Original paper

Non-cycloplegic refractive screening can identify infants whose visual outcome at 4 years is improved by spectacle correction

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Abstract The Second Cambridge Population Infant Vision Screening Programme using the VPR-1 videorefractor without cycloplegia was undertaken in order to identify those infants with refractive errors who were potentially amblyogenic or strabismogenic. Infants identified at eight months were entered into a control trial of treatment with partial spectacle correction and underwent a long-term follow-up that monitored a wide range of visual, visuoperceptual, visuocognitive, visuomotor, linguistic and social development. In the present paper, the authors report on the outcome measures of visual acuity and strabismus. Poor acuity was defined as a best-corrected acuity of 6/12 or worse on crowded letters or 6/9 or worse on single letters, at age 4 years.

Acuity was measured in 79 infants who were significantly hyperopic and/or anisometropic at 11–12 months of age, 23 who showed hyperopia of +3D but less than +3.5D, 196 control subjects, 14 controls with refractive errors, and 126 others who showed an accommodative lag on screening but were not significantly hyperopic on first retinoscopy.

There was a poorer acuity outcome in the untreated group of hyperopes compared to controls (p < 0.0001) and to the children who were compliant in spectacle wear (p < 0.001) or who were prescribed spectacles (p < 0.05). Children who were significantly hyperopic at eight months were also more likely to be strabismic by 5.5 years compared to the emmetropic control group (p < 0.001). However, the present study did not find a significant difference in the incidence of strabismus between corrected and uncorrected hyperopic infants.

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Children who were not refractively corrected for significant hyperopia were four times more likely to have poor acuity at 5.5 years than infants who wore their hyperopic correction, supporting the findings of the First Cambridge Population Infant Vision Screening Programme.

Key words   Accommodation; amblyopia; hyperopia; infant vision; screening; strabismus; videorefraction

Introduction   Strabismus and amblyopia are the most common visual disorders of childhood in developed countries. In the United Kingdom, there have been various estimates of the incidence of these conditions but the consensus is that around 3% of preschool children show a deficit in their visual acuity caused by refractive error and/or strabismus.[1–7]

Amblyopia is a functional loss of vision that can result from degraded image quality in a critical period in early childhood. Strabismus may be associated with accommodative effort necessary in case of hyperopic refraction. Thus, early hyperopic or anisometropic refractive error may be a detectable precursor of these conditions.

Most screening programmes to detect strabismus and amblyopia, or their precursors, have been with children between 3 and 6 years.[8–12] There has been a great deal of debate regarding the optimum time for vision screening and the criteria for referral:[13] should screening be around 4 years when amblyopia and/or squint have developed or should it be earlier to allow pre-school interventions? Amblyopia screening as such is not generally practical in infancy. However, an alternative approach is to screen for early strabismus and strabismogenic and amblyogenic factors that are precursors and predictors of later onset of these problems, namely significant ametropia (high degrees of hyperopia, myopia and anisometropia).[8,14–26] This has been our approach in the two screening programmes we have conducted in the Cambridge Health District;[26] the results from the second programme are reported here.

In the first Cambridge Vision Screening Programme,[17,18,23] we offered screening to the total population of 8–9 month-olds born within the geographical area of the Cambridge Health District, using isotropic photorefraction[17,25] under cycloplegia (1% cyclopentolate hydrochloride). Infants with significant refractive errors on photorefraction were followed up with retinoscopy under cycloplegia. Those with hyperopic refractive errors greater than +3.5D (in one or more axes) on retinoscopy were entered into a randomised control trial of treatment with refractive correction throughout infancy. Untreated infants with significant hyperopia were found to be significantly more likely to become strabismic, and significantly more likely to show poor acuity (amblyopia) at 4 years of age, than infants without refractive errors in infancy. In the randomised control trial, we found that treated infants who wore their spectacles throughout infancy showed a significant reduction in the incidence of these abnormalities (27% poor acuity and/or strabismus by 4 years of age for those who wore spectacles, as opposed to 68% in the untreated group). Furthermore, we found that

hyperopic refractive errors decreased in both treated and untreated groups of infants between 9 and 36 months, although the mean refractive error of both groups remained higher than in the emmetropic control group.[27–31]

Cycloplegic screening presents a number of practical difficulties. As well as being more convenient, non-cycloplegic measures of the refractive state reflect accommodative behaviour as well as the refraction of the eye, which may be of significance in predicting children's visual outcome. In research studies,[32–34] we had previously found that when infants were presented with the demand to accommodate at 75 cm, hyperopic focus of +1.5D or greater predicted a large proportion of those who were significantly hyperopic (+3.5D or more of hyperopia) in one or more axes under cycloplegia on retinoscopy.

The Second Cambridge Infant Vision Screening Programme was carried out to examine (a) the effectiveness of non-cycloplegic refractive screening for errors of accommodation, using videorefraction (rather than cycloplegic photorefraction), in identifying children with significant refractive errors in infancy; (b) whether refractive errors detected in this way are strabismogenic and amblyogenic, i.e. predict outcome in terms of later reduced acuity and binocularity; (c) whether this outcome could be improved by early spectacle correction for the group detected in this programme. This second programme has confirmed, in a screening population, that non-cycloplegic screening for accommodative errors was a predictor of significant refractive errors under cycloplegia.[35] The present paper addresses questions (b) and (c) on outcome in terms of acuity, binocularity and early correction.

