

Late introduction of complementary feeding, rather than duration of breastfeeding, may protect against adult overweight^{1–3}

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ABSTRACT

Background: Early nutrition may affect the risk of overweight in later life.

Objective: The objective was to explore the effect of the duration of breastfeeding (BF) and age at introduction of complementary feeding (CF) on body mass index (BMI) during childhood through adulthood.

Design: The study was based on a subsample of the Copenhagen Perinatal Cohort established in 1959–1961 ($n = 5068$). Information on BF and available information on CF (age of introduction of “spoon-feeding,” “vegetables,” “egg,” “meat,” and “firm food”) and several covariates were collected in infancy and linked with information on BMI from follow-up examinations in childhood and adulthood at age 42 y.

Results: The median (10th, 90th percentiles) durations of any BF and age at introduction of spoon-feeding were 2.50 (0.23, 6.50) and 3.50 (2.00, 6.00) mo, respectively. After 1 y of age and throughout childhood and adolescence, no association between BF and BMI was found in regression models also adjusted for age at introduction of spoon-feeding and covariates. The risk of overweight at age 42 y decreased or tended to decrease with increasing age (in mo) at introduction of spoon-feeding [odds ratio (OR): 0.94; 95% CI: 0.86, 1.02], vegetables (OR: 0.90; 95% CI: 0.81, 0.98), meat (OR: 0.93; 95% CI: 0.87, 1.00), and firm food (OR: 0.92; 95% CI: 0.86, 0.98) but not egg (OR: 0.98; 95% CI: 0.91, 1.05).

Conclusion: The findings of this study suggest that introduction of CF at a later age (within the range of 2 to 6 mo) is protective against overweight in adulthood but do not support a protective effect of a longer duration of BF. *Am J Clin Nutr* 2010;91:619–27.

INTRODUCTION

The obesity epidemic is already evident in early childhood (1, 2) and is increasing at an accelerating rate (3), which highlights the need to identify early determinants. The idea that breastfeeding (BF) protects against obesity has therefore received considerable interest, and BF in the United States is included in recommendations to reduce the prevalence of childhood obesity (4). According to both a review (5) and an intervention study based on a cluster randomization to BF promotion (6), confounding and publication bias could, however, have led to the BF-obesity association. Furthermore, few studies have explored the persistency of the potential BF-obesity association into adulthood. On the basis of the Nurses' Health Study, it was found that BF was associated with a reduced risk of obesity, as assessed by recall of one's own body shape, until 5 y of age, whereas no effect was seen at ages 10, 18, or 37–54 y (7).

A longer duration of BF is associated with a delayed introduction of complementary feeding (CF) (8–12), and an interaction between BF and CF has been reported such that early (<16 wk) introduction of CF was associated with an increased infancy weight gain only for those breastfed <20 wk (8). Despite this and the large number of studies addressing the issue of BF and obesity, only limited knowledge exists regarding the effect of age at introduction of CF on obesity. An analysis of data from 5 randomized trials of different dietary interventions, found infants introduced to CF at <12 wk of age to be heavier at 12 wk than those introduced to food later, but the difference did not persist until 18 mo of age (13). In agreement with this, an intervention study of early (3–4 mo) compared with later (6 mo) introduction to CF, including only formula-fed infants, also showed no differences in weight, length, or percentage body fat at 12 mo of age (14). Interestingly, a cohort study showed no effect of timing of CF on weight at 2 y of age (11), but, at age 7 y, early introduction of CF (<15 wk) was associated with an increased percentage body fat (15). In a study of US children, delayed introduction of CF was associated with a significant, but minor reduction in the risk of overweight (0.1% per month) at age 3–4 y (16). Other studies have not supported an association between timing of CF and body mass index (BMI; in kg/m^2) (10, 17–19) or body fatness in childhood (9), but it is unknown whether an effect is seen after childhood.

In this study, we explored the effect of duration of BF and age at introduction of CF (indicated by age at introduction of “spoon-

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feeding,” “vegetables,” “egg,” “meat,” and “firm food”) in relation to BMI from age 1 through 42 y.

SUBJECTS AND METHODS

The Copenhagen Perinatal Cohort

The Copenhagen Perinatal Cohort consists of 9125 individuals born at the Copenhagen University Hospital from 1959 to 1961 (20). The hospital preferentially admitted mothers for whom home delivery was “inadvisable” (primarily single mothers) and mothers with previous or expected pregnancy or delivery complications. Interviews on social, general medical, and obstetrical history were conducted before delivery when attending the hospital antenatal clinic and during the first few days after birth, when the infants were also examined. The mothers and their offspring were further invited to an examination at ages 1, 3, and 6 y at the hospital (20).

Follow-up examinations

Information on height and weight (7–14 y) was obtained from mandatory school health examinations for those attending school in the municipality of Copenhagen (1, 21) and for men from draft board examinations (mandatory except for men with documented disqualifying illness or disability—not including excess weight) (22). At the age of 20–34 y, a subsample participated in a research program on the effect of prenatal exposure to maternal prescribed medication (22). At the age of 41–43 y (referred to as 42 y), 98% of the study participants surviving infancy were still alive and traceable, and they were sent a questionnaire on lifestyle risk factors and health issues. This included weight, height, and waist circumference measured with an enclosed tape measure. The response rate was 54%. The follow-up examinations were approved by the local ethical committees, and participants gave written informed consent.

