THE EFFECTS OF DELIVERY METHOD AND INFANT FEEDING ON WEIGHT GAIN DURING THE FIRST YEAR OF LIFE

A DISSERTATION SUBMITTED TO THE GRADUATE DIVISION OF THE UNIVERSITY OF HAWAIʻI AT MĀNOA IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN

EPIDEMIOLOGY

MAY 2015

BY

YIHE GOH DAIDA

Dissertation Committee:

Eric Hurwitz, Chairperson

Alan Katz

Robert Cooney

John Grove

Maria Stewart

Keywords: Mode of Delivery, Infant Feeding, Gut Bacteria, Infant Growth

COPY RIGHT PAGE

DEDICATION PAGE

To my parents, who instilled in me the value of hard work, and without whom none of these would be possible.

To Chris, my husband, who guarded my solitude so I may pursue my dreams...

"The point of marriage is not to create a quick commonality by tearing down all boundaries; on the contrary, a good marriage is one in which each partner appoints the other to be the guardian of his solitude, and thus they show each other the greatest possible trust. A merging of two people is an impossibility, and where it seems to exist, it is a hemming-in, a mutual consent that robs one party or both parties of their fullest freedom and development. But once the realization is accepted that even between the closest people infinite distances exist, a marvelous living side-by-side can grow up for them, if they succeed in loving the expanse between them, which gives them the possibility of always seeing each other as a whole and before an immense sky."
― Rainer Maria Rilke, Letters to a Young Poet

To Zoey, who rocks my world. Breastfeeding her is the proudest achievements of my life, which in turn led me to embark on this incredible journey.

ACKNOWLEDGEMENTS

A sincere thank you to my committee members, Dr. Eric Hurwitz, Dr. Al Katz, Dr. Bob Cooney, Dr. John Grove and Dr. Maria Stewart for your mentoring and guidance. I am a better thinker and scientist because of the time you have invested in me. My utmost respect to you for being the academics that you are, and the mentoring heart that each of you possess. Special thanks to Dr. Hurwitz, who provided a safe place to learn, absorb, and thrive.

I'm grateful for the love and support of my sisters and friends, who brought me smiles and hope during this arduous journey.

ABSTRACT

Rapid weight gain in the first year of life sets the growth trajectory and is a risk factor for obesity. New evidence suggests that obesity in mice and humans is characterized by altered gut bacteria, compared to their lean counterparts. Two early factors that influence gut bacteria are delivery method and infant feeding. Since delivery method and infant feeding affect the initial colonization of gut bacteria, and gut bacteria is associated with obesity, the purpose of my dissertation is to study the effects of delivery method, breast feeding intensity, and their joint effects on infant growth in the first year of life.

This is a secondary analysis of data from the Infant Feeding Practices Study II (IFPS), a longitudinal follow-up study of new mothers conducted by the US Food and Drug Administration from 2005-2006. Participants were from a consumer panel of 500,000 households. Survey questionnaires were sent to pregnant women 10 times at regular intervals during the year after they gave birth. All participants were women >18 years of age who delivered a healthy infant. Delivery methods were reported as spontaneous vaginal, induced vaginal, planned C-section and emergency C-section. Breastfeeding intensity was reported at months 1-7, 9, 10 and 12 months.

Emergency C-section and induced vaginal deliveries were associated with lower breastfeeding intensity, compared to women who had spontaneous vaginal delivery. However, no differences in breastfeeding intensity were found between planned C-section and spontaneous vaginal delivery. In the second study, infants who received 0% and 1-49%% milk feeds from formula gained more weight than those fed 100% breast milk. The adjusted weight gain of these 2 groups was also higher than a cut-off point for risk of later obesity. Finally, weight gain was similar for infants born by vaginal deliveries and C-sections. Infants fed at least 50% breast milk gained less weight after 5 months of age. Joint effects of delivery method and breastfeeding intensity did not significantly affect infant weight gain. All three studies provide suggestions for future research needed to fully understand how delivery method and infant feeding affect gut colonization which in turn may affect infant development.

Key Words: Mode of delivery, breastfeeding intensity, weight

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1.

INTRODUCTION

Obesity and the First Year of Life

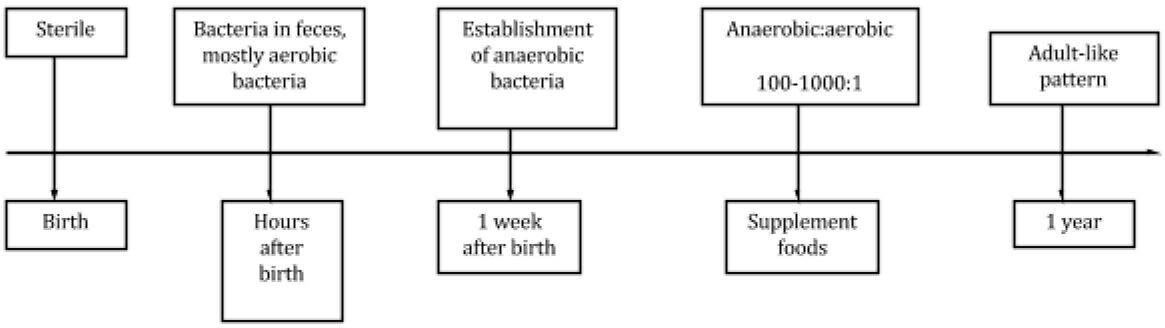
More than one-third (35.7%) of U.S. adults and 17% of children and adolescents are obese, according to Centers for Disease Control and Prevention (CDC) data from 2009–2010.[1] Prevention of obesity can also reduce the incidence of several major causes of death, including heart disease, stroke, type 2 diabetes and certain types of cancer. Obesity is also a major factor driving up health care costs; the annual medical costs for people who are obese were $1,429 higher than those of normal weight, and the estimated annual medical cost of obesity in the U.S. was $147 billion in 2008.[1]

Adult obesity has roots in infancy.[2] Rapid weight gain in the first year of life sets the growth trajectory and is a risk factor for later development of obesity.[3-6] In a meta-analysis by Druet et al.,[7] the authors found that each unit of increase in weight SD scores in the first year of life is associated with a twofold higher risk of childhood obesity (OR = 1.97; 95% CI: 1.83, 2.12), and a 23% higher risk of adult obesity (OR = 1.23; 95% CI: 1.16, 1.30), after adjusting for sex, age and birth weight. In the first prospective cohort of 172 Brazilian boys, Wells et al.[8] found weight gain from 0 to 6 months to be positively associated with BMI at 9 years ($p<0.05$), after adjusting for breastfeeding duration, maternal education, maternal BMI and weight gain during pregnancy, and familial monthly income. A cohort of 559 members[3] from 8 offices of Harvard Vanguard Medical Associates in Massachusetts found a positive change in 6-month weight-for-length *z*- score was associated with higher BMI *z*- scores, higher sums of subscapular and triceps skinfold thicknesses, and increased odds of obesity at 3 years of age. Modifiable factors to optimize infant weight gain patterns in the first year may potentially be intervention points for obesity prevention.

Gut Bacteria

There is growing evidence that gut bacteria have a role in lifelong health. The intestinal gut bacteria serve three major functions: 1) metabolic (e.g. fermentation of non-digestible dietary residue and salvaging of energy as short-chain fatty acids), 2) trophic (control of epithelial cell proliferation and differentiation and 3) barrier effects (development and homoeostasis of the immune system and protective).[9] Because of these functions, gut bacterial composition has been studied as a means for improving health conditions such as atopic diseases[10,11], diabetes[12-14], obesity[15-17], and inflammatory bowel diseases.[18]

Establishment in Early Life



Major changes take place in the composition of the intestinal microbiota during the first year of life. The early gut microbiota of infants begins primarily with aerobic bacteria due to the abundance of oxygen. Mode of delivery is the first source of contamination, after which environmental, oral, and skin microbes from the mother provide the major source of bacteria for the newborn via modes of transfer such as suckling, kissing, and caressing. These bacteria then create an environment that favors anaerobic bacteria until they multiply and outnumber the aerobic species by 100–1000: 1 in adults. The colonization of anaerobic bacteria coincides with the beginning of supplementation and introduction of solid foods so that by one year of age, the infant gut microbiota converges toward an ‘adult-like’ pattern.[19,20]

Early bacteria can modulate expression of genes in host epithelial cells[21] to create a favorable environment for themselves. By doing so, they can also prevent growth of other bacteria introduced later in the ecosystem. Thus, the initial colonization is very relevant to the final composition of the permanent flora in adults.[22] Once established, except under certain circumstances such as acute diarrhea and antibiotic treatment, an individuals’ flora composition pattern usually remains constant in adulthood.[23,24]

Gut Bacteria and Obesity

It is widely acknowledged that a person’s weight and body composition are likely the result of interactions between his/her genetic makeup and social, cultural, behavioral, and environmental factors. New evidence also suggests that obesity in mice and humans is characterized by altered gut bacteria, compared to their lean counterparts.[16,25] Ley et al.[16] found that gut bacteria in the cecum of ob/ob mice had a higher proportion of Firmicutes, a type of bacteria capable of harvesting energy from food that's indigestible in the upper small intestine. In doing so, they produce short-chain fatty acids, that are either used for energy by the colonic cells or absorbed into the bloodstream. Similar results were seen in humans where an increased Firmicutes-to-Bacteroidetes ratio was observed in obese human subjects and the reversal of that ratio when obese subjects lost weight on a low-calorie diet. Backhed et al.[26] was among the first to describe the fattening effects of transplanting gut bacteria from obese mice into their germ-free counterparts. A similar finding was reported by Ley et al.[17] who observed that after controlling for energy intake, germ-free mice receiving the microbes from obese mice gained more weight over a 2-week period compared to germ-free mice that received microbes from lean mice.

The exact mechanism by which gut bacteria influence obesity is unknown, however, current theories center on the "energy harvest" hypothesis, including fermentation of indigestible dietary polysaccharides to absorbable forms and intestinal absorption of monosaccharides and short-chain fatty acids with their subsequent conversion to fat within the liver.[26] Gut bacteria may also influence host genes that promote deposition of fat in lipocytes.[27]

Delivery method and Gut bacteria

One of the first major determinants of the gut microbiota is in the mode of delivery. The birth process begins the bacterial colonization of a previously germ-free gut. Vaginally born infants are colonized at first by fecal and vaginal bacteria from the mother. Vaginal microflora were also shown to be a source of first colonizers in a study reporting that the gastric content of 5- to 10-min-old babies was similar to that of their mothers' cervix.[28] In vaginal delivery, the same serotypes of *Escherichia coli* were found both in babies immediately after birth and in their mothers' feces, suggesting that microbes from mothers' feces also contaminate infants.[29] Term infants who were born vaginally at home and breastfed exclusively not only have the most "beneficial" gut bacteria (highest numbers of bifidobacteria and lowest numbers of *Clostridia difficile* and *E. coli*) compared to those born via Cesarean section (C-section) and exclusively formula-fed, but these differences seem to persist throughout infancy.[30] In contrast, newborns delivered by C-section are exposed initially to bacteria originating from the hospital environment and health care workers and exhibit less variability compared to vaginally-delivered babies.[31,32]

Infant feeding and Gut Bacteria

Following delivery, the second major factor influencing the gut microbiota is infant feeding. Human-milk oligosaccharides can serve as prebiotics on the gut microbiota, enabling desirable bacteria to thrive.[33]

Human milk is species-specific, making it the reference model against which all alternative feeding methods must be measured with regard to growth, health, development, and all other short- and long-term outcomes for infants. The benefits of breastfeeding to both mother and baby are well documented, including prevention of infectious diseases such as bacterial meningitis,[17,18] bacteremia,[18,34] diarrhea, respiratory tract infection and necrotizing enterocolitis.

The American Academy of Pediatrics published a policy statement first in 1997 and an updated policy in 2005, recommending at least 6 months of exclusive breastfeeding and to continue partial breastfeeding up to at least 1 year.[35] WHO also recommends 6 months of exclusive breastfeeding, and to continue partial breastfeeding up to at least 2 years.[36]

Trends in Delivery Method and Infant Feeding

Rates of C-section have been on the increase in the U.S. and also globally.[37] In the U.S., rates increased from 20.7% of all deliveries in 1996 to 32.8% in 2011, prompting The National Institutes of Health, policy leaders, and clinicians to express concern over increasing C-section rates.[38] The Healthy People 2020 initiative recommends a 10% reduction in C-section rates.[39]

Despite well-supported evidence that breastfeeding protects against a host of infant ailments,[16,40,41 42,43] national rates of breastfeeding initiation and duration fall below[35] the targets set by Healthy People 2010 goals.[44] Exclusive breastfeeding rates (no supplementation of any water, juice, nonhuman milk, and no foods except for vitamins, minerals, and medications) are not rising[45,46] even though more women initiate breastfeeding. This shows that formula-supplementing is commonly practiced during the first 6 months of life.[47]

METHODS

Systematic Review

Identification of research articles

All searches were conducted using PubMed, and included all study types made available in English. Narrative reviews and animal studies were excluded. A total of four different literature searches were conducted on the relationships between 1) mode of delivery and infant feeding 2) infant feeding and gut bacteria 3) mode of delivery and gut bacteria 4) infant feeding and infant growth. Combinations of index terms that addressed delivery method (delivery obstetric OR term birth OR childbirth OR birth OR mode of delivery), infant feeding (breast feeding OR breastfed OR breast-fed OR formula fed OR formula-fed OR infant formula), gut bacteria (gut bacteria OR microbiota OR human gut microbiota OR intestinal microbiota) and infant size (body mass index OR body weight) were used. For example, the relationship between delivery method and infant feeding was searched with "delivery obstetric OR term birth OR childbirth OR birth OR mode of delivery AND breast feeding OR breastfed OR breast-fed OR formula fed OR formula-fed OR infant formula."

The *Limits* feature on PubMed was used to confine each search to research articles that included humans of all ages and both sexes, incorporated all study types, and made available in English. Limits for each search are mentioned in each section below. Confidence intervals are reported if available.

Results and Interpretation

Delivery method and breastfeeding

The literature search for the relationship between delivery method and breastfeeding was confined with the limits "0-23 months," "human," "review," and "meta-analysis." There have been 2 cross-sectional, 3 prospective cohort and 1 retrospective cohort studies that examined the relationship between delivery method and breastfeeding.

A study in Istanbul by Cakmak[48] measures LATCH scores as an outcome between women with different delivery methods. The LATCH system is a way by which lactation consultants assign a numerical score of 0, 1, or 2, to five key components of breastfeeding. Each letter of the acronym LATCH denotes an area of assessment. "L" is for how well the infant latches onto the breast. "A" is for the amount of audible swallowing noted. "T" is for the mother's nipple type. "C" is for the mother's level of comfort. "H" is for the amount of help the mother needs to hold her infant to the breast. A total of 201 women, of which 83 had vaginal deliveries and 118 had C-sections were recruited for the study. Inclusion criteria for mothers were ≥ 18-years old, ability to speak and read Turkish, had lived in Istanbul for more than 1 year and had no serious medical condition or obstetrical complications. Their infants had to be ≥ 37 weeks gestation, had an Apgar score of ≥ 8 at 5 minutes postpartum and were breastfed. T-test results showed a lower LATCH score in C-section deliveries at the 1st and 3rd breastfeeding (C-section = 6.27, Vaginal = 7.46, T = 10.48, P<0.001) and (C-section = 8.81, Vaginal = 9.70, T = 7.82, P<0.001), respectively.

The limitations of this study are its cross-sectional design, small sample size and the selection of older, relatively well-educated women. These factors limit the generalizability of the results, making it impossible to know if the same results would hold true for other populations. Outcomes of the study are limited to LATCH scores, and do not include breastfeeding duration. Since no confidence intervals were reported by the authors, the precision of the association is not known. There were also only 2 categories of delivery type, making it impossible to elucidate the differences between elective or emergency C-section, which may be associated with mother's breastfeeding intention.[49]

Perez-Rios[50] used secondary data from the Puerto Rico Reproductive Health Survey, a cross-sectional survey conducted in partnership with the CDC, to investigate breastfeeding differences between C-section and vaginal delivery. Women between 15-49 years who delivered a healthy singleton newborn between 1990 and 1996 were included. The study sample included 1,695 women, 598 of whom had C-section and 1,097 of whom had vaginal delivery. In a multivariate logistic regression predicting breastfeeding initiation (a dichotomous variable yes/no), controlling for education, marital status, profession, Women, Infants, and Children (WIC) participation during pregnancy, breastfeeding persistence, breastfeeding aid, and artificial milk. C-section was associated with a decreased odds ratio (OR) for initiating breastfeeding 0.64 (95% CI: 0.51, 0.81). A strength of this study was the large study population, which yielded narrow confidence intervals. Limitations of the study include its cross-sectional design, and the lack of information on potential confounders such as length of hospital stay, attitudes toward breastfeeding, third party influences, and medication use during or after labor. In addition there was no differentiation between women with different types of C-section (elective vs. emergency C-section).

A prospective study in Australia[51], compared 106 women from 4 hospitals who had spontaneous vaginal delivery, 49 who had instrument-assisted vaginal delivery and 48 who had C-section (emergency C-section = 29, elective C-section = 19). Due to small samples, both types of C-sections were grouped for analyses. Two-way ANOVA comparison between delivery groups and hospitals showed that women who delivered via C-section took approximately 5 more hours after delivery to initiate breastfeeding ($p<0.001$), compared to both types of vaginal delivery. The longitudinal design allowed for causal inferences to be made regarding the relationship between delivery type and breastfeeding. Limitations of the study include the self-section of participants, which may result in selection bias, the mothers who completed the study were older, more educated, and had higher status professions, thus affecting external validity, and the limited sample size did not allow for separation of women who elected to have C-section vs. those who had emergency C-section. Despite a relatively small sample size, the study results were statistically significant, however, since no confidence intervals were reported, the precision of the estimate is unknown.

A prospective cohort study was conducted of 393 women delivering at ≥37 weeks gestation, singleton, live, cephalic births between February 1999 and February 2000.[52] The cohort study was undertaken at two teaching hospitals in Bristol, England. Questionnaires were mailed to participants at 6 weeks and 1 year post-partum. Logistic regression models were used to explore the relationships between infant feeding and mode of delivery, controlling for maternal age, profession, cigarette smoking, parity, duration of second stage, opiate analgesia, admission of baby to special care baby unit and intended breastfeeding. No differences were seen when instrumental vaginal delivery was compared with C-section (adjusted OR = 0.84, 95% CI: 0.50, 1.41 and OR = 1.15 95% CI: 0.69, 1.93 respectively). Breastfeeding rates after failed instrumental delivery were similar to those after immediate C-section (adjusted OR = 0.99, 95% CI: 0.72, 1.38 and OR = 1.28, 95% CI: 0.91, 1.78). Despite a relatively small sample size, the reported confidence intervals were narrow. The limitation of the study, however, is that there were only 2 delivery types.

Using data (2005–2006) from the longitudinal Infant Feeding Practices Study II (N=3,026) Ahluwalia[53] assessed the relationship between delivery method and breastfeeding. Delivery method was classified into 4 categories - spontaneous vaginal (N=1,157), induced vaginal (N=1,017), emergency C-section (N=489), and planned C-section (N=363) and breastfeeding outcome was defined as binary (yes/no) at birth, 4 weeks, 6 months, and overall duration. Spontaneous vaginal delivery was treated as the reference group. Outcomes include breastfeeding at initiation, and at 4 weeks, and at 6 months after delivery, as well as overall breastfeeding duration.

Multivariable analyses were adjusted for maternal age, ethnicity, education, income/poverty level ratio, marital status, parity, and pre-pregnancy BMI category and attitude toward breastfeeding. The authors found an association between delivery method and breastfeeding initiation. Compared to spontaneous vaginal delivery group (reference group), induced vaginal deliveries were less likely to breastfeed 4 weeks postpartum (adjusted odds ratio OR = 0.53, 95% CI: 0.38, 0.71). No difference was observed for those who had planned or emergency C-section deliveries compared to the reference group at 4 weeks. Similar results were seen at six months where, compared with spontaneous vaginal delivery group, those with induced vaginal (adjusted OR = 0.60, 95 % CI 0.47–0.78) and emergency C-section (adjusted OR = 0.68; 95% CI: 0.48, 0.95) deliveries were less likely to breastfeed at 6 months. The adjusted hazard ratios (HRs) indicating time to breastfeeding cessation showed that compared with women who had spontaneous vaginal deliveries, the likelihood of breastfeeding cessation was higher among those who had induced vaginal deliveries (HR = 1.39, 95 % CI: 1.19, 1.62) and those who had emergency C-section deliveries (HR = 1.31, 95 % CI: 1.07–1.60), and those who had planned C-section (HR = 1.16, 95% CI: 0.96, 1.41).

Strengths of this study include its large sample size and longitudinal design. The authors were also able to control for a number of factors that could influence breastfeeding outcomes. Limitations of this study include potential loss to follow-up. As the study progressed, fewer women returned their surveys, and it is impossible to know if women who did not return the surveys had stopped breastfeeding. The authors were also not able to adjust for factors that may predispose women to stop breastfeeding. These factors include complexity or duration of delivery interventions, postpartum fatigue, pain, or delivery-related complications as this information was not collected. Despite the relatively large sample size, it was insufficient to analyze differences between women who were overweight or obese. Finally, IFPS II data originate from a consumer panel survey and therefore have limited generalizability because the participants are more likely to be of higher socio-economic status in general.

Shawky et al.[54] compared 400 women in Saudi Arabia who delivered vaginally (n=348) with those who had C-sections (n=52). These women were recruited from 6 primary care centers in the city of Jeddah, and were selected from attendees of a well-baby clinic, with an infant of ≤ 12 months. Women were identified for recruitment, and a questionnaire captured feeding patterns retrospectively. Duration of breastfeeding was calculated based on answers to the questionnaire. A Cox proportional hazard regression model was used to calculate the adjusted OR for breast-feeding cessation risks, adjusting for maternal age and parity, nationality, education, working status, smoking habits and oral contraceptive. The hazard ratio for women who had a C-section to stop breastfeeding at 12 months postpartum is 1.9 (95% CI: 1.3, 2.8). Data from this study were collected by medical students who gave care to the participants, which may have biased participants' responses. Participants may be more inclined to report longer breastfeeding duration if their own physicians, who advocate for breastfeeding, are collecting the data from them. This could lead to information bias, threatening internal validity. The study also did not differentiate delivery types beyond the standard vaginal and C-section.

Though the outcomes of these studies vary and include breastfeeding initiation, duration and LATCH scores, most studies showed that C-section is associated with adverse breastfeeding outcomes. These results are confirmed by a variety of studies with different study designs as well as populations. None of the existing studies, however, examined the effect of delivery method on the *intensity* of breastfeeding.

Infant feeding and gut bacteria

The literature search for the relationship between infant feeding and gut bacteria was confined with the limits "0-23 months" and "human." There are three cross-sectional studies investigating the relationship between infant feeding and its relationship with gut bacteria.

Fallani et al.[55] conducted a cross-sectional study with 606 infants recruited across five European countries (Glasgow (Scotland), Italy, Stockholm (Sweden), Spain and Germany) from Jan 2003 to June 2006. Of the 606 infants, 312 were exclusively breastfed, 111 had mixed feeding and 183 were formula-fed. Fecal samples were collected at 6 weeks post-partum and analyzed for differences. Approximately 45% of breastfed infants vs. 29% of formula-fed infants were found to have Bifidobacteria in their gut ($p<0.001$). Mixed-fed infants also had higher prevalence of gut Bifidobacteria than formula-fed infants (40.9% vs. 29.9%, $P<0.007$). As this study is cross-sectional, a causal relationship cannot be established, and only an association between infant feeding and gut bacteria may be inferred. The precision of the difference in Bifidobacteria count is also not known as the confidence intervals were not reported.

Another cross-sectional study in Finland[56] compared the gut bacteria of exclusively breastfed, formula-fed, formula with prebiotics, and breastfed infants whose mothers were taking probiotics. There were 8 infants in each of the 4 groups. Inclusion criteria for the study were infants who were 6 months old, had a relative with atopic eczema, allergic rhinitis or asthma and were born between 36 and 42 weeks gestation. The formula group received adapted cow milk-based formula, while group prebiotics + formula consisted of infants given partially hydrolyzed infant formula supplemented with prebiotics. The criteria for inclusion in the study at 6 months of age were that these infants had used the respective formula since at least 2 months of age. The breast milk group were age-matched, exclusively breast-fed infants, and the group probiotics + breast milk were breast-fed infants whose mothers were given probiotics for two weeks before and 2 months after delivery. The authors reported lower count of bifidobacteria in the formula group, 7.6×10^8 (95% CI: 5.5×10^7, 2.2×10^9), than in the groups prebiotics + formula, 2.9×10^9 (95% CI: 2.2×10^9, 3.0×10^9), and breast milk, 2.8×10^9 (95% CI: 2.1×10^9, 3.6×10^9). The count of bifidobacteria in the group prebiotics + breast milk, 2.3×10^9 (95% CI: 1.0×10^9, 3.5×10^9), also tended to be greater than in the formula group. This cross-sectional study does not establish a temporal relationship between feeding type and gut bacteria.

The largest study of the three was also cross-sectional. This study took place in the Netherlands. [30] Penders et al. recruited a total of 1,030 infants, 700 of whom were exclusively breastfed, 232 formula-fed and 98 mixed-fed) from the KOALA Birth Cohort Study. The authors did not find any differences in gut bifidobacteria at day 30 postpartum (99% of all infants were colonized with bifidobacteria). The authors set α at .01 (2-sided) and 99% CI, but do not report either value where no differences were found.

