al (57)	Australia (2000)	40-92 years (n 4721)	Pop	VA < 20/30 with no organic cause	3.1% (2.59-3.53)	140 : 1

Table 1.2: Types of Amblyopia in different populations/ racial groups (1/3)

Study	Country (Year)	Type	Predominant race	Refractive	Strabismus	Combined Refractive-Strabismus
MEPED study (6)	USA (2008)	Pop 30-72m	Hispanic-Latino African-American	77% 84%	13% 16%	7% 0%
BPEDS, Friedman et al (7)	USA (2009)	Pop 30-72m	African-American White	71% 50%	29% 33%	0% 17%
Preslan et al (35)	USA (1996)	School 4-7y	White	66%	34%	0%
SPEDS, Pai et al (6)	Australia (2012)	Pop 30-72m	White	63%	19%	8%
SMS, Robaei et al (44,46)	Australia (2006/8)	Pop 6 & 12y	White	40%	37%	19%
BMS, Attebo et al (36)	Australia (1998)	Pop > 49y	White	50%	19%	27%
ALPSAC, Williams et al (47)	UK (2008)	Pop 7y	White	58%	27%	
Kvarnstrom et al (52)	Sweden (2001)	Pop 4-10y	White	46%	37%	14%

Table 1.2: Types of Amblyopia in different populations/ racial groups (2/3)..continue

Study	Country (Year)	Type	Predominant race	Refractive	Strabismus	Combined Refractive-Strabismus
STARS	Singapore (2010)	Pop 30-72m	Chinese	85%	15%	0%
Rosman et al (42)	Singapore (2005)	Army 18y	Chinese	54%	4%	16%
Quah et al (34)	Singapore (1991)	Army 18y	Chinese	65%	19%	13%
Pi et al (8)	China (2012)	Pop 6-16y	Chinese	75%	3%	0%
Wang et al (50)	China (2011)	Pop 30-80	Chinese	77%	5%	5%
He et al (39)	China (2004)	Pop 5-15y	Chinese	68%	21%	10%
Chang et al (61)	Taiwan (2007)	Pop 3-6y	Chinese	86%	3%	0%
Goh et al (41)	Malaysia (2005)	School 7-17y	Malay	77%	23%	

Table 1.2: Types of Amblyopia in different populations/ racial groups (3/3)..continue

Study	Country (Year)	Type	Predominant race	Refractive	Strabismus	Combined Refractive-Strabismus
Lim et al (40)	Korea (2004)	Preschool 3-5y	Korean	82%	3%	0%
Matsuo et al (54)	Japan (2007)	Pop 6-13y	Japanese	72%	20%	0%
Faghihi et al (51)	Iran (2011)	School 6-21y	Iranian	76%	24%	0%
Yekta el al (48)	Iran (2010)	School 7-17y	Iranian	73%	27%	0%

Note: Percentages may not always add up to 100% because of presence of other causes of amblyopia (eg. deprivational, unknown) and because of missing data.

Table 1.3: Review of literature of risk factors associated with Amblyopia

	Population	**Risk factors associated with Amblyopia** Odd ratio (OR)/Risk Ratio (RR) [95%CI]
ALSPAC (UK), Williams et al (2008) (47)	7825 children born between 1991-1992 aged 7 years; 272 (3.6%) amblyopia	First degree relative with amblyopia or strabismus: OR 2.7 [2.0-3.6]. Council rented housing compared to owned/mortgaged housing: OR 1.5 [1.0-2.2] Maternal smoking: OR 1.4 [1.0-1.9].
SMS (Aust), Robei et al (2006) (44)	1740 6 year old school children examined between 2003-4; 32 (1.8%) amblyopia.	Strabismus: OR 65 [30-144]. Anisometropia>1D: OR 156 [64-382]. Astigmatism>1D OR: 11.0 [5.7-21.1]. BW<2.5kg: OR 4.8 [1.9-11.8]. GA<37weeks: OR 5.4 [2.4-12.3]. Admission to NICU: OR 5.0 [2.1-12.0]. Maternal smoking: OR 2.2 [1.0-5.0].
SPEDS (Aust), Pai et al (2011) (8)	1422 children aged 30-72 months; 27 (1.9%) with amblyopia.	Strabismus: OR 13.1 [4.2-40.3]. Hyperopia≥2D: OR 15.3 [6.5-36.3]. Anisometropia≥1D: OR 27.8 [11.2-69.3]. Astigmatism≥1D: OR 5.7 [2.5-12.7].
STARS (Singapore)	1682 Chinese children aged between 30-72 months. 20 (1.8%) with amblyopia.	Strabismus: OR 18.0 [3.3-97.8] Anisometropia≥1D: OR 20.6 [4.6-91.7]. Astigmatism≥1D: OR 8.9 [2.9-26.8]

Legend: ALSPAC: Avon Longitudinal Study of Parents and Children; SMS: Sydney Myopia study;

SPEDS: Sydney paediatric eye disease study. BW: birth weight, GA: gestational age, NICU: neonatal intensive care unit

Table 1.4: Types of Strabismus (1/2)

Strabismus	Types	Cause or Characteristics
Esotropia	Infantile	Large angle, early onset esotropia (< 6months of age), which do not respond to full cycloplegic spectacle correction.
	Accommodative - Fully - Partially - With high AC/A ratio	Esotropia which responds (decreases in size) with full cycloplegic spectacle correction, either fully or partially. High AC/A if additional plus required for near.
	Late acquired non-accommodative	Late onset (>6months of age), which do not respond to full cycloplegic spectacle correcion
Exotropia	Intermittent exotropia	Comitant exotropia which occurs intermittently
	Constant exotropia	Comitant exotropia present all the time
Ocular motor palsy and other innervation disorders	III nerve, IV nerve, VI nerve Duanes, Mobius syndromes Myasthenia Gravis Progressive external ophthalmolplegia	Due to neurological abnormalities affecting eye muscle movements.

Table 1.4: Types of Strabismus (2/2)..continue

Strabismus	Types	Cause or Characteristics
Restrictive	Thyroid eye disease, myostitis, myopic fixus, congenital fibrosis of extra-ocular muscles, double elevator palsies, Brown's sheath syndrome Blow-out fractures of orbital walls Scleral-buckle retinal detachment surgery Orbital tumours or infections	Due to mechanical restriction of eye movements.
Consecutive		Due to poor vision in one eye
Sensory		Strabismus status post strabismus surgery

Table 1.5: Table of Strabismus Prevalence in Children/Teenagers from selection of Population-based or Large Cohort Studies (ranked according to predominant race and age of subjects) (1/3)

Study	**Country (Year)**	**Study population**	**Type**	**Prevalence**	**XT:ET ratio**
MEPED study (6)	USA (2008)	6 to 72 month old (n 6014) - Hispanic/Latino - African American	pop	 2.4% 2.5%	 1.2: 1 1.1: 1
BPEDS, Friedman et al (7)	USA (2009)	6 to 72 months old (n 2546) - African American - White	pop	 2.1% 3.3%	 1: 1 1.2: 1
Preslan & Novak (35)	USA (1996)	4 to 7 year old preschool/ school children (n 680)	school	3.1%	1: 9
Pathai et al (84)	UK (2010)	3 to 5 year old children (n 14980)	pop	2.1% (1.8-2.4)	-
Kvarnstrom et al (52)	Sweden (2001)	4-10 year old children (n3126)	pop	3.1%	1:2.5
Robaei et al (44)	Australia (2006)	6 year old school children (n 1739)	school	2.8%	1:1.8

Table 1.5: Table of Strabismus Prevalence in Children/Teenagers from selection of Population-based or Large Cohort Studies (ranked according to predominant race and age of subjects) (2/3)..continue

Study	**Country (Year)**	**Study population**	**Type**	**Prevalence**	**XT:ET ratio**
Williams et al (47)	UK (2008)	7 year old (n 7825)	pop	2.3%	1: 3.4
Chew et al (78)	USA (1994)	7 year old (n 39227)	pop	4.2%	1 : 2.4
Donelly et al (43)	Ireland, UK (2005)	8-9 year old (n1582)	pop	4.0%	1:5.0
Ohlsson et al (37)	Sweden (2005)	12 to13 year old school children (n1046)	school	2.7%	1: 2.25
Ohlsson et al (38)	Mexico (2003)	12 to13 year old school children (n1035)	school	2.3%	1: 1.3
Faghihi et al (51)	Iran (2011)	6 to 21 year old school children (n 2150)	school	3.1% (1.3-4.3)	2.3:1
Yekta et al (48)	Iran (2010)	7 to 17 year old school children (n2638)	school	2.02% (1.45-3.16)	2.2:1

Table 1.5: Table of Strabismus Prevalence in Children/Teenagers from selection of Population-based or Large Cohort Studies (ranked according to predominant race and age of subjects) (3/3)..continue

Study	Country (Year)	Study population	Type	Prevalence	XT:ET ratio
STARS	Singapore (2010)	6 to 72 month old Chinese preschool children (n 3009)	pop	0.80%	7: 1
Matsuo et al (53)	Japan (2007)	1.5 & 3 year old (n 6900)	pop	0.01-0.35%	2.4: 1
Fan et al (49)	Hong Kong (2010)	3 to 6 year old preschool children (n 1424)	school	1.70%	6:1
Garvey et al (83)	USA (2010)	3 to 10 year old Native American school children (n 909)	school	1.0%	2.7:1
Yoon et al (82)	Korea (2011)	3 to 18 year old children (n 1811)	pop	1.8%	5.5: 1
Nepal et al (79)	Nepal (2003)	5 to 16 year old school children (n 11100)	school	1.3%	17: 1
Lu et al (45)	Tibet (2008)	6 to 14 year old school children (n 1084)	school	2.49% (1.56-3.42)	5.7:1
Pi et al (56)	China (2012)	6 to 16 year old school children (n 3469)	school	0.28%	1.7:1

Table 1.6: Review of literature of risk factors associated with Strabismus (1/3)

	Population	**Risk factors associated with Strabismus** Odd ratio (OR)/Risk Ratio (RR) [95%CI]
ALSPAC (UK), Williams et al (2008) (47)	7825 children born between 1991-1992 aged 7 years; 211 (2.8%) ET and 45 (0.6%) XT.	Family history of strabismus and amblyopia: OR 2.4 [1.7-3.2]. Prematurity: OR 2.5 [1.6-3.9] for ET. Maternal smoking: OR 2.5 [1.3-4.8]. Intrauterine growth retardation: OR 4.5 [1.8-10.8] for XT.
MCS (UK), Pathai et al (2010) (84)	14980 children born in 2000 aged 3 years; 343 (2.1%) with strabismus.	White compared to South Asian: RR 0.5 [0.3-1.0]. White compared to Black: RR 0.2 [0.1-0.6]. BW<2.5kg & GA<37wks compared to BW≥2.5kg & GA>37wks: RR 2.8 [1.9-4.3] Professional parent compared to technical: RR 0.7 [0.5-1.0]
CPP (USA) Chew et al (1994) (78), Podgor et al (1996) (89)	39227 children of White or Black ethnicity born between 1959 and 1965, screened till age 7 years; 1187 (3.0%) ET and 490 (1.2%) XT.	White ethnicity compared to Black: OR 1.8 [1.5-2.2] for ET. BW<1.5kg compared to BW>4kg: OR 3.3 [2.5-4.2] for ET and OR 4.0 [2.7-5.8] for XT. Maternal smoking >2 packs/day compared to no smoking: OR 1.8 [1.5-2.2] for ET and OR 2.3 [1.7-3.3] for XT Maternal age 30-34years compared to 20-24years: OR 1.4 [1.1-1.7]. Sibling with strabismus: OR 2.0 [1.2-3.2] for ET.

Table 1.6: Review of literature of risk factors associated with Strabismus (2/3)..continue

	Population	**Risk factors associated with Strabismus** Odd ratio (OR)/Risk Ratio (RR) [95%CI]
MEPEDS &BPEDS (USA) Cotter et al (2011) (91)	9970 children of African-American, Hispanic and non-Hispanic White children aged between 6 to 72 months; 102 (1.0%) ET and 102 (1.0%) XT.	GA<33weeks: OR 4.4 [2.1-9.2] for ET and OR 2.5 [1.2-5.3] for XT. Hyperopia>+2D: OR > 6.4. Anisometropia≥1D: OR 2.0 [1.1-3.7] for ET Astigmatism 1.5-2.5D compared to <1.5D: OR 2.5 [1.3-4.8] for XT. Child age >48 months: OR > 7.9 for ET. Female gender: OR 1.6 [1.1-2.4] for XT. Maternal smoking: OR 2.0 [1.2-3.5] for ET and OR 2.9 [1.8-4.6] for XT.
SMS (Aust), Robaei et al (2006) (80,81)	1740 6 year old school children examined between 2003-4; 26 (1.5%) ET and 14 (0.8%) XT.	Non-White: OR 0.3 [0.1-0.8] for ET. BW<2.5kg: OR 3.5 [1.3-9.2]. GA<37weeks: OR 2.8 [1.2-6.3]. Admission to NICU: OR 4.2 [1.6-11.1]. Increase paternal age: OR 4.9 [1.6-15.0]. Amblyopia, hyperopia (≥3D), astigmatism (≥1D) and anisometropia (≥1D) (p<0.001).

Table 1.6: Review of literature of risk factors associated with Strabismus (3/3)..continue

	Population	**Risk factors associated with Strabismus** Odd ratio (OR)/Risk Ratio (RR) [95%CI]
DNBC (Denmark), Torp-Pedersen (2011)(90,93)	96,842 children born between 1996-2003; 649 ET, 183 XT, 488 other strabismus.	BW <2000g: RR 2.2 [1.6-2.0] compared to BW 3000-3499g for ET. Caesarean section: RR: 1.6 [1.1-2.3] for XT Head circumference ≥38cm: RR 1.43 [1.1-1.8] compared to 34-37cm for ET. Maternal smoking: RR 1.2 [1.1-1.4]
STARS (Singapore)	2992 Chinese children aged between 6-72 months; 3 (0.1%) ETand 20 (0.7%) XT.	Sibling with strabismus: OR 41.2 [9.0-188.0]. Astigmatism≥1.0D: OR 4.2 [1.2-14.6]. Amblyopia: OR 12.9 [2.3-71.3]. Paternal education: Tertiary: OR 0.2 [0.07-0.9] and Secondary education: OR 0.1 [0.02-0.8] compared to those with no/Primary education.

Legend: ALSPAC: Avon Longitudinal Study of Parents and Children; MCS: Millennium Cohort Study; CPP: Collaborative Prenatal Project of the National Institute of Neurological Disorders and Stroke; MEPED: Multi-ethnic pediatric eye disease; BPEDS: Baltimore pediatric eye disease study; SPEDS: Sydney paediatric eye disease study. ET: esotropia, XT: exotropia. BW: birth weight, GA: gestational age, NICU: neonatal intensive care unit

Table 1.7: Sensitivity and Specificity of Stereoacuity tests in detection of Amblyopia, Strabismus and Refractive error

	Age /No.	**Test**	**Cut-off**	**Amblyopia** Sen/Spec	**Strabismus** Sen/Spec	**Refractive** Sen/Spec	**All** Sen/Spec
Schmidt 1994 (291)	2-3y/ n30	Random dot E	168s	-	-	-	0.88/0.78
Ruttum 1991 (292)	3-4y/ n 1000	Random dot E	168s	0.54/0.87 (fail vision)			
Hope 1990 (293)	5-15y/ n100	Random dot E	252s 126s	-	-	-	0.53/0.92 0.85/0.53
Moll 2009 (294)	3-6y/ n281	StereoButterfly	Pass	-	0.96/0.86 (constant)	-	-
Chang 2006 (295)	3-6y/ n5232	Random Dot	300s	-	-	0.20/0.89	-
Huynh 2005 (296)	6y/ n1765	Lang II	200s	0.29/0.99	0.29/0.99	0.21/0.99	-
Ohlsson 2002 (297)	12-13y/ n1046	Lang II	200s				0.55/0.96
Williams 1986 (298)	9-11y/ n859	TNO test	240s Qualitative	- -	- -	- -	0.12/0.98 0.33/0.98
Rustein 2000	6-18y/ n 216	Dist B-VAT	Global (120s) Contour (30s)	0.93/0.51 0.91/0.53	0.89/0.30 0.89/0.34	0.90/0.40 0.84/0.42	0.87/0.63 0.84/0.62
STARS	6-72m/ n 1529	Randot Preschool Stereoacuity Test	200s 100s	0.40/0.95 0.80/0.68	0.71/0.95 0.79/0.68	0.12/0.95* 0.60/0.70	0.18/0.95 0.61/0.70

Legend: Sen/Spec: sensivity/specificity. * significant refractive error : anisometropia $\geq$ 2.0D and astigmatism $\geq$ 2.0D

Table 1.8: Vision in Preschooler Study Definitions

Amblyopia Presumed unilateral Suspected unilateral Suspected bilateral 3 year olds 4-5 year olds	 ≥ 3 line difference in VA and unilateral amblyogenic factor 2-line difference in VA and a unilateral amblyogenic factor > 20/50 one eye, > 20/40 in other, and bilat amblyogenic factor > 20/40 one eye, >20/30 in other, and bilat amblyogenic factor
Reduced VA Bilateral 3 year olds 4-5 year olds Unilateral 3 year olds 4-5 year olds	 > 20/50 one eye, > 20/40 in other, no bilat amblyogenic factor > 20/40 one eye, > 20.30 in other, no bilat amblyogenic factor > 20/50 one eye, > 2 line diff (except 20/16 or 20/25) > 20/40 one eye, > 2 line diff (except 20/16 or 20/25)
Strabismus	Any heteropia in primary gaze
Significant refractive error Astigmatism Hyperopia Myopia Anisometropia	cycloplegic refraction >1.50D between principal meridians > 3.25D in any meridian >2.00D in any meridian >1.00D difference in hyperopia, >3.0D in myopia, >1.50D in astigmatism; anitimetropia difference >1.00D and one eye >1.00D of hyperopia, antimetropia difference > 3.00D and one eye >2.00D of myopia.
Amblyogenic Factors Unilateral Bilateral	 Strabismus, anisometropia (as defined above), difference of SE > 0.50D when ≥ 1 eye had >3.50D hyperopia Astigmatism > 2.50D, hyperopia > 5.0D and myopia > 8.5D in each eye

Table 1.9: Sensitivity of various tests in screening of amblyopia, strabismus andreduced visual acuity (VA) when specificity is set at >90% and >94% in the Vision for Preschoolers (VIP) study (135, 136); top 3 tests for each condition in bold

	Specificity > 90%			Specificity >94%		
	Ambly-opia	Reduced VA	Strabis-mus	Ambly-opia	Reduced VA	Strabis-mus
Lea symbols visual acuity	0.76	**0.58**	0.56	0.65	**0.48**	0.48
HOTV visual acuity	0.73	**0.48**	**0.65**	0.52	0.36	0.44
Cover-uncover	0.27	0.06	0.60	0.27	0.06	**0.60**
Randot Dot E	0.63	0.38	0.60	0.28	0.24	0.29
Stereo Smile II	0.77	0.30	**0.68**	0.61	0.27	**0.58**
MTI photoscreener	0.63	0.24	0.65	0.63	0.24	**0.65**
Non-cycloplegic refraction	**0.85**	0.47	0.56	**0.88**	**0.38**	0.50
Retinomax	**0.85**	0.48	**0.67**	**0.78**	**0.39**	0.54
Sure-sight vision screener (VIP criteria)	**0.89**	0.43	0.59	**0.80**	0.35	0.54
Sure-sight vision screener (manufacturer recommendation)	**0.98**	**0.70**	**0.92**	-	-	-

Table 3.1: Snellen visual acuity and LogMar Equivalents

	Snellen		LogMar
4/40	6/60	20/200	1.0
4/32	6/48	20/160	0.9
4/25	6/38	20/125	0.8
4/20	6/30	20/100	0.7
4/16	6/24	20/80	0.6
4/12	6/19	20/63	0.5
4/10	6/15	20/50	0.4
4/8	6/12	20/40	0.3
4/6	6/9.5	20/32	0.2
4/5	6/7.5	20/25	0.1
4/4	6/6	20/20	0

Table 3.2: Summary of items covered by the PedsQL4 and Child Developmental Survey

Pediatric Quality of Life Inventory (PedsQL4):		
	24- 48 months	49- 72 months
Physical functioning	Problems walking, running, participating in active play or exercise, lifting something heavy, bathing, helping picking up toys, hurts or aches and low energy levels	Problems walking more than 1 block, running, participating in sports or exercise, lifting something heavy, taking a bath/shower by themselves, doing chores like picking up their toys, having hurts/aches and low energy levels.
Emotional functioning	Problems feeling afraid/scared, sad/blue, angry, sleeping or worrying	Problems feeling afraid /scared, sad/blue, angry, sleeping and worrying what will happen to them
Social functioning	Problems playing with other children, other children not wanting to play with him/her, getting teased by others, not able to do things that other children their age could do, keep up when playing with other children.	Problems getting along with other children, other children not wanting to be their friend, getting teased by other children, not able to do things that other children their age can do and keeping up when playing with other children
School functioning (applicable only if child was attending school or daycare)	Problems doing the same school activates as peers, missing school/daycare because not feeling well or because they need to go to the doctor or hospital.	Problems paying attention in class, forgetting things, keeping up with school activities, missing school because not feeling well and missing school to go to the doctor or hospital.
Child Development Survey		
Developmental delay	concerns about child's learning, development and behavior	
Speech	concerns about how child talked and made speech sounds	
Comprehension	concerns about how child understood what parents say	
Fine motor skills	concerns about how child used his/her hands and fingers to do things	
Gross motor skills	concerns about how child used his/her arms and legs	
Behavior	concerns about how child behaved)	
Social functioning	concerns about how the child got along with others	
Learning	concerns about how child was learning to do things for themselves	
Preschool skills	concerns about how child was learning preschool or school skills	

Table 3.3. Definition of Amblyopia and Strabismus

Amblyopia	Visual Criteria	Full amblyopic criteria with amblyogenic factors:
Unilateral	• a ≥ 2-line difference in best VA, with visual acuity < 20/30 (logMAR 0.18) in the worse eye	• past or present strabismus, • anisometropia (≥1.00D difference in hyperopia, ≥3.00D difference in myopia, or ≥1.50D difference in astigmatism), and • past or present obstruction of the visual axis
Bilateral	• best VA in both eyes < 20/40 (logMAR 0.3) in children aged 48 to 72 months • best VA in both eyes < 20/50 (logMAR 0.4) in children aged < 48 months	• hyperopia ≥ 4D, • myopia ≤ -6.00D, or • astigmatism ≥2.50D, and • past or present obstruction of the visual axis
Strabismus	any tropia present at distance or near, with or without spectacles	

Table 3.4: Components of the Rasch analysis

	Questions to be addressed	Interpretation/Action
Item fit	Did responders have difficulty differentiating between categories? Were there marked ceiling and floor effects	Are there items that should be removed (ambiguous, ceiling or floor effects)? Should some categories be collapsed?
Person-item targeting (content validity)	Were responses as expected (eg. lower scores for subjects with worse disease)? Was the proper hierarchical ordering observed?	Ideally, the person and item fit residue (mean, SD) close to 0 or 1. If not, instrument not valid
Principal components analysis (PCA) (uni-dimensionality)	Are responses only measuring the condition of interest? Are other random associations which influence responses?	Ideally, PCA should be low ($\leq$50%), and the eigenvalues < 2. If not, there is too much noise in system.
Person separation index (internal reliability)	Was the scale used reliable? (Similar to Cronbach's alpha)	Ideally, PSI $\geq$ 0.7. If not, instrument not reliable

Table 4.1: Distribution of children according to age and gender

Age (months)	n	Male (%)
6.0 - 11.9	190	46.8
12.0 – 23.9	540	57.4
24.0 – 35.9	516	50.9
36.0 - 47.9	579	50.6
48.0 - 59.9	605	53.4
60.0 - 72.0	579	50.4
Total	3009	52.2

Table 4.2: Socioeconomic differences between population within STARS recruitment area and the general population; and between parents of children recruited for study and Singaporean Chinese adults aged 20-40years

	Singapore population (total)*	STARS recruitment area	Singaporean Chinese aged 20-40years*	STARS Fathers	STARS mothers
Education					
- none	19.5%	19.1%	5%	<1%	<1%
- primary	12.1%	12.9%	7%	9%	6%
- secondary	35.5%	35.3%	34%	29%	35%
- polytechnic	21.1%	21.0%	33%	26%	29%
- university	11.7%	11.7%	21%	32%	28%
- unknown				3%	1%
Employment					
- employed	59.4%	60.1%			
- unemployed	3.8%	3.7%			
- inactive	36.8%	36.2%			
Household income				STARS Households	
- < S$1000	12.4%	10.0%	No data	3%	
- S$1000-2999	28%	29.5%	available	21%	
- S$3000-4999	23.5%	25.5%		30%	
- > S$5000	35.6%	35.0%		44%	
- unknown				2%	

Note: * information obtained from Population Census (2000) of persons aged >15 years within different district zones (213)

Table 4.3: Comparison of Responders and non-responders (adapted from table 2 for Dirani et al 2010) (217)

	Non-responders, n (%)	Responders, n (%)	P-value
Study area			
- Bukit Batok	175 (15.1)	408 (13.6)	<0.001
- Clementi	121 (10.5)	209 (6.9)	
- Jurong East	103 (8.9)	366 (12.2)	
- Jurong West	415 (35.9)	1279 (42.5)	
- South Central	336 (29.1)	693 (23.1)	
Gender			
- Male	227 (53.3)	1570 (5.2)	0.668
- Female	199 (46.7)	1439 (47.8)	
Age group			
- 6.0 – 11.9	62 (5.9)	190 (6.3)	0.977
- 12.0 – 23.9	193 (18.5)	540 (17.9)	
- 24.0 – 35.9	183 (17.5)	516 (17.1)	
- 36.0 – 47.9	194 (18.6)	579 (19.2)	
- 48.0 – 59.9	204 (19.6	605 (20.1)	
- 60.0 – 72.0	207 (19.8)	579 (19.2)	
HDB type			
- 3 room	48 (11.6)	70 (6.7)	0.012
- 4 room	122 (29.4)	353 (33.8)	
- 5 room	201 (48.4)	522 (50.1)	
- Executive	44 (10.6)	98 (9.4)	

Note: The nonparticipant group has 929 (80.3%) missing sex data, 112 (9.7%) missing age data, and 740 (64.07%) missing apartment data. The participant group has 1967 (65.37%) missing apartment data.

Table 4.4: Testability of visual acuity tests and numbers who did not meet the amblyopia visual acuity and full criteria.

Age (months)	n	Unable to test	Tested	Fulfill amblyopia visual acuity criteria	Fulfill all amblyopia criteria
30.0 - 35.9	252	169 (67.1%)	83	3 (3.6%)	1 (1.2%)
36.0 - 47.9	579	133 (23.0%)	446	15 (2.4%)	6 (1.3%)
48.0 - 59.9	605	24 (4.0%)	581	21 (3.6%)	9 (1.5%)
60.0 - 72.0	579	7 (1.2%)	572	9 (1.5%)	4 (0.7%)
All	2015	333 (16.5%)	1682	48 (2.9%)	20 (1.2%)

Table 4.5: Refractive errors in those who did and did not complete visual acuity test and in children with and without Amblyopia

	Total (n 2016)	Unable to test VA (n 333)	Able to test VA (n 1682)	P	Amblyopic (n 20)	Non-amblyopic (n 1662)	P
Anisometropia							
- ≥1.0D hyperopia	10 (0.5)	3 (0.9)	7 (0.4)	0.257	2 (10.0)	5 (0.3)	<0.001
- ≥3.0D myopia	3 (0.1)	0 (0)	3 (0.2)	0.440	2 (10.0)	1 (0.1)	<0.001
- ≥1.5D astig	24 (1.2)	2 (0.6)	22 (1.3)	0.278	8 (40.0)	14 (0.8)	<0.001
Bilateral							
Hyperopia ≥ 3.0D	31 (1.5)	4 (1.2)	27 (1.6)	0.572	3 (15.0)	24 (1.4)	<0.001
Myopia ≤ -6.0D	8 (0.4)	1 (0.3)	7 (0.4)	0.759	5 (25.0)	2 (0.1)	<0.001
Astig ≥2.5D	41 (2.0)	8 (2.4)	33 (1.9)	0.603	3 (15.0)	30 (1.8)	<0.001
Total	101 (5.0)	15 (4.5)	86 (5.1)	0.642	17 (85.0)	84 (5.1)	<0.001

Note: Children may have both bilateral high ametropia and anisometropia. Definition of amblyopia is based on both visual acuity and amblyogenic risk factors (including refractive error, strabismus and occlusion of one/both eyes).

Table 4.6: Prevalence of Amblyopia in children aged 30-72 months by age and gender

	N	Any amblyopia n (%, 95% CI)
All children		
Crude rate	1682	20 (1.19, 0.73-1.83)
Adjusted rate+		1.15 (1.12-1.25)
30 to 35 months	83	1 (1.21, 0.03-6.53)
36 to 47 months	446	6 (1.35, 0.50-2.91)
48 to 55 months	581	9 (1.55, 0.71-2.92)
56 to 72 months	572	4 (0.70, 0.19-1.78)
P (trend) †		0.37
Boys (All)	850	12 (1.41, 0.73-2.45)
30 to 47 months	253	2 (0.79, 0.10-2.83)
48 to 72 months	597	10 (1.68, 0.81-3.06)
P (trend) †		0.31
Girls (All)	832	8 (0.96, 0.42-1.89)
30 to 47 months	276	5 (1.81, 0.59-4.180
48 to 72 months	556	3 (0.54, 0.11-1.57)
P (trend) †		0.07

Note: 95% CI = 95% confidence interval (Binomial distribution)

+ weighted to Population Census 2000 (taking into account Location sampling and familial clustering) (213)

Table 4.7: Type of Amblyopia

	Number	Prevalence* (95% CI)
Unilateral	14	0.83% (0.46-1.39)
. Anisometropic	11	0.65% (0.33-1.17)
. Strabismic	3	0.18% (0.04-0.52)
. Combined refractive/strabismus	0	- (0.0 - 0.18)
. Deprivational	0	- (0.0 – 0.18)
Bilateral ametropic	6	0.36% (0.13-0.77)
Total	20	1.19% (0.73-1.83)

Table 4.8: Prevalence of Strabismus in children aged 6 to 72 months by age and gender

	N	Any strabismus*	Exotropia	Esotropia
		n (%, 95% CI)	n (%, 95% CI)	n (%, 95% CI)
All children				
Crude rate	3009	24 (0.80, 0.51-1.19)	20 (0.67, 0.41-1.03)	3 (0.10, 0.02-0.29)
Adjusted rate+		0.84 (0.80-0.88)	0.70 (0.66-0.74)	0.10 (0.086-0.12)
6-11 months	189	0 (-, 0.0 – 1.9)	0 (-, 0.0 – 1.6)	0 (-, 0.0 – 1.6)
12 to 23 months	537	2 (0.37, 0.04 – 1.32)	2 (0.37, 0.04 – 1.32)	0 (-, 0.0 – 0.55)
24 to 35 months	514	5 (0.97, 0.31 – 2.23)	3 (0.58, 0.12 – 1.68)	2 (0.39, 0.005 – 1.07)
36 to 47 months	574	4 (0.69, 0.11 – 1.50)	3 (0.52, 0.11 – 1.50)	1 (0.0, 0.0-0.51)
48 to 59 months	602	7 (1.16, 0.46 – 2.35)	7 (1.16, 0.46 – 2.35)	0 (-, 0.0 – 0.49)
60 to 72 months	576	6 (1.04, 0.38 – 2.23)	5 (0.86, 0.28 – 1.99)	0 (-, 0.0 – 0.95)
P (trend) †		0.08	0.07	0.57
Boys (All)	1561	14 (0.89, 0.44 – 1.41)	12 (0.77, 0.39 – 1.33)	1 (0.064, 0.002-0.36)
6-11 months	88	0 (-, 0.0 – 3.27)	0 (-, 0.0 – 3.27)	0 (-, 0.0 – 3.27)
12 to 23 months	308	1 (0.32, 0.008 – 1.79)	1 (0.33, 0.008 – 1.79)	0 (-, 0.0 -0.96)
24 to 35 months	262	1 (0.38, 0.01 – 2.10)	1 (0.38, 0.01 – 2.10)	0 (-, 0.0 -1.13)
36 to 47 months	291	4 (1.36, 0.21 – 2.94)	3 (1.02, 0.21 – 2.94)	1 (0.34, 0.01-1.89)
48 to 59 months	321	4 (1.24, 0.33 – 3.11)	4 (1.23, 0.33 – 3.11)	0 (-, 0.0 – 0.91)
60 to 72 months	291	4 (1.37, 0.37 – 3.45)	3 (1.03, 0.21 – 2.96)	0 (-, 0.0 – 1.02)
P (trend) †		0.06	0.10	0.92
Girls (All)	1431	10 (0.69, 0.33 – 1.27)	8 (0.56, 0.24 – 1.09)	2 (0.14, 0.02 – 0.50)
6-11 months	101	0 (-, 0.0 – 2.92)	0 (-, 0.0 – 2.92)	0 (-, 0.0 – 2.92)
12 to 23 months	229	1 (0.44, 0.01 – 2.37)	1 (0.44, 0.01 – 2.37)	0 (-, 0.0 – 1.28)
24 to 35 months	252	4 (1.58, 0.43 – 3.95)	2 (0.79, 0.09 – 2.79)	2 (0.80, 0.01 – 2.16)
36 to 47 months	283	0 (-, 0.0 – 1.04)	0 (-, 0.0 – 1.04)	0 (-, 0.0 – 1.04)
48 to 59 months	281	3 (1.06, 0.22 – 3.08)	3 (1.06, 0.22 – 3.08)	0 (-, 0.0 – 1.06)
60 to 72 months	285	2 (0.69, 0.08 – 2.48)	2 (0.70, 0.08 – 2.48)	0 (-, 0.0 – 1.91)
P (trend) †		0.67	0.38	0.43

95% CI = 95% confidence interval (Binomial distribution)

* Includes 1 child, a 71 month old boy, had DVD alone

+ weighted to Singapore Population Census 2000 (taking into account Location sampling and familial clustering) (213)

Table 4.9: Strabismus subtypes and characteristics*

	Number (%)
Strabismus type at distance	
. Intermittent exotropia	12
. Constant exotropia	7
. Intermittent esotropia	0
. Constant esotropia	3
. Strabismus identified only at near	1
Strabismus type at near	
. Intermittent exotropia	12
. Constant exotropia	6
. Intermittent esotropia	0
. Constant esotropia	3
. Strabismus identified only at distance	2
Strabismus magnitude at distance	
. 1-9PD	0
. 10-30PD	5
. > 30PD	6
. Unable to measure	12
Strabismus magnitude at near	
. 1-9PD	0
. 10-30PD	6
. > 30PD	5
. Unable to measure	12

* Not included in this table is data from 1 child with DVD only.

