

Peanut and tree nut consumption during pregnancy and allergic disease in children—should mothers decrease their intake? Longitudinal evidence from the Danish National Birth Cohort

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Background: The relation between maternal peanut intake during pregnancy and allergic disease development in children has been controversial.

Objective: We used data from the Danish National Birth Cohort to examine associations between maternal peanut and tree nut intake during pregnancy and allergic outcomes in children at 18 months and 7 years of age.

Methods: We estimated maternal peanut and tree nut intake ($n = 61,908$) using a validated midpregnancy food frequency questionnaire. At 18 months, we used parental report of childhood asthma diagnosis, wheeze symptoms, and recurrent wheeze (>3 episodes). We defined current asthma at 7 years as doctor-diagnosed asthma plus wheeze in the past 12 months and allergic rhinitis as a self-reported doctor's diagnosis. We also used alternative classifications based on registry-based International Classification of Diseases, Tenth Revision, codes and drug dispensary data. We report here odds ratios (ORs) comparing intake of 1 or more times per week versus no intake. **Results:** We found that maternal intake of peanuts (OR, 0.79; 95% CI, 0.65-0.97) and tree nuts (OR, 0.75; 95% CI, 0.67-0.84) was inversely associated with asthma in children at 18 months of age. Compared with mothers consuming no peanuts, children whose mothers reported eating peanuts 1 or more times per week were 0.66 (95% CI, 0.44-0.98) and 0.83 (95% CI, 0.70-1.00) times as likely to have a registry-based and medication-

related asthma diagnosis, respectively. Higher tree nut intake was inversely associated with a medication-related asthma diagnosis (OR, 0.81; 95% CI, 0.73-0.90) and self-reported allergic rhinitis (OR, 0.80; 95% CI, 0.64-1.01).

Conclusions: Our results do not suggest that women should decrease peanut and tree nut intake during pregnancy; instead, consumption of peanuts and tree nuts during pregnancy might even decrease the risk of allergic disease development in children. (*J Allergy Clin Immunol* 2012;130:724-32.)

Key words: Cohort, pregnancy, peanuts, tree nuts, asthma, wheeze, allergic rhinitis

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The recent increase in morbidity related to asthma and allergies has led to new hypotheses on influential environmental factors that might be acting in early life. Significant controversy exists regarding peanut and tree nut consumption during pregnancy.¹ Many women choose to reduce nut intake during pregnancy to avoid development of allergic disease, primarily peanut/nut allergies, in the child. Yet the current state of knowledge regarding nut consumption on the development of allergic disease is limited, and public policies are conflicting.² Consumption of nuts has even been suggested to be beneficial in avoiding asthma and allergies by promoting immunotolerance.¹ Additionally, avoiding or decreasing intake of peanuts and tree nuts during pregnancy might be compromising the maternal diet because these foods are rich sources of polyunsaturated fatty acids, fiber, micronutrients, and antioxidants.^{3,4}

Few studies have examined maternal nut intake during pregnancy on allergic disease other than food allergies. Two studies showed no association between nut consumption and allergic sensitization and respiratory symptoms.^{5,6} Another study found an increased risk of wheeze and asthma symptoms with daily versus rare nut product consumption.⁷ Other studies done on allergen-restrictive diets during pregnancy⁸⁻¹⁰ or lactation^{11,12} showed either no^{8,12} or protective⁹⁻¹¹ associations for allergic outcomes. However, these studies did not distinguish between prenatal and postnatal effects^{8,11,13} or assess clinical end points.^{11,12} A recent Cochrane review found that avoiding allergenic foods during pregnancy did not appear to be effective for preventing atopic disease.¹⁴

Given the limited and conflicting evidence, especially as it pertains to asthma and allergic rhinitis, more rigorous analyses are warranted, accounting for potential differences between

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Abbreviations used

ALA: α -Linolenic acid
DNPR: Danish National Patient Registry
FFQ: Food frequency questionnaire
LA: Linoleic acid

peanut and tree nut intake, important confounders, and allergic outcomes both in early and later childhood. A better understanding of these relations could better guide maternal dietary decisions during pregnancy.

METHODS

Population and study design

The Danish National Birth Cohort is a prospective cohort study of factors operating prenatally and in early life and diseases in offspring. Participants were enrolled between January 1996 and October 2002 during their first antenatal visit. All women living in Denmark who could speak Danish and were planning to carry to term were eligible for recruitment. About 60% of all eligible women received an invitation from their general practitioner, and of those, 60% chose to participate. A total of 101,045 pregnancies were enrolled. The women participated in 2 telephone interviews during pregnancy at 12 and 30 weeks of gestation. A food frequency questionnaire (FFQ) was administered around the 25th week of gestation. The women were interviewed again after birth when the child was 6 and 18 months old. The mother-child dyads have been followed up through national registries linked by using their unique identity number. We sent an additional questionnaire to the mothers when the child turned 7 years of age.

