

## ORIGINAL STUDY

# The Multi-Ethnic Pediatric Eye Disease Study: Design and Methods

**Rohit Varma, MD, MPH**

Doheny Eye Institute and the Department of Ophthalmology, and Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

**Jennifer Deneen, MPH,  
Susan Cotter, OD, MS,  
and Sylvia H. Paz, MS**

Doheny Eye Institute and the Department of Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

**Stanley P. Azen, PhD**

Doheny Eye Institute and the Department of Ophthalmology, and Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

**Kristina Tarczy-Hornoch, MD, DPhil**

Doheny Eye Institute and the Department of Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

**Peng Zhao, MS**

Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

**The Multi-Ethnic Pediatric Eye Disease Study Group**

See Appendix I

Received 24 October 2005  
Accepted 23 March 2006

Supported by the National Eye Institute, National Institutes of Health, Bethesda, MD (grant nos. EY14472 and EY03040), and an unrestricted grant from the Research to Prevent Blindness, New York, NY. Dr. Varma is a Research to Prevent Blindness Sybil B. Harrington Scholar.

The authors have no proprietary or commercial interest in any materials discussed in the manuscript.

*Correspondence to:* Rohit Varma MD, MPH, Doheny Eye Institute, Department of Ophthalmology, 1450 San Pablo St. Rm. 4900, Los Angeles, CA 90033-9224, USA. Tel.: +1-(323) 442-6411; Fax: +1-(323) 442-6412; E-mail: rvarma@usc.edu

**ABSTRACT** *Purpose:* To summarize the study design of the Multi-Ethnic Pediatric Eye Disease Study (MEPEDS). *Methods:* The objectives of the MEPEDS are to: (1) estimate age- and ethnicity-specific prevalence of strabismus, amblyopia, and refractive error; (2) evaluate the association of selected risk factors with these ocular disorders; and (3) evaluate the association of ocular conditions on limitations in health-related functional status in a population-based sample of 12,000 children aged 6–72 months from four ethnic groups—African-American, Asian-American, Hispanics/Latinos and non-Hispanic White. Each eligible child undergoes an eye examination, which includes an interview with his/her parent. The interview includes an assessment of demographic, behavioral, biological, and ocular risk factors and health-related functional status. The examination includes fixation preference testing, visual acuity, stereoacuity, axial length measurement, cycloplegic refraction, keratometry, eye alignment, and anterior and posterior segment examination.

**KEYWORDS** Epidemiology; pediatric eye disease; population-based study; prevalence of vision disorders; study design

## INTRODUCTION

Vision disorders are the fourth most common class of disability of children in the United States and the leading cause of handicapping conditions in childhood.<sup>1</sup> In infants and young children these vision disorders include significant refractive error, strabismus, and amblyopia, as well as other ocular diseases. Thus the development of vision-screening programs in children has become an important priority since early detection and early treatment of these ocular disorders has beneficial outcomes.<sup>2</sup> While previous studies have examined the prevalence of one or more ocular conditions, none have based prevalence estimates on a comprehensive eye examination, including cycloplegic refraction, in a large sample of African-American, Hispanic/Latino, Asian, and non-Hispanic White children.<sup>3–23</sup>

Extensive research has been conducted over the past three decades on vision disorders in infants and children and has demonstrated that early development of the visual system is critical if infants are to develop normal vision. Any abnormality in the visual system during this early developmental and maturation

phase can modify the normal development of the occipital cortex and cause permanent severe visual loss.<sup>24</sup> However, despite this improved understanding of the underlying mechanisms of vision loss in childhood and improvement in early detection and treatment options, we have little information regarding epidemiological aspects of vision problems in infants and young children and our understanding of ethnic/racial differences among African-Americans, Hispanics/Latinos, Asians, and non-Hispanic Whites is sorely deficient.

The Multi-Ethnic Pediatric Eye Disease Study (MEPEDS) was designed to address this lack of data by estimating the prevalence of strabismus, amblyopia, and refractive error in children six months to 72 months of age in a multiethnic population in Los Angeles County, California. The objective of this article is to summarize the study design and procedures utilized in the MEPEDS.

## MATERIALS AND METHODS

### Study Design

The MEPEDS is a population-based study designed to take advantage of the diversity in ethnic makeup and socioeconomic status in the population found in and around the Los Angeles area. Institutional Review Board/Ethics Committee approval was obtained from the Los Angeles County University of Southern California Medical Center Institutional Review Board.

The specific aims of the MEPEDS are: (1) to estimate and compare the prevalence of strabismus, amblyopia, and refractive error in a population-based sample of African-American, Asian-American, Hispanics/Latinos, and non-Hispanic White children six months through 72 months of age; (2) to evaluate the association of selected demographic, behavioral, biological, and ocular risk factors with these ocular disorders; and (3) to evaluate in children 25 to 72 months of age the association of strabismus, amblyopia, and refractive error on limitations in age-appropriate, health-related, functional status.

In addition to these specific aims we will be examining presenting and best-corrected visual acuity, causes of decreased visual acuity from reasons other than refractive error and amblyopia, such as congenital or acquired conditions, and ocular abnormalities in these ethnic populations.