To date, there are three studies exploring the relationship between infant feeding and gut bacteria, and all three studies are cross-sectional studies. Out of 3 studies, 2 of them found that breast-fed infants have more counts of bifidobacteria. Since bifidobacteria has been found to be beneficial in maintaining a healthy body weight, it is possible that the type of infant feeding may influence the gut bacteria, in turn affecting BMI at 1 year.

Mode of Delivery and Gut Bacteria

The literature search for the relationship between delivery method and gut bacteria was confined with the limits “0-23 months” and “human.” There were a total of 6 studies on delivery method and gut bacteria.

The largest study[10] was a cross-sectional study from the Netherlands, conducted from October 2000 to December 2002. A total of 1,032 infants (103 C-section and 929 vaginal delivery) provided fecal samples at 1 month of age. Bifidobacterial count was the outcome, measured by PCR assays. The study found that compared to vaginally-delivered infants, infants delivered by C-section have fewer counts of bifidobacteria ($p<0.003$), after controlling for maternal education, diet, probiotic and antibiotic use, rupture of membranes, place and mode of delivery, infant gender, gestational age, birth weight and season, hospitalization after birth, type of feeding, infant antibiotic use, fever, siblings, farm residence, furry pets, and total bacterial count. Because this was a cross-sectional study, one limitation is that a temporal relationship cannot be established between delivery method and gut bacteria. Additionally, the KOALA birth cohort was set up to identify factors that influence the clinical expression of atopic disease with a main focus on lifestyle, with participants from a “conventional lifestyle” and “alternative lifestyle.” Although several confounders have been adjusted for, there may be residual confounding factors such as maternal diet that may influence infant gut bacteria.

A second cross-sectional study was conducted across five European countries by Fallani et al.[55] Infants were recruited from the European INFABIO project (http://www.gla.ac.uk/infabio) which has the goal of investigating a better understanding of the relationships between diet, lifestyle and infant feeding practices. A total of 606 infants from Glasgow (n=158), Italy (n=125), Stockholm (n=116), Spain (n=109 and Germany (n=98) were recruited. The study found no effect of the mode of delivery on the relative proportions of bifidobacteria after adjusting for feeding method. Besides the limitation of a cross-sectional design, the heterogeneity of the population across different countries was not well-controlled for (e.g. socioeconomic status was not described).

Biasucci et al.[57] conducted a cross-sectional study in Italy among 46 term infants (23 C-section and 23 vaginal delivery). Recruited infants were from a hospital in Piacenza, Italy, and were screened for maternal infections, clinical illness, diet, antibiotic or probiotic use and maternal or infant antibiotic prophylaxis or therapy. Of the infants delivered vaginally, 57% revealed presence of bifidobacteria compared to 0% in C-section infants. Although the authors reported this difference as significant, no p-value or confidence intervals were reported. This is also the smallest study of the 6 studies retrieved.

A study by Mitsou[58] followed 97 healthy, exclusively breastfed Greek infants (60 C-section and 37 vaginal delivery) prospectively for 90 days. To date, this is the only prospective study that examined the bacterial content of infants. Fecal samples were collected at 4, 30 and 90 days and compared between infants from different delivery methods. Outcome measure was the number of infants with bifidobacterial colonization. The study found restricted bifidobacterial colonization in C-section infants compared to vaginally delivered ones on day 4 and Day 30 (Day 4 = 0% vs. 23%, $p < 0.015$ and Day 30 = 0% vs. 35%, $p < 0.042$). One limitation of the study was that there were no reported data on adherence to exclusive breastfeeding, though this is unlikely to change the direction or magnitude of the results (self-report or otherwise), as exclusive breastfeeding rates usually decline as the infant grows older.

Yap et al.[59] evaluated infant gut bacteria in two Asian populations, Singapore (n = 42) and Indonesia (n = 32) with contrasting socioeconomic development. Stool samples were collected from healthy term babies on day 3, and at 1, 3, and 12 month after birth location. Analyses controlled for mode of delivery (vaginal, emergency C-section or elective C-section), weaning age, number of siblings, total breastfeeding up to 6 month, eczema and prenatal antibiotics. Mode of delivery had the largest effect on stool microbiota signatures influencing the abundance of four bacterial groups. Infants delivered vaginally had more *Bacteroides-Prevotella* (3.016, 95% CI: 0.64, 5.39), Bifidobacterium (16.040, 95% CI: 5.67, 26.41) and Atopobium group (2.53, 95% CI: 0.47, 4.59) when compared to infants delivered via C-section.

Azad et al.[60] characterized the gut microbiota of 24 healthy Canadian infants and described the influence of C-section delivery and formula feeding. Mode of delivery was obtained from medical records, and mothers were asked to report on infant diet and medication use. Fecal samples were collected at 4 months of age. Compared with infants who were delivered vaginally, those born by C-section delivery had bacterial communities with significantly lower abundances of *Escherichia–Shigella* ($p < 0.001$) and an absence of *Bacteroides* ($p < 0.02$).

Cross-sectional and longitudinal studies found greater Bifidobacteria in vaginally-born infants. These results were confirmed in different populations. Although the study by Fallani did not find any difference in gut bacteria between infants born of different delivery types, the study population was also relatively small and population heterogeneous.

Infant feeding and infant growth

The literature search for the relationship between infant feeding and infant size was confined with the limits “0-23 months,” “human,” “review,” “meta-analysis,” and published within the past 10 years.

One systematic review by Arenz et al.[61] investigated the relationship between breast-feeding and obesity in childhood. The outcome measure was odds ratio for obesity in childhood as defined by BMI percentiles. This systematic review included several types of epidemiological studies, including cohort, case–control and cross-sectional studies, that compared types of infant feeding on the BMI percentile after adjusting for potential confounding factors. Calculations of pooled estimates were conducted using fixed- and random-effects models.

Selected studies met the criteria of being 1) population-based cohort, cross sectional or case–control studies 2) children older than 1 year at the last follow-up stage and 3) published in English, French, Italian, Spanish or German. Criteria for meta-analyses were studies that 1) adjusted for at least 3 of the following factors: birth weight, parental overweight, parental smoking, dietary factors, physical activity and socioeconomic status (SES), 2) comparable risk estimates as OR or risk ratio (RR) had to be reported, 3) age at the last follow-up had to be between 5 and 18 years, and 4) had obesity as outcome that defined by BMI percentiles ≥ 90, 95 or 97.. Studies also had to have adjusted for at least 3 of the following factors: birth weight, parental overweight, parental smoking, dietary factors, physical activity and SES. The meta-analyses did not require all studies to use identical reference values.

A total of nine studies with more than 69,000 participants met the inclusion criteria. The meta-analysis showed that breastfeeding reduced the risk of obesity in childhood significantly. The adjusted odds ratio was 0.78 (95% CI: 0.71, 0.85) in the fixed-effects model. The assumption of homogeneity of results of the included studies could not be refuted (Q-test for heterogeneity, P>0.3), stratified analyses showed no differences regarding different study types, age groups, definition of breast-feeding or obesity and number of confounding factors adjusted for. A dose-dependent effect of breast-feeding duration on the prevalence of obesity was reported in four studies. Studies were found to be heterogeneous and no publication biases were found.

Harder et al.[62] published a comprehensive meta-analysis of the existing studies on duration of breastfeeding and risk of overweight. Any definition of overweight was allowed for the analyses of this study. The conclusion of this meta-analysis showed a strong dose-response beneficial effect of breastfeeding. Criteria for inclusion were 1) original report comparing breastfed subjects with exclusively formula-fed subjects (referent group) of any given age, 2) reported the OR and 95% CI (or data to calculate them) of overweight or obesity associated with breastfeeding, and 3) reported the duration of breastfeeding and used exclusively formula-fed subjects as the referent. Seventeen studies met the inclusion criteria. By meta-regression, the duration of breastfeeding was inversely associated with the risk of overweight (0.94, 95% CI: 0.89, 0.98). Categorical analysis confirmed this dose-response association (<1 month of breastfeeding: OR = 1.0, 95% CI: 0.65, 1.55; 1-3 months: OR = 0.81, 95% CI: 0.74, 0.88; 4–6 months: OR = 0.76, 95% CI: 0.67, 0.86; 7–9 months: OR = 0.67, 95% CI: 0.55, 0.82; >9 months: OR = 0.68, 95% CI: 0.50, 0.91). One month of breastfeeding was associated with a 4% decrease in odds of overweight (OR = 0.96/month of breastfeeding, 95% CI: 0.94, 0.98).

Owen et al.[63] examined the influence of initial infant feeding on obesity in later life in a systematic review of published studies. Inclusion criteria are human studies that were based on a larger, inclusive, systematic search of all published articles, letters, abstracts, and review articles on infant feeding and cardiovascular disease, cardiovascular disease risk factors, and growth. Primary outcomes for the meta-analyses were based on the odds of becoming obese or overweight among breastfed subjects, compared with formula-fed subjects. Sixty-one studies reported on the relationship of infant feeding to a measure of obesity in later life; of which 28 (298,900 subjects) provided OR estimates. In these studies, breastfeeding was associated with a reduced risk of obesity, compared with formula feeding (OR = 0.87, 95% CI: 0.85, 0.89). The inverse association between breastfeeding and obesity was particularly strong in 11 small studies of <500 subjects (OR = 0.43, 95% CI: 0.33, 0.55) but was still apparent in larger studies of >500 subjects (OR = 0.88, 95% CI: 0.85, 0.90). When parental obesity, maternal smoking, and social class (the three major potential confounding factors) were adjusted for in 6 studies, the inverse association was still found, though reduced markedly (from an OR of 0.86 to 0.93). Still, the results of these meta-analyses strongly suggest that breastfeeding protects against obesity.

Owen et al.[64] conducted a systematic review to examine whether initial breastfeeding is related to lower mean BMI throughout life. The main outcome of the meta-analysis was the mean difference in BMI between those subjects who were breastfed and those who were formula-fed using fixed-effects models. There were 70 eligible studies, and 36 mean differences in BMI (from 355,301 subjects) were obtained. Results from this study support other findings that breastfeeding has a protective effect on obesity. Subjects who were breastfed had a lower (but small) mean BMI than those who were formula-fed (-0.04 kg/m^2, 95% CI: -0.05, -0.02). Results differed according to study size. In smaller studies (<1000 subjects), a larger difference in mean BMI was found (-0.19 kg/m^2, 95% CI: -0.31, -0.08) and the opposite effect was found in larger studies of ≥1000 subjects (-0.03 kg/m^2, 95% CI: -0.05, -0.02). In 11 studies that adjusted for SES (based on occupation, salary, or education or on all 3 variables), maternal smoking in pregnancy, and maternal BMI, the protective effects of breastfeeding attenuated (-0.10, 95% CI: -0.14, -0.06 before adjustment; -0.01, 95% CI: -0.05, 0.03 after adjustment).

Li et al.[65] tested the hypothesis that infants who were breastfed more intensively during early infancy (<6 months) will be less likely to have excess weight during late infancy (>6 months) using the IFPS II population. They found that infants fed with low (<20% of milk feeds being breast milk) and medium (20%–80%) breastfeeding intensity in the first half of infancy were at least 2 times more likely to have excess weight during the second half of infancy than those breastfed at high intensity (>80%). To our knowledge, this is the only study that treated the breastfeeding variable as "breastfeeding intensity". The study controlled for infant gender, gestational age, birth weight, age at introduction of solids, number of sweet drinks per day, maternal age, parity, education, ethnicity, smoking status, pre-pregnancy BMI, and income.

The anti-obesogenic benefit of breast milk is well-documented, and shown to have a dose-dependent effect in these meta-analyses. None of the studies, however, controlled for mode of delivery. In the current analyses, one would expect that vaginally-delivered infants who were breastfed the longest would have the lowest BMI at 1 year of age.

SUMMARY

Adult obesity, a growing epidemic, has roots in infancy.[2] Rapid weight gain in the first year of life sets the growth trajectory and is a risk factor for later development of obesity.[3-6] This relationship is consistent with growing evidence in both animal and human studies that show a relationship between gut bacteria and adult obesity.

Two early life factors that influence gut bacteria are mode of delivery[29,32] and infant feeding.[30,55] The gut of a newborn infant is sterile until the first microbes that arrive colonize the gut.[28,29,31,32] Studies have shown that C-section and formula-feeding disrupt the establishment of "good" bacteria.[60] Vaginally born infants are colonized at first by the "good" fecal and vaginal bacteria of the mother and oligosaccharides from breast milk are feed for these "good" bacteria, thus enabling them to thrive and grow. Of concern are the facts that C-section rates have been on the rise since 1995, from about 21% all deliveries in 1996 to 33% 2011[38] and breastfeeding rates, while increasing, are not meeting national goals. There is only limited information about the relative impact of mode of delivery and infant feeding on growth during the first year of life.

Purpose of this dissertation

The overall goal of my dissertation is to investigate the relationship between mode of delivery and breastfeeding intensity, and the joint and component effects of mode of delivery and breast feeding intensity on infant growth in the first year of life, which has been shown to be associated with adult obesity. It will be broken down into the following specific aims:

Research Questions

This dissertation includes several research questions that were addressed in three distinct but related studies.

Study 1: To assess the relationship between mode of delivery and breastfeeding intensity during the first year of life.

Study 2: To estimate the effects of breastfeeding intensity on infant weight change from 0-3, 3-5, 5-7 and 7-12 months postpartum.

Study 3: The goal of this paper is to estimate the component and joint effects of mode of delivery and breastfeeding intensity on infant weight gain at 4 time intervals: 0-3, 3-5, 5-7 and 7-12 months postpartum.

CHAPTER 2.
STUDY 1: Breastfeeding Intensity in the First Year of Life: The Impact of Mode of Delivery

ABSTRACT

Background: Breastfeeding is associated with reduced risk of obesity. Mode of delivery affects breastfeeding initiation and duration, but few studies have looked at its effects on breastfeeding intensity.

Objective: To assess the relationship between mode of delivery and breastfeeding intensity during the first year of life.

Methods: Using data (2005–2006) from the longitudinal Infant Feeding Practices Study II (n = 2,762) the relationship between mode of delivery (spontaneous vaginal, induced vaginal, planned C-section and emergency C-section) and breastfeeding intensity at month 1 through 7, 9, 10 and 12 months was assessed. The breastfeeding intensity variable measures percent of all milk feeds that were breast milk. Socio-demographic factors, breastfeeding knowledge and intention to breastfeed among women from different delivery groups were compared using analysis of variance (ANOVA) or Chi-square statistics. Generalized Linear Models were used to compare mean breastfeeding intensity between the delivery groups, adjusting for birth weight, maternal age, pre-pregnancy BMI, smoking, ethnicity, intention to breastfeed, education and income.

Results: Compared to the spontaneous vaginal delivery group, women who had emergency C-sections had lower mean percent of milk feeds that were from breast milk. At 1 month, the difference in means of percent milk feeds that were breast milk between women who had emergency C-sections vs. those in the spontaneous vaginal delivery group was -9.96% (95% CI: -19.15, -0.78) at 1 month ; -14.18% (95% CI: -24.24, -4.13) at 2 months; -14.64), 95% CI: -25.05, -4.23 at 3 months; -14.77%, 95% CI: -25.24, -4.31 at 4 months; -14.86%, 95% CI: -25.57 at 5 months and -4.14%; -13.28, 95% CI: -24.29, -2.27 at 6 months). The induced vaginal delivery group also had lower mean percent milk feeds that were from breast milk compared to the spontaneous vaginal delivery group from months 1-4 (-7.10%, 95% CI: -13.63%, -0.56; -10.22%, 95% CI: -17.18, -3.26; -10.20%, 95% CI: -17.40, -3.01; -9.01%, 95% CI: -16.51, -1.50, respectively). Mean percent milk feeds from breast milk were higher at 4 and 5 months for women with planned C-sections vs. women with emergency C-sections (12.18%, 95% CI: 0.25, 24.11; 13.36%, 95% CI: 1.22, 25.49). No differences were seen between women with planned C-sections and those with spontaneous C-sections.

Conclusion: Mode of delivery has an impact on breastfeeding intensity. Breastfeeding support may benefit from tailoring efforts toward type of delivery.

BACKGROUND

The link between breastfeeding and decreased risk of obesity is well-established.[63] Adult obesity has roots in infancy.[2] Rapid weight gain in the first year of life sets the growth trajectory and is a risk factor for later development of obesity.[3-6] The American Academy of Pediatrics (AAP) reaffirmed its guidelines on breastfeeding in their recent policy statement,[66] recommending at least 6 months of exclusive breastfeeding and to continue breastfeeding up to at least 1 year. Still, national rates of breastfeeding initiation and duration fall below the targets set by Healthy People 2010 goals.[35,44]

Recent studies show that mode of delivery affects breastfeeding practices. The negative relationship between C-section and breastfeeding has been confirmed with different studies with different study designs as well as populations.[48,51-54] Moreover, rates of C-section have been on the increase, not only in the U.S., but also globally.[37,67] In the U.S., rates increased from 20.7% of all deliveries in 1996 to 32.8% in 2011, prompting The National Institutes of Health, policy leaders, and clinicians to express concern over increasing C-section rates.[38] The Healthy People 2020 initiative from the Department of Health and Human Services recommends a 10% reduction in both primary and repeat C-section rates, from 26.5% to 23.9%, and from 90.8%to 81.7%, respectively.[39]

There are several reasons for concern in these rising rates. While it is a necessary and life-saving operation for some,[68,69] medical indications do not fully account for the wide differences in C-section rates observed across states and countries.[70-72] Other than costs associated with this major abdominal surgery,[73] it also carries increased risks to the mother, including greater chance of infection, injury, blood clots, and need for emergency hysterectomy.[68,69] Studies also reported decreased rates of breastfeeding initiation,[51] duration,[52-54,74] exclusivity[52,74] and LATCH scores[48] in different types of studies and populations.

To date, no study has investigated the relationship between mode of delivery and breastfeeding intensity. Breastfeeding intensity, as measured by percent feed that is breast milk, will provide a detailed look into the amount of breast milk intake that other measures do not. Two infants with the same breastfeeding duration (months) may consume different proportions of breast milk. This is important because dose-dependent protection effect of breast milk has been reported.[62,63,64] The goal of this section is to compare infant breastfeeding intensity at months 1 through 7, 9, 10 and 12, among delivery groups: Spontaneous Vaginal (SV), Induced

Vaginal (IV), Planned C-section (PC), and Emergency C-section (EC) and estimate the association between breastfeeding intensity and breastfeeding duration.

METHODS

Study Design

The study is a secondary analysis of data from the Infant Feeding Practices Study (IFPS) II data, focusing on the relationship between type of delivery and breastfeeding intensity during the first year of life. The IFPS II is a longitudinal follow-up study of pregnant women and new mothers conducted by the US Food and Drug Administration (FDA) during 2005 and 2006.

The study sample was obtained from a consumer panel of 500,000 households. Survey questionnaires were sent to pregnant women before their delivery and 10 times at regular intervals during the year after they gave birth. To be eligible to participate in the IFPS II, women had to be >18 years of age and to have delivered a healthy singleton infant who weighed ≥5 pounds at birth, had a gestational age at birth of ≥35 weeks, and spent <3 days in intensive care.

Of the initial panel of 15,147 women identified, 14,618 were mailed a prenatal questionnaire; of these, 4,902 qualified and completed the prenatal questionnaire. All of these women were sent the birth screener and subsequent neonatal survey.[75] Of the total neonatal surveys mailed (n = 4,013), 76.9% (n = 3,033) completed and qualified to participate in the study; additional information about IFPS II methods and response rates for the entire study is available elsewhere.[76] The study sample was limited to women who reported on their method of delivering the index child on their neonatal survey (n = 3,026), which was completed approximately 4 weeks postpartum. Of these women, breastfeeding initiation data were available for more than 99% of the women (n = 3,002); 98% (n = 2,995) were available for 4 weeks and 70% (n = 2,088) for 6 months breastfeeding analyses.

Key Exposure Variable

Mode of delivery was ascertained from responses to the neonatal survey sent to survey participants approximately 4 weeks post-delivery. The mode of delivery categories were spontaneous vaginal (n = 1,058), induced vaginal (n = 923), planned C-section (n = 443), and emergency C-section (n = 328).

Outcome Variable

Breastfeeding intensity at 1 through 7, 9, 10 and 12 months for IV, PC and EC were compared against SV. The breastfeeding intensity variable measures percent of all milk feeds that were breast milk and are not measures of exclusive breastfeeding. Therefore, infants can receive 100 percent of milk feeds as breast milk but not be exclusively breastfed if they also receive any solid foods.

Potential Confounding Variables

To control for confounding, models included adjustment for socio-demographic factors that are associated with both mode of delivery and breastfeeding outcome. Variables considered *a priori* to be potential confounders are summarized in Tables 2.1 and 2.2. Current average daily cigarettes smoked was asked during the prenatal period, and dichotomized into "yes" and "no" categories. Education was operationalized as three categories - "High school and under," "College" and "College/Post graduate." Percent of federal poverty level (FPL) was constructed using household income and household size variables, and categorized into "185% of FPL," "185 – 349% of FPL" and "350% of FPL." Attitude toward breastfeeding was assessed with two questions: 1) mother's strength of agreement toward the statement about benefits of breast milk, and 2) her intention to breastfeed. Maternal understanding of the benefits of breast milk was assessed by how strongly she agreed with the following statement: ''Infant formula is as good as breast milk'' on a 5-point Likert scale (Strongly Disagree, Disagree, Neither Agree nor Disagree, Agree, Strong Agree). Mother's intention to breastfeed was based on their response to a question about how she planned to feed her baby ''in the first few weeks'' after birth with the following response options: ''breastfeed only,'' ''formula feed only,'' ''both breast and formula [feed],'' and ''don't know yet.'' *Statistical Analyses*

SAS 9.3 was used for all analyses. For descriptive statistics, continuous variables were reported as mean ± standard deviation (SD). Analysis of variance (ANOVA) was performed to see if interval-scale (continuous) potential confounders were associated with mode of delivery. Categorical variables were reported as percentages and Chi-square was used to compare differences between modes of delivery.

Generalized linear models were constructed to compare mean and 95% CIs for breastfeeding intensity between delivery groups, adjusting for possible confounders. A multivariable model with interaction term between delivery group and a time variable (breastfeeding intensity variables were collected at months 1 through 7, 9, 10 and 12 months) was used, and adjusted for birth weight and maternal factors (age, pre-pregnancy Body Mass Index [BMI, kg/m^2], smoking, ethnicity, intention to breastfeed, education and income). Age is correlated with parity and breastfeeding knowledge is correlated with intention to breastfeed. The final model adjusted for age and intention to breastfeed as they were better predictors of the outcomes in the multivariable models.

RESULTS

The baseline characteristics of the study population (n = 2,762) are presented in Table 2.1. Women who had a planned C-section were older and had the highest BMI. The emergency C-section group had the highest percent of primigravid women and highest income group. Induced vaginal delivery group and planned C-section had higher percent of White women.

Table 2.2 shows mothers' intention and knowledge. Most women in all delivery groups intended to breastfeed only, and a very small percent of them do not know yet how they will feed their infant. The planned C-section group had the lowest group percent of women intending to breastfeed only, and had the highest percent of women who plan to feed only formula. This group also showed the poorest knowledge of the benefits of breast milk. Interestingly, more women in all delivery groups "somewhat disagree" that infant formula is as good as breast milk than "strongly disagree".

Figure 2.1 shows the mean breastfeeding intensity at months 1 through 7, 9, 10 and 12 for each mode of delivery, adjusting for birth weight, maternal age, pre-pregnancy BMI, smoking, ethnicity, intention to breastfeed and education. Emergency C-section had significantly lower breastfeeding intensity compared to the spontaneous vaginal delivery group from months through 6. Induced vaginal delivery had significantly lower breastfeeding intensity than spontaneous delivery in months 1through 4. Table 2.3 shows the differences in breastfeeding intensity between modes of delivery. Compared to the spontaneous vaginal delivery group, women who had emergency C-sections had lower mean percent of milk feeds that were from breast milk. At 1 month, the difference in means of percent milk feeds that were breast milk between women who had emergency C-sections vs. those in the spontaneous vaginal delivery group was -9.96% (95% CI: -19.15, -0.78) at 1 month ; -14.18% (95% CI: -24.24, -4.13) at 2 months; -14.64), 95% CI: -25.05, -4.23 at 3 months; -14.77%, 95% CI: -25.24, -4.31 at 4 months; -14.86%, 95% CI: -25.57 at 5 months and -4.14%; -13.28, 95% CI: -24.29, -2.27 at 6 months).

The induced vaginal delivery group also had lower mean percent milk feeds that were from breast milk compared to the spontaneous vaginal delivery group from months 1-4 (-7.10%, 95% CI: -13.63%, -0.56; -10.22%, 95% CI: -17.18, -3.26; -10.20%, 95% CI: -17.40, -3.01; -9.01%, 95% CI: -16.51, -1.50, respectively). Mean percent milk feeds from breast milk were higher at 4 and 5 months for women with planned C-sections vs. women with emergency C-sections (12.18%, 95% CI: 0.25, 24.11; 13.36%, 95% CI: 1.22, 25.49). No differences were seen between women with planned C-sections and those with spontaneous C-sections.

