



# Early Weight Gain Forecasts Accelerated Eruption of Deciduous Teeth and Later Overweight Status during the First Year

Julie A. Mennella, PhD<sup>1</sup>, Ashley Reiter, MS<sup>1</sup>, Benjamin Brewer, MS<sup>2</sup>, Ryan T. Pohlig, PhD<sup>2</sup>, Virginia A. Stallings, MD<sup>3</sup>, and Jillian C. Trabulsi, PhD, RD<sup>2</sup>

**Objectives** To determine whether early diet and weight gain velocity have independent or interactive effects on deciduous teeth emergence and overweight status during the first year.

**Study design** Monthly measures of anthropometry and teeth eruption were collected during a 1-year trial (0.5–12.5 months) on formula-fed infants in which the type of randomized infant formula (cow milk or extensively hydrolyzed protein) diet significantly affected early (0.5–4.5 months) weight gain velocity. Generalized linear mixed models determined whether early diet and weight gain velocity had independent or interactive effects on timing and pattern of teeth eruption. Data from a trial on breastfed infants were used to explore effects of breast milk vs infant formula diets on teeth eruption and overweight status at 10.5 months.

**Results** Independent of infant formula diet, velocities of weight gain had direct effects on the age of first deciduous tooth ( $P < .04$ ) and number of erupted teeth over time ( $P < .002$ ). Greater velocity of weight gain from 0.5 to 4.5 months caused earlier and more frequent eruption of deciduous teeth from 4.5 to 12.5 months. Exploratory follow-up analyses on the breastfed and formula-fed diet groups found early weight gain velocity ( $P = .001$ ), but not diet or its interaction, had significant effects. Infants in the upper quartile for weight gain velocity had more primary teeth ( $P = .002$ ), and a greater proportion of them were overweight ( $P < .001$ ) at 10.5 months.

**Conclusions** Faster weight gain accretion forecasted accelerated primary teeth eruption and increased percentage of children who were overweight—risk factors for dental caries and obesity. (*J Pediatr* 2020;225:174–81).

**Trial registration** [ClinicalTrials.gov](https://clinicaltrials.gov): NCT01700205 [2012–2015] and NCT01667549 [2012–2015].

Eruption of deciduous teeth is a regulated process that typically begins during the first and ends by the third year of life.<sup>1</sup> Although this developmental process is heritable,<sup>2,3</sup> metabolic factors during pre- and postnatal life are associated with its timing.<sup>4–6</sup> Teething delays occur among children with hypothyroidism<sup>7,8</sup> or who are undernourished,<sup>9,10</sup> and earlier primary and permanent teeth eruptions occur among children who were or became obese<sup>5,11,12</sup> or were diabetic.<sup>13</sup> In a prospective, birth cohort study of infants of diverse ethnicities, infant weight gain during the first 3 months was significantly associated with earlier eruption of the first tooth, whereas teething delays were characteristic of children of older mothers or those born small for gestational age.<sup>14</sup>

Consistent with the associations between permanent teeth eruption and childhood obesity,<sup>5,11</sup> a study linked the timing of the first deciduous tooth to weight gain in infancy,<sup>14</sup> both of which are influenced by many of the same socioeconomic, nutritional, and metabolic conditions or characteristics of the mother–infant dyad.<sup>4–6,14–18</sup> Nevertheless, after adjusting for confounders, evidence has confirmed the positive association between rapid weight gain in infancy and greater weight status or adiposity later in life.<sup>15,19–22</sup> However, causal links have not been established.

We had the unique opportunity to investigate whether the type of infant diet, patterns of weight gain, or both have independent (causal) or interactive effects on the timing and pattern of deciduous teeth emergence during the first year. The data analyzed come from a randomized controlled trial (RCT) on healthy, formula-fed (FF) infants for whom the experimental diet manipulation—the type of breast milk substitute fed during the first year—produced significant differences in early weight gain velocities.<sup>23</sup> Although their weight was within the range of typically growing infants,<sup>24</sup> the group of infants fed standard cow milk formula (CMF) had significantly greater weight gain velocities (3.9 g/d greater) from 0.5 to 4.5 months than the group fed an isocaloric, extensively hydrolyzed protein

BF	Breastfed
CMF	Cow milk formula
EHF	Extensively hydrolyzed protein formula
FF	Formula fed
RCT	Randomized controlled trial

From the <sup>1</sup>Monell Chemical Senses Center, Philadelphia, PA; <sup>2</sup>University of Delaware, Newark, DE; and <sup>3</sup>Children's Hospital of Philadelphia, Division of Gastroenterology, Hepatology and Nutrition, Philadelphia, PA

Supported by National Institutes of Health grants R01HD072307, R01HD37119, and R03HD94908, from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, United States. The authors declare no conflicts of interest.

Portions of this study were presented at the Annual Meeting of the American Society of Nutrition, June 8–11, 2019, Baltimore, MD.

0022-3476/\$ - see front matter. © 2020 Elsevier Inc. All rights reserved.  
<https://doi.org/10.1016/j.jpeds.2020.06.019>

formula (EHF), due to both energy intake and loss mechanisms.<sup>23</sup> Because the infants were phenotyped monthly for incidence of primary teeth eruption and gross motor milestones, we tested the hypothesis that if early weight gain has direct, causal effects, it should be independent of the type of infant formula diet and specific to teeth eruption. In contrast, if teeth eruption is dependent on the infants' diet, then the effects of the infant formula group should be independent of or interact with trajectories of early weight gain. Anthropometric and teething data collected during a trial on breastfed (BF) infants,<sup>25</sup> most of whom never were fed infant formula and were breastfed for at least 10.5 months, were included to explore the effects of breast milk diet on primary teeth eruption, but at the age of 10.5 months only.

