

Sleep Duration, Current Asthma, and Lung Function in a Nationwide Study of U.S. Adults

To the Editor:

Asthma can affect sleep duration and sleep quality in children. Children with asthma are more likely to have shorter or disrupted sleep due to nocturnal symptoms (1), and children with frequent asthma symptoms report more daytime

tiredness/sleepiness than those with less frequent or no asthma symptoms (2).

The American Academy of Sleep Medicine and the Sleep Research Society recommend that adults should have a regular sleep duration of 7 or more hours per night. Although short sleep duration has been linked to asthma in children and adolescents (3), only a few studies have examined sleep duration and asthma (4, 5) or fractional exhaled nitric oxide (F_{ENO}) (6) in adults. We examined whether short sleep duration is

Table 1. Main Characteristics of the Study Participants (N = 15,442) and Results of the Analysis of the Relation between Sleep Duration and Asthma (National Health and Nutrition Examination Survey 2007–2012)

Characteristics	Control Subjects (n = 14,125)*	Current Asthma* (n = 1,317)	Odds Ratio (95% Confidence Interval)	
			Unadjusted Analysis	Adjusted Analysis
Sleep duration/night, h	6.9 ± 0.02	6.6 ± 0.06 [†]		
6–8 h	11,061 (81.2)	867 (69.9) [†]	1.0	1.0
≤5 h	2,133 (12.7)	348 (23.0)	2.10 (1.78–2.48) [†]	1.73 (1.32–2.27) [†]
≥9 h	931 (6.1)	102 (7.2)	1.37 (1.07–1.76) [‡]	1.02 (0.74–1.41)
Age, yr	45.7 ± 0.4	46.0 ± 0.6	—	0.99 (0.98–0.996) [†]
Male sex	7,107 (49.9)	476 (36.0) [†]	—	0.61 (0.48–0.77) [†]
Race/ethnicity				
Non-Hispanic white	5,785 (66.6)	627 (70.3) [†]	—	1.0
Mexican American	2,447 (9.1)	92 (3.8)	—	0.57 (0.41–0.79) [†]
Other Hispanic	1,538 (5.6)	149 (5.6)	—	0.79 (0.57–1.09)
Non-Hispanic black	3,053 (11.3)	351 (14.6)	—	0.93 (0.73–1.19)
Other	1,302 (7.3)	98 (5.7)	—	0.99 (0.68–1.46)
Marital status				
Married/living together	8,592 (64.9)	671 (56.2) [†]	—	1.0
Divorced/separated	2,031 (12.7)	252 (16.1)	—	0.99 (0.71–1.37)
Widowed/single	3,490 (22.4)	394 (27.6)	—	1.15 (0.92–1.44)
Annual household income ≥ \$20,000	10,511 (85.6)	822 (75.5) [†]	—	1.41 (1.09–1.82) [‡]
Smoking status				
Never/former smokers	11,046 (78.9)	932 (72.9) [†]	—	1.0
Current smokers	3,067 (21.1)	385 (27.1)	—	0.93 (0.67–1.29)
Body mass index, kg/m ²	28.6 ± 0.1	30.9 ± 0.3 [†]	—	1.03 (1.02–1.04) [†]
Serum cotinine level, ng/ml	57.9 ± 2.8	72.3 ± 6.0 [†]	—	1.00 (0.999–1.001)
Family history of asthma	2,294 (16.4)	577 (43.6) [†]	—	2.89 (2.39–3.51) [†]
Use of oral or inhaled steroid in past 2 d	210 (1.9)	373 (37.2) [†]	—	28.68 (21.04–39.10) [†]
Depression severity (PHQ-9 score)	2.9 ± 0.17	4.9 ± 0.21 [†]	—	1.04 (1.01–1.07) [†]
FEV ₁ % predicted	98.0 ± 0.3	88.7 ± 0.8 [†]	—	—
FVC% predicted	101.6 ± 0.2	97.2 ± 0.8 [†]	—	—
FEV ₁ % predicted/FVC	96.1 ± 0.2	90.6 ± 0.5 [†]	—	—
F _{ENO} , ppb	16.8 ± 0.2	22.8 ± 0.9 [†]	—	—
Bronchodilator response	5.6 ± 0.2	10.1 ± 0.9 [†]	—	—

Definition of abbreviations: F_{ENO} = fractional exhaled nitric oxide; PHQ-9 = Patient Health Questionnaire-9.

