# Identification of Infants with Significant Refractive Error and Strabismus in a Population Screening Program using Noncycloplegic Videorefraction and Orthoptic Examination

*Shirley Anker,*[1] *Janette Atkinson,*[1] *Oliver Braddick,*[1,2] *David Ehrlich,*[1,3] *Thomas Hartley,*[1] *Marko Nardini,*[1] *and Jacqueline Wade*[1,4]

**Purpose.** The second Cambridge Infant Vision Screening Program examined whether screening for accommodative errors by using videorefraction without cycloplegia could effectively serve as a first stage of screening for refractive errors, measured by standard cycloplegic retinoscopy. The screening also included an orthoptic examination for detection of strabismus.

**Methods.** All infants born in the Cambridge (UK) Health District, over a 2-year period, were invited for screening. Of those 5142 (76%) with mean age 8.1 ± 0.8 months (SD) attended and received noncycloplegic videorefraction and an orthoptic examination. All those with a focusing error or orthoptic problem, as well as a randomly selected sample of visually normal control subjects, were invited to follow-up a month later for cycloplegic retinoscopy, repeat noncycloplegic videorefraction and orthoptic examination.

**Results.** Of the 5142 screened, 514 had a focusing error or orthoptic problem (positives). Four hundred thirty-nine of these and 284 visually normal control subjects (negatives) attended follow-up. A refractive or orthoptic condition was confirmed in 59.0% of the positive cases, whereas infants in 96.8% of the negative cases were confirmed normal. Adjusting for the proportions of the population represented by those infants seen at follow-up, sensitivity for the screening procedure was calculated at 0.67 and specificity at 0.96. Detailed results are presented in terms of the different conditions detected at screening (far, near, and anisometropic focus and orthoptic error), distribution of greatest axes at screening, and a comparison of initial videorefraction with repeat videorefraction and cycloplegic retinoscopy.

**Conclusions.** A noncycloplegic screening procedure, simpler to perform than cycloplegic screening, succeeded in detecting a large proportion of infants with significant ametropia, particularly those with significant hyperopia, which is considered to be a strabismogenic and amblyogenic risk factor. (*Invest Ophthalmol Vis Sci.* 2003;44:497–504) DOI:10.1167/iovs.02-0070

Strabismus and amblyopia are the commonest visual disorders of childhood in developed countries. Most screening programs to detect these conditions, or their precursors, have been conducted in children between 3 and 6 years of age,[1–4] although a few screening programs have also been conducted in infants.[1,5–10] The evidence for early sensitive periods suggests that the best opportunities for prevention can be expected if screening takes place as early as feasible in infants and young children.[11] However, there has been considerable controversy concerning the efficacy of preschool acuity screening and of occlusion therapy for amblyopia detected at this age.[1,3,4,12–18] An alternative approach is to screen for early strabismus and factors regarded as precursors of strabismus and amblyopia—namely, significant ametropia (high degrees of hyperopia, myopia, and anisometropia).[1,5–9,19–23]

In the first Cambridge Vision Screening Program,[8,9,24] we screened the total population of 8- to 9-month-old infants born within a geographical segment of the Cambridge Health District, using isotropic photorefraction[8,25] 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 +3.5 D (in one or more axes) on retinoscopy were entered into a randomized 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 randomized 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 in the treated group—i.e., those who wore spectacles, as opposed to 68% in the untreated group).

However, the use of cycloplegia in a total-population screening program makes the screening procedure relatively slow for the individual child, with families having to wait for 30 to 40 minutes for the cycloplegia to become effective. It requires a large clinic area to accommodate waiting children and their parents. In addition, the requirement for eye drops may deter some families from attending (although a good attendance of 80% of the total population was achieved in this first program). Use of cycloplegia may also require specific qualifications, conditions or restrictions, depending on the professional regulations in the country concerned, which are not required for a noncycloplegic test.

For these reasons, the Second Cambridge Infant Vision Screening Program was conducted to examine whether noncycloplegic refractive screening for abnormalities of accommodation, using videorefraction, could serve as an effective pre-

From the [1]Visual Development Unit, Department of Psychology, University College London, London, United Kingdom; and the [4]Ophthalmic Department, Addenbrooke's Hospital, Cambridge, United Kingdom.

Present address: [2]Department of Experimental Psychology, University of Oxford, United Kingdom; and [3]Department of Optometry and Vision Sciences, Aston University, Birmingham, United Kingdom.

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Corresponding author: Shirley Anker, Visual Development Unit, Department of Psychology, University College London, Gower Street, London WC1E 6BT, UK; s.anker@ucl.ac.uk.

liminary screening method for identifying children with strabismogenic and amblyogenic refractive errors in infancy. In research studies,[26–28] we found that when infants are presented with the demand to accommodate at 75 cm, hyperopic focus of +1.5 D or greater predicts a large proportion of those who show significant hyperopia (+3.5 D or more of hyperopia) in one or more axes on retinoscopy performed with infants under cycloplegia.

The main purpose of this study was to examine the relationship between poor accommodation detected by noncycloplegic refractive screening, and refractive errors detected by cycloplegic refraction using standard retinoscopy at follow-up, in a large unselected population of infants. The question remains as to whether significant hyperopia, as revealed by accommodative lag detected at screening, is as effective a predictor of later strabismus and amblyopia as screening for refractive errors detected using photorefractive and videorefractive methods in subjects under cycloplegia (as performed in the first Screening Program just described). Some preliminary data on noncycloplegic screening from this program have been published.[9,24,28]

## METHODS

### Screening Population

The target population was all infants born in the Cambridge Health District between July 1992 and July 1994, taken from immunization lists from 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, for infants within the 7- to 9-month age range (calculated from the expected date of birth). Average age at screening was 8.1 ± 0.8 months.

