Modes of Infant Feeding and the Risk of Childhood Asthma: A Prospective Birth Cohort Study

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Objective To determine whether different modes of infant feeding are associated with childhood asthma, including differentiating between direct breastfeeding and expressed breast milk.

Study design We studied 3296 children in the Canadian Healthy Infant Longitudinal Development birth cohort. The primary exposure was infant feeding mode at 3 months, reported by mothers and categorized as direct breastfeeding only, breastfeeding with some expressed breast milk, breast milk and formula, or formula only. The primary outcome was asthma at 3 years of age, diagnosed by trained healthcare professionals.

Results At 3 months of age, the distribution of feeding modes was 27% direct breastfeeding, 32% breastfeeding with some expressed breast milk, 26% breast milk and formula, and 15% formula only. At 3 years of age, 12% of children were diagnosed with possible or probable asthma. Compared with direct breastfeeding, any other mode of infant feeding was associated with an increased risk of asthma. These associations persisted after adjusting for maternal asthma, ethnicity, method of birth, infant sex, gestational age, and daycare attendance (some expressed breast milk: aOR, 1.64, 95% CI, 1.12-2.39; breast milk and formula, aOR, 1.73, 95% CI, 1.17-2.57; formula only: aOR, 2.14, 95% CI, 1.37-3.35). Results were similar after further adjustment for total breastfeeding duration and respiratory infections.

Conclusions Modes of infant feeding are associated with asthma development. Direct breastfeeding is most protective compared with formula feeding; indirect breast milk confers intermediate protection. Policies that facilitate and promote direct breastfeeding could have impact on the primary prevention of asthma. *(J Pediatr 2017;190:192-9).*

B reast milk is widely known to be the optimal source of infant nutrition. The importance of breastfeeding is well-recognized for infants' short-term health with respect to growth, immune function, and gastrointestinal health.[1] In addition to these immediate clinical benefits, there are potential long-term advantages that are realized after the breastfeeding period. An extensive body of literature suggests that breastfeeding may contribute to protection against autoimmune, malignant, and inflammatory diseases, including allergic diseases and asthma.[1-5] However, very few studies distinguish between *breastfeeding*, where the infant suckles directly at the mother's breast, and *consumption of human milk*, which can be expressed and fed from a bottle. This distinction is important because an increasing number of mothers are providing expressed breast milk to their infants.[6,7] For example in the United States, where there is no national policy for paid maternity leave and the average mother returns to work after just 10 weeks,[8] more than 25% of nursing mothers regularly provide expressed breast milk to their infants.[9]

Although several studies,[5,10,11] including our own,[12] have found that breastfeeding is protective against asthma or wheezing disorders, a recent meta-analysis found that evidence for this association was inconsistent across studies, with high heterogeneity ($I^2 = 63\%$ across 29 studies) related to differences in study designs and settings.[13] This inconsistency may also be related to differences in infant feeding modes, which are known to vary widely between countries,[6] but are generally not documented in epidemiologic studies.

To date, only 1 study has examined respiratory health among infants fed direct breast milk versus bottled breast milk[14]; Soto-Ramirez et al found that any mode of infant feeding that included formula or expressed breast milk conferred an increased risk for coughing and wheezing episodes by 1 year of age, compared with direct breastfeeding. A proposed mechanism for this association is the alteration of breast milk components, such as bioactive proteins and microbiota, during the expression and storage of breast milk.[15-17] In addition, during active infection in

CHILD	Canadian Healthy Infant Longitudinal Development

the nursing infant, direct breastfeeding is thought to trigger an increased immune response in the lactating mother, leading to a transfer of protective factors to her relatively immunocompromised offspring.[18] Direct contact through breastfeeding also transmits potentially protective maternal skin microbes,[19] and the physical exercise associated with suckling at the breast is thought to improve airflow and increase lung capacity.[20] However, the potential impact of expressed breast milk on childhood asthma development remains unknown because no studies have examined this association beyond the first year of life.

Using prospective data from the national Canadian Healthy Infant Longitudinal Development (CHILD) population-based birth cohort,[21] we undertook a study to determine the association of infant feeding modes in the first 3 months of life with asthma development by 3 years of age. We hypothesized that any mode of feeding that included expressed breast milk or formula would be associated with an increased risk of asthma compared with direct breastfeeding.

