



Published in final edited form as:

Int J Obes (Lond). 2012 April ; 36(4): 529–534. doi:10.1038/ijo.2011.254.

THE IMPACT OF NEONATAL BREASTFEEDING ON GROWTH TRAJECTORIES OF YOUTH EXPOSED AND UNEXPOSED TO DIABETES IN UTERO: THE EPOCH STUDY

T.L. Crume¹, L.G. Ogden², E.J. Mayer-Davis³, R.F. Hamman¹, J.M. Norris¹, K.J. Bischoff⁴, R. McDuffie⁴, and D. Dabelea¹

¹Department of Epidemiology, Colorado School of Public Health, University of Colorado Denver

²Department of Biostatistics and Informatics, Colorado School of Public Health, University of Colorado Denver

³Departments of Nutrition and Medicine, University of North Carolina Chapel Hill

⁴Kaiser Permanente of Colorado

Abstract

Objective—To evaluate the influence of breastfeeding on the body mass index (BMI) growth trajectory from birth through 13 years of age among offspring of diabetic pregnancies (ODP) and offspring of non-diabetic pregnancies (ONDP) participating in the EPOCH study.

Subjects—There were 94 ODP and 399 ONDP who had multiple BMI measures obtained from birth throughout childhood. A measure of breast milk-months was derived from maternal self-report to categorize breastfeeding status as adequate (≥6 breast milk-months) or low (<6 breast milk-months). Mixed linear effects models were constructed to assess the impact of breastfeeding on the BMI growth curves during infancy (birth to 27 months) and childhood (27 months to 13 years).

Results—ODP who were adequately breastfed had a slower BMI growth trajectory during childhood ($p=0.047$) and slower period-specific growth velocity with significant differences between 4 to 6 years of age ($p=0.03$) and 6 to 9 years of age ($p=0.01$) compared to ODP with low breastfeeding. A similar pattern was seen in the ONDP, with adequate breastfeeding associated with lower average BMI in infancy ($p=0.03$) and childhood ($p=0.0002$) and a slower growth trajectory in childhood ($p=0.0002$). Slower period-specific growth velocity was seen among the ONDP associated with adequate breastfeeding with significant differences between 12–26 months ($p=0.02$), 4–6 years ($p=0.03$), 6–9 years ($p=0.0001$) and 9–13 years of age ($p<.0001$).

Conclusion—Our study provides novel evidence that breastfeeding is associated with long-term effects on childhood BMI growth that extend beyond infancy into early and late childhood.

Users may view, print, copy, download and text and data- mine the content in such documents, for the purposes of academic research, subject always to the full Conditions of use: http://www.nature.com/authors/editorial_policies/license.html#terms

Corresponding Author: Tessa Crume PhD, Assistant Professor, Department of Epidemiology, Colorado School of Public Health, University of Colorado Denver, 13001 East 17th Ave, Box B119, Aurora, CO 80045.

The authors have no conflict of interest to disclose.

Importantly, these effects are also present in the high-risk offspring, exposed to overnutrition during pregnancy. Breastfeeding in the early postnatal period may represent a critical opportunity to reduce the risk of childhood obesity.

Keywords

Breastfeeding; childhood obesity; fetal programming; fetal overnutrition; fetal exposure to diabetes; critical periods; gestational diabetes; BMI; childhood growth trajectories; early infant diet

Introduction

Rates of obesity and overweight are rising in nearly all countries around the globe (1). Obesity in childhood is highly predictive of obesity in adulthood (2). Given the limited success of treating childhood obesity (3), the public health and research community are now intensely focusing on prevention. The gestational and early postnatal periods have both been identified as critical developmental windows for future obesity risk. Previous research suggests that fetal exposure to over-nutrition resulting from maternal diabetes during pregnancy leads to excess fetal growth (4) and an increased risk of obesity in childhood and beyond (5, 6). We recently reported an altered growth trajectory and higher BMI growth velocity during the late childhood period among youth exposed to maternal diabetes *in utero* (7). Early postnatal weight gain is another critical period for determining later overweight and obesity (8, 9). Reports from epidemiologic studies provide strong evidence that breast-fed infants have a lower risk of overweight and obesity in childhood than formula-fed infants (10). Meta-analyses have estimated an effect size of 13–22% reduced odds for overweight or obesity in childhood and later in life associated with having been breast-fed (11). However, it is not clear whether the favorable effects of breastfeeding extend throughout the entire childhood period, and it is not known if such effects are similar in offspring exposed and not-exposed to diabetes *in utero*. The current study explores whether breastfeeding may favorably alter the BMI growth trajectory from birth through 13 years of age among offspring of diabetic pregnancies (ODP) and offspring of non-diabetic pregnancies (ONDP) from Colorado.

METHODS AND PROCEDURES

Study design and participants

This report uses data from a retrospective cohort study conducted in Colorado: Exploring Perinatal Outcomes among Children (EPOCH). Participants were offspring of singleton pregnancies, born at a single hospital in Denver between 1992 and 2002, whose biological mothers were members of the Kaiser Permanente of Colorado Health Plan (KPCO) and who were still KPCO members and living in Colorado over the study period (2006–2009).

Measures

Childhood height and weight measurements—All participants were invited to a research office visit in which standard anthropometric measures were recorded. Current height and weight were measured in light clothing and without shoes. Weight was measured

to the nearest 0.1 kg using an electronic scale. Height was measured to the nearest 0.1 cm using a portable stadiometer. Previously recorded measures of recumbent length (up to age 2 years), standing height (after the child is able to stand) and weight from pediatric office visits were abstracted from the KPCO medical record. For children with an enrollment gap, medical records from non-KPCO providers were obtained. The median number of BMI measurements for subjects was 10 (ranging from 3 to 34). BMI was calculated as kg/m² from weights and heights measured on the same day.

