

The association between family history of asthma and the prevalence of asthma among US adults: National Health and Nutrition Examination Survey, 1999–2004

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Purpose: To assess the overall prevalence of asthma and the association between family history of asthma and the prevalence of asthma among US adults. **Methods:** We analyzed National Health and Nutrition Examination Survey data from 1999 to 2004 for 15,008 respondents aged 20 years or older with no history of emphysema. We divided respondents into three familial risk groups (high, moderate, and average) on the basis of the number and closeness of relatives, that they reported as having asthma and then assessed the asthma prevalence in each. We also assessed associations between asthma prevalence and age, sex, race/ethnicity, income, body mass index, smoking status, household smoking exposure, and physical activity. **Results:** By our definitions, 2.3% of respondents were at high, 13.0% at moderate, and 84.7% at average familial risk for asthma. The crude prevalence of self-reported lifetime asthma was 11.5% (95% confidence interval [CI]: 10.7–12.3%) among all respondents, and 37.6% (95% CI: 30.4–45.4%), 20.4% (95% CI: 18.2–22.7%), and 9.4% (95% CI: 8.7–10.2%) among those at high, moderate, and average familial risk, respectively. Among all risk factors we looked at, family history had the strongest association with lifetime asthma prevalence, and the association remained significant after adjustments for other risk factors. Compared with average familial risk, the adjusted odds ratios for lifetime asthma were 2.4 (95% CI: 2.0–2.8) for moderate and 4.8 (95% CI: 3.5–6.7) for high familial risk. **Conclusion:** Our findings showed that a family history of asthma is an important risk factor for asthma and that familial risk assessments can help identify people at highest risk for developing asthma. Additional research is needed to assess how health care professionals can use family history information in the early detection and management of asthma. *Genet Med* 2009;11(5):323–328.

Key Words: adult, asthma, prevalence, family history, NHANES

In the United States, 34 million people are affected by asthma, a serious chronic lung condition characterized by episodic bronchoconstriction and chronic inflammation of the airways in response to environmental triggers.¹ Earlier data from the Na-

tional Health and Nutrition Examination Survey (NHANES) showed that the prevalence of asthma among 6- to 11-year-old children increased from 4.8% during 1971–1974 to 7.6% during 1976–1980.² Results from other population-based studies among US children of a broader age range have shown that the prevalence of asthma continued to increase between 1980 and 1995 but has remained level since the mid 1990s.^{1,3,4} Even though asthma mortality and hospitalization rates among the US population have decreased within the last few years,¹ asthma is still a significant public health concern and a growing medical burden in the United States. In 2005, lung conditions, including asthma, ranked 8th among the most prevalent conditions causing activity limitations in the United States. In 2007, asthma accounted for \$19.7 billion in direct and indirect health care costs in this country.⁵ Although numerous studies have attempted to identify risk factors for asthma among children, a few have attempted to do so among adults. Those that have focused on adults have identified older age, female sex, obesity, low socioeconomic status, smoking, and physical inactivity as asthma risk factors.^{6–9} Recent studies have also examined genetic risk factors for asthma. In one such study, the *ADAM33* gene was found to be associated with asthma among white residents of the United Kingdom and the United States.¹⁰ This finding was confirmed in a German population study.¹¹ For epidemiological purposes, however, family history of asthma among close relatives is the tool of choice for assessing the combined effect of shared genes and environment on asthma risk.¹² A family history of asthma has been shown to be significantly associated with asthma risk, especially among children.^{13–15} In many of the studies in which this association has been found, however, either the sample size was limited or “family history” was based only on parental history of asthma.⁹ In this study, we estimated the current prevalence of asthma in a nationally representative population of US adults and the accuracy of a three-tiered familial risk hierarchy in predicting the occurrence of asthma. The results of this study may help establish the utility of family history in identifying adults at increased risk for asthma as a targeted health care effort to facilitate early asthma diagnosis and management.

