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Associations between Dietary Factors in Early Life and Childhood Growth

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Associations between Dietary Factors in Early Life and Childhood Growth

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Dedication

To Yadi Hua and Wei Zhu, my parents

&

Ruichen Zhao, my husband

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Associations between Dietary Factors in Early Life and Childhood Growth

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Early life factors play important roles in disease susceptibility in later life. However, the relationship between dietary factors in early life on childhood growth, especially linear growth, remains unclear. This research aimed to improve our understanding of the associations between dietary factors in early life (i.e., infant feeding practices and age of introduction of solid foods) and childhood growth, especially using ulnar length as a surrogate measure of length/height, in a cross-sectional study of 1634 mother-child dyads across eight study centers in the National Children's Study Formative Research in Anthropometry in the United States from 2011-2012 (Chapter 1). Chapter 2 described the data acquisition and preprocessing procedures used in this research and provide practical guidelines of data quality control. In Chapter 3, predictive models for exclusive breastfeeding (XBR) initiation and duration was developed. Discriminant analysis revealed maternal sociodemographic factors had greater discriminating abilities to predict XBR initiation and XBR for 6 months, compared to child birth characteristics and maternal perinatal factors. Chapter 4 demonstrated that ulnar length can serve as an accurate and reliable surrogate measure of recumbent length in healthy infants/children aged 0-1.9 years and of height in healthy children aged 2-5.9 years, respectively. Bland-Altman plots and mixed-effects linear regression analyses showed that the three simple and portable tools (i.e., caliper, ruler, and grid) used to measure ulnar length could be used interchangeably in terms of prediction accuracy. Chapter 5 focused on assessing the interplay among gestational weight gain (GWG), birthweight, infant feeding practices, and childhood anthropometrics. Longer duration of breastfeeding reduced the positive associations of GWG and birthweight with weight-for-age z-scores, weight-for-height/length z-scores, and body mass index-for age z-scores in non-Hispanic Whites. These findings underscore the importance of promoting breastfeeding among women with excessive GWG to mitigate childhood obesity. Longer breastfeeding and a later age at introduction of solid foods had positive effects on ulnar length, a linear growth parameter of upper extremity, in Hispanics. Future prospective research aiming to investigate the underlying mechanisms that drive ethnic variation in these associations between early life dietary factors and childhood growth is warranted (Chapter 6).

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List of Abbreviations

AAP	American Academy of Pediatrics
ANOVA	analysis of variance
ANCOVA	analysis of covariance
AUC	area under the curve
BMI	body mass index
BMIZ	body mass index-for-age z-scores
BrBot	breast-bottle feeding
CI	confidence interval
CV	coefficient of variation
GWG	gestational weight gain
HAZ	height-for-age z-scores
ICC	intraclass correlation coefficient
NCS	National Children’s Study
NHANES	National health and Nutrition Examination Survey
OR	odds ratio
r	Pearson’s correlation coefficient

R^2	coefficients of determination
SD	standard deviation
SE	standard error
SEE	standard error of estimate
ULC	ulnar length by caliper
ULG	ulnar length by grid
ULR	ulnar length by ruler
US	United States
WAZ	weight-for-age z-scores
WHO	World Health Organization
WHZ	weight-for-height z-scores
XBot	exclusive bottle-feeding
XBR	exclusive breastfeeding

Chapter 1: Introduction

BACKGROUND AND SIGNIFICANCE

Recumbent length or standing height is an important measure in the assessment of nutrition and growth status in children (1, 2). Height is fundamental in calculating surface area, body size, and pulmonary function (3-5). Several cohort studies have reported that childhood stature is related to cause-specific morbidity and mortality including stroke, cardiovascular diseases and cancers in adulthood (6-10), suggesting the impact of early life factors on later health. Childhood length/height is influenced by both genetic and environmental factors (11, 12). Potential environmental determinants of childhood length/height include socio-demographic, dietary exposures and other lifestyle factors (12-15). Given genetic disposition and some environmental exposures are difficult to modify, assessment of the association between the most universal and modifiable early life exposures (i.e., dietary practices) and childhood growth is of upmost importance. However, the relationship between dietary factors in early life (i.e., infant feeding practices) on childhood growth, especially linear growth, remains unclear (16-18).

It is difficult to assess recumbent length or standing height in children who are temporarily hospitalized (e.g., children with bone/joint injures or in coma) or have long-term mobility-impairment due to neuromuscular diseases or joint deformities. They are at risk of malnutrition (19, 20) and need special nutritional rehabilitation (21, 22). However, standard anthropometric measures like recumbent length or standing height are usually unobtainable or unreliable in these children (23, 24), hence impeding the assessment of their nutrition and growth status. Therefore, several surrogate measures of length/height have been proposed, including arm span (19, 25-27), lower leg length or knee height (28-32), and segmental lengths of long bones (humerus, radius, ulnar, femur, tibia, and fibula) (33-36), the majority of which have only been tested in adults. Indeed, these children may be unable to have arm span measured due to the difficulty of establishing the outstretched position of both arms. Also, researchers have reported difficulties in measuring lower leg length in children with lower extremity cerebral palsy (31) and acutely ill elderly population (37). In contrast, ulnar length is a potentially optimal surrogate measure for length/height because its measurement is not usually impeded by joint deformity. To date, no study has assessed ulnar length as a surrogate measure for length/height in children aged <6 years in the United States (US) (38-40). In addition, some height/length components or surrogates may be particularly sensitive to early life exposures characterized by distinct growth velocities at different developmental stages (41, 42). However, no research has examined the association between dietary exposures in early life and ulnar length as a surrogate measure of childhood length/height.

On the other hand, despite the mounting evidence that dietary factors in early life varies across populations (43-47), the relative impact of sociodemographics, perinatal factors, and child's birth characteristics on disparities in exclusive breastfeeding (XBR) is not well known. Knowledge and comparison of the relative extent to which these factors contribute to lactation outcomes are of particular importance in formulating effective public health initiatives to promote better lactation performance.

Another factor for consideration relates to ethnic diversity in the US and corresponding ethnic variation in childhood growth [e.g., length/height (48-52) and its components (53-55)] as well as ethnic disparities in disease morbidity and mortality (56-58). Despite the identification of some genetic and early life environmental determinants of childhood length/height (12, 59), the ethnic specific relationships between dietary factors in early life and child growth, especially linear growth, remain to be studied.

OBJECTIVES

Therefore, *the overall objective* of this dissertation was to improve our understanding of the associations between dietary factors in early life and childhood growth, especially linear growth in a cross-sectional study of 1634 mother-child dyads across eight study centers recruited in the National Children's Study (NCS) Formative Research in Anthropometry in the US from 2011-2012. *The specific aims pursued* by this research were as follows:

1) Develop predictive models for XBR initiation and duration that identify women at risk for none or poor lactation performance.

2) Examine the accuracy and reliability of ulnar length measured by different tools as surrogate measures of recumbent length and standing height.

3) Assess the association between dietary factors in early life (i.e., infant feeding practices and) and childhood growth in the total sample and by ethnicity.

Assessment of these relationships (Figure 1.1) would help explain whether ulnar length, as a proxy indicator of childhood linear growth, is sensitive to dietary factors in early life. Ulnar length in turn, serving as an indirect measure or indicator of childhood nutrition and growth status, may provide useful insights into future investigation of the hypothesis of developmental origins of disease (60).

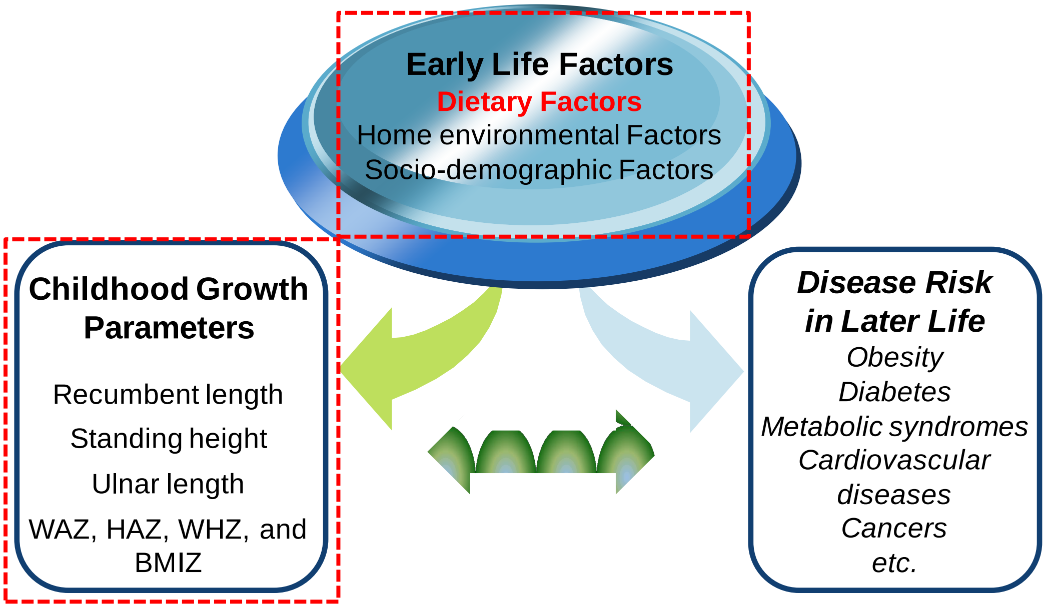

Figure 1.1 The associations among early life factors, childhood growth parameters, and disease risk in later life. This dissertation will focus on the two components in the dotted squares. BMIZ, body mass index-for-age z-scores; HAZ, height-for-length z-scores; WAZ, weight-for-length z-scores; WHZ, weight-for-height z-scores.

LITERATURE REVIEW

Surrogate measures of length/height

Standard anthropometric methods for standing height and recumbent length are not always appropriate and could be difficult to obtain in children who are severely ill, comatose, disabled, injured, skeletal-deformed, or severely retarded. Yousafzai and colleagues reported difficulties in measuring height in 21% of participants aged 2-6 years with disabilities, including amputations, cerebral palsy, post-polio syndrome and clubfoot (61). Spender et al. reported difficulties in measuring recumbent length or standing height in 53% of children with cerebral palsy (24). Under these circumstances, reliable and accurate surrogate measures of length/height are needed either for one-time assessment or long-term follow-up of childhood growth. Moreover, difficulties and problems can be encountered in field studies compared with clinical settings due to the portability, accessibility, and expense of specialized equipment, which may be only available in clinics or research facilities. Therefore, surrogate measures of height and length which can be obtained via simple and portable tools are desirable.

Arm span measured with a flexible measuring tape is a feasible surrogate measure of length/height in both clinical and field settings. Arm span is the distance between the middle finger tip of one hand to the other with arms raised to the shoulder height and fully outstretched with palms facing upward. It has been used as a height surrogate in various age and ethnic groups. The correlation coefficients between arm span and height for Black and White adult females were 0.852 and 0.903, respectively (62). In a population of Malawian children aged 6-15 years, arm span was significantly correlated with height [Pearson's correlation coefficient (r) = 0.986 and 0.983 for girls and boys, respectively] (26). Similarly, linear regression models of height using arm span as a predictor have been established in a population of Chinese children aged 4-16 years [(coefficients of determination (R^2) = 0.972 and 0.965 for girls and boys, respectively] (38). In addition, arm span have been used to estimate height in physically impaired or nonambulatory children. Yousafzai et al. found that arm span was the best predictor of height with the strongest association (R^2 = 0.93) and lowest prediction error [standard error of estimate (SEE) = 3.2 cm), as compared to arm length and tibia length, in both healthy and disabled children aged 2-6 years in India (61). However, it is worth pointing out that the accuracy and reliability of arm span as a length/height surrogate are impaired in children with spasticity or contractures in arms or shoulders, due to the difficulty of establishing the outstretched position of both arms. Measurement difficulties have been documented in physically impaired children in the Philippines (19) and Nigeria (20). Thus, other surrogate measures of length/height are needed in these circumstances.

Lower leg length or knee height is the distance from the posterior surface of the thigh (proximal to the patella) to the sole of the foot when the knee is bent at a 90 degree angle. It can be measured by a caliper (63) or a flexible tape (64). Even though the inter-rater error was smaller when the measurement was taken with the subject lying down than sitting up, there were no systematic differences in measurements between the two positions (63). Thus, flexibility in use of tools and measurement position demonstrates that lower leg length or knee height is a promising alternative measure of length/height in both healthy (30, 39, 65) and mobility-impaired or handicapped populations (28, 31, 32, 37, 66, 67). Studies have examined the relationship between lower leg length and height, with reasonably high correlation of 0.80-0.88 in Caucasian adults (30, 66, 68), 0.83 in Black adults (66), 0.68-0.84 in Asian adults (65, 69), and 0.97-0.98 in White and Black children of 6-18 years (66). However, researchers have also documented difficulties in measuring lower leg length in some populations, e.g., children with lower extremity cerabral palsy (31) and acutely ill elderly population (37).

Segmental lengths of long bones, including humerus, radius, ulnar, femur, tibia and fibula, have also been tested as surrogate measures of length/height. Considering the ease of measurement in bedridden or wheel-chaired people, distal long bones (radius, ulnar, tibia and fibula) are more preferable than proximal ones (humerus and femur). *Tibia length*, the distance from the inner border of the medial condyle to the tip of the medial malleolus (70), is the distal limb measure most studied. Studies have indicated tibia length as a reliable surrogate of length/height with R^2 of 0.77-0.84 in Iranian healthy children aged 7-11 years (71), 0.95-0.96 in Australian children aged 5-19 years, 0.96 in Chinese children aged 3-18 years (72), and 0.72 in Indian children aged 2-6 years (61). However, data about *ulnar length* (from the most proximal point of the olecranon to the most distal point of the styloid process with the forearm flexed at a 90 degree angle) (73), are limited, and not reported in young children in the US. Ulnar length was first described by Valk et al. using a special device called condylograph in assessing children's short term growth (73, 74). Since its measurement is not usually impeded by joint deformity, it is a promising surrogate measure for length/height. Three studies have assessed ulnar length as a length/height proxy measure in children. This measure was shown to be accurate and reproducible in 8-14 year old American children with neuromuscular disease and contractures (r = 0.91) (40), 3-18 year old healthy Chinese children (r = 0.98) (72), and 5-19 year old healthy Australian children (males $R^2 = 0.96$, females $R^2 = 0.94$) (39). To date, no studies have investigated the relationship between ulnar length and length/height in children under age of 6 years in the US across different ethnicities.

Infant Feeding Practices and Childhood Growth

Dietary factors in infancy may include ever breastfeeding or not, XBR, exclusive bottle-feeding (XBot), breast-bottle feeding (BrBot), and age at introduction of solid foods (i.e., solid, semi-solid or soft foods) (75). Regarding breastfeeding, the most recent and updated (2008) World Health Organization (WHO) guideline defines: 1) XBR: infants receiving only breast milk (including milk expressed or from a wet nurse) and nothing else with the exception of oral rehydration salts, drops and syrups (vitamins, minerals, medicines); 2) predominant breastfeeding: differs from XBR by additionally including certain liquids (water, water-based drinks and fruit juice), and breast milk still being the predominant source of nourishment; and 3) breastfeeding: infants receiving breast milk and anything else (76). However, considerable variation exists in the classification of infant feeding practices across studies in terms of the duration and/or exclusiveness of breastfeeding. For instance, in a US national monitoring and surveillance report on breastfeeding, eight out of the eleven datasets collected information on XBR. Five of the eight studies followed the WHO definition (the 1991 version) (77) for XBR and the rest used varied definitions (78). Moreover, researchers may allow consumption of water and other non-milk liquids in the definition of XBR (79). The use of non-standard or arbitrary definitions and inappropriate classification impedes the assessment and comparison of the association between infant feeding practices and health outcomes.

A rich body of studies has documented differences in growth patterns by infant feeding practices. In developed countries, formula-fed infants generally have greater weight gain than breastfed infants during the first year of life (80-84). However, the effect of infant feeding practices on childhood linear growth parameters is less clear and inconsistent. Birkbeck reported that children who received XBR in the first 3 months were significantly taller than exclusively formula-fed children at age 7 years (85), whereas other studies show no association between infant feeding practices and childhood height up to age 7 years (86, 87). Similarly, the relationship between infant feeding practices and childhood length/height components is inconclusive. Martin et al. reported a significantly positive effect of ever breastfeeding on leg length in children aged 2-15 years, controlling for child and parental characteristics (16). In another British national birth cohort, Wadsworth et al. found adults who were breastfed for ≥ 2 weeks had shorter leg length than their bottle-fed counterparts at age 43 years, after adjustment for socioeconomic factors (18). In contrast, Li and colleagues found no association between ever breastfeeding (≥ 1 month) and leg length at 43 years of age, adjusted for parental height, birthweight, family size, and social class (88). However, these studies had no records regarding the exclusiveness of breastfeeding and were based on cohort data between 1930s and 1950s in United Kingdom (16, 18, 88). Since the constitution of commercial infant formula has changed across the late 20th century due to advances in scientific knowledge about essential nutrients in childhood growth, it is uncertain if these relationships would remain the same nowadays. In sum, methodological limitations of these studies include: 1) lack of contemporary data; 2) inconsistent and unclear definitions of infant feeding practices; and 3) failure to adjust for potential confounders including child's birthweight, maternal reproductive factors (e.g., age at childbirth, prepregnancy body mass index (BMI), smoking during pregnancy, and pregnancy complications), and socio-demographic factors. Failure to adjust for residual confounding is of particular concern. In a study of the 1958 British birth cohort, the significant associations of ever breastfeeding with height at 7 years and with leg length at 43 years were attenuated and no longer significant after adjustment for covariates (88).

Besides infant feeding practices as components of early life dietary exposures, the age at introduction of solid foods is also associated with childhood growth (84, 89, 90). However, the relationship between age at introduction of solid foods and childhood linear growth parameters has not been well studied. Given the paucity of such data, the examination of the association between the age at introduction of solid foods and childhood linear growth parameters based on contemporary data is desired.

In addition, ulnar length as a potential length/height surrogate measure might be particularly sensitive to certain early life exposures and hence might assist in assessing the relationships between these early life dietary exposures and childhood growth. Together, the importance of investigating the associations between these dietary factors and early childhood growth parameters is highlighted.

Ethnic variation in Childhood Growth

Length/height may vary by ethnicity across infancy-childhood-puberty stages. Jung et al. reported that Black infants (measured in the 1980s in the US) were significantly taller than White infants between ages of 3-12 months, adjusting for birthweight (49). Additionally, for formula-fed male infants, Black infants showed a faster growth rate than their white counterparts. In an analysis of the National Health and Nutrition Examination Survey (NHANES) in the US, Black children born between 1942-2002 were taller than White children aged 3-11 years by 0.3 standard deviations, whereas White children caught up at ages 14-15 and were taller thereafter (91). The ethnic differences in height between Hispanic and NHW children were observed in the NHANES in 1971-1980 but not in 1999-2004 (48). Similarly, one study done in the late 1980s on US children aged 5-12 years in a poor community revealed that non-Hispanic Black (NHB) children were taller than NHW and Hispanic ones, whereas no significant difference was observed in height between NHW and Hispanic children (52).

Besides ethnic differences in childhood length/height, ethnic differences in height components and surrogates are documented as well. In a group of American children aged 8-18 years, Black children have longer legs and shorter trunks than their white counterparts, adjusted for height (53). In addition, Black children have longer stature-adjusted ulnar and lower leg length (reported as calf length in the study) than White children at 9 years old in a birth cohort in South Africa (55). Mexican American adolescents have shorter leg length than NHW and NHB American adolescents (54). Similarly, Chinese children have shorter height and segmental limb lengths (including humerus, radius, ulna and tibia) than Caucasians (72). Yet, contemporary data comparing length/height and its components or surrogate measures across all the aforementioned ethnicities in one single study of infant/young children are not available. Given the associations between childhood growth and disease susceptibility in later life, identifying determinants to ethnic differences in early childhood growth might improve our understanding of the underlying ethnic specific mechanisms that drive racial/ethnic disparities in disease morbidity and mortality (56-58).

It is well recognized that genetic factors play important roles in determining a child's length/height (92, 93) and adult attained height (94). Maternal height, as an easy-to-obtain measure, serves as a frequently used indicator of genetic influences on childhood height (95). The correlation coefficients of maternal height with children's height ranged between 0.23-0.52 ($P < 0.05$) in NHW and Hispanic children aged 2-9 years using NHANES data (48). Still, a child's genotype potential of length/height is modulated by the restriction of exogenous factors (12, 96). Previous research has identified that these exogenous early life influences may include 1) prenatal and perinatal factors: maternal age at childbirth (12), smoking during pregnancy (97, 98), and child's birthweight (99); and 2) postnatal factors: breastfeeding (96), parental socioeconomic status (99-101), number of siblings (12), and household size (102). However, the relationships between infant feeding practices and childhood growth by ethnicity remains poorly understood. Moreover, although few studies have assessed the effect of these early life factors on height components (leg and trunk length (18, 103, 104)) and other anthropometric measures (foot length (96, 105), shoulder breadth (96), and head circumference (105)), the association with ulnar length as a height surrogate measure has not been investigated. Growth of height surrogate measures occurs with different velocities at different periods throughout infancy and childhood stages (41, 42); thus, some of these length/height surrogates may be particularly sensitive to childhood life exposures.

Understanding the ethnic specific relation between these potentially modifiable early life dietary factors and childhood growth could provide insights into tailored health programs addressing ethnic disparities in health and disease outcomes.

SUMMARY

In summary, evaluation of the relationships between dietary factors in early life (infant feeding practices and age at introduction of solid foods) and childhood growth (especially linear growth) (Figure 1.2) may improve our understanding of the associations between childhood early growth and disease in later life. In addition, exploration of the ethnic specific association between these early life dietary exposures and childhood growth is of great importance regarding the ethnic disparities in disease morbidity and mortality. Surrogate measures of childhood length/height may serve as better indicators than actual length/height in assessing the associations between early growth and later disease susceptibility.

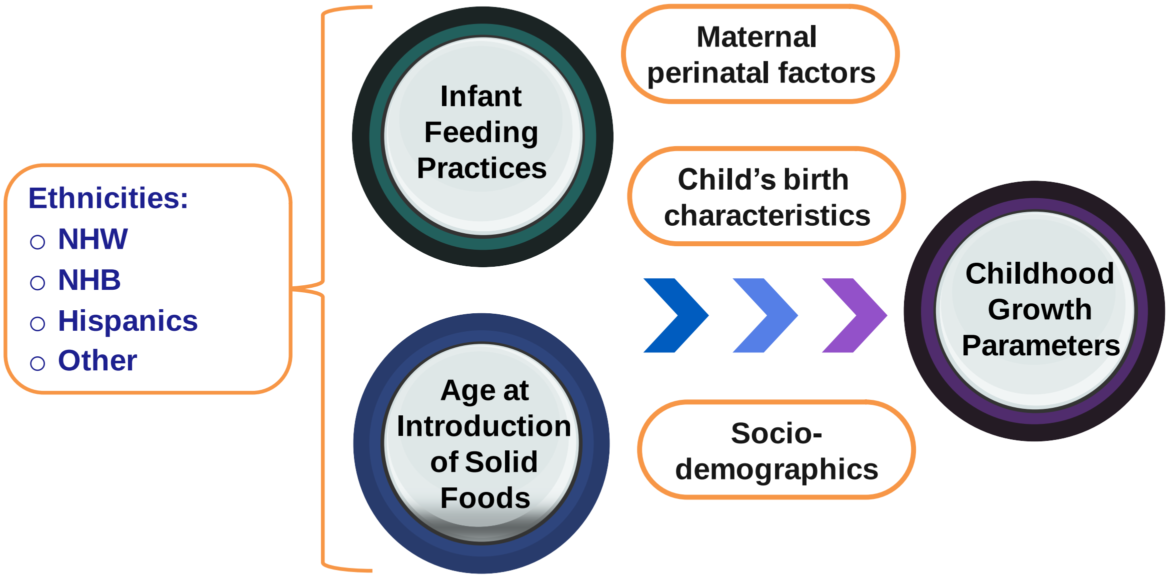

Figure 1.2 The associations between dietary factors in early life with childhood growth parameters may differ by ethnicity after adjustment for maternal and child covariates. NHB, non-Hispanic Black; NHW, non-Hispanic White.

Chapter 2: Quality Control and Assurance in Data Acquisition and Preprocessing[1]

[1] This chapter was previously published as "Zhu Y, Hernandez LM, Mueller P, Dong Y, Forman MR. Data acquisition and preprocessing in studies on humans: What is not taught in statistics classes? The American Statistician 2013;67:235-41." The authors' contributions were as follows: Yeyi Zhu conducted data collection and preprocessing and wrote the manuscript. Ladia M. Hernandez helped supervised the field activities, including data collection, quality assurance and control. Peter Mueller revised the manuscript. Yongquan Dong helped with data management. Michele R. Forman was the Principal Investigator of the study who designed the study; directed its implementation; supervised the field activities, including data collection, quality assurance and control; and revised the manuscript.