*Values are presented as number (%) or mean ± SD. Numbers may vary owing to missing data.

[†]P < 0.01.

[‡]P < 0.05.

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associated with asthma and reduced lung function in a population-based sample of U.S. adults.

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional nationwide survey of the noninstitutionalized U.S. civilian population. Study participants are selected using a stratified multistage probability design and are representative of the U.S. population. As part of its study design, NHANES oversamples persons 60 years and older and ethnic minorities (African Americans and Hispanics) to increase statistical power for data analysis in those subgroups. Subjects 20–79 years of age

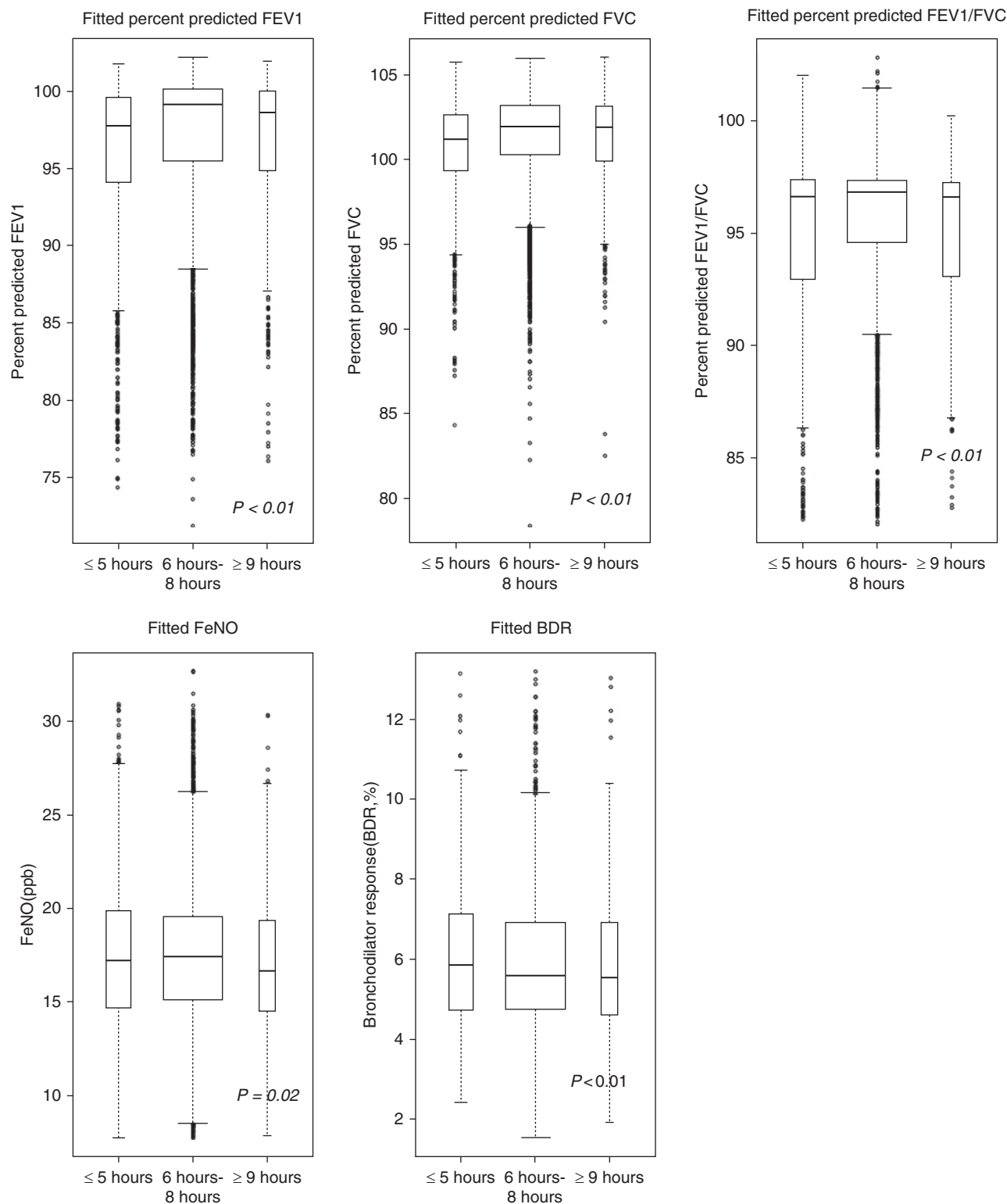


Figure 1. Boxplot of model-fitted values of lung function measures against sleep duration categories (i.e., ≤ 5 h, 6–8 h, and ≥ 9 h). Linear regression was fitted for the analysis of lung function measures (FEV₁% predicted, FVC% predicted, and % predicted FEV₁/FVC), which was adjusted for annual household income, body mass index, current asthma status, smoking status, and use of oral or inhaled steroids in the past 2 days. The models for bronchodilator response (BDR) and fractional exhaled nitric oxide (FeNO) were additionally adjusted for age, sex, and race/ethnicity. P value is for the one-way ANOVA between the three groups. The widths of the boxes are proportional to the sample size in every group.

who had nonmissing values for current asthma and sleep duration were included in the current analysis of the 2007–2012 NHANES dataset. Sleep duration was assessed by household interview using the Computer-Assisted Personal Interviewing system. Subjects were asked the question, “How much sleep (in hours) do you usually get at night on weekdays or workdays?”

Spirometry was performed according to American Thoracic Society recommendations (7). The best FEV₁ and FVC values were selected for data analysis. The analysis of lung function measures was performed using percent predicted values calculated based on the Global Lung Function Initiative (8). FE_{NO} was measured using the Aerocrine NIOX MINO (Aerocrine AB). In a subset of participants whose baseline spirometry showed an FEV₁/FVC ratio below the lower limit of normal and/or below 70%, spirometry was repeated 15 minutes after inhalation of short-acting β₂ agonists. Bronchodilator response (BDR) was expressed as a percentage, calculated as

$$\frac{\text{post-bronchodilator FEV}_1 - \text{baseline FEV}_1}{\text{baseline FEV}_1} \times 100.$$

Current asthma was defined by positive answers to the following questions: 1) “Has a doctor or other health professional ever told you that you have asthma?” and 2) “Do you still have asthma?” Subjects who answered “no” to both questions were selected as control subjects. We categorized weekday sleep duration as ≤5 hours, 6–8 hours (reference group), and ≥9 hours per night.

