

Milk consumption during pregnancy is associated with increased infant size at birth: prospective cohort study¹⁻⁴

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ABSTRACT

Background: Cow milk contains many potentially growth-promoting factors.

Objective: The objective was to examine whether milk consumption during pregnancy is associated with greater infant size at birth.

Design: During 1996–2002, the Danish National Birth Cohort collected data on midpregnancy diet through questionnaires and on covariates through telephone interviews and ascertained birth outcomes through registry linkages. Findings were adjusted for mother's parity, age, height, prepregnant BMI, gestational weight gain, smoking status, and total energy intake; father's height; and family's socioeconomic status. The analyses included data from 50 117 mother-infant pairs.

Results: Mean (\pm SD) consumption of milk was 3.1 ± 2.0 glasses/d. Milk consumption was inversely associated with the risk of small-for-gestational age (SGA) birth and directly with both large-for-gestational age (LGA) birth and mean birth weight (P for trend < 0.001). In a comparison of women drinking ≥ 6 glasses/d with those drinking 0 glasses/d, the odds ratio for SGA was 0.51 (95% CI: 0.39, 0.65) and for LGA was 1.59 (1.16, 2.16); the increment in mean birth weight was 108 g (74, 143 g). We also found graded relations ($P < 0.001$) for abdominal circumference (0.52 cm; 0.35, 0.69 cm), placental weight (26 g; 15, 38 g), birth length (increment: 0.31 cm; 0.15, 0.46 cm), and head circumference (0.13 cm; 0.04, 0.25 cm). Birth weight was related to intake of protein, but not of fat, derived from milk.

Conclusion: Milk intake in pregnancy was associated with higher birth weight for gestational age, lower risk of SGA, and higher risk of LGA. *Am J Clin Nutr* 2007;86:1104–10.

KEY WORDS Pregnancy, milk consumption, birth weight

INTRODUCTION

An infant's weight at birth is associated with survival and long-term health; low birth weight is associated with an increased risk of neonatal death (1) and of developing hypertension and type 2 diabetes as an adult (2, 3). The identification of modifiable factors that influence birth weight may lead to interventions that improve the health of the offspring, but remarkably little has been established regarding specific dietary factors that affect fetal growth.

Cow milk is an efficient vehicle for the delivery of many nutrients essential for fetal development and therefore of potential importance for fetal growth. The cultural trait of milk drinking dates 6000–9000 y back when humans first domesticated

livestock and practiced milk-based pastoralism. Because of contemporary production methods, however, modern cow milk has a high content of sex steroids (4), and estrogen has a known stimulating effect on fetal growth (5). In both children and adults, milk consumption increases blood concentrations of insulin-like growth factor I (IGF-I) (6–12), which is a major determinant of growth during childhood.

The relation between maternal intake of cow milk and measures of infant birth size was studied in 1 randomized controlled trial (13), 4 prospective observational studies (14–17), and 2 retrospective observational studies (18, 19), but the findings are inconsistent and do not provide a clear conclusion. In particular, there is a lack of large prospective studies with a sizeable group of women with zero or low milk consumption. We therefore examined in detail, in a large prospective Danish pregnancy cohort (20), the relations of milk intake and milk constituents with measures reflecting intrauterine growth.

SUBJECTS AND METHODS

The Danish National Birth Cohort

The Danish National Birth Cohort (DNBC) (20) and its dietary component (21) have been described in detail elsewhere. Women were recruited while in early pregnancy during January 1997 to

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October 2002. Data were derived from questionnaires, telephone interviews, and registry linkages.

Exposure variables

A 360-item food-frequency questionnaire (FFQ) was completed at ≈ 25 wk of gestation; it referred to the previous 4 wk. The FFQ was validated against dietary records and biomarkers of particular nutrients (22), but not specifically of milk or milk components; the correlation coefficient for total protein was 0.39. We also asked 100 women to complete the FFQ a second time, at ≈ 35 wk of gestation; we found a correlation coefficient of 0.59 for frequency of milk consumption (glasses/d). Milk consumption was recorded in 8 questions in the FFQ; 2 of these referred to consumption of yogurt, in portions per day (including the percentage of fat) and 6 to the consumption of milk (whole milk, 1.5% milk, 0.5% milk, skim milk, churn buttermilk, and chocolate milk), in glasses/d. We aggregated the milk and yogurt variables to obtain frequency measures; according to a Nordic standard, one glass of milk has been estimated to be 200 mL and one portion of yogurt to 150 mL (23). We also quantified dairy products (in g/d) by summing all milk products other than cheese or ice cream. Consumption of milk and its constituents was also quantified on the basis of standard portion sizes (23) and food-composition tables. Absolute zero consumption did not exist for any of these women because some recipe-based food items, such as sauces or bread, contain small amounts of milk. For the analyses using a quantified amount of milk or quantified amounts of protein, carbohydrates, and fat from milk, we divided the women into deciles of intake.