To avoid dependency among multiple observations, we included only the first Danish National Birth Cohort pregnancy in our study ($n = 89,333$). After limiting our analyses to singletons ($n = 87,090$) and excluding women who had not filled out the FFQ ($n = 25,182$), 61,908 women were available for analysis. Final sample sizes varied based on participant response rate for the outcomes.

We compared participants versus nonparticipants for childhood asthma based on available outcome data at 18 months and 7 years of age. Compared with the 16,018 participants not included at 18 months, the 45,010 participants eligible for the present study were of higher socioeconomic status (higher or medium proficiencies, 54% vs 51%), more likely to be multiparous (48% vs 44%), and less likely to smoke less during pregnancy (12% vs 14%). Compared with the 47,585 participants without data on current asthma at 7 years, the 13,443 participants with asthma data in children were more likely to report maternal asthma (12% vs 8%) and allergy (35% vs 31%). There were also more male children among the participants (57% vs 50%).

Exposure measurement

Peanut and nut intake was assessed during midpregnancy by using a validated 360-item semiquantitative FFQ¹⁵ that covered intake in the past 4 weeks. Specific questions were asked about snack consumption in the past month, separately assessing "peanut and pistachio" intake and the intake of "nuts and almonds." We assumed that most women consumed peanuts rather than pistachios in the "peanut and pistachio" category. Ten different frequency options were given, from "none" to "6 or more times per day." Categories were collapsed at the upper end of intake because few women reported intake of greater than 1 time per week, generating 4 categories (none, 1 time per month, 1-3 times per month, and 1 or more times per week). Women who reported unrealistic energy intake estimates (arbitrarily set to <2500 kJ/d or >25,000 kJ/d) were excluded from statistical analyses.

Outcome measurements

During the 18-month postnatal interview, the mothers were asked about their children's doctor-diagnosed asthma, wheeze symptoms, and number of wheeze episodes since birth. Asthma at 18 months was defined as a positive

response to the question on doctor-diagnosed asthma. Wheeze was similarly assessed by asking about symptoms. Recurrent wheeze was defined as having more than 3 episodes in the first 18 months of life compared with having 3 or less episodes or no reported wheeze.

We used several sources to evaluate asthma and allergic rhinitis diagnosis in later childhood. Asthma at age 7 years was assessed through standardized International Study of Asthma and Allergies in Childhood questions on a questionnaire mailed to all mothers.^{16,17} Asthma cases were defined as having self-reported doctor-diagnosed asthma plus wheezing symptoms in the past 12 months. Cases of ever allergic rhinitis were defined based on reported doctor's diagnosis of hay fever.

We had access to the Danish National Patient Registry (DNPR), which collects data on admissions related to asthma. Information on hospital admissions has been collected since 1977, and information on emergency department and outpatient contacts has been collected since 1995. The DNPR has been found to have excellent sensitivity and specificity when validated against asthma diagnosis from hospital records.¹⁸ Data from the DNPR were extracted in August 2010 and linked to our data by using the Central Person Registry number, a unique identification number given to all Danish citizens. International Classification of Diseases, Tenth Revision, codes for asthma (J45, J45.0, J45.1, J45.8, J45.9, J46, and J46.9) were used to identify first cases in childhood. Allergic rhinitis diagnosis was excluded because of the low number of registry entries (226/47,677).

Furthermore, the Register of Medicinal Product Statistics (RMPS) contains individual-level information on all prescriptions filled at pharmacies that are coded by using the Anatomical Therapeutic Chemical classification system.¹⁹ On the basis of a previous validation study, we used all combinations of drugs for obstructive airway disease to classify asthma cases, except for β_2 -agonists as liquid, inhaled β_2 -agonists only once, or inhaled steroid only once.²⁰ We classified allergic rhinitis cases based on combinations of antiallergy drugs, except for antihistamines only once, eye drops only once, or nasal decongestants only once. As for the DNPR, only the first registered asthma and allergic rhinitis case was used.

Covariates

We obtained information on covariates from the pregnancy interviews. These included socioeconomic status by parental education level and occupation (high-level proficiency, medium-level proficiency, skilled, unskilled, student, and unemployed), maternal age at birth of child, parity (nulliparous and multiparous), maternal prepregnancy body mass index (in kilograms per square meter), maternal smoking during pregnancy (nonsmoker, occasional smoker, or current smoker), maternal exercise during pregnancy, gestational weight gain (in grams per week), breast-feeding duration (none, 0-1, 2-3, 4-6, 7-9, or ≥ 10 months), birth weight (in grams), gestational age (in days since the last menstrual period), child's sex, maternal and paternal history of asthma and allergies, and total energy intake. Furthermore, intake of vitamins A, D, and E; selenium; and zinc from supplements and intake of fruits, vegetables, and alcohol were also considered. All nutrient intakes from diet and alcohol were energy adjusted by using the residual method.²¹

Statistical analysis

The distribution of covariates across categories of peanut and tree nut intake was assessed to identify potential confounding factors. Distributions are presented as age standardized because of significant differences in peanut/tree nut intake across age categories, with "never" consumers being younger compared with higher peanut/tree nut consumers. The final set of covariates was determined by using χ^2 and partial F tests with a P value of less than .10, as well as *a priori* considerations. We excluded covariates deemed to be intermediates on the causal pathways to avoid overadjusting the model. Multivariate logistic regression models with the outcome as a binary variable were evaluated for each and 1 of the outcomes. We assessed 2 models for each outcome, the first adjusting for identified sociodemographic and anthropometric covariates and a second further adjusting for dietary covariates. The peanut and tree nut intakes were entered as indicator variables in categories and compared with the lowest reference category.

