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# Infant diet and subcutaneous fat mass in early childhood.

## The Generation R Study

Running title: infant diet and subcutaneous fat

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1 **ABSTRACT**

2 **Background:** Breastfeeding has a protective effect on childhood obesity, but the influences  
3 on body composition in early childhood are not known.

4 **Objectives:** To assess whether the duration and exclusiveness of breastfeeding, and the  
5 timing of introduction of solid foods are associated with the subcutaneous fat mass in early  
6 childhood.

7 **Methods:** This study was embedded in a population-based prospective cohort study among  
8 779 children. Peripheral (biceps, triceps) and central (suprailiacal and subscapular)  
9 subcutaneous fat mass was measured as skinfold thickness at the ages of 1.5, 6 and 24  
10 months.

11 **Results:** Breastfeeding duration was not associated with subcutaneous fat mass at the age  
12 of 1.5 months. Shorter breastfeeding was associated with higher peripheral and total  
13 subcutaneous fat mass at the age of 6 months (p value for trend <0.05), but not at the age of  
14 24 months. As compared to children who were exclusively breast fed for 4 months, those  
15 who were non-exclusively breast fed had a higher central fat mass at the age of 24 months  
16 (p value for trend <0.01). Timing of introduction of solid foods was not associated with  
17 subcutaneous fat mass.

18 **Conclusion:** Our results suggest that a shorter duration and non-exclusive breastfeeding  
19 affect early body composition during the first 2 years of life. Follow up studies at older ages  
20 are needed to explore the long-term consequences.

**Keywords:** infant feeding, obesity, breastfeeding, solid foods, skinfold, pediatrics

21

## 22 INTRODUCTION

23 Several studies showed a protective effect of breastfeeding on the risk of overweight in  
24 children and adults (Owen *et al.*, 2005; Owen *et al.*, 2005; Harder *et al.*, 2005, Arenz *et al.*,  
25 2004). Although the effect estimates for the associations of breastfeeding with mean body  
26 mass index are generally small, they seem to be consistent (Owen *et al.*, 2005; Owen *et al.*,  
27 2005; Harder *et al.*, 2005; Arenz *et al.*, 2004; Bergmann *et al.*, 2003). An inverse dose-  
28 dependent association has been shown, suggesting that longer duration of breastfeeding is  
29 associated with a lower body mass index (Harder *et al.*, 2005; Arenz *et al.*, 2004). Some  
30 studies have also suggested that early weaning may increase body mass index in childhood,  
31 but results are inconsistent (Wilson *et al.*, 1998; Wright *et al.*, 2004; Forsyth *et al.*, 1993;  
32 Morgan *et al.*, 2004). Body mass index provides only information about body weight,  
33 whereas it does not distinguish between fat and lean mass (Wells and Fewtrell, 2006; Nevill  
34 *et al.*, 2006). Since an unfavorable fat distribution may be stronger related to cardiovascular  
35 and metabolic diseases, it is important to explore the associations of breastfeeding with  
36 measures of fat distribution. Only a few studies have examined the relationships between  
37 breastfeeding in infancy and direct measures of adiposity in childhood, but no consistent  
38 associations were observed (Burdette *et al.*, 2006; Gale *et al.*, 2007). Skinfold thickness is a  
39 valid measurement for subcutaneous fat mass assessment in epidemiological studies (Wells  
40 and Fewtrell, 2006; Nevill *et al.*, 2006). These measurements are quick and simple to obtain  
41 in most age groups, including young infants (Wells and Fewtrell, 2006). We have previously  
42 shown that birth weight is associated with subcutaneous fat mass in early childhood (Ay *et*  
43 *al.*, 2009). Subcutaneous fat mass also tends to track throughout early childhood (Ay *et al.*,  
44 2009).

45 We examined in a population-based prospective cohort study among 779 children,  
46 the associations of breastfeeding duration and exclusivity, and timing of introduction of solid  
47 foods with peripheral, central and total subcutaneous fat mass in early childhood.

