



Influences of Asthma and Household Environment on Lung Function in Children and Adolescents

The Third National Health and Nutrition Examination Survey

Robert S. Chapman¹, Wilbur C. Hadden², and Susan A. Perlin¹

¹ Office of Research and Development, National Center for Environmental Assessment, Environmental Protection Agency, Research Triangle Park, NC.

² National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD.

Received for publication October 8, 2002; accepted for publication January 22, 2003.

The authors examined influences of asthma and household environment (passive smoking, use of a gas stove, and having a dog or cat) on five measures of spirometric lung function among 8- to 16-year-old subjects, as measured cross-sectionally in the Third National Health and Nutrition Examination Survey (NHANES III) (1988–1994). In regression models, independent variables included asthma status, household environmental factors, age, and anthropometric measurements. Regression analyses were weighted by the NHANES III examination sample weighting factor, and results were adjusted for clustering in the sampling design. There were distinct sex differences in the results. In girls, lung function was lowest among active asthmatics taking prescription respiratory medicine, whereas lung function in other active and inactive asthmatics did not differ greatly from that in nonasthmatics. In boys, however, all groups of asthmatics had substantially lower lung function than nonasthmatics. Differences in lung function between active asthmatics and nonasthmatics were stable with increasing age. However, the lung function of inactive asthmatic girls and boys returned to and diverged from nonasthmatics' levels, respectively. In asthmatic girls, passive smoking was associated with reduced lung function; having a dog or cat was associated with increased lung function; and gas stove use was associated with reduced lung function among subjects not taking prescription respiratory medicine.

air pollution, indoor; asthma; environmental health; environmental pollutants; respiratory physiology; spirometry; tobacco smoke pollution

Abbreviations: FEF_{25–75}, forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FEV₁, first-second forced expiratory volume; FVC, forced vital capacity; NHANES III, Third National Health and Nutrition Examination Survey; Th2, T-helper cell type 2.

The National Health and Nutrition Examination Surveys have been conducted since the 1970s by the National Center for Health Statistics. These surveys characterize the health and nutritional status of the US population. They are cross-sectional and employ a complex stratified, multistage probability sampling design. They collect extensive information on health and nutritional status, demographic and socioeconomic factors, household characteristics, and other factors. Thus, they offer investigators the opportunity to assess influences of host and environmental factors on health-related outcomes on a national scale.

The Third National Health and Nutrition Examination Survey (NHANES III) was conducted from 1988 to 1994. A detailed description of the design of NHANES III can be found elsewhere (1). The NHANES III examination included measurement of spirometric lung function, deficits in which can reflect pulmonary air flow limitation (obstruction). In adults, obstructive spirometric deficits are strongly associated with smoking and with premature mortality (2–4). In both children and adults, such deficits are also associated with obstructive respiratory disorders such as asthma and chronic obstructive lung disease. The

Reprint requests to Dr. Susan A. Perlin, National Center for Environmental Assessment, Office of Research and Development (8623-D), Environmental Protection Agency, 1200 Pennsylvania Avenue NW, Washington, DC 20460 (e-mail: perlin.susan@epamail.epa.gov).

TABLE 1. Unweighted and weighted characteristics of all subjects aged 8–16 years included in data analysis, Third National Health and Nutrition Examination Survey ($n = 3,230$), 1988–1994

	Unweighted data (both sexes)		Weighted percentages		
	No.	%	Both sexes	Girls	Boys
Reported ever diagnosis of asthma	309	9.6*	12.1	10.8	13.4
Active asthma	218	6.7	8.9	8.5	9.3
Onset at <3 years of age	83	38.1†	29.9†	25.7†	33.5†
Onset at ≥3 years of age	135	61.9†	70.1†	74.3†	66.5†
Took prescription respiratory medication in past month‡	78	35.8†	41.4†	35.3†	46.8†
Antiasthmatics/bronchodilators	71	32.6†	39.0†	32.8†	44.5†
Steroids	16	7.3†	8.5†	8.4†	8.6†
Inactive asthma	91	2.8	3.2	2.3	4.1
Onset at <3 years of age	47	51.6§	42.8§	55.8§	35.8§
Onset at ≥3 years of age	44	48.4§	57.2§	44.2§	64.2§
Mean age (years)	12.0		12.2		
Sex					
Girls	1,649	51.1	49.0		
Boys	1,581	48.9	51.0		
Ethnicity					
Non-Hispanic White	856	26.5	68.9		
Non-Hispanic Black	1,129	35.0	15.1		
Mexican American	1,119	34.6	8.5		
Non-Mexican Hispanic living in Northeast region	44	1.4	2.1		
Non-Mexican Hispanic not living in Northeast region	43	1.3	2.5		
Other	39	1.2	3.0		
No. of smokers in household					
0	1,973	61.1	62.9		
1	833	25.8	21.9		
≥2	424	13.1	15.1		
Use of a gas stove for cooking					
Does not use gas stove	1,318	40.8	55.5		
Uses gas stove	1,912	59.2	44.5		
Annual income <\$20,000	1,612	49.9	31.2		
Pet ownership					
Dog	734	22.7	33.0		
Cat	523	16.2	26.7		
Involved in ≥3 athletic teams or organized exercise programs	474	14.7	18.8		
FVC¶ or FEV ₁ ¶ not reproducible	190	5.9	3.6		

* Unweighted total asthma prevalences were 7.6% in girls and 11.6% in boys.

† Percentage of active asthmatics.

‡ The types of prescription respiratory medication included were "adrenal corticosteroids" (Food and Drug Administration code 1032), "antiasthmatics/bronchodilators" (code 1940), "respiratory tract" medication (code 1900), and "steroids-inhalation/nasal" (code 1947).

§ Percentage of inactive asthmatics.

¶ FVC, forced vital capacity; FEV₁, first-second forced expiratory volume.

long-term health consequences of stable spirometric deficits in children and adolescents are not fully understood, but available evidence suggests that they signal respiratory health impairment in adulthood (5–8). It is therefore important to understand influences of host and environmental factors on children's and adolescents' lung function and to ascertain the reversibility of lung function deficits in this age group.

In the present study, we examined the influences of asthma and of three household environmental factors (smoking by household members (household passive smoking), use of a gas stove for cooking, and the presence of a dog or cat in the home) on spirometric lung function in nonsmoking NHANES III subjects aged 8–16 years. We also evaluated whether asthmatics' lung function returned to nonasthmatics' levels with increasing age.

TABLE 2. Weighted distributions of characteristics of subjects aged 8–16 years included in data analysis, by sex and asthma status, Third National Health and Nutrition Examination Survey, 1988–1994

	Weighted mean or percentage with indicated characteristic			
	No asthma reported	Active asthma		Inactive asthma*
		Taking prescription respiratory medication	Not taking prescription respiratory medication	
Girls	(n = 1,524)†	(n = 31)†	(n = 64)†	(n = 30)†
Mean age (years)	12.17 (0.06)‡	11.56 (0.52)	13.08 (0.33)	12.87 (0.32)
Mean age (years) at asthma onset		5.86 (0.51)	4.85 (0.50)	3.36 (0.57)
Wheezing in the past 12 months (%)	10.9	94.4	73.0	53.2
Mean no. of days absent from school in the past 12 months§	5.23 (0.17)	9.42 (1.44)	7.38 (0.87)	7.47 (1.08)
Went to physician or emergency room for wheezing in the past 12 months (%)	5.8	66.7	22.6	21.1
Hospitalized for wheezing in the past 12 months (%)	0.1	10.0	1.2	0.0
Asthma or hay fever in one or both parents (%)				
In mother	13.6	46.4	33.8	11.2
In father	10.9	50.2	37.8	21.8
Either parent	21.4	74.4	66.9	32.4
Both parents	3.2	22.2	4.7	0.7
Positive skin test (%)¶				
Any antigen	36.9	85.4	57.8	38.6
Any indoor antigen	26.9	79.2	38.3	33.3
Any outdoor antigen	24.5	65.1	52.7	32.5
Boys	(n = 1,397)†	(n = 47)†	(n = 76)†	(n = 61)†
Mean age (years)	12.20 (0.07)	12.08 (0.33)	12.29 (0.27)	11.65 (0.34)
Mean age (years) at asthma onset		5.84 (0.59)	4.34 (0.37)	4.13 (0.45)
Wheezing in the past 12 months (%)	9.7	95.9	70.6	11.2
Mean no. of days absent from school in the past 12 months§	5.04 (0.32)	11.59 (1.54)	6.35 (0.81)	3.49 (0.62)
Went to physician or emergency room for wheezing in the past 12 months (%)	5.6	88.1	25.3	6.0
Hospitalized for wheezing in the past 12 months (%)	0.2	20.3	0.6	0.6
Asthma or hay fever in one or both parents (%)				
In mother	15.9	31.4	34.6	10.2
In father	10.8	20.7	7.0	17.1
Either parent	25.6	49.2	41.2	17.9
Both parents	1.1	2.9	0.4	9.4
Positive skin test (%)¶				
Any antigen	48.9	64.6	69.6	58.0
Any indoor antigen	38.9	57.6	51.9	36.0
Any outdoor antigen	32.8	44.8	57.4	46.6

* Among inactive asthmatics, no girls and one boy (unweighted) reported taking prescription respiratory medicine in the past month.

