Journal Pre-proof

Effects of Breastfeeding, Formula Feeding, and Complementary Feeding on Rapid Weight Gain in the First Year of Life

Charles T. Wood MD, MPH , Whitney P. Witt PhD, MPH , Asheley C. Skinner PhD , H. Shonna Yin MD, MS , Russell L. Rothman MD, MPP , Lee M. Sanders MD, MPH , Alan M. Delamater PhD , Kori B. Flower MD, MS, MPH , Melissa C. Kay PhD, RD , Eliana M. Perrin MD, MPH

PII: S1876-2859(20)30507-6
DOI: https://doi.org/10.1016/j.acap.2020.09.009
Reference: ACAP 1634

To appear in: *Academic Pediatrics*

Received date: 2 March 2020
Accepted date: 15 September 2020

Please cite this article as: Charles T. Wood MD, MPH , Whitney P. Witt PhD, MPH , Asheley C. Skinner PhD , H. Shonna Yin MD, MS , Russell L. Rothman MD, MPP , Lee M. Sanders MD, MPH , Alan M. Delamater PhD , Kori B. Flower MD, MS, MPH , Melissa C. Kay PhD, RD , Eliana M. Perrin MD, MPH , Effects of Breastfeeding, Formula Feeding, and Complementary Feeding on Rapid Weight Gain in the First Year of Life, *Academic Pediatrics* (2020), doi: https://doi.org/10.1016/j.acap.2020.09.009

TITLE: Effects of Breastfeeding, Formula Feeding, and Complementary Feeding on Rapid Weight Gain in the First Year of Life

AUTHORS: Charles T. Wood, MD, MPH[1], Whitney P. Witt, PhD, MPH[2], Asheley C. Skinner, PhD[3], H. Shonna Yin, MD, MS[4], Russell L. Rothman, MD, MPP[5], Lee M. Sanders, MD, MPH[6], Alan M. Delamater, PhD[7], Kori B. Flower, MD, MS, MPH[8], Melissa C. Kay, PhD, RD[9] Eliana M. Perrin, MD, MPH[1]

AFFILIATION: [1]Division of Primary Care Pediatrics and Duke Center for Childhood Obesity Research, Department of Pediatrics, Duke University School of Medicine, Durham, NC.; [2]Lehigh University, College of Health; [3]Department of Population Health Sciences, Duke University School of Medicine; Duke Clinical Research Institute; [4]Departments of Pediatrics and Population Health, New York University School of Medicine/Bellevue Hospital Center, New York, NY; [5]Center for Health Services Research, Vanderbilt University Medical Center, Nashville, TN; [6]Department of Pediatrics, Center for Policy, Outcomes and Prevention, Stanford University, Stanford, CA; [7]Department of Pediatrics, University of Miami School of Medicine, Miami, FL; [8]Division of General Pediatrics and Adolescent Medicine, Department of Pediatrics, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC. [9]Duke Center for Childhood Obesity Research and Duke Global Digital Health Science Center, Duke University School of Medicine and Duke Global Health Institute, Durham, NC

KEYWORDS: breastfeeding; formula feeding; weight gain

RUNNING TITLE: Infant Feeding and Rapid Weight Gain

CONTACT INFO: Charles Wood, MD, MPH, Division of Primary Care Pediatrics, Department of Pediatrics, Duke University Medical Center, 2213 Elba Street, Durham, NC, USA, 27705.[charles.wood@duke.edu], Phone 919-620-4772 Fax 919-620-4776.

WORD COUNT: 3506

CLINICAL TRIAL REGISTRATION: Addressing Health Literacy and Numeracy to Prevent Childhood Obesity (GreenLight), NCT01040897, ClinicalTrials.gov

FUNDING: Supported by National Institutes of Health (NIH)/Eunice Kennedy Shriver National Institute of Child Health and Human Development grant R01HD059794 with Centers for Disease Control and Prevention supplements 04S1 and 04S2; NIH grant UL1TR001111; NIH/National Center for Advancing Translational Sciences grant UL1TR000445; NIH/National Center for Research Resources grants U54RR023499, UL1RR025747, and UL1TR000038; Robert Wood Johnson Foundation Physician Faculty Scholars program (Dr Yin); and Health Resources and Services Administration grant T32HP014001

DISCLOSURE: No conflicts of interest to disclose.

Abbreviations: WAZ – weight-for-age- z-score; WLZ – weight-for-length z-score; WHO – World Health Organization; TIPP – the Injury Prevention Program; BMI – body mass index

A portion of these analyses was presented at The Obesity Society's annual meeting.

Abstract:

Objective

To determine whether proportion of breast versus formula feeding, and timing of complementary food introduction affect the odds of rapid gain in weight status in a diverse sample of infants.

Methods

Using data from Greenlight Intervention Study, we analyzed the effects of type of milk feeding (breastfeeding, formula, or mixed feeding) from the 2 to 6 month well visits, and the introduction of complementary foods before 4 months on rapid increase in weight-for-age z-score (WAZ) and weight-for-length z-score (WLZ) before 12 months using multivariable logistic regression models.

Results

Of the 865 infants enrolled, 469 had complete data on all variables of interest, and 41% and 33% of those infants had rapid increases in WAZ and WLZ, respectively. Odds of rapid increase in WAZ remained lowest for infants breastfeeding from 2 to 6 months (aOR 0.34; 95% CI: 0.17, 0.69) when compared to infants who were formula fed. Adjusted for feeding, introduction of complementary foods after 4 months was associated with decreased odds of rapid increase in WLZ (aOR 0.64; 95% CI: 0.42, 0.96).

Conclusion

Feeding typified by predominant breastfeeding and delaying introduction of complementary foods after 4 months reduces the odds of rapid increases in WAZ and WLZ in the first year of life.

What's New:
We examined the roles of infant milk and complementary feeding on infant weight gain in an understudied population. Breastfeeding and delaying introduction of complementary foods is associated with lower odds of rapid infant weight gain in this population.

