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Personal and early life factors associated with new-onset asthma, remission, and persistence of asthma in a 2-year follow-up of schoolchildren

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ABSTRACT

Objective: The natural course of childhood asthma, after its onset, is characterized by periods of persistence, relapse and remission. To investigate personal and early life factors associated with new-onset asthma, persistence and remission among children.

Methods: The study was conducted in the province of Saskatchewan, Canada. Children in grades Kindergarten to Grade 8 (ages 5–14 years) participated in a cross-sectional study in 2013. In 2015, we approached those who gave consent in 2013 to be re-contacted, creating a prospective cohort. Data were collected using questionnaires in both years. Participants in 2013 who also had data in 2015 (25%; $n = 324/1,348$) had their asthma status reclassified and longitudinal descriptors were applied: “no asthma”, “new-onset asthma”, “persistent” or “remission”. Personal and early life factors associations with asthma outcomes in 2015 were evaluated.

Results: Among those without asthma in 2013 ($n = 245$), the incidence of new-onset asthma in 2015 was 7.2%. Among those with asthma in 2013 ($n = 79$), 47.1% had remission and 52.9% had persistent asthma in 2015. Parental history of asthma (adjusted odds ratio (aOR): 4.99; 95% confidence interval (CI): 1.88–28.27), early life respiratory infection (aOR: 1.92; 95%CI: 1.47–7.88), early life allergy (aOR: 6.39; 95%CI: 1.34–30.58) and early life infection (aOR: 4.99; 95%CI: 1.19–20.93) were associated with new onset asthma. Similarly, while parental history of asthma (aOR: 1.13; 95%CI: 0.29–4.34), early life respiratory infection (aOR: 2.71; 95%CI: 0.70–10.45), and early life ear infection (aOR: 1.34; 95%CI: 0.36–5.05) were also positively association with persistent asthma, the associations were not statistically significant.

Conclusion: Parental history of asthma, early life respiratory infection and allergy might not only influence the onset of childhood asthma but also be associated with asthma persistence.

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Introduction

Childhood asthma has varied outcomes over the course of life. While asthma may develop in children at any stage of life (1), the possible course of the disease, after its onset, can include remission, persistence, and/or a combination of remission and relapses (2). Factors predicting the natural course and outcomes are unclear.

Several personal [e.g. sex (3), age (4), socio-economic characteristics (5), family history of asthma and allergy (6), and allergic sensitization (7)], and environmental factors [e.g. pet ownership (8), environmental tobacco smoke (9), air pollution especially during pregnancy (10) and early life (11)] have been reported to be associated with development of childhood asthma. However, the relationships between these factors and

asthma remission and persistence are less clear. Since early life infections and the environment are very crucial to the development of respiratory and immune systems in children (12), the outcome of childhood asthma over the course of life could also be linked to exposures occurring in early life (13).

Due to changes in diagnostic patterns, risk factor patterns, socio-economic status, or lifestyles, changes in the clinical manifestations of childhood asthma may occur over a relatively short period. Furthermore, a population-based cohort study in Canada revealed that while the majority of individuals with asthma may have persistent asthma, some had experienced a gap of 2 or more years during which their asthma symptoms were in remission (14). Factors predicting asthma remission were not investigated in this earlier study.

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In the current study, we investigated factors associated with new-onset asthma and persistence of childhood asthma over a 2-year follow-up of schoolchildren. Our aim was to identify baseline characteristics at the time of study entry, personal factors (sex and parental asthma and allergy), and early life characteristics that may be associated with the natural history of asthma in children. Such information may be useful in providing information to anticipate the course of asthma and help parents or healthcare providers to be proactive in the management of the disease in affected children.

Methods

Study design and location

A cross-sectional survey was conducted in the province of Saskatchewan, Canada, in 2013. Participants were followed up in 2015. Methods for the 2013 survey have previously been described (15). Participants were recruited from Regina [population approximately 200 000 (16)], Prince Albert [population approximately 35 000 (17)], and the rural area in the region around Prince Albert (population <2,500 people). In our previous study, we compared children from each of the 3 locations and found several notable differences including age, parental education level, parental smoking, and parental history of allergic disease (18).