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 performed on freely accommodating infants (i.e., without cycloplegia) using the isotropic videorefractor (VPR-1; Clement Clarke Ltd., Harlow, UK). This technique is optically identical with isotropic photorefraction,[25] which has been validated and calibrated against standard measures of refraction[8] for cycloplegic testing. The validity of noncycloplegic measures of refractive state by these techniques, as indicators of cycloplegic refraction, is the concern of the present study. Compared with photorefraction on film, videorefraction has the advantage of capturing digital images from which the operator can make immediate refractive measurements on the screen. This allows the results to be discussed at the time of screening, and an appointment to be arranged for further follow-up when necessary. It also allows for a repeat measure to be made immediately if necessary (if, for example, the infant looks away or becomes fussy).

Published evaluations of the videorefractor (VPR-1; Clement Clarke, Ltd.) by a number of groups have concluded that it provides a valuable screening technique,[29–31] although its use in noncycloplegic screening has been questioned.[30]

In common with other photoscreening methods, the technique involves exposure of the infants' eyes to a number of flashes delivered through a fiber-optic cable at the camera distance. Simons[1] discusses the potential for phototoxicity and concludes that there is no evidence of hazard from light exposure levels in photoscreening procedures, including repeated flashes, but that this issue needs continuing review in the light of any further study.

### Screening Procedure

The screening procedure was performed by a trained senior orthoptist (one of two individuals). On arrival at the clinic, the parents were interviewed for relevant history: the amount of any prematurity, neonatal problems, and any history of strabismus and/or amblyopia or other ocular abnormality in a first-degree relative (either parent or any sibling). Appointments were made at 10- to 15-minute intervals to allow taking the history, the screening test, and explanation of the results. The procedure began with an orthoptic examination to detect any strabismus or ocular motility problems (cover test, ocular movement assessment, convergence to near point, direct and consensual pupil reactions to light, and the 20-D prism base-out test). Four sets of videorefraction measurements were then made. For each measurement, the operator attracted the infant's attention with the help of an illuminated and noise-making toy close to the position of the camera lens. In children of this age, attention to the target was readily gained and maintained, as indicated by the high success rate (see the Results section). Two sets of images were taken with the infant 75 cm from the camera and two at 100 cm. Optical analysis of isotropic photorefraction has indicated that these are the optimal distances for assessment of hyperopic and myopic focusing errors, respectively.

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 refractive state of greater than or equal to +1.5 D in any axis on either set of measures made at a distance of 75 cm between infant and camera focus.
2. Near focus: any infant showing myopic refractive state greater than or equal to −3 D on both measurements made at 100-cm distance.
3. Anisometropia: any infant showing anisometropic defocus of greater than or equal to 1.5 D 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, including manifest strabismus (defined as constant eso- or exotropia detectable on cover test) was detected. When manifest strabismus was present, videorefraction was performed on each eye separately to avoid off-axis errors, with the camera lined up as necessary with the optical axis of the deviating eye.

These infants were referred in to the Visual Development Unit and were entered into the follow-up group.

A control group of infants, who fell into none of the four categories and for whom no problems were reported at birth or in the neonatal period, were also recruited for follow-up. A control child 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 the four criteria.

We have estimated the cost of the screening procedure, including administrative costs, the orthoptist's time, use of premises, and amortization of the equipment, as approximately $12.75(US) per child at 1995 UK prices.[32] The orthoptist's time accounts for approximately $4.75(US) of this total.

### First Follow-up at the Visual Development Unit

The first follow-up after screening occurred at an average age of 9.3 ± 0.9 months (SD)—approximately 1 month after screening—with a maximum interval of 61 days. At follow-up, the information on the child's birth and family history was checked, and each child had a full orthoptic examination and videorefraction without cycloplegia as in the screening procedure. Each child also received retinoscopy under cycloplegia (1% cyclopentolate) and ocular examination from an optometrist or ophthalmologist. Full details of the retinoscopic procedure have been published.[19]

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

1. Significant hyperopia, defined as a cycloplegic refraction of +4.0 D or greater in any axis.
2. Significant myopia of −3.0 D or greater in any axis.
3. Significant anisometropia of 1.5 D or more difference between corresponding axes in the two eyes.
4. No significant refractive error, i.e., children who met none of criteria 1 to 3.

The overlap between categories 1 to 3 is discussed in the Results section.

In addition children were classified according to the presence or absence of constant manifest strabismus or other orthoptic-ophthalmic problems requiring immediate referral to the hospital ophthalmology clinic. The latter group, together with any child showing greater than +7 D hyperopia or 2.5 D anisometropia, were referred immediately to a consultant ophthalmologist. These criteria were agreed to among the ophthalmologists collaborating in the study as sufficient amblyogenic risk factors to necessitate evaluation for immediate treatment. Families of infants so referred were encouraged to continue to attend the Visual Development Unit for further follow-up measures, with their ophthalmic and refractive care being provided by the hospital's ophthalmology team.

## Results

Infants attending the screening numbered 5295, and the procedure was completed on 5142 (97.1% success rate; noncooperation or technical problems account for the failure to complete). Of the 5142 infants screened, 4645 (90.3%) showed normal focusing, whereas 497 (9.7%) met the detection criterion for one or more focusing errors. On the orthoptic examination, 29 cases (0.56% of the screened population) of strabismus or other orthoptic and ophthalmic problems were detected (the overlap between focusing and orthoptic criteria is discussed later).