Outcome variables

Birth weight, birth length, head circumference, abdominal circumference, and placental weight were measured and recorded in birth certificates by the midwives attending child birth according to standard procedures issued by the National Board of Health. Midwives in Denmark are trained to follow standardized procedures: birth weight is measured right after birth; birth length is measured from vertex to heel, with legs stretched; head circumference corresponds to "hat measure"; abdominal circumference is measured just above the navel; and placental weight is measured right after delivery and includes membranes and umbilical cord. Gestational age at birth was primarily assessed from the last menstrual period (LMP) recorded in the recruitment form at ≈ 8 wk of gestation. When the LMP-based estimate was uncertain, gestational age was based on information on the expected date of delivery provided by the women in the second interview, which took place at ≈ 30 wk of gestation. We used growth references provided by the British Child Growth Foundation (24, 25) to identify infants with a birth weight below or above the gestational age and sex-specific 10th and 90th percentiles, respectively.

Mother-child pairs available for analysis

A total of 101 042 women registered in the DNBC, of whom 70 187 completed the FFQ. We restricted our analyses to singletons and term births to eliminate potential confounding by twinning and preterm and postterm delivery, resulting in exclusions of 1724 and 12110 observations, respectively. Of the remaining 56 353 observations, we excluded 290 because of abnormally low or high energy intakes [ie, outside the range 600–6000

kcal/d (2508–25 080 kJ/d)] and 218 had missing birth weight. Of the remaining 55845, 5728 women participated more than once during the recruitment period. The exclusion of later births resulted in the final data set of 50 117 women.

Statistical methods

We adjusted for potential confounding by multiple linear (continuous outcomes) and logistic (dichotomous outcomes) regression. We included the following covariates in the models: infant gestational age (in d); infant's sex; mother's parity (nulliparous versus multiparous), age (<20 , 20–30, 30–40, >40 y), height (<160 , 160–169, 169–179, >179 cm), prepregnant BMI (≤ 18.5 , 18.5–25, 25–30, 30–35, 35–40, ≥ 40), gestational weight gain (in quintiles), smoking status (never, occasional, daily <15 cigarettes, daily ≥ 15 cigarettes), and total energy intake (in quintiles); father's height (170<, 170–179, 180–189, >189 cm); and family's socioeconomic status (6 occupational categories). Missing values were assigned to a "missing" category for each of these covariate variables.

RESULTS

For the 50 117 women included in this analysis, the mean (\pm SD) reported consumption of milk was 3.1 ± 2.0 glasses/d, birth weight was 3596 ± 488 g, birth length was 52.0 ± 2.2 cm, head circumference was 35.0 ± 1.6 cm, abdominal circumference was 32.4 ± 6.6 cm, and placental weight was 662 ± 141 g. For increasing categories of milk consumption, energy intake was greater, whereas the proportion of primiparous women and mean age were lower (**Table 1**). Mother's height and father's height tended to be greater with increasing milk intake, whereas the percentage of smokers and women with low education tended to exhibit a U-shaped relation.

In the univariate analysis, mean birth weight was ≈ 100 g higher among the group that consumed 4–5 glasses of milk/d compared with those who consumed no milk. Above that level no further increments were seen (**Table 2**). When adjusted for potential confounders, a similar maximal increment was observed, but the rise tended to be graded across a broader exposure range, from 0 to ≥ 6 glasses of milk/d (**Table 2**).

The odds of being small-for-gestational age (SGA) declined with increasing consumption of milk, and the adjustment for potential confounding factors did not affect the association (**Table 3**). Compared with women who reported never consuming milk, women consuming >6 glasses/d had a 49% (95% CI: 35%, 61%) lower adjusted odds of having an SGA infant. The odds of having a large-for-gestational age (LGA) increased with exposure ($P < 0.001$), and the adjustment for confounding tended to make the associations somewhat stronger. Compared with women who reported no milk consumption, women who reported consuming >6 glasses of milk/d had a 59% (95% CI: 16%, 116%) higher odds of having an LGA infant.

