

Original article

Timeliness of diagnosis of asthma in children and its predictors

Background: There is a paucity of literature using medical records to evaluate the timeliness of asthma diagnosis in children and the predictors associated with timeliness of asthma diagnosis.

Methods: Subjects were obtained from a convenience sample of 839 children, aged 5–13 years. We conducted comprehensive medical record reviews for these children to determine their asthma status by applying predetermined criteria for asthma. Predictors were evaluated for an association with timeliness of asthma diagnosis.

Results: Of 839 children, 276 children met the criteria for asthma before 18 years of age. Of these subjects, 97 had timely diagnosis of asthma while 179 did not have timely diagnosis of asthma with the median delay of 3.3 years. Children with definite asthma at the time of index date was three times more timely to be diagnosed with asthma [hazard ratios (HR) 3.3, 95% CI: 2.43–4.47, $P < 0.001$], compared to those with probable asthma. Children with a family history of asthma were more timely to be diagnosed with asthma (HR 1.36, 95% CI: 1.03–1.8, $P = 0.031$). Children with exercise-induced wheezing or bronchospasm were more timely to be diagnosed with asthma (HR 1.79, 95% CI: 0.95–3.36, $P = 0.07$), compared to those with spasmodic (or bronchospastic) cough.

Conclusions: Many asthmatic children are not diagnosed with asthma in a timely manner, especially in those without the commonly recognized factors associated with asthma. Health care providers need to be reminded that asthma can still occur in those without commonly recognized risk factors. Asthma guidelines need to emphasize this aspect.

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A number of studies have assessed asthma diagnosis among children and adolescents with asthma symptoms and found that asthma is frequently underdiagnosed (1–5). Despite the availability of the National Asthma Education and Prevention Program (NAEPP) guidelines in the US since 1991 and the Global Initiative for Asthma (GINA) in 1992, underdiagnosis of asthma appears to continue and the national and international efforts to reduce under or untimely diagnosis of asthma appear to have resulted in little impact (6).

However, such an untimely diagnosis of asthma becomes a significant concern if it results in delays in accessing therapeutic and preventive health services for asthma and/or if such a delay in treatment for asthma in children adversely affects asthma morbidity, lung function, and quality of life. Indeed, several studies reported that undiagnosed children with asthma were much less likely to receive appropriate treatments for asthma (1, 4, 6). Although a long-term disease-modifying effect by early treatment with inhaled corticosteroids is still con-

troversial, data from the Childhood Asthma Management Program trial (CAMP) and other studies clearly support that treatments for asthma, e.g. inhaled corticosteroid therapy, provide significant benefits (7–13). Thus, there is evidence that both failure to diagnose and untimely diagnosis of asthma can result in the lack of or the delay in treatment of asthma, which might adversely affect patients' various health outcomes.

However, despite these compelling data about underdiagnosis of asthma and its adverse effects on asthma outcomes, there is a paucity of literature using medical records to evaluate the timeliness of asthma diagnosis in children and the predictors associated with timeliness (or delay in) of asthma diagnosis. Most previous studies, if not all, based their findings on survey data from patients or their parents, not by medical records. This is primarily due to the difficulty determining one's diagnosis of asthma in a setting without a unified, comprehensive medical record system for research among health care providers. Therefore, using medical records in assessing the extent of under or untimely diagnosis of asthma and its associated predictors is necessary and, to our knowledge, this is the first study that examined how timely

Abbreviations: HR, hazard ratios; MMR, measles, mumps, and rubella.

diagnosis of asthma is made and what predictors are associated with such a timeliness of asthma diagnosis.

Patients and methods

Study design and setting

The study was a retrospective cohort study. Rochester, Minnesota, is centrally located in Olmsted County. Olmsted County had a recorded population of 124 277 during the 2000 Census. The population in Olmsted County was 90% white compared to 89% white in Minnesota and 75% in the USA. Characteristics of the City of Rochester and Olmsted County populations were similar to those of the US white population, with the exception of a higher proportion of the working population employed in the health care industry (14, 15). Rochester, Minnesota, is an excellent setting to conduct a retrospective cohort study because medical care is virtually self-contained within the community with a unified medical record system among two medical centers for the past 90 years. This dossier-type medical record contains all inpatient and outpatient data that have been indexed in an automated form since 1935 (16). The recent study on the prevalence of asthma among children and adolescents in kindergarten to 12th grades in Olmsted County, Minnesota showed that 18% of children and adolescents in kindergarten to 12th grades had an asthma diagnosis (17).

