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Abbreviations used: CF (Complementary foods), EDEN (Study of pre- and early postnatal determinants of child health and development), FFQ (Food frequency questionnaire), PCA (principal component analysis)

What is already known about this subject

- While meta-analyses reported small protective effects of breastfeeding on obesity risk, residual confounding remained an issue.
- Whereas breastfeeding and complementary feeding practices are strongly related, they are often analyzed as independent determinants of growth.

What this study adds

- A feeding pattern characterized by "Long breastfeeding, later main meal food introduction and use of home-made foods" is related to slower height and weight growth during the first year and faster height and weight growth from 1 to 5 years, but these associations were mostly driven by breastfeeding duration
- A feeding pattern characterized by "Later dairy products introduction and use of ready-prepared baby foods" is related to a faster height growth from 1 to 3 years.

Abstract

Objectives: As early-life feeding experiences may influence later health, we aimed to examine relations between feeding patterns over the first year of life and child's growth in the first 5 years of life. **Methods:** Our analysis included 1022 children from the EDEN mother-child cohort. Three feeding patterns were previously identified, i.e. "Later dairy products introduction and use of ready-prepared baby foods" (Pattern-1), "Long breastfeeding, later main meal food introduction and use of home-made foods" (Pattern-2), "Use of ready-prepared adult foods" (Pattern-3). Associations between the feeding patterns and growth (weight, height and BMI) were analyzed by multivariable linear regressions. Anthropometric changes were assessed by the final value adjusted for the initial value. **Results**: Even though infant feeding patterns were not related to anthropometric measurements at 1, 3 and 5 y, high scores on pattern-1 were associated with higher 1-3 y weight and height changes. High scores on pattern-2 were related to lower 0-1y weight and height changes, higher 1-5 y weight and height changes but not to BMI changes, after controlling for a wide range of potential confounding variables including parental BMI. Scores on pattern-3 were not significantly related to growth. Additional adjustment for breastfeeding duration reduced the strength of the associations between pattern-2 and growth but not those between pattern-1 and height growth. **Conclusion**: Our findings emphasize the relevance of considering infant feeding patterns including breastfeeding duration, age of complementary foods introduction as well as type of foods used when examining effects of early infant feeding practices on later health.

Introduction

The early programming hypothesis suggests that exposures during fetal and early postnatal life influence infant development and can cause adaptive and permanent changes in physiology and metabolism (1). The perinatal period has been proposed as a critical period for obesity development (2). Early determinants of obesity include early growth trajectories, maternal smoking and maternal weight gain during pregnancy (3). Food intake represents the main determinant of the modified early weight gain as, contrary to energy intake, energy expenditure differences in 3-mo infants are not related to body size at one year (4). Infant diet over the first year of life is characterized by a milk feeding period followed by a progressive transition to complementary foods (CF). Recent findings showed that dietary patterns emerge in early infancy (5), are likely to track into later childhood (6) and are difficult to change once established (7). Besides, early-life feeding experiences contribute to later dietary preferences and habits onset (8, 9).

In the literature, milk feeding and timing of introduction of complementary foods have often been examined as independent determinants of later obesity. In recent years, much of the research has concentrated on breastfeeding. A protective effect of breastfeeding on risk of childhood obesity has been suggested in a number of epidemiologic studies and meta-analyses have summarized the evidence (10). While they reported small protective effects of breastfeeding for obesity risk, residual confounding remained an issue, and heterogeneity between the included studies was highlighted. Moreover, the only trial on breastfeeding promotion did not underline any protective effect on overweight in children (11). The effects of complementary feeding practices on growth have been less studied and there is no clear and consistent association reported with obesity in childhood (12). In practice, breastfeeding and complementary feeding practices are not independent (13, 14) and both are likely to be related with growth (15). There is therefore a need to consider a more comprehensive approach of feeding practices and food intake over the first year of life. The use of an exploratory multidimensional approach to identify infant feeding patterns is interesting as it allows to characterize feeding practices in a global manner, capturing the effects related to each of the practices, but also accounting for their existing covariations.