Thirteen infants screened had already-diagnosed developmental problems (e.g., developmental delay with or without cranial dysmorphia, Down syndrome, hydrocephalus, a dislocated hip, a missing hand). One child with Down syndrome, and 11 children without other developmental problems, had already diagnosed ophthalmic conditions (e.g., entropion, dermoid cyst, anophthalmia, microphthalmia, ptosis, and neurofibromatosis).

Nine percent of the screened group reported a first-degree relative who had received treatment for amblyopia and/or strabismus. Of the total population screened, 7.9% were reported as born 3 weeks or more before term and were deemed premature.

The numbers of children detected by the various screening criteria are listed in Table A1 in the Appendix, which also cross-tabulates the cases that fell into more than one screening category.

In total, 723 of these children attended follow-up: 423 because of potential refractive error related to poor focusing, 16 for orthoptic but not focusing criteria, and 284 in the control group.

### Detection of Far Focus and Confirmation of Hyperopia

By far the largest group detected at screening were those showing far focus—that is, not accommodating fully on the target at 75 cm, which is a potential indicator of hyperopic refractive error. Results for this group will be presented first. The detection criterion for far focus at screening was based on the most hyperopic axis found on noncycloplegic videorefraction. Figure 1 shows the distribution of values for this greatest axis for all infants at screening. The categories used in this distribution are determined by the properties of the videorefractor, as explained in the figure legend. Those with an axis of +1.5 D or more ($n$ = 456, 8.87% of the screened group; shown in black) met the detection criterion for far focus and were invited to attend follow-up. A sample of those who had greatest axis less than +1.5D and were visually normal on all other criteria ($n$ = 4628, 90.00%; white) was invited to attend follow-up as control subjects. The 41 (0.80%) who were detected on other focusing criteria are discussed later.

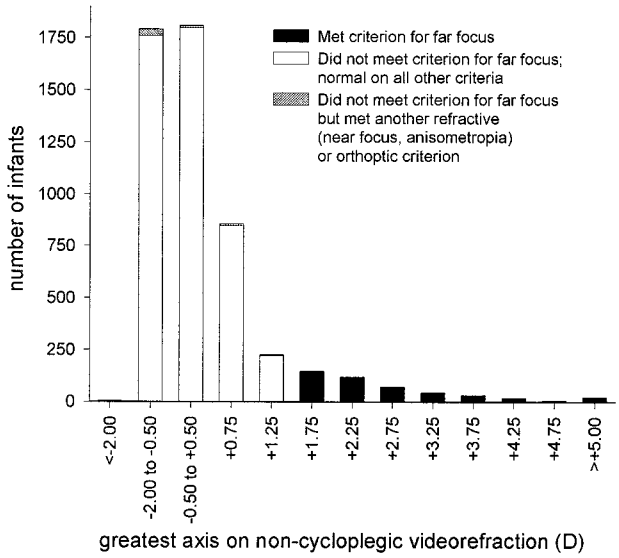


**Figure 1.** Histogram of the most hyperopic axis detected in noncycloplegic videorefraction at screening. The videorefractor outputs values in ranges of 0.5 D. Above +0.5 D the data are organized in bins labeled with the central value of the range. Thus, the +1.25-D bin represents values between 1.0 and 1.5 D. The histogram bins −2.00 to −0.50 D and −0.50 to +0.50 D contain children focused close to the camera whose refractive state within each range is not distinguished by the videorefractor. Similarly, refractive states in the range over +5.0 D are detected but not quantitatively distinguished.

Attending follow-up were 394 infants in the far-focus group and 284 visually normal control subjects. Figure 2 shows the maximum axes on noncycloplegic videorefraction at screening ($x$) and on cycloplegic retinoscopy approximately 1 month later ($y$). Visually normal subjects (+) are distinguished from those who met the detection criterion for a refractive or orthoptic condition (dots). We performed a regression analysis restricted to infants who showed a noncycloplegic refractive state of +0.5 or greater, because this is the range of interest for detection of hyperopia, and the instrument is also less sensitive to small refractive differences in the range around the camera distance. This analysis showed a highly significant relationship ($r = 0.56$, $P < 0.001$), with the regression equation, $y = 1.03x + 1.50$.

Figure 3 shows the distribution of data for the most hyperopic axis, measured by cycloplegic retinoscopy, in each of these groups. To give a picture of the estimated distribution of hyperopic refractive errors in the population, the numbers in these groups have been scaled according to the ratio of those classified in the group at screening to those tested at follow-up. For example, the numbers of the 284 control subjects falling in each band of cycloplegic refractions at follow-up were scaled to represent the total 90% of the screened population who met the same focusing criteria as the control subjects.

Solid histobars represent the number of infants who met the far focus detection criterion at screening and open histobars those who were visually normal on all criteria. A vertical line indicates our confirmation criterion for hyperopia from cycloplegic retinoscopy at follow-up (greatest axis of +4.0 D or