Gestational exposure: *in utero* exposure to maternal diabetes—Physician-diagnosed maternal diabetes status was ascertained from the KPCO Perinatal database, an electronic database linking the neonatal and perinatal medical record. Gestational diabetes (GDM) was coded as present if diagnosed through the standard KPCO screening protocol and absent if screening was negative. Since the 1990s, KPCO has routinely screened for GDM in all non-diabetic pregnancies using a two-step standard protocol. At 24–28 weeks, all pregnant women are offered screening with a 1-h50-g oral glucose tolerance test (OGTT). A value ≥ 140 mg/dl identifies patients who undergo a 3-h 100-g diagnostic OGTT. GDM is diagnosed when two or more glucose values during the diagnostic OGTT meet or exceed the criteria for a positive test, as recommended by the National Diabetes Data Group (12). The KPCO screening and diagnostic protocols have remained constant over time. In addition, birth weight, length and gestational age were also obtained from the database.

Early life exposure: breastfeeding status—At study visit mothers were queried about breast and formula feeding, timing and introduction of other solid foods and beverages. Due to high levels of reported mixed feeding, a previously published (13) measure of breast milk-months was developed that incorporated duration and exclusivity. For exclusively breastfed infants, duration was equal to the age of the child (months) when breastfeeding was stopped. For infants ever fed formula, mothers were asked to classify their infant feeding as: formula only, more formula than breast milk, equal breast milk and formula, or more breast milk than formula. Breastfeeding exclusivity was quantified using weights from 0 and 1, with exclusive breastfeeding having a weight of 1 and exclusive formula feeding having a weight of 0. For infants fed both breast milk and formula, exclusivity was equal to 0.25 for “more formula than breast milk”; 0.50 for “formula and breast milk equally”; 0.75 for and “more breast milk than formula”. The breast milk-months measure incorporated duration and exclusivity to estimate an overall breast milk dose equivalent in months. It was the sum of months of exclusive breastfeeding and the weighted months of mixed breast milk and formula [duration of exclusive breastfeeding (months) + duration of mixed breast and formula feeding (months) * exclusivity weight]. Breast milk-months were categorized as low breastfeeding (< 6 months) and adequate breastfeeding status (≥ 6 months), based on American Academy of Pediatrics (AAP) recommendations (14). Maternal recall of breastfeeding after periods of time spanning between 9 and 20 years has been found to correlate well with infant feeding data obtained from medical records ($r=0.86$) (15) or collected prospectively ($r=0.95$) (16).

Other measurements—Race/ethnicity was self-reported using 2000 U.S. Census-based questions and categorized as Hispanic (any race), non-Hispanic white (NHW), and non-

Hispanic African-American (AA). Children's total energy intake (kcalories/day) was assessed using the Block Kid's Food Questionnaire (17). Self-reported key activities, both sedentary and non-sedentary, performed during the previous 3 days was queried using a 3-day Physical Activity Recall (3DPAR) questionnaire (18). Each 30-minute block of activity was assigned a MET (metabolic equivalent) variable to accommodate the energy expenditure. Results were reported as a percentage of subjects whose number of 30-minute blocks of moderate-to-vigorous and vigorous physical activity (PA) reported over 3 days meet the standard of at least 1 hour of moderate-to-vigorous PA (19) and 20 min of vigorous PA per day (20).

Ethics—The study was approved both by the Colorado Multiple Institutional Review Board and Human Participant Protection Program. All participants provided written informed consent and youth provided written assent.

Data analysis—Mixed effects linear models were constructed to assess differences in BMI and BMI growth velocity for ODP and ONDP according to breastfeeding status: low (<6 breast milk months) versus adequate (≥6 breast milk months). This modeling approach allows for intrasubject correlation of repeated measures on subjects and accounts for an unbalanced design in the number and timing of BMI observations on each subject. Model parameters were estimated using Restricted Maximum Likelihood (PROC MIXED, SAS Version 9.2) and allowed for random intercepts and slopes with an unstructured covariance. Higher order random effects were considered, but covariance parameters were near zero or negative and thus removed from the model. Due to the change in use of recumbent length to standing height around the age of 2 years, two separate growth curves were developed with BMI as the outcome. The first curve was estimated for the infancy period from birth through 26 months and a second curve for the childhood period from 27 months to 13 years (method described in a previous publication (21)). Models were fit separately for ODP and ONDP. The best fitting models, selected using Akaike Information Criteria, used a quadratic polynomial of age and the infancy model included a spline at 11 months. Covariates for the infancy model included breastfeeding status, sex and race/ethnicity as fixed effects. Covariates for the childhood model included breastfeeding status, sex, race/ethnicity, current childhood diet and physical activity levels reported at the EPOCH study office visit as fixed effects. The population BMI growth curve and period-specific BMI growth velocity by adequate and low neonatal breastfeeding in both ODP and ONDP were estimated from the models.

RESULTS

Table 1 shows characteristics of ODP and ONDP according to neonatal breastfeeding status. Of the 94 ODP, 44% had adequate levels of breastfeeding in the neonatal period and NHW youth were more likely to be adequately breastfed than Hispanic or AA ($p=0.0005$). Of the 399 ONDP youth, 47% had adequate levels of neonatal breastfeeding and NHW were more likely to be adequately breastfed than Hispanic or AA youth ($p=0.0002$). Among both ODP and ONDP, sex, tanner stage, current diet and physical activity patterns were not associated with neonatal breastfeeding status.