Introduction

Obesity prevention experts have recently recognized the influence of risk factors for obesity that are present from conception to age 2 (the "first 1000 days").[1] This has prompted renewed examination of risk factors in the early postnatal period. Exclusive breastfeeding and delaying complementary feeding until 6 months are strategies for prevention promoted by national guidelines.[2] Despite recommendations, many infants are consuming complementary foods even before 4 months of age.[3] By 5 months of age, 75% of 5-month-old infants consume complementary foods on a typical day.[4] Complementary feeding involves both the quantity and quality of foods offered as well as the timing of introduction. Given these multiple dimensions of feeding, and their interplay with breastfeeding and bottle feeding, determining the overall effects of the timing of complementary food introduction on subsequent weight gain and obesity has been challenging.

Prospective studies have shown that total daily energy intake generally increases when complementary foods are added, regardless of the month in which an infant begins to consume them.[5] Unlike breastfed infants, who show decreased demand for breast milk once complementary foods are introduced,[6] formula fed infants may not be fed fewer calories from formula despite also receiving calories from complementary foods.[7] Introduction of complementary foods prior to 4 months may increase overweight and obesity risk.[8,9] However, the decision of when to introduce complementary foods and how early introduction influences later weight both vary based on whether the infant was primarily breastfed or formula-fed;[5,10-12] several recent studies concluded that timing of complementary foods introduction was not associated with obesity in early childhood.[13,14]

One difficulty in determining associations between milk feeding type, timing of complementary feeding, and early obesity is the complexity of confounding factors that affect each of these feeding decisions. Many studies have not included analysis for periods of mixed (breast and formula) feeding and fewer have examined early growth patterns such as rapid increases in weight-for-age (WAZ) or weight-for-length (WLZ) z-scores.[12] Rapid gain in weight-for-age in the first 1000 days has been established as a factor related to obesity risk, yet what leads to these increases in weight in the first 2 years of life is unclear.[11,15] Infant growth trajectories likely differ based on multiple genetic and environmental factors, but nutrition plays a significant role, especially in the first year of life when growth is most rapid. In developed countries, infants who are primarily fed formula have slightly more adiposity in later infancy than infants fed exclusively breast milk.[16] Given the need to untangle these influences and identify factors that may attenuate increases in WAZ and WLZ and obesity risk, we aimed to examine correlates of rapid increases in WAZ and WLZ in a diverse group of infants. We hypothesized that increased breastfeeding and delaying complementary foods introduction after 4 months would be associated with reduced odds of rapid increases in WAZ and WLZ in the first year of life.

Methods

We analyzed longitudinal data from the Greenlight Intervention Study, a cluster randomized controlled trial of an obesity prevention intervention during the first two years of life. Detailed methods of the Greenlight study have been published elsewhere.[17] Briefly, the study took place at 4 pediatric resident-based continuity clinics, and enrolled 865 caregiver-infant dyads at the 2-

month preventive visit from December 2009 through June 2014. Caregiver-infant dyads were eligible to be included in the study if the infant was between 6 weeks and 16 weeks of age at the 2-month preventive visit, were born at ≥34 weeks gestational age, weighed ≥ 1500 grams at birth, and had a weight-for-recumbent length at ≥ 3rd percentile, based on World Health Organization (WHO) age- and sex-specific growth standards, and were generally healthy. Dyads were excluded if the caregiver had a significant neurological or mental illness or had uncorrected visual acuity problems. At two of the four clinics a low-literacy toolkit targeting healthy behaviors for optimal growth was delivered at each preventive visit during the first 2 years of life (2, 4, 6, 9, 12, 15-18 months), while participants at the other two clinics received a curriculum from the Injury Prevention Program (TIPP) designed by the American Academy of Pediatrics. The Greenlight intervention toolkit covered a range of topics, including encouraging breastfeeding, recognition of satiety cues, avoidance of sweetened beverages, delaying introduction of complementary foods until at least 4 to 6 months, choosing appropriate solid foods and portion sizes, being active with the infant, and avoiding screen time. The study was approved by the Institutional Review Boards of all four study institutions (University of North Carolina at Chapel Hill, Vanderbilt University, University of Miami, and New York University).

Weight and length information were available from each preventive visit attended, and was measured by clinic staff who were specifically trained in reliable measurement for research studies.[18] Z-scores for both WAZ and WLZ were calculated using sex-specific WHO growth standards. We calculated rapid increases in WAZ and WLZ using the most commonly held definition of ≥ 0.67 U increase in z-score, which has been shown in numerous prospective studies and metanalyses to be associated with childhood obesity.[15,19-21] Changes in z-scores were calculated as the difference between z-score at study initiation (2 month visit) and the z-score at the 12 month visit. Our primary outcome was dichotomous, with $\geq$ 0.67 U change in WAZ or WLZ defined as rapid weight gain.

To examine associations between introduction of complementary foods and milk type on increases in WAZ or WLZ, we used caregiver-reported information from standardized questionnaires collected in the study. At each visit from 2 to 12 months, caregivers answered the questions, “What type of milk does your child drink now?” and “Is your child eating solid foods yet or do you put any solid foods in the bottle?” From these questions, we constructed a 4-category variable for type of milk feeding at the 2 and 6 month visits, with each category representing a different combination of milk feeding between these visits: 1) breast milk only; 2) breast milk at 2 months followed by mixed (i.e., a combination of breast milk and formula) or formula feeding at 6 months; 3) mixed feeding at 2 months followed by mixed or formula feeding at 6 months; and 4) formula feeding only. Formula feeding from 2 to 6 months was the referent category for all analyses. Constructing milk feeding categories in this way highlights the hypothesized protective relationship between the degree and length of breastfeeding with slower growth rates during infancy.[22] Early introduction of complementary foods was defined as reported intake of any foods other than milk consumed by mouth or put in the bottle to drink before the 4 month visit. Introduction of foods prior to 4 months is generally considered to be early.[2,8] Early introduction was analyzed as the referent category in all analyses.