Mean abdominal circumference, placental weight, head circumference, and birth length all showed increases across the whole range of milk intake (P for trend < 0.001 ; **Table 4**). After adjustment for confounding, the total increments were 0.52 cm (0.35–0.69 cm), 26.4 g (15.1–37.7 g), 0.13 cm (0.04–0.25 cm), and 0.31 cm (0.15–0.46 cm) for the 4 measures, respectively.

When we quantified intake of fat and protein from dairy products (excluding cheese and ice cream), no association existed between birth weight and fat from dairy products (**Figure 1**),



TABLE 1Characteristics of women participating in the Danish National Birth Cohort according to frequency of milk consumption ($n = 50\ 117$)

	Median milk consumption [glasses/d (median)]								<i>P</i>
	0 (0)	> 0–1 (0.5)	> 1–2 (1.4)	> 2–3 (2.7)	> 3–4 (3.4)	> 4–5 (4.7)	> 5–6 (5.4)	> 6 (7.2)	
No. of subjects	709	6503	7943	12 721	9181	5550	3789	3721	
Continuous variables									
Gestational age (d)	279.3 ± 8.0 ¹	279.8 ± 7.8	280.0 ± 7.7	280.0 ± 7.8	279.9 ± 7.7	279.9 ± 7.7	279.8 ± 7.7	279.6 ± 7.8	0.50 ²
Mother's age (y)	30.4 ± 4.7	29.4 ± 4.4	29.3 ± 4.4	29.2 ± 4.2	29.1 ± 4.1	28.8 ± 4.1	28.7 ± 4.1	28.2 ± 4.3	<0.001 ²
Mother's height (cm)	168.1 ± 6.3	168.2 ± 6.1	168.7 ± 6.0	168.8 ± 6.0	169.1 ± 6.0	168.9 ± 6.1	169.1 ± 6.1	169.2 ± 6.1	<0.001 ²
Father's height (cm)	181.7 ± 8.3	181.9 ± 7.3	181.9 ± 7.6	181.9 ± 6.9	182.1 ± 7.2	181.9 ± 7.2	182.0 ± 7.1	181.8 ± 7.3	0.14 ²
Prepregnant BMI (kg/m ²)	23.9 ± 4.8	23.6 ± 4.4	23.3 ± 4.0	23.5 ± 4.1	23.2 ± 3.9	23.5 ± 4.0	23.4 ± 4.0	23.6 ± 4.1	0.32 ²
Weight gain (g/wk)	431 ± 263	455 ± 231	467 ± 222	463 ± 219	473 ± 218	480 ± 225	476 ± 232	484 ± 235	<0.001 ²
Energy intake (MJ/d)	8.8 ± 2.9	9.2 ± 2.6	9.6 ± 2.5	10.1 ± 2.5	10.7 ± 2.5	11.1 ± 2.6	11.7 ± 2.7	12.8 ± 3.2	<0.001 ²
Discrete characteristics (%)									
Maternal smoking	26.9	27.4	25.1	24.3	21.8	25.4	25.0	28.6	<0.001 ³
Female births	48.2	50.2	48.7	49.6	48.8	48.0	49.9	47.5	0.08 ³
Multiparity	59.0	51.5	49.2	50.8	46.4	46.6	45.6	43.8	<0.001 ³
Socioeconomic status ⁴									
High status	23.0	23.6	25.1	23.3	25.4	21.6	21.4	17.9	<0.001 ³
Intermediate status	28.8	29.2	30.6	31.2	32.7	31.3	31.3	27.8	
Skilled workers	29.4	26.8	25.5	27.0	24.2	27.2	27.3	30.3	
Unskilled workers	11.9	12.9	11.8	12.2	10.8	12.6	12.5	16.0	
Students	3.8	4.5	4.7	4.1	4.7	4.4	4.0	4.3	
Not working	3.1	3.0	2.5	2.3	2.2	3.0	3.5	3.7	

¹ $\bar{x} \pm SD$ (all such values).² For association as determined by Spearman's correlation coefficient (2-sided *P* value).³ Chi-square tests for measures of an association.⁴ Of the 50 117 women, 23.3% were classified with high status, 30.8% with intermediate status, 26.6% as skilled workers, 12.3% as unskilled workers, 4.4% as students, and 2.7% as not working.