Information on BF and introduction of CF

Information on BF and CF was collected at the 1-y examination by a physician who interviewed the mother. The mothers were asked both about duration of exclusive BF and total duration of BF, but two-thirds of the mothers gave the same answer to these 2 questions. The findings are presented for duration of any BF, but the same pattern was seen when exclusive BF was used in the analysis instead (data not shown). Duration of BF was originally recorded on an 11-category scale, and the middle values were assigned for use in continuous analyses (1 wk, 3 wk, and 1.5, 2.5, 3.5, 4.5, 5.5, 6.5, 8.0, 10.5, and 13.0 mo). Twenty-five percent reported they had stopped BF in the first or second week of life (coded as 1 wk), which included those who did not start BF. It has, however, been reported that only 9% of the infants did not receive any breast milk at the age of 5 d and that the policy of the Maternity Departments at the hospital at that time was to encourage BF from a few hours after delivery, except for mothers with severe mental distress, tuberculosis, some forms of epilepsy, and mothers who had decided to adopt away their child (20). If adequate milk production was not established 3–4 d after birth, supplementary sugar water was given. Mothers of low-birth-weight or ill infants were encouraged to express milk for administration by tube or bottle. Infants who were not breastfed were given formula consisting of either a boiled 50% cow milk

mixture diluted with barley water and added sugar or a commercial butter milk preparation (20).

Regarding CF, questions were asked about the age when the infants were introduced to 1) spoon-feeding, 2) vegetables, 3) egg, 4) meat, and 5) firm food, which was also described as “soaked bread and biscuits.” The age at which the infants started to eat with a spoon was used as the primary CF variable to focus on introduction of CF. Of those with information on all 5 questions ($n = 4143$), 79% were introduced to vegetables at the same age as they started spoon-feeding. Nineteen percent of the children started spoon-feeding before they were introduced to vegetables, egg, meat, or firm food, and they are therefore likely to have been introduced to gruel first.

Outcome variables

BMI from 1 to 42 y and overweight (BMI ≥ 25) at age 42 y were the outcome variables. The age intervals at the preschool follow-up examinations varied and only measurements performed within the age intervals ≥ 10 to <14 mo, ≥ 2.5 to <3.5 y, and ≥ 5.5 to <6.5 y were included and referred to as the 1-, 3-, and 6-y examination, respectively. From the school health records, BMI from age ≥ 6.5 to <7.5 y were included as a 7-y measurement and similarly for the 8–14-y measurements. All childhood BMI measurements were transformed to BMI z scores by using the British 1990 growth references (23) adjusted for sex and exact age. For adults (aged 20–34 and 42 y), no such reference is available; therefore, internal sex-specific BMI- z scores were created. Analyses including BMI at the draft board (range: 16–23 y) and the first adult follow-up examination (range: 20–34 y) were adjusted for current age. Adult waist circumference (42 y) was furthermore used as the outcome variable in both models with and without adjustment for current BMI.

Covariates

Potential confounders included in adjusted analyses were sex, maternal age (y), prepregnant BMI, gestational weight gain (kg, based on the following categories: <6 , 7–8, 9–10, 11–12, 13–15, and ≥ 16 kg as originally recorded), birth weight (g), parental social class (1- to 8-point scale, 8 is the highest), breadwinner’s education (1- to 4-point scale, 4 is the highest), single mother status (yes or no), preterm birth (yes or no, defined as a gestational age ≤ 37 wk due to the original categorization of the variable), and maternal smoking during pregnancy. These variables were all significantly associated with duration of BF, age at introduction of spoon-feeding (the available variable best reflecting introduction of CF) and/or offspring adult BMI (42 y) in bivariate analyses. Preliminary analyses suggested that parity was not a potential confounder, and it was therefore not included in the analyses.

Subjects available for analysis and sample attrition

The original cohort consisted of 9125 infants, of whom 996 were either stillborn, died during infancy, or were from twin or triple births and were excluded. These rates were high because of the hospitals’ admission criteria and high prevalence of preterm births that included infants born as early as 20 wk of gestation. Of the remaining 8129 individuals, this study included the 5068 individuals with information on BF, introduction of spoon-feeding, birth weight, and at least one BMI measurement from 1 y

of age or older (273 subjects did not have such measurements). In a comparison of BMI *z* scores from 3 to 42 y between the 5068 included and the 3061 nonincluded individuals (including all available measurements at all ages), no significant differences were seen (data not shown). Birth weight and 1 y BMI *z* scores were, however, lower among those not included (mean ± SD): 3191 ± 593 compared with 3232 ± 588 g (*P* = 0.003) and 0.09 ± 1.12 compared with 0.26 ± 1.09 (*P* = 0.001), respectively.

Adult BMI (42 y) was considered the most important outcome of the study. Within the included subsample (*n* = 5068), those with information on adult BMI (42 y) had better social conditions in infancy and were breastfed for a longer time, whereas no difference was seen with respect to age at introduction of CF compared with those who did not participate in the last follow-up (Table 1). Birth weight and BMI through childhood did not differ, but at age 20–34 y the prevalence of obesity was lower among the men who participated in the last follow-up than in those who did not.