## Methods

The primary analyses were conducted on data from FF infants who participated in a RCT on the effects of infant formula diet on growth and energy balance from 0.5 to 12.5 months ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01700205) NCT01700205)<sup>23</sup>. Infants (N = 113) were randomized to be fed either CMF (Enfamil; Mead Johnson Nutrition; Evansville, Indiana) or an isocaloric EHF (Nutramigen; Mead Johnson Nutrition) for the first year. Each month, infants were weighed and measured in triplicate by research personnel certified in standard anthropometric techniques and who used calibrated pediatric scales (Scale-Tronix, White Plains, New York) and stadiometers (Harpenden Infantometer 702; Crymych, Dyfed, United Kingdom) that were accurate to 0.001 kg and 0.1 cm, respectively. Anthropometric data were normalized to z scores using World Health Organization growth standards,<sup>24</sup> and the velocities of weight (g/d) and length (cm/d) accretion were calculated by dividing the change of weight in grams or length in centimeters by the change of age in days<sup>26</sup> during 3 time periods: 0.5-4.5 months, >4.5-8.5 months, and >8.5-12.5 months.

For the exploratory follow-up analyses, we included data from a group of BF infants (N = 97) who participated in a RCT investigating the effects of maternal diet from 0.5 to 4.5 months on infants' vegetable acceptance after weaning ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01667549) NCT01667549).<sup>25</sup> The timing of the 3-day vegetable acceptance test varied because it depended on when mothers chose to introduce complementary solids. However, dyads returned for follow-up visits, one of which occurred at 10.5 months. Using methods identical to those used for the FF infants, anthropometric measures were obtained monthly from 0.5 to 4.5 months and then again at 10.5 months.

Inclusion criteria encompassed, for both trials, infants born at term (37-42 weeks) with birth weights within a range considered typical (2500-4500 g),<sup>27</sup> and, for the BF trial only, mothers who intended to exclusively breastfeed (with no formula supplementation) for at least 4 months. Mothers who had gestational diabetes or infants with congenital malformations, systemic or congenital infections, or family history of atopy were excluded. The Office of Regulatory Affairs at

the University of Pennsylvania approved all procedures, and informed consent was obtained from each woman prior to study entry.

The intent-to-treat RCT cohort of 113 FF infants (CMF group = 59; EHF group = 54) was diverse in race/ethnicity, education status, and household income (**Table I**; available at [www.jpeds.com](http://www.jpeds.com)),<sup>23</sup> all of which reflect the urban setting in which they live, the county of Philadelphia.<sup>28</sup> There were no significant differences in birth weights between the CMF (mean: 3292 g, 3181-3402) and EHF (mean: 3304 g, 95% CI 3187-3421;  $P = .87$ ) groups. Neither were there significant group differences in baseline anthropometric characteristics, age of introduction to complementary foods, or energy intake from complementary foods up to 11.5 months.<sup>23</sup> However, as we reported previously<sup>23</sup> and as shown in **Table I**, the type of infant formula that was fed had significant effects on early weight gain velocity from 0.5 to 4.5 months ( $P = .003$ ): the CMF group gained 29.5 g/d (95% CI 28.0-31.0), whereas the EHF group gained 25.7 g/d (95% CI 23.7-27.8). Weight gain velocity from 4.5 to 12.5 months and length gain velocity during the 3 time periods were not statistically different between the 2 infant formula groups (**Table I**). As expected,<sup>29</sup> the comparator group of BF infants (N = 97) differed significantly from the FF group in almost every outcome measured (**Table I**) except velocities of weight gain from 0.5 to 4.5 months (mean: 26.2 g/d, 95% CI 24.8-27.7).

By design, the 2 trials resulted in groups that were dichotomous in infant feeding histories: the FF infants were not fed breast milk and the BF infants never or rarely fed infant formula during the time period (0.5-4.5 months) when velocities of weight and length gain were determined, or thereafter. Although the FF groups were exclusively formula fed, breast milk was the exclusive or predominant source of nourishment for the first 4.5 months for the BF group. After 4.5 months, the majority of BF infants continued to be breastfed: 81% were still breastfeeding and 62% had never been fed infant formula when 10.5 months of age.

For the intent-to-treat FF groups, mothers were queried and infants were observed monthly by study personnel to verify the following milestones: crawling on hands and knees, sitting up independently, standing without assistance, walking with assistance, and the number and location of each tooth, if any. We defined tooth eruption as its apparent penetration through the overlying gingiva, which was verified by visual inspection of the oral cavity. From these data, we determined the timing of each milestone, defined as the age at the study visit during which it was first observed, and the number, location (eg, top, bottom) and type (ie, incisor, molar) of teeth at each monthly visit from 0.5 to 12.5 months. For the BF group, identical methods were used to determine the number of erupted teeth at monthly intervals from 0.5 to 4.5 months and then at 10.5 months.

Descriptive statistics describing characteristics of the FF and BF infant samples used in the primary and follow-up analyses or follow-up analysis only, respectively, are reported.

A  $2 \times 3$  mixed design ANOVA compared groupings of FF infants based on the age of the first deciduous tooth with the number and types of erupted teeth at 12.5 months.

To conduct the primary analyses and test the hypotheses, the gradual progression from exploratory data analysis for identifying covariates to modeling proceeded in a highly procedural manner. First, residuals of all variables were tested for normality using the Shapiro–Wilk test. Second, bivariate relationships of age of first tooth, age of first occurrence of gross motor milestones, and number of primary teeth at 12.5 months with maternal (eg, age, education, body mass index at enrollment, household income) or infant (eg, sex, race/ethnicity, birth weights, anthropometric measures; weight and length gain velocities) characteristics, listed in **Table I**, were examined using *t* tests for group comparisons and Pearson correlations for continuous associations.

Variables that were significant in the bivariate relationships were then included in the full factorial general linear models on the outcomes of age of first tooth eruption and age of first occurrence of each gross motor milestone, and in generalized linear mixed models on the outcome of cumulative number of teeth over time using a Poisson distribution and log link function. A random intercept and random effect for time were used so that trajectories would be permitted to vary across subjects.

For the exploratory follow-up analyses, the sample consisted of the FF infants from the primary analysis plus the group of BF infants. The cross-sectional outcome of number of erupted teeth at 10.5 months was tested using the model established from the bivariate relationships. Lastly, exploratory analysis also evaluated groupings of infants based on overweight status, defined as weight-for-length *z* score >85th percentile (weight-for-length *z* score >1.0),<sup>30</sup> as an additional outcome at 10.5 and 12.5 months.