## Organizational Structure

The MEPEDS resource centers include the Study Coordinating Center, the Survey Research Center (SRC), the Data Management and Analysis Center, and the Local Eye Examination Center (LEEC). Advisory groups include the Internal Advisory Group, which meets on a weekly basis to review study progress and to address scientific and methodological issues as they arise; the Community Advisory Group, which meets twice a year to ensure community involvement and obtain advice from community leaders; and the Data Monitoring and Oversight Committee, which meets once a year to provide additional external oversight to the study.

## Sample Size Considerations

In order to obtain precise age-specific point prevalence estimates for ocular disease we based our sample size estimates on the standard used by the National Center for Health Statistics (NCHS), namely, that the standard error of the prevalence be at most 30% of the point estimate of the prevalence. This is determined by calculating a relative standard error (RSE), which is the ratio of the standard error to the point estimate. The determination of sample size involved an estimate of the prevalence of disease from other studies.<sup>1,4-24</sup>

Table 1 summarizes the range of prevalence rates and corresponding overall and age-specific RSEs for a sample size of 3,000 children per racial/ethnic group. The overall average RSE is based on the prevalence rate of ocular disease in the entire cohort for each racial/ethnic group. The age-specific RSE is based on

**TABLE 1** Range of Prevalence Rates and Corresponding Overall and Age-Specific RSE

Parameter	Amblyopia	Strabismus	Myopia	Astigmatism
Prevalence Rate (%)	0.9-5.7	1.2-5.6	1.2-5.7	2.5-50
Overall Avg. RSE	7.4-19.2	7.4-16.6	7.4-16.6	1.8-11.6
Age-Specific RSE (%)	10.6-38.3	8.4-25.2	10.5-37.5	4.0-16.5

Estimates of the prevalence of ocular disease were obtained from previously published studies.<sup>1,4-24</sup> The RSE is defined as the ratio of the standard error to the point estimate, assuming a sample size of  $n = 3000$  per ethnic group. The age-specific RSE is based on age-specific prevalence rates for each of six age groups (6-11, 12-23, 24-35, 36-47, 48-59, 60-71 months), and assumes  $n = 500$  in each age-group for each ethnic group.

age-specific prevalence rates for each of six age groups (6–11, 12–23, 24–35, 36–47, 48–59, 60–71 months) and assumes a uniform continuous distribution of subjects by age. Because the majority of the age-specific RSEs are within the NCHS standard of 30, we believe that 3,000 children per ethnic group with over 500 children in each age-group (except the youngest age group of 6–11 months) will be sufficient to precisely estimate the prevalence of strabismus, amblyopia, and refractive error.

In addition to allowing precise prevalence estimates of the common childhood ocular disorders the total sample size of 12,000 children will be adequate to detect small relative risks that show associations between various risk factors and ocular disease and will allow the detection of small differences in terms of health-related quality of life between groups of cases and controls. For example, for risk factors with a prevalence rate in the population of 0.2 or greater we can detect odds ratios of 1.8 to 2.2 with adequate power (80%) depending on the frequency of the condition under study.

## Study Area

The study area includes 15 census tracts in Inglewood/Hawthorne, 22 census tracts in Torrance, and 10 census tracts in Monterey Park. These three cities were chosen because of the following characteristics: (1) they are primarily residential areas; (2) collectively, these areas have high proportions of African Americans, Asian Americans, Hispanics/Latinos, and non-Hispanic Whites; and (3) the population of the 47 census tracts provides an optimal number of individuals to ascertain precise prevalence estimates.

## Operational Strategies

### *Ascertainment of Eligibility*

The MEPEDS used the U.S. Census definition of resident to determine residence in the household. A household resident is anyone who considers the household his or her permanent residence, lives and sleeps at the residence most of the time, or lives in the household at least six months of the year. Using this definition, eligibility criteria were based on: (1) age five months to 70 months on the day of the household screening, and (2) parent or legal guardian confirmation that the participant resides in one of the selected MEPEDS census tracts.

## **Recruitment Strategies**

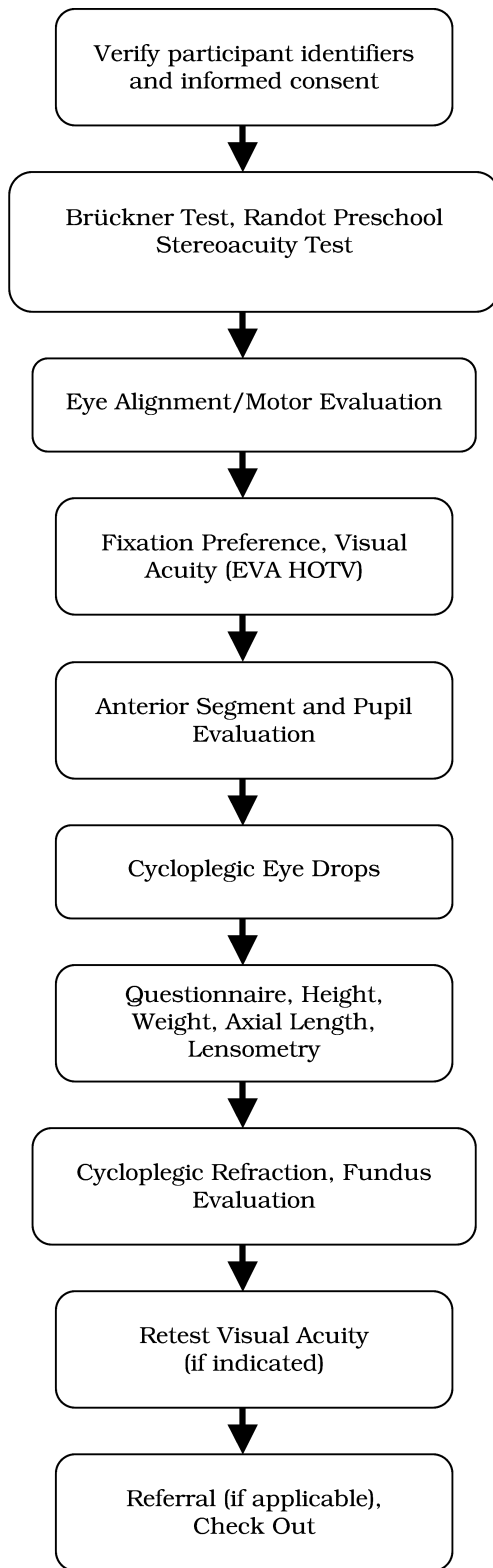
Raising community awareness and support are vital components of our study's recruitment strategies. Prior to beginning a new census tract, households within the census tracts receive (1) an introduction letter by mail; (2) an MEPEDS brochure by mail; (3) a prerecorded follow-up phone call regarding the study; and (4) another brochure distributed via the schools to ensure study visibility. In addition, study brochures are distributed to all preschools, daycare centers, businesses, and churches within the census tract. Collaborative efforts with local community programs and daycare centers are helpful in disseminating information regarding the study to the community.

