Breastfeeding initiation or duration and longitudinal patterns of infections up to 2 years and skin rash and respiratory symptoms up to 8 years in the EDEN mother–child cohort

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Running head

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Ethic Statement

The EDEN mother-child cohort was approved by the Ethics Committee of the University Hospital of Kremlin-Bicêtre on December 12, 2002, and data files were declared to the National Committee for Processed Data and Freedom.

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Availability of data and materials

The data underlying the findings cannot be made freely available because of ethical and legal restrictions because the present study includes an important number of variables that,

together, could be used to re-identify the participants based on a few key characteristics and then be used to access other personal data. Therefore, the French ethical authority strictly forbids making such data freely available. However, they can be obtained upon request from the EDEN principal investigator. Readers may contact barbara.heude@inserm.fr to request the data.

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Abstract

This paper aimed to examine the effect of breastfeeding on longitudinal patterns of common infections up to 2 years and respiratory symptoms up to 8 years. To assess the incidence and reoccurrence of infections and allergic symptoms in the first years of life among 1,603 children from the EDEN mother-child cohort, distinct longitudinal patterns of infectious diseases as well as skin rash and respiratory symptoms were identified by group-based trajectory modeling (GBTM). To characterize infections, we considered the parent-reported number of cold/nasopharyngitis and diarrhea from birth to 12 months and otitis and bronchitis/bronchiolitis from birth to 2 years. To characterize allergy-related symptoms, we considered the parent-reported occurrence of wheezing and skin rash from 8 months to 8 years and asthma from 2 years to 8 years. Then, associations between breastfeeding and these longitudinal patterns were assessed through adjusted multinomial logistic regression. Compared to never-breastfed infants, ever-breastfed infants were at lower risk of diarrhea events in early infancy as well as infrequent events of bronchitis/bronchiolitis throughout infancy. Only predominant breastfeeding duration was related to frequent events of bronchitis/bronchiolitis and infrequent events of otitis. We found no significant protective effect of breastfeeding on longitudinal patterns of cold/nasopharyngitis, skin rash or respiratory symptoms. For an infant population with a short breastfeeding duration, on average, our study confirmed a protective effect of breastfeeding on diarrhea events in early infancy, infrequent bronchitis/bronchiolitis and, to a lesser extent, infrequent otitis events up to 2 years but not on other infections, skin rash or respiratory symptoms.

Introduction

The World Health Organization (WHO) recommends exclusive breastfeeding in the first 6 months of life or at least the first 4 months of life (World Health Organization, 2003). At birth, because of the small in utero exposure to antigens, the newborn's immune system is immature. Human breast milk contains biologically active substances such as lactoferrin, oligosaccharides or maternal leukocytes, which are thought to protect the infant against infections but also promote the immune system's maturation (Field, 2006; Hanson et al., 2003).

A recent review emphasized a protective effect of breastfeeding on diarrhea and respiratory infections (Victora et al., 2016), with an estimated prevention of 72% of hospitalizations for diarrhea and 57% of respiratory infections related to breastfeeding as well as a protective effect on otitis media in children up to 2 years of age. Studies assessing effect of breastfeeding on otitis media were mostly from high-income countries, and those assessing effect of breastfeeding on diarrhea and respiratory infections were mostly from low- and middle-income countries (Bowatte et al., 2015; Horta & Victora, 2013). Concerning allergic disorders, a recent review concluded a protective effect of breastfeeding on asthma, but the evidence was weaker for eczema and allergic rhinitis (Lodge et al., 2015). In this review, the protective effect of breastfeeding on allergic disorders was greater in low- than high-income countries.

In high-income countries, the preventive effect of breastfeeding on respiratory tract infections and allergies is less consistent across studies (Bion et al., 2016; Bowatte et al., 2015; Chiu et al., 2016; Lodge et al., 2015). In a cluster-randomized trial on promotion of breastfeeding (PROBIT), breastfeeding was related to a reduced risk of gastrointestinal infections and atopic eczema in the first year of life (Kramer et al., 2001). However, most studies have

reported infections and allergy-related diseases as outcomes at a specific time point but not their longitudinal pattern throughout infancy and childhood. Assessing association of breastfeeding with a more longitudinal approach could allow for new insights into the timing and duration of the protective effect of breastfeeding on these outcomes.

In this context, the aim of this study was to examine the association between breastfeeding and the trajectories of infections up to 2 years and skin rash or respiratory symptoms up to 8 years.

Methods

Study population

The EDEN mother–child study is a prospective cohort designed to assess prenatal and postnatal determinants of child growth, development and health (Heude et al., 2016). In brief, 2,002 pregnant women were recruited in two French university hospitals, before 24 weeks of amenorrhea. Exclusion criteria were multiple pregnancies, known diabetes before pregnancy, illiteracy and planning to move outside the region in the next 3 years. Written consent was obtained from both parents.

Breastfeeding

Information on breastfeeding was collected by questionnaires given to parents during the maternity stay and at age 4, 8, and 12 months and 2 years of the child. The calculation of breastfeeding duration was previously described in detail (Betoko et al., 2013). For the present analysis, breastfeeding was defined as any breastfeeding when the infant received breast milk and as predominant breastfeeding when the only milk received by the infant was breast milk. Both breastfeeding definitions were assessed through their initiation (never vs ever) and duration. The latter one was assessed as a continuous variable but, as the mean duration of breastfeeding is very short in France (Wagner et al., 2015) and in order to avoid

confusion related to the term "long breastfeeding duration", breastfeeding duration was also assessed as a categorical variable (< 1 month, 1 to < 4 months, ≥ 4 months).

Infections, skin rash and respiratory symptoms

Data on infections, skin rash and respiratory symptoms were collected by questionnaires completed by parents at age 4, 8 and 12 months of the child and then age 2, 3, 4, 5 and 8 years.

For infection-related outcomes, parents could report cold/nasopharyngitis (at age 4, 8 and 12 months), diarrhea (at age 4, 8 and 12 months), otitis (at age 4, 8 and 12 months, 2 years) and bronchitis/bronchiolitis (at age 4, 8 and 12 months, 2 years). For skin rash and respiratory symptoms, parents could report skin rash (at age 8 and 12 months, 2, 3, 4, 5 and 8 years), wheezing (at age 8 and 12 months, 2, 3, 4, 5 and 8 years), and asthma (at age 2, 3, 4, 5 and 8 years). At each of these ages, parents were asked to report whether the event had occurred since the last follow-up and for infections, the number of episodes (1, 2, ≥ 3) during the considered period.

Potential confounders

Family history of allergy is a known risk factor for allergy development (Lack, 2008). Because this family susceptibility results from an inappropriate reaction of the immune system, it is also an important factor to consider when assessing infections in infancy. Parental and sibling history of asthma, eczema, allergic rhinitis and food allergy were collected during a face-to-face interview at 24 to 28 weeks of gestation. Infants were considered at risk of allergy if at least one parent or sibling had one of these allergic symptoms.

During the same interview, data on the study center, maternal education level, family monthly income and smoking status were collected. Parity, sex, gestational age, delivery mode and maternal age were collected at birth from obstetric and pediatric records. The main type of

childcare, age at first attendance at a collective care arrangement in the first year and age at first introduction of solid food were collected from self-administered questionnaires at age 4, 8 and 12 months of the child.