Assumptions for all analyses were evaluated and if violated, remedied appropriately. The nominal alpha (0.05) was used for determining significance. Significant interactions among categorical variables were post-hoc tested using the Fisher least significance difference tests. Significant interactions of continuous and categorical variables were followed up by splitting the continuous variable into meaningful groups to illustrate findings. Data were analyzed using Stata/IC, version 14.2 (Stata Corp., College Station, Texas), Statistica version 13.3 (TIBCO, Tulsa, Oklahoma), and R, version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria), with a significance criterion set at  $P < .05$ , and were expressed as mean (SEM) in **Table I** or mean (95% CI) otherwise.

## Results

Study retention was 81% ( $N = 92$ ) for the FF infants who had data for weight gain velocity (0.5–4.5 months) and 73% ( $N = 83$ ) had data for teeth outcomes at 12.5 months (**Figure 1**; available at [www.jpeds.com](http://www.jpeds.com)). None of the FF infants erupted a tooth before 4.5 months, and all but 3 erupted a tooth by 12.5 months. In all cases, the first tooth was a bottom or top incisor. Grouping infants by the age

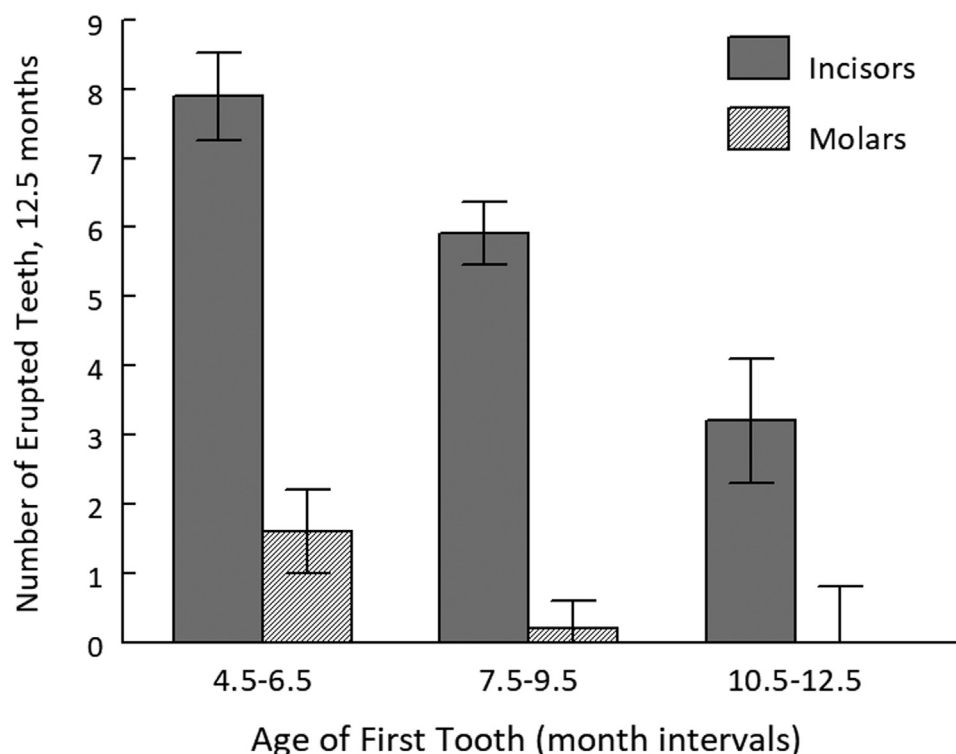
when their first primary tooth erupted (ie, 4.5–6.5 months; 7.5–9.5 months; 10.5–12.5 months) and then analyzing the numbers and types (incisors, molars) of erupted teeth at 12.5 months revealed significant effects of age group ( $P < .001$ ), tooth type ( $P < .001$ ), and age group  $\times$  tooth type interaction ( $P < .001$ ). As shown in **Figure 2**, the group of infants who erupted their first primary tooth the earliest (4.5–6.5 months) had significantly more incisors than the 7.5- to 9.5-month group, who, in turn, had more erupted incisors than the 10.5- to 12.5-month group (all  $P < .001$ ). They also erupted more molars by 12.5 months than the other 2 groups (all  $P < .001$ ), who were not different from each other ( $P = .63$ ).

The timing of first deciduous tooth and the number of erupted teeth at the end of the trial differed based on infant formula group. CMF group had more erupted teeth at 12.5 months (mean: 7.1, 95% CI 6.1–8.2) than did the EHF group (mean 5.5, 95% CI 4.7–6.4;  $P = .02$ ), and they tended to erupt their first tooth at an earlier age (mean: 7.7 months, 95% CI 7.2–8.2) than the EHF group (mean: 8.3 months, 95% CI 7.8–8.9;  $P = .08$ ). In addition, bivariate correlations revealed that weight gain velocity from 0.5 to 4.5 months, but not during later months (>4.5–8.5; >8.5–12.5 months), negatively correlated with age at first tooth ( $P = .02$ ) and positively correlated with number of erupted teeth at 12.5 months ( $P = .03$ ). No other dyad characteristics (listed in **Table I**) or velocity of gains in length significantly correlated with these teething outcomes. Thus, the only significant relationships identified in our bivariate analyses were early weight gain velocity and infant formula group.

In contrast to the timing of first tooth eruption, there were no significant differences between the infant formula groups in the age when infants began sitting independently ( $P = .95$ ), crawling ( $P = .20$ ), standing without assistance ( $P = .08$ ), or walking with assistance ( $P = .40$ ). In addition, early weight gain velocity was not significantly related to the timing of any of these gross motor milestones (ie, sitting [ $P = .67$ ]; crawling [ $P = .58$ ]; standing without assistance [ $P = .82$ ]; walking with assistance [ $P = .12$ ]).

**Table II** summarizes the ANCOVA model findings on the effects of infant formula group, weight gain velocity, and their interaction on the timing of the developmental milestones. When early weight gain velocity was included in the model, infant formula group (CMF, EHF) was no longer significantly associated with age of first tooth ( $P = .24$ ), nor was their interaction ( $P = .34$ ), but early weight gain velocity was significant ( $P = .04$ ). Infant formula treatment group, early weight gain velocity, nor their interaction had any significant effect in any model involving the timing of gross motor milestones.

