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The developmental trajectory of pediatric asthma in 3 to 10 year olds

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To the Editor

Longitudinal studies have suggested that early childhood asthma follows different temporal trajectories.^{1–3} Children with early childhood recurrent wheezing frequently have “symptom or disease-free” periods, followed by “relapse” of disease, or do not have diagnosed asthma for the first time until later childhood. Some children or young adults develop asthma for the first time later in life. However, the childhood trajectory and patterns of disease development and remittance are not well figuratively characterized. The objective of this study was to describe and figuratively present the pattern of first asthma diagnosis and remittance, and to characterize the episodic nature of the disease by gender and race/ethnicity.

We conducted a population-based cohort study of 13,256 children born in the state of Tennessee during a two-year period from 1995–1996 and continuously enrolled in a state-based health insurance plan, Tennessee Medicaid, until age ten years. Asthma was diagnosed in the parent cohort from which this data is derived, during 3.5–5.5 years using an established modified Healthcare Effectiveness Data and Information Set (HEDIS) algorithm incorporating diagnostic coding and asthma specific medication use.^{4,5} Children with an ICD-9-CM diagnosis code of 493 (asthma) or children with asthma-specific prescription use

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in a 365 day period were considered to have asthma as has been previously described in greater detail.^{6–8} Our asthma definition had been validated as both sensitive and specific.⁶ In addition, our algorithm used to diagnose childhood asthma is similar to that used by other US Medicaid systems, a modified algorithm of the Council of State and Territorial Epidemiologists, which has been shown to have 90% sensitivity, 95% specificity, 94% PPV, and 92% NPV in identifying childhood asthma.⁹ In addition, we excluded children with diagnoses of chronic diseases including chronic lung, heart, airway, immunodeficiency or neurologic disease.^{4, 6–7} We further defined asthma period prevalence in 2-year blocks between ages 7–8 (from the 6th to 8th birthday) and 9–10 years (from the 8th to 10th birthday) using the same criteria. As children were classified as either having or not having asthma in each of the three age periods, eight unique asthma diagnosis patterns are possible. Demographic differences in age at first asthma diagnosis were analyzed using Chi-square test. R-software version 2.11.1 (www.r-project.org) was used for analyses and a two-sided 5% significance level was considered for statistical inference. The protocol was approved by the Institutional Review Board of Vanderbilt University and reviewed and approved by the Tennessee Department of Health and Bureau of TennCare.

Among the cohort of 13,256 children, the median gestational age was 39.1 weeks (interquartile range: IQR, 38.1 – 40.1), and the median birth weight was 3,175 grams (IQR, 2,807 – 3,544). Fifty-two percent of children were male gender and 59% had at least one living sibling at birth. The children were from urban (53%), suburban (21%), and rural regions (27%) of the state.

Twenty-five percent (3,352) of the 13,256 children met the asthma definition between ages 3.5 and 10 years, with seven distinct disease development patterns (Fig 1). We figuratively presented these seven patterns using a novel lasagna plot, as the eighth pattern would be that of children never diagnosed with asthma in any of the three time periods. The x axis is the age of follow up, with columns representing the three age periods when asthma was diagnosed. The y axis is the proportion of asthmatics, with height of the row representing the proportion of the children in each disease pattern among children who were ever-diagnosed with asthma. Children with asthma were more likely to be white (57% vs. 46% in children without asthma, $p<.001$), male (58% vs. 50% in children without asthma, $p<.001$), have had at least one bronchiolitis medical encounter during infancy (26% vs. 15% in children without asthma, $p<.001$), and have mothers who smoked during pregnancy (30% vs. 26% in children without asthma, $p<.001$). The proportions of children with asthma during 3.5–5.5, 7–8 and 9–10 years were 14%, 15%, and 16% respectively, which in turn represented 54%, 58%, and 63% of the 3,352 ever-diagnosed asthmatic children by age 10 years. Twenty-four percent of the ever-diagnosed children with asthma had asthma throughout the follow-up period, while 20% were not diagnosed with asthma until age 9–10 years (Fig 1).

The proportion of children with asthma was consistently greater in boys than in girls in each of the seven distinct disease development patterns (Fig 1). We further classified asthmatic children into three mutually exclusive groups by their age at first asthma diagnosis, 60% of children who first developed asthma between age 3.5–5.5 were male gender, while the proportion of male gender decreased to 58% and 53% at ages 7–8 and 9–10 years, respectively. The gender difference shift with increasing female proportion of asthmatic children over increasing age groups was significant ($p=0.01$). Fifty-five percent of children who first developed asthma between age 3.5–5.5 were white, while the proportion of white increased to 61% and 60% at ages 7–8 and 9–10 years, respectively. There was a significant ($p=0.009$) race/ethnicity shift with increasing proportion of white asthmatic children with advancing age, and a decreasing proportion of black asthmatic children (36%, 32%, and 33% respectively) as well as those of other race/ethnicity (9%, 7%, and 7% respectively) with advancing age.

In summary, over half of the children who were ever diagnosed with asthma by age 10 years had the diagnosis by age 5.5, among whom 46% still had an asthma diagnosis at age 10 years. Overall, 24% of children had an asthma diagnosis during the entire study period and 20% were not diagnosed with asthma for the first time until age 9–10 years. Asthmatic children experienced patterns of disease remittance and relapse over time. Male gender is a risk factor for childhood asthma development until at least 10 years of age. However, our study demonstrates the decreasing importance of male gender in asthma development with advancing age of first asthma diagnosis. Studies relying on an asthma diagnosis at a single age or age range would miss children who develop disease later during childhood, or have disease remittance. Because we define children as having asthma using both physician diagnosis and medication use, misclassification from physician's reluctance to label/code a child with asthma, particularly at younger ages, should be minimized. In addition, as asthma was defined consistently over three age periods, misclassification due to diagnostic accuracy would be minimized. While this study is limited in utilizing physician diagnosis and medication utilization to determine asthma diagnosis and activity, it demonstrates the patterns of clinically evident disease and remittance in a population-based sample of children between ages 3.5 to 10 years of age.

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Abbreviations

HEDIS	Healthcare Effectiveness Data and Information Set
IQR	interquartile range

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Fig 1.

Developmental trajectory of asthma among 3,352 children ever-diagnosed with asthma before age 10. Children ever-diagnosed with asthma are included in mutually exclusive disease development patterns. The x-axis represents the age periods during which asthma was diagnosed. The y-axis represents the proportion of children in each asthma diagnosis pattern; the row height represents the proportion of children with each disease pattern.