TABLE I. Age-adjusted distributions of selected covariates across categories of maternal peanut and pistachio intake during pregnancy in the Danish National Birth Cohort (n = 61,026)

Frequency of peanut (and pistachio) intake	No. (%)	Never (n = 37,323)	1 time/mo (n = 13,268)	2-3 times/m (n = 8,797)	≥1 time/wk (n = 1,639)
		Percent or mean (SD)	Percent or mean (SD)	Percent or mean (SD)	Percent or mean (SD)
Maternal age (y)*	61,026	29.0 (4.3)	29.0 (4.3)	29.0 (4.3)	29.0 (4.3)
Socioeconomic position					
High-level proficiencies	12,553 (23)	21	25	27	25
Parity					
Nulliparous	30,826 (53)	51	55	56	55
Prepregnancy BMI (kg/m ²)	57,398	23.7 (4.4)	23.3 (4.0)	23.1 (3.9)	22.9 (4.1)
Physical activity during pregnancy† (yes)	22,586 (39)	37	41	41	41
Smoking in pregnancy					
Current smoker	7,579 (13)	13	12	13	15
Breast-feeding duration					
≥7 mo	25,933 (60)	58	63	63	57
Maternal asthma (yes)	5,356 (9)	9	9	9	11
Maternal allergies (yes)	18,607 (32)	32	33	33	31
Paternal asthma (yes)	4,763 (8)	8	8	8	9
Paternal allergies (yes)	13,860 (24)	23	25	25	25
Child's sex					
Male	31,002 (51)	51	51	51	49
Gestational weight gain (g/wk)	42,054	463 (220)	469 (208)	476 (208)	467 (231)
Birth weight (g)	57,926	3,582 (580)	3,582 (552)	3,571 (575)	3,547 (548)
Gestational age (d)	61,015	280 (14)	280 (13)	280 (14)	280 (17)
Dietary intake					
Energy (kJ/d)	60,772	9,853 (2,655)	10,119 (2,587)	10,613 (2,693)	11,574 (3,264)
Fruit intake (g/d)	61,024	312 (266)	329 (266)	343 (263)	398 (337)
Vegetable intake (g/d)	61,024	122 (95)	131 (95)	144 (107)	179 (157)
Fish fatty acids (mg/d)‡	61,024	0.4 (0.3)	0.4 (0.3)	0.4 (0.3)	0.4 (0.3)
Alcohol (g/d)	60,772	1.4 (2.1)	1.7 (2.3)	2.0 (2.6)	2.0 (2.9)
Intake from supplements					
Vitamin A (RE/d)	61,024	672 (26,504)	671 (28,842)	1,108 (47,421)	423 (629)
Vitamin D (μg/d)	61,024	5.4 (5.1)	5.5 (5.1)	5.6 (5.0)	5.4 (5.1)
Vitamin E (α-TE/d)	61,024	8.2 (18.6)	8.3 (17.5)	8.9 (19.2)	9.6 (28.0)
Selenium (μg/d)	61,024	27.0 (25.9)	27.8 (25.8)	28.4 (25.8)	27.3 (26.5)
Zinc (mg/d)	61,024	7.2 (7.4)	7.4 (7.2)	7.6 (7.3)	7.3 (7.7)

Values are standardized to the age distribution of the study population.

BMI, Body mass index; RE, retinol equivalents; TE, tocopherol equivalents.

*Value not age adjusted.

†Answer to the following question: "Have you been exercising while pregnant?"

‡Eicosapentaenoic acid + docosapentaenoic acid + docosahexaenoic acid.

Estimated odds ratios were reported alongside 95% CIs. The ordinal values for the exposure categories were entered separately into the model as a continuous variable to evaluate the *P* value for trend. All tests were 2-sided, and statistical significance was considered at a *P* value of less than .05. The analyses were performed with SAS software (release 9.2; SAS Institute, Cary, NC).