Statistical analyses

At all ages, all individuals with a BMI measurement were included because the subsample with information on BMI at all ages (*n* = 2) was too small for separate analysis. The estimates are therefore based on differing subsamples. The effects of duration of BF and age at introduction of CF on offspring BMI *z* scores were explored in linear regression models with and without adjustment for covariates. Preliminary analyses and visual inspection indicated that it was appropriate to include BF and CF as linear variables at all ages. Birth weight, maternal prepregnant BMI, and maternal age were also included as continuous variables, whereas the remaining covariates were included as categorical variables with dummy coding. Logistic regression was used to explore the effect of BF and CF on the risk of adult (42 y) overweight and obesity. The regression analyses were conducted by using SPSS (version 15.0; SPSS Inc, Chicago, IL).

TABLE 1
Baseline characteristics of the cohort (*n* = 5068) in relation to participation at the second adult follow-up examination (age 42 y)

	Women				Men			
	Participants		Nonparticipants		Participants		Nonparticipants	
	<i>n</i>	Value	<i>n</i>	Value	<i>n</i>	Value	<i>n</i>	Value
Maternal characteristics								
Age (y)	1544	26.6 ± 6.7 ¹	890	26.0 ± 6.4 ²	1331	26.3 ± 6.4	1276	26.2 ± 6.7
Prepregnancy BMI (kg/m ²)	1433	21.7 ± 2.9	806	21.8 ± 3.0	1244	21.6 ± 2.8	1183	21.8 ± 3.1
BMI ≥ 25 kg/m ² (%)	—	11	—	12	—	10	—	11
BMI ≥ 30 kg/m ² (%)	—	1	—	1	—	1	—	2
Smoking during pregnancy (%)	1516	53	876	53	1318	48	1256	52
Gestational weight gain (kg)	961	11.3 ± 3.6	522	11.3 ± 3.5	839	11.7 ± 3.5	745	11.6 ± 3.6
Social class (1- to 8-point scale)	1482	4.14 ± 1.83	862	3.91 ± 1.75 ³	1268	4.25 ± 1.83	1231	3.91 ± 1.79 ⁴
Breadwinner's education (1- to 4-point scale)	1443	2.42 ± 0.69	832	2.38 ± 0.65	1252	2.48 ± 0.71	1276	2.38 ± 0.68 ⁴
Single mother status (%)	1533	29	883	33 ²	1327	30	1268	34
Offspring characteristics								
Preterm (%) ⁵	1260	17	730	17	1090	20	1014	19
Breastfeeding <2 wk (%) ⁶	1546	15	897	19 ²	1338	17	1287	19
Duration of any breastfeeding (mo) ⁷	1309	3.63 ± 2.78	730	3.24 ± 2.54 ³	1105	3.65 ± 2.77	1045	3.41 ± 2.68
Timing of spoon-feeding (mo)	1546	3.83 ± 1.47	897	3.81 ± 1.51	1338	3.75 ± 1.49	1287	3.80 ± 1.51
Birth weight (g)	1546	3171 ± 555	897	3158 ± 587	1338	3312 ± 583	1287	3273 ± 620
1-y BMI (kg/m ²)	1101	17.67 ± 1.50	691	17.61 ± 1.63	997	18.14 ± 1.51	900	18.15 ± 1.51
3-y BMI (kg/m ²)	758	15.86 ± 1.31	417	15.90 ± 1.40	653	16.03 ± 1.31	555	16.17 ± 1.44
6-y BMI (kg/m ²)	583	15.14 ± 1.40	312	15.27 ± 1.46	512	15.44 ± 1.26	429	15.47 ± 1.41
8-y BMI (kg/m ²)	402	15.61 ± 1.71	256	15.63 ± 1.72	330	15.66 ± 1.30	307	15.75 ± 1.50
11-y BMI (kg/m ²)	402	16.92 ± 2.47	250	16.77 ± 2.21	333	16.75 ± 1.90	299	16.91 ± 2.08
14-y BMI (kg/m ²)	368	18.96 ± 2.47	224	19.02 ± 2.62	298	18.51 ± 2.34	270	18.73 ± 2.54
Draft (16–23 y) BMI (kg/m ²)	—	—	—	—	1115	21.80 ± 2.65	1010	21.69 ± 2.78
Adult (20–34 y) BMI (kg/m ²)	289	22.54 ± 3.76	100	23.16	257	23.64 ± 2.81	150	23.78 ± 3.96
BMI ≥ 25 kg/m ² (%)	—	18	—	25	—	26	—	25
BMI ≥ 30 kg/m ² (%)	—	5	—	7	—	2	—	6 ²
Adult (42 y) BMI (kg/m ²)	1546	24.48 ± 4.88	—	—	1338	25.67 ± 3.69	—	—
BMI ≥ 25 kg/m ² (%)	—	34	—	—	—	51	—	—
BMI ≥ 30 kg/m ² (%)	—	12	—	—	—	11	—	—
Adult waist circumference (cm)	1518	85.9 ± 12.7	—	—	1318	95.2 ± 10.9	—	—

¹ Mean ± SD (all such values).

^{2–4} Significantly different from participants (*t* test, Mann-Whitney *U* test, or chi-square test): ²*P* ≤ 0.05, ³*P* ≤ 0.01, ⁴*P* ≤ 0.001.

