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## **Influence of infant feeding patterns over the first year of life on growth from birth to 5 y**

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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)

1 **What is already known about this subject**

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

6 **What this study adds**

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

13

14

15 **Abstract**

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

35

## 36 **Introduction**

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

49 In the literature, milk feeding and timing of introduction of complementary foods have often  
50 been examined as independent determinants of later obesity. In recent years, much of the  
51 research has concentrated on breastfeeding. A protective effect of breastfeeding on risk of  
52 childhood obesity has been suggested in a number of epidemiologic studies and meta-analyses  
53 have summarized the evidence (10). While they reported small protective effects of  
54 breastfeeding for obesity risk, residual confounding remained an issue, and heterogeneity  
55 between the included studies was highlighted. Moreover, the only trial on breastfeeding  
56 promotion did not underline any protective effect on overweight in children (11). The effects  
57 of complementary feeding practices on growth have been less studied and there is no clear  
58 and consistent association reported with obesity in childhood (12). In practice, breastfeeding  
59 and complementary feeding practices are not independent (13, 14) and both are likely to be

60 related with growth (15). There is therefore a need to consider a more comprehensive  
61 approach of feeding practices and food intake over the first year of life. The use of an  
62 exploratory multidimensional approach to identify infant feeding patterns is interesting as it  
63 allows to characterize feeding practices in a global manner, capturing the effects related to  
64 each of the practices, but also accounting for their existing covariations.

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

## 68 **Material and methods**

### 69 *Study population*

70 The EDEN mother-child study is a prospective cohort aiming to assess pre- and post-natal  
71 determinants of child growth, development and health and it has been described elsewhere  
72 (16). In brief, 2002 pregnant women were recruited in two French university hospitals, before  
73 24 weeks of amenorrhea. Exclusion criteria were multiple pregnancies, known diabetes prior  
74 to pregnancy, illiteracy, planning to move outside the region in the next three years. The study  
75 was approved by the Ethics Committee of the University Hospital of Kremlin-Bicêtre on  
76 December 12, 2002 and data files were declared to the National Committee for Processed  
77 Data and Freedom. Written consent was obtained from both parents (16).

### 78 *Infant feeding patterns*

79 Infant feeding patterns were previously identified using principal component analysis (PCA)  
80 which included data on breastfeeding duration, age of introduction to 14 complementary  
81 foods, type of food (ready-prepared baby-food or adult food or home made) used at 12

82 months (17). Three feeding patterns were characterized: pattern-1, labelled '*Later dairy*  
83 *products introduction and use of ready-prepared baby foods*', pattern-2, labelled '*Long*  
84 *breastfeeding, later main meal food introduction and use of home-made foods*', and pattern-3,  
85 labelled '*Use of ready-prepared adult foods*'. For a given pattern, a score was calculated at  
86 the individual level, a higher score indicating a higher adherence to that particular pattern. A  
87 1-SD increase in the score of pattern-1 corresponded on average to three weeks increase in  
88 breastfeeding duration, three weeks delay in dairy products introduction, two weeks delay in  
89 cheese introduction and a three times more frequent use of ready-prepared baby fruit and  
90 vegetables purees at 12 months. A 1-SD increase in the score of pattern-2 corresponded on  
91 average to eight weeks increase in breastfeeding duration, three weeks delay in fruit,  
92 vegetables and meat introduction, four weeks delay in fish introduction and a four times more  
93 frequent use of home-made fruit and vegetables purees at 12 months. A 1-SD increase in the  
94 score of pattern-3 corresponded on average to two times more frequent use of adult's dairy  
95 products and vegetables purees and two times less frequent use of baby dairy products, home-  
96 made soups, main meals made from fresh meat and fish at 12 months.

### 97 *Child's growth*

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



105 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  
106 birth.

### 107 *Study sample*

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

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

### 121 *Statistical analysis*

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

128 5 years, was estimated with the final value as the outcome, adjusted for the initial value and  
129 other potential confounders. Additional multivariable regression models were run to test the  
130 independent effect of breastfeeding: we first regressed infant feeding pattern scores on  
131 breastfeeding duration and used the residuals as a new variable along with breastfeeding  
132 duration in the models. This allowed studying the independent effect of feeding scores,  
133 adjusted for breastfeeding duration, and breastfeeding duration on growth.

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

144 All analyses were conducted using SAS software version 9.3 (SAS Institute, Inc., Cary, NC).

145 A p-value<0.05 was considered statistically significant.

## 146 **Results**

147 Mothers were on average 29.9 years old and approximately 47% were primiparous (**Table 1**).

148 More than half of the mothers had a university degree. The mean birth weight was 3,299 g  
149 and 4.1% of the infants were born preterm (<37 weeks).