Study samples

Children with missing data on birth weight were excluded from the analyses because they represented early lost to follow-up (n = 103). Because analyses were run separately for infections and skin rash or respiratory symptoms, children with data at only one time point or less regarding any outcome were excluded (n = 232 for infections, n= 465 for skin rash and respiratory symptoms). Children with missing data on any breastfeeding were excluded (n = 1). Finally, we excluded all children with missing data on potential confounding variables (n = 63 for infections, n = 56 for skin rash and respiratory symptoms). Thus, our sample consisted of 1,603 children for the analysis of infections and 1,377 for the analysis of skin rash and respiratory symptoms.

Statistical analyses

Mothers included in the current analysis of infections were compared to their EDEN counterparts by Student *t* test and chi-square test for continuous and categorical data, respectively.

Among children with at least 2 documented time points for the considered outcome, available data for the considered outcome at each time point were used to model the longitudinal patterns, by Nagin's method for group-based trajectory modeling (D. Nagin, 2005). The method is based on the underlying hypothesis that within a population, there are inherent groups that evolve according to different patterns. The groups are not directly identifiable or pre-established by sets of characteristics but are statistically determined by each series of responses. Using the TRAJ procedure from SAS software, multiple models were created, varying in number of groups and shapes (computed by polynomial equations). Age in months

at each time point was the independent variable. For infection patterns, we modeled the number of episodes (none, 1, 2, ≥ 3) during each period (CNORM model). For skin rash and respiratory symptom patterns, we modeled the occurrence of at least one event during each period (LOGIT model). To choose the most suitable model for each outcome, we used 4 decision criteria (**Supplementary tables 2 and 3**). A more complex model (B) has been preferred over an simpler model (A) only in case of higher Bayesian Information Criteria (BIC), defined as follows: $2*(BIC_{modelB}-BIC_{modelA})>10$. Then, to identify the shape of patterns, we considered the Average Posterior Probability (Average PP) (≥ 0.7), the difference between the actual and the estimated prevalence (closest to 0) and the Odds of Correct Classification (OCC) (> 5). As suggested by Nagin and Odgers (D. S. Nagin & Odgers, 2010), we also systematically verified that selected models were plausible in real-life and therefore easily explainable.

Bivariate analyses between breastfeeding initiation or duration (in 3 categories), whatever the definition used, and longitudinal patterns of health outcomes involved chi-square tests and are presented in **Supplementary tables 4 to 7**

The potential links between breastfeeding and longitudinal patterns of health outcomes were assessed using multinomial logistic regression analyses. Analyses were run separately for each definition of breastfeeding and each outcome. All multivariate analyses were adjusted for potential confounding factors, previously identified in literature: family history of allergy (at risk of allergy vs not-at-risk), parity (multiparous vs primiparous), sex (boys vs girls), preterm birth, C-section delivery, age at first attendance at a collective care arrangement (< 4 months, 4 to < 8 months, 8 to 12 months, never attended within the 1st year), age at introduction of solid food (< 4 months, 4 to < 6 months, ≥ 6 months), study center (Nancy vs Poitiers), maternal smoking during pregnancy, maternal education level (secondary school or less, high school, 2-year university degree, 5-year university degree), maternal age at birth (<

25 years, 25 to 29 years, 30 to 34 years, > 34 years) and monthly family income (≤ €1,500, €1,501 to €2,300, €2,301 to €3,000, €3,001 to €3,800, ≥ €3,801).

As no interaction was highlighted between family history of allergies and breastfeeding (all p-value ≥ 0.5), analyses were not stratified on family history of allergies.

P<0.05 was considered statistically significant. All analyses were carried out using SAS version 9.4 (SAS, Cary, NC).

Results

The mothers included in our analyses of infections were compared with their non-included counterparts (**Supplementary table 1**). Briefly, non-included mothers were younger, with lower education level, lower family income and initiate less breastfeeding than mothers included in the analyses. The non-included sample less frequently reported a family history of allergy. The characteristics of the study sample compared by breastfeeding duration categories are available in **Table 1**.

Longitudinal patterns of infections in infancy

The optimal pattern model for describing diarrhea patterns in infancy was a 4-group model with a square shape for each pattern (**Figure 1A**). The first pattern (9% of children) was characterized by only early events, before age 8 months, and labelled "Only early". The second pattern (10% of children) was characterized by recurrent events throughout infancy and labelled "High throughout infancy". The third pattern (43% of children) was characterized by a first event after 4 months and labelled "Lagged occurrence". The last pattern (38% of children) was characterized by no diarrhea and labelled "Never".

The optimal pattern model for describing otitis patterns in infancy was a 4-group model with a constant shape for the first pattern and a square shape for the 3 other patterns (**Figure 1B**). The first pattern (42% of children) was characterized by no otitis event throughout infancy

and labelled “Never”. The second pattern (18% of children) was characterized by a first event after 12 months and labelled “Lagged occurrence”. The third pattern (30% of children) was characterized by increasing events in the first year, with their number remaining moderate up to 2 years, and labelled “Infrequent occurrence”. The last pattern (10% of children) was characterized by increasing events throughout infancy, with a quite high number, and labelled “Increasing throughout infancy”.

The optimal pattern model for describing cold/nasopharyngitis patterns in infancy was a 4-group model with a linear shape for the second and fourth patterns and a square shape for the first and third patterns (**Figure 1C**). The first pattern (31% of children) was characterized by a first event after age 4 months and labelled “Lagged occurrence”. The second pattern (49% of children) was characterized by moderate number of events throughout infancy and labelled “Moderate throughout infancy”. The third pattern (16% of children) was characterized by increased number of events throughout infancy and labelled “Increasing throughout infancy”. The last pattern (4% of children) was characterized by a high number of events in early infancy and labelled “High in early frequency”.

The optimal pattern model for describing bronchitis/bronchiolitis patterns in infancy was a 4-group model with a cubic shape for the first, second and fourth patterns and a square shape for the third (**Figure 1D**). The first pattern (38% of children) was characterized by no event throughout infancy and labelled “Never”. The second pattern (50% of children) was characterized by increasing events, with their number remaining low, and labelled “Infrequent occurrence”. The third pattern (3% of children) was characterized by peak events at 8 months and labelled “Peak in early infancy”. The last pattern (9% of children) was characterized by increasing events throughout infancy and labelled “Increasing throughout infancy”.

Longitudinal patterns of skin rash and respiratory symptoms in childhood

The optimal pattern model for describing skin rash patterns in childhood was a 5-group model with a square shape for all patterns except the fourth one, which had a cubic shape (**Figure 2C**). The first pattern (61% of children) was characterized by no skin rashes throughout childhood and labelled "Never". The second pattern (12% of children) was characterized by a decreasing occurrence of skin rash and labelled "Decreasing throughout childhood". The third pattern (13% of children) was characterized by an increasing occurrence of events and labelled "Increasing throughout childhood". The fourth pattern (4% of children) was characterized by a high peak between 2 and 3 years and labelled "Strong peak in early childhood". The last pattern (10% of children) was characterized by a high occurrence of skin rash throughout childhood and labelled "High throughout childhood".