Table 4.10: Associations of age, gender and basal metabolic index (BMI) with Amblyopia and Strabismus

4.10.1. Amblyopia

Child Risk Factors	**Amblyopia N = 20 n (%)**	**No Amblyopia N = 1662 n (%)**	**OR (95% CI)**	**p-value**
Mean Age(mths) (95% CI)	51.9 (47.7, 56.1)	53.9 (53.4, 54.4)		0.42
Gender – male, n (%)	12 (60.0)	838 (50.4)	1.48 (0.60, 3.63)	0.39
BMI (kg/m^2), mean (95% CI)	16.0 (15.4, 16.7)	15.6 (15.6, 15.8)		0.43
1st quartile	2 (10.0)	302 (18.3)	1	
2nd quartile	3 (15.0)	357 (21.7)	1.27 (2.16, 2.42)	
3rd quartile	7 (35.0)	490 (29.7)	2.16 (0.45, 10.45)	
4th quartile	8 (40.0)	499 (30.3)	2.42 (0.51, 11.48)	0.58

4.10.2. Amblyopia (including past history of amblyopia)

Child Risk Factors	**Amblyopia N = 34 n (%)**	**No Amblyopia N = 1650 n (%)**	**OR (95% CI)**	**p-value**
Mean Age(mths) (95% CI)	54.8 (50.8, 58.8)	53.8 (53.3, 54.4)		0.60
Gender – male, n (%)	20 (58.8)	830 (50.3)	1.41 (0.71, 2.81)	0.33
BMI (kg/m^2) , mean (95% CI)	15.9 (15.2, 16.4)	15.7 (15.6, 15.8)		0.72
1st quartile	5 (14.7)	299 (18.3)	1	
2nd quartile	7 (20.6)	354 (21.6)	1.18 (0.37, 3.76)	
3rd quartile	9 (26.5)	488 (29.8)	1.10 (0.37, 3.32)	
4th quartile	13 (38.2)	495 (30.3)	1.57 (0.55, 4.45)	0.78

4.10.3 Strabismus

Child Risk Factors	Strabismus N = 24 n (%)	No Strabismus N = 2968 n (%)	OR (95% CI)	p-value
Mean Age(mths) (95% CI)	46.5 (39.6, 53.3)	40.4 (39.8, 41.1)		0.11
Gender – male, n (%)	14 (58.3)	1547 (52.1)	1.29 (0.57, 2.9)	0.54
BMI (kg/m^2), mean (95%CI)	16.0 (15.3, 16.8)	15.9 (15.8, 16.1)		0.88
1st quartile	4 (16.7)	580 (19.8)	1	
2nd quartile	2 (8.3)	607 (20.8)	0.49 (0.09, 2.62)	
3rd quartile	9 (37.5)	792 (27.1)	1.65(0.51, 5.38)	
4th quartile	9 (37.5)	946 (32.3)	1.38 (0.42, 4.50)	0.39

Table 4.11: Associations of birth-related factors (ie. birth weight, gestational age, head circumference, body length and admission to neonatal intensive care (NICU)) with Amblyopia and Strabismus

4.11.1. Amblyopia

Birth Factors	**Amblyopia N = 20 n (%)**	**No Amblyopia N = 1662 n (%)**	**OR (95% CI)**	**p-value**
Birth Weight (kg) (BW) Mean (95% CI)	3.09 (2.87, 3.30)	3.11 (3.09, 3.13)		0.81
low BW $\leq$ 2500g	3 (15.0)	130 (8.0)	1	
BW > 2500g	17 (85.0)	1479 (91.1)	0.51 (0.14, 1.72)	0.22
Gestational Period (GA) (wks) Mean (95% CI)	38.3 (37.7, 38.9)	38.5 (38.4, 38.5)		0.65
GA $\leq$ 37 weeks	4(20.0)	306 (19.8)	1	
GA >37 weeks	16 (80.0)	1238 (80.2)	0.90 (0.3, 2.9)	0.93
Birth Length (cm) Mean (95% CI)	49.0 (48.1, 49.8)	49.2 (49.1, 49.4)		0.64
1st quartile (31 - 48.0)	6 (30.0)	545 (31.4)	1	
2nd quartile (48.01 - 49.0)	5 (25.0)	305 (19.1)	1.49 (0.45, 4.92)	
3rd quartile (49.01 - 50.9)	5 (25.0)	311 (19.5)	1.46 (0.44, 4.82)	
4th quartile (51 - 85)	4 (20.0)	436 (27.3)	0.83 (0.23, 2.97)	0.74
Head circumference (cm) Mean (95% CI)	33.3 (32.8, 33.7)	33.6 (33.5, 33.6)		0.21
1st quartile (21.5 - 32.9)	4 (20.0)	386 (24.3)	1	
2nd quartile (33 - 33.5)	10 (50.0)	426 (26.8)	2.27 (0.71, 7.28)	
3rd quartile (33.6 -34.5)	4 (20.0)	419 (26.4)	0.92 (0.23, 3.71)	
4th quartile (34.6 - 52)	2 (10.0)	358 (22.5)	0.54 (0.1, 2.96)	0.12
Admission to NICU	3 (15.0)	88 (5.4)	3.11 (0.89, 10.78)	0.09

4.11.2. Amblyopia (including past history of amblyopia)

Birth Factors	Amblyopia N = 34 n (%)	No Amblyopia N = 1650 n (%)	OR (95% CI)	p-value
Birth Weight (kg) (BW)				
Mean (95% CI)	3.08 (2.91, 3.26)	3.11 (3.09, 3.14)		0.71
low BW ≤ 2500g	5 (15.2)	128 (8)	1	
BW > 2500g	28 (84.8)	1469 (92)	0.49 (0.19, 1.29)	0.18
Gestational Period (GA)				
(wks) Mean (95% CI)	38.0 (37.0, 39.0)	38.5 (38.4, 38.5)		0.39
≤ 37 weeks	7 (21.2)	304 (19.8)	1	
> 37 weeks	26 (78.8)	1228 (80.2)	0.92 (0.4, 2.14)	0.85
Birth Length (cm)				
Mean (95% CI)	48.5 (47.2, 49.8)	49.3 (49.1, 49.4)		0.24
1st quartile (31 - 48.0)	11 (34.1)	541 (34.1)	1	
2nd quartile (48.01 - 49.0)	7 (20.6)	304 (19.2)	1.13 (0.43, 2.95)	
3rd quartile (49.01 - 50.9)	8 (23.5)	308 (19.4)	1.28 (0.51, 3.21)	
4th quartile (51 - 85)	8 (23.5)	432 (27.3)	0.91 (0.36, 2.28)	0.91
Head circumference (cm)				
Mean (95% CI)	32.9 (32.1, 33.8)	33.6 (33.5, 33.6)		**0.03**
1st quartile (21.5 - 32.9)	8 (23.5)	383 (24.3)	1	
2nd quartile (33.0 - 33.5)	13 (38.2)	423 (26.8)	1.47 (0.6, 3.59)	
3rd quartile (33.6 -34.5)	8 (23.5)	415 (26.3)	0.92 (0.34, 2.48)	
4th quartile (34.6 - 52)	5 (14.7)	356 (22.6)	0.67 (0.22, 2.08)	0.45
Admission to NICU	6 (18.2)	86 (5.3)	3.97 (1.61, 9.88)	**0.01**

4.11.3. Strabismus

Birth Factors	Strabismus N = 24 n (%)	No Strabismus N = 2968 n (%)	OR (95% CI)	p-value
Birth Weight (g) (BW)				
Mean (95% CI)	3.05 (2.77, 3.25)	3.09 (3.07, 3.11)		0.36
Low BW ≤ 2500g	4 (16.7)	241 (8.4)	1	
BW > 2500g	20 (83.3)	2637 (91.6)	2.19 (0.74, 6.45)	0.14
Gestational Period (GA)				
(wks) Mean (95% CI)	38.2 (37.5, 38.8)	38.3 (38.3, 38.4)		0.40
GA ≤ 37weeks	5 (20)	626 (22.7)	1	
GA > 37 weeks	19 (79.2)	2128 (77.3)	0.90 (0.33, 2.41)	0.83
Birth Length (cm)				
Mean (95% CI)	48.2 (47.1, 19.2)	49.1 (49.0, 49.2)		0.06
1st quartile (31 - 48.0)	9 (39.1)	1007 (35.2)	1	
2nd quartile (48.01 - 49.0)	6 (26.1)	556 (19.4)	1.21 (0.43, 3.41)	
3rd quartile (49.01 - 50.9)	5 (21.7)	564 (19.7)	0.99 (0.33, 2.97)	
4th quartile (51 - 85)	3 (13.0)	733 (25.6)	0.46 (0.12, 1.70)	0.56
Head circumference (cm)				
Mean (95% CI)	33.6 (32.8, 34.5)	33.5 (33.5, 33.6)		0.72
1st quartile (21.5 - 32.9)	6 (26.1)	691 (24.3)	1	
2nd quartile (33 - 33.5)	5 (21.7)	768 (27.0)	1.21 (0.43, 3.41)	
3rd quartile (33.6 -34.5)	5 (21.7)	750 (26.4)	0.99 (0.33, 2.97)	
4th quartile (34.6 - 52)	7 (30.4)	637 (22.4)	0.46 (0.12, 1.70)	0.78
Admission to NICU	4 (16.7%)	160 (5.5)	3.44 (1.16, 10.2)	**0.02**

Table 4.12: Associations of maternal factors (ie. maternal age, illness, smoking, alcohol use and breast-feeding) with Amblyopia and Strabismus

4.12.1. Amblyopia

Maternal/Prenatal Factors	**Amblyopia N = 20 n (%)**	**No Amblyopia N = 1662 n (%)**	**OR (95% CI)**	**p-value**
Maternal age (years)				
Mean (95% CI)	32.3 (30.4, 33.9)	30.4 (30.2, 30.6)		0.09
≤ 35 years	17 (85)	1444 (88.1)	1	
>35 years	3 (15)	195 (11.9)	1.31 (0.38, 4.51)	0.67
Maternal illness				
Anemia	0	48 (2.9)	-	
High blood pressure	2 (10)	57 (3.5)	3.08 (0.07, 13.6)	0.16
Diabetes	1 (5)	86 (5.2)	0.95 (0.13, 7.18)	0.96
Maternal smoking	0	30 (1.8)	-	
Maternal alcohol use	0	15 (0.9)	-	
Breast Feeding	16 (80)	1258 (76.5)	1.23 (0.41, 3.72)	0.71

4.12.2. Amblyopia (including past history of amblyopia)

Maternal/Prenatal Factors	**Amblyopia N = 34 n (%)**	**No Amblyopia N = 1650 n (%)**	**OR (95% CI)**	**p-value**
Maternal age				
Mean (95% CI)	30.8 (29.3, 32.3)	30.4 (30.2, 30.7)		0.64
≤ 35 years	29 (85.3)	1434 (88.1)	1	
>35 years	5 (14.7)	193 (11.9)	1.28 (0.49, 3.35)	0.60
Maternal illness				
Anemia	0	48 (3)	-	0.62
High blood pressure	2 (5.9)	57 (3.5)	1.72 (0.40, 7.36)	0.34
Diabetes	2 (5.9)	85 (5.2)	1.13 (0.27, 4.81)	0.70
Maternal smoking	0	30 (1.8)	-	
Maternal alcohol	0	15 (0.9)	-	
Breast Feeding	24 (70.6)	1251 (76.6)	0.73 (0.35, 1.55)	0.42

4.12.3 Strabismus

Maternal/Prenatal Factors	**Strabismus N = 24 n (%)**	**No Strabismus N = 2968 n (%)**	**OR (95% CI)**	**p-value**
Maternal age				
Mean (95% CI)	30.0 (27.9, 32.1)	30.6 (30.4, 30.8)		0.52
≤ 35 years	19 (79.2)	2536 (86.6)	1	
>35 years	5 (20.8)	392 (13.4)	1.67 (0.62, 4.49)	0.29
Maternal illness				
Anemia	1 (4.2)	91 (3.1)	1.36 (0.18, 10.15)	0.77
High blood pressure	0	110 (3.8)	--	--
Diabetes	0	165 (5.6)	--	--
Maternal smoking	0	64 (2.2)	-	
Maternal alcohol use	0	30 (1.0)	-	
Breast Feeding	17 (70.8)	2288 (77.8)	0.69 (0.29, 1.68)	0.41

Table 4.13.Correlation between socioeconomic factors (ie. maternal and paternal education, and monthly household income)

		Maternal education			Monthly household income		
		No/Primary	Secondary/ 'O'	'A' /polytechnic /Tertiary	<S$3000	S$3000-4999	≥S$5000
Paternal education	No/Primary	2.9%	5.5%	1.5%	7.3%	2.3%	0.3%
	Secondary/ 'O'	2.7%	17.5%	9.1%	11.6%	11.7%	6.3%
	'A' /polytechnic /Tertiary	0.8%	12.3%	47.6%	4.9%	16.6%	39.1%
Monthly household income	<S$3000	5.0%	13.9%	4.9%			
	S$3000-4999	1.4%	13.9%	15.4%			
	≥ S$5000	0.3%	7.3%	37.8%			

Table 4.14: Associations of socioeconomic factors (ie. maternal and paternal education, and monthly household income) with Amblyopia and Strabismus.

4.14.1. Amblyopia

Socioeconomic Factors	**Amblyopia N = 20 n (%)**	**No Amblyopia N = 1662 n (%)**	**OR (95% CI)**	**p-value**
Maternal Education				
None/Primary School	1 (5.0)	118 (7.2)	1	
Secondary/'O'	10 (50.0)	599 (36.7)	1.99 (0.25, 15.72)	
A'/Polytechnic/Tertiary	9 (45.0)	917 (56.1)	1.19 (0.15, 9.22)	0.45
Paternal Education				
None/Primary School (%)	2 (10.0)	157 (9.6)	1	
Secondary/ 'O' (%)	8 (40.0)	504 (30.8)	1.25 (0.26, 5.93)	
'A'/Polytechnic/University (%)	10 (50.0)	974 (59.6)	0.81 (0.18, 3.71)	0.61
Monthly household income				
< S$3000 (%)	4 (20.0)	378 (23.6)	1	
S$3000 - 4999 (%)	5 (25.0)	488 (30.4)	0.97 (0.26, 5.93)	
$\geq$S$5000 (%)	11 (55.0)	738 (46.0)	1.41 (0.45, 4.45)	0.72

4.14.2. Amblyopia (including past history of amblyopia)

Socioeconomic Factors	Amblyopia N = 34 n (%)	No Amblyopia N = 1650 n (%)	OR (95% CI)	p-value
Maternal Education				
None/Primary School	3 (9.4)	116 (7.2)	1	
Secondary/'O'	15 (46.9)	587 (36.3)	0.98 (0.28, 3.47)	
A'/Polytechnic/Tertiary	14 (43.7)	912 (56.5)	0.59 (0.17, 2.10)	0.35
Paternal Education				
None/Primary School	6 (18.8)	153 (9.5)	1	
Secondary/'O'	10 (31.2)	487 (30.3)	0.52 (0.19, 1.46)	
A'/Polytechnic/Tertiary	16 (50.0)	968 (60.2)	0.42 (0.16, 1.09)	0.19
Monthly household income				
< S$3000	9 (28.1)	373 (23.9)	1	
S$3000 - 49999	7 (21.9)	486 (30.8)	0.60 (0.22, 1.62)	
>S$5000	16 (50.0)	733 (45.3)	0.90 (0.40, 2.07)	0.55

4.14.3 Strabismus

Socioeconomic Factors	Strabismus N = 24 n (%)	No Strabismus N = 2968 n (%)	OR (95% CI)	p-value
Maternal Education				
None/Primary School	6 (25)	194 (6.6)	1	
Secondary/'O'	10 (41.7)	1040 (35.6)	0.24 (0.09, 0.62)	
'A'/Polytechnic/Tertiary	8 (33.3)	1691 (57.8)	0.16 (0.04, 0.56)	**0.001**
Paternal Education				
None/Primary School	8 (33.3)	286 (9.8)	1	
Secondary/'O'	5 (20.8)	878 (35.6)	0.24 (0.09, 0.62)	
'A'/Polytechnic/Tertiary	11 (45.9)	1691 (57.8)	0.16 (0.04, 0.56)	**<0.001**
Monthly household income				
< S$3000	14 (58.3)	684 (23.8)	1	
S$3000 - 49999	4 (16.7)	882 (30.7)	0.22 (0.07, 0.68)	
>S$5000	6 (25.0)	1307 (45.5)	0.22 (0.09, 0.59)	**<0.001**

Table 4.15: Association of ocular factors (ie. hyperopia/myopia, astigmatism, anisometropia and strabismus/amblyopia) with Amblyopia and Strabismus

4.15.1. Amblyopia

Ocular Factors	**Amblyopia N = 20 n (%)**	**No Amblyopia N = 1662 n (%)**	**OR (95% CI)**	**p-value**
Spherical Equivalent (D), Mean (95%CI)	-1.13 (-3.43, 1.17)	0.72(0.67, 0.76)	-	0.11
Hyperopia SE ≥3.0D	4 (20.0)	8 (0.5)	52.9 (13.5,207.7)	**<0.001**
Hyperopia SE 1.0-2.9D	1 (5.0)	55 (3.3)	1.92 (0.17,11.22)	0.74
Emmetropia SE -1.0-1.0D	9 (45.0)	952 (57.3)	1	
Myopia SE -1.0 - -2.9D	3 (15.0)	628 (37.8)	0.50 (0.14,1.87)	0.49
Myopia SE ≤ -3.0D	3 (15.0)	19 (1.1)	16.7 (4.21,66.6)	**<0.001**
Astigmatism (D) Mean (95%CI)	-2.16 (-2.94, -1.39)	-0.67 (-0.70, -0.64)	-	**<0.001**
Cylinder < 1.0D (%)	6 (30.0)	1353 (81.4)	1	
Cylinder 1.0-1.9D (%)	4 (20.0)	235 (14.1)	3.83 (1.07,13.71)	**0.03**
Cylinder ≥2.0D	10 (50.0)	74 (4.5)	30.47 (10.8,86.1)	**<0.001**
Anisometropia (D) (95%CI)				
Mean (95%CI)	1.04 (0.30,1.80)	0.21 (0.20, 0.22)	-	**<0.001**
< 1.0D	16 (80.0)	1637 (98.5)	1	
1.0-1.9D	2 (10.0)	15 (0.9)	13.64 (2.9,64.6)	**0.001**
≥ 2.0D	2 (10.0)	10 (0.6)	20.46 (4.2,100.9)	**<0.001**
Strabismus	3 (15.8)	11 (0,7)	28.07 (7.2,110.3)	**<0.001**

4.15.2. Amblyopia (including past history of amblyopia)

Ocular Factors	Amblyopia N = 34 n (%)	No Amblyopia N = 1650 n (%)	OR (95% CI)	p-value
Spherical Equivalent (D)				
Mean (95%CI)	-0.47 (-1.70,0.83)	0.64 (0.60, 0.68)	-	**<0.001**
Hyperopia SE ≥3.0D	4 (12.5)	12 (0.5)	27.76 (7.6,101.1)	**<0.001**
Hyperopia SE 0.5-2.9D	3 (9.4)	81 (3.2)	3.14 (0.89,11.06)	0.07
Emmetropia SE -0.5-0.5D	17 (53.1)	1144 (57.2)	1.0	
Myopia SE -0.5 - -2.9D	5 (15.6)	725 (37.9)	0.44 (0.16,1.20)	0.112
Myopia SE ≤ -3.0D	3 (9/4)	22 (1.1)	8.76 (2.37,32.45)	**<0.001**
Astigmatism (D)				
Mean (95%CI)	-1.74 (-2.25, -1.22)	-0.59 (-0.61,-0.57)	-	**<0.001**
Cylinder < 1.0D (%)	12 (37.5)	1347 (81.6)	1	
Cylinder 1.0-1.9D (%)	5 (15.6)	234(14.2)	2.40 (0.84,6.87)	0.103
Cylinder ≥2.0D	15 (46.9)	69 (4.2)	24.40 (11.00, 54.13)	**<0.001**
Anisometropia (D)				
Mean(95%CI)	0.90 (0.42,1.39)	0.21 (0.20,0.22)	-	**<0.001**
< 1.0D	26 (81.2)	1627 (98.6)	1	
1.0-1.9D	2 (6.3)	15 (0.9)	8.24 (1.81,38.35)	**0.006**
≥ 2.0D	4 (12.5)	8 (0.5)	31.3 (8.9,110.4)	**<0.001**
Strabismus	5 (15.2)	14 (0.7)	34.9 (10.9,111.5)	**<0.001**

4.15.3. Strabismus

Ocular Factors	Strabismus N = 24 n (%)	No Strabismus N = 2968 n (%)	OR (95% CI)	p-value
Spherical Equivalent (D)				
Mean (95%CI)	0.38 (0.53, 1.29)	0.63 (0.59, 0.67)	-	0.58
Hyperopia SE ≥3.0D	1 (4.2)	19 (0.6)	7.95 (0.98,64.7)	0.05
Hyperopia SE 0.5-2.9D	2 (8.3)	129 (4.3)	2.34 (0.51,10.68)	0.27
Emmetropia SE -0.5-0.5D	11 (45.8)	1662 (56.0)	1	
Myopia SE -0.5 - -2.9D	9 (37.5)	1121 (37.8)	1.21 (0.50,2.95)	0.67
Myopia SE ≤ -3.0D	1 (4.2)	37 (1.2)	4.08 (0.51,32.45)	0.13
Astigmatism (D)				
Mean (95%CI)	-1.26 (-1.70, -0.82)	-0.60 (-0.62, -0.58)	-	**<0.001**
Cylinder < 1.0D (%)	13 (54.2)	2453 (82.6)	1	
Cylinder 1.0-1.9D (%)	6 (25.0)	405 (23.6)	2.79 (1.05,7.39)	**0.04**
Cylinder ≥2.0D	5 (20.8)	110 (3.7)	8.57 (3.00,24.44)	**<0.001**
Anisometropia (D)				
Mean(95%CI)	0.51 (0.16,0.85)	0.22 (0.20,0.23)	-	**<0.001**
< 1.0D	21 (87.5)	2906 (98.0)	1	
1.0-1.9D	1 (4.2)	43 (1.5)	3.21 (0.42,24.47)	0.259
≥ 2.0D	2 (8.3)	15 (0.5)	18.45 (3.90,85.8)	**<0.001**
Amblyopia	3 (21.4)	16 (1.0)	28.1(7.1, 110.3)	**<0.001**

Table 4.16: Associations of family history (ie. parent or sibling with amblyopia or strabismus) with Amblyopia and Strabismus

4.16.1 Amblyopia

Family Factors	**Amblyopia N = 20 n (%)**	**No Amblyopia N = 1662 n (%)**	**OR (95% CI)**	**p-value**
Parent with amblyopia	0	80 (5)	-	0.32
Parent with strabismus	0	14	-	0.68
Sibling with amblyopia	2 (10)	38 (2.3)	4.66 (1.04, 20.78)	**0.03**
Sibling with strabismus	2 (10)	20 (1.2)	8.94 (1.95, 41.14)	**<0.001**

4.16.2. Amblyopia (including past history of amblyopia)

Family Factors	**Amblyopia N = 34 n (%)**	**No Amblyopia N = 1650 n (%)**	**OR (95% CI)**	**p-value**
Parent with amblyopia	3 (9.1)	78 (4.9)	(1.95 (0.58, 6.51)	0.22
Parent with strabismus	0	14 (0.9)	-	0.60
Sibling with amblyopia	15 (44.1)	27 (1.7)	46.52 (21.40, 101.1)	**<0.001**
Sibling with strabismus	3 (8.8)	19 (1.2)	8.14 (2.29, 28.96)	**0.01**

4.16.3. Strabismus

Family Factors	**Strabismus N = 24 n (%)**	**No Strabismus N = 2968 n (%)**	**OR (95% CI)**	**p-value**
Parent with amblyopia	3 (12.5)	145 (5.0)	2.69 (0.79, 9.11)	0.10
Parent with strabismus	1 (4.2)	21 (0.7)	5.91 (0.76, 45.76)	0.17
Sibling with amblyopia	3 (12.5)	55 (1.9)	7.41 (2.15, 25.57)	**0.01**
Sibling with strabismus	7 (29.2)	22 (0.8)	54.10 (20.37, 143.2)	**<0.001**

Table 4.17: Multivariate analysis: Risk factors for Amblyopia

4.17.1. Risk factors for Amblyopia: analysis including age, gender, factors which had a p<0.20 on univariate analysis (ie. maternal age, maternal hypertension, refractive error, strabismus, sibling of amblyopia or strabismus) and factors found to be relevant in literature review (ie. prematurity and socioeconomic status). Maternal smoking was omitted as no child with amblyopia had a mother who smoked during pregnancy.

		Odds Ratio (OR)	**95% C.I. for OR**		**P-value**
			Lower	**Upper**	
Age		0.95	0.89	1.00	**0.07**
Gender	- Girls	1.00			
	- Boys	2.33	0.75	7.2	0.141
Gestational Age (weeks)	> 37 weeks	1.00			
	≤ 37 weeks	1.05	0.30	3.73	0.93
Maternal Age		1.09	0.97	1.22	**0.14**
Paternal Education	- None/Primary	1.00			
	- Secondary/'O'	4.86	0.55	44.92	**0.16**
	- A'/Polytechnic/University	2.23	0.26	19.41	0.46
Refractive error	Myopia (≤ -3.0D)	23.75	4.03	139.7	**<0.001**
	Hyperopia (≥ 3.0D)	16.39	3.21	83.55	**<0.001**
	Astigmatism (≥ 1.0D)	10.31	3.06	34.35	**<0.001**
	Anisometropia (≥ 1.0D)	9.83	1.80	53.78	**0.008**
Concurrent strabismus		10.31	1.49	71.43	**0.018**
Sibling history of amblyopia		2.39	0.38	14.92	0.35
Sibling history of strabismus		6.18	0.52	74.05	**0.15**

Note: This table comprises one multivariate model in which each factor is adjusted for the other factor in this table. Care also taken that highly correlated variables eg. birth weight and gestational age; paternal/maternal education and house hold income were not placed in same model, and various combinations were analysis to determine most parsimonious match.

'O' : General certificate of education Ordinary level; 'A': General certificate of education Advanced level

4.17.2. Risk factors of Amblyopia: most parsimonious model after back-wise elimination of factors, adjusted for age, gender, prematurity (as represented by gestational age) and socioeconomic status (as represented by parental education)

		Odds Ratio (OR)	**95% C.I. for OR**		**P-value**
			Lower	**Upper**	
Age		0.95	0.90	1.00	0.09
Gender	Female	1.00			
	Male	2.05	0.68	6.13	0.20
Gestational age	>37weeks	1.00			
	< 37 weeks	1.14	0.33	3.95	0.828
Paternal education	- None/Primary	1.00			
	- Secondary/'O'	4.77	0.54	42.37	0.16
	- A'/Polytechnic/University	2.13	0.26	17.67	0.48
Refractive error	Myopia (SE $\leq$ -3.0D)	27.60	5.17	147.21	**<0.001**
	Hyperopia (SE $\geq$3.0D)	13.77	2.69	70.55	**0.002**
	Astigmatism ($\geq$ 1.0D)	8.94	2.81	28.46	**0.009**
	Anisometropia ($\geq$ 1.0D)	9.38	1.74	50.51	**<0.001**
Concurrent strabismus		14.54	2.18	96.8	**0.006**

Note: This table comprises one multivariate model in which each factor is adjusted for the other factor in this table. Care also taken that highly correlated variables eg. birth weight and gestational age; paternal/maternal education and house hold income were not placed in same model, and various combinations were analysed to determine most parsimonious match.

'O' : General certificate of education Ordinary level; 'A': General certificate of education Advanced level

Table 4.18: Multivariate analysis: Risk factors for Amblyopia (including past history of amblyopia)

4.18.1. Risk factors for Amblyopia (including past history of amblyopia): analysis including age, gender, factors which had a $p<0.20$ on univariate analysis (ie. maternal age, maternal hypertension, refractive error, strabismus, sibling of amblyopia or strabismus) and factors relevant in literature (ie. prematurity and socioeconomic status). Maternal smoking was omitted as no child with amblyopia had a mother who smoked.

		Odds Ratio (OR)	95% C.I. for OR		P-value
			Lower	Upper	
Age		1.00	0.95	1.05	0.93
Gender	- Girls	1.00			
	- Boys	1.85	0.70	4.85	0.21
Birth weight	> 2500g	1.00			
	≤ 2500g	1.88	0.44	8.00	0.39
Head circumference		0.91	0.66	1.25	0.57
Admission to NICU		3.53	0.84	14.85	0.85
Maternal Age		1.09	0.97	1.22	**0.14**
Paternal Education	- None/Primary	1.00			
	- Secondary/'O'	0.96	0.22	4.12	0.95
	- A'/Polytechnic/University	0.78	0.21	2.97	0.72
Refractive error	Myopia (≤ -3.0D)	6.89	1.16	41.00	**0.03**
	Hyperopia (≥ 3.0D)	8.89	1.90	41.67	**0.006**
	Astigmatism (≥ 1.0D)	8.30	3.12	22.11	**<0.001**
	Anisometropia (≥ 1.0D)	14.45	3.78	55.20	**<0.001**
Concurrent strabismus		10.31	1.49	71.43	**0.018**
Sibling history of amblyopia		50.62	16.39	156.37	**<0.001**
Sibling history of strabismus		0.57	0.05	5.45	0.62

Note: This table comprises one multivariate model whereeach factor is adjusted for other factors in this table. Care was not to place highly correlated variables eg. birth weight/gestational age; paternal/maternal education and house hold income in same model and, various combinations were analysed to determine most parsimonious match. 'O' : General certificate of education Ordinary level; 'A': General certificate of education Advanced level

4.18.2. Risk factors of Amblyopia (including past history of amblyopia): most parsimonious model after back-wise elimination of factors, adjusted for age, gender, prematurity (as represented by birth weight) and socioeconomic status (as represented by parental education)

		Odds Ratio (OR)	95% C.I. for OR		P-value
			Lower	Upper	
Age		1.00	0.96	1.05	0.99
Gender	Female	1.00			
	Male	1.98	0.77	5.12	0.15
Birth weight	>2500g	1.00			
	< 2500g	2.94	0.85	10.10	0.09
Paternal education	- None/Primary	1.00			
	- Secondary/'O'	1.28	0.31	5.37	0.74
	- A'/Polytechnic/University	1.01	0.27	3.82	0.99
Refractive error	Myopia (SE ≤ -3.0D)	8.22	1.29	52.31	**0.03**
	Hyperopia (SE ≥3.0D)	7.83	1.69	36.1	**0.008**
	Astigmatism (≥ 1.0D)	9.14	3.52	23.65	**<0.001**
	Anisometropia (≥ 1.0D)	12.50	3.31	47.16	**<0.001**
Concurrent strabismus		12.49	2.59	60.19	**0.002**
Sibling history of amblyopia		56.39	19.39	163.97	**<0.001**

Note: This table comprises one multivariate model in which each factor is adjusted for the other factor in this table. Care also taken that highly correlated variables eg. birth weight and gestational age; paternal/maternal education and house hold income were not placed in same model, and various combinations were analysed to determine most parsimonious match.

'O' : General certificate of education Ordinary level; 'A': General certificate of education Advanced level

Table 4.19: Multivariate analysis: Risk factors for Strabismus

4.19.1. Risk factors for Strabismus: analysis including age, gender, factors which had a p<0.20 on univariate analysis (ie. admission of NICU, refractive error, socioeconomic status, family history of strabismus /amblyopia) and factors relevant in literature (ie. prematurity and maternal age). Maternal smoking omitted as no child with strabismus had a mother who smoked.

		Odds Ratio (OR)	**95% C.I. for OR**		**P-value**
			Lower	**Upper**	
Age		1.01	0.95	1.07	0.72
Gender	- Girls	1.00			
	- Boys	1.68	0.44	6.37	0.45
Gestational Age (weeks)	> 37 weeks	1.00			
	≤ 37 weeks	0.71	0.12	4.06	0.70
Admission to NICU		1.51	0.17	13.27	0.79
Maternal Age		0.95	0.82	1.10	0.50
Paternal Education	- None/Primary	1.00			
	- Secondary/'O'	0.11	0.01	0.77	**0.03**
	- A'/Polytechnic/University	0.18	0.04	0.76	**0.02**
Refractive error	Myopia (≤ -0.5D)	0.38	0.01	11.27	0.58
	Hyperopia (≥ 0.5D)	3.28	0.25	43.56	0.37
	Astigmatism (≥ 1.0D)	5.66	1.47	21.84	**0.01**
	Anisometropia (≥ 1.0D)	1.46	0.07	31.27	0.81
Concurrent amblyopia		12.69	1.79	89.97	**0.01**
Parental history amblyopia		1.12	0.05	25.28	0.94
Parental history strabismus		47.76	1.89	1205.79	**0.02**
Sibling history of amblyopia		3.89	0.66	23.02	**0.13**
Sibling history of strabismus		44.46	8.54	231.36	**<0.001**

Note: This table comprises one multivariate model in which each factor is adjusted for the other factor in this table. Care also taken that highly correlated variables eg. birth weight and gestational age; paternal/maternal education and house hold income were not placed in same model, and various several combinations were analysed to determine most parsimonious match.

'O' : General certificate of education Ordinary level; 'A': General certificate of education Advanced level

Table 4.19.2: Risk factors for Strabismus: most parsimonious model after back-wise elimination of factors, adjusted for age, gender, prematurity (as represented by gestational age) and socioeconomic status (as represented by parental education)

		Odds Ratio (OR)	**95% C.I. for OR**		**p-value**
			Lower	**Upper**	
Age		1.02	0.96	1.08	0.63
Gender	-Girls	1.00			
	-Boys	1.82	0.50	6.66	0.36
Gestational Age (weeks)	>37 weeks	1.00			
	≤37 weeks	0.82	0.17	3.89	0.80
Father's Education	-None/Primary School	1.00			
	-Secondary/ 'O'	0.07	0.01	0.58	**0.01**
	-'A'/Polytechnic/University	0.23	0.06	0.89	**0.03**
Astigmatism	-Cylinder<1.0D	1.00			
	-Cylinder ≥1.0D	3.50	1.02	12.04	**0.04**
Concurrent amblyopia		15.89	2.72	92.84	**0.002**
Parent history of strabismus		17.92	1.15	278.31	**0.04**
Sibling history of strabismus		38.33	8.72	168.52	**<0.001**

This table comprises one multivariate model in which each factor is adjusted for the other factor in this table. Care also taken that highly correlated variables eg. birth weight and gestational age; paternal/maternal education and house hold income were not placed in same model, and various combinations were analysed to determine most parsimonious match.

NICU: neonatal intensive care unit, 'O' : General certificate of education Ordinary level; 'A': General certificate of education Advanced level

Table 4.20: Demographic, birth and ocular characteristics in children with different stereoacuity levels (1/2)

	Good 40-60sec (n=1034)	Fair 100-200sec (n=464)	Poor 400sec-none (n=30)	P -value	Unable Age<48m (n=410)	Unable Age≥48m (n=71)	P-value
Age (yr) (mean (sd))	57.5 (9.6)	49.4 (10.2)	47.9 (10.9)	**<0.001**	36.9 (4.7)	55.5 (7.2)	**<0.001**
Male (n, %)	519 (50.2%)	228 (49.1%)	17 (56.6%)	0.709	214 (52.2%)	44 (61.9%)	0.127
Birth weight (g) (mean (sd))	3107 (453)	3140 (459)	2943 (483)	**0.023**	3055 (473)	3012 (451)	0.494
Gestational age (wk) (mean (sd))	38.5 (1.5)	38.4 (1.5)	37.7 (1.7)	**0.026**	38.2 (1.6)	38.1 (1.6)	0.607
Spherical equivalent, SE (n,%)							
. Myopia (≤-1D) in at least 1 eye	41 (3.9%)	35 (7.5%)	4 (13.3%)		38 (9.2%)	9 (12.7%)	
. SE -1D to +2D in both eyes	930 (89.9%)	384 (82.8%)	23 (76.7%)	**<0.001**	337 (82.2%)	54 (76.1%)	0.471
. Hyperopia (≥+ 2D) in at least 1 eye	63 (6.1%)	45 (9.7%)	3 (10.0%)		35 (8.5%)	8 (11.2%)	
Anisometropia > 1D (n,%)	5 (0.5%)	14 (3.1%)	2 (6.7%)	**<0.001**	13 (3.2%)	5 (7.1%)	0.101
Astigmatism (n,%)							
. < 1.0D in both eyes	827 (80.0%)	300 (64.7%)	17 (56.7%)		315 (76.8%)	51 (71.8%)	
. 1.0-1.9D in at least 1 eye	167 (16.1%)	116 (25.0%)	7 (23.3%)	**<0.001**	67 (16.3%)	11 (15.5%)	0.233
. > 2.0D in at least 1 eye	40 (3.8%)	48 (10.3%)	6 (20.0%)		28 (6.8%)	9 (12.7%)	
Already wearing glasses	28 (2.7%)	15 (3.2%)	2 (6.7%)	0.408	1 (0.2%)	2 (2.8%)	0.011
Amblyopia (n, %)	3 (0.3%)	7 (1.5%)	5 (16.6%)	**<0.001**	4 (1.0%)	1 (1.4%)	0.101
Strabismus (n, %)	3 (0.3%)	3 (0.6%)	8 (26.6%)	**<0.001**	3 (0.7%)	2 (2.8%)	0.110

Table 4.20: Demographic, birth and ocular characteristics in children with different stereoacuity levels (2/2) ..continue

	Good 40-60sec (n=1034)	Fair 100-200sec (n=464)	Poor 400sec-none (n=30)	P-value	Unable Age<48m (n=410)	Unable Age≥48m (n=71)	P-value
Maternal age (yr) (mean (sd))	30.3 (4.2)	30.6 (4.6)	29.8 (5.5)	0.187	30.2 (4.8)	30.4 (5.5)	0.945
Maternal smoking (n,%)	24 (2.3%)	6 (1.3%)	0 (0%)	0.301	8 (2.0%)	1 (1.4%)	0.778
NICU admission (n,%)	59 (5.7%)	19 (4.2%)	6 (21.4%)	**0.005**	24 (5.9%)	4 (5.8%)	0.989
Breastfeeding (n,%)	773 (75.4%)	356 (77.2%)	19 (63.3%)	0.212	316 (77.8%)	40 (59.7%)	**0.001**
Monthly family income (n,%)							
. < $1000	24 (2.4%)	12 (2.7%)	0 (0%)		10 (2.5%)	6 (9.1%)	
. $1000-2999	213 (21.2%)	89 (20.0%)	10 (33.3%)	0.423	103 (25.7%)	22 (33.3%)	**0.013**
. $3000-4999	312 (31.1%)	131 (29.4%)	11 (36.7%)		128 (32.0%)	20 (30.3%)	
. >S5000	454 (45.3%)	213 (47.9%)	9 (30.0%)		159 (39.8%)	18 (27.3%)	
Paternal educational level (n,%)							
. Primary –none	98 (9.6%)	39 (8.6%)	6 (20.7%)		52 (13.1%)	11 (16.7%)	
. Secondary	318 (31.3%)	139 (31.0%)	10 (34.5%)	0.253	128 (32.2%)	23 (34.8%)	0.592
. College- tertiary	601 (59.1%)	271 (60.4%)	13 (44.8%)		217 (54.7%)	32 (48.5%)	
Maternal educational level (n,%)							
. Primary -none	67 (6.6%)	37 (8.1%)	4 (13.3%)		31 (7.7%)	17 (25.3%)	
. Secondary	379 (37.4%)	158 (34.7%)	15 (50.0%)	0.149	153 (37.9%)	24 (35.8%)	**<0.001**
. College- tertiary	568 (56.0%)	260 (57.2%)	11 (36.7%)		220 (54.4%)	26 (38.8%)	

Note: numbers in each cell may not add up to total due to missing data.

Table 4.21: Binary logistic regression analysis for factors associated with inability to do stereoacuity tests in children aged 30-47months and those aged 48-72months.

	Odds ratio	OR	95%CI	p
Age 30-47m:				
Age	Older	0.82	0.79-0.85	**<0.001**
Gender	Male	1.30	0.92-1.86	**0.013**
Paternal education	- GCE 'A'/polytechnic/tertiary	1.00		
	- secondary/GCE 'O'	1.30	0.92-1.86	**0.140**
	- none-primary	3.29	1.83-5.91	**<0.001**
Spherical equivalent	- Emmetropia (-1.0D to +2.0D)	1.00		
	- Hyperopia (≥2.0D) in at least 1 eye	2.54	1.32-4.89	**0.005**
	- Myopia (≤1.0D) in at least 1 eye	1.59	0.86–2.89	0.133
Birth weight	- ≥3000g	1.00		
	- <3000g	1.44	1.04-2.01	**0.030**
Aged 48-72m:				
Age	Older	0.90	0.87-0.94	**<0.001**
Anisometropia	- <1.0D	1.00		
	- 1.0D-1.9D	4.97	0.98-26.0	0.057
	- ≥2.0D	8.75	2.00-38.2	**0.004**
Maternal education	- GCE ' A'/polytechnic / tertiary	1.00		
	- secondary and GCE 'O	1.32	0.74-2.36	0.057
	- none-primary	5.21	2.00-38.2	**0.004**

Note: factors assessed and eliminated included child's gestational age, maternal age at child's birth, history of maternal smoking, history of breastfeeding, diagnosis of amblyopia or strabismus, presence of astigmatism, presence of child's pre-existing glasses wear and the household monthly income.

OR: Odds ratio; GCE: general certificate of education; 'O' level: ordinary level (equivalent to high school); 'A level': advanced level (equivalent to college).

Table 4.22: Ordered logistic analysis of factors which result in poorer stereoacuity in children able to co-operate with Randot preschool stereoacuity test; with stereoacuity graded from good (40-60sec) to fair (100-200sec) to poor (400sec to none).

	Odds ratio	OR	95%CI	p
Age	Older	0.91	0.91-0.93	**<0.001**
Anisometropia	- <1.0D	1.00		
	- 1.0-1.9D	1.23	0.37-4.07	0.736
	- ≥ 2.0D	12.35	2.58-59.07	**0.002**
Astigmatism	- <1.0D in both eyes	1.00		
	- 1.0-1.9D in at least 1 eye	1.57	1.18-2.08	**0.002**
	- ≥ 2.0D in at least 1 eye	3.15	2.00-4.95	**<0.001**
Spherical equivalent	- Emmetropia (-1.0D to +2.0D)	1.00		
	- Hyperopia (≥2.0D) in at least 1 eye	1.71	1.12-2.62	**0.014**
	- Myopia (≤1.0D) in at least 1 eye	1.20	0.70-2.04	0.507
Amblyopia		6.33	1.81-20.93	**0.002**
Strabismus		37.69	10.98-129.42	**<0.001**
Maternal education	- GCE 'A'/polytechnic/tertiary	1.00		
	- secondary/GCE 'O'	1.08	0.84-1.39	0.554
	- none-primary	1.76	1.12-2.78	**0.015**

OR: odds ratio

Table 4.23: Area under the curve (auc) for Receiving Operator curves in the detection of ocular disease using stereoacuity as the classification variable.

	Area under curve	95% confidence intervals	Cut-off for specificity >90%	PPV
Amblyopia	0.775	0.631 – 0.920	200s	17%
Strabismus	0.823	0.658 - 0.988	200s	27%
Anisometropia $\geq$ 1.0D	0.750	0.627 – 0.872	200s	7%
Anisometropia $\geq$ 2.0D	0.836	0.723 – 0.549	200s	7%
Astigmatism $\geq$ 1.0D	0.617	0.588 – 0.646	200s	47%
Astigmatism $\geq$ 2.0D	0.674	0.627 – 0.721	200s	20%
Hyperopia $\geq$ 2.0D	0.553	0.497 – 0.609	200s	7%
Myopia $\leq$ -1.0D	0.623	0.564 – 0.681	200s	14%
Refractive error (astig $\geq$2D, aniso $\geq$2D)	0.697	0.651 - 0.743	200s	27%
Refractive error plus amblyopia/strabismus	0.688	0.642 – 0.733	200s	43%

Note: PPV: positive predictive value

Table 4.24: Sensitivity and Specificity of Randot Preschool Stereoacuity Test in detection of eye disorders.