whereas birth weight showed a relation with protein from dairy products (Figure 1), which resembled its relation with milk exposure expressed in glasses/d (Table 2), although the total increment in birth weight across the full exposure range of protein from dairy products was somewhat smaller (65 compared with 100 g; Figure 1 compared with Table 2). Birth weight was constant across quintiles of nondairy protein (Figure 2), which suggests that the association with dairy protein is unlikely to reflect a general effect of protein. Cheese protein predicted only

a slight increase in birth weight, but the range of intake was much narrower than that for milk protein.

DISCUSSION

We found that maternal milk intake during pregnancy was associated with a reduced risk of SGA, an increased risk of LGA, and an increased mean birth weight, abdominal circumference,

TABLE 2Unadjusted and adjusted differences in mean birth weight increment according to frequency of milk consumption in the Danish National Birth Cohort ($n = 50\ 117$)¹

Milk intake (glasses/d)	Difference in birth weight, unadjusted			Difference in birth weight, adjusted ³		
	<i>g</i>	95% CI	<i>P</i> ²	<i>g</i>	95% CI	<i>P</i> ²
0 ($n = 709$)	Referent	—	—	Referent	—	—
> 0–1 ($n = 6503$)	44.8	(7.0, 82.6)	0.020	48.2	(15.5, 80.9)	0.004
> 1–2 ($n = 7943$)	66.2	(28.8, 103.7)	0.001	57.2	(24.7, 89.6)	0.001
> 2–3 ($n = 12\ 721$)	79.0	(42.1, 115.8)	<0.001	66.3	(34.3, 98.3)	<0.001
> 3–4 ($n = 9181$)	89.7	(52.5, 127.0)	<0.001	78.5	(46.0, 110.9)	<0.001
> 4–5 ($n = 5550$)	103.0	(64.8, 141.1)	<0.001	91.0	(57.8, 124.1)	<0.001
> 5–6 ($n = 3789$)	105.2	(66.1, 144.3)	<0.001	100.5	(66.4, 134.6)	<0.001
> 6 ($n = 3721$)	105.2	(66.2, 144.5)	<0.001	107.8	(73.5, 142.5)	<0.001
<i>P</i> for trend ⁴	<0.001			<0.001		

¹ The group of women who consumed zero glasses of milk was used as a reference for each pairwise comparison.² Student's *t* test.³ Adjusted for gestational age; infant's sex; mother's parity, age, height, prepregnant BMI, gestational-weight gain, smoking status, and total energy intake; father's height; and family's socioeconomic status.⁴ Student's *t* test for regression coefficient (continuous variable).

TABLE 3

Unadjusted and adjusted odds ratios for the risk of small-for-gestational age (SGA) birth according to frequency of milk intake in the Danish National Birth Cohort ($n = 50\ 117$)¹

Milk intake (glasses/d)	No. of cases <i>n</i> (%)	Unadjusted odds ratios (95% CI)	Adjusted odds ratios (95% CI) ²
SGA 10th percentile			
0 ($n = 709$)	104 (14.7)	1.00	1.00
> 0–1 ($n = 6503$)	700 (10.7)	0.70 (0.56; 0.88)	0.67 (0.54; 0.85)
> 1–2 ($n = 7944$)	766 (9.6)	0.62 (0.50; 0.77)	0.62 (0.49; 0.78)
> 2–3 ($n = 12\ 721$)	1204 (9.5)	0.61 (0.49; 0.76)	0.62 (0.49; 0.77)
> 3–4 ($n = 9181$)	832 (9.1)	0.58 (0.47; 0.72)	0.59 (0.47; 0.74)
> 4–5 ($n = 5551$)	469 (8.5)	0.54 (0.43; 0.68)	0.53 (0.42; 0.67)
> 5–6 ($n = 3789$)	313 (8.3)	0.52 (0.41; 0.67)	0.51 (0.40; 0.65)
> 6 ($n = 3721$)	324 (8.7)	0.56 (0.44; 0.70)	0.51 (0.39; 0.65)
<i>P</i> for trend ³		< 0.001	< 0.001
LGA, 90th percentile			
0 ($n = 709$)	53 (7.5)	1.00	1.00
> 0–1 ($n = 6503$)	592 (9.1)	1.24 (0.93; 1.66)	1.37 (1.01; 1.84)
> 1–2 ($n = 7944$)	670 (8.4)	1.14 (0.85; 1.52)	1.24 (0.92; 1.68)
> 2–3 ($n = 12721$)	1234 (9.7)	1.33 (1.00; 1.77)	1.42 (1.06; 1.91)
> 3–4 ($n = 9181$)	939 (10.2)	1.41 (1.06; 1.88)	1.54 (1.15; 2.07)
> 4–5 ($n = 5551$)	573 (10.3)	1.42 (1.06; 1.91)	1.54 (1.14; 2.08)
> 5–6 ($n = 3789$)	390 (10.3)	1.42 (1.05; 1.91)	1.4 (1.13; 2.10)
> 6 ($n = 3721$)	392 (10.5)	1.46 (1.08; 1.96)	1.59 (1.16; 2.16)
<i>P</i> for trend ³		< 0.001	< 0.001