The optimal pattern model for describing wheezing patterns in childhood was a 5-group model with a square shape for each pattern (**Figure 2A**). The first pattern (13% of children) was characterized by low occurrence of events throughout childhood and labelled "Low occurrence". The second pattern (11% of children) was characterized by a small peak between 12 months and 2 years and labelled "Peak in early childhood". The third pattern (66% of children) was characterized by no wheezing event throughout childhood and labelled "Never". The fourth pattern (3% of children) was characterized by decreasing occurrence of wheezing throughout childhood and labelled "Decreasing throughout childhood". The last pattern (7% of children) was characterized by high occurrence throughout childhood and labelled "High throughout childhood".

The optimal pattern model for describing asthma attack patterns in childhood was a three-group model with a square shape for all patterns (**Figure 2B**). The first pattern (6% of children) was characterized by increasing occurrence of asthma attack throughout childhood and labelled "Increasing throughout childhood". The second pattern (91% of children) was

characterized by no asthma attack and labelled “Never”. The third pattern (3% of children) was characterized by a peak in asthma attacks between 2 and 3 years followed by a relatively steady frequency and labelled “Strong peak in early childhood”.

Breastfeeding and longitudinal patterns of infectious diseases up to 2 years

Both any and predominant breastfeeding were negatively associated with longitudinal patterns of early episodes (<4 months) of diarrhea in the first year of life, whether these episodes persisted or not thereafter. Predominant breastfeeding duration, considered as a continuous variable, was also associated with lower risk of late episodes of diarrhea (Table 2).

Any breastfeeding was not associated with otitis events in the first 2 years of life. Nonetheless, predominant breastfeeding duration, considered as a continuous variable, was associated with a lower risk of belonging to the otitis pattern “infrequent occurrence”. The same trend was observed for long duration (≥ 4 months) of predominant breastfeeding (Table 2).

Breastfeeding was not associated with longitudinal trajectories of colds / nasopharyngitis (Table 3).

Predominant breastfeeding and, to a lesser extent, any breastfeeding were both negatively associated with the risk of infrequent occurrence of bronchitis / bronchiolitis in the first 2 years of life. Long duration of predominant breastfeeding (≥ 4 months) was also associated with a lower risk of belonging to the trajectory “increasing throughout infancy” of bronchitis / bronchiolitis. The association was not significant when any breastfeeding duration was considered (Table 3).

Breastfeeding and longitudinal patterns of skin rash and respiratory symptoms up to 8 years

Ever breastfeeding and breastfeeding duration were not related to the longitudinal patterns of skin rash and respiratory symptoms up to 8 years (**Tables 4 and 5**).

Discussion

In the EDEN mother–child cohort, we confirmed that breastfeeding was related to lower risk of diarrhea events in early infancy and infrequent occurrence of bronchitis/bronchiolitis up to 2 years. Moreover, predominant breastfeeding duration was negatively related to the risk of diarrhea events in late infancy, of infrequent otitis occurrence, and of repeated bronchitis/bronchiolitis events throughout infancy. However, we were not able to highlight association between breastfeeding and longitudinal patterns of cold/nasopharyngitis, skin rash or respiratory symptoms.

Most of the studies regarding the association between breastfeeding and diarrhea or respiratory infections were conducted in low- and middle-income countries (Horta & Victora, 2013), but even in high-income countries, where hygienic conditions do not benefit the development of germs, breastmilk has a protective role. However, the protective role of breastfeeding on gastrointestinal infections may last only while the infant is breastfed and shortly after (Kramer et al., 2003; Quigley, Kelly, & Sacker, 2007). Consistent with these findings, in the EDEN mother–child cohort, ever-breastfed infants were less likely to show longitudinal patterns of diarrhea characterized by increased number of diarrheas in early infancy.

Concerning respiratory infections, the last meta-analysis concluded a clear protective effect of breastfeeding (Horta & Victora, 2013). The latter finding was also highlighted in a systematic review of data from high-income countries (Duijts, Ramadhani, & Moll, 2009). In the present study, we did not find such a protective effect on cold/nasopharyngitis. Breastfed children seemed less likely to have infrequent occurrence of bronchitis/bronchiolitis (as compared with never occurrence), whatever the definition used for breastfeeding, whereas only predominantly breastfed infants, especially those breastfed for ≥ 4 months, seemed less likely to have frequent occurrence of bronchitis/bronchiolitis. Our results suggest that breastfeeding

may be related to the incidence of respiratory symptoms but also to the reoccurrence of these symptoms throughout infancy. Frequent episodes of bronchiolitis are known to predispose to asthma in the early years of life, so low-frequency bronchitis/bronchiolitis may rely more on infectious origins, whereas high-frequency bronchitis/bronchiolitis may be related to the allergic background of the child. Thus, our results would suggest a protective effect of breastfeeding on respiratory infections. Using other statistical methods, the PARIS cohort highlighted that children who were breastfed for at least 6 months were less likely to have the cough/rhinitis phenotype in the first 4 years of life (Ranciere, Nikasinovic, Bousquet, & Momas, 2013).

Concerning ear infections, a recent meta-analysis of studies from the United States and Europe found consistent evidence of a protective effect of breastfeeding on acute otitis media occurrence during the first 2 years of life (Bowatte et al., 2015). In this meta-analysis, the protective effect was clearer when considering exclusive breastfeeding for the first 6 months (odds ratio=0.57 [95% confidence interval 0.44-0.75]) than when considering any breastfeeding for > 3 to 4 months (0.71 [0.42-1.20]). In line with these findings, we did not find any association between any breastfeeding and longitudinal trajectories of otitis but predominant breastfeeding duration was negatively related to the risk of infrequent occurrence of otitis events.

The protective effect of breastfeeding on the development of allergic symptoms remains controversial (Victora et al., 2016). Exclusive breastfeeding was found associated with reduced eczema prevalence at age 1 year in the cluster-randomized trial PROBIT (Kramer et al., 2001), but a recent meta-analyses found no evidence of an association with eczema incidence and inconclusive evidence for an association with asthma or wheezing (Kramer & Kakuma, 2012; Lodge et al., 2015). In these meta-analyses, asthma was not considered for children under age 5 in order to avoid misclassification of infants with transient wheezing.

Our results agree with these findings despite some noticeable differences in the definition of allergic symptoms. In our study, we used skin rash instead of eczema, which widened the definition of this outcome. Moreover, eczema, wheezing and asthma attacks do not always have an allergic origin. Finally, the EDEN mother–child cohort recorded a wide range of confounding factors such as family history of allergy or age at introduction of solid foods, which did not change the results when adjusted for in the analyses.

Beyond nutrients, breast milk transmits immunomodulatory components such as secretory immunoglobulin A, lactoferrin, food antigens or oligosaccharides and microorganisms (Berdi et al., 2018; Hanson et al., 2003; Hoppu, Kalliomaki, Laiho, & Isolauri, 2001; Petherick, 2010). These components may influence gut microbiota as human milk oligosaccharides are substrates for the development of certain beneficial bacterial strains (Coppa, Bruni, Morelli, Soldi, & Gabrielli, 2004) and microorganisms may colonize the infant's digestive tract and prevent the development of other potentially harmful strains (Petherick, 2010).

To our knowledge, few studies have used group-based trajectory modeling to assess infection and allergic development. The method allows for longitudinal classification of infants and discrimination between transient and regular outbreaks, which can reflect the infant’s susceptibility to infections and allergic profile. As any statistical method, the GBTM method is not perfect. It is not always easy to find the optimal number of groups or the right shape for each pattern. Criteria such as BIC, averagePP or OCC are useful objective tools for decision making regarding the choice of number of groups but the consistency of these groups with real life must not be neglected. Nonetheless, when assessing the links between breastfeeding and these patterns, the method brings additional information such as whether a potential association is found only when the infant is still breastfed or even after breastfeeding cessation or whether breastfeeding is associated with the temporal evolution of a symptom. Comparison of the same patterns from larger and foreign cohorts would give good

information on the development of these outcomes and may lead to targeted interventions to prevent them.