Children with incomplete data for weight, length and/or age at the 2 and 12 month well visits (n=240), missing responses to the question of milk type feeding at both the 2 and 6 month well visits (n=110), and missing responses to the introduction of complementary foods at the 4 month well visit (n=46), were excluded, leaving a total sample of 469 caregiver-child dyads. We used logistic regression to examine whether characteristics of missing data differed from our analytic sample.

To examine predictors of rapid increases in WAZ or WLZ, we tested continuous variables with t-tests and categorical variables with Pearson's chi-square tests. Polychoric correlation matrices were used to test for collinearity among predictors. No predictors were significantly correlated. We constructed logistic regression models assessing the effects of milk feeding type, complementary feeding before 4 months, and potential confounders on rapid weight gain between the 2 and 12-month visits. A series of regression analyses were conducted to determine whether milk feeding type and early introduction of complementary foods were independently associated with rapid increases in WAZ or WLZ. Model 1 examined the relationship between milk feeding type and rapid increases in WAZ or WLZ, with no adjustments for covariates. For model 2, we added early introduction of complementary foods to Model 1 to test whether early introduction of foods attenuated the relationship between milk feeding and rapid increases in WAZ or WLZ. We added potential confounders to Model 3, to assess whether associations with these increases were affected by known and hypothesized covariates. These covariates included caregiver BMI, race/ethnicity and education and infant birth weight, gestational age at birth, age at the 2 month visit, sex, whether the infant received less than 30 minutes of tummy time, and 30 minutes or more of active TV watching (caregivers directly responded with the number of minutes and hours their infant spent watching TV) at the 2 month visit. We tested the Greenlight intervention effect on our outcomes, which did not reveal a significant effect. As there may be differences in decisions regarding complementary feeding based on milk feeding type, we assessed but did not find any significant statistical interaction between milk feeding type and timing of complementary foods introduction (data not shown).

Results

Out of 865 infants enrolled, 469 had complete data on all variables of interest. Of these infants, 41% and 33% gained $\geq$0.67 U in WAZ and WLZ, respectively (Tables 2 and 3). Infants were on average 3.3 kg (SD 0.5 kg) at birth and 9 weeks old (SD 1.7 weeks) at the 2-month well visit; half were female (51%, Table 1). Caregivers in our sample were mostly mothers (96%), Hispanic (52%) or non-Hispanic black (26%), on average overweight (mean BMI 28.4 (SD 6.7)), and over a quarter (26%) had less than a high school education. Nearly half (40%) of the infants were fed formula only between their 2 and 6-month well visit and 16% were fed breast milk only (no formula). A third of infants (34%) had complementary foods introduced before 4 months; most had less than 30 minutes per day of tummy time (69%) and nearly a quarter watched 30 minutes or more of television (24%) at the 2-month visit.

Infants who were excluded from analyses due to missing information were more likely to have been born at an earlier gestational age (p=0.02) and fed formula at 2 months (p=0.03) or switched to mixed feeding at 6 months (p=0.04) compared to those fed breast milk only through 6 months. Early introduction of complementary foods was independently associated with increased odds of rapid increase in WLZ (OR 1.70 95% CI: 1.14, 2.54) and WAZ (OR 1.63 95% CI: 1.10, 2.40; data not shown).

Infants with rapid increase in WAZ (depicted in Table 2) were significantly smaller at birth (3.2 kg vs. 3.4 kg, p<0.001) and at their 2-month visit (5.2 kg vs. 5.5 kg, p<0.001), and were born at earlier gestational age (38.6 weeks vs. 39.3 weeks, p=0.01), compared to those without rapid gain. Caregivers of infants with rapid increases in WAZ had a significantly higher BMI (29.2 vs. 27.8, p=0.03). There were significant differences in distributions of race/ethnicity and milk feeding type at 2 and 6 months among those infants with rapid increases in WAZ. Significantly more infants with rapid increase in WAZ had foods introduced before 4 months (40% vs. 29%, p=0.01) and watched 30 minutes or more of television (30% vs 20%, p=0.01).

There were slight differences in the characteristics of infants with rapid increases in WLZ (Table 3). These infants, unlike those with rapid increases in WAZ, had a similar weight at their 2-month visit, but weighed more at birth (3.4 kg vs. 3.2 kg, p<.001) and had later gestational age (39.3 vs. 38.9, p=0.01) compared to those with no rapid increase in WLZ. There were no significant relationships between milk feeding type from the 2 to 6-month visits or television watching and rapid increase in WLZ. There were differences in the relationship between race/ethnicity and WLZ, with more non-Hispanic black (29% vs. 26%) and non-Hispanic white infants (23% vs. 18%) having rapid increases in WLZ than their respective overall samples. Infants with rapid increases in WLZ were more likely to have foods introduced before the 4-month visit (42% vs. 30%, p=0.01).

In Model 1, we observed a dose-response relationship in the odds of rapid increase in WAZ, with progressively decreased odds of rapid increase in WAZ for each category of increasing breast milk (Table 4 and Figure 1). Infants who had feedings that were mixed breast milk and formula between the 2 and 6-month visits had 50% lower odds, those having breast milk at 2 months and mixed feeding at 6 months had 68% lower odds, and those having breast milk from 2 to 6 months with no formula had 73% decreased odds of rapid increases in WAZ. However, there was no significant relationship between type of milk feeding and rapid increase in WLZ.

In Model 2, when adjusting for categories of milk feeding between 2 and 6 months and interaction between milk feeding category and timing of complementary introduction, introduction of complementary foods before the 4 month visit increased the odds of rapid increases in WLZ (aOR 1.57 95% CI: 1.04, 2.37), but the relationship was no longer significant with WAZ increases (aOR 1.38 95% CI: 0.92, 2.07) (Table 4 and Figure 1). Point estimates for the associations between rapid increase in WAZ and categories of milk feeding changed slightly when adjusting for the timing of complementary foods introduction. The odds of rapid increase in WAZ maintained a dose-response relationship; feeding breast milk (both mixed at 6 months and only from 2 to 6 months) was associated with lower odds of rapid weight gain at 12 months compared to feeding formula (aOR 0.32 95% CI: 0.14, 0.73, and aOR 0.30 95% CI: 0.16, 0.55, respectively). Mixed feeding was also significantly associated with decreased odds of rapid increase in WAZ when compared to formula feeding (OR 0.53 95% CI: 0.395 0.81). Relationships between rapid increases in WLZ and milk feeding type were no longer statistically significant when adjusting for timing of complementary foods introduction.