Study subjects

The study protocol was approved by the Institutional Review Boards at both the Mayo Clinic and at the Olmsted Medical Center. Study subjects were obtained from a sample of 876 children who were enrolled in the Rochester Family Measles Project, which was a convenience sample recruited from the Rochester School District in Rochester, Minnesota and the details about the original subjects were described in a previous study (18). Briefly, the original study cohort ages 5–13 years were enrolled in the study from schools in Rochester, Minnesota, in 1993. At the time of our study between 2002 and 2006, the study subjects were 14 years or older. Overall, the gender and ethnic distribution of the study cohort are very similar to the demographic characteristics of the 1990 Olmsted County population, where 51% of the residents were female, and 96% were white (19).

Ascertainment of asthma cases

We conducted comprehensive medical record reviews for these children to determine their asthma status by applying predetermined criteria for asthma. These criteria are detailed in Table 1. The criteria for asthma based on medical record review were developed during a previous study by Yunginger et al. (14) and in the original study, to assess the reliability of the criteria, random samples of records were reviewed by different nurse abstractors and analyzed for inter-observer reliability and agreement rates between abstractors and a high degree of concordance was found (20). Previous literatures on asthma epidemiology research have used these criteria to define asthma (18, 21, 22). Briefly, for criterion 1 of the criteria, we reviewed the entire medical records to identify a history of cough with wheezing and/or shortness of breath documented by physicians OR documented wheezing episodes on examination with cough and/or shortness of breathing. Criterion 2 of the criteria was considered to be met when a history of the constellation of the above asthma symptoms or signs had occurred at least twice or more in 3-year periods within the first episode with the documented interim periods without asthma symptoms. When two of eight items of the third criterion were

Table 1. Asthma criteria

Patients were considered to have *definite* asthma if a physician had made a diagnosis of asthma and/or if each of the following three conditions were present. They were considered to have *probable* asthma if only the first two conditions were present:

1. History of cough, dyspnea, and/or wheezing, OR history of cough and/or dyspnea plus wheezing on examination and
2. Substantial variability in symptoms from time to time, or periods of weeks or more when symptoms were absent and
3. Two or more of the following:
 - Sleep disturbance by nocturnal cough and wheeze
 - Nonsmoker (14 years of age or older)
 - Nasal polyps
 - Blood eosinophilia > 300/ μ l
 - Positive wheal and flare skin tests or elevated serum IgE
 - History of hay fever or infantile eczema or Cough, dyspnea, and wheezing regularly on exposure to an antigen
 - Pulmonary function tests showing one FEV₁ or FVC < 70% predicted and another with at least 12% AND 200 ml improvement to an FEV₁, of > 70% predicted
 - Or A methacholine challenge test showing 20% or greater fall in FEV₁
 - Favorable clinical response to bronchodilator

Patients were excluded from the study if any of these conditions were present:

- Pulmonary function tests that showed FEV₁ to be consistently below 50% predicted or diminished DLCO (diffusion capacity)
- Tracheobronchial foreign body at or about the incidence date
 - Hypogammaglobulinemia (IgG < 2.0 mg/ml) or other immunodeficiency disorder
 - Wheezing occurring only in response to anesthesia or medications

The following diseases excluded the patient from study if they occurred prior to the incidence date:

- Bullous emphysema or pulmonary fibrosis on chest radiograph
- PiZZ alpha₁-antitrypsin
- Cystic fibrosis
- Other major chest disease such as juvenile kyphoscoliosis, or bronchiectasis

documented in medical records, we considered the third criterion was met. The dependent variable in this study is whether asthma diagnosis is made at the time when a subject met the asthma criteria. Asthma status, as defined above, was determined first. Subsequently, specific asthma index date and asthma diagnosis date were determined. Asthma index date was defined as the earliest constellation of symptoms, including cough, dyspnea, and/or wheeze, found in the medical record that met the predetermined criteria for asthma in Table 1. Take, for example, a patient with a history of infantile eczema who was seen by a physician for a first episode of upper respiratory infection (URI)-associated wheezing, who at that visit was diagnosed with 'bronchospasm.' The patient did well for several months until their next URI, when they again developed wheezing. They were seen by a physician, responded well to an inhaled bronchodilator, and were diagnosed with URI-associated wheezing. For this particular patient, the time of that second physician visit would be the asthma index date, because they met the following criteria for asthma listed in Table 1: history of wheezing, periods of weeks or more when symptoms were absent, history of infantile eczema, and had a favorable clinical response to bronchodilator.

