Breast-feeding in relation to asthma, lung function, and sensitization in young schoolchildren

Inger Kull, PhD,[a,b] Erik Melen, MD,[a,d] Johan Alm, MD,[e,f] Jenny Hallberg, PhD,[e] Magnus Svartengren, MD,[c] Marianne van Hage, MD,[g] Göran Pershagen, MD,[a] Magnus Wickman, MD,[a,e] and Anna Bergström, PhD[a] *Stockholm, Sweden*

Background: The evidence from previous studies on beneficial effects of breast-feeding in relation to development of asthma is conflicting.

Objective: To investigate the relation between breast-feeding and asthma and/or sensitization during the first 8 years of life.

Method: In a birth cohort, children were followed up to 8 years by questionnaires at ages 2 months and 1, 2, 4, and 8 years to collect information on exposures and health effects. Determination of serum IgE antibodies to common inhalant and food allergens was performed at 4 and 8 years. Longitudinal analyses were applied by using general estimated equations. The study population consisted of 3825 children (93% of the original cohort), of whom 2370 gave blood and 2564 performed lung function measurements at 8 years.

Results: Children exclusively breast-fed 4 months or more had a reduced risk of asthma during the first 8 years of life (adjusted odds ratio [OR], 0.63; 95% CI, 0.50-0.78) compared with children breast-fed less than 4 months. At 8 years, reduced risks of sensitization (adjusted OR, 0.79; 95% CI, 0.64-0.99) and asthma in combination with sensitization (adjusted OR, 0.59; 95% CI, 0.37-0.93) were seen among children exclusively breast-fed 4 months or more. This group also had a significantly better lung function measured with peak expiratory flow.

Conclusion: Breast-feeding for 4 months or more seems to reduce the risk of asthma up to 8 years. At this age, a reduced risk was observed particularly for asthma combined with sensitization. Furthermore, breast-feeding seems to have a beneficial effect on lung function. (J Allergy Clin Immunol 2010;125:1013-9.)

Key words: *Breast-feeding, asthma, sensitization, lung function, infant feeding, prevention, BAMSE*

Human milk contains high amounts of IgA, cytokines, and long-chain fatty acids as well as indigestible oligosaccharides that promote colonization of a healthy gut flora. These factors stimulate the development of the infant's own immune system.[1] Previous studies on the relation between breast-feeding and asthma give conflicting results.[2-8] The discrepancy between studies may partly be explained by differences in study design or measurement of exposure and outcome, or in differences in duration of breast-feeding between populations and selection of the reference group.[9]

Despite the large number of studies on this topic, few of them have distinguished between allergic and nonallergic asthma. We have previously shown that exclusive breast-feeding for 4 months or more lowers the risk of asthma and reduced lung function up to 4 years of age, in particular when taking the effects of reverse causation into consideration.[10] In the current study, we investigate the relation between breast-feeding (exclusive or partial) and asthma during the first 8 years of life, particularly in relation to IgE sensitization.

METHODS

The Children Allergy Milieu Stockholm an Epidemiological Study (BAMSE) study is an unselected, population-based cohort study designed to assess risk factors for allergic diseases in childhood, among others short duration of breast-feeding. In total, 4089 newborn children from 4 municipalities in Stockholm County were enrolled from 1994 to 1996. The study has been described in detail elsewhere.[11,12] Briefly, at a median age of 2 months, data on family history of allergic disease and various exposures were obtained by parental questionnaires. Follow-up questionnaires focusing on symptoms related to allergic diseases and key exposures such as diet, parental tobacco smoke, and so forth were answered by the parents when the child was 1, 2, 4, and 8 years old. The response rates were 96%, 94%, 92%, and 84%, respectively. Information on breast-feeding and age for introduction of complementary feeding was assessed by the questionnaire at age 1 year.