48

49

50 **METHODS**

51 **Design**

52 This study was embedded in the Generation R Study, a population-based prospective cohort  
53 study of pregnant women and their children from fetal life onwards in Rotterdam, the  
54 Netherlands (Jaddoe *et al.*, 2010). Enrollment in the study was aimed at early pregnancy  
55 (gestational age <18 weeks) but was possible until birth of the child. All children were born  
56 between April 2002 and January 2006, and form a prenatally enrolled birth-cohort that is  
57 currently followed until young adulthood. Additional detailed assessments of postnatal growth  
58 and development were conducted in a subgroup of 1106 Dutch mothers and their children  
59 from late pregnancy (Jaddoe *et al.*, 2010). Between February 2003 and April 2005, all  
60 pregnant mothers participating in the Generation R study, who met this criterion, were  
61 approached for additional measurements (Jaddoe *et al.*, 2010). Of all approached women,  
62 80% agreed to participate in the subgroup study. The study protocol was approved by the  
63 Medical Ethical Committee of the Erasmus Medical Centre, Rotterdam. Written informed  
64 consent was obtained from all parents.

65

66 **Population for analysis**

67 From the total of 1106 children, 1039 children participated in at least one of the postnatal  
68 assessments at the ages of 1.5, 6 and 24 months (Figure 1). Children without complete  
69 information on breastfeeding (n = 225) were excluded from the analyses. Of the remaining  
70 814 live births with complete data on breastfeeding, skinfold measurements were measured  
71 in at least one of the three visits in 799 children. Next, twins (n = 20) were excluded from the  
72 analyses since twins are correlated and may differ from other children in the relation between  
73 breastfeeding and subcutaneous fat mass. Missing skinfold measurements were mainly due  
74 to crying behavior. No differences in child and maternal characteristics were found between  
75 children with and without skinfold measurements (n = 779 versus n = 1106).

76

77 **Duration and exclusiveness of breastfeeding and solids foods introduction**

78 Information about breastfeeding initiation and continuation was obtained from delivery  
79 reports and postal questionnaires at the ages of 2, 6 and 12 months after birth, as previously  
80 described (Durmuş *et al.*, 2011). Mothers were asked whether they ever breast fed their child  
81 (yes; no) and at what age they quit breastfeeding. Subsequently, breastfeeding duration was  
82 categorized into three groups: 1) never; 2) less than 4 months; 3) 4 months or longer.

83 Duration of exclusive breastfeeding was defined by using information about at what age  
84 other types of milk and/or solids were introduced in the first 6 months of life, according to a  
85 short food frequency questionnaire. The information about duration and exclusiveness of  
86 breastfeeding was combined and categorized into the following three categories: 1) never; 2)  
87 non-exclusive breast fed until 4 months; and 3) exclusive breast fed until 4 months. Never  
88 indicates infants who were never breast fed. Non-exclusive indicates infants receiving both  
89 breastfeeding, and formula feeding or solids during the first four months. Exclusive indicates  
90 infants who have been breast fed, without any other milk, solids or fluids during the first four  
91 months. Information about timing of introduction solid foods like fruit- and vegetable snacks  
92 was obtained from the same short food frequency questionnaire. Starting solid foods was  
93 defined as the age that a fruit- or vegetable snack was given for the first time (< 4 months; 4-  
94 5 months; and > 5 months).

95

96 **Subcutaneous fat mass measurements and anthropometrics**

97 Subcutaneous fat mass was measured as skinfold thicknesses (SFT) in millimeters at the  
98 ages of 1.5, 6 and 24 months on the left side of the body at four different sites (biceps,  
99 triceps, suprailiacal and subscapular) according to standard procedures by using a skinfold  
100 caliper (Slim Guide, Creative Health Products) (Lohman *et al.*, 1991). Four well-trained  
101 medical assistants performed all measurements (WHO, 2006). The consensus between and  
102 among observers for the medical assistants was analyzed using the intraclass correlation  
103 coefficient (ICC) (Bland and Altman, 1986; Shrout and Fleiss, 1979). Intraobserver ICC was  
104 0.88 and interobserver ICC was 0.76. Total subcutaneous fat mass was calculated from the

105 sum of biceps SFT + triceps SFT + suprailiacal SFT + subscapular SFT. Central  
106 subcutaneous fat mass was calculated from the sum of suprailiacal SFT + subscapular SFT.  
107 Peripheral subcutaneous fat mass was calculated from the sum of triceps SFT + biceps SFT  
108 (Ketel *et al.*, 2007; Birmingham *et al.*, 1993). Body length at the age of 1.5 and 6 months was  
109 measured in supine position to the nearest millimeter using a neonatometer and in 24-month  
110 olds height was measured in standing position by a Harpenden stadiometer (Holtain Limited,  
111 Dyfed, U.K.). Weight was measured to the nearest grams in naked infants at the age of 1.5  
112 and 6 months by using an electronic infant scale (SECA) and in 24-month olds by a  
113 mechanical personal scale (SECA).