Methods

This study included 3296 infants from the CHILD study,[21] a general population-based national birth cohort that recruited pregnant women from Toronto, Winnipeg, Edmonton, and Vancouver from 2009 to 2012. The CHILD Study enrolled women at least 18 years of age in their second or third trimester of pregnancy with proficiency in English and residing within reasonable proximity to a recruitment center. Exclusion criteria for the CHILD study were children with major congenital anomalies, born preterm ($<35^{6/7}$ weeks of gestation), of multiple births, or resulting from in vitro fertilization. Written informed consent was obtained by caregivers at enrollment and the study was approved by the Human Research Ethics Boards of the Universities of Alberta, British Columbia, Manitoba, Toronto and McMaster University.

Modes of feeding were reported by mothers at 3 months and infants were classified into 4 categories: (1) breast milk only—all direct breastfeeding (no expressed milk or formula from birth to 3 months of age); (2) breast milk only—some expressed breast milk (received some breast milk expressed with a pump before 3 months of age, but no formula); (3) formula and breast milk (formula introduced before 3 months of age, but still receiving some direct or expressed breast milk at 3 months of age); or (4) formula only (not receiving any breast milk at 3 months of age).

A semistructured assessment of asthma was performed at 3 years of age. The diagnosis of asthma was made after a focused history and physical examination by a limited number of well-trained healthcare professionals (2 or 3 physicians, nurses, or clinical research associates at each site) and classified for this analysis as possible or probable asthma or no asthma. In a sensitivity analysis, we evaluated the modified Asthma Predictive Index as an alternative outcome, adapted from Guilbert et al[22] and defined as a diagnosis of possible or probable asthma plus one of the following: diagnosed atopic dermatitis,[21] positive skin prick test to any allergen (wheal diameter ≥2 mm

greater than the response to the negative control),[21] or parental history of diagnosed asthma (self-reported by parents).

Infant sex, gestational age, method of birth, maternal age, and number of older siblings (parity) were documented from hospital records. Maternal ethnicity, history of asthma, and tobacco smoking during pregnancy and infancy were self-reported by standardized questionnaire. Maternal education and home ownership were also self-reported during pregnancy, and assessed as measures of socioeconomic status. Daycare attendance at 1 year of age was defined as spending 7 or more hours a week with at least 3 other children at a location away from home. The total duration of any breastfeeding (infant age at breastfeeding cessation) and number of respiratory infections (colds) were documented from maternal questionnaires completed at 3, 6, 12, 18, and 24 months postpartum.

Statistical Analyses

Logistic regression was used to investigate associations between modes of infant feeding and asthma. First, potential confounders (listed above) were tabulated against infant feeding mode and asthma. Those found to be significantly associated with both feeding mode and asthma ($P < .05$ by χ^2 test) were subsequently included in logistic regression models. Regression models were also adjusted for 3 established asthma risk factors selected a priori (infant sex, maternal ethnicity, and maternal asthma). Results are presented as crude odds ratios (ORs) and adjusted ORs (aORs) with 95% confidence intervals (CI). Analyses were conducted for the 2534 children with complete data for infant feeding, asthma diagnosis, and essential covariates (**Figure 1**; available at www.jpeds.com). Children who were lost to follow-up or had incomplete feeding data (n = 762) were similar to those with complete data (n = 2534) with respect to infant feeding patterns, maternal asthma, and child asthma (**Table I**). Mothers of children with complete data were more likely to be white and have a higher socioeconomic status, and less likely to smoke. To address potential bias from incomplete data and loss to follow-up, a sensitivity analysis was performed in the full cohort after multiple imputation of missing feeding, asthma, and covariate data. Multiple imputation (n = 20 imputed datasets) was performed with fully conditional specification (chained equations) using all essential covariates plus the following auxiliary variables: maternal age, parity, and post-secondary education; history of prenatal smoke exposure; and study site. We present results from the imputed data as the main findings because they are adjusted (through multiple imputation) for potential bias from missing data. Additional sensitivity analyses were performed to evaluate an alternative outcome definition (modified Asthma Predictive Index, as defined), and to adjust for respiratory infections (among all infants) and breastfeeding duration (excluding infants in the formula-only group). All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

Results

Among 2534 infants with complete feeding and asthma data, the distribution of feeding modes at 3 months of age was: 60%