ABSTRACT

The aim of this chapter is to address issues in research that may be missing from statistics classes and important for (bio-)statistics and epidemiology students. In the context of the NCS Formative Research in Anthropometry as a case study, this chapter discusses data acquisition and preprocessing steps that fill the gap between research questions posed by subject matter scientists and statistical methodology for formal inference. Issues include participant recruitment, data collection standardization, variable coding, and data review, verification, cleaning, editing, and documentation. Despite the critical importance of these details in research, most of these issues are rarely discussed in an applied statistics program. One reason for the lack of more formal training is the difficulty in addressing the many challenges that can possibly arise in the course of a study in a systematic way. This chapter can help to bridge this gap between research questions and formal statistical inference by using an illustrative case study for a further discussion. It is hoped that reading and discussing this chapter and practicing data preprocessing exercises will sensitize statistics students and researchers to these important issues and achieve optimal conduct, quality control, analysis, and interpretation of a study.

Keywords: Quality control; data collection; data cleaning; data code book; data dictionary.

INTRODUCTION

Statistics classes focus on mathematical, statistical, and computational theories and methods. However, before researchers reach the first step of formal statistical analysis, many data errors and data quality issues may arise of which a researcher needs to be aware. Data errors and problems may include entry errors, missing values, duplicates, outliers, and data inconsistencies and discrepancies, any of which may affect the validity, reproducibility, and thus the quality of studies. In large-scale studies, budgets may be allocated for personnel with distinct roles, including principal investigators, study coordinators, data collectors, database managers, and statisticians. More often than not, researchers may need to play multiple roles in certain study settings, thereby increasing the demands on researchers to oversee quality control over the whole study flow from study design to data acquisition, preprocessing, and analysis. The importance of quality control over data acquisition is well recognized, but is usually not discussed in applied statistics classes. Furthermore, data preprocessing bridges the gap from data acquisition to statistical analysis but has not been championed as a relevant component in statistics curricula.

This chapter reviews some critical issues in quality control and assurance of which statistics students should be aware but that are typically not taught in statistics courses. The aim of this chapter is to address these issues in the context of the NCS Formative Research in Anthropometry. It is hoped that introducing the concepts and practical approaches of data acquisition and preprocessing using NCS as a case study will sensitize statistics students and researchers to these important issues in quality control and encourage more related discussions.

WHY DO WE CARE ABOUT DATA ACQUISITION AND PREPROCESSING?

Data errors may appear at any stage of data acquisition and preprocessing, which could affect study results and lead to erroneous statistical interpretation and conclusions. Goldberg, Niemierko, and Turchin (106) reported error rates of 2.3 - 5.2% for demographic data and 10 - 26.9% for clinical data in oncology patients, which could be attributed to data entry errors and researchers' misinterpretation of tumor treatment outcomes due to missing and inconsistent data. These data errors could significantly affect the results by increasing the standard errors of the mean and decreasing the statistical power (107). Data errors could also lead to erroneous findings. An erratum to a published paper (108) on risk assessment of disease burden reported that an error in the estimates of burden for alcohol use led to incorrect estimates of mortality and morbidity from ischaemic heart disease attributable to alcohol use, which required corrections in the Summary, Results, and Discussion sections, three tables, all figures, and the appendix. This type of data error could be due to: conversion errors from ounces to grams as the measure of alcohol use in different countries/regions; miscoding of alcohol use as some other risk factors of interest in the study; or errors when data were merged from different sources. With proper data preprocessing, these errors could be avoided before the formal analysis and reporting. Moreover, data errors could result in opposite conclusions. In a clinical study comparing the effect of two treatment protocols on patients with Hodgkin's disease, Levitt et al. (109) demonstrated that omission of one select patient from one treatment group (n = 37) changed the comparison results from statistical insignificance to significance.

Despite recognition of these data issues and adverse consequences, data preprocessing has received relatively little attention in instructional environments, compared to the emphasis on optimal study design and adherence to research protocols. Students or researchers who are new but want to perform data preprocessing may be challenged by limited and difficult-to-access resources. Although the Ethical Guidelines for Statistical Practice by the American Statistical Association state that researchers should report “the data cleaning and screening procedures used, including any imputation” in publications (110), it is uncommon to see all information reported in publications. Some universities and institutes do provide online information about data acquisition and preprocessing but they are usually request-based services. Indeed, it is difficult for students to find comprehensive manuals or guidelines regarding these issues. Therefore, given the significance of data acquisition and preprocessing in relation to data quality control, it is important that applied statistics curricula provide students a platform to learn, discuss, and practice data acquisition and preprocessing skills in a systematic and planned way.

STEPS TO DATA ACQUISITION AND PREPROCESSING USING A CASE STUDY AS AN ILLUSTRATION

The data acquisition process in studies involving human subjects typically includes participant recruitment, screening, consent, and data collection. Data preprocessing usually has five steps: data review; entry and verification; cleaning; editing; and documentation (111). Given the large variability in data issues within study-specific contexts, it is impossible to enumerate all possible data errors and corresponding preprocessing strategies. Instead, this chapter uses an epidemiological study of infant feeding practices and childhood growth to illustrate common approaches to data acquisition and preprocessing in order to improve data quality and integrity.

Background: Study Description

The case study based on the NCS Formative Research in Anthropometry, is a cross-sectional study involving 1634 mother-child dyads across eight study sites in the US. Mothers were administered a perinatal history questionnaire on socio-demographic, reproductive, and child feeding factors (*see* Appendix A). Children aged <6 years were measured for standard anthropometrics (length, height, and weight) and ulnar length by different tools (caliper, ruler, and paper grid). The primary objective of this study was to evaluate ulnar lengths measured by different tools as surrogate measures of body length and height by age, sex, and ethnicity in infants and children aged 0-5.9 years. A secondary goal was to examine the associations between infant feeding practices and childhood growth in this sample. The following discussion is based on data acquisition and preprocessing procedures used in this study.

Quality Control in Data Acquisition

Participant Recruitment, Screening, and Consent. Statistical classes usually do not discuss participant recruitment, screening, or consent. However, it is important that statisticians are aware of these procedures so that they can provide feedback for study design before actual data collection begins. For example, this NCS formative research involved multi-site data collection. After participant recruitment, researchers examined subject characteristics in each site to determine whether a study site effect was present and whether a mixed-effects linear regression model with study site as a random effect was appropriate. In addition, according to subject eligibility criteria, researchers created filters to exclude ineligible participants although prescreened and observed in the dataset. It is also worth noting that any study that depends on volunteer participants is subject to a possible selection bias. It is important that the statistical collaborators are aware of these challenges and can sensitize study investigators to these problems in the study design phase. In our case, to reduce the impact of possible selection bias inherent to this convenience sample, researchers collected relevant covariates of childhood growth and infant feeding to compare participants by selective characteristics that might bias results, e.g. ethnicity, maternal prepregnancy BMI, perinatal morbidity, and child's birthweight.

Staff Training and Data Collection Standardization. In order to implement effective quality control, a set of procedures should be established prior to data collection to ensure the staff adheres to the defined set of quality control criteria. In this NCS study, researchers at each study center were *initially trained* by experienced principal investigators with hands-on practice of measurements on young children volunteers. *A manual of procedures for anthropometric measurements* was provided to the staff with detailed steps for conducting the standardized measurements. *A training video* was provided to each study center for subsequent re-training in anthropometrics to standardize collection procedures. *Webinars* describing interview procedures were held by principal investigators to all study sites. *Weekly conference calls* were held to discuss and share field experiences regarding participant recruitment, data collection, interaction with participants, and field conditions. *Daily calibration of equipment* was required and recorded on forms.

Actual data collection required careful attention to the administration of the study questionnaire(s) by interviewers and completion by participants. In our study, despite the preferred mode of administration by in-person interview, approximately 11% of the mothers self-completed the questionnaire at one site due to logistical issues. Self-administration compared to interviewer-guided administration could potentially affect data quality due to participants' misinterpretation of questions, thus requiring special attention during data preprocessing. In addition, comments regarding logistical conditions during measurement, participants' compliance to the measurement protocol, and reasons for measurement interruption or failure were documented on the anthropometric form. If statisticians identify invalid or implausible values during the data cleaning stage, these comments may help data evaluation and interpretation.

Variable Coding and a Data Code Book. Variable coding is a process that distills and aggregates useful information from the original data and assigns codes to make data analyzable. A data code book describes the content of the dataset and typically has information including original survey questions and skip patterns; variable definitions; variable name, type, label, and values; code for missing data; and other characteristics of each variable. In this study, researchers collected a series of open-ended and multiple choice questions about whether the mother has ever fed the child in the study on breast milk and/or formula, age started and stopped feeding breast milk and/or formula, and age at introduction of solid foods. As illustrated in Table 2.1, a data code book documents

Table 2.1 An example of variable coding documented in a data code book

Survey questions *[responses]*	Variable definitions	Variable name	Label	Codes	Type
18. Was XXX ever fed breast milk? *[Yes/No]* 19. How old was XXX when s/he completely stopped being fed breast milk? *[Age A]* 20. How old was XXX when s/he was first fed something other than breast milk or water? *[Age B]* 21. Was XXX ever fed formula? *[Yes/No]*	a) Exclusive breastfeeding (XBR): *Yes* to Q18 & *No* to Q21; or *Yes* to Q18 and Q21 & *Age A* < *Age B* b) Breast-bottle feeding (BrBot): *Yes* to Q18 and Q21 & *Age A* ≥ *Age B* c) Exclusive bottle-feeding (XBot): *No* to Q18 & *Yes* to Q21	IF practices	Infant feeding practices	1 = XBR 2 = BrBot 3 = XBot 97 = Refused 98 = Don't know 99 = Missing	Nominal

Age A: age stopped breastfeeding, Age B: age started feeding something other than breast milk or water, IF: infant feeding.

variable definitions, derivations from the original data, and variable coding. Besides the use of a word document or a spreadsheet, there are software programs available for recording data and developing a data code book, such as IBM SPSS, SAS, and STATA.

Quality Control in Data Preprocessing

Data errors and issues are prone to arise at any stage even in carefully planned studies. Thus, a systematic and thorough preprocessing approach developed before data analysis is critical to enhance overall data quality and integrity. Data preprocessing can be delineated into a series of five steps as follows:

Step 1: Data Review. As a front-end process, data review of forms and questionnaires by trained researchers is critical to reduce errors and evaluate data integrity. In this study, *a data review guidebook* was developed to identify and describe the errors and solutions. Detectable errors at the data review stage could be due to, but not limited to: misinterpretation of survey questions by interviewers and/or interviewees; conversion errors due to the use of different metric units in measurements; transcription errors from measurement equipment to forms; and correct values recorded in wrong boxes. Error screening methods at this phase are not necessarily restricted to the statistical. These errors can be detected usually based on study-specific expected ranges; researchers' knowledge of the subject; and common sense. For example, data collection of the study occurred between June 2011 and August 2012; thus dates out of this range must be errors. If not corrected before data entry, these errors could be very difficult to detect and could subsequently result in errors for age calculated as the difference between study date and birth date. Another example is that a child aged 22 months was measured for recumbent length but the value was recorded in the box for standing height while only measurement for the former was expected. In some circumstances, a data reviewer may be able to requery participants or research collaborators to correct errors; however, considering the increasing difficulty of requerying as time goes by and the relevant person becomes unreachable, it is highly recommended to initiate the data review process as early as possible, ideally soon after data collection begins.

Step 2: Data Entry and Verification. Several approaches could be used for data entry, for example, manual entry of paper records, data transfer from handheld computers used for data collection, and optical scanning (112). Researchers manually entered values from measurement forms and questionnaires into an informatics platform. When additional data errors were discovered at this stage, researchers implemented rules in the *data review guidebook* and documented the changes. Despite careful entry by well-trained staff, data entry is inevitably prone to errors. Based on study-specific features of data, investigators might choose different data verification methods including double data entry or visual comparison (113, 114). In this study, due to the unavailability of double entry in the informatics platform, a different person from that of the data enterer verified entries by visual comparison, following specific guidelines for error detection, correction, and documentation in the *data review guidebook.*

Step 3: Data Cleaning. Although many data errors can be detected by initial review, as a good practice, it would be important for researchers to pre-establish or define rules for data cleaning and editing. In this study, researchers cleaned demographic, anthropometric, and infant feeding data using the following checks for logic and consistency, outliers, and missing data.

(a) Logic and Consistency Checks. Compared to outliers, erroneous data within the expected range are more difficult to distinguish from valid data (115). In this study, given the logic behind maternal responses to infant feeding practices, two types of checks were performed as below. First, researchers performed cross-checks on the same variable measured on repeated occasions using different questions. For example, alerts were triggered when the child was reported as being currently formula-fed but not fed formula in the past 7 days based on responses to two separate questions. The second type was pairwise and multivariable cross-checks among variables that should be internally related. An example for pairwise cross-checks was to compare the ages when formula feeding started and stopped. Flags were created if the age started was later than the age ended. An example for multivariable cross-checks was to examine whether those breast-bottle fed children (categorized using multiple questions shown in Table 2.1) were reported as being fed formula only or both formula and breast milk during the mixed feeding period. Obviously, maternal report of feeding formula only was inconsistent with the practice of mixed feeding.

In short, the logic and consistency checks are essential to data cleaning and facilitate the identification of suspected erroneous data which otherwise would be difficult to locate using regular statistical methods for outlier checks as discussed below.

In addition, data cleaning is highly recommended in the early stage of a study in order to provide feedback about data error sources to investigators and develop study-tailored quality control strategies for data collection.

(b) *Outlier Detection.* Screening approaches for outlier detection can be statistical and/or empirical. Statistical packages usually have functions to perform univariate outlier detection, such as frequency checks using histograms or frequency distribution tables; range checks using box plots and stem-and-leaf plots; and central tendency and dispersion checks calculating the mean, median, and standard deviation for example. Also, multivariate outlier detection with the assistance of graphics can assist outlier detection via data visualization. For example, a scatter plot stratified by child's age group (Figure 2.1) and Bland-Altman plot (Figure 2.2) of two related measures visually identified potential outliers which could be difficult to detect using univariate statistical methods.

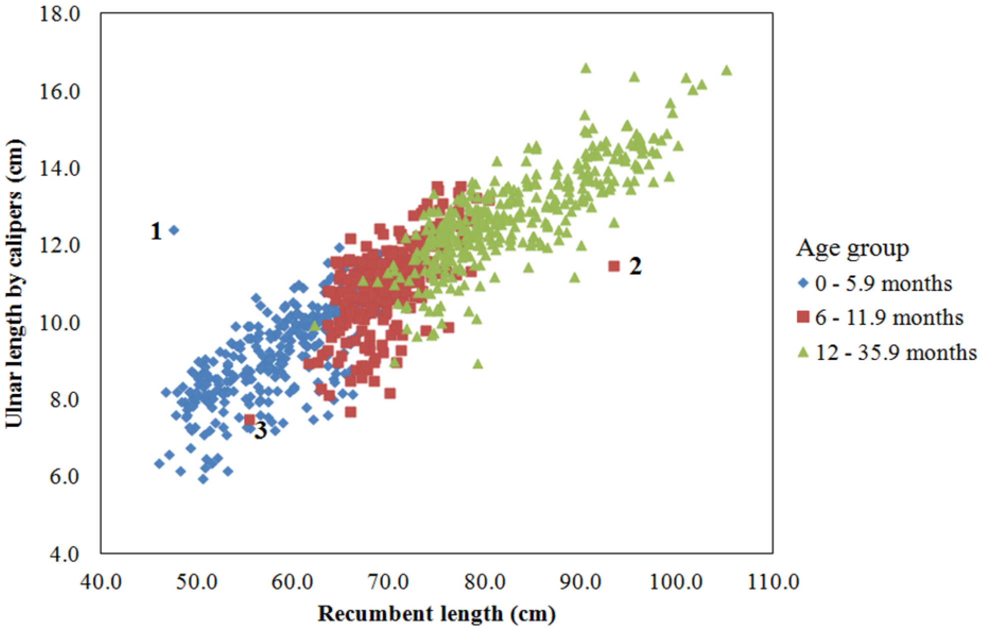

Figure 2.1 An example of multivariate outlier detection using a scatter plot of ulnar length versus recumbent length by age group. Potential outliers are flagged with numbers.

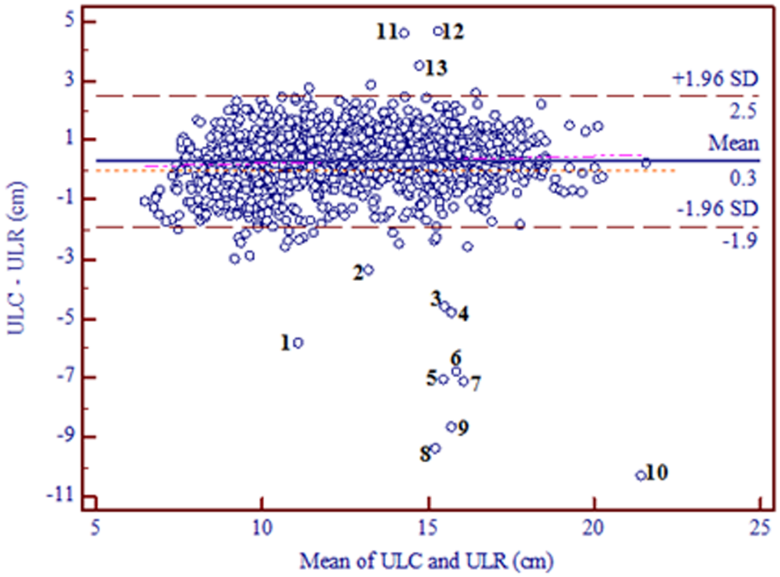

Figure 2.2 An example of multivariate outlier detection using a Bland-Altman plot of ulnar length measured by caliper versus ulnar length by rulers. Potential outliers are flagged with numbers. ULC, ulnar length by caliper; ULR, ulnar length by ruler.

Outlier screening can also be based on researchers' knowledge and experience. One example in our study is outlier checks on maternal-reported birthweight of the child. The quality of maternal-reported birth data could be compromised by recall bias and conversion errors due to different metric units used by mothers of different ethnicities. For example, a birthweight of 5000 g would be about 3.5 standard deviations above the reported national mean (mean = 3389 g, standard deviation = 466 g) (116) and hence would be flagged as an unusual observation. In order to screen further, it was necessary to take relevant maternal characteristics into consideration. If the infant mentioned above was born to a mother who had severe anemia and smoked frequently during pregnancy, it would trigger an alert because these maternal complications are risk factors for low birthweight (117). In addition, if other data such as newborn's birth length were available, further reviews of the data would provide helpful information for consideration as birthweight and length are positively correlated. For example, an infant boy with a high birthweight of 5000 g and a short birth length of 45 cm would be a potential outlier based on the weight-for-length growth chart (118).

(c) Missing Data Preprocessing. Missing data are a common issue for most studies. Before statisticians apply approaches to address this issue in the analysis phase, it is important to understand why data are missing and be aware of the approaches to avoid missingness. Besides participants' failure to provide responses, missing values could be due to incomplete data forms sent by study coordinators, data entry errors, or interruptions of data transmission from informatics to personal computers, which could

be avoided by re-sending forms, correcting entry errors, and careful data transmission, respectively. In addition, missing data may be avoided by abstracting the same or relevant information collected from different questions on other forms. For instance in this study, child’s birth date should be reported on both anthropometric measurement form and maternal questionnaire. In case one was missing, the same information reported in the other source could be used to fill in the blank.

Step 4: Data Editing. Following data cleaning, researchers need to clarify and determine whether the suspected data errors or issues detected at step 3 are real errors, true extremes, or unable to be verified. In this study, authors applied diagnostic procedures as follows. First, researchers checked for data entry accuracy and corrected entry errors. Second, for data errors that did not pass checks for entry accuracy (which could be due to errors in data collection), researchers contacted the corresponding study site coordinators for subject requerying. If no further confirmation or requery was obtained, the suspected erroneous variables were re-coded as missing values. Finally, data editing rules were established according to the consensus reached in laboratory meetings based on the investigators’ research experience and knowledge. All the comments, flags, and corrections were documented accordingly.

Step 5: Documentation in a Data Dictionary. Clear and detailed documentation for data preprocessing is important for data integrity and serves as a useful tool for statistical analysis and interpretation. Different from a data code book described above, a data dictionary has detailed documentation on suspected errors including: diagnostic strategies for data cleaning; justification and rules for data editing; decisions for error treatment; and information on dates and personnel involved with specific data preprocessing steps. Such information from the data dictionary should also be reported in the final publication as an essential component of quality and validity assessment as suggested by the American Statistical Association (110). Furthermore, the data dictionary provides important feedback about data error sources to study investigators, which could assist researchers in improving research protocols and training procedures and in harmonizing data across studies to improve data quality control.

RECOMMENDATIONS TO CONDUCT QUALITY CONTROL IN DATA ACQUISITION AND PREPROCESSING

Although the importance of data acquisition and preprocessing in terms of quality control and assessment is well recognized, these concepts are rarely introduced in statistics classes. Some practical recommendations as a beginners' guide are provided for those who are interested in adding these concepts in a statistics curriculum.

Conduct a Case Study

Students new to the topic of data acquisition and preprocessing might be challenged by the question "Where and what to start with?" Given data preprocessing issues vary considerably by subject-specific research area, it is advocated that instructors begin by selecting research topics and associated datasets of interest and conduct a case study in class. For example, the NCS formative research discussed in this chapter could be an example of an in-class case study in epidemiological research. Instructors can either lecture about the case study or conduct interactive class discussions with students. Outside speakers with access to an actual dataset and experiences in data acquisition and preprocessing are recommended to be invited for an in-class talk as well.

Assign a Data Preprocessing Exercise

To better motivate and involve students in real data preprocessing practices, it is recommended that a class project or assignment for data preprocessing be supplemented with case study discussions. Real case exercises give students an opportunity to better understand the components of preprocessing through examples of data collection. Within the context of a specific research question, students may need to design and implement tailored preprocessing approaches that might have not been discussed in this chapter. For purposes of practicing data preprocessing using a real, unprocessed dataset, a series of five key steps can be provided to students as guidelines (Table 2.2). It is important for students and researchers to realize that each step alone is insufficient while the entirety of steps creates a platform for data quality control via optimal data acquisition and systematic preprocessing approaches.

Table 2.2 Practical approaches and guidelines to implement data preprocessing using real, unprocessed data

Steps	Objectives	Data preprocessing guidelines
1. Get to know the study	(1) Assess the quality and integrity of collected data by looking into data acquisition process (2) Get a sense of potential bias or data issues in the dataset	(1) Learn details about the study: • What is the research question and study design? • What are the subject recruitment criteria? • How and what data are collected? (2) Check whether subjects in the dataset meet the eligibility criteria. If not, exclude them and document the changes in the *data dictionary*.
2. Assess the validity of variable coding	Ensure the variables of interest are coded in a meaningful and clear language	(1) Check how variables are coded and assess if the coding is appropriate according to the sampling distribution, specific research question, and coding methods used in related literature. (2) If the current coding is inappropriate, recode the variable and document justifications for recoding in the *data code book*.
3. Assess data entry accuracy	Make sure information in the dataset is valid and accurate	(1) If original data are accessible, review and verify data entry (assuming data are already entered and electronically available). (2) If data entry errors are detected, correct the invalid entries and document the changes or comments in the *data dictionary*.
4. Perform data cleaning	Detect suspected data errors	(1) Perform logic and consistency checks: • Cross-check the same variable collected and measured using different questions. • Conduct pairwise and multivariable cross-checks among variables that are internally related. (2) Review for outliers: • Statistical methods: univariate (frequency, range, and central tendency and dispersion) and multivariate checks (graphics plotting multiple related measures). • Empirical methods based on related knowledge or experience. (3) Look for missing data and assess if missingness can be avoided. (4) Document suspected data errors in the *data dictionary*.
5. Edit identified data errors	Improve data quality by addressing data errors	(1) Re-check data entry accuracy and correct errors if necessary. (2) Requery study coordinators or participants for problematic data. (3) Edit data for suspected errors: deletion, correction, or no change. (4) Document data editing rules and decisions in the *data dictionary*.

CONCLUDING REMARKS

In a typical statistics curriculum, the primary focus is usually on study design, statistical theories and methods, and the use of statistical packages with either a brief or even absent description of data acquisition and preprocessing. This chapter uses a real life example to illustrate the process of data acquisition with respect to quality control, and the need for and approaches to data preprocessing in an epidemiological study involving human subjects. It also demonstrates data preprocessing as a pivotal component in the interactive feedback system among study design, data acquisition, statistical analysis, and publication (Figure 2.3). Each component in the system has a unique contribution in terms of improving overall data quality control and cannot be removed. This real case scenario may provide insights into data quality control via optimal data acquisition and systematic data preprocessing for teachers and students in applied statistics related disciplines. It is advocated that instructors incorporate data acquisition and preprocessing components into current statistics curricula by introducing a case study discussion or lecture and supplement it with a real case data preprocessing exercise. It is hoped that data acquisition and preprocessing can serve to more closely bridge the phase of study design to the phase of statistical analysis, and ultimately help both investigators and statisticians to achieve optimal conduct, quality control, data analysis, and interpretation of a study.