150 The associations between the infant feeding patterns and anthropometrics at 1, 3 or 5 y, and  
151 changes from birth to 5 y are depicted in **Figures 1** and **2** respectively. The infant feeding

152 pattern-1 was neither significantly related to child's weight at 1, 3 or 5 y, nor to weight  
153 change from birth to 1 y or from 3 to 5 y. It was positively related to weight change from 1 to  
154 3 y ( $p=0.045$ ). However, this association was no longer significant when looking at the  
155 patterns residuals adjusted for any breastfeeding duration. The infant feeding pattern-2 was  
156 not related to weight at 1 y, 3 or 5 y, but was negatively related to weight change from birth to  
157 1 y. It was positively related to weight gain from 1 to 3 y and from 3 to 5 y. These  
158 associations also disappeared when looking at the feeding patterns residuals adjusted for  
159 breastfeeding duration, but in these models, breastfeeding duration was negatively related to  
160 weight change from birth to 1 y and positively related to weight change from 1 to 3 y, and  
161 from 3 to 5 y. The infant feeding pattern-3 was not associated with child's weight or weight  
162 changes during the first 5 y of life.

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

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

172 We obtained very similar results in analyses based on multiple imputation of missing data. In  
173 the sample with data on infant feeding patterns ( $n=1022$ ), the differences between non-  
174 imputed and imputed effect size were less than 0.01 points for all adjusted-estimates. In the  
175 larger sample ( $n=1763$ ), where missing data on infant feeding patterns were also imputed,

176 results were very similar but the association between infant feeding pattern-2 and height  
177 change from 1 to 3 y remained significant after adjustment for any breastfeeding duration ( $\beta$   
178 [95%CI] = 0.11 [0.01;0.20]).

## 179 **Discussion**

180 Infant feeding patterns were not significantly related to anthropometric measurements at 1, 3  
181 and 5 y, but they were related to height and weight growth both during the first year and from  
182 1 to 3 years. High scores on infant feeding pattern characterized by *long breastfeeding, later*  
183 *main meal food introduction and use of home-made foods* were related to significant lower 0-  
184 1 years and higher 1-3 years or 3-5 years increase in weight and height. This specific growth  
185 pattern was explained by the long breastfeeding duration. None of the feeding patterns was  
186 related to a significant BMI change.

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

199 in Belarusia did not show any protective effect of exclusive breastfeeding on obesity at 11.5  
200 years (11).

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

215 A major strength of our study was the population-based cohort, with mothers being followed  
216 up from the third trimester of pregnancy onwards, the carefully collected and modeled data  
217 on growth and information about a large number of possible confounders such as parental  
218 characteristics. The use of feeding patterns derived from PCA allowed us to account for  
219 breastfeeding and complementary feeding practices over the first year of life simultaneously.  
220 The PCA-derived infant feeding patterns were related to growth. However, additional  
221 adjustment highlighted that some associations, especially those between pattern-2 and growth,  
222 were more strongly related to breastfeeding than to the other pattern-specific feeding

223 practices, whereas associations between pattern-1 and growth were less impaired by the  
224 additional adjustment for breastfeeding. This emphasizes the need to consider all infant  
225 feeding practices over the first year of life when examining effects of early infant feeding  
226 practices on later growth.

227 Our study has however some limitations. Because PCA is a data-driven approach, patterns  
228 identified in our cohort might not be reproducible in other populations, and therefore limit  
229 replication of results in other studies. The EDEN population is not representative of the  
230 French general population. Compared to the French national perinatal survey carried out in  
231 2003 (30), women included in EDEN study were slightly older, more educated and more  
232 often employed. Infants born premature or with a low birth weight were also more likely to be  
233 lost to follow-up. However, we believe that the relationships observed are of interest for the  
234 general population of healthy infants born in France from middle class parents.

## 235 **Conclusion**

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

244

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269 the present analyses. AB analyzed and interpreted the data and wrote the initial draft of the  
270 manuscript. SL, BH, SC, RH, NR, JB and all the co-authors critically reviewed all sections of  
271 the text for important intellectual content. MAC is the guarantor of the study. All authors had  
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273 and the accuracy of the data analysis. All the authors read and approved the final version of  
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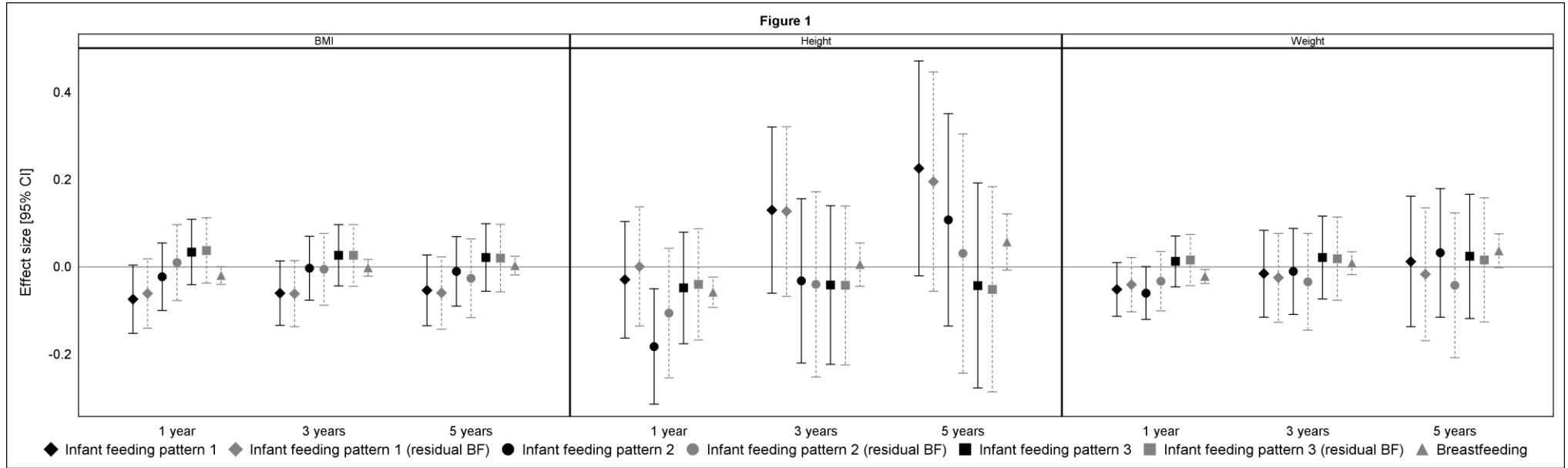
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**Table 1: Characteristics of parents and offspring (n=1022).**