Cut-off	Amblyopia Sen /Spec(LR+/LR-)	Strabismus Sen /Spec(LR+/LR-)	Anisometropia ≥1D Sen /Spec(LR+/LR-)	Anisometropia ≥2D Sens /Spec(LR+/LR-)
40	1.00/0.00 (1.0/-)	1.00/ 0.00 (1.0/-)	1.00/ 0.00 (1.0/-)	1.00/0.00 (1.0/-)
60	0.86/0.31 (1.3/0.4)	0.86/ 0.31 (1.2/0.5)	0.86/0.31 (1.2/0.5)	1.00/0.31 (1.3/0.0)
100	0.80/0.68 (2.5/0.3)	0.79/ 0.68 (2.5/0.3)	0.76/0.68 (2.4/0.3)	0.87/0.68 (2.7/0.2)
200	0.40/0.95 (7.7/0.6)	0.71/ 0.95 (14.4/0.3)	0.38/0.95 (7.5/0.7)	0.38/0.95 (6.9/0.7)
400	0.33/0.98 (20.2/0.7)	0.57/ 0.98 (39.3/0.4)	0.10/0.98 (5.1/0.9)	0.25/0.98 (13.6/0.9)
800	0.27/0.99 (22.8/0.7)	0.36/0.99 (67.6/0.6)	0.05/0.99 (6.0/0.9)	0.13/0.99 (15.8/0.9)
none	0.20/1.00 (75.7/0.8)	0.36/1.00 (270.4/0.6)	0.00/0.99 (0.0/1.0)	0.00/0.99 (0.0/1.0)
	Astigmatism ≥1.D Sen /Spec(LR+/LR-)	Astigmatism ≥2D Sen /Spec(LR+/LR-)	Hyperopia >2D Sen /Spec(LR+/LR-)	Myopia (≤-1D) Sen / Spec
40	1.00/0.00 (1.0/-)	1.00/0.00 (1.0/-)	1.00/0.00 (1.0/-)	1.00/0.00 (1.0/-)
60	0.82/0.35 (1.3/0.5)	0.90/0.32 (1.3/0.3)	0.72/0.31 (1.0/0.9)	0.85/0.31 (1.2/0.5)
100	0.44/0.73 (1.6/0.8)	0.58/0.70 (1.9/0.6)	0.43/0.69 (1.4/0.8)	0.49/0.69 (1.6/0.7)
200	0.07/95.1 (1.4/0.9)	0.10/0.95 (2.0/0.9)	0.09/0.95 (1.7/0.9)	0.13/0.95 (2.4/0.9)
400	0.03/0.98 (2.2/1.0)	0.06/0.98 (3.4/0.9)	0.03/0.98 (1.4/1.0)	0.05/0.98 (2.8/1.0)
800	0.02/0.99 (3.0/1.0)	0.03/0.99 (4.1/1.0)	0.01/0.99 (1.1/1.0)	0.03/0.99 (3.3/1.0)
none	0.01/1.00 (3.4/1.0)	0.02/0.99 (5.4/1.0)	0.00/1.00 (0.0/1.0)	0.01/1.00 (3.0/1.0)
	Refractive error (astig ≥2D, aniso ≥2D) Sen / Spec (LR+/LR-)		Refractive error plus amblyopia/strabismus Sen / Spec (LR+/LR-)	
40	1.00 / 0.00 (1.0/-)		1.00 / 0.00 (1.0/-)	
60	0.89 / 0.32 (1.3/0.3)		0.91 / 0.32 (1.3/0.3)	
100	0.61 / 0.70 (2.1/0.6)		0.60 / 0.70 (2.0/0.6)	
200	0.18 / 0.96 (3.9/0.9)		0.13 / 0.95 (2.5/0.9)	
400	0.10 / 0.99 (8.7/0.9)		0.07 / 0.98 (4.6/0.9)	
800	0.06 / 0.99 (18.1/0.9)		0.04 / 0.99 (5.7/1.0)	
none	0.05 / 1.00 (67.9/0.9)		0.02 / 1.00 (5.1/1.0)	

Table 4.25: Area under the curve (auc) for Receiving Operator curves in the detection of ocular disease using refractive error as the classification variable; with cut-off for best balance sensitivity/specificity, and for specificity >90% (1/2)

	Area under curve	95% confidence intervals	Cut-off	Sen /Spec (LR+/LR-)	Cut-off when specificity >90%	Sen /Spec (LR+/LR-)	PPV
VA <20/40 in at least 1 eye							
- Anisometropia	0.532	0.502 - 0.563	1.0D	0.17 / 0.89 (1.5/0.9)	1.5D	0.06/0.98 (3.9/0.9)	44%
- Asisometropic astigmatism	0.614	0.575 – 0.653	1.0D	0.38/0.84 (2.3/0.7)	1.5D	0.13/0.97 (4.6/0.9)	32%
- Hyperopia	0.523	0.467 – 0.580	1.5D	0.56/0.45 (1.0/0.9)	2.0D	0.15/0.91 (1.7/0.9)	33%
- Myopia	0.583	0.520 – 0.646	-2.0D	0.36/0.79 (1.7/0.8)	-3.0D	0.13/0.96 (2.6/0.9)	44%
- Astigmatism	0.703	0.659 – 0.748	1.5D	0.58 / 0.75 (2.3/0.6)	2.0D	0.40/0.90 (4.1/0.6)	35%
VA ≤20/50 in at least 1 eye							
- Anisometropia	0.571	0.519 – 0.623	1.0D	0.25/0.89 (2.2/0.8)	1.5D	0.08/0.99 (5.6/0.9)	38%
- Anisometropic astigmatism	0.705	0.644 – 0.766	1.0D	0.56 / 0.83 (3.3/0.5)	1.5D	0.22/0.97 (7.7/0.8)	26%
- Hyperopia	0.503	0.421 – 0.585	1.5D	0.52/0.45 (0.9/1.0)	2.0D	0.15/0.91 (1.6/0.9)	15%
- Myopia	0.677	0.577 – 0.777	-2.0D	0.53 / 0.78 (2.5/0.6)	-3.0D	0.27/0.95 (5.8/0.7)	38%
- Astigmatism	0.748	0.688 – 0.808	1.5D	0.67 / 0.74 (2.6/0.4)	2.5D	0.28/0.94 (4.6/0.7)	20%

Sen: Sensitivity, Spec: Specificity, LR+: positive likelihood ratio, LR-: negative likelihood ratio, PPV: positive predictive value

Table 4.25: Area under the curve (auc) for Receiving Operator curves in the detection of ocular disease using refractive error as the classification variable; with cut-off for best balance sensitivity/specificity, and for specificity >90%. (2/2)

	Area under curve	95% confidence intervals	Cut-off	Sen /Spec (LR+/LR-)	Cut-off when specificity >90%	Sen /Spec (LR+/LR-)	PPV
Amblyopia							
- Anisometropia	0.725	0.610 – 0.841	1.0D	0.55 / 0.86 (4.8/0.5)	1.5D	0.20/0.99 (14.2.0.8)	23%
- Anisometropic astigmatism	0.821	0.714 – 0.929	1.0D	0.75 / 0.82 (4.3/0.3)	1.5D	0.50/0.97 (16.0/0.5)	26%
- Hyperopia	0.628	0.444 – 0.812	1.5D	0.33 / 0.91 (3.6/0.7)	2.0D	0.33/0.91 (3.6/0.7)	12%
- Myopia	0.777	0.583 – 0.972	-3.0D	0.56 / 0.95 (10.6/0.5)	-3.0D	0.56/0.95 (10/0.5)	36%
- Astigmatism	0.876	0.804 – 0.948	2.0D	0.70 / 0.88 (5.6/0.3)	2.5D	0.65/0.94 (10.5/0.4)	13%
Strabismus							
- Anisometropia	0.588	0.491 – 0.685	1.0D	0.29 / 0.87 (2.3/0.8)	1.5D	0.12/0.98 (6.4/0.9)	12%
- Anisometropic astigmatism	0.607	0.515 – 0.709	1.0D	0.37/0.83 (2.2/0.7)	1.5D	0.13/0.97 (4.5/0.9)	0%
- Hyperopia	0.511	0.371 – 0.652	2.0D	0.21 / 0.89 (1.9/0.9)	3.0D	0.11/0.98 (5.5/0.9)	6%
- Myopia	0.650	0.443 – 0.857	-2.0D	0.57 / 0.72 (2.0/0.6)	-3.0D	0.14/0.94 (2.3/0.9)	4%
- Astigmatism	0.687	0.571 – 0.803	1.5D	0.54/0.75 (2.2/0.6)	2.5D	0.25/0.94 (4.6/0.8)	5%

Sen: Sensitivity, Spec: Specificity, LR+: positive likelihood ratio, LR-: negative likelihood ratio, PPV: positive predictive value

Table 4.26: PedsQL4 scores adjusted for age, gender and socioeconomic status in children with and without strabismus and amblyopia

	No strabismus (n 1902) Mean (95%CI)	Strabismus (n 22) Mean (95%CI)	P^1	Unable to assess (n 12) Mean (95%CI)	P^2
Physical HSS	98.0 (97.7-98.2)	97.2 (95.2-99.2)	0.30	96.5 (91.8-101.2)	0.43
Emotional function	93.0 (93.3-94.3)	90.3 (85.9-94.7)	0.65	93.4 (84.7-102.1)	0.97
School function	94.4 (93.8-94.9)	95.1 (90.3-99.8)	0.82	84.3 (68.5-100.0)	**0.01**
Social function	98.2 (97.9-98.5)	99.6 (97.1-102.2)	0.36	88.9 (75.9-101.9)	**<0.001**
Psychological HSS	95.6 (95.3-95.9)	94.8 (92.0-97.7)	0.48	89.7 (80.6-98.8)	**0.03**
Total score	96.5 (96.2-96.7)	95.7 (93.5-98.0)	0.34	92.1 (85.5-98.8)	**0.04**
	No Amblyopia (n 1437) Mean (95%CI)	Amblyopia (n19) Mean (95%CI)	P^3	Unable to assess (n 285) Mean (95CI)	P^4
Physical HSS	97.9 (97.7-98.2)	99.1 (96.9-101.2)	0.30	98.1 (97.5-98.6)	0.68
Emotional function	93.7 (93.2-94.3)	94.8 (90.1-99.5)	0.65	94.3 (92.9-95.2)	0.39
School function	94.2 (93.6-94.8)	94.7 (90.0-99.5)	0.82	95.9 (94.3-96.9)	**0.04**
Social function	98.3 (97.9-98.6)	99.6 (96.7-102.4)	0.36	98.0 (96.9-98.6)	0.59
Psychological HSS	95.5 (95.1-95.8)	96.6 (93.5-99.6)	0.48	96.1 (95.1-96.6)	0.12
Total score	96.4 (96.1-96.7)	97.6 (95.1-100.0)	0.34	96.9 (96.1-97.6)	0.11

Note: p: p-value. p^1 is comparison between non-strabismus and strabismus children, and p^2 is comparison between non-strabismus children and those who could not be assess for strabismus. p^3 is comparison between non-amblyopia and amblyopia children, and p^4 is comparison between non-amblyopia children and those who could not be assess for amblyopia.

Table 4.27: Problems reported in childhood development survey in children with or without amblyopia and strabismus.

Problems with		No Amblyopia (n 1437)	Amblyopia (n19)	p	No Strabismus (n 1904)	Strabismus (n22)	p
Development	Yes	80 (5.5)	0	0.15	106 (5.6)	2 (9.0)	0.93
	A little	126 (8.7)	0		159 (8.4)	2 (9.0)	
	No	1226 (85.3)	19 (100)		1633 (85.9)	18 (82.0)	
Speech	Yes	48 (3.3)	0	0.11	72 (3.8)	4 (18.0)	**0.001**
	A little	67 (4.6)	1 (5.3)		99 (5.2)	0	
	No	1309 (91.1)	18 (94.7)		1721 (90.4)	18 (82.0)	
Comprehension	Yes	6 (0.4)	0	0.42	9 (0.5)	0	**<0.001**
	A little	12 (0.8)	1 (5.3)		18 (0.9)	2 (9.0)	
	No	1406 (97.8)	18 (94.7)		1862 (97.8)	20 (91.0)	
Fine Motor skills	Yes	9 (0.6)	0	0.76	11 (0.5)	1 (4.5)	0.21
	A little	8 (0.6)	0		13 (0.7)	0	
	No	1411 (98.1)	19 (100)		1869 (98.1)	21 (95.5)	
Gross Motor skills	Yes	9 (0.6)	0	0.39	11 (0.6)	0	0.47
	A little	9 (0.6)	0		13 (0.7)	0	
	No	1407 (97.9)	19 (100)		1862 (97.8)	22 (100)	
Behavior	Yes	178 (12.3)	2 (10.5)	0.77	246 (13.9)	2 (9.0)	0.93
	A little	278 (19.3)	4 (21.0)		370 (19.4)	4 (18.0)	
	No	972 (67.6)	13 (68.4)		1277 (66.9)	16 (73.0)	
Social functioning	Yes	34 (2.3)	0	0.36	48 (2.5)	0	**0.003**
	A little	72 (5.0)	1 (5.3)		105 (5.5)	0	
	No	1317 (91.6)	18 (94.7)		1734 (90.9)	22 (100)	
Learning	Yes	14 (0.9)	0	-	19 (1.0)	1 (4.5)	0.06
	A little	20 (1.4)	0		36 (1.9)	1 (4.5)	
	No	1391 (96.8)	19 (100)		1832 (96.1)	20 (91.0)	
Preschool skills	Yes	29 (2.0)	0	**<0.001**	37 (1.9)	0	0.13
	A little	72 (5.0)	0		79 (4.1)	1 (4.5)	
	No	1261 (87.7)	19 (100)		1533 (80.4)	16 (72.7)	
Other	Yes	197 (13.7)	5 (26.3)	0.44	255 (13.4)	6 (27.3)	0.09
	A little	179 (12.4)	3 (15.8)		231 (13.5)	5 (22.7)	
	No	1048 (72.9)	11 (57.9)		1403 (82.1)	11 (50.0)	

Note: numbers of subject in each column may not add up because of missing data. In all groups, missing date accounted for <0.5% except in the pre-school skills group where 13% of parents either declined to answer or felt that the question was not applicable.

Table 4.28: Performance summary of the PedsQL4 using Rasch analysis in the Amblyopia population (n=1936)

Functioning	Physical	Emotional	Social	School		Psychological	
				25-48mths	49-72mths	25-48mths	49-72mths
Number of items	8	5	5	3	5	13	13
Number of question/response category formats	5	5	5	5	5	5	5
Number of response categories needing reordering	2	1	1	None	None	1	2
Number of misfitting items	0	1	0	All	0	1	1
Misfitting items	N/A	Q11	N/A	Q19-Q21	N/A	Q12	Q18
Person separation index, person reliability	Near 0	Near 0	Near 0	1.06, 0.53	Near 0	Near 0	Near 0
Targeting - Mean ±SD person measure (logits)	5.43±0.54	5.31±1.25	3.99±0.70	12.32±3.44	4.53±1.01	6.13±1.12	4.82±0.96
Principal Component Analysis – raw variance by first contrast: eigenvalue (%)	34.3%:1.6	43.3%:1.8	30.2%:1.6	74.4%:3.0	28.5%:1.5	40.9%:1.7	21.4%:1.6
Loading items (>0.4) removed	0	0	0	0	0	4 (Q16, Q18, Q20, Q21)	5 (Q9, Q10, Q11, Q23, Q24)

Table 4.29.Performance summary of the PedsQL4 using Rasch analysis in the Strabismus population (n=1742)

Functioning	Physical	Emotional	Social	School		Psychological	
				25-48mths	49-72mths	25-48mths	49-72mths
Number of items	8	5	5	5	5	13	13
Number of question/response category formats	5	5	5	5	5	5	5
Number of response categories needing reordering	2	1	1	None	None	1	2
Number of misfitting items	0	1	1	All	0	2	4
Misfitting items	N/A	Q11	Q18 (not removed)	Q22-Q26	N/A	Q17, Q12	Q9, Q10, Q23, Q24
Person separation index, person reliability	Near 0	Near 0	Near 0	Near 0	Near 0	Near 0	Near 0
Targeting - Mean ±SD person measure (logits)	5.01±0.97	5.26±1.25	4.31±0.54	4.21±0.37	4.55±1.04	6.36±1.47	5.00±1.09
Principal Component Analysis – raw variance by first contrast: eigenvalue (%)	34.4%:1.6	43.1%:1.8	23.8%:1.6	57.4%:1.8	28.7%:1.5	41.2%:1.7	22.9%:1.6
Loading items (>0.4) removed	0	0	0	0	1 (Q23)	0	1 (Q18)

Table 4.30A: Difference in Rasch score between children with and without Strabismus adjusted for age, gender and socioeconomic group

	No strabismus (n 1902) Mean (95%CI)	Strabismus (n 22) Mean (95%CI)	P[1]	Unable to assess (n 12) Mean (95%CI)	P[2]
Physical HSS	5.01 (4.97-5.05)	4.85 (4.43-5.25)	0.425	4.83 (4.25-5.41)	0.543
Emotional	5.26 (5.20-5.32)	4.88 (4.35-5.41)	0.165	5.21 (4.46-5.96)	0.898
Social	4.30 (4.27-4.33)	4.46 (4.22-4.70)	0.211	3.84 (3.50-4.18)	**0.009**
School					
- 24-48months	4.19 (4.09-4.30)	4.27 (3.31-5.22)	0.877	4.19 (2.85-5.54)	0.997
- 49-72months	4.53 (4.47-4.59)	5.16 (4.54-5.78)	**0.049**	2.39 (1.41-3.37)	**<0.001**
Psychological HSS					
- 24-48months	6.35 (6.25-6.45)	6.02 (5.17-6.86)	0.443	6.35 (5.25-7.45)	0.993
- 49-72months	5.01 (4.94-5.08)	5.44 (4.77-6.11)	0.215	3.44 (2.49-4.39)	**<0.001**

P1: p-value between no strabismus and strabismus, p2: p-value between no strabismus and unable to assess group

Table 4.30B: Difference in Rasch score between children with and without Strabismus and Amblyopia adjusted for age, gender and socioeconomic group

	No Amblyopia (n 1437) Mean (95%CI)	Amblyopia (n19) Mean (95%CI)	P[3]	Unable to assess (n 285) Mean (95%CI)	P[4]
Physical HSS	4.99 (4.94-5.04)	5.26 (4.82-5.69)	0.231	5.06 (4.93-5.19)	0.341
Emotional	5.28 (5.22-5.35)	5.40 (4.82-5.98)	0.715	5.32 (5.14-5.49)	0.788
Social	4.31 (4.28-4.34)	4.46 (3.81-5.12)	0.646	4.25 (4.18-4.33)	0.216
School					
- 24-48months	12.19 (11.82-12.56)	11.84 (9.21-14.47)	0.797	12.65 (12.00-13.30)	0.243
- 49-72months	4.53 (4.46-4.60)	4.64 (3.98-5.30)	0.742	4.16 (3.69-4.64)	0.135
Psychological HSS					
- 24-48months	6.19 (6.07-6.30)	6.29 (5.58-7.01)	0.770	5.98 (5.83-6.14)	0.053
- 49-72months	4.82 (4.76-4.89)	5.07 (4.44-5.70)	0.437	4.43 (3.99-4.87)	0.084

P3: p-value between no amblyopia and amblyopia, p2: p-value between no amblyopia and unable to assess group

Table 5.1: Comparison of STARS, MEPEDS, BPEDS and SPEDS studies

	STARS	MEPEDS	BPEDS	SPEDS
Prevalence Amblyopia	Chinese 1.19 (0.73-1.83)	Hispanic Latino: 2.6 (1.8-3.4) African American: 1.5 (0.9-2.1)	White: 1.8 (0.9-3.1) African American: 0.8 (0.3-1.6)	Australian (mix) 1.9
Strabismus	Chinese 0.80 (0.51-1.19)	Hispanic Latino: 2.4 (1.9-3.0) African American: 2.5 (2.0-3.1)	White: 2.1 (1.3-3.0) African American: 3.3 (2.3-4.6)	-
Risk associations Amblyopia	Strabismus, Anisometropia≥1D, Astigmatism ≥1D.	-		Strabismus, Hyperopia≥2D, Anisometropia≥1D, Astigmatism ≥1D.
Strabismus	Sibling with strab, Astigmatism≥1.0D, Amblyopia, Lower paternal education	Prematurity, Hyperopia ≥2D, Anisometropia≥1.5D for ET, Astigmatism ≥1.5D for XT, Child > 48months for ET, female for XT.		-

Table 5.2: Odd ratios required to achieve significance (calculated using PS version 3.0.43; http://biostat.mc.vanderbilt.edu/PowerSampleSize)

	MEPEDS presuming cases 3%		STARS if cases 3%	STARS if cases 1%, and with variable of exposure in controls			
Cases	360 (3%)	360 (3%)	120 (3%)	30 (1%)	30 (1%)	30 (1%)	30 (1%)
Controls	11640	11640	2880	2970	2970	2970	2970
Alpha	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Power	0.80	0.80	0.80	0.80	0.80	0.80	0.80
Exposure in controls	0.20	0.10	0.20	0.20	0.10	0.05	0.02
OR	1.43	1.57	2.12	2.90	3.46	4.45	6.80

Note: MEPEDS: Multiethnic Pediatric Eye Disease Study; OR: odds ratio

Table 5.3: Risk factor exposure within different population/cohort studies
(as estimated from data provided in published literature).

Prevalence	STARS	MCS	SMS	ALSPAC	CPP	MEPEDS
Country	Singapore	UK	Australia	UK	Europe	US
BW < 2500g	8%	7%	5%	3%	13%	-
GA < 37wks	21%	9%	7%	6%	-	9%
Admission to NICU	6%	9%	5%	-	-	-
Maternal smoking	2%	9%	11%	18%	50%	9%
Maternal alcohol	1%	18%	-	-	-	-
Maternal age >35	13%	16%	-	-	9%	13%
Family with strabismus	1%	-	-	16%	-	6%
Family with amblyopia	2%	-	-	(famHx)	-	1%

Note: STAR: Strabismus, Amblyopia and Refractive Error in Singaporean Preschoolers Study; MCS: Millennium Cohort Study; SMS: Sydney Myopia study; ALSPAC: Avon Longitudinal Study of Parents and Children; CPP: Collaborative Prenatal Project of the National Institute of Neurological Disorders and Stroke; MEPEDS: Multiethnic Pediatric Eye Disease Study; BW: birth weight, GA: gestational age, NICU: neonatal intensive care unit

Table 5.4: Screening Programs in different countries

Country	Age (year)	Type of visual screening test	Person applying test
Singapore	Infancy	General eye check	Doctors
	4-16 years	Visual acuity	Nurses
	6 years	Cover test, Color test, Firsby near stereoacuity	Nurses
USA (variable according to state)	0-2 years	General eye check +/- Bruckners, cover test, visual acuity, refraction	Doctors, orthoptists, nurses
	4-5 years	Visual acuity +/- cover test, stereopsis, refraction	Orthoptists, nurses
	6-8 years	Visual acuity, refraction, ocular motility	Orthoptists, nurses
Canada	Infancy	General eye check	Doctors
	4.5-5.5 years	Visual acuity, ocular alignment, stereoactuiy	Nurses
UK	3.5-4.5 years	General eye check, Hirschberg, cover test, visual acuity	Orthoptist
Australia	Infancy, 0.5, 1.5, 2 and 3.5 years	General eye check+/- Hirschberg, Bruckner, cover test or parental questionnaire	Doctors/Orthoptist/Nurses
	3.5-5, 6-12 years	Visual acuity	Orthoptic/Nurses
Sweden, Denmark	Infancy, 0.5, 1.5, 2 and 3 years	General visual and behaviour check	Doctors/Nurses
	4, 5.5, 7, 10 years	Visual acuity	Nurses
Korea, Japan, Taiwan	4 years	Visual acuity (home-visual screening kit)	Parents

Figure 3.1: Study population as located on the Singapore map

Figure 3.2: The Strabismus, Amblyopia, Refractive Error in Singaporean Preschoolers (STARS) Study process

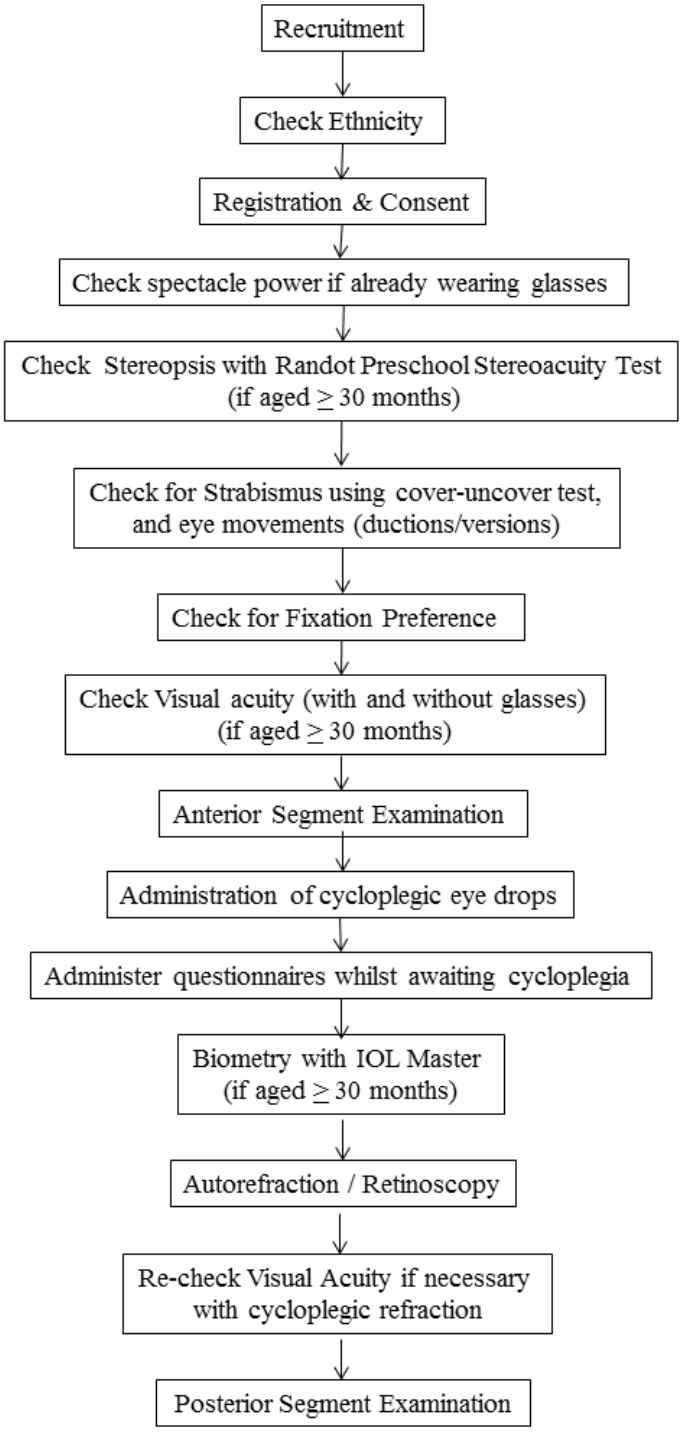
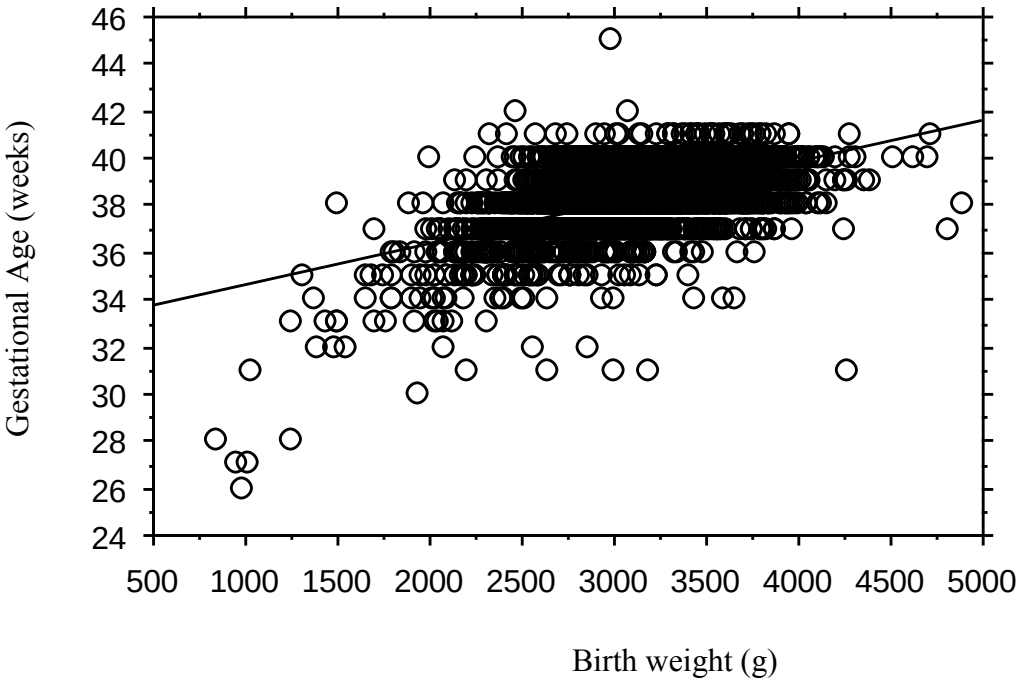


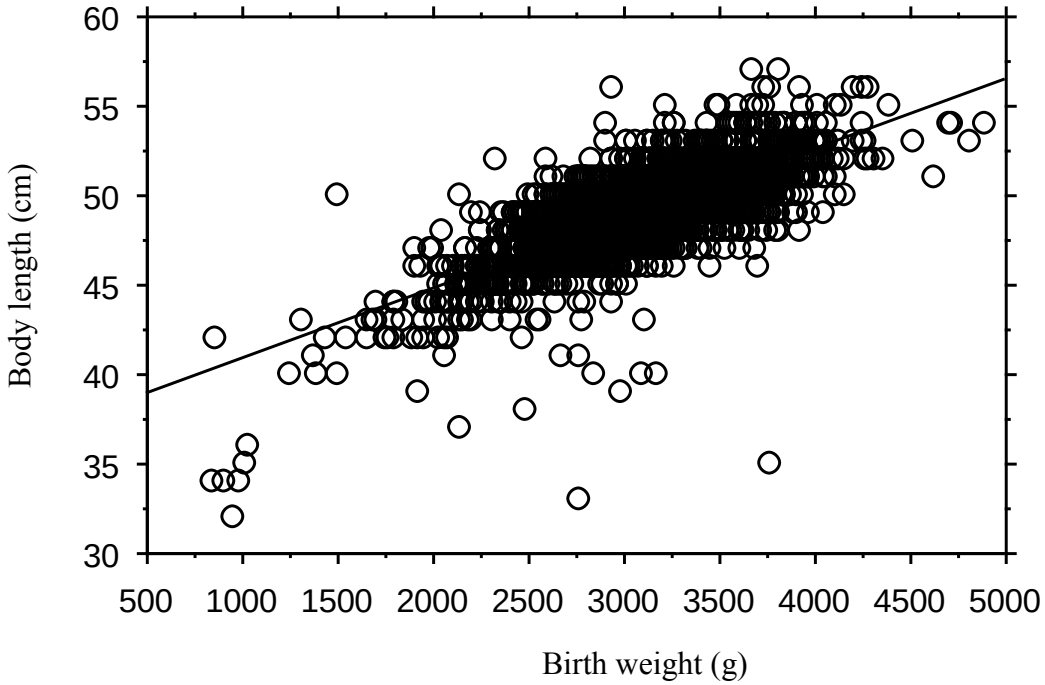
Figure 4.1: Scatterplots of Birth-weight (BW) vs Gestational Age (GA), Body-Length (BL) and Head Circumference (HC) at birth.

4.1.1: Birth-weight versus Gestational Age



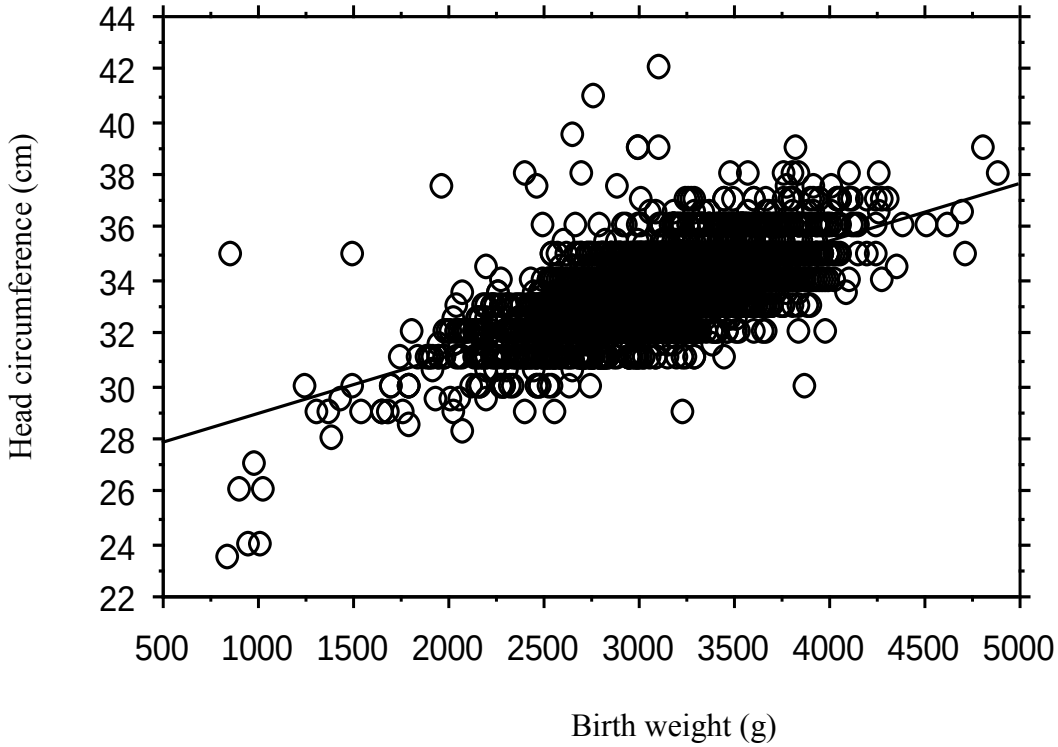
GA= 32.98 +0.002 BW, R2=0.271

4.1.2: Birth-weight versus Body Length at birth



BL=39.1+0.004BW, R2=0.55

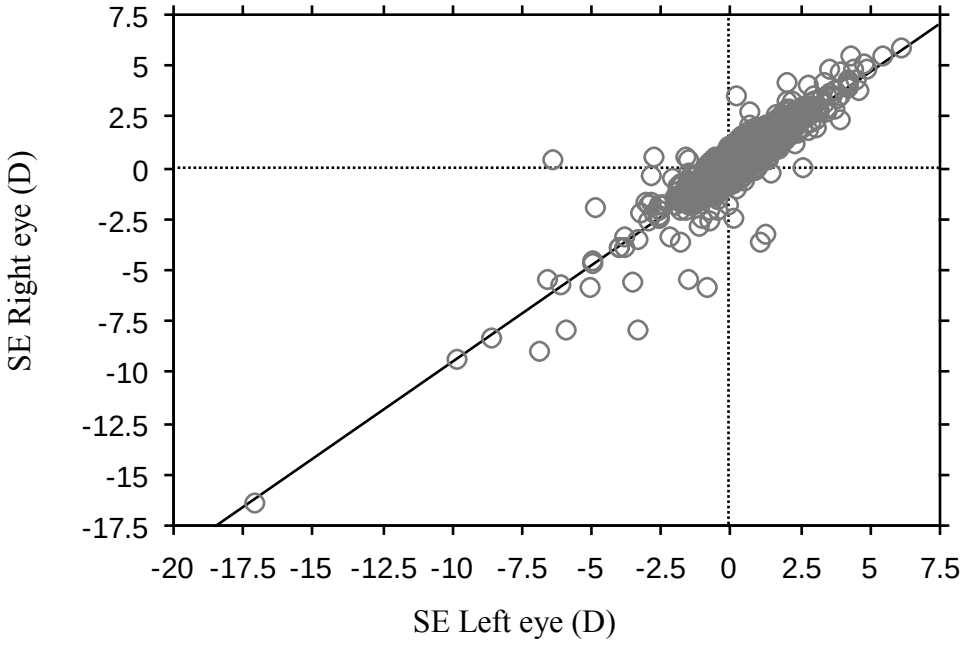
4.1.3: Birth-weight versus Head Circumference at birth



HC=26.8+0.002BW; R2=0.42

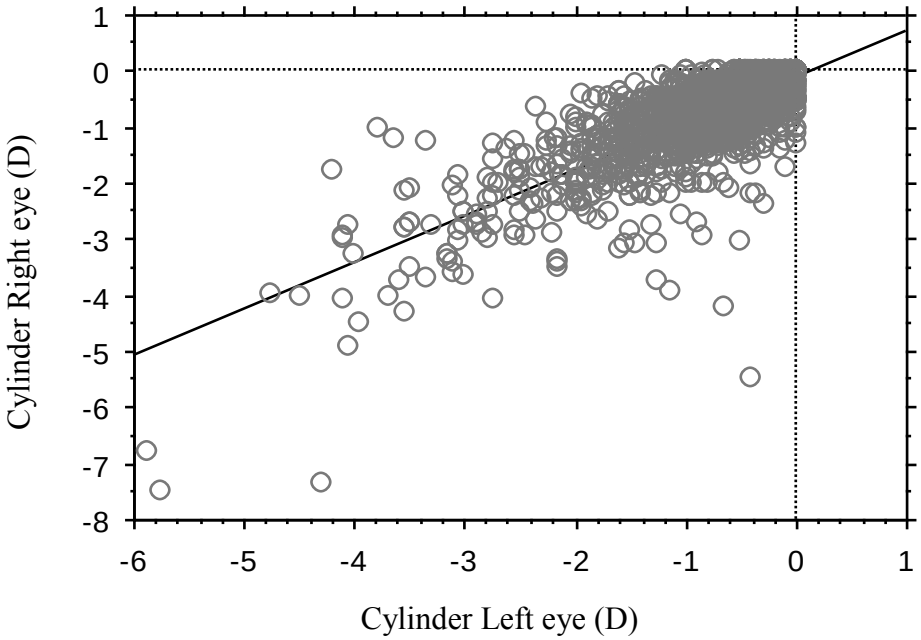
Figure 4.2: Scatterplot of Refractive Errors between Right and Left Eyes

4.2.1: Spherical Equivalent of Right and Left Eyes



SE RE=0.015+0.95SE LE, R2=0.87

4.2.2: Cylindrical Power of Right and Left Eyes



Cyl RE=0.11+0.83CylLE; R2=0.66

Figure 4.3: Stereoacuity levels in children, as measured by Randot Preschool Stereoacutiy Test, within different age groups

Figure 4.3.1: All children who were tested (including those unable to do test)

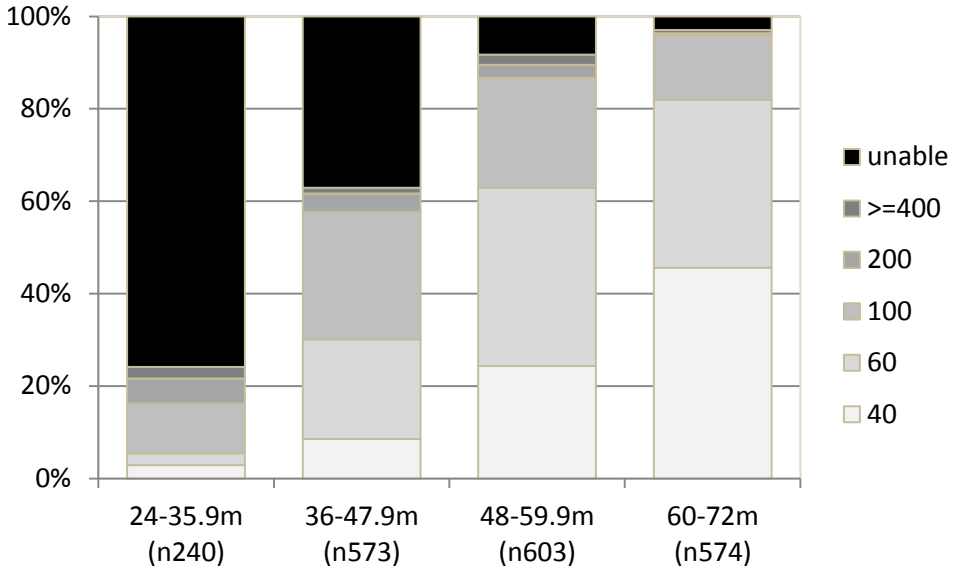


Figure 4.3.2: Stereoacuity levels in children able to perform Randot Preschool Stereoacuity Test

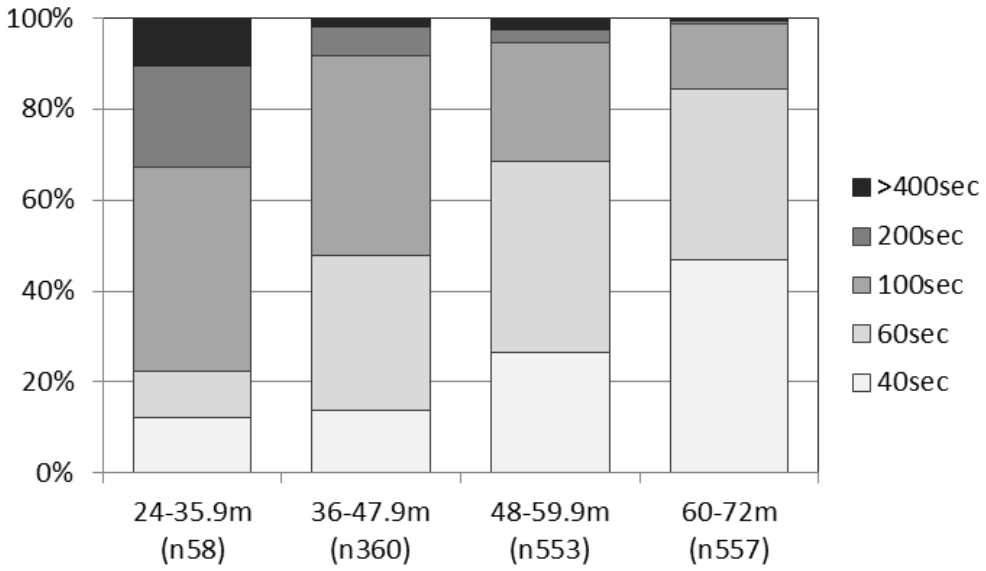


Figure 4.4: Stereoacuity levels in children able to perform test with different ocular abnormalities compared to normal children (without amblyopia, strabismus, anisometropia, high ametropia or astigmatism).

