

# Implementation of the WHO Multicentre Growth Reference Study in the United States

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## Abstract

*The World Health Organization (WHO) Multicentre Growth Reference Study (MGRS) North American site was Davis, California. For the longitudinal cohort (0–24 months), 208 infants were enrolled between January and December 1999 from five area hospitals at which nearly all Davis women give birth. The target sample size was lower in the United States than in the other sites, because recruitment in the United States was restricted to mothers who were willing to exclusively breastfeed for at least 4 months and continue breastfeeding for at least 12 months. For the cross-sectional component, a mixed-longitudinal design was used, which required approximately 500 subjects. The subjects were recruited by going door-to-door, with the sampling scheme based on the distribution of the subjects of the longitudinal study within the city. The cross-sectional sample was recruited between January and July 2001. Major challenges during implementation were maintaining daily communication with hospital personnel and scheduling home visits.*

**Key words:** Anthropometry, breastfeeding, child health, child nutrition, growth, growth monitoring, growth references, infant feeding practices, United States

## Introduction

The World Health Organization (WHO) Multicentre

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Growth Reference Study (MGRS) North American site was Davis, California, in the United States. Davis is a university town. Its average educational level is high. More than 95% of mothers initiate breastfeeding, and support services for breastfeeding are available. The altitude is about 15 m. The mobility of the student population is high, but for the longitudinal study, only mothers who planned to remain in Davis for at least 24 months were included. Five hospitals collectively account for more than 95% of all births to women residing in Davis: Sutter Davis Hospital, Woodland Memorial Hospital, and three hospitals in Sacramento, California—the University of California at Davis (UC Davis) Medical Center and two Kaiser Permanente hospitals. Prior to initiating this study, the research team had had extensive experience with studies on infant nutrition and growth in the community. Thus, the study site fulfilled the criteria for inclusion in the MGRS described elsewhere in this supplement [1].

## Planning phase

### Study timeline and preparatory activities

The timeline of the study is summarized in figure 1. During the first two months, the study team met with representatives from the five hospitals listed above and arranged for letters to be sent to potential subjects when they registered to give birth at each hospital. Permission to recruit newborns from the hospitals and conduct specific activities was obtained from the administrators of the hospitals. Letters to the patients described the study and indicated that study personnel would visit the mothers in the hospital shortly after delivery. Members of the study team met with the physicians in charge of each hospital's maternity ward and other relevant hospital personnel to explain the logistics of the study, introduce team members, and discuss study procedures. Letters introducing the study and explaining its logistics were sent to local physicians. During the longitudinal recruitment phase of the study,

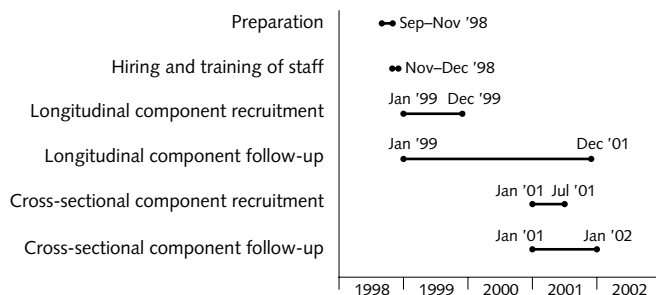


FIG. 1. Study timeline

letters were mailed to the physicians of enrolled subjects explaining the study and describing the lactation counseling services of the study.

Institutional ethical approval was obtained from the University of California Human Subjects Review Committee and the Kaiser Permanente Northern California Health Services Institutional Review Board.

### Study teams

There were three study teams for the longitudinal study: the coordination, neonatal, and follow-up teams. The coordination team consisted of the site's principal investigator, three supervisors, a study secretary, and two data entry clerks. This team had the general responsibility of overseeing all study activities. Two supervisors were International Board Certified Lactation Consultants (IBCLCs). These supervisors jointly managed the neonatal team, and one of them also served as the data manager. The third supervisor was in charge of anthropometric training and supervised the follow-up team. All three supervisors served as backup data collectors for the neonatal and follow-up teams. The neonatal team, composed of two IBCLC lactation counselors and two research assistants, was responsible for screening, lactation counseling, and data collection through day 14 of each subject's participation. The follow-up team was responsible for data collection from 1 to 24 months. They referred mothers to the lactation counselors of the neonatal team as needed. This team consisted of four research assistants.