The MEPEDS interviewers are trained to minimize and convert refusals whenever feasible. Interviewers wear identification badges with the University of Southern California, Doheny Eye Institute and the MEPEDS logos and carry an official letter from the principal investigator and copies of the study brochure to reinforce the legitimacy of the study. Interviewer badges, the letter, and the brochure contain two local telephone numbers that prospective respondents may call to inquire further about the study and verify that it is legitimate. When a respondent is reluctant to participate in the screener or is reluctant to allow his/her child to participate in the eye exam, interviewers explain the importance of the study and how the respondent cannot be replaced. Further refusals are then referred to the field supervisor, who determines how best to deal with each respondent on a case-by-case basis.

To accommodate the large proportion of respondents of working age both field and clinic schedules include weekdays, weekday evenings, and weekends. To facilitate respondent comprehensibility and remove language barriers the MEPEDS has field interviewers who are bilingual. To overcome transportation barriers respondents are offered free transportation to and from the clinic. In addition, each participant is given a \$25 gift certificate to a local store to reimburse them for travel time to the clinic as well as the time that they spend participating in the study.

## **Field Work and In-Home Survey Procedures**

The SRC oversees and is responsible for listing all households in the 47 MEPEDS census tracts, screening each household to identify eligible children,



**FIGURE 1** Flowchart of Clinic Procedures (Clinical Examination/Questionnaire).

obtaining informed consent for each eligible participant, conducting an in-home interview (average time 15 minutes), and scheduling eligible participants to complete a comprehensive eye examination at the

LEEC. Computer-assisted in-person interviewing systems (CAPIs) are used to collect all screener and home interview data. Interviewers use the preferred language (English, Spanish, Cantonese, or Mandarin) of each individual to complete the screening and interview. Once the screener has determined that eligible children reside in the household, home questionnaires are completed on each eligible child. Upon completion of the home questionnaire, appointments are scheduled for each participant to receive a free comprehensive eye examination at the LEEC.

## In-Clinic Ocular Examination and Interview Procedures

The in-clinic procedures include a comprehensive ocular examination and in-clinic interview/questionnaire. Clinic staff includes pediatric ophthalmologists and pediatric optometrists, an ophthalmic technician, and two project assistants. The ophthalmologists, optometrists, and technician are all trained and certified prior to data collection. Data is entered directly into the MEPEDS web-based database system as it is collected. Figure 1 depicts the flow of the data collection process; Table 2 summarizes the in-home screener and in-clinic questionnaire components.

The clinical examination includes the following procedures:

- 1) verification of the participant's name, date of birth, gender, and informed consent completion;
- 2) Brückner test. The Brückner test is a light reflex test that is useful in the diagnosis of small-angle strabismus in young uncooperative children. This test uses the coaxial light source of a direct ophthalmoscope to compare brightness (and whiteness) of fundus reflexes seen through the pupils of both eyes.<sup>25,26</sup>
- 3) Randot Preschool Stereoacuity test (Stereo Optical Company, Chicago, IL); The Randot Preschool Stereoacuity test, which measures random dot stereoacuity from 800 to 40 arc seconds (800, 400, 200, 100, 60, 40), is performed in all participants 30 months of age or older.
- 4) uncover cover testing;
- 5) simultaneous prism cover test (SPCT) measurement of any strabismus present;
- 6) prism and alternate cover test measurement of any strabismus or phoria present;