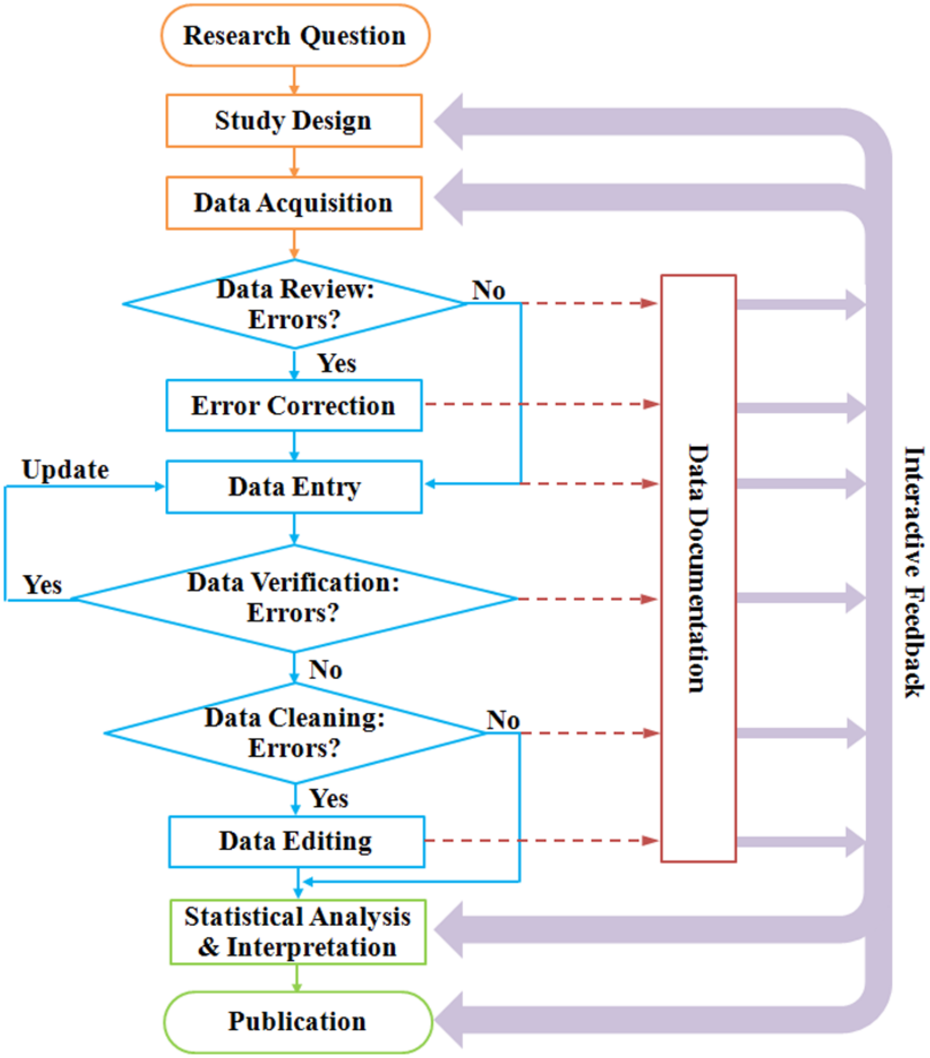

Figure 2.3 The interactive feedback system including study design, data acquisition, preprocessing, statistical analysis, and publication.

Chapter 3: Predictive Models for Exclusive Breastfeeding Initiation and Duration

ABSTRACT

Maternal lactation performance varies across populations, yet the relative impact of maternal sociodemographic and reproductive factors and child's birth characteristics on disparities in exclusive breastfeeding (XBR) is not well known. This chapter aimed to develop predictive models for XBR initiation and duration that identify women at risk for none or poor lactation performance. Infant feeding data were obtained from women with infants and children aged <6 years in a multi-center multi-ethnic cross-sectional study in the US (2011–2012). Discriminant function analyses were used to develop and validate predictive models for XBR initiation and duration ≥6 months. Mixed-effects multivariate logistic regression analyses were completed to calculate adjusted odds ratio (OR) for factors associated with XBR initiation and duration. Among 1471 children, 76.6% of them were ever breastfed and 15.3% exclusively breastfed for ≥6 months. Maternal sociodemographics (education level, marital status, nativity, and age at childbirth) had larger standardized discriminant function coefficients than birth characteristics and perinatal factors in models predicting ever XBR and XBR ≥6 months. Multivariate logistic regression analyses demonstrated significant ethnic disparities in XBR performance. Non-Hispanic Black mothers were less likely to ever XBR or extend it to 6 months versus non-Hispanic White counterparts. The areas under the receiver operating characteristic curves for models predicting ever XBR and XBR ≥6 months were 0.88 (95% CI 0.85, 0.91) and 0.90 (95% CI 0.88, 0.93), respectively. Maternal age at childbirth was consistently associated with ever XBR, XBR ≥6 months, and BrBot subgroups. In conclusion, maternal sociodemographics have greater discriminating abilities in predicting XBR performance than birth and perinatal factors. Findings suggest the importance of educational, clinical, and social support to promote XBR in mothers with sociodemographic factors predictive of none or poor XBR outcomes.

Keywords: Birth characteristics; breast-bottle feeding; discriminant analysis; exclusive breastfeeding; exclusive bottle feeding; maternal perinatal factors; prediction model.

INTRODUCTION

Breastfeeding has both short-term and long-term health benefits for mothers and infants (119, 120). Indeed, both the WHO and the American Academy of Pediatrics (AAP) recommend infants should be exclusively breastfed for 6 months with introduction of complementary foods and continued breastfeeding thereafter (75, 121). Despite the rising rates of breastfeeding in the US (122), the latest reported rates of ever breastfeeding (76.9%) and exclusive breastfeeding (XBR) for 6 months (16.3%) among births in 2009 (123) are lower than the Healthy People 2020 Targets of 81.9% and 25.5%, respectively (124). However, it is worth noting that the reported overall rates obscure sociodemographic and cultural disparities in breastfeeding practices (125-127). Therefore, it is important for healthcare and public health professionals to understand how these disparities influence mothers' lactation performance.

In addition, the trend of mothers returning to work within a short time period after childbirth is on the rise in the past decades (128). Cumulatively, 44.2% of new mothers returned to work by 3 months after childbirth in 2005-2007, compared to 32.9% in 1981-1984 (129). Consequently, some mothers who initiate XBR may have to supplement breast milk with formula or completely switch to formula feeding. Studies investigating factors associated with breast-bottle feeding (BrBot) are warranted to help health practitioners identify women at risk of early determination of XBR.

Despite a rich body of literature on the factors associated with breastfeeding initiation and duration (43-47), determinants of XBR initiation and duration have been less studied (130-138). Moreover, comparisons across previous studies are limited by inconsistent or unclear definitions of XBR, failure to adjust for potential confounding factors, and varied sociocultural context. For example, among three studies assessing factors associated with XBR using nationally representative survey data in the US (134-136), one failed to apply the WHO recommendation of XBR for 6 months (136); all three collected breastfeeding data from survey respondents rather than exclusively from biological mothers; and none included maternal reproductive factors (i.e., prepregnancy BMI, gestational weight gain, and pregnancy complications) as covariates, which are associated with XBR (46, 139). Additionally, in spite of factors identified to be associated with XBR, there is a paucity of data on the relative extent to which these factors contribute to the performance of XBR initiation and duration ≥6 months. Knowledge of the relative impact of XBR determinants is of particular importance in formulating effective public health initiatives to promote better compliance to the WHO and AAP recommendation.

Therefore, the objectives of this study were to 1) develop predictive models for ever XBR since birth and XBR ≥6 months; 2) compare the relative discriminant ability of predictors for ever XBR and XBR ≥6 months; and 3) explore factors associated with BrBot subgroups by the relative frequency of each feeding in a multi-ethnic sample of mother-child dyads in the US.

METHODS

Study design and population

Data for this study were collected during the NCS Formative Research in Anthropometry, a cross-sectional study across eight study sites in the US (2011-2012). Mother-offspring dyads were recruited at daycare centers, churches, clinics, and community centers by study coordinators, word of mouth, and referral. Eligibility criteria included: mothers aged 18-49 years and non-institutionalized; and children who were aged 0-5.9 years, healthy, of the same ethnicity as and living with the mother, had not suffered from an acute illness associated with weight loss within the past week, and were afebrile at the time of study visit. Among 1634 eligible dyads, this analysis only included those with complete infant feeding data (*n* = 1538). If more than one infant/child of the same mother was recruited, the youngest one was included in this analysis to reduce the cluster effect from shared infant feeding practices in children of the same mother (*n* = 1471). Data preprocessing approaches applied in this study were reported previously in Chapter 2 (140). This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Institutional Review Boards at the University of Texas at Austin and all other seven participating sites. Written informed consent was obtained from mothers.

Infant feeding practices

During the study visit, trained researchers administered a questionnaire to the mother about socio-demographics, child's early life factors, and maternal reproductive characteristics. As part of the questionnaire, items about infant feeding practices were answered from a series of open-ended and multiple-choice questions (Figure 3.1). Specifically, infant feeding practices were classified as: 1) XBR (by the WHO definition) (76): if the mother reported she had only fed the child breast milk (including milk expressed or from a wet nurse) without anything else except for drops and syrups containing vitamins, minerals, and medicines; 2) BrBot: if the mother reported breastfeeding and formula-feeding her child at the same time; or 3) exclusive bottle-feeding (XBot): if the mother reported she had fed her child formula (or any other non-human milk liquid) from a bottle but never fed breast milk. The BrBot group was further stratified into three subgroups based on the question about the relative frequency of breast milk versus formula feedings to the child: 1) breast milk > formula; 2) breast milk = formula; and 3) breast milk < formula. Duration of XBR was defined as the age before introduction of anything else other than breast milk if the child was exclusively breastfed since birth. If the child was still being breastfed at the time of interview, the age when breastfeeding stopped was re-coded as the age of the child at study visit.

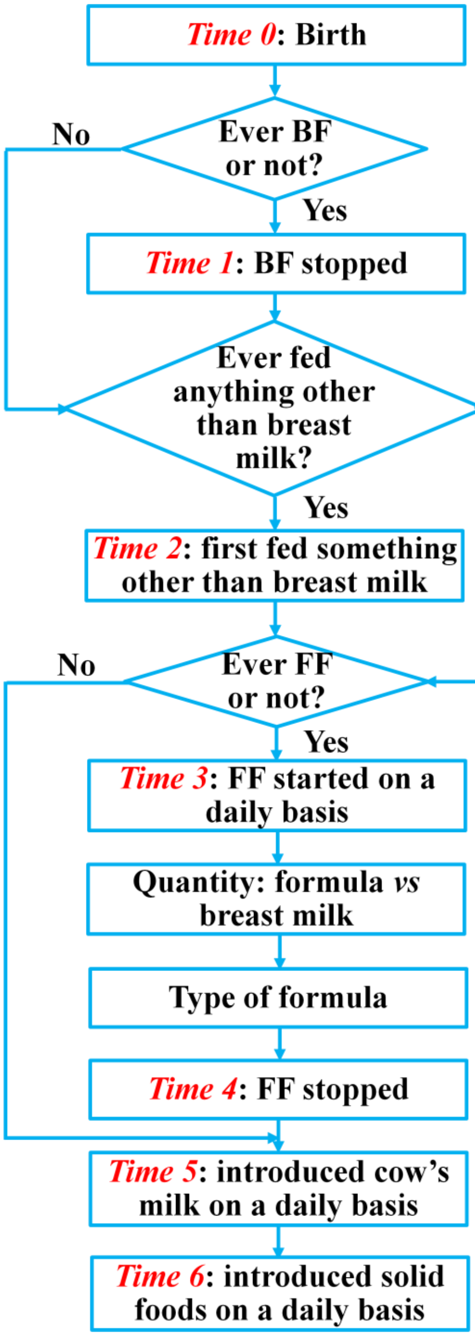

Figure 3.1 Development of an infant feeding algorithm based on maternal recalls. BF: breastfeeding; BM: breast milk; BrBot: breast-bottle feeding; FF: formula feeding; XBot: exclusive bottle feeding; XBR: exclusive breastfeeding.

Covariates

Based on previous literature and knowledge, factors considered as potential determinants of XBR outcomes included: 1) maternal characteristics: ethnicity, education level, marital status, nativity, employment status at the time of the interview, age at the index child's birth, prepregnancy BMI (self-reported prepregnancy weight [kg]/height[m]^2), weight gain and smoking during pregnancy, and pregnancy complications (gestational diabetes, high blood pressure, pre-eclampsia/eclampsia, and only proteinuria); 2) child characteristics: age, sex, birth year, birthweight, gestational age, and birth order; and 3) household number. These variables were collected via maternal-reported responses from the interviewer-administered questionnaire.

Statistical analysis

Descriptive statistics of continuous and categorical variables were presented as the mean (SD) or frequency, respectively. Bivariate associations between infant feeding practices (XBR, BrBot, and XBot) and maternal/child factors were assessed by ANOVA or the χ^2 test.

Discriminant analysis for ordinal responses was used to develop predictive models discriminating mothers who initiated XBR since birth or maintained XBR for 6 months versus those who initiated XBot since birth, respectively. Factors associated with infant feeding practices in the bivariate analyses meeting the confounder selection criteria (P <0.25) (141) were included in the initial multivariate discriminant model for ever XBR since birth, along with child's birth year (range 2005-2012) based on the secular trend of increasing XBR rates over time(122). Stepwise selection using entry (*P* = 0.10) and removal (*P* = 0.05) criteria were then used to identify variables that contributed significantly to the final discriminant function for XBR since birth. These factors were also used to build a predictive model for XBR duration ≥6 months. Of particular note, although discriminant analysis is less preferable than logistic regression for classification due to the difficulty in meeting the multivariate normality assumption (142), it provides an approach to assess the relative discriminant ability of predictors by comparing the size of standardized canonical discriminant function coefficients. In addition, these standardized coefficients and their 95% CIs were derived based on 1000-fold bootstrap samples, which can improve model robustness against sensitivity to multivariate normality (143).

To assess the independent associations of predictors included in the final discriminant functions with the endpoints of XBR since birth, XBR duration ≥6 months, and BrBot subgroups (ie, breast milk > formula, breast milk = formula, and breast milk <formula), mixed-effects logistic regression with study center as a random effect was used to estimate the unadjusted and adjusted ORs of each endpoint. Only variables reaching *P* <0.25(141) in univariate analysis were included in the multivariate logistic regression model. Because maternal reproductive factors and child characteristics at birth are often correlated, variance inflation factors (VIFs) were calculated to assess the multicollinearity of covariates. Results indicated no concerns about multicollinearity with

VIFs all below 2.5. The area under the curve (AUC) statistic of the receiver operating characteristic curve was calculated to quantify the ability of the multivariate logistic models to discriminate mothers who exclusively breastfed the child since birth or for ≥6 months from those who exclusively bottle-fed the child since birth. All analyses were conducted with IBM SPSS 20 (IBM Corp, Armonk, New York). Statistical significance was set at a 2-tailed $P < 0.05$.

RESULTS

Study population

Among the 1471 children included in this analysis, 256 (17.4%) were exclusively breastfed since birth, 871 (59.2%) exclusively bottle-fed, and the remainder (23.4%) mixed fed with both breast milk and formula (Table 3.1). Of the 1127 (76.6% of 1471) mothers who ever breastfed, the rates of XBR ≥6 months were 15.3%. Infant feeding practices varied by several maternal and child characteristics. Compared to mothers in the XBot group, mothers in the XBR group were more likely to be non-Hispanic White (NHW), have more than a high school education, be partnered (married or living with a partner), foreign-born, and older at the child's birth, have a lower prepregnancy BMI, fewer pregnancy complications, not smoked in pregnancy, and an index child weighing more at birth. Also, more BrBot mothers were employed at the time of interview compared to XBR or XBot mothers.

Discriminant function analyses

The variable reduction procedure via stepwise selection resulted in a final predictive model of ten variables for initiating XBR since birth. These variables were ordered by the size of standardized canonical discriminant coefficients (Table 3.2). Maternal education had the greatest discriminating ability while prepregnancy BMI had the least impact on predicting mothers in the XBR group versus the XBot group. Similarly, the same variables except child's birth year were in a final predictive model discriminating mothers who extended XBR to 6 or more months from those who initiated XBot since birth.

Mixed-effects logistic regression analyses

Logistic regression analyses revealed associations of individual variables with breastfeeding outcomes (i.e., ever XBR since birth, XBR duration ≥6 months, and BrBot subgroups). Non-Hispanic Black (NHB) mothers were least likely to initiate XBR since birth or prolong it to 6 or more months in either unadjusted or adjusted analyses compared to their NHW counterparts (Table 3.3). In unadjusted analyses, the likelihoods of initiating XBR since birth were higher among mothers who had more than a high school education, who were married or living with a partner, born in foreign countries, older at childbirth, and whose index child was born more recently (range 2005-2012); whereas the likelihoods were lower among those who were obese before pregnancy, had more than one pregnancy complication, smoked in pregnancy, and had an index child born <2500 g. These maternal and child factors were also independently associated with ever XBR in the adjusted model, except for maternal prepregnancy obesity and pregnancy complications.

Overall, the ORs of factors associated with XBR ≥6 months were of similar magnitude and statistical significance as those for ever XBR. However, consistent with the results from the discriminant function analysis, birth year was significantly associated with ever XBR but not with XBR duration in either unadjusted or adjusted analyses. In addition, the significant associations of maternal nativity, prepregnancy BMI, and pregnancy complications with XBR duration in the crude analysis did not remain in the adjusted model. The AUC statistics of the receiver operating characteristic curves for initiating XBR since birth and XBR ≥6 months based on the multivariate logistic regression models were 0.88 (95% CI 0.85, 0.91) and 0.90 (95% CI 0.88, 0.93), respectively (Figure 3.2a and 3.2b).

Among 871 children who were breast-bottle fed, the majority was fed less breast milk than formula, while 191 were fed more breast milk than formula and 154 were fed the two milks equally. Factors associated with feeding the child “breast milk > formula” differed from those associated with “breast milk = formula” (Table 3.4). Mothers who were married or living with a partner were more likely to feed the child more breast milk than formula rather than feeding the two milks equally. Maternal age at childbirth was positively associated with increased likelihoods of both “breast milk > formula” and “breast milk = formula”. Although mothers who were obese before pregnancy were 51% less likely to feed the child more breast milk than formula compared to their normal weight counterparts after adjusting for covariates, the ORs of “breast milk = formula” did not vary by prepregnancy BMI. For children born more recently (range 2005-2012), their mothers were 27% more likely to feed the two milks equally versus feeding more formula after adjusting for covariates.

DISCUSSION

Among the 1471 mothers of children born in 2005-2012 in this study, 76.6% reported ever breastfeeding and 15.3% reported XBR for 6 or more months, which are comparable to the reported rates of 76.9% and 16.3% for births in 2009 based on nationally representative survey data (123). The predictive models for ever XBR and XBR $\geq$6 months included maternal sociodemographic factors (education level, marital status, nativity, and age at childbirth) with greater discriminating abilities than child characteristics (birthweight) and perinatal factors (complications and smoking during pregnancy and prepregnancy BMI). Amongst the predictors, obese women before pregnancy and pregnant smokers are women who can be targeted for strategies to promote breastfeeding from their first prenatal visit, whereas those who experience complications in pregnancy can be targeted upon diagnosis. Additionally, although most sociodemographic factors are difficult to modify, identification of these predictors provide potential targets for effective interventions. For instance, breastfeeding education and counseling provided to mothers with low educational attainments, clinical and familial support offered to single mothers, or a combination of both strategies might be used to promote XBR. Thus the predictive models are empirically driven by variables with strong potential for public health interventions.

There could be several reasons why less educated, young, and single mothers were less likely to initiate or prolong XBR to 6 or more months. Previous data show 66.3% of mothers with a bachelor’s degree or more enjoyed paid leave compared to

18.5% of mothers with less than a high school education level (129). Educated and older mothers were more likely to be aware of the WHO/AAP recommendation of XBR for 6 months and had greater intention to meet the recommendation (144). Also, given that paternal knowledge of breastfeeding recommendations (145), preference for breastfeeding (146), and ability to help mothers prevent and manage lactation difficulties (147) are positively associated with the likelihoods of breastfeeding initiation and duration, lack of such support from a spouse or partner may compromise lactation performance in single mothers. Indeed, most of these maternal sociodemographic characteristics are difficult to ameliorate; however, these factors might be indicators of the underlying psychosocial mechanisms of poor lactation performance. Future research investigating determinants of these related psychosocial factors is important to better our understanding in structuring effective interventions.

Our results revealed substantial ethnic disparities in infant feeding practices. In this study, NHB mothers were least likely to initiate XBR since birth or prolong the duration for 6 or more months among all ethnic groups. These findings are consistent with previous results of nationally representative surveys in the US (135, 136, 148). In contrast with previous observations, Hispanic mothers were less likely to ever exclusively breastfeed or extend XBR to 6 months compared to their NHW counterparts. This could be due to the larger number of Hispanic participants in our study, especially at one study center where 79.8% of all participants were Hispanic. Compared to NHW mothers, Hispanic women in the study were younger at the birth of the index child, more obese before pregnancy, and less educated (data not shown). As shown in the predictive models (Table 3.2), these characteristics are negatively associated with XBR since birth or XBR ≥6 months. In addition, the reasons behind the ethnic disparities could also be behavioral, cultural, and/or psychosocial. A study of low-income mothers in the US revealed Hispanic mothers were more likely to report perceptions of infant breast refusal and milk insufficiency than their non-Hispanic counterparts; while NHW and NHB mothers were more likely to cease breastfeeding due to breast discomfort or pain (149). Thus, future breastfeeding promotion programs incorporating both identified determinants in our study and potential psychosocial factors are warranted to optimize intervention strategies.

As reported previously, high prepregnancy BMI was associated with poor lactation performance (150-153). Likewise, our results showed prepregnancy obesity was associated with reduced likelihoods of ever XBR and XBR ≥6 months in unadjusted analyses. However, the association did not remain after adjusting for other covariates in the model. Similarly, pregnancy complication was associated with XBR outcomes in the unadjusted but not in the adjusted model. These differences between the crude and adjusted models could be due to the intercorrelation between the prepregnancy BMI and pregnancy complications (data not shown; Spearman's rho = 0.24, P <0.01). Indeed, obese women have a higher risk of pregnancy complications such as gestational diabetes, hypertension, and pre-eclampsia (154-156). However, few studies have included pregnancy complications as a potential confounder of the association between maternal prepregnancy obesity and breastfeeding outcomes (46, 138, 157). Kitsantas and Pawloski reported an independent effect of prepregnancy overweight/obesity on breastfeeding initiation only among mothers with pregnancy and/or birth complications but not among healthy ones (157). Collectively, these findings suggest pregnancy complication is an important covariate to address when assessing the association between maternal prepregnancy BMI and breastfeeding/XBR outcomes.

In agreement with previous observations on XBR determinants (134, 136, 158), our results also indicated that maternal smoking during pregnancy and child's low birthweight (<2500 g) decreased the likelihood of ever XBR and XBR for 6 months, respectively. A review of maternal smoking and breastfeeding suggested psychosocial factors rather than physiological ones are largely responsible for poor lactation performance in mothers who smoked (159), who perceive smoking as a barrier to breastfeeding (160) and are less likely to seek help for breastfeeding problems (161). Thus, efforts to address these challenges are needed in XBR promotion initiatives. As for child's low birthweight, one major contributor is preterm birth (162). The separation between mothers and their hospitalized infants in the neonatal intensive care unit could contribute to the difficulty in initiating XBR. Given the environment of the neonatal intensive care unit, special clinical support is of upmost importance to promote XBR in this particular population.

Our study also revealed immigrant women were more likely to exclusively breastfeed the child since birth but not necessarily for 6 or more months compared to US-born women. Similarly, the 2007 National Survey of Children's Health reported increased likelihood of ever breastfeeding but not 6-month XBR in foreign-born women relative to US-born women (134). It is speculated that whilst cultural traditions and beliefs inherent to the mother's origin could influence the mothers' decision to initiate XBR, social support or the lack thereof from families and health professionals would influence the duration of XBR. Future studies to identify barriers to prolonging XBR among women who initiate XBR in a culturally sensitive approach are warranted.

In addition, the factors associated with BrBot subgroups in this study differed from those associated with XBR outcomes, whereas older maternal age at childbirth was the only factor consistently associated with ever XBR, XBR $\geq$6 months, and BrBot subgroups. Given that pediatricians in 2004 versus 1995 were five times more likely to recommend against breastfeeding for mothers who were perceived as "too young or immature" (163), it is of particular importance to provide appropriate clinical support to young mothers.