Study population, selection and recruitment

Participants were schoolchildren (ages 5–14 years) attending Kindergarten to Grade 8 in 2013 ($n = 3,509$) and were targeted for follow-up in 2015. In the 2013 survey, study packages, including an information letter, and survey were distributed to students to take home for self-completion by their parents. Surveys were then returned to the school and were collected by research personnel. The participation rate in the 2013 survey was approximately 28% (15). In 2015, we approached those who gave consent ($n = 1,348$) to be re-contacted based on a question in the 2013 survey creating a prospective cohort. In 2015, study packages were mailed to parents for self-completion. In addition to the survey, children also underwent lung function testing in 2015 but not in 2013.

The study was approved by the University of Saskatchewan Biomedical Research Ethics Board (Bio #: 14–162). Completion and return of the survey implied voluntary consent for the study. Children and parents also provided written assent and consent, respectively, prior to clinical testing. Furthermore, all school divisions involved approved the study.

Data collection and operational definition of asthma at baseline

Data collection was performed based on the standardized International Study of Asthma and Allergy in Childhood (19), the American Thoracic Society Children's Respiratory Disease (20), and questionnaires used previously in Saskatchewan lung health studies (21,22). The survey included questions on respiratory health, general health, parental health history, early life respiratory illness and allergy, environmental exposures, and socio-demographic factors as well as indoor environment characteristics. Active physician-diagnosed asthma at baseline (2013) was based on a positive response to the question: "Has this child ever been diagnosed as having asthma by a doctor?" along with a report of any of the following in the past 12 months: (i) wheeze, (ii) prescribed asthma medication use, (iii) ≥ 1 asthma episodes, and (iv) ≥ 1 healthcare service use for asthma (hospitalization, emergency room or physician visits).

Operational definition of asthma status at follow-up (2015)

Similar questionnaires were used for obtaining participants' information in both 2013 and 2015 surveys. Modifications to the 2015 questionnaire occurred only when a particular question was needed to more fully investigate various aspects of health and exposure (e.g. asthma symptoms severity or healthcare service use). In 2015, a participant's asthma status was reclassified and longitudinal descriptors were applied including "remission", "persistent", "new-onset asthma" or "no asthma". A child was defined as being in "remission" if the child had active asthma in 2013 but did not report signs of active asthma (absence of wheeze, asthma episodes, asthma medication use, or healthcare utilization for asthma in the past 12 months) in 2015. Subjects identified as having "Persistent asthma" had active asthma in 2013 and continued to have active asthma in 2015. "New-onset asthma" was defined as no report of "active asthma" in the 2013 survey but had active asthma in 2015. "No asthma" was defined as no reports of "active asthma" in either 2013 or 2015. It is possible that a child had a diagnosis of asthma prior to 2013 but was not considered active in 2013. Based on our operational definition of "active asthma", 8 children were excluded. The 8 children had been diagnosed to have asthma before 2013 but as of 2013, their asthma was no longer active asthma based on the criteria above.

Operational definitions of covariates

We obtained information on several covariates at baseline and assessed their relationships with asthma outcomes in the follow-up survey. Covariates of interest included were age, sex, ethnicity (Caucasian vs. others), parental education levels ($\leq$ high school education vs. $>$ high school education), place of residence (urban vs. rural), parental smoking (yes vs. no), indoor characteristics, parental history of asthma and allergy (yes vs. no), and early life respiratory illness and allergy (yes vs. no). These covariates were selected based on their potential for predicting the course of childhood asthma (2,23–25).

Indoor characteristics assessed included: pet ownership defined as presence of either a cat or dog past 12 months; presence of mold or dampness in home defined as positive response to “Does your house have any damage caused by dampness (e.g. wet spots on walls, floor)?” “Are there signs of mold or mildew in any living areas in your home?” A history of early life respiratory illness was considered positive if a child reported physician-diagnosed bronchitis, pneumonia, whooping cough or croup (26) before the age of 3 years while early life allergy was defined as a positive report of physician-diagnosed eczema or hay fever (27) before the age of 3 years.