**TABLE 2** Questionnaire Administered in the Multiethnic Pediatric Eye Disease Study

Sections	Questions
<b>SCREENER</b>	
I. Demographics	Date of birth, gender, birth place, ethnic identification information of participant and participant's parents, maternal/paternal education level, country of birth, parents' marital status, parents' occupation, parents' education level.
II. General Health	Self-reported general health. Utilization of health services and health insurance coverage. Disability at birth.
III. Ocular Health/Ocular Disease History	Self-reported general vision. History of amblyopia, strabismus, and other eye or vision problems.
IV. Stereoacuity Test	Randot Preschool Stereoacuity Test
V. Clinic Eye Appointment	Eye examination appointment
<b>IN-CLINIC</b>	
I. General Health Service Use	Utilization of health services, barriers to care, health insurance coverage, vision insurance coverage.
II. Pregnancy History	Maternal/paternal age at child's birth, maturity of child at birth, low birth weight, prenatal care, history of delivery, breast feeding, maternal history during pregnancy.
III. Smoking/Alcohol	History of maternal tobacco and alcohol usage during pregnancy.
IV. General Health	History of asthma, allergies, mental retardation, cerebral palsy, Down Syndrome, high fever, seizures, coordination problem, heart condition, fetal alcohol syndrome, speech or hearing problems, attention or learning problems, developmental delay, diabetes, tumor or cancer, meningitis or encephalitis, flu, other major health problems. History of accidents or injuries.
V. Ocular Disease History	Self-reported ocular history. History of strabismus, amblyopia, myopia, cataracts, glaucoma, retinopathy of prematurity, or other eye or vision problem. Family history of strabismus, amblyopia, and myopia.
VI. Developmental Delay	Parents' Evaluation of Developmental Status
VII. Motor Milestones	WHO Motor Milestone Evaluation
VIII. Quality of Life	Pediatric Quality of Life Inventory. Amblyopia Treatment Index
IX. Income and Income Assistance	Household income, use of government assistance
X. Future Contact	Future contact information

- 7) assessment of versions and ductions;
- 8) alternate cover test for comitancy, if indicated;
- 9) Hirschberg and Krimsky tests if required: The Hirschberg test is indicated when the examiner (1) is unable to perform cover/uncover testing at near to determine the presence, direction, and/or laterality of strabismus, or (2) is unable to obtain SPCT measurements at near. These tests are light reflex tests and assess the position of the corneal light reflexes when a penlight is placed approximately 40 cm in front of the participant. The relative position of the Purkinje light reflexes are noted with respect to the centers of the pupils. If the relative positions are symmetric and centered in the pupil, then it is assumed that no strabismus is present.

If the light reflexes are asymmetric, the Krimsky test is performed to measure the magnitude of the strabismus. In primary gaze, a correcting prism is placed over the participants' fixating eye to center the corneal light reflex. The magnitude and direction of the prism determines the magnitude of the strabismus.

- 10) fixation preference testing;
- 11) single surrounded HOTV visual acuity testing using the Electronic Visual Acuity (EVA) system<sup>27</sup> is performed. The ATS visual acuity testing protocol includes a pretest to assess testability, a rapid screening to obtain an approximation of the acuity threshold, and threshold testing using single surrounded optotypes for the complete test.<sup>28</sup>

- 12) Color Vision Testing Made Easy<sup>®</sup> Test and Waggoner Color Vision Testing (Home Vision Care, Gulf Breeze, FL) if 30 months of age or older. The Color Vision Testing Made Easy<sup>®</sup> Test is a pseudo-isochromatic color plate test that uses the identification of simple shapes and objects to detect red-green deficiencies.<sup>29</sup> The Waggoner Color Vision Test is a pseudo-isochromatic plate test that uses simple symbols to detect, classify, and estimate the degree of defective color vision.
- 13) anterior segment and pupil evaluation. The anterior segment is evaluated using a handheld or mountable slit lamp. A direct ophthalmoscope and hand light can also be used.
- 14) cycloplegia. Each child receives one drop of 0.5% proparacaine, one drop of cyclopentolate (0.5% if child is  $\leq 1$  year and 1.0% if child is  $> 1$  year), one drop of phenylephrine, and one additional drop of cyclopentolate (concentration dependent on age) after waiting 5 min.
- 15) height and weight measurements. Height and length is measured using a Shorr length board/stadiometer (Shorr Productions, Olney, MD). Length is measured in children less than 24 months of age and height is measured in children 24 months and older. Weight is measured using a Seca 4802 digital floor scale (Scale-tronix, White Plains, NY).
- 16) lensometry if applicable;
- 17) axial length measurement using IOLMaster (Carl Zeiss Meditec, Dublin, CA), if 30 months of age or older;
- 18) cycloplegic autorefractometry using the Retinomax autorefractor (Nikon, Inc, Melville, NY);
- 19) cycloplegic retinoscopy performed, if cycloplegic autorefractometry cannot be obtained;
- 20) noncycloplegic retinoscopy, if cycloplegic drops cannot be administered;
- 21) fundus examination; and
- 22) visual acuity retesting if indicated. Visual acuity retesting is indicated in children who meet the following criteria: (1) Any child with 20/32 or worse (including “unables”) in one eye and two lines or greater intraocular difference in visual acuity in the presence of a unilateral or bilateral amblyogenic factor; and (2) children with or without an identified amblyogenic factor and visual acuity in one or both eyes of: 20/60 or worse (including “unables”)

when  $< 4$  years of age or 20/50 or worse (including “unables”) when  $\geq 4$  years of age.

At the conclusion of the examination the clinician discusses the results of all testing and diagnoses with the participant’s parent/guardian. Two reports are provided before participants leave the clinic: one in lay language, including referral recommendations, and one for the participant’s parent/guardian to take to the child’s eye care provider or primary care physician. If a referral is needed, a list of local providers is supplied.