There are a number of strengths of our study. To our knowledge, it is the first study exploring factors associated with BrBot subgroups, which contribute to better understanding of mothers who feed both breast milk and formula to different extents. Also, this study applied the WHO definition of XBR and recommendation of XBR for 6 months based on breastfeeding data obtained from biological mothers. In discriminant function analysis, a comparison of standardized discriminant coefficients revealed the relative contribution and discriminant ability of each determinant, which is of great significance in designing effective public health initiatives to address disparities in lactation performance.

However, there are several limitations to the study. First, infant feeding behaviors were based on maternal recalls; thus, recall bias may exist. Li et al (164) reported maternal recall on breastfeeding initiation and duration were valid and reliable especially within 3 years after the practice; however, our study included children up to 5.9 years of age. In addition, maternal recall for food and fluids other than breast milk are less accurate (164, 165), which could compromise the reliability of data on XBR performance. Second, some factors which may influence mother's choice of infant feeding practices are not available in this study, e.g. maternal prior lactation experience, knowledge of breastfeeding recommendations and benefits, mental health, social support, and maternity leave during the infant feeding period. In addition, besides breastfeeding directly from the breast, recent data predominantly in the US Caucasian population revealed that infants were also frequently fed expressed breast milk from the bottle (166, 167). Future research to investigate the determinants of not only the type and duration of milk fed to the child but also the mode of milk delivery in a multi-ethnic population is warranted. Finally, the study population was not sampled to be nationally representative which would limit generalizability.

In conclusion, the present study revealed predictive models for ever XBR and XBR ≥6 months. Maternal sociodemographic factors had greater discriminating abilities to predict ever XBR and XBR ≥6 months compared to child birth characteristics and maternal perinatal factors. Maternal age at the birth of the index child was the consistently associated with ever XBR, XBR ≥6 months, and BrBot subgroups. Our findings can help healthcare and public health professionals identify mothers at increased risk of not initiating XBR, early termination of XBR, and breastfeeding to a less extent among BrBot mothers, with an ultimate goal to help reduce disparities in lactation performance in different populations.

Table 3.1 Characteristics of the study population by infant feeding practices[1]

	XBR (*n* = 256)	BrBot (*n* = 871)	XBot (*n* = 344)	*P* value[2]
Maternal characteristics				
Ethnicity, %				<0.001
Non-Hispanic White	40.6	18.0	9.9	
Hispanic	32.4	49.7	43.0	
Non-Hispanic Black	11.0	23.3	44.2	
Other	16.0	9.0	2.9	
Education, %				<0.001
< High school	11.7	18.4	28.9	
= High school	8.6	17.9	30.3	
> High school	79.7	63.7	40.8	
Employed, %	43.9	50.5	43.1	0.036
Marital status (single mother), %	11.3	27.2	50.0	<0.001
Nativity (US born), %	70.8	70.8	87.5	<0.001
Age at childbirth, y, mean ± SD	29.9 ± 5.3	28.6 ± 6.2	26.6 ± 6.4	<0.001
Prepregnancy BMI, kg/m^2, mean ± SD	25.3 ± 6.7	26.3 ± 6.4	27.4 ± 6.9	<0.001
Gestational weight gain, %				<0.001
<14 lbs	9.5	15.2	21.9	
15-19 lbs	9.1	11.4	9.8	
20-29 lbs	27.7	29.2	26.9	
30-40 lbs	38.7	27.8	26.0	
>40 lbs	15.0	16.4	15.4	
Pregnancy complications (≥1), %	20.7	23.7	31.8	0.003
Smoking during pregnancy, %	1.6	4.7	12.0	<0.001
Primiparous, %	39.5	39.0	35.1	0.270
Mother-child dyad characteristics				
Household number, mean ± SD	4.5 ± 1.6	4.4 ± 1.5	4.6 ± 1.8	0.410
Child characteristics				
Age, y, mean ± SD	1.8 ± 1.7	2.0 ± 1.7	2.1 ± 1.7	0.055
Males, %	52.0	51.2	53.2	0.763
Birthweight, kg, mean ± SD	3.4 ± 0.6	3.2 ± 0.6	3.1 ± 0.6	<0.001
Preterm birth (<37 wk), %	9.0	10.3	14.0	0.059

[1] *n* = 1471. BrBot, breast-bottle feeding; XBot, exclusive bottle-feeding; XBR, exclusive breastfeeding.
[2] ANOVA for continuous variables and χ^2 tests for categorical variables.

Table 3.2 Standardized canonical discriminant function coefficients of factors predicting ever exclusive breastfeeding since birth and exclusive breastfeeding duration ≥6 months[1]

	Any XBR[2]	XBR ≥6 months[3]
	Coefficient (95% CI)	Coefficient (95% CI)
Maternal education (> high school)	0.50 (0.35, 0.63)	0.49 (0.35, 0.62)
Marital status (single mother)	0.42 (0.29, 0.55)	0.38 (0.24, 0.50)
Maternal nativity (foreign born)	0.28 (0.11, 0.42)	0.24 (0.05, 0.42)
Maternal age at childbirth, y	0.27 (0.13, 0.41)	0.30 (0.16, 0.44)
Child's birthweight, g	0.25 (0.10, 0.39)	0.29 (0.16, 0.42)
Child's birth year, years	0.24 (0.10, 0.38)	0.004 (-0.13, 0.16)
Pregnancy complications (none)	0.21 (0.05, 0.35)	0.19 (0.03, 0.35)
Maternal ethnicity (non-Hispanic)	0.18 (0.03, 0.33)	0.26 (0.11, 0.40)
Smoking during pregnancy (no)	0.17 (0.04, 0.29)	0.14 (0.01, 0.26)
Maternal prepregnancy BMI, kg/m^2	-0.16 (-0.32, -0.01)	-0.26 (-0.41, -0.11)

[1] XBR, exclusive breastfeeding.

[2] Sample size for the model predicting ever XBR (*n* = 256) versus exclusively bottle-feeding (*n* = 344) is 600.

[3] Sample size for the model predicting XBR ≥6 months (*n* = 172) versus exclusively bottle-feeding (*n* = 344) is 516.

Table 3.3 Unadjusted and adjusted odds ratios of factors associated with ever exclusive breastfeeding since birth and exclusive breastfeeding duration[1]

	Ever XBR		XBR ≥6 months	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[2]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[2]
Maternal ethnicity				
Non-Hispanic White	1.00	1.00	1.00	1.00
Hispanic	0.19 (0.10, 0.34)[5]	0.27 (0.13, 0.56)[5]	0.14 (0.07, 0.26)[5]	0.28 (0.12, 0.63)[3]
Non-Hispanic Black	0.07 (0.04, 0.13)[5]	0.12 (0.06, 0.25)[5]	0.05 (0.02, 0.10)[5]	0.11 (0.05, 0.25)[5]
Other	1.10 (0.44, 2.79)	0.77 (0.24, 2.45)	0.88 (0.32, 2.37)	0.85 (0.25, 2.88)
Maternal education				
< High school	1.00	1.00	1.00	1.00
High school graduate or equivalent	0.75 (0.39, 1.42)	0.89 (0.42, 1.87)	0.61 (0.24, 1.48)	0.63 (0.22, 1.77)
> High school	4.37 (2.64, 7.24)[5]	2.99 (1.54, 5.80)[4]	5.76 (3.02, 11.00)[5]	3.41 (1.48, 7.83)[4]
Married/ living with a partner	6.09 (3.82, 9.72)[5]	2.38 (1.36, 4.15)[4]	6.17 (3.54, 10.74)[5]	2.22 (1.14, 4.33)[3]
Maternal nativity (foreign born)	2.54 (1.61, 4.03)[5]	2.44 (1.29, 4.59)[4]	2.15 (1.25, 3.69)[4]	2.01 (0.91, 4.44)
Maternal age at childbirth, years	1.07 (1.04, 1.11)[5]	1.05 (1.01, 1.10)[3]	1.08 (1.04, 1.12)[5]	1.07 (1.02, 1.12)[4]
Maternal prepregnancy BMI, kg/m^2				
Underweight (<18.5)	0.94 (0.43, 2.04)	1.15 (0.42, 3.20)	0.88 (0.36, 2.12)	1.02 (0.32, 3.230)
Normal (18.5-24.9)	1.00	1.00	1.00	1.00
Overweight (25.0-29.9)	0.66 (0.41, 1.05)	0.59 (0.33, 1.07)	0.70 (0.41, 1.18)	0.59 (0.31, 1.14)
Obese (≥30.0)	0.44 (0.28, 0.69)[5]	0.66 (0.37, 1.19)	0.33 (0.19, 0.58)[5]	0.50 (0.24, 1.04)
Pregnancy complications (≥1)	0.65 (0.43, 0.97)[3]	0.63 (0.37, 1.08)	0.56 (0.34, 0.90)[3]	0.64 (0.34, 1.21)
Smoking during pregnancy	0.13 (0.04, 0.38)[4]	0.16 (0.04, 0.55)[4]	0.14 (0.04, 0.49)[4]	0.23 (0.06, 0.89)[3]
Child's birthweight, g				
Low (<2500)	0.30 (0.15, 0.60)[4]	0.44 (0.20, 0.98)[3]	0.25 (0.11, 0.60)[4]	0.30 (0.11, 0.83)[3]
Normal (2500-3999)	1.00	1.00	1.00	1.00
High (≥4000)	1.49 (0.79, 2.80)	1.28 (0.57, 2.84)	1.70 (0.85, 3.42)	1.49 (0.60, 3.75)
Child’s birth year (2005-2012)	1.19 (1.06, 1.32)[4]	1.33 (1.16, 1.53)[5]	0.94 (0.83, 1.06)	1.10 (0.93, 1.30)

[1] Sample size for the model predicting ever XBR (*n* = 256) versus exclusively bottle-feeding (*n* = 344) is 600. Sample size for the model predicting XBR ≥6 months (*n* = 172) versus exclusively bottle-feeding (*n* = 344) is 516. XBR, exclusive breastfeeding.

[2] Adjusted for all other variables in the table.

[3] $P < 0.05$.

[4] $P < 0.01$.

[5] $P < 0.001$.

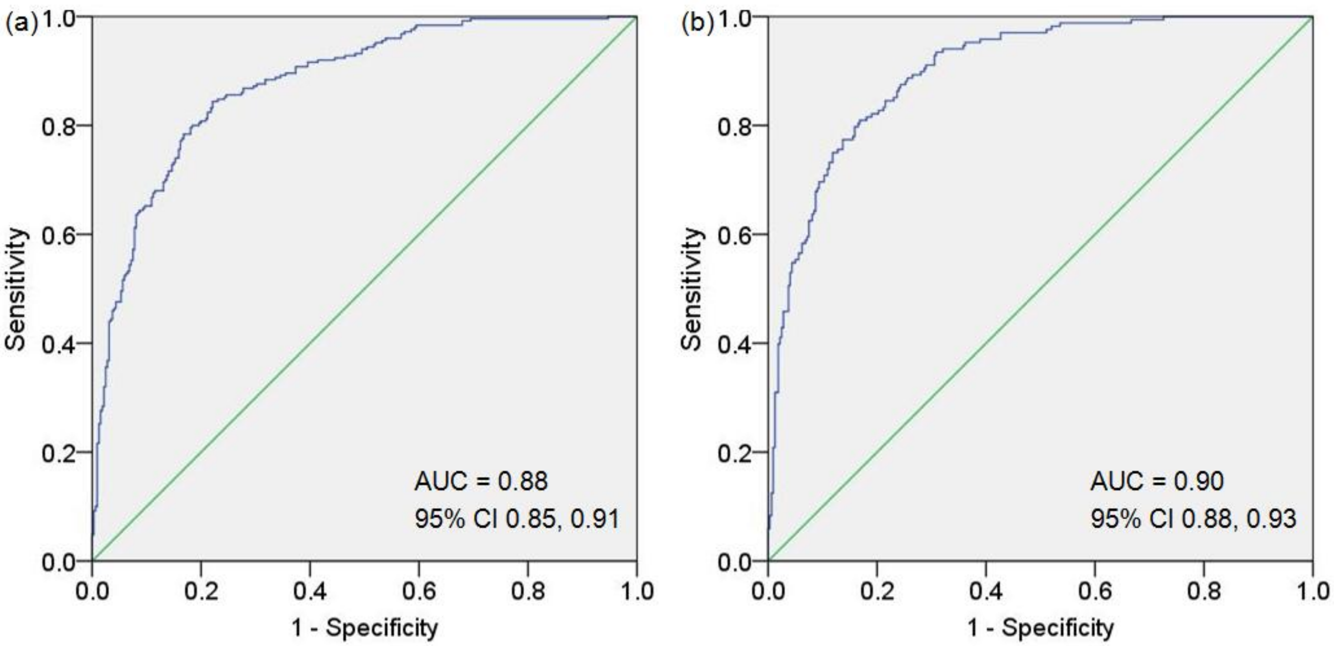

Figure 3.2 Receiver operating characteristic curves of the multivariate mixed-effects logistic regression models for (a) ever exclusive breastfeeding since birth and (b) exclusive breastfeeding ≥ 6 months. AUC, area under the curve.

Table 3.4 Unadjusted and adjusted odds ratios of factors associated with breast-bottle feeding subgroups[1]

	Breast milk > formula		Breast milk = formula	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[2]	Unadjusted OR (95% CI)	Adjusted OR (95% CI) [2]
Maternal Ethnicity				
Non-Hispanic White	1.00	1.00	1.00	1.00
Hispanic	0.80 (0.51, 1.28)	1.00 (0.62, 1.61)	1.37 (0.78, 2.44)	1.47 (0.79, 2.74)
Non-Hispanic Black	0.48 (0.28, 0.83)[4]	0.69 (0.39, 1.22)	1.16 (0.62, 2.18)	1.56 (0.80, 3.05)
Other	0.94 (0.47, 1.89)	1.04 (0.50, 2.18)	2.10 (0.96, 4.61)	1.94 (0.80, 4.70)
Married/ living with a partner	2.31 (1.52, 3.51)[5]	1.81 (1.15, 2.85)[3]	1.81 (1.17, 2.79)[4]	1.52 (0.95, 2.43)
Maternal nativity (foreign born)	1.04 (0.71, 1.52)	0.83 (0.53, 1.29)	1.55 (1.05, 2.28)[3]	1.13 (0.71, 1.79)
Maternal age at childbirth, years	1.06 (1.03, 1.09)[5]	1.06 (1.03, 1.09)[5]	1.06 (1.03, 1.10)[5]	1.06 (1.03, 1.10)[5]
Maternal prepregnancy BMI, kg/m^2				
Underweight (<18.5)	1.21 (0.50, 2.96)	1.23 (0.49, 3.01)	2.08 (0.84, 5.17)	1.75 (0.67, 4.53)
Normal (18.5-24.9)	1.00	1.00	1.00	1.00
Overweight (25.0-29.9)	0.97 (0.63, 1.49)	0.89 (0.57, 1.40)	1.63 (1.04, 2.58)[3]	1.49(0.92, 2.41)
Obese (≥30.0)	0.56 (0.36, 0.87)[3]	0.49 (0.31, 0.79)[4]	1.00 (0.62, 1.56)	0.78 (0.47, 1.30)
Child's birth year (2005-2012)	1.10 (0.99, 1.23)	1.10 (1.00, 1.23)	1.25 (1.11, 1.42)[5]	1.27 (1.12, 1.45)[5]

[1] Sample size for the model predicting "breast milk > formula" (*n* = 191) versus "breast milk < formula" (*n* = 526) is 717. Sample size for the model predicting "breast milk = formula" (*n* = 154) versus "breast milk < formula" (*n* = 526) is 680.

[2] Adjusted for all other variables in the table.

[3] $P < 0.05$.

[4] $P < 0.01$.

[5] $P < 0.001$.

Chapter 4: Estimation of Recumbent Length and Height from Ulnar Length and Arm Span among Infants and Children Aged 0-5.9 Years

ABSTRACT

Surrogate measures are needed when recumbent length or height is unobtainable or unreliable. Arm span has been used as a surrogate but is not feasible in children with shoulder or arm contractures. The measurement of ulnar length is not usually impaired by joint deformities, yet its utility as a surrogate has not been adequately studied. This study aimed to examine the accuracy and reliability of ulnar length measured by different tools as surrogate measures of length and height. In this cross-sectional study, anthropometrics (weight, recumbent length, height, ulnar length by caliper [ULC], ruler [ULR], and grid [ULG], and arm span) were measured in 1479 healthy infants and children aged <6 years across eight study centers in the US. Multivariate mixed-effects linear regression models for length and height were developed using ulnar length and arm span as surrogate measures. The agreement between the measured length or height and the predicted values by ULC, ULR, ULG, and arm span were examined by Bland-Altman plots. All three measures of ulnar length and arm span were highly correlated with length and height. Linear regression models of length prediction by ULC (R^2 = 0.928), ULR (R^2 = 0.915), and ULG (R^2 = 0.914) using age, sex, and ethnicity as covariates were comparable to that by arm span (R^2 = 0.914); however, height prediction by ULC (R^2 = 0.866), ULR (R^2 = 0.846), and ULR (R^2 = 0.872) were less comparable to arm span (R^2 = 0.945). Overestimation of predicted length was observed using ULC or ULR in young infants. In conclusion, ulnar length by caliper, ruler, or grid can serve as an accurate and reliable surrogate measure of recumbent length and height. Further testing of ulnar length as a surrogate is warranted in physically impaired or nonambulatory children.

Keywords: Arm span; Bland-Altman plot; recumbent length; prediction equation; standing height; surrogate measure; ulnar length.

INTRODUCTION

Recumbent length or standing height is an essential measure in the assessment and management of nutrition and growth in children (1, 2). Length or height is fundamental in calculating BMI and body surface area (168) and in estimating medication dosage (169), blood pressure (170), renal function (171), and pulmonary function (5, 172). Length and height are important surveillance tools for public health monitoring (173, 174) and in chronic disease research (8-10). Despite the importance of length and height in assessing nutritional and growth status, length and height are usually unobtainable or unreliable in children who are temporarily hospitalized or who have long-term mobility-impairment due to neuromuscular diseases or joint deformities (23, 24). Thus, a surrogate measure of length or height is needed, whether at a single point in time to estimate length or height for acute care management, or at consecutive clinic visits to monitor linear growth over time.

Linear growth of the body and its segments undergo transformations from birth to adulthood (175, 176). Understanding these anthropometric changes offers insight into possible effects of genetics, environment, and pathologic states. Surrogate measures of length and height are thus desirable in that they may: 1) serve as clinical substitutes; 2) permit an estimate of length or height through a formula calculation; 3) provide in some cases greater accuracy than traditional length or height measurements; and/or 4) offer insight about the differential growth of body segments as a function of age, sex, ethnicity, and pathologic conditions. Moreover, difficulties and problems in linear measurement can be encountered in field studies compared with clinical settings due to the portability, accessibility and expense of specialized equipment. Therefore, surrogate measures of length and height which can be obtained via simple and portable tools are desirable.

Examples of surrogate measures of length or height include arm span (25-27), lower leg length or knee height (29, 30), and segmental lengths of long bones (humerus, radius, ulnar, femur, tibia, and fibula) (33-35), the majority of which have only been evaluated in adults. Of particular note, arm span may be unobtainable or inaccurate due to the difficulty of maintaining the outstretched position of both arms. In addition, researchers have reported difficulties in measuring lower leg length in children with lower extremity cerebral palsy (31) and in the acutely ill elderly population (37). In contrast, ulnar length is a potential surrogate measure of length and height because its measurement is not usually impeded by joint deformity.

Ulnar length was first described by Valk et al (73) using a special device called the condylograph to assess children's short term growth. Two studies have subsequently assessed ulnar length as a surrogate measure of height in children using the Harpenden anthropometer (i.e., a counter-type anthropometric caliper) which is less bulky and easier to use than the condylograph. Ulnar length was demonstrated as an accurate and reproducible surrogate measure of height in healthy Chinese children aged 3-18 years (r = 0.98) (72) and in healthy Australian children aged 5-19 years (males R^2 = 0.96, females R^2 = 0.94) (39). To date, no studies have investigated the relationship between ulnar length and recumbent length in children <3 years nor has the relationship with height been assessed in children aged 2- 5.9 years across different ethnicities in the US.

As part of formative research for the NCS, a cross-sectional study of healthy infants and children aged <6 years was conducted to determine whether ulnar length can serve as a surrogate measure of recumbent length and height and whether one of three simple and portable tools (i.e., caliper, ruler, or paper grid) for ulnar length measurement is a more optimal surrogate. In particular, principle investigators (Drs. Michele R. Forman, Himes H. John, and Robert K. Danish) developed a paper and pencil grid to measure ulnar length and considered whether a simple straight steel ruler would be a feasible surrogate for ulnar length as measured by caliper when length or height could not be measured, e.g., children with cerebral palsy or temporarily injured.

METHODS

Subjects

This research was a one-point in time cross-sectional study of anthropometric status of infants and children aged <6 years across eight study centers (*see* Appendix B) in the US between June 2011 and September 2012. Mother-offspring dyads were recruited at daycare centers, churches, clinics, and community centers by study coordinators, word of mouth, and referral (*n* = 1634). Eligibility criteria included: mothers aged 18-49 years and non-institutionalized; and offspring who were aged 0-5.9 y, healthy, of the same ethnicity (categorized as NHW, Hispanic, NHB, or other based on mothers' responses) and living with the mother, had not suffered from any illness associated with weight loss nor acutely ill within the past week, and were afebrile at the time of study visit. The analysis was restricted to infants and children with at least one anthropometric measurement and one infant/child of each mother to avoid cluster effects from shared sociodemographic characteristics and genetics (*n* = 1479) of children in the same household. The study was approved by the Institutional Review Boards at the Eunice Kennedy Shriver National Institute of Child Health and Human Development and by those at each study center. Written informed consent was obtained from the mothers.

Anthropometric Measurements

A team of two trained researchers (one measurer and one recorder) obtained anthropometric measurements in the home, community center, church, or clinic. Quality control and data collection standardization procedures were reported previously (140). Weight, recumbent length, and standing height were measured using standard anthropometric protocols (177). Weight in kg was measured to the nearest 0.01 kg in infants wearing dry diaper or in children wearing underpants on an electronic scale (SECA, Germany) that was calibrated daily using a Tromer® weight. Recumbent length in cm was measured to the nearest 0.1 cm in infants and children aged <3 years in supine position with body extended, head held steady facing upward and knees held down using an infantometer (Ellard Instrumentation Ltd, Monroe, WA). Height in cm was measured to the nearest 0.1 cm in children aged 2.0-5.9 years using a portable stadiometer (SECA, Germany) while the child was standing in bare feet with head (after removal of hair piece where applicable), shoulders, buttocks, and heels touching the vertical plate and head in the Frankfort plane.

Ulnar length was measured on the right arm using different tools to compare as surrogate measures of recumbent length and height. First, the measurer palpated and marked in ink a line of about 1 cm at the distal end of the ulna (i.e., the styloid process) while the infant/child was in the sitting position with the right elbow flexed approximately 90 degrees (touching the table and arm and hand pointing upward), the wrist straight, and the fingers extended. The proximal end of the ulna, the olecranon, was identified by palpation with the elbow flexed 90 degrees. Ulnar length in cm was measured to the nearest 0.1 cm using three methods with the elbow flexed approximately 90 degrees using a : 1) caliper (Rosscraft Innovations Inc, Vancouver, Canada): placed the tips of the caliper against both end points of the forearm (i.e., the olecranon and styloid process) with the arm placed in a horizontal plane (*see* Appendix C1); 2) ruler: measured the distance between the two end points of the forearm using a steel or hard plastic ruler with the elbow touching the table and arm pointing upward in a vertical plane (*see* Appendix C2); and 3) grid: marked the location of the two end points of the ulna which was secured on a rigid board or on the table (*see* Appendix C3). The grid method was performed in infants and children aged ≥3 months. The grid was developed on graph paper that has uniform dimensions and is colored across rows/units of ten boxes to facilitate reading the measurements. The colorful nature of the grid facilitated its use because children enjoyed its rainbow effect.

Arm span was measured while the subject lay supine on a piece of paper on the floor, with shoulders flat against the surface and the body extended. Both arms were stretched laterally outward and perpendicular to the long axis of the body with palms facing upward. The measurer and observer worked synchronously and gently pressed their hands against the subject's elbow at the same time to maximize arm extension and to extend the fingers maximally on each side. Each then notified the other and simultaneously marked the most distal points of the middle finger of each hand on the paper by pencil or pen. After releasing the child from the position, the distance between the two points was measured to the nearest 0.1 cm by a steel or plastic (non-stretch) measuring tape.

Each measurement was taken in duplicate. The mean value of each anthropometric measurement was calculated if the two initial measurements agreed within 0.2 kg for weight or within 0.2 cm for length, height, ulnar length, and arm span. Otherwise, an additional measurement was taken and the mean of the two closest recordings was used. To determine the inter-observer measurement reliability, replicate measures were taken by the staff team reversing their positions as measurer and recorder in an approximately 10% random sub-sample (*n* = 119).