There were two teams for the cross-sectional study: one for recruitment and a second for obtaining anthropometric measurements. The recruitment team was responsible for going door-to-door to screen and enroll subjects. This team consisted of five individuals, most of whom worked part-time. The measurement team subsequently contacted each family to complete the cross-sectional visit and take the anthropometric measurements. The team consisted of three research assistants.

All members of the data collection teams had at least a four-year college degree in a related field and qualifications consistent with the duties they would perform.

### Training and initial standardization

The study teams received training in accordance with the MGRS Manual of Operations. The breastfeeding observation protocol was standardized among the lactation counselors and the two IBCLC supervisors. The follow-up team was given instructions on the referral system to be used for women experiencing breastfeeding problems. The cross-sectional study recruitment personnel received instructions on the neighborhood recruitment scheme and the screening protocol.

### Adaptation of study materials and procedures

The Manual of Operations was adapted to reflect the team configuration implemented at this site. A home visit was added on day 3 postpartum to optimize the successful establishment of breastfeeding, in accordance with the recommendations of the American Academy of Pediatrics [2].

Minor adaptations were made to the baseline and follow-up questionnaires. Several questions were added to document socioeconomic status. In recording educational status, the number of years of higher education was "capped" at a predetermined maximum, depending on the degree obtained. The list of potential responses to selected questions was expanded (e.g., site-specific foods for the food frequency and dietary recall questions).

### Public relations activities

Study displays and informational brochures were placed in clinics and offices of physicians likely to have patients interested in the study. Study personnel visited local childbirth classes and mothers' support groups to introduce and explain the aims and procedures of the study.

The Davis, Sacramento, and UC Davis newspapers published several articles with photographs about the study, and two television segments publicizing the study were aired on local channels. The mothers and infants received a matching set of T-shirts with the local study logo as a means of thanking the participants, publicly acknowledging their participation, and

introducing the study to the wider community. Local merchants were also solicited to offer discounts and gift certificates to subjects as a means of encouraging wider community involvement.

The cross-sectional study was publicized in the local newspaper prior to the commencement of recruitment. Pediatricians were contacted and asked to encourage their patients to participate in the study. Flyers to parents were distributed through local day-care centers and kindergarten classes. A publicity table also was set up at the Davis Farmer's Market.

## Implementation of the longitudinal study

### Sampling strategy

All infants born during the enrollment period to mothers who planned to remain in Davis for at least 24 months were potentially eligible for the longitudinal study. Most subjects (95%) were recruited from the five hospitals listed above. Each of these hospitals was contacted daily, seven days a week, to identify potential subjects. Potential subjects were visited in the hospital within 24 hours of delivery by a member of the research team. Mothers who resided in Davis and gave birth at home or at other hospitals were also eligible to participate if the research team was notified and the mother could be reached within 24 hours after delivery. Women who planned to have a home birth were contacted prenatally via the designated midwife.

Eligibility criteria specific to the US site are shown in table 1. The target sample size for the longitudinal study at the US site was 200 (as compared with 300 in the other sites). The sample size was judged adequate based on the documented research experience in this community. This experience indicated that the desired final sample size (at least 70 infants) could be attained if recruitment was restricted to mothers who were willing to breastfeed exclusively for at least 4 months and continue breastfeeding for at least 12 months.