All children with answered questionnaires at 8 years were invited to a clinical investigation including blood sampling and lung function measurement. Sera of 2370 children were analyzed for the presence of IgE antibodies to a mix of common inhalant allergens with Phadiatop (cat, dog, horse, birch, timothy, mugwort, *Dermatophagoides pteronyssinus*, and *Cladosporium herbarum*) and to a mix of common food allergens with fx5 (cow's milk, hen's egg, cod fish, soy bean, peanut, and wheat) by using the ImmunoCAP System (Phadia AB, Uppsala, Sweden). Single allergens were analyzed if Phadiatop or fx5 tested positive (≥0.35 kU_A/L). For single allergens, the lower detection level was set at ≥0.35 kU_A/L.

Lung function was measured by peak expiratory flow (PEF) using the normal range Ferraris Peak Flow Meter (Ferraris Medical Limited, Hertford, United Kingdom). Each child performed 3 PEF readings according to European Respiratory Society guidelines.[13] Exclusion criteria were poor quality reported by the test leader and inability to perform 2 reproducible PEF values (at least 100 L/min and within 15%).[14] The largest PEF reading

From [a]the Institute of Environmental Medicine, [b]the Center for Allergy Research, and [c]the Department of Public Health Sciences, Karolinska Institutet, Stockholm; [d]Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm; [e]the Department of Pediatrics, Sachs' Children's Hospital, Stockholm; [f]the Department of Clinical Science and Education, Karolinska Institutet, Södersjukhuset; and [g]the Clinical Immunology and Allergy Unit, Department of Medicine Solna, Karolinska Institutet and University Hospital.

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Reprint requests: Inger Kull, PhD, Institute of Environmental Medicine, Karolinska Institutet, Norrbacka 3rd Level, SE-171 76 Stockholm, Sweden. E-mail: inger.kull@ki.se.

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Abbreviations used
BAMSE: Children, Allergy, Milieu, Stockholm an Epidemiological Study
GEE: General estimated equation
MEFV: Maximum expiratory flow volume
OR: Odds ratio
PEF: Peak expiratory flow

was used for analysis. Maximum expiratory flow volumes (MEFVs) were measured by using a spirometer (2200 Pulmonary Function Laboratory; Sensormedics, Anaheim, Calif). All children performed several MEFV measurements sitting, using a nose clip. The highest values of FEV_1 were extracted and used for analysis provided that the child's effort was coded as being maximal by the test leader, the MEFV curve passed visual quality inspection, and the 2 highest readings were reproducible according to American Thoracic Society/ERS criteria.[15]

The Ethics Committee of Karolinska Institutet, Stockholm, Sweden, approved the study.

Classification of exposure

Exclusive breast-feeding denotes that the infants were given only breast milk, and no formula, cow's milk, or solid foods had been introduced.[10] *Partial breast-feeding* implies that the child in addition to breast milk also received infant formula or solid food.[10]

Definition of health outcomes

Recurrent wheeze meant the child had at least 3 episodes of wheeze in the last 12 months at 1, 2, 4, or 8 years.[16] At 1 and 2 years, *asthma* was defined as at least 3 episodes of wheeze and signs of bronchial hyperreactivity without concomitant respiratory infection, or 1 episode of wheeze in combination with inhaled corticosteroids.[16] At 4 and 8 years, at least 4 episodes of wheeze in the last 12 months or 1 episode in combination with inhaled corticosteroids was required.[10]

Sensitization was defined as a positive Phadiatop and/or fx5 (specific IgE ≥ 0.35 kU_A/L).

The terms *allergic* and *nonallergic asthma* were used if the child fulfilled the criteria of asthma at 4 and/or 8 years and was or was not sensitized to common food and/or inhalant allergens (a positive Phadiatop and/or fx5).