Lung function assessment

Children underwent lung function testing during home or school visits according to recommended standards (28) using the Easy-on PC spirometer (ndd Medical Technologies, Zurich, Switzerland). Of the 335 children who responded to the follow-up survey in 2015, 288 (86%) performed spirometry testing. Measurements of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, and forced expiratory flow (FEF25–75%) were obtained. Predicted values were based on the all-age, multi-ethnic Global Lung Function Initiative (GLI) reference Equation (29).

Statistical analysis

Statistical analyses were completed with the Statistical Package for the Social Sciences (SPSS) Version 24 (SPSS Inc. Armonk, NY: IBM Corp.). Participants' characteristics between 2013 and 2015 were compared using the McNemar test or Paired *t*-test as appropriate. The Chi-squared test (χ^2) test or Fisher's exact test (for categorical variables) was used to compare baseline factors and early life characteristics by asthma

outcome groups in 2015. Analysis of variance (ANOVA) was conducted to compare differences in mean values for lung function between asthma outcome groups in 2015 as well as mean difference in age and body mass index at baseline. Because the survey was conducted at two time periods (2013 and 2015) on the same participants, we accounted for repeated outcomes and time-dependent predictors within subjects using a generalized estimating equation (GEE) analysis with asthma as the outcome of interest. To show the sequential effects of personal and early life characteristics with new-onset asthma and persistent asthma in 2015, two separate multivariate logistic regression analyses were performed. Model I examined the relationships between personal, demographic, and environmental factors at baseline as well as early life characteristics with new-onset asthma in 2015 among children with no asthma in 2013 using “No asthma” as the reference group. Model II examined associations with persistent asthma in 2015 among children with report of active asthma in 2013 using “Remission” as the reference group. Variables were included in the final model based on statistical significance, clinical/biological importance, and potential confounding (30). Following model fitting, Goodness-of-Fit testing was assessed. The strength of the associations were assessed using odds ratios (ORs) and their 95% confidence interval (CI). Statistical significance was defined by an alpha level of $p \leq 0.05$.

Results

Of the 1,348 participants who gave consent to be re-contacted in 2013, a total of 335 (24.8%) responded to the 2015 follow-up survey (Table 1). Identified reasons for the low participation rate in 2015 were relocation without knowledge of new address ($n=154$), refusal ($n=257$), and non-response ($n=602$). Participants' characteristics in both the 2013 and 2015 surveys were similar except children participating in 2015 were older (mean $\pm$ SD age: 9.3 ± 2.5 vs. 11.1 ± 2.7 years, respectively; $p < 0.05$), less likely to own a pet (49.5% vs. 53.2%, respectively; $p = 0.03$), or live in damp housing (22.5% vs. 30.0%, respectively; $p = 0.01$). Of the 335 participants who responded to follow-up survey in 2015, 324 (96.7%) had information on asthma status in the 2013 survey (Active asthma = 87; No asthma = 237) and formed the study population used in the current analysis.

Of the 237 children with “No asthma” in 2013, 7.2% developed asthma by 2015 (17 new cases). Also, of the 87 children with asthma in 2013, 47.1% (41 participants) had remission in 2015.

Table 1. Baseline characteristics in 2013 by asthma outcome at end of study in 2015 ($n = 324$).