TABLE 1. Longitudinal study selection criteria specific to the USA site

Davis resident: mailing address in Davis or El Macero (a subdivision of Davis)
Perinatal morbidity: any condition that was serious enough for the infant to be kept in the intensive care unit for more than 24 hours led to exclusion. This included conditions such as respiratory illnesses, congenital malformations, maternal drug abuse, Down syndrome, and nervous system disorders
Intention to breastfeed: mother was willing to exclusively breastfeed for at least 4 months and continue breastfeeding for at least 12 months
Socioeconomic status: telephone in the home

### Screening and enrollment of children

Informed written consent was obtained from the mother after eligibility was established. If she was unwilling or ineligible, or wanted to discuss her participation in the study with her partner, written consent was obtained for the neonatal measurements only. All newborns of interviewed mothers were measured if consent for those measurements was obtained, irrespective of enrollment in the full study. Eligible mothers wishing to postpone their decision kept the consent form until the first follow-up visit at home.

### Follow-up logistics

Subjects were given the option of having home visits or going to the site's central facility. The majority preferred home visits. The neonatal team conducted home visits on days 3, 7, and 14 and at week 4 to all mothers who experienced breastfeeding problems on day 14. This allowed the lactation counselor to evaluate whether breastfeeding problems had been resolved and offer further assistance if needed. In cases where such follow-up was required, the neonatal team continued to follow the subject until week 4. Otherwise, the follow-up team initiated follow-up after the day 14 visit and conducted all home visits from four weeks to 24 months. Whenever mothers experienced breastfeeding problems after four weeks, the follow-up team contacted the neonatal team supervisor to arrange for lactation counseling. Figure 2 illustrates coordination among the teams.

The motor development assessment began at four months, according to the MGRS protocol described elsewhere in this supplement [3]. The implementation of the 12-month study visit to those who were ineligible owing to breastfeeding intention, refusal, or dropout followed the standard protocol [1]. All children who completed the study were given a certificate of completion at 24 months.

### Lactation support and complementary feeding

The lactation counselors provided breastfeeding guidance to all mothers during the first 24 hours after birth and on days 3, 7, and 14, and were available for home consultations at other times. A telephone hotline was made available for emergency support seven days a week from 8 am to 5 pm. At three and six months, the mothers were contacted by telephone by one of the supervisors or lactation counselors. At three months exclusive breastfeeding was encouraged, and at six months the mother was encouraged to continue breastfeeding and given advice on complementary feeding. If a mother planned to start working outside the home and would not have the baby with her, a lactation counselor made an appointment to teach

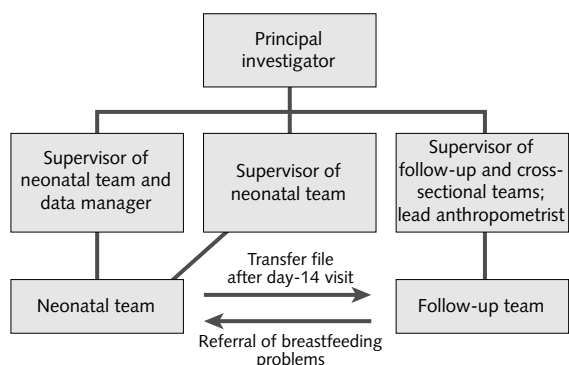


FIG. 2. Organizational and team coordination chart

her how to extract breastmilk (and, if necessary, left a breast pump with her). A counselor also contacted a mother when she experienced breastfeeding problems or the follow-up team was concerned that breastfeeding might be terminated before 12 months.

Complementary feeding guidelines were developed by the site's coordination team. Draft guidelines were sent to local pediatricians for comment and subsequently were revised based on their input (table 2). The guidelines were provided to all mothers. If a mother asked for advice on complementary feeding, the assistant referred to the guidelines but did not interfere with her physician's advice.

## Implementation of the cross-sectional study

### Sampling strategy

The limited population of Davis and the MGRS protocol requirement to minimize subject participation in both the longitudinal and cross-sectional components required local adaptations. The cross-sectional study adopted a mixed-longitudinal design, in which each child would be measured three different times at three-month intervals. Also, because of funding delays, the cross-sectional study at the United States site could not begin until after the longitudinal study subjects began to enter the age range of the cross-sectional study (18–71 months), and for this reason the target age range was restricted to 27 to 71 months. The mixed-longitudinal design and likely attrition rates set the target sample size at 483.

