1040-5488/07/8402-0084/0 VOL. 84, NO. 2, PP. 84–96
OPTOMETRY AND VISION SCIENCE

FEATURE ARTICLE ON LINE

Infant Hyperopia: Detection, Distribution, Changes and Correlates—Outcomes From the Cambridge Infant Screening Programs

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ABSTRACT

Purpose. To report on two population screening programs designed to detect significant refractive errors in 8308 8- to 9-month-old infants, examine the sequelae of infant hyperopia, and test whether early partial spectacle correction improved visual outcome (strabismus and acuity). The second program also examined whether infant hyperopia was associated with developmental differences across various domains such as language, cognition, attention, and visuomotor competences up to age 7 years. Linked programs in six European countries assessed costs of infant refractive screening.

Method. In the first program, screening included an orthoptic examination and isotropic photorefraction, with cycloplegia. In the second program we carried out the same screening procedure without cycloplegia. Hyperopic infants (≥+4 D) were followed up alongside an emmetropic control group, with visual and developmental measures up to age 7 years, and entered a controlled trial of partial spectacle correction.

Results. The second program showed that accommodative lag during photorefraction with a target at 75 cm (focus ≥+1.5 D) was a marker for significant hyperopia. In each program, prevalence of significant hyperopia at 9 to 11 months was around 5%; manifest strabismus was 0.3% at 9 months and 1.5 to 2.0% by school age. Infant hyperopia was associated with increased strabismus and poor acuity at 4 years. Spectacle wear by infant hyperopes produced better visual outcome than in uncorrected infants, although an improvement in strabismus was found in the first program only. The corrections did not affect emmetropization to 3.5 years; however, both corrected and uncorrected groups remained more hyperopic than controls in the preschool years. The hyperopic group showed poorer overall performance than controls between 1 and 7 years on visuoperceptual, cognitive, motor, and attention tests, but showed no consistent differences in early language or phonological awareness. Relative cost estimates suggest that refractive screening programs can detect visual problems in infancy at lower overall cost than surveillance in primary care.

Conclusions. Photo/videorefraction can successfully screen infants for refractive errors, with visual outcomes improved through early refractive correction. Infant hyperopia is associated with mild delays across many aspects of visuocognitive and visuomotor development. These studies raise the possibility that infant refractive screening can identify not only visual problems, but also potential developmental and learning difficulties.

(Optom Vis Sci 2007;84:84–96)

Key Words: infant vision, hyperopia, vision screening, strabismus, photorefraction, cognitive correlates of hyperopia, emmetropization

Hyperopia has a high prevalence among young children, and is commonly found in association with the early development of strabismus and amblyopia. It has therefore been suggested that screening for significant hyperopia during infancy has the potential for early detection, and preventive measures, for these disorders.[1–7] However, retinoscopic screening of infants demands full optometric or ophthalmic training, together with experience of testing very young children, and these professional skills are in limited supply in many health contexts and make screening relatively expensive.

Alternatively, autorefractors typically require co-operation, not found in infants, for looking through an eyepiece and fixating a small static target. However, the development of photo- and videorefractive methods,[8–14] which can assess the refractive state of an infant's eyes rapidly from a distance, has made non-invasive screening a practical possibility.

We have carried out two programs in which photo- or videorefractive screening was offered to all children around 8 to 9 months of age, living within a defined geographical area in Cambridgeshire, England. Detailed descriptions of components of these programs, and their results, have been published elsewhere.[10,15–22] In this paper, therefore, we review the main findings and bring together related results from the first and second programs. We also present some previously unpublished data related to each program.

Each of these programs screened about 75% of a total population cohort, and so has provided a unique sample for the study of the natural history, correlates, and consequences of infant hyperopia. The large majority of infants in this screened population (around 85%) were white of British or other European ethnic origin. We will review the data which these programs have provided on the prevalence and distribution of refractive errors in infancy in this population.[10,16–18] For each program, the study design also included an extensive longitudinal follow-up, to school age, of infants detected with hyperopia, alongside a control group of children from the same clinics who did not have a significant refractive error (or any ophthalmological problem) at screening. This follow-up examined a range of visual sequelae, including refractive change (emmetropization), visual acuity, and strabismus.[15,16]

The design of both programs also incorporated a controlled trial of the effects on visual development of early spectacle correction of refractive errors, testing the hypothesis that adverse effects of early hyperopia could be counteracted by reducing the accommodative effort required to overcome image blur. The possibility of effective treatment is an important element in evaluating refractive screening as a preventative healthcare measure.

Such evaluation needs also to consider the costs of a screening program, relative to established systems based in primary care for identifying children who develop visual problems. These relative costs will depend on the way healthcare is organized in different national systems. The Cambridge screening program was linked to a set of pilot projects co-ordinated across six European countries[23]; this experience has allowed an initial analysis of comparative costs in a variety of different health care environments.

Observations during the first program suggested the possibility that children who had been hyperopic in infancy differed from controls not only in purely visual measures, but also in terms of a broader spectrum of cognitive and visuomotor development. Consequently, the second program included in the design of its follow-up a range of tests of attention, visual perception, spatial cognition, language, and visuomotor competence appropriate to the ages of follow-up sessions between 12 months and 7 years. We will review the evidence[19,20] provided by these tests that infant hyperopia is indeed statistically associated with a range of mild but significant delays in development, but that these delays are concentrated in certain visual, spatial, attentional, and visuomotor aspects, rather than reflecting a global cognitive or developmental delay.

Populations, Methods, and Protocols in the Cambridge Screening Programs

First Cambridge Screening Program (Cycloplegic). Every infant living in the City of Cambridge (England) over a 2.5 year period (1981–1983) was sent an appointment to attend at one of eight local Well Baby Clinics when the infant was between 7 and 8 months of age. A total of 3166 infants (74% attendance) were screened by a trained orthoptist. The screening procedure included a basic orthoptic examination (cover test, 20 dioptre prism base out test, convergence to near point and Hirschberg test) and isotropic photorefraction[8–10] following cycloplegia with one or two drops of 1% cyclopentolate. The photorefractive procedure requires three 35-mm photographs with different camera settings; one focused on the child's eyes at 75 cm, and the other two focused at 150 and 50 cm (i.e., 0.67 diopters in front and behind the child). A measure of defocus is derived from the dimensions of the blur ellipses in the latter two images, and the pupil size derived from the first.

Infants were referred for follow-up on the following criteria:

Hyperopia: refraction exceeding +3.5 D in one or more meridians.
Myopia: myopia exceeding –2 D in one or more meridians.
Anisometropia: more than 1.0 D difference between equivalent meridians of the two eyes.
Orthoptic: strabismus or any other ocular pathology evident in the orthoptic examination conducted at screening.
Control group: for each of the refractive conditions above, the next infant to be screened after the infant with the "condition."

Overall, 9.3% of the screened infants were followed-up in one or other of these groups. The first follow-up occurred by age 9 months and included a full orthoptic examination, photorefraction (before and after cycloplegia), acuity (using forced choice preferential looking), ophthalmic examination of the fundus, and cycloplegic retinoscopy. Where a significant refractive error was confirmed, and for the control group, follow-up appointments were made at regular intervals up to age 4 years; the overall plan is indicated in Fig. 1.