Timeliness of asthma diagnosis, duration from index date to asthma diagnosis (dependent variable)

We developed specific criteria regarding the time of asthma index date, and these criteria were used to estimate an approximate index

date in cases where the onset of asthma was described in general terms. One example could be a patient who was described as having asthma for a few years. In this study, we consistently considered 'a few years' to indicate 3 years prior to the date of the current physician encounter.

Date of asthma diagnosis was defined as the date of the earliest diagnosis of asthma documented in medical record. We considered asthma diagnosis to be a physician diagnosis of asthma, bronchial asthma, asthmatic bronchitis, allergic or exogenous or extrinsic asthma, intrinsic or endogenous or nonallergic asthma, infectious asthma, or reactive airway disease. An example of the date of asthma diagnosis would be a patient who had recurrent wheezing associated with exercise. The point in time at which the physician lists one of the above asthma diagnoses was considered to be the date of asthma diagnosis.

Independent variables

The independent variables in this study included likelihood of asthma, gender of the study subject, maternal education level, and earliest asthma symptom diagnosis.

Likelihood of asthma. To determine the likelihood of asthma, we further classified the status of asthma at the time the criteria for asthma were met inside the medical record. Patients were classified as having definite or probable asthma, and the criteria for these are also listed in Table 1.

Gender of the study subject. Gender of the study subject was determined by the medical records.

Earliest asthma symptom diagnosis. The medical records for each subject were examined for diagnoses suggestive of asthma but without using the word 'asthma'. These symptom diagnoses included wheezing or bronchospasm, URI-induced wheezing or bronchospasm, exercise-induced wheezing or bronchospasm, and spasmodic (bronchospastic) cough.

Maternal education level. The medicals records for each subject were examined to determine the highest level of education achieved by the subject's mother.

Statistical analysis

The event of interest was the diagnosis of asthma documented in the medical record by a health care provider. Subjects were followed from their asthma index date to the date of their asthma diagnosis or last follow-up prior to 18 years of age and, thus, the subjects were censored at the time of asthma diagnosis, last follow-up day, and 18th birthday. Subjects who met the asthma criteria on the same day as their asthma diagnosis were assigned a duration of 0.5 days. Univariate Cox proportional hazards model were fit to evaluate the association of demographic, family history, asthma symptom-related factors with time to asthma diagnosis. Associations were summarized by calculating hazard ratios (HR) and corresponding ninety-five confidence intervals (95% CI). In this study, because of a relatively small sample size in categories of each variable and being the first (exploratory) study that examined associated predictors with time-liness of diagnosis of asthma based on medical records, we did not run a multivariate model. All calculated p-values were two-sided and P-values less than 0.05 were considered statistically significant. Statistical analyses were performed using the SAS software package (SAS version 8.2; SAS Institute Inc., Cary, NC, USA).

Results

Study cohort

Of the 876 children enrolled in the Rochester Family Measles Project, 839 had research authorization and complete information for this study (Fig. 1). At the time of the original study enrollment of the subjects in the Rochester Family Measles Project, the prevalence of asthma among the subjects was 19% (156 of 839) and 120