† Unweighted number of subjects.

‡ Numbers in parentheses, standard error.

§ Among an unweighted total of 3,230 subjects, 18 (0.6%) had missing values for days absent from school in the past 12 months.

¶ The allergy skin-test battery included the following 10 antigens: indoor antigens—cat, cockroach, dust mite (*Dermaphagoides fariniae*); outdoor antigens—*Alternaria*, Bermuda grass, ragweed, Russian thistle, rye grass, white oak; food antigen—peanuts. Among an unweighted total of 3,230 subjects, 223 (6.9%) had missing values for allergy skin-test results.

MATERIALS AND METHODS

Data collection

In NHANES III, standardized questionnaire interviews were administered to subjects in their homes and at mobile examination centers, and extensive physical and laboratory examinations were carried out at the mobile examination

centers. Lung function was measured in subjects aged ≥ 8 years. For child subjects aged birth to 16 years, most questionnaire information, including asthma history, was provided by a surrogate respondent, usually the mother. Subjects over the age of 16 years responded for themselves. Preliminary analyses suggested that there were systematic differences between surrogate-reported asthma prevalences

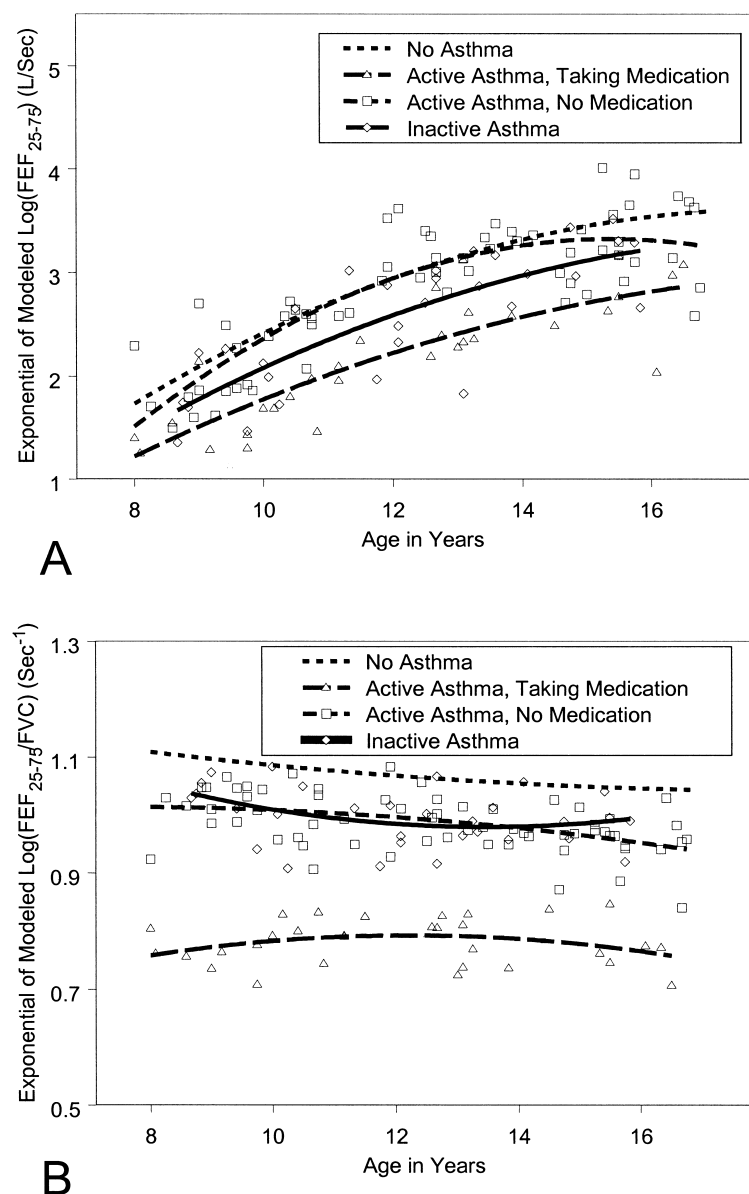


FIGURE 1. Model-predicted lung function among girls aged 8–16 years, by asthma status and age, Third National Health and Nutrition Examination Survey, 1988–1994. Group-specific quadratic regression curves are shown for FEF₂₅₋₇₅ (panel A) and FEF₂₅₋₇₅/FVC (panel B). Individual predictions are shown only for asthmatics. FEF₂₅₋₇₅, forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FVC, forced vital capacity; L/Sec, liters/second.

and self-reported asthma prevalences. Therefore, in this report we consider only subjects aged 8–16 years.

The spirometric testing protocol and quality control procedures followed the spirometry guidelines issued by the American Thoracic Society in 1987 (9). Lung function was measured at the mobile examination centers with dry rolling-seal volume spirometers that recorded data electronically. Subjects performed a minimum of five and a maximum of eight forced vital capacity (FVC) maneuvers. Spirometry was quality-controlled by the National Institute of Occupational Safety and Health (Morgantown, West Virginia) (10). Measurements of FVC and first-second forced expiratory

volume (FEV₁) were judged reproducible if their largest and second-largest values from acceptable maneuvers were within the greater of 5 percent or 100 ml.

Five lung function metrics were examined in data analysis: FVC; FEV₁; forced expiratory flow between 25 percent and 75 percent of FVC (FEF₂₅₋₇₅); and the ratios of FEV₁ and FEF₂₅₋₇₅ to FVC (FEV₁/FVC and FEF₂₅₋₇₅/FVC, respectively). The analyzed FVC and FEV₁ values were the largest volumes achieved in any acceptable FVC maneuver. The FEF₂₅₋₇₅ was taken from the acceptable maneuver with the largest sum of FVC and FEV₁.