Statistical Analysis

Data preprocessing approaches applied in this study were reported previously (140). Descriptive statistics of anthropometrics were presented as the mean ± SD or the frequency as appropriate by age, sex, and ethnicity. Differences of anthropometrics were assessed by ANOVA or Student's t test across age groups or analysis of covariance (ANCOVA) among sex and ethnicity groups with age as the covariate and study center as a random effect. Post hoc tests were adjusted by Bonferroni correction. Inter-observer and intra-observer variability were analyzed by calculating the coefficients of variation (CVs) for each anthropometric measure in the random sub-sample of repeat measurements in 119 infants/children, respectively. In addition, the intraclass correlation coefficients (ICCs) using a one-way random model and absolute agreement type were calculated to assess the inter-observer and intra-observer reliability. Paired *t* tests with

Bonferroni adjustment were computed to assess significant differences between ulnar length by caliper (ULC), ulnar length by ruler (ULR), and ulnar length by grid (ULG) in the total population and by age, sex, and ethnicity. Pearson's correlation coefficients were calculated to assess the bivariate associations between length/height and surrogate anthropometrics (i.e., ULC, ULR, ULG, and arm span) by age, sex, and ethnicity. Spearman's rank-order correlation coefficients were also computed to assess the comparability by using the ranks of each anthropometric variable.

Prediction equations for length and height by surrogate measures and covariates (age, sex, and ethnicity) were derived using multivariate mixed-effects linear regression with study center as a random effect. To quantify the goodness-of-fit of the prediction models, the marginal R^2 proposed by Nakagawa and Schielzeth (178) was calculated to represent the proportion of variance explained by fixed effects. SEE was computed for each equation. According to the validation criteria recommended by Lohman et al (177), SEE of valid prediction equations should be less than 3.5 and R^2 be greater than 0.7. To assess the agreement between the measured length/height and the predicted values by each prediction equation, the difference between the 2 measurements (i.e., predicted and measured length/height) against the mean of the 2 measurements was plotted as described by Bland and Altman (179). The limits of agreement were defined as the mean difference ± 1.96 SD. The Bland-Altman plots can identify whether the tools/methods can be used interchangeably by visually examining the relationship between the differences of measurements from two tools/methods and the magnitude of the measurements.

All analyses were conducted with IBM SPSS 21 (IBM Corp, Armonk, New York) and R Statistical Software (Foundation for Statistical Computing, Vienna, Austria). Records with missing values for one or more of the predictors were excluded from each analysis and noted in the tables. Statistical significance was set at a 2-tailed $P < 0.05$.

RESULTS

Of the 1479 mother-offspring dyads, the mean age ± SD of the offspring was 23.7 ± 20.0 months and 51.8% were boys (Table 4.1). Three ethnic groups were well-represented: 45% Hispanic (largely Mexican American), 26% NHB, 20% NHW, and 8.7% other ethnic groups. Among the others, 72 (55.8%) were Chinese American and the remainder were largely other Asians (data not shown). As expected, all anthropometric values increased with increasing age. All anthropometrics were consistently lower in girls than boys after age adjustment. Ethnic differences were observed for many anthropometrics after age adjustment, with the highest values consistently appearing among the NHB across the measures. Conversely, the other ethnic groups weighed the least, were the shortest, and had the shortest ulnar and arm span measurements among all ethnic groups. The Hispanics compared with the NHW did not differ in weight, length, ULC, ULR, and arm span, but were shorter in height and ULG.

The CVs for inter-observer variability were consistently greater than CVs for intra-observer variability for all measures in a random sub-sample of 119 subjects (Table 4.2). Weight had the least intra-observer variability, followed by height, length, arm span, and ulnar length measured by different tools. Similarly, weight had the least inter-observer variability, followed by height, arm span, length, and ulnar length measured by different tools. Intra-observer reliability evaluated by ICCs was consistently greater than inter-observer ICCs for all measures except for weight and arm span being equivalent. Consistent with the observation that ULG had the highest inter- and intra-observer variability assessed by CVs, ULG had the lowest inter- and intra-observer reliability evaluated by ICCs among ulnar length measured by the three tools.

The mean paired differences between ULC, ULR, and ULG by sex, age, and ethnicity were calculated with Bonferroni adjustment for multiple comparisons (Table 4.3). The mean paired differences for ULC-ULR ranged from 0.04 to 0.30 cm with consistently higher ULC than ULR values for the total. Similarly, ULC values were higher than ULR in girls, by age except among infants, and by ethnicity in the NHW and other ethnic groups. The mean paired differences for ULC-ULG ranged from -0.03 to 0.16 cm, with higher ULC than ULG values for the total, among infants, and in Hispanics. The mean paired differences for ULR-ULG ranged from -0.31 to 0.13 cm with differences higher for ULG than ULR for the total, among children aged ≥ 2 y, and in the NHW. In summary, among the three tools measuring ulnar length, the calipers and the grid were more comparable than the ruler.

Correlation coefficients between surrogate measures and length/height were always highest in arm span (Table 4.4). Among surrogate measures beside arm span, the correlation coefficients between ULC and length were always higher than ULR or ULG while the coefficients between height and ULC were similar to ULG and higher than ULR. These findings were similar to the results using Spearman’s rho correlation (data not shown).

In predictive equations developed from multivariate mixed-effects linear regression analysis (Table 4.5), ulnar length measured by different tools (i.e., ULC, ULR, and ULG), age, and sex were significant predictors of recumbent length in children aged 0-3 years (Models 1-3). On the other hand, arm span and age, but regardless of sex, were significant predictors of recumbent length (Model 4). In equations for height in children aged 3.0-5.9 y, age and surrogate measures (i.e., ULC, ULR, ULG, and arm span) were consistently significant (Models 5-8). Ethnicity was included as a predictor in all equations due to significant ethnic differences in length and height as observed in this study (Table 4.1) and previously (49, 55, 91, 180); however, ethnicity was significant in only some equations after inclusion of surrogate measures, age, and sex (Models 4, 6-8). The proportions of variation in length accounted for by fixed effects in Models 1-3 were similar to that in Model 4 when arm span was a predictor. In contrast, the proportions of variation in standing height accounted for by fixed effects in Models 5-7 were less than that in Model 8 (94.5%).

In Bland-Altman plots assessing the concordance between the lengths predicted by surrogate measures and measured length, patterns were observed for ULC and ULR (Figures 4.1 A1-A3). Specifically, ULC and ULR tended to overestimate recumbent length of younger infants (noted as the smaller mean values on X-axis) by using predictive Models 1-2 shown in Table 4.5. No curved pattern appeared for ULG because infants aged <3 months were not measured. In contrast, the left-handed curved pattern was not apparent for arm span compared to ULC and ULR (Figure 4.1 A4). Bland-Altman plots for the measured and predicted height by surrogate measures did not reveal a pattern or bias attributable to ULC, ULR, ULG, or arm span (Figures 4.1 B1-B4).

DISCUSSION

In this study potential surrogate measures of recumbent length and standing height in children, utilizing different methods were accurate and reproducible in healthy neonates, infants, and children aged <6 years. The values of CVs and ICCs are comparable to or better than those reported previously (39, 181, 182). Thus, obtaining these surrogate measures in a variety of clinical settings is feasible and reliable using trained personnel. Ulnar length and arm span were highly correlated with length in infants/children aged 0-3 years and with height in children aged 2-5.9 years. Multivariate mixed-effects linear regression analyses demonstrated both ulnar length and arm span were significant predictors of recumbent length and standing height. Therefore, ulnar length and arm span can be used to estimate length and height using prediction models in Table 4.5 when actual length and height cannot be obtained accurately or reliably.

Paired *t* test computed differences of the mean ulnar measurements across the tools (i.e., caliper, ruler, and grid) and showed little variation by age, sex, and ethnicity. Overall, the mean ULC was larger than the mean ULG which in turn was larger than the mean ULR. Since all three measures of ulnar length were obtained using the same landmarks on the forearm (i.e., the olecranon and styloid process), variations between different measurement methods could be due to tool-specific postural issues. For example, measurement accuracy could be compromised if the caliper was not held steady or parallel to the floor; if the ruler was not touching against the arm in a vertical plane; or if the arm rolled during the grid measurement. Indeed, a challenge in use of the grid was the ability to mark the grid as proximally as possible to the marks for the olecranon and styloid process of the ulna. Even the width of the pen point could alter the location of and the size of the mark on the page; thus, training how to and where to make a mark is necessary. In stratification analysis by age, values of ULG were shorter than ULC in newborns and infants aged <1 y whereas the two measures did not differ in children aged 1.0-5.9 years (Table 4.3). Given the tool-specific issues, a combination of tools to use in specific age groups and/or in different field conditions (e.g., home versus clinic) might optimize the measurement accuracy and reliability.

To our knowledge, this study for the first time reports correlation coefficients between ulnar length measured by different tools and length/height in infants/children <6 years in the US. Pearson’s correlation coefficients between length/height and arm span(r = 0.98 for length; r = 0.96 for height) were greater compared to ulnar length. Similarly, Miller and Koreska reported the correlation coefficient of arm span with standing height (r = 0.97) was greater than the coefficient of ulnar length (r = 0.91) in normal children (183), based on anthropometric data of children aged 8-14 years in the US (184). However, in children with Duchenne muscular dystrophy with contractures who could not fully extend their arms or fingers, arm span did not correlate well with height (r = 0.47) while ulnar length measurement was not impeded by wrist or finger contractures and its accuracy was thus not impaired (183).

Several studies have developed prediction equations for height from arm span. Arm span is an accurate and strong predictor of height in healthy Chinese children aged

4-16 years (males $R^2 = 0.965$, females $R^2 = 0.972$; SEE not reported) (38), in Malawian children aged 6-15 years without any physical deformities ($R^2 = 0.988$ with age as a covariate; SEE = 0.76 cm) (26), and in nondisabled children aged 2-6 years in India ($R^2 = 0.93$; SEE = 3.2 cm) (61). Fewer data are available for the ability of ulnar length to predict length/height. Agnihotri et al developed a prediction model of height from ULC in college students in Mauritius ($R^2 = 0.74$; SEE not reported) (185). In a sample of healthy Australian children aged 5-19 years (39), ulnar length measured by a Harpenden anthropometer and age explained 96% (root mean square of error= 3.896 cm) and 94% (root mean square of error = 3.785 cm) of variation in height, respectively. In contrast, the SEEs of length and height prediction using ULC, ULR, and ULG as surrogates ranged from 2.80-3.42 cm in our study, all below the recommended validation criteria of less than 3.5 cm by Lohman et al (177).

To date, this is the first study that developed prediction equations for length and height from ulnar length in infants/children aged <6 years in the US. Results demonstrated that the accuracy of length prediction by ULC, ULR, and ULG was comparable to that by arm span, whereas height prediction by ULC, ULR, and ULG was less accurate than that by arm span in terms of the proportion of variation in length/height explained by these surrogate measures and covariates (age, sex, and ethnicity) (61). However, the accuracy and reliability of arm span as a length/height proxy may be impaired in children with shoulder or arm spasticity or contractures due to the difficulty in establishing an outstretched position of both arms (19, 20). Under these circumstances, ulnar length is probably the best measure available that can provide reasonably high prediction accuracy. In addition, each of the three tools for ulnar length measurement may be used interchangeably as their respective values of marginal R^2 in predicting length/height varied little in terms of prediction accuracy.

In Bland-Altman plots examining the agreement between the predicted and measured length/height, a trend toward overestimation of recumbent length predicted from ULC and ULR was observed in newborns and young infants. Given the postural difficulty in maintaining newborns and infants in a properly extended supine position, the overestimation of predicted length versus measured length could be partially attributable to measurement errors inherent in recumbent length (i.e., measured length smaller than the actual value). Indeed, the trend toward overestimation disappeared in Bland-Altman plots for height in older children aged 2.0-5.9 years. In contrast to ULC and ULR measured in the whole sample, ULG was only obtained in infants/children aged ≥ 3 months due to the difficulty of maintaining a steady posture of the forearm on the grid in newborns and young infants. The absence of ULG measurements in young infants could largely explain the absence of a curved pattern in ULG. In addition, the 95% limits of agreement were smaller for the difference between the measured length and length predicted from arm span (± 3.5 cm) compared to any of the ulnar length measured by different tools (±5.91, ±5.57, and ±5.01 cm for ULC, ULR, and ULG, respectively). A similar magnitude of the 95% limits of agreement was observed for height, which is considerably smaller than those reported previously (186-188). For instance, the 95%

limits of agreement of the difference between the predicted height by ulnar length measured using an anthropometric tape and measured height were (-10.0, 13.8) cm and (-9.0, 9.8) cm in 30 White men and 35 White women aged 21-62 years in the United Kingdom, respectively (187). Despite the high accuracy of length/height prediction by these surrogate measures at the group level, caution should be exercised when using surrogate measures for estimation of length/height in individuals because a 3 or 5 cm difference could potentially alter clinical assessment or management based on the calculation of BMI or estimation of renal or pulmonary function via length/height.

In conclusion, ulnar length measurements by three different tools (i.e., caliper, ruler, and paper grid) and arm span can serve as accurate and reliable surrogate measures of recumbent length and standing height in neonates, infants, and children aged <6 years across eight study centers in the US. Prediction equations developed from these surrogate measures using age, sex, and ethnicity as covariates can be used to estimate length or height when actual length or height is not measured or cannot be obtained accurately or reliably due to postural problems or subjects' noncompliance. Arm span exhibited a greater level of accuracy in predicting height compared to ulnar length, while ulnar length may serve as a better surrogate in children with postural problems (e.g., joint deformities or chondrodysplasia). The prediction equations developed in this sample of healthy neonates, infants, and children aged <6 years require further testing in children who are physically impaired or nonambulatory. Moreover, ulnar length provides an option for estimating length or height in field settings where the use of an infantometer or a stadiometer could be limited due to the portability, accessibility, and/or expense issues.

Table 4.1 Anthropometrics by age, sex, and ethnicity[1]

	n (%)[2]	Weight	Length	Height	ULC	ULR	ULG	Arm span
		kg	cm	cm	cm	cm	cm	cm
Overall	1479 (100)	11.7 ± 5.4	71.1 ± 12.0	100.7 ± 8.7	12.8 ± 2.9	12.7 ± 2.9	13.3 ± 2.6	82.5 ± 19.6
Age (mo)[3]								
0-11.9	574 (38.8)	7.0 ± 0.2^{a}	65.3 ± 0.5^{a}	NA	10.1 ± 0.08^{a}	9.8 ± 0.08^{a}	10.5 ± 0.08^{a}	62.8 ± 0.4^{a}
12-23.9	299 (20.2)	10.7 ± 0.2^{b}	79.8 ± 0.5^{b}	NA	12.4 ± 0.09^{b}	12.0 ± 0.10^{b}	12.3 ± 0.09^{b}	78.0 ± 0.5^{b}
24-35.9	193 (13.0)	14.1 ± 0.2^{c}	91.9 ± 0.7^{c}	91.3 ± 0.5^{a}	14.2 ± 0.11^{c}	13.8 ± 0.11^{c}	14.0 ± 0.10^{c}	91.6 ± 0.6^{c}
36-71.9	413 (27.9)	18.1 ± 0.2^{d}	NA	104.4 ± 0.4^{b}	16.3 ± 0.08^{d}	16.0 ± 0.08^{d}	16.1 ± 0.08^{d}	105.8 ± 0.4^{d}
P[4]		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Sex[3]								
Boys	766 (51.8)	12.1 ± 0.1	71.6 ± 0.3^{a}	101.4 ± 0.3	13.0 ± 0.06^{a}	12.9 ± 0.06^{a}	13.4 ± 0.06	84.3 ± 0.3^{a}
Girls	713 (48.2)	11.6 ± 0.1	69.9 ± 0.3^{b}	100.5 ± 0.3	12.7 ± 0.06^{b}	12.5 ± 0.06^{b}	13.1 ± 0.06	82.7 ± 0.3^{b}
P[5]		0.001	<0.001	0.007	<0.001	<0.001	<0.001	<0.001
Ethnicity[3]								
NHW	296 (20.0)	12.0 ± 0.2^{a}	70.6 ± 0.4	101.4 ± 0.4^{a}	12.7 ± 0.09^{a}	12.5 ± 0.09^{a}	13.3 ± 0.09^{a}	83.2 ± 0.5^{a}
Hispanic	665 (45.0)	12.0 ± 0.2^{a}	70.6 ± 0.4	99.9 ± 0.5^{b}	12.7 ± 0.09^{a}	12.5 ± 0.10^{a}	13.0 ± 0.09^{b}	$82.8 \pm 0.5^{a,b}$
NHB	385 (26.0)	12.2 ± 0.2^{a}	71.5 ± 0.4^{a}	$102.5 \pm 0.4^{a,c}$	13.3 ± 0.08^{b}	13.2 ± 0.09^{b}	13.7 ± 0.08^{c}	86.3 ± 0.4^{c}
Other	129 (8.7)	10.9 ± 0.3^{b}	70.1 ± 0.6^{b}	98.9 ± 0.6^{b}	12.5 ± 0.13^{a}	12.3 ± 0.13^{a}	$12.8 \pm 0.13^{b,d}$	$81.1 \pm 0.6^{b,d}$
P[6]		0.004	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 4.1 Anthropometrics by age, sex, and ethnicity (continued)[1]

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[1] $n = 1479$. Length was measured in children aged ≤ 36 months ($n = 1206$). Height was measured in children aged 24-71.9 months ($n = 486$). Ulnar length by grid, was measured in children 3-71.9 months (n = 1296). NA, not available; NHB, non-Hispanic Black; NHW, non-Hispanic White; ULC, ulnar length by caliper; ULG, ulnar length by grid; ULR, ulnar length by ruler. Values with different superscript letters in a column are significantly different, $P < 0.05$ (Bonferroni post hoc test).

[2] Totals may be <1479 due to missing values.

[3] Values are $\bar{x} \pm$ SEs.

[4] ANOVA or student's t test with study center as a random effect.

[5] Student's t test with study center as a random effect, adjusting for age.

[6] ANCOVA with study center as a random effect, adjusting for age.

Table 4.2 Intra-observer and inter-observer reliability of anthropometric measurements assessed by coefficient of variation and intraclass correlation coefficient in a sub-sample of infants/children[1]

	Intra-observer reliability			Inter-observer reliability		
	n[2]	CV (%)	ICC (95% CI)	*n*[3]	CV (%)	ICC (95% CI)
Weight	119	0.08	1.000 (1.000, 1.000)	119	0.24	1.000 (1.000, 1.000)
Length	58	0.2	1.000 (0.999, 1.000)	56	0.53	0.999 (0.998, 0.999)
Height	66	0.12	0.999 (0.999, 1.000)	64	0.29	0.999 (0.998, 0.999)
ULC	119	0.62	0.999 (0.998, 0.999)	117	1.48	0.996 (0.984, 0.997)
ULR	113	0.49	0.999 (0.998, 0.999)	112	1.78	0.993 (0.990, 0.995)
ULG	108	0.9	0.997 (0.995, 0.998)	105	2.33	0.989 (0.983, 0.992)
Arm span	109	0.26	1.000 (1.000, 1.000)	105	0.34	1.000 (1.000, 1.000)

[1] CV, coefficient of variation; ICC, intraclass correlation coefficient; ULC, ulnar length by caliper; ULG, ulnar length by grid; ULR, ulnar length by ruler. *n* = 119.

[2] *n* for intra-observer CV.

[3] *n* for inter-observer CV.

Table 4.3 Mean differences between ulnar length by caliper, ulnar length by ruler, and ulnar length by grid by age, sex, and ethnicity[1]

	ULC - ULR		ULC - ULG		ULR - ULG	
	n[2]	Paired difference	*n*[2]	Paired difference	*n*[2]	Paired difference
Overall	1362	0.16 ± 1.04[3]	1249	0.07 ± 0.65[4]	1196	-0.11 ± 1.16[5]
Age (mo)[6]						
0-11.9	515	0.04 ± 1.13	375	0.15 ± 0.70[4]	349	0.13 ± 1.13
12-23.9	260	0.23 ± 1.05[5]	282	0.05 ± 0.68	263	-0.18 ± 1.15
24-35.9	175	0.27 ± 0.86[4]	182	0.01 ± 0.62	174	-0.27 ± 0.88[4]
36-71.9	412	0.23 ± 0.96[3]	410	0.05 ± 0.59	410	-0.18 ± 1.09[5]
Sex[7]						
Boys	712	0.12 ± 0.04	650	0.07 ± 0.03	623	-0.07 ± 0.05
Girls	650	0.21 ± 0.04[3]	599	0.08 ± 0.03	573	-0.14 ± 0.05
Ethnicity[7]						
NHW	278	0.28 ± 0.06[3]	252	-0.03 ± 0.04	249	-0.31 ± 0.07[4]
Hispanic	610	0.08 ± 0.04	537	0.12 ± 0.03[3]	517	-0.03 ± 0.05
NHB	352	0.17 ± 0.06	341	0.04 ± 0.04	317	-0.14 ± 0.07
Other	122	0.30 ± 0.09[5]	116	0.16 ± 0.06	113	-0.18 ± 0.11

[1] *n* = 1479. Paired difference is by paired *t* test. NHB, non-Hispanic Black; NHW, non-Hispanic White; ULC, ulnar length by caliper; ULG, ulnar length by grid; ULR, ulnar length by ruler.

[2] Totals may be <1479 due to missing values.

[3] Significantly different from zero, $P < 0.001$ (with Bonferroni adjustment).

[4] Significantly different from zero, $P < 0.01$(with Bonferroni adjustment).

[5] Significantly different from zero, $P < 0.05$(with Bonferroni adjustment).

[6] Values are $\bar{x}$ ± SDs.

[7] Values are $\bar{x}$ ± SEs, adjusted for age.

Table 4.4 Pearson's correlation coefficients between ulnar length by caliper, ulnar length by ruler, and ulnar length by grid, and arm span, and length and height by age, sex, and ethnicity[1]

	ULC	ULR	ULG	Arm span
Length (*n* = 941)	0.90[2]	0.85[2]	0.86[2]	0.98[2]
Age (mo)				
0-11.9 (*n* = 567)	0.81[2]	0.75[2]	0.65[2]	0.95[2]
12-23.9 (*n* = 272)	0.77[2]	0.68[2]	0.77[2]	0.95[2]
24-35.9 (*n* = 102)	0.74[2]	0.71[2]	0.73[2]	0.86[2]
Sex				
Boys (*n* = 497)	0.89[2]	0.87[2]	0.85[2]	0.98[2]
Girls (*n* = 444)	0.91[2]	0.84[2]	0.87[2]	0.99[2]
Ethnicity				
NHW (*n* = 172)	0.91[2]	0.88[2]	0.86[2]	0.99[2]
Hispanic (*n* = 458)	0.87[2]	0.90[2]	0.83[2]	0.98[2]
NHB (*n* = 242)	0.94[2]	0.74[2]	0.89[2]	0.98[2]
Other (*n* = 66)	0.97[2]	0.94[2]	0.91[2]	0.99[2]
Height (*n* = 578)	0.87[2]	0.82[2]	0.87[2]	0.96[2]
Age (mo)				
24-35.9 (*n* = 166)	0.75[2]	0.57[2]	0.73[2]	0.92[2]
36-71.9 (*n* = 412)	0.82[2]	0.75[2]	0.82[2]	0.94[2]
Sex				
Boys (*n* =286)	0.87[2]	0.79[2]	0.87[2]	0.96[2]
Girls (*n* = 292)	0.87[2]	0.85[2]	0.87[2]	0.96[2]
Ethnicity				
NHW (*n* = 142)	0.90[2]	0.83[2]	0.88[2]	0.96[2]
Hispanic (*n* = 194)	0.82[2]	0.77[2]	0.86[2]	0.97[2]
NHB (*n* = 165)	0.91[2]	0.86[2]	0.88[2]	0.97[2]
Other (*n* = 77)	0.88[2]	0.89[2]	0.86[2]	0.94[2]

[1] Length was measured in children aged ≤ 36 months. Height was measured in children aged 24-71.9 months. NHB, non-Hispanic Black; NHW, non-Hispanic White; ULC, ulnar length by caliper; ULG, ulnar length by grid; ULR, ulnar length by ruler.

[2] P <0.001.