Table I. Characteristics of CHILD study dyads with complete versus incomplete data

	Dyads with complete feeding and asthma data (n = 2534)		Dyads with incomplete data (n = 762)		
	n	(%)	n	(%)	P value
Maternal asthma					
No	1961	(78.9)	557	(79.6)	.569
Yes	526	(21.1)	143	(20.4)	
Missing	47		77		
Maternal ethnicity					
Asian	404	(16.0)	106	(14.8)	<.001
White	1866	(74.0)	492	(68.5)	
First Nations	96	(3.8)	48	(6.7)	
Other	155	(6.1)	72	(10.0)	
Missing	13		59		
Socioeconomic status: maternal education					
Did not complete post-secondary	550	(22.3)	191	(28.4)	.001
Completed post-secondary	1914	(77.7)	481	(71.6)	
Missing	70		90		
Socioeconomic status: home ownership					
Family owns home	1875	(76.0)	435	(64.8)	<.001
Family rents home	591	(24.0)	236	(35.2)	
Missing	68		91		
Maternal smoking during pregnancy					
No	2305	(92.6)	581	(85.2)	<.001
Yes	184	(7.4)	101	(14.8)	
Missing	45		80		
Maternal smoking during infancy					
No	2077	(94.6)	331	(89.0)	<.001
Yes	118	(5.4)	41	(11.0)	
Missing	339		390		
Method of birth					
Vaginal	1877	(75.2)	536	(73.6)	.296
Cesarean	620	(24.8)	192	(26.4)	
Missing	37		49		
Infant gestational age (wk)					
<37	111	(4.5)	30	(4.2)	.026
37-38	145	(5.8)	59	(8.2)	
38-39	420	(16.9)	137	(19.1)	
≥39	1815	(72.9)	493	(68.6)	
Missing	43		58		
Number of older siblings					
0	1369	(54.0)	392	(53.0)	.520
1	838	(33.1)	260	(35.1)	
≥2	327	(12.9)	88	(11.9)	
Missing	0		22		
Infant sex					
Female	1187	(46.8)	376	(48.4)	.319
Male	1347	(53.2)	401	(51.6)	
Missing	0		0		
Daycare attendance by 1 year					
No	1760	(80.5)	309	(81.3)	.715
Yes	426	(19.5)	71	(18.7)	
Missing	348		397		
Feeding mode at 3 months					
Breast milk only: all direct breastfeeding	690	(27.2)	126	(25.6)	.153
Breast milk only: some expressed breast milk	831	(32.8)	144	(29.3)	
Breast milk + formula	659	(26.0)	137	(27.8)	
Formula only	354	(14.0)	85	(17.3)	
Missing	0		285		
Possible or probable asthma at 3 years of age					
No	2215	(87.4)	105	(92.9)	.082
Yes	319	(12.6)	8	(7.1)	
Missing	0		664		
Modified asthma predictive index at 3 years of age					
Negative	2308	(91.4)	106	(94.6)	.228
Positive	217	(8.6)	6	(5.4)	
Missing	9		665		

Percentages reflect proportion of nonmissing data. Comparisons by χ^2 test.

breast milk only (27% all direct breastfeeding, 33% with some expressed breast milk), 26% breast milk and formula, and 14% formula only (**Table I**). By 3 years of age, 319 (12.6%) were diagnosed with possible or probable asthma and 217 (8.6%) had a positive modified Asthma Predictive Index. Risk factors for possible or probable asthma diagnosis included male sex, gestational age of less than 37 weeks, maternal asthma, caesarean section delivery, and daycare attendance by 1 year of age (**Table II**). Number of siblings, maternal education, and maternal smoking were not associated with asthma.

Mode of infant feeding was associated with several maternal and infant characteristics (**Table II**). Direct breastfeeding was associated with higher maternal education, Asian and white ethnicity, vaginal delivery, and gestational age of 39 weeks or greater. Firstborn infants received less direct breast milk and more expressed milk compared with those with older siblings, although the proportion receiving formula was similar regardless of birth order. Mothers who smoked were less likely to provide direct or expressed breast milk and more likely to provide formula. Infants who attended daycare were less likely to receive direct breast milk exclusively.