The effects of spectacle correction were evaluated in the hyperopic group who had refractions under +6 D. (More extreme hyperopes were considered to require correction as conventional clinical practice, which was carried out in the regular ophthalmological clinic; their outcome is however included in the overall group results discussed below.) Of this hyperopic group, 50% (randomly selected) were prescribed a partial spectacle correction based on the following protocol. This was a consensus protocol, based on the goal of minimizing the risk of any child becoming overcorrected in the interval between visits, in particular with respect to astigmatism which frequently reduces rapidly over the first years of life[24,25]:

Sphere: 1.0 D less than the least hyperopic meridian (corrections $<$1.5 D were not prescribed).
Cylinder: up to 2 years of age, half of astigmatic error if $>$2.5 D; at 2 to 3.5 years, half of any astigmatic error (as a positive cylinder added to any spherical correction); over 3.5 years, full correction.

On each visit, families whose children had been prescribed spectacles were carefully questioned about compliance (wearing

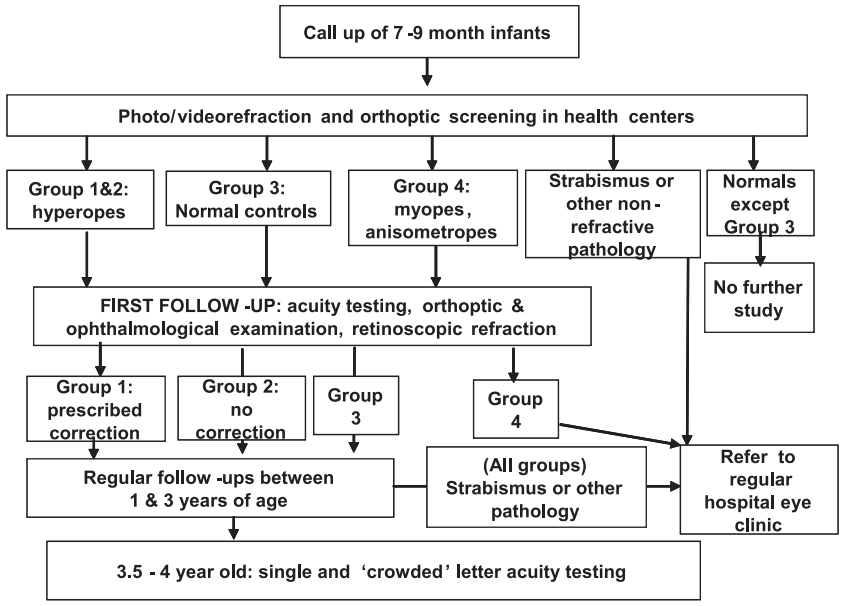

FIGURE 1.

Scheme of the first Cambridge refractive screening program. The second program differed in that (a) the groups were initially selected for follow-up on the basis of noncycloplegic focus; (b) the first follow-up then selected groups similar to 1 to 4 above, on the basis of cycloplegic retinoscopy; (c) continuing visual, motor, and cognitive measures continued in follow-ups to ages 6 to 7 (Table 1).

spectacles for more than 50% of waking hours was deemed "compliant").

Second (Noncycloplegic) Cambridge Screening Program. This second program differed from the first principally in the use of a noncycloplegic screening procedure, and in the wider range of follow-up measures. Its target population was all infants born in the Cambridge Health District between July 1992 and July 1994 (a somewhat a larger region than the City on which the first program was based), derived from Child Health immunization lists from the Cambridge Lifespan Community Trust (Primary Health Care in the UK National Health Service). At one of eight locations in Cambridgeshire, 5142 infants (76%) attended for screening at an average age of 8.1 months. The screening procedure was similar to the first program, except that no cycloplegia was administered, and photorefraction on film was replaced by the VPR-1 videorefractor (Clement Clarke International Ltd.), which uses the same optical configuration as isotropic photorefraction, but captures the images in a digital framestore from which immediate computer-based measurements of the blur ellipse are made. The procedure, including repeated videorefraction at 75 and 100 cm distances, is described fully in ref. 16.

In this program, initial follow-up was on the basis of accommodative state without cycloplegia, when the child's attention was attracted to an illuminated toy at the camera distance. The criteria for follow-up were as follows:

Far focus: any infant showing a (freely accommodating) hyperopic focus of $\geq +1.5$ D in any meridian on either of the 75 cm measures. This criterion was selected on the basis of pilot work[26] which suggested that it would yield a manageable proportion of cases to follow-up (of the order of 5%) and that it would correspond to a similar cycloplegic refraction to that selected in the first program (cycloplegic refraction of +4 D or more in at least one meridian).

Near focus: any infant showing a (freely accommodating) myopic refractive focus of ≥ -3 D on both measures made at 100 cm distance (the optical theory of photorefraction[8] and empirical calibration, show that this camera distance of 100 cm gives greater differentiation of myopic errors than at 75 cm).

Anisometropia: any infant showing anisometropic defocus of $\geq$1.5 D in parallel meridians of the two eyes, on any two or more of the four videorefractive measures.

Controls: recruited in the same manner as for the first program.

Orthoptic failure: any infant in whom an orthoptic or ophthalmic problem (e.g., esotropia, exotropia, Duane's syndrome, ptosis, lens opacities, iris remnants) was detected.

At the first follow-up (mean age 9.1 months), cycloplegic refraction was checked (two drops cyclopentolate hydrochloride 1%), and used to define refractive groups on a similar basis as the first program, except that a +4 D threshold was taken to define the hyperopic group for the general analysis.

The group reaching this criterion for significant hyperopia was given a second follow-up approximately 6 weeks to 2 months after their initial follow-up (at 10 to 11 months of age). At this follow-up, half of the confirmed hyperopic group were given a partial correction for their hyperopic refractive error using the same prescription protocol as in the first program.

The schedule of the follow-up to age 7 years, including the cognitive and behavioral testing, is tabulated in Table 1. The tests in the follow-up program are not described in full detail here, but may be found in the referenced sources. They included functional visual measures from the Atkinson Battery of Child Development for Examining Functional Vision (ABCDEFV) battery devised and standardized in the Visual Development Unit.[27] This includes a set of age-appropriate Core Vision Tests [e.g., acuity from Forced Choice Preferential Looking (FPL) or the Cambridge Crowding cards,[28] and measures of binocularity (Lang, TNO)], plus addi-

TABLE 1.
Follow-up schedule in the second screening program

Age (months)	Follow-up number	Procedures
7–9	Screening	Noncyclo videorefraction and orthoptic
9–11	1	Refraction, orthoptic, binocular acuity
11–13	2a	(Treatment group only) Cyclo refraction, binoc and monoc acuity, first spectacle prescription given
	2b	(Treatment group only) Spectacles checked
13–15	3	Refraction, orthoptic, binoc acuity, MCDI, ABCDEFV, head circumference
19–21	4	Refraction, orthoptic, binoc and monoc acuity, ABCDEFV (part)
24–27	5	Refraction, orthoptic, acuity, ABCDEFV
30–33	6	(Hyperopic groups only) Refraction, orthoptic, acuity, ABCDEFV, MCDI
36–39	7a	Final cycloplegic refraction, orthoptic, binoc and monoc acuity (single optotype)
	7b	(Treatment group only) Spectacles checked, binoc and monoc acuity
42–45	8	Griffiths test, ABCDEFV, movement ABC
48–52	9	Orthoptic incl. stereo test, binoc and monoc acuity (crowding cards)
63–72	10a/b	Orthoptic, acuity, WPPSI object assembly, block construction from ABCDEFV (timed), movement ABC, BPVS, Griffiths performance test, CN-Rep, Rutter, PAT
72–84	11	TEA-Ch

'Refraction', unless stated otherwise, included noncycloplegic videorefraction as well as cycloplegic retinoscopy and videorefraction. 'Orthoptic' tests included age-appropriate stereo testing.