Table 4.5 Regression equations to estimate recumbent length in children aged 0-3 years and height in children aged 2-5.9 years using ulnar length by caliper, ulnar length by ruler, and ulnar length by grid, or arm span[1]

	n	Equation	$R^2_{marginal}$	SEE
Length				
Model 1	918	$L=35.17+2.35\times ULC^{*}+0.84\times A^{*}+0.70\times Boy+0.07\times NHW^{\dagger}-0.05\times Hispanic+0.21\times NHB$	0.928	3.22
Model 2	864	$L=39.21+1.88\times ULR^{*}+0.94\times A^{*}+0.94\times Boy^{*}+0.54\times NHW+0.52\times Hispanic+0.31\times NHB$	0.915	3.42
Model 3	741	$L=44.51+1.63\times ULG^{*}+0.83\times A^{*}+0.90\times Boy^{*}+0.26\times NHW-0.04\times Hispanic+0.07\times NHB$	0.914	2.80
Model 4	784	$L=13.13+0.80\times AS^{*}+0.22\times A^{*}-0.12\times Boy+0.21\times NHW+0.02\times Hispanic-0.86\times NHB^{\ddagger}$	0.914	2.09
Height				
Model 5	577	$H=43.18+2.70\times ULC^{*}+0.33\times A^{*}+0.22\times Boy+0.85\times NHW-0.54\times Hispanic-0.18\times NHB$	0.866	3.14
Model 6	571	$H=48.17+2.27\times ULR^{*}+0.38\times A^{*}+0.05\times Boy+1.35\times NHW^{\ddagger}-0.27\times Hispanic+0.59\times NHB$	0.846	3.28
Model 7	573	$H=44.07+2.64\times ULG^{*}+0.34\times A^{*}+0.37\times Boy+0.19\times NHW-0.90\times Hispanic^{\ddagger}-0.70\times NHB$	0.872	3.13
Model 8	551	$H=21.44+0.71\times AS^{*}+0.16\times A^{*}-0.11\times Boy+0.70\times NHW^{\ddagger}-0.41\times Hispanic-1.15\times NHB^{\dagger}$	0.945	2.04

[1] Mixed-effects linear regression analysis using study center as a random effect. A, age (mo); AS, arm span (mo); H, height (cm); L, length (cm); NHB, non-Hispanic Black; NHW, non-Hispanic White; $R^2_{marginal}$, coefficient of determination for fixed effects; SEE, standard error of estimate (cm); ULC, ulnar length by caliper (cm); ULG, ulnar length by grid (cm); ULR, ulnar length by ruler (cm) between measured and predicted length or height;.

* *P* <0.001

† *P* <0.01.

‡ *P* <0.05.

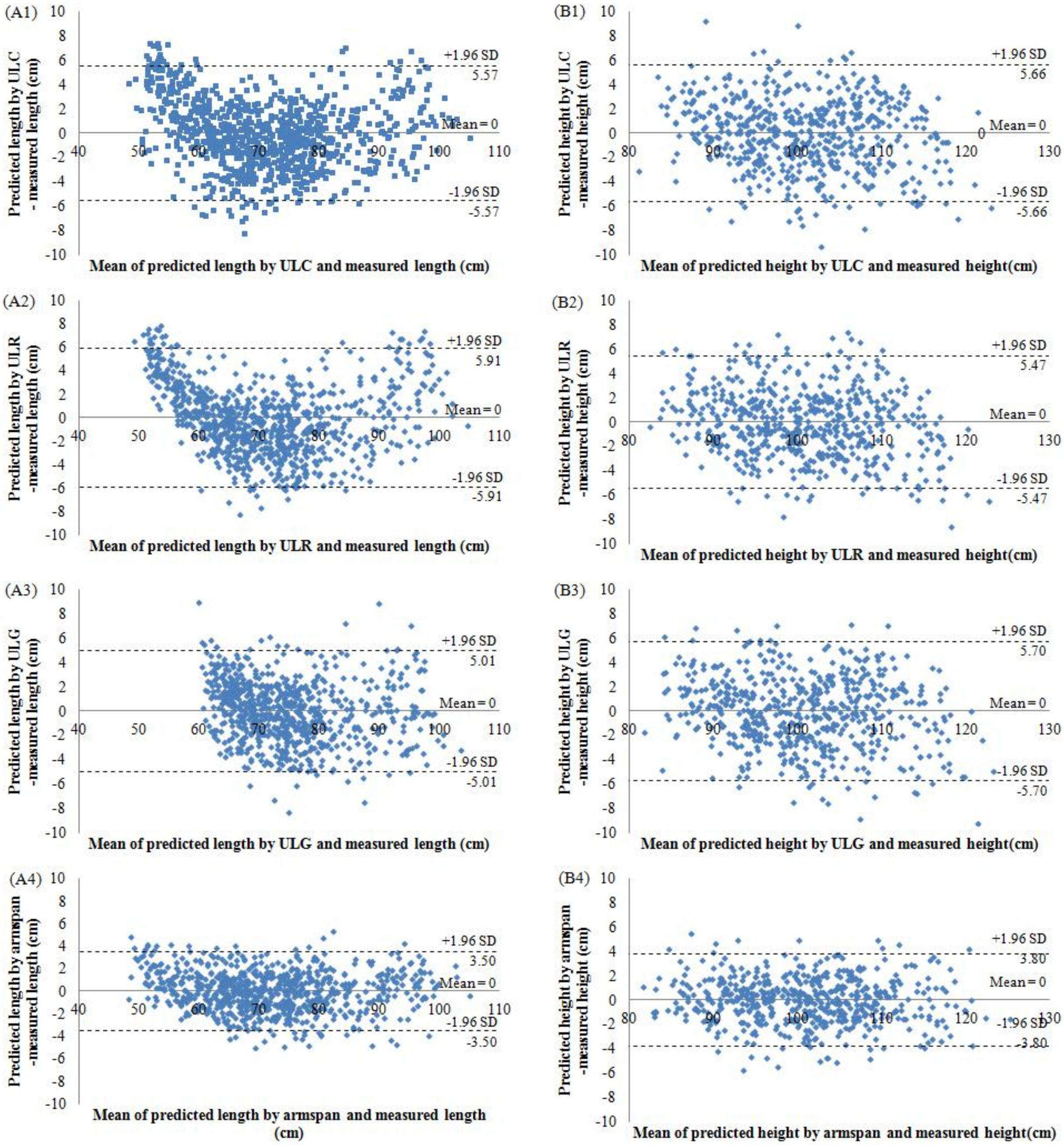


Figure 4.1 Bland-Altman plots: the difference between predicted and measured length in children aged 0-3 years (A1-A4) or height in children aged 2-5.9 years (B1-B4) plotted against the mean of predicted and measured length or height. Solid lines represent the mean difference. Dashed lines represent the 95% limits of agreement (i.e. mean difference ± 1.96 SD). ULC, ulnar length by caliper; ULG, ulnar length by grid; ULR, ulnar length by ruler.

Chapter 5: Longer Length of Breastfeeding Reduces the Positive Relationships among Gestational Weight Gain, Birthweight, and Childhood Anthropometrics

ABSTRACT

The relationship between gestational weight gain (GWG) and childhood growth remains controversial; thus an examination whether early life nutrition mediates this relationship may improve our understanding. This study investigated whether the relationships among GWG, birthweight, and childhood anthropometrics were mediated through breastfeeding duration and age at introduction of solid foods in a cross-sectional study of 1387 mothers and their children aged 0-5.9 years in the US (2011-2012). Child anthropometrics included age-/sex-specific z-scores for: weight-for-age (WAZ), height/length-for-age (HAZ), weight-for-height/length (WHZ) and body mass index (BMIZ); and ulnar length, a marker for limb growth. Using structural equation modeling, GWG had a consistent positive effect on all anthropometrics mediated via birthweight, whereas longer breastfeeding duration reduced the positive effects of GWG and birthweight on WAZ, WHZ, and BMIZ (β = -0.076, -0.062, and -0.124, respectively) in non-Hispanics. Longer breastfeeding duration and introducing solid foods at a later age were positively associated with ulnar length (β = 0.021 and 0.030, respectively) not HAZ, suggesting a distinct effect for the first time on limb growth. Findings suggest promoting longer breastfeeding duration among women with excessive GWG may mitigate offspring obesity. Future prospective research investigating ethnic-specific interrelationships among GWG, birthweight, infant feeding, and postnatal growth are warranted.

Keywords: Age at introduction of solid foods; birthweight; breastfeeding duration; child growth; gestational weigh gain; mediation analysis; structural equation model.

INTRODUCTION

Fetal life and early childhood are critical life stages during which developmental adaptations to environmental exposures may have profound impact on health outcomes in later life as illustrated by the effect of nutrition and growth status in early life on disease susceptibility throughout later life stages (8, 10, 17, 189-193). In particular, observational evidence indicates that the obesity epidemic may have developmental origins as early as *in utero*, infancy, and/or early childhood (175, 194). Given that gestational weight gain (GWG) may have substantial impact on intrauterine nutrition and growth, the relationship between GWG and offspring's obesity risk is of particular interest.

Previous studies indicate that GWG was either positively associated with offspring's obesity throughout the lifespan (195-200) or a null association was observed after adjusting for confounders (201-204), while others reported a U-shaped relationship (205, 206). Low birthweight (<2500 g) infants born to mothers with inadequate GWG may have undergone intrauterine growth restriction. As proposed by Dulloo et al (207), these infants may exhibit a thrifty phenotype characterized by catch-up growth and an early adiposity rebound as compensatory growth, leading to obesity and metabolic syndrome in later life. On the other hand, high birthweight (>4000 g) as a marker of intrauterine over-nutrition is associated with metabolic abnormities and subsequently an increased risk of obesity and metabolic disease (208). Indeed, birthweight, as a proxy of *in utero* nutrition and growth status, is associated with both maternal GWG (209-212) and adiposity and body composition in later life (213-216). However, less knowledge is available whether birthweight mediates the association between GWG and childhood growth.

The intergenerational impact of maternal GWG on offspring weight status and obesity may act through direct and/or indirect pathways. Maternal GWG may directly program fetal development and child adiposity by disturbing lipid, insulin, energy, and leptin dynamics (208, 217-219). An indirect effect of maternal GWG on child adiposity may be attributable to shared genetics (202), obesity-related behaviors (220, 221), and environment (222). Yet, it is not well-known whether early life nutrition mediates the pathway from GWG to childhood growth. Since infant feeding practices are associated with maternal pre-pregnancy obesity and GWG (138, 223) as well as childhood growth and obesity (193, 224, 225), investigation of the mediation effect of infant feeding practices is warranted. Such research could identify a modifiable early nutrition factor for obesity prevention strategies. Furthermore, despite numerous studies of GWG and child obesity, there is a scarcity of data on the impact of GWG on childhood linear growth. Height/length surrogates may be particularly sensitive to early life exposures with distinct growth velocities at different developmental stages (41, 42), therein suggesting the need for investigation.

Therefore, this study aimed to 1) investigate the mediation effects of birthweight and infant feeding practices (i.e., breastfeeding duration and age at introduction of solid foods) on the relationship between maternal GWG and childhood growth; and 2) compare the direct and indirect effects of GWG on childhood growth in the total sample and by ethnicity via structural equation modeling (SEM). This study also examined the interplay among GWG, birthweight, infant feeding, and ulnar length, an upper limb segment that is both a reliable and valid surrogate for length/height**.**

METHODS

Subjects

A cross-sectional study of anthropometric status of infants and children aged <6 years was conducted across eight study sites in the NCS Formative Research in Anthropometry in the United States from 2011-2012. Mother-offspring dyads were recruited at daycare centers, churches, clinics, and community centers by study coordinators, word of mouth, and referral (*n* = 1634). Eligibility criteria included: mothers aged 18-49 years and non-institutionalized; and offspring who were aged 0-5.9 years, healthy, of the same ethnicity as and living with the mother, had not suffered from any illness associated with weight loss nor acutely ill within the past week, and were afebrile at the time of study visit. If more than one infant/child of the same mother was recruited, the youngest one was included in this analysis to reduce the cluster effect from shared socio-demographic characteristics, infant feeding practices, and genetics of the children in the same family (*n* = 1479). Complete information on all variables and at least one anthropometric measurement were available for 1387 infants and children. The study was approved by the Institutional Review Boards at the Eunice Kennedy Shriver National Institute of Child Health and Human Development and each study center. Informed consent was obtained from the mothers.

Anthropometric measurements

Trained researchers collected anthropometric measurements in the daycare center, church, clinic, or community center. Quality control procedures were described previously (140). Weight, recumbent length, and height were measured using standard anthropometric protocols (177). Weight was measured to the nearest 0.01 kg in infants wearing dry diaper or in children wearing underpants on an electronic scale (SECA, Germany) calibrated daily using a Tromer® weight. Recumbent length was measured to the nearest 0.1 cm in infants and children aged <3 years in a supine position using an infantometer (Ellard Instrumentation Ltd, Monroe, WA). Height was measured to the nearest 0.1 cm in children aged 2-5.9 years using a portable stadiometer (SECA, Germany). After marking the two end points of the ulna (i.e., the styloid and olecranon process) on the right arm, ulnar length was measured to the nearest 0.1 cm using a caliper (Rosscraft Innovations Inc, Vancouver, Canada) while the arm was placed in a horizontal plane with the elbow flexed ~90 degrees. Each measurement was taken in duplicate. The mean value of each anthropometric was calculated if the two initial measurements agreed within 0.2 kg for weight or within 0.2 cm for length, height, and ulnar length. Otherwise, an additional measurement was obtained and the mean of the two closest recordings was used. The age- and sex-specific z-scores for weight-for-age (WAZ), height/length-for-age (HAZ), weight-for-height/length (WHZ) among infants/children aged 0-5.9 years, and body mass index-for-age z-scores (BMIZ) among children aged 2-5.9 years were calculated using the Centers for Disease Control and Prevention reference data (226). For height-related z-scores, recumbent length and height were used in infants/children aged <2 years and children aged 2-5.9 years, respectively.

Gestational weight gain

Maternal GWG was self-reported as a categorical variable using an interviewer-administered questionnaire in the following categories: <14, 15-19, 20-29, 30-40, >40 pounds (lb) based on previous research (205).

Mediating variables

Birthweight in lb and ounces was reported by the mother to an open-ended question in the interviewer administered questionnaire and converted to kg for analysis. Infant feeding practices reported by mothers during the interview included 1) breastfeeding duration (i.e., the age in months when the mother stopped feeding the child any breast milk assuming the child was breastfed since birth); and 2) age at introduction of solid (or semi-solid) foods in months. If the child was still being breastfed at the time of interview, the age when breastfeeding stopped was re-coded as the age of the child at study visit.

Covariates

Based on the interviewer-administered questionnaire, variables that were both correlated with GWG and anthropometrics with a P value <0.20 were included as covariates (227). Specifically, pre-pregnancy BMI was calculated as self-reported pre-pregnancy weight (kg)/height^2 (m^2). Maternal age at the birth of the index child was reported in years. Maternal educational level was categorized as <high school, high school degree or equivalent, and >high school. Marital status was categorized as married/living with a partner or single. Ethnicity was dichotomized as Hispanic and non-Hispanic based on mothers' responses whether they consider themselves Hispanic or Latina. The number of pregnancy complications (i.e., gestational diabetes, high blood pressure, pre-eclampsia/eclampsia, and only proteinuria) was coded as 0 to 4. Maternal smoking during pregnancy was dichotomized as yes or no.

Statistical analysis

Data preprocessing approaches applied in this study were reported previously (140). Descriptive statistics of continuous or categorical maternal and child characteristics by GWG were presented as the mean (SD) or frequency, respectively. Differences in maternal/child characteristics across GWG categories were assessed by analyses of variance, analyses of covariance, or χ^2 test.

A theoretical framework to test the associations among GWG, birthweight, infant feeding, and childhood growth is depicted in Figure 5.1. Given SEM performs better than regression analysis in terms of unveiling complex interrelationships among variables of interest (228), SEM was used to test whether the associations between GWG and childhood anthropometrics may be direct or indirect (i.e., mediated by birthweight, breastfeeding duration, and/or age at introduction of solid foods) after adjustment for covariates.

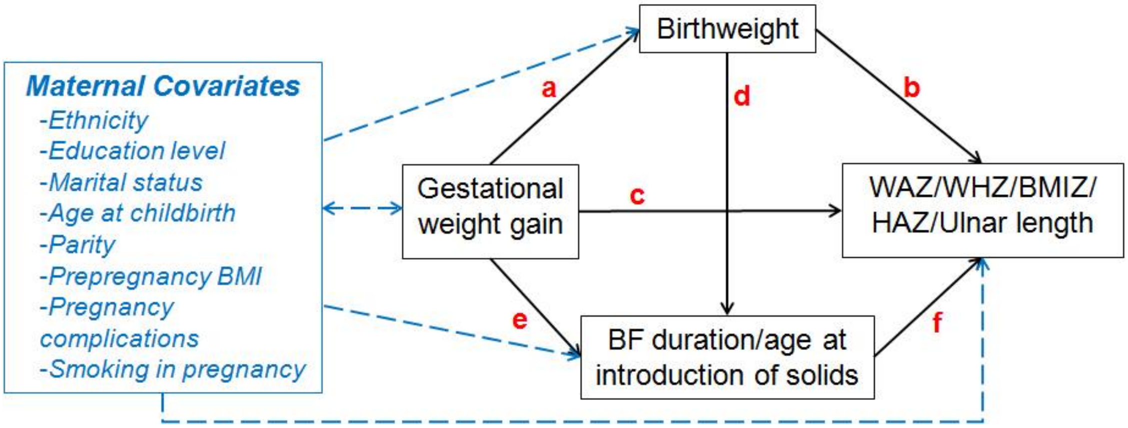


Figure 5.1 A theoretical model to test the associations among maternal gestational weight gain, child's birthweight, breastfeeding duration/age at introduction of solid foods, and childhood growth parameters [weight-for-age z-score (WAZ), weight-for-length/height z-score (WHZ), body mass index z-score (BMIZ), length/height-for-age z-score (HAZ), and ulnar length]. Covariates include maternal ethnicity, education level, marital status, age at childbirth, parity, prepregnancy BMI, pregnancy complications, and smoking in pregnancy. Paths are presented by letters from a-f.

Complete case analyses were performed for each anthropometric measure (*n* = 1387, 1338, 1330, and 1368 for WAZ, WHZ, HAZ, and ulnar length in infants/children aged 0-5.9 y, respectively; *n* = 554 for BMIZ in children aged 2-5.9 years). Maternal and child characteristics of the complete cases were similar to those excluded cases due to missing data. Ordinal variables like maternal GWG were natural log-transformed and treated as continuous variables. The standardized coefficient of each path was calculated. Standardized total, direct, and indirect effects of GWG, birthweight, and breastfeeding duration on each childhood anthropometric measure (i.e., WAZ, WHZ, BMIZ, HAZ, and ulnar length) were calculated, respectively. To test the stability of parameter estimates when the assumption of multivariate normality may be violated, 95% bias-corrected bootstrap confidence intervals were calculated based on 500-fold bootstrap samples. Model fit was assessed by the model χ^2 test, root mean square error of approximation, comparative fit index, and Tucker-Lewis index, using cut-offs of 0.06, 0.95, and 0.95, respectively (229).

Another set of models replaced breastfeeding duration with the age at introduction of solid foods as a mediator. All models were also stratified by ethnicity (ie, Hispanics and non-Hispanics) to test for ethnic-specific interrelationships among path variables. All analyses were conducted with IBM SPSS 21 and Amos 20 (IBM Corp, Armonk, New York). Statistical significance was set at a 2-tailed $P < 0.05$.

RESULTS

Maternal and child characteristics by GWG categories are shown in Table 5.1. Among mothers who gained <14 lb during pregnancy, 60.8% were Hispanic, whereas among those who gained >40 lb, the highest percentage was non-Hispanic black (32.3%). Primiparous mothers had greater GWG than the multiparous. Pre-pregnancy BMI co-varied inversely with GWG. Of 1387 infants/children, the mean duration of breastfeeding was longest or shortest in those born to mothers who gained 15-19 lb or <14 lb during pregnancy, respectively; however, the difference was marginally significant. Mothers who gained 20-29 lb during pregnancy introduced solid foods to their children at a later age than those who gained >40 lb (6.9 versus 6.1 months, $P = 0.04$ by Bonferroni adjustment). Maternal GWG exhibited a U-shaped but not significant relationship with WAZ, WHZ, and BMIZ. Child's HAZ was positively associated with GWG in a monotonic pattern; whereas ulnar length did not vary by GWG.

In SEM models (Figure 5.2), the direct effect of GWG was significant and negative for WHZ but positive for HAZ (path c). On the other hand, GWG's indirect effects on anthropometrics were mediated through several pathways. Path a→b (GWG-birthweight-anthropometrics) was positive across all anthropometrics. Path a→d→f (GWG-birthweight-breastfeeding duration-anthropometrics) was significant in all except for HAZ; however, path f was negative for WAZ, WHZ, and BMIZ and positive for ulnar length. Ethnic-stratified analysis illustrated that the negative effects of breastfeeding duration on WAZ, WHZ, and BMIZ were only significant in non-Hispanics, whereas the positive effect of breastfeeding duration on ulnar length was significant in Hispanics (Table 5.3). Path e→f (GWG-breastfeeding duration-anthropometrics) was not a significant contributor to the indirect effect of GWG on anthropometrics. Model fit statistics all met the respective cut-off criteria in each SEM model (data not shown).

Table 5.2 presents the beta coefficients for the total, direct (also shown in Figure 5.2), and indirect effects and their 95% CIs of GWG, birthweight, and breastfeeding duration on anthropometrics. Maternal GWG had a positive total effect on HAZ and a consistent positive indirect effect on all anthropometrics. Birthweight had positive total and direct effects on all anthropometrics. Regarding weight status, birthweight had greater total and direct effects on WAZ than on WHZ as illustrated by larger beta coefficients and non-overlapping 95% CIs. For linear growth, birthweight had greater total and direct effects on HAZ than on ulnar length. Breastfeeding had no indirect effect on anthropometrics.

Regarding complementary feeding, despite a consistent positive path a→b across all models (Figure 5.3), the birthweight-anthropometrics association was not mediated via age at introduction of solid foods (path d→f). Also, ethnic-stratified analysis indicated that age at introduction of solid foods had a significantly positive direct effect on ulnar length in the total sample and in Hispanics, respectively (data not shown). As demonstrated in Table 5.4, although the total effect of GWG was only positive on HAZ, GWG had a constantly positive indirect effect on each anthropometric. The positive total effects of birthweight on anthropometrics were largely attributable to direct rather than indirect effects.

DISCUSSION

Among 1387 mother-child dyads in the NCS Formative Research in Anthropometry in the United States, a consistent positive indirect effect of GWG on childhood anthropometrics was observed via birthweight (path a→b). Breastfeeding duration displayed a protective effect by suppressing the positive associations of GWG and birthweight with WAZ, WHZ, and BMIZ (path a→d→f). In contrast, age at introduction of solid foods did not mediate the relationship between birthweight and most anthropometrics except ulnar length. Longer duration of breastfeeding and a later age at introduction of solid foods were positively associated with ulnar length but not with HAZ in a direct path (f), indicating a distinct growth pattern of the upper limb segment compared to total height.

Results showed GWG was positively associated with childhood anthropometrics via indirect pathways mainly through birthweight. Similarly, previous studies reported that adjustments for birthweight attenuated the positive associations of GWG with BMIZ (201) and excessive fat mass (230) at 4 years, respectively. Given data available in this study, it is not clear whether birthweight is a predominant mediator of the relationship between GWG and child anthropometrics, or rather an indicator of intrauterine programming of metabolic profiles (217-219). Further investigation on the effect of GWG on postnatal growth and disease susceptibility is warranted to identify underlying neuro-endocrine pathways.

Of particular note, although the total effects of GWG on most anthropometrics (except HAZ) were insignificant, there is no need to establish mediation from a significant zero-order (total) effect (231). Since the direct and indirect effects of GWG on anthropometrics (except HAZ) were of opposite signs, the total effects were more close to zero, which formulated a competitive mediation model as proposed by Zhao et al (231). On the other hand, the direct and indirect effects of GWG on HAZ were both positive, thus creating a complementary mediation model. Besides a positive indirect path from GWG to WHZ via birthweight, the negative direct effect of GWG on WHZ might indicate an additional J-shaped relationship bypassing birthweight. Specifically, infants born to mothers who had a low GWG might have experienced catch-up growth as compensation to early intrauterine growth retardation. This finding provides some supporting evidence to the thrifty phenotype hypothesis (232). Indeed, children with intrauterine malnutrition and growth restriction due to inadequate GWG may be programmed to a disturbed endocrine axis (233), energy and metabolic homeostasis (217-219, 234), and appetite control (220).

The results suggest that longer breastfeeding duration suppresses the positive effects of GWG and birthweight on WAZ, WHZ, and BMIZ via an indirect pathway (a→d→f). The protective effect of longer breastfeeding duration on child WAZ, WHZ, and BMIZ might act by several mechanisms. Breastfeeding infants have lower energy and protein intakes than formula-fed ones at 3, 6, and 9 months of age (235). Breastfeeding mothers might be more responsive to infants' cues of hunger and satiety (236). Thus, they may have less feeding restrictions on the child's feeding frequency and volume, which in turn may allow breastfed infants to better self-regulate their energy intake. As compared to breastfeeding directly at the breast, formula-fed infants might lack self-regulation of milk intake (166) and are at a higher risk of rapid weight gain during the first year of life (237). Besides behavioral pathways, breastfeeding may be negatively linked with later obesity via metabolic mechanisms. Formula-fed infants have a greater insulin response and lactate and pyruvate rise after feeding, compared with their breastfed counterparts (238, 239). Breastfed infants had lower plasma concentrations of insulin-like growth factors I than non-breastfed infants at 9 months of age (240). In addition, human milk intake in early life may impact obesity until adolescence by lowering leptin concentrations relative to fat mass (241). Together, these data suggest that endocrine programming in early life may serve as a link between early nutrition exposures and later obesity risk.