An extensive follow-up programme to 7 years of age studied all development through a wide range of measures including visual, visuoperceptual, visuocognitive (including attention), visuomotor, linguistic and social. Each child followed up was seen at intervals of 4–6 months for the first 4.5 years of life. We have already reported a significant relationship between early refractive status and preschool measures of development in visuocognitive and visuomotor preschool tests and in tests of attention at 6 years.[36] Infants were identified at 8 months by non-cycloplegic videorefractive screening as showing a focussing error requiring further investigation by means of cycloplegic refraction (on average 2 weeks later). A group of control infants, who did not show accommodative errors or strabismus at screening, was recruited at the same time for follow-up alongside the group whose refractive errors were confirmed following screening.

In this paper, we report detailed visual outcome measures for children with different refractive histories and the effects of refractive correction on visual outcome. In particular, we compare the visual outcome at 3.25–6 years in children who were detected by non-cycloplegic screening and confirmed as significantly hyperopic and/or anisometropic at 9–11 months of age (i.e. at their second follow-up visit to the Visual Development Unit) with that of the control group, identified and confirmed as infants who did not have strabismus or significant refractive errors; and within the group with infant refractive error we examine the effects of partial refractive correction.

Material and methods

SCREENING POPULATION   The screening population consisted of all infants born in the Cambridge Health District between July 1992 and July 1994, taken from immunisation lists of Community Child Health in the Cambridge Lifespan Community Trust.

During the screening period, 6732 infants were sent appointments and 5142 (76%) attended and completed screening. Appointments were arranged, at one of eight locations (usually Well Baby Clinics) in the Cambridge Health District, within the 7–9 month-old age range (calculated from the expected date of birth). Average age at the initial non-cycloplegic screening was 8.1 months (s.d. 0.8 months). This paper is concerned with the 784 children who were followed-up from this screening with the cycloplegic examination.

The research protocol adhered to the Declaration of Helsinki for research involving human subjects. All parents or guardians of the infants studied provided written consent to the screening and follow-up assessments.

ISOTROPIC VIDEOREFRACTION   Refractive screening was carried out on freely accommodating infants (i.e. without cycloplegia) using the VPR-1 isotropic videorefractor [Clement Clarke Ltd]. This technique is optically identical to isotropic photorefraction,[25] which has been validated and calibrated against standard measures of refraction[17] for cycloplegic testing. Published evaluations of the VPR-1 by a number of groups have concluded that it provides a valuable screening technique.[37–39]

SCREENING PROCEDURE   The screening procedure has been described fully elsewhere.[23,32–34] The protocol used for screening and follow-up is shown in Appendix 1. At screening, infants were referred for follow-up at the Visual Development Unit if they fell into any of the following categories:

1. *Far focus* Any infant showing hyperopic focus greater than or equal to +1.5D in any axis on either of the two measures made with the infant at a distance of 75 cm from the camera. (This measure has been shown to be optimal for indicating the presence of significant amounts of hyperopia[32]).

2. *Near focus* Any infant showing myopic focus greater than or equal to −3D on both the measurements made at 100 cm distance. This criterion was selected to distinguish small degrees of overaccommodation (common in young infants) from established myopia.

3. *Anisometropia* Any infant showing difference of focus greater than or equal to 1.5D in parallel axes of the two eyes on any two of the four videorefractive measures.

4. *Orthoptic failure* Any infant in whom an orthoptic or ophthalmic problem was detected, including manifest strabismus (defined as constant esotropia or exotropia detectable on cover test).

5. *Control group* A control group of infants who fell into none of the above four categories and who reported no problems at birth or in the neonatal period was also recruited for follow-up. A control child

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was recruited as the next available child with a normal screening outcome from the same clinic as each of the children referred for follow-up under criteria 1–4 above.

FIRST FOLLOW-UP EXAMINATION INCLUDING CYCLOPLEGIC REFRACTION   The first follow-up after screening occurred at average age 9.3 months (s.d. 0.9 months) – i.e., approximately one month after screening (maximum interval = 61 days). At follow-up, the information on the child's birth history and family history was checked and the occurrence of treated strabismus or amblyopia in any first-degree relative was recorded. Each child had a full orthoptic examination and also received retinoscopy under cycloplegia (1% cyclopentolate), as well as an ocular examination from an ophthalmologist. Full details of the retinoscopic procedure have been published.[18]

This served as the basis for the classification of confirmed refractive error:

1. Significant hyperopia, defined as a cycloplegic refraction of +4D or more in any axis. (Infants with hyperopia of 3.5 or 3.75D were classed as 'borderline hyperopes').
2. Significant myopia defined as −3.0D or more in any axis.
3. Significant anisometropia, i.e. 1.5D or more difference between corresponding axes in the two eyes.
4. Emmetropic controls – infants who were selected to be part of the control group at screening and were confirmed on cycloplegic retinoscopy to have no significant refractive errors (i.e., met none of the criteria 1–3).

These groups have been described in greater detail elsewhere.[35]

SECOND FOLLOW-UP   To confirm the group appropriate for refractive correction, a second follow-up examination with cycloplegic retinoscopy was carried out on infants in all the refractive error groups (average age 11.1 months (s.d. 0.64 months)). Infants were retained in the hyperopic group and entered into the trial of refractive correction if their most hyperopic axis remained as +4.0D or greater. Those who remained above +3.0D but below +4.0D were designated as 'borderline hyperopes'.