Statistical analyses

General estimated equations (GEEs) with an unstructured correlation matrix were used to assess the association between breast-feeding and the selected health outcomes. The GEE model calculates population average risk taking the correlation within individuals into account and provides estimates when missing observations are unequally spaced.[17] The model incorporated an interaction between time and exposure to evaluate the effect of exposure over time.[17]

Exclusive breast-feeding was analyzed as a dichotomized variable (<4 months compared with ≥4 months). This cut-off corresponded to the 25th percentile and was also in agreement with the national recommendations for breast-feeding at the time of the study, as well as with current international recommendations.[18,19] Further, to disentangle the effects of exclusive and partial breast-feeding, the durations of exclusive and partial breast-feeding were each grouped into 3 categories (0 to <2, 2 to <4, ≥4 months). Results are presented as adjusted odds ratios (ORs) with 95% CIs. In the multivariate analyses, adjustments were made for sex, birth weight (<2600 g vs ≥2600 g), parental history of allergic disease (defined as doctor diagnosed asthma and/or allergic rhinitis in combination with reported allergy to pollen or pets in any parent or both parents), maternal smoking during pregnancy and/or at birth (yes vs no), and maternal age (<26 years vs ≥26 years at enrollment). However, all these factors changed the risk estimate less than 3%. The Wald test was used to assess interaction between breast-feeding and other covariates (departure from a multiplicative model) and to assess differences between the subgroups of additional partial breast-feeding within groups of exclusive breast-feeding.

To examine effects caused by disease-related modification of exposure, the effect of breast-feeding was analyses in 2 different modes.[10] First, the association between breast-feeding and the selected health outcomes was analyzed in the whole study population. Second, the same association was assessed after exclusion of children with onset of wheeze and/or eczema during the period of breast-feeding (n = 474). To investigate the association between breast-feeding and allergic/nonallergic asthma at 8 years, logistic regression was used with the same set of confounding variables as used for the GEE analysis. Linear regression was used to test differences in PEF and FEV_1 values in relation to duration of breast-feeding, and adjustments were made for sex, age, and height.[14] All statistical analyses were performed with STATA, Statistical Software release 9.0 (College Station, Tex).

Children with information on breast-feeding, possible confounding factors, and relevant outcomes were included in this study. Thus, the final study population was composed of 3825 children for the analyses of asthma, whereas 2370 children were included in the analyses of asthma in combination with IgE sensitization. In the analyses of breast-feeding and lung function, 2564 children were included when PEF was used as the outcome measurement, whereas 1838 children were included in the analyses of FEV_1.

RESULTS

In total, 99% of the children in our study were breast-fed to some extent. The majority of the children (80%) were exclusively breast-fed during the first 4 months of life, whereas 5% received breast milk in combination with formula from the start. The mean duration of exclusive breast-feeding was 5.1 months (SD, 2.5 months), and partial breast-feeding, 3.5 months (SD, 2.7 months). Exclusive and partial breast-feeding correlated only weakly ($r = -0.16$).

Exposure to parental tobacco smoke at birth, maternal age less than 25 years, low birth weight, and low parental socioeconomic status were associated with a shorter breast-feeding period (Table I). Compared with the original cohort, there were no major differences regarding distribution of background exposures among children included in the study population, children who provided blood samples, and children who participated in the lung function measurements (data not shown). Although 84% of our cohort answered the questionnaire at age 8 years, missing information on disease status was somewhat more common among children breast-fed less than 4 months (20.0%) compared with children breast-fed 4 months or more (13.7%; $P < .05$).

At 8 years of age, 6.3% of the children fulfilled the criteria for asthma, compared with 7.0% at 4 years, 5.7% at 2 years, and 3.8% at 1 year of age. The corresponding frequencies for recurrent wheeze were 3.5% at 8 years, 4.6% at 4 years, 10% at 2 years, and 6.9% at 1 year.