¹ The group of women who consumed zero glasses of milk was used as a reference for each pairwise comparison.

² Adjusted for mother's parity, age, height, prepregnant BMI, gestational weight gain, smoking status, and total energy intake; father's height; and family's socioeconomic status.

³ Chi-square test for regression coefficient (continuous variable).

placental weight, birth length, and head circumference adjusted for gestational age at birth.

The strengths of our study included its size and prospective design (20, 21). Milk intake was assessed in midpregnancy, which is long before birth weight or the other growth measures were evaluated, because only term deliveries were included in the analysis. A potential limitation of our study was that milk intake was measured during a narrow time window of pregnancy, 1 mo in midpregnancy; however, our milk measure will also closely reflect milk intake during other periods of pregnancy because dietary patterns are rather constant throughout pregnancy (26). Other potential limitations were the nonparticipation of women eligible for recruitment and attrition among the women recruited. During 1996–2002, 30–40% of all women who got pregnant in Denmark were recruited for the DNBC. Because all women getting pregnant in the country were in principle eligible, this might have caused selection bias. This was addressed in an analysis based on data from a particular geographic area in Denmark, where it was possible to compare odds ratios for selected exposure-outcome relations (including between smoking status and risk of SGA) among women who were recruited and those who were not; notably, only minor differences in the odds ratios were detected between participants and nonparticipants (27). Of 101 042 women recruited in early pregnancy for the cohort, 50 117 were included in the present analyses. This attrition was caused by several different mechanisms, but none of them is likely to have resulted in any serious distortion of the associations that we observed because decisions regarding participation occurred before participants or their care providers knew their birth outcomes. Of those women in the cohort who participated with

more than one pregnancy, we only included their first participation in our analyses; this was done for statistical reasons to exclude interdependent observations. Finally, we restricted our analyses to include only singleton infants born at term; therefore, this was the target population for which we made our statistical inference.

Some, but not all, results from earlier studies are in line with our findings. A reanalysis of an early randomized controlled trial found an increase in mean birth weight of 53 g in mothers who could buy one pint of milk per day at half price (13) (95% CI: –6, 111 g) (intention-to-treat analysis; Y Ben-Shlomo, personal communication, 2005). A small randomized controlled trial conducted in adolescent women reported a higher birth weight after supplementation (3717 g) than after no supplementation (3277 g) with dairy products and calcium during the latter half of the pregnancy; however, the trial findings were difficult to interpret because of the dubious quality of the trial (28). Furthermore, in a study in which women completed a few food frequency questions after delivery, mean birth weight increased by 134 g, and the risk of SGA declined by 80% in women who consumed ≥ 1 L/d compared with no milk during pregnancy (18). However, the study was retrospective, and no data were available at the nutrient level. In a prospective study in India, birth weight, birth length, head circumference, and placental weight were directly associated with frequency of milk intake assessed at 18 wk of gestation, but no associations were detected for milk intake assessed at 28 wk (14), for abdominal circumference, or for dairy protein and birth weight (14). In a prospective study in Canadian women, overrepresented by women who restricted their milk intake, low milk intake tended to be associated with lower mean birth weight,

TABLE 4

Unadjusted and adjusted differences in mean increment in abdominal circumference, placental weight, head circumference, and birth length according to frequency of milk intake in the Danish National Birth Cohort ($n = 50\ 117$)¹