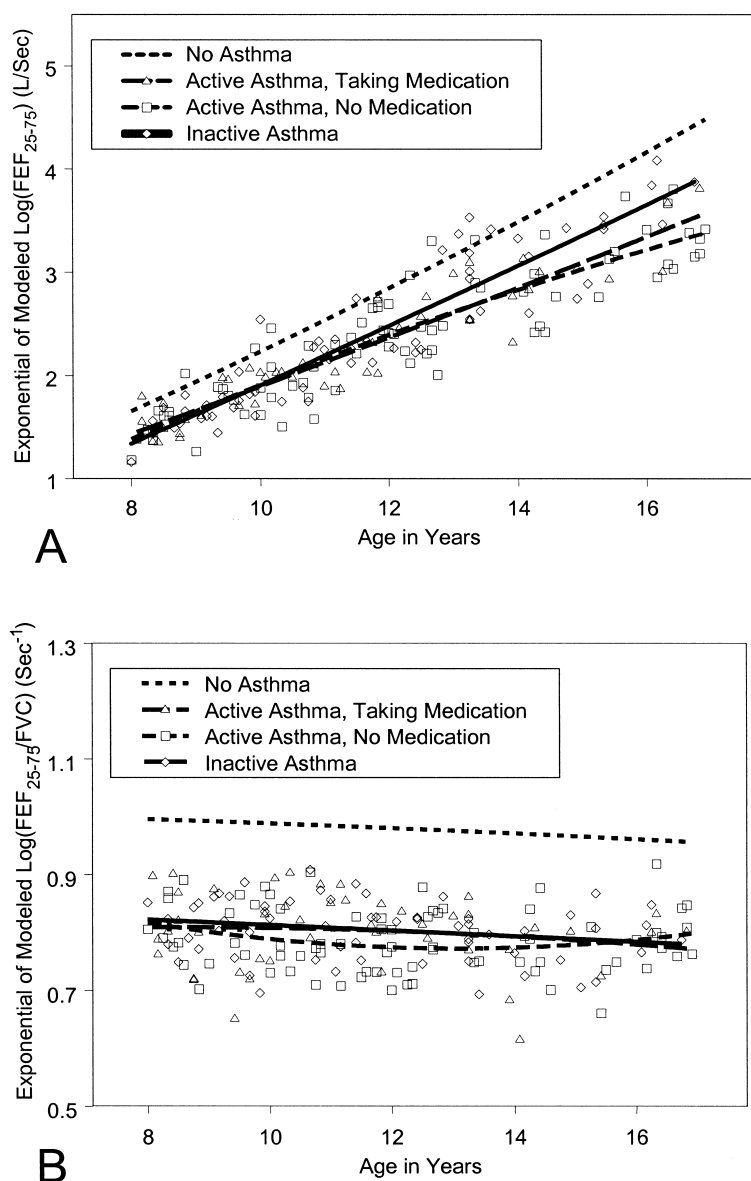


FIGURE 2. Model-predicted lung function among boys aged 8–16 years, by asthma status and age, Third National Health and Nutrition Examination Survey, 1988–1994. Group-specific quadratic regression curves are shown for FEF_{25-75} (panel A) and FEF_{25-75}/FVC (panel B). Individual predictions are shown only for asthmatics. FEF_{25-75} , forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FVC, forced vital capacity; L/Sec, liters per second.

Deficits in all of these metrics except FVC reflect reduced patency of the lung's airways, with resulting air flow limitation (obstruction). A selective deficit in FEV_1 reflects obstruction mainly of larger (proximal) airways. FEF_{25-75} detects small-airways obstruction more sensitively than does FEV_1 . Persons with purely obstructive airways disorders generally achieve normal FVC, though slowly. Division of FEV_1 and FEF_{25-75} by FVC provides standardization for lung size beyond that provided by statistical adjustment for age and anthropometric measurements.

Data analysis

Questionnaire respondents were asked whether a doctor had ever told them that they had asthma and, if so, whether they still had asthma. Subjects who answered "yes, yes" and "yes, no" were classified as having active and inactive asthma, respectively. Data inspection revealed that mothers reported a higher prevalence of active asthma than did other questionnaire respondents. Analysis was thus restricted to subjects for whom the mother responded. Nonasthmatic subjects for whom the mother reported wheezing without

TABLE 3. Model-predicted lung function among non-Hispanic White girls and boys aged 8–16 years, by asthma status, Third National Health and Nutrition Examination Survey, 1988–1994†

	No asthma	Active asthma		Inactive asthma
		Taking prescription respiratory medication	Not taking prescription respiratory medication	
Girls	(n = 1,524)‡	(n = 31)‡	(n = 64)‡	(n = 30)‡
FVC§ (liters)	2.757	2.763	2.831	2.549***
FEV ₁ § (liters)	2.440	2.249**	2.456	2.221***
FEF _{25–75} § (liters/second)	2.869	2.142***	2.749	2.464***
FEV ₁ /FVC (%)	88.5	81.3***	86.7	87.1
FEF _{25–75} /FVC (per second)	1.040	0.775***	0.971	0.966
Boys	(n = 1,397)‡	(n = 47)‡	(n = 76)‡	(n = 61)‡
FVC (liters)	3.029	3.031	3.050	3.126*
FEV ₁ (liters)	2.622	2.483**	2.482**	2.555
FEF _{25–75} (liters/second)	2.887	2.409***	2.376***	2.478***
FEV ₁ /FVC (%)	86.6	81.9***	81.4***	81.7***
FEF _{25–75} /FVC (per second)	0.953	0.795***	0.779***	0.793***

* $0.05 \leq p < 0.10$; ** $0.01 \leq p < 0.05$; *** $p < 0.01$ (p value for the designated lung function metric and asthma status in relation to no asthma).

† Exponentials of model-predicted values are given at the weighted means of the natural logs of age, standing height, and body mass for Non-Hispanic Whites with triceps skinfold thickness at <90th percentile, no smokers in the home, no use of a gas stove, negative parental history of asthma/hay fever in nonasthmatics, no wheezing in nonasthmatics, annual income $\geq \$20,000$, no dog or cat, and no participation in ≥ 3 organized physical activities, with reproducible FVC and FEV₁ values.

‡ Unweighted number of subjects.

§ FVC, forced vital capacity; FEV₁, first-second forced expiratory volume; FEF_{25–75}, forced expiratory flow between 25 percent and 75 percent of forced vital capacity.

colds but no wheezing in the past 12 months were also excluded.

Respondents were asked about use of prescription respiratory medication in the past month. A history was considered positive if the subject reported taking any of the following: “adrenal corticosteroids” (Food and Drug Administration code 1032), “antiasthmatics/bronchodilators” (code 1940), “respiratory tract” medication (code 1900), or “steroids-inhalation/nasal” (code 1947). Under code 1940, approximately 65 percent, 25 percent, and 10 percent of positive responses were for beta agonists (bronchodilators), theophylline and its derivatives, and cromolyn sodium, respectively.

Information on personal smoking history was obtained through confidential interviews with subjects. The prevalence of personal smoking was strongly positively associated with age. We excluded subjects who were current smokers or had smoked ≥ 5 packs of cigarettes during their lifetime, to avoid the potential confounding of personal smoking effects with effects of age on lung function.

Previous studies have shown sex differences in the effects of asthma and of host and environmental factors on lung function and respiratory symptom prevalence (11–14). We therefore conducted sex-specific analyses. Preliminary analyses showed no appreciable effects of urban versus rural status, day-care attendance, or the presence of any siblings, older siblings, or younger siblings in the NHANES III data

set. Reported use of an exhaust fan had no discernible influence on the effect of using a gas stove for cooking. Among nonasthmatics, there were no appreciable effects of prescription respiratory medication use, wheezing in the past 12 months, or parental history of asthma or hay fever. Therefore, these characteristics were not considered in the final models.

Regression models were constructed. Outcome variables were the natural logarithms of lung function metrics. Data analysis was conducted in three steps. Step 1 was intended to characterize overall influences of asthma on girls’ and boys’ lung function. Step 1 models included three 0/1 dummy variables (main effects) for active asthmatics taking and not taking prescription respiratory medication and for inactive asthmatics. Models also included the following independent covariates: 1) natural log of age in years (age in months/12); 2) anthropometric measures—the natural logs of standing height (cm) and body mass index (weight (kg)/height (m)²) and a dummy variable for exceeding the age- and sex-specific 90th percentile value for triceps skinfold thickness; 3) household environmental factors (all dummy variables)—having one smoker in the home, having two or more smokers in the home, use of a gas stove for cooking, having a dog, and having a cat; 4) ethnicity (all dummy variables)—non-Hispanic Black, Mexican American, non-Mexican Hispanic American living in the Northeast census region (where about half of all Hispanic Americans were Puerto Rican Amer-