Given that specific height components may be more sensitive to disease susceptibility in later life than height itself (7, 242), this study explored the interrelationships among GWG, birthweight, infant feeding practices, and ulnar length, a linear growth parameter for upper extremity. Unlike most height components or surrogates (e.g., arm span and lower leg length), ulnar length may serve as a better surrogate because its measurement is not impeded by joint deformity. It has been demonstrated that ulnar length can serve as an accurate and reliable surrogate for length/height using simple and portable tools (caliper, ruler, or paper grid) (*submitted*). In this study, although birthweight had greater direct effects on HAZ than ulnar length, the indirect effect of birthweight mediated via breastfeeding duration was only observed in ulnar length. Additionally, both longer duration of breastfeeding and a later age at introduction of solid foods had positive effects on ulnar length but not on HAZ. Future research investigating contributors to distinct growth patterns of ulnar or another bone length versus height is warranted. In addition, the protective effects of breastfeeding on WAZ, WHZ, and BMIZ were only significant in non-Hispanics. According to Davis et al., the absence of a protective effect of breastfeeding on child obesity might be masked by high sugar intake in Hispanic toddlers (243). Given the associations between childhood growth and disease risk in later life, identifying contributors to these ethnic variations might enhance our understanding of the underlying mechanisms that drive ethnic disparities in disease morbidity and mortality.

There are a number of strengths of our study. The SEM approach is superior to conventional linear regression analysis in terms of delineating multiple pathways by which variables may influence outcomes of interest. In addition, this study adds to the limited literature of the associations among GWG, birthweight, infant feeding, and early postnatal growth (especially linear growth) rather than only BMIZ or BMI percentile. Last, this analysis included a series of important maternal socio-demographic and reproductive factors as covariates. Failure to adjust for residual confounding is of particular concern, which may contribute to the inconsistent findings across studies. In a study of 2758 mother-child dyads in the Collaborative Perinatal Project, the positive association between GWG and child BMIZ at age 4 years was attenuated and no longer significant after adjusting for shared family factors (201). In contrast to our findings, a stronger direct than indirect effect of GWG on child BMIZ at 5 years was observed in

3600 mother-child dyads in the Early Childhood Longitudinal Study-Birth Cohort (244). However, beside socio-demographic and family lifestyle covariates, no maternal perinatal covariates were included (244); thus the discordant findings might be partially attributable to residual confounding.

Certain limitations of this study need to be noted. First, significant paths identified in SEM do not establish causal effects. Due to the absence of temporal precedence in this cross-sectional study, further investigation using a longitudinal study design is needed to confirm our findings. Second, maternal recall of GWG and infant feeding practices may be subject to bias from memory and social desirability. However, Li et al (164) reported maternal recall of breastfeeding initiation and duration were valid and reliable especially within 3 years after the practice. In addition, residual confounding might exist in this analysis, e.g. child physical activity, television watching, and other lifestyle factors. Finally, the study population was not sampled to be nationally representative which would limit generalizability.

In conclusion, findings from this study suggest a stronger indirect effect (via birthweight and breastfeeding) than direct effect of maternal GWG on childhood anthropometrics, independent of maternal socio-demographic and reproductive factors. Longer breastfeeding duration reduces the positive associations of GWG and birthweight with WAZ, WHZ, and BMIZ, suggesting promoting longer breastfeeding may be a strategy for women with excessive GWG to mitigate offspring obesity. The positive direct effects of longer breastfeeding duration and later introduction of solid foods on ulnar length are significant in Hispanics. Future prospective research is warranted to investigate the ethnic-specific path variables and childhood growth trajectories.

Table 5.1 Characteristics of 1387 mother-child dyads by maternal gestational weight gain in the National Children's Study Formative Research in Anthropometrics, United States, 2011-2012[1]

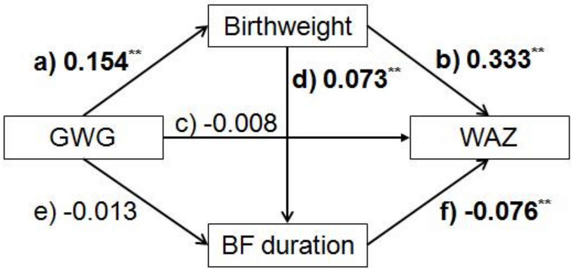
	Gestational weight gain					*P* value[2]
	<14 lbs	15-19 lbs	20-29 lbs	30-40 lbs	>40 lbs	
n	217	144	397	412	217	
Maternal characteristics						
Ethnicity						<0.001
Non-Hispanic White	9.7	9.7	18.9	26.5	30.9	
Hispanic	60.8	57.6	47.4	41.7	29.5	
Non-Hispanic Black	24.9	25.7	22.7	24.3	32.3	
Other	4.6	6.9	11.1	7.5	7.4	
Education						<0.001
< High school	26.3	23.6	17.1	19.2	13.8	
= High school	28.1	20.8	20.2	15.3	14.3	
> High school	45.6	55.6	62.7	65.5	71.9	
Single mother	53.9	51.4	47.4	42	47.5	0.04
Age at childbirth, y	28.2 (6.1)	28.5 (6.2)	29.1 (6.4)	27.9 (6.0)	27.8 (6.0)	0.02
Parity (primiparous)	25.8	30.6	38	41.5	51.2	<0.001
Prepregnancy BMI, kg/m^2	29.4 (7.3)	27.4 (6.3)	26.5 (7.0)	25.1 (5.7)	24.9 (5.1)	<0.001
Pregnancy complications	32.3	26.4	23.4	21.1	26.7	0.03
Smoking in pregnancy	7.4	3.5	3.8	5.6	9.7	0.02
Child characteristics						
Age, months	23.1 (20.1)	24.6 (21.1)	24.6 (20.7)	21.6 (19.1)	27.3 (20.3)	0.01
Males	42.9	45.8	50.6	59.5	57.6	<0.001
Birthweight, kg	3.1 (0.6)	3.1 (0.6)	3.3 (0.6)	3.3 (0.6)	3.2 (0.6)	<0.001
Breastfeeding duration, mo	3.4 (4.7)	5.0 (6.9)	4.6 (5.9)	4.6 (5.5)	4.4 (5.7)	0.06
Age at introduction of solid foods, mo	6.6 (3.3)	6.7 (3.0)	6.9 (3.4)	6.2 (2.5)	6.1 (3.0)	<0.01
WAZ	0.01 (1.26)	-0.04 (1.09)	0.11 (1.25)	0.1 (1.19)	0.13 (1.06)	0.56
WHZ	0.35 (1.06)	0.21 (1.10)	0.23 (1.21)	0.18 (1.35)	0.22 (0.99)	0.56
BIMZ	0.54 (1.15)	0.26 (1.16)	0.29 (1.37)	0.11 (1.35)	0.38 (1.03)	0.15
HAZ	-0.15 (1.07)	-0.1 (0.95)	0.02 (0.98)	0.12 (1.06)	0.17 (0.98)	<0.01
Ulnar length, cm	12.8 (2.9)	12.6 (3.3)	12.7 (1.9)	12. 8 (1.8)	12.9 (2.5)	0.34[3]

[1] Values are mean (SD) for continuous variables or % for categorical variables. BMI, body mass index; BMIZ, body mass index-for-age z-score; HAZ, height/length-for-age z-score; SD, standard deviation; WAZ, weight-for-age z-score; WHZ, weight-for-height/length z-score.

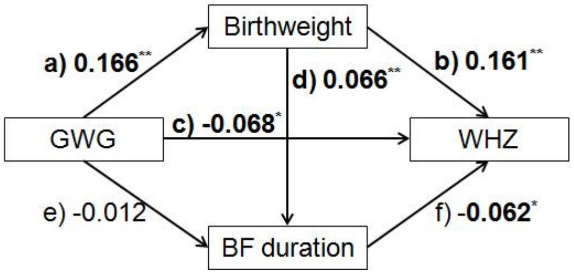
[2] Based on ANOVA for continuous variables and χ^2 tests for categorical variables unless otherwise stated.

[3] Based on ANCOVA with age and sex as covariates.

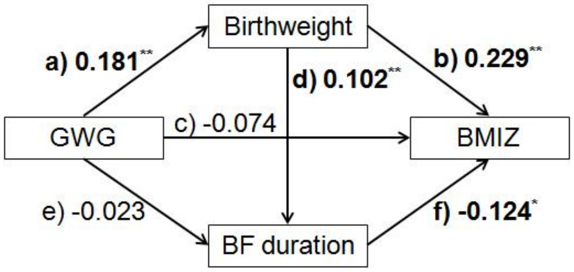
A) SEM model 1(*n* = 1387)



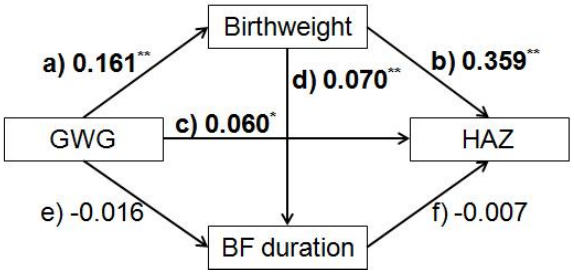
B) SEM model 2 (*n* = 1330)



C) SEM model 3 (*n* = 554)



D) SEM model 4 (*n* = 1338)



E) SEM model 5 (*n* = 1368)

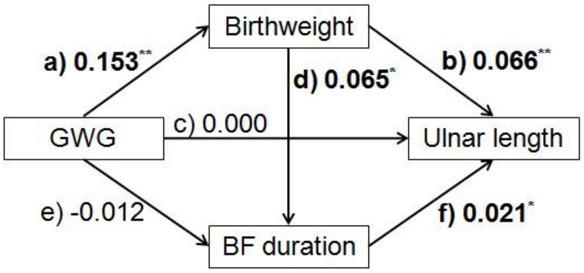


Figure 5.2 Structural equation models with standardized path coefficients for the relationships among maternal gestational weight gain (GWG), child's birthweight, breastfeeding (BF) duration, and weight-for-age z-score (WAZ) (A), weight-for-length/height z-score (WHZ) (B), body mass index-for-age z-score (BMIZ) (C), length/height-for-age z-score (HAZ) (D), and ulnar length (E). All models were adjusted for maternal ethnicity, education level, marital status, age at childbirth, parity, prepregnancy BMI, pregnancy complications, and smoking in pregnancy. * Ulnar length was additionally adjusted for child's age and sex. P <0.05; ** P <0.01.

Table 5.2 Standardized total, direct, and indirect effects of gestational weight gain, child's birthweight, and breastfeeding duration on childhood anthropometric measures in the National Children's Study Formative Research in Anthropometrics, United States, 2011-2012[1]

	WAZ (*n* = 1387)		WHZ (*n* = 1330)		BMIZ (*n* = 554)[2]		HAZ (*n* = 1338)		Ulnar length (*n* = 1368)	
	β	95% CI	*β*	95% CI	*β*	95% CI	*β*	95% CI	*β*	95% CI
Gestational weight gain										
Total effect	0.044	-0.005, 0.095	-0.041	-0.086, 0.013	-0.038	-0.113, 0.039	**0.118**	**0.066, 0.176**	0.010	-0.010, 0.032
Direct effect	-0.008	-0.052, 0.045	**-0.068**	**-0.113, -0.014**	-0.074	-0.158, 0.005	**0.060**	**0.007, 0.116**	0.000	-0.020, 0.022
Indirect effect	**0.052**	**0.033, 0.072**	**0.027**	**0.015, 0.042**	**0.036**	**0.013, 0.070**	**0.058**	**0.038, 0.078**	**0.010**	**0.006, 0.017**
Child's birthweight										
Total effect	**0.328**	**0.265, 0.397**	**0.157**	**0.088, 0.216**	**0.216**	**0.126, 0.301**	**0.359**	**0.294, 0.418**	**0.067**	**0.046, 0.091**
Direct effect	**0.333**	**0.272, 0.399**	**0.161**	**0.092, 0.219**	**0.229**	**0.136, 0.309**	**0.359**	**0.295, 0.421**	**0.066**	**0.045, 0.089**
Indirect effect	**-0.005**	**-0.014, -0.001**	-0.004	-0.012, 0.000	**-0.013**	**-0.032, -0.003**	0.000	-0.005, 0.004	**0.001**	**0.000, 0.004**
Breastfeeding duration										
Total effect	**-0.076**	**-0.132, -0.022**	**-0.062**	**-0.123, 0.000**	**-0.124**	**-0.216, -0.040**	-0.007	-0.064, 0.050	**0.021**	**0.001, 0.041**
Direct effect	**-0.076**	**-0.132, -0.022**	**-0.062**	**-0.123, 0.000**	**-0.124**	**-0.216, -0.040**	-0.007	-0.064, 0.050	**0.021**	**0.001, 0.041**
Indirect effect	–	–	–	–	–	–	–	–	–	–

[1] Adjusted for maternal ethnicity, education level, marital status, age at childbirth, parity, prepregnancy BMI, pregnancy complications, and smoking in pregnancy. Ulnar length was additionally adjusted for child's age and sex. 95% CIs were bias-corrected bootstrap CIs. *β*, standardized coefficient; BMIZ, body mass index-for-age z-score; CI, confidence interval; HAZ, height/length-for-age z-score; WAZ, weight-for-age z-score; WHZ, weight-for-height/length z-score.

[2] Among children aged 2-5.9 years in the study.

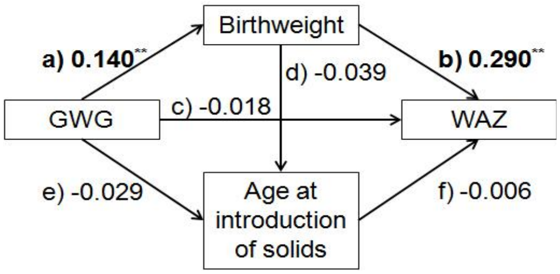
Table 5.3 Standardized path coefficients for childhood anthropometric measures derived from structural equation modeling by ethnicity in the National Children's Study Formative Research in Anthropometrics, United States, 2011-2012[1]

			WAZ		WHZ		BMIZ[2]		HAZ		Ulnar length	
Path			NH	H	NH	H	NH	H	NH	H	NH	H
n			748	639	722	608	361	193	730	608	740	628
a) Birthweight	←	GWG	**0.192****	**0.113****	**0.202****	**0.125****	**0.179****	**0.190****	**0.194****	**0.125****	**0.193****	**0.110****
b) Anthropometrics	←	Birthweight	**0.359****	**0.306****	**0.207*****	**0.120*****	**0.249****	**0.207***	**0.324****	**0.410*****	**0.055****	**0.081****
c) Anthropometrics	←	GWG	0.009	**0.113****	-0.039	-0.046	-0.063	-0.038	0.045	0.032	0.001	-0.017
d) BF duration	←	Birthweight	**0.098****	0.038	**0.092***	0.042	**0.131****	0.064	**0.092***	0.042	**0.096****	0.035
e) BF duration	←	GWG	-0.026	0.003	-0.022	-0.005	-0.015	0.071	-0.028	-0.005	-0.025	0.004
f) Anthropometrics	←	BF duration	**-0.080****	-0.071	**-0.052***	-0.061	**-0.115***	-0.122	-0.017	-0.008	-0.014	**0.066****
P-value for model χ^2			0.005		<0.001		<0.001		0.003		<0.001	
RMSEA			0.026		0.033		0.054		0.019		0.039	
CFI			0.984		0.974		0.945		0.993		0.966	
TLI			0.970		0.960		0.935		0.979		0.951	

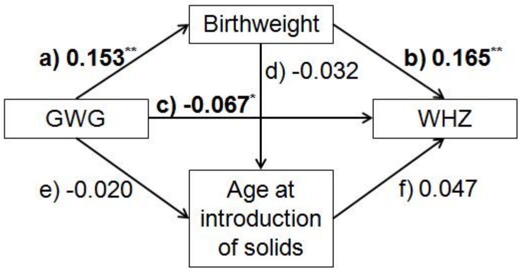
[1] Adjusted for maternal prepregnancy body mass index, education level, marital status, ethnicity, pregnancy complications, and smoking during pregnancy. Ulnar length was additionally adjusted for child's age and sex. BF, breastfeeding; BMIZ, body mass index-for-age z-score; CFI, goodness-of-fit statistic; GWG, gestational weight gain; H, Hispanic; HAZ, height/length-for-age z-score; NH, non-Hispanic; RMSEA, root mean square error of approximation; TLI, Tucker-Lewis index; WAZ, weight-for-age z-score; WHZ, weight-for-height/length z-score.

[2] Among children aged 2-5.9 years in the study.

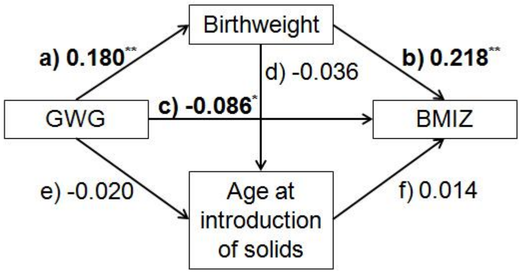
A) SEM model 1(*n* = 1107)



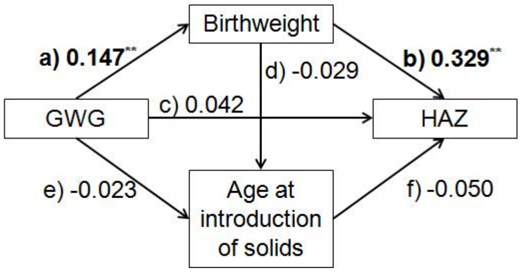
B) SEM model 2 (*n* = 1056)



C) SEM model 3 (*n* = 551)



D) SEM model 4 (*n* = 1064)



E) SEM model 5 (*n* = 1095)

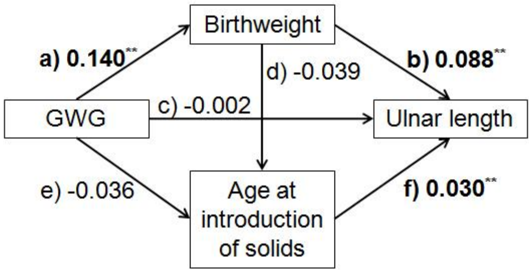


Figure 5.3 Structural equation models with standardized path coefficients for the relationships among maternal gestational weight gain (GWG), child's birthweight, age at introduction of solids, and weight-for-age z-score (WAZ) (A), weight-for-length/height z-score (WHZ) (B), body mass index z-score (BMIZ) (C), length/height-for-age z-score (HAZ) (D), and ulnar length (E). All models were adjusted for maternal ethnicity, education level, marital status, age at childbirth, parity, prepregnancy BMI, pregnancy complications, and smoking in pregnancy. Ulnar length was additionally adjusted for child's age and sex. * P <0.05; ** P <0.01.

Table 5.4 Standardized total, direct, and indirect effects of gestational weight gain, child's birthweight, and age at introduction of solid foods on childhood anthropometric measures in the National Children's Study Formative Research in Anthropometrics, United States, 2011-2012[1]

	WAZ (*n* = 1107)		WHZ (*n* = 1056)		BMIZ (*n* = 551)[2]		HAZ (*n* = 1064)		Ulnar length (*n* = 1095)	
	β	95% CI	*β*	95% CI	*β*	95% CI	*β*	95% CI	*β*	95% CI
Gestational weight gain										
Total effect	0.023	-0.032, 0.074	-0.043	-0.095, 0.008	-0.047	-0.118, 0.030	**0.092**	**0.032, 0.146**	0.009	-0.015, 0.031
Direct effect	-0.018	-0.073, 0.034	**-0.067**	**-0.121, -0.018**	**-0.086**	**-0.156, -0.003**	0.042	-0.016, 0.104	-0.002	-0.027, 0.020
Indirect effect	**0.041**	**0.021, 0.062**	**0.060**	**0.029, 0.109**	**0.039**	**0.017, 0.068**	**0.050**	**0.030, 0.077**	**0.011**	**0.004, 0.019**
Child's birthweight										
Total effect	**0.290**	**0.224, 0.364**	**0.164**	**0.082, 0.240**	**0.217**	**0.126, 0.293**	**0.331**	**0.265, 0.386**	**0.087**	**0.056, 0.113**
Direct effect	**0.290**	**0.222, 0.363**	**0.165**	**0.084, 0.244**	**0.218**	**0.126, 0.302**	**0.329**	**0.266, 0.384**	**0.088**	**0.058, 0.115**
Indirect effect	0.000	-0.002, 0.006	-0.003	-0.020, 0.001	0.000	-0.011, 0.004	0.001	-0.001, 0.010	-0.001	-0.005, 0.001
Age at introduction of solids										
Total effect	-0.006	-0.068, 0.060	0.047	-0.024, 0.130	0.014	-0.081, 0.123	-0.050	-0.122, 0.009	**0.030**	**0.002, 0.057**
Direct effect	-0.006	-0.068, 0.060	0.047	-0.024, 0.130	0.014	-0.081, 0.123	-0.050	-0.122, 0.009	**0.030**	**0.002, 0.057**
Indirect effect	–	–	–	–	–	–	–	–	–	–

[1] Adjusted for maternal ethnicity, education level, marital status, age at childbirth, parity, prepregnancy BMI, pregnancy complications, and smoking in pregnancy. Ulnar length was additionally adjusted for child's age and sex. 95% CIs were bias-corrected bootstrap CIs. *β*, standardized coefficient; BMIZ, body mass index-for-age z-score; CI, confidence interval; HAZ, height/length-for-age z-score; WAZ, weight-for-age z-score; WHZ, weight-for-height/length z-score.

[2] Among children aged 2-5.9 years in the study.

Chapter 6: Conclusions

RESEARCH FINDINGS AND PUBLIC HEALTH SIGNIFICANCE

This research used data from a multi-center multi-ethnic population of mother-child dyads in the NCS Formative Research in Anthropometry in the US from 2011-2012. The overall objective of this research was to improve our understanding of the associations between dietary factors in early life and childhood growth. Based on quality control strategies used in this research, Chapter 2 provided a summary and beginners' guidelines to perform data management and preprocessing procedures in human studies. Predictive models for ever XBR since birth and XBR duration ≥6 months were developed using sociodemographics, maternal perinatal factors, and child birth characteristics to identify women at risk for none or poor lactation performance (Chapter 3). In Chapter 4, the accuracy and reliability of ulnar length measured by different tools (i.e., caliper, ruler, and paper grid) was examined as surrogate measures of recumbent length in infants and children aged 0-2.9 years and standing height in children aged 2-5.9 years, respectively. Finally, the interrelationships among maternal GWG, child birthweight, infant feeding practices (breastfeeding duration and age at introduction of solid foods), and childhood anthropometric outcomes in the total sample and by ethnicity were investigated via an SEM approach (Chapter 5).

Predictive Models for XBR Initiation and Duration

A wide selection of sociodemographic, perinatal, and birth outcome factors was used to develop predictive models for XBR initiation and duration ≥6 months. The final models identified ten independent determinants of XBR performance: maternal education level, marital status, nativity, age at birth of the index child, prepregnancy complications, ethnicity, smoking during pregnancy, prepregnancy BMI, child’s birthweight, and child’s birth year. Maternal socio-demographic factors (education level, marital status, nativity, and age at childbirth) had greater discriminating abilities to predict ever XBR since birth and XBR duration ≥6 months, compared to child birth characteristics (birthweight and birth year) and maternal perinatal factors (complications and smoking during pregnancy and prepregnancy BMI). Since most of these socio-demographic factors are not amenable, the differences observed may be attributable to not only cultural and psychosocial factors, but also to environmental support provided to and received by the mothers. Therefore, breastfeeding education and counseling provided to mothers with low educational attainments, clinical and familial support offered to single mothers, or a combination of both strategies might be used to promote XBR. Of particular note, maternal age at childbirth was the only factor consistently associated with XBR initiation, XBR duration, and BrBot subgroups. Given that pediatrician in 2004 were five times more likely than ten years ago to recommend against breastfeeding for mothers who were perceived as “too young or immature” (163), it is of particular importance to provide appropriate clinical support to younger mothers. In addition, based on the identified predictors, obese women before pregnancy and pregnant smokers can be targeted for strategies to promote breastfeeding from their first prenatal visit; whereas those who suffer from pregnancy complications can be targeted upon diagnosis. In summary, the predictive models are empirically driven by variables with strong potential for public health interventions.

Considering maternal lactation performance including duration varies across populations, our findings can help health professionals identify mothers at increased risk of not initiating/continuing XBR and breastfeeding to a less extent among BrBot mothers. The ultimate goal must be to help reduce disparities in lactation performance in different populations.