MCDI, MacArthur Communicative Development Inventory; ABCDEFV, Atkinson Battery of Child Development for Examining Functional Vision; Rutter, Rutter Parental Report Inventory; CN-Rep, Test of Non-word Repetition; PAT, Phonemic Awareness Test; TEA-Ch, Test of Everyday Attention for Children. See text for references.

tional tests of visual perception, visuomotor behavior, and spatial cognition. It also included standardized measures of early language development (the Macarthur Communication Development Inventory,[29] adapted for British English; British Picture Vocabulary Scales (BPVS)[30]; CN-Rep Non-Word Repetition Test[31]; Phonological Abilities Test[32]; the Movement ABC battery,[33] which assesses both fine and gross motor development; the Griffiths pediatric development test[34]; the Rutter Parental Report Inventory[35] (hyperactivity scale), and subtests of the Test of Everyday Attention for Children[36]). If a child had a prescribed correction at the time of testing, it was worn for these tests. Following the cycloplegic refraction at visit 7 (36 to 39 months) any children from the untreated group who still had a refractive error requiring correction were prescribed it, and wore their correction for the subsequent follow-up testing.

Both programs were approved through the Research Ethical Review procedures prevailing at the time of the work. Informed consent was gained from all participating families, and the research followed the tenets of the Declaration of Helsinki.

RESULTS

Prevalence of Refractive Errors and Strabismus in Infancy

Both programs indicated that within the population screened, 4 to 5.5% of 6- to 9-month olds have +3.5 D or more of hyperopia, <1% have anisometropia of 1.5 D or greater, and very few (0.25%) have myopia −3 D or greater. Strabismus is seen in <1%.[16,18] Fig. 2 shows the proportions detected and confirmed in these ametropic groups in the two screening programs.

For most analyses from the second program a criterion of +4.0 D on retinoscopy was used to define significant hyperopia. For comparability with data from the second program, Fig. 2 plots confirmation rates for both +3.5 and +4.0 D criteria.

For the second program, cycloplegic refraction is available only for the groups who were followed-up. As discussed below, initial selection for these groups, based on noncycloplegic refractive state, is not perfectly correlated with cycloplegic refractive error. Nonetheless, the number in the population having a certain degree of hyperopia can be estimated by combining (a) the number of infants with that refraction found to fail screening on the "far focus" criterion, with (b) the number with the same refraction initially selected in the control group, scaled up from this sample to reflect the size of the population from which the controls were drawn.[18] Fig. 3 plots in detail the distribution of hyperopia at 9 months determined from (a) and (b), measured as greatest meridian on cycloplegic retinoscopy, in the second screening program.

This figure makes clear that the distribution is skewed, with a modal value of the most hyperopic meridian at this age between +1.5 and +1.75 D, and a long tail extending to +9 D. Many of the infants in this hyperopic tail of the distribution have significant astigmatism, and some are anisometropic; information about the distribution of these aspects of refraction in the followed-up sample is reported in full in ref. 17.

In summary, data from the two programs agree that most 8- to 9-month-old infants in an unselected, largely white population have a small degree of hyperopia, often including some astigmatism. About 5% have a hyperopic meridian of +4 D or greater, considered appropriate for follow-up in these programs.

Cycloplegic and Noncycloplegic Videorefraction as Predictors of Refractive Error

In the first screening program, initial screening was by cycloplegic photorefraction. As the cycloplegic procedure adds to the time

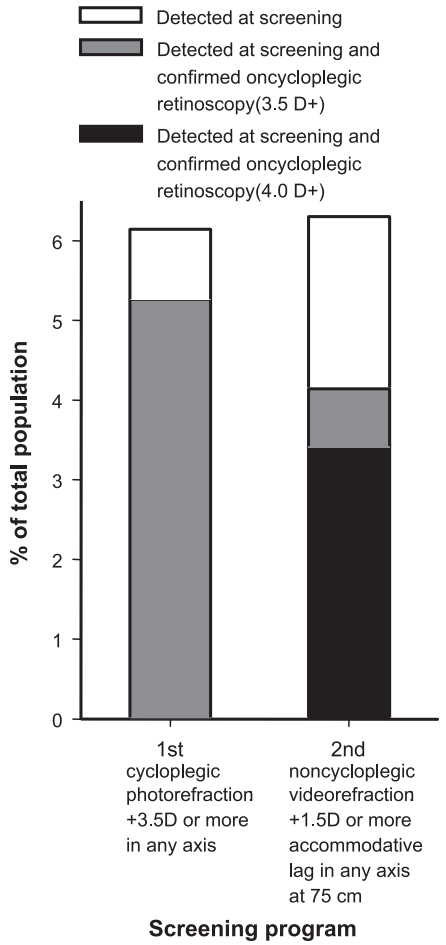

FIGURE 2.

Histograms showing the prevalence of hyperopic focus on cycloplegic photorefraction (first screening program) and accommodative lag on noncycloplegic videorefraction (second screening program) in the population at 6 to 8 months. Rates confirmed hyperopic on subsequent cycloplegic videorefraction at 9 months are shaded: greatest meridian confirmed 3.5 D+ (gray); 4.0 D+ (black, second program only).

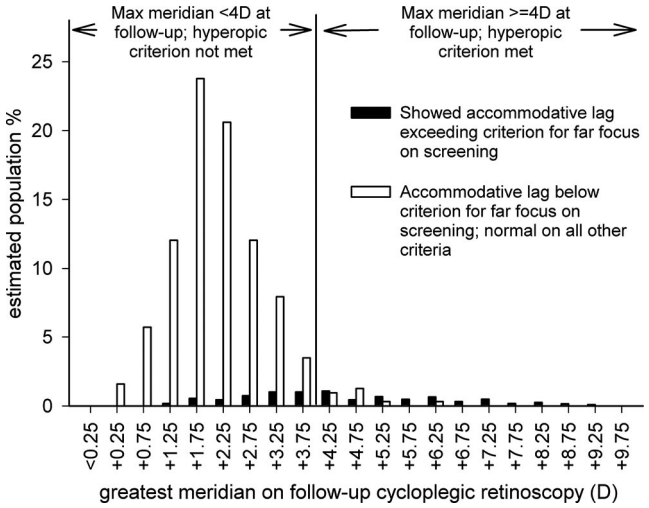

FIGURE 3.