	No Asthma ($n = 220$)	New cases ($n = 17$)	Remission ($n = 41$)	Persistent ($n = 46$)	p
Personal characteristics					
Age, mean (SD), years	8.99 (2.58)	8.87 (2.23)	9.48 (2.38)	8.87 (2.37)	0.785
Body mass index, mean (SD), kgm^{-2}	4.79 (3.74)	4.96 (2.05)	3.97 (1.17)	4.57 (1.97)	0.750
Female (%)	50.0	29.4	46.3	39.1	0.255
> High school parental education (%)	88.1	88.2	85.4	77.3	0.298
Caucasian (%)	78.9	80.0	92.3	74.4	0.195
Urban residence (%)	85.9	94.1	97.6	89.1	0.158
Parental smoking (%)	11.9	17.6	14.6	17.4	0.707
Indoor characteristics					
Pet ownership (%)	50.9	58.8	65.9	45.7	0.232
Dampness in home (%)	20.5	17.6	18.9	15.6	0.892
Home mold (%)	9.0	6.7	17.9	13.6	0.335
Parental history of asthma and allergies					
Asthma (%)	10.5	35.3	36.6	54.3	<0.001
Allergy (%)	42.3	41.2	70.7	76.1	<0.001
Early life characteristics					
Respiratory infection ^{§†} (%)	14.1	29.4	34.1	43.5	<0.001
Allergy ^{††} (%)	11.4	29.4	31.7	39.1	<0.001
Ear infection [†] (%)	30.9	70.6	43.9	37.0	0.006
Tonsillitis [†] (%)	6.8	11.8	17.1	6.5	0.156
Breastfed (%)	91.8	100.0	83.3	86.8	0.224
Daycare attendance	56.8	75.0	69.2	64.3	0.250

p -value based on analysis of variance (continuous variables) and χ^2 (categorical variables) tests.

SD: Standard Deviation.

[§]Diagnosed bronchitis, pneumonia, whooping cough or croup.

[†]Diagnosed eczema or hay fever.

^{††}Condition diagnosed before the age of 3 years.

Table 2. Mean (SD) lung function results by asthma outcomes at follow-up ($n = 278$).

	No asthma ($n = 186$)	New cases ($n = 15$)	Remission ($n = 35$)	Persistent ($n = 42$)	p
FVC (% predicted)	98.2 (12.0)	101.5 (16.8)	97.2 (9.7)	101.4 (13.1)	0.296
FEV ₁ (% predicted)	95.6 (13.0)	93.3 (19.2)	93.2 (9.7)	92.9 (15.6)	0.471
FEV ₁ /FVC (% predicted)	97.2 (7.0)	94.7 (10.1)	96.6 (6.9)	93.3 (7.2) ^a	0.014
FEF _{25%-75%} (% predicted)	89.9 (22.6)	88.6 (27.8)	85.9 (16.8)	81.1 (24.1)	0.130

p -value based on analysis of variance (ANOVA).

SD: Standard Deviation.

^a $p < 0.05$: Persistent asthma compared to no asthma.

Table 3. Association between personal and early life characteristics and asthma accounting for repeated observations at baseline and follow-up using generalized estimating equation.

	No asthma (Reference)	Asthma aOR (95%CI)
Age (years)	1.00	1.08 (0.97–1.19)
Body mass index, mean (SD), kgm^{-2}	1.00	0.99 (0.97–1.01)
Sex (ref: female)	1.00	1.82 (1.05–3.15) ^a
Maternal education (ref: $\leq$ high school)	1.00	0.36 (0.15–0.85) ^b
Parental smoking (ref: no)	1.00	1.09 (0.42–2.81)
Parental history of asthma (ref: no)	1.00	3.74 (2.06–6.77) ^a
Parental history of allergy (ref: no)	1.00	2.05 (1.13–3.72) ^a
Early life respiratory infection ^{§†} (ref: no)	1.00	1.86 (1.09–3.18) ^a
Early life allergy ^{††} (ref: no)	1.00	1.86 (1.12–3.06) ^a
Early life ear infection [†] (ref: no)	1.00	0.71 (0.50–1.00)
Early life tonsillitis [†] (ref: no)	1.00	0.68 (0.38–1.23)
Daycare attendance (ref: no)	1.00	1.68 (0.94–3.01)

aOR: Adjusted odds ratio. Model adjusted for each variable in the table as well as pet ownership.

[§]Diagnosed bronchitis, pneumonia, whooping cough or croup infection.