⁵ Born at gestational week ≤37 as explained in Subjects and Methods.

⁶ Presented separately because those not establishing breastfeeding were included in this group.

⁷ Does not include those who breastfed for <2 wk.

TABLE 2Spearman correlation coefficients between duration of any breastfeeding (in mo) and age (in mo) at the time of introduction of complementary feeding¹

	Spoon-feeding	Vegetables	Egg	Meat	Firm food
Breastfeeding	0.17 (5068)	0.20 (4898)	0.06 (4392)	0.07 (5444)	0.02 (4339) ²
Spoon-feeding		0.80 (4898)	0.30 (4392)	0.24 (4544)	0.17 (4339)
Vegetables			0.34 (4291)	0.28 (4455)	0.17 (3967)
Egg				0.57 (4216)	0.28 (3967)
Meat					0.37 (4130)

¹ *n* in parentheses. *P* < 0.001 for all, except where otherwise indicated.² *P* = 0.163.**RESULTS**

The characteristics of the study participants and their mothers are shown in Table 1. The prevalence of overweight was low among the mothers (11%), but had increased to 34% and 51% in the adult (42 y) women and men, respectively. On the basis of the International Obesity Task Force's criteria for childhood overweight (24), the prevalence ranged from 3% to 5% in both girls and boys during the school years.

The median (10th, 90th percentiles) durations of any BF and age at introduction of spoon-feeding were 2.50 (0.23, 6.50) and 3.50 (2.00, 6.00) mo, respectively. The mean (\pm SD) age at introduction of CF for spoon-feeding, vegetables, egg, meat, and firm food were 3.80 ± 1.49 , 4.05 ± 1.34 , 6.08 ± 1.84 , 6.87 ± 1.92 , and 8.10 ± 2.08 mo, respectively. Duration of BF was positively correlated with introduction of all CF food items except firm food. Age at introduction of spoon-feeding, vegetables, egg, meat, and firm food were all positively correlated, but the correlations between spoon-feeding and vegetables ($r = 0.80$) and between egg and meat ($r = 0.57$) were especially high (Table 2). Duration of BF and age at introduction of spoon-feeding were not similarly related to covariates (data not shown). Mothers with high prepregnancy BMI breastfed for a shorter time and tended to start spoon-feeding at an earlier age. Infants from a high social class were breastfed longer, but were also introduced earlier to spoon-feeding. The same was seen for

infants with the highest birth weight; they were breastfed for a longer period, but were also introduced earlier to spoon-feeding. Compared with normal-weight subjects, participants who were overweight or obese as adults (42 y) had a higher birth weight, had mothers who were younger, had mothers who were heavier before pregnancy, and had mothers from a lower social class (Table 3).

The longest duration of BF ($P < 0.001$) and latest introduction of spoon-feeding ($P = 0.082$) were seen among the normal-weight subjects (Table 3). When BMI *z* scores were regressed from 1 to 42 y on duration of BF and only adjusted for sex, a significant inverse association was seen at 1 y (β : -0.018 ; 95% CI: -0.032 , -0.007) and at 42 y (β : -0.019 ; 95% CI: -0.031 , -0.006) for BMI *z* scores per month of BF at 1 and 42 y, respectively. Restricting the same analyses to the sample with information on all covariates and age at introduction of spoon-feeding (but not adjusting for it), the associations persisted for BMI *z* scores at 1 y (β : -0.025 ; 95% CI: -0.043 , -0.007), but not for those at 42 y (β : -0.005 ; 95% CI: -0.024 , 0.013). When covariates were adjusted for the age at introduction of spoon-feeding, only the inverse association at 1 y remained significant (β : -0.022 ; 95% CI: -0.041 , -0.003) (Figure 1).

When BMI *z* scores were regressed from 1 to 42 y on age at introduction of spoon-feeding and adjusted for only sex, significant or borderline significant inverse associations were seen

TABLE 3

Relation between covariates and offspring adult BMI category (age 42 y)

	<i>n</i>	Offspring adult BMI (kg/m ²)				<i>P</i> ¹
		<18.5	≥ 18.5 to <25	≥ 25 to <30	≥ 30	
Total sample (%)	2884	2	56	31	11	
Maternal characteristics						
Age (y)	2875	28.2 ± 7.9^2	26.7 ± 6.6	26.3 ± 6.5	25.4 ± 6.2	0.004
Maternal BMI (kg/m ²)	2677	20.5 ± 2.0	21.4 ± 2.7	21.8 ± 2.8	23.1 ± 3.6	<0.001
Gestational weight gain (kg)	1800	10.4 ± 3.9	11.4 ± 3.5	11.6 ± 3.6	11.9 ± 3.5	0.067
Social status at birth (1- to 8-point scale)	2750	4.53 ± 1.99	4.36 ± 1.88	4.09 ± 1.78	3.56 ± 1.56	<0.001
Breadwinner's education (1- to 4-point scale)	2695	2.43 ± 0.65	2.51 ± 0.73	2.41 ± 0.68	2.25 ± 0.58	<0.001
Single mother (%)	2860	17	28	31	34	0.041
Smoking in pregnancy (%)	2834	61	50	50	55	0.158
Infant characteristics						
Preterm (%) ³	2350	19	17	20	19	0.363
Birth weight (g)	2842	2974 ± 537	3222 ± 563	3255 ± 582	3294 ± 586	0.002
Duration of breastfeeding (mo)	2884	2.32 ± 2.0	3.24 ± 2.90	2.97 ± 2.80	2.73 ± 2.58	<0.001
Timing of spoon-feeding (mo)	2884	3.70 ± 1.26	3.85 ± 1.52	3.75 ± 1.42	3.64 ± 1.40	0.082