The aim of the present study was to examine relations between infant feeding patterns over the first year of life derived by principal component analysis and anthropometric changes in the first five years of life.

Material and methods

Study population

The EDEN mother-child study is a prospective cohort aiming to assess pre- and post-natal determinants of child growth, development and health and it has been described elsewhere (16). In brief, 2002 pregnant women were recruited in two French university hospitals, before 24 weeks of amenorrhea. Exclusion criteria were multiple pregnancies, known diabetes prior to pregnancy, illiteracy, planning to move outside the region in the next three years. The study was approved by the Ethics Committee of the University Hospital of Kremlin-Bicêtre on December 12, 2002 and data files were declared to the National Committee for Processed Data and Freedom. Written consent was obtained from both parents (16).

Infant feeding patterns

Infant feeding patterns were previously identified using principal component analysis (PCA) which included data on breastfeeding duration, age of introduction to 14 complementary foods, type of food (ready-prepared baby-food or adult food or home made) used at 12 months (17). Three feeding patterns were characterized: pattern-1, labelled '*Later dairy products introduction and use of ready-prepared baby foods*', pattern-2, labelled '*Long breastfeeding, later main meal food introduction and use of home-made foods*', and pattern-3, labelled '*Use of ready-prepared adult foods'*. For a given pattern, a score was calculated at the individual level, a higher score indicating a higher adherence to that particular pattern. A 1-SD increase in the score of pattern-1 corresponded on average to three weeks increase in breastfeeding duration, three weeks delay in dairy products introduction, two weeks delay in cheese introduction and a three times more frequent use of ready-prepared baby fruit and vegetables purees at 12 months. A 1-SD increase in the score of pattern-2 corresponded on average to eight weeks increase in breastfeeding duration, three weeks delay in fruit, vegetables and meat introduction, four weeks delay in fish introduction and a four times more frequent use of home-made fruit and vegetables purees at 12 months. A 1-SD increase in the score of pattern-3 corresponded on average to two times more frequent use of adult's dairy products and vegetables purees and two times less frequent use of baby dairy products, home-made soups, main meals made from fresh meat and fish at 12 months.

Child's growth

At each clinical examination, child's weight and height were measured. In between, weight and height data were collected from self-administered EDEN questionnaires and from measurements noted in the child's health booklet by health professionals. Children had on average 22 weight measurements (interquartile range 16–26) from birth to 5–6 years. Individual growth curves of weight and height were obtained using the Jenss growth curve model (18). This method allows parameters on individual growth patterns to be predicted, such as weight, height and BMI at any age (18). We used the predicted values of height and

BMI at birth, 1 y, 3 y and 5 y, weight at 1 y, 3 y and 5 y and observed values of weight at birth.

Study sample

Of the 2 002 recruited women, 96 were excluded because they left the study upon delivery for personal reasons, 4 because of intra-uterine death, 3 because they delivered outside the study hospitals. Birth weight was available for 1 899 newborns. Weight and height individual growth curves were obtained among 1763 children. Due to the late introduction of the questionnaire inquiring about type of food used at 12 months, feeding patterns scores could be derived only for 1 022 infants.

When compared to the 1022 included, the 980 excluded children had slightly lower birth weight and gestational age (3,255g *vs*. 3,299g, p=0.06; 39.1 *vs*. 39.4 weeks, p<0.001). The mothers of the excluded children were younger (29.0 *vs*. 29.9 years old, p<0.001), more often multiparous (58% *vs*. 53%, p=0.02) and had lower social conditions (46% *vs*. 60% university degree, p<0.001 and 24% *vs*. 11% with family income <1501€/month, p<0.001). There was no significant difference for maternal pre-pregnancy BMI (p=0.15), birth length (p=0.46) and newborn's sex (p=0.17).