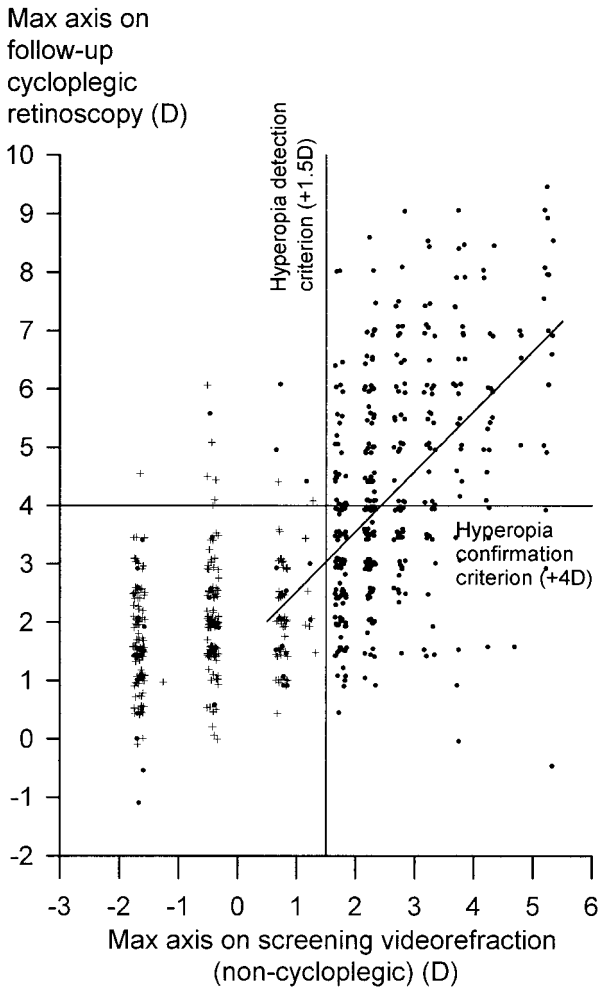


**FIGURE 2.** Scatterplot showing the relation between greatest axes on noncycloplegic videorefraction at screening ($x$) and on cycloplegic retinoscopy approximately 1 month later ($y$) for negative (no condition detected at screening; +) and positive (at least one refractive or orthoptic condition detected; •) subjects. Data points are jittered by ± 0.1 D to reduce overlap. The regression line shown is the result of linear regression analysis for cases in the precycloplegic range of +1.5 D and higher.

more). Solid histobars to the right of the line thus represent far-focus infants who were confirmed as hyperopic (true positive), whereas open histobars to the left represent refractively normal infants confirmed not hyperopic (true negative). Solid histobars to the left of the line represent false positives, whereas open histobars on the right represent false negatives. Alternative positions of the vertical line would indicate the efficacy of the screening procedure in detecting different levels of hyperopia.

The elapsed time between screening and follow-up means that the underlying refraction may have changed between these occasions. Data bearing on this possibility are discussed in a later section.

## Detection and Confirmation of All Refractive Errors and Strabismus

The different conditions detected at screening may overlap. For instance, most infants who met the detection criterion for anisometropia also met the detection criterion for far focus, and many with an orthoptic problem also had a refractive error. Although the same child may have more than one condition, the most useful description of our results is in terms of individual children rather than individual conditions. We therefore present our results in the form of categories that are mutually exclusive (i.e., each child can be counted only once). The cross-tabulation in Table A1 (Appendix) indicates the co-occurrence of different conditions in individual infants.

Table 1 presents a first categorization by focusing error. Any infant with anisometropia of 1.5 D or more detected at screening was classified as anisometropic (including anisometropic infants who also met the detection criterion for far or near focus). The far-focus and near-focus groups in this table thus exclude infants meeting the detection criterion for anisometropia. The remaining group (normal focus) showed no focusing error at screening on any of these criteria, but include children who failed on orthoptic criteria only. For each category, the number at screening is given and also the number of these who attended follow-up. Of those followed up, Table 1 gives the number confirmed with the refractive error corresponding to the screening category, (as described in detail in the table legend), and the number confirmed in any category of refractive error. In particular, a number of infants with anisometropic focus at screening did not appear anisometropic on cycloplegic retinoscopy, but were nevertheless significantly hyperopic on follow-up: these appear in the column confirmed in any category.

At follow-up there were 284 designated control subjects of whom 275 were confirmed as refractively normal and 9 who had significant refractive errors (false negatives). In addition, 2 of 16 children detected with orthoptic problems, but focusing normally at screening, were found to have refractive errors at follow-up.

Table 2 categorizes all screened children according to orthoptic results, in a format similar to that of Table 1. Only one infant who failed the orthoptic tests at screening was not confirmed at follow-up, whereas no orthoptic problems were found at follow-up among the infants who had had no orthoptic condition detected at screening. Conditions confirmed were esotropia ($n$ = 9), exotropia ($n$ = 4), Duane syndrome ($n$ = 2), Brown syndrome ($n$ = 2), oculomotor apraxia ($n$ = 1), bilateral ptosis ($n$ = 3), Waardenburg's syndrome ($n$ = 1), and

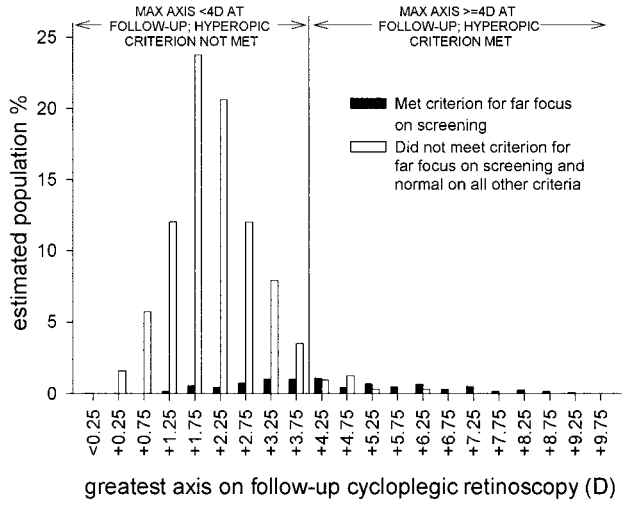


**FIGURE 3.** Histogram of most hyperopic axis detected by cycloplegic retinoscopy at follow-up. The bin labeled 1.75 D includes values of 1.5 D and 1.75 D, and so forth. Subjects in the far-focus category by noncycloplegic videorefraction at screening ($n$ = 394) are distinguished from normal-focus subjects ($n$ = 284). Data plotted for each group are scaled in line with the overall proportion of far-focus/normal-focus infants found in the population. *Vertical line*: confirmation criterion for hyperopia at follow-up (maximum axis, ≥4.0 D).