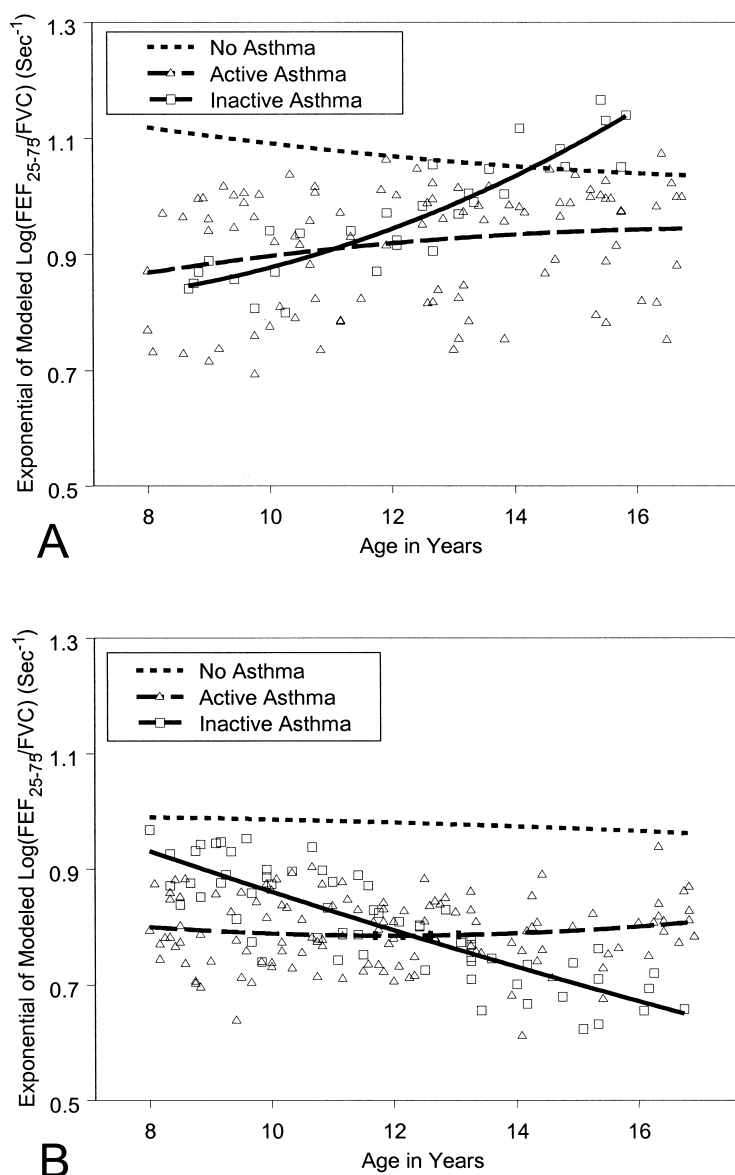


FIGURE 3. Model-predicted FEV_{25-75}/FVC among subjects aged 8–16 years, by asthma status and age, Third National Health and Nutrition Examination Survey, 1988–1994. Group-specific quadratic regression curves, from models with age interaction terms for active asthma and inactive asthma, are shown for girls (panel A) and boys (panel B). Individual predictions are shown only for asthmatics. FEV_{25-75} , forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FVC, forced vital capacity.

ican), non-Mexican Hispanic American living outside the Northeast region (where there were relatively few Puerto Rican Americans), and any other ethnic group except non-Hispanic White; and 5) other dummy variables—annual family income <\$20,000, involvement in ≥ 3 athletic teams or organized exercise programs in the past year, and nonreproducible FVC or FEV_1 .

Step 2 was intended to assess whether active and inactive asthmatic girls' and boys' lung function returned to nonasthmatics' levels with increasing age. Step 2 models included dummy variables and age interaction terms for active and inactive asthmatics and a dummy variable for use of respira-

tory medication in asthmatics. Other covariates were defined as in the step 1 models.

Step 3 was intended to examine influences of household environment on lung function. Factors of interest were household passive smoking, use of a gas stove for cooking, and having a dog or cat. Separate models were constructed for asthmatics and nonasthmatics. Asthmatics' models included dummy variables for inactive asthma and age at asthma onset <3 years among active and inactive asthmatics. These models included dummy variables for use of respiratory medication, using a gas stove and taking respiratory medication, using a gas stove and not taking respiratory

TABLE 4. Model-predicted lung function among non-Hispanic White asthmatic girls and boys aged 8–16 years from models including all asthmatics, by number of smokers in the home, Third National Health and Nutrition Examination Survey, 1988–1994†

	No. of smokers in the home		
	0	1	≥2
Girls	(n = 74)‡	(n = 32)‡	(n = 19)‡
FVC§ (liters)	3.133	3.240	3.058
FEV ₁ § (liters)	2.917	3.021	2.717*
FEF _{25–75} § (liters/second)	3.962	4.027	3.224**
FEV ₁ /FVC (%)	93.1	93.2	88.9*
FEF _{25–75} /FVC (per second)	1.265	1.243	1.054**
Boys	(n = 110)‡	(n = 43)‡	(n = 31)‡
FVC (liters)	3.158	3.213	2.932*
FEV ₁ (liters)	2.609	2.651	2.390*
FEF _{25–75} (liters/second)	2.497	2.651	2.334
FEV ₁ /FVC (%)	82.6	82.5	81.5
FEF _{25–75} /FVC (per second)	0.791	0.771	0.796

* $0.05 \leq p < 0.10$; ** $0.01 \leq p < 0.05$; *** $p < 0.01$ (p value for the designated lung function metric and home smoking category in relation to no smokers in the home).

† Exponentials of model-predicted values are given at the weighted means of the natural logs of age, standing height, and body mass for Non-Hispanic Whites with triceps skinfold thickness at <90th percentile, no use of a gas stove, annual income $\geq \$20,000$, no dog or cat, and no participation in ≥ 3 organized physical activities, with reproducible FVC and FEV₁ values.

‡ Unweighted number of subjects.

§ FVC, forced vital capacity; FEV₁, first-second forced expiratory volume; FEF_{25–75}, forced expiratory flow between 25 percent and 75 percent of forced vital capacity.

medication, and having a dog or cat. Other covariates were defined as in the step 1 models. Nonasthmatics' step 3 models were identical to those of the step 1 models, except that they did not include terms for asthma status or respiratory medication.

All regression analyses employed SUDAAN software (Research Triangle Institute, Research Triangle Park, North Carolina), which calculates sample variances to adjust for stratification and geographic clustering in the sampling design. Regression analyses were weighted by the examination sample weighting factor, which corrects for nonrepresentative sampling on ethnicity, age, sex, and other factors.

Predicted lung function was depicted for selected models; exponentials (antilogs) of modeled log(lung function) were plotted by age using S-Plus 2000 software (Insightful Corporation, Seattle, Washington). Category-specific exponentials were fitted with quadratic regression curves.

RESULTS

Subjects' characteristics are shown in table 1. Weighted ethnic distributions differed from unweighted ones, because Blacks and Mexican Americans were intentionally oversampled in NHANES III. In the analyzed weighted sample, 68.9 percent of subjects were non-Hispanic White, 15.1 percent were non-Hispanic Black, and 8.5 percent were Mexican American. Weighted prevalences of active and inactive asthma were higher in boys than in girls. Weighted preva-

lences of use of prescription respiratory medication in the past month were 1.4 percent, 41.4 percent, and 0.4 percent in nonasthmatics, active asthmatics, and inactive asthmatics, respectively. Among active asthmatics, the weighted prevalence of prescription antiasthmatic/bronchodilator use was substantially higher in boys than in girls. Only 8.5 percent (weighted) of active asthmatics reported using steroids in the past month.

Weighted characteristics are shown, by asthma status, in table 2. Among girls, prevalences of asthma-associated characteristics were quite consistently highest in active asthmatics taking prescription respiratory medicine, second-highest in other active asthmatics, second-lowest in inactive asthmatics, and lowest in nonasthmatics. Among boys, this tendency was less consistent, though prevalences of these characteristics were generally highest in active asthmatics. In both sexes, prevalences of wheezing, visiting a physician or an emergency room for wheezing, and hospitalization for wheezing in the past year were distinctly highest in active asthmatics taking prescription respiratory medication. Among inactive asthmatics, wheezing was more prevalent in girls (53.2 percent) than in boys (11.2 percent).

Results of the step 1 analyses are summarized in table 3 and figures 1 and 2. Table 3 shows model-predicted lung function for non-Hispanic Whites and p value levels for each lung function metric in each asthmatic group in relation to nonasthmatics. Figures 1 and 2 show predicted FEF_{25–75} and FEF_{25–75}/FVC values in all girls and boys, respectively.