Histogram of most hyperopic meridian measured by cycloplegic retinoscopy at follow-up, age 9 months, in the second screening program.[18] Black bars: those initially meeting the videorefraction criterion for "far focus" at screening. White bars: control group with normal focus. The figures in each group are scaled to reflect the overall proportions of "far focus" and "normal focus" infants in the population at screening. Vertical line: +4.0 D confirmation criterion for hyperopia at follow-up.

and waiting facilities required, and the qualifications needed for the screening personnel, the second program was designed to evaluate whether infants with hyperopic refractions could be detected when they were allowed to accommodate freely and tested with noncycloplegic videorefraction.

The positive predictive value of the noncycloplegic procedure is illustrated by the right-hand bar of Fig. 2, where the shaded region shows the proportion of far-focus infants who were confirmed to be hyperopic under cycloplegia. A fuller picture is given in Fig. 3, in which black bars right of the 4 D line show the extent of this "true positive" group. White bars to the right of the line provide an estimate, based on the control group, of the proportion of children who accommodated closer to the camera than +1.5 D but nonetheless proved to be significantly hyperopic (false negatives).

In addition to hyperopia, this screening program detected anisometropia (usually, but not always accompanied by hyperopia) as well as, in a small proportion of infants, myopia and orthoptic problems including strabismus. We calculated the overall sensitivity and specificity of the screening procedure as a whole, using the proportions of children detected and confirmed with *any* of these refractive or orthoptic conditions. It should be noted however that among children detected with at least one condition in screening, this included far focus in more than 90% of cases. (Near focus proved not to be a particularly useful indicator; only 0.3% of the screened population were in this category, and only 46% of these were confirmed in any category.) This overall analysis yielded a sensitivity of 0.67, specificity 0.96, and positive predictive value 0.60.[18] In other words, children who are within the "normal range" of refraction will have a very high probability of passing the test (i.e., do not show accommodative lag $\geq +1.5$ D); but a significant proportion of hyperopic infants also manage to accommodate on the target to this criterion.

The cycloplegic refraction followed the screening by about 1 month. In noncycloplegic videorefraction at this visit ("FU-1" in Table 1), about 25% of the children who had met the far-focus criterion at screening no longer showed this amount of accommodative lag. In this group whose lag had reduced there was a much lower proportion of hyperopes (27%) than those who still showed the lag (62%; see Fig. 4 in ref. 18). This is consistent with the idea that the former group may have been hyperopic, with consequent lag, at the age of screening, with significant reduction of both hyperopia and lag in the following 1 to 2 months. If this is correct, the positive predictive value of noncycloplegic screening would have been higher if the comparison had been made with an immediate cycloplegic refraction.

Prediction and Prevention of Strabismus and Amblyopia

The justification for screening would not be strong if simple detection of hyperopic refractive errors was its end point. Screening gains its value from the ability to detect potentially amblyogenic and strabismogenic conditions, and particularly if it provides the opportunity for effective intervention. The two programs provided evidence on both these points.

In the first screening program, infants with +3.5 D or more of hyperopia who did not wear a spectacle correction had, by 4 years, a high prevalence of strabismus (21%), compared with emmetropic controls (1.6%). Amblyopia was measured as failure on the Cambridge Crowding Cards acuity test[28,35]; for detection of amblyopia, crowded acuity is a more sensitive measure than single-letter tests at the same age.[37] Note that, as explained in the description of the follow-up procedure, in both programs any children requiring refractive correction (whether or not they had been part of the "treated" group) wore it for the vision testing at 4 years. In the hyperopic group, 68% failed the crowded acuity test at 4 years, compared with 11.1% in the control group.[15,16] These results confirmed that infant hyperopes are significantly "at risk" for later strabismus and amblyopia.

However, wearing a spectacle correction reduced these risks significantly. In infant hyperopes who wore a partial spectacle correction, the prevalence of strabismus was reduced to 6.3%, and for amblyopia to 28.6%.

In the second screening program[18,21] infant hyperopes greater than +4 D who were not corrected showed much higher prevalence of later strabismus (17%) and amblyopia (68%) than emmetropic controls (0.5 and 0.5% respectively). Those who wore a spectacle correction had a significantly reduced rate of amblyopia (17.1%); however in this program the prevalence of strabismus was not significantly reduced in the treated group.

These results as stated are for the group of children who actually wore their prescribed correction, i.e., were reported as compliant for 50% or more of their waking hours. To answer the scientific question of whether refractive correction is an effective preventive measure, this is a relevant comparison. However, to evaluate refractive screening from a public health point of view, the significant question is whether the overall system of assigning treatment on the basis of screening results leads to improved outcome. This question must be answered by comparing groups on the basis of intention to treat rather than on whether spectacles were actually worn. In both programs, such a comparison on the basis of "intention to treat" showed significantly improved acuity results for the group assigned spectacle correction, irrespective of compliance (see ref. 15 for the first program, and ref. 21 for the full details of the second program). The effect of spectacle correction on strabismus found in the first program was also significant if the comparison was made between intention to treat (8.8% of infant hyperopes became strabismic) and "no intention to treat" (23.2% became strabismic). As expected, the effects on acuity and strabismus were greater if children who actually wore their correction were evaluated against the untreated group.

The compliance rates achieved in the two programs were 71 and 62% respectively. Compliance rate in any program of this kind is likely to be sensitive to a number of factors, including the age at which spectacles are first prescribed, the care with which appropriate frames for very young children are selected and fitted, and the degree to which families are convinced of the value of the treatment. Thus the success of any program will depend heavily on these factors which reflect the skills and personal approach of all those involved, as much as the formal protocol of the screening and follow-up.

Data from the second program allow us to consider whether accommodative lag, resulting in a habitually blurred image, or habitual accommodation of marked hyperopes, were predictors of visual outcome. The numbers are relatively small, but the results showed no indication that hyperopic children who accommodated at the camera distance for screening were thereby at greater risk of amblyopia or strabismus.

They showed better acuity outcome than children who showed an accommodative lag, but the numbers did not allow these groups to be matched for the degree of initial hyperopia.[21]

In summary, both programs found that the wearing of a spectacle correction in infancy improves the chances of infant hyperopes having normal vision at age 4 and beyond. However, compared with the improvement of acuity, the effect on strabismus is less consistent between the programs; possible reasons for this are considered in the discussion.

Survey of the Screened Population at School Age

The geographical nature of this population who participated in the second program allowed us to investigate the general visual outcome, in terms of acuity (Cambridge Crowding cards) and stereo testing (Lang) in a school population at average age 6.9 years (SD 0.5 years).[38] These tests were conducted in Cambridgeshire schools over a period such that one group of children were too old to have been included in the screened population, while a later group had been in the appropriate age cohort. Of 5915 children tested, 2292 turned out to have been screened. Fig. 4 presents the test outcome in these two groups, and shows that on both acuity (near and distance) and stereo measures, the screened population show a better school-age vision outcome than the preceding cohort who had not received screening. We do not know how far this is attributable to successful treatment within the groups detected in screening, and how far to an increased awareness of eye care needs in families who had attended the screening with their infants.