**TABLE 1.** Confirmation of Refractive Conditions Detected at Screening

| | Focusing Error Detected at Screening | | Refractive Error Confirmed at Follow-up | | | | |
|---|---|---|---|---|---|---|---|
| Screening Category | *n* | % of Screened Population | Followed Up (*n*) | Confirmed in Same Category (*n*) | Confirmed in Any Category (*n*) | % Confirmed in Same Category | % Confirmed in Any Category |
| Anisometropic | 108 | 2.1 | 89 | 45 | 60 | 50.6 | 67.4 |
| Far focus* | 376 | 7.3 | 323 | 167 | 173 | 51.7 | 53.6 |
| Near focus* | 13 | 0.3 | 11 | 2 | 4 | 18.2 | 36.4 |
| Normal focus | 4645 | 90.3 | 300 | 289 | — | 96.3 confirmed no significant refractive error | — |

Children were classified into mutually exclusive refractive conditions at screening. Number confirmed in same category refers to those anisometropic at screening who were anisometropic on cycloplegic retinoscopy at follow-up, those who were far focus (not anisometropic) at screening and were hyperopic (not anisometropic) on follow-up, and those who were near focus (not anisometropic) at screening and myopic (not anisometropic) at follow-up. For the normal-focus group, number confirmed in same category refers to those who were not found to be in any of the defined ametropic categories. The classification is solely on refractive criteria at screening. Children who failed on orthoptic criteria may appear in any row (see Table 1A, Appendix for overlap); those who were normal focus, are indicated in the fourth row.

* Not anisometropic.

ocular abnormalities ($n = 7$; lens opacities, iris remnants or abnormalities).

Table 3 evaluates the overall outcome of screening, in terms of whether any condition—orthoptic or refractive—was detected. Infants with at least one condition detected were classified positive and those with none, negative, for calculation of the overall sensitivity and specificity of our screening procedure. A child who was positive at screening and met any of the refractive or orthoptic criteria at follow-up therefore counted as having a true-positive classification, whereas one who met none of these criteria had a false-positive classification. A control child who met any of the positive criteria at follow-up had a false-negative classification.

However, because the control subjects represent only a sample of those who were negative at screening, the number of true and false negatives must be estimated for the screening population on the basis of the percentage of true and false negatives among the control subjects. This is shown, with an analogous estimate for the positive cases, in the final two columns of Table 3. Using these proportions in the standard formulas, we calculate an overall sensitivity for our screening procedure of 0.67, specificity of 0.96, and positive predictive value of 0.60.

It should be noted that in those in the control group (negatives) who were followed up, the false negatives are numerically few, and so the figures for sensitivity and specificity obtained by estimating proportions in the population are subject to sampling error.

## Noncycloplegic Videorefraction at Follow-up

As well as cycloplegic retinoscopy, the follow-up protocol included a repeat of the noncycloplegic videorefraction procedure used at screening. This provided an opportunity to consider whether the measure used at screening may have altered in the intervening period. Figure 4 shows the proportions of those subjects distinguished as far focus or normal focus at screening who appeared in the same focusing category at follow-up. These subjects were confirmed hyperopic or otherwise by retinoscopy. Among those who were deemed far focus at screening, almost a quarter did not show far focus at the follow-up examination. This is a systematic change rather than just a reflection of the intrinsic variability of infants' focusing behavior, because the mean value of the most hyperopic axis in noncycloplegic videorefraction declined from 2.64 to 2.17 D (significant reduction on paired-samples *t*-test, $t = 8.19$, $P < 0.001$). The group who no longer met the far-focus criterion showed a much lower proportion of subjects confirmed as hyperopic under cycloplegia, compared with those who showed far focus on the second test. Thus, far focus was a more reliable indicator of hyperopic refraction measured at the same time, than it was of refraction measured after approxi-

**TABLE 2.** Confirmation of Orthoptic Problems Detected at Screening

| | Orthoptic/Ophthalmic Condition Detected at Screening | | Orthoptic/Ophthalmic Condition Confirmed at Follow-up | | |
|---|---|---|---|---|---|
| | *n* | % of Screened Population | Followed Up (*n*) | Confirmed (*n*) | % Confirmed |
| Condition detected | 29 | 0.6 | 28 | 27 | 96.4 |
| No condition detected | 5113 | 99.4 | 695 | 695 | 100.0 |

All children were classified into exclusive categories: orthoptic/ophthalmic and not orthoptic/ophthalmic. The number at follow-up confirmed with/without an orthoptic and/or ophthalmic problem, and the confirmation percentage applied to the orthoptic/nonorthoptic proportions in the screening population are shown. The classification was based solely on orthoptic criteria at screening. Children who failed on focusing criteria may appear in either row (see Table A1, Appendix for overlap).

**TABLE 3.** Confirmation of Any Condition Detected at Screening

| | Any Condition Detected at Screening | | Confirmation of Any Condition at Follow-up | | | Estimated % in Screened Population | |
|---|---|---|---|---|---|---|---|
| | *n* | % of Screened Population | Followed Up (*n*) | Confirmed (*n*) | % Confirmed | % Confirmed (True) | % Not Confirmed (False) |
| Positive | 514 | 10.0 | 439 | 259 | 59.0 | 5.9 | 4.1 |
| Negative | 4628 | 90.0 | 284 | 275 | 96.8 | 87.2 | 2.9 |

The proportion of positive (any condition, refractive or orthoptic/ophthalmic) and negative (no condition) subjects at screening who were confirmed (true) at follow-up are shown. The criterion for confirmation is any condition at follow-up for positives, no condition at follow-up for negatives. The proportions confirmed are converted to estimated percentages in the total population and the not-confirmed (false) percentage is also shown for each group. These figures served as the basis for sensitivity and specificity estimates.

mately a 1-month interval. This is consistent with the possibility that there is significant refractive change (emmetropization) over this interval, although these data do not allow us to separate the contributions of changes in refraction and accommodative behavior.