Impact of Breastfeeding on Growth during the Infancy Period

Figure 1 (Panels A and B) shows the modeled BMI growth trajectory for the infancy period from birth through 26 months for low and adequate neonatal breastfeeding in ODP (Panel A) and ONDP (Panel B). In both groups, the BMI at birth was not significantly different for those with adequate and low breastfeeding status. Also in both groups, the average BMI tended to be lower and the BMI trajectory slower among those in the adequate breastfeeding category; however differences only reached statistical significance for average BMI in the ONDP group ($p=0.03$). Table 2 displays the period-specific BMI growth velocity of ODP and ONDP by breastfeeding status, as well as the number of BMI observations in each period. Based on the quadratic spline model it is estimate that, on average, ODP who had adequate neonatal breastfeeding gained 1.72 kg/m^2 between birth and 9 months of age compared with 2.83 kg/m^2 among those low breastfeeding, a difference of -1.11 kg/m^2 that was borderline statistically significant ($p=0.07$). In both the ODP and ONDP, there were no differences in growth velocity by breastfeeding status between 9–12 months. Between 12 and 26 months, the ONDP with adequate breastfeeding status had negative BMI growth velocity compared to BMI gains among those with low breastfeeding status (-0.56 vs. 0.32 kg/m^2 , $p=0.02$). Differences in growth velocity by breastfeeding status among the ODP were not detected in this period. There were no significant interactions between exposure to diabetes *in utero* and breastfeeding status.

Impact of Breastfeeding on Growth in the Childhood Period

Figure 2 shows the BMI growth trajectory from 27 months through 13 years of age for ODP (Panel A) and ONDP (Panel B). During the childhood period, ODP (Panel A) with adequate neonatal breastfeeding status had a significantly lower average BMI ($p=0.034$) and a slower BMI growth trajectory ($p=0.047$) compared to those with low neonatal breastfeeding status, independent of sex, race/ethnicity, current childhood diet and physical activity levels. A similar pattern is seen in the ONDP (Panel B), with average lower BMI over this period ($p=0.0002$) and a slower BMI growth trajectory ($p=0.0002$) associated with adequate compared to low neonatal breastfeeding, independent of sex, race/ethnicity, and current childhood diet and physical activity levels.

Table 2 shows the period specific BMI growth velocity of ODP and ONDP who had adequate or low neonatal breastfeeding status from the quadratic model. BMI growth velocity was not significantly different by breastfeeding status from 27 months through 4 years in either the ODP and ONDP. However, between 4 and 6 years, BMI growth velocity was significantly lower for the adequately breastfed among both ODP (0.11 vs. 0.68 kg/m^2 , $p=0.03$) and ONDP (0.26 vs. 0.53 kg/m^2 , $p=0.03$). Similar patterns were seen in both ODP and ONDP between 6 and 9 years of age (1.30 vs. 2.21 kg/m^2 , $p=0.01$ in ODP; 1.10 vs. 1.73 kg/m^2 , $p=0.0001$ in ONDP) for adequate vs. low breastfeeding status, respectively). Between 9 and 13 years of age, ONDP with adequate breastfeeding status also had slower BMI growth compared to those with low breastfeeding (2.80 vs. 4.05 kg/m^2 , $p<0.0001$) and significant differences were not detected by breastfeeding status among the ODP. There were no significant interactions between exposure to diabetes *in utero* and breastfeeding status.

DISCUSSION

We found that adequate breastfeeding (≥ 6 breast milk-months) reduces the overall body size and slows BMI growth velocity both during infancy as well as in the childhood period. These effects were similar in offspring of diabetic and non-diabetic pregnancies, and independent of sex, race/ethnicity, current childhood diet and physical activity levels. Our data provide additional evidence that early infant diet represents a critical period for influencing childhood obesity risk. Moreover, our study indicates that the favorable effects of breastfeeding on BMI growth patterns extend throughout the entire childhood period, and are also present in youth at increased risk for obesity due to intrauterine exposure to maternal diabetes.

While height and weight trajectories increase linearly from birth throughout childhood, the normal development of adiposity, assessed by BMI, is characterized by several phases of overall adiposity gains and losses reflected by negative and positive BMI growth velocity (22). In the ONDP we found positive growth velocity between 12 and 26 months among subjects with low breastfeeding compared to negative velocity in the adequately breastfed. This represents an accelerated growth pattern where children with suboptimal early life nutrition are accumulating adiposity at an age range when it is waning in their adequately breastfed peers. Subsequently, low vs. adequate breastfeeding was associated with higher BMI growth velocity in both the ONDP and ODP starting at 4 years of age indicating this acceleration of BMI growth extends into childhood. Slower growth in infancy and lower percent body fat composition among breastfed compared to formula-fed infants has been reported in a number of studies (23, 24). Rzehak et al (25) developed growth trajectories of weight, length and BMI from birth to age 6 in a large population-based birth cohort in Germany to assess the effect of breastfeeding on childhood growth. The authors reported that infants who were fully breastfed for at least 4 months gained less in the first 12 months of life compared to mixed- or formula-fed children. The DARLING Study (26) found a similar pattern of increased weight-for-length *z* scores between 4 and 18 months of age among formula-fed infants compared to those breastfed for 1 year.