RESULTS

Study cohort

Table I shows age-standardized participant characteristics among the mother-child pairs with peanut intake data. Mean maternal age was 29.0 ± 4.0 years, most were from higher socioeconomic backgrounds (high-level proficiencies, 23%), and 53% were expecting their first child. The mean prepregnancy body mass index was 23.5 ± 4.2 kg/m², and the mean gestational weight gain was 467 ± 216 g/wk. About 13% smoked during pregnancy, and more than 60% reported no recreational physical

activity during the pregnancy. Breast-feeding rates were high, with 60% of women breast-feeding for 7 or more months. The prevalence of maternal asthma and allergies was 9% and 32%, respectively. Paternal asthma and allergies were found in 8% and 24% of men, respectively. The average birth weight and gestational age were 3580 ± 573 g and 280 ± 14 days, respectively.

A total of 61% of women reported no peanut and tree nut intake during pregnancy. Three percent consumed peanuts and 9% consumed tree nuts 1 or more times per week.

Multivariate analysis

Child's asthma, ever wheeze, and recurrent wheeze at the 18-month follow-up. Among women with peanut and tree nut intake, a total of 17.1% (n = 7,803/45,635) of mothers reported an asthma diagnosis in their child, 26.7% (n = 12,259/45,844) reported ever wheeze, and 8.6% (n = 3,948/45,747)

TABLE II. Association between maternal peanut and pistachio intake during pregnancy and asthma, wheeze, and recurrent wheeze in children at the 18-month follow-up in the Danish National Birth Cohort

Frequency of peanut (and pistachio) Intake	Cases/no.	Asthma (n = 45,010),		Cases/no.	Wheeze symptoms (n = 45,215),		Cases/no.	Recurrent wheeze (>3 episodes [n = 45,120]),	
		OR (95% CI)	P value for trend		OR (95% CI)	P value for trend		OR (95% CI)	P value for trend
Never									
Crude	4,873/27,648	1.00 (reference)	.0001	7,545/27,788	1.00 (reference)	.02	2,476/27,736	1.00 (reference)	.05
Adjusted*			.02			.52			.99
1 time/mo									
Crude	1,609/9,837	0.91 (0.84-0.97)		2,556/9,873	0.94 (0.89-0.99)		777/9,845	0.87 (0.80-0.95)	
Adjusted*		0.94 (0.87-1.01)			0.98 (0.92-1.04)			0.94 (0.85-1.04)	
2-3 times/mo									
Crude	1,033/6,397	0.90 (0.84-0.97)		1,677/6,421	0.95 (0.89-1.01)		544/6,410	0.95 (0.86-1.04)	
Adjusted*		0.96 (0.88-1.05)			0.99 (0.92-1.06)			1.04 (0.93-1.17)	
≥1 time/wk									
Crude	172/1,128	0.84 (0.71-0.99)		296/1,133	0.95 (0.83-1.09)		96/1,129	0.95 (0.77-1.17)	
Adjusted*		0.79 (0.65-0.97)			0.97 (0.83-1.14)			0.95 (0.74-1.23)	

OR, Odds ratio.

*Adjusted for maternal age, smoking, parity, prepregnancy body mass index, physical activity, breast-feeding, socioeconomic status, maternal history of asthma, paternal history of asthma and allergies, and total energy intake.

TABLE III. Association between maternal tree nut intake during pregnancy and asthma, wheeze, and recurrent wheeze in children at the 18-month follow-up in the Danish National Birth Cohort

Frequency of tree nut Intake	Cases/no.	Asthma (n = 44,956),		Cases/no.	Wheeze symptoms (n = 45,161),		Cases/no.	Recurrent wheeze (>3 episodes [n = 45,067]),	
		OR (95% CI)	P value for trend		OR (95% CI)	P value for trend		OR (95% CI)	P value for trend
Never									
Crude	5,012/27,310	1.00 (reference)	<.0001	7,614/27,431	1.00 (reference)	<.0001	2,553/27,368	1.00 (reference)	<.0001
Adjusted*			<.0001			<.0001			.001
1 time/mo									
Crude	1,111/6,971	0.84 (0.79-0.91)		1,865/7,013	0.94 (0.89-1.00)		568/7,001	0.86 (0.78-0.94)	
Adjusted*		0.91 (0.83-0.99)			0.99 (0.93-1.07)			0.94 (0.84-1.05)	
2-3 times/mo									
Crude	1,014/6,703	0.79 (0.74-0.85)		1,656/6,734	0.85 (0.80-0.90)		512/6,721	0.80 (0.73-0.89)	
Adjusted*		0.89 (0.82-0.97)			0.90 (0.84-0.97)			0.90 (0.80-1.01)	
≥1 time/wk									
Crude	534/3,972	0.69 (0.63-0.76)		927/3,983	0.79 (0.73-0.85)		260/3,977	0.68 (0.60-0.78)	
Adjusted*		0.75 (0.67-0.84)			0.85 (0.78-0.93)			0.77 (0.66-0.90)	

OR, Odds ratio.

*Adjusted for maternal age, smoking, parity, prepregnancy body mass index, physical activity, breast-feeding, socioeconomic status, maternal history of asthma, paternal history of asthma and allergies, and total energy intake.

reported more than 3 wheezing episodes in the first 18 months of life.