The sampling strategy was based on the index household method. Index households were defined as those that had been screened for the longitudinal study. Because nearly all births to Davis mothers in 1999 were screened for the longitudinal study, this approach did not bias the sample. The city was divided into 83 neighborhoods. The number of cross-sectional study subjects to be recruited from each neighborhood was based on its number of index households.

TABLE 2. Complementary feeding guidelines at the USA site

<p>Introduce solids, starting with small amounts, one or two times per day and gradually increase to three meals per day by 12 months, with additional snacks as desired</p> <p>The order of introduction of solids doesn't seem to matter, but start one new food at a time and allow four to seven days to watch for any reaction</p> <p>Baby cereals that are iron fortified are a good source of iron and therefore are often recommended as one of the first foods.</p> <p>After the transition period (when new foods are introduced), include fruits, vegetables, and high-protein foods (meat, fish, or eggs) every day. Include vitamin A-rich fruits and vegetables</p> <p>Do not feed more than 8 ounces of juice per day</p> <p>If there is a family history of allergies, don't feed eggs until the child is two years old, and don't feed peanuts, nuts, or fish until the child is three years old</p> <p>Continue to breastfeed as often as your baby wants. If you supplement, use cow's milk formula, NOT regular cow's, goat's, or soy milk before 12 months</p> <p>Start with pureed or strained foods, then mashed or finely chopped foods at 8 to 10 months, and most family food after 12 months (when more teeth are in)</p> <p>Fluoride drops are recommended where nonfluoridated water is used</p> <p>Iron drops are recommended for low-birthweight infants (beginning at 1 month, through 12 months)</p> <p>Vitamin D supplements are recommended for dark-skinned infants or those who get insufficient sunlight</p> <p>For those children who eat few or no animal products and show signs of poor appetite, a multivitamin (containing zinc) is recommended</p> <p>Make mealtime a happy, pleasant experience. Do not force your child to eat certain foods or finish everything on the plate</p>
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The recruiters identified each index household and went door-to-door in a clockwise direction to obtain information on the households closest to each index household. To determine the order of potential enrollment, the index households within each neighborhood were randomized. After the eligible children from the index households had been recruited, the children from nearby households were enrolled, starting with the household closest to the first index household, then the household closest to the second index household, and so on. The children in the set of next closest households were then enrolled. This continued, moving further and further from each index household, until the target number of subjects for each neighborhood was reached.

The selection criteria were consistent with the general MGRS protocol, except that children born outside of Davis were not excluded. Children enrolled in the longitudinal study were potentially eligible for the cross-sectional study, but a "cap" was placed on the percentage in the youngest age ranges that could participate in both components. The cap was based

on the estimated proportion of cross-sectional study children who, given the city's demographics, would have been in the longitudinal study. The maximum allowable percentage of longitudinal study children was 17% in the 27- to 30-month interval, 11% in the 30- to 33-month interval, and 6% in the 33- to 36-month interval. There were no longitudinal study subjects in the cross-sectional sample other than in those age groups.

If a household had more than one child who qualified, all were selected. The only exception was for siblings of subjects screened for the longitudinal study. We selected one such sibling for every third household screened for the longitudinal study that had more than one child who qualified (based on achieving a similar proportion in the cross-sectional study sample as these siblings would represent in the general population of Davis children 27–71 months of age).

#### **Screening, enrollment, and survey logistics**

The cross-sectional study recruiters went door-to-door during the daytime and early evening hours seven days a week. Flyers with a postage-paid reply form were left at homes where no contact was made. If the form was not returned, up to two additional attempts were made (at least one of which was after 5 pm or on a weekend) to find someone at home. Neighbors were also asked about whether there were any children under six in the targeted households. If at least one neighbor was sure that no child in that age range was part of that household, the household was excluded.

In each neighborhood, the five households closest to each index household were contacted initially. On the first visit, the eligible children in the index household or the next closest household were enrolled, but children in all other households were put on a waiting list until complete information was available for all five households nearest to each index household. If at this point the target number for the neighborhood had not been reached, the process was repeated with the next closest set of five households.

