

Prospective Cohort Study of Breastfeeding and the Risk of Childhood Asthma

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Objectives To study whether the duration of breastfeeding and time for introduction of complementary foods was associated with the risk of childhood asthma.

Study design We used data from the Norwegian Mother and Child Study, a nationwide prospective cohort study that recruited pregnant women from across Norway between 1999 and 2008. Children with complete data of breastfeeding up to 18 months and current age >7 years were eligible (n = 41 020). Asthma as the primary outcome was defined based on ≥2 dispensed asthma medications at age 7 years registered in the Norwegian Prescription Database. We used log-binomial regression models to obtain crude relative risks (RRs) in the main analysis, and adjusted for selected confounders in multivariable analyses.

Results For duration of any breastfeeding, 5.9% of infants breastfed <6 months (adjusted RR [aRR] 1.05, 0.93-1.19) and 4.6% breastfed 6-11 months (aRR 0.96, 0.87-1.07) had dispensed asthma medications at age 7 years compared with 4.6% of infants breastfed ≥12 months (P_{trend} .62). Infants still breastfed at 6 months, but introduced to complementary foods <4 months and 4-6 months, had an aRR of 1.15 (0.98-1.36) and 1.09 (0.94-1.27) respectively, compared with infants fully breastfed for 6 months (P_{trend} .09). Ages at introduction of solids or formula separately were not significant predictors (P_{trend} .16 and .08, respectively).

Conclusions We found no association between duration of breastfeeding or age of introduction to complementary foods and asthma at age 7 years. (*J Pediatr* 2017;■■:■■-■■).

The World Health Organization recommends continuing full breastfeeding during the first 6 months of life, a recommendation that has been adopted by several countries.¹ The World Health Organization, furthermore, recommends partial breastfeeding up to the age of 2 years, but it is unclear if this is associated with further health, growth, and developmental benefits for children in high-income countries.^{2,3}

The prevalence of asthma in children has increased in the second half of the 20th century.⁴ Rapid changes in occurrence of disease suggest a potential role for environmental factors, though diagnostic practices may contribute to changing prevalence. Environmental factors in pregnancy and infancy may increase a child's susceptibility to develop asthma.⁵

The role of breastfeeding and the appropriate age for introduction of complementary foods in the prevention of asthma is controversial. Some studies show a reduced risk for asthma in children who are breastfed, whereas others show no association, or even increased risk.⁶⁻⁹ Published reviews include a spectrum of different studies, in addition to cohort studies, also cross-sectional and case control studies. The heterogeneity of previously conducted studies with regard to design, outcome classification, and age at outcome classification is likely to influence any pooled measures of association, calling for large cohort studies.

The associations tend to be weaker for asthma defined at an older age compared with early wheezing.¹⁰⁻¹⁵ Asthma before school age likely includes a large proportion of wheezing because of lower respiratory tract infection, although asthma that persists in school age consists of a greater number of children with allergic respiratory symptoms.¹⁶ Based on the current evidence, it remains unclear whether the associations differ by asthma phenotypes, defined by age and associated atopic disease.

The aim of this prospective cohort study was, therefore, to investigate the association of duration of breastfeeding with asthma at age 7 years. We further aimed to study whether the age for introduction of complementary foods was associated with later asthma. Asthma at age 3 years was studied as a secondary outcome.

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aRR	Adjusted relative risk
BMI	Body mass index
MoBa	The Norwegian Mother and Child Cohort Study
NorPD	The Norwegian Prescription Database
RR	Relative risk

Methods

The Norwegian Mother and Child Cohort Study (MoBa) is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health.¹⁷ Pregnant women were recruited from all over Norway from 1999 to 2008 at approximately 18 gestational weeks. The participation rate was 41%, and all participants provided a written informed consent. Follow-up was conducted by mailed questionnaires at regular intervals.

The study is based on version VIII of the quality-assured data files released for research on February 14, 2014. In the current study, we use information from 6 questionnaires; the baseline questionnaire completed at approximately week 18 of pregnancy, questionnaires at child age 6, 18, and 36 months and 7 years, and the father's questionnaire (completed at recruitment; questionnaires are available at www.fhi.no/moba). Information gathered through questionnaires was linked to the Medical Birth Registry of Norway and the Norwegian Prescription Database (NorPD) using unique national identification numbers. The current study was approved by the Norwegian Data Inspectorate and the Regional Committee for Medical and Health Research Ethics of South-East Norway.