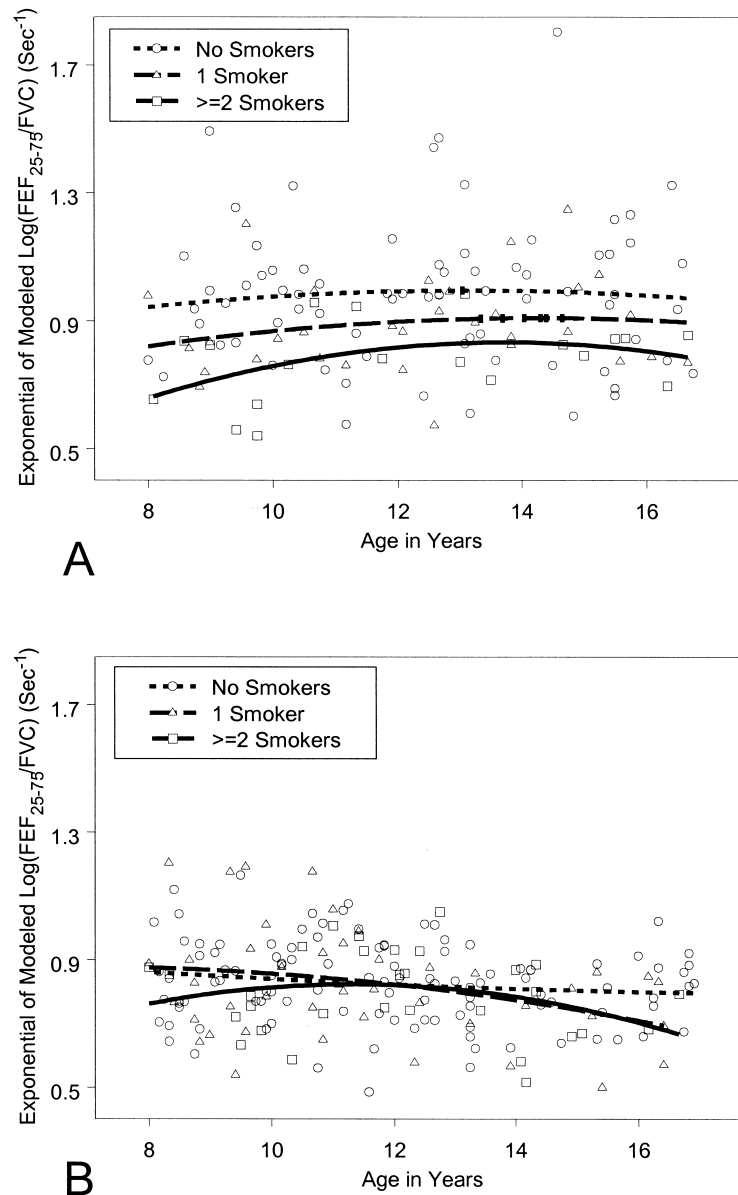


FIGURE 4. Model-predicted FEF_{25-75}/FVC among asthmatics aged 8–16 years, by number of smokers in the home and age, Third National Health and Nutrition Examination Survey, 1988–1994. Group-specific quadratic regression curves are shown for girls (panel A) and boys (panel B). FEF_{25-75} , forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FVC, forced vital capacity.

Predicted levels of all metrics but FVC were lower in asthmatics than in nonasthmatics. Effects of asthma were generally clearest in the ratio metrics $\log(FEV_1/FVC)$ and $\log(FEF_{25-75}/FVC)$. Among girls, predicted ratio metrics were clearly lowest in asthmatics taking prescription medication. Among other active and inactive asthmatic girls, these metrics generally did not differ greatly from those in nonasthmatics. Among boys, however, these metrics were distinctly and statistically significantly lower (at $\alpha = 0.05$) in all asthmatic groups than in nonasthmatics and did not differ appreciably among asthmatic groups.

In step 2 analyses, differences between the lung function of active asthmatics and that of nonasthmatics were reasonably stable with age (for the interaction of active asthma with age across all sex-specific lung function metrics, $p \geq 0.436$). In contrast, the lung function of inactive asthmatic girls tended to return to nonasthmatics' levels, and that of inactive asthmatic boys tended to diverge from nonasthmatics' levels, with increasing age. In girls, the sign of the interaction of inactive asthma with age was positive for all metrics but FVC. In boys, this interaction was negative for all metrics but FVC. Among girls, p values for this interaction were 0.175, 0.030, 0.081, and 0.047 for $\log(FEV_1)$,

TABLE 5. Model-predicted lung function among non-Hispanic White asthmatic girls and boys aged 8–16 years from models including all asthmatics, by use of a gas stove for cooking, Third National Health and Nutrition Examination Survey, 1988–1994†

	No use of a gas stove for cooking	Use of a gas stove for cooking	
		Taking prescription respiratory medication	Not taking prescription respiratory medication
Girls	(n = 50)‡	(n = 14)‡	(n = 61)‡
FVC§ (liters)	3.133	2.943	3.029
FEV ₁ § (liters)	2.917	2.824	2.653***
FEF _{25–75} § (liters/second)	3.962	3.889	3.141***
FEV ₁ /FVC (%)	93.1	95.9	87.6***
FEF _{25–75} /FVC (per second)	1.265	1.321	1.037***
Boys	(n = 85)‡	(n = 22)‡	(n = 77)‡
FVC (liters)	3.158	3.486***	3.202
FEV ₁ (liters)	2.609	2.837*	2.655
FEF _{25–75} (liters/second)	2.497	2.619	2.566
FEV ₁ /FVC (%)	82.6	81.4	82.9
FEF _{25–75} /FVC (per second)	0.791	0.751	0.802

* $0.05 \leq p < 0.10$; ** $0.01 \leq p < 0.05$; *** $p < 0.01$ (p value for the designated lung function metric and gas stove use category in relation to no use of a gas stove).

† Exponentials of model-predicted values are given at the weighted means of the natural logs of age, standing height, and body mass for Non-Hispanic Whites with skinfold thickness at <90th percentile, no smokers in the home, annual income $\geq \$20,000$, no dog or cat, and no participation in ≥ 3 organized physical activities, with reproducible FVC and FEV₁ values.

‡ Unweighted number of subjects.

§ FVC, forced vital capacity; FEV₁, first-second forced expiratory volume; FEF_{25–75}, forced expiratory flow between 25 percent and 75 percent of forced vital capacity.

$\log(\text{FEF}_{25-75})$, $\log(\text{FEV}_1/\text{FVC})$, and $\log(\text{FEF}_{25-75}/\text{FVC})$, respectively. Among boys, the corresponding p values were 0.825, 0.127, 0.069, and 0.014. Figure 3 shows predicted FEF_{25–75}/FVC by age in nonasthmatics, active asthmatics, and inactive asthmatics, as derived in step 2 models.

In step 3 analyses, household environmental factors consistently influenced lung function in asthmatic girls but not in other sex-asthma groups. In asthmatic girls, the presence of two or more smokers in the home was associated with reduced lung function (table 4 and figure 4). This association was statistically significant for $\log(\text{FEF}_{25-75})$ and $\log(\text{FEF}_{25-75}/\text{FVC})$ and was marginally significant for $\log(\text{FEV}_1)$ and $\log(\text{FEV}_1/\text{FVC})$. In asthmatic boys, modeled lung function was also generally lowest in the presence of two or more smokers but not significantly so. In asthmatic girls, use of a gas stove in the absence of prescription respiratory medication was consistently associated with reduced lung function (table 5 and figure 5). No such association was observed for gas stove use when respiratory medication was taken. There was no consistent influence of gas stove use on asthmatic boys' lung function. The presence of a dog or cat in the home was consistently and significantly associated with increased lung function in asthmatic girls but not in asthmatic boys (table 6 and figure 6).

Among nonasthmatics, the presence of two or more smokers in the home was associated with significantly increased predicted FVC ($p = 0.011$) in boys and with

nonsignificantly increased predicted FEV₁ ($p = 0.274$) in boys. Otherwise, the presence of two or more smokers was associated with nonsignificant reductions in nonasthmatics' lung function. There were no appreciable effects of gas stove use, having a dog, or having a cat on predicted lung function in nonasthmatics (data not shown).

DISCUSSION

When interpreting these results, it is important to note that different subpopulations were present in different proportions in the US population and the weighted NHANES III sample. For example, non-Hispanic Whites constituted over two thirds of our weighted analytical sample. Therefore, this group counted more heavily than other ethnic groups in the computation of effect estimates. The estimates derived in our models should be regarded as composite nationwide estimates for persons aged 8–16 years. They should not be generalized beyond this age group, and they may not be equally applicable to all ethnic groups.

