positive specific IgE against *P. pratense* (≥0.7 kU/L); and a forced expiratory volume in 1 second at least 70% of the predicted value at screening and randomization visits.

**METHODS.** The subjects (85% polysensitized, 25% with asthma) were randomized 1:1 to receive once-daily MK-7243 (2800 BAU *P. pratense*) or placebo. The first dose was given at the investigator’s office; subsequent doses were self-administered at home. The primary end point was total combined score (TCS) (composed of rhinoconjunctivitis daily symptom score plus daily medication score) over the entire grass pollen season. Key secondary end points included entire-season daily symptom score, daily medication score, peak-season TCS, and rhinoconjunctivitis quality-of-life questionnaire scores. Safety outcomes included adverse events (AEs).

**RESULTS.** MK-7243 yielded improvements over placebo across all end points measured, with similar efficacy noted between children and adults. Specifically, there was a 23% improvement in entire-season TCS (median difference: −0.98, *P* < .001), 29% in peak-season TCS (median difference: −1.33, *P* < .001), 20% in entire-season daily symptom score (median difference: −0.64, *P* = .001), 35% in entire-season daily medication score (mean difference: −0.48, *P* < .001), and 12% in the peak-season rhinoconjunctivitis quality-of-life questionnaire (median difference: −0.13, *P* = .027). Most AEs were transient, local application-site reactions, with no serious treatment-related AEs or anaphylactic shock. Three subjects (1 receiving placebo, 2 receiving MK-7243) had moderate systemic allergic reactions.

**CONCLUSIONS.** This study found that MK-7243 was effective in polysensitized, grass-allergic North American children and adults with allergic rhinoconjunctivitis, confirming findings from previous studies.

**REVIEWER COMMENTS.** This study is the first large, randomized trial in North America analyzing the safety and efficacy of grass sublingual immunotherapy in both adults and children who had multiple allergies. Its results confirm the earlier findings of 2 smaller, North American, randomized, placebo-controlled studies (Blais M, Maloney J, Nolte H, Gawchik S, Yao R, Skoner DP. Efficacy and safety of timothy grass allergy immunotherapy tablets in North American children and adolescents. *J Allergy Clin Immunol*. 2011;127[1]:64–71 and Nelson HS, Nolte H, Creticos J, et al. Efficacy and safety of timothy grass allergy immunotherapy tablet treatment in North American adults. *J Allergy Clin Immunol*. 2011;127[1]:72–80). Looking at the efficacy of MK-7243 versus placebo in improving TCS. These accumulated data provide strong evidence of MK-7243’s efficacy in treating subjects who have allergic rhinoconjunctivitis due to grass pollen. This approach will provide children with an additional option for the management of seasonal allergies. It is important to remember, however, that these results apply only to sublingual therapy with this product and may not apply to other products or doses of sublingual immunotherapy.


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**Early-Life Risk Factors for Childhood Wheeze Phenotypes in a High-Risk Birth Cohort**

**PURPOSE OF THE STUDY.** The goal of this study was to identify asthma phenotypes in a prospective birth cohort study based on age of onset and clinical evolution and to characterize their respective associated risk factors.

**STUDY POPULATION.** The study population included members of MACS (Melbourne Atopy Cohort Study), a birth cohort at high risk for allergy consisting of 620 children who were followed up prospectively at defined time points during the first 7 years of life. An additional evaluation was conducted at 12 years of age.

**METHODS.** Latent class analysis was used to categorize asthma phenotypes in the context of wheeze patterns between 4 weeks and 7 years of age. Relative contributions of known clinical and demographic characteristics to the defined clusters of wheeze phenotypes were also evaluated in a logistic regression analysis.