METHODS

National Health and Nutrition Examination Survey

The NHANES is a national survey conducted annually to assess the health and nutritional status of noninstitutionalized children and adults in the United States. The survey, consisting of an interview and a physical examination, is conducted among a nationally representative sample of approximately 5000 people each year. The interview includes demographic, socioeconomic, dietary, and health-related questions, and the physical examination includes medical, dental, and physiological measurements, as well as diagnostic laboratory tests. The survey has been conducted continuously since 1999, and data are released

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as public-use data files in 2-year increments. For this study, we combined data from six surveys conducted from 1999 to 2004.

The NHANES uses a complex sampling scheme in which participants are randomly selected, although the probability of selection is not the same for all potential participants. For example, those aged 60 years or older, African Americans, and Hispanics are oversampled. To account for the differences in the probability of selection and participation in the different sections of the survey, NHANES assigns participants with statistical weights that must be properly included in the analyses to obtain unbiased estimates. In this study, we first limited potential study subjects to adult NHANES participants aged 20 or older who completed household interview ($N = 15332$). Those who answered “don’t know” to the question about whether they had ever been diagnosed with asthma or “yes” to the question “Has a doctor or other health professional ever told you that you had emphysema?” ($N = 324$) were excluded. Among eligible interview samples, 13,925 also participated in the subsequent physical examination. The sample used in the final model in multivariate analysis consisted of 11,202 participants with non-missing data on lifetime asthma question, race/ethnicity, body mass index (BMI), physical activity, smoking, poverty income ratio, and family history of asthma.

Variables

Lifetime asthma

Respondents’ “lifetime asthma” status was based on their answer to the question, “Has a doctor or other health professional ever told you that you have asthma?”

Age at onset of asthma

This variable was based on participants’ response to the question “How old were you when you were first told that you had asthma?”

Familial risk of asthma

Participants aged 20 years or older were asked, “Including living and deceased [relatives], were any of your biological, that is blood, relatives, including grandparents, parents, brothers, or sisters, ever told by a health professional that they had asthma?” Those who answered “yes” were then asked, “Which biological [blood] family member?” Response options were mother, father, mother’s mother, mother’s father, father’s mother, father’s father, brother, sister, other, refused, and do not know. On the basis of these responses, we divided respondents into three familial risk categories: (1) high: those with at least two first-degree relatives with asthma and those with one first-degree and two second-degree relatives with asthma from the same lineage (i.e., either both from their mother’s side or both from their father’s side of the family); (2) moderate: those with one first-degree relative and one second-degree relative with asthma or those with only one first-degree relative with asthma, or those with at least two second-degree relatives with asthma from the same lineage; (3) average: those with no known blood relative or only one second-degree relative with diagnosed asthma.¹⁶

Covariates

Covariates were age (six age groups, by decade, from 20 to 29 to ≥ 70 years); race/ethnicity (non-Hispanic white, non-Hispanic black, and Mexican American); poverty income ratio (ratio of family income to federal poverty level for pertinent family size (≤ 1 and > 1)); BMI category (< 18.5 , 18.5 – 24.9 , 25 – 29.9 , and ≥ 30); leisure time physical activity level in the previous 30 days (inactive [no LPTA], somewhat active

[weekly, < 60 minutes of vigorous activity or < 150 minutes of moderate activity], and active [weekly, ≥ 60 minutes of vigorous activity or ≥ 150 minutes of moderate activity]); education (less than high school, high school, and more than high school); smoking status (nonsmoker [smoked fewer than 100 cigarettes in lifetime], former smoker [smoked at least 100 cigarettes in lifetime but was not smoking at the time of the interview], and current smoker [smoked at least 100 cigarettes in lifetime and smoking at time of interview]); and household smoking exposure (yes, no).