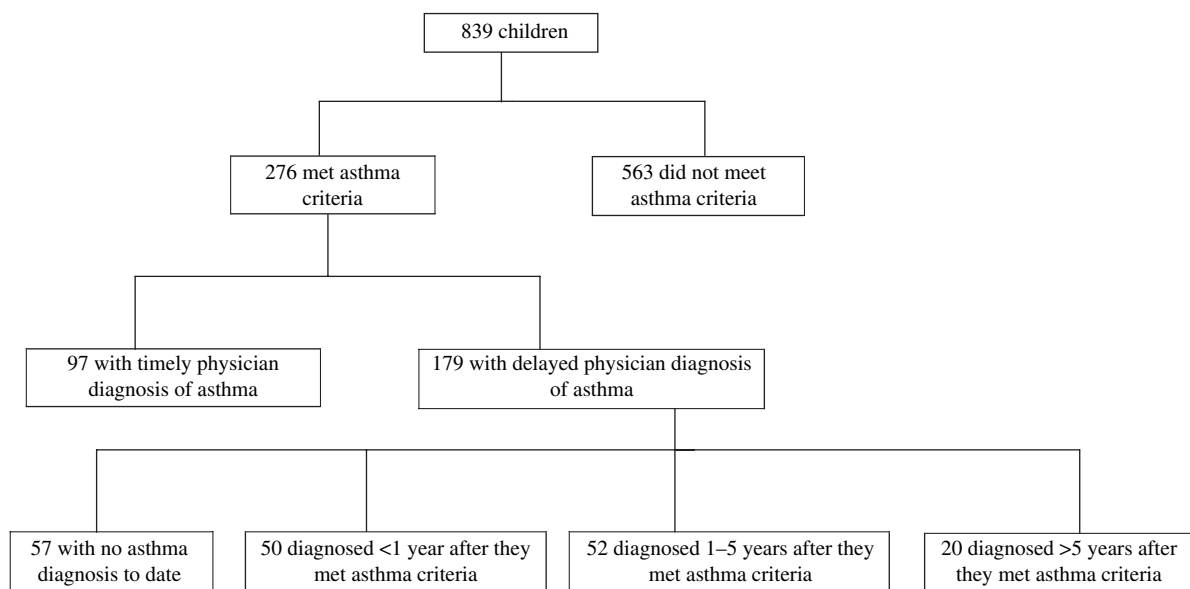


Figure 1. Timely and delayed diagnoses of asthma among study subjects.

additional subjects developed asthma afterward. Thus, of the 839 children, a total of 276 met the criteria for asthma prior to 18 years of age (median age at the index date, 7.9 years; range 0.2–17.7 years), including 150 (54%) males and 259 (94%) Caucasians. Among the 276 children, 97 met the criteria for asthma at the time of their diagnosis (i.e. these children were timely diagnosed) while 179 were not timely diagnosed (i.e. a delay in diagnosis) (65%). Of the 179 children with a median delay of 3.3 years, 57 (32%) had not yet received an asthma diagnosis [27 of the 57 (47%) were followed through age 18], and the median delay for the other 122 children was 1.4 years (mean 2.6 years, interquartile range 0.2–3.8 years).

Table 2 summarizes the demographic and asthma-related variables of patients that were evaluated for an association with timeliness of diagnosis of asthma, based on fitting a Cox proportional hazards model in which patients who have not yet received a diagnosis were censored at the date of their last follow-up prior to age 18. Children who met the criteria for definite asthma were more timely to be diagnosed with asthma (HR = 3.30; 95% CI 2.43–4.47; $P < 0.001$), compared to those with probable asthma. Subjects with a family history of asthma were 1.36 (95% CI 1.03–1.80; $P = 0.031$) times more timely to receive a diagnosis of asthma than those without a family history. The type of earliest asthma symptom was associated with timeliness of asthma diagnosis. Children who presented with exercise-induced wheezing or bronchospasm had a more timely diagnosis of asthma (HR 1.79, 95% CI 1.17–3.61, $P = 0.07$), compared to spasmodic (bronchospastic) cough, whereas the subject who presented with URI-induced wheezing (HR 0.6, 95% CI 0.38–0.96, $P = 0.033$), wheezing or bronchospasm (HR 0.58, 95% CI 0.34–1, $P = 0.049$) were less timely to reach asthma diagnosis, compared to spasmodic (bronchospastic) cough. Children with a more severe asthma (moderate or severe asthma by the NAEPP guidelines) at the time of index date approached to statistical significance in association with more timely diagnosis of asthma (HR 1.59, 95% CI 0.92–2.67, $P = 0.081$), compared to those with mild intermittent asthma. Although not statistically significant, subjects with a family history of atopy were 1.24 (95% CI 0.94–1.65; $P = 0.13$) times more timely to receive a diagnosis than those without a family history of atopy.

Discussion

Our study results demonstrate that a significant proportion of asthmatic children are not timely diagnosed with asthma and the duration of this delay in diagnosis of asthma is concerning. Predictors for timeliness in diagnosis of asthma include likelihood of asthma (meeting definite vs probable asthma criteria), family history of

Table 2. List of predictors evaluated for an association with timeliness of diagnosis of asthma