SPECTACLE CORRECTION   Spectacle correction was tested as an intervention by assigning infants into 'treated' and 'untreated' groups. Infants who met the criterion for hyperopia in the first 12 months of the study were assigned as 'untreated' and in the second 12 months as 'treated'. Comparison of the hyperopes included in our analysis of acuity outcome shows that those screened in the first 12 months had a mean greatest axis of +6.0D (s.d. 1.3D) on cycloplegic retinoscopy at the first follow-up, while those screened in the following 12 months had +5.9D (s.d. 1.1D); the difference was not significant (t = 0.55, p > 0.5). Comparing controls in the same way, we see that the mean greatest axes were +1.8D (s.d. 0.9) for the group screened in the first 12 months and +1.8D (s.d. 0.7) for the following 12 months; the difference was not significant (t = 0.63, p > 0.6). Thus, the groups followed-up from the first and second years appear to be comparable in terms of refraction.

Spectacles were prescribed based on the outcome of cycloplegic retinoscopy according to the following protocol:

• Sphere: 1 dioptre less than the least hyperopic meridian (corrections less than +1.5D were not prescribed);
• Cylinder: up to 2 years of age – half of the astigmatic error if >2.5D 2–3.5 years – half of any astigmatic error after 3.5 years – full correction

The prescriptions and refractions were checked at 4-monthly intervals and adjusted whenever necessary. At each of these follow-ups the length of time that the child wore the spectacles was recorded after questioning the carer/parent. This record allowed a compliance measure to be defined. The child was deemed a 'compliant' spectacle wearer if they were reported as wearing their prescribed spectacles for at least 50% of their waking hours on average through the years of this study (11 months to 4 years of age).

VISUAL OUTCOME MEASURES Each child who was followed-up entered an extensive programme including tests assessing all aspects of visual development and tests of cognitive, linguistic and social development.[36] Here we will discuss the visual outcome measures.

At each follow-up the children were examined by a trained senior orthoptist and their binocular status was recorded. If the child presented with strabismus at any stage of follow-up (from initial screening to the final follow-up visit at 6+ years) they were referred immediately to their local hospital ophthalmology department for treatment, but were encouraged to continue to attend the Unit to participate in the full follow-up programme.

At age 3–3.25 years all children were tested monocularly with the Cambridge Crowding Cards[40–42] using single optotypes at the prescribed distance of 3 metres, with and without spectacle correction if worn. Any child with over +1.5D of hyperopia was given a correction prior to testing at the 3+ year follow-up and beyond. At age 4–4.5 years, the crowded test cards were also included. The Cambridge Crowding Cards are designed to provide a measure of crowding equivalent to a linear Snellen Chart for preschool children. The child has to identify the central letter from an array of 5 letters whose separation is always half of one letter-width for all letter sizes, which range from 6/60 (0.1, 20/200) to 6/3 (2.0, 20/10) Snellen equivalents. The child may either name the central letter or match it against samples on a board. At the last Unit visit at age 5.25 years, crowded acuity was again tested monocularly with and without the appropriate spectacle correction using the Cambridge Crowding Cards.

The visual acuity outcome has been categorised as 'pass' or 'fail' using the following criteria for 'pass':

age 3.0–3.25 yrs, vision at least 6/9 (0.67, 20/30) on single optotype
age 4.0–4.5 yrs, vision at least 6/6 (1.0, 20/20) on single optotype and/or 6/9 (0.67, 20/30) on crowded optotype
age 5.25–6 yrs, vision at least 6/6 (1.0, 20/20) on single optotype and/or 6/9 (0.67, 20/30) on crowded optotype

Children were tested with and without their spectacle correction, with the pass/fail categorisation based on the better of the two acuities

recorded. Children failing on these criteria were referred to the oph-thalmic team for continuing management of the visual deficit. We have taken the crowded acuity as the preferred measure, and used single optotype acuity when crowded acuity was unable to be tested. The cat-egorised acuity is ideally taken from the measure at age 4.0–4.5 years, but if the child did not attend for that appointment then we have used the later measure, and if the child did not attend for either of those later measures then we have used the acuity data from age 3.0–3.25 years (comprising 80 out of 449 children).

The visual acuity was tested by a qualified senior orthoptist who also carried out an orthoptic examination to identify whether strabismus was present. This examination included a cover test with and without spectacles, ocular movements, convergence to near point, the 20-dioptre prism base-out test, and either the Lang or TNO stereotest.

We will present the visual outcome in terms of visual acuity and the occurrence of manifest strabismus separately.

Results

VISUAL ACUITY   Only children who completed at least one reliable acuity measure between the ages of 3 and 5 years were considered for this analysis. We compared visual outcomes across the following groups, using the Cambridge Crowding Cards acuity measure at >4 years (described above) whenever available – these constituted 83.1% of our acuity measures. Acuity measures on the remaining children were recorded using single-letter optotypes at either 3.25 years (14.3%) or >5 years (2.6%).

There are 10 groups to be considered, as indicated in Figure 1 (Appendix 1). The N-values given below refer to the number from each of those groups for whom outcome data are available.