In Model 3, we analyzed the relationship between rapid increases in WAZ and WLZ separately, adjusting for caregiver obesity and race/ethnicity, birth weight, gestational age at birth, age at the 2-month visit, and caregiver-reported infant activity (tummy time) and TV watching. We found that odds of rapid increase in WAZ for infants receiving mixed feedings at 2 and 6 months remained significantly lower when compared to formula feeding (aOR 0.55; 95% CI: 0.34, 0.91). Receiving breast milk at 2 months and mixed feeds or formula at 6 months (aOR 0.40; 95% CI: 0.16, 0.99), and receiving breast milk only from 2 to 6 months (aOR 0.34; 95% CI: 0.17, 0.69) were also associated with decreased odds of rapid increases in WAZ compared to formula feeding. Odds of rapid increase in WLZ were lower for increasing level of breast milk consumption, but estimates for each category of milk feeding were not statistically significant. Even when adjusting for confounders, introducing complementary foods before the 4-month visit was associated with higher odds of rapid gain in WLZ (aOR 1.61; 95% CI: 1.01, 2.55) than delaying introduction (Table 4).

Discussion

Our analysis indicates that maintaining breastfeeding and delaying introduction of complementary foods beyond 4 months are associated with lower odds of rapid increases in weight-for-age and weight-for-length, respectively. As hypothesized, we found that increasing levels of breast milk as the main source of milk between the 2 and 6-month well visits reduced the odds of rapid increase in weight-for-age z-scores in the first year of life in a stepwise manner. Similarly, delaying introduction of complementary foods until after the 4-month visit was associated with reduced odds of rapid increase in weight-for-length z-scores in the first year of life. Our findings suggest that the type of milk feeding and timing of complementary foods introduction are associated with differential accelerated growth in early life in this low-income, diverse sample of infants.

In our study sample, parental report of delayed introduction of complementary foods beyond 4 months was associated with reduced odds of rapid increases in weight-for-length over the first year of life. One study found six-fold increased odds of childhood obesity among formula fed, but not breastfed, infants receiving solid foods before 4 months.[9] Although that study population had much higher levels of education and income compared with our analysis, the results suggest that decisions to wean infants before 6 months may confound relationships between introduction of solid food and obesity. Parents of both breastfed and formula fed infants may perceive the infant to need more calories than breast milk or formula provides. Such reverse causation, especially among infants weaned from breastfeeding due to concerns about intake, has been shown in studies investigating the role of breastfeeding on subsequent obesity.[23] Infant appetite remains an area of active exploration.[24,25]

While previous studies demonstrated interaction between breastfeeding duration and the timing of introduction of complementary foods, [8,26] we did not find a significant interaction in our sample. Others have shown that introduction of solid foods before 4 months, compared to after 6 months, is associated with increased BMI for infants breastfed for < 4 months as well as those breastfed for ≥ 4 months.[8] Delaying introduction of solids after 7 months, compared to 5-6 months, is also associated with increased BMI for infants breastfed for < 4 months, but not for infants breastfed ≥ 4 months of age. A U-shaped relationship between the timing of complementary foods introduction and BMI suggests 4-6 months to be an appropriate time to introduce foods. This conveniently corresponds to recommendations for prevention of atopic disease.[27]

The timing of introduction varies widely among cultures.[28,29] Although early introduction of foods has been shown to affect obesity differentially by ethnic group,[30] most cohorts investigating factors related to rapid weight gain and obesity have not been as racially, ethnically, and economically diverse as ours. Our sample is not representative of the US, as it is more racially and ethnically diverse and is much poorer than many other study populations. However, understanding these interplays in this population is critically important since this is the population at greatest risk for childhood obesity, which may be driven by the fact that milk feeding type differs by racial and ethnic group.[31] The strengths of our analysis include prospective data collection of repeated feeding characteristics in a clinical setting, and the analysis by both weight-for-age and weight-for-length to describe differences in these measures.

Given that weight and length provide an incomplete, albeit practically useful, measure of obesity risk, we decided, as others have,[32-34] to report associations between both weight-for-age and weight-for-length. Differences in body composition attributed to milk type may explain our observed differences between WAZ changes and WLZ changes. Increases in WAZ may be attributed to fat mass or fat free mass and include increases in height, whereas increases in WLZ are likely to represent adipose tissue deposits.[35] Therefore, these changes contribute to different mechanisms of growth, both of which play roles in future health. Changes in body composition in infancy differ between breastfed and formula-fed infants. In our analysis, breastfeeding may have influenced increases in both weight and length differently than timing of complementary foods, due to hormonal influences on growth or specific macronutrient content .[36] Understanding how different exposures to different milk feeding influences fat-free mass and fat-mass accrual will be important for prevention efforts.[25]

Limitations

Our analysis was limited in that we only looked at the growth changes between 2 and 12 months to assess the outcome of rapid weight gain during this period. Most missing data was due to attrition from the study, and we felt imputation would not have yielded an appropriate representation of this diverse sample. However, attrition may have affected the interpretation and generalizability of our findings. A different approach might yield important evidence on specific periods of time, or other measures such as peak weight velocity, or peak BMI that could signal later cardiometabolic disease risk.[37] Feeding in the first week and month of life influence weight gain and obesity risk,[38,39] and we did not collect detailed information on feeding prior to the 2 month visit. Although reasons for early introduction were not assessed, 12% of caregivers in our sample had already introduced solid foods at enrollment (2 month preventive visit).[31] Roughly half of our analysis sample were exposed to the study intervention, although our analyses accounted for both receipt of the intervention and the site at which the participant was enrolled. Desirability bias, or participants answering questions based on their knowledge of the intervention content, could also play a role in our findings. Finally, given the potential for unmeasured confounding, we cannot fully establish causation between feeding and weight changes in this sample.