Milk intake (glasses/d)	Not adjusted for covariates			Adjusted for covariates ³			
	Increment	95% CI	P^2	Increment	95% CI	P^2	
Abdominal circumference (cm)							
0	676	Referent	—	Referent	—	—	
> 0–1	6255	0.17	(0.002, 0.34)	0.048	0.20	(0.04, 0.36)	0.012
> 1–2	7656	0.26	(0.09, 0.42)	0.003	0.26	(0.10, 0.42)	0.001
> 2–3	12 273	0.31	(0.15, 0.48)	<0.001	0.30	(0.15, 0.46)	<0.001
> 3–4	8853	0.33	(0.16, 0.50)	<0.001	0.34	(0.18, 0.50)	<0.001
> 4–5	5342	0.42	(0.25, 0.59)	<0.001	0.43	(0.26, 0.59)	<0.001
> 5–6	3658	0.39	(0.21, 0.56)	<0.001	0.42	(0.26, 0.59)	<0.001
> 6	2609	0.46	(0.29, 0.64)	<0.001	0.52	(0.35, 0.69)	<0.001
P for trend ⁴		<0.001			<0.001		
Placental weight (g)							
0	686	Referent	—	Referent	—	—	
> 0–1	6274	10.4	(−0.7, 21.6)	0.067	13.3	(2.5, 24.1)	0.016
> 1–2	7678	12.4	(1.3, 23.5)	0.028	14.9	(4.2, 25.6)	0.006
> 2–3	12 310	13.7	(2.8, 24.6)	0.014	15.4	(4.9, 25.9)	0.004
> 3–4	8907	15.9	(4.9, 26.9)	0.005	19.4	(8.7, 30.1)	<0.001
> 4–5	5362	20.1	(8.8, 31.3)	<0.001	22.4	(11.5, 33.4)	<0.001
> 5–6	3658	20.3	(8.7, 31.8)	<0.001	24.1	(12.9, 35.4)	<0.001
> 6	3620	22.0	(10.4, 33.6)	<0.001	26.4	(15.1, 37.7)	<0.001
P for trend ⁴		<0.001			<0.001		
Head circumference (cm)							
0	689	Referent	—	Referent	—	—	
> 0–1	6401	0.01	(−0.11, 0.13)	0.87	0.03	(−0.08, 0.15)	0.60
> 1–2	7795	0.05	(−0.08, 0.17)	0.45	0.04	(−0.07, 0.16)	0.48
> 2–3	12 489	0.08	(−0.04, 0.20)	0.20	0.07	(−0.04, 0.18)	0.23
> 3–4	9018	0.08	(−0.04, 0.20)	0.20	0.07	(−0.01, 0.22)	0.22
> 4–5	5449	0.12	(−0.01, 0.25)	0.06	0.11	(−0.01, 0.24)	0.07
> 5–6	3723	0.10	(−0.03, 0.23)	0.07	0.12	(0.00, 0.24)	0.06
> 6	3659	0.11	(−0.02, 0.23)	0.06	0.13	(0.04, 0.25)	0.04
P for trend ⁴		<0.001			<0.001		
Birth length (cm)							
0	706	Referent	—	Referent	—	—	
> 0–1	6468	0.13	(−0.04, 0.30)	0.14	0.13	(−0.017, 0.28)	0.082
> 1–2	7901	0.22	(0.05, 0.39)	0.001	0.16	(0.01, 0.31)	0.034
> 2–3	12 672	0.26	(0.10, 0.43)	0.001	0.20	(0.05, 0.35)	0.007
> 3–4	9146	0.29	(0.12, 0.46)	<0.001	0.22	(0.07, 0.36)	0.004
> 4–5	5534	0.34	(0.17, 0.51)	<0.001	0.27	(0.12, 0.42)	<0.001
> 5–6	3770	0.33	(0.15, 0.51)	<0.001	0.29	(0.14, 0.45)	<0.001
> 6	3713	0.31	(0.13, 0.48)	<0.001	0.31	(0.15, 0.46)	<0.001
P for trend ⁴		<0.001			<0.001		

¹ The group of women who consumed zero glasses of milk was used as a reference for each pairwise comparison.

² Student's t test.

³ Adjusted for gestational age; infant's sex; mother's parity, age, height, prepregnant BMI, gestational weight gain, smoking status, and total energy intake; father's height; and family's socioeconomic status.