For the analysis on the cumulative number of erupted teeth from 4.5 to 12.5 months, the generalized linear mixed models found no significant effects of infant formula group ( $P = .17$ ) or any of its interactions (group  $\times$  time interaction,  $P = .25$ ; group  $\times$  velocity interaction  $P = .27$ ; group  $\times$  velocity  $\times$  time interaction,  $P = .32$ ). Rather, early weight gain velocity ( $\beta = 0.06$ ; 95% CI 0.023–0.101;



**Figure 2.** Association between grouping based on age at first tooth eruption and numbers and type (incisors, molars) of erupted deciduous teeth at 12.5 months (mean ± 95% CI) among FF infants (age group × tooth type interaction;  $P < .001$ ).

$P = .002$ ), time ( $\beta = 0.542$ ; 95% CI 0.423-0.660;  $P < .001$ ), and their interaction ( $\beta = -0.005$ , 95% CI  $-0.009, -0.001$ ;  $P = .020$ ) were significant. This interaction suggests that greater velocity of weight gain during the first 4.5 months accelerates the eruption of teeth. Over time, this acceleration will become less pronounced because all will eventually erupt the same number of deciduous teeth.

To further probe this significant interaction, FF infants were categorized based on weight gain velocities into 3 groups. Those in the >75th percentile group gained >30.7 g/d from 0.5 to 4.5 months, whereas the 25th-75th percentiles group gained 23.2-30.7 g/d and the <25th percentile group gained <23.2 g/d. As shown in Figure 3, FF infants in the >75th percentile group erupted more teeth over time

than the others ( $P < .02$ ). In addition, a greater proportion of them were categorized as overweight at 12.5 months (80.0% overweight;  $N = 20$ ) compared with the 25th-75th (28% overweight;  $N = 43$ ) and <25th (10% overweight;  $N = 20$ ) percentile ( $P < .001$ ) groups.

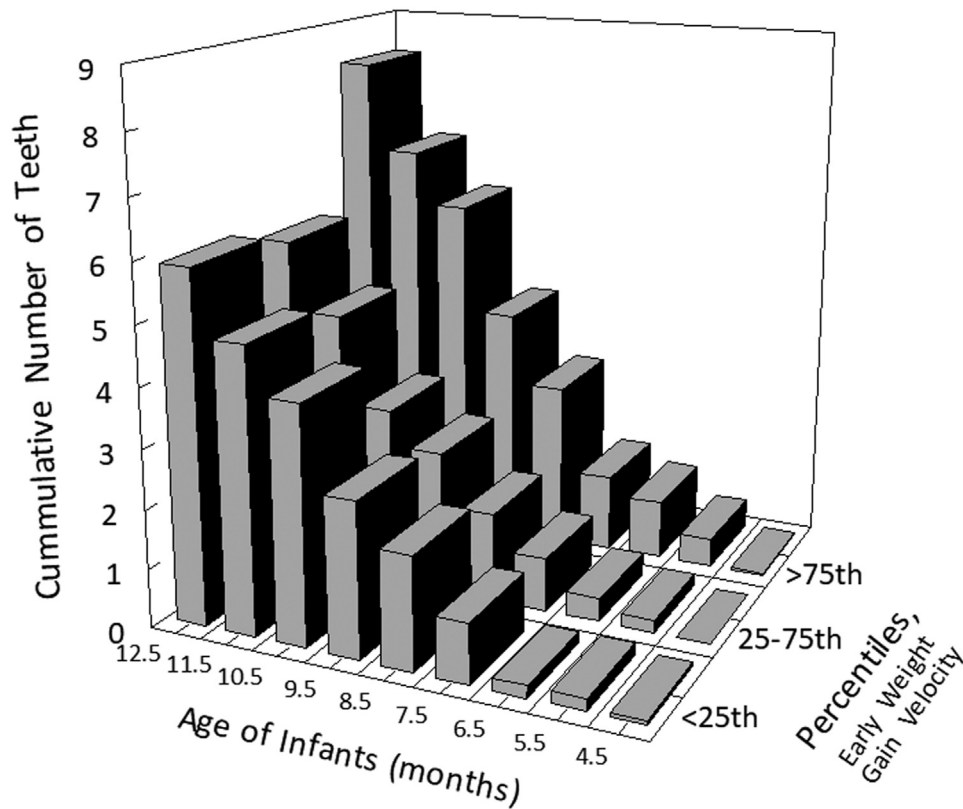
As shown in Figure 1, 80% ( $N = 78$ ) of the BF and 75% ( $n = 85$ ) of the FF infants were still enrolled at 10.5 months. Although only 1 BF infant erupted a tooth by 4.5 months, 94% of the BF infants and 91% of the FF infants had erupted at least 1 tooth by 10.5 months. The distribution of the total number of teeth at 10.5 months was non-normal; therefore, a Poisson regression with logit link function was used in lieu of an ANCOVA. We found no significant effect of diet group ( $P = .17$ ) or diet

**Table II. Timing of developmental milestones: effects of infant formula treatment group with significant covariate—early weight gain velocity (0.5-4.5 months)**

Outcomes, age in mo	P value*		
	Infant formula treatment group	Weight gain velocity	Infant formula treatment group × weight gain velocity
First tooth eruption†	.24	.04	.34
Sits up	.36	.74	.35
Crawls	.17	.15	.11
Walks with assistance	.71	.53	.60
Stands without assistance	.13	.17	.22

\*P values for effects of infant formula treatment group (CMF, EHF), early weight gain velocity (0.5-4.5 months), and their interaction from ANCOVA. All outcomes normally distributed.

†Three infants had no teeth at 12.5 months.



**Figure 3.** Cumulative number of teeth (y-axis) by percentile category of early weight gain velocity (z-axis) from 4.5 to 12.5 months (x-axis) among FF infants. Generalized linear mixed models revealed significant weight gain velocity ( $P = .002$ ), time ( $P < .001$ ), and velocity  $\times$  time interaction ( $P = .02$ ).

group  $\times$  weight gain velocity interaction ( $P = .15$ ) on the number of teeth. However, the main effect of early weight gain velocity was significant ( $P < .001$ ). The results remained the same when we compared the BF group with each FF (CMF, EHF) group separately.