Conclusion

In a diverse, multicenter cohort of infants, we show that two early parent feeding behaviors are associated with decreased odds of rapid increases in either WAZ or WLZ: (1) increased breast milk feeding before age 6 months and (2) delayed introduction of complementary foods until after age 4 months. These findings suggest that each of these factors may play a critical role in early risk for obesity, and may be key targets for early childhood obesity prevention efforts in clinical community-based settings.

References

1. Taveras EM. Childhood Obesity Risk and Prevention: Shining a Lens on the First 1000 Days. *Child Obes.* 2016;12(3):159-161.
2. Institute of Medicine Committee on Prevention of Obesity in C, Youth. The National Academies Collection: Reports funded by National Institutes of Health. In: Koplan JP, Liverman CT, Kraak VI, eds. *Preventing Childhood Obesity: Health in the Balance.* Washington (DC): National Academies Press (US); 2005.
3. Kuo AA, Inkelas M, Slusser WM, Maidenberg M, Halfon N. Introduction of solid food to young infants. *Maternal and child health journal.* 2011;15(8):1185-1194.
4. Miles G, Siega-Riz AM. Trends in Food and Beverage Consumption Among Infants and Toddlers: 2005–2012. *Pediatrics.* 2017;139(6).
5. Grote V, Schiess SA, Closa-Monasterolo R, et al. The introduction of solid food and growth in the first 2 y of life in formula-fed children: analysis of data from a European cohort study. *Am J Clin Nutr.* 2011;94(6 Suppl):1785s-1793s.
6. Cohen RJ, Brown KH, Canahuati J, Rivera LL, Dewey KG. Effects of age of introduction of complementary foods on infant breast milk intake, total energy intake, and growth: a randomised intervention study in Honduras. *Lancet.* 1994;344(8918):288-293.
7. Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B, Dewey KG. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: the DARLING Study. *Am J Clin Nutr.* 1993;58(2):152-161.
8. Sun C, Foskey RJ, Allen KJ, et al. The Impact of Timing of Introduction of Solids on Infant Body Mass Index. *J Pediatr.* 2016;179:104-110.e101.
9. Huh SY, Rifas-Shiman SL, Taveras EM, Oken E, Gillman MW. Timing of solid food introduction and risk of obesity in preschool-aged children. *Pediatrics.* 2011;127(3):e544-551.
10. Pearce J, Langley-Evans SC. The types of food introduced during complementary feeding and risk of childhood obesity: a systematic review. *Int J Obes (Lond).* 2013;37(4):477-485.
11. Woo Baidal JA, Locks LM, Cheng ER, Blake-Lamb TL, Perkins ME, Taveras EM. Risk Factors for Childhood Obesity in the First 1,000 Days: A Systematic Review. *Am J Prev Med.* 2016;50(6):761-779.
12. Pearce J, Taylor MA, Langley-Evans SC. Timing of the introduction of complementary feeding and risk of childhood obesity: a systematic review. *Int J Obes (Lond).* 2013;37(10):1295-1306.
13. Barrera CM, Perrine CG, Li R, Scanlon KS. Age at Introduction to Solid Foods and Child Obesity at 6 Years. *Child Obes.* 2016;12(3):188-192.
14. Lin SL, Leung GM, Lam TH, Schooling CM. Timing of Solid Food Introduction and Obesity: Hong Kong's "Children of 1997" Birth Cohort. *Pediatrics.* 2013;131(5):e1459-e1467.
15. Druet C, Stettler N, Sharp S, et al. Prediction of childhood obesity by infancy weight gain: an individual-level meta-analysis. *Paediatr Perinat Epidemiol.* 2012;26(1):19-26.

16. 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):1035-1041.
17. Sanders LM, Perrin EM, Yin HS, Bronaugh A, Rothman RL. "Greenlight study": a controlled trial of low-literacy, early childhood obesity prevention. *Pediatrics.* 2014;133(6):e1724-1737.
18. Bureau UDoHaHSMaCH. Growth chart training. http://depts.washington.edu/growth/module5/text/page4a.htm. Published 2008. Accessed October 13, 2013.
19. Ekelund U, Ong K, Linne Y, et al. Upward weight percentile crossing in infancy and early childhood independently predicts fat mass in young adults: the Stockholm Weight Development Study (SWEDES). *Am J Clin Nutr.* 2006;83(2):324-330.
20. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life--a systematic review. *Obes Rev.* 2005;6(2):143-154.
21. Ong KK, Loos RJ. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatr.* 2006;95(8):904-908.
22. Grummer-Strawn LM, Mei Z. Does breastfeeding protect against pediatric overweight? Analysis of longitudinal data from the Centers for Disease Control and Prevention Pediatric Nutrition Surveillance System. *Pediatrics.* 2004;113(2):e81-86.
23. Kramer MS, Moodie EE, Dahhou M, Platt RW. Breastfeeding and infant size: evidence of reverse causality. *Am J Epidemiol.* 2011;173(9):978-983.
24. Fildes A, van Jaarsveld CH, Llewellyn C, Wardle J, Fisher A. Parental control over feeding in infancy. Influence of infant weight, appetite and feeding method. *Appetite.* 2015;91:101-106.
25. Lumeng JC, Taveras EM, Birch L, Yanovski SZ. Prevention of Obesity in Infancy and Early Childhood: A National Institutes of Health Workshop. *JAMA Pediatr.* 2015.
26. Baker JL, Michaelsen KF, Rasmussen KM, Sorensen TI. Maternal prepregnant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. *Am J Clin Nutr.* 2004;80(6):1579-1588.
27. Greer FR, Sicherer SH, Burks AW. The Effects of Early Nutritional Interventions on the Development of Atopic Disease in Infants and Children: The Role of Maternal Dietary Restriction, Breastfeeding, Hydrolyzed Formulas, and Timing of Introduction of Allergenic Complementary Foods. *Pediatrics.* 2019;143(4):e20190281.
28. Schiess S, Grote V, Scaglioni S, et al. Introduction of complementary feeding in 5 European countries. *J Pediatr Gastroenterol Nutr.* 2010;50(1):92-98.
29. Woo JG, Guerrero ML, Ruiz-Palacios GM, et al. Specific infant feeding practices do not consistently explain variation in anthropometry at age 1 year in urban United States, Mexico, and China cohorts. *J Nutr.* 2013;143(2):166-174.
30. Brophy S, Cooksey R, Gravenor MB, et al. Risk factors for childhood obesity at age 5: analysis of the millennium cohort study. *BMC Public Health.* 2009;9:467.
31. Perrin EM, Rothman RL, Sanders LM, et al. Racial and Ethnic Differences Associated With Feeding- and Activity-Related Behaviors in Infants. *Pediatrics.* 2014.
32. Lavner JA, Stansfield BK, Beach SRH, Brody GH, Birch LL. Sleep SAAF: a responsive parenting intervention to prevent excessive weight gain and obesity among African American infants. *BMC Pediatr.* 2019;19(1):224.