114

#### 115 **Covariates**

116 Gestational age at birth, birth weight and sex were obtained from midwife and hospital  
117 registries at birth. Information about highest attained maternal educational level and parity  
118 were obtained at enrollment in the study. Educational level of the parents was defined  
119 according to the classification of Statistics Netherlands (Statistics Netherlands, 2004).  
120 Information on maternal smoking during pregnancy (yes; no) was retrieved from the prenatal  
121 questionnaire. Maternal height and weight were measured at enrollment while the mother  
122 stood without shoes and heavy clothing, and body mass index was calculated ( $\text{kg}/\text{m}^2$ ).

123 **Statistical analysis**

124 Differences in baseline characteristics between the breastfeeding variables ever (never;  
125 ever), duration (< 4 months; >4 months) and exclusivity (non-exclusive breast fed until 4  
126 months; exclusively breastfed until 4 months) were compared with Student's t-test for  
127 continuous variables and Chi-square tests for categorical variables. The associations of  
128 breastfeeding (never; ever), breastfeeding duration (never; < 4 months; and > 4 months),  
129 breastfeeding exclusivity (never; non-exclusive until 4 months; and exclusive until 4 months),  
130 and timing of introduction of fruit-and vegetable snacks (< 4 months; 4- 5 months; and > 5  
131 months) with peripheral, central, and total subcutaneous fat mass at the ages of 1.5, 6 and  
132 24 months, were assessed using multiple linear regression models. The reference groups of  
133 these regression models were ever breast fed, breastfeeding duration of >4 months,  
134 exclusive breast fed until 4 months, respectively. In these models, breastfeeding categories  
135 were used as predictor variables and peripheral, central and total fat as outcome variables.  
136 The models were adjusted for potential confounders including child's age at visit, sex,  
137 maternal education, maternal body mass index, smoking and parity, gestational age, birth  
138 weight, current height and observer. The models focused on the role of timing of introduction  
139 of solid foods, were additionally adjusted for breastfeeding duration. Tests for trends were  
140 performed by treating each categorized variable as a continuous term and by entering the  
141 variable into the fully adjusted linear regression model. To handle missing values in  
142 covariates, we performed multiple imputations by generating 5 independent datasets for all  
143 analyses using the Markov Chain Monte Carlo method. Imputations were based on the  
144 relationships between all covariates included in this study. All measures of association are  
145 presented with their 95% confidence intervals (CI). Statistical analyses were performed using  
146 the Statistical Package of Social Sciences version 17.0 for Windows (SPSS Inc., Chicago, IL,  
147 USA).

148

149

150



151 **Results**

152 Subject characteristics are given in Table 1. Of the total group of 779 children, 87.9% had  
153 ever been breastfed with a mean duration of 4.5 months (range 0.5 – 12.0). Differences  
154 between the breastfeeding categories are given in the Supplementary material (Tables S1,  
155 S2, S3). As compared to mothers who never breast fed their children, those who breast fed  
156 their children had more frequently a higher educational level, were more likely to consume  
157 alcohol during pregnancy but less likely to smoke (Table S1). Mothers who breast fed their  
158 children for more than 4 months, compared to mothers who breast fed their children shorter  
159 than 4 months, were older and had a lower body mass index (Table S2). Mothers who  
160 exclusively breast fed their children had a lower weight, were more likely to have more than  
161 one child and had children with a higher birth weight (Table S3).

162 The associations of ever breastfeeding, breastfeeding duration and exclusivity with  
163 peripheral, central and total fat mass at the ages of 1.5, 6 and 24 months are shown in Table  
164 2. Breastfeeding duration was not associated with subcutaneous fat mass at the age of 1.5  
165 months. Shorter breastfeeding was associated with higher peripheral and total subcutaneous  
166 fat mass at the age of 6 months ( $p$  value for trend  $<0.05$ ), but not at the age of 24 months. As  
167 compared to children who were breast fed exclusively for 4 months, those who were never  
168 breast fed had a higher peripheral and total subcutaneous fat mass at the age of 6 months  
169 and higher central fat mass at the age of 24 months ( $p$  value for trend  $<0.01$ ).