## DISCUSSION

### Detection of Refractive Error

A screening program depending on noncycloplegic videorefraction has been shown to have high specificity for the detection of refractive error in infants. In particular, in the criteria used, accommodative lag is an indicator of hyperopic refraction. The quantitative relationship underlying this prediction is demonstrated by the regression line in Figure 2.

The false negatives in our screening procedure primarily included children who had hyperopia but did not meet the screening criterion of accommodative lag. These children accommodated well, despite showing hyperopic refractive errors under cycloplegia.

We defined hyperopia by a particular cutoff point (+4.0 D, vertical line, Fig. 3) on the continuous scale of refractions. Figure 3 indicates that a lower cutoff (e.g., +3.5 D) would disproportionately increase the number of false negatives, given the accommodative criterion we selected. A lower criterion for accommodative lag would also be possible, but Figure 1 shows that this would substantially increase the number of children who needed follow-up, an unknown number of whom would be false positives. Conversely, the regression equation in Figure 2 implies that a mean cycloplegic refraction of +4 D would be predicted by a noncycloplegic measurement of +2.4 D—that is, selecting this as a screening criterion would miss approximately half the infants with +4 D hyperopia.

We believe that the criteria we selected are appropriate, in that they require follow-up of a manageable proportion of the population (10%) and yield an acceptable sensitivity.

The most fully evaluated other screening method is the PhotoScreener (Medical Technology Inc. [MTI], Lancaster, PA).[20,33,34] These reports cover a population with a broader age range (1–48 months, median, 21) and differently selected (attending a pediatric ophthalmology practice, and consequently a high incidence of strabismus) compared with the present study. On the original manufacturers' criteria,[20,33] they report a markedly lower sensitivity and specificity, especially for refractive error in the absence of strabismus. However, an analysis of the latter group with revised criteria[34] showed high sensitivity for a small group of hyperopic children (8/8 over +3.5 D detected) but lower specificity than our study (88%). With these numbers, definitive comparison cannot be made. It is possible that accommodative behavior is more consistently related to refraction in the toddler age group than in our 8-month-old infants.

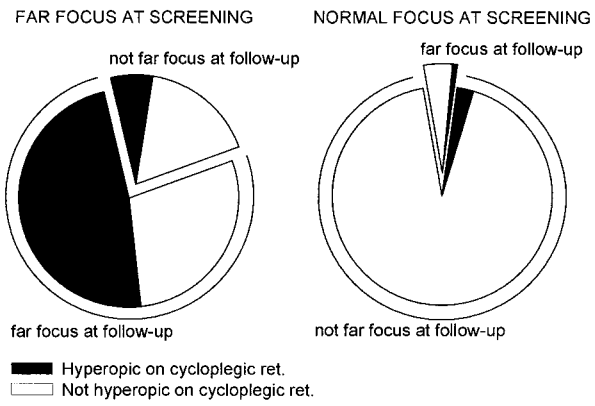


**FIGURE 4.** Pie charts showing proportions of far-focus and normal-focus infants from screening who were (*left*) confirmed in the same focusing category by repeat noncycloplegic videorefraction (*wedge* on each chart); (*right*) found to be hyperopic or not hyperopic by cycloplegic retinoscopy. The normal-focus group plotted excludes any infants found to have had orthoptic or ophthalmic problems.

### Changes of Category

Table 1 shows that some children who were detected with an indicator of one category of refractive error were confirmed in a different category. This primarily reflects variations in the assessment of anisometropia, resulting either from off-axis videorefraction[35] or from cases of anisometropia that may be more readily detected in the videorefractive images from the two eyes on the same screen than in retinoscopy with young infants. Because the goal of screening is not diagnosis, but rather to detect cases that require more definitive investigation, we believe that the analysis we report of screened positive subjects confirmed in any diagnostic category is the appropriate one. Studies with the PhotoScreener (MTI)[20,33] have used a similar approach, although in those studies, the major issue was the interaction of detection of strabismus and refractive error, a minor aspect of our data, given the low incidence of strabismus in the general population.

### Incidence of Strabismus

Almost all orthoptic problems detected at screening were confirmed at follow-up. This reflects the fact that, unlike the refractive testing, the procedures at screening and follow-up were very similar. Because our screening was performed by orthoptists, we did not use a protocol that required nonspecialist personnel to detect strabismus from the corneal reflexes

visible on the videorefraction images. Experience in other programs[33] suggests that the reliability of detecting strabismus would be considerably lower with such a protocol. However, our data include the children who met criteria for refractive error in the presence of strabismus.

Although the detection of strabismus and other orthoptic conditions in a community setting is undoubtedly valuable, it is notable that the number of such children at 8 to 9 months is low, well under 1% of the population. This figure is consistent with the first Cambridge screening program,[9,24] which also suggests that manifest strabismus develops in a larger number of children after 8 to 9 months, but before school age. Consequently, the main justification for a large-scale infant screening program must be in terms of the detection of strabismogenic and amblyogenic conditions, rather than of manifest strabismus itself, although the latter relatively small category is important to detect as early in life as possible.