#### **Standardization, quality control, and data management activities**

##### **Anthropometric standardization sessions**

Initial anthropometric training was conducted by the local lead anthropometrist, whose measurement techniques were standardized against the WHO lead anthropometrist before the initiation of the study [4]. The members of the neonatal and follow-up teams participated in standardization sessions with the cosupervisors and the local lead anthropometrist.

The neonatal team standardization sessions could

not be conducted in hospital newborn nurseries. Therefore, the mothers of young infants not enrolled in the longitudinal study were recruited to participate in specially conducted standardization sessions held at the site's coordination center. To ensure that the measurement techniques used with newborns did not differ from those used during standardization sessions, the lead anthropometrist observed at least one newborn measurement per week at the local hospital. During the first year of the study, neonatal team standardization sessions were held on a weekly basis for eight consecutive weeks to accumulate the data required for calculating reliability (precision and accuracy) statistics. Because the team was large, an algorithm was designed by the site statistician that permitted each infant to be measured by only four observers. This required 21 infants over a period of eight weeks, with each observer measuring 12 infants. This design allowed estimates of accuracy and precision similar to those required by the standard MGRS design [4].

The alternative algorithm described above was not required for the follow-up team. Standardization sessions were held at the coordination center or at local day-care centers. In general, five children aged 2 to 66 months were measured at each session. The data from two sessions were combined to obtain the required estimates of accuracy and precision. The accuracy and precision of each team member's measurements were reviewed after each standardization period, and corrective standardization sessions were scheduled for individuals whose measurement techniques needed improvement.

When the cross-sectional study began, the team participating in this component joined the remaining follow-up team members for anthropometric standardization sessions. Because the follow-up team helped out with the cross-sectional measurements, all personnel at that time were trained and standardized for measurement of height.

##### **Motor development standardization sessions**

To ensure standardized data collection, the sites were required to conduct regular motor development standardization sessions [3]. However, by the time the standardization protocol was finalized, the US site had nearly completed collecting motor development data. Thus, only one standardization session was held following the standardized protocol. The initial training and standardization at this site were conducted at local day-care centers prior to the initiation of data collection with the assistance of a local expert (Dr. Ernesto Pollitt).

##### **Quality control activities**

All quality control procedures in the MGRS protocol were followed [1]. During the first few weeks of the

study, the supervisors accompanied the fieldworkers on several home visits. Thereafter, random monitoring of data collection (10% of all interviews) was conducted by telephone. The supervisors served as backup data collectors and routinely observed the interviewing and measurement techniques of all study assistants.

The questionnaires were turned in to the supervisor daily and checked for completeness and consistency. Corrections were made when necessary. This sometimes required telephoning the mother or remeasuring a child. Any problems found during routine questionnaire checks were discussed at the next team meeting.

All team members attended regular staff meetings. In the longitudinal study, each team met with the supervisor weekly in the first few months and at least once every two weeks thereafter. These operational procedures provided abundant opportunities to oversee the quality of the work being performed.

#### Data management

After reviewing all questionnaires, the supervisors coded the responses to any open-ended questions and forwarded the forms to data clerks. The data manager conducted data cleaning and validation (e.g., checking for outliers, data entry errors, and out-of-range values), completed preliminary data analyses, and prepared

the data files for transfer to the MGRS Coordinating Centre in Geneva.

#### Conclusions

There were several challenges in implementing the MGRS protocol at this site, particularly during the neonatal phase. First, maintaining adequate daily communication with hospital staff was sometimes difficult. It required building good working relationships and perseverance. Mothers were sometimes not receptive to being screened so soon after delivery. This required making all mothers (and their physicians) aware of the study before hospitalization. Performing infant length measurements in the hospital was sometimes difficult when the infant became agitated. The mothers were reassured that the procedure was brief and not painful. In general, the mothers needed frequent breastfeeding support and assistance, and therefore additional lactation consultants were hired. During the follow-up phase, scheduling visits was a challenge that required persistence and flexibility. For example, if mothers were working outside the home, visits were scheduled at day-care centers. In terms of overall management, the greatest challenges were scheduling standardization sessions and mastering the data management system.

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