Infant feeding mode was associated significantly with possible or probable asthma diagnosis at 3 years of age (**Table III**). Compared with direct breastfeeding, any mode of infant feeding that included expressed milk or formula was associated with an increased risk of possible or probable asthma diagnosis (**Figure 2**). The lowest prevalence (8.8%) was observed among infants who received direct breast milk only. Prevalence was higher among infants receiving some expressed breast milk (12.5%) or breast milk and formula (14.9%), and was highest among exclusively formula-fed infants (15.8%). Associations persisted after multiple imputation of missing data and adjustment for infant sex, maternal asthma, ethnicity, method of birth, daycare attendance, and gestational age (some expressed breast milk: aOR, 1.43, 95% CI, 1.04-1.97; breast milk and formula: aOR, 1.56, 95% CI, 1.12-2.18; formula only: aOR, 1.79, 95% CI, 1.23-2.61). Similar patterns of association were found for the alternative outcome definition of the modified Asthma Predictive Index (**Table III**). Sensitivity analyses adjusting for frequent respiratory infections yielded similar results, while adjustment for total breastfeeding duration resulted in slightly attenuated associations (**Table III**).

Discussion

Our research in the population-based CHILD birth cohort indicates that any mode of infant feeding other than direct breastfeeding is associated with an increased likelihood of possible or probable asthma by 3 years of age. Compared with infants who received direct breast milk only, those who received some expressed milk had a 43% increased odds of this diagnosis, and those who received only formula had a 79% increased odds. These associations were independent of established maternal, socioeconomic, and environmental risk factors.

Although several studies have examined the association between infant feeding and asthma,[5,10,11,13,23] the present study uniquely distinguishes between direct breastfeeding and expressed breast milk. Our results suggest that feeding mode differences could help to explain the apparently inconsistent results observed in "breastfeeding" studies across different populations and settings. Our study also extends recent findings by Soto-Ramirez et al,[14] who reported that American infants fed bottled breast milk or formula have an increased risk of coughing and wheezing episodes by 1 year of age compared with those who were directly breastfed. Finally, our results add to recent evidence that feeding expressed breast milk is associated with increased odds of otitis media[24] and rapid infant weight gain,[25] compared with direct breastfeeding.

There are several possible explanations for the apparently differential effects of direct breastfeeding and expressed breast milk. One involves the alteration of breast milk components, such as immune cells, cytokines, and microbiota, during the expression and storage of breast milk.[15-17] For example, freezing or processing human milk has been shown to diminish its antioxidative properties,[16] decrease vitamin levels, and reduce immunoglobulin A activity.[17] Expressed milk could also contain asthmogenic chemicals used in the manufacturing or cleaning of breast pumps or storage containers, including phthalates, bisphenols, or triclosan.[26]

Another hypothesis is that, when a nursing infant is sick, direct breastfeeding triggers an increased immune response in the lactating mother to provide her infant with a more effective immunologic defense. Riskin et al showed that white blood cells and cytokines were increased in breast milk collected from mothers when their nursing infants were infected, even when the mothers themselves were asymptomatic.[18] Although the mechanism explaining this phenomenon is not fully understood, there appears to be a bidirectional exchange of immune factors between mother and infant during direct breastfeeding.

In addition to the bioactive factors in breast milk, the physical act of breastfeeding may also play a role in asthma prevention. There is increasing evidence that commensal bacteria are essential to health,[19] and the direct skin-to-skin contact during breastfeeding provides a source of potentially protective maternal microbes to the nursing infant. Moreover, Ogbuanu et al[20] showed that breastfed children have increased lung volumes by 10 years of age and attributed this advantage to the mechanical stimulus and "physical training" associated with sucking at the breast in early life.

Our results have implications for health and social policy. Breastfeeding is a societal responsibility that must be supported by government initiatives,[27] including paid maternity leaves that facilitate direct breastfeeding. In the American Infant Feeding Practices Study II, maternal employment was the strongest predictor of infant feeding mode between 1 and 5 months of age, with working mothers being twice as likely to provide expressed milk compared with those who were not working.[9] The US is 1 of only 4 countries worldwide without a national policy requiring paid maternity leave,[28] and even among countries that do have policies, only 53% meet the International Labor Organization's minimum recommendation of 14