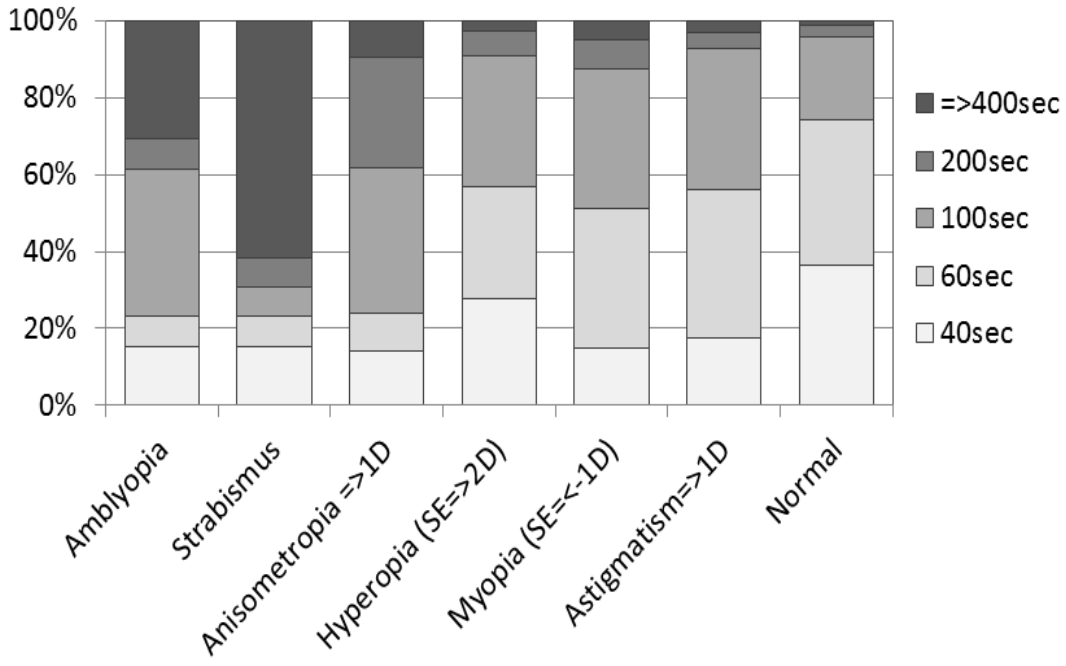


Figure 4.5.1. Receiver Operator Characteristics (ROC) curves with stereoacuity cut-offs of 40, 60, 100, 200, 400, 800 seconds and no stereoacutiy for detection of amblyopia and strabismus.

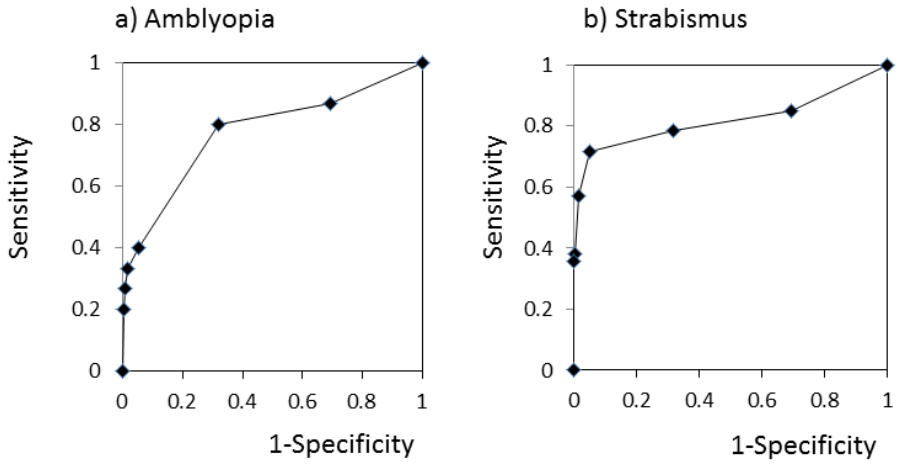
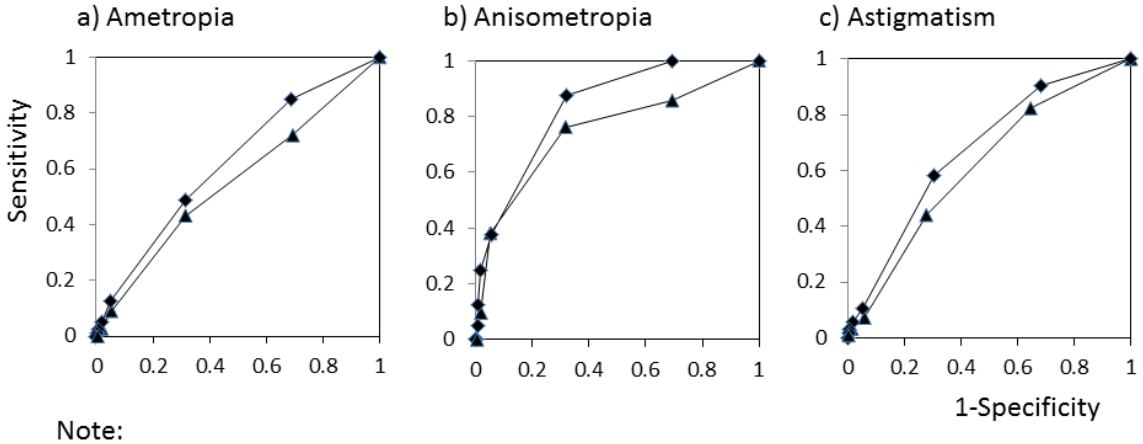


Figure 4.5.2. Receiver Operator Characteristics (ROC) curves with stereoacuity cut-offs of 40, 60, 100, 200, 400, 800 seconds and no stereoacuity for detection of refractive errors.



Note:

a) Triangles denotes hyperopia ≥ +2.0D in at least 1 eye. Diamonds denotes myopia ≤ -1.0D in at least 1 eye.
b) Triangles denotes anisometropia ≥ 1.0D. Diamonds denotes anisometropia ≥ 2.0D.
c) Triangles denotes astigmatism ≥ 1.0D. Diamonds denotes astigmatism ≥ 2.0D.

Figure 4.6.1.Receiver Operator Characteristic (ROC) curves with anisometropia cut-offs of 1.00D, 1.50D, 2.00D and 2.50D for detection of impaired visual acuity (i.e. VA ≤20/40 or≤20/50 in at least one eye), amblyopia and strabismus.

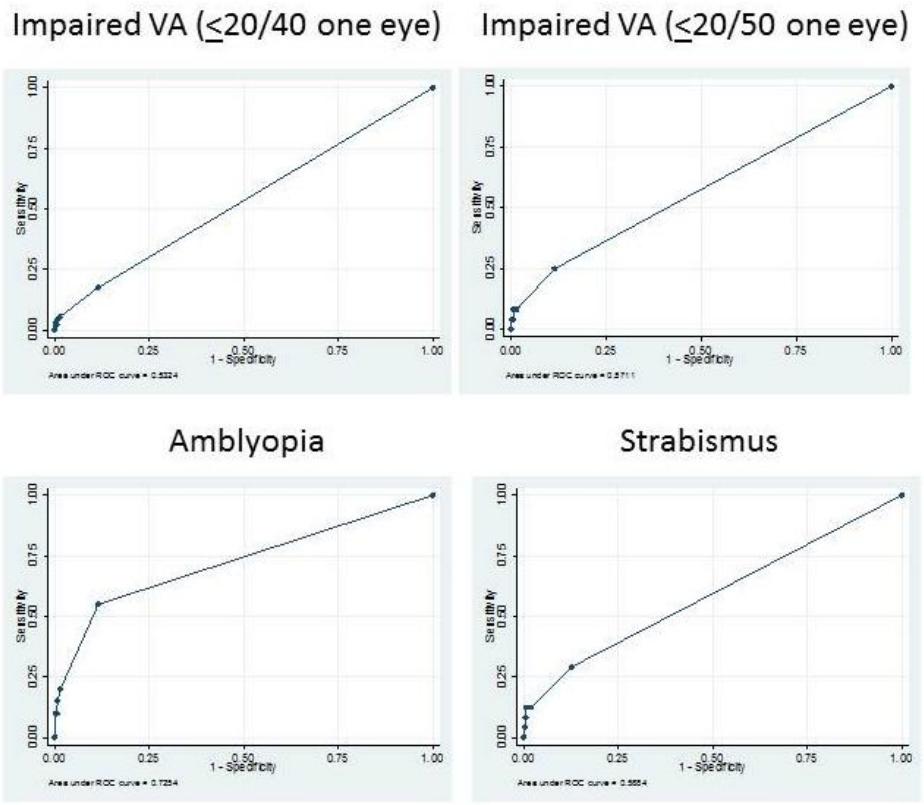


Figure 4.6.2. Receiver Operator Characteristic (ROC) curves with anisometropic astigmatism cut-offs of 0.50D, 1,00D, 1.50D, 2.00D and 2.5D for detection of impaired visual acuity (i.e. VA ≤20/40 or≤20/50 in at least one eye), amblyopia and strabismus.

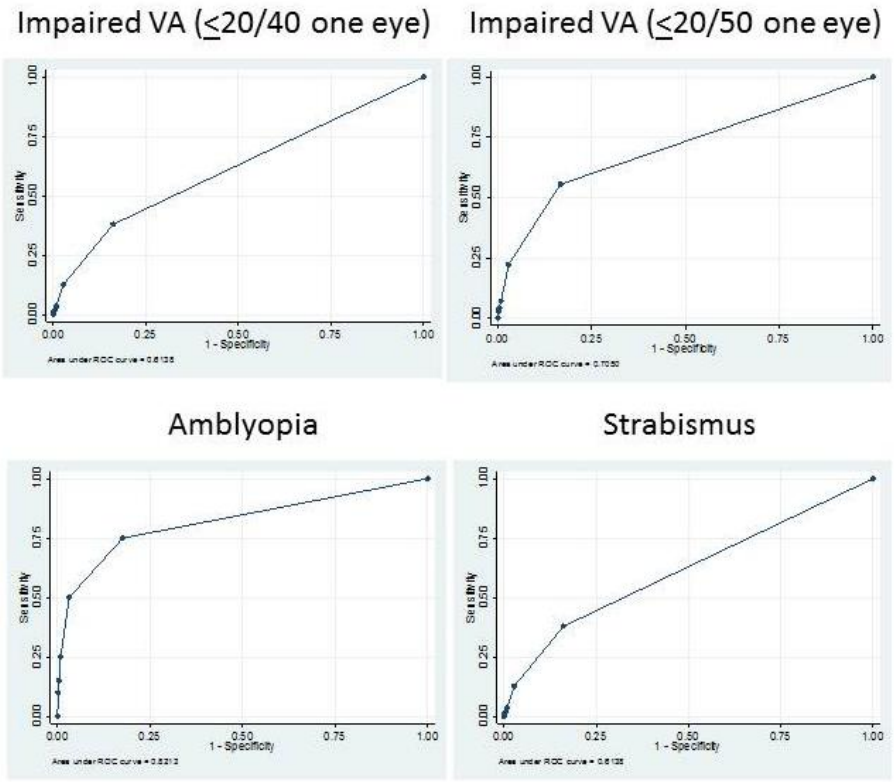


Figure 4.6.3. Receiver Operator Characteristic (ROC) curves with hyperopia in more hyperopic eye cut-offs of 1.00D, 2.00D, 3.00D, 4.00D and 5.00D for detection of impaired visual acuity (i.e. VA ≤20/40 or≤20/50 in at least one eye), amblyopia and strabismus.

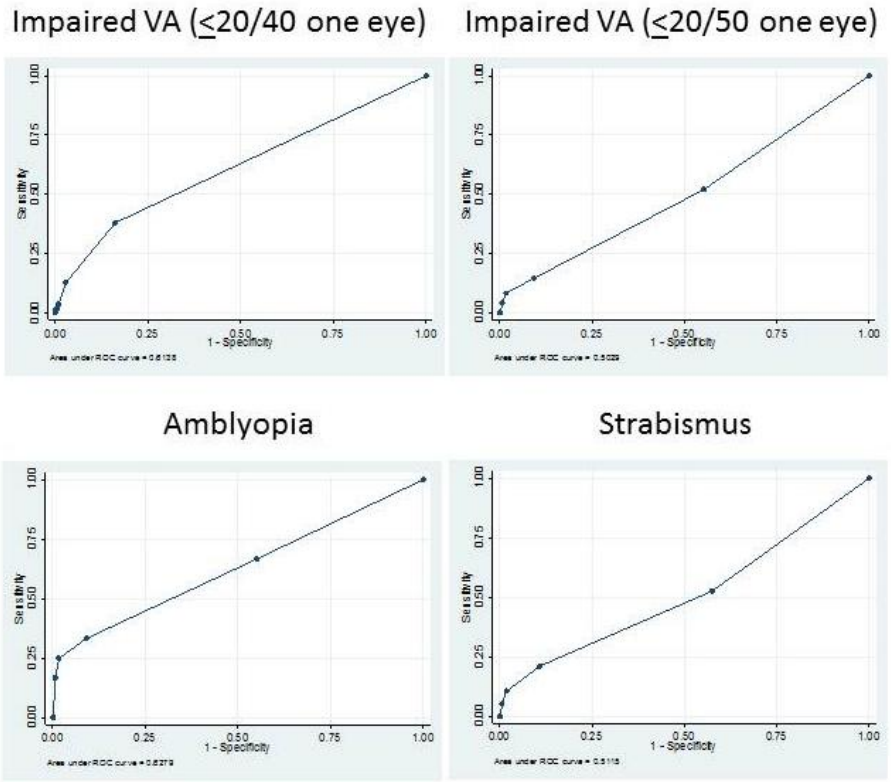


Figure 4.6.4.Receiver Operator Characteristic (ROC) curves with myopia in more myopic eye of -1.00D, -2.00D, -3.00D, -4.00D and -5.00D for detection of impaired visual acuity (i.e. VA ≤20/40 or≤20/50 in at least one eye), amblyopia and strabismus.

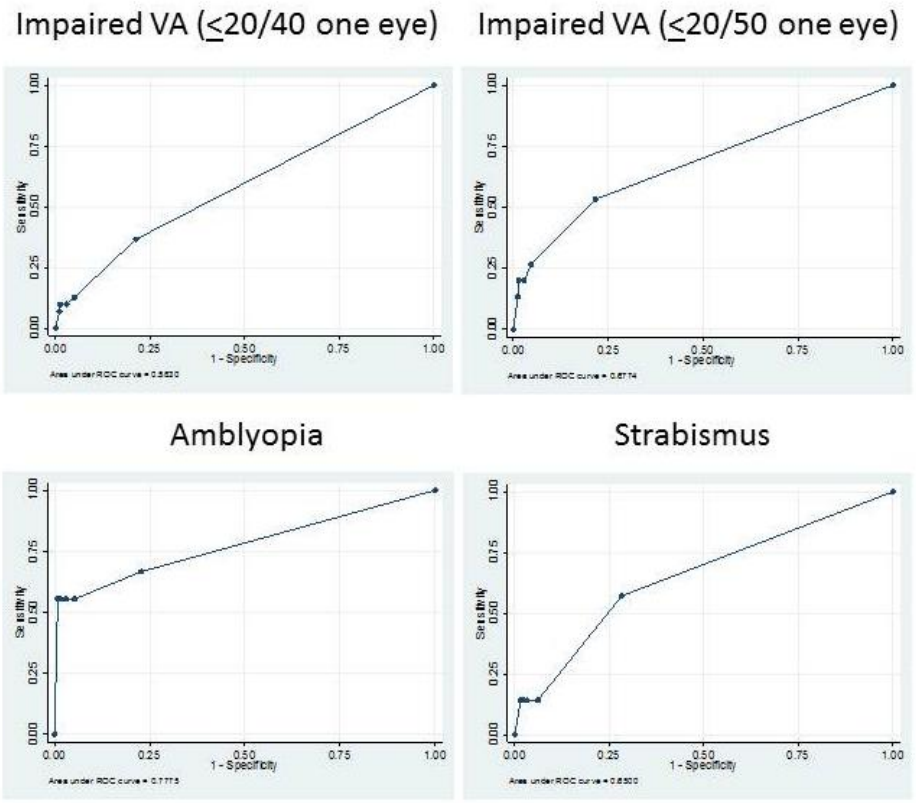


Figure 4.6.5.Receiver Operator Characteristic (ROC) curves with astigmatism in more astigmatic eye of 0.50D, 1.00D, 1.50D, 2.00D and 2.5D for detection of impaired visual acuity (i.e. VA ≤20/40 or≤20/50 in at least one eye), amblyopia and strabismus.

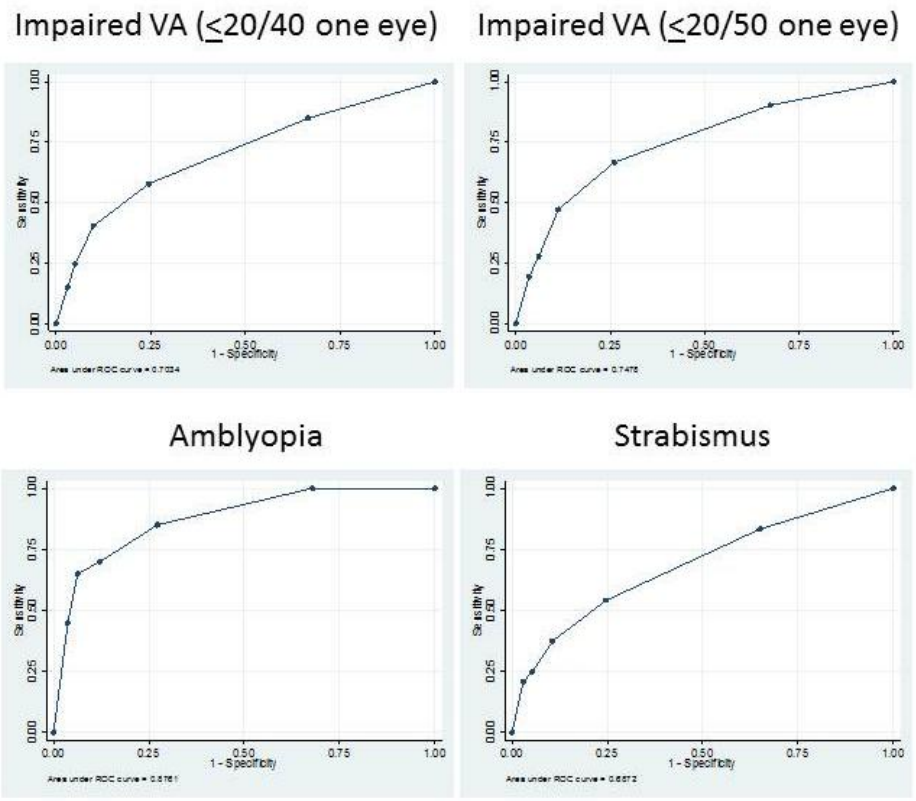


Figure 4.7 PedsQL scores for children without amblyopia or strabismus and in children with amblyopia and strabismus (1/2)

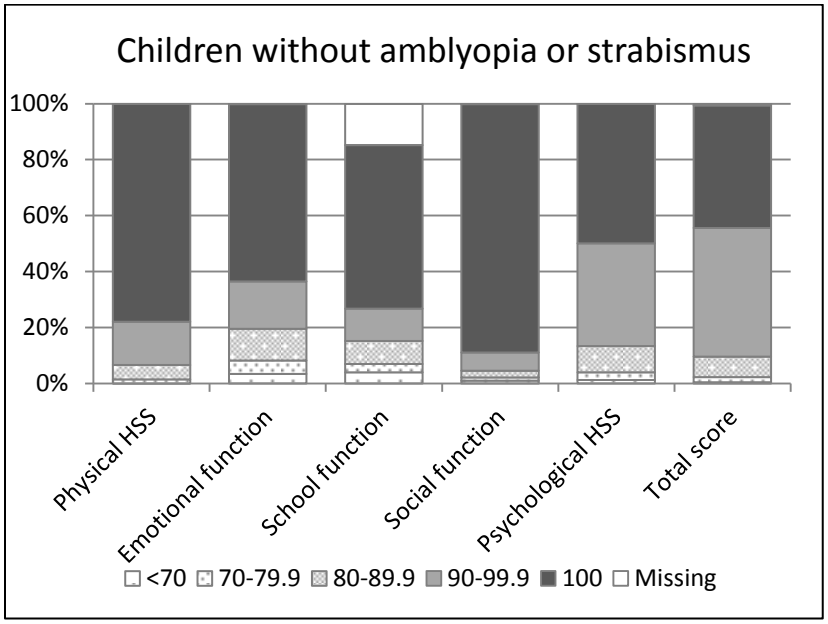
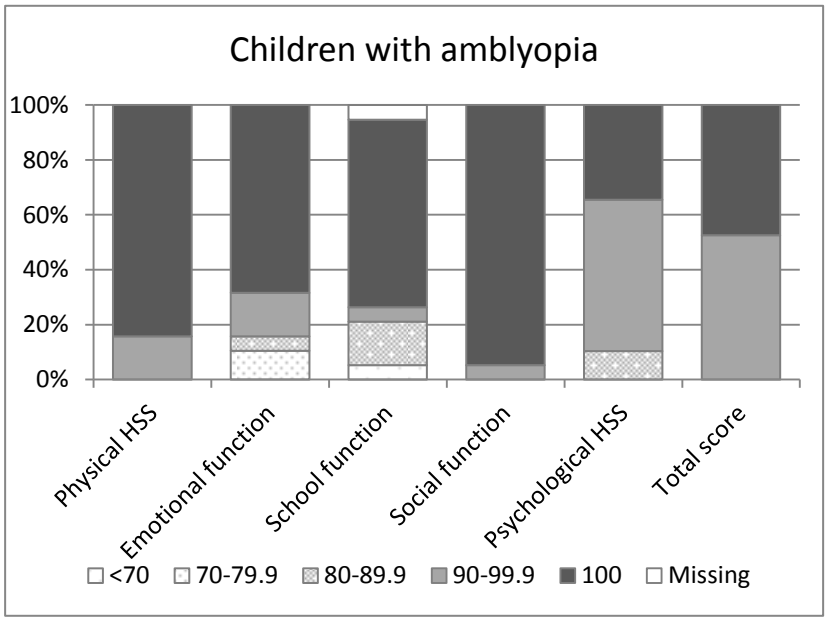


Figure 4.7 PedsQL scores for children without amblyopia or strabismus and in children with amblyopia and strabismus (2/2)



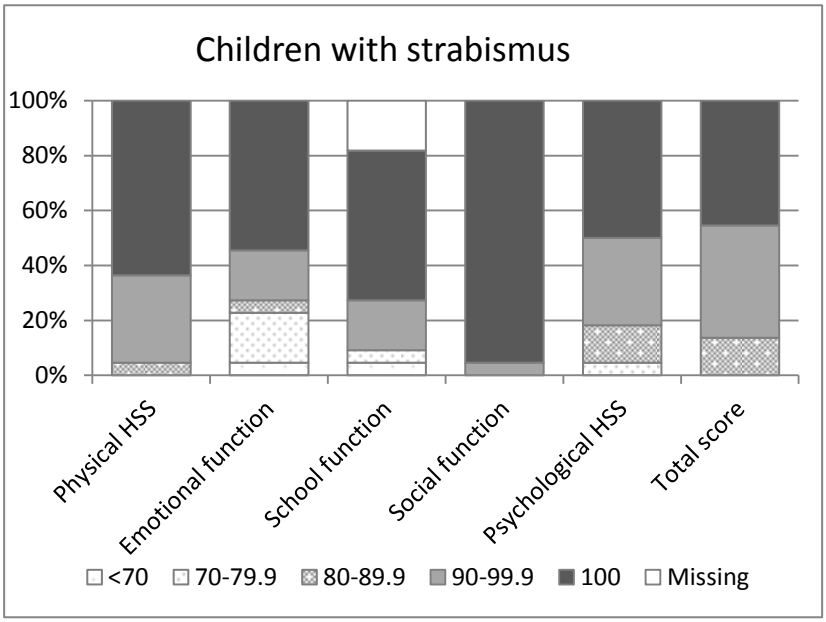
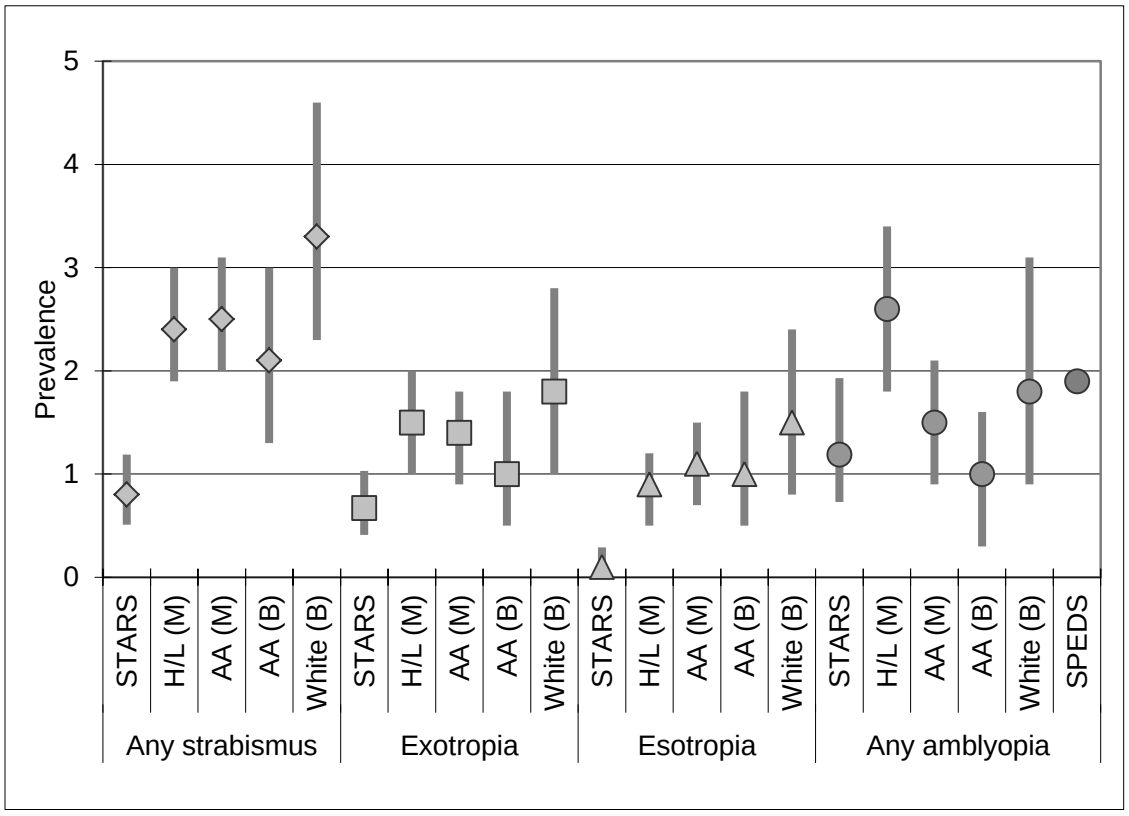


Figure 5.1: Comparison of strabismus and amblyopia prevalence in Singaporean Chinese children in the STARS study, with Hispanic/Latino and African American children from MEPEDS, African American and White children from BPEDS , and Australian children from the SPEDS studies



H/L (M) denotes Hispanic/Latino and AA (M) denotes African American children in the MEPEDS, while AA (B) denotes African American and White (B) denotes White children in the BPEDS.

Central symbol denotes prevalence, with lines denoting 95% confident interval limits.

Figure 5.2: Sensitivity, Specificity and Likelihood ratios

	Disease	No Disease	
Positive Test	True positive (TP)	False positive (FP)	Positive PV = TP/(TP+FP)
Negative Test	False negative (FN)	True negative (TN)	Negative PV = TN/(FN+TN)
	Sensitivity = TP/(TP+FN)	Specificity = TN/(FP+TN)	

Likelihood ratio for positive test (LR+) = Sensitivity/ (1-Specificity)

Likelihood ratio for negative test (LR-) = (1-Sensitivity)/Specificity

LR-	LR+	Change in pre- to post-test probability
<0.1	>10	Large, often conclusive
0.1-0.2	5-10	Moderate
0.2-0.5	2-5	Small, sometimes important
0.5-1.0	1-2	Small, rarely important

8.2.Appendix:

8.2.1. STARS data collection forms

STUDY ID: _____

DATE: _____

A Study on Strabismus, Amblyopia and Refractive Error in Singapore (STARS) Preschoolers

Sticky Label with following info:

1. Study No.[sno]
2. Name
3. BC number
4. Age
5. Gender {gender)
6. Address
7. DOB {dob}

DATE: {date}_____

ARRIVAL TIME: [timea] _____
(24-hr system)

	Tick when Completed	Investigator Code	Time Completed
1. Registration 2. Consent	☐ ☐	☐☐ ☐☐	☐☐:☐☐
3. Test for Glasses 4. Stereopsis / Randot Preschool Stereoacuity Test 5. Eye Alignment 6. Ductions / Versions 7. Bruckner Test: 8. Fixation Preference Test 9. Colour Vision 10. Visual Acuity (With & without Glasses) 11. Test for Pupil 12. Anterior Segment Evaluation	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐	☐☐:☐☐
13. Eye Drops	☐	☐☐	☐☐:☐☐
14. Measure Weight, Length and Height 15. Measure BP and Skin Fold	☐	☐☐	☐☐:☐☐
16. Interview	☐	☐☐	☐☐:☐☐
17. Axial length 18. Auto-refraction 19. Retinoscopy	☐ ☐ ☐	☐☐ ☐☐ ☐☐	☐☐:☐☐
19. Visual Acuity (Same-day) Retest	☐	☐☐	☐☐:☐☐
20. Fundus Evaluation 21. Diagnosis	☐ ☐	☐☐ ☐☐	☐☐:☐☐
22. Sub-Studies	☐	☐☐	☐☐:☐☐
23. Case File Completed/Checked	☐	☐☐	☐☐:☐☐

STUDY ID: _____

DATE: _____

CLINICAL EXAMINATION: SHORT FORM

(1) Glasses: [gl] **Yes** 1. ☐ **RX: OD** _____sph _____cyl ___axis **OS** _____sph _____cyl ___axis
N0 2. ☐ **[glsphr] [glcylr] [glaxr] [glsphl] [glcyll] [glaxl]**

(2) Stereopsis: [stereo]

Randot Preschool Stereoacuity Test (aged 30 months or older only)

800"	400"	200"	100"	60"	40"	No stereopsis	Unable	N/A
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9

(3) Accommodative lag [acclag] 1 ☐ **Applicable** 0 ☐ **Not Applicable**
(≥ 42 months)

1. Eye **[aclag]** ☐ 1 Right ☐ 2 Left ☐ 3 Unable
2. Glasses **[acglas]** ☐ 1 with ☐ 2 without ☐ 3 Unable
3. Lag

variable name		lag	RE	LE
lagr1	**lagl1**	1		
lagr2	**lagl2**	2		
lagr3	**lagl3**	3		

(4) Bruckner Test: (Red Reflex)

[redrfl]

Symmetry ……1. ☐
Asymmetry……...2. ☐
Unable ……...3. ☐

(4.1) Nystagmus : [nstg]

Present ……1. ☐
Absent ……...2. ☐
If present, type:
[nstgyp]_____

STUDY ID: _____

DATE: _____

(5) Eye Alignment (UCT): [align] Non-Strabismic 1. ☐ Strabismic 2. ☐ Can't determine 3. ☐

If Strabismic, tick the abnormalities present (5.1 to 5.6):

Items	1. Distance		2. Near	
	With correction	**Without correction**	**With correction**	**Without correction**
5.1 frequency	Constant 1. ☐ Intermittent 2. ☐ **[dcfr]**	Constant 1. ☐ Intermittent 2. ☐ **[dwcfr]**	Constant 1. ☐ Intermittent 2. ☐ **[ncfr]**	Constant 1. ☐ Intermittent 2. ☐ **[nwcfr]**
5.2 Laterality	RE 1. ☐ LE 2. ☐ alt 3. ☐ **[dclt]**	RE 1. ☐ LE 2. ☐ alt 3. ☐ **[dwclt]**	RE 1. ☐ LE 2. ☐ alt 3. ☐ **[nclt]**	RE 1. ☐ LE 2. ☐ alt 3. ☐ **[nwclt]**
5.3 Horizontal Direction	ET 1. ☐ XT 2. ☐ **[dchd]**	ET 1. ☐ XT 2. ☐ **[dwchd]**	ET 1. ☐ XT 2. ☐ **[nchd]**	ET 1. ☐ XT 2. ☐ **[nwchd]**
5.4 Vertical Direction	**Hyper T:** RE 1. ☐ LE 2. ☐ **[dcvd]**	**Hyper T:** RE 1. ☐ LE 2. ☐ **[dwcvd]**	**Hyper T:** RE 1. ☐ LE 2. ☐ **[ncvd]**	**Hyper T:** RE 1. ☐ LE 2. ☐ **[nwcvd]**
5.5. Alternate Prism Cover Test 1. Horizontal magnitude 2. Vertical magnitude	(1) _____ pd Unable (99) ☐ **[dchm]** (1) _____ pd Unable (99) ☐ **[dcvm]**	(1) _____ pd Unable (99) ☐ **[dwchm]** (1) _____ pd Unable (99) ☐ **[dwcvm]**	(1) _____ pd Unable (99) ☐ **[nchm]** (1) _____ pd Unable (99) ☐ **[ncvm]**	(1) _____ pd Unable (99) ☐ **[nwchm]** (1) _____ pd Unable (99) ☐ **[nwcvm]**
5.6 Dissociate Vertical Deviation (DVD) **[dvd1]**	Yes 1. ☐ No 2. ☐ If "Yes" please specify the effected eyes: **[dvdeye1]** RE 1. ☐ LE 2. ☐ BE 3. ☐			

STUDY ID: _____

DATE: _____

(6) Ductions/Versions: [duction]

All Normal 1. ☐

Abnormality present 2. ☐

*** If abnormality presence; please fill in the following: (6.1 to 6.6)**

Muscle	(1) RE	(2) LE
6.1 Superior Oblique (In and Down)	Over Action 1. ☐ [so_rt] Under Action 2. ☐ [so_rt1]	Over Action 1. ☐ [so_lt] Under Action 2. ☐ [so_lt1]
6.2 Inferior Oblique (In & Up)	Over Action 1. ☐ [io_rt] Under Action 2. ☐ [io_rt1]	Over Action 1. ☐ [io_lt] Under Action 2. ☐ [io_lt1]
6.3 Superior Rectus (Out & Up)	Over Action 1. ☐ [sr_rt] Under Action 2. ☐ [sr_rt1]	Over Action 1. ☐ [sr_lt] Under Action 2. ☐ [sr_lt1]
6.4 Inferior Rectus (Out and Down)	Over Action 1. ☐ [ir_rt] Under Action 2. ☐ [ir_rt1]	Over Action 1. ☐ [ir_lt] Under Action 2. ☐ [ir_lt1]
6.5 Medial Rectus (In)	Over Action 1. ☐ [mr_rt] Under Action 2. ☐ [mr_rt1]	Over Action 1. ☐ [mr_lt] Under Action 2. ☐ [mr_lt1]
6.6 Lateral Rectus (Out)	Over Action 1. ☐ [lr_rt] Under Action 2. ☐ [lr_rt1]	Over Action 1. ☐ [lr_lt] Under Action 2. ☐ [lr_lt1]

**possible answers are 0, 1, 2, 3, 4, or unable (9).*

GRADE OF FIXATION PREFERENCE:

(7) Fixation Preference test: [prefer]

(Place 12△ base-down loose prism in front of the Rt eye – observe the response, then repeat this step to the Lt eye)

Alternates	Holds well	Holds fair (1-3 sec)	No Hold (< 1 sec)	Unable
A (1)	B (2)	C (3)	D (4)	E (5)

(1) RE Preference ☐

(2) LE Preference ☐

(3) NO Preference ☐ **[eprefer]**

STUDY ID: _____

DATE: _____

(8) Color Vision: [cv] 1☐ Applicable 0☐ Not Applicable

(30 months or older only)

Ishihara at 40 cm (Per Eye):

Indicate only numbers that are not given by normal person response in RE / LE column, respectively.

RE	LE	Plate	Normal Response	R-G Deficiencies Responses				RE	LE
ihhr1	ihhl1	1	12	12					
ihhr2	ihhl2	2	8	3					
ihhr3	ihhl3	3	29	70					
ihhr4	ihhl4	4	5	2					
ihhr5	ihhl5	5	3	5					
ihhr6	ihhl6	6	15	17					
ihhr7	ihhl7	7	74	21					
ihhr8	ihhl8	8	6	X					
ihhr9	ihhl9	9	45	X					
ihhr10	ihhl10	10	5	X					
ihhr11	ihhl11	11	7	X					
ihhr12	ihhl12	12	16	X					
ihhr13	ihhl13	13	73	X					
ihhr14	ihhl14	14	X	5					
ihhr15	ihhl15	15	X	45					
				Protan		Deutan			
				Strong	Mild	Strong	Mild		
ihhr16	ihhl16	16	26	6	(2) 6	2	2 (6)		
ihhr17	ihhl17	17	42	2	(4) 2	4	4 (2)		

Note:

- The mark „X" shows that the plate cannot be read. **Data key in as "100"**
- The numerals in „( )" show that they can be read but they are comparatively unclear.
- Number of errors allowed to consider no colour deficiencies = 5 errors
- The mark „√" shows that the plate can be read, Data key in as "888"

1. Right: [cvr]	**2. Left:** [cvl]
Normal 1.☐	Normal 1.☐
Abnormal 2.☐	Abnormal 2.☐
Unable 3.☐	Unable 3.☐
Please specify: [cvrspf]_____)	Please specify: ([cvlspf]_____)

STUDY ID: _____

DATE: _____

(9) Visual Acuity [va] 1 ☐ **Applicable** 0 ☐ **Not Applicable**
(30 months or older only):

1. Without Glasses :

VR [var]_____ **VL [val]**_____

Unable 99 ☐ Unable 99 ☐

2. With Glasses (if any):

VR [glvar]_____ **VL[glval]**_____

Unable 99 ☐ Unable 99 ☐

(10) Pupils: **[pupil]**

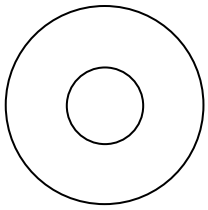
(1) ☐ Normal
(2) ☐ Afferent pupillary defect (OD)
(3) ☐ Afferent pupillary defect (OS)
(4) ☐ Other. Please specify**: [pupilo]**
_____

STUDY ID: _____

DATE: _____

(11) Anterior segment evaluation :

(RE)

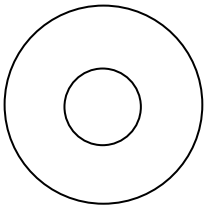


9.1 (Right) [as_rt]

Normal **1.** ☐

Abnormal **2.** ☐

(LE)



9.2 (Left) [as_lt]

Normal **1.** ☐

Abnormal **2.** ☐

For abnormal finding(s), please complete the followings:

	1. Yes	2. No		1. Yes	2. No
11.3. Ptosis **[rptosis]**	☐	☐	**[lptosis]**	☐	☐
11.4 Cataract **[rcat]**	☐	☐	**[lcat]**	☐	☐
11.5 Epiblepharon **[repiblep]**	☐	☐	**[lepiblep]**	☐	☐
11.6 Others **[rasoths]**	☐	☐	**[lasoths]**	☐	☐

(Please specify):

[rasspf] _____ _____

[lasspf] _____ _____

STUDY ID: _____

DATE: _____

(12) OCULAR DOMINANCE [od]

1 ☐ **Applicable** 0 ☐ **Not Applicable**

2 ☐ **Applicable but Unable**

≥ 48 months and above
> non-cylopleged eye

1. "Hole in the card" Test _____

Right Eye- Object seen through the hole (Left eye covered) **[odr1]** ☐1Yes ☐0 No

Left Eye- Object seen through the hole (Right eye covered) **[odl1]** ☐1Yes ☐0 No

2. "Hole in the card" Test _____

Right Eye- Object seen through the hole (Left eye covered) **[odr2]** ☐1Yes ☐0 No

Left Eye- Object seen through the hole (Right eye covered) **[odl2]** ☐1Yes ☐0 No

3. "Hole in the card" Test _____

Right Eye- Object seen through the hole (Left eye covered) **[odr3]** ☐1Yes ☐0 No

Left Eye- Object seen through the hole (Right eye covered) **[odl3]** ☐1Yes ☐0 No

4. "Tube" Test **[odtube]** ☐1Right eye ☐2 Left Eye

5. Observation

1. Hand used for drawing\coloring **[drawing]** ☐1Right hand ☐2 Left hand

2. Hand used for picking up a toy **[picking]** ☐1Right hand ☐2 Left hand

STUDY ID: _____

DATE: _____

(13) <u>Eyedrops:</u>	0.5% proparacaine	@ _____H _____
	1.0% cyclopentolate (0.5% if child ≤ 1 year)	@ _____H _____
	2.5% pheynyephrine **[mydfrin]**	@ _____H _____
	(5 minutes later administer) ↓	
	1.0% cyclopentolate (0.5 % if child ≤ 1 year)	@ _____H _____
	(5 minutes later administer) ↓	
	1.0% cyclopentolate (0.5 % if child ≤ 1 year)	@ _____H _____

Comment: _____
[comeye]

Total number of cyclopentolate eyedrop installed **[eyedrno]:** ☐
**possible answers are 0, 1, 2, 3*

(14) IOL Master (Biometry) [iol] **(30 months or older only)**	1. ☐ Done 2. ☐ Refused 3 ☐ Unable 4. ☐ Not Applicable Comments **[iolcom]** _____ **(Staple IOLMaster paper here and write the child's name)**

(15) REFRACTION: [auto] (30 minutes after last drop of cyclopentolate)

A. Autorefraction (for 24 months or older)

B. Retinomax (for less than 24 months)

1. ☐ Done 2. ☐ Refused 3. ☐ Unable 4. ☐ Not Applicable

Comments **[comauto]**

Retinomax : **[retinomax]** 1 ☐ **Applicable** 0 ☐ **Not Applicable** 2. ☐ **Unable**

Check the following:

- Ensure best readings.
- Cross – out readings with * and extra readings in excess of 5.
- Retake if more than 1 * or SD > ± 0.25.
- Write down comments for any rejections or unsuccessful attempts.