To our knowledge, this is the first study that longitudinally assessed the impact of breastfeeding on BMI growth trajectories among offspring who are exposed fetal overnutrition from maternal diabetes *in utero*. Some researchers have expressed concern that breast milk of diabetic mothers could have increased glucose or insulin concentrations that would in fact contribute to fetal programming for future obesity, though the macro-nutrient content of breast milk among well-controlled diabetic mothers has not been demonstrated to be different (27). Plagemann et al (28) reported that offspring of mothers with type 1 diabetes who consumed the highest tertile of breast milk in the first week of life were more likely to be overweight and have a worse metabolic profile at 2 years of age compared to those who consumed banked milk. However, a follow-up study by Rodekamp et al. (29) accounted for intake in the 2nd to 4th weeks of life and found that neither dose nor duration of breastfeeding among offspring women with type 1 diabetes was associated with increased risk of overweight or impaired glucose tolerance at 2 years of age. Among Pima Indian youth exposed to maternal type 2 diabetes or GDM *in utero*, Pettitt et al (30) reported a reduction in diabetes risk if the offspring were breastfed for at least 2 months compared to

those who were formula-fed (30.1 vs. 43.6%). In the Growing up Today Study (GUTS), Mayer-Davis et al (31) reported a reduced odds ratio (OR) for risk of overweight at 9–14 years of 0.66 (95%CI 0.53–0.82) associated with exclusive breastfeeding versus exclusive formula feeding among all subjects and a OR of 0.62 (95% C.I.: 0.24–1.60) among youth exposed to maternal diabetes *in utero*. And recently, in a cross-sectional analysis of youth enrolled in the EPOCH cohort, we found lower adiposity levels and a less centralized body fat distribution pattern among youth exposed to diabetes *in utero* who had adequate neonatal breastfeeding levels (≥ 6 breast milk months) compared to those with low breastfeeding status. The current study adds an important dimension to our understanding of the influence of early infant diet on the growth and development of children who may be programmed for a faster growth trajectory due to *in utero* exposure to over-nutrition from a diabetic pregnancy.

The mechanisms responsible for the favorable long-term effects of breastfeeding on infant and childhood growth patterns are likely multiple. Formula and other types of milk feedings (besides human) have growth accelerating properties on infant weight, length, body fatness and growth velocity (32). The macronutrient composition of breast milk (i.e., proteins, fat, carbohydrate) and bioactive substances not present in formula may have a protective influence on metabolic programming and regulation of body fatness and growth rates. Another group of potential mechanisms relate to breastfeeding behaviors. For example, smaller or slower growing infants may be deliberately weaned while fast-growing infants would more often be placed on supplementation to reduce crying related to their greater hunger demands (33). In the current study we found shorter birth length ($p=0.03$) and smaller birth weight ($p=0.07$) were associated with low levels of breastfeeding among ONDP which suggests that size at birth may influence breastfeeding behaviors. Additional factors related to breastfeeding that may affect the rate of infant growth include parental control of intake patterns as they can visually assess consumption and want to ‘finish the bottle’, thereby overriding an infant’s innate ability to regulate their meal size and interval based on satiety cues.

Our study has several limitations. Our smaller sample of ODP ($n=94$) may have limited our ability to detect significant differences in the overall growth trajectory or period-specific growth velocity by neonatal breastfeeding. Information on childhood diet and physical activity patterns were only collected once during the research visit, so adjustment for current behaviors may not have adequately removed potential confounding for the entire childhood period. Given the epidemiological nature of this study we were not able to adequately explore the mechanisms responsible for these long-term favorable effects. However, our study also has important strengths including a longitudinal study design and analysis using mixed linear methods which allowed us to explore the effect of breastfeeding on the growth trajectory in infancy and childhood as well as period specific growth. Our cohort was diverse in racial and ethnic youth including non-Hispanic white, Hispanic, and African American. Our assessment of exposure to diabetes *in utero* was based on clinical records from a large Health Maintenance Organization. And finally, our measure of early infant diet was based on a breastfeeding score which incorporated mixed feeding.

In conclusion, this study provides novel evidence that optimal nutrition the early post-natal period is an important strategy to reduce the risk of childhood obesity. Importantly, this strategy appears to be as effective among offspring of diabetic pregnancies, who are at high risk for becoming overweight or obese early in life, as it is in the larger pediatric population. Moreover, these data support the notion that early postnatal life has long-term influences on growth and development.

Acknowledgments

This work was supported by RO1 DK068001. The study sponsor had no role in the study.

Abbreviations

EPOCH	Exploring Perinatal Outcomes Among Children Study
KPCO	Kaiser Permanente
GDM	gestational diabetes mellitus
OGTT	oral glucose tolerance test
AAP	American Academy of Pediatrics
PA	physical activity
HMO	health maintenance organization

Reference List

1. de Onis M, Blossner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr.* 2010; 92(5):1257–64. [PubMed: 20861173]
2. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med.* 1997; 337(13):869–73. [PubMed: 9302300]
3. Whitlock EP, Williams SB, Gold R, Smith PR, Shipman SA. Screening and interventions for childhood overweight: a summary of evidence for the US Preventive Services Task Force. *Pediatrics.* 2005; 116(1):e125–e144. [PubMed: 15995013]
4. Catalano PM, Thomas A, Huston-Presley L, Amini SB. Increased fetal adiposity: a very sensitive marker of abnormal in utero development. *Am J Obstet Gynecol.* 2003; 189(6):1698–704. [PubMed: 14710101]
5. Hillier TA, Pedula KL, Schmidt MM, Mullen JA, Charles MA, Pettitt DJ. Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. *Diabetes Care.* 2007; 30(9):2287–92. [PubMed: 17519427]
6. Silverman BL, Rizzo T, Green OC, et al. Long-term prospective evaluation of offspring of diabetic mothers. *Diabetes.* 1991; 40 (Suppl 2):121–5. [PubMed: 1748240]
7. Crume TL, Ogden L, Daniels S, Hamman RF, Norris JM, Dabelea D. The Impact of In Utero Exposure to Diabetes on Childhood Body Mass Index Growth Trajectories: The EPOCH Study. *J Pediatr.* 2011; 158(6):941–6. [PubMed: 21238981]
8. Sachdev HS, Fall CH, Osmond C, et al. Anthropometric indicators of body composition in young adults: relation to size at birth and serial measurements of body mass index in childhood in the New Delhi birth cohort. *Am J Clin Nutr.* 2005; 82(2):456–66. [PubMed: 16087993]
9. McCarthy A, Hughes R, Tilling K, Davies D, Smith GD, Ben-Shlomo Y. Birth weight; postnatal, infant, and childhood growth; and obesity in young adulthood: evidence from the Barry Caerphilly Growth Study. *Am J Clin Nutr.* 2007; 86(4):907–13. [PubMed: 17921364]