After multivariate adjustment, we found an inverse association between maternal peanut intake and child's asthma (≥1 time per week vs never, 0.79; 95% CI, 0.65-0.97), but no association with either ever or recurrent wheeze (Table II). Compared with mothers who consumed no tree nuts during pregnancy, those whose tree nut intake was 1 or more times per week were only 0.75 (95% CI, 0.67-0.84) times as likely to report asthma in their children, 0.85 (95% CI, 0.78-0.93) times as likely to report wheeze symptoms, and 0.77 (95% CI, 0.66-0.90) times as likely to report 3 or more wheeze episodes in the first 18 months of life (Table III). Adding dietary covariates into the model did not alter the effect estimates.

The correlation between tree nut and peanut intake was moderate (Spearman $r = 0.27$, $P < .0001$). When the peanut and tree nut

intake were put in the same model, the effect estimates did not change substantially for either exposure. The CIs widened for peanut intake only and crossed the null value for child's asthma diagnosis (≥1 times per week vs never, 0.85; 95% CI, 0.69-1.04; data not shown).

Ever and current asthma in children at the 7-year follow-up. A total of 6.0% (2,316/39,057) children were classified as registry asthma cases, 31.8% (12,419/39,039) as medication-related asthma cases, and 11.5% (1,574/13,634) as having current asthma based on the 7-year questionnaire.

We found that children whose mothers consumed peanuts at least 1 time per week were only 0.66 as likely to have a registry asthma diagnosis (95% CI, 0.44-0.98) as never consumers (Table IV). The association for a medication-related diagnosis was slightly weaker but still significant (≥1 time per week vs never, 0.83; 95% CI, 0.70-1.00). Likewise, tree nut intake was inversely

TABLE IV. Association between maternal peanut and pistachio intake during pregnancy and asthma in children in the Danish National Birth Cohort

Frequency of peanut (and pistachio) intake	Ever asthma (DNPR [n = 38,570]),			Ever asthma (RMPS [n = 38,552]),			Current asthma at 7 y (questionnaire [n = 13,443]),		
	Cases/no.	OR (95% CI)	P value for trend	Cases/no.	OR (95% CI)	P value for trend	Cases/no.	OR (95% CI)	P value for trend
Never									
Crude	1,482/23,656	1.00 (reference)	.0003	7,670/23,649	1.00 (reference)	.0002	990/8,301	1.00 (reference)	.29
Adjusted*			.002			.29			.27
1 time/mo									
Crude	462/8,496	0.86 (0.77-0.96)		2,640/8,490	0.94 (0.89-0.99)		316/2,901	0.90 (0.79-1.03)	
Adjusted*		0.90 (0.79-1.03)			1.03 (0.96-1.10)			0.89 (0.75-1.05)	
2-3 times/mo									
Crude	288/5,427	0.84 (0.74-0.96)		1,659/5,422	0.92 (0.86-0.98)		202/1,898	0.88 (0.75-1.03)	
Adjusted*		0.82 (0.69-0.97)			0.98 (0.90-1.06)			0.87 (0.70-1.06)	
≥1 time/wk									
Crude	48/991	0.76 (0.57-1.02)		283/991	0.83 (0.72-0.96)		47/343	1.17 (0.86-1.61)	
Adjusted*		0.66 (0.44-0.98)			0.83 (0.70-1.00)			1.15 (0.75-1.74)	

OR, Odds ratio; RMPS, Register of Medicinal Product Statistics.

*Adjusted for maternal age, smoking during pregnancy, parity, prepregnancy body mass index, physical activity during pregnancy, breast-feeding, socioeconomic status, maternal history of asthma and allergies, paternal history of asthma and allergies, and total energy intake.

TABLE V. Association between maternal tree nut intake during pregnancy and asthma in children in the Danish National Birth Cohort

Frequency of tree nut intake	Ever asthma (DNPR [n = 38,512]),			Ever asthma (RMPS [n = 38,494]),			Current asthma at 7 y (questionnaire [n = 13,415]),		
	Cases/no.	OR (95% CI)	P value for trend	Cases/no.	OR (95% CI)	P value for trend	Cases/no.	OR (95% CI)	P value for trend
Never									
Crude	1,447/23,248	1.00 (reference)	.001	7,725/23,247	1.00 (reference)	<.0001	947/8,220	1.00 (reference)	.38
Adjusted*			.19			.0003			.99
1 time/mo									
Crude	343/6,133	0.89 (0.79-1.01)		1,847/6,127	0.87 (0.82-0.92)		223/2,093	0.92 (0.79-1.07)	
Adjusted*		0.92 (0.79-1.08)			0.91 (0.84-0.98)			0.84 (0.69-1.03)	
2-3 times/mo									
Crude	309/5,739	0.86 (0.76-0.97)		1,739/5,733	0.88 (0.82-0.93)		237/1,935	1.07 (0.92-1.25)	
Adjusted*		0.95 (0.81-1.11)			0.97 (0.89-1.05)			0.98 (0.80-1.19)	
≥1 time/wk									
Crude	176/3,392	0.83 (0.70-0.97)		925/3,387	0.76 (0.70-0.82)		143/1,167	1.07 (0.89-1.29)	
Adjusted*		0.89 (0.72-1.09)			0.81 (0.73-0.90)			1.06 (0.83-1.36)	

OR, Odds ratio; RMPS, Register of Medicinal Product Statistics.