(Staple paper here and write the child's name)

OD _____

OS_____

(16) Retinoscopy:

(If autorefraction/ retinomax fails or if no cyclo done)

[retiscopy] 1☐ **Applicable** 0 ☐ **Not Applicable** 2. ☐ **Unable**

[stsphr] [stcylr] [staxr]
[stsphl] [stcyll] [staxl]

OD: _____sph_____cyl_____axis

OS: _____sph_____cyl_____axis

STUDY ID: _____

DATE: _____

(17) Visual Acuity Re-Testing:

VA RETEST CRITERIA

Criteria Set #1		Criteria Se t#2
1. 20/30 or worse (or unable) in one eye AND 2. ≥ 2 line IOD AND 3. Unilateral or bilateral amblyogenic factor*	or	VA decrease: a. <4 years of age: 20/60 or worse (or unable) in one or both eyes b. ≥4 years of age: 20/50 or worse (or unable) in one or both eyes

Amblyogenic Factors

Unilateral	Bilateral
1. Anisometropia (*spherical equivalent): ➢ 1.00D* Hyperopic anisometropia ➢ 3.00D* Myopic anisometropia ➢ 1.50D* Astigmatic anisometropia 2. Antimetropia (*spherical equivalent): Eye with the greater refractive error has: ≥1.00D* of Hyperopia or ≥3.00D* of Myopia 3. History of physical obstruction along the line of sight of one eye 4. Strabismus in primary gaze at distance and/or near fixation or a history of strabismus surgery (or botulinium)	1. Isometropia: ≥4.00D Hyperopia ≥6.00D Myopia ≥2.50D Astigmatism 2. History of physical obstruction along the line of sight in both eyes

Same-day retest (Cyclopleged)

OD: _____sph _____cyl _____axis VA _____ Unable(99) ☐

[resphr] [recylr] [reaxr] **[revar]**

OS: _____sph _____cyl _____axis VA _____ Unable(99) ☐

[resphl] [recyll] [reaxl] **[reval]**

[return] Passed Criteria ☐ 1

For Return-Visit Retest (Non-cyclopleged) ☐ 2

STUDY ID: _____

DATE: _____

(18) Blood Pressure and Skin Fold: [BP]

1☐ **Applicable** 0☐ **Not Applicable**
2☐ **Applicable but Refused**

1. **48 months and above**
2. **BP with 1 minute interval**

BLOOD PRESSURE **PULSE RATE**

Systolic *Diastolic*

{bpsys1} {bpdia1} 1ST Reading ☐☐☐/☐☐☐mmHg {bppul1}☐☐☐beats/min

{bpsys2} {bpdia2} 2ND Reading ☐☐☐/☐☐☐mmHg {bppul2}☐☐☐beats/min

{method12} Measuring method ☐0 Dinamap ☐1 Manual ☐2 Omron

Note:

If the difference between the 2 readings are **greater than** 10mmHg **SBP** and / or 5mmHg **DBP**, take a 3rd reading. Accept the two closest readings for data entry.

{bpsys3} {bpdia3} 3RD Reading ☐☐☐/☐☐☐mmHg {bppul3}☐☐☐beats/min

{method3} Measuring method ☐0 Dinamap ☐1 Manual ☐2 Omron

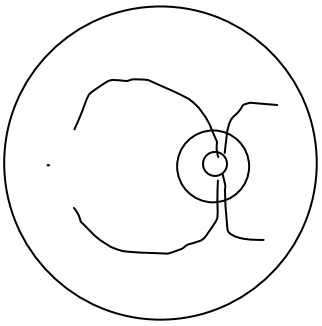
SKIN FOLD (mm) [sf] 1☐ **Applicable** 0☐ **Not Applicable** 2☐ **Applicable but Refused**

1. ☐☐.☐ [skfo1] **2.** ☐☐.☐ [skfo2] **3.** ☐☐.☐ [skfo3]

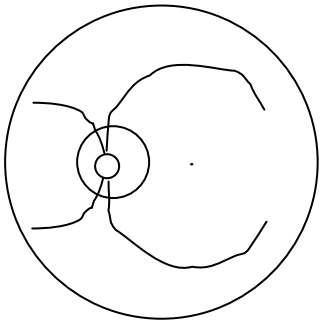
(19) Height (cm) (24 months or older) [htcm]	☐☐☐.☐ cm
Or	
(20) Length (cm) (if < 24 months): [ltcm]	☐☐☐.☐ cm

(21) Weight (kg): [wtchild] [wtparent] [wtcomb]	21.1. Weight of child (only) = ☐☐.☐ (kg) **If child < 24 months** 21.2. Weight of **parent** = ☐☐.☐ (kg) 21.3. Weight of **child and parent** = ☐☐.☐ (kg)

(22) Fundus:



(RE)



(LE)

	1. Normal	2.Abnormal	3. Unable	1. Normal	2.Abnormal	3. Unable
1.Macular **[macular]**	☐	☐	☐	☐ **[macula]**	☐	☐
2. Disc **[discr]**	☐	☐	☐	☐ **[discl]**	☐	☐
3. Media **[mediar]**	☐	☐	☐	☐ **[medial]**	☐	☐
4.Posterior pole of retina **[postretr]**	☐	☐	☐	☐ [postretl]	☐	☐
5.Peripheral retina **[periretr]**	☐	☐	☐	☐ **[periretl]**	☐	☐
6. Describe lesions: **[desbr]**	_____			_____ **[desbl]**		

[comfun] _____

OTHER TEST

1. Fundus Photo [funpto] (>47 months) Taken ☐ **1** Not Taken ☐ **0** Not Applicable ☐ **2**

2. ORA **[ora]** Done ☐ **1** Not Done ☐ **0** Not Applicable ☐ **2**

3. DNA/Saliva **[dna]** Collected ☐ **1** Not Collected ☐ **0**

4.. Peripheral Refraction **[prp]** (≥48 months, right eye only, after cycloplegia) Done ☐ **1** Not Applicable ☐ **2** Unable ☐ **99**

23. DIAGNOSIS: Please (✔) the appropriate clinical diagnosis and their sub-clinical diagnosis

1. **Amblyopia and Decreased Visual Acuity** .....Yes 1. ☐
   [dxamdva] No 2. ☐
   Unclassified 3. ☐

*** If it is "Amblyopia and Decreased Visual Acuity", please (✔) the appropriate**
[amdva]

1.1. Unilateral Amblyopia .....1. ☐
1.2. Suspected Unilateral Amblyopia ..... 2. ☐
1.3 Suspected Bilateral Amblyopia ..... 3. ☐
1.4. Unilateral Decreased Visual Acuity; Not Amblyopia ..... 4. ☐
1.5. Bilateral Amblyopia ..... 5. ☐
1.6. Bilateral Decreased Visual Acuity; Not Amblyopia ..... 6. ☐
1.7. Normal Visual Acuity ..... 7. ☐

2. **Amblyopia** .....Yes 1. ☐
   [dxambly] No. 2. ☐

If it is "Amblyopia", please (✔) the appropriate diagnosis
[ambly]

(1) Strabismic amblyopia ..... 1. ☐
(2) Anisometropic amblyopia ..... 2. ☐
(3) Combined strabismic/ anisometropic amblyopia .....3. ☐
(4) Isoametropic amblyopia .....4. ☐
(5) Deprivation amblyopia ..... 5. ☐

3. **Strabismus** .....Yes 1. ☐
[dxstrab] No. 2. ☐ **(Skip to 4)**

If it is "Strabismus", please (✔) the appropriate diagnosis.

3.1. **Esotropia** .....Yes 1. ☐
[esotrop] No 2. ☐

[esotype] If "yes" to # (3.1), **please (✔) one of the followings:**

3.1.1. Esotropia, Refractive Accommodative .....1. ☐
3.1.1.a Partially Accommodative.....a. ☐ [18]
3.1.1.b Complete Accommodative .....b. ☐ [19]
3.1.2. Esotropia, Non- Refractive Accommodative .....2. ☐
3.1.3. Esotropia, Mixed Accommodative .....3. ☐
3.1.4. Esotropia, Non-Accommodative (Basic) .....4. ☐
3.1.5. Sensory Esotropia ..... .5 ☐

3.1.6. Esotropia, Non-comitant .....6. ☐
3.1.7. Infantile Esotropia Syndrome ..... 7. ☐

3.2. **Exotropia** .....Yes 1.☐
[dxexop] No 2. ☐

If it is **"Exotropia"**, **please (✔) one of the followings:**

[exotrop]

3.2.1. Intermittent Exotropia .....1. ☐
3.2.2. Constant Exotropia .....2. ☐
3.2.3. Sensory Exotropia .....3. ☐
3.2.4. Exotropia, Non-comitant ..... 4. ☐
[exospf] (Please Specify type _____)

3.3. **Hypertropia** .....Yes 1. ☐
[hyptrop] No 2. ☐

3.4. **Microtropia** .....Yes 1. ☐
[mictrop] No 2. ☐

3.5. **DVD** .....Yes 1. ☐
[dxdvd] No 2. ☐
If it is **"DVD"**, **please (✔) one of the followings:**

[dvdeye]

3.5.1. Right Eye.....1. ☐
3.5.2 Left Eye.....2. ☐
3.5.3 Both Eye..... .....3. ☐

4. **Nystagmus** ..... Yes 1. ☐
[dxnyst] No. 2. ☐
If it is **"Nystagmus"** , **please (✔) one of the followings:**

[nystyp]

5.1. Manifest.....1. ☐
5.2. Latent .....2. ☐

5. **Any other clinical Diagnosis** .....Yes 1. ☐
[othdx] No 2. ☐

If "yes" please specify. **[othdxspf]**

_____-

Finish Time: _____ **[timef]**
(24-hr system)

STUDY ID: _____

DATE: _____

STUDY ID: ☐☐☐☐ _ ☐ _ ☐☐
(Home ID) (Fam ID) (Child ID)

[sno]

INTERVIEWER ID: ☐☐☐

[invest2]

DATE OF INTERVIEW: _____

[date2] (DD – MM – YYYY)

Sticky Label with following information:

1. Name: [name]
2. BC number: [bcno]
2. Age: [agemth]
3. Gender: [gender]

A Study on Strabismus, Amblyopia and Refractive Error in Singapore Preschoolers

新加坡学前孩童于折射误差，弱视和斜视方面的研究

Clinic Questionnaire
诊所问卷

(1 Interview / Child)
(1 采访 / 儿童)

Remarks 备注:

_____

_____

_____

_____

START TIME ☐☐:☐☐ AM/PM

STUDY ID: _____

DATE: _____

OBTAIN INFORMED CONSENT FROM A PARENT OR LEGAL GUARDIAN FOR EACH CHILD BEFORE PROCEEDING WITH INTERVIEW FOR THAT CHILD.

在进行这项访问之前，必须得到每个孩童的父母或合法监护人的同意。

While your child is participating in the eye exam today I would like to ask you to fill in some questions to help researchers learn more about the eye health of children living in Singapore.
All the information you provide will be kept strictly confidential. You may choose not to answer any questions that you do not want to answer.
当您孩子今天在接受视力检查的同时，我想请您填写这份问卷以帮助研究人员了解更多有关新加坡孩童的视力健康问题。
您的作答将完全被保密。您可拒绝回答您不想回答的任何问题。

SECTION A: Healthcare Utilization
A 项：保健的使用

		NAME 1
A1. What is your relationship to the children? 你和这孩子的关系是什么？	[childrel]	BIOLOGICAL MOTHER 亲生母亲 ..... 1. ☐ BIOLOGICAL FATHER 亲生父亲 ..... 2. ☐ STEP ADOPTIVE MOTHER 继母 ..... 3. ☐ STEP ADOPTIVE FATHER 继父 ..... 4. ☐ GRANDMOTHER 祖母 ..... 5. ☐ GRANDFATHER 祖父 ..... 6. ☐ AUNT 姑母 ..... 7. ☐ UNCLE 姑父 ..... 8. ☐
	[femrel]	OTHER FEMALE RELATIVE 其他女性亲戚..... 9. ☐ (Specify) (说明) _____
	[malerel]	OTHER MALE RELATIVE 其他男性亲戚..... 10. ☐ (Specify) (说明) _____
	[fnonrel]	OTHER FEMALE NON-RELATIVE 其他女性但不是亲戚 ..... 11. ☐ (Specify) (说明) _____
	[mnonrel]	OTHER MALE NON-RELATIVE 其他男性但不是亲戚 ..... 12. ☐ (Specify) (说明) _____
		RF 拒绝回答 ..... 98. ☐ DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

A2. In what country was the child born?

您的孩子在哪里出世?

[country]

SINGAPORE 新加坡.....**(SKIP TO A 3)**.....1. ☐

MALAYSIA 马来西亚 .....**(GO TO A2 a)**.....2. ☐

OTHER (SPECIFY)

其它 (说明) ..... **(GO TO A2 a)**.....3. ☐

[cntyspf]

Specify 请说明: _____

RF 88. ☐ DK 99. ☐

RF 拒绝回答.....98. ☐

DK 不知道 .....99. ☐

A2. a When did your child move to Singapore?

您的孩子在哪一年移居新加坡?

[yrmove]

|_|_|_|_| .....YEAR 年

A3. Where was the child born?

您的孩子在哪里出生?

[hospital]

KKH 竹脚妇幼医院.....1. ☐

NUH 国立医院.....2. ☐

SGH 中央医院.....3. ☐

GLENEAGLES HOSPITAL 鹰阁医院 .....4. ☐

MOUNT AVERNIA.....5. ☐

THOMSON MEDICAL CENTER 康生 .....6. ☐

HOME 家里.....7. ☐

GP CLINIC 普通医生诊所 .....8. ☐

[hosspf]

OTHER 其它 .....9. ☐

Specify 请说明: _____

RF 88. ☐ DK 99. ☐

RF 拒绝回答.....98. ☐

DK 不知道 .....99. ☐

STUDY ID: _____

DATE: _____

SECTION B: Pregnancy History
B 项：怀孕的经历

B1. How old were you when the child was born?

当您的孩子出生时，您多少岁？

[pregyear] ☐☐ ..... YEARS OLD 岁

RF 拒绝回答 ..... 98. ☐

DK 不知道 ..... 99. ☐

B2. Was the child admitted to the neonatal intensive care unit?

您的孩子有否进入新生儿的加护病房？

[neonate]

YES 是 ..... **(GO TO B2 a)** ..... 1. ☐

NO 没有 ..... **(SKIP TO B3)** ..... 0. ☐

RF 拒绝回答 ..... **(SKIP TO B3)** ..... 98. ☐

DK 不知道 ..... **(SKIP TO B3)** ..... 99. ☐

B2. a If YES, Why? (Specify reason)

[neonarey]

_____

_____

_____

B3. During the pregnancy with the child, did a doctor ever tell you that you had? (**READ LIST**)

在怀着您的孩子时，医生有否曾经告诉您有关（**请读出**）？

(RF = 98, DK = 99)
(拒绝回答 = 98, 不知道 = 99)

		YES 有	NO 没有	DK 不知道	During what month of pregnancy did the doctor first tell her this? 在怀孕期间的第几个月，医生第一次告诉他以下 (RF = 98, DK = 99) (拒绝回答 = 98, 不知道 = 99) **MONTH 月**
1)	anemia or low blood count 贫血症或血球计数低 ..... [anemia]	1	0	99	☐ [anemth]
2)	high blood pressure that developed during pregnancy, but went away after the pregnancy was over 怀孕期间产生的高血压，但是怀孕后将不存在 ..... [hibp]	1	0	99	☐ [hibpmth]
3)	diabetes that developed during pregnancy, but went away after the pregnancy was over 怀孕期间产生的糖尿病，但是怀孕后将不存在 ..... [db]	1	0	99	☐ [dbmth]
4)	any other problem during the pregnancy 在怀孕期间的其它问题..... Specify 请说明: _____ [pregspf] [pregoth]	1	0	99	☐ [othmth]

SECTION C: Smoking and Alcohol Intake During Pregnancy for this particular Child.
C 项：在怀着这孩子期间吃药、抽烟和喝酒

C 0. Is the person who answering the questionnaire the biological mother of the child?

受采访者是否是孩子的亲生母亲？

[biomo]

YES 是 .... 1. ☐
NO 不是..... ..... 0. ☐

C 1. Did you take any medicines or traditional medicines during your pregnancy?

在怀孕的时候，您是否有吃药或传统中药？

[tradmed]

YES 有 .....**(GO TO C 1a)** ..... 1. ☐
NO 没有..... **(SKIP TO C 2)** ..... 0. ☐
RF 拒绝回答..... **(SKIP TO C 2)** .... 98. ☐
DK 不知道 ..... **(SKIP TO C 2)** .... 99. ☐

C 1a. If YES, name all medicines

如果有，请列出药物的名称

[medspf]

SPECIFY 请说明:

(If traditional medicine, please list down the names of the medicines. If not, please write down herbs, e.g. Chinese herbs, Malay herbs.)

C 2. At any time during the pregnancy with the child, did you smoke?

在怀着您的孩子的任何时候，您有否抽烟？

[pregsmk]

YES 有 .....**(GO TO C 2a)** ..... 1. ☐
NO 沒有..... **(SKIP TO C 3)** ..... 0. ☐
RF 拒绝回答..... **(SKIP TO C 3)** .... 98. ☐
DK 不知道 ..... **(SKIP TO C 3)** .... 99. ☐

C 2a. During which months of the pregnancy with the child did you smoke?

CODE ALL THAT APPLY.

在怀着您的孩子的哪一个月，您有抽烟？

记录所有选项。

[smkmth]

MONTH 1 第一个月 ..... 1. ☐
MONTH 2 第二个月 ..... 2. ☐
MONTH 3 第三个月 ..... 3. ☐
MONTH 4 第四个月 ..... 4. ☐
MONTH 5 第五个月 ..... 5. ☐
MONTH 6 第六个月 ..... 6. ☐
MONTH 7 第七个月 ..... 7. ☐
MONTH 8 第八个月 ..... 8. ☐
MONTH 9 第九个月 ..... 9. ☐
RF 拒绝回答..... 98. ☐
DK 不知道 ..... 99. ☐

C 2b. On average, how many cigarettes per day did you smoke?

您平均每天抽多少支香烟？

[smkno]

└┴┘..... # CIGS PER DAY 每天多少支香
RF 拒绝回答..... 98. ☐
DK 不知道 ..... 99. ☐

C 3. At any time during the pregnancy with the child, did you drink alcohol?

在怀着您的孩子的任何时候，您有否喝酒？

[pregalc]

YES 有 ..... **(GO TO C 3a)** ..... 1. ☐
NO 沒有 ..... **(SKIP TO D)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO D)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO D)** ..... 99. ☐

C 3a. During which months of the pregnancy with the child did you drink alcohol?

CODE ALL THAT APPLY.

在怀着您的孩子的哪一个月，您有喝酒？

记录所有选项。

[alcmth]

MONTH 1 第一个月 ..... 1. ☐
MONTH 2 第二个月 ..... 2. ☐
MONTH 3 第三个月 ..... 3. ☐
MONTH 4 第四个月 ..... 4. ☐
MONTH 5 第五个月 ..... 5. ☐
MONTH 6 第六个月 ..... 6. ☐
MONTH 7 第七个月 ..... 7. ☐
MONTH 8 第八个月 ..... 8. ☐
MONTH 9 第九个月 ..... 9. ☐
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

C 3b. During an average month during your pregnancy with the child, how many days in a week did you drink alcohol?

在怀着您孩子的期间，您平均每星期有多少天喝酒？

[alcdays]

└─┘ ..... # OF DAYS A WEEK 每星期多少天
OCCASIONAL DRINK / NO AVERAGE PATTERN
偶尔喝 / 不固定 ..... 0. ☐
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

C 3c. On average, how many drinks per day did you have?

您平均每天喝多少杯酒？

[alcdrink]

└─┴─┘ . # DRINKS PER DAY 每天多少杯
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

SECTION D: History of Health Conditions
D 项: 健康病历

D1. Has a doctor ever said that your child had (**READ LIST**)?

医生是否曾经说过您孩子有以下病症？（**读出以下各项**）？

		NAME1 姓名 1			
		YES 有	NO 没有	RF 拒绝回答	DK 不知道
1. Asthma 哮喘……	[asthma]	1. ☐	2. ☐	98. ☐	99. ☐
2. Chronic allergies or sinus trouble 长期的过敏症或额窦性问题……	[allergy]	1. ☐	2. ☐	98. ☐	99. ☐
3. Mental retardation 智力迟钝 ……	[retard]	1. ☐	2. ☐	98. ☐	99. ☐
4. Very high fever that caused convulsions or seizures 高烧所引起的抽搐或癫痫……	[fits]	1. ☐	2. ☐	98. ☐	99. ☐
5. Coordination problem, motor delay, muscle weakness or paralysis 协调问题，运动神经迟缓，肌肉无力或瘫痪……	[paralyse]	1. ☐	2. ☐	98. ☐	99. ☐
6. Any heart condition 任何心脏问题 ……	[heart]	1. ☐	2. ☐	98. ☐	99. ☐
7. Speech or hearing problems 说话或听觉问题 ……	[speech]	1. ☐	2. ☐	98. ☐	99. ☐
8. Attention or learning problems 注意力或学习问……	[learning]	1. ☐	2. ☐	98. ☐	99. ☐
9. Developmental delay 成长的延误 ……	[dvpdl]	1. ☐	2. ☐	98. ☐	99. ☐
10. Diabetes 糖尿病……	[diab]	1. ☐	2. ☐	98. ☐	99. ☐
11. Other problems 其它问题 ……	[othsprob]	1. ☐	2. ☐	98. ☐	99. ☐

SPECIFY 详细说明:

[probspf1] [probspf2] [probspf3]

_____

_____

STUDY ID: _____

DATE: _____

SECTION E: History of BREAST FEEDING: 哺乳的历史

E1. Was your child ever breastfed or fed breast milk? 您的孩子是否曾经被喂以母奶？

[bf]

0. ☐ No (If no, go to Section F) 没有（如果没有，请到 F 项）

99. ☐ Don't Know (If DK, go to Section F) 不知道（如果不知道，请到 F 项）

1. ☐ Yes (If yes, go to Question E2) 有（如果有，请回答问题 E2）

E2 How old was your child when (he/she) was first fed breast milk?
您的孩子第一次被喂以母奶时，他多大？

If < 1 month old 如果小过一个月 ☐☐ [bfday] days old 天大

If started breastfeeding 1 month or older 如果在一个月或以后开始喂以母奶 ☐☐ [bfmth] months old 个月大

E3 How long did you breastfeed this child? (For how long was your child breastfed or received breast milk?)
您喂母奶给这孩子多久了？（您的孩子喝多久的母奶？）

[bfdur]

1. ☐ Less than 1 week 少过一个星期
2. ☐ 1 to 4 weeks 一至四个星期
3. ☐ 1 to 3 months 一至三个月
4. ☐ 4 to 6 months 四至六个月
5. ☐ 6 to 12 months 六至十二个月
6. ☐ More than 12 months 多过十二个月
7. ☐ Still breastfeeding 还在喂以母奶

E4 Which type of breastfeeding best describes what you practiced at that time?
(Which type of breastfeeding best described what your child received at that time?)
哪一种喂以母奶的方式最适合形容您那个时候的做法？
（哪一种喂以母奶的方式最适合形容您孩子那个时候所得到的？）

[bfmtd1]

1. ☐ Exclusive breastfeeding (Only breast milk – may include medicines & vitamins) 纯粹喂以母奶 (只有母奶 – 可能包括药物或维他命)
2. ☐ Mostly breastfeeding (Breast milk and water, sweetened water, or juices– NO formula milk) 大部分喂以母奶 (母奶和水，糖水，或果汁 – 没有婴儿奶粉)
3. ☐ Partly breastfeeding (Breast milk AND formula milk or other complementary foods) 部分喂以母奶 (母奶和婴儿奶粉或其它补充的食物)

E5 How did you feed your child breast milk? (How did the mother feed the child breast milk?)
您怎样喂母奶给您孩子？（妈妈怎样喂母奶给孩子？）

[bfmtd2]

1. ☐ Directly from the breast (direct breastfeeding)
直接从乳房 (直接喂以母奶)

2. ☐ Expressed breast milk feedings without progression to direct breastfeeding
挤出母奶后才喂（不是直接喂以母奶）

3. ☐ Partial direct breastfeeding and partial expressed breast milk feedings
部分直接从乳房喂以母奶和部分挤出母奶后才喂

STUDY ID: _____

DATE: _____

SECTION F: History of Ocular Conditions for the CHILD
F 项: 视觉病历

F1 During the past 12 months have you noticed that your child frequently squinting? (i.e. eye turns in/out)
在过去的 12 个月里，您有否察觉您的孩子经常斜着眼看东西？(即当一只眼睛看向前面但另一只眼睛交叉或目光无目的地移动)

[squint]

YES 有 .....1. ☐
NO 没有 .....0. ☐
RF 拒绝回答 .....98. ☐
DK 不知道 .....99. ☐

IF CHILD IS < 24 MONTHS, SKIP TO F3.
如果孩子小于 24 个月，请跳到 F3

F2 During the past 12 months has your child had difficulty drawing or coloring, besides not staying in the lines?

在过去的 12 个月里，您的孩子有否绘画或填色方面的困难（不包括填色时越过线）？

[drawing]

NOT APPLICABLE 不适合.....2. ☐
YES 有 .....1. ☐
NO 没有 .....0. ☐
RF 拒绝回答 .....98. ☐
DK 不知道 .....99. ☐

F3 Does your child close one eye when (he/she) is in bright sun light?

当您的孩子在强烈阳光下时，（他/她）有否闭上一只眼睛？

[sunlight]

YES 有 .....1. ☐
NO 没有 .....0. ☐
RF 拒绝回答 .....98. ☐
DK 不知道 .....99. ☐

F4 Does your child close or cover one eye when (he/she) is concentrating on a task?

当他正专心做一件事情时，您的孩子有否闭上或遮盖一只眼睛？

[task]

YES 有 .....1. ☐
NO 没有 .....0. ☐
RF 拒绝回答 .....98. ☐
DK 不知道 .....99. ☐

F5 How often are your child's eyes checked?

您孩子的眼睛是否经常接受检查？

[eyechk]

This is the first time 这是第一次 .....1. ☐
6 months 6 个月 .....2. ☐
Once a year 一年一次.....3. ☐
Once in 2 years 两年一次 .....4. ☐
Once in 3 years 三年一次 .....5. ☐
Once in 4 years 四年一次 .....6. ☐
Once in 5 years or more
五年一次或更多 .....7. ☐
RF 拒绝回答 .....98. ☐
DK 不知道 .....99. ☐

F6 Has a doctor told you that your child needs to wear glasses or contact lenses?

医生有否说过您的孩子需要佩戴眼镜或隐形眼镜？

[needglas]

YES 有 ..... **(GO TO F6 a)** .....1. ☐
NO 没有 .....**(SKIP F 7)** .....0. ☐
RF 拒绝回答 .....**(SKIP F 7)** .....98. ☐
DK 不知道 .....**(SKIP F 7)** .....99. ☐

STUDY ID: _____

DATE: _____

F6a. And when?

什么时候？

[galsyrs]

☐☐ ..... YEARS AGO 年前

RF 拒绝回答 ....98. ☐

DK 不知道 .....99. ☐

F6b. Did your child get them?

您的孩子是否有佩戴?

[glasyes]

YES 有 .....**(GO TO F6 d)**.....1. ☐

NO 没有 .. **(GO TO F6c, THEN F 8)**0. ☐

RF 拒绝回答 .....**(GO TO F 7)**.....98. ☐

DK 不知道 .....**(GO TO F 7)**.....99. ☐

F6c. If not, why?

若没有，为什么？

[glasnot]

Adopt a wait and see approach because the prescription is too low

再观望一阵子，因为度数太低.....1. ☐

Doctor / optometrist advice against glasses as they do not see the need for the child to wear glasses yet

医生 / 验光师反对佩戴眼睛，因为他们认为孩子还不需要配戴眼镜 .....2. ☐

Child does not like the idea of wearing glasses

孩子不喜欢配戴眼镜. .....3. ☐

The price of the spectacles was too expensive

眼镜的价格太昂贵.....4. ☐

Cannot find any suitable frame

找不到适合的镜框.....5. ☐

RF 拒绝回答 .....98. ☐

DK 不知道 .....99. ☐

F6d. When did your child first begin wearing glasses or contact lenses?

在什么时候，您的孩子第一次佩戴眼 镜或隐形眼镜？

[wearmth] [wearyrs]

☐☐ MONTH 月

☐ RF 88 拒绝回答

☐ DK 99 不知道

☐☐☐☐ YEAR 年

☐ RF 88 拒绝回答

☐ DK 99 不知道

IF RF, PROBE:
How old was your child when he/she first began wearing glasses or contact lenses?

如果拒绝回答, 调查:
您的孩子是在几岁时第一次佩戴眼镜或隐性眼镜？

[wearage]

OR 或

AGE 年龄 ☐☐

☐ RF 拒绝回答

☐ DK 不知道

STUDY ID: _____

DATE: _____

F7 a) Does your child wear spectacles?

您的孩子是否有佩戴眼镜?

[wrspec]

YES 有 .....**(GO TO F7 b)**.....1. ☐
NO 没有 ..... **(SKIP TO F 8)** .....0. ☐
RF 拒绝回答 .... **(SKIP TO F 8)** .....98. ☐
DK 不知道 ..... **(SKIP TO F 8)** .....99. ☐

b) Does s/he need glasses primarily for:
(CHECK ONLY ONE)

他需要眼镜的主要目的是:
(只能选一项)

[specneed]

Viewing things clearly in the distance (eg, television or the blackboard
能在一定距离内看清事物（例如：电视或黑板）.....1. ☐
Reading or other close work
阅读或看清其它较近的事物 .....2. ☐
Equally important for distance and close work
以上两项都一样重要 .....3. ☐
RF 拒绝回答 .....98. ☐
DK 不知道 .....99. ☐

c) Is the prescription fitted in the lenses the same as the prescription prescribed?

镜片的度数是否和验眼的度数是一样的?

[sameprsc]

YES 是 ..... **(SKIP TO F7 d)** .....1. ☐
NO 不是 ..... **(Go TO F7 c) i)**.....0. ☐
RF 拒绝回答 ... **(SKIP TO F7 d)**.....98. ☐
DK 不知道 ..... **(SKIP TO F7 d)**.....99. ☐

i. If NO, is it generally lower?

若不是，是不是比一般的低呢?

[prscblow]

YES 是 ..... **(SKIP TO F7 c) ii)** ....1. ☐
NO 不是 ..... **(SKIP TO F7 d)** .....0. ☐
RF 拒绝回答 ... **(SKIP TO F7 d)**.....98. ☐
DK 不知道 ..... **(SKIP TO F7 d)**.... 99. ☐

ii. If lower, who requested it?

如较低，是谁要求的呢?

[prscreq]

Prescriber 给与处方的人.....1. ☐
Parents 家长 ....0. ☐
RF 拒绝回答 ....98. ☐
DK 不知道 .....99. ☐

d) On an average day, how many hours per day does your child wear glasses?

平均一天里，你的孩子会戴眼镜几个小时?

[glashrs]

☐☐ ..... Hours / Day 小时/天
RF 拒绝回答 ....98. ☐
DK 不知道 .....99. ☐

e) If your child wears spectacles, does your child wear glasses when playing sports?

如果您的孩子有佩戴眼镜，在运动时，他有否戴着眼镜 ?

[glasplay]

YES 有 .....1. ☐
NO 没有 ....0. ☐
RF 拒绝回答 ....98. ☐
DK 不知道 .... 90. ☐

STUDY ID: _____

DATE: _____

Amblyopia is poor vision in an eye that cannot be corrected with glasses or contact lenses and the eye looks normal.

弱视是一种视力的缺陷，不能即由眼镜或隐性眼镜而矫正，而眼睛也看似正常。

F8 1) Has a doctor ever told you that your child had amblyopia? [ambly]

医生有否说过您的孩子有弱视的问题？

YES 有 .....**(GO TO F8 (2))**.....1. ☐
NO 没有 .....**(SKIP TO F 9)** .....0. ☐
RF 拒绝回答 ....**(SKIP TO F 9)** .....98. ☐
DK 不知道 .....**(SKIP TO F 9)** .....99. ☐

2) When was your child first diagnosed as having amblyobia? [amblymth] [amblyyrs]

在什么时候，您的孩子第一次被诊断出患有弱视？

MONTH 月 ☐☐ YEAR 年 ☐☐☐☐
☐ RF 拒绝回答 ☐ RF 拒绝回答
☐ DK 不知道 ☐ DK 不知道

IF RF, PROBE:
How old was your child when he/she was first diagnosed? [amblyage]

如果拒绝回答, 调查:
您的孩子是在几岁时第一次被诊断出患有弱视？

OR 或 AGE 年龄 ☐☐
☐ RF 拒绝回答
☐ DK 不知道

3) Was that in your child's right eye, left eye, or both eyes? [amblyeye]

您孩子的右眼，左眼或双眼患有弱视？

RIGHT EYE 右眼 .....1. ☐
LEFT EYE 左眼 .....2. ☐
BOTH EYES 双眼.....3. ☐
RF 拒绝回答 ....98. ☐
DK 不知道 ....99. ☐

4) Has your child ever been treated for amblyopia? [amblytx]

您的孩子有否接受过弱视的治疗？

YES 有 .....**(GO TO F8 (5))** .....1. ☐
NO 没有 .....**(SKIP TO F 9)** .....0. ☐
RF 拒绝回答 .....**(SKIP TO F 9)** .....98. ☐
DK 不知道 .....**(SKIP TO F 9)** .....99. ☐

5) What treatment or treatments did your child receive?
READ ITEMS.
以下哪些是您的孩子接受过的治疗?
读出以下各项

		YES 有	NO 没有	RF 拒绝回答	DK 不知道
a) Glasses or contact lenses 眼镜或隐形眼镜	[txglass]	1. ☐	0. ☐	98. ☐	99. ☐
b) Patching (保護病傷眼睛用的)眼罩 ...	[txpatch]	1. ☐	0. ☐	98. ☐	99. ☐
c) Eye drops 眼药水	[txdrops]	1. ☐	0. ☐	98. ☐	99. ☐
d) Vision therapy 视力疗法	[txvision]	1. ☐	0. ☐	98. ☐	99. ☐
e) Other 其它.....	[txoths]	1. ☐	0. ☐	98. ☐	99. ☐

SPECIFY 详细说明: [txspec]

_____

6) How long did your child receive treatments? [txdur]

您的孩子接受治疗有几年了？

└┘└┘ .....YEARS 年
RF 拒绝回答 ....98. ☐
DK 不知道 .....99. ☐

7) Is the child still undergoing the treatment or has it been stopped? [txstatus]

您的孩子还继续接受治疗吗？还是已经停止了？

STILL UNDERGOING 还继续接受治疗
.....**(SKIP TO F 9)**.....1. ☐
STOPPED 已经停止了
.....**(GO TO F 8 (8))**.....2. ☐
RF 拒绝回答 ....98. ☐
DK 不知道..... .....99. ☐

8) If stopped, why was the treatment stopped? [txstop]

若已经停止了，是什么原因呢？

_____
_____
_____
RF 拒绝回答 ....98. ☐
DK 不知道..... .....99. ☐

STUDY ID: _____

DATE: _____

Strabismus – Eyes that are not properly lined up. This happens when one eye looks straight ahead and the other eye crosses in or wanders out.
斜视 – 两只眼睛不能完全地列好，即当一只眼睛看向前面但另一只眼睛交叉或目光无目的地移动。

F9 1) Does your child have Strabismus?

您的孩子有否患上斜视？

[strab]

YES 有 .....**(GO TO F9 (2))** .....1. ☐
NO 没有 ..... **(SKIP TO G 1)** .....0. ☐
RF 拒绝回答 .... **(SKIP TO G 1)** .....98. ☐
DK 不知道 ..... **(SKIP TO G 1)** .....99. ☐

2) When was your child first diagnosed as having strabismus?

在什么时候，您的孩子第一次被诊断出患有斜视？

[strabmth] [strabyrs]

MONTH 月 ☐☐ YEAR 年 ☐☐☐☐

☐ RF 拒绝回答 ☐ RF 拒绝回答

☐ DK 不知道 ☐ DK 不知道

IF RF, PROBE:
How old was your child when he/she was first diagnosed?

如果拒绝回答, 调查:
您的孩子是在几岁时第一次被诊断出患有斜视？

[strabage]

OR 或 AGE 年龄 ☐☐

☐ RF 拒绝回答

☐ DK 不知道

3) Was that in your child's right eye, left eye, or both eyes?

您孩子的右眼，左眼或双眼患有斜视？

[strabeye]

RIGHT EYE 右眼 .....1. ☐
LEFT EYE 左眼 .....2. ☐
BOTH EYES 双眼 .....3. ☐
RF 拒绝回答 ....98. ☐
DK 不知道 ....99. ☐

4) Has your child ever been treated for Strabismus?

您的孩子有否接受过斜视的治疗？

[strabtx]

YES 有 .....**(GO TO F9 (5))** .....1. ☐
NO 没有 ..... **(SKIP TO G 1)** .....0. ☐
RF 拒绝回答 ..... **(SKIP TO G 1)** .....98. ☐
DK 不知道 ..... **(SKIP TO G 1)** .....99. ☐

5) What kind of treatment did your child receive?

您的孩子接受过什么治疗？

[stratxtyp]

_____

_____

_____

RF 拒绝回答 ....98. ☐
DK 不知道 .....99. ☐

STUDY ID: _____

DATE: _____

Section G: Outdoor and indoor and pre-school activities
G 项: 室外、室内及就学前的活动

For Question G 1a, 1b and 1c, the total time spend should be *24* hours.
问题 G 1a，1b 和 1c，其时间的和应为 *24* 小时。

G1 a) On a normal 24 hour day, how many hours per day does your child spend sleeping?

一天 24 小时里，您的孩子睡多少个小时？

[sleep]

每天 ☐☐ 小时 hrs per day
RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

b) On a normal 24 hour day, How many hours per day does your child spend indoors (example at home, friend's house, shopping) ?

一天 24 小时里，您的孩子花在室内的时间有几个小时？（例如在家、朋友的家、逛街）

[indoor]

每天 ☐☐ 小时 hrs per day
RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

c) On a normal 24 hour day, how many hours per day does your child spend outdoors (i.e. not in an enclosed space)?

一天 24 小时里，您的孩子花在户外的时间有几个小时?（室外:不在密闭的空间）

[outdoor]

每天 ☐☐ 小时 hrs per day
RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

Please specify the sports (e.g. swimming, Tennis) your child do and the **number of hours per week** during the school term that your child spend doing the activity.