Statistical analysis

The examination sample weights were used in most analyses. For the initial bivariate analyses of lifetime asthma and variables that had been collected in the household interview, the interview weights were used as recommended in the NHANES analytic guidelines.¹⁷ We used SAS version 9.1 (SAS Institute Inc., Cary, NC) to conduct data management and SUDAAN (Research Triangle release 9.0.1, Research Triangle Park, NC, 2007) to account for the complex sample design of the survey in our statistical analyses. We constructed multiple linear regression models to assess the association between family history of asthma and age of asthma onset and estimated predicted marginals (adjusted means) for respondents’ age at the time of asthma onset. A test for linear trend was used to assess the adjusted mean age at asthma onset among people with asthma at each increasing level of familial risk. We used logistic regression models to estimate odds ratios and produced 95% confidence intervals (95% CIs) for all odds ratios and prevalence estimates. In all multiple logistic regression models, age, BMI, and poverty income ratio were included as continuous variables.

RESULTS

Of the 15,008 respondents in our study sample, 1,549 recalled having been diagnosed with asthma during their lifetime. The estimated crude prevalence of lifetime asthma was 11.5% (95% CI: 10.7–12.3%); however, as expected, the prevalence varied significantly by familial risk category: 9.4% (95% CI: 8.7–10.2%) among those at average familial risk, 20.4% (95% CI: 18.2–22.7%) among those at moderate familial risk, and 37.6% (95% CI: 30.4–45.4%) among those at high familial risk. Risk for asthma was also positively associated with being young, being female, being a non-Hispanic black, having a family income below the poverty threshold, having a BMI of 30 or above, living with a smoker, being a smoker, and being physically inactive (Table 1).

The results of the univariate logistic regression modeling showed that the crude odds of having a history of asthma were 2.5 (95% CI: 2.1–2.9) times higher among people at moderate familial risk and 5.8 (95% CI: 4.2–8.0) times higher among those at high familial risk than it was among those at average familial risk.

We estimated that 84.7% of US adults had an average, 13.0% had a moderate, and 2.3% had a high familial risk for asthma. As shown in Figure 1, familial risk was also positively associated with asthma prevalence in all risk-factor subgroups, indicating familial risk for asthma did not interact with other asthma risk factors. (There were no participants with a BMI < 18.5 and high familial risk of asthma.)

Figure 2 shows how estimated adjusted odds ratios produced with our multiple logistic regression models changed little as we added covariates to the model in the following order: race/ethnicity, sex, BMI, age, physical activity level, smoking status, and poverty/income ratio. The relative stability of the estimated adjusted odds ratios indicates that the risk factors considered

Table 1 Crude prevalence of lifetime asthma among US adults by demographic factors and familial risk, NHANES 1999–2004