1. Infants with significant hyperopia ≥+4.0D at the second follow-up who were not given a spectacle correction at 12 months (hyperope not treated (**Hnt**)). These make up the 'untreated' group. N = 18

2. Infants with significant hyperopia ≥+4.0D at the second follow-up who were given a spectacle correction, but who on average wore them for less than 50% of their waking hours throughout the first three years of life. These make up the 'hyperopic treated non-com-pliant (**Htnc**)' group. N = 23

3. Infants with significant hyperopia ≥+4.0D at the second follow-up who were given a spectacle correction at 12 months and who wore the spectacles for ≥50% of their waking hours (hyperope treated compliant (**Htc**)). N = 35

4. Infants who showed an anisometropia (**Anc**) of ≥1.5D between the eyes at the second follow-up, and who wore their spectacles for ≥50% of their waking hours. N = 13

5. Infants who showed an anisometropia of ≥1.5D between the eyes at the second follow-up, and who did not wear their spectacles for ≥50% of their waking hours (**Annc**). N = 7

6. Infants who appeared to have an accommodative lag on screening but were not confirmed as significantly hyperopic (+4.0D) at the

Identified at screening for follow-up

age 8 months
non-cycloplegic videorefraction

1st follow-up

age 9 months
cycloplegic retinoscopy

2nd follow-up

age 10 months
cycloplegic retinoscopy

spectacle correction

age 11-12 months

| screened | n=5142 |

near focus
any axis
<=-3.0D
n=20

aniso.
diff. betw
parallel axes
>=1.5D; not
near focus
n=101

far focus
any axis
>=+1.5D; not
aniso.
n=376

control
none of these;
no orth. or
opthalm.
problem
n=287

unconfirmed
myopia; no
aniso.
all axes
>-3.0D; diff
betw parallel
axes <1.5D
n=10

unconfirmed
aniso.; no
hyperopia
diff. betw
parallel axes
<1.5D; max
axis <+4.0D
n=27

unconfirmed
hyperopia
[uH]
all axes
<+4.0D
n=155 (126)

control w/
refractive
error [Ce]
any axis
>=+3.5D
n=20 (14)

unconfirmed
myopia; sig.
aniso.
all axes
>-3.0D; diff.
>=1.5D
n=2

unconfirmed
aniso; sig.
hyperopia
diff. <1.5D;
max axis
>=+4.0D
n=15

significant
myopia
any axis
<=-3.0D
n=6

significant
aniso.
diff. betw
parallel axes
>=1.5D
n=41

significant
hyperopia
any axis
>=+4.0D
n=168*

emmetropic
control [C]
all axes
<+3.5D
n=267 (196)

reducing
myopia
all axes
>-3.0D
n=1

reducing
aniso.; no
hyperopia
diff. betw
parallel axes
<1.5D; max
<+4.0D
n=4

reducing
hyperopia
all axes
<+3.0D
n=1

*33 did not have
2nd follow-up
retinoscopy within
a period of 3
months from 1st
follow-up, and
therefore could
not be considered
for the trial of
spectacle
correction

reducing
aniso.; sig.
hyperopia
diff. betw
parallel axes
<1.5D; max
>=+4.0D
n=3

borderline
hyperopia
[bH]
greatest axis
>=3.0D but
<+4.0D
n=32 (23)

significant
myopia
any axis
<=-3.0D
n=2

significant
aniso.
diff. betw
parallel axes
>=+1.5D
n=20

significant
hyperopia
greatest axis
>=+4.0D
n=94

myope,
treated
n=2

aniso., treated
[Anc; Annc]
n=20 (20)

hyp, not
treated [Hnt]
n=36 (18)

hyp, treated
[Htc; Htnc]
(see text for
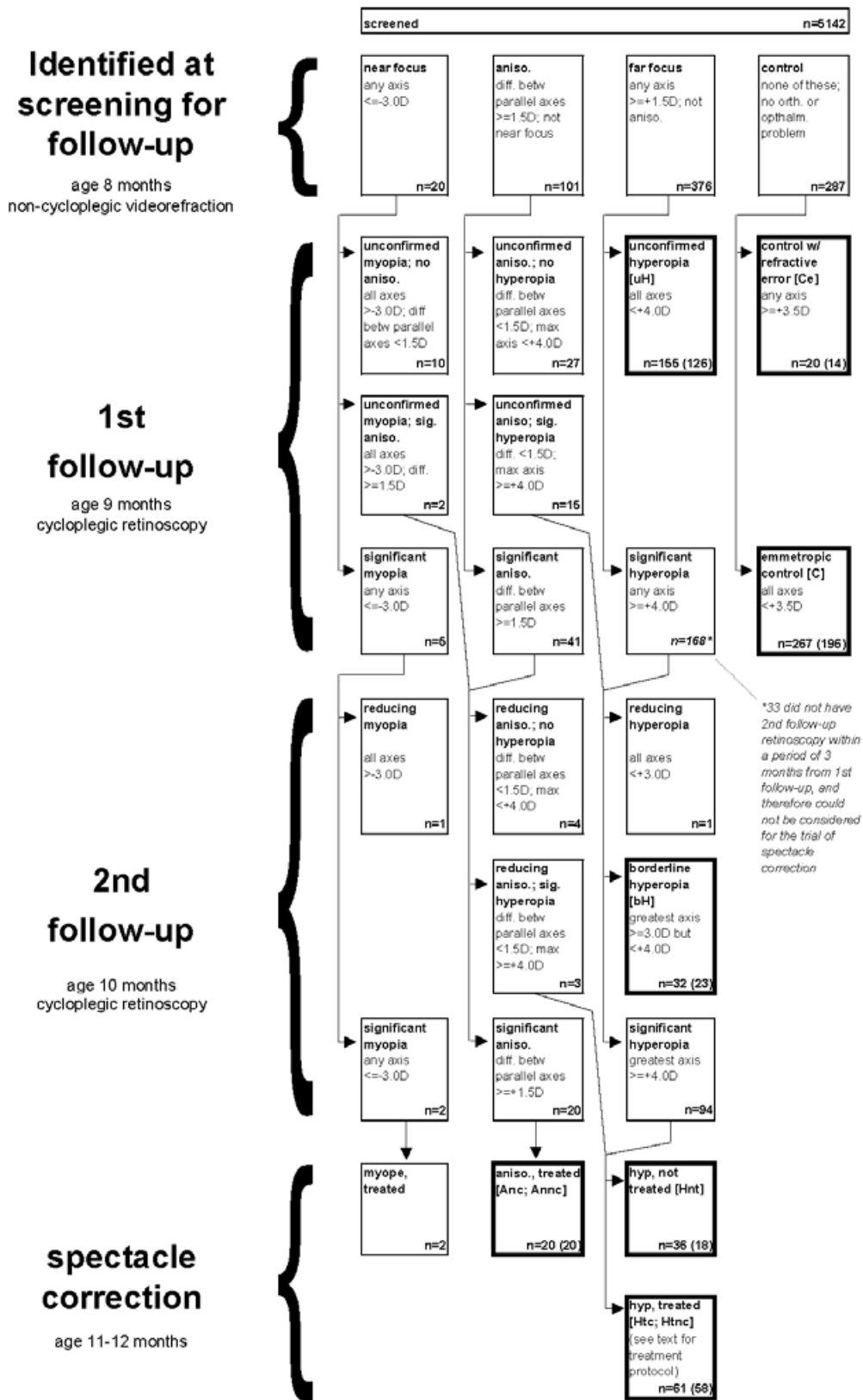treatment
protocol)
n=61 (58)