The EDEN mother–child cohort is a French ongoing regional observational study. Due to the sample selection and attrition issues, these results cannot be generalized to the whole population. In high-income countries, wealthy families are more likely to breastfed their infants and these infants are at lower risk of infections, which can lead to a probable overestimation of the associations between breastfeeding and lower risk of infection. Therefore, further studies need to be conducted, especially in disadvantaged families. However, the insights and long-term follow-up of our results represent a major asset. Recent data from a French nationwide birth cohort reported 70% breastfeeding initiation and 22% breastfeeding rates at 4 months (Wagner et al., 2015), whereas in the EDEN mother–child cohort, 74% of children were ever breastfed and 36% were breastfed for at least 4 months. Breastfeeding rates in the EDEN cohort are higher than national ones, but still below guidelines.

Conclusion

Despite a context of low rate and duration of breastfeeding and high hygienic conditions, we found, using a longitudinal approach, a beneficial association between breastfeeding and diarrhea, bronchitis/bronchiolitis and, to a lesser extent, otitis during infancy. The use of longitudinal patterns of infections allowed us to confirm that the potential protective effect of breastfeeding on diarrhea events seems to be maximized when breastfeeding is still ongoing. However, we were not able to highlight any association between breastfeeding and skin rash or respiratory symptoms. These results and particularly the use of group-based trajectory modeling need to be replicated in larger and representative cohorts. Nonetheless, the promotion and facilitation of breastfeeding initiation and duration are part of prevention of the

401 occurrence of infections and hence reduce their economic cost due to health care system
402 usage (hospitalization, medication etc.) and parental leave from work.

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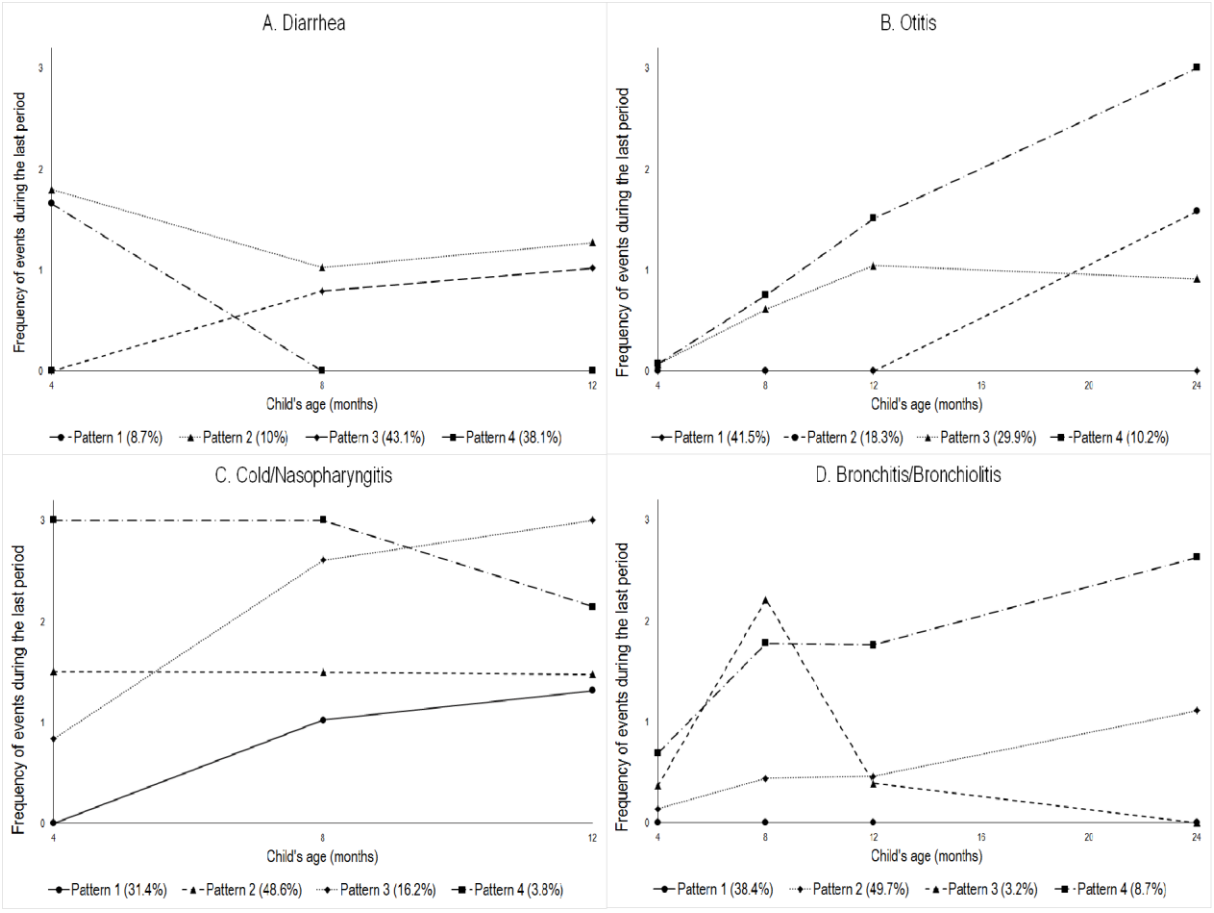
481 **Table 1:** Characteristics of the study sample according to any breastfeeding duration (n=1,603 children)

	Any breastfeeding duration		
	<1 month	**1 to 4 months**	**≥4 months**
N	**523**	**510**	**570**
Recruitment in Poitiers	63.7% (333)	42.2% (215)	38.8% (221)
Familial history of allergy	49.7% (260)	52.7% (269)	54.7% (312)
Primiparous mother	44.2% (231)	50.2% (256)	43.9% (250)
Maternal smoking during pregnancy	31.5% (165)	25.1% (128)	15.1% (86)
Maternal master's degree	22.0% (115)	33.5% (171)	47.9% (273)
Maternal age at birth (years)	29.4 (± 4.9)	29.3 (± 4.7)	30.5 (± 4.6)
Family monthly income			
≤€ 1,500	17.0% (89)	11.2% (57)	12.3% (70)
€ 1,501 - 2,300	37.3% (195)	29.8% (152)	22.8% (130)
€ 2,301 - 3,000	25.8% (135)	28.4% (145)	28.4% (162)
€ 3,001 - 3,800	13.0% (68)	17.8% (91)	19.6% (112)
€ 3,801	6.9% (36)	12.7% (65)	16.8% (96)
Boy	53.2% (278)	54.5% (278)	48.9% (279)
Preterm birth	5.2% (27)	6.9% (35)	4.0% (23)
C-section delivery	16.6% (87)	16.5% (84)	14.7% (84)
Age at first attendance to collective care arrangement			
Before 4 months	16.4% (86)	21.4% (109)	15.1% (86)
Between 4 and 8 months	6.9% (36)	11.6% (59)	17.5% (100)
Between 8 and 12 years	2.1% (11)	4.1% (21)	5.3% (30)
Never	74.6% (390)	62.9% (321)	62.1% (354)
Age at solid food introduction	3.9 (± 1.7)	4.2 (± 1.6)	5.0 (± 1.4)