### Refractive and Accommodative Change in Infancy

The data shown in Figure 4 suggest that the specificity of noncycloplegic testing would be higher if associated with immediate cycloplegic refraction. One possible interpretation is that some infants who had hyperopia at the time of screening had shifted significantly towards emmetropia by the time of follow-up. Because it is presumably most important to detect relatively long-lasting refractive errors, this could be offered as an argument for screening later in infancy. Against this argument should be set the desirability of undertaking any preventive measures as early as possible and the fact that, toward and beyond 1 year of age, children become progressively more active and less cooperative, both in test procedures and in complying with spectacle wear.

### Noncycloplegic Screening and Later Outcome

Our screening procedure detected infant hyperopes who did not habitually accommodate to overcome their hyperopic defocus. What are the implications of detecting this group, but not the minority who show no accommodative lag? On the one hand, the detected group includes those who have blur due to defocus, and correction would improve their image quality. Such blur may also have amblyogenic effects.

On the other hand, hyperopia is associated with strabismus, which is commonly attributed to overaccommodation leading to a breakdown in the accommodative convergence synergy.[36–38] This theory implies that the risk of strabismus might be less in those children who habitually underaccommodate. Although it has been frequent experience that reduced accommodative demand alleviates manifest esotropic strabismus, it is not yet known whether the level of accommodation in infancy predicts later strabismus. Data from the follow-up of the present sample to 4 years and beyond will provide information on this question.

## Conclusions

We have demonstrated that a noncycloplegic videorefractive procedure, combined with orthoptic examination, is a feasible method for large-scale population screening and detects a large proportion of significantly ametropic infants—in particular, hyperopes. Our previous (cycloplegic) program[9,24] showed that hyperopic infants were at risk of strabismus and poor vision that can be alleviated by early intervention. Analysis of the later follow-up of the screened group in this second program will indicate whether a similar effect can be achieved after noncycloplegic screening. The program also provides data from a population study on whether infant refractive error shows associations with broader visuospatial, visuomotor, and cognitive development through the preschool years. Our initial analysis of these data shows a significant relationship between visual screening results and these broader aspects of development.[39,40]

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### *References*

1. Simons, K. Preschool vision screening: rationale, methodology, and outcome. *Surv Ophthalmol.* 1996;41:3–30.
2. Hartmann EE, Dobson V, Hainline L, et al. Preschool vision screening: summary of a task force report. *Ophthalmology.* 2001; 108:479–486.
3. Kemper AR, Margolis PA, Downs SM, Bordley WC. A systematic review of vision screening tests for the detection of amblyopia. *Pediatrics.* 1999;104:1220–1222.
4. Ciner EB, Schmidt PP, Orel-Bixler D, et al. Vision screening of preschool children: evaluating the past, looking toward the future. *Optom Vis Sci.* 1998;75:571–584.
5. Ingram RM. Screening for refractive errors at age 1 year: a pilot study. *Br J Ophthalmol.* 1979;63:243–250.
6. Ingram RM. Prediction of amblyopia and squint by means of refraction at age 1 year. *Br J Ophthalmol.* 1986;70:12–15.
7. Ingram RM. Results of a randomised trial of treating abnormal hypermetropia from the age of 6 months. *Br J Ophthalmol.* 1990; 74:158–159.
8. Atkinson J, Braddick OJ, Durden K, Watson PG. Atkinson S. Screening for refractive errors in 6-9 months old infants by photorefraction. *Br J Ophthalmol.* 1984;68:105–112.
9. Atkinson J, Braddick O, Bobier B, et al. Two infant vision screening programmes: prediction and prevention of strabismus and amblyopia from photo- and videorefractive screening. *Eye.* 1996;10:189–198.
10. Spierer A, Royzman Z, Chetrit A, Novikov I, Barkay A. Vision screening of preverbal children with Teller acuity cards. *Ophthalmology.* 1999;106:849–854.
11. Daw NW. *Visual Development.* New York: Plenum Press; 1995.
12. Jarvis SN, Tamhne RC, Thompson L, Francis PM, Anderson J, Colver AF. Preschool vision screening. *Arch Dis Child.* 1991;66: 288–294.
13. Bray LC, Clarke MP, Jarvis SN, Francis PM, Colver A. Preschool vision screening: a prospective comparative evaluation. *Eye.* 1996; 10:714–718.
14. Newman DK, East MM. Preschool vision screening: negative predictive value for amblyopia. *Br J Ophthalmol.* 1999;83:676–679.
15. Snowdon SK, Stewart-Brown SL. Pre-school vision screening. *Health Technol Assess.* 1997;1:1–75.
16. Robinson B, Bobier WR, Martin E, Bryant L. Measurement of the validity of a preschool vision screening program. *Am J Pub Health.* 1999;89:193–198.
17. Kvarnstrom G, Jakobsson P, Lennerstrand G. Visual screening of Swedish children: an ophthalmological outcome. *Acta Ophthalmol Scand.* 2001;79:240–244.
18. Kvarnstrom G, Jakobsson P, Lennerstrand G. Screening for visual disorders in children: evaluation of the system in Sweden. *Acta Paediatr.* 1998;87:1173–1179.
19. Ehrlich D, Braddick O, Atkinson J, et al. Infant emmetropization: a longitudinal study of refraction components from 9 months of age. *Optom Vis Sci.* 1997;74:822–843.
20. Tong PY, Bassin RE, Enke-Miyazaki E, et al. Screening for amblyopia in preverbal children with photoscreening photographs. II. Sensitivity and specificity of the MTI PhotoScreener. *Ophthalmology.* 2000;107:1623–1629.
21. Miller JM, Harvey EM, Dobson V. Visual acuity screening versus noncycloplegic autorefraction screening for astigmatism in native