Table II. Distribution of infant feeding modes at 3 months and prevalence of possible or probable asthma at 3 years, according to maternal and infant characteristics in the CHILD cohort

| | | Feeding mode at 3 months | | | | | | | | | Possible or probable asthma at 3 years | | |
| | | Breast milk only: direct breastfeeding | | Breast milk only: some expressed milk | | Breast milk and formula | | Formula only | | | | | |
	N	n	(%)	n	(%)	n	(%)	n	(%)	P	n/N	(%)	P
Maternal asthma										.055			**.004**
No	2338	650	(27.8)	747	(32.0)	623	(26.6)	318	(13.6)		235/2042	(11.5)	
Yes	622	146	(23.5)	212	(34.1)	160	(25.7)	104	(16.7)		88/547	(16.1)	
Maternal ethnicity										<.001			.152
Asian	474	137	(28.9)	132	(27.8)	149	(31.4)	56	(11.8)		60/419	(14.3)	
White	2204	602	(27.3)	754	(34.2)	539	(24.5)	309	(14.0)		227/1936	(11.7)	
First Nations	123	25	(20.3)	32	(26.0)	31	(25.2)	35	(28.5)		11/105	(14.5)	
Other	199	45	(22.6)	54	(27.1)	70	(35.2)	30	(15.1)		28/169	(16.6)	
SES: maternal education										<.001			.866
Did not complete postsecondary	673	164	(24.4)	172	(25.6)	166	(24.7)	171	(25.4)		71/585	(12.1)	
Completed postsecondary	2264	625	(27.6)	781	(34.5)	610	(26.9)	248	(11.0)		245/1976	(12.4)	
SES: home ownership										<.001			.632
Family owns home	2183	589	(27.0)	734	(33.6)	583	(26.7)	277	(12.7)		243/1937	(12.6)	
Family rents home	754	200	(26.5)	219	(29.0)	193	(25.6)	142	(18.8)		74/626	(11.8)	
Maternal smoking during pregnancy										<.001			.624
No	2713	759	(28.0)	912	(33.6)	711	(26.2)	331	(12.2)		296/2392	(12.4)	
Yes	250	39	(15.6)	48	(19.2)	72	(28.8)	91	(36.4)		27/199	(13.6)	
Maternal smoking during infancy										<.001			.896
No	2326	648	(27.9)	807	(34.7)	595	(25.6)	276	(11.9)		251/2144	(11.7)	
Yes	150	33	(22.0)	15	(10.0)	42	(28.0)	60	(40.0)		15/124	(12.1)	
Method of birth										**.003**			**.009**
Vaginal	2220	623	(28.1)	730	(32.9)	567	(25.5)	300	(13.5)		225/1960	(11.5)	
Cesarean	756	176	(23.3)	232	(30.7)	216	(28.6)	132	(17.5)		100/649	(15.4)	
Infant gestational age (wk)										<.001			**.007**
<37	125	22	(17.6)	39	(31.2)	44	(35.2)	20	(16.0)		21/116	(18.1)	
37-38	182	48	(26.4)	45	(24.7)	52	(28.6)	37	(20.3)		21/153	(13.7)	
38-39	516	116	(22.5)	150	(29.1)	157	(30.4)	93	(18.0)		71/438	(16.2)	
≥39	2144	610	(28.5)	725	(33.8)	527	(24.6)	282	(13.2)		211/1894	(11.1)	
Number of older siblings										<.001			.645
0	1640	345	(21.0)	611	(37.3)	432	(26.3)	252	(15.4)		183/1418	(12.9)	
1	1002	326	(32.5)	275	(27.4)	264	(26.3)	137	(13.7)		103/883	(11.7)	
≥2	382	144	(37.7)	89	(23.3)	100	(26.2)	49	(12.8)		41/346	(11.9)	
Infant sex										.001			**.008**
Female	1430	417	(29.2)	468	(32.7)	329	(23.0)	216	(15.1)		131/1241	(10.6)	
Male	1596	399	(25.0)	507	(31.8)	467	(29.3)	223	(14.0)		196/1406	(13.9)	
Daycare at 1 year										**.026**			**.024**
No	1994	565	(28.3)	671	(33.7)	500	(25.1)	258	(12.9)		200/1821	(11.0)	
Yes	482	110	(22.8)	156	(32.4)	139	(28.8)	77	(16.0)		65/438	(14.8)	

SES, Socioeconomic status.
Comparisons by χ^2 test. Significant associations ($P < .05$) in bold.