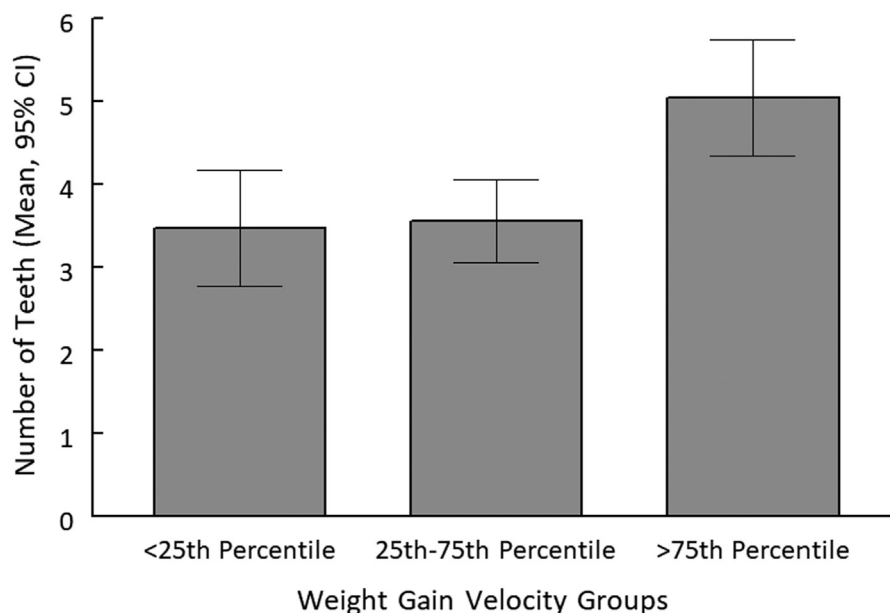
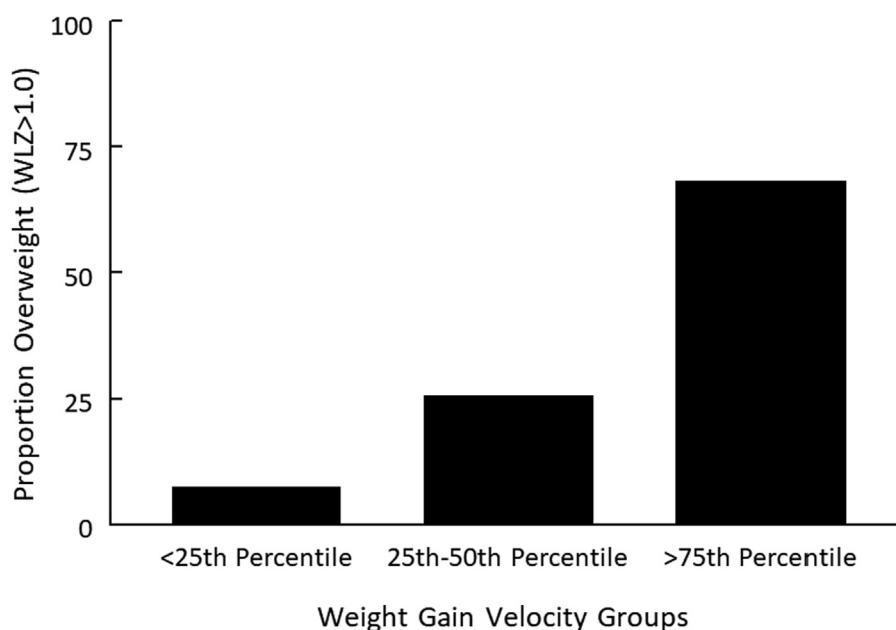
We used the same procedure described previously to further probe this significant interaction; FF and BF infants were categorized into 3 groups based on early weight gain velocities (Figure 4). The group in the >75th percentile for early weight gain velocity ( $N = 41$ ) had more erupted primary teeth ( $P = .002$ ; Figure 4, A), and a greater proportion of them were overweight ( $P < .001$ ; Figure 4, B) at 10.5 months compared with the <25th ( $N = 40$ ) and 25th-75th ( $N = 82$ ) percentile groups.

## Discussion

The present findings provide evidence that the timing and pattern of primary teeth eruption during the first year was directly affected by early rapid weight gain and forecasted overweight status several months later. Variation in how fast infants gained weight during the first 4.5 months, but not how fast they grew in length, had significant effects on the age of the first deciduous tooth, which did not generalize

to the age of the first occurrence of several gross motor milestones, findings that were consistent with previous associational studies.<sup>14,31</sup> In addition to earlier eruption of the first tooth, greater velocity of weight gain from 0.5 to 4.5 months caused more frequent eruption of deciduous teeth from 4.5 to 12.5 months.

For the primary analyses, we focused on data collected during a trial in which FF infants who were randomized to be fed CMF had greater velocities of early weight gain than those randomized to be fed EHF.<sup>23</sup> When we focused solely on differences in the eruption of deciduous teeth between the randomized groups, we found that the CMF group tended to erupt their first primary tooth earlier and had more teeth at 1 year than did those randomized to EHF. However, when the statistical models also factored in early weight gain velocity and its interaction with infant formula group, infant formula group did not explain the variation in the timing of the first tooth or cumulative teeth eruption during the first year. Rather, independent of formula group, weight gain velocity occurring before any FF infant erupted a tooth was significantly related to both the timing and patterning of primary teeth eruption. In other words, the effects of being fed different types of infant formulas (CMF, EHF) on teething were secondary to their differential effects on weight gain velocity.

**A** Deciduous Teeth, 10.5 months**B** Overweight, 10.5 months

**Figure 4.** **A**, Number of erupted deciduous teeth (mean  $\pm$  95% CI) and **B**, proportion of infants who were overweight at 10.5 months, by percentile category of early weight gain velocity among FF and BF infants. Greater weight gain velocity (>75th percentiles) associated with more deciduous teeth ( $P = .001$ ) and greater proportion of overweight children ( $P < .001$ ).