Statistical analysis

Multivariable linear regression models were used to examine the associations between child's weight, height and BMI at ages 1, 3 and 5 years respectively and the feeding patterns scores adjusted for parental (maternal age, education, and employment status, maternal smoking during pregnancy, family income, parity, and parental BMI and height) and child (gestational age, sex and child care attendance) characteristics. The effect of the feeding patterns on the change in anthropometric measurements, from birth to 1 year, from 1 to 3 years and from 3 to

5 years, was estimated with the final value as the outcome, adjusted for the initial value and other potential confounders. Additional multivariable regression models were run to test the independent effect of breastfeeding: we first regressed infant feeding pattern scores on breastfeeding duration and used the residuals as a new variable along with breastfeeding duration in the models. This allowed studying the independent effect of feeding scores, adjusted for breastfeeding duration, and breastfeeding duration on growth.

Missing data on covariates were handled as follows: the modal class value was imputed when the percentage of missing values was lower than 5%, (maternal education, BMI and smoking status, family income, parity). Otherwise, individuals with missing values were grouped into a separate category (paternal BMI, childcare attendance). To assess the potential impact of these missing measurements, we conducted multiple imputations as a sensitivity analysis. We assumed that data were missing at random and generated five independent datasets using the Markov Chain Monte Carlo method (SAS MI procedure, NIMPUTE option, Yuan 2000), and then calculated pooled effect estimates (SAS MIANALYSE procedure). These sensitivity analyses were run on the sample with data on infant feeding pattern (n=1022) but also on the sample without exclusion of missing data on infant feeding pattern (n=1763).

All analyses were conducted using SAS software version 9.3 (SAS Institute, Inc., Cary, NC). A p-value<0.05 was considered statistically significant.

Results

Mothers were on average 29.9 years old and approximately 47% were primiparous (**Table 1**). More than half of the mothers had a university degree. The mean birth weight was 3,299 g and 4.1% of the infants were born preterm (<37 weeks).

The associations between the infant feeding patterns and anthropometrics at 1, 3 or 5 y, and changes from birth to 5 y are depicted in **Figures 1** and **2** respectively. The infant feeding pattern-1 was neither significantly related to child's weight at 1, 3 or 5 y, nor to weight change from birth to 1 y or from 3 to 5 y. It was positively related to weight change from 1 to 3 y (p=0.045). However, this association was no longer significant when looking at the patterns residuals adjusted for any breastfeeding duration. The infant feeding pattern-2 was not related to weight at 1 y, 3 or 5 y, but was negatively related to weight change from birth to 1 y. It was positively related to weight gain from 1 to 3 y and from 3 to 5 y. These associations also disappeared when looking at the feeding patterns residuals adjusted for breastfeeding duration, but in these models, breastfeeding duration was negatively related to weight change from birth to 1 y and positively related to weight change from 1 to 3 y, and from 3 to 5 y. The infant feeding pattern-3 was not associated with child's weight or weight changes during the first 5 y of life.

We found similar associations between infant feeding patterns and child's height or height changes during the first 5 y of life, to the exception that the association between the infant feeding pattern-1 residuals and height change from 1 to 3 y remained significant after adjustment for breastfeeding duration.

None of the infant feeding patterns was related to child's BMI from 1 to 5 y or to BMI change from birth to 5 y. This was not modified by additional adjustment for any breastfeeding duration. However, breastfeeding duration, after adjustment for the residuals of other feeding practices, was negatively related to BMI change from birth to 1 y, positively from 1 to 3 y, and no longer associated from 3 to 5 y.

We obtained very similar results in analyses based on multiple imputation of missing data. In the sample with data on infant feeding patterns (n=1022), the differences between non-imputed and imputed effect size were less than 0.01 points for all adjusted-estimates. In the larger sample (n=1763), where missing data on infant feeding patterns were also imputed, results were very similar but the association between infant feeding pattern-2 and height change from 1 to 3 y remained significant after adjustment for any breastfeeding duration (β [95%CI] = 0.11 [0.01;0.20]).

Discussion

Infant feeding patterns were not significantly related to anthropometric measurements at 1, 3 and 5 y, but they were related to height and weight growth both during the first year and from 1 to 3 years. High scores on infant feeding pattern characterized by *long breastfeeding, later main meal food introduction and use of home-made foods* were related to significant lower 0-1 years and higher 1-3 years or 3-5 years increase in weight and height. This specific growth pattern was explained by the long breastfeeding duration. None of the feeding patterns was related to a significant BMI change.