These results raise the possibility that infant screening not only provides a window of opportunity for early detection and treatment of visual problems and early treatment, but may also raise awareness of

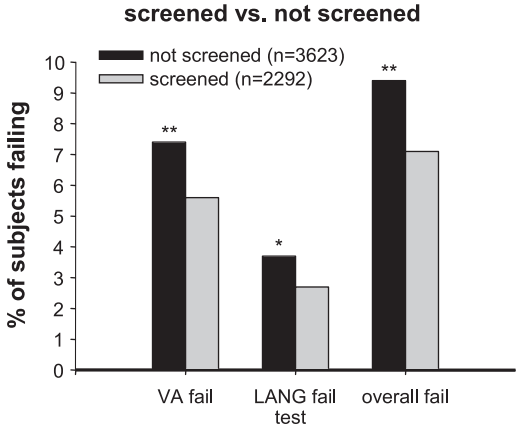

FIGURE 4.

Rate of children's failures on vision tests conducted in Cambridgeshire schools, at average age 6.9 years on a cohort who had participated in the second Cambridge screening program as 8 to 9-month-old infants, and cohort who were 1 year too old to have done so. VA fail = acuity worse than 6/9, in either eye or at least a two line difference between eyes, using Cambridge Crowding Cards at 3 m, or worse than 6/12 equivalent with a near version of the cards at 30 cm. Lang fail = could not identify at least two of three stimuli (i.e., disparity >600 sec of arc) on the Lang stereotest.

the possibility of visual problems early in life and encourage parents who detect a possible problem to bring young children into the eye clinic.

Emmetropization With and Without Spectacle Correction

A possible concern with early spectacle correction is that it could impede the normal process of emmetropization, which is partly driven by optical defocus.[39–44] To minimize this risk, the prescription protocol defined above gave only a partial spectacle correction for hyperopia, and the frequent follow-up intervals were intended to ensure that children did not become overcorrected due to reducing hyperopia between refractions. These repeated measurements of refraction allowed us to assess whether the reduced blur and accommodative requirement for children wearing their correction compromised their natural process of emmetropization.

In the first screening program, mean hyperopia (most hyperopic meridian) for infant hyperopes who were not treated with spectacle correction fell from +4.3 D at 9 months to +3.1 D at 36 months (Fig. 5). Over the same period, mean hyperopia in those who wore a partial correction reduced from +4.6 to +3.4 D. Both groups thus showed an average reduction of +1.2 D. Wearing spectacles therefore did not impede infant hyperopes' emmetropization by 36 months. Fig. 5 also shows (previously unpublished) data from the second program which show a very similar pattern of results; in neither case was there a statistically significant difference between the refractions of the treated and untreated groups at 36 months.

More detailed emmetropization results from the first program can be found in ref. 22, including an analysis based on intention to treat. This analysis, like that shown in Fig. 5, found no final difference for hyperopic infants assigned versus not assigned to treatment. However, in either analysis, initial emmetropization in the treated group was slower. Fig. 5 shows that, at 18 months, the untreated group had reached the mean which they retained to 36 months, whereas hyperopia in the treated group was significantly higher and still reducing. By 36 months, the treated group had "caught up," and the two did not differ. This is consistent with emmetropization being accelerated by greater degrees of optical defocus, but shows that the protocol for partial correction used in this program did not prevent normal emmetropization by 36 months. The temporary disadvantage of a slower emmetropization should be set against the greatly reduced prevalence of strabismus and amblyopia in the treated group.

A fuller analysis of the early stage of emmetropization in the second program is presented in ref. 17, including a detailed consideration of early changes in cylinder as well as spherical components. This showed that spherical hyperopia and astigmatism both reduce during infancy, but that the processes determining these appear to be largely independent. This may have significant implications for understanding the mechanisms of emmetropization, which affect both the axial length of the eye and corneal curvature.

Early Visuoperceptual, Visuocognitive, and Visuomotor Correlates of Infant Hyperopia

During the first program we observed that children in the hyperopic group often showed signs of mild developmental delays. This could potentially be because hyperopia is a "soft sign" of other developmental anomalies, or because poor early vision itself leads to abnormal development. In the second program we compared, over a series of follow-up visits, a wide range of measures of visuomotor and cognitive development (Table 1) in the groups who had been identified as infant hyperopes and emmetropic controls. The data presented in this and the two following sections comes entirely from the second program.

Children were tested between 13 months and 5.5 years with the ABCDEFV,[27] the Movement ABC,[33] and the Griffiths Child Development Scales.[34]

We found[19] that 14-month-old infants with hyperopia were twice as likely as controls to fail one or more of the visuocognitive and visuomotor tests of the ABCDEFV which at that age includes, apart from core sensory visual tests, retrieval of totally and partially covered objects (Piagetian test of cognitive object permanence), picking up black and white cotton using a pincer grasp, and stack-

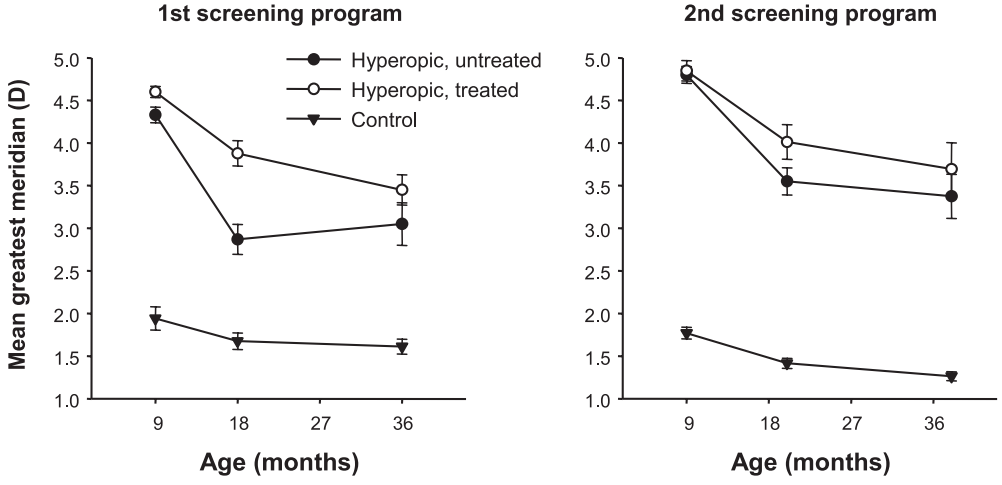

FIGURE 5.

Mean changes of refraction in hyperopic treated, hyperopic untreated, and control groups in each of the two screening programs. "Treated" is here defined as the group who were assigned for spectacle correction, and complied by wearing their correction at least 50% of waking time during the period. "Untreated" combines children in the hyperopic group who were not assigned for treatment, and those who were assigned for correction but were not compliant in wearing their prescribed spectacles by the above criterion.