¹ ANOVA, chi-square test, or Kruskal-Wallis test.² Mean \pm SD (all such values).³ Born at gestational week ≤ 37 as explained in Subjects and Methods.

at all ages ($P < 0.100$) at 1, 7, 8, 9, 11, 12, and 14 y; draft board; 20–34 y, and 42-y follow-up. Only the associations at age 14, 20–34, and 42 y persisted in unadjusted analyses of the reduced sample with information on all covariates (data not shown). When adjustment for covariates was carried out together with inclusion of BF, the inverse association at 20–34 y ($P = 0.07$) and 42 y persisted ($P = 0.03$) (Figure 1).

Although age at introduction of spoon-feeding did not seem to influence 1-y BMI z scores, it was explored whether the effect

of spoon-feeding on adult BMI (42 y) was explained by an effect of infancy weight gain by including 1-y weight and exact age at the measurement in the model. With adult BMI z scores (42 y) as the dependent variable, the effect (β) of spoon-feeding was -0.048 (95% CI: $-0.088, -0.007$) and -0.046 (95% CI: $-0.086, -0.006$) when weight at 1 y was also included in the model ($n = 992$ in both models).

In the regression models shown in Figure 1, no significant interactions between duration of BF and age at introduction of

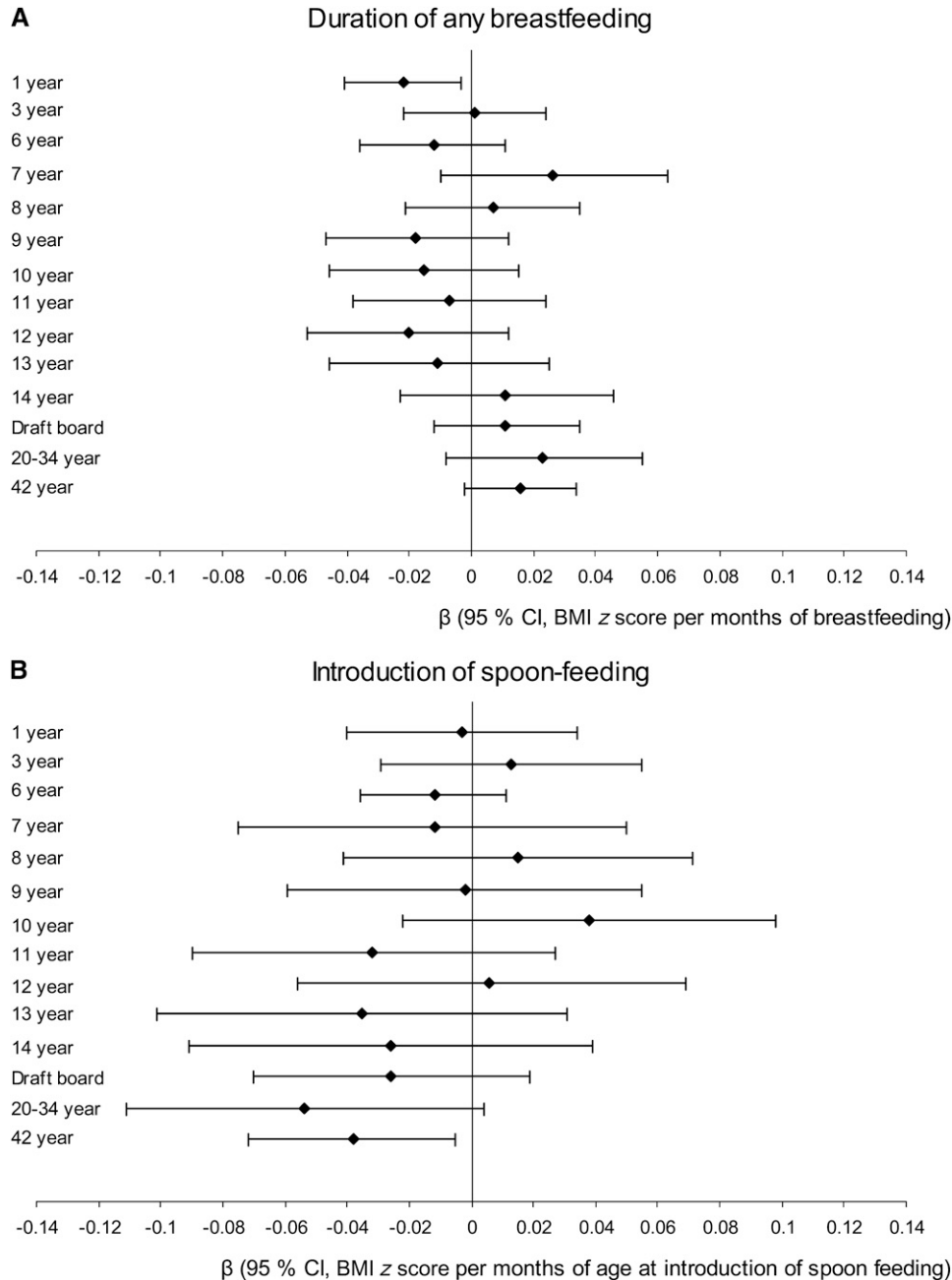


FIGURE 1. Results from regression analyses with BMI z scores from age 1 to 42 y as dependent variables and the duration of breastfeeding (A) and age at introduction of complementary feeding (B) as independent variables included in the same analysis. Each line represents the β coefficient with 95% CI from a single analysis. All models were further adjusted for sex, maternal age at birth, prepregnancy BMI, gestational weight gain, smoking during pregnancy, social class, breadwinner’s education, single mother status, prematurity, and birth weight. The number of subjects varied from 367 (BMI at 7 y) to 1675 (BMI at 1 y).

TABLE 4Estimates from logistic regression analyses with adult (age 42 y) overweight and obesity as outcomes¹

	n	OR (95% CI)	
		Overweight	Obesity
Age (mo) at introduction of spoon-feeding	1305	0.94 (0.86, 1.02)	0.94 (0.83, 1.08)
Duration of breastfeeding		1.00 (0.96, 1.05)	1.05 (0.98, 1.12)
Age (mo) at introduction of vegetables	1270	0.90 (0.81, 0.98)	0.89 (0.76, 1.03)
Duration of breastfeeding		1.01 (0.97, 1.06)	1.06 (0.99, 1.14)
Age (mo) at introduction of eggs	1146	0.98 (0.91, 1.05)	1.06 (0.96, 1.18)
Duration of breastfeeding		0.99 (0.97, 1.06)	1.02 (0.95, 1.10)
Age (mo) at introduction of meat	1188	0.93 (0.87, 1.00)	0.97 (0.87, 1.08)
Duration of breastfeeding		0.99 (0.95, 1.04)	1.03 (0.96, 1.10)
Age (mo) at introduction of firm food	1132	0.92 (0.86, 0.98)	1.00 (0.90, 1.11)
Duration of breastfeeding		0.99 (0.94, 1.03)	1.03 (0.95, 1.11)

¹ OR, odds ratio. All models were further adjusted for sex, maternal age at birth, prepregnancy BMI, gestational weight gain, smoking during pregnancy, social class, breadwinner's education, single mother status, prematurity, and birth weight. When the analyses were conducted with only the 1009 subjects for whom information on age at introduction of spoon-feeding, vegetables, eggs, meat, and firm food were available, the findings did not change.