Characteristics and risk factors	Sample, N (%)	Lifetime asthma	
		Prevalence (95% CI)	Crude odds ratio (95% CI)
Age (yr)			
20–29	2,793 (18.6)	14.4 (12.4–16.7)	2.0 (1.6–2.6)
30–39	2,557 (17.0)	11.7 (10.2–13.4)	1.6 (1.2–2.0)
40–49	2,461 (16.4)	11.3 (9.8–13.1)	1.5 (1.2–2.0)
50–59	1,836 (12.2)	11.2 (9.8–12.9)	1.5 (1.2–1.9)
60–69	2,266 (15.1)	10.6 (9.1–12.3)	1.4 (1.2–1.8)
≥70 ^a	3,095 (20.6)	7.7 (6.5–9.1)	
Sex			
Male ^a	7,034 (46.9)	9.7 (9.0–10.5)	
Female	7,974 (53.1)	13.2 (12.1–14.3)	1.4 (1.3–1.6)
Race/ethnicity			
Non-Hispanic white	7,583 (54.7)	11.8 (10.9–12.8)	2.1 (1.6–2.6)
Non-Hispanic black	2,920 (21.1)	13.0 (11.8–14.4)	2.3 (1.8–3.0)
Mexican American ^a	3,352 (24.2)	6.1 (5.0–7.5)	
Education			
Less than high school	4,886 (32.7)	10.3 (9.0–11.8)	0.8 (0.7–1.0)
High school	3,558 (23.8)	10.7 (9.6–12.0)	0.9 (0.7–1.0)
More than high school ^a	6,506 (43.5)	12.3 (11.2–13.6)	
Poverty income ratio			
≤1	2,556 (18.9)	14.6 (12.9–16.4)	1.4 (1.2–1.6)
>1 ^a	10,982 (81.1)	11.1 (10.4–11.9)	
BMI			
<18.5	205 (1.5)	13.0 (7.6–21.3)	1.2 (0.7–2.2)
18.5–24.9 ^a	4,085 (30.4)	11.0 (9.8–12.4)	
25.0–29.9	4,821 (35.9)	9.9 (8.8–11.1)	0.9 (0.7–1.1)
≥30.0	4,324 (32.2)	14.4 (12.9–15.9)	1.4 (1.1–1.6)
Smoking in household			
Yes	2,973 (20.1)	12.7 (11.2–14.4)	1.2 (1.0–1.4)
No ^a	11,798 (79.9)	11.1 (10.3–12.0)	
Smoking status			
Current smoker	3,201 (21.4)	11.8 (10.4–13.3)	1.1 (1.0–1.3)
Former smoker	3,908 (26.1)	13.1 (11.9–14.4)	1.3 (1.1–1.5)
Nonsmoker ^a	7,862 (52.5)	10.6 (9.6–11.6)	
Leisure time physical activity			
Inactive	3,507 (24.0)	12.0 (10.4–13.7)	1.6 (1.2–2.1)
Somewhat active	9,919 (67.8)	11.7 (10.8–12.6)	1.6 (1.2–2.1)
Active ^a	1,202 (8.2)	7.7 (6.1–9.7)	
Familial risk for asthma			
High	300 (2.0)	37.6 (30.4–45.4)	5.8 (4.2–8.0)
Moderate	1,778 (11.8)	20.4 (18.2–22.7)	2.5 (2.1–2.9)
Average ^a	12,927 (86.2)	9.4 (8.7–10.2)	
Overall	15,008	11.5 (10.7–12.3)	

^aReference group.