Unlike retrospective and prospective observational studies, which cannot elucidate causal relationships, the use of an RCT design in the FF study provided a longitudinal perspective and thus enabled the determination of the effects of infant formula diet, early weight gain velocity, and its interaction, whereas other variables were randomly distributed. The infant formula treatment

groups did not differ in mother–infant characteristics known to be associated with the timing of teeth eruption (eg, maternal age, prepregnancy weight gain, race/ethnicity, birth weight, maternal body mass index).<sup>4-6,14,18</sup> Although none of these potential confounders related to the teething outcomes and thus were not included in the model, early weight gain velocity—a known associate in the timing of

primary dentition eruption<sup>14</sup>—predicted the number of erupted teeth over the first year and was independent of infant formula treatment group.

Further support of the hypothesis that early weight gain velocity impacts later teeth eruption and is independent of diet came from our follow-up exploratory analysis on the FF group studied in the primary analysis and a group of BF infants for whom breastfeeding was exclusive or predominant for the first 4.5 months and for the majority continued for more than 10 months (and without infant formula supplementation). Independent of diet group, early weight gain velocity significantly associated with number of erupted teeth by 10.5 months. Further, BF and FF infants in the >75th percentile for early weight gain velocity not only had more erupted teeth but also more than two-thirds of them were categorized as overweight at this time.

Although the BF and FF groups were dichotomous in early feeding histories, we acknowledge several limitations. Teething data for the BF group were available for only one age (10.5 months) and did not include the timing of the eruption of the first deciduous tooth or other developmental milestones. The small sample size did not allow us to factor in the many baseline maternal and infant characteristics that significantly differed between the BF and FF groups and are due, in part, to the psychosocial, economic, and demographic influences on mothers' decision to breastfeed or formula feed.<sup>32</sup> Nevertheless, when the BF infants were included in the exploratory follow-up analyses, the findings were consistent with those obtained from the randomized FF groups alone, suggesting that it is not diet per se that causes changes teeth eruption, it is how the infants respond to the diet in terms of weight gain. Further, the period of rapid weight gain occurred before the eruption of the first deciduous tooth and during the formation and mineralization of the crowns of developing teeth.<sup>33</sup>

Taken together with the rich findings from prospective and retrospective studies, the present findings suggest that metabolic factors during early postnatal life can accelerate the cascade of events surrounding primary teeth eruption.<sup>4,5,7-9,11,13,14</sup> Both acceleration in deciduous teeth emergence and greater overweight status at the end of the first year are of concern because of their associations with increased risk for dental caries<sup>34</sup> and obesity<sup>35</sup>—prevalent diseases of childhood. Whether RCT interventions that successfully reduce rapid infancy weight gain<sup>36</sup> also alter the timing and patterning of primary teeth emergence and reduce these risks is an important hypothesis yet to be explored. ■

*We acknowledge the expert technical assistance of Loma Inamdar, MS, Naomi Pressman, MS, RD, and Loran Daniels, MS, and we thank Drs Deborah Young-Hyman and Ann Griffen for valuable discussions and insights.*

Submitted for publication Feb 3, 2020; last revision received Jun 2, 2020; accepted Jun 5, 2020.

Reprint requests: Julie A. Mennella, PhD, 3500 Market St, Philadelphia, PA 19104-3308. E-mail: mennella@monell.org

## Data Statement

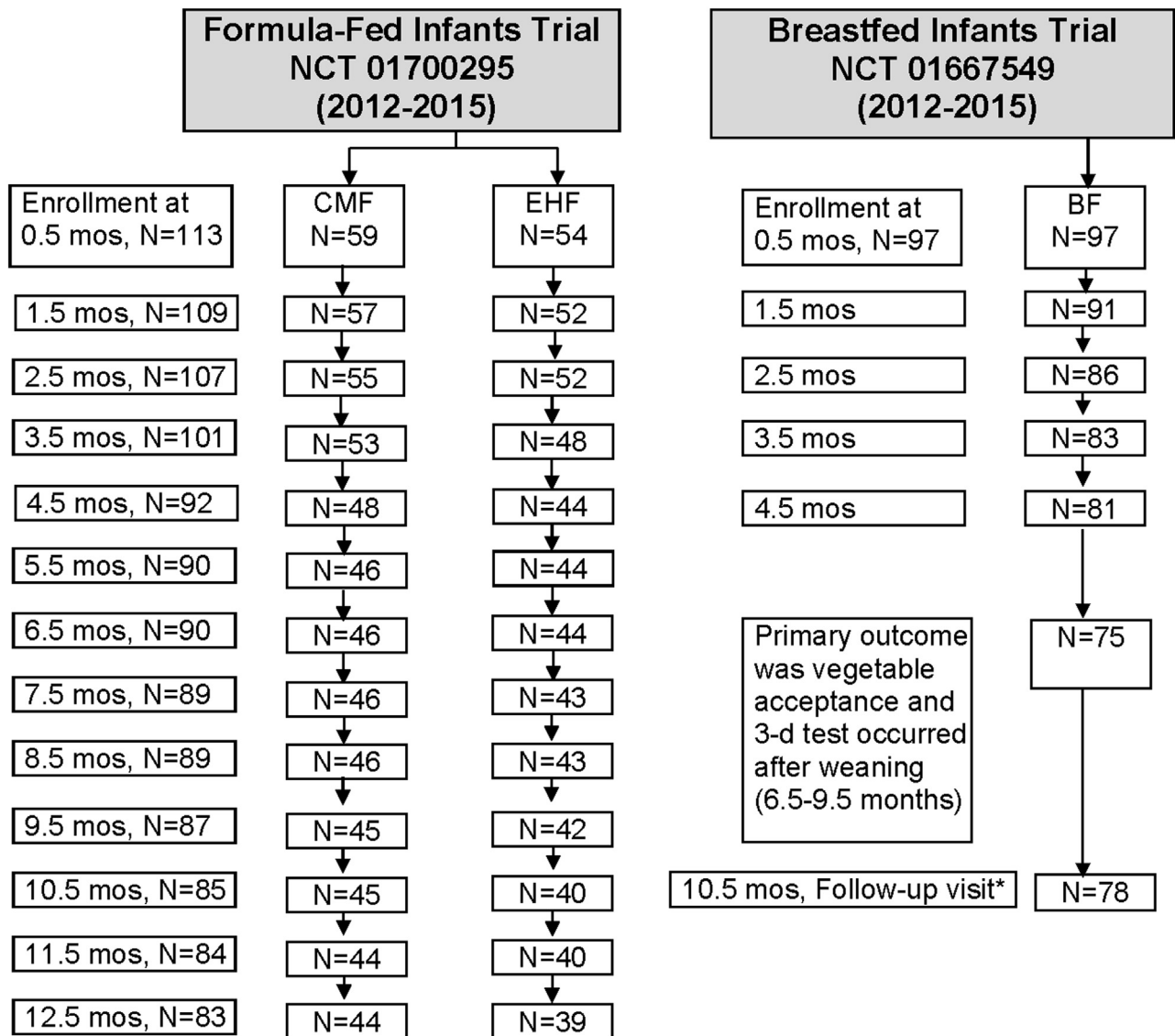
Data sharing statement available at [www.jpeds.com](http://www.jpeds.com).