We included individuals with information from the questionnaire completed at 18 gestational weeks, in addition to questionnaire completed when the child was 6 and 18 months of age, who had reached age 7 years by December 31, 2013 (n = 41 020, [Figure 1](#)). We decided to use information about asthma medication from the NorPD as the primary outcome

to reduce the impact of self-selection at age 7 years. Out of the parents who received the age 7-year questionnaire, 54% answered and returned it to MoBa. Characteristics of participants with missing exposure information up to age 18 months and, thus, not included are presented in [Table I](#).

The primary outcome was current asthma at age 7 years as defined based on dispensed prescriptions in the NorPD, which contains information regarding all dispensed medications in Norway from January 2004 and onward, and classifies medications according to the Anatomical Therapeutic Chemical classification system. Medications classified as asthma medications were inhaled short- and long-acting beta2-agonists (R03 AC), inhaled corticosteroids (R03 BA), fixed-dose combinations of inhaled beta2-agonists and corticosteroids (R03 AK), and leukotriene antagonists (R03 DC). Children who had at least 1 dispensed prescription for asthma medications in the past year at the age of 7 years, in addition to a second dispensed prescription within 12 months of the first, were defined as asthma cases.

As secondary outcomes, we defined current asthma at age 3 and 7 years based on maternal report through questionnaires. Current asthma was defined based on maternal "yes, has now" in response to the question if the child suffered from asthma and reported use of inhaled glucocorticoids and/or beta2-agonists the last 12 months. Positive answers to both asthma diagnosis and use of medications were required for our definition of current asthma.

We classified children with asthma into 3 groups; early transient (asthma at only age 3 years), late-onset (asthma onset after age 3 years), and persistent asthma (asthma at both age 3 and

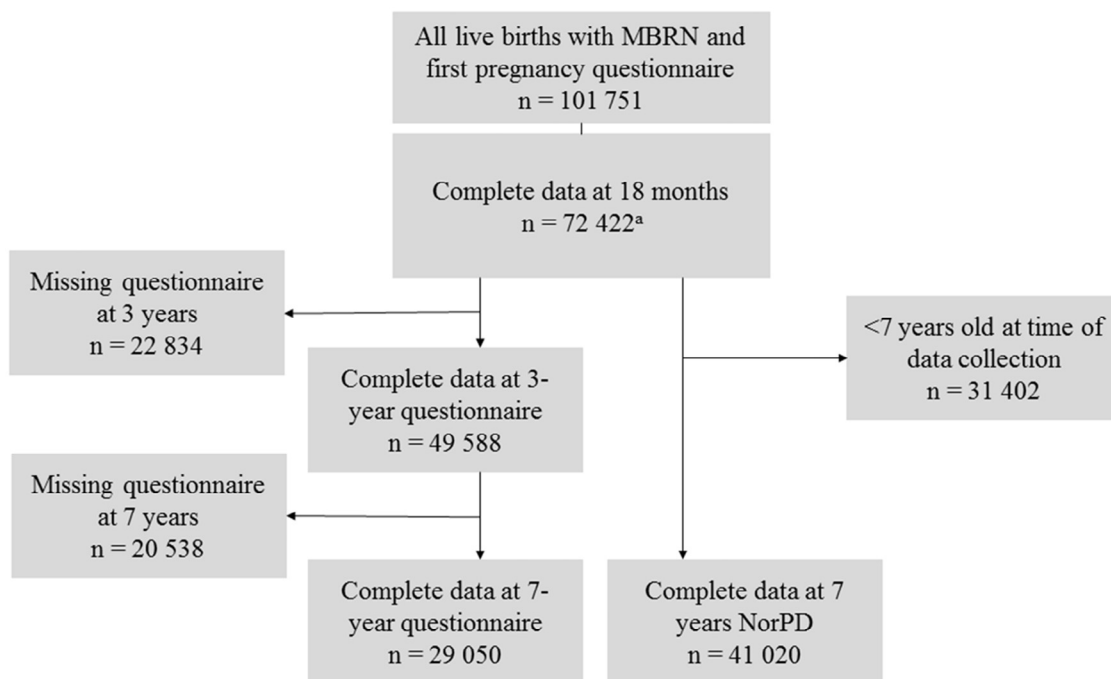


Figure 1. Flow chart of participants in the study. *MBRN*, Medical Birth Registry of Norway; *NorPD*, Norwegian Prescription Database. ^aMissing 6-month and/or 18-month questionnaire (n = 29 329).

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