33. Skilton MR, Marks GB, Ayer JG, et al. Weight gain in infancy and vascular risk factors in later childhood. *Pediatrics.* 2013;131(6):e1821-1828.
34. Lucas K, James P, Choh AC, et al. The positive association of infant weight gain with adulthood body mass index has strengthened over time in the Fels Longitudinal Study. *Pediatr Obes.* 2018;13(8):476-484.
35. Stettler N, Baumann M. Excess weight gain in the first 18 months of life is associated with later childhood overweight, obesity and greater arterial wall thickness. *Evid Based Nurs.* 2014;17(3):85.
36. Gale C, Logan KM, Santhakumaran S, Parkinson JR, Hyde MJ, Modi N. Effect of breastfeeding compared with formula feeding on infant body composition: a systematic review and meta-analysis. *Am J Clin Nutr.* 2012;95(3):656-669.
37. Woo JG. Fast, Slow, High, and Low: Infant and Childhood Growth as Predictors of Cardiometabolic Outcomes. *J Pediatr.* 2017.
38. Feldman-Winter L, Burnham L, Grossman X, Matlak S, Chen N, Merewood A. Weight gain in the first week of life predicts overweight at 2 years: A prospective cohort study. *Matern Child Nutr.* 2017.
39. Stettler N, Stallings VA, Troxel AB, et al. Weight gain in the first week of life and overweight in adulthood: a cohort study of European American subjects fed infant formula. *Circulation.* 2005;111(15):1897-1903.

Table 1. Demographics and Descriptive Characteristics of Dyads in Analysis Sample from Greenlight Intervention Study, n=469

Mean (SD), % (n)		Overall
Birth weight, kg (n=468)		3.3 (0.5)
Gestational age, wk (n=467)		39.1 (1.5)
Age at 2 mo visit, wk		9.3 (1.7)
Weight 2 mo visit, kg		5.4 (0.7)
Female		50.8 (238)
Caregiver type (Mother)		96.4 (452)
Caregiver BMI, (n=432)		28.4 (6.7)
Caregiver Race/Ethnicity	Non-Hispanic Black	26.4 (124)
	Hispanic	51.8 (243)
	Non-Hispanic White	17.5 (82)
	Non-Hispanic Other	4.3 (20)
Caregiver education (n=468)	Less than high school	26.1 (122)
	High school graduate	33.1 (155)
	Some college	22.7 (106)
	College graduate	18.2 (85)
Milk Type (at 2 and 6 months)	Formula, formula	39.9 (187)
	Mixed, formula	37.3 (175)
	Breast, mixed	7.0 (33)
	Breast, breast	15.8 (74)
Complementary foods before 4 month visit		33.5 (157)
Tummy time < 30 min/day (n=466)		69.3 (323)

TV watching >=30 min/day	23.9 (112)

*p < 0.05 within indicated sociodemographic characteristics; WAZ – weight-for-age z-score; WLZ – weight-for-length z-score

Table 2. Demographics and Descriptive Characteristics by Weight-for-age (WAZ) Change Category

		No Rapid WAZ Change	Rapid WAZ Change
Mean (SD), % (n)		58.9 (276)	41.2 (193)
Birth weight, kg (n=468)		3.4 (0.5)	3.2 (0.5)*
Gestational age, wk (n=467)		39.3 (1.3)	38.6 (1.6)*
Age at 2 mo visit, wk		9.4 (1.7)	9.2 (1.6)
Weight 2 mo visit, kg		5.5 (0.7)	5.2 (0.7)*
Female		51.5 (142)	49.7 (96)
Caregiver type (Mother)		96.4 (266)	96.4 (186)
Caregiver BMI, (n=432)		27.8 (6.2)	29.2 (7.2)*
Caregiver Race/Ethnicity	Non-Hispanic Black	20.3 (56)	35.2 (68)*
	Hispanic	57.3 (158)	44.0 (85)
	Non-Hispanic White	17.8 (49)	17.1 (33)
	Non-Hispanic Other	4.7 (13)	3.6 (7)
Caregiver education (n=468)	Less than high school	26.8 (74)	25.0 (48)
	High school graduate	32.3 (89)	34.4 (66)
	Some college	19.9 (55)	26.6 (51)
	College graduate	21.0 (58)	14.1 (27)
Milk Type (at 2 and 6 months)	Formula, formula	31.2 (86)	52.3 (101)*
	Mixed, formula	39.9 (110)	33.7 (65)
	Breast, mixed	8.7 (24)	4.7 (9)
	Breast, breast	20.3 (56)	9.3 (18)