Logistic or linear regression was used for the analysis of sleep duration and current asthma, percent predicted lung function measures, BDR, and FE_{NO}. All multivariable models were adjusted for annual household income, body mass index, family history of asthma, marital status, serum cotinine, smoking status, use of oral or inhaled steroids in the past 2 days, and depression severity. Models for current asthma, FE_{NO}, and BDR were additionally adjusted for age, sex, and race/ethnicity.

Table 1 shows the main characteristics of the study participants and the results of the analysis of the relation between sleep duration and current asthma. Compared with control subjects, subjects with current asthma were more likely to sleep ≤5 hours or ≥9 hours per night and to be female, non-Hispanic white, and current smokers. They were also more likely to have an annual household income of <\$20,000; higher body mass index and serum cotinine; a family history of asthma; used oral or inhaled steroids in the past 2 days; shorter sleep duration; greater depression severity; lower FEV₁, FVC, and FEV₁/FVC; and higher FE_{NO} and BDR. In a multivariable analysis adjusting for depression severity and other covariates, a sleep duration of no more than 5 hours per night was significantly associated with 1.7 times increased odds of current asthma, but there was no significant association between sleeping at least 9 hours per night and current asthma. We found no significant interaction between sleep duration and other covariates on current asthma. Similar results were obtained in a secondary analysis of sleep duration and lifetime asthma (defined as a positive answer to physician-diagnosed asthma but a negative answer to still having asthma [data not shown]).

Figure 1 shows the results of the multivariable analysis of sleep duration and lung function, BDR, and FE_{NO}. In this analysis, both short and long sleep durations were associated with lower percent predicted lung function measures (FEV₁, FVC, and FEV₁/FVC [*P* < 0.01 in all instances]) and FE_{NO} (*P* = 0.02),

and short sleep duration was associated with increased BDR (*P* < 0.01).

A population-based study of young Korean adults and a hospital-based study of U.S. adults previously reported a U-shaped association between sleep duration and asthma (4, 5). Our study differs from prior studies of asthma (3, 5, 9) with regard to geographic location (5), age range of the study participants (3, 5, 9), mode of ascertainment of asthma diagnosis (4, 5), and ability to adjust for potential confounders such as depression severity and use of inhaled steroids (4). Moreover, we found no significant evidence of modification of the estimated effect of sleep duration on current asthma by sex or overweight/obesity.