Fig. 1.

first follow-up. These are the 'unconfirmed hyperopic' group (**uH**). N = 126

7. Infants who were at least +3D but <+4.0D at the second follow-up and therefore not hyperopic enough to be entered into the treated or untreated groups. These are the 'borderline hyperopes' (**bH**). N = 23

8. Infants who were none of the above and deemed to be 'controls' (**C**). N = 196

9. Infants who focused normally on screening and were recruited into the control group, but met the criterion for refractive error (anisometropia, hyperopia or myopia) at the first follow-up (**Ce**). N = 14

10. Infants who presented with strabismus, other ophthalmological problems, or developmental delay at screening and were therefore referred to the ophthalmic clinic at ≥9 months. The early strabismics detected at screening are deemed infantile strabismics and a further set who developed strabismus later are included in this group of orthoptic failures (**O**).

There were very few significant myopes in the population, and as such there were too few to use for statistical analysis. Five myopes were confirmed at first follow-up, and three of these attended the second follow-up. On the outcome measures, two passed acuity and one failed and developed strabismus.

Comparison of the final numbers in brackets with numbers in the boxes from earlier stages of the protocol indicates the drop-out rates. To consider whether differential drop out may have any effect on our results comparing the hyperopic group with controls, we need to consider drop-out rates between the second follow-up, at which the groups were defined, and the outcome measures. These drop-out rates were 19% and 27%, respectively. The figures do not differ significantly on Fisher's test of exact probabilities (p = 0.17).

COMPARISON OF GROUPS BY ACUITY PASS/FAIL   Table 1 shows the number in each group who passed or failed on visual acuity, and the results of statistical comparisons (chi square, or Fisher's exact test where appropriate) between groups. A number of comparisons are possible, testing related but distinct questions.

1. *Do children who were still significantly hyperopic at 11 months of age, and were not corrected, show worse visual outcome at 4 years than children who were emmetropic? Comparison of the Hnt and C groups.*

    Only 1 of 196 children in the C group (0.5%) failed on acuity, compared to 12 of 18 (66.7%) in the Hnt group; the difference was significant (p < 0.0001). Children with significant hyperopia under cycloplegia at 11 months, and who were not treated, were much more likely to develop poor visual acuity than those who were emmetropic at the same age.

2. *Do children who were significantly hyperopic at 11 months of age, and were not corrected, show worse visual outcome at 4 years than hyperopic infants who were treated and compliant? Comparison of the Hnt and Htc groups.*

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Six of 35 hyperopic children (17.1%) who wore spectacles for at least 50% of their waking hours failed on acuity, compared with 66.7% of those who were hyperopic but not treated; this difference was significant (p < 0.001).

3. *Do children who were significantly hyperopic at 11 months of age and were not corrected show worse visual outcome at 4 years than those who were prescribed a correction, irrespective of compliance? Comparison of the Hnt and (Htc + Htnc) groups.*

Irrespective of compliance, visual outcome was significantly better in the treated hyperopic groups (22 failures in 58 children; 37.9%) than in the untreated hyperopic group (66.7%) (p < 0.05).

4. *Do children who were prescribed a partial spectacle correction have the same visual outcome as their emmetropic controls? Comparison of the Htc and Htnc groups with C.*

Only one of the C children from a total of 196 failed on the acuity test compared to 16 out of 23 Htnc children; the difference was significant (p < 0.0001). Group C also differed significantly from group Htc, where 6 out of 35 children failed (p < 0.0001).

5. *Was visual outcome worse in infant anisometropes than in those who had been emmetropic? Comparison of group C with the Anc and Annc groups.*

Controls were significantly better than compliant anisometropes (2 acuity failures in 13 children, p < 0.05); they were also better than the non-compliant anisometropes (5 acuity failures in 7 children, p < 0.0001).