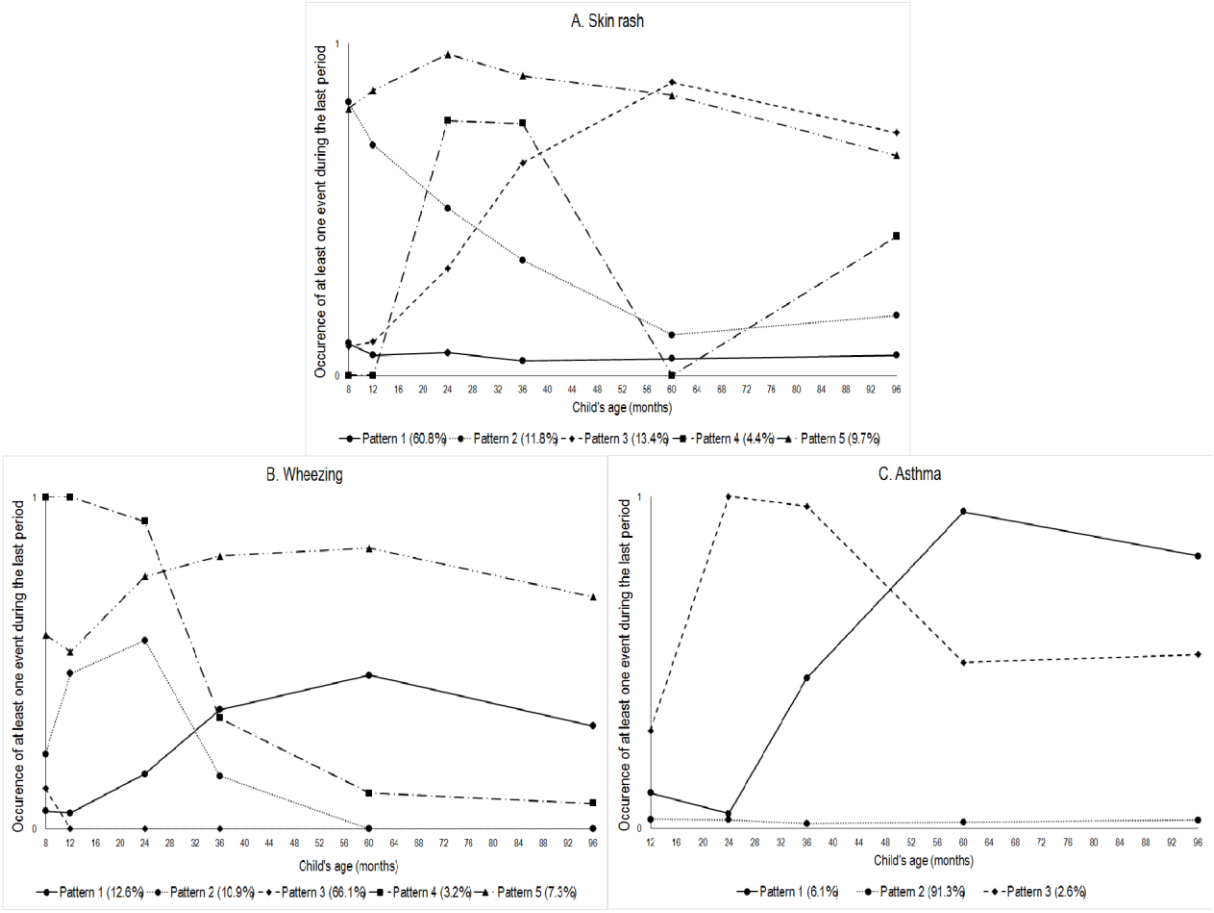
% (n) or mean (± sd)

Figure 1: Longitudinal patterns of diarrhea, otitis, cold/nasopharyngitis and bronchitis/bronchiolitis up to 2 years (n = 1,603)



Pattern legend. A-Diarrhea: 1) "Only early", 2) "High throughout infancy", 3) "Lagged occurrence", 4) "Never"; B-Otitis: 1) "Never", 2) "Lagged occurence", 3) "Infrequent occurrence", 4) "Increasing throughout infancy"; C-Cold/nasopharyngitis: 1) "Lagged occurrence", 2) "Moderate throughout infancy", 3) "Increasing throughout infancy", 4) "High throughout infancy"; D-Bronchitis/bronchiolitis: 1) "Never", 2) "Infrequent occurrence", 3) "Peak in early infancy", 4) "Increasing throughout infancy".

Figure 2: Longitudinal patterns of skin rash, wheezing and asthma attack up to 8 years (n = 1,377)



Pattern legend. A-Skin rash: 1) "Never". 2) "Decreasing throughout childhood", 3) "Increasing throughout childhood", 4) "Strong peak in early childhood", 5) "High throughout childhood"; B-Wheezing: 1) "Low occurrence", 2) "Peak in early childhood", 3) "Never", 4) "Decreasing throughout childhood", 5) "High throughout childhood"; C-Asthma attack: 1) "Increasing throughout childhood", 2) "Never", 3) "Strong peak in early childhood".

Table 2. Adjusted associations between breastfeeding status and longitudinal patterns of diarrhea up to 1 year and otitis up to 2 years (n = 1,603)

	Diarrhea (ref: never)				**Otitis** (ref: never)			
	Only early	High throughout infancy	Lagged occurrence	*p*	Lagged occurrence	Infrequent occurrence	Increasing throughout infancy	*p*
Any breastfeeding				*<1.10-4*				*0.3*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
Ever breastfed	0.51 [0.33 ; 0.78]	0.41 [0.27 ; 0.60]	1.09 [0.82 ; 1.43]		0.81 [0.58 ; 1.15]	0.87 [0.65 ; 1.16]	0.68 [0.45 ; 1.03]	
Any breastfeeding duration (months)	0.86 [0.80 ; 0.92]	0.85 [0.80 ; 0.91]	0.99 [0.96 ; 1.02]	*<1.10-4*	1.00 [0.96 ; 1.04]	0.97 [0.94 ; 1.01]	0.96 [0.91 ; 1.01]	*0,2*
Any breastfeeding duration				*<1.10-4*				*0.5*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
1 to < 4 months	0.52 [0.33 ; 0.81]	0.42 [0.27 ; 0.65]	0.90 [0.67 ; 1.20]		0.93 [0.65 ; 1.34]	0.96 [0.71 ; 1.30]	0.77 [0.49 ; 1.20]	
≥ 4 months	0.27 [0.16 ; 0.46]	0.28 [0.17 ; 0.45]	1.02 [0.76 ; 1.37]		0.88 [0.61 ; 1.27]	0.76 [0.55 ; 1.04]	0.69 [0.43 ; 1.09]	
Predominant breastfeeding				*< 1.10-4*				*0,2*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
Ever breastfed	0.48 [0.33 ; 0.72]	0.41 [0.28 ; 0.59]	0.95 [0.74 ; 1.21]		0.81 [0.59 ; 1.10]	0.87 [0.67 ; 1.14]	0.70 [0.48 ; 1.02]	
Predominant breastfeeding duration (months)	0.85 [0.77 ; 0.93]	0.79 [0.72 ; 0.88]	0.95 [0.91 ; 0.99]	*<1.10-4*	0.97 [0.92 ; 1.02]	0.93 [0.88 ; 0.97]	0.96 [0.89 ; 1.03]	*0,03*
Predominant breastfeeding duration				*< 1.10-4*				*0,08*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
1 to < 4 months	0.42 [0.27 ; 0.65]	0.43 [0.28 ; 0.64]	0.96 [0.75 ; 1.23]		0.87 [0.63 ; 1.19]	0.85 [0.65 ; 1.11]	0.75 [0.50 ; 1.11]	
≥ 4 months	0.35 [0.19 ; 0.65]	0.25 [0.13 ; 0.47]	0.75 [0.54 ; 1.04]		0.72 [0.47 ; 1.09]	0.54 [0.37 ; 0.80]	0.70 [0.42 ; 1.19]	