*Adjusted for maternal age, smoking during pregnancy, parity, prepregnancy body mass index, physical activity during pregnancy, breast-feeding, socioeconomic status, maternal history of asthma and allergies, paternal history of asthma and allergies, and total energy intake.

related to having a registry diagnosis (≥1 time per week vs never, 0.89; 95% CI, 0.72-1.09) and a medication-related diagnosis (≥1 time per week vs never, 0.81; 95% CI, 0.73-0.90), although only the latter reached statistical significance (Table V). The effect estimates for current asthma as assessed by using the questionnaire were slightly greater than 1 but did not reach statistical significance. Adding dietary covariates into the model did not alter the effect estimates.

The independent associations of peanut and tree nut intake remained similar. The CIs widened for a registry (≥1 time per week vs never, 0.68; 95% CI, 0.46-1.02) and medication-related diagnosis (≥1 time per week vs never, 0.89; 95% CI, 0.74-1.07) with peanut intake, crossing the null value (data not shown).

We also examined DNPR asthma diagnosis by patient type (inpatient, outpatient, and emergency department) at first diagnosis. The strongest association was found for peanut intake among inpatient visits (≥1 time per week vs never, 0.41; 95% CI, 0.21-0.80). We also found inverse associations for outpatient

visits with tree nut intake (≥1 time per week vs never, 0.78; 95% CI, 0.57-1.06).

Ever allergic rhinitis in children at the 7-year follow-up. The prevalence of medication-related allergic rhinitis was 7.8% (3,040/39,039) and 4.9% (1,887/38,761) by self-reported doctor's diagnosis. There was no association between self-reported allergic rhinitis diagnosis and peanut intake (Table VI). We did find an inverse association with higher tree nut consumption during pregnancy (≥1 time per week vs never, 0.80; 95% CI, 0.64-1.01; Table VII). Again, adding dietary covariates into the model did not alter the effect estimates.

For independent associations, the odds ratios remained similar, whereas the CIs were somewhat broadened (data not shown).

Sensitivity analyses

We excluded women who reported other food allergies (2,155/21,475 = 0.10), but this did not alter the results. For example, higher maternal peanut intake was still significantly related to

TABLE VI. Association between maternal peanut and pistachio intake during pregnancy and allergic rhinitis in children in the Danish National Birth Cohort

Frequency of peanut (and pistachio) intake	Cases/no.	Ever allergic rhinitis (RMPS [n = 38,552]),* OR (95% CI)	P value for trend	Cases/no.	Ever allergic rhinitis (questionnaire [n = 38,279]),* OR (95% CI)	P value for trend
Never						
Crude adjusted†	1,949/23,649	1.00 (reference)	.0002	1,165/23,484	1.00 (reference)	.46
			.001			.06
1 time/mo						
Crude adjusted†	601/8,490	0.85 (0.77-0.93)		395/8,430	0.94 (0.84-1.06)	
		0.84 (0.75-0.95)			0.88 (0.76-1.02)	
2-3 times/mo						
Crude adjusted†	392/5,422	0.87 (0.78-0.97)		262/5,383	0.98 (0.85-1.13)	
		0.83 (0.71-0.96)			0.87 (0.73-1.04)	
≥1 time/wk						
Crude adjusted†	64/991	0.77 (0.59-1.00)		45/982	0.92 (0.68-1.25)	
		0.78 (0.57-1.08)			0.89 (0.59-1.32)	

OR, Odds ratio; RMPS, Register of Medicinal Product Statistics.

*Total might be less than sum of nos. because of missing values.

†Adjusted for maternal age, smoking during pregnancy, parity, prepregnancy body mass index, physical activity during pregnancy, breast-feeding, socioeconomic status, maternal history of asthma and allergies, paternal history of asthma and allergies, and total energy intake.

TABLE VII. Association between maternal tree nut intake during pregnancy and allergic rhinitis in childhood in the Danish National Birth Cohort

Frequency of tree nut intake	Cases/no.	Ever allergic rhinitis (RMPS [n = 38,494]),* OR (95% CI)	P value for trend	Cases/no.	Ever allergic rhinitis (questionnaire [n = 38,223]),* OR (95% CI)	P value for trend
Never						
Crude adjusted†	1,857/23,247	1.00 (reference)	.22	1,137/23,074	1.00 (reference)	.14
			.39			.21
1 time/mo						
Crude adjusted†	446/6,127	0.90 (0.81-1.01)		306/6,088	1.02 (0.90-1.16)	
		0.95 (0.83-1.08)			1.01 (0.85-1.19)	
2-3 times/mo						
Crude adjusted†	446/5,733	0.97 (0.87-1.08)		283/5,699	1.01 (0.88-1.15)	
		0.99 (0.86-1.14)			1.01 (0.85-1.20)	
≥1 time/wk						
Crude adjusted†	254/3,387	0.93 (0.82-1.07)		136/3,362	0.81 (0.68-0.98)	
		0.92 (0.77-1.10)			0.80 (0.64-1.01)	

OR, Odds ratio; RMPS, Register of Medicinal Product Statistics.