	<b>Values</b>
<b>Parental characteristics</b>	
Maternal education (% university degree)	388 (38%)
Monthly family income > 3,000 €	316 (31%)
Primiparous	480 (47%)
Maternal pre-pregnancy BMI < 25 kg/m <sup>2</sup>	775 (76%)
Paternal BMI < 25 kg/m <sup>2</sup>	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%)
<b>Child characteristics</b>	
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/m <sup>2</sup> )	16.8 ± 1.2
At 3y of age	
Weight (kg)	14.5 ± 1.6
Height (cm)	95.3 ± 3.4
BMI (kg/m <sup>2</sup> )	15.9 ± 1.2
At 5y of age	
Weight (kg)	18.8 ± 2.3
Height (cm)	110.3 ± 4.4
BMI (kg/m <sup>2</sup> )	15.4 ± 1.3
<b>Other variables</b>	
Recruitment center (% Poitiers)	578 (57%)

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

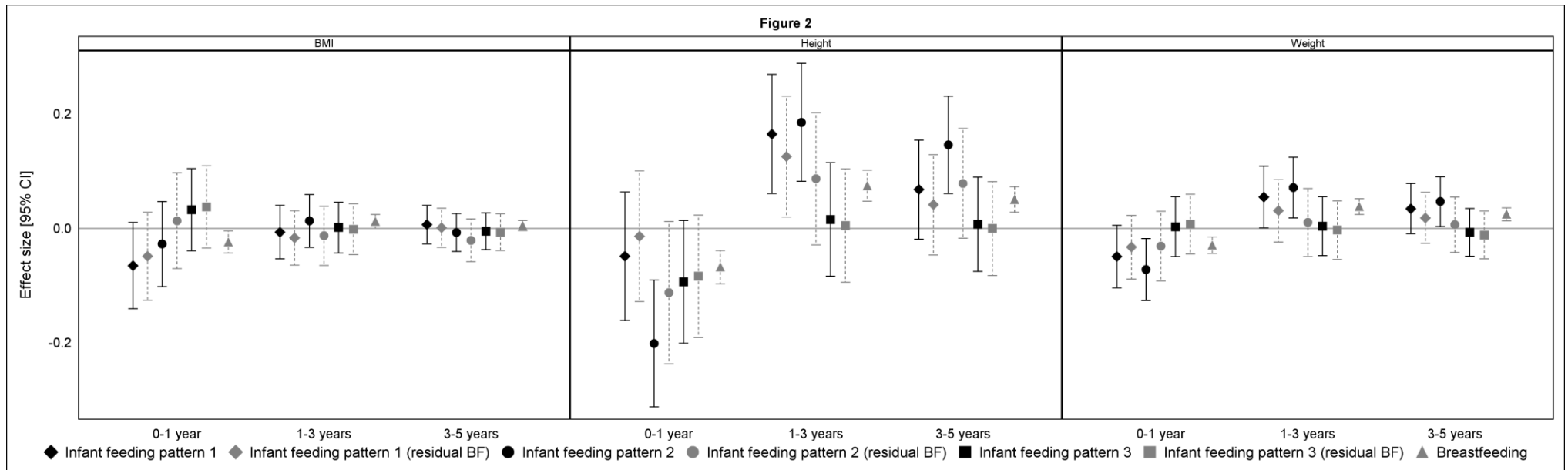


4 Model 1, in black, included all three infant feeding patterns in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal  
 5 education level, family income, parity, maternal smoking, maternal pre-pregnancy BMI, paternal BMI, maternal return to work at 4 mo, infant's age at first  
 6 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  
 7 and breastfeeding in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal education level, family income, parity,  
 8 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  
 9 age and, for model on height, parental height.

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

12

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



14

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

16 Model 1, in black, included all three infant feeding pattern in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal  
 17 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  
 18 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  
 19 and breastfeeding in multivariable linear regressions, also adjusted for recruitment center, maternal age, maternal education level, family income, parity,  
 20 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  
 21 age and, for model on height, parental height.

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

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