Data are multinomial OR [95% CI], adjusted for center, family history of allergy, parity, smoking status during pregnancy, maternal education level, maternal age at birth, family monthly income, sex, gestational age, caesarean section, age at first attendance to collective care arrangement, age at introduction of solid food. Separate models were conducted for each breastfeeding exposure and for each outcome, diarrhea or otitis.

Table 3. Adjusted associations between breastfeeding status and longitudinal patterns of respiratory infections in infancy (n = 1,603)

	Cold/nasopharyngitis (ref: moderate throughout infancy)				**Bronchitis/bronchiolitis** (ref: never)			
	Lagged occurrence	Increasing throughout infancy	High in early infancy	*p*	Infrequent occurrence	Peak in early infancy	Increasing throughout infancy	*p*
Any breastfeeding				*0.3*				*0.1*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
Ever breastfed	1.02 [0.77 ; 1.35]	1.34 [0.94 ; 1.93]	1.36 [0.71 ; 2.59]		0.75 [0.58 ; 0.98]	0.53 [0.27 ; 1.06]	0.82 [0.52 ; 1.30]	
Any breastfeeding duration (months)	1.00 [0.97 ; 1.03]	0.98 [0.94 ; 1.02]	0.98 [0.90 ; 1.06]	*0.7*	0.96 [0.93 ; 0.99]	0.95 [0.87 ; 1.04]	0.95 [0.90 ; 1.01]	*0.06*
Any breastfeeding duration				*0.9*				*0.2*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
1 to < 4 months	1.14 [0.85 ; 1.53]	1.02 [0.70 ; 1.47]	1.21 [0.63 ; 2.32]		0.71 [0.54 ; 0.94]	0.83 [0.40 ; 1.73]	0.81 [0.50 ; 1.29]	
≥ 4 months	1.15 [0.85 ; 1.55]	1.04 [0.71 ; 1.52]	0.81 [0.39 ; 1.68]		0.75 [0.56 ; 0.99]	0.59 [0.27 ; 1.31]	0.64 [0.38 ; 1.07]	
Predominant breastfeeding				*0.8*				*0.04*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
Ever breastfed	1.13 [0.88 ; 1.46]	1.01 [0.74 ; 1.39]	1.12 [0.62 ; 2.02]		0.74 [0.58 ; 0.94]	0.57 [0.30 ; 1.07]	0.69 [0.45 ; 1.04]	
Predominant breastfeeding duration (months)	1.03 [0.99 ; 1.08]	0.95 [0.89 ; 1.01]	1.01 [0.90 ; 1.13]	*0.1*	0.93 [0.90 ; 0.97]	0.94 [0.84 ; 1.06]	0.88 [0.80 ; 0.96]	*0.003*
Predominant breastfeeding duration				*0.6*				*0.07*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	1 [Ref]	
1 to < 4 months	1.12 [0.87 ; 1.46]	0.80 [0.58 ; 1.11]	1.04 [0.57 ; 1.89]		0.89 [0.70 ; 1.14]	0.98 [0.51 ; 1.88]	0.73 [0.48 ; 1.12]	
≥ 4 months	1.11 [0.79 ; 1.57]	0.75 [0.48 ; 1.18]	1.11 [0.48 ; 2.56]		0.64 [0.46 ; 0.88]	0.57 [0.23 ; 1.43]	0.44 [0.23 ; 0.83]	

Data are multinomial OR [95% CI], adjusted for center, family history of allergy, parity, smoking status during pregnancy, maternal education level, maternal age at birth, family monthly income, sex, gestational age, caesarean section, age at first attendance to collective care arrangement, age at introduction of solid food. Separate models were conducted for each breastfeeding exposure and for each outcome, cold/nasopharyngitis or bronchitis/bronchiolitis.

Table 4. Adjusted associations between breastfeeding status and longitudinal patterns of skin rash in childhood (n = 1,377)

	Skin rash (ref: never)				
	Decreasing throughout childhood	Increasing throughout childhood	Strong peak in early childhood	High throughout childhood	*p*
Any breastfeeding					*0.5*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	
Ever breastfed	0.81 [0.54 ; 1.20]	0.96 [0.65 ; 1.42]	1.70 [0.81 ; 3.55]	1.04 [0.66 ; 1.64]	
Any breastfeeding duration (months)	1.00 [0.95 ; 1.05]	0.99 [0.94 ; 1.04]	1.03 [0.96 ; 1.11]	0.97 [0.91 ; 1.02]	*0.7*
Any breastfeeding duration					*0.5*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	
1 to < 4 months	0.99 [0.65 ; 1.53]	0.96 [0.63 ; 1.47]	2.22 [1.06 ; 4.65]	1.24 [0.78 ; 1.98]	
≥ 4 months	0.95 [0.61 ; 1.49]	0.98 [0.64 ; 1.50]	1.76 [0.81 ; 3.80]	0.82 [0.49 ; 1.36]	
Predominant breastfeeding					*0.8*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	
Ever breastfed	0.89 [0.62 ; 1.29]	0.91 [0.64 ; 1.30]	1.37 [0.73 ; 2.58]	1.07 [0.70 ; 1.63]	
Predominant breastfeeding duration (months)	0.96 [0.89 ; 1.03]	1.00 [0.94 ; 1.07]	0.85 [0.71 ; 1.01]	0.99 [0.91 ; 1.07]	*0.3*
Predominant breastfeeding duration					*0.8*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	
1 to < 4 months	1.03 [0.70 ; 1.51]	0.89 [0.61 ; 1.28]	1.31 [0.71 ; 2.41]	1.21 [0.80 ; 1.84]	
≥ 4 months	1.13 [0.66 ; 1.92]	1.23 [0.77 ; 1.99]	1.38 [0.63 ; 3.01]	0.91 [0.50 ; 1.66]	

Data are multinomial OR [95% CI], adjusted for center, family history of allergy, parity, smoking status during pregnancy, maternal education level, maternal age at birth, family monthly income, sex, gestational age, caesarean section, age at first attendance to collective care arrangement, age at introduction of solid food. . Separate models were conducted for each breastfeeding exposure.