In the literature, it has been shown that growth in the first year of life differs according to milk feeding mode. Indeed, compared to formula-fed infants, breastfed infants show slower weight and length gains from the 3rd month to the 12th month of life (19) and lower BMI at 1 year of age (20, 21). As in a previous paper (17), birth weight was related to none of the three infant feeding patterns, associations found with 0-1 year growth were not assumed to reflect association with birth size. Studies that examined the influence of breastfeeding on BMI trajectories tend to show that the protective effect found in infancy disappeared in toddlerhood (20) and then reappeared later in childhood (22, 23). Most meta-analyses suggested a protective effect of breastfeeding on childhood obesity (10, 24) but the effect was of small magnitude (25) and the meta-analyses also underlined that potential residual confounding cannot be excluded. Breastfeeding promotion interventions were related to a modest reduction in BMI or weight-for-height z-scores in childhood (26). The large randomized trial conducted in Belarusia did not show any protective effect of exclusive breastfeeding on obesity at 11.5 years (11).

Few studies have examined the effects of timing of CF introduction on growth and suggested, consistent with our study, small and transient effects on early growth that were no longer apparent by 2 years of age (27). Interestingly, Wilson et al (28) reported an increased percentage body fat in 7-year-old children among children introduced early to CF, Seach et al (29) found that delayed CF introduction was associated with reduced odds of being overweight/obese at 10 years of age and Schack-Nielsen et al (21) showed a decrease of the risk of overweight at age 42 years with increasing age at CF introduction despite no effect on weight in infancy. Therefore, there may be a transient effect in infancy and re-emergence of associations later in childhood. In our study, both longer breastfeeding and delayed introduction of complementary food characterized the second infant feeding pattern. It would be of interest to test the association between these feeding practices and overweight/obesity risk after the adiposity rebound, occurring around 6 y of age, as well as during puberty. However, a causal link between infant feeding pattern and a latent obesity effect will be difficult to establish.

A major strength of our study was the population-based cohort, with mothers being followed up from the third trimester of pregnancy onwards, the carefully collected and modelized data on growth and information about a large number of possible confounders such as parental characteristics. The use of feeding patterns derived from PCA allowed us to account for breastfeeding and complementary feeding practices over the first year of life simultaneously. The PCA-derived infant feeding patterns were related to growth. However, additional adjustment highlighted that some associations, especially those between pattern-2 and growth, were more strongly related to breastfeeding than to the other pattern-specific feeding practices, whereas associations between pattern-1 and growth were less impaired by the additional adjustment for breastfeeding. This emphasizes the need to consider all infant feeding practices over the first year of life when examining effects of early infant feeding practices on later growth.

Our study has however some limitations. Because PCA is a data-driven approach, patterns identified in our cohort might not be reproducible in other populations, and therefore limit replication of results in other studies. The EDEN population is not representative of the French general population. Compared to the French national perinatal survey carried out in 2003 (30), women included in EDEN study were slightly older, more educated and more often employed. Infants born premature or with a low birth weight were also more likely to be lost to follow-up. However, we believe that the relationships observed are of interest for the general population of healthy infants born in France from middle class parents.

Conclusion

In our study, early feeding practices characterized by '*Long breastfeeding, later main meal food introduction and use of home-made foods*' were related to slower growth over the first year and faster growth from 1 to 5 year, whereas early feeding practices characterized by "*Later dairy products introduction and use of ready-prepared baby foods*" were related to faster growth from 1 and 3 years. The potential effects of early feeding practices on later risk of overweight and obesity may be mediated, at least in part, through an early programming of later dietary habits, as we previously demonstrated that early feeding practices are associated with diet in childhood (8, 6).