Variables that impact diagnosis of asthma	<i>n</i> (%)	HR (95% CI)†	<i>P</i> -value‡
Gender			
Male	150 (54.4)	1.00 (0.76–1.31)	0.99
Female	126 (45.6)	Referent	
Age met asthma criteria (years)			
<4	72 (26.1)	Referent	
4 to <8	67 (24.3)	0.83 (0.56–1.20)	0.31
8 to <12	73 (26.4)	0.77 (0.53–1.12)	0.18
≥12	64 (23.2)	1.01 (0.69–1.47)	0.98
Caucasian			
Unknown	8	n/e	
No	9 (3.4)	Referent	
Yes	259 (96.6)	1.00 (0.45–2.26)	0.99
Low birth weight (<2500 g)			
Unknown	65	n/e	
No	204 (96.7)	1.49 (0.61–3.62)	0.38
Yes	7 (3.3)	Referent	
Season of birth			
Winter	93 (33.7)	1.13 (0.79–1.63)	0.50
Spring	71 (25.7)	1.10 (0.75–1.62)	0.63
Summer	63 (22.8)	Referent	
Fall	49 (17.8)	1.03 (0.67–1.59)	0.89
Education of mother			
Unknown	105	n/e	
Less than high school	2 (1.2)	n/e	
High school graduate	21 (12.3)	1.04 (0.59–1.82)	0.90
Some college	81 (47.4)	1.03 (0.71–1.49)	0.86
College degree	67 (39.2)	Referent	
Family history of asthma			
Unknown	16	n/e	
No	126 (48.5)	Referent	
Yes	134 (51.5)	1.36 (1.03–1.80)	0.031
Family history of atopy			
Unknown	21	n/e	
No	111 (43.5)	Referent	
Yes	144 (56.5)	1.24 (0.94–1.65)	0.13
Likelihood of asthma			
Probable	115 (41.7)	Referent	
Definite	161 (58.3)	3.30 (2.43–4.47)	<0.001
Asthma severity at date met criteria			
Unknown	31	n/e	
Mild intermittent	151 (61.6)	Referent	
Mild persistent	77 (31.4)	1.11 (0.82–1.50)	0.51
Moderate (<i>n</i> = 13) or severe (<i>n</i> = 4)	17 (6.9)	1.59 (0.95–2.67)	0.081
Earliest symptom diagnosis			
Unknown	125	n/e	
Wheezing or bronchospasm	33 (21.9)	0.58 (0.34–1.00)	0.049
URI-induced wheezing or bronchospasm	55 (36.4)	0.60 (0.38–0.96)	0.033
Exercise-induced wheezing or bronchospasm	15 (9.9)	1.79 (0.95–3.36)	0.070
Spasmodic (bronchospastic) cough	41 (27.2)	Referent	
Other	7 (4.6)	0.61 (0.24–1.55)	0.30

n/e = not evaluated.

†Obtained from fitting univariate Cox proportional hazards models (the higher hazard ratio is, the more timely the diagnosis of asthma is made).

asthma, and the type of earliest symptoms of asthma at the time of index date.

We found that almost 65% of the children in our study had a delay in asthma diagnosis, and of those, 32% remained undiagnosed whose asthma status had not been documented as of their last follow up day documented in medical records or 18th birthday. Of those with a known duration of delay in asthma diagnosis, the median delay were 1.4–3.3 years, which is concerning. Our study results were based on medical records and support previous observations that a number of children experience a delay in asthma diagnosis (1–4, 23). Previous studies suggest that underdiagnosis of asthma varied significantly ranging from less than 5% to 95% depending on gender, age, socioeconomic status, ethnicity, symptom frequency, atopic status, and asthma severity (2–4, 6, 24, 25). Because most previous studies were based on surveys, there are limited data on the specific duration in a lag between index date of asthma and the date for diagnosis of asthma documented in medical records. Although our data did not examine the duration between the onset of asthma symptoms and the diagnosis of asthma, Wright et al. reported that among their study subjects (the Tucson Children's Respiratory Study Cohort) with asthma, there was a significant delay between the onset of asthma symptoms, e.g. wheezing episodes, and diagnosis of asthma (9.0 ± 5 vs 7.3 ± 4.5 years for girls and boys, respectively) based on their survey data. Also, they reported that there was a significant lag between age at first onset of wheezing episode and first use of asthma medication among their study subjects (2.8 vs 1.6 years for girls and boys, respectively). In the literature for adult asthma, a diagnosis of occupational asthma has been reported to be delayed by more than 4 years (26). Therefore, delay in diagnosis of asthma in clinical practice appears to be a real phenomenon underlying delay in treatment for asthma.