Table 5. Adjusted associations between breastfeeding status and longitudinal patterns of respiratory allergic symptoms in childhood (n = 1,377**)**

	Wheezing (ref: never)					**Asthma attack** (ref: never)		
	Low occurrence	Peak in early childhood	Decreasing throughout childhood	High throughout childhood	*p*	Increasing throughout childhood	Strong peak in early childhood	*p*
Any breastfeeding					*0.9*			*0.4*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	
Ever breastfed	1.04 [0.70 ; 1.55]	0.94 [0.61 ; 1.44]	0.74 [0.36 ; 1.52]	0.94 [0.57 ; 1.55]		1.30 [0.76 ; 2.24]	0.69 [0.32 ; 1.47]	
Any breastfeeding duration (months)	0.97 [0.92 ; 1.02]	1.00 [0.95 ; 1.05]	0.91 [0.82 ; 1.02]	1.01 [0.95 ; 1.08]	*0.3*	1.00 [0.94 ; 1.07]	1.01 [0.91 ; 1.12]	*1*
Any breastfeeding duration					*0.6*			*0.7*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	
1 to < 4 months	1.27 [0.84 ; 1.93]	0.89 [0.57 ; 1.41]	0.70 [0.32 ; 1.50]	0.77 [0.44 ; 1.34]		1.01 [0.56 ; 1.82]	0.65 [0.27 ; 1.56]	
≥ 4 months	0.93 [0.60 ; 1.46]	0.95 [0.60 ; 1.51]	0.56 [0.24 ; 1.27]	1.03 [0.60 ; 1.77]		1.34 [0.75 ; 2.40]	1.04 [0.44 ; 2.46]	
Predominant breastfeeding								*1*
Never breastfed	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]	*0.4*	1 [Ref]	1 [Ref]	
Ever breastfed	1.01 [0.70 ; 1.46]	0.81 [0.55 ; 1.20]	0.56 [0.29 ; 1.09]	0.96 [0.60 ; 1.53]		1.05 [0.64 ; 1.71]	1.03 [0.50 ; 2.14]	
Predominant breastfeeding duration (months)	1.02 [0.96 ; 1.09]	0.99 [0.93 ; 1.06]	1.04 [0.95 ; 1.15]	0.96 [0.89 ; 1.04]	*0.6*	1.01 [0.92 ; 1.10]	1.08 [0.94 ; 1.24]	*0.6*
Predominant breastfeeding duration					*0.2*			*1*
< 1 month	1 [Ref]	1 [Ref]	1 [Ref]	1 [Ref]		1 [Ref]	1 [Ref]	
1 to < 4 months	1.23 [0.85 ; 1.77]	0.89 [0.60 ; 1.32]	0.55 [0.27 ; 1.10]	0.98 [0.62 ; 1.56]		1.03 [0.62 ; 1.72]	0.75 [0.35 ; 1.62]	
≥ 4 months	0.71 [0.41 ; 1.22]	0.8 [0.47 ; 1.35]	0.40 [0.14 ; 1.16]	0.60 [0.30 ; 1.22]		0.97 [0.48 ; 1.97]	0.97 [0.33 ; 2.89]	

Data are multinomial OR [95% CI], adjusted for center, family history of allergy, parity, smoking status during pregnancy, maternal education level, maternal age at birth, family monthly income, sex, gestational age, caesarean section, age at first attendance to collective care arrangement, age at introduction of solid food. Separate models were conducted for each breastfeeding exposure and for each outcome, wheezing or asthma attack.

SUPPORTING INFORMATION

Supplementary table 1: Comparison of included and excluded families (Chi2 and Student t-tests)

	Selected	Excluded	p
Recruitment in Poitiers	48.0% (769)	49.9% (199)	0.500
Familial history of allergy	52.5% (841)	36.8% (147)	0.000
Primiparous mother	46.0% (737)	37.0% (111)	0.004
Maternal smoking during pregnancy	23.6% (379)	43.0% (105)	0.000
Maternal master's degree	34.9% (559)	15.6% (48)	0.000
Maternal age at birth (years)	29.8 (± 4.8)	28.0 (± 5.2)	0.000
Family monthly income			0.000
≤€ 1,500	13.5% (216)	35.8% (111)	
€ 1,501 – 2,300	29.8% (477)	29.4% (91)	
€ 2,301 – 3,000	27.6% (442)	19.0% (59)	
€ 3,001 – 3,800	16.9% (271)	7.4% (23)	
€ 3,801	12.3% (197)	8.4% (26)	
Boy	52.1% (835)	55.0% (165)	0.350
Preterm birth	5.3% (85)	8.3% (25)	0.040
C-section delivery	15.9% (255)	14.9% (44)	0.650
Age at first attendance to collective care arrangement			0.001
Before 4 months	17.5% (281)	7.6% (9)	
Between 4 and 8 months	12.2% (195)	6.8% (8)	
Between 8 and 12 years	3.9% (62)	1.7% (2)	
Never	66.4% (1065)	83.9% (99)	
Age at solid food introduction	4.4 (± 1.6)	4.6 (± 1.9)	0.13

% (n) or mean (± sd)

Supplementary table 2: Model criteria for longitudinal patterns of infection

	Diarrhea	*Otitis*	*Cold/ nasopharyngitis*	*Bronchitis/ bronchiolitis*
Pattern model criteria				
BIC	-4217.93	-4548.05	-5091.26	-6830.17
Estimated prevalence				
First group	0.108	0.282	0.245	0.293
Second group	0.174	0.214	0.584	0.510
Third group	0.487	0.404	0.142	0.091
Fourth group	0.231	0.101	0.029	0.107
Actual prevalence				
First group	0.087	0.415	0.314	0.384
Second group	0.1	0.183	0.486	0.497
Third group	0.431	0.299	0.162	0.032
Fourth group	0.381	0.102	0.038	0.087
Average PP				
First group	0.743	0.679	0.712	0.717
Second group	0.986	0.687	0.932	0.797
Third group	0.828	0.943	0.687	0.569
Fourth group	0.541	0.777	0.697	0.825
OCC				
First group	23.878	5.386	7.618	6.113
Second group	334.333	8.062	9.763	3.772
Third group	5.071	24.406	13.262	13.187
Fourth group	3.924	31.014	77.021	39.344

BIC, Bayesian Information Criteria; PP, Posterior Probability; OCC, Odds of Correct Classification

Supplementary table 3: Model criteria for longitudinal patterns of allergic symptoms

	Wheezing	*Skin rash*	*Asthma attack*
Pattern model criteria			
BIC	-2911.67	-4055.77	-1146.49
Estimated prevalence			
First group	0.188	0.563	0.067
Second group	0.212	0.137	0.904
Third group	0.488	0.141	0.029
Fourth group	0.035	0.062	
Fifth group	0.077	0.097	
Actual prevalence			
First group	0.126	0.608	0.061
Second group	0.109	0.118	0.913
Third group	0.661	0.134	0.026
Fourth group	0.032	0.044	
Fifth group	0.073	0.097	
Average PP			
First group	0.815	0.868	0.860
Second group	0.727	0.703	0.985
Third group	0.738	0.744	0.916
Fourth group	0.773	0.561	
Fifth group	0.812	0.812	
OCC			
First group	19.028	5.104	85.542
Second group	9.898	14.910	6.973
Third group	2.955	17.705	365.122
Fourth group	93.889	19.333	
Fifth group	51.774	40.208	

BIC, Bayesian Information Criteria; PP, Posterior Probability; OCC, Odds of Correct Classification

Supplementary table 4: Non-adjusted association between breastfeeding, any or predominant, and diarrhea and otitis in infancy (n = 1,603, chi-square test)