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Contributors: The EDEN mother-child Study Group, coordinated by MAC and BH, was responsible for study design and data collection. MAC and BLG were involved in all aspects from study conception to manuscript writing. AB and AF participated in data management for the present analyses. AB analyzed and interpreted the data and wrote the initial draft of the manuscript. SL, BH, SC, RH, NR, JB and all the co-authors critically reviewed all sections of the text for important intellectual content. MAC is the guarantor of the study. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All the authors read and approved the final version of the paper.

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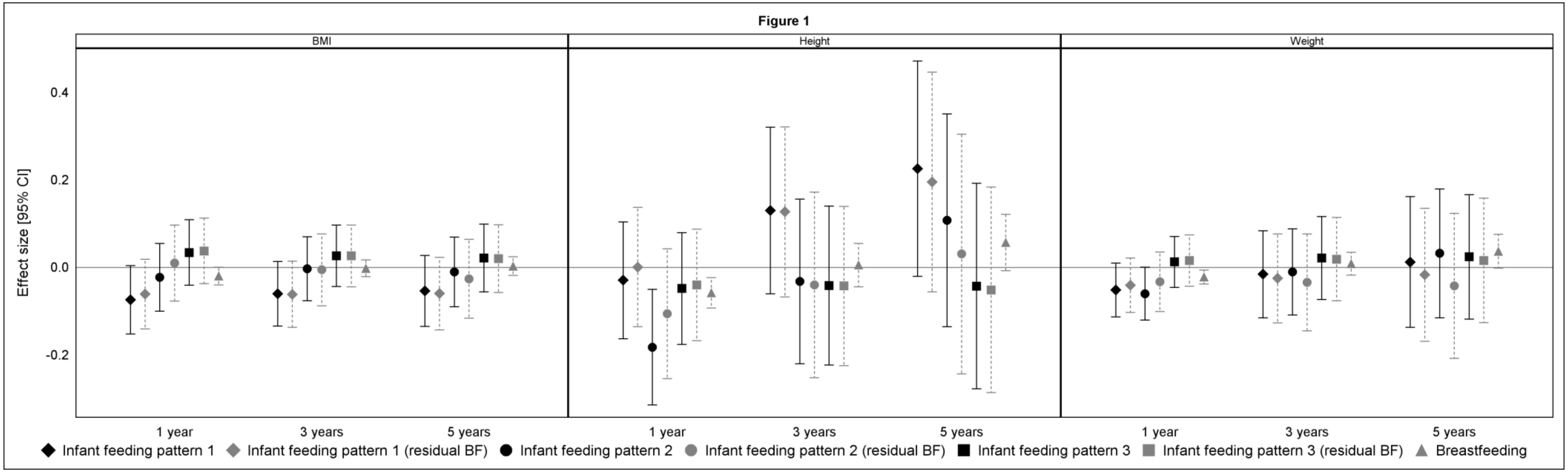
Table 1: Characteristics of parents and offspring (n=1022).

	Values
Parental characteristics	
Maternal education (% university degree)	388 (38%)
Monthly family income > 3,000 €	316 (31%)
Primiparous	480 (47%)
Maternal pre-pregnancy BMI < 25 kg/m²	775 (76%)
Paternal BMI < 25 kg/m²	493 (48%)
Maternal age at child's birth (yrs)	29.9 ± 4.7
The mother worked in the first 4 months	430 (42%)
Maternal smoking during pregnancy	219 (21%)
Child characteristics	
Female sex	500 (49%)
Gestational age (weeks of amenorrhea)	39.4 ± 1.5
Birth weight (g)	3299± 488
Birth length (cm)	50.3 ± 2.1
Never attended to child-care in the first year of life	112 (11%)
At 1y of age	
Weight (kg)	9.6 ± 1.0
Height (cm)	75.7 ± 2.5
BMI (kg/m²)	16.8 ± 1.2
At 3y of age	
Weight (kg)	14.5 ± 1.6
Height (cm)	95.3 ± 3.4
BMI (kg/m²)	15.9 ± 1.2
At 5y of age	
Weight (kg)	18.8 ± 2.3
Height (cm)	110.3 ± 4.4
BMI (kg/m²)	15.4 ± 1.3
Other variables	
Recruitment center (% Poitiers)	578 (57%)