An increase in maternal age is associated with decreased odds of being lost to follow-up at all time intervals (Table 2.4), and between months 7 to 12, the odds of lost to follow-up is 1.43 (95% CI: 1.03, 1.99) for the induced vaginal delivery group compared to the spontaneous vaginal delivery group. The odds of being lost to follow-up is 1.74 (95% CI: 1.09, 2.79) for the emergency C-section group, compared to the spontaneous vaginal delivery group.

Table 2.1. Frequency Distributions (in Percent) or Means ± Standard Deviations (SD) of Selected Socio-Demographic and Birth Characteristics by Mode of Delivery among Participants in the Infant Feeding Practices Survey II (N = 2,762)

		Spontaneous Vaginal (n = 1,060)	Induced Vaginal (n = 928)	Planned C-section (n = 445)	Emergency C-section (n = 329)
Birth Weight, grams (Mean ± SD)		3458.9 ± 453.2	3433.3 ± 457.1	3497.6 ± 465.1	3466.3 ± 521.8
Gestational age, weeks (Mean ± SD)[1]		39.4 ± 1.4	39. 4± 1.2	39.1 ±1.0	39.4 ± 1.6
Gender (%)[2]	Boy	49.6	45.4	50.8	54. 3
	Girl	50.4	54.6	49.2	45.7
Age, years (Mean ± SD)[3]		28.4 ± 5.4	28.4 ± 5.2	30.6 ± 4.9	28.9 ± 6.3
BMI, kg/m^2 (Mean ± SD)[4]		25.1 ± 5.5	26.4 ± 6.5	29.2 ± 8.2	28.4 ± 7.3
Parity (%) [5]	First child	27.4	27.1	11.1	63.3
	More than one child	72.6	72.9	88.9	36.7
Ethnicity (%)[6]	White	83.8	86.1	87.4	79.6
	Black	4.5	4.5	2.5	9.1
	Hispanic	7.3	5.4	5.2	5.2
	Asian/Pacific Islander	2.7	2.2	2.5	4.3
	Other	1.7	1.8	2.5	1.8

Table 2.1. (Continued) Frequency Distributions (in Percent) or Means ± Standard Deviations (SD) of Selected Socio-Demographic and Birth Characteristics by Mode of Delivery among Participants in the Infant Feeding Practices Survey II (N = 2,762)

		Spontaneous Vaginal (n = 1,060)	Induced Vaginal (n = 928)	Planned C-section (n = 445)	Emergency C-section (n = 329)
% Federal Poverty Level (%)[7]	185% of FPL	41.6	45.0	35.7	38.3
	185 – 349% of FPL	36.7	33.9	42.9	29.2
	350% of FPL	21.7	21.0	21.4	32.5
Smoking (%)	Yes	9.7	9.4	9.7	11.6
	No	90.3	90.6	90.3	88.5
Education (%)	High School and under	20.2	22.6	17.7	17.8
	1-3 year of College	39.1	40.7	42.7	40.6
	College/Grad school	40.8	36.8	39.6	41.6
Marital Status (%)[8]	Married	78.5	80.7	85.5	73.3
	Not married	21.5	19.3	14.5	26.7

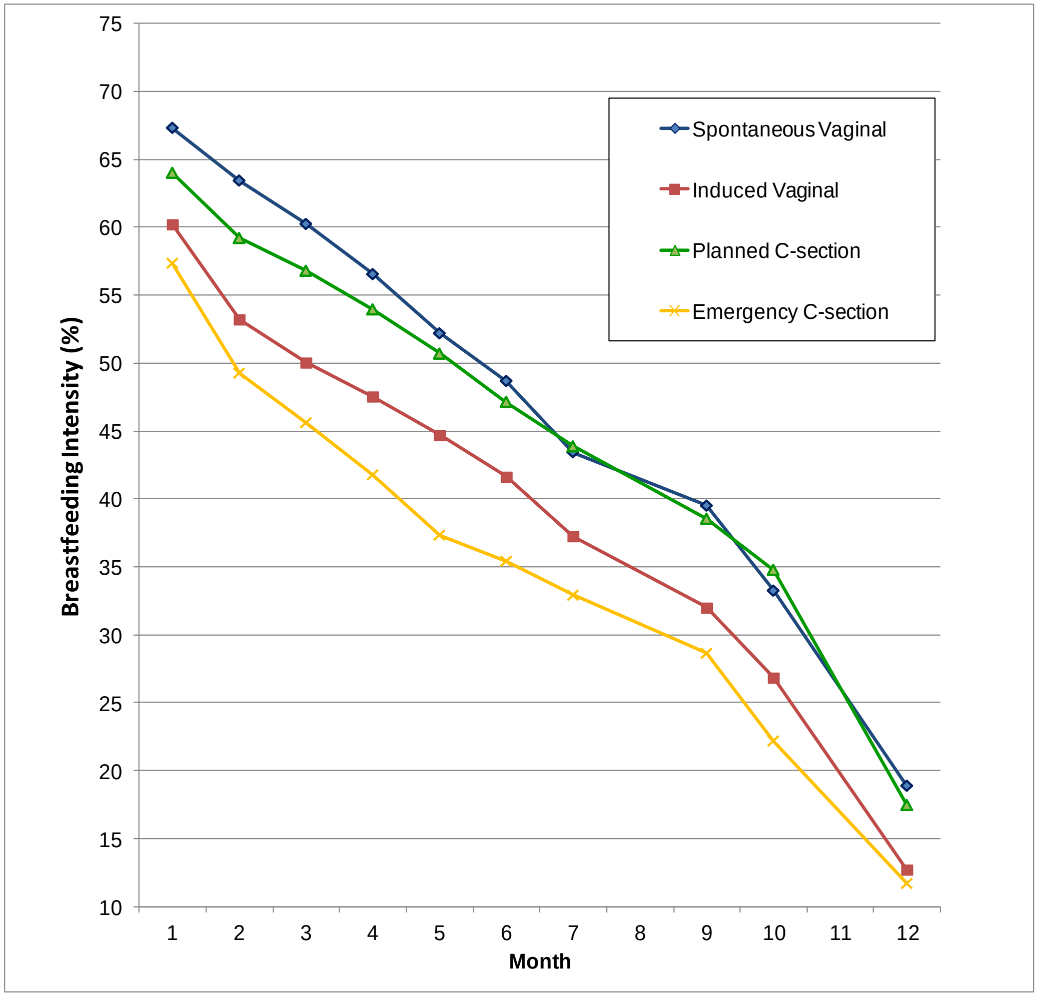
[1] F-value = 4.04, *df* = 3p = 0.007; [2] $\chi^2 = 9.25$, $p < 0.05$; [3] F-value = 18.95, *df* = 3, $p < 0.0001$; [4] F-value = 50.21, *df* = 3, $p < 0.0001$; [5] $\chi^2 = 253.45$, $p < 0.0001$; [6] $\chi^2 = 29.39$, $p < 0.003$; [7] $\chi^2 = 34.61$, $p < 0.0001$; [8] $\chi^2 = 29.34$, $p < 0.004$

Table 2.2. Distribution of Breastfeeding Knowledge and Intention to Breastfeed by Mode of Delivery among Participants in the Infant Feeding Practices Survey II (n=2, 762)

	Spontaneous Vaginal (n = 1,058)	Induced Vaginal (n = 923)	Planned C-section (n = 443)	Emergency C-section (n = 328)
Intention to breastfeed in the first few weeks after birth[1]				
Breastfeed only (%)	63.7	60.9	51.7	61.0
Formula feed only (%)	12.2	12.5	18.9	12.8
Both (%)	20.8	24.0	24.5	22.3
Don't know yet (%)	3.2	2.6	4.9	4.0
"Infant formula is as good as breast milk"[2]				
Strongly Disagree (%)	31.3	28.5	21.4	24.7
Somewhat Disagree (%)	31.6	33.9	32.1	35.1
Neither Agree nor Disagree (%)	10.3	11.9	14.5	14.0
Somewhat Agree (%)	19.2	20.2	21.2	18.9
Strong Agree (%)	7.7	5.5	10.8	7.3

[1] $\chi^2 = 27.45$, $p < 0.001$; [2] $\chi^2 = 31.92$, $p < 0.001$

Figure 2.1. Estimated Adjusted[1] Effects (Breastfeeding Intensity, Percent) and 95% Confidence Intervals by Mode, among Participants in the Infant Feeding Practices Survey II (N = 2,762)



[1] Results of multivariate regression analyses, adjusted for birth weight, maternal age, pre-pregnancy BMI, smoking, ethnicity, intention to breastfeed and education

Table 2.3. Differences in Breastfeeding Intensity (in Percent) Between Modes of Delivery, among Participants in the Infant Feeding Practices Survey II (N = 2, 762)

	Mode of Delivery	β	SE	Adjusted P value[2]	95% CI	
MONTH 1 (n= 2,762)	Induced Vaginal vs. Spontaneous Vaginal	-7.10	1.68	**0.01**	-13.63	-0.56
	Planned C-section vs. Spontaneous Vaginal	-3.31	2.12	1.00	-11.55	4.93
	Emergency C-section vs. Spontaneous Vaginal	-9.96	2.36	**0.01**	-19.15	-0.78
	Induced Vaginal vs. Planned C-section	-3.79	2.16	1.00	-12.19	4.61
	Induced Vaginal vs. Emergency C-section	2.86	2.40	1.00	-6.47	12.20
	Planned C-section vs. Emergency C-section	6.65	2.72	0.91	-3.92	17.23
MONTH 2 (n= 2,418)	Induced Vaginal vs. Spontaneous Vaginal	-10.22	1.79	**<.0001**	-17.18	-3.26
	Planned C-section vs. Spontaneous Vaginal	-4.23	2.25	1.00	-12.96	4.50
	Emergency C-section vs. Spontaneous Vaginal	-14.18	2.59	**<.0001**	-24.24	-4.13
	Induced Vaginal vs. Planned C-section	-5.99	2.29	0.82	-14.88	2.91
	Induced Vaginal vs. Emergency C-section	3.96	2.62	1.00	-6.24	14.16
	Planned C-section vs. Emergency C-section	9.95	2.95	0.24	-1.51	21.41

Table 2.3. (Continued) Differences in Breastfeeding Intensity (in Percent) Between Modes of Delivery, among Participants in the Infant Feeding Practices Survey II (N = 2, 762)

	Mode of Delivery	β	SE	Adjusted P value[2]	95% CI	
MONTH 3 (n = 2,265)	Induced Vaginal vs. Spontaneous Vaginal	-10.20	1.85	**<.0001**	-17.40	-3.01
	Planned C-section vs. Spontaneous Vaginal	-3.44	2.32	1.00	-12.45	5.56
	Emergency C-section vs. Spontaneous Vaginal	-14.64	2.68	**<.0001**	-25.05	-4.23
	Induced Vaginal vs. Planned C-section	-6.76	2.37	0.64	-15.97	2.45
	Induced Vaginal vs. Emergency C-section	4.44	2.72	1.00	-6.15	15.02
	Planned C-section vs. Emergency C-section	11.19	3.05	0.10	-0.68	23.06
MONTH 4 (n = 2,124)	Induced Vaginal vs. Spontaneous Vaginal	-9.01	1.93	**0.002**	-16.51	-1.50
	Planned C-section vs. Spontaneous Vaginal	-2.59	2.37	1.00	-11.81	6.62
	Emergency C-section vs. Spontaneous Vaginal	-14.77	2.69	**<.0001**	-25.24	-4.31
	Induced Vaginal vs. Planned C-section	-6.41	2.43	0.81	-15.87	3.04
	Induced Vaginal vs. Emergency C-section	5.77	2.75	0.99	-4.91	16.45
	Planned C-section vs. Emergency C-section	12.18	3.07	**0.04**	0.25	24.11

Table 2.3. (Continued) Differences in Breastfeeding Intensity (in Percent) Between Modes of Delivery, among Participants in the Infant Feeding Practices Survey II (N = 2, 762)

	Mode of Delivery	β	SE	Adjusted P value[2]	95% CI	
MONTH 5 (n = 2,071)	Induced Vaginal vs. Spontaneous Vaginal	-7.47	1.95	0.06	-15.06	0.11
	Planned C-section vs. Spontaneous Vaginal	-1.50	2.40	1.00	-10.82	7.82
	Emergency C-section vs. Spontaneous Vaginal	-14.86	2.76	**<.0001**	-25.57	-4.14
	Induced Vaginal vs. Planned C-section	-5.98	2.45	0.91	-15.49	3.53
	Induced Vaginal vs. Emergency C-section	7.38	2.80	0.81	-3.50	18.26
	Planned C-section vs. Emergency C-section	13.36	3.12	**0.01**	1.22	25.49
MONTH 6 (n = 1,994)	Induced Vaginal vs. Spontaneous Vaginal	-7.05	1.99	0.15	-14.78	0.69
	Planned C-section vs. Spontaneous Vaginal	-1.54	2.42	1.00	-10.96	7.88
	Emergency C-section vs. Spontaneous Vaginal	-13.28	2.83	**0.002**	-24.29	-2.27
	Induced Vaginal vs. Planned C-section	-5.51	2.48	0.98	-15.16	4.14
	Induced Vaginal vs. Emergency C-section	6.23	2.88	0.98	-4.98	17.44
	Planned C-section vs. Emergency C-section	11.74	3.19	0.10	-0.68	24.16

Table 2.3. (Continued) Differences in Breastfeeding Intensity (in Percent) Between Modes of Delivery, among Participants in the Infant Feeding Practices Survey II (N = 2, 762)

	Mode of Delivery	β	SE	Adjusted P value[2]	95% CI	
MONTH 7 (n = 1,930)	Induced Vaginal vs. Spontaneous Vaginal	-6.18	2.02	0.47	-14.05	1.68
	Planned C-section vs. Spontaneous Vaginal	0.43	2.46	1.00	-9.12	9.97
	Emergency C-section vs. Spontaneous Vaginal	-10.53	2.90	0.12	-21.80	0.75
	Induced Vaginal vs. Planned C-section	-6.61	2.52	0.82	-16.41	3.19
	Induced Vaginal vs. Emergency C-section	4.34	2.96	1.00	-7.15	15.84
	Planned C-section vs. Emergency C-section	10.96	3.26	0.25	-1.73	23.65
MONTH 9 (n = 1,821)	Induced Vaginal vs. Spontaneous Vaginal	-7.51	2.09	0.13	-15.62	0.60
	Planned C-section vs. Spontaneous Vaginal	-0.97	2.52	1.00	-10.75	8.82
	Emergency C-section vs. Spontaneous Vaginal	-10.88	2.98	0.11	-22.48	0.73
	Induced Vaginal vs. Planned C-section	-6.54	2.60	0.88	-16.66	3.57
	Induced Vaginal vs. Emergency C-section	3.37	3.06	1.00	-8.53	15.26
	Planned C-section vs. Emergency C-section	9.91	3.36	0.56	-3.16	22.98

Table 2.3. (Continued) Differences in Breastfeeding Intensity (in Percent) Between Modes of Delivery, among Participants in the Infant Feeding Practices Survey II (N = 2, 762)

	Mode of Delivery	β	SE	Adjusted P value[2]	95% CI	
MONTH 10 (n = 1,709)	Induced Vaginal vs. Spontaneous Vaginal	-6.40	2.16	0.55	-14.78	1.98
	Planned C-section vs. Spontaneous Vaginal	1.53	2.61	1.00	-8.61	11.67
	Emergency C-section vs. Spontaneous Vaginal	-11.07	3.04	0.11	-22.88	0.74
	Induced Vaginal vs. Planned C-section	-7.93	2.68	0.56	-18.36	2.50
	Induced Vaginal vs. Emergency C-section	4.67	3.10	1.00	-7.39	16.74
	Planned C-section vs. Emergency C-section	12.60	3.43	0.10	-0.72	25.93
MONTH 12 (n = 1,700)	Induced Vaginal vs. Spontaneous Vaginal	-6.17	2.17	0.65	-14.59	2.25
	Planned C-section vs. Spontaneous Vaginal	-1.41	2.60	1.00	-11.51	8.68
	Emergency C-section vs. Spontaneous Vaginal	-7.19	3.07	0.95	-19.12	4.74
	Induced Vaginal vs. Planned C-section	-4.75	2.70	1.00	-15.26	5.76
	Induced Vaginal vs. Emergency C-section	1.03	3.16	1.00	-11.26	13.31
	Planned C-section vs. Emergency C-section	5.78	3.47	1.00	-7.69	19.25

[1] Results of multivariate regression analyses, adjusted for weight, maternal age, pre-pregnancy BMI, smoking, ethnicity, intention to breastfeed and education; [2] Tukey test for comparison of least square means; SE = Standard Error; 95% CI = 95% Confidence Interval

Table 2.4. Logistic Regression Model Predicting Odds of Loss to Follow-up among Participants between 1-7, 7-9, 9-10 and 10-12 months in the Infant Feeding Practices Survey II

	1-2 Months (n = 2,536)				2-3 Months (n = 2,250)				3-4 Months (n = 2,109)			
	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value
Gender (Male/Female)[1]	1.07	0.85	1.34	0.56	0.91	0.71	1.16	0.44	1.06	0.83	1.37	0.64
Gestational age (weeks)	1.02	0.94	1.12	0.59	1.05	0.95	1.16	0.33	1.07	0.96	1.18	0.22
Black[2]	1.71	1.05	2.77	**0.03**	0.70	0.34	1.46	0.34	1.06	0.58	1.95	0.85
Hispanic[2]	1.59	1.05	2.41	**0.03**	1.32	0.81	2.15	0.27	1.20	0.71	2.01	0.49
Asian Pacific Islander[2]	1.47	0.75	2.87	0.27	0.86	0.36	2.04	0.73	1.04	0.46	2.34	0.93
Other[2]	1.37	0.65	2.91	0.41	1.73	0.80	3.75	0.17	1.12	0.45	2.80	0.81
Parity[3]	1.04	0.78	1.40	0.78	1.31	0.94	1.82	0.11	1.22	0.87	1.72	0.25
Pre-pregnancy smoking[4]	0.72	0.50	1.03	0.08	0.67	0.45	1.00	**0.05**	1.25	0.77	2.02	0.37
185 – 349% of FPL[5]	0.97	0.75	1.26	0.84	1.04	0.78	1.39	0.78	0.99	0.74	1.32	0.92
350% of FPL[5]	0.60	0.42	0.86	**0.01**	0.75	0.51	1.11	0.15	0.79	0.54	1.17	0.24
Maternal BMI (kg/m^2)	1.01	0.99	1.02	0.43	0.99	0.97	1.01	0.21	1.00	0.99	1.02	0.67
Maternal age (years)	0.97	0.95	1.00	**0.03**	0.95	0.92	0.97	**0.0001**	0.96	0.93	0.98	**0.001**
Marital status (married/not)[6]	1.07	0.99	1.15	0.11	1.05	0.96	1.15	0.28	1.14	1.04	1.24	**0.01**
Spontaneous vaginal	***Reference***											
Induced vaginal	0.99	0.76	1.29	0.93	1.19	0.88	1.60	0.26	1.19	0.89	1.59	0.23
Planned C-section	1.05	0.74	1.47	0.80	1.30	0.89	1.89	0.18	0.95	0.65	1.40	0.80
Emergency C-section	1.30	0.89	1.90	0.18	2.02	1.32	3.07	**0.001**	0.66	0.39	1.12	0.12

Table 2.4. (Continued) Logistic Regression Model Predicting Odds of Loss to Follow-up among Participants between 1-7, 7-9, 9-10 and 10-12 months in the Infant Feeding Practices Survey II

	4-5 Months (n = 2,000)				5-6 Months (n = 1,944)				6-7 Months (n = 1,881)			
	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value
Gender (Male/Female)[1]	0.96	0.73	1.25	0.75	1.05	0.80	1.39	0.71	1.05	0.79	1.40	0.73
Gestational age (weeks)	0.99	0.89	1.10	0.85	0.97	0.87	1.09	0.64	0.97	0.87	1.09	0.60
Black[2]	1.66	0.91	3.03	0.10	1.64	0.86	3.13	0.14	1.12	0.54	2.35	0.76
Hispanic[2]	1.68	1.01	2.79	**0.05**	1.20	0.66	2.17	0.54	1.25	0.68	2.27	0.47
Asian Pacific Islander[2]	1.44	0.66	3.13	0.36	1.00	0.39	2.57	1.00	1.55	0.68	3.55	0.30
Other[2]	0.89	0.31	2.61	0.84	1.23	0.46	3.27	0.68	2.57	1.10	6.03	**0.03**
Parity[3]	0.97	0.69	1.37	0.87	1.10	0.76	1.58	0.62	1.39	0.95	2.04	0.09
Pre-pregnancy smoking[4]	0.48	0.32	0.72	**0.0003**	0.59	0.37	0.93	**0.02**	0.57	0.36	0.90	**0.02**
185 – 349% of FPL[5]	0.90	0.66	1.24	0.52	1.00	0.72	1.37	0.98	0.72	0.51	1.02	0.06
350% of FPL[5]	0.82	0.55	1.23	0.34	0.78	0.51	1.20	0.25	0.85	0.55	1.30	0.45
Maternal BMI (kg/m^2)	1.00	0.98	1.02	0.88	1.02	1.00	1.04	0.06	1.01	0.99	1.04	0.23
Maternal age (years)	0.95	0.92	0.98	**0.0004**	0.95	0.93	0.98	**0.002**	0.94	0.91	0.97	**0.0003**
Marital status (married/not)[6]	1.07	0.97	1.17	0.17	1.04	0.94	1.16	0.41	1.12	1.01	1.23	**0.03**
Spontaneous vaginal	***Reference***											
Induced vaginal	0.84	0.62	1.15	0.28	1.11	0.81	1.53	0.52	1.10	0.78	1.55	0.59
Planned C-section	0.78	0.51	1.18	0.24	0.69	0.44	1.09	0.11	0.96	0.62	1.50	0.86
Emergency C-section	0.92	0.58	1.47	0.73	1.09	0.67	1.78	0.73	1.53	0.94	2.50	0.09

Table 2.4. (Continued) Logistic Regression Model Predicting Odds of Loss to Follow-up among Participants between 1-7, 7-9, 9-10 and 10-12 months in the Infant Feeding Practices Survey II

	7-9 Months (n = 1,810)				9-10 Months (n = 1,722)				10-12 Months (n = 1,617)			
	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value
Gender (Male/Female)[1]	0.94	0.72	1.24	0.66	0.94	0.72	1.21	0.61	0.87	0.66	1.15	0.34
Gestational age (weeks)	1.10	0.99	1.23	0.09	1.02	0.91	1.13	0.79	1.02	0.91	1.14	0.75
Black[2]	2.18	1.18	4.00	**0.01**	0.69	0.31	1.53	0.36	2.30	1.25	4.23	**0.01**
Hispanic[2]	0.89	0.47	1.67	0.71	1.51	0.91	2.51	0.11	1.16	0.62	2.16	0.65
Asian Pacific Islander[2]	0.87	0.34	2.26	0.78	1.08	0.47	2.46	0.85	1.02	0.42	2.49	0.97
Other[2]	2.87	1.19	6.90	**0.02**	1.57	0.55	4.46	0.40	2.14	0.86	5.34	0.10
Parity[3]	1.05	0.73	1.50	0.81	1.34	0.95	1.89	0.10	0.93	0.65	1.33	0.68
Pre-pregnancy smoking[4]	0.62	0.39	0.99	**0.05**	0.90	0.55	1.48	0.67	0.75	0.46	1.22	0.24
185 – 349% of FPL[5]	0.77	0.56	1.06	0.11	0.92	0.68	1.26	0.61	0.62	0.45	0.86	**0.004**
350% of FPL[5]	0.64	0.42	0.97	0.04	1.10	0.75	1.60	0.63	0.51	0.34	0.78	**0.002**
Maternal BMI (kg/m^2)	1.00	0.98	1.02	0.96	1.03	1.01	1.05	**0.001**	0.99	0.97	1.01	0.34
Maternal age (years)	0.95	0.92	0.98	**0.001**	0.96	0.94	0.99	**0.01**	0.94	0.92	0.97	**0.0002**
Marital status (married/not)[6]	1.00	0.91	1.11	0.95	1.11	1.01	1.22	**0.03**	0.94	0.85	1.05	0.26
Spontaneous vaginal	***Reference***											
Induced vaginal	1.27	0.92	1.76	0.15	0.81	0.60	1.11	0.19	1.43	1.03	1.99	**0.03**
Planned C-section	1.47	0.98	2.19	0.06	0.86	0.59	1.25	0.42	1.12	0.72	1.74	0.62
Emergency C-section	1.03	0.61	1.74	0.90	0.83	0.52	1.34	0.45	1.74	1.09	2.79	**0.02**

[1] Reference = Female; [2] Reference = White; [3] Reference = More than 1 child; [4] Reference = Not smoking; [5] Reference = 185% of FPL; [6]Reference = Married; SE = Standard Error; FPL = Federal Poverty Level; BMI = Body Mass Index; 95% CI = 95% Confidence Interval

DISCUSSION

In this study of women across the U.S., it was found that having either an emergency C-section or induced vaginal delivery was associated with lower breastfeeding intensity, compared to women who had spontaneous vaginal delivery. Breastfeeding intensity for the planned C-section group was more like that observed for spontaneous vaginal delivery, and at months 4 and 5, was higher than breastfeeding intensity following emergency C-section.