	Diarrhea					Otitis				
	Never	Only early	High throughout infancy	Lagged occurrence	*p*	Never	Lagged occurrence	Infrequent occurence	Increasing throughout infancy	*p*
Any breastfeeding					*<10-4*					*0.5*
Never breastfed	23% (139)	39% (54)	43% (69)	22% (149)		24% (161)	25% (73)	27% (129)	29% (48)	
Breastfed	77% (472)	61% (86)	57% (92)	78% (542)		76% (504)	75% (221)	73% (351)	71% (116)	
Any breastfeeding duration					*<10-4*					*0.7*
< 1 month	28% (171)	50% (70)	52% (84)	29% (198)		32% (213)	30% (89)	34% (163)	35% (58)	
1 to < 4 months	34% (205)	31% (43)	27% (44)	32% (218)		31% (207)	32% (93)	34% (161)	30% (49)	
≥ 4 months	38% (235)	19% (27)	21% (33)	40% (275)		37% (245)	38% (112)	33% (156)	35% (57)	
Predominant breastfeeding					*<10-4*					*0.7*
Never breastfed	30% (181)	47% (66)	52% (83)	30% (209)		32% (215)	33% (98)	34% (165)	37% (61)	
Ever breastfed	70% (429)	53% (74)	48% (78)	70% (482)		68% (449)	67% (196)	66% (315)	63% (103)	
Predominant breastfeeding duration					*<10-4*					*0.2*
< 1 month	40% (242)	61% (86)	64% (103)	42% (288)		43% (285)	44% (129)	48% (229)	46% (76)	
1 to < 4 months	40% (244)	27% (38)	28% (45)	42% (289)		38% (252)	39% (115)	40% (190)	36% (59)	
≥ 4 months	20% (124)	12% (16)	8% (13)	16% (114)		19% (127)	17% (50)	12% (61)	18% (29)	

% (n)

Supplementary table 5: Non-adjusted association between breastfeeding, any or predominant, and cold/nasopharyngitis and bronchitis/bronchiolitis in infancy (n = 1,603, chi-square test)

	Cold/nasopharyngitis					Bronchitis/bronchiolitis				
	Lagged occurrence	Moderate throughout infancy	Increasing throughout infancy	High in early infancy	*p*	Never	Infrequent occurrence	Peak in early infancy	Increasing throughout infancy	*p*
Any breastfeeding					*0.1*					*0.1*
Never breastfed	23.7% (119)	28.2% (220)	21.5% (56)	26.2% (16)		22% (138)	28% (221)	29% (15)	27% (37)	
Breastfed	76.3% (384)	71.8% (559)	78.5% (204)	73.8% (45)		78% (478)	72% (575)	71% (37)	73% (102)	
Any breastfeeding duration					*0.2*					*0.1*
< 1 month	28% (144)	35% (275)	32% (82)	36% (22)		29% (176)	35% (282)	31% (16)	35% (49)	
1 to < 4 months	32% (163)	31% (242)	32% (83)	36% (22)		33% (203)	30% (239)	37% (19)	35% (49)	
≥ 4 months	39% (196)	34% (262)	37% (95)	28% (17)		38% (237)	35% (275)	33% (17)	30% (41)	
Predominant breastfeeding					*0.3*					*0.03*
Never breastfed	30% (153)	36% (278)	34% (87)	34% (21)		29% (180)	36% (286)	38.5% (20)	38.1% (53)	
Ever breastfed	70% (350)	64% (501)	66% (172)	66% (40)		71% (436)	64% (509)	61.5% (32)	61.9% (86)	
Predominant breastfeeding duration					*0.6*					*0.04*
< 1 month	41% (208)	46% (358)	49% (126)	44% (27)		41% (254)	46% (370)	42% (22)	52% (73)	
1 to < 4 months	41% (203)	38% (295)	36% (94)	39% (24)		39% (237)	39% (307)	42% (22)	36% (50)	
≥ 4 months	18% (92)	16% (126)	15% (39)	16% (10)		20% (125)	15% (118)	16% (8)	12% (16)	

% (n)

Supplementary table 6: Non-adjusted association between breastfeeding, any or predominant, and skin rash in infancy (n = 1,377, chi-square test)

	Skin rash					
	Never	Decreasing throughout childhood	Increasing throughout childhood	Strong peak in early childhood	High throughout childhood	*p*
Any breastfeeding						
Never breastfed	24% (205)	32% (52)	27% (49)	16% (10)	26% (34)	*0,1*
Breastfed	76% (632)	68% (110)	73% (135)	84% (51)	74% (99)	
Any breastfeeding duration						
< 1 month	32% (268)	36% (59)	33% (61)	20% (12)	34% (45)	*0,3*
1 to < 4 months	31% (258)	31% (50)	29% (53)	39% (24)	36% (48)	
≥ 4 months	37% (311)	33% (53)	38% (70)	41% (25)	30% (40)	
Predominant breastfeeding						*0.4*
Never breastfed	33% (274)	38% (61)	35% (64)	25% (15)	32% (43)	
Ever breastfed	67% (562)	62% (101)	65% (120)	75% (46)	68% (90)	
Predominant breastfeeding duration						*0.8*
< 1 month	45% (374)	46% (75)	45% (82)	36% (22)	44% (58)	
1 to < 4 months	39% (326)	38% (62)	36% (66)	42% (26)	42% (56)	
≥ 4 months	16% (136)	15% (25)	19% (36)	21% (13)	14% (19)	

% (n)

Supplementary table 7: Non-adjusted association between breastfeeding, any or predominant, and wheezing and asthma in infancy (n = 1,377, chi-square test)

	Wheezing						Asthma attack			
	Never	Low occurrence	Peak in early childhood	Decreasing throughout childhood	High throughout childhood	*p*	Never	Increasing throughout childhood	Strong peak in early childhood	*p*
Any breastfeeding status						*0,9*				*0,3*
Never breastfed	25% (227)	26% (45)	25% (37)	30% (13)	28% (28)		25% (315)	26% (22)	36% (13)	
Breastfed	75% (683)	74% (128)	75% (113)	70% (31)	72% (72)		75% (942)	74% (62)	64% (23)	
Any breastfeeding duration						*0,8*				*0,9*
< 1 month	32% (291)	31% (54)	32% (48)	39% (17)	35% (35)		32% (401)	35% (29)	42% (15)	
1 to < 4 months	31% (284)	36% (63)	30% (45)	32% (14)	27% (27)		32% (400)	29% (24)	25% (9)	
≥ 4 months	37% (335)	32% (56)	38% (57)	30% (13)	28% (38)		36% (456)	37% (31)	33% (12)	
Predominant breastfeeding						*0.7*				*0.7*
Never breastfed	32% (293)	34% (58)	36% (54)	41% (18)	34% (34)		33% (413)	37% (31)	36% (13)	
Ever breastfed	68% (616)	66% (115)	64% (96)	59% (26)	66% (66)		67% (843)	63% (53)	64% (23)	
Predominant breastfeeding duration						*0.4*				*0.8*
< 1 month	44% (397)	43% (74)	46% (69)	55% (24)	47% (47)		44% (552)	48% (40)	53% (19)	
1 to < 4 months	38% (348)	4% (77)	37% (55)	34% (15)	41% (41)		39% (493)	37% (31)	33% (12)	
≥ 4 months	18% (164)	13% (22)	17% (26)	11% (5)	12% (12)		17% (211)	15% (13)	14% (5)	

% (n)