The NHANES III data set does not provide information on mother's smoking, the number or ages of siblings, or the specific ethnicity of Hispanic Americans other than Mexican Americans. In addition, breastfeeding influences the development of asthma and wheezing (15) and a mother's smoking during pregnancy influences children's lung function (16). In NHANES III, this information was collected

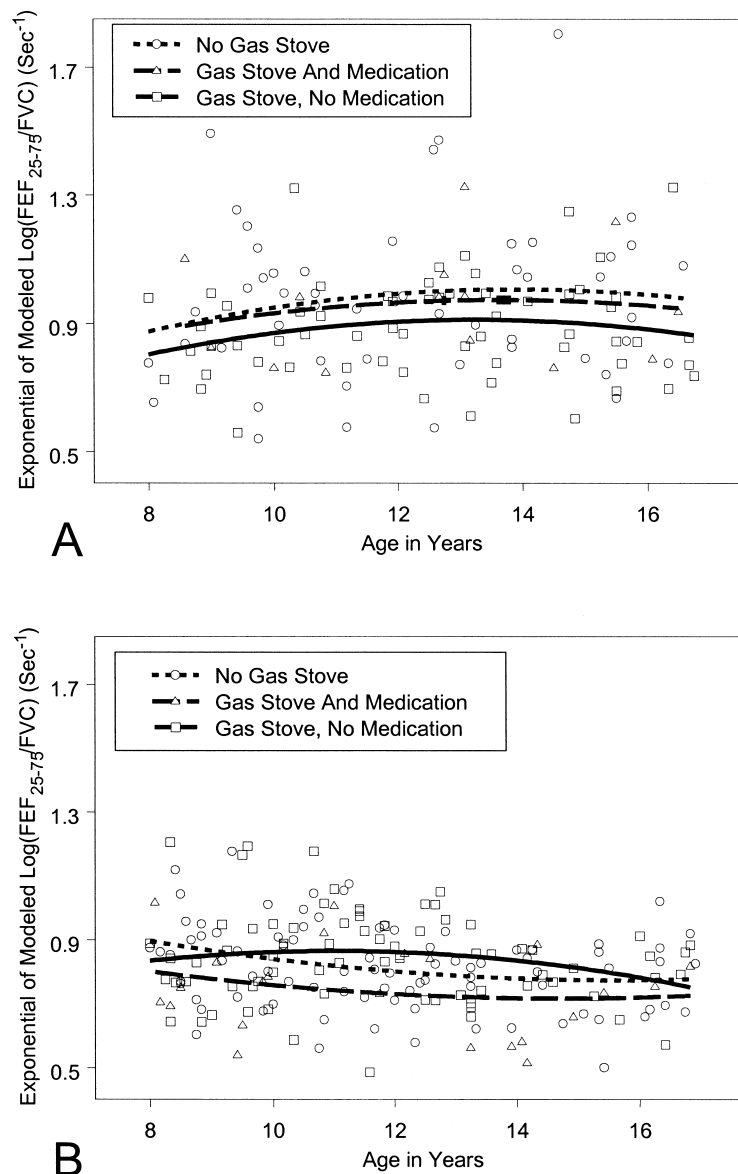


FIGURE 5. Model-predicted FEF_{25-75}/FVC among asthmatics aged 8–16 years, by use of a gas stove for cooking and age, Third National Health and Nutrition Examination Survey, 1988–1994. Group-specific quadratic regression curves are shown for girls (panel A) and boys (panel B). FEF_{25-75} , forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FVC, forced vital capacity.

only for children aged birth to 5 years and children aged birth to 11 years, respectively. Inability to adjust the analytical models for these factors limits interpretation of these findings somewhat.

Use of prescription respiratory medication was associated with clinically severe asthma, especially in girls (table 2). Deficits in lung function were especially pronounced among asthmatic girls who took such medication (table 3). Other investigators have also observed larger lung function deficits in asthmatics taking such medication than in those not taking it (11, 12). Overall, the literature suggests strongly that medical treatment does not yet compensate for lung function deficits in asthmatic children and adolescents. It would be

highly desirable to assess whether the effectiveness and accessibility of asthma treatment are improving over time. The National Health and Nutrition Examination Surveys provide the opportunity to conduct such assessment nationally, although the current survey does not include lung function testing.

Asthmatic subjects were classified as active or inactive according to their mothers' perceptions. This classification is subject to some uncertainty, especially in girls, in whom wheezing during the past 12 months was reported for over half of inactive asthmatics and in whom the frequency of school absence was nearly as high in inactive asthmatics as in active asthmatics (table 2). Nevertheless, in both girls and

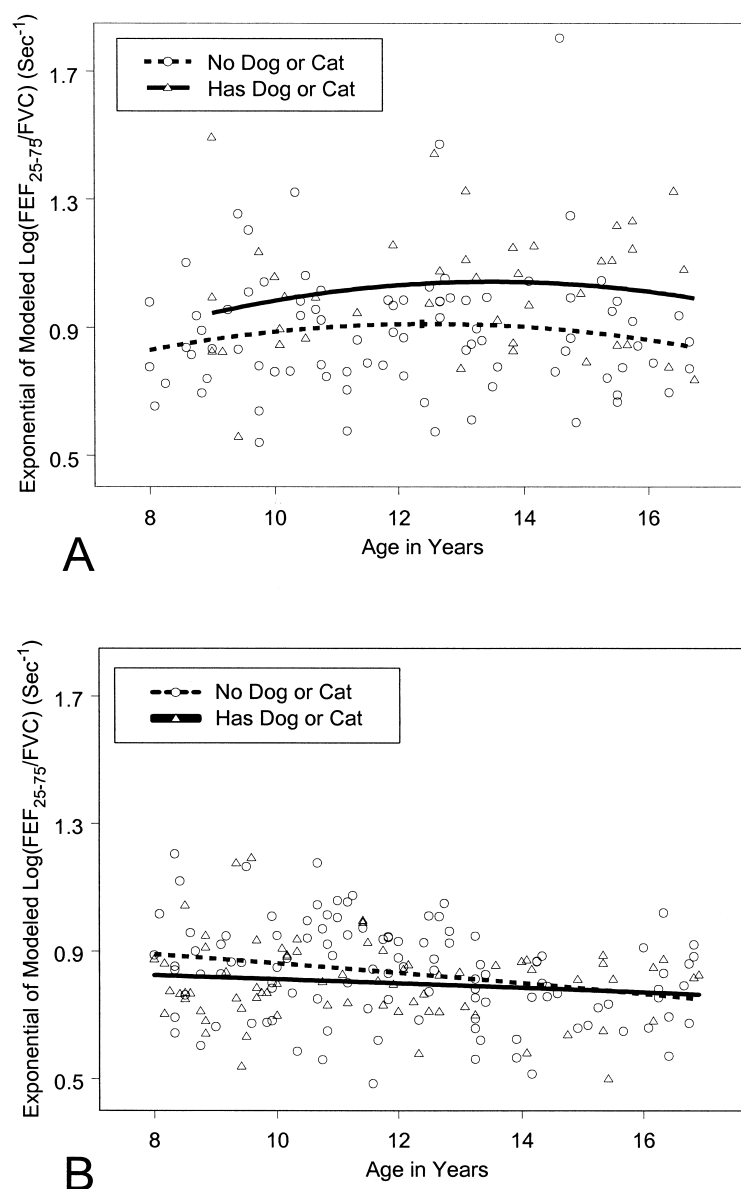


FIGURE 6. Model-predicted $\text{FEF}_{25-75}/\text{FVC}$ among asthmatics aged 8–16 years, by the presence of a dog or cat in the home and age, Third National Health and Nutrition Examination Survey, 1988–1994. Group-specific quadratic regression curves are shown for girls (panel A) and boys (panel B). FEF_{25-75} , forced expiratory flow between 25 percent and 75 percent of forced vital capacity; FVC, forced vital capacity.

boys, weighted frequencies of most asthma-related characteristics were appreciably lower in inactive asthmatics than in active asthmatics. This was true even for wheezing in girls. In addition, among inactive asthmatics, no girls and only one boy had taken prescription respiratory medication in the past month. On balance, we believe that the chosen classification method is reasonable.

Absolute differences between the lung function of active asthmatics and the lung function of nonasthmatics were quite stable with age. This observation is broadly consistent with

the literature, which suggests that lung function deficits associated with childhood asthma sometimes improve after childhood but do not disappear entirely. Among children aged 6–18 years, Gold et al. (11) observed that absolute deficits in lung function associated with asthma and wheezing increased with age. Percentage deficits did not change substantially with age. In southern California, Berhane et al. (12) made similar findings in asthmatic children and adolescents; asthma-associated deficits were somewhat larger in boys than in girls.