Our finding that emergency C-section has a negative impact on breastfeeding is consistent with current literature. Though the outcomes of these studies vary and include breastfeeding initiation, duration and LATCH scores, most studies showed that C-section is associated with adverse breastfeeding outcomes.[48,50-52,54,74] Medical interventions during the birth process have been shown to interfere with the mother-infant bonding experience, which in turn affects breastfeeding outcomes.[77] The administration of intrapartum opioids is also linked to lower incidence of breastfeeding.[78, 79]

Previous studies that differentiated between planned or emergency C-section, emergency C-section found shorter breastfeeding duration and exclusivity.[53,80] Since both planned C-section and emergency C-section utilize the same drugs and procedures but have different breastfeeding intensities, our results, and that of others,[53,80,32,33] suggest that trauma during birth may be a more powerful deterrent to breastfeeding. Fetal or maternal distress, and mechanical impedance to the progress of labor are possible indications for emergency C-section, and women often undergo emergency C-section after going through long, difficult labor. One study reported that women's perceived lack of control during labor, and the discrepancy between their expectations vs. what actually took place during the birthing event predicted self-reported birthing trauma.[81] Stress during delivery delays breastfeeding initiation and affects breastfeeding outcomes,[52,82,83] and may be what differentiates breastfeeding outcomes between planned vs. emergency C-section.

A limitation of this study is that the sample population, although well distributed throughout the United States, is not representative of the US population. However, it is not expected that the effects of mode of delivery and breastfeeding intensity will be very different across different populations. In addition, all data are self-reported by the mother. The reasons for breastfeeding outcome may also be associated with other effects of delivery that were not captured by the questionnaires, such as the duration of delivery interventions, postpartum fatigue, pain, or delivery-related complications. Older maternal age has decreased odds of being lost to follow-up. As age is positively associated with breastfeeding intensity, our estimates might have been higher due to more older women staying in the study. However, women in the induced vaginal delivery group and emergency C-section groups were more likely to be lost to follow-up, and both of these groups have lower breastfeeding intensities than the spontaneous delivery group. As a consequence, the observed difference between feeding groups may have been larger, if they had stayed in the study.

The prospective design of this study is a strength. This study followed up mother-infant pairs from the last trimester of pregnancy until 12 months. The richness of the data includes infants' feeding patterns, the frequency with which data were collected, four categories of delivery method, attitude toward breastfeeding, and several additional possible confounders. Lastly, the study's large sample size allowed for better precision when estimating parameters of interest.

CONCLUSION

Compared to spontaneous vaginal delivery, women who underwent induced vaginal delivery and emergency C-section had lower breastfeeding intensities compared to women who had spontaneous vaginal deliveries. No differences were seen between planned C-section and spontaneous C-section. Future research should explore the psychological factors associated with intrapartum interventions such as mothers' level of comfort with change in birth plans and its possible implications on breastfeeding outcomes. Details surrounding the birth process, such as length of labor may also help us better define "trauma." Lastly, breastfeeding support may benefit from tailoring efforts toward type of delivery.

CHAPTER 3.

STUDY 2: The Effect of Breastfeeding Intensity on Weight Gain in the First Year of Life

ABSTRACT

Background: Most studies on breastfeeding and weight gain measure breastfeeding as duration or exclusivity and present infant growth over a 6- or 12-month period.

Objectives: To estimate the effects of breastfeeding intensity on infant weight change from 0-3, 3-5, 5-7 and 7-12 months postpartum.

Methods: The sample included 1,710 mothers who participated in postpartum surveys of the Infant Feeding Practice Study II and provided weight measurement of their infants at 3 months. Breastfeeding intensity was divided into 4 categories: 0%, 1-49%, 50-99% and 100% breast milk. The main outcome variable is infant weight change at 4 time intervals: 0-3, 3-5, 5-7 and 7-12 months. Multiple regression was used to estimate mean weight change by breastfeeding intensity, adjusted for infant gender, gestational age, at time of survey, change in infant length, solid intake, and maternal ethnicity, pre-pregnancy smoking, mode of delivery and exposure to antibiotics.

Results: Compared to infants who received 100% breast milk, those who received 50-99% gained less (-156.4 grams, 95% CI: -254.4, -58.5) from 0-3 months. Infants who received 0% breast milk gained more than infants fed 100%: 132.6 grams (95% CI: 26.3, 239.0) from 3-5 months; 291.7 grams (95% CI: 162.8, 420.6) from 5-7 months and 515.6 grams (95% CI: 234.3, 796.9) from 7-12 months. At the 7-12 months interval, infants who received 1-49% breast milk also gained more than infants who received 100% (411.1 grams, 95% CI: 79.3, 742.9). Among all infants who had no or some breast milk, those fed 50-99% gained less than infants fed 0% breast milk from months at 0-3, 3-5, 5-7 and 7-12 months.

Conclusions: Even among mothers who are not able to feed 100% breast milk, increasing breastfeeding intensity should be part of the strategy to prevent childhood obesity.

Key Words: Breastfeeding, intensity, weight change

BACKGROUND

More than one-third (35.7%) of U.S. adults and 17% of children and adolescents are obese, according to CDC's data from 2009–2010.[1] Preventing obesity can avert several major causes of death, including heart disease, stroke, type 2 diabetes and certain types of cancer.[1]

Adult obesity has roots in infancy.[2] Rapid weight gain in the first year of life sets the growth trajectory and is a risk factor for obesity later in life.[3-6] Some evidence suggest that the rate of weight gain during the first few months of life may influence weight status later in childhood[84-86] as well as the later development of adult cardiovascular disease.[87, 88]

Infants who received breast milk are at lower risk for later childhood obesity than infants who did not.[61,63,89,90] Breastfeeding duration is also associated with lower rates of childhood obesity.[62,84,91,92] However, most studies on breastfeeding and weight gain measure breastfeeding as duration or exclusivity - few studies have attempted to quantify breastfeeding *intensity*, a measures that better captures a "dose" effect among infants who are not exclusively breastfed. At a time when banked breast milk was commonly available, and randomization of infants to donor breast milk or formula was feasible and ethical, Singhal et al.[93] investigated the dose-response effect of breast milk and lipoprotein profile at age 13-16. The authors were able to quantify the exact volume of early breast milk intake, and showed prospectively that increased consumption of human milk was associated with reduced ratios of LDL to HDL cholesterol. Also, most studies also present infant growth over a 6- or 12-month period, because more detailed infant growth records are rarely available.

The goal of this paper is to estimate the effects of breastfeeding intensity on infant weight change at 4 time intervals during the first year of life: 0-3, 3-5, 5-7 and 7-12 months postpartum.

METHODS

Study Design

The proposed study is a secondary analysis of data from the Infant Feeding Practices Study (IFPS) II data, focusing on the relationship between type of delivery and breastfeeding intensity during the first year of life. The IFPS II is a longitudinal follow-up study of pregnant women and new mothers conducted by the US Food and Drug Administration and Centers for Disease Control and Prevention during 2005 and 2006.

Study Population

The IFPS II study sample was obtained from a consumer panel of 500,000 households. Survey questionnaires were sent to pregnant women before their delivery and 10 times at regular intervals during the year after they gave birth. To be eligible to participate in the IFPS II, women had to be ≥18 years of age and to have delivered a healthy singleton infant who weighed ≥5 pounds at birth, had a gestational age at birth of ≥35 weeks, and spent <3 days in intensive care. Of the initial panel of 15,147 women identified, 14,618 were mailed a prenatal questionnaire, of these 4,902 qualified and completed the prenatal questionnaire; all of these women were sent the birth screener and subsequent neonatal survey.[94] Of the total neonatal surveys mailed (n = 4,013), 76.9% (n = 3,033) completed and qualified to participate in the study; additional information about IFPS II methods and response rates for the entire study is available.[94] Our study sample includes 1,710 of these women who provided their infants' weight at 3 months. Due to loss to follow-up and missing data, sample size was 1,106 at 5 months, 875 at 7 months and 679 at 12 months.

Key Exposure Variable

Breastfeeding intensity measures percent of all milk feeds that were breast milk (number of breast milk feeds ÷ all other milk feeds x 100) from maternal self-report of infant milk intake "in the past 7 days". Women answered these questions in the postnatal questionnaire at months 2-7 and months 9, 10 and 12. Mothers self-reported all milk intake. Tests for linearity of the effect of breastfeeding intensity use breastfeeding percent as a continuous variable and including its squared and cubed terms in the model. The cubed term was not significant at $p < 0.05$, suggesting that a quadratic model is appropriate. Hence breastfeeding intensity was divided into 4 categories: 0% breast milk, 1-49% breast milk, 50-99% breast milk <100% and 100% breast milk. It is important to note that the breastfeeding intensity measure was not a measure of exclusive breastfeeding. Therefore, infants can receive 100% of milk feeds as breast milk but not be exclusively breastfed if they also receive any solid foods.

Outcome Variable

Infant weight change was calculated from the difference between weight during the current month and the last reported weight. Infant weights were reported at 0, 3, 5, 7 and 12.

From these reported weights, 4 time intervals outcomes were derived - weight change from 0-3, 3-5, 5-7 and 7-12 months. All weights were reported in grams.

Potential Confounding Variables

Variables considered *a priori* to be potential confounders were use of solids (yes/no), gender), age of infant at time of survey, change in length (cm), gestational age ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), federal poverty level (%), parity, maternal age (years), body mass index (BMI, kg/m^2), marital status (married/single), pre-pregnancy smoking (yes/no) and education (high school and under, 1-3 year of college, and college/graduate school).

Because recent studies showed an association between gut bacteria and obesity, [95,96] the models included adjustment for mode of delivery and use of antibiotics in our analyses. The method of delivery categories were spontaneous vaginal, induced vaginal, planned C-section, and emergency C-section. Antibiotic use was reported as a dichotomous variable ("Baby received antibiotics past 2 weeks") from months 2 through 7, 9, 10 and 12. A cumulative variable of whether the infant had ever received antibiotics was created and used in analyses.

Statistical Analyses

SAS 9.3 was used for all analyses. For descriptive statistics, continuous variables are reported as mean ± standard deviation (SD). Categorical variables are reported as frequencies and percentages.

A series of multiple linear regression models were fit to estimate mean weight change at each time interval and 95% confidence interval (CI) by breastfeeding intensity category. For example, mean weight change from 0-3 months was estimated by breastfeeding intensity category at 3 months.

To accomplish this, first univariate models regressing each interval mean weight change on each confounder (separately at each of the 4 time intervals: 0-3, 3-5, 5-7 and 7-12 months) were fit. Variables that reached a p-value of ≤ 0.20 in at least one of the time intervals were kept and fitted into a multiple regression model to predict weight change. Variables that were not significant ($p > 0.05$) at all 4 time intervals were then removed from the model. The remaining variables made up the final model that was used to predict weight change at each time interval. The final model includes infant gender (male or female), gestational age (weeks), at time of survey (months), change in infant length (cm), solid intake (yes/no), and maternal ethnicity

(White, Black, Hispanic, Asian/Pacific Islander and Other), pre-pregnancy smoking (yes/no), mode of delivery and exposure to antibiotics.

To explore difference in weight change among infants who were not fed 100% breast milk, weight change in infants fed 1-49% and 50-99% were compared with those who did not receive any breast milk. Infants who received 100% breast milk were excluded in this analysis. Logistic regression was used to determine which baseline factors were associated with loss to follow-up from 3-5 months, 5-7 months and 7-12 months.

RESULTS

The baseline characteristics of the study population (N = 1,710) are presented in Table 3.1. Mean maternal age was 29.5 ± 5.4 years and 69.6% had at least one child prior to this pregnancy. 87.1% were White, 3.5% were Black, 5.2% were Hispanic, and 2.9% Asian and Pacific Islander and 1.4% were another race. Most of these women were married (82.5%) and 16.8% completed no more than high school, 39.2% completed 1 to 3 years of college and 44.0% had a college or graduate degree.

Results of multivariable analyses are in Table 3.2 show that from months 0-3 months, infants fed 50-99% breast milk gained less weight **(**-156.4 grams, 95% CI: -254.4, -58.5) than those who were fed 100% breast milk. From 3-5 months, infants who received no breast milk gained 132.6 grams more (95% CI**:** 26.3, 239.0)**,** 291.7 grams more (95% CI: 162.8, 420.6) from 5-7 and 515.6 grams (95% CI: 234.3, 796.9) from 7-12 months. From 7-12 months, there was higher weight gain in infants who received 1-49% breast milk vs. 100% breast milk-fed infants *(*411.1 grams**,** 95% CI: 79.3, 742.9). In the first months postpartum, male infants gained less weight than females, but the gender effect does not persist after 3 months of age. Infants with lower gestational age also gained less weight between 0-3 months but gained significantly more after 3 months. Table 3.3 shows the estimate and standard error for each feeding group. The standard errors of the difference with the reference group were large, making it impossible to estimate a dose-response effect. Table 3.3 shows the weight gain for each of the 4 feeding groups, and Figure 3.1 summarized these same data in a bar graph.

Table 3.4 shows the adjusted mean weight change of infants who were fed 1-49% or 50-99% breast milk, compared to those who received no breast milk. Increased breastfeeding intensity was associated with less weight gain at months at 0-3, 5-7 and 7-12. Infants fed 50-99% breast milk gained less weight than infants who received 0% -113.97 grams (95% CI -217.91, -

10.03) between 0-3 months; -197.37grams (95% CI: -387.36, -7.38) between 5-7 months; and -372.45 grams (95% CI: -546.62, -198.28) between 7-12 months. Figure 3.2 summarized the weight gain for each of the 3 feeding groups.

Most literature investigating weight gain in infancy with later risk of obesity reported weight gain from 0-12 months. To compare these results with other studies, the effects of infant feeding with weight gain from 0-12 months were also reported. The results were similar to weight changes at each time interval –there was an inverse relationship between breastfeeding intensity and weight gain (Figure 3.3).

Primigravid women were more likely to be lost to follow-up (Table 3.5) between 3-5, 5-7 and 7-12 months (OR = 1.38, 95% CI: 1.04, 1.83; OR = 1.58, 95% CI: 1.09, 12.29 and OR = 1.62, 95% CI: 1.09, 2.41 respectively). Although women with increased maternal age were less likely to be lost to follow-up at months 3-5 and 7-12, the ORs and confidence intervals were close to null (OR = 0.97, 95% CI: 0.94, 0.99; OR = 0.97, 95% CI: 0.94, 1.00 respectively). Black women were more likely to be lost to follow-up at 3-5 months (OR = 2.06, 95% CI: 1.16, 3.67) and between 7-12 months (OR = 2.82, 95% CI: 1.11, 7.21).

Table 3.1. Frequency Distributions (in Percent) or Means (± Standard Deviations) of Selected Socio-Demographic and Birth Characteristics (n = 1,710)

	Infant Characteristics	
Gender (%)	Boy	48.7
	Girl	51.3
Gestational age, weeks (Mean ± SD)		39.3 ± 1. 3
Birth Weight, grams (Mean ± SD)		3,474.9 ± 457.8
	Maternal Characteristics	
Age, years (Mean ± SD)		29.5 ± 5.4
Maternal pregnancy BMI, kg/m^2 (Mean ± SD)		26.7 ± 6.9
Marital Status (%)	Married	82.5
	Single	17.5
Parity (%)	First child	30.4
	One or more child	69.6
Mode of Delivery (%)	Spontaneous vaginal	38.1
	Induced vaginal	34.3
	Planned C-section	16.5
	Emergency C-section	11.1
Education (%)	High School and under	16.8
	1-3 year of College	39.2
	College / Graduate school	44.0
% Federal Poverty Level (%)	185% of FPL	37.0
	185 – 349% of FPL	36.9
	350% of FPL	26.1
Ethnicity (%)	White	87.1
	Black	3.5
	Hispanic	5.2
	Asian Pacific Islander	2.9
	Other	1.4
Pre-pregnancy Smoking (%)	No	91.8
	Yes	8.1

BMI = Body Mass Index; SD = Standard Deviation

Table 3.2. Estimated Adjusted Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals (CI) of Infants Who Were Fed None or Some Breast Milk, Compared to Infants Fed 100% Breast Milk, among Participants in the Infant Feeding Practices Survey II

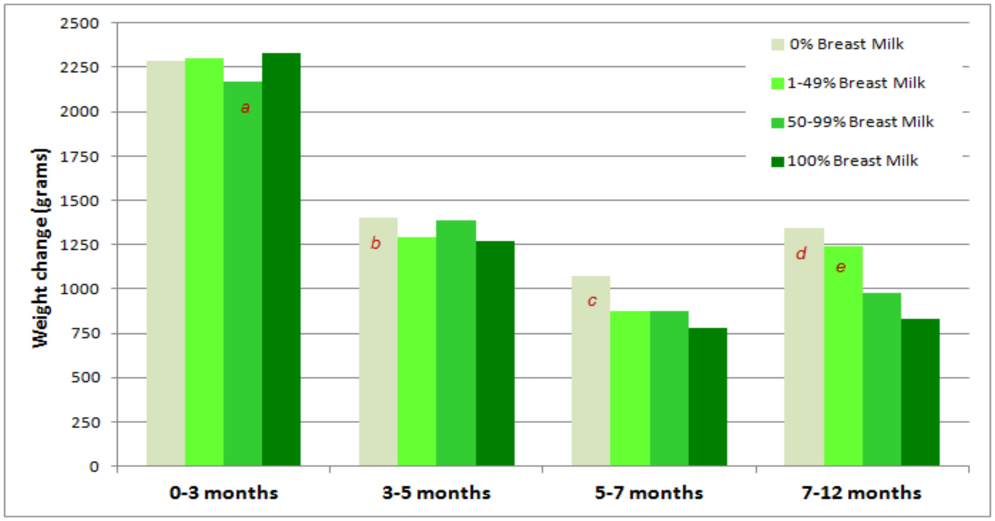
	MONTH 0-3 (n = 1,710) (Unadjusted weight gain = 2,101.4 grams)					MONTH 3-5 (n = 1,106) (Unadjusted weight gain = 1,244.0 grams)				
	β	SE	P Value	95% CI		β	SE	P Value	95% CI	
Intercept	2883.6	580.5	<0.0001	1745.1	4022.1	1942.6	809.1	0.02	354.9	3530.3
Gender (male/female)[1]	-414.5	33.5	<0.0001	-480.1	-348.8	-63.3	45.2	0.16	-152.0	25.3
Infant age (months)	362.9	38.2	<0.0001	288.0	437.8	22.0	56.8	0.70	-89.3	133.4
Gestational age (weeks)	-55.3	13.6	<0.0001	-82.0	-28.6	28.5	5.1	<0.0001	18.6	38.4
Change in length (cm)	53.3	4.5	<0.0001	44.4	62.3	-23.5	18.3	0.20	-59.5	12.4
Solid intake (yes/no)[2]	-8.4	43.8	0.85	-94.2	77.5	139.6	56.7	0.01	28.3	251.0
Black[3]	188.3	91.8	0.04	8.2	368.5	239.9	144.7	0.10	-44.0	523.8
Hispanic[3]	140.0	75.4	0.06	-8.0	287.9	-152.3	106.5	0.15	-361.2	56.5
Asian/Pacific Islander[3]	4.8	98.6	0.96	-188.7	198.2	22.6	126.3	0.86	-225.1	270.3
Other[3]	34.4	140.8	0.81	-241.7	310.5	54.4	189.5	0.77	-317.4	426.1
Pre-pregnancy smoking (yes/no)[4]	1.9	62.5	0.98	-120.8	124.6	-157.8	90.2	0.08	-334.8	19.2
Induced vaginal[5]	26.5	39.5	0.50	-51.0	104.0	-30.2	54.2	0.58	-136.6	76.3
Planned C-section[5]	4.7	48.6	0.92	-90.7	100.1	-44.4	66.0	0.50	-173.9	85.0
Emergency C-section[5]	-54.1	55.3	0.33	-162.5	54.3	-12.8	74.4	0.86	-158.7	133.2
Antibiotic exposure (yes/no)[4]	-212.6	58.5	0.0003	-327.5	-97.8	37.9	57.0	0.51	-73.9	149.7
0% Breast Milk	-40.6	40.5	0.32	-120.1	38.8	132.6	54.2	0.01	26.3	239.0
1-49% Breast Milk	-27.9	72.6	0.70	-170.3	114.4	25.3	99.3	0.80	-169.4	220.1
50-99% Breast Milk	-156.4	50.0	0.002	-254.4	-58.5	120.0	72.0	0.10	-21.3	261.3
100% Breast Milk	*Reference*									

Table 3.2. (Continued) Estimated Adjusted Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals (CI) of Infants Who Were Fed None or Some Breast Milk, Compared to Infants Fed 100% Breast Milk, among Participants in the Infant Feeding Practices Survey II

	MONTH 5-7 (n = 875) Unadjusted weight gain = 1,074.1 grams)					MONTH 7-12 (n = 679) Unadjusted weight gain = 1,805.7 grams)				
	β	SE	P Value	95% CI		β	SE	P Value	95% CI	
Intercept	-830.4	1124.2	0.46	-3036.8	1376.1	629.5	1600.3	0.70	-2512.8	3771.9
Gender (male/female)[1]	-34.4	56.3	0.54	-144.8	76.1	-53.9	57.7	0.35	-167.2	59.5
Infant age (months)	172.4	70.3	0.01	34.5	310.4	53.4	75.1	0.48	-94.1	200.9
Gestational age (weeks)	17.8	5.0	0.0003	8.1	27.6	20.5	4.3	<0.0001	12.1	28.9
Change in length (cm)	4.8	22.6	0.83	-39.5	49.2	-17.5	22.4	0.44	-61.4	26.5
Solid intake (yes/no)[2]	-257.6	265.6	0.33	-779.0	263.7	681.8	747.1	0.36	-785.2	2148.9
Black[3]	117.8	179.8	0.51	-235.0	470.7	101.9	219.4	0.64	-328.8	532.6
Hispanic[3]	98.4	142.0	0.49	-180.2	377.1	-144.5	134.4	0.28	-408.5	119.5
Asian/Pacific Islander[3]	-108.9	157.8	0.49	-418.6	200.9	-145.6	162.8	0.37	-465.2	174.1
Other[3]	-28.2	240.9	0.91	-501.1	444.6	-36.5	218.2	0.87	-465.0	391.9
Pre-preg smoking (yes/no)[4]	437.2	115.5	0.0002	210.5	663.9	-153.6	123.8	0.22	-396.7	89.4
Induced vaginal[5]	-63.8	68.4	0.35	-198.1	70.5	60.4	70.2	0.39	-77.4	198.2
Planned C-section[5]	77.8	80.9	0.34	-81.0	236.7	86.9	81.2	0.28	-72.5	246.3
Emergency C-section[5]	-119.2	91.2	0.19	-298.2	59.9	-20.7	94.8	0.83	-206.9	165.6
Antibiotic exposure (yes/no)[4]	-51.7	60.7	0.40	-170.9	67.5	-12.4	58.0	0.83	-126.3	101.5
0% Breast Milk	291.7	65.7	<0.0001	162.8	420.6	515.6	143.3	0.0003	234.3	796.9
1-49% Breast Milk	97.7	136.3	0.47	-169.8	365.1	411.1	169.0	0.02	79.3	742.9
50-99% Breast Milk	96.3	93.1	0.30	-86.4	279.0	144.8	160.4	0.37	-170.1	459.8
100% Breast Milk	*Reference*									

[1] Reference group = Female; [2] Reference group = "Yes"; [3]Reference group = White; [4] Reference group = "No"; SE = Standard Error; 95% CI = 95% Confidence Interval

Figure 3.1 Estimated Adjusted[1] Mean Weight Change (grams) at 0-3, 3-5, 5-7 and 7-12 months of Infants in all Breastfeeding Groups, among Participants in the Infant Feeding Practices Survey II



	MONTH 0-3 (n = 1,710) (Unadjusted weight gain = 2,101.4 grams)		MONTH 3-5 (n = 1,106) (Unadjusted weight gain = 1,244.0 grams)		MONTH 5-7 (n = 875) (Unadjusted weight gain = 1,074.1 grams)		MONTH 7-12 (n = 679) (Unadjusted weight gain = 1,805.7 grams)	
	β	SE	β	SE	β	SE	β	SE
0% Breast Milk	2286.1	68.7	1402.5	107.2	1069.5	292.8	1346.4	756.9
1-49% Breast Milk	2298.8	94.9	1295.1	136.0	875.5	316.5	1241.9	765.1
50-99% Breast Milk	2170.3	77.3	1389.9	119.4	874.2	302.3	975.7	763.1
100% Breast Milk	2326.7	69.9	1269.8	105.7	777.8	289.9	830.8	772.1