⁴ Student's t test for regression coefficient (continuous variable).

but no association was seen with birth length or head circumference (17). Finally, 2 prospective studies (15, 16) and a case-control study (19) were unable to detect significant associations between birth weight and SGA and maternal milk intake; one reason might have been the lack of a sufficiently large reference group with low milk intake.

Many factors in milk could promote fetal growth. Calcium supplementation in pregnancy may reduce the risk of low birth weight (29). Because of a high degree of collinearity in our data (Spearman $r = 0.89$) between intake of milk and total dietary calcium, we were unable in our analysis to evaluate this issue

critically, and calcium remains a possibility. Mannion et al (17, 30) suggested vitamin D as the factor underlying the association observed between birth weight and milk intake in Canadian women. Our observation that protein, but not fat, from milk was related to birth weight suggests that the potentially causative constituents in milk are unlikely to be part of the lipid component of milk, which does not support vitamin D as having been an underlying factor.

Modern cow milk, because of the way it is produced, may have a high content of estrogen and probably other sex steroids (4), and estrogen has a known stimulating effect on fetal growth (5). However, as mentioned above, our data do not support a

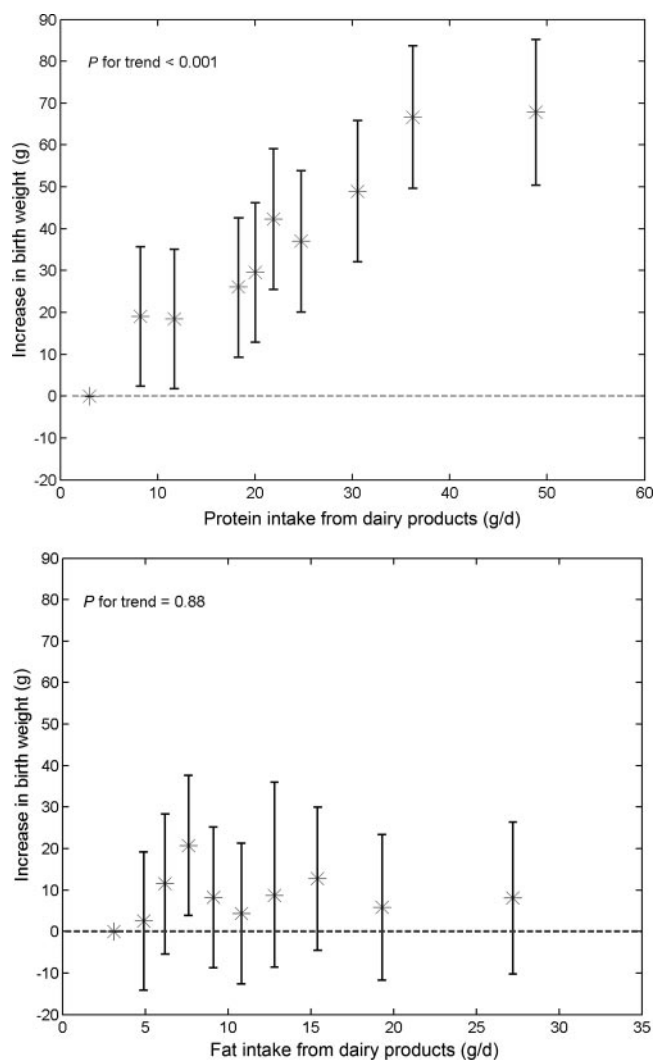


FIGURE 1. Associations between quantified intakes of protein and fat from dairy products (excluding cheese and ice cream) and birth weight ($n = 50\,117$). The dietary variables are divided into deciles. The increase in birth weight (95% CI) for each decile compared with the lowest decile is shown. Estimates are adjusted for covariates (gestational age; infant's sex; mother's parity, age, height, prepregnant BMI, gestational weight gain, smoking status, and total energy intake; father's height; and family's socioeconomic status). The P for trend refers to Student's t test for the regression coefficient (continuous variable).

fat-soluble substance as the causative factor. Protein from milk was associated with birth weight, whereas nondairy protein was not, which points away from a general protein effect. Another potential candidate is the peptide hormone, IGF-I, which is a major determinant of growth velocity in children. In cross-sectional studies of children (12) and adults (9–11), milk consumption has been shown to be associated with higher blood concentrations of IGF-I, and higher milk intakes have been shown in intervention trials to increase IGF-I concentrations in both children (8, 31) and adults (7). Milk consumption has also been directly associated with height in children (12, 32). A high intake of milk elevated blood concentrations of IGF-I in Danish boys (12). Whether the elevation in IGF-I due to milk consumption results from direct absorption of this hormone in milk or from stimulation of endogenous production is not clear. Evidence indicates that the biologic activity of IGF-I, and probably