spoon-feeding were seen ($P > 0.05$ at all ages) as explored by including the product of BF (mo) and spoon-feeding (mo) or the interaction term of BF < 2 mo (46%) or ≥ 2 mo (54%) and spoon-feeding (mo). An analysis stratified on duration of BF further confirmed this finding: at 42 y, the association (β) of spoon-feeding (age in mo) with BMI (kg/m^2) was -0.151 (95% CI: $-0.369, 0.068$) and -0.101 (95% CI: $-0.304, 0.100$) for individuals with BF < 3 mo compared with ≥ 3 mo, respectively (P for interaction = 0.644)

The analyses with BMI z scores from 1 to 42 y as outcome were repeated with age at introduction of vegetables, egg, meat, and firm food as independent variables and adjusted for covariates and duration of BF. In these analyses, BF was again not associated with BMI after age 1 y (data not shown). Age at introduction of vegetables was inversely associated with BMI z scores at 20–34 y (β : -0.072 ; 95% CI: $-0.133, -0.010$) and 42 y (β : -0.064 ; 95% CI: $-0.101, -0.027$). Age at introduction of egg was not associated with BMI z scores at any age (data not shown). Age at introduction of meat was inversely associated with BMI z scores at age 42 y (β : -0.032 ; 95% CI: $-0.059, -0.005$). Age at introduction of firm food was inversely associated with BMI z scores at 1 y (β : -0.053 ; 95% CI: $-0.082, -0.024$), 10 y (β : -0.054 ; 95% CI: $-0.096, -0.012$), 11 y (β : -0.057 ; 95% CI: $-0.101, -0.013$), and borderline significant ($P = 0.097$) at 42 y (β : -0.022 ; 95% CI: $-0.048, 0.004$).

Waist circumference at age 42 y was also used as the outcome, with adjustment for all covariates and both with and without simultaneous adjustment for current BMI. Duration of BF was not associated with waist circumference in any of the models. Early introduction of CF (spoon-feeding and vegetables) was associated with larger waist circumference when not adjusted for BMI. After adjustment for BMI, the effect was reduced (data not shown) but remained significant for spoon-feeding (β : -0.25 ; 95% CI: $-0.49, -0.01$; waist circumference in cm per month of age at introduction of spoon-feeding).

Logistic regression analyses with overweight and obesity at 42 y as outcome variables confirmed the findings from the linear regression analyses. In adjusted models, no effect was seen for duration of BF, whereas risk of overweight decreased with in-

creasing age (mo) at introduction of vegetables ($P = 0.014$), meat ($P = 0.044$), and firm food ($P = 0.012$), but not spoon-feeding ($P = 0.112$) and egg ($P = 0.527$; **Table 4**). In a comparison of the effect of early (< 4 mo) compared with late (≥ 4 mo) introduction of CF, a protective effect of late introduction was seen for vegetables ($P = 0.046$) and a similar trend was seen for spoon-feeding ($P = 0.053$; **Figure 2**).