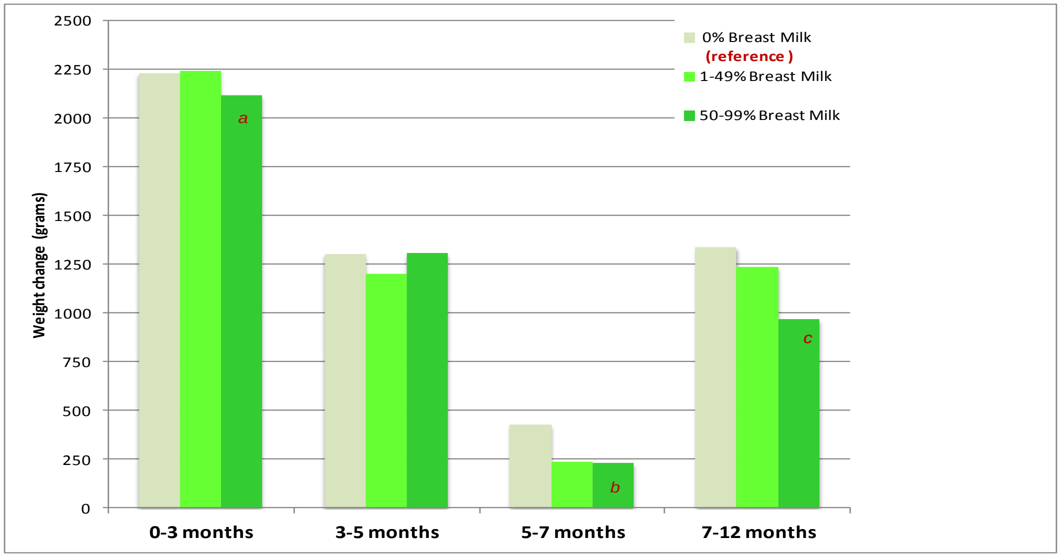
[1] Results of multivariate regression analyses, adjusted for gender, infant age, infant change in length, gestational age, solid intake, ethnicity, smoking, antibiotic use and mode of delivery; [a] p = 0.002; [b] p = 0.02; [c] p < 0.0001; [d] p = 0.0003; [e] p = 002

Table 3.3. Estimated Adjusted[1] and Unadjusted Mean Weight Change (grams) at 0-3, 3-5, 5-7 and 7-12 months of Infants in <u>all Breastfeeding Groups</u>, among Participants in the Infant Feeding Practices Survey II

	Variable	β	SE	Unadjusted Mean Weight gain (Mean ± SD)	Unadjusted Mean Weight gain (Mean ± SD)
0-3 MONTHS (n = 1,710)	**0% Breast Milk** (n = 782)	2286.10	68.65	2139.00 ± 781.27	2101.35 ± 781.69
	1-49% Breast Milk (n = 122)	2298.82	94.92	2137.87 ± 801.02	
	50-99% Breast Milk (n = 308)	2170.30	77.29	1996.45 ± 825.51	
	100% Breast Milk (n = 829)	2326.74	69.89	2100.59 ± 760.50	
3-5 MONTHS (n = 1, 106)	**0% Breast Milk** (n = 659)	1402.46	107.19	1328.81 ± 830.56	1244.03 ± 762.28
	1-49% Breast Milk (n = 90)	1295.12	136.05	1220.23 ± 1017.43	
	50-99% Breast Milk (n = 195)	1389.86	119.41	1273.24 ± 598.20	
	100% Breast Milk (n = 561)	1269.82	105.65	1144.35 ± 672.48	
5-7 MONTHS (n = 875)	**0% Breast Milk** (n = 675)	1069.50	292.75	1190.18 ± 937.80	1074.23 ± 844.74
	1-49% Breast Milk (n = 62)	875.51	316.52	1017.63 ± 506.89	
	50-99% Breast Milk (n = 153)	874.16	302.32	1005.44 ± 905.25	
	100% Breast Milk (n = 423)	777.84	289.93	933.45 ± 672.63	
7-12 MONTHS (n = 679)	**0% Breast Milk** (n = 825)	1346.44	756.95	1886.92 ± 776.71	1805.70 ± 767.68
	1-49% Breast Milk (n = 99)	1241.92	765.10	1789.57 ± 727.10	
	50-99% Breast Milk (n = 140)	975.66	763.14	1492.1 ± 664.32	
	100% Breast Milk (n = 46)	830.83	772.11	1343.73 ± 578.09	

[1] Results of multivariate regression analyses, adjusted for gender, infant age, infant change in length, gestational age, solid intake, ethnicity, smoking, antibiotic use and mode of delivery; SE = Standard Error; SD = Standard Deviation

Figure 3.2 Estimated Adjusted[1] Mean Weight Change (grams) at 0-3, 3-5, 5-7 and 7-12 months of Infants Not Exclusively Breastfed, among Participants in the Infant Feeding Practices Survey II



	MONTH 0-3 (n = 1,710) (Unadjusted weight gain = 2,101.4 grams)		MONTH 3-5 (n = 1,106) (Unadjusted weight gain = 1,244.0 grams)		MONTH 5-7 (n = 875) (Unadjusted weight gain = 1,074.1 grams)		MONTH 7-12 (n = 679) (Unadjusted weight gain = 1,805.7 grams)	
	β	SE	β	SE	β	SE	β	SE
0% Breast Milk	2232.6	79.2	1305.7	138.9	429.7	907.1	1339.9	763.8
1-49% Breast Milk	2242.2	104.8	1203.4	163.2	237.8	918.6	1235.3	772.0
50-99% Breast Milk	2118.6	86.8	1307.0	145.9	232.3	913.1	967.4	770.1
100% Breast Milk	2232.6	79.2	1305.7	138.9	429.7	907.1	1339.9	763.8

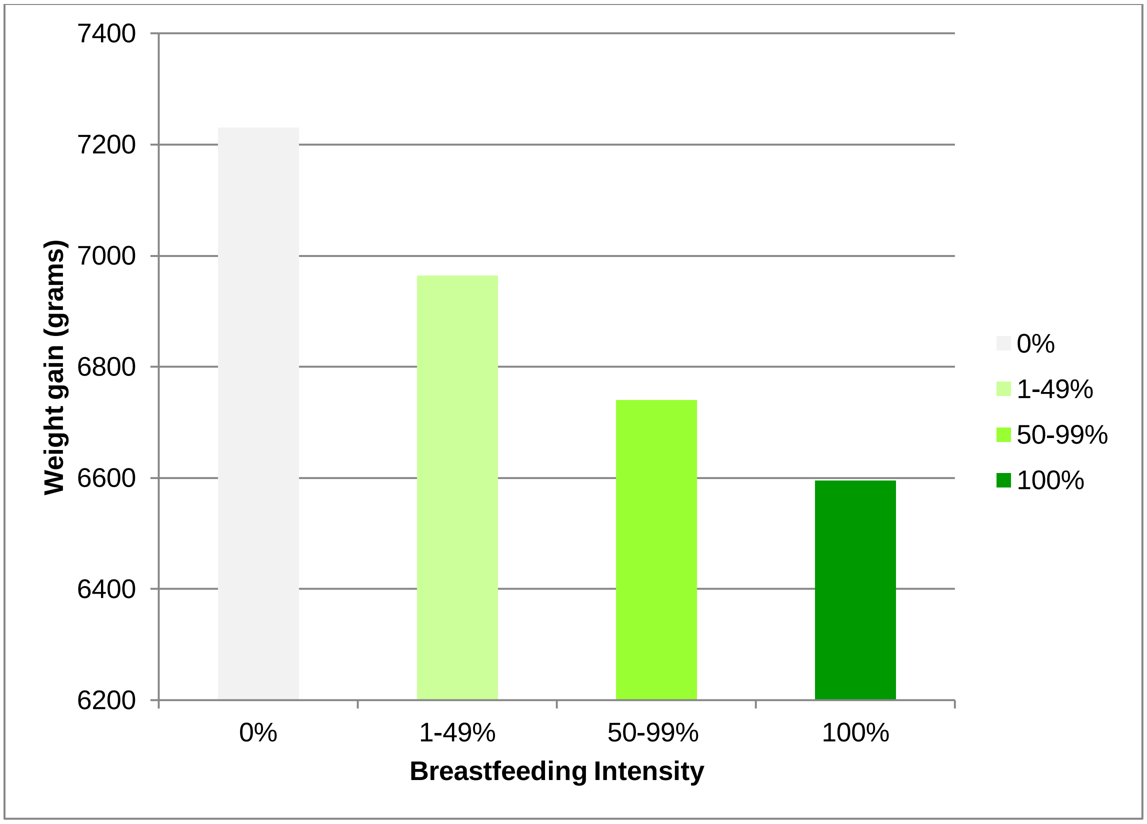
[1] Results of multivariate regression analyses, adjusted for gender, infant age, infant change in length, gestational age, solid intake, ethnicity, smoking, antibiotic use and mode of delivery; [a] $p = 0.03$; [b] $p = 0.04$; [c] $p < 0.0001$

Table 3.4. Estimated Adjusted[1,2] Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals of Infants Who Were Fed Some Breast Milk, Compared to Infants Who Were Not Fed Any Breast Milk, among Participants in the Infant Feeding Practices Survey II

		β	SE	P value	95% CI		Unadjusted Mean Weight gain (Mean ± SD)	Unadjusted Mean Weight gain (Mean ± SD)
0-3 MONTHS (n = 1,002)	**0% Breast Milk[1]** (n = 572)	3050.63	745.07	**<0.0001**	1588.52	4512.74	2139.00 ± 781.27	2101,89 ± 796.70
	1-49% Breast Milk (n = 122)	9.56	74.20	0.90	-136.04	155.16	2137.87 ± 801.02	
	50-99% Breast Milk (n = 308)	-113.97	52.97	**0.03**	-217.91	-10.03	1996.45 ± 825.51	
3-5 MONTHS (n = 682)	**0% Breast Milk[1]** (n = 397)	2248.96	1081.33	0.04	125.73	4372.20	1328.81 ± 830.56	1306.01 ± 807.42
	1-49% Breast Milk (n = 90)	-102.23	103.74	0.32	-305.93	101.47	1220.23 ± 1017.43	
	50-99% Breast Milk (n = 195)	1.36	77.22	0.99	-150.27	152.99	1273.24 ± 598.20	
5-7 MONTHS (n = 589)	**0% Breast Milk[1]** (n = 374)	-2278.83	1701.85	0.18	-5621.46	1063.80	1190.18 ± 937.80	1142.45 ± 909.44
	1-49% Breast Milk (n = 62)	-191.85	144.24	0.18	-475.16	91.47	1017.63 ± 506.89	
	50-99% Breast Milk (n = 153)	-197.37	96.73	**0.04**	-387.36	-7.38	1005.44 ± 905.24	
7-12 MONTHS (n = 650)	**0% Breast Milk[1]** (n = 411)	1013.84	1637.78	0.54	-2202.30	4229.98	1886.92 ± 776.71	1826.31 ± 768.95
	1-49% Breast Milk (n = 99)	-104.59	103.57	0.31	-307.97	98.79	1789.57 ± 727.10	
	50-99% Breast Milk (n =140)	-372.45	88.70	**<0.0001**	-546.62	-198.28	1492.10 ± 664.32	

[1] Results of multivariate regression analyses, adjusted for gender, infant age, infant change in length, gestational age, solid intake, ethnicity, smoking, antibiotic use and mode of delivery; [2] Reference group = infants who did not receive any breast milk; SE = Standard Error; SD = Standard Deviation; 95% CI = 95% Confidence Interval

Figure 3.3. Estimated Adjusted[1] Mean Weight Change (grams) from <u>0-12 months</u> of Infants by Breastfeeding Intensity Group, among Participants in the Infant Feeding Practices Survey II



	MONTH 0-12 (n = 679) Unadjusted weight gain = 6262.6 grams)	
	β	**SE**
0% Breast Milk (n = 825)	7231.0	1152.5
1-49% Breast Milk (n = 99)	6964.4	1164.7
50-99% Breast Milk (n = 140)	6740.0	1161.6
100% Breast Milk (n = 46)	6595.0	1175.3

[1]Adjusted for breast milk%, infant gender (male or female), gestational age (weeks), at time of survey (months), change in infant length (cm), solid intake (yes/no), and maternal ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), pre-pregnancy smoking (yes/no), and exposure to antibiotics (yes/no); SE = Standard Error

Table 3.5. Logistic Regression Model Predicting Odds of Loss to Follow-up among Participants between 3-5, 5-7 and 7-12 months in the Infant Feeding Practices Survey II

	Loss to Follow up											
	3-5 months (n = 1,595)				**5-7 months (n = 1,050)**				**7-12 months (n = 833)**			
	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value
Gender (Male/Female)[1]	1.07	0.87	1.32	0.53	1.21	0.93	1.59	0.16	1.03	0.77	1.39	0.84
Gestational age (weeks)	1.00	0.92	1.08	0.92	1.01	0.91	1.13	0.82	0.98	0.87	1.11	0.78
Black[2]	2.06	1.16	3.67	**0.01**	1.05	0.43	2.54	0.92	2.82	1.11	7.21	**0.03**
Hispanic[2]	1.14	0.71	1.85	0.58	1.68	0.91	3.10	0.10	0.70	0.32	1.54	0.37
Asian Pacific Islander[2]	0.95	0.49	1.82	0.87	1.12	0.51	2.50	0.77	0.99	0.42	2.34	0.98
Other[2]	0.67	0.26	1.77	0.42	1.36	0.48	3.83	0.56	0.34	0.07	1.61	0.18
Parity[3]	1.38	1.04	1.83	**0.03**	1.58	1.09	2.29	**0.02**	1.62	1.09	2.41	**0.02**
Pre-pregnancy smoking[4]	0.81	0.55	1.20	0.30	0.70	0.42	1.17	0.18	0.86	0.47	1.60	0.64
185 – 349% of FPL[5]	0.93	0.73	1.20	0.59	0.92	0.66	1.27	0.61	0.81	0.56	1.17	0.25
350% of FPL[5]	0.82	0.60	1.11	0.20	0.76	0.51	1.13	0.18	0.85	0.56	1.30	0.46
Maternal BMI (kg/m^2)	0.99	0.98	1.01	0.35	1.01	0.99	1.03	0.58	1.01	0.99	1.03	0.42
Maternal age (years)	0.97	0.94	0.99	**0.003**	0.98	0.95	1.01	0.13	0.97	0.94	1.00	**0.05**
Marital status (married/not)[6]	1.04	0.96	1.12	0.40	1.02	0.91	1.13	0.74	1.05	0.93	1.19	0.41
Spontaneous vaginal	***Reference***											
Induced vaginal[7]	**0.91**	**0.71**	**1.16**	**0.43**	**0.95**	**0.69**	**1.30**	**0.73**	**1.10**	**0.77**	**1.57**	**0.60**
Planned C-section[7]	0.80	0.58	1.09	0.16	0.80	0.53	1.19	0.27	0.97	0.63	1.50	0.91
Emergency C-section[7]	0.91	0.62	1.32	0.61	0.81	0.49	1.33	0.40	1.38	0.82	2.30	0.22

[1] Reference = Female; [2] Reference = White; [3] Reference = More than 1 child; [4] Reference = Not smoking; [5] Reference = 185% of FPL; [6] Reference = Married; SE = Standard Error; FPL = Federal Poverty Level; BMI = Body Mass Index; 95% CI = 95% Confidence Interval

DISCUSSION

Our findings show that having 100% milk feed from formula is associated with increased infant weight gain in later infancy, babies fed only formula exclusively gained more weight than those who received 100% breast milk. From month 7-12, infants who received some (but less than 50%) breast milk also gained more weight than those who received 100% breast milk. Though there was not a clear dose-response relationship, predominantly breastfed infants generally gained less than those who were fed formula exclusively.

The results of our study are similar to previous studies on exclusive breast or formula feeding. Dewey et al.[97] reported that exclusively breastfed infants gained significantly less weight than exclusively formula-fed infants at 3-6, 6-9, and 9-12 months. In addition, they found breastfeeding intensity at the lower end of the spectrum to be associated with increased weight gain at 12 months. It is interesting that at month 3, there were no differences between 0% and 100%. Instead differences were seen between 50-99% and 100%. It is possible that breastfeeding challenges during the early months led to less weight gain in this group, and that while breastfeeding intensity was high, the net amount of milk intake was low.

Toschke et al.,[98] reported a weight gain in first 12 months of more than 6,933 grams, as a predictor of overweight at 5-7 years of age in 4,235 German infants. Comparing our data to theirs, spontaneous vaginal deliveries have the lowest weight gain in between 0 to 12 months, and closest to the 6,933 grams reported by Toschke. For the group with breastfeeding intensity 0% and 1-49% groups, the adjusted weight gain from 0-12 months were higher than the cut-off point reported by Toschke, hence suggesting that regardless of delivery type, infants with lower breast milk intake in our population are more likely to be overweight in later childhood.

Several theories attempt to explain the biological mechanisms by which breastfeeding might protect against high growth rates. One possible mechanism is that high protein intake in formula-feeding stimulates the secretion of insulin-like growth factor I, which accelerates growth and increases muscle mass and adipose tissue.[99] In addition, two hormones related to the etiology of childhood obesity are leptin and adiponectin, both of which are found in breast milk but not in infant formulas.[100,101] Leptin may help regulate appetite and energy metabolism, and adiponectin may cause weight loss by raising metabolic rates without affecting appetite.[102]

It has also been theorized that infants' learned self-regulation of energy intake is related to breastfeeding. In theory, breastfed infants may be better able to control the amount of milk they consume in response to their internal satiety cues than bottle-fed infants, who might be encouraged to finish a bottle even if they are already full. While the flow from a milk bottle is continuous, infants fed from the breast have to work for several let-downs during a feeding session, making them more likely to stop when full.[103] Studies have also found a negative correlation between the energy density of breast milk and the amount of milk consumed by exclusively breastfed infants.[104,105] This correlation presumably reflects the ability of breastfed infants to self-regulate their milk consumption to match their energy needs.[106]

The strengths of our study include its prospective design. This study followed up mother-infant pairs from the last trimester of pregnancy until 12 months following birth with extensive testing of survey questions. The richness of the data includes the details of infants' feeding patterns and the frequency at which the data were collected. Lastly, the study's large sample size allows for better precision when estimating parameters of interest.

Limitations of the study include small numbers in some breastfeeding groups, making it difficult to see a clearer dose-response relationship between breastfeeding intensity and weight change. Also, underlying assumption in calculating breastfeeding intensity was that the reported intensity in the past 7 days was representative of other weeks. In a second evaluation, the previous month breastfeeding intensity was used in the analyses (with the exception of month 12, where the last reported breastfeeding intensity was 10 months), similar results were obtained. This suggests that breastfeeding intensities were similar between the current and previous month.

In addition, all data are self-reported by the mother; no medical records were examined to confirm infant health, weight, length, or any other characteristic. As the study progressed, the number of women available for analysis decreased, potentially leading to selection bias. Loss to follow-up of primigravid women is consistent across all time intervals. However, since parity did not have an effect on weight change independent of breastfeeding intensity, the loss of follow-up of primigravid women is not likely to have changed our results. Lastly, even though the richness of the data allowed for controlling of several potential confounders, residual confounding is still possible given that there is no way to quantify the net amount of breast milk and its bioactive components consumed by the infants.

CONCLUSION

Because the prevalence of childhood obesity has increased dramatically in the United States, increasing breastfeeding intensity if a mother is unable to provide 100% breast milk is a modifiable factor that should be part of a public health campaign to prevent childhood obesity. To further quantify the dose-response relationship using breastfeeding intensity, future larger studies with minimal attrition rates are needed. Longer follow-up period of infants and measurements taken by trained study staff will provide prospective, standardized measures.

CHAPTER 4.
STUDY 3: Growth in the First Year of Life: Effects of Mode of Delivery and Breastfeeding Intensity

ABSTRACT

Background: Mode of delivery and infant feeding are the first determinants of the gut bacterial composition, which may contribute to the development of obesity.

Objectives: The goal of this paper is to estimate the component and joint effects of mode of delivery and breastfeeding intensity on infant weight gain at 4 time intervals: 0-3, 3-5, 5-7 and 7-12 months postpartum.

Methods: The sample consisted of 1,710 women who participated in postpartum surveys of the Infant Feeding Practice Study II and provided their infants' 3-month weight. Breastfeeding intensity was divided into 2 categories: <50% breast milk and ≥50% breast milk. Delivery method was classified into vaginal and C-section delivery and the main outcome is infant weight change from 0-3, 3-5, 5-7 and 7-12 months. Multiple regression models were used to estimate the effects of breastfeeding intensity and delivery method on mean weight change, adjusted for potential confounders. Using dummy variables, interaction terms were created between each delivery group and feeding group, yielding a total of 4 unique groups. The group of infants born via spontaneous vaginal delivery and fed 100% breast milk was used as the reference group.

Results: The effect of C-section delivery on weight change is similar to vaginal delivery after adjusting for infant feeding, gender, age, gestational age, change in length, solid intake, ethnicity, antibiotic exposure and maternal pre-pregnancy smoking. Infants who were fed <50% breast milk gained significantly more weight than those fed ≥ 50% breast milk. The interaction term between delivery method and feeding was not statistically significant. Exploratory analyses of the effects of the interaction term, using "Vaginal*Breast Milk ≥ 50%" as the reference group, "Vaginal*Breast Milk < 50%" gained more between 5-7 and 7-12 months (248.0 grams, 95% CI: 112.2, 383.8; 367.8 grams, 95% CI: 199.0, 536.6). Similarly, "C-section*Breast Milk < 50%" gained more than the reference group: 261.0 grams (95% CI: 96.1, 425.8) between months 5-7 and 393.7 grams (95% CI: 207.5, 580.0) between 7-12 months.

Conclusion: Weight gain was similar between vaginal deliveries and C-sections. Infants fed at least 50% breast milk gain less weight after 5 months of age. Although the joint effects of delivery method and feeding was not statistically significant, our exploratory analyses suggest that infants who were fed <50% breast milk gained more than those who were fed more regardless of delivery types.

Key Words: Breastfeeding, intensity, mode of delivery, weight change

BACKGROUND

More than one-third (35.7%) of U.S. adults and 17% of children and adolescents are obese, according to Centers for Disease Control and Prevention (CDC) data from 2009–2010.[1] Prevention of obesity can also prevent several major causes of death, including heart disease, stroke, type 2 diabetes, and certain types of cancer.[1] Adult obesity has roots in infancy.[2] Rapid weight gain in the first year of life sets the growth trajectory and is a risk factor for obesity later in life.[3-6] Some evidence suggest that the rate of weight gain during the first few months of life may influence weight status later in childhood[84-86] as well as the later development of adult cardiovascular disease.[87, 88]

There is increasing evidence that gut bacteria is associated with obesity.[26,17] Two early determinants of gut bacteria are mode of delivery and infant feeding. The birth process begins the bacterial colonization of a previously germ-free gut begins. Vaginally born infants are colonized at first by fecal and vaginal bacteria of the mother. Term infants who were born vaginally at home and were breastfed exclusively not only have the most "beneficial" gut bacteria (highest numbers of bifidobacteria and lowest numbers of *C. difficile* and *E. coli*), but these differences seem to persist throughout infancy.[30] One of the theories for how breast milk might prevent obesity is that oligosaccharides from breast milk then serve as prebiotics for the gut microbiota, enabling desirable bacteria to thrive.[17, 33] Hence, the interplay between an emerging gut microbial ecology and the availability of human-milk oligosaccharides which serve as prebiotics may have synergistic effects on infant growth.[33]

The relationship between mode of delivery and later obesity has been explored by several recent studies.[96,107-111] However, some did not adjust for breastfeeding, and only one reported on weight change within the first year of life. The goal of this paper is to estimate the component and joint effects of mode of delivery and breastfeeding intensity on infant weight gain at 4 time intervals during the first year of life: 0-3, 3-5, 5-7 and 7-12 months postpartum.

METHODS

Study Design

The proposed study is a secondary analysis of data from the Infant Feeding Practices Study (IFPS) II data, focusing on the relationship between type of delivery and breastfeeding intensity during the first year of life. The IFPS II is a longitudinal follow-up study of pregnant women and new mothers conducted by the US Food and Drug Administration and Centers for Disease Control and Prevention during 2005 and 2006.

Study Population

The IFPS II study sample was obtained from a consumer panel of 500,000 households. Survey questionnaires were sent to pregnant women before their delivery and 10 times at regular intervals during the year after they gave birth. To be eligible to participate in the IFPS II, women had to be ≥18 years of age and to have delivered a healthy singleton infant who weighed ≥5 pounds at birth, had a gestational age at birth of ≥35 weeks, and spent <3 days in intensive care. Of the initial panel of 15,147 women identified, 14,618 were mailed a prenatal questionnaire, of these 4,902 qualified and completed the prenatal questionnaire; all of these women were sent the birth screener and subsequent neonatal survey.[94] Of the total neonatal surveys mailed (n = 4,013), 76.9% (n = 3,033) completed and qualified to participate in the study; additional information about IFPS II methods and response rates for the entire study is available.[94] Our study sample includes 1,873 of these women who provided their infants' weight at 3 months.

Key Exposure Variable

Breastfeeding intensity measures percent of all milk feeds that were breast milk (number of breast milk feeds ÷ all other milk feeds x 100) from maternal self-report of infant milk intake "in the past 7 days." Women answered these questions in the postnatal questionnaire at months 2-7 and months 9, 10 and 12. Mothers self-reported all milk intake. Breastfeeding intensity was divided into 2 categories: <50% breast milk and ≥50% breast milk. It is important to note that the breastfeeding intensity measure was not a measure of exclusive breastfeeding. Therefore, infants can receive 100% of milk feeds as breast milk but not be exclusively breastfed if they also receive any solid foods.

Mode of delivery was ascertained from responses to the neonatal survey sent to survey participants approximately 4 weeks post-delivery. The method of delivery was classified into vaginal and C-section delivery.

Outcome Variable

Infant weight change was calculated from the difference between weight during the current month and the last reported weight. Infant weights were reported at 0, 3, 5, 7 and 12. From these reported weights, four time intervals outcomes were derived - weight change from 0-3, 3-5, 5-7 and 7-12 months. For comparison with other studies, weight change from birth to 12 months was also calculated. All weights were reported in grams.