[†]Diagnosed eczema or hay fever.

^{††}Conditions diagnosed before the age of 3 years.

^a $p < 0.05$.

^b $p < 0.001$.

The proportion of parents with a report of history of asthma or allergy was significantly higher in

children with persistent asthma compared to children with no asthma. With regard to early life characteristics, children with persistent asthma were more likely to have early life respiratory infection and allergy compared to those with no asthma while early life ear infection was significantly higher in those with new onset asthma compared to those with no asthma.

Clinical parameters assessed in 2015 are shown in Table 2. Mean percent predicted FEV₁/FVC ratio was lower in children with persistent asthma (93.3%) compared to children with no asthma (97.2%).

Table 3 presents the results of associations between independent variables and asthma outcomes in 2015 using the GEE to account for repeated outcomes and time-dependent predictors. The results show that being male, having parents with history of asthma and allergy, early life respiratory infection, and early life allergy were all positively associated with asthma while higher maternal education was associated with a lower risk of asthma. Table 4 shows the sequential results

Table 4. Associations between baseline and early life characteristics and asthma outcomes at follow-up.

	Model I		Model II	
	No asthma (Reference)	New-onset asthma aOR (95%CI)	Remission (Reference)	Persistent aOR (95%CI)
Age (years)	1.00	1.08 (0.81–1.44)	1.00	1.36 (0.83–2.24)
Sex (ref: male)	1.00	1.62 (0.40–6.58)	1.00	2.08 (0.58–7.46)
Parental smoking (ref: no)	1.00	0.96 (0.11–8.27)	1.00	1.18 (0.14–10.22)
Parental history of asthma (ref: no)	1.00	4.99 (1.88–28.27)^a	1.00	1.13 (0.29–4.34)
Parental history of allergy (ref: no)	1.00	0.53 (0.11–2.65)	1.00	3.89 (0.72–20.95)
Early life respiratory infection ^{§†} (ref: no)	1.00	1.92 (1.47–7.88)^a	1.00	2.71 (0.70–10.45)
Early life allergy ^{††} (ref: no)	1.00	6.39 (1.34–30.58)^a	1.00	1.34 (0.36–5.05)
Early life ear infection [†] (ref: no)	1.00	4.99 (1.19–20.93)^a	1.00	0.36 (0.09–1.40)
Daycare attendance (ref: no)	1.00	2.45 (0.53–11.37)	1.00	0.65 (0.16–2.57)

aOR: Adjusted odds ratio. Model adjusted for each variable in the table as well as maternal education level and body mass index.

§Diagnosed bronchitis, pneumonia, whooping cough or croup infection.

†Diagnosed eczema or hay fever.

††Conditions diagnosed before the age of 3 years.

^a $p < 0.05$.

for the associations between personal and early life characteristics and new-onset asthma and persistent asthma. Parental history of asthma (aOR: 4.99; 95%CI: 1.88–28.27), early life respiratory infection (aOR: 1.92; 95%CI: 1.47–7.88), early life allergy [aOR: 6.39; 95%CI: 1.34–30.58] and early life infection (aOR: 4.99; 95%CI: 1.19–20.93) were associated with new onset asthma.

Discussion

We worked with a cohort of schoolchildren to determine factors associated with new-onset asthma and persistence of asthma over a 2-year follow-up period in Saskatchewan, Canada. Overall, the incidence of new-onset asthma in this cohort was low (7.1%). Asthma remission was 47.1% among those with asthma in 2013 with the majority of children with asthma falling into the persistent group (52.9%). Parental history of asthma, early life respiratory infections, early life allergy and early life ear infection were risk factors for new onset asthma.

The associations between parental history of asthma with asthma development (6) and persistence (31) have been reported in previous studies. While there may be some differences in the association observed, the overall evidence suggest that children with a parental history of asthma are at risk of developing asthma compared to those without a parent with history of asthma (6). In the Prevention and Incidence of Asthma and Mite Allergy (31) and the German Multicenter Allergy (32) cohort studies, parental history of asthma was significantly associated with more than 2 folds increase in risk of persistent asthma. The present study confirmed results from these previous studies.