## References

- Pavcin IS, Dumancic J, Badel T, Vodanovic M. Timing of emergence of the first primary tooth in preterm and full-term infants. *Ann Anat* 2016;203:19-23.
- Hughes TE, Bockmann MR, Seow K, Gotjamanos T, Gully N, Richards LC, et al. Strong genetic control of emergence of human primary incisors. *J Dent Res* 2007;86:1160-5.
- Fatemifar G, Hoggart CJ, Paternoster L, Kemp JP, Prokopenko I, Horikoshi M, et al. Genome-wide association study of primary tooth eruption identifies pleiotropic loci associated with height and craniofacial distances. *Hum Mol Genet* 2013;22:3807-17.
- Ntani G, Day PF, Baird J, Godfrey KM, Robinson SM, Cooper C, et al. Maternal and early life factors of tooth emergence patterns and number of teeth at 1 and 2 years of age. *J Dev Orig Health Dis* 2015;6:299-307.
- Must A, Phillips SM, Tybor DJ, Lividini K, Hayes C. The association between childhood obesity and tooth eruption. *Obesity* 2012;20:2070-4.
- Zadzinska E, Sitek A, Rosset I. Relationship between pre-natal factors, the perinatal environment, motor development in the first year of life and the timing of first deciduous tooth emergence. *Ann Hum Biol* 2016;43:25-33.
- Loevy HT, Aduss H, Rosenthal IM. Tooth eruption and craniofacial development in congenital hypothyroidism: report of case. *J Am Dent Assoc* 1987;115:429-31.
- Reuland-Bosma W, Reuland MC, Bronkhorst E, Phoa KH. Patterns of tooth agenesis in patients with Down syndrome in relation to hypothyroidism and congenital heart disease: an aid for treatment planning. *Am J Orthod Dentofacial Orthop* 2010;137:584.e1-9.
- Gaur R, Kumar P. Effect of undernutrition on deciduous tooth emergence among Rajput children of Shimla District of Himachal Pradesh, India. *Am J Phys Anthropol* 2012;148:54-61.
- Holman DJ, Yamaguchi K. Longitudinal analysis of deciduous tooth emergence: IV. Covariate effects in Japanese children. *Am J Phys Anthropol* 2005;126:352-8.
- Nicholas CL, Kadavy K, Holton NE, Marshall T, Richter A, Southard T. Childhood body mass index is associated with early dental development and eruption in a longitudinal sample from the Iowa Facial Growth Study. *Am J Orthod Dentofacial Orthop* 2018;154:72-81.
- Fatemifar G, Evans DM, Tobias JH. The association between primary tooth emergence and anthropometric measures in young adults: findings from a large prospective cohort study. *PLoS One* 2014;9:e96355.
- Lal S, Cheng B, Kaplan S, Softness B, Greenberg E, Goland RS, et al. Accelerated tooth eruption in children with diabetes mellitus. *Pediatrics* 2008;121:e1139-43.
- Un Lam C, Hsu CS, Yee R, Koh D, Lee YS, Chong MF, et al. Influence of metabolic-linked early life factors on the eruption timing of the first primary tooth. *Clin Oral Investig* 2016;20:1871-9.
- Zheng M, Lamb KE, Grimes C, Laws R, Bolton K, Ong KK, et al. Rapid weight gain during infancy and subsequent adiposity: a systematic review and meta-analysis of evidence. *Obes Rev* 2018;19:321-32.
- Wijlaars LP, Johnson L, van Jaarsveld CH, Wardle J. Socioeconomic status and weight gain in early infancy. *Int J Obes (Lond)* 2011;35:963-70.
- Mihrshahi S, Battistutta D, Magarey A, Daniels LA. Determinants of rapid weight gain during infancy: baseline results from the NOURISH randomised controlled trial. *BMC Pediatr* 2011;11:99.
- Wu H, Chen T, Ma Q, Xu X, Xie K, Chen Y. Associations of maternal, perinatal and postnatal factors with the eruption timing of the first primary tooth. *Sci Rep* 2019;9:2645.
- Singhal A. Long-term adverse effects of early growth acceleration or catch-up growth. *Ann Nutr Metab* 2017;70:236-40.
- Fabricius-Bjerre S, Jensen RB, Faerch K, Larsen T, Molgaard C, Michaelsen KF, et al. Impact of birth weight and early infant weight