Potential Confounding Variables

Variables considered *a priori* to be potential confounders were use of solids (yes/no), gender, age of infant at time of survey, change in length (cm), gestational age, ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), antibiotic exposure, federal poverty level (%), parity, maternal age (years), body mass index (BMI, kg/m^2), marital status (married/single), pre-pregnancy smoking (yes/no) and education (high school and under, 1-3 year of college, and college/graduate school).

Statistical Analyses

SAS 9.3 was used for all analyses. For descriptive statistics, continuous variables were reported as mean ± standard deviation (SD). Analysis of variance (ANOVA) was performed to see if interval-scale (continuous) potential confounders were associated with mode of delivery. Categorical variables were reported as percentages and Chi-square was used to compare differences between modes of delivery.

A series of multiple linear regression models were estimated to estimate mean weight change at each time interval and 95% confidence interval (CI) by breastfeeding intensity category. For example, mean weight change from 0-3 months by breastfeeding intensity category was estimated using the data at age 3 months. First, univariate models for the regression of weight change on each confounder were estimated separately at each of the 4 time intervals: 0-3, 3-5, 5-7 and 7-12 months. Variables that reached a p-value of ≤ 0.20 in at least one of the time intervals were kept and fitted into a multiple regression model along with breastfeeding intensity, mode of delivery and their interaction term to predict interval mean weight change. Potential confounding variables that were not significant ($p < 0.05$) at all 4 time intervals were then removed from the model. The remaining variables made up the final model that was used to predict weight change at each time interval. The final model includes delivery method, infant feeding, infant gender (male or female), gestational age (weeks), at time of survey (months), change in infant length (cm), solid intake (yes/no), and maternal ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), pre-pregnancy smoking (yes/no) and exposure to antibiotics.

To investigate the joint effects of delivery and breastfeeding intensity, interaction terms were created between each delivery group and feeding group, yielding a total of 16 unique groups. The group of infants born via spontaneous vaginal delivery and fed 100% breast milk was used as the reference category. Logistic regression was used to determine which baseline factors were associated with loss to follow-up from 3-5 months, 5-7 months and 7-12 months.

In order to compare our weight change with previous studies that investigated the association between weight gain and alter risk for obesity, weight gain between birth to month 12 was regressed on delivery method and infant feeding in two separate models, adjusted only for infant gender, gestational age, at time of survey (months), solid intake (yes/no), and maternal ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), pre-pregnancy smoking (yes/no), and exposure to antibiotics, and with no intercept.

RESULTS

The baseline characteristics of the study population (N = 1,170) are presented in Table 4.1. Birth weight and gestational age were similar across delivery types. Women who had planned C-sections were older and weighed the most while those who had spontaneous vaginal delivery weighed the least. Most women who underwent emergency C-sections had the highest percentage of women in the highest income group.

Breastfeeding intensity group by type of delivery is presented in Table 4.2. At 3, 5, 7 and 12 months, spontaneous vaginal had the highest percent of women who exclusively breastfed while emergency C-section had the highest percent of women who did not breastfeed at all. As the infants grow older, fewer women had breastfeeding intensity between 50-99% and 100% groups. This was true in all delivery types.

The effect of C-section delivery on weight change is similar to vaginal delivery after adjusting for infant feeding, gender, age, gestational age, change in length, solid intake, ethnicity, antibiotic exposure and maternal pre-pregnancy smoking (Table 4.3). Infants who were fed <50% breast milk gained significantly more weight than those fed ≥ 50% breast milk. Figure 4.1, is a graphical representation of weight gain for each vaginal vs. C-section delivery category. The differences in mean weight change between feeding groups are also shown in Figure 4.2. Infants receiving <50% breast milk initially gained less than those fed ≥50%, but gained significantly more after that. The interaction between delivery method and feeding was not statistically significant (results not shown).

The effects of the interaction terms on weight change to explore differences between these groups were compared. Using infants from vaginal births who were breast fed at least 50% of the time as the reference group, infants from vaginal birth and were fed < 50% breast milk gained more between 5-7 and 7-12 months (248.0 grams, 95% CI: 112.2, 383.8; 367.8 grams, 95% CI: 199.0, 536.6). Similarly, infants from C-section birth and fed < 50% breast milk gained more than the reference group: 261.0 grams (95% CI: 96.1, 425.8) between months 5-7 and 393.7 grams (95% CI: 207.5, 580.0) between 7-12 months. The differences between each of the groups increase after 3 months, especially after 5 months. After 5 months, weight gain between feeding groups are higher for those fed <50% breast milk when compared to those fed ≥50%, regardless of delivery type.

As most literature that investigated weight gain in infancy with later risk of obesity, the effects of delivery method, infant feeding and their interaction on weight change between 0 to 12 months were investigated in order to make meaningful comparisons of our results. The results are similar to weight changes at each time interval - no differences were seen between delivery method on weight change (Table 4.5 and Figure 4.4). Infants fed <50% gained more in 12 months than those fed ≥50% breast milk (Table 4.5 and Figure 4.5).

Primigravid women are more likely to be lost to follow-up (Table 4.6) between 3-5, 5-7 and 7-12 months (OR = 1.38, 95% CI: 1.04, 1.83; OR = 1.58, 95% CI: 1.09, 12.29 and OR = 1.62, 95% CI: 1.09, 2.41 respectively). Although women with increased maternal age were less likely to be lost to follow-up at months 3-5 and 7-12, the ORs and confidence intervals were close to null (OR = 0.97, 95% CI: 0.94, 0.99; OR = 0.97, 95% CI: 0.94, 1.00 respectively). Black women have increased odds of loss to follow-up at 3-5 months (OR = 2.06, 95% CI: 1.16, 3.67) and between 7-12 months (OR = 2.82, 95% CI: 1.11, 7.21). There were no differences in loss to follow-up between modes of delivery.

Table 4.1. Frequency Distributions (in Percent) or Means ± Standard Deviations of Selected Socio-Demographic and Birth Characteristics by Mode of Delivery among Participants in the Infant Feeding Practices Survey II (N = 1,170)

		Spontaneous Vaginal (n = 7647)	Induced Vaginal (n = 571)	Planned C-section (n = 288)	Emergency C-section (n = 204)
Birth Weight, grams (Mean ± SD)		3,486.3 ± 448.2	3,445.5 ± 438.2	3,515.1 ± 471.0	3,464.0 ± 516.8
Gestational age, weeks (Mean ± SD)		39.3 ± 1.3	39.3 ± 1.2	39.2 ± 0.9	39.3 ± 1.7
Gender (%)	Boy	51.2	45.5	47.6	51.5
	Girl	48.8	54.5	52.4	48.5
Age, years (Mean ± SD)[1]		29.1 ± 5.5	29.1 ± 5.1	31.0 ± 4.8	29.7 ± 6.1
Maternal pre-pregnancy BMI, kg/m^2 (Mean ± SD)[2]		25.1 ± 5.6	26.7 ± 6.7	29.2 ± 8.4	28.5 ± 7.3
Parity (%)[3]	First child	27.4	28.9	11.5	71.9
	More than one	72.6	71.2	88.5	28.1
Ethnicity (%)	White	87.5	87.6	87.9	83.3
	Black	3.1	3.0	2.4	7.4
	Hispanic	5.0	5.4	5.9	3.9
	Asian/Pacific Is	3.4	2.5	2.1	3.9
	Other	1.1	1.6	1.7	1.5
Federal Poverty Level (%)[4]	185% FPL	37.7	39.2	32.3	34.8
	185 – 349% FPL	38.6	35.2	43.4	27.0
	350% FPL	23.7	25.6	24.3	38.2
Smoking (%)	Yes	91.19	92.47	93.4	90.2
	No	8.8	7.5	6.6	9.8
Education (%)	High School/under	16.9	18.2	15.4	14.9
	1-3 year College	38.7	40.6	38.9	36.9
	College/Graduate	44.4	41.2	45.7	48.2
Marital Status (%)[5]	Married	81.5	83.8	88.2	74.1
	Not married	18.6	16.2	11.8	25.9

[1] F-value = 30.82, *df* = 3, p < 0.0001; [2] F-value = 10.54, *df* = 3, p <0 .0001; [3] χ^2 = 211.69, p < 0.0001; [4] χ^2 = 26.00, p = 0 .002; [5] χ^2 = 23.57, p = 0 .02

Table 4.2. Crosstabulation of Mode of Delivery and Breastfeeding Intensity among Participants in the Infant Feeding Practices Survey II

			Spontaneous Vaginal	Induced Vaginal	Planned C-section	Emergency C-section
3 MONTHS[1] (n = 1,710)	**0% Breast Milk** (n = 636)	N	193	235	115	93
		%	29.83	41.16	39.93	45.59
	1-49% Breast Milk (n = 106)	N	35	41	14	16
		%	5.41	7.18	4.86	7.84
	50-99% Breast Milk (n = 260)	N	107	77	45	31
		%	16.54	13.49	15.63	15.2
	100% Breast Milk (n = 708)	N	312	218	114	64
		%	48.22	38.18	39.58	31.37
	TOTAL		647	571	288	204
5 MONTHS[2] (n = 1, 106)	**0% Breast Milk** (n = 467)	N	147	170	86	64
		%	36.75	45.70	43.65	46.72
	1-49% Breast Milk (n = 68)	N	17	24	16	11
		%	4.25	6.45	8.12	8.03
	50-99% Breast Milk (n = 147)	N	56	47	28	16
		%	14.00	12.63	14.21	11.68
	100% Breast Milk (n = 424)	N	180	131	67	46
		%	45.00	35.22	34.01	33.58
	TOTAL		400	372	197	137
7 MONTHS[3] (n = 875)	**0% Breast Milk** (n = 434)	N	127	160	82	65
		%	40.97	55.56	50.31	57.02
	1-49% Breast Milk (n = 43)	N	17	12	8	6
		%	5.48	4.17	4.91	5.26
	50-99% Breast Milk (n = 112)	N	40	32	27	13
		%	12.9	11.11	16.56	11.4
	100% Breast Milk (n = 286)	N	126	84	46	30
		%	40.65	29.17	28.22	26.32
	TOTAL		310	288	163	114
12 MONTHS (n = 679)	**0% Breast Milk** (n = 505)	N	168	170	98	69
		%	68.29	78.34	74.24	82.14
	1-49% Breast Milk (n = 60)	N	25	17	14	4
		%	10.16	7.83	10.61	4.76
	50-99% Breast Milk (n = 85)	N	40	22	15	8
		%	16.26	10.14	11.36	9.52
	100% Breast Milk (n = 29)	N	13	8	5	3
		%	5.28	3.69	3.79	3.57
	TOTAL		246	217	132	84

[1] $\chi^2 = 35.34$, $p < 0.0001$; [2] $\chi^2 = 17.10$, $p = 0.05$; [2] $\chi^2 = 20.69$, $p = 0.01$

Table 4.3. Estimated Adjusted Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals (CI) Delivery Method and Breastfeeding Intensity, among Participants in the Infant Feeding Practices Survey II

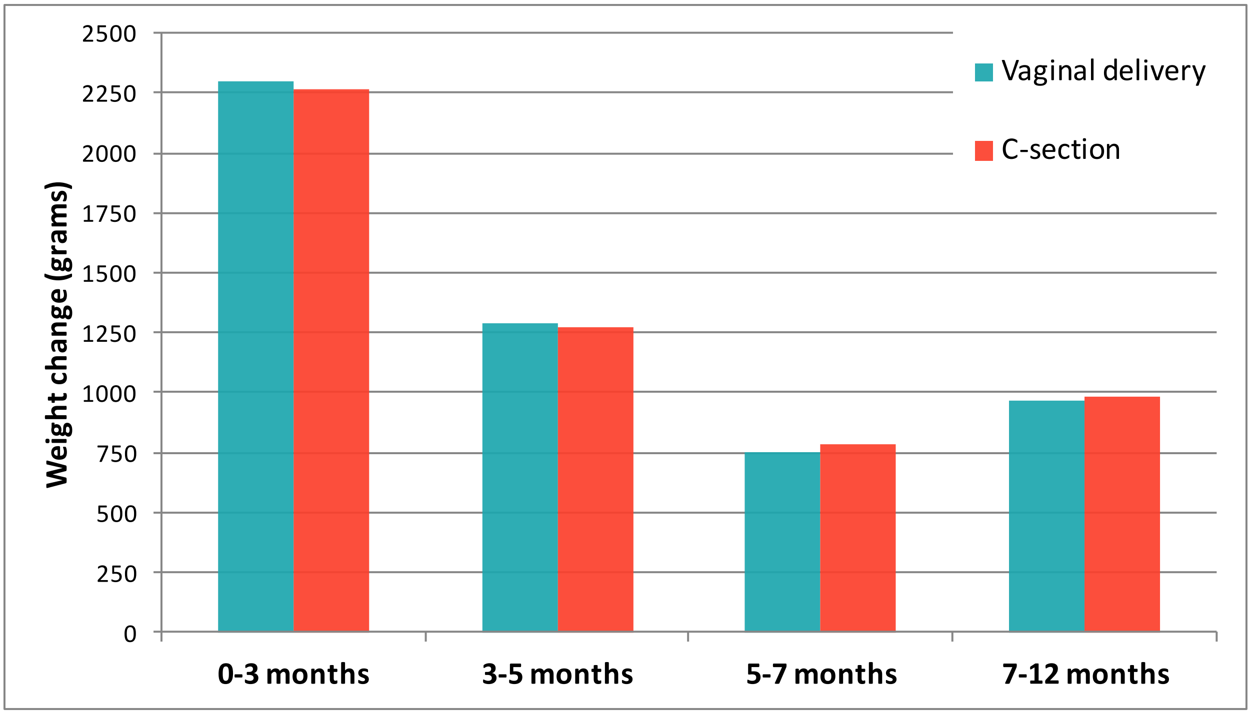
	MONTH 0-3 (n = 1,710) Unadjusted weight gain = 2,101.4 grams)					MONTH 3-5 (n = 1,106) Unadjusted weight gain = 1,244.0 grams)				
	β	SE	P Value	95% CI		β	SE	P Value	95% CI	
Intercept	2297.7	67.1	**<0.0001**	2166.1	2429.3	1289.2	103.5	**<0.0001**	1086.1	1492.2
Gender (male/female)[1]	-413.4	33.5	**<0.0001**	-479.0	-347.8	-62.3	45.1	0.17	-150.9	26.2
Infant age (months)	358.7	38.2	**<0.0001**	283.7	433.7	25.4	56.7	0.65	-85.9	136.7
Gestational age (weeks)	-53.8	13.6	**<0.0001**	-80.5	-27.2	-24.7	18.3	0.18	-60.6	11.3
Change in length (cm)	53.5	4.6	**<0.0001**	44.5	62.4	28.4	5.0	**<0.0001**	18.5	38.3
Solid intake (yes/no)[2]	-14.6	43.7	0.74	-100.2	71.1	156.3	56.0	**0.01**	46.3	266.2
Black[3]	175.9	91.5	**0.05**	-3.5	355.4	241.8	143.8	0.09	-40.3	523.8
Hispanic[3]	135.2	75.5	0.07	-12.8	283.3	-146.5	106.4	0.17	-355.3	62.3
Asian/Pacific Islander[3]	-13.8	98.6	0.89	-207.2	179.6	35.9	125.9	0.78	-211.2	282.9
Other[3]	50.2	141.0	0.72	-226.4	326.8	46.1	189.4	0.81	-325.6	417.9
Antibiotic exposure (yes/no)[4]	211.2	58.6	**0.0003**	96.2	326.1	-34.1	57.0	0.55	-145.9	77.7
Pre-pregnancy smoking (yes/no)[4]	8.2	62.5	0.90	-114.3	130.8	-167.0	90.2	0.06	-344.0	10.0
Vaginal delivery	*Reference*									
C-section	-35.1	36.7	0.34	-107.1	36.9	-15.8	49.3	0.75	-112.4	80.9
Breast Milk ≥50%	Reference									
Breast Milk <50%	-5.3	36.1	0.88	-76.1	65.4	71.7	48.1	0.14	-22.8	166.1

Table 4.3. (Continued) Estimated Adjusted Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals (CI) of Delivery Method and Breastfeeding Intensity, among Participants in the Infant Feeding Practices Survey II

	MONTH 5-7 (n = 875) Unadjusted weight gain = 1,074.1 grams)					MONTH 7-12 (n = 679) Unadjusted weight gain = 1,805.7 grams)				
	β	SE	P Value	95% CI		β	SE	P Value	95% CI	
Intercept	750.5	289.4	**0.01**	182.5	1318.6	963.6	761.1	0.21	-530.8	2458.0
Gender (male/female)[1]	-33.6	56.2	0.55	-143.9	76.7	-49.0	57.5	0.39	-161.9	63.8
Infant age (months)	172.1	70.4	**0.01**	34.0	310.3	59.1	75.0	0.43	-88.2	206.5
Gestational age (weeks)	4.5	22.6	0.84	-40.0	48.9	-19.3	22.4	0.39	-63.3	24.6
Change in length (cm)	18.0	5.0	**0.0003**	8.2	27.7	20.8	4.3	**<0.0001**	12.4	29.2
Solid intake (yes/no)[2]	-218.0	265.1	0.41	-738.2	302.2	703.2	745.9	0.35	-761.5	2167.9
Black[3]	106.3	179.5	0.55	-246.0	458.7	97.1	219.0	0.66	-333.0	527.2
Hispanic[3]	104.3	142.3	0.46	-175.0	383.5	-127.9	133.6	0.34	-390.2	134.4
Asian/Pacific Islander[3]	-131.2	157.1	0.40	-439.4	177.1	-166.3	162.1	0.31	-484.5	152.0
Other[3]	-44.2	241.0	0.85	-517.2	428.9	-48.7	217.3	0.82	-475.4	378.1
Antibiotic exposure (yes/no)[4]	53.1	60.8	0.38	-66.4	172.5	12.5	57.9	0.83	-101.2	126.1
Pre-pregnancy smoking (yes/no)[4]	428.8	115.3	**0.0002**	202.5	655.1	-149.2	123.3	0.23	-391.3	92.9
Vaginal delivery	*Reference*									
C-section	32.2	60.7	0.60	-86.9	151.4	18.9	61.8	0.76	-102.4	140.2
Breast Milk ≥50%	Reference									
Breast Milk <50%	234.6	57.9	**<0.0001**	120.9	348.3	378.9	72.6	**<0.0001**	236.3	521.4

[1] Reference group = Female; [2] Reference group = "Yes"; [3] Reference group = White; [4] Reference group = "No"; SE = Standard Error; 95% CI = 95% Confidence Interval

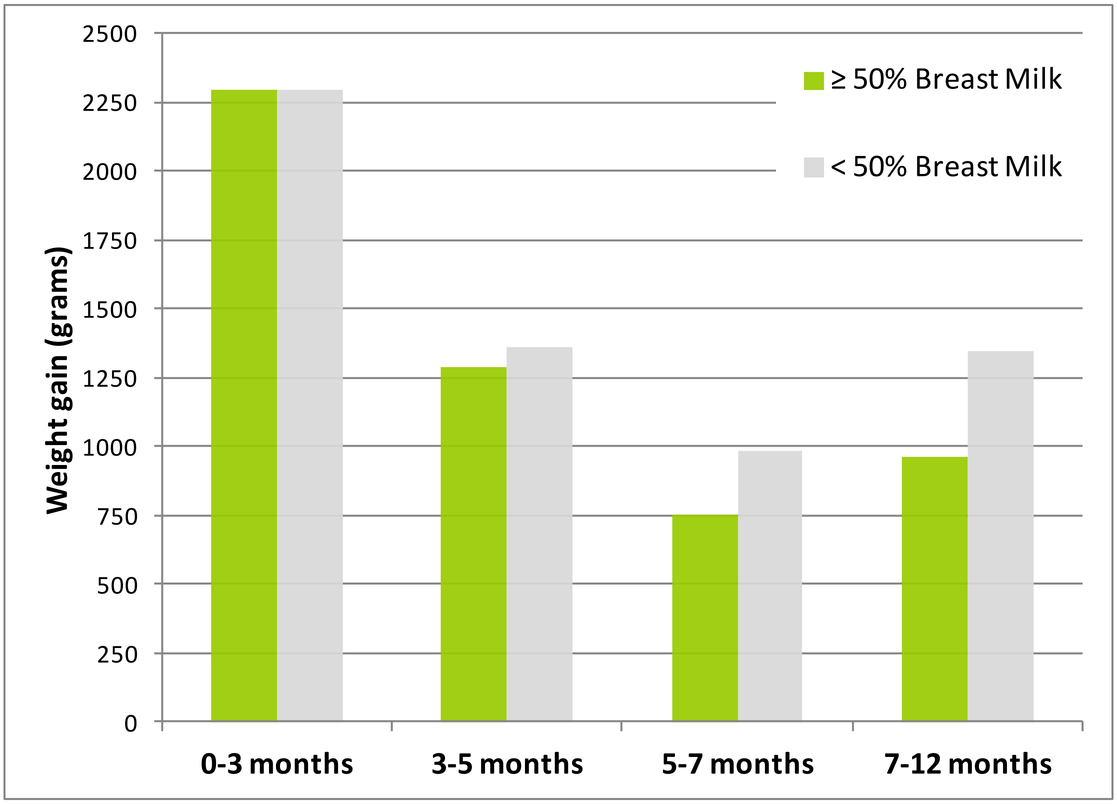
Figure 4.1 Estimated Adjusted[1] Mean Weight Change (grams) at 0-3, 3-5, 5-7 and 7-12 months of Infants Born via Vaginal Delivery vs. via C-section, among Participants in the Infant Feeding Practices Survey II



	0-3 months		3-5 months		5-7 months		7-12 months	
	β	SE	β	SE	β	SE	β	SE
Vaginal delivery	2297.7	67.1	1289.2	103.5	750.5	289.4	963.6	761.1
C-section	2262.6	71.9	1273.4	109.9	782.8	294.2	982.5	764.5

[1] Reference group = Female; [2] Reference group = "Yes"; [3] Reference group = White; [4] Reference group = "No"; [5] Reference group = Spontaneous vaginal delivery; [6] Reference group = Infants consuming 100% breast milk; SE = Standard Error; 95% CI = 95% Confidence Interval; Adjusted for breast milk%, infant gender (male or female), gestational age (weeks), at time of survey (months), change in infant length (cm), solid intake (yes/no), and maternal ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), pre-pregnancy smoking (yes/no), and exposure to antibiotics (yes/no)

Figure 4.2 Estimated Adjusted[1] Mean Weight Change (grams) at 0-3, 3-5, 5-7 and 7-12 months of Infants Fed <50% Breast Milk vs. 100% Breast Milk, among Participants in the Infant Feeding Practices Survey II



	0-3 months		3-5 months		5-7 months		7-12 months	
	β	SE	β	SE	β	SE	β	SE
≥ 50% Breast Milk	2297.7	67.1	1289.2	103.5	750.5	289.4	963.6	761.1
< 50% Breast Milk	2292.4	66.4	1360.8	104.0	985.1	290.9	1342.5	756.5

[1] Reference group = Female; [2] Reference group = "Yes"; [3] Reference group = White; [4] Reference group = "No"; [5] Reference group = Spontaneous vaginal delivery; [6] Reference group = Infants consuming 100% breast milk; SE = Standard Error; 95% CI = 95% Confidence Interval; Adjusted for delivery method, infant gender (male or female), gestational age (weeks), at time of survey (months), change in infant length (cm), solid intake (yes/no), and maternal ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), pre-pregnancy smoking (yes/no), and exposure to antibiotics (yes/no)

Table 4.4. Estimated Adjusted Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals (CI) of the Interactions Between Delivery Method and Breastfeeding Intensity, among Participants in the Infant Feeding Practices Survey II