请指名那些运动（例如游泳，网球）您孩子（姓名）参与的及在学校里每星期有多少小时参与这些运动。

G 2. OUTDOOR SPORTS DURING THE 7 DAYS OF THE WEEK {for your child (NAME)}
您孩子（姓名）在一星期七天内的室外运动

	Name of the outdoor sports 室外运动的名称	Number of hours per week spent in this activity 每星期多少小时参与这项运动
1	[sports1]	每星期 ☐☐ 小时 hrs per week [spthrs1]
2	[sports2]	每星期 ☐☐ 小时 hrs per week [spthrs2]
3	[sports3]	每星期 ☐☐ 小时 hrs per week [spthrs3]
4	[sports4]	每星期 ☐☐ 小时 hrs per week [spthrs4]

STUDY ID: _____

DATE: _____

G 3. **During the school year, how many hours per day (outside of regular school hours) would you estimate your child:**
在上学学年里，您的孩子每天大约花多少小时（不包括正规的上课时间）：

(PLEASE tick ✓ "Not Applicable" if your child does not perform this activity)
(请画 ✓ "不适当" 如果您的孩子没有参与此项活动)

	On the weekdays (Mon.-Fri.) 周日（星期一至五)	On the weekend (Sat. & Sun.) 周末（星期六及日)	Not applicable 不适当	Refused 拒绝	DK 不知道
a) Reading and writing (school work & read for pleasure) 读书和写字(课业及娱乐)	⌊__⌋ hours/day 小时/天 **[wdrw]**	⌊__⌋ hours/day 小时/天 **[wkrw]**	0	98	99
b) Colors, or draws for fun (pleasure) 填色，画画（娱乐）	⌊__⌋ hours/day 小时/天 **[wdcolor]**	⌊__⌋ hours/day 小时/天 **[wecolor]**	0	98	99
c) Watches television 看电视	⌊__⌋ hours/day 小时/天 **[wdtv]**	⌊__⌋ hours/day 小时/天 **[wetv]**	0	98	99
d) Playing television games (e.g. play station) 玩电子游戏 (例如：play station)	⌊__⌋ hours/day 小时/天 **[wdtvgame]**	⌊__⌋ hours/day 小时/天 **[wetvgame]**	0	98	99
e) Uses a computer / plays computers 用电脑 / 玩电脑	⌊__⌋ hours/day 小时/天 **[wdcomp]**	⌊__⌋ hours/day 小时/天 **[wecomp]**	0	98	99
f) Plays hand held video games (e.g. gameboy, handphone games). 玩手提式电动游戏（例如：gameboy, 电话游戏)	⌊__⌋ hours/day 小时/天 **[wdvideo]**	⌊__⌋ hours/day 小时/天 **[wevideo]**	0	98	99
g) Other near work activities, please describe below: (e.g. cutting paper, playing with toys) 其它活动，请说明（如剪纸，玩具）： **[nwtype]** _____ _____	⌊__⌋ hours/day 小时/天 **[wdoths]**	⌊__⌋ hours/day 小时/天 **[weoths]**	0	98	99
Time Spent outside 室外活动的时间：					
h) Playing out of doors (In a backyard, walk, bike riding) 室外游戏 (在后院, 散步, 骑脚车)	⌊__⌋ hours/day 小时/天 **[wdplay]**	⌊__⌋ hours/day 小时/天 **[weplay]**	0	98	99
i) Out door leisure activities (Family BBQs, Park, Picnic, Beach) 室外闲暇活动 (家庭烤肉, 公园, 野餐, 海边)	⌊__⌋ hours/day 小时/天 **[wdleis]**	⌊__⌋ hours/day 小时/天 **[weleis]**	0	98	99

G 4. Is there a park or garden near to your home where your child could play outdoors?

在您家附近是否有公园或花园（您孩子可到那里去玩）？

[garden]

YES 有	**(GO TO G4 a)** 1. ☐
NO 没有	**(SKIP TO G 5)** 0. ☐
RF 拒绝回答	**(SKIP TO G 5)** 98. ☐
DK 不知道	**(SKIP TO G 5)** 99. ☐

G 4a. If YES, does your child play in the nearby park or garden at least once a week?

若是，您的孩子是否至少一个星期到该公园或花园玩一次？

[freqgdn]

YES 有	1. ☐
NO 没有	0. ☐
RF 拒绝回答	98. ☐
DK 不知道	99. ☐

G 5. Does your child read words by himself or herself?
(A "word" can be a letter (e.g. A, B, C) or a word (e.g. Apple))

您的孩子有否自行阅读单字？
（（一个单字可以是一个字母（如：A，B，C）或一个字（如：Apple））

[wordslf]

YES 有	1. ☐
NO 没有	0. ☐
RF 拒绝回答	98. ☐
DK 不知道	99. ☐

G 6. Does your child read picture books by himself or herself

您的孩子有否自行阅读图画书？

[pictslf]

YES 有	1. ☐
NO 没有	0. ☐
RF 拒绝回答	98. ☐
DK 不知道	99. ☐

G 7. How often does your child read for fun (outside of school)?
(CHECK ONLY ONE BOX)

您的孩子是否经常自行阅读（在学校以外）？
(只能选一项)

[funread]

Never 从来没有	**(SKIP TO G 12)** 1. ☐
Rarely 很少	2. ☐
Sometimes 有时	3. ☐
Often 经常	4. ☐
Child doesn't read yet 还未开始阅读	**(SKIP TO G 12)** 5. ☐
RF 拒绝回答	**(SKIP TO G 12)** 98. ☐
DK 不知道	**(SKIP TO G 12)** 99. ☐

G 8. How long on average does your child read before taking a break?

您孩子平均会阅读多久才休息一会儿？

[readhrs]

0 – 10 minutes 分钟	1. ☐
11 – 20 minutes 分钟	2. ☐
21 – 30 minutes 分钟	3. ☐
31 – 40 minutes 分钟	4. ☐
41 – 50 minutes 分钟	5. ☐
51 – 60 minutes 分钟	6. ☐
> 60 minutes 超过 60 分钟	7. ☐
RF 拒绝回答	98. ☐
DK 不知道	99. ☐

G 9. How frequently does your child read with the book close to his or her face? (Demonstrate reading at ~ 33 cm)

您孩子有否经常在阅读时把书靠近他的脸？（示范读书在~ 33 cm）

[readclse]

NEVER 从未	0. ☐
SELDOM 很少	1. ☐
OFTEN 经常	2. ☐
NA 不适当	3. ☐
RF 拒绝回答	98. ☐
DK 不知道	99. ☐

	Has not started this activity 还没开始这项活动	RF 拒绝回答	DK 不知道
G 10. At what age did your child first start reading books by himself / herself on a regular basis 您的孩子多少岁开始自行地及习惯性地阅读 ␣␣ years old 岁 [agebook]	97. ☐	98. ☐	99. ☐
G 11. Number of books read per week {**Read by the Child**} 一星期读多少本书{由孩子读} ␣␣ books per week 本/每星期 [nobkwk]	97. ☐	98. ☐	99. ☐
G 12. Number of hours of academic tuition classes (e.g. school related subjects such as English. Math, Chinese) outside school hours 一星期多少小时的课外补习课（例如：英文科目数学、中文） ␣ hours per week 小时/每星期 [hrtuitn]	97. ☐	98. ☐	99. ☐
G 13. At what age did your child start attending a pre-school centre (includes kindergarten, childcare and montessori centers) 您的孩子多少岁开始进入就学前的学习中心（例如：幼稚园、育幼院和蒙特梭利中心） ␣ years old 岁 [preschyr]	97. ☐ **SKIP TO H**	98. ☐	99. ☐

G 14. What type of preschool is your child attending?

现在您的孩子进入那一种就学前的学习中心？

[presch]

[prespf]

KINDERGARDEN 幼儿园	1. ☐
CHILDCARE 育幼院	2. ☐
NURSERY 托儿所	3. ☐
OTHERS 其它 **(SPECIFY)**	4. ☐
SPECIFY 请说明: _____	
NONE 没有 **(SKIP TO H)**	5. ☐
RF 拒绝回答 **(SKIP TO H)**	98. ☐
DK 不知道 **(SKIP TO H)**	99. ☐

G 15. How many hours per day does your child spend in pre-school?

您孩子每天多少个小时在就学前的学习中心？

[preschhr]

␣␣ hours per day 小时/每天	
RF 拒绝回答	98. ☐
DK 不知道	99. ☐

STUDY ID: _____

DATE: _____

SECTION H
H 项

			NAME1 姓名 1			
					I.	II.
H	Has a doctor ever told you that your child ever had (**READ LIST**)? 医生是否曾经说过您的孩子有以下病症？（读出以下各项） **RF=98, DK=99.** **拒绝回答=98, 不知道=99.**		YES (ASK I & II) 是 (发问 I & II)	NO 不是	What treatment was received? **IF NONE, SKIP TO NEXT CONDITION.** 接受什么治疗？ **如果没有，跳到下一项.**	When was this? 什么时候？
[cat]	1)	Cataracts 白內障.....	1	0	_____ [cattx]	_____ [catdur]
[glau]	2)	Glaucoma 青光眼，綠內障	1	0	_____ [glautx]	_____ [glaudur]
[ret]	3)	Retinopathy of prematurity..... 早产儿视网膜病	1	0	_____ [rettx]	_____ [retdur]
[tumor]	4)	Eye tumor or retinoblastoma..... 眼睛肿瘤或視網膜神經膠質瘤（即眼癌，遗传性）	1	0	_____ [tumortx]	_____ [tumordur]
[opticnr]	5)	Optic nerve hypoplasia ..... 视力神经发育不全	1	0	_____ [optictx]	_____ [opticdur]
[ductob]	6)	Nasolacrimal duct obstruction..... 属于鼻与泪器的輸送管梗塞	1	0	_____ [ducttx]	_____ [ductdur]
[cortvi]	7)	Cortical visual impairment..... 皮层视力损伤	1	0	_____ [corttx]	_____ [cortdur]
[eyeoths]	8)	Others. Please specify: 其它（请详细说明） _____	1	0	_____ [eyeothtx]	_____ [eyeotdur]

STUDY ID: _____

DATE: _____

SECTION I (I 项):

Developmental Delay: 成长的延误

[dvpln] 1) Do you have any concerns about your child's learning, development, and behavior?

您是否担心您孩子的学习，成长及行为?

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NO 不是 ..... **(SKIP TO I 3)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO I 3)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO I 3)** ..... 99. ☐

[lrncrn] 2) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么？
记录所有选项。

SEEMS BEHIND
似乎落后 ..... 1. ☐
CAN'T DO WHAT OTHER KIDS CAN
不可以做其他孩子做的事 ..... 2. ☐
SLOW AND BEHIND OTHER KIDS
比其他孩子慢及落后 ..... 3. ☐
IMMATURE
不成熟 ..... 4. ☐
LEARNS SLOWLY
学习能力慢 ..... 5. ☐
LATE TO LEARN TO DO THINGS
迟开始学习 ..... 6. ☐
LEARNS BUT TAKES A LONG TIME
需要较长的时间学习 ..... 7. ☐
PROBLEMS LEARNING EVERYTHING
学习任何事情都有问题 ..... 8. ☐
OTHER (SPECIFY)
其它 (请说明) ..... 9. ☐

[lrncrn1] SPECIFY: _____
请说明

RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

SPEECH : 说话及发音

[dvpsph] 3) Do you have any concerns about how your child talks and makes speech sounds?

您是否担心您孩子的说话及发音？

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NO 不是 ..... **(SKIP TO I 5)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO I 5)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO I 5)** ..... 99. ☐

[sphcrn] 4) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么？
记录所有选项。

NOT TALKING LIKE HE/SHE SHOULD
不能照他的方式说话 ..... 1. ☐
USES SHORT SENTENCES
用缩短的句子表达 ..... 2. ☐
CAN'T ALWAYS SAY WHAT HE/SHE MEANS
不能表达他要表达的意思 ..... 3. ☐
DOESN'T ALWAYS MAKE SENSE
不能让人明白 ..... 4. ☐
CAN'T TALK CLEARLY
不能清楚地说话 ..... 5. ☐
NOBODY UNDERSTANDS WHAT HE/SHE IS SAYING EXCEPT FAMILY MEMBERS
没有人了解他说什么，除了他的家人 ..... 6. ☐
OTHER (SPECIFY)
其它 (请说明) ..... 7. ☐
[sphcrn1] SPECIFY: _____
请说明
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

COMPREHENSION : 领悟能力

[dvpund] 5) Do you have any concerns about how your child understands what you say?

您是否担心您孩子能否了解您说的话？

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NO 不是 ..... **(SKIP TO I 7)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO I 7)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO I 7)** ..... 99. ☐

[undcrn] 6) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么？
记录所有选项。

DOESN'T UNDERSTAND WHAT YOU SAY
不明白你说什么 ..... 1. ☐
DOESN'T LISTEN WELL
不能听好 ..... 2. ☐
OTHER (SPECIFY)
其它 (请说明) ..... 3. ☐
[undcrn1] SPECIFY: _____
请说明
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

FINE MOTOR SKILLS: 精细的运动技巧

[dvphnd] 7) Do you have any concerns about how your child uses his or her hands and fingers to do things?

您是否担心您孩子怎样使用他的手和手指做事？

- YES 是 ..... 1. ☐
- A LITTLE 一点 ..... 2. ☐
- NO 不是 ..... **(SKIP TO I 9)** ..... 0. ☐
- RF 拒绝回答 ..... **(SKIP TO I 9)** ..... 98. ☐
- DK 不知道 ..... **(SKIP TO I 9)** ..... 99. ☐

[hndcrn] 8) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么？ **记录所有选项。**

- CAN'T STAY IN LINES WHEN COLORS 填色时超越线 ..... 1. ☐
- CAN'T WRITE NAME 不能写自己的名字 ..... 2. ☐
- CAN'T DRAW SHAPES 不能画形状 ..... 3. ☐
- CAN'T HOLD A PENCIL RIGHT 不能正确地握笔 ..... 4. ☐
- CAN'T GET FOOD TO MOUTH/MESSY EATER 不能把食物送进嘴里 ..... 5. ☐
- OTHER (SPECIFY) 其它 (请说明) ..... 6. ☐

[hndcrn1] SPECIFY: _____ 请说明

- RF 拒绝回答 ..... 98. ☐
- DK 不知道 ..... 99. ☐

GROSS MOTOR SKILLS : 整体的运动技巧

[dvparm] 9) Do you have any concerns about how your child uses his or her arms and legs?

您是否担心您孩子怎样使用他的手臂和脚？

- YES 是 ..... 1. ☐
- A LITTLE 一点 ..... 2. ☐
- NO 不是 ..... **(SKIP TO I 11)** ..... 0. ☐
- RF 拒绝回答 ..... **(SKIP TO I 11)** ..... 98. ☐
- DK 不知道 ..... **(SKIP TO I 11)** ..... 99. ☐

[armcrn] 10) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么？ **记录所有选项。**

- CLUMSY 笨拙 ..... 1. ☐
- WALKS FUNNY 走路滑稽 ..... 2. ☐
- CAN'T RIDE A BIKE YET 还不能骑脚踏车 .. 3. ☐
- FALLS A LOT 时常跌倒 ..... 4. ☐
- LIMPS 跛行 ..... 5. ☐
- POOR BALANCE 平衡能力差 ..... 6. ☐
- OTHER (SPECIFY) 其它 (请说明) ..... 7. ☐

[armcrn1] SPECIFY: _____ 请说明

- RF 拒绝回答 ..... 98. ☐
- DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

BEHAVIOUR : 行为

[dvpbhv] 11) Do you have any concerns about how your child behaves?

您是否担心您孩子的行为?

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NO 不是 ..... **(SKIP TO I 13)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO I 13)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO I 13)** ..... 99. ☐

[bhvcrn] 12) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么?
记录所有选项。

STUBBORN 固执 ..... 1. ☐
OVER-ACTIVE 过动 ..... 2. ☐
SHORT ATTENTION SPAN 三分钟热度 ..... 3. ☐
SPOILED 被宠坏 ..... 4. ☐
AGGRAVATING 可恼的、讨厌的 ..... 5. ☐
THROWS FITS 痉攣 ..... 6. ☐
ONLY DOES WHAT HE/SHE WANTS
只做他想做的 ..... 7. ☐
OTHER (SPECIFY) 其它 (请说明) ..... 8. ☐
SPECIFY: _____ [bhvcrn1]
请说明
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

SOCIAL FUNCTIONING : 社交技巧

[dvpgot] 13) Do you have any concerns about how your child gets along with others?

您是否担心您孩子怎么与人相处?

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NO 不是 ..... **(SKIP TO I 15)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO I 15)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO I 15)** ..... 99. ☐

[gotcrn] 14) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么?
记录所有选项。

WANTS TO BE LEFT ALONE 只想一人独处 1. ☐
MOOD SWINGS, CLINGY
心情摇摆不定，缠着人 ..... 2. ☐
WHINY 爱抱怨 ..... 3. ☐
BOTHERED BY CHANGES 由于改变而烦恼 4. ☐
ANGRY, DISINTERESTED IN USUAL THINGS
生气，对平常事没有兴趣 ..... 5. ☐
EASILY LEAD 容易被人带坏 ..... 6. ☐
ACTS MEAN 行为小气 ..... 7. ☐
EASILY FRUSTRATED 容易发怒 ..... 8. ☐
BOSSY 爱指挥他人的 ..... 9. ☐
SHY 害羞 ..... 10. ☐
CLASS CLOWN 诙谐的人 ..... 11. ☐
ANGRY 生气 ..... 12. ☐
MEAN 吝啬 ..... 13. ☐
HATES ME 讨厌我 ..... 14. ☐

OTHER (SPECIFY) 其它 (请说明)..... 15. ☐
SPECIFY: _____
请说明
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

[gotcrn1]

LEARNING：学习做事

[dvpthgs] 15) Do you have any concerns about how your child is learning to do things for (himself/herself)?

否担心您孩子怎么为他们自己学习做事？

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NO 不是 ..... **(SKIP TO I 17)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO I 17)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO I 17)** ..... 99. ☐

[thgscrn] 16) What are your concerns?
CODE ALL THAT APPLY.

您担心的是什么？
记录所有选项。

WON'T DO THINGS FOR HIM/HERSELF
不会为他们自己做事 ..... 1. ☐
WON'T TELL ME WHEN HE/SHE IS WET
当他撒尿他不会告诉我..... 2. ☐
NOT TOILET TRAINED YET
还没训练他上厕所..... 3. ☐
STILL WANTS A BOTTLE
还是要奶瓶..... 4. ☐
CAN'T GET DRESSED BY HIM/HERSELF
不会自己穿衣 ..... 5. ☐
OTHER (SPECIFY)
其它 (请说明) ..... 15. ☐
SPECIFY: _____
请说明
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

[thgscrn1]

PRESCHOOL SKILLS : 学前技能

[dvpprsch] 17) Do you have any concerns about how your child is learning preschool or school skills?

您是否担心您孩子怎么在学习中心学习？

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NOT APPLICABLE 不适合 ..... 3. ☐
NO 不是 ..... **(SKIP TO I 19)** ..... 0. ☐
RF 拒绝回答 ..... **(SKIP TO I 19)** ..... 98. ☐
DK 不知道 ..... **(SKIP TO I 19)** ..... 99. ☐

[prschcrn] 18) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么？
记录所有选项。

CAN'T WRITE HIS/HER NAME
不会写他的名字 ..... 1. ☐
DOESN'T KNOW COLORS OR NUMBERS
不会辨认颜色和数字 ..... 2. ☐
JUST NOT LEARNING TO READ
不愿学习阅读 ..... 3. ☐
CAN'T REMEMBER LETTER SOUNDS
不记得字母的发音 ..... 4. ☐
KNOWS SPELLING WORDS ONE DAY BUT NOT THE NEXT
今天知道字的发音，第二天就忘了 ..... 5. ☐
OTHER (SPECIFY)
其它 (请说明) ..... 15. ☐

[prschcn1] SPECIFY: _____
请说明

RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

Other Concerns : 其它担心的事情

[dvpoth] 19) Do you have any other concerns about your child?

您是否在其它事情上也担心您的孩子？

YES 是 ..... 1. ☐
A LITTLE 一点 ..... 2. ☐
NO 不是 .....**(SKIP TO SECTION J)** ..... 0. ☐
RF 拒绝回答 ..**(SKIP TO SECTION J)** ..... 98. ☐
DK 不知道 .....**(SKIP TO SECTION J)** ..... 99. ☐

[othcrn] 20) What are your concerns? **CODE ALL THAT APPLY.**

您担心的是什么？
记录所有选项。

EAR INFECTIONS 耳朵传染 ..... 1. ☐
ASTHMA 哮喘 ..... 2. ☐
SMALL FOR AGE
身材比实际年龄矮小 ..... 3. ☐
SICK A LOT 经常生病 ..... 4. ☐
I DON'T THINK HE/SHE HEARS WELL
我不认为他听觉好 ..... 5. ☐
HE/SHE GETS UP TOO CLOSE TO THE TV AND I WORRY ABOUT HIS/HER SIGHT
太靠近电视机，我担心他的视力 ..... 6. ☐
OTHER (SPECIFY) 其它 (请说明)..... 15. ☐

[othcrn1] SPECIFY: _____
请说明

RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

SECTION J: Please collect the following data from Health Booklet

J 项: 请从健康手册集合以下资料

J1 How much did your child weigh at birth?
在出世时，您的孩子的重量是多少？

[bthwt] WEIGHT AT BIRTH ..... ☐☐☐☐ gm
出世时的重量
RF 拒绝回答 .....98. ☐
DK 不知道 ....99. ☐

J2 What was your child's gestational age at birth?
在出世前，您的孩子在母体内待了多少个星期？

[gesage] ☐☐+☐ ..... # WEEKS 星期
RF 拒绝回答 .....98. ☐
DK 不知道.....99. ☐

J3 What was your child's length at birth?
在出世时，您的孩子的身长是多少？

[blength] ☐☐.☐ Cm 公分
RF 拒绝回答....98. ☐
DK 不知道.....99. ☐

J4 What was your child's Head circumference at birth?
在出世时，您的孩子的头的周长是多少？

[hdcf] ☐☐.☐ Cm 公分
RF 拒绝回答....98. ☐
DK 不知道.....99. ☐

INTERVIEWER ID: ☐☐☐ **END TIME** ☐☐:☐☐ AM/PM

STUDY ID: _____

DATE: _____

STUDY ID: ☐☐☐☐ _ ☐ _ ☐☐
[sno] (Home ID) (Fam ID) (Child ID)

INTERVIEWER ID: ☐☐☐
[invest1]
Date of Interview: _____
[date1] (DD – MM – YYYY)

A Study on Strabismus, Amblyopia and Refractive Error in Singapore Preschoolers (STARS Study)

新加坡学龄前孩童于斜视，弱视和折射误差方面的研究

Family History
家庭的来历

(1 Interview / Household)
(1 采访 / 家庭)

CHILD Sticky Label Here

Remarks 备注:

_____

_____

_____

STUDY ID: _____

DATE: _____

A: Income and Educational Status
A 项: 收入和学历

A.1 What is child's father dialect group?
孩子爸爸的籍贯？

[fadial]

HOKKIEN 福建人 ..... 1. ☐
TEOCHEW 潮州人 ..... 2. ☐
CANTONESE 广东人 ..... 3. ☐
HAKKA 客家人 ..... 4. ☐
HAINANESE 海南人 ..... 5. ☐
HOKCHEW 福州人 ..... 6. ☐
OTHER **(SPECIFY)** 其他（请说明）
..... 7. ☐

[fadialsp]

Specify: _____
请说明

RF 88. ☐ DK 99. ☐

RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

A.2 What is child's mother dialect group?
孩子妈妈的籍贯？

[modial]

HOKKIEN 福建人 ..... 1. ☐
TEOCHEW 潮州人 ..... 2. ☐
CANTONESE 广东人 ..... 3. ☐
HAKKA 客家人 ..... 4. ☐
HAINANESE 海南人 ..... 5. ☐
HOKCHEW 福州人 ..... 6. ☐
OTHER **(SPECIFY)** 其他（请说明）
..... 7. ☐

[modialsp]

Specify: _____
请说明

RF 88. ☐ DK 99. ☐

RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

A.3 What is your total combined monthly household income? (Singapore dollars)

您每月的家庭总收入是多少？
（以新元计算）

[income]

Less than S$1,000 少过 S$1,000.. 1. ☐
S$1,000 – S$2,999 ..... 2. ☐
S$3,000 – S$4,999 ..... 3. ☐
S$5,000 and above
S$5,000 及以上 ..... 4. ☐
RF 拒绝回答 ..... 98. ☐
DK 不知道 ..... 99. ☐

A.4 What's the child father's completed educational level?

孩子父亲的学历

[faedu]

None 没有 ..... 1. ☐
Primary 小学 ..... 2. ☐
Secondary 中学..... 3. ☐
"O" / "N" Levels "O" / "N" 水准 ..... 4. ☐
"A" Levels / Polytechnic / Diploma / ITE / Certificate
"A" 水准 / 理工学院 / 学位文凭 / 工艺教育学院 / 文凭
..... 5. ☐
University education (degree and above, including bachelor, master and PhD)
大学教育 (学位及以上，包括学士、硕士和博士) ..... 6. ☐
Others 其它 ..... 7. ☐

[faedspf]

Specify: _____
请说明：

RF 拒绝回答..... 98. ☐
DK 不知道 ..... 99. ☐

A.5 What's the child mother's completed educational level?

孩子母亲的学历

[moedu]

None 没有 ..... 1. ☐
Primary 小学 ..... 2. ☐
Secondary 中学..... 3. ☐
"O" / "N" Levels "O" / "N" 水准 ..... 4. ☐
"A" Levels / Polytechnic / Diploma / ITE / Certificate
"A" 水准 / 理工学院 / 学位文凭 / 工艺教育学院 / 文凭
..... 5. ☐
University education (degree and above, including bachelor, master and PhD)
大学教育 (学位及以上，包括学士、硕士和博士) ..... 6. ☐
Others 其它 ..... 7. ☐

[moedspf]

Specify: _____
请说明

RF 拒绝回答..... 98. ☐
DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

SECTION B: Mother's Smoking History.

B 项: 孩子母亲吸烟的历史

B1 Has the mother ever smoked?
(At least one cigarette a day for 1 year or longer)

您可曾吸烟?
(每天至少吸一支香烟有整年或更长的时间)

[mosmoke]

NO 没有 ..... **(SKIP TO 到 C 1)** ..... 0. ☐

YES, and she currently still smokes
有，目前还在吸烟
..... **(SKIP TO 到 B 3)** ..... 1. ☐

YES, but she quit smoking
有，目前已戒烟
.....**(GO TO 到 B 2)** ..... 2. ☐

RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

B2 If the mother quit smoking, how long ago did she quit?

如果已戒烟，那是多久的事?

[moquit]

└┴┘ .....YEARS AGO 年前
RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

B3 At what age did the mother start smoking cigarettes on a regular basis?

您几岁开始有规律性地吸烟?

[mosmkage]

└┴┘ .....YEARS OLD 岁
RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

B4 If the mother smokes / used to smoke manufactured cigarettes, what is the number of cigarettes that he smoked per day?

如果您是吸烟者/ 习惯吸香烟厂的香烟，一天吸多少支香烟?

[mosmkno]

6 cigarettes or less
6 支香烟或更少..... 1. ☐
7 – 12 cigarettes 7 – 12 支香烟..... 2. ☐
13 – 22 cigarettes 13 – 22 支香烟.. 3. ☐
23 – 32 cigarettes 23 – 32 支香烟.. 4. ☐
33 – 42 cigarettes 33 – 42 支香烟.. 5. ☐
43 cigarettes or more
43 支香烟或更多..... 6. ☐
RF 拒绝回答..... ..... 98. ☐
DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

SECTION C: Father's Smoking History.

C 项: 孩子父亲吸烟的历史

C1 Has the father ever smoked?
(At least one cigarette a day for 1 year or longer)

您可曾吸烟?
(每天至少吸一支香烟有整年或更长的时间)

[fasmoke]

NO 没有 ..... **(SKIP TO 到 D)**..... 0. ☐

YES, and he currently still smokes
有，目前还在吸烟
..... **(SKIP TO 到 C 3)**..... 1. ☐

YES, but he quit smoking
有，目前已戒烟
.....**(GO TO 到 C 2)** ..... 2. ☐

RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

C2 If the father quit smoking, how long ago did he quit?

如果已戒烟，那是多久的事?

[faquit]

└┴┘ .....YEARS AGO 年前
RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

C3 At what age did the father start smoking cigarettes on a regular basis?

您几岁开始有规律性地吸烟?

[fasmkage]

└┴┘ .....YEARS OLD 岁
RF 拒绝回答..... ..... 98. ☐
DK 不知道 .... 99. ☐

C4 If the father smokes / used to smoke manufactured cigarettes, what is the number of cigarettes that he smoked per day?

如果您是吸烟者/ 习惯吸香烟厂的香烟，一天吸多少支香烟?

[fasmkno]

6 cigarettes or less
6 支香烟或更少..... 1. ☐
7 – 12 cigarettes 7 – 12 支香烟..... 2. ☐
13 – 22 cigarettes 13 – 22 支香烟.. 3. ☐
23 – 32 cigarettes 23 – 32 支香烟.. 4. ☐
33 – 42 cigarettes 33 – 42 支香烟.. 5. ☐
43 cigarettes or more
43 支香烟或更多..... 6. ☐
RF 拒绝回答..... ..... 98. ☐
DK 不知道 ..... 99. ☐

STUDY ID: _____

DATE: _____

SECTION D: Contact Details
D 项: 联络方式

This section can be completed by the respondent (这个部分可以由受访者完成)

		Home Tel 住家电话	Office Tel 办公室电话	Pager no 传呼机	Hand-phone 手提电话	Email 电子邮件
D.1. [faname]	Father's name: 父亲的名字: _____	[fatelh]	[fatelo]	[fapager]	[fahp]	[faemail]
D.2. [moname]	Mother's name: 母亲的名字 _____	[motelh]	[motelo]	[mopager]	[mohp]	[moemail]
D.3. [carename]	Other Care Giver 其他看护人 (Please Specify) （请说明） _____	[telhcl]	[telocl]	[pagercl]	[hpcl]	[emaicl]

1. Other Care Giver may be grandparents, baby sitter, maid etc. (其他看护者可以是祖父母，保姆，佣人)

STUDY ID: _____

DATE: _____

E. This section can be completed by the respondent. (这个部分可以由受访者完成)

Now I'd like to get the names, addresses, and telephone numbers of one person who does not live with you now but who would know how to reach you if you move. Anyone we contact would be asked only if they know how to reach you. They won't be asked anything else, and they won't be given any information about you. Please try to include at least one close relative/friend who lives in the Singapore but does not live with you.

请提供至少一个不与您居住在一起，但居住在新加坡并时常与您保持联络的亲戚/朋友的联络资料。如果您搬家，我们将会联络他，而唯一的目的就是为了联络你，我们将不会问他其它的问题。

[crname] 1. FULL NAME 全名:

_____

[crrelate] 2. PERSON'S RELATIONSHIP TO YOU 你们两人的关系:

_____

[cradd] 3. PRESENT ADDRESS 现在的住址:

_____

[crpcode] _____S( )

[crtelh] 4. HOME TELEPHONE NUMBER 住家电话 ..... |_|_|_|_|_|_|_|_|

[crtelo] 5. WORK TELEPHONE NUMBER 办公室电话 ..... |_|_|_|_|_|_|_|_|

[crtelhp] 6. HANDPHONE NUMBER 手提电话..... |_|_|_|_|_|_|_|_|

STUDY ID: _____

DATE: _____

Family History (Immediate Family: Father, Mother, and Children) of wearing glasses, contact lens and eye related diseases
家庭背景(直属亲人：父亲，母亲和孩子) 有 戴眼镜，隐形眼镜和有关眼睛的疾病

(1) Name 姓名	(2) Relationship 关系	(3) Gender 性别 1 = Male 男 2 = Female 女	(4) History of wearing glasses/contact lens/laser surgery 是否曾配戴眼镜或隐形眼镜/激光手术 1 = Yes 是 0 = NO 不是	(4.1) If Yes for previous question (who had a history of wearing any glasses/contact lens) 如果曾配戴眼镜或隐形眼镜，请回答以下问题		(5) Do you have any of the following eye diseases? 是否患上以下眼疾？		Child participating in the study 孩子是否参与这项研究 1 = Yes 是 0 = No 不是	If the child is participating in the study, please provide child study ID 如果孩子参与这项研究，请提供他的研究编号。
				(4.1.1) Age first wore glasses (yrs) 一开始配戴眼镜的年龄（岁数）	(4.1.2) Glasses are for 眼镜是用来： 1 = Distance 远距离 2 = Close 近距离 3 = Both Distance and close 远和近距离 4 = Contact Lens 隐形眼镜 5 = Astigmatism 散光	(5.1) **Amblyopia 弱视** 1 =Yes 是 0 = No 不是	(5.2) **Strabismus 斜视** 1 = Yes 是 0 = No 不是		
[faname]	**Father 父亲**	**1** [fagender]	[glassfa]	[glagefa]	[gltypfa]	[ambfa]	[strabfa]	**NA**	**NA**
[moname]	**Mother 母亲**	**2** [mogender]	[glassmo]	[glagemo]	[gltypmo]	[ambmo]	[strabmo]	**NA**	**NA**
Name of child(ren):									
[sib1nam]	Child1 孩子 1	[sibgen1]	[glassib1]	[glagesb1]	[gltypsb1]	[ambsb1]	[strabsb1]	[sibptp1]	[sibid1]
[sib2nam]	Child2 孩子 2	[sibgen2]	[glassib2]	[glagesb2]	[gltypsb2]	[ambsb2]	[strabsb2]	[sibptp2]	[sibid2]
[sib3nam]	Child3 孩子 3	[sibgen3]	[glassib3]	[glagesb3]	[gltypsb3]	[ambsb3]	[strabsb3]	[sibptp3]	[sibid3]
[sib4nam]	Child4 孩子 4	[sibgen4]	[glassib4]	[glagesb4]	[gltypsb4]	[ambsb4]	[strabsb4]	[sibptp4]	[sibid4]
[sib5nam]	Child 5 孩子 5	[sibgen5]	[glassib5]	[glagesb5]	[gltypsb5]	[ambsb5]	[strabsb5]	[sibptp5]	[sibid5]

1. **Amblyopia: Amblyopia is poor vision in an eye that can not be corrected with glasses or contact lenses and the eye looks normal.**
   弱视是一种视力的缺陷，不能即由眼镜或隐性眼镜而矫正，而眼睛也看似正常。
2. **Myopia: Myopia or nearsightedness or needs to wear glasses to see far away.**
   近视是需要戴眼镜才能看清远距离的东西。
3. **Strabismus is when the eyes are not properly lined – up. This happens when one eye looks straight ahead and the other eye crosses in or wanders out.**
   斜视 – 两只眼睛不能完全地列好，即当一只眼睛看向前面但另一只眼睛交叉或目光无目的地移动。

8.2.2. Manuscripts

Manuscripts from this thesis:

1. Chia A, Dirani M, Chan YH, Gazzard G, Au Eong KG, Selvaraj P, Ling Y, Quah BL,Young TL, Mitchell P, Varma R, Wong TY, Saw SM. Prevalence of amblyopia and strabismus in young singaporean chinese children. Invest Ophthalmol Vis Sci 2010; 51: 3411-7. [copyright ARVO]

2. Chia A, Lin XY, Dirani M, Gazzard G, Ramamurthy D, Quah BL, Chang B, Ling Y, Leo SW, Wong TY, Saw SM. Risk factors for Strabismus and Amblyopia in young Singapore Chinese children. Ophthalmic Epidemiol. 2013 Jun;20(3):138-47.

3. Chia A, Dirani M, Haaland B, Wong TY, Varma R, Saw SM. Assessment of Screening Performance of Stereoacuity Tests in Preschool Children.
- Submitted to Ophthalmic Epidemiology Dec 2012.

4. Chia A, Chan YH, Lamoureux E, Chiang P, Thumboo J, Wong TY, Saw SM.
Effect of Strabismus and Amblyopia on Quality-of-life and Development in young Singaporean children.
- Submitted to Optometry and Visual Science Dec 2012

Prevalence of Amblyopia and Strabismus in Young Singaporean Chinese Children

Audrey Chia,[1,2] *Mohamed Dirani,*[3] *Yiong-Huak Chan,*[4] *Gus Gazzard,*[5,6] *Kah-Guan Au Eong,*[7,8,9,10] *Prabakaran Selvaraj,*[4] *Yvonne Ling,*[1,2] *Boon-Long Quah,*[1,2] *Terri L. Young,*[11,12] *Paul Mitchell,*[13] *Rohit Varma,*[14] *Tien-Yin Wong,*[1,2,3,9] *and Seang-Mei Saw*[2,4,11]

Purpose. To determine the prevalence of amblyopia and strabismus in young Singaporean Chinese children.

Methods. Enrolled in the study were 3009 Singaporean children, aged 6 to 72 months. All underwent complete eye examinations and cycloplegic refraction. Visual acuity (VA) was measured with a logMAR chart when possible and the Sheridan-Gardner test when not. Strabismus was defined as any manifest tropia. Unilateral amblyopia was defined as a 2-line difference between eyes with VA < 20/30 in the worse eye and with coexisting anisometropia (≥1.00 D for hyperopia, ≥3.00 D for myopia, and ≥1.50 D for astigmatism), strabismus, or past or present visual axis obstruction. Bilateral amblyopia was defined as VA in both eyes <20/40 (in children 48–72 months) and <20/50 (<48 months), with coexisting hyperopia ≥4.00 D, myopia ≤ −6.00 D, and astigmatism ≥2.50 D, or past or present visual axis obstruction.

Results. The amblyopia prevalence in children aged 30 to 72 months was 1.19% (95% confidence interval [CI], 0.73–1.83) with no age ($P = 0.37$) or sex ($P = 0.22$) differences. Unilateral amblyopia (0.83%) was twice as frequent as bilateral amblyopia (0.36%). The most frequent causes of amblyopia were refractive error (85%) and strabismus (15%); anisometropic astigmatism >1.50 D (42%) and isometropic astigmatism >2.50 D (29%) were frequent refractive errors. The prevalence of strabismus in children aged 6 to 72 months was 0.80% (95% CI, 0.51–1.19), with no sex ($P = 0.52$) or age ($P = 0.08$) effects. The exotropia-esotropia ratio was 7:1, with most exotropia being intermittent (63%). Of children with amblyopia, 15.0% had strabismus, whereas 12.5% of children with strabismus had amblyopia.

Conclusions. The prevalence of amblyopia was similar, whereas the prevalence of strabismus was lower than in other populations. (*Invest Ophthalmol Vis Sci.* 2010;51:3411–3417) DOI:10.1167/iovs.09-4461

Amblyopia and strabismus are two common pediatric eye conditions with functional and cosmetic consequences. Amblyopia is associated with suboptimal vision, despite best spectacle correction in the absence of any other ocular and neural abnormality.[1] Failure to diagnose and manage amblyopia before the age of 8 years can result in life-long visual impairment.[1] Strabismus is the misalignment of the eyes, and if left untreated, may result in loss of binocularity and depth perception.[1]

Overall, global estimates of the prevalence of amblyopia and strabismus in children and teenagers range from 0.20% to 6.2% and 0.13% to 4.7%, respectively.[1–29] However, few studies have been performed on population-based samples, so that variation in study design and disease classification could account for some of the disparity noted, making direct comparison between studies difficult (Table 1).[30,31]

Most past studies of amblyopia and strabismus have involved older school-age children, when therapeutic and preventive strategies are less successful. In a study of 7843 children 7 years of age in the 1991 to 1992 birth cohort in Avon, United Kingdom, a 3.6% prevalence of past or present amblyopia was recorded, with most having had treatment, thus leaving only 0.6% with impaired vision.[28] In this study, a strabismus prevalence of 2.3% was recorded, including 73.4% of cases that were convergent, 21.4% divergent, and 5.2% vertical. In contrast, in an Australian study in which 1736 children aged 6 years were examined, amblyopia was reported in 0.7%, most of which was related to strabismus (37.5%), anisometropia (34.4%), or both (18.8%).[17] Strabismus was present in 2.8% (54% esotropia and 29% exotropia) with even lower rates, particularly of esotropia, noted in the East Asian children included in the study.[16]

Few studies have involved East Asian children, in which the prevalence of myopia is highest. Matsuo et al.,[21,22] in a questionnaire-based study of Japanese children aged between 1.5 and 12 years, the reported prevalence rate of amblyopia and strabismus ranging between 0% to 0.2% and 0.01% to 0.99%, respectively. Most such studies, however, were handicapped by their dependence on the return of questionnaires and variability in family or ophthalmologist definitions of amblyopia

From the [1]Singapore National Eye Center and the [2]Singapore Eye Research Institute, Singapore; the [3]Center for Eye Research Australia, Department of Ophthalmology, University of Melbourne, Melbourne, Victoria, Australia; the Departments of [4]Epidemiology and Public Health and [9]Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; the [5]Institute of Ophthalmology, London, United Kingdom; [6]Moorfields Eye Hospital, London, United Kingdom; the [7]Department of Ophthalmology and Visual Sciences, Alexandra Hospital, Singapore; the [8]Eye Clinic, Jurong Medical Center, Singapore; the [10]Singapore International Eye Cataract Retina Center, Mount Elizabeth Medical Centre, Singapore; [11]Duke-National University of Singapore Graduate Medical School, Singapore; the [12]Department of Ophthalmology, Duke University Medical Center, Durham, North Carolina; the [13]Centre for Vision Research (Westmead Millennium Institute), University of Sydney, Sydney, New South Wales, Australia; and the [14]Doheny Eye Institute, University of Southern California, Los Angeles, California.