10. Harder T, Bergmann R, Kallischnigg G, Plagemann A. Duration of breastfeeding and risk of overweight: a meta-analysis. *Am J Epidemiol.* 2005; 162:397–403. [PubMed: 16076830]
11. Arenz S, Ruckerl R, Koletzko B, von Kries R. Breast-feeding and childhood obesity—a systematic review. *International Journal of Obesity.* 2004; 28:1247–1256. [PubMed: 15314625]
12. National Diabetes in Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes.* 1979; 28:1039–57. [PubMed: 510803]
13. Crume TL, Ogden L, Maligie M, et al. Long-term impact of neonatal breastfeeding on childhood adiposity and fat distribution among children exposed to diabetes in utero. *Diabetes Care.* 2011; 34(3):641–5. [PubMed: 21357361]
14. Gartner LM, Morton J, Lawrence RA, et al. Breastfeeding and the use of human milk. *Pediatrics.* 2005; 115(2):496–506. [PubMed: 15687461]
15. Kark JD, Troya G, Friedlander Y, Slater PE, Stein Y. Validity of maternal reporting of breast feeding history and the association with blood lipids in 17 year olds in Jerusalem. *J Epidemiol Community Health.* 1984; 38(3):218–25. [PubMed: 6470599]
16. Vobecky JS, Vobecky J, Froda S. The reliability of the maternal memory in a retrospective assessment of nutritional status. *J Clin Epidemiol.* 1988; 41(3):261–5. [PubMed: 3339379]
17. Block, G.; Murphy, M.; Roullet, J., et al. Pilot validation of a FFQ for children 8–10 years. *The Fourth International Conference on Dietary Assessment Methods*; 2000.
18. Pate R, Ross R, Dowda F, et al. Validation of a three-day physical activity recall instrument in female youth. *Pediatr Exerc Sci.* 2003; 15:257–65.
19. Strong WB, Malina RM, Blimkie CJ, et al. Evidence based physical activity for school-age youth. *J Pediatr.* 2005; 146(6):732–7. [PubMed: 15973308]
20. U.S. Department of Health and Human Services. *Healthy People 2010. 2.* Washington, D.C: U.S. Government Printing Office; 2000.
21. Crume TL, Ogden L, Daniels S, Hamman RF, Norris JM, Dabelea D. The Impact of In Utero Exposure to Diabetes on Childhood Body Mass Index Growth Trajectories: The EPOCH Study. *J Pediatr.* 2011; 158(6):941–6. [PubMed: 21238981]
22. Rolland-Cachera MF, Deheeger M, Guilloud-Bataille M, Avons P, Patois E, Sempe M. Tracking the development of adiposity from one month of age to adulthood. *Ann Hum Biol.* 1987; 14(3): 219–29. [PubMed: 3662424]
23. Dewey KG, Peerson JM, Brown KH, et al. Growth of breast-fed infants deviates from current reference data: a pooled analysis of US, Canadian, and European data sets. *World Health Organization Working Group on Infant Growth. Pediatrics.* 1995; 96(3 Pt 1):495–503. [PubMed: 7651784]
24. 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.* 1992; 89(6 Pt 1):1035–41. [PubMed: 1594343]
25. Rzehak P, Sausenthaler S, Koletzko S, et al. Period-specific growth, overweight and modification by breastfeeding in the GINI and LISA birth cohorts up to age 6 years. *Eur J Epidemiol.* 2009; 24(8):449–67. [PubMed: 19521784]
26. 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.* 1992; 89(6 Pt 1):1035–41. [PubMed: 1594343]
27. van Beusekom CM, Zeegers TA, Martini IA, et al. Milk of patients with tightly controlled insulin-dependent diabetes mellitus has normal macronutrient and fatty acid composition. *Am J Clin Nutr.* 1993; 57(6):938–43. [PubMed: 8503365]
28. Plagemann A, Harder T, Franke K, Kohlhoff R. Long-term impact of neonatal breast-feeding on body weight and glucose tolerance in children of diabetic mothers. *Diabetes Care.* 2002; 25(1):16–22. [PubMed: 11772895]
29. Rodekamp E, Harder T, Kohlhoff R, Franke K, Dudenhausen JW, Plagemann A. Long-term impact of breast-feeding on body weight and glucose tolerance in children of diabetic mothers: role of the late neonatal period and early infancy. *Diabetes Care.* 2005; 28(6):1457–62. [PubMed: 15920068]

30. Pettitt DJ, Knowler WC. Long-term effects of the intrauterine environment, birth weight, and breast-feeding in Pima Indians. *Diabetes Care*. 1998; 21 (Suppl 2):B138–B141. [PubMed: 9704241]
31. Mayer-Davis EJ, Rifas-Shiman SL, Zhou L, Hu FB, Colditz GA, Gillman MW. Breast-feeding and risk for childhood obesity: does maternal diabetes or obesity status matter? *Diabetes Care*. 2006; 29(10):2231–7. [PubMed: 17003298]
32. Kramer MS, Guo T, Platt RW, et al. Feeding effects on growth during infancy. *J Pediatr*. 2004; 145(5):600–5. [PubMed: 15520757]
33. Kramer MS, Matush L, Vanilovich I, et al. Effects of prolonged and exclusive breastfeeding on child height, weight, adiposity, and blood pressure at age 6.5 y: evidence from a large randomized trial. *Am J Clin Nutr*. 2007; 86(6):1717–21. [PubMed: 18065591]