Early life respiratory infections (33) and allergy (34) have been shown to be major drivers of asthma

development in children. In a birth cohort study in the Netherlands, respiratory tract infection (reports of serious respiratory, throat, nose, and/or ear infections, bronchitis or pneumonia in the last 12 months) of at least once per year between birth and the first 4 years of life nearly double the risk of developing asthma at age 7–8 years while eczema before the age of 4 years more than doubled the risk of asthma development (35). In the current study, we showed that early life infection and early life allergy were predictors of new-onset asthma and also increased likelihood of persistent asthma at follow-up. These findings are consistent with the results from the Isle of Wight birth cohort study in the United Kingdom where the risk of persistent wheeze from the first 4 years of life to age 10 years was significantly doubled in children with respiratory chest infections at 2 years of age and also increased more than 5 times in risk if they were atopic at 4 years of age (36). The results are also in agreement with the prevailing theories that factors occurring prenatally (10) and at infancy (11,13,37) might have a strong effect in influencing the natural course of childhood asthma.

Early life environments are critical in the development of respiratory symptoms (38) during which the developing immune system may be primed toward allergic diseases (13). For example, recent evidence indicated that environmental exposure during pregnancy (13,38) and early life (11,13,38) can be early life risk factors for respiratory symptoms possibly due to increased vulnerability in the development of lungs (39) and the immune systems (40). Therefore, the most likely mechanism for explaining the effect of early life respiratory infection on asthma development could be the diminished production of anti-inflammatory cytokines such as interferon-gamma (IFN- γ) and interleukin-10 (IL-10), postnatally (41), which subsequently increased production of TH2 cytokine (42); leading to a more

persistent risk of asthma and allergy in susceptible individuals. For this reason, it is possible that children who developed a respiratory infection at infancy may be more likely to have recurrent respiratory symptoms of infections in later life, thus contributing to recurrent asthma episodes and long term asthma morbidity.

The current study has some limitations to be considered. Asthma remission was defined as absence of asthma symptoms and without use of breathing medications or health care visits in the past 12 months. A more stringent definition (complete or physiologic remission) could require an objective demonstration of normal lung function and absence of airway hyperresponsiveness (AHR) in addition to absence of symptoms and medication use (43,44). While our definition of remission could be viewed as fulfilling clinical remission, but not necessarily physiologic remission, it is consistent with the definition most commonly used in epidemiological studies of childhood asthma (43,45).

We could not exclude the possibility of a relapse among children with clinically remitted asthma if the children were followed further. Studies have shown that subjects with clinical remission from asthma may have continuous and sustained airway obstruction (46) and AHR which may predispose to a relapse of asthma symptoms after a period of remission (47). In the current study, all asthma groups had normal lung function. While FEV₁/FVC ratio was significantly higher in children with remission compared to those with persistent asthma, the difference observed may only reflect statistical significance and not necessarily clinical significance due to the very small difference in FEV₁/FVC values between the two groups. Another limitation of the study is that we did not assess the impact of asthma medication use, as a separate variable, because it was used as part of the operational definition for asthma outcomes. However, a study in the USA where children with asthma were randomly assigned into inhaled corticosteroid and placebo groups and followed for 4–6 years to determine the natural course of asthma showed equal percentages of remission and persistence in all treatment groups (48). This suggests that while asthma medication use may serve as an important controller therapy for persistent asthma, the long-term treatment may not necessarily influence the natural outcome of the disease and may not necessarily be a predictor of remitting asthma. The participation rate at follow-up was low (25% follow-up rate; Table S1, [Supplementary material](#)). Despite strong associations for parental history of allergy and early life respiratory infections in relation to persistent asthma, these were not statistically