Children exclusively breast-fed 4 months or more had an overall reduced risk of asthma during the first 8 years of life (adjusted OR, 0.63; 95% CI, 0.50-0.78) with similar results for recurrent wheeze compared with children breast-fed less than 4 months (Fig 1). At each follow up—that is, at 1, 2, 4, and 8 years—asthma and recurrent wheeze were less prevalent in children exclusively breast-fed for the first 4 months of life or longer. The association diminished with age and was no longer statistically significant at 8 years. Controlling for disease-related modification of exposure by excluding children with symptoms of wheeze and/or eczema during the breast-feeding period had

TABLE I. Distribution of exposure characteristics at birth in relation to exclusive breastfeeding (≥4 months) in a birth cohort from Stockholm, Sweden (N = 3825)

		<4 mo		≥4 mo		
	N	n	%	n	%	95% CI
Study population	3825	774	20.2	3051	79.8	78.5–81.0
Birth weight						
≥2600 g	3650	683	18.7	2967	81.3	80.0–82.5
<2600 g	175	91	52.0	84	48.0	40.5–55.0
Sex						
Female	1885	391	20.7	1494	79.3	77.4–81.1
Male	1940	383	19.7	1557	80.3	78.4–82.0
Parental history of allergic disease*						
None	2690	558	20.7	2132	79.3	77.7–80.8
Any	1014	199	19.6	815	80.4	78.0–82.8
Both	119	17	14.5	102	85.7	79.3–92.1
Maternal age at enrollment						
≥25 y	3531	687	19.4	2844	80.5	79.2–81.8
<25 y	294	87	29.9	207	70.4	65.1–75.6
Socioeconomic status						
Blue collar workers	633	168	26.5	465	73.5	70.0–76.9
White collar workers	3140	592	18.8	2548	81.1	79.8–82.5
Parental tobacco smoke at enrollment†						
No	3031	568	18.7	2463	81.3	79.1–82.6
Yes	794	206	25.9	588	74.1	71.0–77.1
Older siblings						
No	1990	391	19.6	1599	80.3	78.6–82.1
Yes	1835	383	20.9	1452	79.1	77.3–81.0

*Doctor's diagnosis of asthma and/or rhinitis in combination with reported allergy to pollen or pets in any parent or both.
†Any parent smoked at least 1 cigarette at the time of enrollment.

some impact on the overall risk reduction (adjusted OR, 0.50; 95% CI, 0.39-0.69).

To examine the temporal trends further, we classified children with asthma at any time between age 3 months and 8 years into transient (asthma during age 1-4 years but not later), late onset (after age 4 years), and persistent asthma (at age 1-4 years and after 4 years). The effect of breast-feeding for 4 months or more was significant for children with transient (adjusted OR, 0.67; 95% CI, 0.49-0.91) and persistent asthma (adjusted OR, 0.63; 95% CI, 0.41-0.98) but not late onset of asthma (adjusted OR, 0.78; 95% CI, 0.46-1.30). The effect of breast-feeding did not differ in relation to sex, parental history of allergic disease, maternal asthma, or parental smoking ($P > .05$ for all tests of interaction).

To try to disentangle the effects of exclusive and partial breast-feeding, the duration of each type of breast-feeding was each grouped into 3 categories (0 to <2, 2 to <4, ≥4 months; Table II). For recurrent wheeze, a reduced risk was observed among children exclusively breast-fed for 2 to 4 months. Although subsequent partial breast-feeding tended to provide additional protection, the effect was not statistically significant ($P > .05$ for all subgroups). For asthma, a reduced risk was suggested among children exclusively breast-fed for 2 months or more, but statistically significant associations were consistently seen only for at least 4 months of exclusive breast-feeding.

The association between exclusive breast-feeding and lung function at 8 years of age is shown in Table III. Children exclusively breast-fed for 4 months or more had significantly better lung function at 8 years as measured with PEF. Even after adjustment for asthma at the age of 8 years, similar results were observed (ΔPEF, 4.1; 95% CI, 0.43-7.86). Although not statistically significant, the same tendencies were seen for FEV_1.