170 Table 3 presents the associations between age at introduction of solid foods and  
171 peripheral, central and total fat mass at the ages of 1.5, 6 and 24 months. As compared to  
172 children who received solid foods after the age of 5 months, those receiving solid foods  
173 before the age of 5 months, tended to have increased subcutaneous fat mass measures, but  
174 these associations were not significant.

175 **DISCUSSION**

176

177 **Main findings**

178 Results from this study suggest that a shorter duration and non-exclusive breast fed affect  
179 early body composition during the first 2 years of life. A shorter duration of breastfeeding was  
180 associated with higher peripheral and total subcutaneous fat mass at the age of 6 months,  
181 whereas non-exclusive breast fed was associated with higher central subcutaneous fat mass  
182 at the age 24 months. Early introduction of solid foods was not associated with subcutaneous  
183 fat mass measures.

184

185 **Strengths and weaknesses**

186 The most important strengths of this study are the population-based prospective design with  
187 a relatively large number of subjects being studied from early pregnancy onwards, and  
188 information about a large number of potential confounders available. Our analyses were  
189 based on 799 children with skinfold thickness measurements. Furthermore, information was  
190 available about duration and exclusivity of breastfeeding. Some methodological issues need  
191 to be considered. Of the total group of 1039 children, breastfeeding information was available  
192 in 78%. This non-response would lead to biased effect estimates if the associations of  
193 breastfeeding duration and exclusivity with skinfold thickness measurements would be  
194 different between those included and not included in the analyses. This seems unlikely  
195 because biased estimates in cohort studies mainly arise from loss to follow-up rather than  
196 from non-response at baseline (Nohr *et al.*, 2006). Information about breastfeeding was  
197 prospectively collected by questionnaires without direct reference to any skinfold  
198 measurement. Although assessing breastfeeding by questionnaires seems to be a valid  
199 method, misclassification may occur (Li *et al.*, 2005). We estimated breastfeeding exclusivity  
200 according to whether the child received breastfeeding without any other infant formula, milk  
201 or solids according to the short food frequency questionnaire. This definition does not cover  
202 the strict criteria used by the World Health Organization (WHO), which suggest that even the

203 use of water in combination with breastfeeding does not fulfill the definition of exclusivity.  
204 However, we did ask for the most commonly introduced solids and fluids. Furthermore, in  
205 The Netherlands it is not common that children receive breastfeeding in combination with the  
206 use of water to prevent dehydration. Therefore, we consider our measurement of exclusive  
207 breast fed as a good proxy for exclusive breast fed according to the World Health  
208 Organization criteria. Our definition of solid foods included only fruit or vegetable snacks.  
209 However in the first months of life it is not likely that other products were introduced. We  
210 created our specific duration, exclusivity and solid foods categories based on the collected  
211 data and growth measurements. These categories do not enable direct comparison with the  
212 widely used categories (6 months) of the WHO. Furthermore, our study group was ethnically  
213 homogenous and the mothers were highly educated. We were not able to assess the effect  
214 of breastfeeding on subcutaneous fat mass development in children with different ethnic and  
215 social backgrounds. Finally, we used skinfold thickness as a measure of subcutaneous fat  
216 mass because of the limited use of body mass index as a direct measure of adiposity in early  
217 childhood. Skinfold thickness provide a simple, easy, and quick yet highly informative  
218 assessment of regional fatness in most age groups and can be used in large-scale  
219 epidemiological studies (Wells and Fewtrell, 2006). In general, intraobserver and  
220 interobserver error are low compared to between-subject variability, but in obese children  
221 accuracy and precision are poorer (Wells and Fewtrell, 2006; Nevill *et al.*, 2006).  
222 Furthermore, skinfold thickness has a limitation in assessing lean and fat mass of the whole  
223 body (Wells and Fewtrell, 2006).