Supported by Grant NMRC/1009/2005 from the National Medical Research Council, Singapore.

Submitted for publication August 11, 2009; revised October 2 and November 20, 2009, and January 5, 2010; accepted February 5, 2010.

Disclosure: **A. Chia**, None; **M. Dirani**, None; **Y.-H. Chan**, None; **G. Gazzard**, None; **K.-G. Au Eong**, None; **P. Selvaraj**, None; **Y. Ling**, None; **B.-L. Quah**, None; **T.L. Young**, None; **P. Mitchell**, None; **R. Varma**, None; **T.-Y. Wong**, None; **S.-M. Saw**, None

Corresponding author: Audrey Chia, Singapore Eye Center, 11 Third Hospital Road, Singapore 168751; wla_chia@yahoo.com.

Table 1. Table of Strabismus and Amblyopia Prevalence in Children/Teenagers from Selection of Population-Based or Large Cohort Studies, Ranked According to Age of Subjects

Study	Country (y)	Study Population Age (*n*)	Strabismus (%)	XT:ET Ratio*	Definition of Amblyopia Used	Amblyopia (%)
STARS	Singapore	6–72 mo† (3,009)	0.80	7:1	Unilateral: VA <20/30 in the worse eye, 2-line difference and	1.19
MEPED study group[26]	United States (2008)	6–72 mo† (6,014)				
		Hispanic/Latino	2.4	1.2:1	amblyogenic factors.	2.6
		African American	2.5	1.1:1	Bilateral: VA both eyes <20/40	1.5
Friedman et al.[29]	United States (2009)	6–72 mo† (2,546)			(age 48–72 mo) or <20/50 (age	
		White	3.3	1.2:1	<48 mo), and amblyogenic	1.8
		African American	2.1	1:1	factors.	0.8
Matsuo et al.[22]‡	Japan (2007)	1.5 and 3 y† (6,900)	0.01–0.35	2.4:1	As determined by ophthalmologist.	0–0.18
Chang et al.[20]	Taiwan (2007)	3 to 6 y† (5,232)	—	—	VA <20/20 with amblyogenic risk factors.	2.2
Lim et al.[11]	Korea (2004)	3 to 5 y; kindergarten children (36,973)	—	—	VA <20/40 (age, ≤3 y), <20/32 (age, >3 y) or 2-line difference.	0.42
Preslan and Novak[6]	United States (1996)	4 to 7 y; preschool/ school children (680)	3.1	1:9	VA <20/30 with amblyogenic factors.	3.9
Robaei et al.[17,18]	Australia (2006)	6 y; school children (1,739)	2.8	1:1.8	VA <20/40 or 2-line difference.	0.7–1.8
Williams et al.[28]	United Kingdom (2008)	7 y (7,825)†	2.3	1:3.4	VA <20/40, 2-line difference or history.	3.6
He et al.[10]	China (2004)	5–15 y† (4,364)	1.9	4:1	VA ≤20/32 and other factors.	0.87
Matsuo and Matsuo[21]‡	Japan (2007)	6–13 y† (113,763)	0.99–1.28	2.8:1	As determined by ophthalmologist.	0.14–0.20
Goh et al.[14]	Malaysia (2005)	7–15 y† (4,634)	—	—	VA ≤20/32 and other factors.	2.0
Robei et al.[18,27]	Australia (2006, 2008)	12 y; school children (2,353)	2.7	1.3:1	VA <20/40 or 2-line difference.	0.4
Ohlsson et al.[9]	Mexico (2003)	12 to 13 y; school children (1,035)	2.3	1:1.8	VA ≤20/40 or 2-line difference and amblyogenic factors.	2.5
Ohlsson et al.[8]	Sweden (2001)	12 to 13 y; school children (1,046)	2.7	1:2.2	VA ≤20/40, 2-line difference with no organic cause.	1.1
Yassur et al.[2]	Rwanda (1972)	10 to 18 y; school children (1,550)	NA	—	VA ≤20/40.	1.2
Quah et al.[4]	Singapore (1991)	18 y; army recruits (6,556)			VA ≤20/40 with no organic cause.	0.73
Rosman et al.[15]	Singapore (2005)	18 y; army recruits (122,596)	NA	—	VA ≤20/40 with no organic cause.	0.34

XT, exotropia; ET, esotropia.
* XT:ET ratio calculated from data presented in the papers.
† Population-based studies.
‡ Studies from Matsuo et al.[22] and Matsuo and Matsuo[21] based on questionnaire responses.

and strabismus. Lim et al. used a home screening unit to identify at risk Korean children aged 3 to 5 years. These children were then referred to an ophthalmologist and amblyopia, mostly refractive, was detected in 0.4% of the 43% who responded.[11] In Taiwan, Lai et al.[24] reviewed visual screening records of 625 preschool children and identified amblyopia, using various definitions, in approximately 5% and strabismus in 9.6% of children. He et al.,[10] primarily assessing visual impairment in 4368 children, aged 5 to 15 years, in Guangzhou, China, reported amblyopia in 1.9%, and near and distant tropia in 1.9% and 3% of their subjects, respectively.

Few population-based studies have focused on eye disease in younger children aged <6 years. The Multiethnic Pediatric Eye Disease Study (MEPEDS) and Baltimore Pediatric Eye Disease Study (BPEDS) are two large studies designed to determine the prevalence of decreased visual acuity (VA), strabismus, amblyopia, and refractive errors in children aged 6 to 72 months.[26,29,32] In 2008, the MEPEDS study group reported an amblyopia prevalence of 2.6% and 1.5% and a strabismus prevalence of 2.4% and 2.5% in 3007 Hispanic/Latino and 3007 African-American children, respectively.[26] In 2009, Friedman et al.[29] reported the BEPDS findings on 2546 children, with amblyopia prevalence rates of 1.8% and 0.8%, and strabismus prevalence rates of 3.3% and 2.1% in Caucasian and African-American children, respectively. These data are not generalizable to Asian populations.

The purpose of the Strabismus, Amblyopia, and Refractive Error in Singapore (STARS) study was to determine the prevalence of amblyopia and strabismus in young Chinese preschool children in Singapore. Methods and definitions used in the STARS study are similar to those used in the BPEDS and MEPEDS studies, so that comparisons can readily be made between these studies.[32]

Methods

Sample Population

Chinese children aged 6 to 72 months were recruited from Housing Development Board townships through a door-to-door recruitment exercise. The study area included a large part of the South-Western region of Singapore. The majority of the population (84%) live in such townships, and there are no distinctive demographic differences between this region of Singapore and the rest of the island (Table 2).[33] However, parents of children recruited for this study were generally better educated with higher incomes than other young Singaporean adults aged between the ages of 20 to 40 years, suggesting some underrepresentation of the poorer, less educated, and lower income

TABLE 2. Socioeconomic Differences between Populations within the STARS Recruitment Area and the General Population and between Parents of Children Recruited for the Study and Singaporean Chinese Adults Aged 20–40 y

	Singapore Population (Total %)*	STARS Recruitment Area (%)*	Singaporean Chinese Aged 20–40 y (%)*	STARS Fathers (%)	STARS Mothers (%)
Education					
None	19.5	19.1	5	<1	<1
Primary	12.1	12.9	7	9	6
Secondary	35.5	35.3	34	29	35
Polytechnic	21.1	21.0	33	26	29
University	11.7	11.7	21	32	28
Unknown				3	1
Employment					
Employed	59.4	60.1			
Unemployed	3.8	3.7			
Inactive	36.8	36.2			
Household income				STARS Households	
<S$1000	12.4	10.0	No data available	3	
S$1000–2999	28.0	29.5		21	
S$3000–4999	23.5	25.5		30	
>S$5000	35.6	35.0		44	
Unknown				2	

* Information obtained from Population Census (2000) of persons aged >15 years within different district zones.[33]

groups within the population. Parents were invited to bring their children to one of two visual screening sites. Children of non-Chinese or mixed ethnicity were excluded from the study. Disproportionate stratified sampling by 6-month age groups was performed with an almost equal number of children in each 6-month age group. A total of 4162 Chinese children were eligible to participate in the study, with 3009 examined (response rate 72.3%). There were no significant sex ($P = 0.65$) or age ($P = 0.18$) differences between participants and nonparticipants. Response rates in different age groups were similar and ranged between 71% and 74%. There were, however, significant area differences ($P < 0.001$), with participation rates of districts closer to examination sites being greater than those located farther away.

This study was approved by the National Medical Research Council (NMRC) in Singapore, and all procedures adhered to the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians before any tests were conducted.

Examination of Alignment and VA

Ocular Motility. Ocular alignment was assessed by using the Hirschberg light reflex, cover test, and prism cover–uncover tests. Cover tests were performed by using fixation targets at both distance (6 m) and near (30 cm). The presence of strabismus, its characteristics (constant or intermittent), type (exotropia, esotropia, hyper/hypotropia or dissociated vertical deviation), and size (prism diopters) were also recorded.

Visual Acuity. VA was measured in children aged 30 to 72 months with a logarithm of the minimum angle of resolution (logMAR) distance vision chart. If this was not possible, single-letter Sheridan-Gardner tests were used. When initial VA was < 20/30 (logMAR 0.18) in either eye, it was retested. If the results were still poor, or if the children were unable to co-operate with the VA testing, they were given Sheridan-Gardner single letters to learn, and a retest date was scheduled.

Pupil Dilation. Cycloplegic refraction was performed 30 minutes after the use of 3 drops of cyclopentolate 1% (Cyclogyl; Alcon-Couvreur, Purrs, Belgium) administered at 5-minute intervals, with 0.5% cyclopentolate used for children aged <12 months. Refraction was measured with a table-mounted autorefractor (model RKF-1; Canon, Ltd., Tochigiken, Japan) or a handheld autorefractor (Retinomax; Nikon Corp., Tokyo, Japan) whenever possible, or streak retinoscopy when not possible. Five consecutive autorefractor readings were obtained from each subject, all of which had to be within 0.25 D of each other. Spherical equivalent (SE) was calculated as the sum of the spherical plus half the cylindrical error.

Ocular Examination. The children underwent a full ocular examination, and any pathology involving the anterior and posterior ocular segments was documented.

Interview

Parents were asked a series of questions about their children, including questions on the past or present history of amblyopia and strabismus, the type and duration of any treatment provided for amblyopia or strabismus, and the presence of any other past or present ocular problems.

Definitions

Children were classified as having strabismus if any tropia was present at distance or near, with or without spectacles.

Anisometropia, the presence of significant refractive error differences between eyes, was defined as spherical when there was a difference in spherical equivalent, or astigmatic when there were differences in cylinder power. Isometropia occurred when less-significant refractive differences were present between the eyes. Levels of amblyogenic anisometropia and isometropia varied for both ametropia (myopia or hyperopia) and astigmatism, depending on whether the children had unilateral or bilateral amblyopia.

Unilateral amblyopia was defined, as in the MEPEDS, as a ≥2-line difference in best VA, when <20/30 (logMAR 0.18) in the worse eye, and with amblyogenic factors such as past or present strabismus, anisometropia (≥1.00 D difference in hyperopia, ≥3.00 D difference in myopia, or ≥1.50 D difference in astigmatism), and past or present obstruction of the visual axis.[26,32]

Bilateral amblyopia was defined as best VA in both eyes <20/40 (logMAR 0.3) in children aged 48 to 72 months or <20/50 (logMAR 0.4) in children aged <48 months, in the presence of amblyogenic factors such as hyperopia ≥4 D, myopia ≤ −6.00 D, or astigmatism ≥2.50 D, or past or present obstruction of the visual axis.[26,32]

Statistical Analyses

Age and sex-specific prevalence rates for strabismus and amblyopia were calculated. Poisson distribution was used to construct 95% CIs for all prevalence estimates. Data were weighted to the Singapore Popu-

Table 3. Prevalence of Strabismus in Children Aged 6 to 72 Months

	n	Any Strabismus* *n* (%, 95% CI)	Exotropia *n* (%, 95% CI)	Esotropia *n* (%, 95% CI)
All children				
Crude rate	3009	24 (0.80, 0.51–1.19)	20 (0.67, 0.41–1.03)	3 (0.10, 0.02–0.29)
Adjusted rate†		(0.84, 0.80–0.88)	(0.70, 0.66–0.74)	(0.10, 0.086–0.12)
6–11 mo	189	0 (0, 0.0–1.9)	0 (0, 0.0–1.6)	0 (0, 0.0–1.6)
12–23 mo	537	2 (0.37, 0.04–1.32)	2 (0.37, 0.04–1.32)	0 (0, 0.0–0.55)
24–35 mo	514	5 (0.97, 0.31–2.23)	3 (0.58, 0.12–1.68)	2 (0.39, 0.005–1.07)
36–47 mo	574	4 (0.69, 0.11–1.50)	3 (0.52, 0.11–1.50)	1 (0, 0.0–0.51)
48–59 mo	602	7 (1.16, 0.46–2.35)	7 (1.16, 0.46–2.35)	0 (0, 0.0–0.49)
60–72 mo	576	6 (1.04, 0.38–2.23)	5 (0.86, 0.28–1.99)	0 (0, 0.0–0.95)
P (trend)		0.08	0.07	0.57
Boys (all)	1561	14 (0.89, 0.44–1.41)	12 (0.77, 0.39–1.33)	1 (0.064, 0.002–0.36)
6–11 mo	88	0 (0, 0.0–3.27)	0 (0, 0.0–3.27)	0 (0, 0.0–3.27)
12–23 mo	308	1 (0.32, 0.008–1.79)	1 (0.33, 0.008–1.79)	0 (0, 0.0–0.96)
24–35 mo	262	1 (0.38, 0.01–2.10)	1 (0.38, 0.01–2.10)	0 (0, 0.0–1.13)
36–47 mo	291	4 (1.36, 0.21–2.94)	3 (1.02, 0.21–2.94)	1 (0.34, 0.01–1.89)
48–59 mo	321	4 (1.24, 0.33–3.11)	4 (1.23, 0.33–3.11)	0 (0, 0.0–0.91)
60–72 mo	291	4 (1.37, 0.37–3.45)	3 (1.03, 0.21–2.96)	0 (0, 0.0–1.02)
P (trend)		0.06	0.10	0.92
Girls (all)	1431	10 (0.69, 0.33–1.27)	8 (0.56, 0.24–1.09)	2 (0.14, 0.02–0.50)
6–11 mo	101	0 (0, 0.0–2.92)	0 (0, 0.0–2.92)	0 (0, 0.0–2.92)
12–23 mo	229	1 (0.44, 0.01–2.37)	1 (0.44, 0.01–2.37)	0 (0, 0.0–1.28)
24–35 mo	252	4 (1.58, 0.43–3.95)	2 (0.79, 0.09–2.79)	2 (0.80, 0.01–2.16)
36–47 mo	283	0 (0, 0.0–1.04)	0 (0, 0.0–1.04)	0 (0, 0.0–1.04)
48–59 mo	281	3 (1.06, 0.22–3.08)	3 (1.06, 0.22–3.08)	0 (0, 0.0–1.06)
60–72 mo	285	2 (0.69, 0.08–2.48)	2 (0.70, 0.08–2.48)	0 (0, 0.0–1.91)
P (trend)		0.67	0.38	0.43

95% CI, binomial distribution.

* Includes 1 child, a 71-month-old boy, who had DVD alone.

† Weighted to Census of Population 2000 (taking into account Location sampling and familial clustering).[33]

lation Census 2000, taking into account disproportionate age sampling and familial clustering[33] (Stata 10; StataCorp, College Station, TX).

Results

Prevalence of Strabismus

A total of 3009 children aged 6 to 72 months were recruited, of which 17 (0.5%) were excluded because of an inability to perform motility assessments. These included one child (0.5%) aged 6 to 11 months, three children (0.5%) aged 12 to 23 months, two (0.4%) aged 24 to 35 months, five (0.8%) aged 36 to 47 months, three (0.5%) aged 48 to 59 months, and three (0.5%) aged 60 to 72 months.

The overall prevalence of strabismus in children aged 6 to 72 months was 0.80%, with exotropia exceeding esotropia by a ratio of 7:1 (Table 3). There was no significant difference in strabismus prevalence between the boys and the girls ($P = 0.52$), and there were no age trends ($P = 0.08$).

The most frequent strabismus type was intermittent exotropia (58%), followed by constant exotropia (25%) and constant esotropia (12%). One subject, a 71-month-old boy, had an isolated dissociated vertical deviation (DVD; Table 4). Three children (12%) with strabismus also had amblyopia.

Prevalence of Amblyopia

Of the 2015 children aged 30 to 72 months, 333 (16.5%) were excluded because of an inability to complete VA testing. Excluded were 169 (67%) children aged 30 to 35 months, 133 (23%) aged 36 to 47 months, 24 (4%) aged 48 to 59 months, and 7 (1%) aged 60 to 72 months.

Cycloplegic refraction was available in 1796 (89.1%) of the 2015 children aged 30 to 72 months and in 1521 (90.5%) of the 1682 children in whom VA could be tested. Noncycloplegic autorefraction and manifest refraction were available for the remaining children. The mean SE in those who were able and unable to complete the VA test was 0.69 ± 1.12 and 0.41 ± 1.24 D respectively ($P < 0.0001$). However, there was no significant difference between children who were or were not able to complete the VA testing, in terms of the proportion with hyperopia ≥3.00 D (1.6% vs. 1.2%, $P = 0.58$), myopia ≤−6.00 D (0.3% vs. 0.4%, $P = 0.76$), or astigmatism ≥2.50 D (3.6% vs. 4.5%, $P = 0.57$). Overall, significant bilateral amblyo-

Table 4. Strabismus Subtypes and Characteristics*

	n
Strabismus type at distance	
Intermittent exotropia	12
Constant exotropia	7
Intermittent esotropia	0
Constant esotropia	3
Strabismus identified only at near	1
Strabismus type at near	
Intermittent exotropia	12
Constant exotropia	6
Intermittent esotropia	0
Constant esotropia	3
Strabismus identified only at distance	2
Strabismus magnitude at distance	
1–9 PD	0
10–30 PD	5
>30 PD	6
Unable to measure	12
Strabismus magnitude at near	
1–9 PD	0
10–30 PD	6
>30 PD	5
Unable to measure	12

* Data from one child with DVD are not included.

TABLE 5. Prevalence of Amblyopia by Sex and Age

	n	Any Amblyopia *n* (%, 95% CI)
All children		
Crude rate	1682	20 (1.19, 0.73–1.83)
Adjusted rate*		(1.15, 1.12–1.25)
30–35 mo	83	1 (1.21, 0.03–6.53)
36–47 mo	446	6 (1.35, 0.50–2.91)
48–55 mo	581	9 (1.55, 0.71–2.92)
56–72 mo	572	4 (0.70, 0.19–1.78)
P (trend)		0.37
Boys (all)	850	12 (1.41, 0.73–2.45)
30–47 mo	253	2 (0.79, 0.10–2.83)
48–72 mo	597	10 (1.68, 0.81–3.06)
P (trend)		0.31
Girls (All)	832	8 (0.96, 0.42–1.89)
30–47 mo	276	5 (1.81, 0.59–4.180)
48–72 mo	556	3 (0.54, 0.11–1.57)
P (trend)		0.07

95% CI, binomial distribution.

* Weighted to Census of Population 2000 (taking into account location sampling and familial clustering).[33]

genic refractive risk factors were identified in 19 (5.7%) of the 333 children unable to complete the VA screening testing, and in 100 (5.9%) in whom VA could be assessed ($P = 0.86$).

Of the 1682 children in whom VA assessment was possible, 48 (2.8%) met the VA criteria for amblyopia, but of these, 28 (58%) were not considered amblyopic because insufficient amblyogenic risk factors were identified. In these 28 subjects, 19 (67%) had minimal refractive error, with no past or present strabismus or visual obstruction. Nine children, however, missed refractive cutoff levels by smaller margins; four children with potential unilateral amblyopia had astigmatism between 1.50 and 4.00 D, but with anisometropic astigmatism <1.50 D; and five children with potential bilateral amblyopia had astigmatism between 1.45 and 2.50 D.

Twenty children satisfied all amblyopic requirements, so that the overall amblyopia prevalence in this study among children aged 30 to 72 months was 1.19% (Table 5). There was no significant difference in amblyopia prevalence between boys and girls ($P = 0.22$), and no age trend was evident ($P = 0.37$).

Amblyopia was attributed to refractive error in 17 children (85%) and to strabismus in 3 (15%; Table 6). Among children with unilateral amblyopia, refractive error was most frequently associated with anisometropic astigmatism ≥1.50 D ($n = 7$), followed by anisometropic myopia ≥3.00 D ($n = 2$) and anisometropic hyperopia ≥1.00 D ($n = 2$). In the bilateral amblyopia group, refractive errors recorded included astigmatism ≥2.50 D ($n = 2$), combined astigmatism and myopia ≤ −6.00 D ($n = 2$), combined astigmatism and hyperopia ≥4.00 D ($n = 1$) and myopia ≤ −6.00 D ($n = 1$). Of the three children in whom amblyopia was attributed to strabismus, two had intermittent exotropia and one had a constant esotropia.

Based on questionnaire information, 15 children, aged 30 to 72 months, had previously had a diagnosis and treatment of amblyopia. One child was unable to co-operate with the VA testing and two were found to be still amblyopic at our examination. The remaining 12 children (with presumably successfully treated amblyopia) were aged 63.5 ± 9.7 months (range, 53.2–72.0 months): six had high astigmatism ≥1.50 D, two had anisometropia ≥1.00 D, one had strabismus, and three had no identifiable cause.

DISCUSSION

In this study of young Singaporean Chinese children, we report an 0.80% prevalence of strabismus in children aged 6 to 72 months and a 1.19% prevalence of amblyopia in children aged 30 to 72 months. The overall exotropia and esotropia prevalence rates were 0.70% and 0.10%, respectively. Unilateral amblyopia was twice as frequent as bilateral amblyopia, whereas amblyopia was associated with a refractive error in >90% of the children, with astigmatism the most frequent amblyogenic risk factor.

Our prevalence estimate (0.80%; 95% CI, 0.51–1.19) for strabismus in young Chinese children was much lower than in Hispanic/Latino (2.4%; 95% CI, 1.9–3.0) and African-American (2.5%, 95% CI, 2.0–3.1) children who participated in the MEPEDS and also compared with Caucasian (3.3%, 95% CI, 2.3–4.6) and African-American (2.1%, 95% CI, 1.3–3.0) children in the BPEDS (Fig. 1).[26,29] It was also lower than in children aged between 4 and 7 years in the United States, United Kingdom, and Australia where the reported prevalence has ranged from 2.3% to 3.4% (Table 1).[7,17,18] Similar lower strabismus prevalence rates have been reported in other East Asian communities, such as those in Australia, Japan, and China.[10,16,21,22]

In regard to strabismus type, the prevalence of esotropia in young Singaporean Chinese children was much lower, whereas the prevalence of exotropia was only half that reported in Hispanic/Latino, African-American, and white American children in the MEPEDS and BPEDS (Fig. 1). The cause of this difference is uncertain, and although lower hyperopia rates in East Asian populations may be partly responsible, genetic and ethnic differences may also exist. Indeed, studies suggest that the strabismus risk is greater in those with a positive family history, and twin studies indicate that genetic liabilities exceed environmental ones.[34,35] The resultant high exotropia-esotropia ratio is typical of East Asian populations where it is often greater than 2:1.[10,21,22,36–39] In contrast, the ratio in many Caucasian studies is frequently reversed (Table 1).[8,16,17,18,28] More recently, Yu et al.[36] and Matsuo et al.[37] reported that the exotropia-esotropia ratio appears to be increasing in Hong Kong and Japan presumably as their populations become less hyperopic. A similar shift may also be occurring in the West as the exotropia-esotropia ratio in white children in the BPEDS study and 12-year-old children in Australia were recently reported to be 1.2:1 and 1.3:1, respectively.[18,29]

The prevalence of amblyopia in our Singaporean preschool sample was 1.19% (95% CI, 0.73–1.83). Compared with children in the MEPEDS and BPEDS, this prevalence was less than for Hispanic/Latino (2.6%, 95% CI, 1.8–3.4) and more similar to that found in white (1.8%, 95% CI, 0.9–3.1) and African-American (0.8%, 95% CI, 0.3–1.6, in the MEPEDS, and 1.5%, 95% CI, 0.9–2.1, in the BPEDS) children (Fig. 1).[26,29] Unfortunately, differences in study design and the lack of a consistent definition of amblyopia makes comparison with other studies difficult (Table 1).[40] Some of these studies have used definitions

TABLE 6. Type of Amblyopia

	n	Prevalence (%) (95% CI)
Unilateral	14	0.83 (0.46–1.39)
Anisometropic	11	0.65 (0.33–1.17)
Strabismic	3	0.18 (0.04–0.52)
Combined refractive/strabismus	0	0.0 (0.0–0.18)
Deprivational	0	0.0 (0.0–0.18)
Bilateral ametropic	6	0.36 (0.13–0.77)
Total	20	1.19 (0.73–1.83)

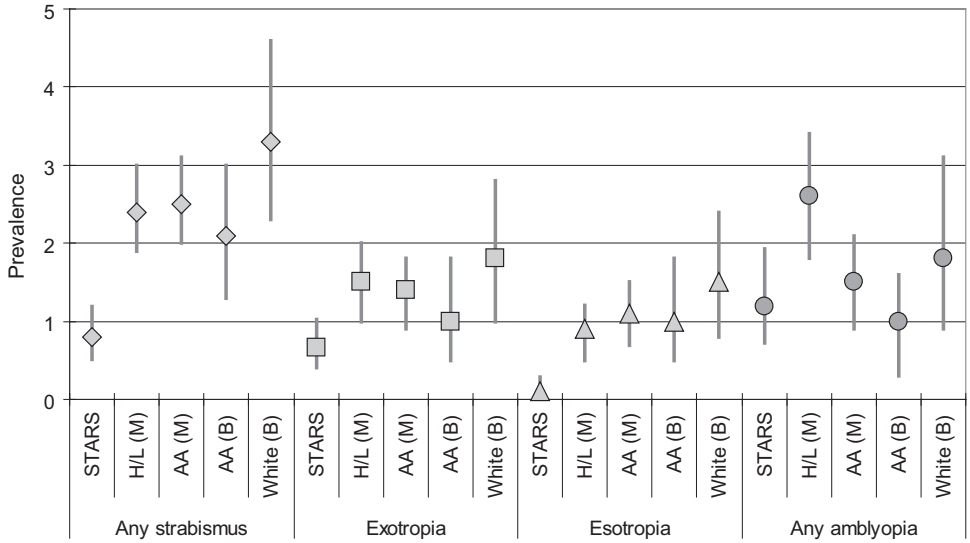


FIGURE 1. Comparison of strabismus and amblyopia prevalence in Singaporean Chinese children in the STARS study with Hispanic/Latino and African-American children from MEPEDS (M) and African-American and white children from BPEDS (B) studies.[26,29] H/L (M) denotes Hispanic/Latino and AA (M) denotes African-American children in the MEPEDS, and AA (B) denotes African-American and White (B) denotes white children in the BPEDS. *Central symbol*: prevalence; *vertical lines*: 95% CI.

similar to those of the American Association of Pediatric Ophthalmology and Strabismus (AAPOS), which classify suspected amblyopia as VA <20/40 in at least one eye in children aged 30 to 59 months and <20/30 in children aged over 60 months; a 2-line difference between eyes, even if vision is within the passing range; and the presence of amblyogenic risk factors including anisometropia >1.5 D, hyperopia >3.50 D, myopia < −3.00 D, astigmatism >1.50 D at the 90° or 180° meridian or >1.00 D in the oblique meridian, any manifest strabismus, media opacity >1 mm, and ptosis with a pupillary margin reflex ≤1 mm.[41,42] If we had used these more liberal criteria in our study, the amblyopia prevalence would increase 2.7-fold to 3.27%, with rates of 2.41%, 4.26%, 2.75%, and 3.15% in the 30- to 35-month, 36- to 47-month, 48- to 59-month, and 60- to 72-month age groups, respectively.

In terms of amblyopia type, Singapore preschool children were more likely to have refractive rather than strabismic amblyopia. Lower levels of strabismic amblyopia have also been noted in preschool children in other East Asian countries such as Korea (12.8%) and Taiwan (2.6%).[11,20] Hispanic/Latino and African-American children in the MEPEDS study were also more likely to have refractive amblyopic (80%) compared with strabismic amblyopia.[26] In contrast, amblyopia in Caucasian children in the United States, United Kingdom, and Australia was more likely to be associated with strabismus alone (26%–44%) or combined strabismus and refractive error (20%), rather than refractive error alone (40%–50%).[6,7,17,27–29]

There are several limitations to this study. It is possible that children already receiving ophthalmic care did not attend, resulting in an underestimation of prevalence. Conversely, families in whom parents suspected disease, or in whom there was a strong family history of eye disorders may have been more motivated to participate. There was also difficulty in determining whether a child was truly amblyopic. Half of the children aged 30 to 48 months were unable to co-operate with the optotype identification tests used, making any estimation of amblyopia prevalence in this group unreliable.[20,26] Children who were unable to perform the VA test were excluded from the study, but it is uncertain how many failed to co-operate because they were amblyopic. Children who cooperated but failed the VA test were also required to have certain levels of amblyogenic risk factors to be considered amblyopic; some of these children may have had past amblyogenic factors that lessened over time or milder levels or combinations of amblyogenic influences that were sufficiently amblyogenic in their case.[26]

CONCLUSIONS

In summary, the prevalence of amblyopia in Singaporean Chinese preschool children appears to be similar and that of strabismus much lower than that in Hispanic/Latino, white, and African-American children in the MEPEDS and BPEDS cohorts.

References

1. Carlton J, Karnon J, Czoski-Murray C, Smith KJ, Marr J. The clinical effective and cost-effectiveness of screening programs for amblyopia and strabismus in children up to the age of 4–5 years; a systemic review and economic evaluation. *Health Technol Assess.* 2008;12(25):1–194.
2. Yassur Y, Yassur S, Zifrani S, Sachs U, Ben-Sira I. Amblyopia among African pupils in Rwanda. *Br J Ophthalmol.* 1972;56:368–370.
3. Stayte M, Johnson A, Wortham C. Ocular and visual defects in a geographically defined population of 2-year-old children. *Br J Ophthalmol.* 1990;74:465–468.
4. Quah BL, Tay MT, Chew SJ, Lee LK. A study of amblyopia in 18–19 year old males. *Singapore Med J.* 1991;32:126–129.
5. Williamson TH, Andrews R, Dutton GN, Murray G, Graham N. Assessment of an inner city visual screening program for preschool children. *Br J Ophthalmol.* 1995;79:1068–1073.
6. Preslan NW, Novak AS. Baltimore Visual Screening Project. *Ophthalmology.* 1996;103:105–109.
7. Newman DK, Hitchcock A, McCarthy H, Keast-Butler J, Moore AT. Preschool vision screening: outcome of children referred to the hospital eye service. *Br J Ophthalmol.* 1996;80:1077–1082.
8. Ohlsson J, Villarreal G, Sjostrom A, Abrahamsson M, Sjostrand J. Visual acuity, residue amblyopia and ocular pathology in a screening population of 12–13-year-old children in Sweden. *Acta Ophthalmol Scand.* 2001;79:589–585.
9. Ohlsson J, Villarreal G, Sjostrom A, Cavazos H, Abrahamsson M, Sjostrand J. Visual acuity, amblyopia, and other ocular pathology in 12- to 13-year-old children in Northern Mexico. *J APPOS.* 2003; 7(1):47–53.
10. He M, Zeng J, LiuY, Xu J, Pokbarel GP, Ellwein LB. Refractive error and visual impairment in urban children in Southern China. *Invest Ophthalmol Vis Sci.* 2004;45:793–799.
11. Lim HT, Yu YS, Park SH, et al. The Seoul Metropolitan Preschool vision screening programs: result for South Korea. *Br J Ophthalmol.* 2004;88(7):929–933.
12. Tananuvat N, Manassakorn A, Worapong A, Kupat J, Chuwuttayakorn J, Wattananikorn S. Vision screening in schoolchildren: two years result. *J Med Assoc Thai.* 2004;87(6):679–684.

13. Donelly UM, Stewart NM, Hollinger M. Prevalence and outcomes of childhood visual disorders. *Ophthalmic Epidemiol.* 2005;12(4): 243–250.
14. Goh PP, Abqariyah Y, Pokharel GP, Ellwin LB. Refractive error and visual impairment in school-aged children in Gombak District. *Malaysia Ophthalmol.* 2005;112:678–685.
15. Rosman M, Wong TY, Koh CLK, Tan DTH. Prevalence and causes of amblyopia in a population-based study of young adult men in Singapore. *Am J Ophthalmol.* 2005;140(1):551–552.
16. Robaei D, Rose KA, Kifley A, Cosstick M, Ip JM, Mitchell P. Factors associated with childhood strabismus: findings from a population-based study. *Ophthalmology.* 2006;113(7):1146–1153.
17. Robaei D, Rose KA, Ojaimi E, Kifley A. Martin FJ, Mitchell P. Causes and associations of amblyopia in a population-based sample of 6-year-old Australian children. *Arch Ophthalmol.* 2006;124(6): 878–884.
18. Robaei D, Kifley A, Mitchell P. Factors associated with a previous diagnosis of strabismus in a population based sample of 12-year old Australian children. *Am J Ophthalmol.* 2006;142(6):1085–1088.
19. Gronlund MA, Andersson S, Aring E, Hard AL, Hellstrom A. Ophthalmological findings in a sample of Swedish children aged 4–15 years. *Acta Ophthalmol Scand.* 2006;84(2):169–176.
20. Chang CH, Tsai RK, Sheu MM. Screening amblyopia of preschool children with uncorrected vision and stereopsis tests in Eastern Taiwan. *Eye.* 2007;21:1482–1488.
21. Matsuo T, Matsuo C. Comparison of prevalence rates of strabismus and amblyopia in Japanese elementary school children between the years 2003 and 2005. *Acta Med Okayama.* 2007;61(6):329–334.
22. Matsuo T, Matsuo C, Matsuoka H, Kio K. Detection of strabismus and amblyopia in 1.5- and 3-year-old children by a preschool vision screening program in Japan. *Acta Med Okayama.* 2007;61:9–16.
23. Drover JR, Kean PG, Courage ML, Adaims RJ. Prevalence of amblyopia and other vision disorders in young Newfoundland and Labrador children. *Can J Ophthalmol.* 2008;43(1):89–94.
24. Lai YH, Hsu HT, Wang HZZ, Chang SJ, Wu WC. The visual status of children ages 3 to 6 years in the vision screening program in Taiwan. *J APPOS.* 2009;13(1):8–62.
25. Lu P, Chen X, Zhang W, Chen S, Shu L. Prevalence of ocular disease in Tibetan primary school children. *Can J Ophthalmol.* 2008;43(1):95–99.
26. Multi-ethnic Pediatric Eye Disease Study Group. Prevalence of amblyopia and strabismus in African American and Hispanic children aged 6 to 72 months. *Ophthalmology.* 2008;115(7):1229–1236.
27. Robaei D, Kifley A, Rose KA, Mitchell P. Impact of amblyopia on vision at age 12 years: findings from a population-based study. *Eye.* 2008;22(4):496–502.
28. Williams C, Northstone K, Howard M, Harvey I, Harrad RA, Sparrow JM. Prevalence and risk factors for common visual problems in children: data from the ALSPAC study. *Br J Ophthalmol.* 2008; 92(7):959–964.
29. Friedman DS, Repka MX, Katz J, et al. Prevalence of amblyopia and strabismus in white and African-American children aged 6 through 71 months: The Baltimore Pediatric Eye Disease Study. *Ophthalmology.* 2009;116(11):2128–2134.
30. Donahue SP, Arnold RW, Ruben JB. Preschool vision screening: what should we be detecting and how should we report it?—uniform guidelines for reporting of results of preschool vision screening studies *J AAPOS.* 2003;7(5):314–315.
31. Ohlsson J. Defining amblyopia: the need for a joint classification. *Strabismus.* 2005;13:15–20.
32. Varma R, Deneen J, Cotter S, et al. The multiethnic pediatric eye disease study: design and methods. *Ophthalmic Epidemiol.* 2006; 13(4):253–262.
33. Leow BG. *Singapore: Census of Population 2000*. Singapore: Department of Statistics; 2001.
34. Michaelides M, Moore AT. The genetics of strabismus. *J Med Genet.* 2004;41:641–646.
35. Wilner JB, Backus BT. Genetic and environmental contributions to strabismus and phorias: evidence from twins. *Vision Res.* 2009;49: 2485–2493.
36. Yu CB, Fan DS, Wong VM, et al. Changing patterns of strabismus: a decade of experience in Hong Kong. *Br J Ophthalmol.* 2002;86: 854–856.
37. Matsuo T, Matsuo O. The prevalence of strabismus and amblyopia in Japanese elementary school children. *Ophthalmic Epidemiol.* 2005;12:31–36.
38. Chia A, Seenyen L, Quah BL. A retrospective review of 287 consecutive children presenting with intermittent exotropia in Singapore. *J APPOS.* 2005;9:257–263.
39. Chia A, Roy L, Seenyen L. Horizontal comitant strabismus in Singapore. *Br J Ophthalmol.* 2007;91(10):1337–1340.
40. Arnold RW. Amblyopia and strabismus prevalence (letter). *Ophthalmology.* 2009;116(2):365–366.
41. Committee on Practice and Ambulatory Medicine, Section on Ophthalmology. Eye examination and vision screening in infants, children, and young adults. *Pediatrics.* 2006;98(1):153–157.
42. Simons K. Preschool vision screening: rationale, methodology and outcome. *Surv Ophthalmol.* 1996;41(1):3–30.

Ophthalmic Epidemiology, 2013; 20(3): 138–147

ISSN: 0928-6586 print / 1744-5086 online
DOI: 10.3109/09286586.2013.767354

informa
healthcare

ORIGINAL ARTICLE

Risk Factors for Strabismus and Amblyopia in Young Singapore Chinese Children

Audrey Chia[1,2], XiaoYu Lin[3], Mohamed Dirani[4], Gus Gazzard[5,6], Dharani Ramamurthy[3], Boon-Long Quah[1,2], Benjamin Chang[7,8], Yvonne Ling[1,2], Seo-Wei Leo[9], Tien-Yin Wong[1,2,10], and Seang-Mei Saw[3]

[1]Singapore National Eye Center, Singapore, [2]Singapore Eye Research Institute, Singapore, [3]Department of Community, Occupational & Family Medicine, National University of Singapore, Singapore, [4]Center for Eye Research Australia, Department of Ophthalmology, University of Melbourne, Victoria, Australia, [5]Institute of Ophthalmology, London, UK, [6]Moorfields Eye Hospital, London, UK, [7]Department of Ophthalmology and Visual Sciences, Khoo Teck Puat Hospital, Singapore, [8]Eye Clinic, Jurong Medical Center, Singapore, [9]Department of Ophthalmology, Tan Tock Seng Hospital, Singapore, and [10]Department of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

ABSTRACT

Purpose: To determine the risk factors for strabismus and amblyopia in young Singapore Chinese children.

Methods: A total of 3009 children were recruited for the population-based cross-sectional Strabismus, Amblyopia and Refractive Error in Singaporean Preschoolers Study (STARS). Strabismus was defined as any tropia identified on cover test. Visual acuity was measured in children aged 30–72 months with a logMAR chart where possible and the Sheridan-Gardiner test if not. Amblyopia was defined based on visual acuity and refractive error or presence of strabismus or past/present visual axis obstruction. Parents completed questionnaires on family, prenatal and birth histories.

Results: Our study showed that 24 children aged 6–72 months (1.2%) had strabismus (20 with exotropia), and 20 children aged 30–72 months (0.8%) were amblyopic. After multivariate analysis, strabismus was associated with astigmatism ≥1.00 diopter (D; $p = 0.03$), amblyopia ($p = 0.003$), a sibling with strabismus ($p < 0.001$), and families with lower parental education ($p = 0.04$). In addition to strabismus, amblyopia was associated with anisometropia ≥1.00 D ($p < 0.001$) and astigmatism ≥1.00 D ($p < 0.001$). No association was noted between either strabismus or amblyopia and prematurity, maternal age or smoking.

Conclusion: This study highlights the importance of family history in strabismus, and the close associations between refractive error and strabismus with amblyopia. These factors play a more important role in young Singapore Chinese children.