Table III. Association of infant feeding modes and possible or probable asthma at 3 years in the CHILD cohort

| Modes of infant feeding at 3 months | Possible or probable asthma at 3 years of age | Crude association | Adjusted for covariates* | Sensitivity analyses (all adjusted for covariates*) | | | |
| | | | | Alternative outcome definition: positive mAPI | MI of missing data | MI + adjusted for respiratory infections† | MI + adjusted for breast feeding duration (breastfed infants only) |
	n/N (%) n = 2534	OR (95% CI) n = 2534	aOR (95% CI) n = 2102	aOR (95% CI) n = 2099	aOR (95% CI) n = 3296	aOR (95% CI) n = 3296	aOR (95% CI) n = 2839
Breast milk only: direct breastfeeding	61/690 (8.8)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Breast milk only: some expressed breast milk	104/831 (12.5)	1.48 (1.06-2.06)	1.64 (1.12-2.39)	1.79 (1.13-2.83)	1.43 (1.04-1.97)	1.45 (1.05-2.01)	1.39 (1.02-1.92)
Breast milk and formula	98/659 (14.9)	1.80 (1.28-2.53)	1.73 (1.17-2.57)	1.76 (1.09-2.84)	1.56 (1.12-2.18)	1.61 (1.15-2.25)	1.44 (1.00-2.07)
Formula only	56/354 (15.8)	1.94 (1.32-2.86)	2.14 (1.37-3.35)	1.80 (1.03-3.14)	1.79 (1.23-2.61)	1.86 (1.28-2.71)	-

mAPI, Modified Asthma Predictive Index; *MI*, multiple imputation.
*Adjusted for infant sex, maternal diagnosis of asthma, ethnicity, method of birth, daycare attendance, and gestational age.
†Frequent colds (≥4 in the first year of life).

weeks.[28] Our results suggest that programs and policies to support direct breastfeeding could have a meaningful impact on asthma prevention at the population level.

It is important to acknowledge that mothers often express milk owing to logistic and physical barriers to breastfeeding, and these challenges should not be dismissed. Expression can help mothers to continue providing breast milk when breastfeeding is difficult or contraindicated, and during times of separation. Recognizing the many challenges new mothers encounter, our goal is not to discourage those who cannot provide direct breast milk exclusively, but rather to highlight the underappreciated differences between direct breastfeeding and expressed breast milk, guide further research, and inform societal policies and individual decisions about infant feeding.

The major strengths of our study are the standardized prospective assessment of infant feeding in a large birth cohort,
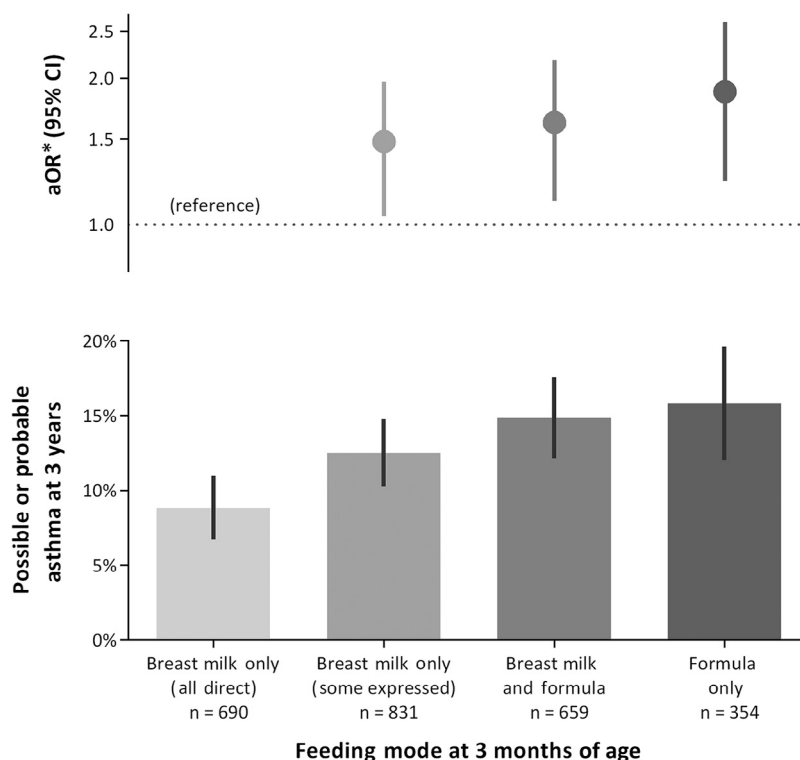