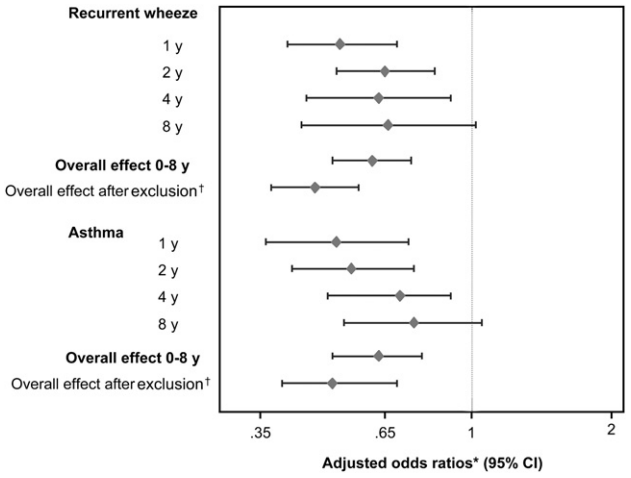

FIG 1. Exclusive breast-feeding (≥4 months) and asthma during the first 8 years of life among children in a birth cohort from Stockholm (N = 3825). *Adjusted for sex, birth weight, parental history of allergic disease, maternal smoking during pregnancy and/or at birth, and maternal age. ORs and 95% CIs were estimated by using GEEs. †After exclusion of 474 children with symptoms of wheeze or eczema during the breast-feeding period.

The association between exclusive breast-feeding and sensitization at 8 years is explored in Table IV. A reduced risk of sensitization to common inhalant and/or food allergens was observed among children breast-fed 4 months or more (adjusted OR, 0.79; 95% CI, 0.64-0.99). A similar pattern was seen after exclusion of children with early symptoms of wheeze and/or eczema.

TABLE II. Association between patterns of breast-feeding (exclusive and partial in combination) and development of recurrent wheeze and asthma up to 8 years* in a birth cohort from Stockholm, Sweden (N = 3825)

	Overall effect 0-8 y* Recurrent wheeze		Asthma	
Exclusive and partial breast-feeding	Adjusted OR†	(95% CI)	Adjusted OR†	(95% CI)
Exclusive 0-2 mo + partial 0-2 mo (n = 246)	Reference		Reference	
Exclusive 0-2 mo + partial 2-4 mo (n = 113)	0.79	(0.47-1.33)	0.89	(0.50-1.56)
Exclusive 0-2 mo + partial >4 mo (n = 204)	0.71	(0.46-1.10)	0.73	(0.45-1.21)
Exclusive >2-4 mo + partial 0-2 mo (n = 254)	0.59	(0.39-0.90)	0.63	(0.39-1.01)
Exclusive >2-4 mo + partial >2-4 mo (n = 154)	0.45	(0.26-0.78)	0.55	(0.31-0.99)
Exclusive >2-4 mo + partial >4 mo (n = 199)	0.47	(0.29-0.76)	0.69	(0.42-1.14)
Exclusive >4 mo + partial 0-2 mo (n = 1058)	0.55	(0.40-0.75)	0.58	(0.41-0.83)
Exclusive >4 mo + partial >2-4 mo (n = 676)	0.48	(0.33-0.68)	0.54	(0.37-0.80)
Exclusive >4 mo + partial >4 mo (n = 983)	0.46	(0.33-0.64)	0.48	(0.33-0.70)

*OR obtained by GEEs.

†Adjusted for parental sex, birth weight, history of allergic disease, maternal smoking during pregnancy and/or at birth, and maternal age.

At 4 years of age, 43% (n = 80) of the children with asthma were sensitized compared with 67% (n = 115) at 8 years of age. These children were defined as having allergic asthma. At 4 years, similar risks were indicated for allergic (adjusted OR, 0.69; 95% CI, 0.37-1.29) and nonallergic asthma (adjusted OR, 0.80; 95% CI, 0.45-1.40; Fig 2). At the age of 8 years, exclusive breast-feeding for 4 months or more was associated with a reduced risk of allergic asthma (adjusted OR, 0.59; 95% CI, 0.37-0.93) but not of nonallergic asthma (adjusted OR, 1.18; 95% CI, 0.56-2.48).