*Total might be less than sum of nos. because of missing values.

†Adjusted for maternal age, smoking during pregnancy, parity, prepregnancy body mass index, physical activity during pregnancy, breast-feeding, socioeconomic status, maternal history of asthma and allergies, paternal history of asthma and allergies, and total energy intake.

child's asthma at 18 months (≥1 time per week vs never, 0.80; 95% CI, 0.66-0.98), registry asthma diagnosis (≥1 time per week vs never, 0.68; 95% CI, 0.44-1.00), and medication-related asthma diagnosis (≥1 time per week vs never, 0.86; 95% CI, 0.71-1.03).

Given that early respiratory symptoms and clinical asthma might involve different pathologies and causes, we excluded the first 3 years of life from the registries. The sample size decreased, primarily because of a reduced number of cases. The number of registry cases more than halved, and the number of medication-related cases was reduced by close to 80%. However, no substantial differences were observed in the results for tree nut intake. The effect estimates did become more inverse for peanut intake both for the registry diagnosis (≥1 time per week vs never, 0.57; 95% CI, 0.29-1.12) and the medication-related diagnosis (≥1 time per week vs never, 0.59; 95% CI, 0.40-0.87).

We furthermore examined the relation to doctor-diagnosed eczema in children, which was self-reported at 18 months and 7

years, in support of the atopic march. The prevalence of eczema was 14% at 18 months and 20% at 7 years. We did not find any associations with the outcome at either time point.

DISCUSSION

In this study we examined the relation between maternal peanut and tree nut intake during pregnancy and allergic disease outcomes in early and later childhood. We found that higher peanut and tree nut intake was inversely associated with asthma diagnosis and wheeze at 18 months. Furthermore, higher peanut intake was inversely associated with a registry diagnosis of asthma. The associations weakened for peanut intake with asthma in children at 18 months of age and for medication-related asthma diagnosis when examined independently of tree nut intake.

We could not explain these results by other lifestyle behaviors, food and nutrient intakes, or avoidance of allergens in the high nut

consumption groups. Behaviors observed in the highest peanut intake category have been associated with increased risk of allergic disease (maternal smoking²²). Factors that have been suggested to confer some benefit against allergic disease, such as maternal dairy intake,²³ use of hypoallergenic formula,²⁴ child day care attendance,²⁵ and pet ownership,^{26,27} were less common in this group compared with never consumers.

These results support the recent withdrawal of United Kingdom recommendations to avoid peanuts during pregnancy,²⁸ as well as a report from the American Academy of Pediatrics²⁹ that did not find any benefits of maternal dietary restrictions during pregnancy. Earlier recommendations were primarily based on development of peanut allergy in children, for which the evidence, although not firmly established, is more comprehensive than for asthma and allergic rhinitis. Studies on the relation between maternal diet during pregnancy and peanut sensitization/allergy have been inconsistent, with some studies showing a direct association^{30,31} and others showing a null association.³²⁻³⁴ To the best of our knowledge, there is currently only 1 study that has specifically examined the association between nut intake during pregnancy and childhood asthma. Willers et al⁷ found an increased risk of self-reported wheeze and asthma symptoms with daily consumption of nut products (eg, peanut butter), but not whole nut intake, during the first 8 years of life. Similarly, we did not find any associations for self-reported asthma at 7 years. Although the effect estimates were greater than 1, the CIs were wide and not statistically significant. This suggests that the registries are important resources for capturing clinically relevant asthma. Other explanations of the differences between our and the above studies could be inadequate separation of low- versus high-frequency consumers and low power; we were able to assess detailed diet information in a large cohort. Studies that examined the relation between maternal intake of nuts, pulses, or both and allergic outcomes did not find any associations.^{5,6} These differences could have been due to numerous factors, including a small sample size, a lack of assessment of clinical end points, crude intake categories, differences in nut intake between populations, and conglomeration of food items with potentially different etiologic pathways.