The questionnaire includes assessment queries regarding: (1) health care coverage and utilization; (2) basic medical history; (3) ocular history; (4) pregnancy and neonatal history; (5) tobacco and alcohol use during pregnancy (questions adapted from HHANES); (6) age-appropriate quality of life (PedsQL 4.0 Measurement Model for the Pediatric Quality of Life Inventory developed by James W. Varni, Children’s Hospital and Health Center, San Diego, CA)<sup>30,31</sup>; (7) presence or absence of developmental delay; (8) motor milestones; and (9) socioeconomic status. The questionnaire has been translated and back-translated into Spanish and Chinese (simplified and traditional). To ensure that translated questionnaires are culturally appropriate as well as linguistically accurate, the questionnaires were pilot tested in a sample of Spanish-speaking and Chinese-speaking (Cantonese and Mandarin) groups. At the beginning of each questionnaire, the respondents are given the choice of having the interview conducted in English, Spanish, or Chinese (Cantonese or Mandarin).

## Primary Outcome Measures

*Amblyopia* is defined as follows: *Unilateral amblyopia* is a  $\geq 2$  line interocular difference in best visual acuity, after testing with refractive error correction, with vision of 20/32 or worse in the worse eye in the presence of a unilateral amblyogenic factor consistent with the affected eye. Amblyogenic factors are strabismus at distance and/or near fixation with or without spectacle correction, a history of strabismus surgery (or botulinum toxin injection), anisometropia ( $\geq 1.00$  D difference in hypermetropia,  $\geq 3.00$  D difference in myopia, or  $\geq 1.50$  D difference in astigmatism in any meridian, evidence of past or present obstruction of the visual axis on examination (e.g., cataract, intraocular

lens, aphakia, corneal opacity, ptosis, or hemangioma) or a history of obstruction of the visual axis (e.g., ptosis or hemangioma). If visual acuity measurements are not obtained for both eyes (e.g., child is under 30 months of age), unilateral amblyopia is defined to be a strong fixation preference with no ability to hold fixation with the nonpreferred eye in the presence of a unilateral amblyogenic factor.

*Suspected unilateral amblyopia* is diagnosed only in the absence of visual acuity measurements in both eyes and when there is a strong fixation preference with inability to hold fixation more than momentarily with the nonpreferred eye in the presence of a unilateral amblyogenic factor.

*Bilateral amblyopia* is reduced ( $<20/40$  in both eyes for ages 48 to 72 months, or  $<20/50$  in both eyes for ages  $<48$  months) best-corrected visual acuity in the presence of a bilateral amblyogenic factor (defined as bilateral high ametropia of hypermetropia  $\geq 4.00$  D, myopia  $\geq 6.00$  D, or astigmatism  $\geq 2.50$  D, or bilateral evidence of past or present obstruction of the visual axes). Visual acuity retesting with a trial lens spectacle correction, according to the cycloplegic refraction performed during the clinical examination, is required whenever initial visual acuity testing (without correction or with patient's own spectacles, if worn) shows bilaterally decreased visual acuity or a two-line interocular visual acuity difference with vision of  $20/32$  or worse in the worse eye, so that diagnosis of unilateral or bilateral amblyopia is based on the best visual acuity measures obtained in each eye after testing with refractive error correction.

*Strabismus* is defined as a heterotropia at distance and/or near fixation with or without spectacle correction and is classified as esotropia, exotropia, or hypertropia, and as constant or intermittent.

*Refractive error* (hypermetropia, myopia, astigmatism, anisometropia) is defined based on the measurements made with the Retinomax autorefractor, which is performed with cycloplegia. If automated results are unreliable for either eye, cycloplegic refraction is determined using cycloplegic retinoscopy, performed in both eyes for the purposes of assessing for anisometropia. Non-cycloplegic retinoscopy is performed only rarely, when cycloplegic drops are refused. Full distributions of refractive parameters will be reported so that the data may be evaluated using a variety of different definitions of the refractive errors of interest.

## MEPEDS Clinical Information System

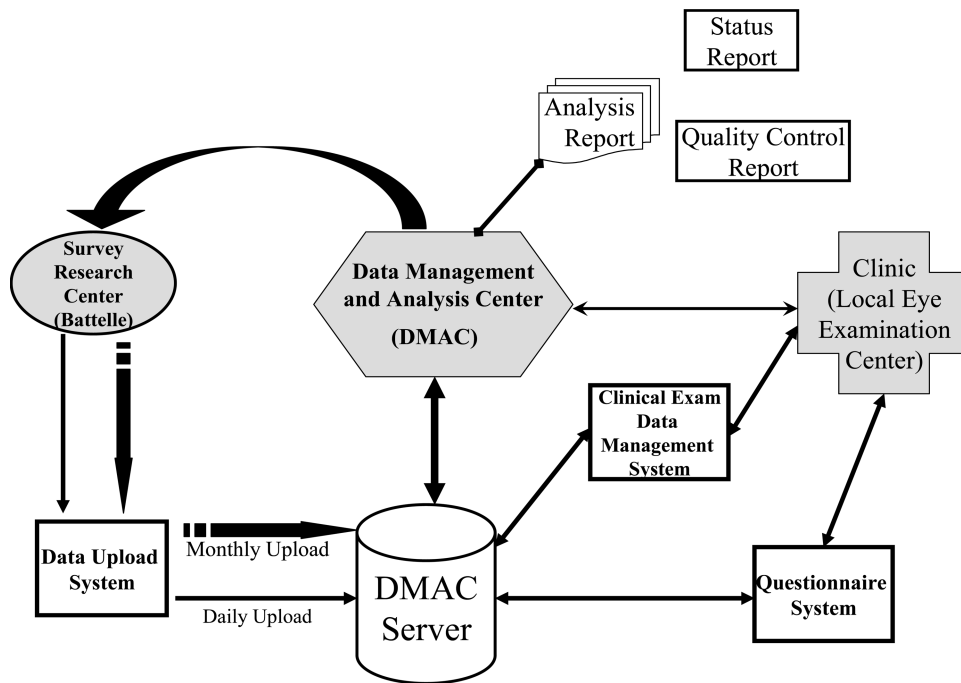
The MEPEDS Clinical Information System integrates data from two sources, namely, (1) the Battelle SRC home interview using the Battelle BLAISE/ACCESS database system (Battelle, St. Louis, MO), and (2) the LEEC clinical examination and clinical questionnaire using the MEPEDS web-based database system (Figure 2).