Recumbent Length and Height Prediction from Ulnar Length

In this study, it is demonstrated that ulnar length can serve as an accurate and reliable surrogate measure of recumbent length in healthy infants/children aged 0-1.9 years and of standing height in healthy children aged 2-5.9 years in the US, respectively. Although arm span as a surrogate measure of length/height had higher prediction accuracy compared to ulnar length, its use might be limited in children with postural problems (e.g., joint deformities or chondrodysplasia). In contrast, ulnar length might serve as a better surrogate of linear growth in these children because its measurement is not usually impeded by joint deformities.

Results from the Bland-Altman plots and mixed-effects linear regression models showed that the three simple and portable tools (i.e., caliper, ruler, and grid) used to measure ulnar length can be interchangeable in terms of prediction accuracy. Considering the special needs of portable, easily accessible and inexpensive measurement tools of anthropometrics in certain field studies, ulnar length measured by these three tools could serve as practical alternatives for standard measurement of length/height using infantomer/stadiometer. However, it is worth noting that tool-specific issues exist when measuring ulnar length using caliper, ruler, and grid. For instance, ulnar length might be overestimated if the caliper is angled either horizontally or vertically away from the long axis of the ulna (i.e., not parallel with either the line of the ulna or with the tabletop). Measurers might obtain a shorter ulnar length than the real value if either the ruler or the ulnar is not placed vertically against the table. The grid method might generate more measurement difficulties because it involves separate marking of the two ulnar points (i.e., the styloid and olecranon process) with accuracy compromised if the arm moves. Additionally, a challenge in use of the grid is the ability to mark the grid with a pen as proximally as possible to the marks for the olecranon and styloid process of the ulna. Even the width of the pen point could alter the location of and the size of the mark on the page; thus, careful training and administration regarding the marking process is essential. Given these tool-specific issues, a combination of tools in specific age groups and field settings might optimize the measurement accuracy and reliability and alleviate or ameliorate field conditions (e.g., home versus clinic) that could hamper the accuracy of one approach over another.

Given the importance of length and height in assessing nutritional and growth status in both healthy and physically impaired children, future research is warranted assessing ulnar length by the three tools in children who are temporarily hospitalized or who have long-term mobility-impairment due to neuromuscular diseases or joint deformities. Ulnar length as a potential surrogate measure of length/height in these children may not only contribute to a single point in time estimation of linear growth for acute care management, but also to long-term monitoring of growth trajectories.

Infant Feeding as a Mediator of the GWG-Childhood Growth Association

Applying the SEM approach, it is demonstrated that maternal GWG had a greater indirect than direct effect on child anthropometric outcomes. Several indirect pathways were observed by which maternal GWG imposed its effects on child linear growth and adiposity parameters. Child’s birthweight, as a mediator, led the most prominent indirect pathway from maternal GWG to all child anthropometrics. Dietary factors in early life were also significant mediators in certain pathways. Specifically, longer duration of breastfeeding showed reduced the positive associations among GWG, birthweight, and certain anthropometrics (i.e., WAZ, WHZ, and BMIZ). On the other hand, age at introduction of solid foods did not mediate the relationship between birthweight and anthropometric outcomes except ulnar length. These findings underscore the importance of promoting longer breastfeeding duration among women with excessive GWG to mitigate childhood obesity.

Ulnar length, as a linear growth parameter of upper extremity, was sensitive to both breastfeeding duration and age at introduction of solid foods, independent of maternal sociodemographic, perinatal factors, and child’s age and sex. This finding may suggest a distinct growth pattern of the upper limb segment compared to the total length/height in early life. Similarly, previous studies revealed that certain specific height components or surrogates (e.g., leg length and trunk length) may be more sensitive to disease susceptibility in later life than height itself (7, 242). Our findings add to the literature that ulnar length as a proxy of upper extremity growth may serve as a better indicator of childhood nutrition and growth status, which might provide unique insights into future investigation of the associations between early life factors and later disease risk.

In addition, ethnic-specific interplay was observed among maternal GWG, birthweight, infant feeding, and childhood anthropometrics. In stratification analysis by ethnicity, the negative effects of longer length of breastfeeding on child's WAZ, WHZ, and BMIZ were only evident in non-Hispanic White infants and children. In contrast, the positive association between better performance of infant feeding practices (i.e., longer length of breastfeeding and a later age at introduction of solid foods) and ulnar length was only significant in Hispanics. Future research aiming to study the underlying mechanisms that drive ethnic variation in the associations between dietary factors in early life and childhood growth is needed to enhance our understanding of the ethnic specific disparities in disease morbidity and mortality.

DIRECTIONS FOR FUTURE RESEARCH

This research could be extended to further understand the role of early life dietary factors in child growth trajectories and subsequent disease risk in later life. Our analysis was based on a cross-sectional study of child anthropometrics in the US from 2011-2012. The absence of temporal precedence of dietary factors in early life and child anthropometric outcomes in this study limited our ability to establish causal relationships. Future studies using a longitudinal study design are needed to verify our findings. In addition, inclusion of other environmental exposures in early life including lifestyle, home environmental, and psychosocial factors would allow researchers to account for potential residual confounding not addressed in this study.

Considering ulnar length is an accurate and reliable surrogate measure of linear growth in healthy infants and children aged <6 years, an extension of the assessment of this surrogate in both short- and long-term physically impaired children is warranted. In addition, SEM results revealed ulnar length is more sensitive to certain dietary factors in early life (i.e., breastfeeding duration and age at introduction of solid foods) than HAZ. Research aiming to assess the association between ulnar length and disease susceptibility in later life might benefit from the long-term monitoring of the distinct growth pattern of this surrogate measure.

Another methodological consideration relates to the use of maternal recall data of infant feeding practices. Despite the challenges in longitudinal studies involving postpartum women who might be overloaded with burden from both the family and society, frequent recalls at certain time points along with the mother’s lactation practice would largely reduce the systematic error attributed to long-term recall bias. In addition, recent data predominantly in Caucasian population in the US revealed that infants fed expressed breast milk from the bottle exhibited similar growth patterns as those who were formula-fed from the bottle (237). Future research focusing on the association between dietary factors in early life and child growth could be further extended to investigate not only the type and duration of milk fed to the child but also the mode of milk delivery.

Appendix A Perinatal History Questionnaire

(affix label here)

PERINATAL HISTORY

The purpose of this questionnaire is to learn more about food intake and growth among newborns, infants, and children. This questionnaire needs to be completed by the mother of the newborn, infant, or child.

SOCIO-DEMOGRAPHICS

1. How many people, both children and adults, live in your household? Include any persons who usually stay but are temporarily away on business, vacation, or students living temporarily away from home. Including yourself, what is the total number of people who live in your household?

|___|___|

REFUSED	9--97
DON'T KNOW	9--98

2. Now I'd like to ask about your marital status. What is your current marital status? Are you:

Married	1
Not married but living together with a partner	2
Widowed	4
Divorced	5
Separated	6
Never been married	7
REFUSED	9--97
DON'T KNOW	9--98

3. Do you consider yourself to be Hispanic, or Latina?

YES	1
NO	2
REFUSED	9--97
DON'T KNOW	9--98

4. What race do you consider yourself to be? You may select one or more.

SELECT ALL THAT APPLY.

White,	1
Black or African American,	2
Filipino	3
Chinese	4
Native Hawaiian	5
Other Pacific Islander	6
South East Indian	7
SOME OTHER RACE (SPECIFY): ______________________	8
REFUSED	9--97
DON'T KNOW	9--98

5. Is the father of the newborn, infant, or child considered to be Hispanic, or Latino?

YES	1
NO	2
REFUSED	9--97
DON'T KNOW	9--98

6. What race is the father of the newborn, infant, or child considered to be? You may select one or more.

SELECT ALL THAT APPLY.

White,	1
Black or African American,	2
Filipino	3
Chinese	4
Native Hawaiian	5
Other Pacific Islander	6
South East Indian	7
SOME OTHER RACE (SPECIFY): ______________________	8
REFUSED	9--97
DON'T KNOW	9--98

7. Please look at the card and tell me what is the highest degree or level of school that you have completed?

NO SCHOOL	1
ELEMENTARY	
NURSERY SCHOOL TO 4TH GRADE	2
5TH-6TH GRADE	3
7TH-8TH GRADE	4
HIGH SCHOOL	
9TH GRADE	5
10TH GRADE	6
11TH GRADE	7
12TH GRADE (NO DIPLOMA)	8
HIGH SCHOOL DIPLOMA	9
GED OR EQUIVALENT	10
COLLEGE	
SOME COLLEGE CREDITS, BUT LESS THAN 1 YEAR	11
1 OR MORE YEARS OF COLLEGE, BUT NO DEGREE	12
ASSOCIATE DEGREE: OCCUPATIONAL, TECHNICAL, OR VOCATIONAL PROGRAM	13
ASSOCIATE DEGREE: ACADEMIC PROGRAM	14
BACHELOR'S DEGREE (e.g., BA, BS)	15
GRADUATE	
MASTER'S DEGREE (e.g., MA, MS, MSW, MEng, MBA)	16
PROFESSIONAL SCHOOL DEGREE (e.g., MD, DDS, DVM, JD)	17
DOCTORAL DEGREE (e.g., Ph.D., Ed.D.)	18
REFUSED	9--97
DON'T KNOW	9--98

8. Are you currently a full- or part-time student? This includes vocational or technical schooling that may not be done in a classroom.

NO, NOT A STUDENT	1	(skip to Q10)
YES, FULL-TIME STUDENT	2	
YES, PART-TIME STUDENT	3	
REFUSED	9--97	(skip to Q10)
DON'T KNOW	9--98	(skip to Q10)

9. What type or types of school are you currently attending?

HIGH SCHOOL	1
TECHNICAL SCHOOL	2
COLLEGE OR UNIVERSITY	3
GRADUATE SCHOOL	4
PROFESSIONAL SCHOOL (E.G., MEDICAL, LAW, DENTAL)	5
OTHER (SPECIFY): ______________________________	6
REFUSED	9--97
DON'T KNOW	9--98

10. Are you currently employed?

YES	1
NO	2
REFUSED	9--97
DON'T KNOW	9--98

11. Were you born in the United States?

YES	1
NO	2
REFUSED	9--97
DON'T KNOW	9--98

This part of this questionnaire asks about newborn, infant, or child's birth weight, length and type of feeding received during early life.

Child's History

12. What is [PARTICIPANT]'s birth name? (Last name, First name and Middle name)

13. What is [PARTICIPANT]'s gender?

Male	1
Female	2

14. What is [PARTICIPANT]'s date of birth?

|___|___| |___|___| |___|___|___|___|

Month Day Year

15. What was [PARTICIPANT]'s weight at birth?

|___|___| |___|___|
Pounds Ounces

16. What was [PARTICIPANT]'s length at birth?

|___|___| . |___|___|
Inches

17. Was [PARTICIPANT] born earlier or later than expected?

On time	1
Less than 2 weeks late	2
More than 2 weeks late	3
Less than 2 weeks early	4
More than 2 weeks early	5
REFUSED	9--97
DON'T KNOW	9--98

18. Was [PARTICIPANT] ever fed breast milk?

YES	1	
NO	2	(skip to Q20)
REFUSED	9--97	(skip to Q20)
DON'T KNOW	9--98	(skip to Q20)

19. How old was [PARTICIPANT] when s/he **completely** stopped being fed breast milk?

Please enter age in days, weeks, months and years or if currently breastfeeding, circle 5 below.

Age |___|___|___|

Please circle the time unit that applies:

Days	1
Weeks	2
Months	3
Years	4
Currently breastfeeding	5
REFUSED	9--97
DON'T KNOW	9--98

20. How old was [PARTICIPANT] when s/he was **first** fed something other than breast milk or water? (Include formula, juice, cow’s milk, solid foods).

Please enter age in days, weeks, months and years.

Age |___|___|___|

Please circle the time unit that applies:

Days	1
Weeks	2
Months	3
Years	4
Exclusively breastfed	5
REFUSED	9--97
DON’T KNOW	9--98

21. Was [PARTICIPANT] ever fed formula?

YES	1	
NO	2	(skip to Q27)
REFUSED	9--97	(skip to Q27)
DON’T KNOW	9--98	(skip to Q27)

22. How old was [PARTICIPANT] when s/he was first fed formula **on a daily basis**? (Include receiving formula and breast milk at the same time).

Please enter age in days, weeks, months and years.

Age |___|___|___|

Please circle the time unit that applies:

Days	1
Weeks	2
Months	3
Years	4
Never on a daily basis	5
REFUSED	9--97
DON’T KNOW	9--98

23. While [PARTICIPANT] received formula, was s/he fed . . .

Formula only	1
Formula and breast milk equally	2
More formula than breast milk	3
More breast milk than formula	4
REFUSED	9--97
DON'T KNOW	9--98

24. What type of infant formula was s/he fed most often?

Regular, cow's milk-based (SMA, Similac, Enfamil)	1
Soy or soybean based (Isomil, ProSobee, Nursoy)	2
Other (rice-based, elemental)	3
REFUSED	9--97
DON'T KNOW	9—98

25. How old was [PARTICIPANT] when s/he **completely** stopped drinking formula?

Please enter age in days, weeks, months and years.

Age |___|___|___|

Please circle the time unit that applies:

Days	1	
Weeks	2	
Months	3	
Years	4	
Currently fed formula	5	
Never fed formula	6	(skip to Q27)
REFUSED	9--97	
DON'T KNOW	9--98	

26. What kind of formula was [PARTICIPANT] fed in the <u>past 7 days</u>? Infant formulas are listed alphabetically in the chart below. [PRESENT CARD TO MOTHER] Please put an X in the box next to the name of each infant formula your baby was fed. (MARK ALL THAT APPLY)

Did not feed formula in the past 7 days .... ☐ ➔**SKIP TO Q25**

Formula Name		**Formula Name**	
EleCare..	☐ 1	Enfagrow Soy Toddler..	☐ 29
Enfamil..	☐ 2	Enfaport LIPIL	☐ 30
Enfamil AR.......................................	☐ 3	Gerber Good Start Essentials	☐ 31
Enfamil Enfacare	☐ 4	Gerber Good Start 2 Essentials	☐ 32
Enfamil Gentlease	☐ 5	Gerber Good Start Essentials Soy	☐ 33
Enfamil Gentlease Toddler................	☐ 6	Gerber Good Start 2 Essentials Soy	☐ 34
Enfamil LactoFree LIPIL...................	☐ 7	Gerber Good Start Essentials Soy DHA and ARA..	☐ 35
Enfamil LIPIL	☐ 8	Gerber Good Start Supreme	☐ 36
Enfamil Next Step LIPIL	☐ 9	Gerber Good Start Supreme DHA and ARA..........	☐ 37
Enfamil NextStep ProSobee LIPIL....	☐ 10	Gerber Good Start Supreme 2 DHA and ARA.......	☐ 38
Enfamil Premature LIPIL	☐ 11	Gerber NAN DHA and ARA	☐ 39
Enfamil Premature Newborn	☐ 12	Horizon Organic	☐ 40
Enfamil Premature Infant..................	☐ 13	Similac Soy Isomil	☐ 41
Enfamil Premium Toddler..................	☐ 14	Isomil Advance...	☐ 42
Enfamil Premium Older Toddler........	☐ 15	Isomil 2	☐ 43
Enfamil ProSobee	☐ 16	Isomil 2 Advance..	☐ 44
Enfamil ProSobee LIPIL...................	☐ 17	Isomil DF	☐ 45
Enfamil Nutramigen AA LIPIL...........	☐ 18	Similac..	☐ 46
Enfamil Pregestimil LIPIL	☐ 19	Similac Advance...	☐ 47
Enfamil Restful LIPIL........................	☐ 20	Similac Advance Organic	☐ 48
Similac 2	☐ 21	Similac Human Milk Fortifier	☐ 49
Similac 2 Advance	☐ 22	Similac Sensitive	☐ 50
Similac Expert Care Alimentum.........	☐ 23	Similac Sensitive for Spit-up	☐ 51
Similac Lactose Free Advance..........	☐ 24	Store Brand milk based without DHA and ARA......	☐ 52
Similac Expert Care Neosure	☐ 25	Store Brand milk based with DHA and ARA LIPID	☐ 53
Similac Expert Care for Diarrhea.......	☐ 26	Store Brand soy based without DHA and ARA.......	☐ 54
Similac Go & Grow – milk based.......	☐ 27	Store Brand soy based with DHA and ARA LIPID..	☐ 55
Similac Go & Grow – soy based........	☐ 28	Other (specify)___________________________	☐ 56

27. How old was [PARTICIPANT] when s/he started drinking cow's milk (i.e. not in formula or breast milk) **on a daily or almost daily basis?**

Please enter age in days, weeks, months and years.

Age |___|___|___|

Please circle the time unit that applies:

Days	1
Weeks	2
Months	3
Years	4
Never on a daily or almost daily basis	5
REFUSED	9--97
DON'T KNOW	9--98

28. How old was [PARTICIPANT] when s/he started eating solid foods (e.g. rice cereal, baby food, crackers or any non-liquid foods) **on a daily or almost daily basis**?

Please enter age in days, weeks, months and years.

Age |___|___|___|

Please circle the time unit that applies:

Days	1
Weeks	2
Months	3
Years	4
Never on a daily or almost daily basis	5
REFUSED	9--97
DON'T KNOW	9--98

Since your baby/child [PARTICIPANT] was born, has your baby/child taken any…

	YES/NO	IF YES: When did your baby/child start taking them?	Is your baby/ child still taking them?	IF NO: When did your baby/child stop taking them?	ALL: On average, how many times per week has your baby/ child taken during this time period?
29. Flouride drops, for example, Tri-Vi-Flor or Poly-Vi-Flor	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	I___I___I / WK
30. Multi-vitamin drops such as Tri-Vit (Tri-Vi-Sol) or Poly-Vi-Sol	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	I___I___I / WK
31. Multi-vitamin chewable or gummies	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	I___I___I / WK
32. Iron drops	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	I___I___I / WK
33. Other vitamins or supplements: Specify___________	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	☐$_1$ Yes ☐$_2$ No	I___I___I Weeks$_2$ OR I___I___I Months$_3$ OR I___I___I Years$_4$	I___I___I / WK

A1. What type of restraint do you currently use for your child when riding in a vehicle?

Please circle the type of restraint that applies:

Car seat	1
Booster seat	2
Seat belt	3
No restraint	4
REFUSED	9–97
DON'T KNOW	9--98

A2. Which picture best represents your child's restraint type?

Please circle the type of restraint that applies:

REFUSED	9–97
DON'T KNOW	9--98

A3. At what age did your child progress from a car or booster seat to a standard seat belt?

Please enter age in months or years.

Age |___|___|___|

Months	1
Years	2
My child has not started using a standard seat belt	3
REFUSED	9--97
DON'T KNOW	9--98

The next part of the questionnaire asks about your pregnancy with [PARTICIPANT].

Mother's History

34. What is your date of birth?

|___|___| |___|___| |___|___|___|___|
Month Day Year

35. How tall are you without shoes?

|___|___| |___|___|
Feet Inches

36. What was your birth weight in pounds (lbs)?

Less than 5.5 lbs	1
5.5 – 6.9 lbs	2
7-8.4 lbs	3
8.5-9.9 lbs	4
10 lbs or more	5
REFUSED	9--97
DON'T KNOW	9--98

37. How much do you weigh without shoes and in no/light clothing?

|___|___|___|
Pounds

38. Just before you got pregnant with [PARTICIPANT], how much did you weigh?

|___|___|___|
Pounds

39. Approximately, how much weight did you gain during this pregnancy? (Mark one)

Less than 10 pounds	1
10-14 pounds	2
15-19 pounds	3
20-29 pounds	4
30-40 pounds	5
More than 40 pounds	6
REFUSED	9--97
DON'T KNOW	9--98

40. Did you smoke at any time in your life?

YES	1	
NO	2	(skip to Q46)

41. Did you smoke at any time while you were pregnant with [PARTICIPANT]?

YES	1	
NO	2	(skip to Q45)
REFUSED	9--97	(skip to Q45)
DON'T KNOW	9--98	(skip to Q45)

42. If yes, how many cigarettes did you smoke on an average day during your pregnancy with [PARTICIPANT]?

Less than 10	1
10-20	2
Over 20	3
REFUSED	9--97
DON'T KNOW	9--98

43. At any time while you were pregnant did you stop smoking for the rest of the pregnancy with [PARTICIPANT]?

YES	1	
NO	2	(skip to Q45)
REFUSED	9--97	(skip to Q45)
DON'T KNOW	9--98	(skip to Q45)

44. If yes, about what month of the pregnancy with [PARTICIPANT] did you stop smoking?

|___|___| Months

I did not stop	1

45. Did you smoke at any time while you were breastfeeding [PARTICIPANT]?

YES	1
NO	2
I did not breast feed	3
REFUSED	9--97
DON'T KNOW	9--98

46. While you were pregnant with [PARTICIPANT], were you ever told by a health care provider that you had one or more of the following conditions?
(mark all that apply)

a)	Anemia$_1$	Yes$_1$ No$_2$	→ **If yes**, did you take iron supplements? ○ Yes$_1$ ○ No$_2$
b)	Diabetes$_2$	Yes$_1$ No$_2$	→ **If yes**, did you take insulin? ○ Yes$_1$ ○ No$_2$
c)	High blood pressure$_3$	Yes$_1$ No$_2$	
d)	Pre-eclampsia or eclampsia (toxemia)$_4$	Yes$_1$ No$_2$	
e)	Proteinuria (protein in the urine)$_5$	Yes$_1$ No$_2$	
f)	Infection (kidneys, respiratory, etc.)$_6$	Yes$_1$ No$_2$	

47. If yes to Q46b, did your diabetes go away after [PARTICIPANT] was born?

YES	1
NO	2
REFUSED	9--97
DON'T KNOW	9--98

48. If yes to Q46b, do you have diabetes now?

YES	1	
NO	2	(skip to Q51)
REFUSED	9--97	(skip to Q51)
DON'T KNOW	9--98	(skip to Q51)

49. If yes to Q48, how old were you when you were first told you got diabetes?

|___|___| Years old (skip to 51)

DON'T KNOW	9--98

50. If you don't know, were you told you got diabetes before you were pregnant with [PARTICIPANT]?

YES	1
NO	2
REFUSED	9--97
DON'T KNOW	9--98

51. During your pregnancy with [PARTICIPANT], did you take a multiple or prenatal vitamin?

YES............................1
NO..............................2

→**If yes,** did you take them regularly?
○ Yes$_1$ ○ No$_2$

<table>
<tr><th colspan="3">52. Childbirth History</th><th colspan="3">Include all pregnancies lasting 6 months or longer. Include [PARTICIPANT] as well as twins. Answer one line apiece for each twin.</th></tr>
<tr><th colspan="3">Date of Birth</th><th>Outcome</th><th>Gender</th><th>Born Preterm (>3 wks before due date)</th></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
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|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
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|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
<tr><td>Month
|___|___|</td><td>Day
|___|___|</td><td>Year
|___|___|</td><td>○ Stillbirth$_1$
○ Live birth$_2$</td><td>○ Male$_1$
○ Female$_2$</td><td>○ Yes$_1$
○ No$_2$</td></tr>
</table>

53. Did you ever have a miscarriage?

YES............................1
NO 2

→**If yes,** how many?
○ 1 ○ 2 ○ 3 ○ 4 ○ 5 or more

◆ **This is the end of the interview. Do you have any questions or comments?**

1☐ No

2☐ Yes, no review needed

3☐ Yes, review needed

Comments:

◆ **Thank you for completing this interview.**

FOR STUDY USE ONLY

Interview Assessment:

1. How much difficulty did the Patient have in understanding the interview questions?

1☐ None 2☐ Slight 3☐ Moderate 4☐ A Great Deal 5☐ Don't know

2. Were there significant problems with the interview?

1☐ Yes 2☐ No

If yes describe: →

Date Completed ☐☐ ☐☐ ☐☐☐☐ Completed by ☐☐☐
Month Day Year

Mode of Administration 1☐ In-Person 2 ☐ Telephone 3 ☐ Self-complete

Date Reviewed ☐☐ ☐☐ ☐☐☐☐ Reviewer Code ☐☐☐
Month Day Year

Date Entered ☐☐ ☐☐ ☐☐☐☐ Data Entry Code ☐☐☐
Month Day Year

Appendix B Number and Percent of Participants by Study Center

Study Center	*n*	%
University of Texas at Austin/Baylor College of Medicine	288	19.5
Johns Hopkins University	89	6.0
Michigan State University	226	15.3
Saint Louis University	23	1.6
University of California, Irvine	45	3.0
University of California, Los Angeles	40	2.7
University of Minnesota	51	3.4
University of Texas Health Science Center at San Antonio	717	48.5

Appendix C Ulnar Length Measured by Caliper, Ruler, and Paper Grid

Appendix C1 Ulnar length measured by caliper

Appendix C2 Ulnar length measured by ruler

Appendix C3 Ulnar length measured by paper grid

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