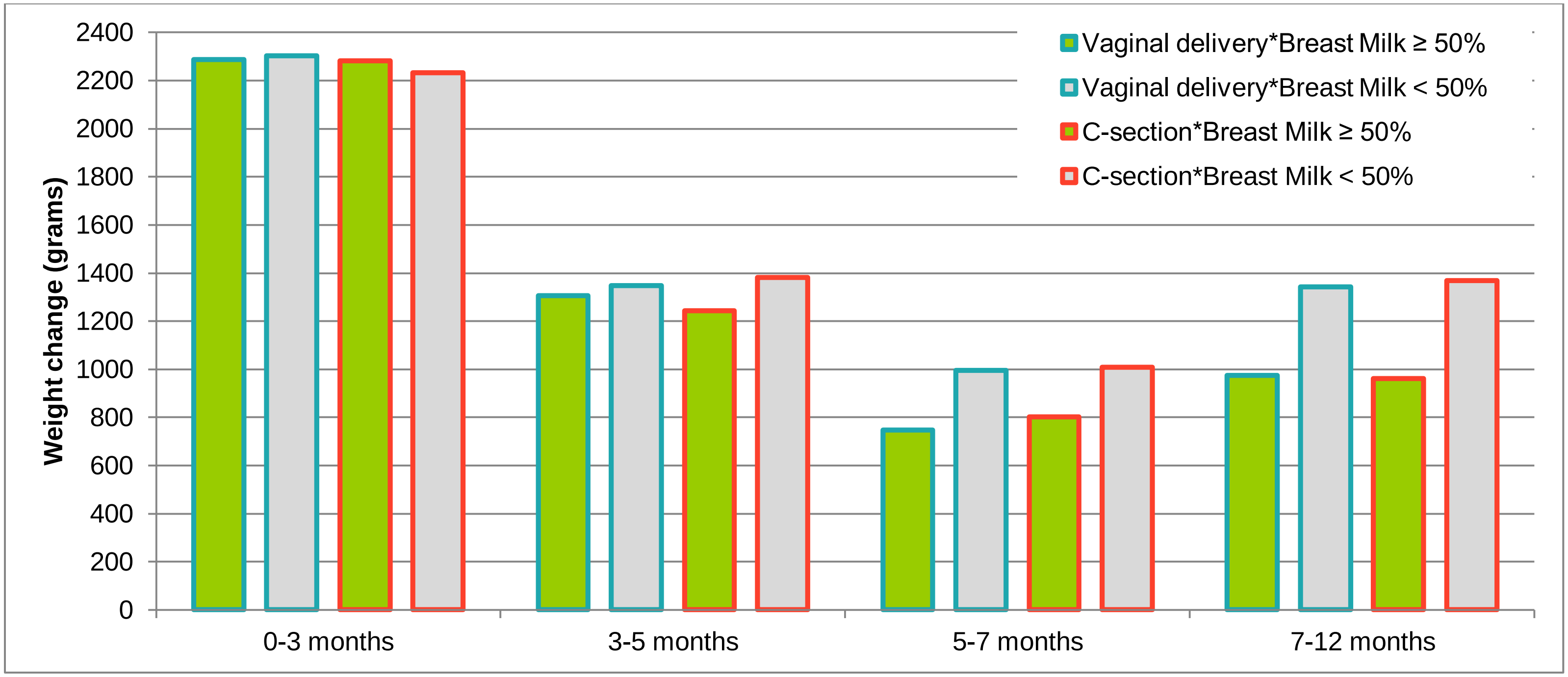
	MONTH 0-3 (n = 1,710) Unadjusted weight gain = 2,101.4 grams)					MONTH 3-5 (n = 1,106) Unadjusted weight gain = 1,244.0 grams)				
	β	SE	P Value	95% CI		β	SE	P Value	95% CI	
Intercept	2794.1	579.9	**<.0001**	1656.8	3931.4	1970.7	809.3	**0.02**	382.7	3558.8
Gender (male/female)[1]	-413.6	33.5	**<.0001**	-479.3	-348.0	-61.3	45.1	0.17	-149.8	27.2
Infant age (months)	358.5	38.2	**<.0001**	283.5	433.5	27.8	56.8	0.62	-83.6	139.2
Gestational age (weeks)	-53.7	13.6	**<.0001**	-80.4	-27.0	-24.1	18.3	0.19	-60.1	11.9
Change in length (cm)	53.7	4.6	**<.0001**	44.7	62.6	28.4	5.0	**<.0001**	18.5	38.3
Solid intake (yes/no)[2]	-15.5	43.7	0.72	-101.2	70.2	154.9	56.1	**0.01**	44.9	264.9
Black[3]	180.0	91.6	**0.05**	0.3	359.7	238.5	143.8	0.10	-43.7	520.6
Hispanic[3]	137.0	75.5	0.07	-11.1	285.1	-147.3	106.4	0.17	-356.1	61.5
Asian/Pacific Islander[3]	-17.3	98.7	0.86	-210.8	176.3	39.1	126.0	0.76	-208.0	286.3
Other[3]	53.2	141.1	0.71	-223.4	329.9	35.4	189.8	0.85	-337.0	407.7
Antibiotic exposure (yes/no)[4]	213.0	58.7	**0.0003**	98.0	328.1	-36.7	57.0	0.52	-148.6	75.2
Pre-pregnancy smoking (yes/no)[4]	10.4	62.5	0.87	-112.3	133.0	-169.8	90.3	0.06	-346.9	7.3
Vaginal delivery*Breast Milk < 50%	14.0	42.3	0.74	-69.1	97.0	42.4	56.5	0.45	-68.5	153.4
C-section*Breast Milk ≥ 50%	-6.2	49.5	0.90	-103.2	90.8	-62.8	68.5	0.36	-197.3	71.7
C-section*Breast Milk < 50%	-56.6	53.0	0.29	-160.5	47.3	76.8	70.6	0.28	-61.7	215.2

Table 4.4. (Continued) Estimated Adjusted Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals (CI) of the Interactions Between Delivery Method and Breastfeeding Intensity, among Participants in the Infant Feeding Practices Survey II

	MONTH 5-7 (n = 875) Unadjusted weight gain = 1,074.1 grams)					MONTH 7-12 (n = 679) Unadjusted weight gain = 1,805.7 grams)				
	β	SE	P Value	95% CI		β	SE	P Value	95% CI	
Intercept	746.9	289.8	**0.01**	178.1	1315.6	765.0	1594.5	0.63	-2365.8	3895.9
Gender (male/female)[1]	-34.2	56.2	0.54	-144.6	76.2	-49.4	57.5	0.39	-162.3	63.6
Infant age (months)	172.2	70.4	**0.01**	33.9	310.4	59.1	75.1	0.43	-88.4	206.5
Gestational age (weeks)	4.3	22.7	0.85	-40.2	48.8	-19.3	22.4	0.39	-63.2	24.7
Change in length (cm)	18.0	5.0	**0.0003**	8.2	27.7	20.8	4.3	**<0.0001**	12.4	29.2
Solid intake (yes/no)[2]	-221.8	265.4	0.40	-742.7	299.1	700.7	746.5	0.35	-765.1	2166.6
Black[3]	107.0	179.6	0.55	-245.6	459.5	96.2	219.2	0.66	-334.3	526.6
Hispanic[3]	103.7	142.4	0.47	-175.7	383.2	-128.6	133.7	0.34	-391.1	134.0
Asian/Pacific Islander[3]	-132.5	157.2	0.40	-440.9	176.0	-165.8	162.2	0.31	-484.3	152.7
Other[3]	-41.4	241.2	0.86	-514.9	432.1	-49.3	217.5	0.82	-476.4	377.8
Antibiotic exposure (yes/no)[4]	54.7	61.0	0.37	-65.2	174.5	11.9	57.9	0.84	-101.8	125.7
Pre-pregnancy smoking (yes/no)[4]	429.1	115.4	**0.0002**	202.7	655.5	-148.8	123.4	0.23	-391.1	93.4
Vaginal*Breast Milk < 50%	248.0	69.2	**0.0004**	112.2	383.8	367.8	86.0	**<0.0001**	199.0	536.6
C-section*Breast Milk ≥ 50%	56.3	90.8	0.54	-122.0	234.6	-12.5	144.1	0.93	-295.5	270.5
C-section*Breast Milk < 50%	261.0	84.0	**0.002**	96.1	425.8	393.7	94.9	**<0.0001**	207.4	580.0

[1] Reference group = Female; [2] Reference group = "Yes"; [3] Reference group = White; [4] Reference group = "No"; [5] Reference group = Spontaneous vaginal delivery*Breast Milk ≥ 50%; [6] Reference group = Infants consuming 100% breast milk; SE = Standard Error; 95% CI = 95% Confidence Interval

Figure 4.3. Estimated Adjusted Effects (Mean Weight Change at 0-3, 3-5, 5-7 and 7-12 months in grams) and 95% Confidence Intervals (CI) of the Interactions Between Delivery Method and Breastfeeding Intensity, among Participants in the Infant Feeding Practices Survey II



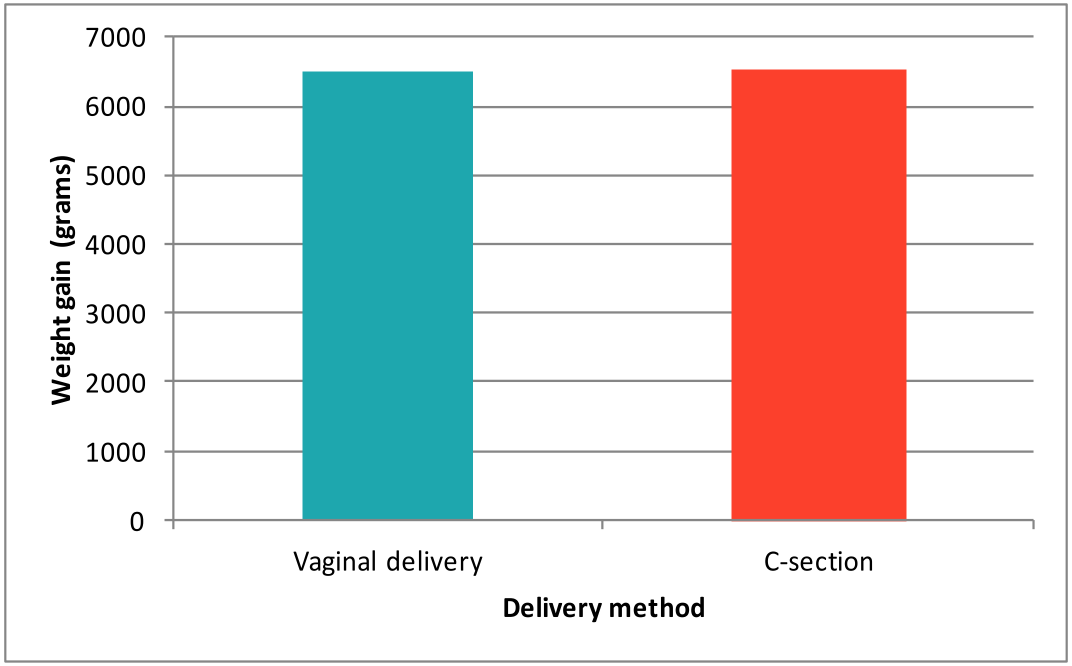
	MONTH 0-3 (n = 1,710) Unadjusted weight gain = 2,101.4 grams)		MONTH 3-5 (n = 1,106) Unadjusted weight gain = 1,244.0 grams)		MONTH 5-7 (n = 875) Unadjusted weight gain = 1,074.1 grams)		MONTH 7-12 (n = 679) Unadjusted weight gain = 1,805.7 grams)	
	β	SE	β	SE	β	SE	β	SE
Vaginal*Breast Milk ≥50%[3]	2288.0	68.0	1306.0	104.9	746.9	289.8	975.0	763.1
Vaginal*Breast Milk <50%[3]	2302.0	67.3	1348.4	104.7	994.9	292.3	1342.8	757.1
C-section*Breast Milk ≥50%[3]	2281.9	75.3	1243.2	114.1	803.1	299.8	962.5	769.5
C-section*Breast Milk <50%[3]	2231.4	76.0	1382.7	115.9	1007.8	296.6	1368.7	760.9

[1]All models adjusted for infant gender (male or female), gestational age (weeks), at time of survey (months), change in infant length (cm), solid intake (yes/no), and maternal ethnicity (White, Black, Hispanic, Asian/Pacific Islander and Other), pre-pregnancy smoking (yes/no), and exposure to antibiotics (yes/no); [2]Model 1; [3]Model 2

Table 4.5. Estimated Adjusted Effects (Mean Weight Change between 0-12 months in grams) and 95% Confidence Intervals (CI) of Delivery Method and Breastfeeding Intensity, among Participants in the Infant Feeding Practices Survey II

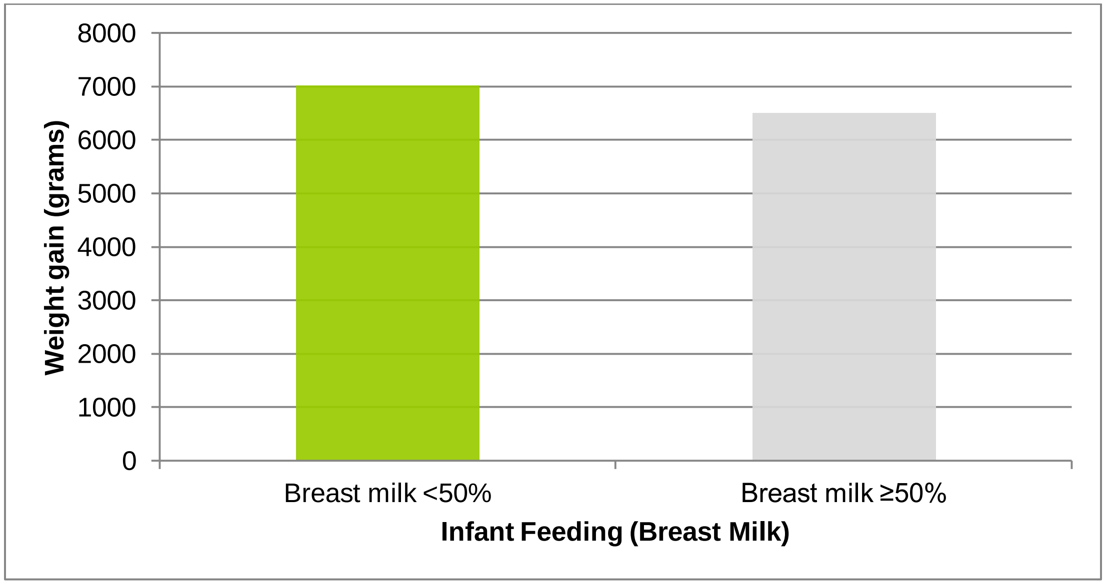
	MONTH 0-12 (n = 875) (Unadjusted weight gain = 6262.6 grams)				
	β	SE	P Value	95% CI	
Intercept	6507.8	1165.7	**<0.0001**	4218.9	8796.6
Gender (male/female)[1]	-563.5	88.2	**<0.0001**	-736.6	-390.4
Infant age (months)	239.1	115.1	**0.04**	13.1	465.2
Gestational age (weeks)	-143.4	34.3	**<0.0001**	-210.8	-76.0
Solid intake (yes/no)[2]	-211.9	1142.3	0.85	-2454.9	2031.1
Black[3]	428.9	335.9	0.20	-230.6	1088.4
Hispanic[3]	-46.9	204.9	0.82	-449.2	355.4
Asian/Pacific Islander[3]	-206.1	248.5	0.41	-694.1	281.8
Other[3]	-173.3	333.4	0.60	-827.9	481.3
Antibiotic exposure (yes/no)[4]	143.3	88.6	0.11	-30.7	317.4
Pre-pregnancy smoking (yes/no)[4]	-242.7	189.2	0.20	-614.2	128.8
Vaginal delivery	***Reference***				
C-section	20.9	94.6	0.83	-164.9	206.7
Breast Milk ≥50%	***Reference***				
Breast Milk <50%	6507.8	1165.7	**<0.0001**	4218.9	8796.6

Figure 4.4. Estimated Adjusted[1] Mean Weight Change (grams) between 0-12 months of Infants Born via Vaginal Delivery vs. C-section, among Participants in the Infant Feeding Practices Survey II



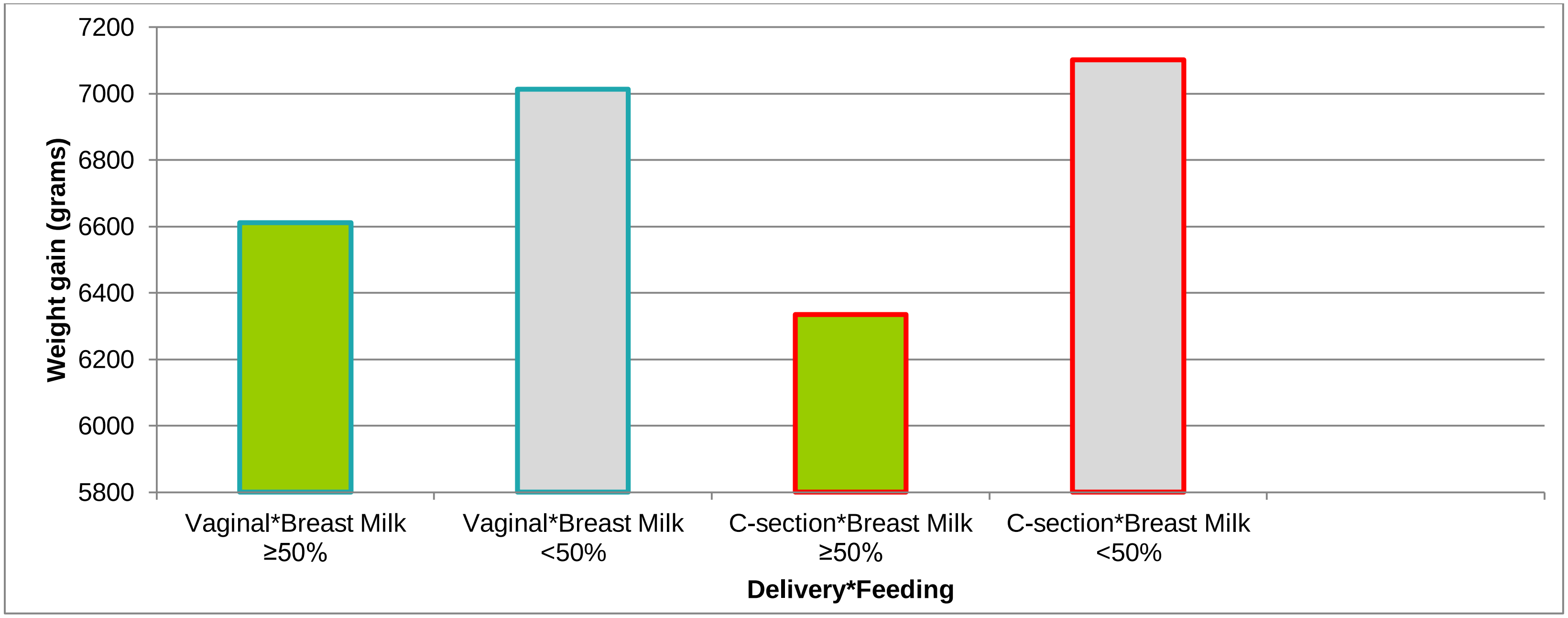
	MONTH 0-12 (n = 679) (Unadjusted weight gain = 6262.6 grams)	
	β	**SE**
Vaginal delivery	6507.8	1165.7
C-section	6528.7	1170.6

Figure 4.5. Estimated Adjusted[1] Mean Weight Change (grams) from <u>0-12 months</u> of Infants Fed <50% Breast Milk vs. 100% Breast Milk, among Participants in the Infant Feeding Practices Survey II



	MONTH 0-12 (n = 679) (Unadjusted weight gain = 6262.6 grams)	
	β	**SE**
Breast milk <50%	7015.3	1158.9
Breast milk ≥50%	6507.8	1165.7

Figure 4.6. Estimated Adjusted[1] Effects (Mean Weight Change from <u>0-12 months</u> in grams) and 95% Confidence Intervals (CI) of Interaction Between Delivery Method and Breastfeeding Intensity, among Participants in the Infant Feeding Practices Survey II (n=679)



	MONTH 0-12 (n = 679) (Unadjusted weight gain = 6262.6 grams)	
	β	**SE**
Vaginal*Breast Milk ≥50%	6612.0	1166.7
Vaginal*Breast Milk <50%	7014.5	1157.8
C-section*Breast Milk ≥50%	6334.5	1176.7
C-section*Breast Milk <50%	7101.9	1163.2

Table 4.6. Logistic Regression Model Predicting Odds of Loss to Follow-up among Participants between 3-5, 5-7 and 7-12 months in the Infant Feeding Practices Survey II

	Loss to Follow up											
	3-5 months (n = 1,595)				5-7 months (n = 1,050)				7-12 months (n = 833)			
	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value	Odds Ratio	95% CI		P value
Gender (Male/Female)[1]	1.07	0.87	1.32	0.53	1.21	0.93	1.59	0.16	1.03	0.77	1.39	0.84
Gestational age (weeks)	1.00	0.92	1.08	0.92	1.01	0.91	1.13	0.82	0.98	0.87	1.11	0.78
Black[2]	2.06	1.16	3.67	**0.01**	1.05	0.43	2.54	0.92	2.82	1.11	7.21	**0.03**
Hispanic[2]	1.14	0.71	1.85	0.58	1.68	0.91	3.10	0.10	0.70	0.32	1.54	0.37
Asian Pacific Islander[2]	0.95	0.49	1.82	0.87	1.12	0.51	2.50	0.77	0.99	0.42	2.34	0.98
Other[2]	0.67	0.26	1.77	0.42	1.36	0.48	3.83	0.56	0.34	0.07	1.61	0.18
Parity[3]	1.38	1.04	1.83	**0.03**	1.58	1.09	2.29	**0.02**	1.62	1.09	2.41	**0.02**
Pre-pregnancy smoking[4]	0.81	0.55	1.20	0.30	0.70	0.42	1.17	0.18	0.86	0.47	1.60	0.64
185 – 349% FPL[5]	0.93	0.73	1.20	0.59	0.92	0.66	1.27	0.61	0.81	0.56	1.17	0.25
350% FPL[5]	0.82	0.60	1.11	0.20	0.76	0.51	1.13	0.18	0.85	0.56	1.30	0.46
Maternal BMI (kg/m^2)	0.99	0.98	1.01	0.35	1.01	0.99	1.03	0.58	1.01	0.99	1.03	0.42
Maternal age (years)	0.97	0.94	0.99	**0.003**	0.98	0.95	1.01	0.13	0.97	0.94	1.00	**0.05**
Marital status (married/not)	1.04	0.96	1.12	0.40	1.02	0.91	1.13	0.74	1.05	0.93	1.19	0.41
Spontaneous vaginal	***Reference***											
Induced vaginal	0.91	0.71	1.16	0.43	0.95	0.69	1.30	0.73	1.10	0.77	1.57	0.60
Planned C-section	0.80	0.58	1.09	0.16	0.80	0.53	1.19	0.27	0.97	0.63	1.50	0.91
Emergency C-section	0.91	0.62	1.32	0.61	0.81	0.49	1.33	0.40	1.38	0.82	2.30	0.22

[1] Reference = Female; [2] Reference = White; [3] Reference = More than 1 child; [4] Reference = Not smoking; [5] Reference = 185% FPL; [6] Reference = Married; SE = Standard Error; FPL = Federal Poverty Level; BMI = Body Mass Index; 95% CI = 95% Confidence Interval

DISCUSSION

In this longitudinal follow-up study of pregnant women across the United States, weight gain was found to be similar between vaginal deliveries and C-sections. Infants fed at least 50% breast milk gain less weight after 5 months of age. Although the joint effects of delivery method and feeding was not statistically significant, our exploratory analyses suggest that infants who were fed <50% breast milk gained more than those who were fed more regardless of delivery types.

Our results are similar to a large population-representative birth cohort of Chinese children from a developed non-Western setting in Hong Kong.[110] To the best of our knowledge, this is the only other study that investigated mode of delivery and infant feeding with weight change for the months during the first year of life. The authors estimated the association of mode of delivery (vaginal or cesarean) with body mass index (BMI) z-score and overweight (including obesity) from 3 months to 13 years. This was a large cohort of 7,809 term birth with 94% follow-up from a population-representative Chinese birth cohort. The authors did not find C-section to be associated with BMI z-score from 3 months to 13 years (mean difference, 0.03; 95% CI: 0.02, 0.09) or overweight from 3 years to 13 years (OR = 0.98; 95% CI: 0.77, 1.25) after adjusting for infant and maternal characteristics and family socioeconomic position.

The finding that C-section was not associated with higher weight gain when compared to vaginal delivery was not an expected finding. As indicated by previous studies, C-section was associated with colonization of different gut bacteria.[30,55,57-59] Similarly, the lack of significance of the interaction between delivery method and feeding was also not expected. Since breast milk acts as a prebiotic to enable the growth of healthy gut bacteria after they have been established during vaginal delivery, one would expect that the effect of delivery method on the weight change is different at different feeding levels. However, recent studies suggest that gut bacteria differs more on a geographic level than individual levels, due to settings such as host genetics and diet.[55,112,113] Our study may not have detected a significant difference between delivery and infant weight change because of lack of differences in environmental factors in our study population. Lack of sample size, as indicated by the large standard errors, may have also led to our non-significant finding.

Toschke et al.,[98] reported a weight gain in first 12 months of more than 6,933 grams, as a predictor of overweight at 5-7 years of age in 4,235 German infants. Comparing our data to theirs, spontaneous vaginal deliveries have the lowest weight gain in between 0 to 12 months, and closest to the 6,933 grams reported by Toschke. For the group with breastfeeding intensity <50% breastfeeding intensity, the adjusted weight gain from 0-12 months of 7,014.5 grams was higher than the cut-off point reported by Toschke, hence suggesting that regardless of delivery type, lower breast milk intake in our population are more likely to be overweight in later childhood.

Limitations of the study include small sample size, making it difficult get precise estimates of weight change. Also, underlying assumption in calculating breastfeeding intensity was that the reported intensity in the past 7 days was representative of other weeks. In a second evaluation, previous month breastfeeding intensity were used in the analyses (with the exception month 12, where the last reported breastfeeding intensity was 10 months), and similar results were obtained. This suggests that breastfeeding intensities were similar between the current and previous month. In addition, all data are self-reported by the mother; no medical records were examined to confirm infant health, weight, length, or any other characteristic. As the study progressed, the number of women available for analysis decreased, potentially leading to selection bias. Loss to follow-up of primigravid women is consistent across all time intervals. However, since parity did not have an effect on weight change independent of breastfeeding intensity, the loss of follow-up of primigravid women is not likely to have changed our results. Lastly, even though the richness of the data allowed for controlling of several potential confounders, residual confounding is still possible given that there is no way to quantify the net amount of breast milk and its bioactive components consumed by the infants.

The richness of the data is a strength of this study – its longitudinal design which included many birth and maternal socio-demographic characteristics. Details of infants' feeding patterns were available, and these data were collected frequently albeit self-reported. Even though adjustments for many potential confounders were made, infant weight gain is a multi-factorial and dynamic process, and there might be residual confounding that still exists.