TABLE 2.
Tests of visuomotor and visuocognitive development on groups of hyperopic and control infants followed up from the second screening program, age 14 months–5.5 years

Test	Age	Hyperopes	Controls
% Passing ABCDEFV (three subtests)	14 mo	66	85
% Passing ABCDEFV (>2/4 subtests, excl block constructions)	2 yr	76	83
ABCDEFV (four subtest, excl block constructions)	3.5 yr	87	98
Movement ABC overall z-score	3.5 yr	−0.23	0.00
Movement ABC overall z-score	5.5 yr	−0.34	0.00
MCDI vocabulary size	2 yr	57.1	57.2

ing two blocks. At 2 and 3.5 years, the ABCDEFV visual perception tests include shape matching in a form board and finding embedded animal figures in a drawing; these did not show significant differences at 2 years, but at 3.5 years, children in the hyperopic group showed a greater number of failures on these items than did controls. However, none of the items on the Griffiths scales of pediatric development showed a difference, arguing against the idea that this is a general delay in development at this age. Overall, these results indicate mild deficits in the hyperopic group, concentrated in areas of visual perception and visuomotor control, which in some tests are apparent as early as 14 months, and on others as late as 5.5 years. The numerical results for these tests are summarized in Table 2.

The difference between the hyperopic group and controls remained even when children who were strabismic or failed the acuity test at 4 years were taken out of each group. We also examined the comparison between the hyperopes who had worn a spectacle correction and those who had not. The differences in ABCDEFV scores between these groups were not consistent and were far from statistical significance, at any of the three ages tested. We conclude that although visuocognitive problems are associated with the group of infant hyperopes, they do not seem to be a consequence of the visual conditions which are also found in this group, and we have no evidence that they are improved by refractive correction of the hyperopia.

Deficits on the Movement ABC

Most striking were differences in the two groups' performance on the Movement ABC, a standardized assessment of everyday visuomotor and spatial competence.[33] We compared infant hyperopes with emmetropic controls at 3.5 and 5.5 years.[20]

The Movement ABC includes tasks to assess motor development within three categories: manual dexterity, balance, and ball skills. It is normalized for ages 4 to 12 years, over which scores on individual tests can be converted to "impairment scores" corresponding to percentiles. For age 3.5 years, slightly below that for which there were previously published norms, we analyzed raw scores on individual tests and an overall z-score. For age 5.5 years, we analyzed these (as the most sensitive measures of difference between groups), as well as standardized impairment scores, which are used to identify clinically significant motor impairments.

At 3.5 years, the hyperopic group scored significantly lower on three of the 12 tests, including one from each category, as well as on mean performance over all tests expressed as a z-score.[20] (No test showed better performance by the hyperopes.) At 5.5 years the hyperopic group scored significantly lower on five of the twelve tests, as well as on overall z-score. (Only one test showed a nonsignificant advantage for the hyperopes.) Overall results are summarized in Table 2. At this age children's scores were also converted to standardized impairment scores, again showing a significant difference between the hyperopic and control groups. Against norms for 4 to 5 year olds, the control group's median impairment score corresponded to the 56th centile, while the hyperopic group's corresponded to the 42nd.

This overall difference between the control and hyperopic groups could potentially be explained by a poorly performing subgroup within the hyperopic group, whose scores would skew the data. However, an analysis of distributions of scores did not find evidence for such a subgroup; the hyperopic distribution was simply shifted down with respect to control distribution, and only 5.1% of children of the former fell below the fifth centile of the norms (the usual criterion for a clinically significant motor difficulty). The evidence indicates a deficit that was mild but widespread, rather than a subgroup of severely impaired children.

One possible subgroup would be strabismic children. Indeed, at 5.5 years the strabismic children in the hyperopic group did have significantly poorer scores than the nonstrabismic children (mean z-scores −0.62 and −0.23 respectively) suggesting that strabismus is associated with poor motor performance. However, even the latter figure is significantly different from performance of the control group, and so the association of the deficit with hyperopia is not simply a secondary effect of the problems of strabismic children.

The results for children in the hyperopic group who wore a spectacle correction did not differ significantly from those who had not (mean z-scores −0.30 and −0.37 respectively).[20] Thus the data does not provide support for the idea that the spectacle correction was an effective therapy for the visuomotor associates of hyperopia, as distinct from the acuity which was improved by spectacle correction in these children.

Taken together, these tests show a pattern of mild but persistent visuomotor and spatial deficits in children who had been identified with significant hyperopia in infancy, lasting at least until school age (6 years). This is unlikely to be a direct consequence of strabismus or of uncorrected refractive error, as in general both the strabismic and nonstrabismic groups and the compliant corrected and not corrected groups show similar degrees of deficit.

Tests of Language and Attention

Were the visuomotor and perceptual deficits associated with infant hyperopia paralleled by developmental delays in other domains, such as language and attention? On the whole, we found language development in the hyperopic group to be normal. At 2 years, hyperopes did not differ from controls on an early checklist of vocabulary by parental report, the MacArthur Communicative

TABLE 3.
Tests of language and attention on hyperopic and control groups from the second screening program, age 7 years

Number of children	Test	Hyperope group score		Control group score		Test of difference
		Mean	SD	Mean	SD	
n = 171	BPVS	107.7	14.4	112.6	13.7	t = 2.30, p < 0.02*
n = 171	CNRep	33.2	5.3	33.8	4.5	t = 0.85, p > 0.1
n = 171	PAT rhyme	9 (median)		9 (median)		U = 3612.5, p > 0.4
n = 171	PAT letter knowledge	25 (median)		25 (median)		U = 3618.5; p > 0.4
n = 147	PAT end deletion	7 (median)		7 (median)		U = 2595; p > 0.3
n = 147	PAT beginning deletion	7 (median)		8 (median)		U = 2448, p > 0.1
n = 118	TEA-Ch Sky Search	9.6	3.4	11.0	3.8	t = 2.00, p < 0.03*
n = 118	TEA-Ch Opposite worlds	10.4	2.6	11.6	3.2	t = 2.08, p < 0.03*
n = 118	TEA-Ch Score	10.2	4.1	11.0	4.0	t = 0.98, p > 0.1
n = 118	TEA-Ch Walk Don't Walk	8.0	3.5	8.3	3.4	t = 0.47, p > 0.3
n = 147	Rutter hyperactivity	1 (median)		0 (median)		U = 2341.5; p = 0.07

*Difference is significant at the 5% level.

Development Inventory[29] adapted for British English in our unit[19] (Table 2).

At 5.5 years we tested children on a fuller set of measures of language development. The British Picture Vocabulary Scale (BPVS) short form[30] requires children to select line drawings that match the meaning of single spoken words. From the Phonological Abilities Test (PAT), we used rhyming, letter knowledge, and segmentation tasks; these assess phonological awareness, which has been found to be a predictor of later reading and spelling difficulties.[32] The Children's Test of Nonword Repetition (CNREP)[31] is a short-term memory test for language processing at 4 to 8 years; poor performance is associated with poor vocabulary, and reduced ability to acquire reading skills.[45] Results of these tests are included in Table 3.