Peanuts and tree nuts are foods with complex nutrient profiles comprising many potential candidates that could account for our results. The biological mechanism behind our results is poorly understood and involves numerous hypotheses and paradigms. Both peanuts and tree nuts are rich in α -linolenic acid (ALA), linoleic acid (LA), vitamin E, magnesium, selenium, zinc, folate, and other micronutrients. Peanuts tend to be richer in niacin, folate, and vitamin E, whereas tree nuts contain, on average, more ALA, LA, selenium, zinc, and magnesium.³ Further complexity is added because nutrient profiles vary between peanuts and tree nuts, as well as between individual tree nuts.^{4,35} Beneficial relations have been demonstrated for a number of these nutrients with allergic outcomes, including ALA intake in relation to wheeze,³⁶ vitamin E and wheeze and asthma,³⁷⁻³⁹ zinc and wheeze and asthma,^{37,38} and selenium and wheeze/persistent wheeze,^{40,41} whereas a direct association was found for LA intake with eczema.³⁶ These nutrients have been hypothesized to influence lung growth^{42,43} and airway development,^{44,45} improving the T_H1/T_H2 ratio by altering cytokine secretions,^{39,46-48} influencing eicosanoid production,⁴⁹ and reducing eosinophilia.⁵⁰ From this study, we are unable to determine which of these nutrients might be acting either independently or in concert, producing

synergistic effects on immune system development, maturation, or function in the growing fetus. However, they stress the importance of consuming whole foods during pregnancy and might be more relevant for future recommendations on pregnancy diet.

This study adds to the literature on dietary exposure during pregnancy and allergic disease development in children. With our prospective study design, we followed a large cohort for the first 7 years of life. We collected detailed information on maternal peanut and tree nut intake during pregnancy and related this to outcomes at 2 time points in childhood, allowing for potential change in risk across time and by different allergic disease manifestations. We adjusted for numerous sociodemographic and dietary confounders, reducing the potential for residual confounding. We took advantage of both self-reported data and national registries. The self-reported outcome assessment might be subject to misclassification but is more useful for outcomes, such as allergic rhinitis, which are unlikely to result in hospitalizations and use of prescription medication because of more moderate symptoms and use of over-the-counter drugs. The International Classification of Diseases, Tenth Revision, classification could be limited by miscoding; however, a recent validation study in Danish male conscripts against medical examination suggested that any misclassification was small.⁵¹ Differences in disease severity based on the reporting method could have etiologic relevance. From our sensitivity analyses by type of admission, it appears the results for peanut intake are stronger for more severe asthma that was diagnosed in inpatient versus outpatient care. This finding needs to be examined further to better understand the role of severity in asthma development.

The principal limitations of this study relate to the self-reporting of exposure and outcomes. We expect any exposure misclassification to have been nondifferential, thus leading to underestimates of associations. We were also not able to access risk for processed nut products, such as peanut butter and peanut/tree nut residues in chocolate bars, cereals, and desserts, although we do not suspect them of being significant dietary contributors in Denmark. In addition, we could not evaluate the associations for specific nut species or differentiate between peanut and pistachio intake. Early introduction of peanuts into the child's diet has been associated with lower development of peanut allergies.⁵² Although the influence of peanut and tree nut intake by children on the development of asthma and allergic rhinitis has not been thoroughly examined, it remains plausible that some of our association might be accounted for by intake by children. Furthermore, we could not examine the associations independent of peanut/tree nut during lactation because of the unavailability of these data, although adjusting our analyses for breast-feeding duration might have reduced any potential confounding. Our analyses were limited by the absence of information on diet during lactation and childhood, and therefore we cannot exclude the possibility that maternal peanut and tree nut intake might be acting as a marker for intake of these foods. Nevertheless, our findings make it unlikely that maternal consumption during pregnancy leads to a greater risk of childhood allergic disease.

Misclassification is plausible for questionnaire-assessed outcomes. This could explain the failure to detect an association for self-reported asthma. The sample size was also smaller for the self-reported outcomes, especially in the high-intake categories, and could explain why they did not reach statistical significance.

As part of a sensitivity analysis, we excluded women who reported any food allergies to avoid reverse causation. We were unable to exclude women with peanut/tree nuts allergies only. Assuming that women with peanut/tree nut allergies avoided or reduced their intake of these foods, excluding these women would have attenuated our results to null. Inclusion of women with other food allergies and sensitivities in this group would be expected to reduce such an attenuation, thereby overestimating our results. However, we expect that women with peanut/tree nut allergies make up a very small sample of the study population (peanut allergy prevalence in Denmark is reported at <1%⁵³); therefore we would not expect substantial changes to our results, even if only maternal peanut/tree nuts allergies were excluded.

Finally, attrition is always a concern in longitudinal studies in regard to potential for selection bias. A detailed examination of population characteristics of participants with outcome data at the 18-month and 7-year assessments did not show any substantial differences to suggest selection bias.

In this study we did not find any suggestion that peanut and tree nut consumption in pregnancy increases the risks of asthma. Instead, higher consumption of these foods was associated with lower risk of early wheeze and asthma and possibly an even lower risk of later, more severe asthma.

Clinical implications: In this prospective cohort study we found that maternal peanut and tree nut intake 1 or more times per week during pregnancy decreases the risk of allergic disease in childhood. These results do not support avoidance of nuts during pregnancy.

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