The Battelle BLAISE/ACCESS database system allows interviewers to collect screener questionnaires via CAPI. When an interview is administered using a CAPI system, all question and answer categories appear on the computer screen, optional phrasing for questions are automatically tailored by the computer for each interview, and skip logic and consistency checks are built directly into the system to reduce the number of errors. All data that is collected on this database system is uploaded and cleaned before being delivered to the MEPEDS database.

The MEPEDS server is configured to utilize transaction logging for auditing and recovery purposes, and is configured to provide commercial-grade encryption via Secure Sockets Layer and Transport Layer Security. Static and dynamic protection (including preassigned user IDs, user-specified passwords, and a preassigned range of server-specified IP addresses) is employed to ensure confidentiality, data integrity, and data security. The secure clinical and questionnaire database system utilizes Microsoft<sup>®</sup> SQL Server 2000 Standard Edition.

Data entry computers use an Internet browser to access clinical and questionnaire data in the MEPEDS web-based entry system. The clinical data system permits on-line data entry for each child participant, replacing paper medical records, and supports the acquisition, storage, manipulation, and distribution of participant information. Quality control features for the clinical data include: (1) range checks based on allowable values, (2) pop-up flags for required data fields, (3) "use-case" scenarios to permit skipping data items that are not needed/appropriate for a specific child participant, and (4) pop-up flags for ocular retesting for quality control purposes. In addition, a summary report of ocular and clinical findings is provided and given to the parent by the examining clinician.

In order to expedite the collection of questionnaire data for multiple children within a single family the



**FIGURE 2** Flowchart of the MEPEDS web-based database system.

computerized questionnaire data system also permits on-line data entry, but on a family basis (rather than on a child participant basis); therefore, the family representative (e.g., parent) answers each question for all of the participating children within that family, rather than answering the questions for the first child, then the second child, etc. The MEPEDS system then restructures the child within the family questionnaire database in order to integrate it with the per-child clinical database.

The databases are then exported to an SAS (ODBC-compliant) database, merged, and quality controlled using an SAS program, such as checking of commonly shared variables across all databases, checking dates, and sorting and checking the data for duplicate records. Summary reports of home interview, clinical, and questionnaire data are generated on a weekly basis to be reviewed by the study investigators and staff.

## Quality Control Procedures

Quality control (QC) measures are implemented and followed throughout the entire study and in all resource centers in order to ensure that all data collected and analyzed are as accurate and complete as possible. Prior to the beginning of data collection a comprehensive Manual of Procedures (MOP) was written. This MOP

contains detailed instructions on fieldwork procedures, clinical examination procedures, and data collection and entry procedures.

*Fieldwork Quality Control.* All SRC staff are certified on all fieldwork procedures outlined in the MOP and are provided with retraining workshops throughout the study to ensure that these procedures are followed accurately. The SRC conducts a 100% verification of the dwelling units listed in the selected census tract area to assure that all dwelling units are identified during the initial listing process. This is completed as the sample is confirmed and the screening process begins. In addition, the SRC conducts a 5% validation of each interviewer's work to ensure that each interviewer is collecting data in an accurate, professional manner.

## Clinical Examination and Questionnaire Quality Control

All examiners at the MEPEDS LEEC are trained and certified on examination protocols as described in the MOP. Examiners are certified every six months to ensure that examination protocols are being followed in a standardized and accurate manner. In addition to the certification process, quality control measures are in place to ensure inter-examiner reliability. The first two normal patients each day are retested for one of three outcome variables (cover testing, fixation preference testing, or visual acuity) that are rotated each

month. All “abnormals” are retested. A 5% random sample of all participants are called and asked a series of interviewer performance and questionnaire verification questions. These procedures allow us to ensure that the questionnaire data collected at the time of the clinical examination is accurate and being properly collected.

### **Data Entry Quality Control**

The database at the LEEC was developed to help ensure data accuracy by including data range checks and error-trapping procedures. In addition to the built-in QC each month, 5% of the participants are randomly selected and their data is re-entered to assess data entry accuracy.

At the Data Management and Analysis Center, data from the SRC and LEEC are merged. Once merged, additional QC is performed using SAS programs to check commonly shared variables across all databases, checking dates, and sorting and checking the data for duplicate records.