DISCUSSION

In this prospective cohort including 3825 Swedish children followed from birth, children exclusively breast-fed for 4 months or more had a reduced risk of asthma during the first 8 years of life. This group of children also had a reduced risk of sensitization to common inhalant or food allergens at 8 years. When we assessed the association between breast-feeding among children with allergic and nonallergic asthma at 8 years, a risk reduction was seen for allergic asthma only. Moreover, children breast-fed 4 months or more had in general a slightly better lung function measured as PEF.

The strengths of the current study include its prospective design, the large number of participants, limited loss to follow-up, detailed and repeated assessment of recurrent wheeze and asthma through questionnaires, and phenotyping of children with asthma by the presence of allergen-specific IgE antibodies and by measurement of lung function. Moreover, we have detailed assessment of parental history of allergic disease and various exposures collected at 2 months of age. Breast-feeding was reported by the parents when the child was 1 year old. The average duration of breast-feeding was relatively long compared with other studies,[4,7] and only 1% of the children were not breast-fed at all. The high prevalence of breast-feeding in our study makes it impossible to provide risk estimates for breast-feeding *per se* (ie, breast-fed children vs not breast-fed children).[20]

Recall bias is a potential weakness in our study. Although we assessed breast-feeding at age 1 year, some misclassification of exposure cannot be excluded. If the misclassification is independent of disease status, it will generally lead to a dilution of the risk estimates.[21]

A more important concern is the risk of disease-related modification of exposure (also called reverse causality).[22] This might be a problem also in prospective studies because early symptoms of allergic disease might occur already during breast-feeding and may encourage the mother to continue to breast-feed.[23] Also, parental history of allergic disease has been reported to influence breast-feeding habits.[24,25] We tried to assess effects of such bias by performing analyses also with exclusion of children with symptoms during the breast-feeding period, as well as testing for interaction with parental history of asthma and other allergic diseases. These analyses showed that, to some degree, reverse causality exists within our study.

An additional problem in prospective studies is missing data over time (eg, loss to follow-up) that may be related to the exposure and outcome of interest. In the current study, we observed a higher occurrence of missing information on disease status at age 8 years among children with shorter breast-feeding duration. These children are more exposed to environmental tobacco smoke at birth and have a younger mother. Both these exposures have been identified as risk factors for asthma in our cohort. Consequently, a higher loss to follow-up in this group will likely dilute the risk estimates observed in our analyses.

In our study, a certain period of exclusive breast-feeding was associated with an overall reduced risk of asthma up to age 8 years, which is in concordance with results from the Prevention and Incidence of Asthma and Mite Allergy study.[26] However, the literature on breast-feeding in relation to asthma appears inconclusive, which to some extent may be explained by differences in study design as well as in measurement of exposure and outcome.[9] In addition, differences in duration of breast-feeding between populations may contribute to differences in risk. In the study by Sears et al,[4] 51% of the children were not breast-fed or were breast-fed less than 4 weeks, and the remaining 49% were breast-fed 4 weeks or more in comparison with the current study, in which almost all children were breast-fed to some extent. Moreover, some studies provide evidence of effect modification by sex and parental history of allergic disease.[27,28] No such effect modification was evident in our study.

The conditions for breast-feeding vary, and for many reasons it is difficult for mothers to breast-feed for a longer period in some parts of the world. Therefore, we would like to emphasize that in the current study also, a rather short period of exclusive breast-feeding in combination with an additional period of partial breast-feeding seemed to reduce the risk of asthma and recurrent wheeze, which is important from a public health point of view.[9]

TABLE III. Lung function at 8 years in relation to duration of breast-feeding among children in a cohort from Stockholm, Sweden (N = 2564 in the analyses of PEF and N = 1838 in the analyses of FEV_1)