224

### 225 **Comparison with other studies**

226 Several studies have shown that breastfeeding is associated with a lower risk of later  
227 overweight and obesity (Owen *et al.*, 2005; Owen *et al.*, 2005; Harder *et al.*, 2005, Arenz *et*  
228 *al.*, 2004). Body mass index is a poor outcome due to its low predictive value and lack of  
229 information about fat distribution (Wells *et al.*, 2007). Studies focusing on the association  
230 between breastfeeding and body composition instead of body mass index did show

231 inconsistent associations (Burdette *et al.*, 2006; Gale *et al.*, 2007). This may be due to  
232 differences in body measurements, ages and samples sizes. A study among adult males  
233 from Brazil did not show an association between breastfeeding and adult body fat, measured  
234 by skinfolds and fat mass using a bio-impedance scale (Victora *et al.*, 2003), while a large  
235 study in the UK reported a negligible protective effect of breastfeeding duration for more than  
236 6 months on mean body fat measured with Dual Energy X-ray Absorptiometry (DEXA) in  
237 children aged 9-10 years (Toschke *et al.*, 2007). Any association was attenuated after  
238 adjustment for confounders. One study in Southampton reported a graded association  
239 between shorter breastfeeding duration and higher DXA- derived fat mass in children aged 4  
240 years (Robinson *et al.*, 2009). In contrast, two studies, assessing the associations of  
241 breastfeeding and direct measures of body composition using DEXA at ages of 2 and 5  
242 years, did not show any association (Burdette *et al.*, 2006; Tull Dahl *et al.*, 1999). We used  
243 skinfold thickness as measures of subcutaneous fat mass at younger ages, but the results  
244 are in line with these previous studies. Only at the age of 6 months we found that shorter  
245 breastfeeding duration leads to higher peripheral and total fat mass. Our study was the first  
246 study that used both breastfeeding duration and exclusivity, to examine the effect on  
247 subcutaneous fat mass. We showed that non- exclusive breast fed was associated with  
248 higher peripheral and total subcutaneous fat mass at the age of 1.5 months and higher  
249 central fat mass at the age of 24 months. We cannot explain these differences. However,  
250 central fat mass might be stronger related to adverse cardiovascular and metabolic health  
251 outcomes (Fox *et al.*, 2007; Pischon *et al.*, 2008). Although the effect estimates were small,  
252 exclusive breast fed might affect subcutaneous fat mass development in early childhood.

253           The European Society for Pediatric Gastroenterology, Hepatology and Nutrition  
254 (ESPGHAN) Nutrition Committee recommended in 2008 that complementary foods (solid  
255 foods and liquids other than breastfeeding or formula) should not be introduced before 4  
256 months and not later than 6 months (Agostoni *et al.*, 2008). Many studies in industrialized  
257 countries showed non-adherence to these recommendations (Noble and Emmett, 2006;  
258 Scott *et al.*, 2009). In our Dutch study population, we found that most mothers introduced

259 solid foods mainly after the age of 4 months. There is conflicting evidence about the relation  
260 between timing of introduction of solid foods and adiposity in childhood. A few studies did not  
261 show differences in adiposity between early and delayed introduction of solid foods (Kramer,  
262 1981; Zive *et al.*, 1992). One recent study suggested that a diet based on fruit, vegetables,  
263 and home-prepared foods in the first year of life is associated with a higher lean and lower fat  
264 mass measured with DXA at the age of 4 years (Robinson *et al.*, 2009). The same study  
265 group reported a greater gain in both weight and skinfold thickness between 6 and 12  
266 months among infants who received the same diet with fruit, vegetables and home-prepared  
267 foods at the age of 6 months (Baird *et al.*, 2008). We did not observe significant associations  
268 between early introduction of solid foods and subcutaneous fat mass measures.

269

## 270 **Conclusion**

271 Our results suggest that a shorter duration and non- exclusive breast fed affect early body  
272 composition during the first 2 years of life. Early introduction of solid foods was not  
273 associated with subcutaneous fat mass measures. Follow-up studies are needed to assess  
274 whether breastfeeding duration and exclusivity affect subcutaneous fat mass and other  
275 measures of body composition at older ages.

276

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283 general practitioners, hospitals, midwives and pharmacies in Rotterdam.