Figure 2. Modes of infant feeding at 3 months and possible or probable asthma at 3 years in the CHILD cohort. *ORs adjusted for infant sex, maternal asthma, ethnicity, method of birth, daycare attendance, and gestational age, with multiple imputation of missing data; lines represent 95% CIs.

and the distinction of direct breastfeeding from expressed breast milk. Although 24% of eligible infants had incomplete feeding data or were lost to follow-up, our sensitivity analysis demonstrated that results were robust to multiple imputation of missing data. A limitation of our study is our inability to quantify the relative proportion of direct breast milk, expressed breast milk, and formula provided, which precludes evaluation of dose effects. Also, the frequency and timing of expressed milk feeding within the first 3 months was not reported, leading to potential exposure misclassification for feeding mode "at 3 months of age." Although our asthma diagnosis was based on a structured history and physical examination by trained healthcare professionals, we acknowledge that diagnostic uncertainty is an important concern at this age. Further research is required to establish associations with confirmed asthma later in childhood and to determine the underlying mechanisms (eg, through formal mediation analyses accounting for early life infections classified by type, timing, and severity and analysis of breast milk bioactivity after expression and storage). Finally, as in all observational studies, we cannot exclude the possibility that our results may be influenced by unmeasured confounders, although we have controlled for multiple maternal and socioeconomic factors known to influence feeding practices and asthma development.

In summary, our findings demonstrate that modes of infant feeding in the first 3 months of life are associated with a diagnosis of possible or probable asthma by 3 years of age. Compared with formula feeding, direct breastfeeding seems to be most protective, whereas expressed breast milk may confer intermediate levels of protection. Further research is warranted to confirm and explain the differential effects of direct breastfeeding and expressed breast milk. Meanwhile, policies that facilitate and promote direct breastfeeding could have a significant impact on the primary prevention of asthma. ■

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Appendix

Additional members of the Canadian Healthy Infant Longidutinal Development (CHILD) Study Investigators are listed below.

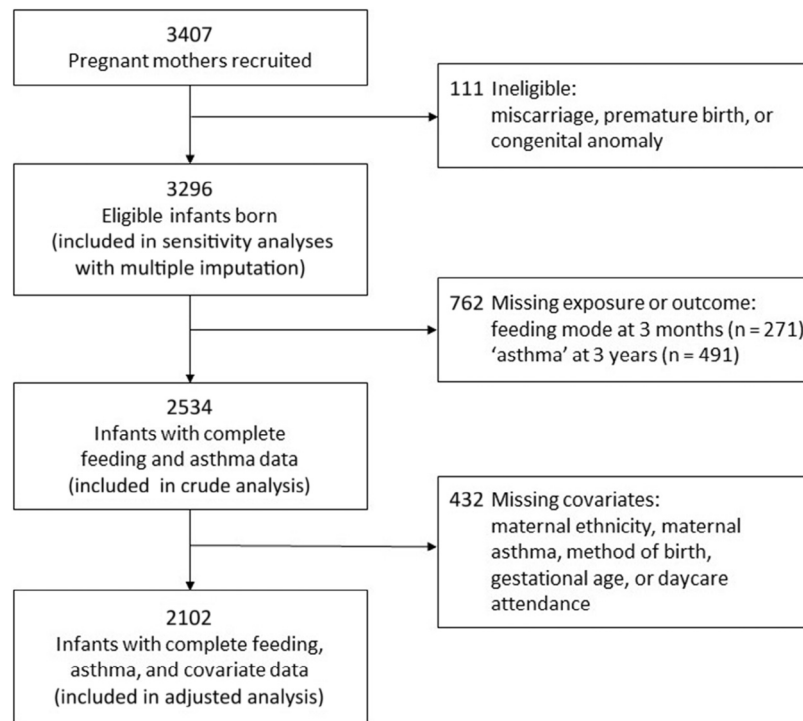|	Full Name and Email Address	University	Degrees
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Figure 1. CONSORT flow diagram.