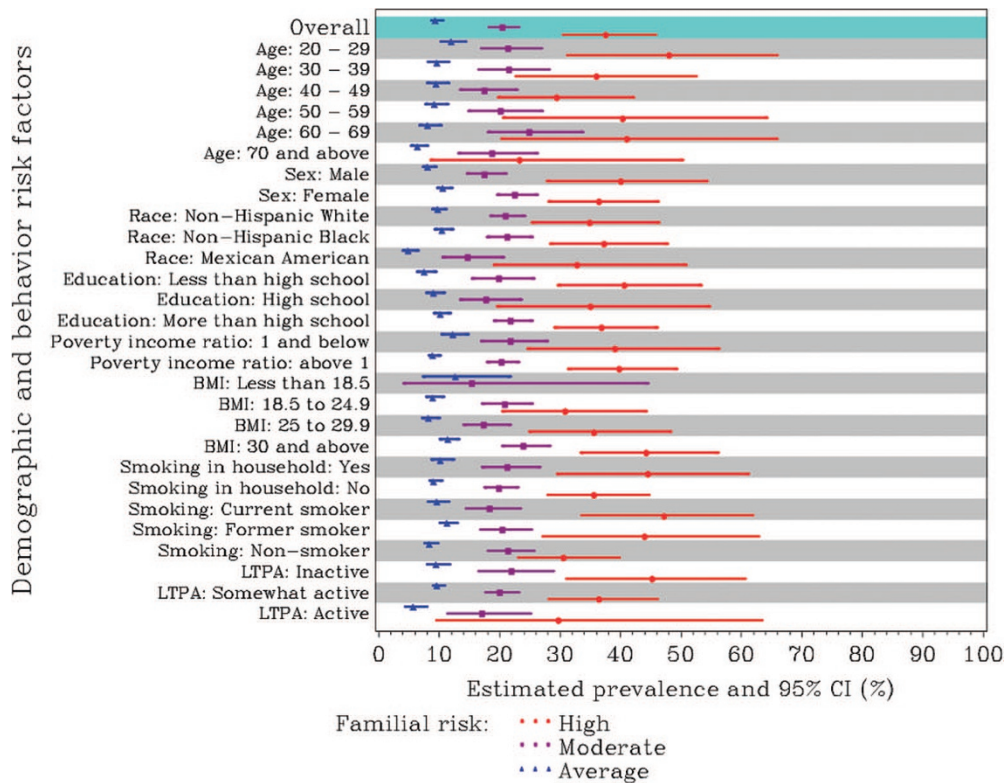


Fig. 1. Prevalence of lifetime asthma and 95% CI according to three risk levels of family history and risk factors in US adults aged 20 and older (NHANES, 1999–2004). There were no participants in the lowest BMI category with a high familial risk. Blue triangles and bars = average familial risk; purple squares and bars = moderate familial risk; red dots and bars = high familial risk.

had little effect on the association between familial risk for asthma and the risk of having the disease. After adjusting for all of these risk factors, we found that, people at moderate and high familial risk for asthma were 2.4 (95% CI: 2.0–2.8) times and 4.8 (95% CI: 3.5–6.7) times more likely to suffer from asthma, respectively, than were people at average familial risk.

We also found that the mean age of people with asthma at the time of the onset of their asthma varied significantly by familial risk category: 17.0 years among those at high familial risk, 19.4 years among those at moderate familial risk, and 22.3 years among those at average familial risk (*P* value for trend, 0.008) after adjustments for other variables (Fig. 3).

DISCUSSION

Our estimate of the overall prevalence of asthma among US adults during 1999–2004 (11.5%) was comparable with previous national estimates. For example, the American Lung Association, using Behavioral Risk Factor Surveillance System (BRFSS) data, estimated that the annual prevalence ranged from 10.4% in 2000 to 13.3% in 2004,¹ and annual estimates based on National Health Interview Survey (NHIS) data for 2000 through 2004 ranged from 9.3 to 9.9%.^{18–22} Moreover, the American Lung Association’s 2006 estimate that 4.2% of the US population (children and adults) had experienced an asthma attack¹ within the preceding year was exactly the same percentage we estimated on the basis of 1999–2004 NHANES data (data not shown). The BRFSS and the NHIS datasets, however, do not include data on family history of asthma. Using the

NHANES data, we were able to stratify people’s familial risk for asthma according to the number and lineage (maternal, paternal) of their first- and second-degree relatives with asthma. The three-tiered familial risk methodology that we used was first introduced by Scheuner et al.¹⁶ in 1997 and has since been used with NHANES data to assess familial risk for diabetes^{23,24} and osteoporosis.²⁵ Our finding that the prevalence of asthma was two times higher among US adults with a moderate familial risk and six times higher among those with a high familial risk than it was among those with an average familial risk suggests that family history of asthma can be a useful tool in identifying people most likely to benefit from asthma early detection.

Asthma is often overlooked in adults and therefore diagnosed late. Identifying people with a family history may facilitate their earlier diagnosis and treatment. In a study among children, London et al.²⁶ found that early-onset persistent asthma was strongly associated with a parental history of asthma and allergy. Our similar finding that familial risk for asthma was inversely related to the age of people with asthma at the onset of their condition suggests that information about family history of asthma could help identify people at elevated risk for early onset of the disease. The inverse association between familial risk and people’s age at asthma onset may reflect an actual earlier occurrence of asthma among asthma patients with a stronger genetic component, a greater likelihood that the disease will be identified early by people with a strong family history of asthma because they are likely more aware of symptoms, or both. This association could also be affected by survey respondents’ age at interview because we found that, among people with