Finally, the pattern of introduction of CF was described by the number of food items (spoon-feeding, vegetables, egg, meat, and firm food) introduced at 3, 4, 5, and 6 mo of age (**Table 5**). The OR for overweight increased with increasing number of food items introduced, but it was not significant.

DISCUSSION

Our study suggests that a longer duration of BF was associated with a lower BMI at 1 y of age, but no effect was seen later in childhood or in adulthood. A late introduction of CF was

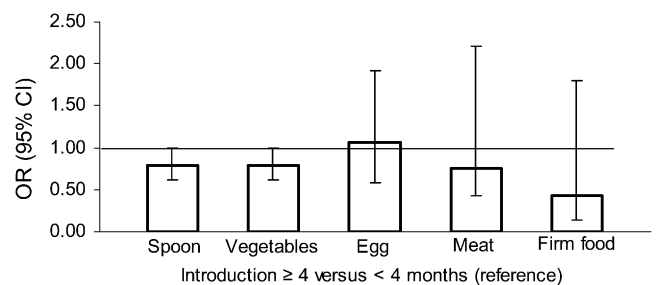


FIGURE 2. Results from logistic regression analyses with overweight [BMI ($\text{in kg}/\text{m}^2$) ≥ 25] at age 42 y as the outcome variable and age ≥ 4 mo compared with < 4 mo of age (reference) at the time of introduction of complementary feeding (spoon, vegetables, eggs, meat, and firm food) as independent variables in separate analyses [odds ratios (ORs) and 95% CIs]. All models were further adjusted for sex, maternal age at birth, prepregnancy BMI, gestational weight gain, smoking during pregnancy, social class, breadwinner's education, single mother status, prematurity, birth weight, and duration of breastfeeding. The numbers of subjects in each analysis were as follows: 1305 for spoon-feeding, 1270 for vegetables, 1146 for egg, 1188 for meat, and 1132 for firm food.

TABLE 5

Frequency distribution of the number of food items introduced at different ages and the association with risk of overweight at age 42 y¹

Number of food items	3 mo (n = 1009)	4 mo (n = 1009)	5 mo (n = 1009)	6 mo (n = 1009)
	%	%	%	%
0	52	25	12	2
1	11	7	5	1
2	33	53	49	21
3	3	10	20	28
4	1	4	14	33
5	0	1	2	15
OR (95% CI) for overweight (42 y) ²	1.10 (0.97, 1.26)	1.08 (0.95, 1.22)	1.06 (0.94, 1.20)	1.09 (0.97, 1.23)

¹ Values were calculated as the sum of spoon-feeding, vegetables, egg, meat, and firm food. OR, odds ratio.

² All models were further adjusted for sex, maternal age at birth, prepregnancy BMI, gestational weight gain, smoking during pregnancy, social class, breadwinner's education, single mother status, prematurity, birth weight, and duration of breastfeeding.

associated with a lower BMI at age 42 y, but, earlier in life, no effect of age at introduction of CF was seen.

Breastfeeding and obesity

Because most of the subjects in our cohort were breastfed for at least some days and because we do not have detailed information on who was never breastfed, our study explored the effect of duration of BF. A longer duration of BF was associated with a lower BMI at age 1y, which agrees with more recent studies (25). The associations we found between duration of BF and covariates were also as in more recent cohorts (26–28); a longer duration of BF was associated with better social conditions in infancy (higher social class, higher breadwinner's education, fewer single mothers), a lower prevalence of smoking during pregnancy, and a lower maternal prepregnancy BMI.

Our finding of no association between BF and obesity in adulthood is in line with other studies of varying size, design, and confounder control (7, 29–34), although one study suggested that BF was associated with an increased risk of obesity (35). Compared with many of these studies, an advantage of our study was the use of information on BF collected at the end of infancy compared with maternal recall later in childhood (31, 33, 34) or in adulthood (7, 35).

One important difference between studies with follow-up in childhood and adulthood relates to the increasing prevalence of obesity among children (2). In our study, the prevalence of overweight according to International Obesity Task Force criteria was 3–5% during the school years, which increased to 35% and 51% for women and men, respectively, at age 42 y. In our sample, overweight was therefore primarily developed in adulthood, and different mechanisms may exist for this compared with overweight developed during childhood in contemporary children. Some studies of contemporary children suggest that BF has its most protective effect in the upper end of the BMI distribution (36), with only a minor—if any—effect on the mean BMI (37, 38). Among children, the obesity epidemic is characterized by an increase in the upper end of the BMI distribution (39); consequently, we found that the possibility of a protective effect of BF in contemporary children should not be excluded. The composition of the current formula is closer to human milk than is the formula used in the 1960s; therefore, it does not seem likely that

a change in formula composition explains the possible protective effect of BF in contemporary children.

Complementary feeding and obesity

At the 1-y examination, questions were asked about age at introduction of spoon-feeding, vegetables, egg, meat, and firm food. Except for egg, later introduction of CF was associated with a lower adult mean BMI (only borderline significant for meat) and a 6–10% lower risk of overweight per 1-mo delay (only borderline significant for spoon-feeding).