TABLE 6. Model-predicted lung function among non-Hispanic White asthmatic girls and boys aged 8–16 years from models including all asthmatics, by the presence of a pet dog or cat, Third National Health and Nutrition Examination Survey, 1988–1994†

	Presence of a dog or cat	
	No	Yes
Girls	(n = 84)‡	(n = 41)‡
FVC§ (liters)	3.133	3.158
FEV ₁ § (liters)	2.917	3.103**
FEF _{25–75} § (liters/second)	3.962	4.590**
FEV ₁ /FVC (%)	93.1	98.3***
FEF _{25–75} /FVC (per second)	1.265	1.454**
Boys	(n = 111)‡	(n = 73)‡
FVC (liters)	3.158	3.259
FEV ₁ (liters)	2.609	2.644
FEF _{25–75} (liters/second)	2.497	2.442
FEV ₁ /FVC (%)	82.6	81.1
FEF _{25–75} /FVC (per second)	0.791	0.749

* $0.05 \leq p < 0.10$; ** $0.01 \leq p < 0.05$; *** $p < 0.01$ (p value for the designated lung function metric and having a dog or cat in relation to not having a dog or cat).

† Exponentials of model-predicted values are given at the weighted means of the natural logs of age, standing height, and body mass for Non-Hispanic Whites with triceps skinfold thickness at the <90th percentile, no smokers in the home, annual income $\geq \$20,000$, no use of a gas stove, and no participation in ≥ 3 organized physical activities, with reproducible FVC and FEV₁ values.

‡ Unweighted number of subjects.

§ FVC, forced vital capacity; FEV₁, first-second forced expiratory volume; FEF_{25–75}, forced expiratory flow between 25 percent and 75 percent of forced vital capacity.

In our analyses, inactive asthmatic girls' lung function appeared to "catch up" with nonasthmatics' lung function, whereas inactive asthmatic boys' lung function diverged from nonasthmatics' lung function as age increased. These trends were observed for multiple lung function metrics and were often statistically significant. These trends are subject to uncertainty, because unweighted sample sizes were small and because the NHANES III data are cross-sectional. Age trends observed in cross-sectional studies can differ from those in longitudinal ones (17, 18), largely because of unadjusted birth cohort effects in cross-sectional data. We cannot rule out the possibility of subtle cohort effects in the present study.

In addition, one might expect wheezing to be associated with worsening, not improving, lung function. Wheezing was reported for more than half of the inactive asthmatic girls, so the observed age trends might seem counterintuitive. Even so, these trends persisted when additional dummy variables for wheezing in nonasthmatics and asthmatics were entered into the step 2 model. This caused the absolute magnitudes of effect estimates for the interaction of inactive asthma with age to diminish by less than 10 percent, with no

changes in their signs and only small changes in p values. When variables for age at asthma onset were entered into the step 2 model, the inactive asthma-age interaction tended to increase, and its p value to decrease, in girls. Furthermore, in separate models, the interaction of wheezing with age in ever-asthmatics was positive for all metrics but FVC in girls and was negative for all metrics in boys.

Thus, we submit that the observed age trends in inactive asthmatics may well reflect actual sex differences in the natural history of asthma between the ages of 8 and 16 years. Long-term deficits in asthmatics' lung function may result from permanent restructuring of the airways (airway remodeling) (19, 20), which may be mediated in turn by chronic airway inflammation (21, 22). Conceivably, among inactive asthmatics, 8- to 16-year-old boys might be more susceptible than girls to these processes, even though the girls have a higher prevalence of wheezing. The prevalence of positive skin tests was higher in inactive asthmatic boys than in inactive asthmatic girls. In addition, the prevalence of a positive history of asthma or hay fever in both parents was substantially higher among inactive asthmatic boys than among inactive asthmatic girls or active asthmatic boys (table 2). Therefore, one might hypothesize that in the studied age group, susceptibility to airway remodeling could be more closely associated with one or both of these characteristics than with wheezing.

We examined five lung function metrics, including the ratios of FEV₁ and FEF_{25–75} to FVC. Our results underscore the importance of considering such ratios. O'Connor et al. (23) reported that FEF_{25–75}/FVC is particularly effective in detecting effects of asthma and maternal smoking on children's lung function. In our analyses, ratio metrics generally provided the clearest distinctions not only regarding the effects of asthma and passive smoking on lung function but also regarding the effects of gas stove use and having a dog or cat in asthmatic girls.

In the present study, the lung function of asthmatic girls was influenced, negatively and positively, by exposure to household environmental factors. Household passive smoking was clearly associated with reduced lung function in this group, as was gas stove use in asthmatic girls not taking prescription respiratory medication. It appeared that use of such medication conferred protection against the effects of gas stove use, even though overall, asthma was most clinically severe among asthmatic girls taking such medication.

The presence of a dog or cat in the home was consistently associated with increased lung function in asthmatic girls. Previous studies suggest that the presence of animals in the home can protect against incident asthma (24–27). It has also been proposed that such protection may be conferred by a modified T-helper cell type 2 (Th2) response to cat antigen. Such a modified Th2 response might stimulate production of immunoglobulin G and not of immunoglobulin E as usually associated with the Th2 response. Such a modified response might lead in turn to reduced skin-test sensitivity to cat antigen (28). It is not known whether such a "desensitization" response could reduce clinical severity or lung function deficits in preexisting asthma. If so, it might be more likely to occur in girls than in boys and it might progress with

increasing age or increasing duration of pet ownership. In the present study, there were too few asthmatics for us to test these hypotheses reliably or to test the separate effects of having a dog and having a cat.

In asthmatic girls, the association of having a dog or cat with increased lung function could reflect selective avoidance of pets (29, 30). If so, the prevalence of having a dog or cat should be lower in asthmatic girls than in nonasthmatic girls. In fact, weighted prevalences were very similar in asthmatic and nonasthmatic girls (47.3 percent and 48.3 percent, respectively). Thus, we doubt whether avoidance of pets accounted for this association.

To assess the sensitivity of household environmental effects to model specification, we constructed several additional models. Specifically, we entered a term for wheezing in separate models. We also constructed a model with no adjustment for nonreproducibility of FVC or FEV₁ and another excluding nonreproducible measurements. Household environmental effects were actually somewhat stronger in the model with an additional term for wheezing than in the step 3 model.

Use of a gas stove and having a dog or cat had little or no influence on lung function in asthmatic boys or in nonasthmatics of either sex. In addition, modeled lung function was usually lowest, though not statistically significantly so, among subjects with two or more smokers in the home. We reran the analytical models as weighted mixed models (the MIXED procedure in SAS/STAT software; SAS Institute, Inc., Cary, North Carolina), treating strata and clusters as random effects. In nonasthmatic girls, for all metrics but log(FVC), there were significant or marginally significant associations of the presence of two or more household smokers with reduced lung function ($p < 0.054$). In nonasthmatic boys, the presence of two or more smokers was significantly associated with increased log(FVC) and log(FEV₁) and with reduced log(FEV₁/FVC) and log(FEF₂₅₋₇₅/FVC) (data not shown). Thus, SUDAAN may yield somewhat conservative results regarding the effects of passive smoking.

Mannino et al. (31, 32) investigated the effects of passive smoking among children and adolescents in NHANES III. They excluded subjects who reported active smoking and whose serum cotinine level was greater than 20 ng/ml; they then divided subjects into tertiles of cotinine level as a metric of passive smoking. In both the whole sample (31) and the sample of asthmatics (32), Mannino et al. reported significantly lower lung function in the high-cotinine tertile than in the low-cotinine tertile. Our results regarding the effects of passive smoking are qualitatively similar to those of Mannino et al., although we observed a statistically significant effect only in asthmatic girls. Differences between results may well reflect differences in analytical strategy. For example, Mannino et al. used serum cotinine as the metric for passive smoking, whereas we used questionnaire responses. In addition, Mannino et al. appear to have combined both sexes into single models, with adjustment for sex. In view of the marked sex differences in the effects of covariates in this age group, we conducted sex-specific analyses.