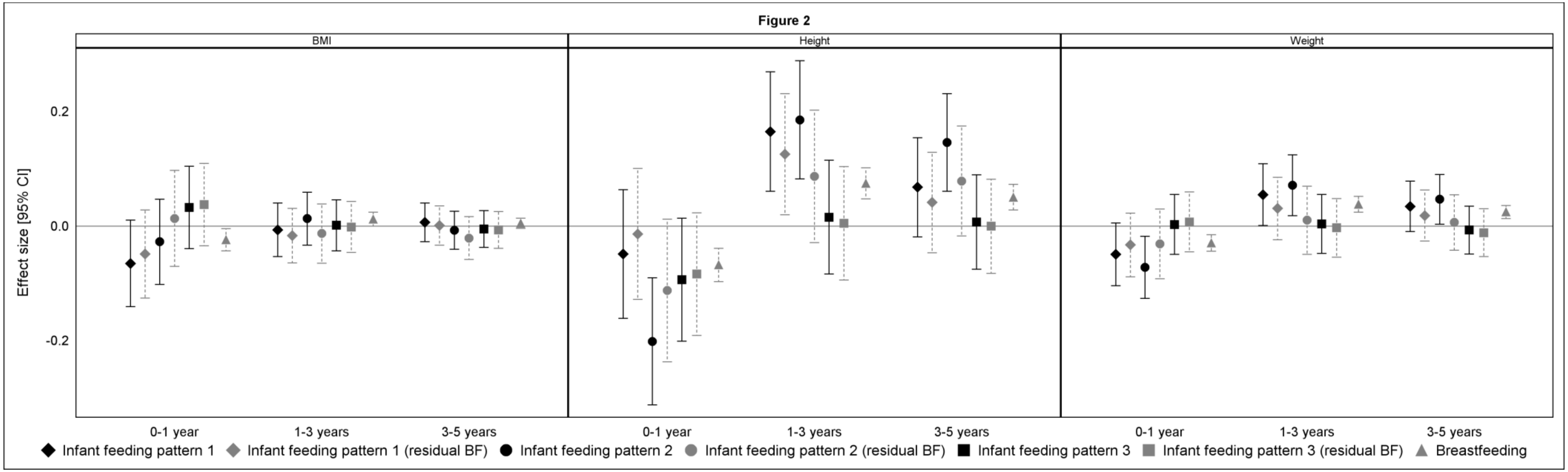
Figure 1: Associations between infant feeding practices and anthropometric measurements at 1, 3 and 5 y (n=1022).



Model 1, in black, included all three infant feeding patterns in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal education level, family income, parity, maternal smoking, maternal pre-pregnancy BMI, paternal BMI, maternal return to work at 4 mo, infant's age at first attendance to child care, sex, gestational age and, for model on height, parental height. Model 2; in gray, included residuals of all three infant feeding pattern and breastfeeding in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal education level, family income, parity, maternal smoking, maternal pre-pregnancy BMI, paternal BMI, maternal return to work at 4 mo, infant's age at first attendance to child care, sex, gestational age and, for model on height, parental height.

Infant feeding pattern 1: Later dairy products introduction and use of ready-prepared baby foods; Infant feeding pattern 2: Long breastfeeding, later main meal food introduction and use of home-made foods; Infant feeding pattern 3: Use of ready-prepared adult foods.

Figure 2: Associations between infant feeding practices and change in anthropometric measurements from birth to 5 y (n=1022).



Change in anthropometric measurements was assessed by the final value, adjusted for the initial value.

Model 1, in black, included all three infant feeding pattern in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal education level, family income, parity, maternal smoking, maternal pre-pregnancy BMI, paternal BMI, maternal return to work at 4 mo, infant's age at first attendance to child care, sex, gestational age and, for model on height, parental height. Model 2; in gray, included residuals of all three infant feeding pattern and breastfeeding in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal education level, family income, parity, maternal smoking, maternal pre-pregnancy BMI, paternal BMI, maternal return to work at 4 mo, infant's age at first attendance to child care, sex, gestational age and, for model on height, parental height.

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