On these tests, only the BPVS showed a small deficit in the hyperopic group relative to controls. On the CNREP and PAT however, the two groups showed no differences.

Overall, these data show little evidence for a language delay in the hyperopic group. It is of note that the only test that showed a difference, the BPVS, has significant visual, cognitive, and attentional components. Children must select a line drawing that matches a word, and on some of the more complex items the understanding of the mappings between drawings and words requires cognitive interpretation of the depicted events as well as vocabulary knowledge. There is also an important "response-selection" component: the task is to select which of four drawings best matches the spoken word, and therefore to inhibit inappropriate responses to items that may initially appear to match but are erroneous. We investigated these response-selection and inhibition abilities in the hyperopic group in more detail using early tests of attention (described in the following paragraphs).

In a final follow-up at 6 to 7 years, by which time children were already at school, we compared former infant hyperopes and emmetropic controls on four standardized subtests from the Test of Everyday Attention for Children (TEA-Ch).[36,46] These results are summarized in Table 3. On "Sky Search," a test of selective visual attention in which children find targets embedded in an array of distractors, standardized scores were significantly lower for the hyperopic group. As children's motor speed at the test is subtracted before calculating the final score, the difference reflects specifically a deficit in visual attention in the hyperopic group. On "Opposite worlds," a test of attentional control and inhibition of a prepotent verbal response, the hyperopic group likewise scored significantly lower. The two other tests from this battery "Score" (sustained auditory attention) and "Walk don't walk" (a test of sustained attention and motor inhibition) did not show a difference between the groups.

These results show persisting deficits in selective visual attention and attentional control and inhibition in the hyperopic group at 6 to 7 years. Interestingly, these tests require the integration of visual information with selection and executive control functions associated with the frontal lobes. In contrast, the tests in which the information to be processed was auditory, rather than visual, did not show poorer results for the hyperopic group.

As for the visuocognitive and visuomotor effects described above, any differences in attention scores between hyperopic children who had versus had not worn a spectacle correction, either overall or for the separate subtests, were far from statistical significance. The association of poorer scores with refractive error is not apparently reduced by optical correction of that refractive error.

Costs and Benefits of Refractive Screening

The studies described above demonstrate that refractive screening can be an effective measure for detecting hyperopia and anisometropia in infancy, and thereby predicting and treating subsequent childhood problems of acuity and binocularity. However, screening requires human and other resources, and for a large majority of screened infants, no visual problems are detected. Screening must therefore be evaluated in health-economic terms, as to the cost per case detected. This can be compared with the cost per case of infant ocular problems that would be detected without screening, i.e., through conventional primary care surveillance. Either method will send to the ophthalmology clinic a certain number of false referrals, and the cost of examining these must be included in the overall cost of the program.

These costs will be dependent on the organization and costs of primary care in a particular health care system. The opportunity to examine this issue in a range of different systems was provided by

TABLE 4.
Illustration of calculated screening cost per child (1996 US$ equivalent)

Component costs of screening (UK example)	Cost per child screened ($)
Provision of list from immunization register	0.92
Clerical cost of making appointment	0.76
Orthoptist time (fraction of salary cost for 15 minutes per child)	4.82
Use of building (rental costs charged by health centre)	5.12
Equipment—videorefractor written off over 10,000 tests	1.53
Total	*13.15*

TABLE 6.
Calculation of cost per case confirmed

Screening:
Cost per case confirmed = $(N_sC_s + N_{ds}C_o)/N_{cs}$ where
- N_s = number screened
- C_s = screening cost per child
- N_{ds} = number detected in screening
- C_o = cost per case in ophthalmology clinic
- N_{cs} = number confirmed from screening at follow-up in ophthalmology clinic

Surveillance by primary care physician:
Cost per case confirmed = $(N_pC_p + N_{rp}C_o)/N_{cp}$ where
- N_p = number seen for surveillance in primary care
- C_p = cost of primary care surveillance per child
- N_{rp} = number referred from primary care surveillance
- C_o = cost per case in ophthalmology clinic
- N_{cp} = number confirmed from primary care surveillance at follow-up in ophthalmology clinic

our collaboration between centers in six European countries that carried out pilot videorefractive infant screening programs.[23]

Tables 4 to 7 illustrate our methodology. In all cases costs have been taken, and translated into U.S. dollars, at the rates prevailing at the time the data were gathered (1996). Table 4 indicates the component costs of screening as conducted in the UK. The corresponding figure is presented in Table 5 for the six countries. Table 5 also presents the cost of a specialist appointment (with an ophthalmologist in the systems prevailing in these countries), required to confirm the presence of a condition (refractive or strabismic) suspected from either screening or surveillance. We also used figures on the costs of the visual components specified in each country's program of child health surveillance at the time.

The calculation also requires us to know (i) how many children were detected at screening (on the criteria described for the second program above); (ii) what proportion were confirmed as ametropic and/or strabismic; (iii) how many children would be referred from surveillance *on the same population*; and (iv) what proportion of these were confirmed in the ophthalmology clinic. (The latter figures could be obtained from ophthalmology clinic records for the year before the pilot screening program; the referral criterion would in this case almost always be suspected strabismus). Table 6 defines how these figures can be used to obtain comparable values of "cost per case detected." The figures required were available for this comparison in three of the centers (UK, Italy, Spain), in which the screening population was defined in such a way (e.g., as the catchment area of a specific hospital) that the surveillance results could be calculated.

Table 7 gives the figures calculated on this basis. Surveillance of one child is usually substantially cheaper than refractive screening, since the time spent by the general physician on vision checks is very brief, but the number of false referrals is generally much higher. The end result is that the overall cost per case detected, including ophthalmology clinic time, is substantially lower for screening, by a factor ranging from 1.5:1 to 3.2:1.

The conclusion that screening is economically advantageous must be qualified in several ways. First, the "cases" detected are different; in particular, the screening will detect infants with significant hyperopia, straight-eyed at the time of screening, who would almost certainly not be detected in surveillance. Second, because screening detects cases that would not otherwise come to light, the total cost may be increased, and this must be weighed against the benefits of early detection of refractive errors. The value of detecting cases depends on the success of subsequent treatment or preventive measures; we know something about this for the partial refractive correction in our trial, but do not have figures available for the success of any treatment following detection in surveillance. Nonetheless, apart from the benefits of detection, the figures emphasize the advantage of screening, in examining infants, and reassuring their families, who would otherwise occupy expensive specialist time with unconfirmed strabismus suspected in primary care.