### **Statistical Analysis**

SAS Version 9.1.3 (Cary, NC) is used for all statistical analyzes. Age-specific prevalence estimates for strabismus, amblyopia, and refractive error will be calculated as the ratio of the number of cases to the number of subjects who completed the clinical examination within a given age group. The direct standardization method will be used to determine age-adjusted prevalence estimates of strabismus, amblyopia, and refractive error. We will use the age distribution of Hispanics/Latino, African-American, Asian, and non-Hispanic white children in the U.S. as the standard age distribution. Interactions between age groups and race will also be evaluated.

Risk factors will be assessed using prevalent cases and all noncases in the population. Conditional logistic regression analyses (both univariate and stepwise) will be conducted to relate the likelihood of strabismus, amblyopia, and refractive error with demographic factors (e.g., age, sex, race, socioeconomic status), maternal alcohol and tobacco use during pregnancy, eye care and healthcare utilization, and characteristics of the birth (e.g., birth weight, gestational age). To measure functional status, the Pediatric Quality of Life Inventory will be scored according to standard algorithms. Analysis of variance will be used to contrast the average subscales and composite scores across strata defined by demographic and ocular characteristics.

## **STUDY STRENGTHS AND LIMITATIONS**

The MEPEDS is the first population-based study to comprehensively examine the prevalence of ocular conditions in a multi-ethnic cohort of infants and young children. In addition, the MEPEDS is the first study to examine risk indicators of ocular conditions, as well as the impact of ocular conditions on health-related functional status/quality of life. Study strengths include the standardization of the study protocol across ethnic and age groups, cultural tailoring of study methods, and the numerous quality control protocol-driven and computer-based procedures to minimize error rates. The comprehensive and standardized questionnaire will facilitate the assessment of risk indicators, as well as the impact of ocular conditions on quality of life. In addition, the fact that the MEPEDS is population-based facilitates the generalizability of the findings. A study limitation is inaccurate self-reporting of treatment history and risk exposures. With regard to inaccurate self-reporting of treatment history, history of patching, strabismus surgery, and other ocular surgery will be validated by obtaining medical records from the eye care providers to confirm the nature, timing, and duration of treatment. This validation will help minimize errors in self-reporting these treatment variables. Additionally, self-reporting has been found to be reasonably accurate when assessing alcohol use, healthcare utilization, and the number of comorbidities.<sup>32–34</sup> Another limitation of our study is the likelihood of familial household clustering effects as we include all siblings in a household and, thus, common environmental risk exposures are likely to bias prevalence estimates. We plan to assess the magnitude of the bias in our prevalence by comparing the variance in our prevalence estimates of specific eye disorders both with and without familial household clustering using a mixed effects model approach with the random factor in the model being the household.

To our knowledge the MEPEDS is the largest population-based study of eye health in infants and young children. The data obtained from the MEPEDS should help inform vision scientists, eye care providers, pediatricians, community health educators, and health policy makers on the burden of eye problems in infants and young children and help focus resources on the most pressing, treatable conditions in this vulnerable group.

## ACKNOWLEDGEMENTS

The authors thank the MEPEDS Data Monitoring and Oversight Committee for their advice and contributions: Jonathan Holmes, MD (Chairman); Natalie Kurinij, PhD; Eileen Birch, PhD; Karen Cruickshanks, PhD; Maureen Maguire, PhD; Joseph Miller, MD; Graham Quinn, MD; and Karla Zadnik, OD, PhD.

## REFERENCES

- [1] Gerali P, Flom MC, Raab EL. *Report of Children's Vision Screening Task Force*. Schaumburg, IL: National Society to Prevent Blindness, 1990.
- [2] Healthy People 2010: Vision and Hearing. National Institutes of Health. 2005. 7–22–2005.
- [3] Attkinson J. Infant vision screening: Prediction and prevention of strabismus and amblyopia from refractive screening in the Cambridge Photorefractive Program. In: Simons K, editor. *Early Visual Development, Normal and Abnormal*. New York: Oxford University Press, 1993.
- [4] Atkison J, Braddick OJ, Durden K, Watson K, Atkinson S. Screening for refractive errors in 6–9 month old infants by photorefractometry. *Br J Ophthalmol*. 1984;68:105–12.
- [5] Chew E, Remaley NA, Tamboli A, et al. Risk factors for esotropia and exotropia. *Arch Ophthalmol*. 1994;112:1349–1355.
- [6] DaCunha, Jenkins EM. Amblyopia in three-year-olds. *Med Officer* 1961;106:146–148.
- [7] Dobson V, Fulton AB, Sebris SL. Cycloplegic refractions of infants and young children: The axis of astigmatism. *Invest Ophthalmol Vis Sci*. 1984;25:83–87.
- [8] Flom MC, Bedell HE. Identifying amblyopia using associated conditions, acuity, and nonacuity features. *Am J Optom Physiol Opt*. 1985;62:153–160.
- [9] Flom MC, Neumaier RW. Prevalence of amblyopia. *Public Health Rep*. 1966;81:329–341.
- [10] Gwiazda J, Scheiman M, Mohindra I, Held R. Astigmatism in children: Changes in axis and amount from birth to six years. *Invest Ophthalmol Vis Sci*. 1984;25:88–92.
- [11] Ingram RM, Barr A. Changes in refraction between the ages of 1 and 3 1/2 years. *Br J Ophthalmol*. 1979;63:339–342.
- [12] Kvarnstrom G, Jakobsson P, Lennerstrand G. Visual screening of Swedish children: An ophthalmological evaluation. *Acta Ophthalmol Scand*. 2001;79:240–244.
- [13] MacFarlane DJ, Fitzgerald WJ, Stark DJ. The prevalence of ocular disorders in 1000 Queensland primary school children. *Aust NZ J Ophthalmol*. 1987;15:161–174.
- [14] Mayer DL, Hansen RM, Moore BD, et al. Cycloplegic refractions in healthy children aged 1 through 48 months. *Arch Ophthalmol*. 2001;119:1625–1628.
- [15] McBride WG, Black BP, Brown CJ, Dolby RM, Murray AD, Thomas DB. Method of delivery and developmental outcome at five years of age. *Med J Aust*. 1979;1:301–304.
- [16] Nawratzki I, Oliver M, Neumann E. Screening for amblyopia in children under three years of age. *Sight Sav Rev*. 1972;42:15–19.
- [17] Oliver M, Nawratzki I. Screening of pre-school children for ocular anomalies. II. Amblyopia. Prevalence and therapeutic results at different ages. *Br J Ophthalmol*. 1971;55:467–471.
- [18] McNeil NL. Patterns of visual defects in children. *Br J Ophthalmol*. 1955;39:688–701.
- [19] Preslan MW, Novak A. Baltimore vision screening project. *Ophthalmology*. 1996;103:105–109.
- [20] Preslan MW, Novak A. Baltimore vision screening project. Phase 2. *Ophthalmology*. 1998;105:150–153.
- [21] Russel EL, Kada JM, Huffhines DM. Orange County vision screening project, Part 2. *Sight Sav Rev*. 1961;31:215–219.