CONCLUSION

Infant feeding has a strong effect on weight change during the first year, and efforts to prevent obesity should start with increasing breastfeeding intensity. Future studies should seek to have a larger number of participants with minimal loss to follow-up in order to better quantify the dose-response relationship using breastfeeding intensity. The potential of mode of delivery effect on infant weight gain needs to be further researched using data that includes women from different geographical regions and information on maternal gut bacteria profile. Follow-up past the first year of life will also give valuable information on how the infants develop in childhood years.

CHAPTER 5.
CONCLUSION

Recent studies on obesity have shown obesity to be associated with bacteria in the gut, both in humans and animal models. Since gut bacteria profile does not change easily after establishment, and mode of delivery and gut bacteria are the first factors that influence the gut colonization, the goal of my dissertation was to study the effects that they have on infant weight gain during the first year of life.

The aim of the first study was to see if delivery method affects breastfeeding intensity. Breastfeeding intensity between planned C-section and spontaneous vaginal delivery was very similar, and that induced vaginal delivery and emergency C-section was associated with lower breastfeeding intensity. Results from this study gave insights into the dynamic nature of breastfeeding behavior. It would be reasonable to expect that a major surgery like C-section with a longer recovery time will affect breastfeeding behavior. However, this data suggests that the trauma that mothers undergo during the intrapartum process is what determines breastfeeding outcomes. To better understand breastfeeding outcomes in relationship to mode of delivery, future research should explore the psychological factors associated with intrapartum interventions such as mothers' level of comfort with change in birth plans. Details surrounding the birth process may provide a more comprehensive understanding of the factors that can influence breastfeeding outcome.

The second study focused on breastfeeding intensity as a predictor of infant weight gain. The vast majority of studies on the benefits of breastfeeding define breastfeeding as either initiation, exclusivity or duration. Breastfeeding intensity captures more details on "dose" among infants who are not exclusively breastfed or formula-fed. Although a clear dose-dependent effect was not observed, breastfeeding intensity at the lower end (< 50%) was associated with higher weight gain by the end of the first year. Even if infants were not exclusively breastfed, having more proportions of their milk feeds from breast milk was associated with less weight gain. This is informative for breastfeeding support - that even if a mother is unable to exclusively breastfeed, more breast milk is better than less, even if breastfeeding duration is the same. A clearer dose-dependent effect of breastfeeding may be possible if future studies are larger, longer, with minimal loss to follow-up.

Finally, although breastfeeding had an effect on weight gain, delivery itself did not have a significant effect on infant weight gain. Though not statistically significant, infants from vaginal deliveries had less infant weight gain at a level associated with overweight in later childhood, as was a greater percent of breast milk that is fed to the infant. Recent studies suggest that gut bacteria differs more on a geographic level than individual levels, due to settings such as host genetics and diet.[55,112,113] It is possible that statistically significant associations between delivery and infant weight change were not observed due to of lack of differences in environmental factors in our study population. Larger studies that span across continents, with a larger number of participants with minimal loss to follow-up are needed. Study population should also include women from different geographical regions and information on maternal gut bacteria profile.

How gut bacteria is affected by delivery and feeding method, and what or how long their effects, if any, lasts, may shed important information on how we can prevent obesity starting at the intrapartum period.

REFERENCES

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. *Prevalence of obesity in the United States, 2009-2010* Hyattsville, MD: National Center for Health Statistics 2012.

2. Singhal A, Lucas A. Early origins of cardiovascular disease: is there a unifying hypothesis? *Lancet.* May 15 2004;363(9421):1642-1645.

3. Taveras EM, Rifas-Shiman SL, Belfort MB, Kleinman KP, Oken E, Gillman MW. Weight status in the first 6 months of life and obesity at 3 years of age. *Pediatrics.* Apr 2009;123(4):1177-1183.

4. Oken E, Gillman MW. Fetal origins of obesity. *Obes Res.* Apr 2003;11(4):496-506.

5. Gillman MW, Rifas-Shiman SL, Belfort MB, Kleinman K, Oken E, Taveras EM. Size at birth, infant growth, and obesity at age 3 years. *Early Hum Dev.* 2007;83:S160-S160.

6. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ.* Oct 22 2005;331(7522):929-934.

7. Druet C, Stettler N, Sharp S, et al. Prediction of childhood obesity by infancy weight gain: an individual-level meta-analysis. *Paediatr Perinat Epidemiol.* Jan 2012;26(1):19-26.

8. Wells JC, Hallal PC, Wright A, Singhal A, Victora CG. Fetal, infant and childhood growth: relationships with body composition in Brazilian boys aged 9 years. *Int J Obes (Lond).* Oct 2005;29(10):1192-1198.

9. Guarner F, Malagelada JR. Gut flora in health and disease. *Lancet.* Feb 8 2003;361(9356):512-519.

10. Penders J, Stobberingh EE, Thijs C, et al. Molecular fingerprinting of the intestinal microbiota of infants in whom atopic eczema was or was not developing. *Clin Exp Allergy.* Dec 2006;36(12):1602-1608.

11. Penders J, Stobberingh EE, van den Brandt PA, Thijs C. The role of the intestinal microbiota in the development of atopic disorders. *Allergy.* Nov 2007;62(11):1223-1236.

12. Creely SJ, McTernan PG, Kusminski CM, et al. Lipopolysaccharide activates an innate immune system response in human adipose tissue in obesity and type 2 diabetes. *Am J Physiol Endocrinol Metab.* Mar 2007;292(3):E740-747.

13. Brugman S, Klatter FA, Visser JT, et al. Antibiotic treatment partially protects against type 1 diabetes in the Bio-Breeding diabetes-prone rat. Is the gut flora involved in the development of type 1 diabetes? *Diabetologia.* Sep 2006;49(9):2105-2108.

14. Cani PD, Amar J, Iglesias MA, et al. Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes.* Jul 2007;56(7):1761-1772.

15. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature.* Dec 21 2006;444(7122):1027-1031.

16. Ley RE, Backhed F, Turnbaugh P, Lozupone CA, Knight RD, Gordon JI. Obesity alters gut microbial ecology. *Proc Natl Acad Sci U S A.* Aug 2 2005;102(31):11070-11075.

17. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature.* Dec 21 2006;444(7122):1022-1023.

18. Vanderploeg R, Panaccione R, Ghosh S, Rioux K. Influences of intestinal bacteria in human inflammatory bowel disease. *Infect Dis Clin North Am.* Dec;24(4):977-993, ix.

19. Mackie RI, Sghir A, Gaskins HR. Developmental microbial ecology of the neonatal gastrointestinal tract. *Am J Clin Nutr.* May 1999;69(5):1035S-1045S.

20. Palmer C, Bik EM, DiGiulio DB, Relman DA, Brown PO. Development of the human infant intestinal microbiota. *PLoS Biol.* Jul 2007;5(7):e177.

21. Hooper LV, Wong MH, Thelin A, Hansson L, Falk PG, Gordon JI. Molecular analysis of commensal host-microbial relationships in the intestine. *Science.* Feb 2 2001;291(5505):881-884.

22. Ducluzeau R. [Development, equilibrium and role of microbial flora in the newborn]. *Ann Pediatr (Paris).* Jan 1993;40(1):13-22.

23. Simon GL, Gorbach SL. Intestinal flora in health and disease. *Gastroenterology.* Jan 1984;86(1):174-193.

24. Moore WE, Moore LH. Intestinal floras of populations that have a high risk of colon cancer. *Appl Environ Microbiol.* Sep 1995;61(9):3202-3207.

25. Schwiertz A, Taras D, Schafer K, et al. Microbiota and SCFA in lean and overweight healthy subjects. *Obesity (Silver Spring).* Jan 2010;18(1):190-195.

26. Backhed F, Ding H, Wang T, et al. The gut microbiota as an environmental factor that regulates fat storage. *Proc Natl Acad Sci U S A.* Nov 2 2004;101(44):15718-15723.

27. Backhed F, Manchester JK, Semenkovich CF, Gordon JI. Mechanisms underlying the resistance to diet-induced obesity in germ-free mice. *Proc Natl Acad Sci U S A.* Jan 16 2007;104(3):979-984.

28. Brook I, Barrett CT, Brinkman CR, 3rd, Martin WJ, Finegold SM. Aerobic and anaerobic bacterial flora of the maternal cervix and newborn gastric fluid and conjunctiva: a prospective study. *Pediatrics.* Mar 1979;63(3):451-455.

29. Bettelheim KA, Breadon A, Faiers MC, O'Farrell SM, Shooter RA. The origin of O serotypes of Escherichia coli in babies after normal delivery. *J Hyg (Lond).* Feb 1974;72(1):67-70.

30. Penders J, Thijs C, Vink C, et al. Factors influencing the composition of the intestinal microbiota in early infancy. *Pediatrics.* Aug 2006;118(2):511-521.

31. Bezirtzoglou E. The intestinal microflora during the first weeks of life. *Anaerobe.* Apr-Jun 1997;3(2-3):173-177.

32. Gronlund MM, Lehtonen OP, Eerola E, Kero P. Fecal microflora in healthy infants born by different methods of delivery: permanent changes in intestinal flora after cesarean delivery. *J Pediatr Gastroenterol Nutr.* Jan 1999;28(1):19-25.

33. Jeurink PV, van Esch BC, Rijnierse A, Garssen J, Knippels LM. Mechanisms underlying immune effects of dietary oligosaccharides. *Am J Clin Nutr.* Aug 2013;98(2):572S-577S.

34. Salminen S, Bouley C, Boutron-Ruault MC, et al. Functional food science and gastrointestinal physiology and function. *Br J Nutr.* Aug 1998;80 Suppl 1:S147-171.

35. American Academy of Pediatrics. Breastfeeding and the Use of Human Milk. *Pediatrics.* 2005;115:496-506.

36. World Health Organization. Infant and young child nutrition: Global strategy on infant and young child feeding 2002. http://apps.who.int/gb/archive/pdf_files/WHA55/ea5515.pdf.

37. Betran AP, Merialdi M, Lauer JA, et al. Rates of caesarean section: analysis of global, regional and national estimates. *Paediatr Perinat Epidemiol.* Mar 2007;21(2):98-113.

38. Spong CY, Berghella V, Wenstrom KD, Mercer BM, Saade GR. Preventing the first cesarean delivery: summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, and American

College of Obstetricians and Gynecologists Workshop. *Obstet Gynecol.* Nov 2012;120(5):1181-1193.

39. Department of Health and Human Services H. Healthy People 2020 summary of objectives, maternal, infant, and child health [Internet]. 2012 [cited 2013 Oct 11]. Available from: http://www.healthypeople.gov/2020/topicsobjectives2020/pdfs/MaternalChildHealth.pdf.

40. Heinig MJ. Host defense benefits of breastfeeding for the infant. Effect of breastfeeding duration and exclusivity. *Pediatr Clin North Am.* Feb 2001;48(1):105-123, ix.

41. Takala AK, Eskola J, Palmgren J, et al. Risk factors of invasive Haemophilus influenzae type b disease among children in Finland. *J Pediatr.* Nov 1989;115(5 Pt 1):694-701.

42. Lucas A, Cole TJ. Breast milk and neonatal necrotising enterocolitis. *Lancet.* Dec 22-29 1990;336(8730):1519-1523.

43. Chulada PC, Arbes SJ, Jr., Dunson D, Zeldin DC. Breast-feeding and the prevalence of asthma and wheeze in children: analyses from the Third National Health and Nutrition Examination Survey, 1988-1994. *J Allergy Clin Immunol.* Feb 2003;111(2):328-336.

44. US Department of Health and Human Services. Healthy People 2010: Conference Edition-Volumes I and II. 2000; Washington, DC.

45. US Department of Health and Human Services. HHS Blueprint for Action on Breastfeeding 2000; http://www.womenshealth.gov/archive/breastfeeding/programs/blueprints/bluprntbk2.pdf . Accessed Oct 19, 2011.

46. Ryan AS. The resurgence of breastfeeding in the United States. *Pediatrics.* Apr 1997;99(4):E12.

47. Gartner LM, Morton J, Lawrence RA, et al. Breastfeeding and the use of human milk. *Pediatrics.* Feb 2005;115(2):496-506.

48. Cakmak H, Kuguoglu S. Comparison of the breastfeeding patterns of mothers who delivered their babies per vagina and via cesarean section: an observational study using the LATCH breastfeeding charting system. *Int J Nurs Stud.* Sep 2007;44(7):1128-1137.

49. Zanardo V, Pigozzo A, Wainer G, et al. Early lactation failure and formula adoption after elective caesarean delivery: cohort study. *Arch Dis Child Fetal Neonatal Ed.* Jan 2013;98(1):F37-41.

50. Perez-Rios M, Santiago-Perez MI, Alonso B, Malvar A, Hervada X. Exposure to second-hand smoke: a population-based survey in Spain. *Eur Respir J.* Apr 2007;29(4):818-819.

51. Rowe-Murray HJ, Fisher JR. Baby friendly hospital practices: cesarean section is a persistent barrier to early initiation of breastfeeding. *Birth.* Jun 2002;29(2):124-131.

52. Patel RR, Liebling RE, Murphy DJ. Effect of operative delivery in the second stage of labor on breastfeeding success. *Birth.* Dec 2003;30(4):255-260.

53. Ahluwalia IB, Li R, Morrow B. Breastfeeding practices: does method of delivery matter? *Matern Child Health J.* Dec 2012;16 Suppl 2:231-237.

54. Shawky S, Abalkhail BA. Maternal factors associated with the duration of breast feeding in Jeddah, Saudi Arabia. *Paediatr Perinat Epidemiol.* Jan 2003;17(1):91-96.

55. Fallani M, Young D, Scott J, et al. Intestinal microbiota of 6-week-old infants across Europe: geographic influence beyond delivery mode, breast-feeding, and antibiotics. *J Pediatr Gastroenterol Nutr.* Jul 2010;51(1):77-84.

56. Rinne MM, Gueimonde M, Kalliomaki M, Hoppu U, Salminen SJ, Isolauri E. Similar bifidogenic effects of prebiotic-supplemented partially hydrolyzed infant formula and breastfeeding on infant gut microbiota. *FEMS Immunol Med Microbiol.* Jan 1 2005;43(1):59-65.

57. Biasucci G, Benenati B, Morelli L, Bessi E, Boehm G. Cesarean delivery may affect the early biodiversity of intestinal bacteria. *J Nutr.* 2008;138(9):1796s-1800s.

58. Mitsou EK, Kirtzalidou E, Oikonomou I, Liosis G, Kyriacou A. Fecal microflora of Greek healthy neonates. *Anaerobe.* Apr 2008;14(2):94-101.

59. Yap GC, Chee KK, Hong PY, et al. Evaluation of stool microbiota signatures in two cohorts of Asian (Singapore and Indonesia) newborns at risk of atopy. *BMC Microbiol.* 2011;11:193.

60. Azad MB, Konya T, Maughan H, et al. Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months. *CMAJ.* Mar 19 2013;185(5):385-394.

61. Arenz S, Ruckerl R, Koletzko B, von Kries R. Breast-feeding and childhood obesity--a systematic review. *Int J Obes Relat Metab Disord.* Oct 2004;28(10):1247-1256.

62. Harder T, Bergmann R, Kallischnigg G, Plagemann A. Duration of breastfeeding and risk of overweight: a meta-analysis. *Am J Epidemiol.* Sep 1 2005;162(5):397-403.

63. Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG. Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. *Pediatrics.* May 2005;115(5):1367-1377.

64. Owen CG, Martin RM, Whincup PH, Davey-Smith G, Gillman MW, Cook DG. The effect of breastfeeding on mean body mass index throughout life: a quantitative review of published and unpublished observational evidence. *Am J Clin Nutr.* Dec 2005;82(6):1298-1307.

65. Li R, Fein SB, Grummer-Strawn LM. Association of breastfeeding intensity and bottle-emptying behaviors at early infancy with infants' risk for excess weight at late infancy. *Pediatrics.* Oct 2008;122 Suppl 2:S77-84.

66. American Academy of Pediatrics. Breastfeeding and the Use of Human Milk. *Pediatrics.* 2012;129:e827-841.

67. Declercq E, Young R, Cabral H, Ecker J. Is a rising cesarean delivery rate inevitable? Trends in industrialized countries, 1987 to 2007. *Birth.* Jun 2011;38(2):99-104.

68. Ecker JL, Frigoletto FD, Jr. Cesarean delivery and the risk-benefit calculus. *N Engl J Med.* Mar 1 2007;356(9):885-888.

69. Freeman RK CA, Depp R,, Frigoletto FD HG, Lieberman E. *Evaluation of cesarean delivery.* Washington (DC): American College of Obstetricians and Gynecologists;2000.

70. Bailit JL, Love TE, Mercer B. Rising cesarean rates: are patients sicker? *Am J Obstet Gynecol.* Sep 2004;191(3):800-803.

71. Baicker K, Buckles KS, Chandra A. Geographic variation in the appropriate use of cesarean delivery. *Health Aff (Millwood).* Sep-Oct 2006;25(5):w355-367.

72. Clark SL, Belfort MA, Hankins GD, Meyers JA, Houser FM. Variation in the rates of operative delivery in the United States. *Am J Obstet Gynecol.* Jun 2007;196(6):526 e521-525.

73. Truven Health Analytics. *The cost ofhaving a baby in the United States.* Greenwood Village (CO): Truven Health Analytics;2013.

74. Chalmers B, Kaczorowski J, Darling E, et al. Cesarean and vaginal birth in canadian women: a comparison of experiences. *Birth.* Mar;37(1):44-49.

75. Fein SB, Labiner-Wolfe J, Shealy KR, Li R, Chen J, Grummer-Strawn LM. Infant Feeding Practices Study II: study methods. *Pediatrics.* Oct 2008;122 Suppl 2:S28-35.

76. Fein SB, Grummer-Strawn LM, Raju TN. Infant feeding and care practices in the United States: results from the Infant Feeding Practices Study II. *Pediatrics.* Oct 2008;122 Suppl 2:S25-27.

77. Zanardo V, Svegliado G, Cavallin F, et al. Elective cesarean delivery: does it have a negative effect on breastfeeding? *Birth.* Dec 2010;37(4):275-279.

78. Rajan L. The impact of obstetric procedures and analgesia/anaesthesia during labour and delivery on breast feeding. *Midwifery.* Jun 1994;10(2):87-103.

79. Jordan S, Emery S, Bradshaw C, Watkins A, Friswell W. The impact of intrapartum analgesia on infant feeding. *BJOG.* Jul 2005;112(7):927-934.

80. Bai DL, Wu KM, Tarrant M. Association between intrapartum interventions and breastfeeding duration. *J Midwifery Womens Health.* Jan-Feb 2013;58(1):25-32.

81. O'Donovan A, Alcorn KL, Patrick JC, Creedy DK, Dawe S, Devilly GJ. Predicting posttraumatic stress disorder after childbirth. *Midwifery.* Aug 2014;30(8):935-941.

82. Rowe-Murray HJ, Fisher JR. Operative intervention in delivery is associated with compromised early mother-infant interaction. *BJOG.* Oct 2001;108(10):1068-1075.

83. Dewey KG, Nommsen-Rivers LA, Heinig MJ, Cohen RJ. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. *Pediatrics.* Sep 2003;112(3 Pt 1):607-619.

84. von Kries R, Koletko B, Sauerwald T, et al. Breast feeding and obesity: cross sectional study. *BMJ.* 1999;319:147-150.

85. Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. *BMJ.* 2000;320:967-971.

86. Eid E. Follow-up study of physical growth of children who had excessive weight gain in first six months of life. *Br Med J.* Apr 11 1970;2(5701):74-76.

87. Eriksson JG, Forsen T, Tuomilehto J, Winter PD, Osmond C, Barker DJ. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. *BMJ.* Feb 13 1999;318(7181):427-431.

88. Stettler N, Zemel BS, Kumanyika S, Stallings VA. Infant weight gain and childhood overweight status in a multicenter, cohort study. *Pediatrics.* Feb 2002;109(2):194-199.

89. Singhal A, Lanigan J. Breastfeeding, early growth and later obesity. *Obes Rev.* Mar 2007;8 Suppl 1:51-54.

90. Dewey KG, Heinig MJ, Nommsen-Rivers LA. Differences in morbidity between breast-fed and formula-fed infants. *J Pediatr.* May 1995;126(5 Pt 1):696-702.

91. Gillman MW, Rifas-Shiman SL, Camargo CA, Jr., et al. Risk of overweight among adolescents who were breastfed as infants. *JAMA.* May 16 2001;285(19):2461-2467.

92. Grummer-Strawn LM, Scanlon KS, Fein SB. Infant feeding and feeding transitions during the first year of life. *Pediatrics.* Oct 2008;122 Suppl 2:S36-42.

93. Singhal A, Cole TJ, Fewtrell M, Lucas A. Breastmilk feeding and lipoprotein profile in adolescents born preterm: follow-up of a prospective randomised study. *Lancet.* May 15 2004;363(9421):1571-1578.

94. U.S. Department of Health and Human Services. *The surgeon general's call to action to support breastfeeding* Washington, DC: US Department of Health and Human Services, Office of the Surgeon General 2011.

95. Bodner K, Wierrani F, Grunberger W, Bodner-Adler B. Influence of the mode of delivery on maternal and neonatal outcomes: a comparison between elective cesarean section and planned vaginal delivery in a low-risk obstetric population. *Arch Gynecol Obstet.* Jun 2011;283(6):1193-1198.

96. Huh SY, Rifas-Shiman SL, Zera CA, et al. Delivery by caesarean section and risk of obesity in preschool age children: a prospective cohort study. *Arch Dis Child.* Jul 2012;97(7):610-616.

97. Dewey KG, Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B. Growth of breast-fed and formula-fed infants from 0 to 18 months: the DARLING Study. *Pediatrics.* Jun 1992;89(6 Pt 1):1035-1041.

98. Toschke AM, Grote V, Koletzko B, von Kries R. Identifying children at high risk for overweight at school entry by weight gain during the first 2 years. *Arch Pediatr Adolesc Med.* May 2004;158(5):449-452.

99. Singhal A, Wells J, Cole TJ, Fewtrell M, Lucas A. Programming of lean body mass: a link between birth weight, obesity, and cardiovascular disease? *Am J Clin Nutr.* Mar 2003;77(3):726-730.

100. Houseknecht KL, McGuire MK, Portocarrero CP, McGuire MA, Beerman K. Leptin is present in human milk and is related to maternal plasma leptin concentration and adiposity. *Biochem Biophys Res Commun.* 1997;240(3):742–747.

101. Martin LJ, Woo JG, Geraghty SR, et al. Adiponectin is present in human milk and is associated with maternal factors. *Am J Clin Nutr.* May 2006;83(5):1106-1111.

102. Qi Y, Takahashi N, Hileman SM, et al. Adiponectin acts in the brain to decrease body weight. *Nat Med.* May 2004;10(5):524-529.

103. Li R, Fein SB, Grummer-Strawn LM. Do infants fed from bottles lack self-regulation of milk intake compared with directly breastfed infants? *Pediatrics.* Jun 2010;125(6):e1386-1393.

104. Nommsen LA, Lovelady CA, Heinig MJ, Lonnerdal B, Dewey KG. Determinants of energy, protein, lipid, and lactose concentrations in human milk during the first 12 mo of lactation: the DARLING Study. *Am J Clin Nutr.* Feb 1991;53(2):457-465.

105. Perez-Escamilla R, Cohen RJ, Brown KH, Rivera LL, Canahuati J, Dewey KG. Maternal anthropometric status and lactation performance in a low-income Honduran population: evidence for the role of infants. *Am J Clin Nutr.* Mar 1995;61(3):528-534.

106. Dewey KG, Lonnerdal B. Infant self-regulation of breast milk intake. *Acta Paediatr Scand.* Nov 1986;75(6):893-898.

107. Mamun AA, Sutharsan R, O'Callaghan M, et al. Cesarean delivery and the long-term risk of offspring obesity. *Obstet Gynecol.* Dec 2013;122(6):1176-1183.

108. Li H, Ye R, Pei L, Ren A, Zheng X, Liu J. Caesarean delivery, caesarean delivery on maternal request and childhood overweight: a Chinese birth cohort study of 181 380 children. *Pediatr Obes.* Feb 2014;9(1):10-16.

109. Blustein J, Attina T, Liu M, et al. Association of caesarean delivery with child adiposity from age 6 weeks to 15 years. *Int J Obes (Lond).* Jul 2013;37(7):900-906.

110. Lin SL, Leung GM, Schooling CM. Mode of delivery and adiposity: Hong Kong's "Children of 1997" birth cohort. *Ann Epidemiol.* Nov 2013;23(11):693-699.

111. Goldani MZ, Barbieri MA, da Silva AA, Gutierrez MR, Bettiol H, Goldani HA. Cesarean section and increased body mass index in school children: two cohort studies from distinct socioeconomic background areas in Brazil. *Nutr J.* 2013;12(1):104.

112. Grzeskowiak L, Collado MC, Mangani C, et al. Distinct gut microbiota in southeastern African and northern European infants. *J Pediatr Gastroenterol Nutr.* Jun 2012;54(6):812-816.

113. Nam YD, Jung MJ, Roh SW, Kim MS, Bae JW. Comparative analysis of Korean human gut microbiota by barcoded pyrosequencing. *PLoS One.* 2011;6(7):1-15.