6. *Do children who were only mildly hyperopic, or who focussed normally on screening but were hyperopic on subsequent retinoscopy, have a poorer acuity outcome than children in the emmetropic control group? Comparison of the bH and Ce groups with the C group.*

Borderline hyperopes, who had not met the criteria for treatment (n = 23), had no acuity failures. Similarly, children who focussed normally on screening but had a hyperopic axis of +3.5D or greater on subsequent retinoscopy (n = 14) had no acuity failures – neither group differed significantly from the control group.

7. *Do children who focussed normally on screening but were hyperopic on subsequent cycloplegic retinoscopy (Ce) have better acuity outcome than those children who were confirmed hyperopic at the first follow-up, whose far focus had been detected at screening and who had no correction (Hnt, Htnc)? Comparison of the Ce group with the Hnt and Htnc groups.*

The rate of acuity failure in the Ce group (none of 14 children failed) was significantly lower than in the Hnt group (6 out of 35 failed, p < 0.001) and the Htnc group (7 out of 23 failed, p < 0.0001); it was also significantly lower than that of all hyperopes considered together (34 out of 76 failed, p < 0.001). Thus, those infants who were able to overcome their hyperopic defocus at 8 months performed better than those who were hyperopic and who did not accommodate accurately.

8. *Do children with far focus on screening who were not confirmed +4D hyperopic on subsequent retinoscopy (uH) differ from children who were confirmed borderline hyperopic on retinoscopy (bH) and from*

emmetropic controls (C) who were not hyperopic and had not had a far focus on screening? Comparison of the uH group with the bH and C groups.

Ten of 126 unconfirmed hyperopes (7.9%) failed on visual acuity; this rate was significantly higher than the failure rate in the control group (1 in 196 failed, p < 0.001). It did not differ significantly from the failure rate in the borderline hyperopic group, where none of 23 children failed.

BINOCULARITY OUTCOME   At screening, seven infants were strabismic without an accompanying accommodative problem, of whom one had a congenital divergent strabismus. Three of these seven infants (43%) had a history of strabismus and/or amblyopia in a first-degree relative.

The low number of strabismics suggests that many children who were to become strabismic had not done so before 8 months of age. There were eight children that were not straightforward strabismics: six had congenital musculo-fascial anomalies or ptosis (Duane syndrome (2), Brown syndrome (1), ptosis (2), oculomotor apraxia (1)); two children also had retarded development, and one child was delayed without strabismus being present.

Thirty-three infants developed strabismus after the screening appointment, and 7 of these 33 (21%) had a history of strabismus and/or amblyopia in a first-degree relative compared to 9% in the whole screened population. Of these 33 infants, 28 (85%) had been identified as being significantly hyperopic or anisometropic at the first follow-up visit; 14 of these 28 (50%) developed an accommodative strabismus (average age of onset 3.18 years, range 1.3 to 5.2 years). Four of the remaining 19 became divergent. All infants followed the same protocol of correction of refractive error, whereby a partial correction was given for the hyperopia until they were older than 3.5 years.[26]

INCIDENCE OF STRABISMUS   Table 2 shows the incidence of strabismus in each group and the results of statistical comparisons (chi square, or Fisher's exact test where appropriate) between groups. Again, several comparisons could be made.

1. *Do children who were significantly hyperopic at 11 months of age show a greater incidence of strabismus at 4 years than children who were emmetropic? Comparison of the Hnt, Htc and Htnc groups with the C group.*

The incidence of strabismus was significantly higher in each of the hyperopic groups than in the control group. One of 196 emmetropic controls (0.5%) developed strabismus, compared with two of 18 children in the hyperopic not-treated group (p < 0.001), 7 of 35 in the treated compliant group (p < 0.001) and 5 of 23 in the treated non-compliant group (p < 0.001). The incidence of strabismus in all three hyperopic groups considered together (14 in 76 children, 18.4%) was also significantly higher than in the control group (p < 0.0001). Children in the hyperopic group who were compliant in their spectacle wear were later on average in developing strabismus, i.e. they were never under the age of two years, whereas the non-compliant and

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TABLE 1. Numbers of children who attended at +3 years or more and passed/failed on the visual outcome measure, and results of statistical comparisons between groups (chi square or Fisher's exact test).

Group	n passed	n failed	Emmetropic control [C]	Control w/ refractive error [Ce]	Hyperope, not treated [Hnt]	Hyperope, treated, compliant [Htc]	Hyperope, treated, not compliant [Htnc]	unconfirmed Hyperope [uH]	borderline Hyperope [bH]	Anisometrope, treated, compliant [Anc]
Emmetropic control [C]	195	1								
Control w/ refractive error [Ce]	14	0	n.s.							
Hyperope, not treated [Hnt]	6	12	****	***						
Hyperope, treated, compliant [Htc]	29	6	****	****	***					
Hyperope, treated, not compliant [Htnc]	7	16	***	-	-	*				
unconfirmed Hyperope [uH]	116	10	n.s.	-	-	-	-			
borderline Hyperope [bH]	23	0	*	-	-	-	-	n.s.		
Anisometrope, treated, compliant [Anc]	11	2	****	-	-	-	-	-	-	
Anisometrope, treated, non-compliant [Annc]	2	5	-	-	-	-	-	-	-	-

**** p<0.0001
*** p<0.001
** p<0.01
* p<0.05
n.s. not significant
- groups not compared

TABLE 2. Numbers of children who attended at +3 years or more with/without strabismus, and results of statistical comparisons between groups (chi square or Fisher's exact test).