**RESULTS.** The study identified 5 distinct wheeze phenotypes: never/infrequent, early transient (appeared in first 12 months and resolved by 3 years), early persistent (wheezing appeared in the first 6 months), intermediate onset (wheezing onset at ~18 months), and late onset (occurred at ~4 years); the latter 3 groups were associated with increased risk of current wheeze at 12 years. Consistent with previous observations, an increased propensity to childhood wheeze was noted with lower respiratory tract infection before 1 year. However, this risk was abrogated when adjusted for aeroallergen and food sensitization, and the strength of this association declined over time, becoming nonsignificant in the late-onset group. The study found protective effects of dog exposure at baseline and first-born status against intermediate-onset wheezing. Breastfeeding for >3 months reduced the risk of both early transient and late-onset wheezing. Parental smoking was a risk factor associated with late-onset wheeze.

**CONCLUSIONS.** The study confirmed the contributory role of various early-life exposures to the generation of distinct childhood wheeze phenotypes in a birth cohort at high risk of allergy.

**REVIEWER COMMENTS.** The heterogeneity of childhood asthma is being increasingly recognized, as determined by
using multiple environmental and biological factors. The study reinforced known clinical and demographic associations with early-life wheeze. However, the definition of wheeze phenotypes was largely based on the empirical categorization of the investigators. In addition, further information regarding disease course and outcomes was not available, and future longitudinal studies are necessary to determine the clinical relevance of the identified phenotypes in terms of stability over time and also in predicting severity and treatment response.


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The Burden of Childhood Asthma and Late Preterm and Early Term Births

PURPOSE OF THE STUDY. The goal of this study was to evaluate the association between gestational age at birth and the risk of subsequent development of childhood asthma.

STUDY POPULATION. The study population was derived from a clinical birth database of 45,030 infants born after 22 weeks’ gestation at a university hospital in Finland between 1989 and 2008. Women with live-born infants without asthma served as control subjects.

METHODS. This trial was a retrospective, observational, hospital-based birth case-controlled study in which data on 44,173 women with live-born infants were linked with data from the register for reimbursement for asthma medication for their offspring. Pregnancy factors consisting of 75 background items were recorded during pregnancy. Health care workers added information on pregnancy complications, pregnancy outcomes, and the neonatal period. The main outcome measure was asthma among the infants.

RESULTS. The study found that the risk of asthma was highest in children born before 32 weeks’ gestation compared with control subjects, and it remained high in those born up to 38 weeks. Delivery after 41 weeks seemed to protect against the development of asthma. The magnitude of the risk decrease depends on gestational age at birth.

REVIEWER COMMENTS. Reduction in risk of asthma development is a key goal of asthma management. This study confirmed previous reports of the association between preterm delivery and asthma in offspring. A novel finding is that the risk is still almost double in those born late preterm and that it remains significant even in those born early term compared with children born at term. This knowledge can help guide the avoidance of iatrogenic early term/late preterm deliveries, especially in pregnant women with asthma. A limitation of the study is that prenatal and environmental factors after birth, which are potential risk factors for asthma development in children, were not controlled. In addition, asthma severity was not taken into account.


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Parental Psychological Distress During Pregnancy and Wheezing in Preschool Children: The Generation R Study

PURPOSE OF THE STUDY. The goal of this study was to evaluate the associations of maternal psychological distress during pregnancy with childhood wheezing in the first 6 years of life.

STUDY POPULATION. In this study, 4848 children were evaluated from the Generation R Study, a population-based cohort trial from fetal life onward in Rotterdam, the Netherlands. Subjects were born between April 2002 and January 2006.

METHODS. The Brief Symptom Inventory was used to assess maternal and paternal psychological distress at 20 weeks of gestation and 3 years after delivery. Maternal psychological distress was also assessed at 2 and 6 months after delivery. Information on wheezing was obtained annually at ages 1, 2, 3, and 4 years by using the asthma questionnaire from the International Study on Asthma and Allergy in Childhood, and information on physician-diagnosed (ever) asthma was obtained by using a questionnaire at 6 years.

RESULTS. Of mothers, 7.8% had overall psychological distress during pregnancy. Children had an increased odds ratio (OR) of wheezing overall from 1 to 4 years of life if
Early-Life Risk Factors for Childhood Wheeze Phenotypes in a High-Risk Birth Cohort

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