significant, likely due to the low sample size for this group. Furthermore, we observed some differences in participants' characteristics in the current study compared to the original group in 2013 (e.g. age, parental education, tobacco smoke exposure, and parental history of allergy; Table S2, [Supplementary material](#)). The low follow-up rate and differences between the baseline and follow-up groups might have resulted in biased values obtained for incident asthma and persistence in the current study when compared to the general study population; warranting caution in interpreting the results. The incidence of new-onset asthma in this cohort was low (7.1%). This may reflect potential sample bias in which children with asthma or asthma-related symptoms at baseline were more likely to agree to participate in the follow-up survey in 2015 thereby underestimating asthma incidence rate in this population. On the other hands, this may also reflect the reported decreasing trends in asthma incidence rates among pediatric population in Canada (49). Finally, incidence rate for asthma may vary across age group with peak incidence likely to occur at earlier age (49). Participants for this study were children aged 5–14 years old and likely to have varied patterns of asthma outcomes across age group. Due to the relatively small sample size, especially for incident asthma and remission, we were not able to determine patterns of incidence and remission by age groups in this study.

One of the strengths of the study was the prospective study design with a short interval which minimized parental recall bias of their child's asthma conditions. We also used standardized questionnaires. Furthermore, the study participants were from large urban, small urban and rural areas with similar distributions in both the 2013 and 2015 surveys supporting participant's representativeness from a variety of sociodemographic and environmental backgrounds.

Conclusion

In summary, our results showed some insights into modifiable (particularly early life infections) and non-modifiable hereditary (parental history of asthma) factors that may help in providing useful information for predicting prognosis of asthma in children. We demonstrated that parental history of asthma and early life respiratory infection and allergy might not only influence the onset of childhood asthma, but also be associated with persistent asthma; adding further information to the importance of personal factors and early life events in the natural course of asthma.

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Disclosure statement

The authors have no conflict of interest related to this study to disclose.

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Table S1: Comparison of participants' characteristics in 2013 and 2015 surveys

	2013 (n=335)	2015 (n=335)	<i>p</i>
Personal characteristics			
Age, mean (SD), years	9.03 (2.52)	11.12 (2.69)	0.001
Female (%)	47.2	47.2	1.000
> high school, maternal (%)	86.1	86.1	1.000
Ethnic background (%)			
Caucasian	79.8	79.8	1.000
Other ethnic background	20.2	20.2	
Place of residence			
Urban (%)	88.1	87.2	<0.001
Rural (%)	11.9	12.8	
Tobacco smoke exposure			
Maternal smoking (%)	4.6	4.7	<0.001
Paternal smoking (%)	11.9	9.6	<0.001
Indoor characteristics			
Pet ownership (%)	53.2	49.5	0.034
Dampness in home (%)	19.2	22.5	0.010
Home mold (%)	11.0	12.3	0.576
Asthma-related symptoms			
Parental history of asthma (%)	20.9	20.9	1.000
Parental history of allergy (%)	50.1	50.1	1.000

Table S2: Comparison of characteristics between those who participated in the 2013 baseline survey and those who participated in the 2015 follow-up study

	Participated in the 2013 baseline survey (n = 3338)	Participated in the 2015 follow-up survey (n = 335)	<i>p</i>
Personal characteristics			
Age, mean (SD), years	9.52 (2.76)	9.03 (2.52)	0.001
Female (%)	50.6	47.2	0.231
> high school, maternal (%)	73.7	86.1	<0.001
Ethnic background (%)	62.6	79.8	
Caucasian	37.4	20.2	<0.001
Others			
Place of residence			
Urban (%)	85.5	88.1	0.197
Rural (%)	14.5	11.9	
Tobacco smoke exposure			
Maternal smoking (%)	18.7	4.6	<0.001
Paternal smoking (%)	22.0	1.2	<0.001
Indoor characteristics			
Pet ownership (%)	52.2	53.2	0.731
Dampness in home (%)	16.3	19.2	0.182
Home mold (%)	12.2	11.0	0.546
Parental history of asthma and allergies			
Parental history of asthma (%)	16.9	20.9	0.067
Parental history of allergy (%)	37.3	50.1	<0.001