Keywords: Amblyopia, Asia, risks, Singapore, strabismus

INTRODUCTION

Strabismus and amblyopia are common childhood eye conditions with prevalence ranging between 0.13–4.7% and 0.20–6.2%, respectively.[1–9] Ocular and medical associations with these conditions are well known. Strabismus can be infantile, refractive, sensory, and less commonly, neurological, syndromic or due to orbital disorders. Amblyopia is often associated with extremes in refractive error, anisometropia, strabismus or visual obstruction.[1–13] The few studies that have focused on perinatal, demographic and socioeconomic risks, suggest that there are associations between strabismus and prematurity, maternal smoking, increased maternal age and a familial predisposition (Table 1),[1,2,4,7,10–12,14–20] while

Received 25 January 2012; Revised 22 August 2012; Accepted 30 August 2012; Published online 28 May 2013
Correspondence: Audrey Chia, Singapore National Eye Center, 11 Third Hospital Avenue, Singapore 168751. Tel: +65 63228800. Fax: +65 62263395. E-mail: wla_chia@yahoo.com

TABLE 1. Review of the literature of risk factors associated with strabismus and amblyopia.

	Population	Risk factors associated with strabismus Odd ratio (OR)/Risk Ratio (RR) (95%CI)	Risk factors associated with amblyopia Odd ratio (OR)/Risk Ratio (RR) (95%CI)
ALSPAC (UK), Williams (2008)[4]	7825 children born between 1991–1992 aged 7 years; 211 (2.8%) with esotropia, 45 (0.6%) with exotropia and 272 (3.6%) with amblyopia	Family history of strabismus and amblyopia: OR 2.4 (95% CI 1.7–3.2). Prematurity: OR 2.5 (95% CI 1.6–3.9) for ET. Maternal smoking: OR 2.5 (95% CI 1.3–4.8) Intrauterine growth retardation: OR 4.5 (95% CI 1.8–10.8) for XT.	First degree relative with amblyopia or strabismus: OR 2.7 (95% CI 2.0–3.6) Council rented housing compared to owned/mortgaged housing: OR 1.5 (95% CI 1.0–2.2) Maternal smoking: OR 1.4 (95% CI 1.0–1.9)
MCS (UK), Pathai (2010)[7]	14,980 children born in 2000 aged 3 years; 343 (2.1%) with strabismus	South Asians compared to White: RR 0.5 (95% CI 0.3–1.0). Black compared to White: RR 0.2 (95% CI 0.1–0.6) BW < 2.5 kg & GA < 37 weeks compared to BW ≥ 2.5 kg & GA > 37 weeks: RR 2.8 (95% CI 1.9–4.3) Professional parent compared to technical: RR 0.7 (95% CI 0.5–1.0)	–
CPP (USA) Chew (1994)[9], Podgor (1996)[10]	39,227 children of white or black ethnicity born between 1959 and 1965, screened till age 7 years; 1187 (3.0%) with esotropia and 490 (1.2%) with exotropia	White ethnicity compared to black: OR 1.8 (95% CI 1.5–2.2) for ET BW < 1.5 kg compared to BW > 4 kg: OR 3.3 (95% CI 2.5–4.2) for ET and OR 4.0 (95% CI 2.7–5.8) for XT Maternal smoking >2 packs/day compared to no smoking: OR 1.8 (95% CI 1.5–2.2) for ET and OR 2.3 (95% CI 1.7–3.3) for XT Maternal age 30–34 years compared to 20–24 years: OR 1.4 (95% CI 1.1–1.7) Sibling with strabismus: OR 2.0 (95% CI 1.2–3.2) for ET	–
MEPEDS & BPEDS (USA) Cotter (2011)[11]	9970 children of African-American, Hispanic and non-Hispanic white children aged 6–72 months; 102 (1.0%) with esotropia and 102 (1.0%) with exotropia	GA < 33weeks: OR 4.4 (95% CI 2.1–9.2) for ET and OR 2.5 (95% CI 1.2–5.3) for XT Hyperopia >2 D: OR > 6.4 Anisometropia ≥1 D: OR 2.0 (95% CI 1.1–3.7) for ET Astigmatism 1.5–2.5 D compared to <1.5 D: OR 2.5 (95% CI 1.3–4.8) for XT Child age >48 months: OR > 7.9 for ET Female sex: OR 1.6 (95% CI 1.1–2.4) for XT Maternal smoking: OR 2.0 (95% CI 1.2–3.5) for ET and OR 2.9 (95% CI 1.8–4.6) for XT	

(continued)

TABLE 1. Continued

	Population	Risk factors associated with strabismus Odd ratio (OR)/Risk Ratio (RR) (95%CI)	Risk factors associated with amblyopia Odd ratio (OR)/Risk Ratio (RR) (95%CI)
SMS (Australia), Robaei (2006)[1,2]	1740 6-year-old school children examined between 2003–4; 26 (1.5%) with esotropia, 14 (0.8%) with exotropia and 32 (1.8%) with amblyopia	Non-white: OR 0.3 (95% CI 0.1–0.8) for ET BW <2.5 kg: OR 3.5 (95% CI 1.3–9.2) GA <37weeks: OR 2.8 (95% CI 1.2–6.3) Admission to NICU: OR 4.2 (95% CI 1.6–11.1) Increase paternal age: OR 4.9 (95% CI 1.6–15.0) Amblyopia, hyperopia (≥3 D), astigmatism (≥1 D) and anisometropia (≥1D) $p<0.001$	Strabismus: OR 65 (95% CI 30–144) Anisometropia >1D: OR 156 (95% CI 64–382) Astigmatism >1D OR: 11.0 (95% CI 5.7–21.1) BW <2.5 kg: OR 4.8 (95% CI 1.9–11.8) GA <27 weeks: OR 5.4 (95% CI 2.4–12.3) Admission to NICU: OR 5.0 (95% CI 2.1–12.0) Maternal smoking: OR 2.2 (95% CI 1.0–5.0)
SPEDS (Australia), Pai (2011)[12]	1422 children aged 30–72 months; 27 (1.9%) with amblyopia	–	Strabismus: OR 13.1 (95% CI 4.2–40.3). Hyperopia ≥2D: OR 15.3 (95% CI 6.5–36.3). Anismetropia ≥1D: OR 27.8 (95% CI 11.2–69.3). Astigmatism ≥1 D: OR 5.7 (95% CI 2.5–12.7).
DNBC (Denmark), Torp-Pedersen (2011)[19,20]	96,842 children born between 1996–2003; 649 with esotropia, 183 with exotropia, 488 with other strabismus	BW <2000 g: RR 2.2 (95% CI 1.6–2.0) compared to BW 3000–3499 g for ET Caesarean section: RR 1.6 (95% CI 1.1–2.3) for XT Head circumference ≥38 cm: RR 1.43 (95% CI 1.1–1.8) compared to 34–37 cm for ET Maternal smoking: RR 1.2 (95% CI 1.1–1.4)	–
This study (Singapore)	2992 Chinese children aged 6–72 months; 3 (0.1%) with esotropia and 20 (0.7%) with exotropia. 1682 children aged 30–72 months: 20 (1.8%) with amblyopia	Sibling with strabismus: OR 41.2 (95% CI 9.0–188.0). Astigmatism ≥1.0 D: OR 4.2 (95% CI 1.2–14.6). Amblyopia: OR 12.9 (95% CI 2.3 71.3). Paternal education: tertiary: OR 0.2 (95% CI 0.07–0.9) and secondary education: OR 0.1 (95% CI 0.02–0.8) compared to those with no/primary education	Strabismus: OR 18.0 (95% CI 3.3–97.8) Anisometropia ≥1 D: OR 20.6 (95% CI 4.6–91.7). Astigmatism ≥1 D: OR 8.9 (95% CI 2.9–26.8)

ALSPAC, Avon Longitudinal Study of Parents and Children; MCS, Millennium Cohort Study; CPP, Collaborative Prenatal Project of the National Institute of Neurological Disorders and Stroke; MEPEDS, Multi-ethnic Pediatric Eye Disease Study; BPEDS, Baltimore Pediatric Eye Disease Study; SMS, Sydney Myopia Study; SPEDS, Sydney Paediatric Eye Disease Study. ET: esotropia, XT: exotropia. BW: birth weight, GA: gestational age, NICU: neonatal intensive care unit, CI: confidence interval, D: diopters

amblyopia has been associated with prematurity, admission to a neonatal intensive care unit (NICU) and maternal smoking.[4] Most large population-based studies are based in the United States of America, the United Kingdom, Denmark and Australia, with few based in Asia.

The aim of this study was to determine a range of ocular, growth, perinatal, demographic and socio-economic risk factors associated with strabismus and amblyopia in this cohort of young Singapore Chinese children.

MATERIALS AND METHODS

A total of 3009 Chinese children aged 6–72 months (response rate 74%) were recruited for the cross-sectional population-based Strabismus, Amblyopia and Refractive Error in Singaporean Preschoolers Study (STARS). Full descriptions of recruitment, methods and study population are detailed elsewhere[3,6,21–25] Briefly, Chinese children from South-West Singapore were identified through a door-to-door recruitment exercise and invited to attend two assessment clinics from 2006–2009. Analysis showed that there were no demographic differences between the recruitment area and the rest of Singapore. However, parents of children attending clinics were more likely to be better educated, have higher income and live closer to the assessment centers.[6]

Ethics approval was obtained from the Singapore Eye Research Institute Institutional Review Board in Singapore, and all procedures adhered to the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians before any tests were conducted.

Eye Examinations

All children underwent a detailed ophthalmological assessment. Hirschberg light reflex, cover test and prism cover-uncover tests for distance and near, assessment of extraocular eye movement and cycloplegic refraction were performed by an orthoptist and an optometrist, and anterior and posterior segment examinations were performed by an ophthalmologist.[6,21–25]

In children aged over 30 months, visual acuity (VA) was tested by an optometrist or orthoptist using a logarithm of the minimum angle of resolution (logMAR) 4 m Early Treatment Diabetic Retinopathy Study (ETDRS) chart, where five optotypes were presented on each line.[23] Scoring was based on the line where the child failed to read three or more letters, with an additional 0.02 added for each optotype missed. When logMAR visual testing was not possible, children were tested with Sheridan-Gardiner matching test where single uncrowded optotypes were presented at 4 m and children were asked to find the same letter on the matching card. Smaller optotypes were presented till mistakes were made on two attempts at the same level. A larger optotype was presented and if the child was able to read this correctly, that was taken as the child's visual acuity. If not, the process was repeated and progressively larger optotypes were presented until the child was able to identify at least two optotypes correctly at a similar level. Vision was measured in terms of Snellen visual acuity and converted to LogMAR equivalents. When initial VA was less than 20/30 (logMAR 0.18) in either eye, best-corrected VA was re-tested again at cycloplegic refraction. If vision remained poor, or if children were unable to co-operate with the VA testing, the children were given Sheridan-Gardiner single letters to learn, and a re-test date organized.

Cycloplegic refraction was performed 30 minutes after instillation of three drops of cyclopentolate 1% spaced 5 minutes apart using a table-mounted Canon Autorefractor RK-F1 (Japan) when possible, or hand-held Retinomax K-Plus 2 Autorefractor (Japan) and streak retinoscopy (Welch Allyn, France) if not. Subjective refraction was then obtained with best-corrected VA recorded. Spherical equivalent refraction (SEq) was calculated as sphere plus half cylinder.

Questionnaire

The questionnaire started with confirmation of the Chinese dialect group of each parent to ensure ethnicity. Details regarding total combined monthly income (<S$1000, S$1000–2999, S$3000–4999 and ≥S$5000), father's and mother's highest completed education level (none, primary, secondary, general certificate of education (GCE) ordinary (O) or advanced (A) levels, polytechnic or university) were collected. The GCE "O" is equivalent to a junior high-school qualification, while the GCE "A" and polytechnic are equivalent to senior high school qualifications. Parents were asked if they themselves or their other children wore glasses, contact lenses or had undergone refractive laser surgery. Parents were also asked if they or their other children had a history of amblyopia or lazy eye (yes/no), and strabismus or squinting eye (yes/no).

Pregnancy history included maternal age (in years), maternal prenatal medical history and whether the child was admitted to the NICU and if so, the reasons why. Parents were asked if the child's mother smoked or drank alcohol during pregnancy, and if so, the months (first-ninth) of exposure and the average number of cigarettes smoked or drinks per day was determined.

Children's gestational age (in weeks) and birth weight (in grams) were recorded from each child's health booklet. If children were breastfed, parents were questioned about the age when breastfeeding was commenced and the duration for which the child was breastfed. Details were asked of the child's ocular condition such as whether he/she had problems with visual tasks (eg, drawing and coloring); been prescribed glasses and if so, when and why; and, whether a doctor had ever told them that their child had amblyopia or strabismus and if so, when the diagnosis was made, how this had been treated and whether treatment had been completed or was ongoing.

Definitions

Definitions used were similar to those used by the Multi-Ethnic Pediatric Eye Disease Study (MEPEDS) and the Baltimore Pediatric Eye Disease Study (BPEDS).[3,5,18] Children were categorized based only on findings noted during the study visit.

Strabismus was defined as any manifest tropia identified on cover test and was classified by frequency (constant or intermittent) and type (exotropia, esotropia, hyper/hypotropia or dissociated vertical deviation).

Unilateral amblyopia was defined as a 2-line difference between eyes with VA<20/30 in the worse eye, and with coexisting anisometropia (≥1.00 diopters (D) for hyperopia, ≤−3.00 D for myopia, ≥1.50 D for astigmatism), strabismus or past/present visual axis obstruction. Bilateral amblyopia was defined as VA in both eyes <20/40 (in children 48–72 months) or <20/50 (30–47.9 months), with coexisting hyperopia ≥4.00 D, myopia ≤−6.00 D and astigmatism ≥2.50 D, or past/present visual axis obstruction.

Statistical Analysis

Potential risk factors were first analyzed by comparing children with and without strabismus or amblyopia in bivariate models using either the *t*-test, non-parametric Wilcoxon rank or the χ^2 test. If significant differences ($p<0.20$) were shown in the univariate models, these risk factors were included together with all known risk factors based on prior evidence in multiple logistic regression models with either strabismus or amblyopia as dependent variables. Care was taken not to include highly correlated factors such as birth weight and gestational age, paternal and maternal education levels, and parental education levels and household income in the same model. Manual backward stepwise elimination procedures were performed to choose the most parsimonious model. Statistical analyses were performed in SPSS (PASW Statistics for Windows V18.0, SPSS Inc., Chicago, IL). Two-tailed p values less than 0.05 were considered statistically significant. Odds ratios (ORs) and 95% confidence intervals (CIs) of ORs are presented.

RESULTS

A total of 3009 Chinese Singaporean children were recruited for this study. Assessment for strabismus was attempted in all children, and assessment of visual impairment was undertaken in the 2015 children aged between 30 and 72 months.

Factors Associated with Strabismus

Assessment for strabismus was possible in 2992 (99.4%) children. Those unable to co-operate were not significantly different in terms of age, birthweight, gestational age, maternal perinatal factors, socioeconomic status, and refractive error. A total of 24 children (1.2%) were found to have strabismus; 20 with exotropia, three with esotropia, and one with dissociated vertical deviation (DVD). There were no sib-pairs.

As most had exotropia (83%), the comparison of children with and without strabismus was mainly a comparison of children with and without exotropia (Table 2). Only three children had esotropia; all were hyperopic between 1.00 and 2.00 D, had low levels of anisometropia (0–0.50 D) and astigmatism ≤1.00 D. They came from a slightly lower socioeconomic group with parents achieving primary/secondary education and with a monthly household income <S$3000. The child with DVD was also from a lower socioeconomic group, had a SEq of −9.00 D and astigmatism of 4.10 D in the worse eye and anisometropia of 2.10 D.

A multivariate model adjusting for age, sex, past admission to a NICU, socioeconomic factors, maternal age, prematurity and maternal smoking found that children with strabismus were more likely to have amblyopia ($p=0.003$), astigmatism ($p=0.03$), have fathers with lower education ($p=0.04$) and a sibling with strabismus ($p<0.001$; Table 3).

Factors Associated with Amblyopia

Visual assessment was possible in 1682 (83.5%) of the 2015 children aged between 30 and 72 months. Children able to co-operate were more likely to be older ($p<0.001$), female ($p=0.03$), have parents with higher education levels ($p=0.02$) and were less likely to be myopic (<−3.00 D; $p=0.01$). A total of

TABLE 2. Risk factors associated with children with strabismus compared to those without strabismus.

Risk factors	No strabismus ($n=2968$)	All strabismus ($n=24$)	Crude Odds Ratio, (95% CI)	p value
Age, mean months (95% CI)	40.4 (39.8–41.1)	46.5 (39.6–53.3)	–	0.11
Male, *n* (%)	1547 (52.1)	14 (58.3)	1.29 (0.57–2.90)	0.54
BMI, mean kg/m^2 (95% CI)	15.9 (15.8–16.1)	16.0 (15.3–16.8)	–	0.88
Gestational factors				
Birth weight, mean kg (95% CI)	3.09 (3.07–3.10)	3.04 (2.76–3.25)	–	0.36
>2.5 kg, *n* (%)	2637 (91.6)	20 (83.3)	1	
≤2.5 kg, *n* (%)	241 (8.4)	4 (16.7)	2.19 (0.74–6.45)	0.14
Gestational age, mean weeks (95% CI)	38.3 (38.2–38.4)	38.2 (37.3–38.8)	–	0.40
>37 weeks, *n* (%)	2128 (77.3)	19 (79.2)	1	
≤37 weeks, *n* (%)	626 (22.7)	5 (20.8)	0.9 (0.33–2.41)	0.83
Admission to NICU, *n* (%)	160 (5.5)	4 (16.7)	3.44 (1.16–10.19)	0.02
Maternal factors				
Maternal age, mean years, (95% CI)	30.6 (30.4–30.8)	30.0 (27.9–32.1)	–	0.52
Smoking during pregnancy, *n* (%)	64 (2.2)	0	–	–
Alcohol during pregnancy, *n* (%)	30 (1.0)	0	–	–
Breast feeding, *n* (%)	2288 (77.8)	17 (70.8)	–	0.41
Socioeconomic factors				
Maternal education				
None/Primary School, *n* (%)	194 (6.6)	6 (25.0)	1	
Secondary/"O", *n* (%)	1040 (35.6)	10 (41.7)	0.24 (0.09–0.62)	
"A"/Polytechnic/University, *n* (%)	1691 (57.8)	8 (33.3)	0.16 (0.04–0.56)	0.001
Paternal education				
None/Primary School, *n* (%)	286 (9.8)	8 (33.3)	1	
Secondary/"O", *n* (%)	878 (30.2)	5 (20.8)	0.31 (0.11–0.87)	
"A"/Polytechnic/University, *n* (%)	1748 (60.0)	11 (45.8)	0.16 (0.04–0.56)	<0.001
Monthly household income				
<S$3000, *n* (%)	684 (23.8)	14 (58.3)	1	
S$3000–4999, *n* (%)	882 (30.7)	4 (16.7)	0.22 (0.07–0.68)	
≥S$5000, *n* (%)	1307 (45.5)	6 (25.0)	0.22 (0.09–0.59)	<0.001
Refractive/ocular factors				
Spherical equivalent refraction, mean D (95%CI)	+0.63 (+0.59–+0.67)	+0.38 (−0.53–+1.29)		0.57
−0.5 to +0.5 D (emmetropia), *n* (%)	821 (27.7)	8(33.3)	1	
≤−0.5 D (myopia), *n* (%)	399 (13.5)	5(20.8)	1.29 (0.42–3.96)	0.66
>+0.5 D (hyperopia), *n* (%)	1744 (58.8)	11(45.8)	0.65 (0.26–1.62)	0.35
Astigmatism, mean D (95% CI)	−0.60 (−0.62–−0.58)	−1.26 (−1.70– −0.82)		<0.001
Cylinder <1.0 D, *n* (%)	2449 (82.6)	13 (54.2)	1	
Cylinder ≥1.0 D, *n* (%)	515 (17.4)	11 (45.8)	4.02 (1.79–9.03)	0.001
Anisometropia (≥1.0 D), *n* (%)	58 (2.0)	3 (12.5)	7.16 (2.08–24.67)	0.002
Concurrent amblyopia, *n* (%)	16 (1.0)	3 (21.4)	–	<0.001
Family history				
Parent with amblyopia, *n* (%)	145 (5.0)	3 (12.5)	2.69 (0.79–9.11)	0.10
Parent with strabismus, *n* (%)	21 (0.7)	1 (4.2)	5.91 (0.76–45.76)	0.17
Sibling with amblyopia, *n* (%)	55 (1.9)	3 (12.5)	7.41 (2.15–25.57)	0.01
Sibling with strabismus, *n* (%)	22 (0.8)	7 (29.2)	54 (20.37–143.16)	<0.001

CI, confidence interval; OR, odds ratio; D, diopter; BMI, body mass index; NICU, neonatal intensive care; "O", General certificate of education Ordinary level; "A", General certificate of education Advanced level

20 children (0.8%, 17 with refractive and three strabismic amblyopia) fulfilled the requirements for amblyopia. Factors associated with children with and without amblyopia are presented in Table 4.

Unilateral amblyopia ($n=14$) was most frequently associated with anisometopic astigmatism ≥1.50 D (50%), followed by anisometropic myopia ≤−3.00 D (14%) and anisometropic hyperopia ≥1.00 D (14%) (Table 4). Two children were exotropic while one was esotropic. In the bilateral amblyopia group ($n=6$), refractive errors recorded included astigmatism ≥2.50 D (33%), combined astigmatism and myopia ≤−6.00 D (33%), combined astigmatism and hyperopia ≥4.00 D (16%) and myopia ≤−6.00 D (16%).

In a multivariate regression model including age, sex, socioeconomic factors and family history of strabismus and amblyopia, prematurity, admission to neonatal intensive care and maternal smoking, amblyopia was associated with strabismus ($p=0.001$), anisometropia ≥1.00 D ($p<0.001$) and astigmatism ≥1.00 D ($p<0.001$; Table 5).

DISCUSSION

In this study involving young Chinese children, strabismus was associated with astigmatism, amblyopia, a sibling with strabismus and families with

TABLE 3. Multivariate analysis: Strabismus.

	Odds Ratio	95% CI Lower	95% CI Upper	*p* value
Age	1.02	0.96	1.08	0.61
Sex				
Girls	1.00			
Boys	1.44	0.41	5.03	0.57
Gestational age				
>37 weeks	1.00			
≤37 weeks	0.82	0.17	4.11	0.81
Admission to NICU	1.50	0.20	11.38	0.69
Father's education				
None/Primary School	1.00			
Secondary/"O"	0.12	0.02	0.77	0.03
"A"/Polytechnic/University	0.25	0.07	0.96	0.04
Sibling with strabismus	41.20	9.03	188.00	<0.001
Astigmatism				
Cylinder <1.0D	1.00			
Cylinder ≥1.0D	4.19	1.20	14.65	0.03
Concurrent amblyopia	12.85	2.32	71.27	0.003

This table comprises one multivariate model in which each factor is adjusted for the other factor in this table.
NICU, neonatal intensive care unit; "O", General certificate of education Ordinary level; "A", General certificate of education Advanced level; CI, confidence interval; D, diopter

lower parental education, while amblyopia was associated with strabismus, anisometropia and astigmatism. Prematurity, maternal age and maternal smoking were not associated with strabismus or amblyopia.

There are several birth cohort and population-based cross-sectional studies such as the Avon Longitudinal Study of Parents and Children (ALSPAC) and the Millennium Cohort Study (MCS) based in the UK, the Collaborative Prenatal Project of the National Institute of Neurological Disorders and Stroke (CPP) study, MEPEDS and BPEDS based in the USA, the Sydney Myopia Study (SMS) and Sydney Paediatric Eye Disease Study (SPEDS) based in Australia, and the Danish National Birth Cohort (DNBC) Study based in Denmark.[1–12,18–20]

These studies showed associations between amblyopia and strabismus and prematurity, family history of strabismus or amblyopia, maternal smoking, increased maternal age, concurrent strabismus or amblyopia and occasionally lower socioeconomic status (Table 1).[1–12,18–20] Differences in age, ethnicity, disease definitions and data collection make direct comparisons between some studies difficult. None of these studies were based in East Asia where the prevalence of exotropia and myopia are higher.[1–12] Other factors unique to the Singapore cohort include the relatively low maternal smoking (2%) and alcohol intake (1%) rates and high breast-feeding (77%) rate (Table 2).

There is increasing evidence that family history of strabismus or amblyopia is associated with strabismus and possibly amblyopia.[11,16–18] Children with strabismus were more likely to have a sibling with strabismus (OR 41.2) in the STARS, as well as in the CPP and ALSPAC studies (OR 2.0–2.4; Table 3). In a review of 96 strabismic children, Ziakas et al. found that 67% of those with accommodative esotropia (33/49), 42% with infantile esotropia (11/26), 33% with anisometropic esotropia (5/15) and 17% with exotropia (1/6) had at least one first degree relative with strabismus.[17] Likewise, in a longitudinal study, Aurell and Norrsell found that strabismus developed in 6 of 34 (17%) of children with a parent or older sibling with strabismus.[25] Matsuo et al. also found a higher familial concordance with accommodative esotropia and intermittent exotropia.[16] With regards to amblyopia, Williams et al. also noted increased amblyopia risk with family history of amblyopia.[4] In our Singaporean subjects, children with amblyopia were more likely to have a sibling with amblyopia (10% vs 2.3%) and strabismus (10% vs 1.2%), but this association was not statistically significant.

Another common finding among studies was the association between refractive error, strabismus and amblyopia.[1,2,9,12] Previous studies suggest that amblyopia tended to be due more to refractive errors (70–80%) in East Asian, Hispanic/Latino and African American children and was more strabismic (40–50%) or refractive-strabismic (20%) in white children.[2–4,6,8–10] However, the associations between astigmatism and exotropia in MEPEDS, and the associations between strabismus, astigmatism or anisometropia and amblyopia in SPEDS was quite similar to that in STARS (Table 1).[1,2,9] Hyperopia was less relevant in STARS, probably because of the lower rates of esotropia and hyperopia in the Singaporean children.

The effect of socioeconomic factors was more controversial. Children with strabismus in STARS and MCS were more likely to have parents with lower educational levels and household incomes (Table 1).[7] There may indeed be environmental, developmental or neurological factors which predispose to strabismus. However, as there is a genetic predisposition, there may be family groups who are trapped within a lower socioeconomic level by the social, psychological and cosmetic disadvantages associated with strabismus. Parental education and socioeconomic status were, however, not found to be significantly associated with amblyopia or strabismus in the SMS, ALSPAC and MEPEDS/BPEDS studies.[1,4,12]

We also did not find an association with prematurity and maternal smoking as noted in other studies. Prematurity was associated with strabismus in many studies (Table 1).[1,2,4,7,9–12,18,19] O'Connor et al. found that 39 of 572 (20%) children with birth weight <1701g had strabismus at age 10–12 years compared to only 3% in a similar-age school cohort.[15] A 2.5 to 4.4-times increase in strabismus was also noted in premature

TABLE 4. Risk factors associated with children with amblyopia compared to those without amblyopia.

Risk factors	No amblyopia ($n = 1662$)	Amblyopia ($n = 20$)	Crude Odds Ratio (95% CI)	p value
Age, mean months (95% CI)	53.9 (53.4–54.4)	51.9 (47.7–56.1)	–	0.42
BMI, mean kg/m^2 (95% CI)	15.6 (15.6–15.8)	16.0 (15.3–16.8)	–	0.39
Male sex, *n* (%)	838 (50.4)	12 (60.0)	1.48 (0.60–3.63)	0.43
Gestational factors				
Birth weight, mean kg (95% CI)	3.11 (3.09–3.13)	3.09 (2.87–3.31)	–	0.81
≤2.5 kg, *n* (%)	130 (8.1)	3 (15.0)	2.01 (0.58–6.94)	
>2.5 kg, *n* (%)	1479 (91.9)	17 (85.0)	1	0.22
Gestational age, mean weeks (95% CI)	38.5 (38.4–38.5)	38.3 (37.7–38.9)	–	0.65
>37 weeks, *n* (%)	1238 (80.2)	16 (80.0)	1	
≤37 weeks, *n* (%)	306 (19.8)	4 (20.0)	1.01 (0.34–3.05)	0.93
Admission to NICU, *n* (%)	88 (5.4)	3 (15.0)	3.1 (0.89–10.78)	0.09
Maternal factors				
Maternal age, mean years) (95% CI)	30.4 (30.2–30.6)	32.3 (30.4–33.9)	–	0.09
Smoking during pregnancy, *n* (%)	30 (1.8)	0	–	–
Alcohol during pregnancy, *n* (%)	15 (0.9)	0	–	–
Breast feeding, *n* (%)	1258 (76.5)	16 (80.0)	1.23 (0.41–3.70)	0.71
Socioeconomic factors				
Maternal education				
None/primary school, *n* (%)	118 (7.2)	1 (5.0)	1	
Secondary/"O", *n* (%)	599 (36.7)	10 (50.0)	1.97 (0.25–15.54)	
"A"/Polytechnic/University, *n* (%)	917 (56.1)	9 (45.0)	1.16 (0.15–9.22)	0.67
Paternal education				
None/primary school, *n* (%)	157 (9.6)	2 (10.0)	1	
Secondary/"O", *n* (%)	504 (30.8)	8 (40.0)	1.25 (0.26–5.93)	
"A"/polytechnic/university, *n* (%)	974 (59.6)	10 (50.0)	0.81 (0.18–3.71)	0.72
Monthly household income				
<S$3000, *n* (%)	378 (23.6)	4 (20.0)	1	
S$3000–4999, *n* (%)	488 (30.4)	5 (25.0)	0.97 (0.26–5.93)	
≥S$5000, *n* (%)	738 (46.0)	11 (55.0)	1.41 (0.45–4.45)	0.73
Refractive/ocular factors				
Spherical equivalent refraction, mean D (95%CI)	+0.72(+0.67–+0.76)	−1.13 (−3.43–+1.17)	–	0.11
−0.5–0.05 D (emmetropia), *n* (%)	463 (27.9)	4 (20.0)	1	
≤−0.5 D (myopia), *n* (%)	144 (8.7)	7 (35.0)	5.63 (1.62–19.50)	0.01
>0.5 D (Hyperopia), *n* (%)	1055 (63.5)	9 (45.0)	0.99 (0.30–3.22)	0.98
Astigmatism, mean D (95%CI)	−0.67 (−0.70–−0.64)	−2.16 (−2.94–−1.39)	–	<0.001
Cylinder <1.0 D, *n* (%)	1353 (81.4)	6 (30)	1	
Cylinder ≥1.0 D, *n* (%)	309 (18.6)	14 (70.0)	10.22 (3.90–26.80)	<0.001
Anisometropia (≥1.0 D), *n* (%)	25 (1.5)	4 (20.0)	16.37 (5.11–52.46)	<0.001
Concurrent strabismus, *n* (%)	11 (0.7)	3 (15.8)	28.07 (7.15–110.29)	<0.001
Family history				
Parent with amblyopia, *n* (%)	80 (5.0)	0	–	0.32
Parent with strabismus, *n* (%)	14 (0.9)	0	–	0.68
Sibling with amblyopia, *n* (%)	38 (2.3)	2 (10.0)	4.66 (1.04–20.78)	0.03
Sibling with strabismus, *n* (%)	20 (1.2)	2 (10.0)	8.94 (7.15–110.29)	<0.001

BMI, body mass index; NICU, neonatal intensive care; "O", General certificate of education Ordinary level; "A", General certificate of education Advanced level; CI, confidence interval; D, diopter

children in the SMS, CPP, DNBC and MEPEDS/BPEDS studies (Table 1).[1,10,18] In STARS, 16.7% and 20.8% of children with strabismus had birth weights ≤2500 g and gestational age ≤37 weeks, respectively, compared to 8.4% and 22.7% of children with no strabismus, but these differences were not statistically significant ($p = 0.14$). Prematurity was associated with amblyopia in the ALSPAC (OR 2.5) and SMS (OR 5.0) studies (Table 1).[2,4] There are several reasons why no association with prematurity was seen in STARS. Active ophthalmological follow-up of premature children (<32 weeks and <1500 g) in Singapore means that those with strabismus and amblyopia may already be under care, and thus not present for the study. Alternatively, prematurity may be less associated with exotropia than esotropia.[19] Advances in neonatal care may also have altered risk.

Maternal smoking was associated with strabismus in the CPP, ALSPAC, MEPEDS/BPEDS and DNBC studies, and for amblyopia in the ALSPAC study.[4,9,12,19,20] Maternal smoking was not associated with amblyopia or strabismus in the MCS, SMS or STARS studies.[1,2,7] Hakim and Tielsch, in a USA cohort, found that smoking during pregnancy was associated with esotropia (OR 1.8, 95% CI 1.1–2.8) but not exotropia.[14] Similarly, Torp-Pederson et al., in the

TABLE 5. Multivariate analysis: Amblyopia.

	Odds Ratio	95% CI Lower	95% CI Upper	*p* value
Age	0.97	0.92	1.02	0.19
Sex				
Girls	1.00			
Boys	1.41	0.51	3.90	0.51
Gestational age				
>37 weeks	1.00			
≤37 weeks	1.18	0.36	3.89	0.78
Paternal education				
None/Primary	1.00			
Secondary/"O"	3.87	0.45	32.96	0.22
"A"/Polytechnic/University	2.32	0.30	18.00	0.42
Sibling history of amblyopia	3.59	0.71	18.14	0.12
Concurrent strabismus	18.00	3.31	97.76	0.001
Refractive error				
Anisometropia (≥1.0 D)	20.65	4.65	91.75	<0.001
Astigmatism (≥1.0 D)	8.95	2.99	26.81	<0.001
Myopia (≤-0.5 D)	1.52	0.46	5.07	0.50

This table comprises one multivariate model in which each factor is adjusted for the other factor in this table.
"O", General certificate of education Ordinary level; "A", General certificate of education Advanced level; CI, confidence interval

DNBC study, found an association between congenital esotropia (RR 1.66, 95% CI 1.00–2.75) and accommodative esotropia (RR 1.52, 95% CI 1.07–2.18) and those children whose mothers who had smoked 5–10 cigarettes per day, and an association between exotropia (RR 1.60, 95% CI 1.45–2.68) and children whose mothers had smoked >10 cigarettes per day.[20] Smoking <5 cigarettes per day, however, was less likely to be associated with strabismus.[20] This may explain why no association was found in STARS where maternal smoking rates, and presumably number of cigarettes smoked per day, were low (2.1%); none of the mothers of children with strabismus or amblyopia smoked.

Studies have also demonstrated possible associations between strabismus and parental age. Chew et al. noted an increased maternal age with esotropia in the CPP study, while Robaei et al. noted an increased association with increasing paternal but not maternal age in the SMS (Table 1).[1,9] There was, however, no association between maternal age and strabismus in the MEPEDS/BPEDS and STARS studies.[11]

The main strength of this study is the use of a large population-based cross-sectional design consisting of a single ethnicity. There are, however, several limitations. First, with low numbers of strabismus and amblyopia cases, the power of our study was low for a number of risk factor variables examined. Second, even though our response rate was reasonably good (74%), there may still be differences between the non-responder and responder group. Some children with strabismus and amblyopia who are already under care may not have presented for the study. There were also 12 children, whose parents reported as having had previous diagnosis of amblyopia, who were not identified as being amblyopic in our study. As it was uncertain if these children ever had amblyopia, they were not classified as such but some may have had amblyopia which had been successfully treated in the past. Third, as the study population was very young, the assessment of amblyopia was at times difficult, as children may fail vision tests for reasons other than amblyopia. In this study, VA was tested either with the ETDRS chart or the Sheridan Gardner cards. Use of the latter 'easier' test, may lead to an underestimation of amblyopia. The use of a refractive component to define amblyopia also meant any analysis of refractive components and its role in amblyopia may be biased. Finally, parental responses to some questions (eg, maternal illness, smoking or drug use, or family history of strabismus and amblyopia) may be subject to recall bias and error.

This study highlights the importance of family history in the development of strabismus, and the close associations between refractive error and strabismus with amblyopia.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

The study was funded by the National Medical Research Council, Singapore NMRC/1009/2005.

REFERENCES

1. Robaei D, Rose KA, Kifley A, et al. Factors associated with childhood strabismus: findings from a population-based study. *Ophthalmology* 2006;113:1146–1153.
2. Robaei D, Rose KA, Ojaimi E, et al. Causes and associations of amblyopia in a population-based sample of 6-year-old Australian children. *Arch Ophthalmology* 2006;124:878–884.
3. Multi-ethnic Pediatric Eye Disease Study Group. Prevalence of amblyopia and strabismus in African American and Hispanic children aged 6–72 months. *Ophthalmology* 2008;115(7):1229–1236.
4. Williams C, Northstone K, Howard M, et al. Prevalence and risk factors for common vision problems in children: data from ALSPAC study. *Br J Ophthalmol* 2008;92:959–964.
5. Friedman DS, Repka MX, Katz J, et al. Prevalence of amblyopia and strabismus in white and African American children aged 6 through 71 months: the Baltimore Pediatric Eye Disease Study. *Ophthalmology* 2009;116(11):2128–2134.
6. Chia A, Dirani M, Chan YH, et al. Prevalence of amblyopia and strabismus in young Singaporean children. *IOVS* 2010;51:3411–3417.
7. Pathai S, Cumberland PM, Rahi JS. Prevalence of and early-life influences on childhood strabismus: findings from the Millennium Cohort Study. *Arch Pediatr Adolesc Med* 2010;164(3):250–257.

8. Cumberland PM, Pathai S, Rahi JS, Millennium Cohort Study Child Health Group. Prevalence of eye disease in early childhood and associated factors. Findings from the Millennium Cohort Study. *Ophthalmology* 2010;117: 2184–2190.
9. Chew E, Remaley NA, Tamboli A, et al. Risk factors for esotropia and exotropia. *Arch Ophthalmol* 1994;112: 1349–1355.
10. Podgor MJ, Remaley NA, Chew E. Associations between siblings for esotropia and exotropia. *Arch Ophthalmol* 1996;114:739–744.
11. Cotter SA, Varma R, Tarczy-Hornoch K, et al., the joint writing committee for the Multi-ethnic Pediatric Eye Disease Study and the Baltimore Pediatric Eye Disease Study Group. Risk factors associated with childhood strabismus. *Ophthalmology* 2011;118:2251–2261.
12. Pai AS, Rose KA, Leone JF, et al. Amblyopia prevalence and risk factors in Australia preschool children. *Opthalmology* 2012;119:138–144.
13. Weakley DR, Birch E. The role of anisometropia in the development of accommodative esotropia. *Tr Am Ophth Soc* 2000; 98:71–79.
14. Hakim RB, Tielsch KM. Maternal cigarette smoking during pregnancy: a risk factor for childhood strabismus. *Arch Ophthalmol* 1992;110:1459–1462.
15. O'Connor AR, Stephenson TJ, Johnson A, et al. Strabismus in children of birth weight less than 1701g. *Arch Ophthalmol* 2002;120(6):767–773.
16. Matsuo T, Hayashi M, Fujiwara H, et al. Concordance of strabismic phenotypes in monozygotic versus multizygotic twins and other multiple births. *Jpn J Ophthalmol* 2002;46(1):59–64.
17. Ziakas NG, Woodruff G, Smith LK, Thompson JR. A study of heredity as a risk factor in strabismus. *Eye* 2002;16: 519–521.
18. Varma R, Deneen J, Cotter S, et al; the Multi-Ethnic Pediatric Eye Disease Study Group. The multi-ethnic pediatric eye disease study: design and methods. *Ophthalmic Epidemiol* 2006;13:253–262.
19. Torp-Pederson T, Boyd HA, Poulsen G, et al. Perinatal risk factors for strabismus. *Int J Epidemiology* 2010;39:1229–1239.
20. Torp-Pederson T, Boyd HA, Poulsen G, et al. In-utero exposure to smoking, alcohol, coffee, and tea and risk of strabismus. *Am J Epidemiology* 2010;171:868–875.
21. Prabakaran S, Dirani M, Chia A, et al. Cycloplegic refraction in preschool children: comparisons between the hand-held autorefractor, table-mounted autorefractor and retinoscopy. *Ophthalmic Physiol Opt* 2009;29:422–426.
22. Trager MJ, Dirani M, Fan Q, et al. Testability of vision and refraction in preschoolers: the strabismus, amblyopia, and refractive error study in Singaporean children. *Am J Ophthalmol* 2009;148:235–241.
23. Dirani M, Zhou B, Hornbeak D, et al. Prevalence and causes of decreased visual acuity in Singaporean Chinese preschoolers. *Br J Ophthalmol* 2010;94:1561–1565.
24. Dirani M, Chan YH, Gazzard G, et al. Prevalence of refractive error in Singaporean Chinese children: the strabismus, amblyopia, and refractive error in young Singaporean Children (STARS) study. *Invest Ophthalmol Vis Sci* 2010;51:1348–1355.
25. Aurell E, Norrsell K. A longitudinal study of children with a family history of strabismus: factors determining the incidence of strabismus. *Br J Ophthalmol* 1990;74: 589–594.