	PEF (L/min)				FEV1 (mL)			
Duration of exclusive breast-feeding	**N**	**Unadjusted Mean PEF (sd)**	**ΔPEF***	**(95% CI)**	**n**	**Mean FEV_1**	**ΔFEV_1***	**(95% CI)**
All children	2564	291 (41.4)			1837	1776		
Breast-feeding								
<4 mo	467	286 (43.4)	Referent		332	1759	Referent	
≥4 mo	2033	292 (40.6)	4.4	(0.72 to 8.12)	1611	1780	17.2	(–5.1.1 to 39.4)
All children after exclusion†	2168	292 (41.0)			1550	1780		
Breast-feeding								
<4 mo	438	288 (42.7)	Referent		311	1767	Referent	
≥4 mo	1730	293 (40.5)	4.5	(0.62 to 8.29)	1369	1783	17.4	(–5.7 to 40.5)

*Adjusted for sex, birth weight, sex, and length of the child.
†After exclusion of 474 children with symptoms during the breast-feeding period.

TABLE IV. Breast-feeding and allergen-specific IgE (≥0.35 kU_A/L) to common allergens at 8 years of age among children in a birth cohort from Stockholm, Sweden (N = 2370)

	All children Exclusive breast-feeding ≥4 mo				After exclusion* Exclusive breast-feeding ≥4 mo			
Positive test At 8 y	**N**	**n**	**Adjusted OR†**	**(95% CI)**	**N**	**n**	**Adjusted OR†**	**(95% CI)**
Phadiatop or fx5	1915	654	0.79	(0.64-0.99)	1629	498	0.71	(0.55-0.89)
Inhalant allergens								
Phadiatop	1918	494	0.81	(0.63-1.03)	1632	365	0.71	(0.56-0.92)
Cat	1916	226	0.71	(0.52-0.97)	1630	159	0.63	(0.45-0.88)
Dog	1913	214	0.79	(0.58-1.09)	1629	147	0.68	(0.47-0.97)
Horse	1911	122	0.77	(0.52-1.15)	1628	72	0.55	(0.36-0.91)
Timothy	1909	268	0.73	(0.55-0.98)	1624	185	0.60	(0.43-0.83)
Birch	1908	299	0.87	(0.65-1.17)	1624	209	0.74	(0.55-1.02)
Dust Mite	1907	68	0.52	(0.32-0.84)	1624	49	0.46	(0.28-0.77)
Mugwort	1903	143	0.96	(0.65-1.43)	1623	96	0.73	(0.47-1.13)
Mold	1904	40	0.68	(0.35-1.30)	1623	19	0.42	(0.19-0.92)
Food allergens								
fx5	1916	379	0.93	(0.72-1.21)	1630	282	0.83	(0.63-1.10)
Egg white	1912	117	1.30	(0.81-2.09)	1628	82	1.22	(0.73-2.07)
Cow's milk	1907	178	0.78	(0.55-1.07)	1623	132	0.66	(0.47-0.94)
Fish	1905	9	‡		1621	5	‡	
Wheat	1907	111	0.83	(0.54-1.26)	1623	72	0.62	(0.39-0.98)
Peanut	1910	156	1.01	(0.68-1.50)	1626	101	0.88	(0.56-1.37)
Soy	1908	96	0.96	(0.59-1.55)	1624	64	0.82	(0.48-1.41)

*After exclusion of 474 children with symptoms during the breast-feeding period.
†Adjusted for parental history of allergic disease, maternal age, any parent smoking at baseline, birth weight, and sex.
‡Too few children in the analyses.