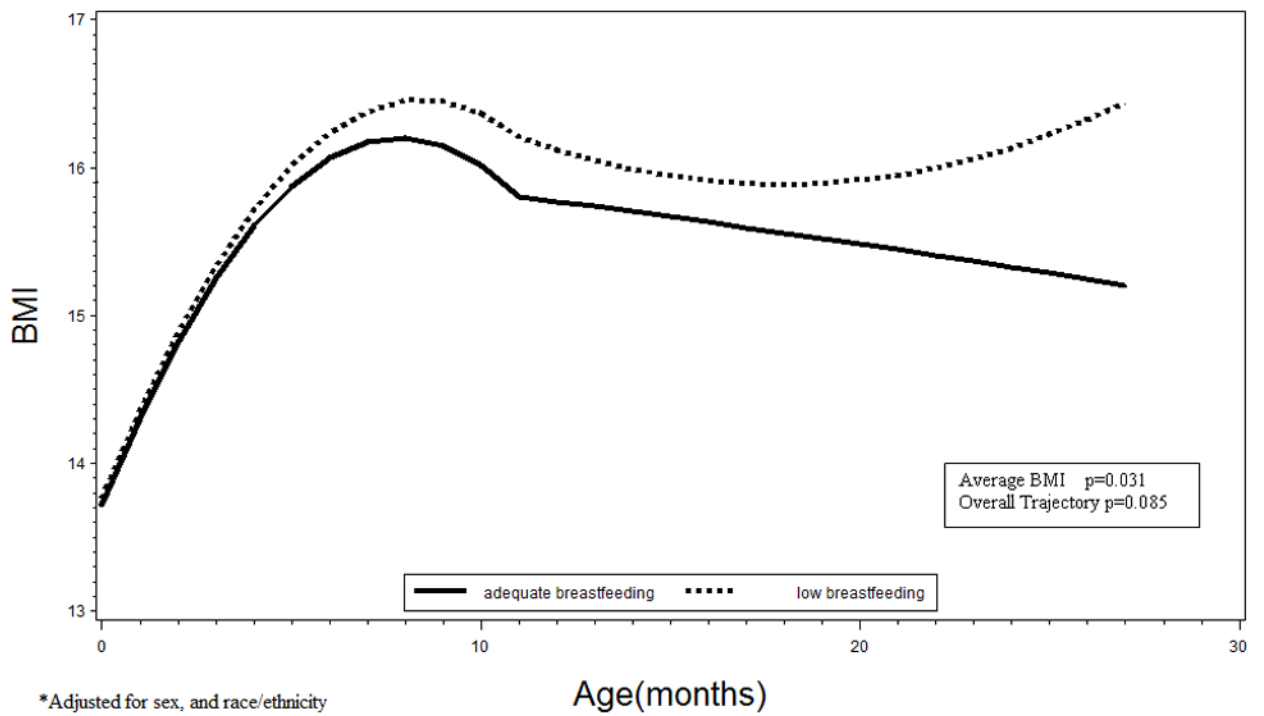
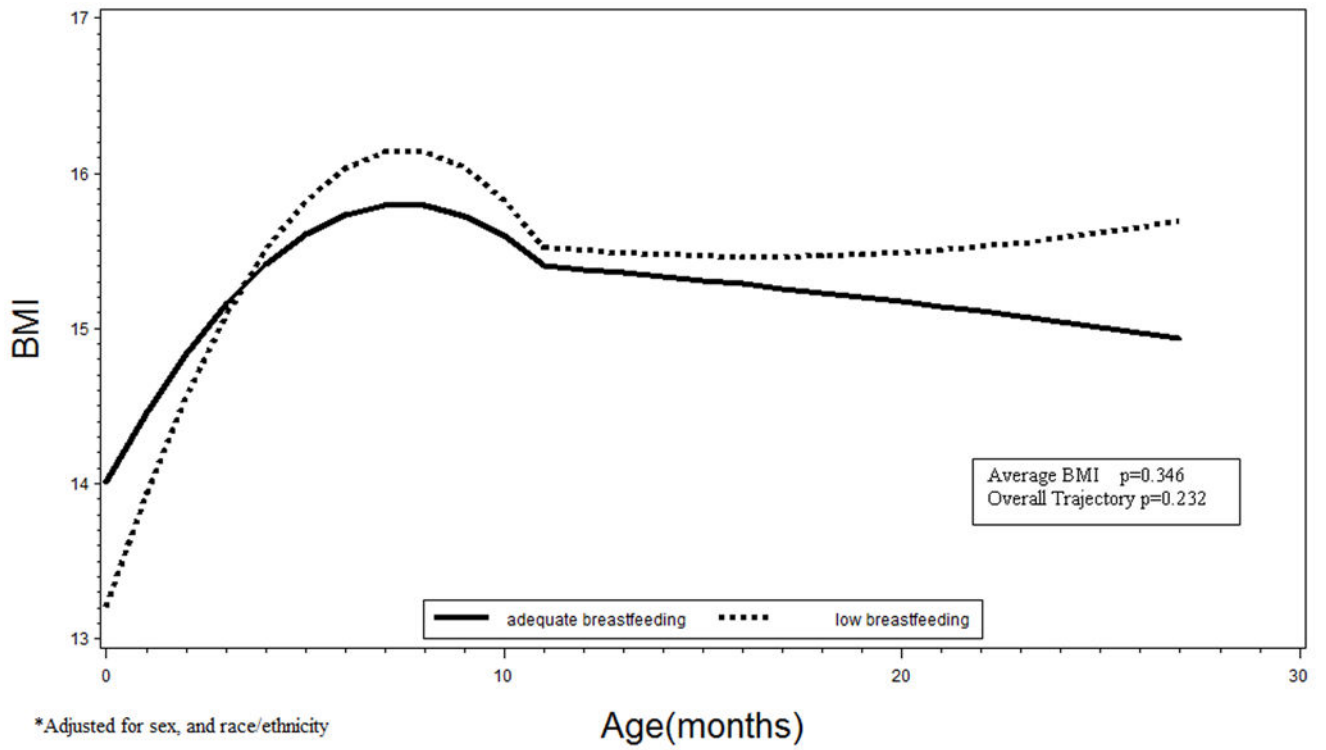