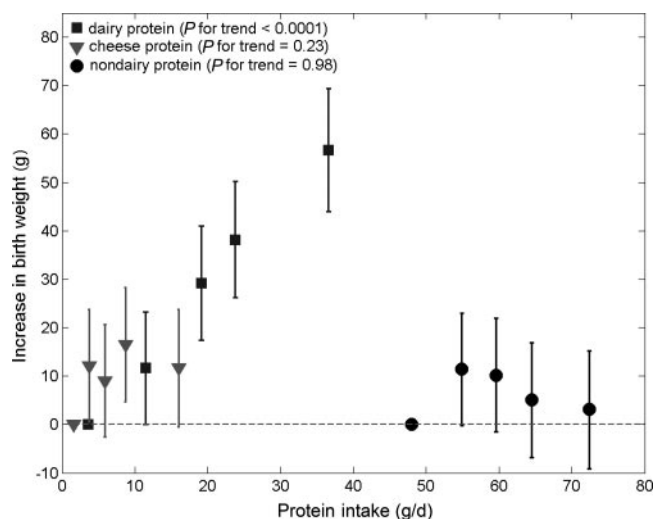


FIGURE 2. Associations between birth weight ($n = 50\,117$) and quantified intakes of protein from dairy products (excluding cheese and ice cream), protein from cheese, and protein from nondairy products. The dietary variables are divided into quintiles and were mutually adjusted for one another. The total protein intakes in the referent groups were 81, 75, and 80 g/d for dairy, cheese, and nondairy protein, respectively. The increment in birth weight (95% CI) for each quintile compared with the lowest quintile (plotted on the dashed line) is shown. Estimates were adjusted for covariates (gestational age; infant's sex; mother's parity, age, height, prepregnant BMI, gestational weight gain, smoking status, and total energy intake; father's height; and family's socioeconomic status). The P for trend refers to Student's t test for the regression coefficient (continuous variable).

of other peptide hormones, in dairy products is altered during fermentation (33). The weaker association of birth weight with protein from fermented milk products than with milk-derived protein observed in our study is therefore compatible with the possibility that IGF-I or other peptide hormones may be the underlying factor accounting for the association between milk and birth weight. However, the intake range for cheese protein was much more limited than that for milk protein.

In conclusion, the data presented herein lead us to hypothesize that water-soluble substances in milk increase fetal growth. The implications that such increases in growth could have for newborn health depend on the underlying factors and mechanisms. Identifying means to increase fetal growth rate may lead to new measures for the prevention of neonatal mortality and morbidity (1) and possibly of adult cardiovascular diseases and type 2 diabetes associated with low birth weight (2, 3). However, milk intake was associated not only with a decreased risk of SGA but also with an increased risk of LGA, and a rapid early growth rate may be a risk factor for obesity (34), cancer of the breast (35–37), and reduced longevity (35, 36). More research is needed to identify the causative factors in cow milk and to examine whether the possible growth-stimulating effect of cow milk is beneficial or deleterious to the health of the fetus in the short term as well.

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The authors' responsibilities were as follows—SFO (guarantor of the study, had full access to all of the data, and takes responsibility for the integrity of the data and the accuracy of the data analysis); conceived the idea and was responsible for designing the dietary component and for acquiring

the dietary data of the DNBC; TIH: conducted the statistical analyses and helped interpret the data; WCW: helped design the dietary component of the DNBC and interpreted the data; VKK, and TBM: helped acquire the dietary data; JO: led the overall data acquisition of the DNBC; SFO: drafted the article; TIH, WCW, VKK, MWG, TBM, and JO: contributed to revising the manuscript critically. The NUTRIX consortium (internet: <http://www.nutrix.be/>) members (Claude Remacle, coordinator; Bernadette Bréant, the late C Nicolas Hales, Sjurður F Olsen, Susan Ozanne, William D Rees, and Brigitte Reusens) helped interpret the data and revise the manuscript critically. The funding agencies had no involvement in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; or the preparation, review, and approval of the manuscript. None of the authors had a conflict of interest to declare.

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