The literature is somewhat inconsistent regarding effects of household environmental factors on respiratory health and regarding sex differences in sensitivity to these factors. In the Netherlands, Cuijpers et al. (13) reported that boys' lung function was negatively associated with passive smoking but was not affected by the presence of unvented gas-fueled kitchen geysers (water heaters) or pets. In girls, passive smoking and the presence of geysers exhibited limited negative associations with lung function. In southern California, Peters et al. (33) observed reduced lung function among children living in homes with gas stoves. In Italy, among households using gas stoves, Corbo et al. (34) observed a significant negative association of time spent in the kitchen with girls' lung function but not boys'.

Gas stoves emit the air pollutant nitrogen dioxide. In the United States, Neas et al. (35) observed no consistent association of indoor nitrogen dioxide with children's lung function, but they did observe a statistically significant positive association with respiratory symptoms, including wheezing, in girls. In Japan, Shima and Adachi (36) also observed a stronger association of indoor nitrogen dioxide with respiratory symptoms in girls than in boys. Overall, the current literature, like the present study, suggests that there are stronger respiratory effects of gas cooking among girls than among boys. Further research is needed to ascertain why effects of household environmental factors differ across locations and subpopulations.

ACKNOWLEDGMENTS

Drs. Scott Kegler (Centers for Disease Control and Prevention) and William McDonnell (Environmental Protection Agency) gave valuable advice on statistical and epidemiologic aspects of data analysis and interpretation. Jennifer Aliftiras and Nataliya Kravets (National Center for Health Statistics) provided expert assistance in data programming.

This paper does not necessarily reflect Environmental Protection Agency policy. Mention of commercial products does not constitute endorsement for their use.

REFERENCES

1. National Center for Health Statistics. Plan and operation of the Third National Health and Nutrition Examination Survey, 1988–94. (Vital and health statistics, series 1, no. 32). Hyattsville, MD: National Center for Health Statistics, 1994. (DHHS publication no. (PHS) 94-1308).
2. Beaty TH, Newill CA, Cohen BH, et al. Effects of pulmonary function on mortality. *J Chronic Dis* 1985;38:703–10.
3. Neas LM, Schwartz J. Pulmonary function levels as predictors of mortality in a national sample of U.S. adults. *Am J Epidemiol* 1998;147:1011–18.
4. Truelson T, Prescott E, Lange P, et al. Lung function and risk of fatal and non-fatal stroke: The Copenhagen City Heart Study. *Int J Epidemiol* 2001;30:145–51.
5. Kelly WJ, Hudson I, Raven J, et al. Childhood asthma and adult lung function. *Am Rev Respir Dis* 1988;138:26–30.

6. Roorda RJ, Gerritsen J, van Aalderen WM, et al. Follow-up of asthma from childhood to adulthood: influence of potential childhood risk factors on the outcome of pulmonary function and bronchial responsiveness in adulthood. *J Allergy Clin Immunol* 1994;93:575–84.
7. Godden DJ, Ross S, Abdalla M, et al. Outcome of wheeze in childhood: symptoms and pulmonary function 25 years later. *Am J Respir Crit Care Med* 1994;149:106–12.
8. Strachan DP, Griffiths JM, Johnston ID, et al. Ventilatory function in British adults after asthma or wheezing illness at ages 0–35. *Am J Respir Crit Care Med* 1996;154:1629–35.
9. American Thoracic Society. Standardization of spirometry: 1987 update. ATS statement. *Am Rev Respir Dis* 1987;136:1285–98.
10. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 1999;159:179–87.
11. Gold DR, Wypij D, Wang X, et al. Gender- and race-specific effects of asthma and wheeze on level and growth of lung function in children in six U.S. cities. *Am J Respir Crit Care Med* 1994;149:1198–208.
12. Berhane K, McConnell R, Gilliland F, et al. Sex-specific effects of asthma on pulmonary function in children. *Am J Respir Crit Care Med* 2000;162:1723–30.
13. Cuijpers CE, Swaen GM, Wesseling G, et al. Adverse effects of the indoor environment on respiratory health in primary school children. *Environ Res* 1995;68:11–23.
14. Jarvis D, Chinn S, Luczynska C, et al. Association of respiratory symptoms and lung function in young adults with use of domestic gas appliances. *Lancet* 1996;347:426–31.
15. Wright AL, Holberg CJ, Taussig LM, et al. Factors influencing the relation of infant feeding to asthma and recurrent wheeze in childhood. *Thorax* 2001;56:192–7.
16. Li Y-F, Gilliland FD, Berhane K, et al. Effects of in utero and environmental tobacco smoke exposure on lung function of boys and girls with and without asthma. *Am J Respir Crit Care Med* 2000;162:2097–104.
17. Louis TA, Robins J, Dockery DW, et al. Explaining discrepancies between longitudinal and cross-sectional models. *J Chronic Dis* 1986;39:831–9.
18. Ware JH, Dockery DW, Louis TA, et al. Longitudinal and cross-sectional estimates of pulmonary function decline in never-smoking adults. *Am J Epidemiol* 1990;132:685–700.
19. Paganin F, S  neterre E, Chanez P, et al. Computed tomography of the lungs in asthma: influence of disease severity and etiology. *Am J Respir Crit Care Med* 1996;153:110–14.
20. Wilson JW. What causes airway remodelling in asthma? *Clin Exp Allergy* 1998;28:534–6.
21. van den Toorn LM, Prins J-B, Overbeek SE, et al. Adolescents in clinical remission of atopic asthma have elevated exhaled nitric oxide levels and bronchial hyperresponsiveness. *Am J Respir Crit Care Med* 2000;162:953–7.
22. van den Toorn LM, Overbeek SE, De Jongste JC, et al. Airway inflammation is present during clinical remission of atopic asthma. *Am J Respir Crit Care Med* 2001;164:2107–13.
23. O'Connor GT, Sparrow D, Demolles D, et al. Maximal and partial expiratory flow rates in a population sample of 10- to 11-year old schoolchildren. *Am J Respir Crit Care Med* 2000;162:436–9.
24. Hesselmar B, Aberg N, Eriksson B, et al. Does early exposure to cat or dog protect against later allergy development? *Clin Exp Allergy* 1999;29:611–17.
25. Roost HP, Kunzli N, Schindler C, et al. Role of current and childhood exposure to cat and atopic sensitization. *J Allergy Clin Immunol* 1999;104:941–7.
26. Sporik R, Squillance SP, Ingram JM, et al. Mite, cat, and cockroach exposure, allergen sensitization, and asthma in children: a case-control study of three schools. *Thorax* 1999;54:675–80.
27. Ronmark E, Jonsson E, Platts-Mills T, et al. Incidence and remission of asthma in schoolchildren: report from the Obstructive Lung Disease in Northern Sweden Studies. *Pediatrics* 2001;107:E37.
28. Platts-Mills T, Vaughan J, Squillance S, et al. Sensitization, asthma, and a modified Th2 response in children exposed to cat allergen: a population-based cross-sectional study. *Lancet* 2001;357:752–6.
29. Brunekreef B, Groot B, Hoek G. Pets, allergy and respiratory symptoms in children. *Int J Epidemiol* 1992;21:338–42.
30. Anyo G, Brunekreef B, de Meer G, et al. Early, current and past pet ownership: associations with sensitization, bronchial responsiveness and allergic symptoms in school children. *Clin Exp Allergy* 2002;32:361–6.
31. Mannino DM, Moorman JE, Kingsley B, et al. Health effects related to environmental tobacco smoke exposure in children in the United States: data from the Third National Health and Nutrition Examination Survey. *Arch Pediatr Adolesc Med* 2001;155:36–41.
32. Mannino DM, Homa DM, Redd SC. Involuntary smoking and asthma severity in children: data from the Third National Health and Nutrition Examination Survey. *Chest* 2002;122:409–15.
33. Peters JM, Avol E, Gauderman WJ, et al. A study of twelve southern California communities with differing levels and types of air pollution. II. Effects on pulmonary function. *Am J Respir Crit Care Med* 1999;159:768–75.
34. Corbo GM, Forastiere F, Agabiti N, et al. Effect of gas cooking on lung function in adolescents: modifying role of sex and immunoglobulin E. *Thorax* 2001;56:536–40.
35. Neas LM, Dockery DW, Ware JH, et al. Association of indoor nitrogen dioxide with respiratory symptoms and pulmonary function in children. *Am J Epidemiol* 1991;134:204–19.
36. Shima M, Adachi M. Effect of outdoor and indoor nitrogen dioxide on respiratory symptoms in schoolchildren. *Int J Epidemiol* 2000;29:862–70.