Group	no strab.	strab.	Emmetropic control [C]	Control w/ refractive error [Ce]	Hyperope, not treated [Hnt]	Hyperope, treated, compliant [Htc]	Hyperope, treated, not compliant [Htnc]	unconfirmed Hyperope [uH]	borderline Hyperope [bH]	Anisometrope, treated, compliant [Anc]
Emmetropic control [C]	195	1								
Control w/ refractive error [Ce]	14	0	n.s. / ***							
Hyperope, not treated [Hnt]	16	2	**** / ***	n.s. / n.s.						
Hyperope, treated, compliant [Htc]	28	7	**** / ***	- / -	n.s. / n.s.					
Hyperope, treated, not compliant [Htnc]	18	5	** / ***	- / -	-	n.s.				
unconfirmed Hyperope [uH]	118	8	n.s. / n.s.	- / -	-	-	-			
borderline Hyperope [bH]	23	0	**** / ***	- / -	-	-	-	n.s. / n.s.		
Anisometrope, treated, compliant [Anc]	10	3	**** / ***	- / -	-	-	-	-	-	
Anisometrope, treated, non-compliant [Annc]	4	3	-	-	-	-	-	-	-	n.s.

**** p<0.0001
*** p<0.001
** p<0.01
* p<0.05
n.s. not significant
- groups not compared

untreated groups were less than two years of age at the onset of strabismus.

2. *Did treatment with spectacles improved the likelihood of developing good binocular function in children who were significantly hyperopic at 11 months? Comparison of the Hnt, Htc and Htnc groups.*

    The rate of strabismus was not significantly different in the untreated and the treated (compliant + non-compliant) hyperopic groups. Furthermore, there was no significant difference between the compliant hyperopes and the non-compliant hyperopes.

3. *Is the incidence of strabismus higher in infant anisometropes compared to children who had been emmetropic? Will comparison of the Anc and Annc groups show whether incidence of strabismus was higher in infant anisometropes who did not wear their spectacles? Comparison of C with the Anc and Annc groups.*

    Three of 13 children (23.1%) in the compliant and 3 of 7 (42.9%) in the non-compliant anisometropic group had strabismus; these incidences were significantly higher than one in 196 (0.5%) in the control group ($p < 0.001$; $p < 0.001$, respectively). Both anisometropic groups considered together also had a significantly higher rate of strabismus than the control group ($p < 0.0001$), but the difference between the compliant and non-compliant anisometropic groups was not significant.

4. *Did children who were only mildly hyperopic, or who focussed normally on screening but were hyperopic on cycloplegic retinoscopy, show a poorer binocular outcome than children in the control group? Comparison of the bH and Ce groups with the C group.*

    The group of borderline hyperopes, who had not met the criteria for treatment (n = 23), contained no instances of strabismus. Children who focussed normally on screening but had a hyperopic axis of +3.5D or greater on subsequent retinoscopy (n = 14) also had no incidence of strabismus – neither group differed significantly from the control group We found that infants who were significantly hyperopic at first follow-up but who were able to overcome their hyperopia did not differ significantly from those who were not hyperopic and did not show a lag of accommodation.

5. *Do the hyperopes who present with an accommodative lag (Hnt, Htc and Htnc groups) show a greater incidence of strabismus than the 'failed controls' (Ce), i.e. those hyperopes who were able to accommodate to overcome their hyperopia?*

    The incidence of strabismus in the untreated hyperopic group, 2 of 18, was not significantly higher than that in the Ce group (n = 14, none strabismic). The incidence of strabismus in the Hnt, Htc and Htnc groups considered together, 14 out of 76, did not differ significantly from that in the Ce group. However, the numbers in these groups mean that little weight can be placed on this comparison; it should also be noted that the H groups contain more large hyperopic refractions than the Ce group.

6. *Do children with far focus on screening who were not confirmed + 4D hyperopic on subsequent retinoscopy (uH) show a different binocular status from children who were confirmed borderline hyperopic on retinoscopy (bH), or from controls (C) who did not show*

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far focus on screening? Comparison of the uH and bH groups with C.

In the unconfirmed hyperopic group, 8 of 118 children (6.8%) developed strabismus; this rate was significantly higher than the one of 196 in the control group (p < 0.01). In the borderline hyperopic group (n = 23) no children developed strabismus, but the difference between this group and the unconfirmed hyperopic group was not significant.

Discussion The main findings from this study can be summarised as follows:

1. Poor hyperopic accommodation, measured using non-cycloplegic videorefractive screening, is an indicator of significant hyperopic refractive error in infancy. The refractive errors detected in this way predict a high incidence of reduced acuity and strabismus by 5.5 years, compared to controls without significant refractive error in infancy.

2. The compliant wearing of a partial correction of significant hyperopia and anisometropia throughout infancy reduces the incidence of poorer than average acuity in 3–5.5 year-olds. In this programme, the spectacle correction was given on average at around one year of age. This effect is statistically apparent even if children are classified by 'intention to treat' rather than by whether they actually complied fully with the spectacle correction.

3. Compliant spectacle wear for hyperopic refractive error throughout infancy from 1 to 3 years did not significantly reduce the incidence of strabismus (including accommodative strabismus). However, in children in the compliant group who developed accommodative strabismus, their strabismus was controlled by subsequent refractive correction.