- gain on insulin resistance and associated cardiovascular risk factors in adolescence. *PLoS One* 2011;6:e20595.
21. 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* 2009;123:1177-83.
  22. Wang G, Johnson S, Gong Y, Polk S, Divall S, Radovick S, et al. Weight gain in infancy and overweight or obesity in childhood across the gestational spectrum: a prospective birth cohort study. *Sci Rep* 2016;6:29867.
  23. Mennella JA, Inamdar L, Pressman N, Schall J, Papas MA, Schoeller D, et al. Type of infant formula increases early weight gain and impacts energy balance: a randomized controlled trial. *Am J Clin Nutr* 2018;108:1015-25.
  24. WHO Multicentre Growth Reference Study Group. WHO child growth standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development. Geneva (Switzerland): WHO; 2006.
  25. Mennella JA, Daniels LM, Reiter AR. Learning to like vegetables during breastfeeding: a randomized clinical trial of lactating mothers and infants. *Am J Clin Nutr* 2017;106:67-76.
  26. Butte NF, Wong WW, Hopkinson JM, Smith EO, Ellis KJ. Infant feeding mode affects early growth and body composition. *Pediatrics* 2000;106:1355-66.
  27. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Division of Vital Statistics. Births: Final data for 2018. *Natl Vital Stat Rep* 2019;60:1-46.
  28. Pew Charitable Trusts [homepage on the internet]. Philadelphia 2019 The State of the City. Philadelphia. PA: The Trusts; 2019 [updated 2019 April 30]. <https://www.pewtrusts.org/en/research-and-analysis/reports/2019/04/11/philadelphia-2019>. Accessed February 20, 2020.
  29. Hendricks K, Briefel R, Novak T, Ziegler P. Maternal and child characteristics associated with infant and toddler feeding practices. *J Am Diet Assoc* 2006;106(1 suppl 1):S135-48.
  30. Roy SM, Spivack JG, Faith MS, Chesi A, Mitchell JA, Kelly A, et al. Infant BMI or weight-for-length and obesity risk in early childhood. *Pediatrics* 2016;137:e20153492.
  31. Shaweesh AI, Al-Batayneh OB. Association of weight and height with timing of deciduous tooth emergence. *Arch Oral Biol* 2018;87:168-71.
  32. Mercier RJ. Identifying risk factors for not breastfeeding: the interaction of race and economic factors: A case for seeking a local perspective. *Breastfeed Med* 2018;13:544-8.
  33. AlQahtani SJ, Hector MP, Liversidge HM. Brief communication: the London atlas of human tooth development and eruption. *Am J Phys Anthropol* 2010;142:481-90.
  34. Heng C. Tooth decay is the most prevalent disease. *Fed Pract* 2016;33:31-3.
  35. 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* 2005;331:929.
  36. Savage JS, Birch LL, Marini M, Anzman-Frasca S, Paul IM. Effect of the INSIGHT responsive parenting intervention on rapid infant weight gain and overweight status at age 1 year: a randomized clinical trial. *JAMA Pediatr* 2016;170:742-9.





**Figure 1.** Trial profiles: Flow of participants from enrollment at 0.5 months to 12.5 months in the trial on FF infants and to 10.5 months in the trial on BF infants. \*Three mother–infant dyads in the BF group who did not complete the primary outcome visits (vegetable acceptance test) returned for follow-up at 10.5 months. *NCT*, National Clinical Trial.

**Table I.** Dyad characteristics by infant formula treatment groups and by diet groups

Characteristics*	Infant formula treatment groups			Diet groups		FF vs BF, P value <sup>†</sup>
	CMF	EHF	CMF vs EHF, P value <sup>†</sup>	Combined FF	BF	
Number of dyads enrolled	59	54		113	97	
Infants						
Female, n (%)	28 (47%)	29 (54%)	.51	57 (50%)	50 (52%)	.87
Race, n (%)			.14			<.001
Black	35 (59%)	35 (65%)		70 (62%)	31 (32%)	
White	17 (29%)	8 (15%)		25 (22%)	49 (51%)	
Other/more than 1 race	7 (12%)	11 (20%)		18 (16%)	17 (18%)	
Anthropometry at 0.5 mo, z scores						
Weight for age, 0.5 mo	-0.36 ± 0.11	-0.25 ± 0.11	.49	-0.30 ± 0.1	0.11 ± 0.1	<.001
Length for age, 0.5 mo	-0.49 ± 0.14	-0.46 ± 0.14	.91	-0.48 ± 0.1	0.11 ± 0.1	<.001
Weight for length, 0.5 mo	-0.26 ± 0.12	-0.12 ± 0.13	.43	-0.19 ± 0.1	-0.26 ± 0.1	.62
Weight gain velocity, g/d <sup>‡</sup>						
0.5-4.5 mo	29.5 ± 0.9	25.7 ± 0.9	.003	27.7 ± 0.7	26.2 ± 0.1	.10
>4.5-8.5 mo	15.9 ± 0.6	15.2 ± 0.7	.46			
>8.5-12.5 mo	9.0 ± 0.5	10.1 ± 0.5	.13			
Length gain velocity, cm/d <sup>‡</sup>						
0.5-4.5 mo	0.103 ± 0.002	0.103 ± 0.002	.97	0.102 ± 0.001	0.095 ± 0.001	<.001
>4.5-8.5 mo	0.056 ± 0.002	0.053 ± 0.002	.13			
>8.5-12.5 mo	0.043 ± 0.002	0.042 ± 0.002	.76			
Mothers						
Age, y	27.1 ± 0.7	27.0 ± 0.8	.89	27.1 ± 0.5	30.8 ± 0.5	<.001
Body mass index at 0.5 mo, kg/m <sup>2</sup>	30.7 ± 1.0	31.4 ± 1.1	.61	31.1 ± 0.7	28.3 ± 0.7	.008
Primiparous, n (%)	12 (20%)	11 (20%)	1.00	23 (20%)	33 (34%)	.03
Household income, n (%)			.70			<.001
<\$35 000	44 (76%)	37 (70%)		81 (73%)	40 (41%)	
\$35 000-75 000	5 (9%)	7 (13%)		12 (11%)	21 (22%)	
>\$75 000	9 (15%)	9 (17%)		18 (16%)	36 (37%)	
Education level, n (%)			.21			<.001
Primary school	12 (20%)	5 (9%)		17 (15%)	5 (5%)	
High school/technical school	32 (54%)	36 (67%)		68 (60%)	32 (33%)	
College degree or greater	15 (26%)	13 (24%)		28 (25%)	60 (62%)	

Values are mean ± SEM or n (%).

BMI, body mass index.

\*Some values do not sum to total because of missing data: gestational weight gain (FF: n = 111; BF: n = 96); maternal BMI (FF: n = 112; BF: n = 96); household income (FF: n = 111).

†P values for main effect of infant formula treatment (CMF vs EHF) or diet (FF vs BF) groups for categorical variables obtained from Pearson  $\chi^2$  tests or 1-way ANOVA for continuous variables with group as between-subjects factor. Comparison of CMF and EHF published previously.<sup>23</sup>

‡Comparisons of weight and length gain velocities between BF and FF groups could only be made for the 0.5- to 4.5-month time period, because these data were not available for subsequent time periods for the BF group.