In the current study, children breast-fed for 4 months or more had better lung function at 8 years as measured with PEF, and there was a tendency in the same direction for FEV_1. This is in agreement with results from our previous follow-up at age 4 years.[10] Likewise, data from a British birth cohort show that children breast-fed at least 4 months had better lung function measured as forced vital capacity, FEV_1, and PEF at age 10 years compared with children who were not breast-fed.[29] Longer duration of breast-feeding was also associated with improved lung growth both at age 11 and 16 years in a US cohort, although only in the absence of maternal asthma.[30]

Interestingly, we observed a reduced risk for sensitization associated with exclusive breast-feeding for 4 months or more in the current follow-up at 8 years, but not in our previous follow-up at 4 years.[10] This is in agreement with an intervention study from Isle of Wight in which a combination of breast-feeding, diet, and house dust mite reduction lowered the risk of atopy at 8 years,[31] whereas most previous studies have not observed any association between breast-feeding and sensitization.[32,33]

When stratifying children with asthma into sensitized or not at 8 years, we observed a reduced risk for allergic asthma, whereas at age 4 years, the risk reduction appeared similar in both groups. This might be explained by the natural course of asthma development, because the proportion of children with allergic asthma increases with age.[34] This is reflected in our cohort, in which about one third of the children with asthma were sensitized at 4 years,[10] in comparison with two thirds at 8 years. Few studies on breast-feeding and asthma have distinguished between allergic

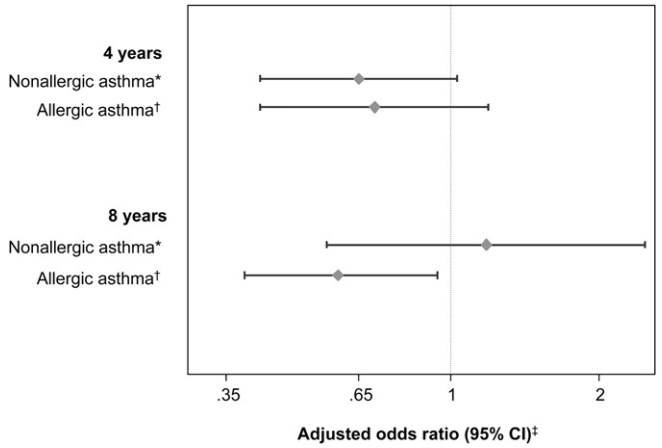

FIG 2. Exclusive breast-feeding (≥4 months) and asthma and sensitization in combination at 4 and 8 years among children in a birth cohort from Stockholm (N = 2370). *Asthma in combination with a negative Phadiatop and a negative fx5. †Asthma in combination with a positive Phadiatop and/or a positive fx5. ‡ORs and 95% CIs were estimated by using logistic regression.

and nonallergic asthma. In a cross-sectional study from Northern Sweden, breast-feeding during the first 3 months or more was associated with a reduced risk of asthma, but in stratified analyses, this reduction in risk was confined to the nonatopic subjects with asthma.[33] In the Isle of Wight birth cohort study, exclusive breast-feeding in the first 3 months of life reduced the risk of wheeze during the first 10 years in life in never-atopics and in early childhood atopics.[35] A plausible explanation for these apparently contrasting results is the different reference groups and different outcome definitions used in these studies. In the current study, we combined a strict definition of asthma at 8 years with sensitization at the same age using a reference group consisting of children with no asthma and no sensitization.

The evidence that breast-feeding for the first months of life reduced the risk of virus-induced wheeze during infancy is substantial.[36] However, it is also biologically plausible that exclusive breast-feeding for the first months of life may reduce the risk of asthma and allergy because breast milk contains components that have a beneficial effect on the infant's immune system such as high amounts of IgA, cytokines, and prebiotica.[1] Furthermore, exclusive breast-feeding for the first 4 months of life followed by a gradual introduction of complementary food while breast-feeding is maintained has been suggested as a way to achieve immune tolerance.[37]

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Clinical implications: Exclusive breast-feeding for 4 months or more reduces the risk of asthma up to 8 years compared with a shorter duration of breast-feeding.

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Correction

With regard to the October 2009 article entitled “Analysis of behavior-related adverse experiences in clinical trials of montelukast” (J Allergy Clin Immunol 2009;124:699-706), two protocol numbers in Table E1 are incorrect as given. Under “Adult Studies,” protocol number “202” should read “A202,” and protocol number “402” should read “A402.”