CYCLOPLEGIC AND NON-CYCLOPLEGIC SCREENING Cycloplegic screening gives a direct measure of infants' refractions, but is a longer screening procedure and because of the requirement to administer cyclopentolate, restricts the personnel who can carry out screening. Thus, non-cycloplegic screening is an important goal if it is effective in detecting the required conditions. In a previous study,[35] we showed that non-cycloplegic screening was effective at picking up the majority of infants with potentially amblyogenic and strabismogenic refractive errors. In the First Cambridge Refractive Screening Programme,[25,26] we showed that infant hyperopia and anisometropia detected under cycloplegia was a predictor of strabismus and reduced acuity. Our present results show that those infant hyperopes and anisometropes detected by non-cycloplegic screening similarly show the increased risk of these visual problems during early childhood.

A subset of hyperopes will not be detected by non-cycloplegic screening because they accommodate to a sufficient degree that they do not meet the criterion for the 'far focus' group. Our knowledge of the development of this group has to come from the Ce group, who were selected as controls but showed hyperopic refractive errors on follow-up. The 14 children from this group who completed follow-up showed no

failures on either the acuity or strabismus criteria. Thus, apparently, the fact that non-cycloplegic screening fails to unmask some hyperopic refractions does not lead to substantial numbers of potential visual problems being missed.

The hyperopic and Ce groups differ (a) in that the Ce group shows enough accommodation to reduce the accommodative lag below 1.5D; (b) in that the hyperopic group experiences a greater degree of optical blur during infancy. Either of these differences might be expected to impair visual development. From (a), the theory of accommodative esotropia might suggest that the Ce group ought to be at greater risk of strabismus due to their habitual accommodation. Our data give no support to this view. However, it must be noted that the number in the Ce group is small, and also that the children with large degrees of hyperopia are more likely to be detected in the far-focus group (the distribution is apparent in Figure 3 of our previous paper[35]). Thus, it is possible that the far-focus group were showing as much or more habitual accommodation as the children whose hyperopia went undetected. By definition, however, they were suffering any effects of optical blur to a greater degree.

EFFICACY OF PREVENTIVE TREATMENT Regarding the prevention of acuity deficits, the results of this programme are consistent with the beneficial effects of early spectacle correction found in our first programme based on cycloplegic screening at 8 months.[23,26] However, that programme was also effective in reducing the incidence of strabismus, which we have not found in the present study. In the earlier programme, we gave the spectacle correction two months earlier on average than in this second programme. We also achieved a slightly higher level of compliance in the first programme than in the second.

These results taken together suggest that earlier treatment, in the form of a partial spectacle correction by 10 months of age, may be more effective than at 12 months of age or later, both in terms of compliance and visual outcome. They suggest that early screening and treatment before 9 months of age is likely to be the most effective way of preventing strabismus and amblyopia. However, given the rapid rate of refractive change during the first year of life, early screening will inevitably pick up a substantial number of children whose hyperopia reduces greatly in the following months. The comparison of our findings for acuity and strabismus suggests that the age of treatment is less critical for the prevention of poor acuity; it may be that the sensitive period for development of high acuity is more prolonged than for the establishment of binocularity.

However, a crucial factor is the level of compliance with spectacle wear. If this is low for any reason then no amount of well-run screening, identification of risk factors and offer of treatment will be cost-effective. Compliance may depend on the spectacles being first accepted at an early age, the physical convenience of spectacle frames prescribed for infants, the amount and nature of support given to families by clinic staff, and social factors within the families.

Spectacle correction must also be seen in the context of the process of emmetropisation. Our protocol, in which hyperopic and especially

astigmatic errors are undercorrected, was designed to minimise the risk that children became over-corrected through the progression of refractive change, but it is important to check children's refractions and update corrections regularly to ensure that this risk is avoided. Our earlier results[27] suggest that correction according to this protocol does not counteract the natural reduction of hyperopic refractive errors between ages 9 months to 3 years.

In summary, non-cycloplegic refractive screening in infancy is an effective method for detecting amblyogenic and strabismogenic conditions, and can lead to significant prevention of later acuity deficits. Most strabismus is not yet manifest at the age when screening was first conducted; many of the children who will become strabismic are detected by this procedure. However, prevention of strabismus may only be feasible if spectacle corrections are prescribed early and a high level of compliance is achieved.

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Appendix 1. Screening and follow-up protocol up to 12 months

In the following chart, the sequence of visits is ordered vertically. Refractive categories of interest at each visit are arranged horizontally. Each box details the criterion a child had to meet for inclusion in that category at that age, and the number of children who met that criterion.

A child's inclusion in a particular refractive category at one visit determined the range of categories in which they could be placed at the following visit. Arrows between categories represent an exhaustive account of possible category changes from visit to visit. The number of children in each category who failed to attend a subsequent follow-up is not indicated, but is given by the difference between the number of children in a category C at a given visit and the total number of children in all categories to which members of C were assigned at the following visit. For example, 20 children had near-focus at screening (row 1); 17 of these appear in the categories below at first follow-up, leaving three who did not attend follow-up.

Bold boxes denote the final refractive groups whose later acuity and binocular outcomes we compare. The number of children in each group who had acuity and orthoptic measures available after age 3 years, and were therefore included in our analysis, is given in round brackets. The abbreviation we use in the text for each group is given in square brackets. Compliant and noncompliant anisometropes (Anc, Annc) and treated hyperopes (Htc, Htnc) occupy the same boxes in the diagram, but were subsequently grouped according to their pattern of spectacle wear, with 50% wear the criterion for compliance.