We examined what predictors are associated with timeliness of diagnosis of asthma to explore the potential reasons for delay in or timeliness of diagnosis of asthma. We found that definite asthma as a likelihood of asthma status according to our asthma criteria, the presence of family history of asthma, and exercised-induced asthma symptoms as the type of earliest symptoms of asthma at the time of index date were associated with a timely diagnosis of asthma. These appear to be quite understandable. For example, health care providers may feel more comfortable diagnosing a child with asthma symptoms, e.g. exercise-induced wheezing episodes with a family history of asthma/atopy. Castro-Rodriguez et al. formulated a clinical index predicting a risk of asthma in children, which included doctor diagnosed parental history of asthma as a major criteria for asthma (27). There are numerous studies that have reported family history of asthma or atopy as a risk factor for asthma. Thus, children with family history of asthma or atopy are more likely to be diagnosed with asthma by health care

providers whose clinical decisions appear to reflect evidence supported by the literature for some degree. Along these lines, severity of asthma at index date and likelihood of asthma might help clinicians diagnose asthma more promptly, compared to those with mild presentations of asthma symptoms or probable asthma because the components (history of eczema or allergic rhinitis, eosinophilia, and asthma symptoms, wheezing episodes) of the clinical index for asthma formulated by Castro-Rodriguez et al. overlap with our criteria. However, health care providers need to be reminded that, as asthma and atopy can be inherited independently, asthma can occur in children without family history of asthma or atopy and other risk factors listed above (28, 29). In this respect, the conceptual definition of asthma was greatly enhanced in the newly released National Asthma Education and Prevention Program in 2007 but the practical ways to help health care providers make a timely diagnosis of asthma are yet to be addressed. Considering a possibility to operationalize our criteria for asthma, a criteria-based asthma questionnaire or decision-support system facilitating health care providers to make a timely diagnosis of asthma can be considered. A set of questions for parents or health care providers can be developed to determine the asthma diagnosis of a child based on the clinical definition of asthma.

An unexpected finding in this study was a high cumulative incidence of asthma in the study cohort (33% during the first 18 years of life). However, at the time of the original study enrollment of the Rochester Family Measles Project, the prevalence of asthma was 19% (156 of 839) which is close to the prevalence of asthma (18%) among K-12 children and adolescents in our community (17). The reason for the increased identification of asthma status after the study enrollment is not entirely clear. However a recent study by Bisgaard and Szefer et al. reported that a significant proportion of preschool children (32%) experience recurrent clinically-significant asthma-like symptoms (cough, wheezing, and breathlessness) in European countries and the US based on 2700 pediatric subjects. In their study, only 20% of the study population were diagnosed with asthma (30). Thus, our study may not necessarily overrepresent children with asthma and our sampling approach is unlikely to affect our study results.

Other predictors associated with timeliness of diagnosis of asthma such as gender, ethnicity, and socioeconomic status reported by previous studies (4, 6) were not associated with timeliness of diagnosis of asthma in our study. This observation could be a discrepancy in the diagnosis status of asthma between parental report and medical records, although other explanations are possible. In our study setting, sociodemographic factors (i.e. maternal educational level) do not seem to influence the timeliness of diagnosis of asthma by health care providers. Along these lines, the insurance status is unlikely to affect our study results, albeit not available for this study,

because of the less diverse and relatively more affluent nature of our community compared to the general population in the state of Minnesota and the USA.

Strengths of our study include ascertainment of asthma status, index date (incidence date) of asthma, and diagnosis date of asthma by predetermined, established criteria based on comprehensive medical record reviews. We also had the advantage of access to thorough, comprehensive, medical records in a self-contained health care environment with unified medical records systems among health care providers in our community.

There are also, however, limitations in our study. Some limitations are inherent to its retrospective design. Estimating the index date of asthma using the criteria for vague terms for time in our study may not be entirely accurate. However, we believe that medical record reviews are still more accurate and reliable in assessing delay in diagnosis of asthma than parents' self report and it is unlikely to affect the study results because the criteria were applied to both groups of asthmatic children with and without a delay in diagnosis of asthma (i.e. nondifferential misclassification bias). A long-term large prospective study might be difficult and costly in the general pediatric population. It would be worth examining physician-specific variables, such as physician age, number of years in practice, type of training program attended, level of understanding about asthma guidelines, and continuity of care in relation to study outcomes. As

our study population is predominantly Caucasian (94%), our results also may not be generalizable to populations of other races or ethnicity.

In conclusion, diagnosis of asthma is not timely made in children and adolescents and the duration of delay in diagnosis of asthma is concerning. However, untimely diagnosis of asthma appears to occur primarily in children and adolescents who lack the commonly-recognized risk factors for asthma. Thus, health care providers need to be cognizant that asthma can still occur in children without major risk factors for asthma and the new asthma guidelines need to emphasize this aspect.

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Conflicts of interest

The study investigators have nothing to disclose that poses a conflict of interest.

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