Figure 1.
Infancy BMI Growth Trajectory for Offspring of Diabetic Pregnancies. Panel A.
Infancy BMI Growth Trajectory for Offspring of Non-Diabetic Pregnancies. Panel B.

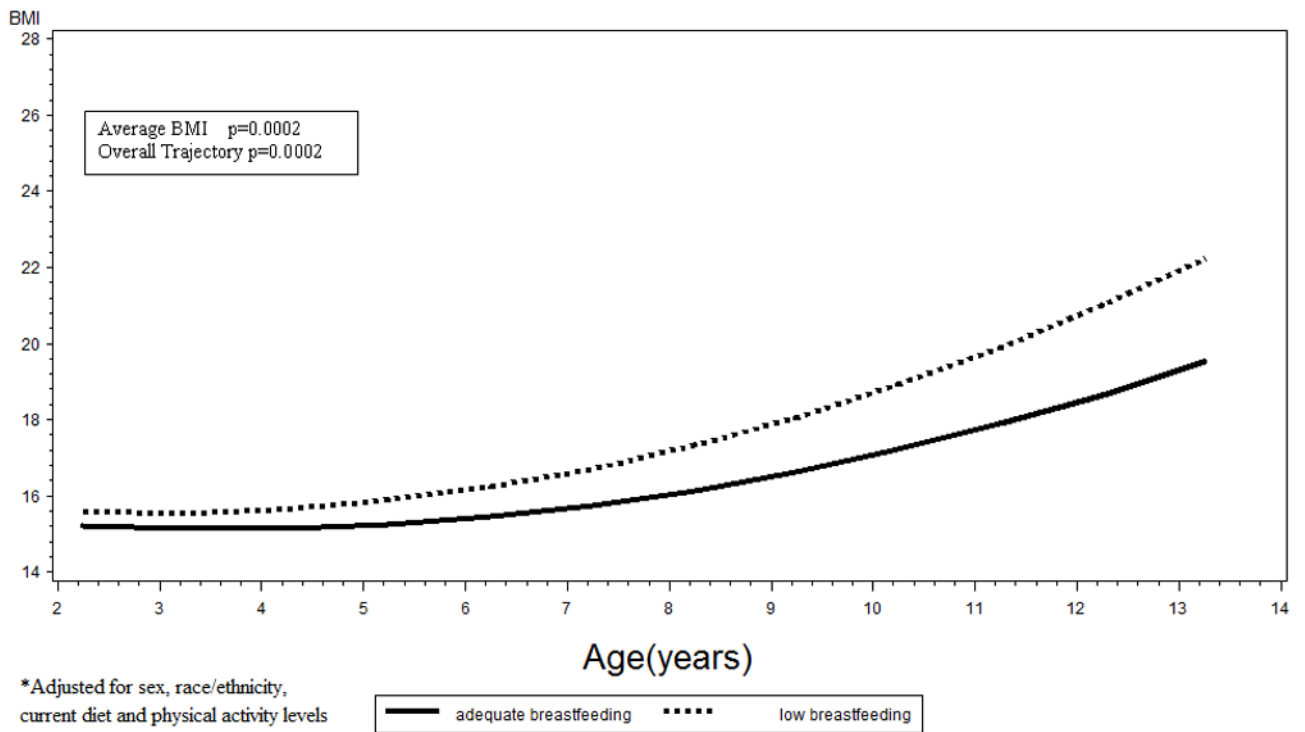
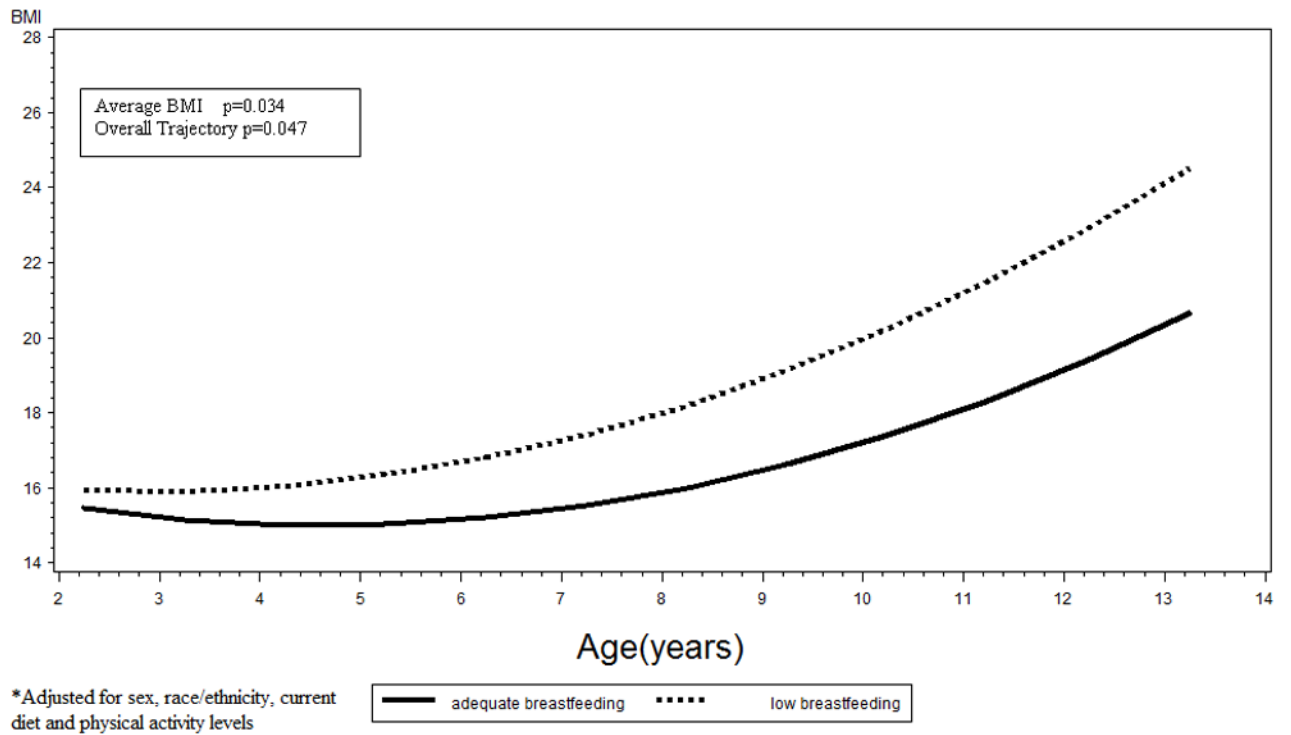