Complementary foods before 4 month visit	29.0 (80)	39.9 (77)*
Tummy time < 30 min/day (n=466)	72 (198)	65.5 (125)
TV watching >=30 min/day	19.6 (54)	30.1 (58)*
*p < 0.05 within indicated sociodemographic characteristics; WAZ – weight-for-age z-score; WLZ – weight-for-length z-score		

Table 3. Demographics and Descriptive Characteristics by Weight-for-length (WLZ) Change Category

		No Rapid WLZ Change	Rapid WLZ Change
Mean (SD), % (n)		67.2 (315)	32.8 (154)
Birth weight, kg (n=468)		3.2 (0.5)	3.4 (0.5)*
Gestational age, wk (n=467)		38.9 (1.5)	39.3 (1.3)*
Age at 2 mo visit, wk		9.4 (1.7)	9.0 (1.6)*
Weight 2 mo visit, kg		5.4 (0.7)	5.4 (0.8)
Female		49.5 (156)	53.3 (82)
Caregiver type (Mother)		96.2 (303)	96.8 (149)
Caregiver BMI, (n=432)		28.0 (6.5)	29.2 (6.9)
Caregiver Race/Ethnicity	Non-Hispanic Black	25.4 (80)	28.6 (44)*
	Hispanic	56.2 (177)	42.9 (66)
	Non-Hispanic White	14.9 (47)	22.7 (35)
	Non-Hispanic Other	3.5 (11)	5.8 (9)
Caregiver education (n=468)	Less than high school	28.6 (90)	20.9 (32)
	High school graduate	31.8 (100)	36.0 (55)
	Some college	20.3 (64)	27.5 (42)
	College graduate	19.4 (61)	15.7 (24)
Milk Type (at 2 and 6 months)	Formula, formula	36.5 (115)	46.8 (72)

	Mixed, formula	39.1 (123)	33.8 (52)
	Breast, mixed	7.0 (22)	7.1 (11)
	Breast, breast	17.5 (55)	12.3 (19)
Complementary foods before 4 month visit		29.5 (93)	41.6 (64)*
Tummy time < 30 min/day (n=466)		70.5 (222)	66.0 (101)
TV watching >=30 min/day		23.2 (73)	25.3 (39)
*p < 0.05 within indicated sociodemographic characteristics; WAZ – weight-for-age z-score; WLZ – weight-for-length z-score			

Table 4. Multivariate Odds of Rapid Infant Gain in Weight-for-age (WAZ) and Weight-for-length (WLZ) among infants in the Greenlight Intervention Study (n=469).

	Model 1, OR (95% CI)		Model 2, AOR (95% CI)		Model 3, AOR (95% CI)	
Variable	Rapid Gain WAZ	Rapid Gain WLZ	Rapid Gain WAZ	Rapid Gain WLZ	Rapid Gain WAZ	Rapid Gain WLZ
Milk Type						
Formula	--	--	--	--	--	--
Mixed* from 2 to 6 mos.	0.50** (0.33, 0.77)	0.68 (0.44, 1.05)	0.53** (0.35, 0.81)	0.73 (0.46, 1.13)	0.55** (0.34, 0.91)	0.71 (0.42, 1.19)
Breast 2 mos., mixed* 6 mos.	0.32 ** (0.14, 0.72)	0.80 (0.37, 1.74)	0.32** (0.14, 0.73)	0.81 (0.37, 1.79)	0.40** (0.16, 0.99)	0.82 (0.33, 2.01)
Breast, no	0.27**	0.55	0.30**	0.63	0.34**	0.53

formula 2 to 6 months	(0.15, 0.50)	(0.30, 1.00)	(0.16, 0.55)	(0.34, 1.15)	(0.17, 0.69)	(0.26, 1.07)
Early Introduction of Complementary Foods						
No			--	--	--	--
Yes			1.38 (0.92, 2.07)	1.57** (1.04, 2.37)	1.34 (0.85, 2.10)	1.61** (1.01, 2.55)
Maternal BMI						
Obese (BMI ≥ 30 kg/m^2)					--	--
Not obese (BMI <30kg/m^2)					0.91 (0.58, 1.43)	0.90 (0.57, 1.43)
Birthweight (kg)					0.76 (0.47, 1.24)	2.77** (1.65, 4.64)
Gestational Age (weeks)					0.74 (0.62, 0.87)	1.08 (0.90, 1.29)
Age at 2 mos. visit (weeks)					0.87 (0.77, 1.00)	0.84** (0.73, 0.97)
Sex, female					1.30 (0.85, 1.97)	0.94 (0.61, 1.45)
Race/ethnicity						
White, non-Hispanic					--	--

Black, non-Hispanic					1.35 (0.72, 2.55)	0.93 (0.49, 1.78)
Hispanic					1.08 (0.58, 1.99)	0.71 (0.38, 1.32)
Other					1.25 (0.42, 3.77)	1.61 (0.55, 4.75)
Tummy Time						
> 30 min/day					--	--
≤ 30 min/day					0.85 (0.53, 1.36)	0.81 (0.50, 1.31)
Active TV watching by infant						
> 30 min/day					--	--
≤ 30 min/day					0.74 (0.44, 1.24)	1.18 (0.68, 2.03)