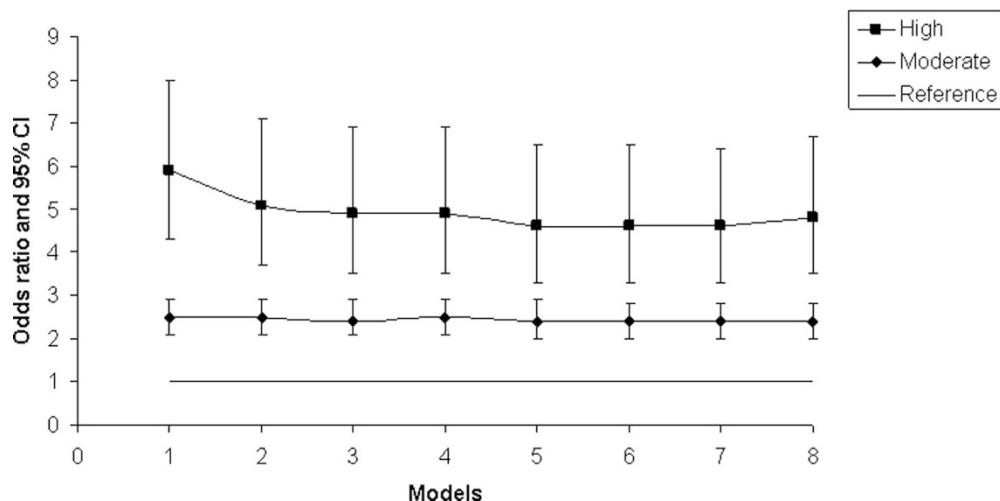


Fig. 2. Adjusted odds ratios according to familial risk level of asthma (NHANES, 1999–2004). The models are (adjusted for): Model 1 (unadjusted); Model 2 (race/ethnicity); Model 3 (race/ethnicity, sex); Model 4 (race/ethnicity, sex, BMI); Model 5 (race/ethnicity, sex, BMI, age); Model 6 (race/ethnicity, sex, BMI, age, leisure time physical activities); Model 7 (race/ethnicity, sex, BMI, age, leisure time physical activities, smoking status); Model 8 (race/ethnicity, sex, BMI, age, leisure time physical activities, smoking status, poverty income ratio). Squares = high familial risk; diamonds = moderate familial risk; continuous line = average familial risk (reference).

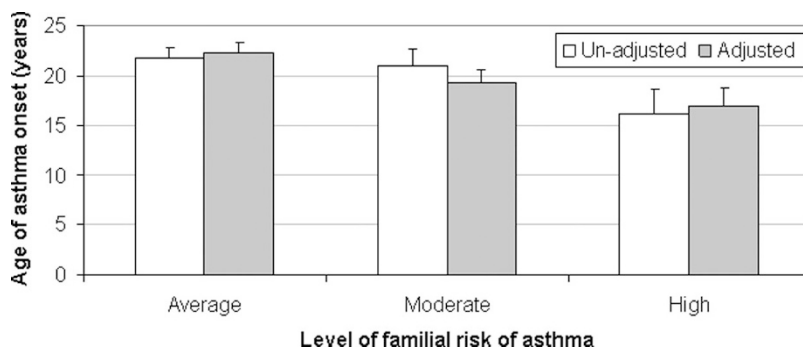


Fig. 3. Adjusted and unadjusted mean age of asthma onset by familial risk of asthma in adults aged 20+ years with a history of asthma, NHANES 1999–2004. The multiple linear regression model is adjusted for age, race, gender, BMI, poverty income ratio, smoking status, and leisure time physical activity level. Empty bars = unadjusted estimates of mean age of asthma onset; light gray bars = adjusted estimates of mean age of asthma onset.

lifetime asthma, age was positively associated with age at asthma onset (asthma is now diagnosed at younger ages than in the past, data not shown); however, the inverse association between age at onset and familial risk for asthma remained statistically significant even after adjustments for age and other influential factors in our multiple regression model. Longitudinal studies, however, will be necessary to confirm the relationship between family history of asthma and how soon the onset of asthma occurs.