American preschool children. *J Am Acad Pediatr Ophthalmol Strabismus.*. 1999;3:160–165.
22. Miller JM, Dobson V, Harvey EM, Sherrill DL. Comparison of preschool vision screening methods in a population with a high prevalence of astigmatism. *Invest Ophthalmol Vis Sci.* 2001;42: 917–924.
23. Sjostrand J, Abrahamsson M. Can we identify risk populations for development of amblyopia and strabismus? *Klin Monatsbl Augenheilkd.* 1996;208:23–26.
24. Atkinson, J. Infant vision screening: prediction and prevention of strabismus and amblyopia from refractive screening in the Cambridge photorefraction programme. In: Simons K, ed. *Early Visual Development: Normal and Abnormal.* New York: Oxford University Press; 1993:335–347.
25. Howland HC, Braddick OJ, Atkinson J, Howland B. Optics of photorefraction: orthogonal and isotropic methods. *J Opt Soc Am A.* 1983;73:1701–1708.
26. Braddick OJ, Atkinson J, Wattam-Bell J, Anker S, Norris V. Videorefractive screening of accommodative performance in infants. *Invest Ophthalmol Vis Sci.* 1988;29(4):**S**60. Abstract nr 15.
27. Atkinson J, Anker S, Braddick O, Ehrlich DL, Wattam-Bell J. Noncycloplegic videorefraction: applications to infant refractive screening (Abstract). *Strabismus.* 1994;2:42.
28. Ehrlich DL, Anker S, Atkinson J, Braddick OJ, Weeks F, Wade J. Infant VPR-1 video-refraction and ocular characteristics of those "far-focussing" at 75cm. *Invest Ophthalmol Vis Sci*. 1995;36(4): **S**48. Abstract nr 232.
29. Bobier WR, Schmitz P, Strong G, Knight J, Widdersheim K, Howland HC. Comparison of three photorefractive methods in a study of a developmentally handicapped population. *Clin Vision Sci.* 1992;7:225–235.
30. Hodi S, Wood ICJ. Comparison of the techniques of videorefraction and static retinoscopy in the measurement of refractive errors in infants. *Ophthalmic Physiol Opt.* 1994;14:21–24.
31. Bischoff P, Althaus, K. Wie genau ist die Videorefraktionsmessung beim Kleinkind im Vergleich zur Skiaskopie? *Klin Monatsbl Augenheilkd.* 1994;205:128–132.
32. Atkinson J, Braddick O, Anker S, et al. Co-ordinated infant videorefractive screening programmes in six European centres [ARVO Abstract]. *Invest Ophthalmol Vis Sci.* 1996;37(3):**S**1111. Abstract nr 5115.
33. Tong PY, Enke-Miyazaki E, Bassin RE, et al. Screening for amblyopia in preschool children with photoscreening photographs. *Ophthalmology*. 1998;105:856–863.
34. Tong PY, Macke JP, Bassin RE, et al. Screening for amblyopia in preschool children with photoscreening photographs. III. Improved grading criteria for hyperopia. *Ophthalmology*. 2000;107: 1630–1636.
35. Ehrlich DL, Anker S, Braddick OJ. On- and off- axis refractions of infants [ARVO Abstract]. *Invest Ophthalmol Vis Sci*. 1994;35: 1806. Abstract nr 2571.
36. Von Noorden GK. *Binocular Vision and Ocular Motility: Theory and Management of Strabismus.* 5th ed. St. Louis: Mosby; 1996.
37. Thorn F. Development of refraction and strabismus. *Curr Opin Ophthalmol.* 2000;11:301–305.
38. Abrahamsson M, Fabian G, Sjostrand J. Refraction in children developing convergent or divergent strabismus. *Br J Ophthalmol.* 1992;76:723–727.
39. Atkinson J, Anker S, Nardini M, Braddick O, Rae S, Hughes C. Do infant hyperopia and poor accommodation predict deficits in later cognitive and neurological development? *Invest Ophthalmol Vis Sci.* 2000;41(4):**S**327. Abstract nr 1720.
40. Atkinson J, Anker S, Nardini M, et al. Infant vision screening predicts failures on motor and cognitive tests up to school age. *Strabismus*. 2002;10:187–198.

## APPENDIX

**TABLE A1.** Cross-tabulation of Infants Detected in Screening to Be Normal or to Have Different Orthoptic/Ophthalmic Conditions

| Condition | Orthoptic, Not Aniso. | Aniso., Not Orthoptic | Orthoptic and Aniso. | Not Orthoptic, Not Aniso. | Total |
|---|---|---|---|---|---|
| Far focus, not near | 8 | 76 | 2 | 368 | 454 |
| Near focus, not far | 1 | 5 | 0 | 12 | 18 |
| Near focus and far focus | 0 | 2 | 0 | 0 | 2 |
| Anisometropic, not near, not far focus | — | 22 | 1 | — | 23 |
| Orthoptic only | 17 | — | — | — | 17 |
| Normal | — | — | — | 4628 | 4628 |
| Total | 26 | 105 | 3 | 5008 | 5142 |

The categories in each row are mutually exclusive: Normal refers to children who met none of the refractive or orthoptic/ophthalmic criteria. The columns are also mutually exclusive and define how the criteria for anisometropia (Aniso.) and orthoptic/ophthalmic conditions intersect with the different refractive categories. For brevity, orthoptic refers to any of the orthoptic or ocular conditions detected in the orthoptic examination at screening. Combinations of the column totals show that 29 children met the orthoptic criteria and a total of 108 on the anisometropic criterion.