*Mixed = formula and breast milk; **95% CI does not cross 1.0

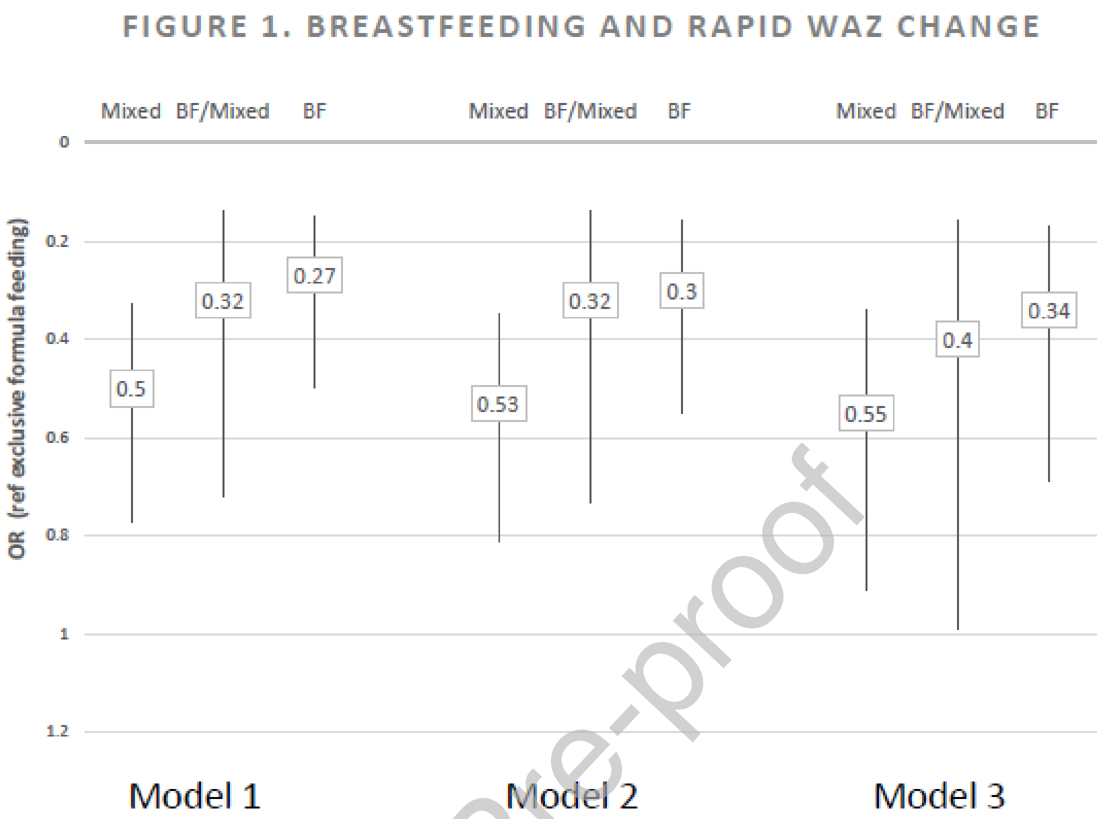

Figure 1. Odds of rapid gain in weight-for-age z-scores in the first year of life by milk feeding category in 3 models.

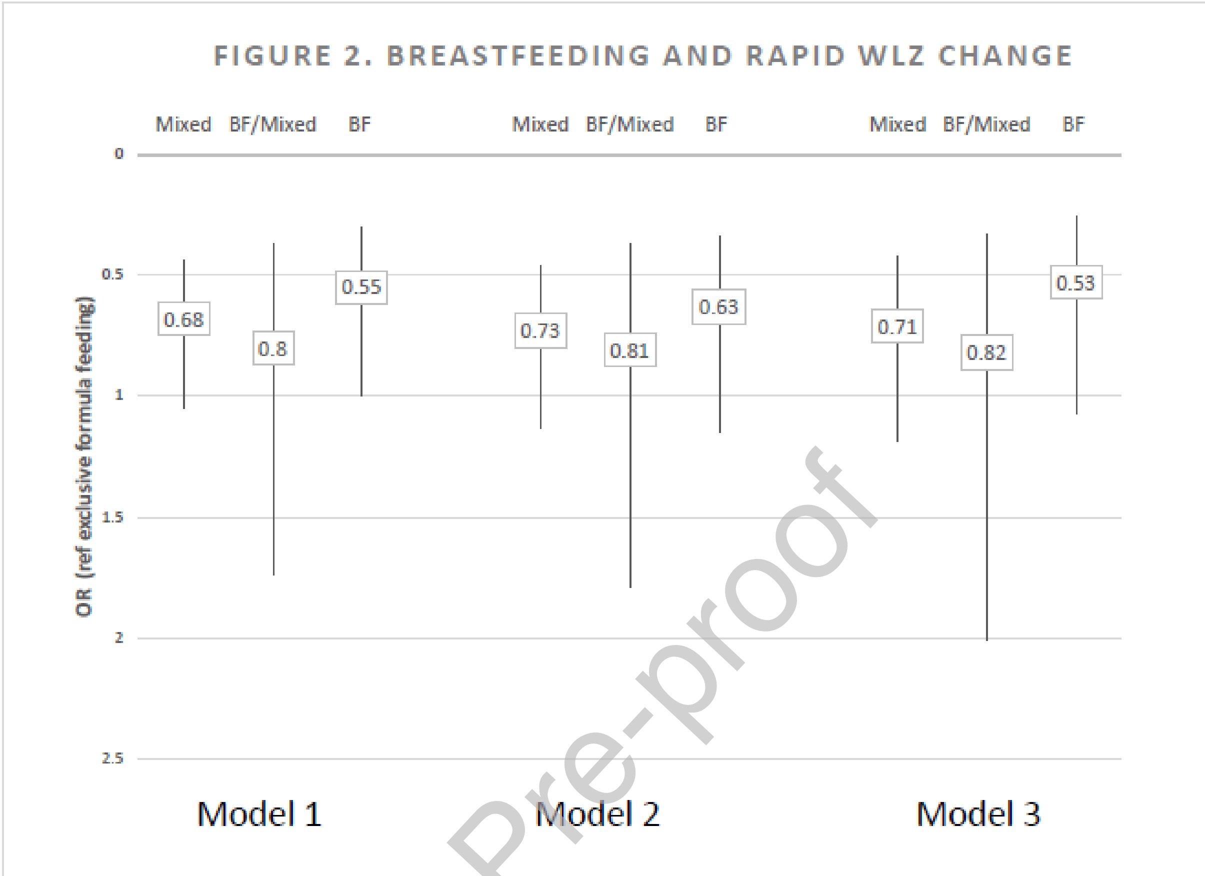

Figure 2. Odds of rapid gain in weight-for-length z-scores in the first year of life by milk feeding category in 3 models.