- [22] Vereecken E, Feron A, Evens L. Importance de la detection precoce du strabisme et de l'amblyopie. *Bull Soc Belge Ophthalmol*. 1966;143:729–742.
- [23] Woodruff ME. Vision and refractive status among grade 1 children of the province of New Brunswick. *Am J Optom Physiol Opt*. 1986;63:545–552.
- [24] Simons K. *Early Visual Development, Normal and Abnormal*. New York: Oxford University Press, 1993.
- [25] Griffin JR, Cotter SA. The Brückner Test: Evaluation of clinical usefulness. *Am J Optom Physiol Opt*. 1986;63(12):957–961.
- [26] Tongue AC, Cibis GW. Brückner Test. *Ophthalmology*. 1981;88(10):1041–1044.
- [27] Moke PS, Turpin AH. Computerized method of visual acuity testing: Adaptation of the amblyopia treatment study visual acuity testing protocol. *Am J Ophthalmol* 2001;132:903–909.
- [28] Holmes JM, Beck RW, Repka MX, Leske DA, Kraker RT, Blair RC, Moke PS, Birch EE, Saunders RA, Hertle RW, Quinn GE, Simons KA, Miller JM, and Pediatric Eye Disease Investigator Group. The Amblyopia Treatment Study Visual Acuity Testing Protocol. *Arch Ophthalmol*. 2001;119:1345–1353.
- [29] Cotter SA, Lee DY, French AL. Evaluation of a new color vision test: "Color Vision Testing Made Easy<sup>®</sup>." *Optom Vis Sci*. 1999;76:631–636.
- [30] Varni JW, Burwinkle TM, Seid M. The PedsQL<sup>™</sup> as a pediatric patient-reported outcome: Reliability and validity of the PedsQL<sup>™</sup> Measurement Model in 25,000 children. *Expert Review of Pharmacoeconomics and Outcomes Research*. 2005;5:705–719.
- [31] Varni JW, Seid M, Kurtin PS. PedsQL<sup>™</sup> 4.0: Reliability and validity of the Pediatric Quality of Life Inventory<sup>™</sup> Version 4.0 Generic Core Scales in healthy and patient populations. *Medical Care* 2001;39(8):800–812.
- [32] Kehoe R, Wu SY, Leske MC, Chylack LT Jr. Comparing self-reported and physician-reported medical history. *Am J Epidemiol*. 1994;139:813–818.
- [33] Ritter P, Stewart AL, Kaymaz H, Sobel DS, Block DA, Lorig KR. Self-reports of health care utilization compared to provider records. *J Clin Epidemiol*. 2001;54:136–141.
- [34] Lee DJ, Markides K, Ray LA. Epidemiology of self-reported past heavy drinking in Hispanic adults. *Ethn Health*. 1997;2:77–88.

## APPENDIX

### THE MULTI ETHNIC PEDIATRIC EYE DISEASE STUDY GROUP

#### University of Southern California

Rohit Varma, MD, MPH (Principal Investigator); Jennifer Deneen, MPH (Project Director); LaVina Abbott; Stanley P. Azen, PhD; Tal Barak, OD; Mark Borchert, MD; Jessica Chang, OD; Susan Cotter, OD (Co-Principal Investigator); Ivania Cuzul; Jackie Diaz; Anne DiLauro, MPH; Jill Donofrio, MPH; Claudia Dozal; James Gardner; Felicia Kang, OD; Jesse Lin, MS; George Martinez; Roberta McKean, PhD; Sylvia Paz, MS; Erin Song, OD; Kristina Tarczy-Hornoch, MD, DPhil; Mina Torres, MS; Natalia Uribe, OD; Peng Zhao, MS

#### Battelle Survey Research Center

Charles Aders; Candace Kwong, MPH; Nancy Noedel; Michael Preciado; Hugo Skandrani; Karen Tucker, MA.