Some studies have shown that a maternal family history of asthma is associated with a stronger risk for asthma than a paternal family history.^{27,28} However, we found no significant difference in asthma prevalence between people with a maternal family history and those with a paternal family history of asthma, although the sample size was too small for us to make any definitive conclusions about the relative importance of maternal and paternal family histories.

Knowledge of the risk associated with a family history of asthma might help those with a moderate or high familial risk and their health care providers to be alert for early signs of

asthma and to respond quickly with treatment and amelioration of environmental risk factors. According to the Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR 3) by the National Heart, Lung, and Blood Institute, family history can help physicians to distinguish infants whose wheezing is the temporary result of viral infections from infants whose wheezing is indicative of the future development of chronic asthma and thus to help reduce the exposure of high-risk infants to environmental triggers that exacerbate asthma.²⁹ However, the EPR 3 also states that although a family history of asthma or atopic diseases is associated with asthma, it is not the major indicator of asthma risk. Part of the reason that the EPR 3 does not consider family history to be a key indicator of asthma risk is because of its low positive predictive value. In our study, the a priori chance of a person having asthma in the general US adult population is 11.5%. When factoring in family history, this chance increases to 23.0% for moderate or high and 37.6% for just high familial risk. The diagnosis of asthma is often delayed because its most common

symptoms are nonspecific and often attributed to respiratory infections. If clinicians are aware that patients have a family history of asthma they may be more likely to ask patients about asthma symptoms that may have otherwise gone undetected and thus to diagnose asthma and initiate asthma treatment and environmental controls earlier. Two recent long-term observational studies have shown that early diagnosis of asthma and initiation of inhaled corticosteroids among adults may prevent subsequent declines in lung function.^{30,31}

The main strength of this study was our use of data from a nationally representative survey of the US population, which allowed us to produce reliable population estimates. However, within the period of 1999–2004, NHANES data did not include objective measures of asthma severity such as the skin test sensitization and pulmonary function test results, which would have been useful in our study. The major limitations of our study are the completeness and the validity of the measurement of family history of asthma. In adults this is particularly difficult because NHANES did not sample extended families, and most second degree relatives were not included in the survey. In addition, asthma is often under diagnosed because of the intermittent nature of its symptoms which often recede before the patient is examined by a medical professional and because the most common asthma symptoms, cough and wheeze, are often attributed to respiratory infections. These limitations might bias our associations, but we think they would make them weaker not stronger. Another limitation is that most of the data we used were based on self-reports of survey participants and therefore subject to recall bias. For example, those with physician-diagnosed asthma may have been more likely to identify relatives with asthma and therefore provide more detailed family history data. Finally, although we excluded respondents with emphysema, we did not exclude those with chronic bronchitis because the diagnoses of asthma and chronic bronchitis may overlap. Approximately 2.1% of study subjects reported that they had been diagnosed with both asthma and chronic bronchitis. Although our inclusion of people with chronic bronchitis may have introduced some bias into our results, this bias should have been quite small after we controlled for smoking in the logistic regression models, given that 80–90% of chronic bronchitis cases are due to smoking.³²

Our finding that family history of asthma is an independent risk factor for the disease suggests that family history is one of a number of important tools in identifying at-risk populations most likely to benefit from preventive efforts to reduce their risk of asthma through proper environmental modifications. It could be especially valuable in helping clinical practitioners decide whether to diagnose isolated wheezing episodes as asthma. However, more empirical evidence is needed on how to use family history as a tool for the early diagnosis and management of asthma and whether the use of family history in identifying patients at high risk for asthma will lead to overall reduction in rates of asthma-related morbidity and mortality.

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