284

285 **Conflict of interest**

286 The authors declare no conflict of interest.

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383

**Legend for Figure 1**

Flow chart of participants in study

**Table 1 Subject characteristics <sup>a</sup>**

	<b>Total (n = 779)</b>
<b>Maternal characteristics</b>	
Age (years)	32.3 (24.9 – 37.9)
Height (cm)	170.8 (6.3)
Weight (kg)	72.0 (13.4)
Body Mass Index (kg/m <sup>2</sup> )	24.7 (4.4)
Highest educational level (%)	
Low	1.8
Moderate	34.5
High	63.7
Smoking in pregnancy (%)	
Ever	22.2
Never	77.8
Alcohol consumption in pregnancy (%)	
Ever	70.1
Never	29.9
Parity (%)	
0	62.5
≥1	37.5
<b>Birth characteristics</b>	
Males (%)	51
Gestational age (weeks)	40.3 (37.1 – 42.1)
Weight (grams)	3515 (549)
Small for gestational age (<5%)	4.9

Low birth weight (<2500 g) (%)	3.6
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Preterm birth (%)	4.1
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**Breastfeeding**

Ever (%)	87.5
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Duration (months)	4.5 (0.0 – 12.0)
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**Solid foods (fruit- or vegetables)**

< 4 months introduced (%)	7.7
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> 4-5 months introduced (%)	60.4
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> 5 months introduced (%)	31.9
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<sup>a</sup>Values are means (SD), percentages or medians (90% range) for variables with skewed distribution. Of the total group, data were missing on maternal anthropometrics (n = 5), maternal education (n = 9), maternal smoking (n = 98), maternal alcohol use (n = 93), parity (n = 1), breastfeeding duration (n = 141), introduction solid foods (n = 153).



4 months <sup>c</sup>

(n = 210)

*P for trend*

*P = 0.07*

*P = 0.41*

*P = 0.16*

***P < 0.01***

*P = 0.13*

***P = 0.02***

*P = 0.38*

***P < 0.01***

*P = 0.06*

---

<sup>a</sup>Values are unstandardized regression coefficients (95% confidence interval).

<sup>b</sup>\*  $P < 0.05$  and \*\*  $P < 0.01$  using multiple linear regression models. Models are adjusted for child's age at visit, sex, birth weight, maternal education, maternal body mass index, smoking and parity, gestational age, current height and observer.

<sup>c</sup>Non-exclusive breastfeeding until 4 months includes partial until 4 months, partial thereafter; and partial until 4 months, not thereafter. Exclusive breastfeeding until 4 months includes exclusive until 6 months; exclusive until 4 months, partial thereafter; exclusive until 4 months, not thereafter.

**Table 3 Age at introduction of solid foods and subcutaneous skinfolds (mm) in early childhood <sup>a b c</sup>**

Solid foods (fruit- or vegetables)	Age 6 months			Age 24 months		
	Peripheral fat (mm) (95% CI)	Central fat (mm) (95% CI)	Total fat (mm) (95% CI)	Peripheral fat (mm) (95% CI)	Central fat (mm) (95% CI)	Total fat (mm) (95% CI)
N = 779	N = 486	N = 484	N = 484	N = 476	N = 469	N = 469
< 4 months (n = 48)	0.23 (-1.11, 1.56)	0.96 (-0.30, 2.21)	1.18 (-1.04, 3.40)	1.66 (-0.11, 3.42)	-0.09 (-1.39, 1.21)	1.29 (-1.46, 4.04)
> 4-5 months (n = 378)	-0.06 (-0.79, 0.67)	0.45 (-0.24, 1.14)	0.40 (-0.82, 1.61)	0.82 (-0.09, 1.73)	0.66 (-0.01, 1.33)	1.46 (0.05, 2.88)*
>5 months (n = 200)	<b>Reference</b>	<b>Reference</b>	<b>Reference</b>	<b>Reference</b>	<b>Reference</b>	<b>Reference</b>
<i>P for trend</i>	<i>P = 0.89</i>	<i>P = 0.10</i>	<i>P = 0.31</i>	<b><i>P = 0.03</i></b>	<i>P = 0.29</i>	<i>P = 0.08</i>

<sup>a</sup>Values are unstandardized regression coefficients (95% confidence interval) using multiple linear regression models.

<sup>b</sup>Models are adjusted for child's age at visit, sex, maternal education, maternal body mass index, smoking and parity, gestational age, birth weight, current height, observer and breastfeeding duration.

<sup>c</sup> \* P < 0.05





**Figure 1 Flow chart of participants in study**