From this analysis we suggest that the savings made by early effective screening and treatment can be substantial, provided the screening procedure is effective and does not have high false referral

TABLE 5.
Costs of screening and ophthalmology clinic visit in six European countries (all costs at 1996 levels and exchange rates)

Country	Cost per ophthalmology clinic visit ($)	Basis	Cost per videorefractive screening by orthoptist ($)
UK	61.60	Hospital charge to purchasing health authority	13.15
Spain	22.95	Health insurance approved charge	5.62
France	46.20	State health insurance approved charge	15.40
Italy	34.80	Public health charge	8.47
Portugal	28.77	National health service costing	5.50
Germany	64.22	State health insurance approved charge	16.79

TABLE 7.
Overall cost per case detected, by methodology of Table 5, in three European countries

	Surveillance		Screening	
Center	Cost per case detected ($)	% cases in population	Cost per case detected ($)	% Cases in population
Britain (Cambridge)	1100	1.3	337	5.2
Italy (Padova)	935	3.3	299	3.7
Spain (Barcelona)	172	3.0	112	11

rates, and the after-care and treatment is robust, with well-trained eye specialists with effective methods and procedures for examining very young children.

In applying this analysis elsewhere, the cost of the training of the individuals carrying out the screening and the accuracy of screening are crucial variables, as are the prevalence of strabismus and amblyopia in the particular population.

It should be noted that this is not a full cost-benefit analysis, in the sense that it does not attempt to quantify the benefits of different outcomes in economic terms. For instance, "false negatives" or missed cases place no cost burden on the healthcare system beyond their initial screening and thus play no special part in the analysis. However, whatever screening or surveillance method is used, it is important to state clear to parents that, even if no ocular abnormality is detected at that time, such problems may arise later in the child's life, and that they should seek professional advice if they suspect any problem in the future. More broadly, a full cost-benefit analysis would need to evaluate the effect on quality of life, and cost of subsequent health care, of strabismus and vision loss which is not effectively treated in childhood.

DISCUSSION AND CONCLUSIONS

In this population, the typical state of the infant eye around 8 to 9 months of age is modest hyperopia (+1.5 D on average), although there is a long tail of significantly hyperopic refractions in the distribution, with about 5% showing +4 D or more in one or more meridians in this particular population. This refraction identifies a group who are at increased risk of strabismus and relatively poorer acuity, by age 4 years.

The theory of accommodative strabismus would suggest that the group at greatest risk would be those showing habitual accommodation in the face of their hyperopia. Our data do not support this conclusion; they suggest that on the contrary accommodative lag at age 9 months may be an indicator of poor visual outcome, although this point needs further study. What we can say is that in this study, noncycloplegic screening effectively identified many infant hyperopes, including a group at high risk of strabismus and reduced acuity.

A partial spectacle correction for significant hyperopia in infancy yields a marked improvement in visual outcome, although even children who are compliant in wearing their correction do not on average achieve as good a result as emmetropic controls. However, the second screening program did not achieve the prevention of strabismus seen in the first program. This was not an effect of differential compliance since the prevention was not found even among those children who wore their correction. The lack of effect may be attributable to the fact that corrections were given approximately 2 months later in the second program than the first. If so, it suggests that treatment before the end of the first year may be necessary to prevent the onset of strabismus; the timing of treatment appears to be less critical for improving acuity outcome.

Ingram[3,47] has also conducted trials of correcting hyperopic refractive errors detected in infant screening. His initial trial[47] found no effect on strabismus of prescribing corrections after screening at 1 year, which would be consistent with the program above on timing. However, in his later trial,[3] in which screening took place at 6 months, he also found no preventive effect. For comparison with our results, it would be of interest to know at what age the prescriptions were filled, and the subsequent level of compliance which is not in the published data.

The study in schools within the screened district from the second program showed that, overall, the screened cohort showed a better visual outcome at age 7 years than an immediately preceding cohort from the same population who had not been offered screening. This suggests that screening provides a general benefit of raising awareness in families of the possibility of early detection of visual problems and earlier treatment.

Hyperopic infants show small but reliable deficits in many visuocognitive, spatial, visuomotor, and attention tests, first identifiable in the second year of life and with persisting effects at the beginning school years. This is not a general developmental delay, since no effect is apparent in most language and auditory attention tests. There is no evidence that it is a result of strabismus, or that it can be reduced by optical correction. The deficit may be particularly associated with fronto-parietal systems for spatial cognition and attention. The basis of this association is not yet known; it is as likely to be a common neurodevelopmental origin, as to be a visual consequence of hyperopia on cognitive and motor development. It offers the possibility of early identification of children at risk of preschool visuocognitive problems, in particular attention deficits which may be a significant factor for educational achievement. However, considerably more work is required to investigate whether these deficits are particularly associated with accommodative lag in infancy (perhaps itself an indicator of attention), and/or with high levels of hyperopia persisting beyond infancy, or to a third more general factor such as a small delay in all neural circuitry controlling visual behavior.

We conclude that infant refractive screening with spectacle correction is a potentially valuable and cost-effective preventive measure for children's visual problems. However, this depends on adequate skills and organization, not only for delivering the screening procedure to the target population, but also in the follow-up

that confirms refractions, prescribes corrections, and encourages and monitors compliance in the correction being worn. It is well known that there are marked differences in the prevalence of specific refractive errors in different ethnic populations, and the pattern found in this population would not necessarily be the same elsewhere. Furthermore, participation rates and compliance are likely to depend on the socioeconomic makeup of the screened population; while this program covered the whole range within the target population, the high attendance rate for screening and relatively good compliance achieved here would be considerably more challenging in a mixed inner-urban population, and in the context of a sustained service delivery rather than a research-oriented screening program.

We hope that these programs can serve as a starting point, which will inspire other teams to develop further carefully controlled studies of early hyperopia and its consequences across different populations and social and healthcare contexts, with the goal of improving not only children's vision but also a wider range of behavioral and cognitive function related to early visual brain development, so that children can achieve their true potential at school.

ACKNOWLEDGMENTS

This work has been supported by grant G7908507 from the Medical Research Council of Great Britain, a grant from the East Anglia Regional Health Authority, and under a Concerted Action of the BIOMED program of the European Community.

We acknowledge the help and support of present and past members of the Visual Development Unit in the two screening programs. Bill Bobier, Kim Durden, and David Ehrlich carried out the great majority of the retinoscopic refractions. Jackie Day, Kim Durden, David Ehrlich, Carol Evans, Clare Hughes, Ann Macintyre, Fiona Macpherson, Francoise Mathieu, Elizabeth Pimm-Smith, Sarah Rae, Jackie Wade, John Wattam-Bell, and Frank Weeks made substantial contributions to testing, organization, and data analysis. Katrina Richards carried out the great majority of the testing in schools. The screening programs were run with the collaboration and support of Mr. P. G. Watson and Mr. A. T. Moore, Consultant Ophthalmologists at Addenbrooke's Hospital Cambridge, and Dr. D. Vickers and colleagues, Lifespan Community Child Health, Cambridge Health District. We thank Sue Atkinson and Robert Ingram for helpful discussions in the planning of these programs. The co-ordinated European study was possible through the collaboration of Orlando Alves da Silva (Lisbon), Mario Angi (Padua), Alfonso Castanera de Molina (Barcelona), Ruxandra Sireteanu (Frankfurt), and François Vital-Durand (Lyon).

Received June 12, 2006; accepted November 7, 2006.

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