Figure 2. Childhood BMI Growth Trajectory for Offspring of Diabetic Pregnancies. Panel A. Childhood BMI Growth Trajectory for Offspring of Non-Diabetic Pregnancies. Panel B.

Table 1
 Characteristics of ODP and ONDP Participating in EPOCH, According to Breastfeeding Status

	ODP			ONDP		
	Adequate Breastfeeding N=41	Low Breastfeeding N=53	P	Adequate Breastfeeding N=187	Low Breastfeeding N=212	P
Sex (proportion male)	51.2 (21)	56.6 (30)	0.6	44.5 (85)	51.9 (110)	0.20
Race/ethnicity						
NHW	85.4 (35)	47.2 (25)	0.0005	58.8 (110)	38.2 (81)	0.0002
Hispanic	14.6 (6)	43.4 (23)		34.8 (65)	50.5 (107)	
AA	0	9.4 (5)		6.4 (12)	11.3 (24)	
Birth weight (grams)	3377.0±441.1	3326.7±620.4	0.6	3354.0±486.6	3256.2±593.0	0.07
Birth length (cm)	49.3±4.1	49.8±2.6	0.6	50.4±4.0	49.6±2.7	0.02
Tanner stage <2*	73.2 (30)	69.8 (37)	0.7	51.1 (95)	49.1 (104)	0.6
Total calories (/day)*	1833.3±473.5	1690.2±466.6	0.1	1786.6±543.2	1815±539.9	0.60
Physical activity percentage score*†	46.5 (33)	53.5 (38)	0.5	47.3 (151)	52.7 (168)	0.60

Data are % (n) or means ± SD

† Percentage of subjects meeting physical activity standards for moderate-to-vigorous and vigorous PA

* self-reported at the EPOCH office visit at 6–13 years of age

Adequate breastfeeding 6 breast milk-months, low breastfeeding <6 breast milk-months

Table 2

BMI growth velocity for ODP and ONDP according to breastfeeding status

	ODP				ONDP			
	# Obs	Adequate Breastfeeding N=41	Low Breastfeeding N=57	P	# Obs	Adequate Breastfeeding N=187	Low Breastfeeding N=212	P
birth-9m	364	1.72 (0.43)	2.83 (0.43)	0.07	1040	2.43 (0.25)	2.69 (0.25)	0.48
9-12m	125	-0.34 (0.13)	-0.03 (0.20)	0.20	396	-0.38 (0.07)	-0.18 (0.12)	0.114
12-26m	308	-0.44 (0.50)	0.19 (0.43)	0.34	719	-0.56 (0.26)	0.32 (0.27)	0.02
27m-3.99y	275	-0.41 (0.20)	0.07 (0.19)	0.09	850	-0.08 (0.10)	0.05 (0.10)	0.34
4-5.99y	407	0.11 (0.19)	0.68 (0.17)	0.03	1172	0.26 (0.09)	0.53 (0.09)	0.03
6-8.99y	540	1.30 (0.28)	2.21 (0.25)	0.01	1640	1.10 (0.12)	1.73 (0.11)	0.0001
9-13y	323	3.88 (0.51)	5.21 (0.47)	0.06	1648	2.80 (0.23)	4.05 (0.21)	<.0001

Estimates expressed as change in kg/m² during the indicated period

* Adjusted for sex, race/ethnicity.

** Adjusted for sex, race/ethnicity, childhood diet and physical activity level.

Breast milk months=Weighted months of mixed breast milk and formula, [duration of exclusive breast feeding (months) + duration mixed breast and formula feeding (months) * exclusivity weight].

Adequate breastfeeding < 6 breast milk-months, low breastfeeding < 6 breast milk-months