Food items introduced late in the weaning period (meat and firm food) were also associated with later obesity in separate analyses. This may have been due to the significant associations between the ages at the time of introduction of the different food items. Another interpretation is that early introduction of meat and firm food is a marker of a high intake of CF. The effect of early introduction of CF could then be more due to an adverse effect of eating a large quantity of CF at an early age than to an effect of age at which CF is introduced. The analyses exploring the effect of number of food items introduced at a specific age showed a pattern consistent with the latter hypothesis, but it was not significant. Our finding also suggests that early introduction of CF (only seen for the variable spoon-feeding) was associated with increased waist circumference, even after adjustment for BMI at age 42 y.

Other studies that explored a potential effect of age at introduction of CF on risk of obesity have included follow-up in childhood, the majority of which found no effects (9, 10, 17–19). Correspondingly, we found no consistent effect of age at introduction of CF on BMI in childhood. It may be that the effect of CF is at least partly expressed already during adolescence and that the effect did not become statistically significant because of a lower number of individuals than at the 42-y follow-up examination. Additional analyses of skewness to explore an effect on the distribution not reflected in the mean (based on the residuals from adjusted regression analyses; data not shown) of the BMI distributions at different ages showed no skewness during childhood but a marked skewness at the later follow-up examinations. There were, however, no difference in this skewness pattern between subjects introduced to CF at <4 mo and those introduced to CF at ≥4 mo.

Interestingly, and in support of a potential programming effect, a prospective Scottish study found that introduction of CF before 15 wk of age was associated with increased weight and percentage body fat at 7 y of age, whereas no effect on weight was seen at the age of 2 y (11). The analysis was adjusted for body weight at the age of introduction of CF, because weight at this time may be a potential confounder because heavier infants are introduced earlier to CF (11–13, 40). Similarly, it appeared in our cohort that an increase in infancy weight gain was not part of a mechanism explaining the association between CF and adult obesity.

It is possible that the early introduction of CF makes individuals more susceptible to an obesogenic environment, which would imply that the expression of the effect is dependent on environmental factors. The mechanism may involve permanent biological changes directly related to weight regulation, such as adipogenesis, appetite control, or effects on the central nervous system that are later associated with behavior leading to overweight and obesity. In a broader perspective, we believe that the observation fits well into other recent findings of obesity risk factors that act during fetal life and are not expressed until later in life. For example, in the same cohort, we reported a positive association between gestational weight gain and offspring BMI, which was not fully expressed until adulthood (41). It has also been reported that maternal smoking during pregnancy results in lower birth weight, but an increased risk of obesity later in childhood (42).

Regarding composition of CF and later obesity, interest has focused on the protein-adiposity hypothesis; ie, a high protein intake in early childhood increases the risk of adiposity in childhood (43). This hypothesis was supported by some studies that explored the role of protein intake at 12 mo of age (44, 45), but not by other studies of protein intake at 6 (44) or 9 (46) mo. In agreement with this finding, our data did not suggest a particular role of the food items egg and meat, which are more protein rich than the other food items. However, we did not have sufficient information on protein intake because the quantity of milk was not recorded.

Whereas residual confounding remains a major concern when addressing the effect of BF on obesity risk, it seems different with respect to CF, because later introduction of CF was associated with lower social class in infancy and not with maternal smoking during pregnancy. A high maternal prepregnancy BMI was associated with an earlier introduction of CF, but only weakly so. Therefore, it seems unlikely that residual confounding by social class, maternal smoking, or maternal BMI explained the observed association between introduction of CF and later obesity. A limitation of our data regarding adult BMI (42 y) was that weight and height were self-reported, and participation may be subject to some bias because of a lower participation rate among overweight subjects (Table 1). Selective underreporting by the heaviest subjects, however, is expected to lead to a weakening of the association. The potential bias with respect to participating in the follow-up will only affect the association if it is different among participants and nonparticipants, which we find unlikely.

According to current recommendations from the World Health Organization (WHO), infants should be exclusively breastfed for the first 6 mo of life, with introduction of CF and continued BF thereafter. It has been argued that the evidence for the benefits of this change in recommendation for infants in high-income countries compared with the previous WHO recommendation of

exclusive BF for 4 to 6 mo is not strong, and that there is a need for more studies (47). One concern has been that exclusive BF may not provide sufficient energy at the age of 6 mo (48). Whether 6 mo is also the optimal time to introduce CF in formula-fed infants has received little attention (49). In our study, 17% of the participants were introduced to spoon-feeding before 3 mo, and 46% did not start until 4 mo of age or later. Our study therefore suggests that postponing the introduction of CF to the recommended 6 mo will be beneficial with respect to risk of later overweight. Too late an introduction of CF (>6 mo) may compromise the supply of total energy, protein, and some micronutrients (50, 51) and might also result in problems with acceptance of new tastes and textures (52).

Conclusions

In the Copenhagen Perinatal Cohort, born in 1959–1961 and followed into adulthood, longer duration of BF was associated with a lower BMI at the age of 1 y after several covariates and age at introduction of CF were taken into account; thereafter, however, the effect disappeared. The present study indicates that early introduction of CF may be associated with an increased BMI and risk of overweight in adulthood independent of BF and several covariates.

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