A prior study in NHANES showed a U-shaped relationship between sleep duration and FE_{NO} but did not adjust for depression severity (6). Our novel finding of a U-shaped association between sleep duration and lung function measures or BDR may be explained by increased airway inflammation in subjects reporting sleep deprivation or excessive sleep.

We acknowledge several study limitations. First, we cannot determine temporal relationships in a cross-sectional study. Second, self-reported sleep duration is not as accurate as objective gold standards. However, our findings were essentially unchanged in a sensitivity analysis excluding 921 subjects who reported less than 4 hours of sleep (data not shown). Third, using weekday sleep duration may have led to underestimation of the true effect of insufficient sleep on asthma or lung function. Fourth, we lacked data on potential confounders of the relation between sleep duration and asthma, including sleep apnea, sleep hygiene, and insomnia (10). Lastly, misclassification of chronic obstructive pulmonary disease as asthma is possible in a study of adults.

In summary, we found that short and long sleep durations were significantly associated with reduced lung function measures and FE_{NO} in a sample of U.S. adults, in whom short sleep duration was also associated with current asthma and increased BDR. Our findings support conducting prospective studies of sleep duration, asthma, and lung function in adults. ■

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Trends in Idiopathic Pulmonary Fibrosis-related Mortality in the United States: 2000–2017

To the Editor:

Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic lung disease of unknown etiology and poor prognosis, with a median survival of 2.5–3.5 years (1, 2). The epidemiology of this disease has been challenging to study as it is a relatively uncommon disease with evolving diagnostic criteria. Because the disease is uniformly fatal, a more comprehensive characterization remains a priority for clinical and epidemiological research.

Evolving diagnostic and treatment guidelines for IPF in recent years (3, 4) have impacted classification of this disease and therefore its epidemiological profile. Recent epidemiological studies have suggested that IPF rates are increasing both in the United States and abroad (5–8). Whether this increase reflects a true rise in

IPF incidence or is due to increased clinical recognition of the disease is undetermined.

In this study we evaluated IPF mortality rates in the United States for the period of 2000–2017. We examined temporal mortality trends and conducted subanalyses based on sex, age group, and race. The study provides a national-level, contemporary assessment of IPF epidemiology and identifies several demographic groups at increased risk.

Methods

We analyzed national death certificate data from the U.S. National Vital Statistics System, which aggregates decedent data using ICD-10 codes representing underlying cause of death and contributing conditions.

Cases containing ICD-10 codes for pulmonary fibrosis (J84.1 or J84.9) were included in the study. To approximate IPF, we excluded records containing ICD-10 codes for diseases known to have a component of pulmonary fibrosis, using criteria similar to those used in previous studies (8, 9). We included records of decedents 45 years of age and older because IPF is exceedingly rare outside of this population. Our exclusion criteria led to broad and strict IPF case definitions.

Age-adjusted mortality rates were obtained via CDC WONDER (10), which uses direct standardization to the 2000 U.S. Standard Population. Rates were expressed per 100,000 persons. We stratified rates by sex, race, and age group. We conducted a statistical analysis using JMP Pro 14 to calculate odds ratios (ORs) and analyze temporal trends via Poisson regression.

Results

Overall mortality. We identified 420,479 records containing a diagnostic code for our broad definition of pulmonary fibrosis. After we applied exclusion criteria, 401,567 decedent records remained. The overall age-adjusted mortality rate per 100,000 persons was 18.81 in 2000 and 20.66 in 2017 (Table 1). Regression analysis showed a positive temporal trend over the study period ($P < 0.0001$).

Sex. Mortality rates among males and females rose over the study period (Table 1). Among males, regression showed a positive temporal trend for the study period ($P < 0.0001$); however, the trend among females was not statistically significant. Overall rates were significantly higher among males than among females (OR, 1.63; 95% confidence interval [CI], 1.60–1.66) across all racial subgroups studied (Table 1).

Race. Mortality rates by racial group varied over the study period (Table 1). Among white individuals, a positive temporal trend for the study period was observed ($P < 0.0001$). Among American Indians/Alaska Natives, the temporal trend was not statistically significant. Among Asian/Pacific Islanders and black/African American individuals, a negative temporal trend for the study period ($P < 0.0001$) was observed (Table 1).

Significant differences in rates were observed between racial groups (Table 1). American Indians/Alaska Natives had the highest rate of all racial subgroups at 26.57 per 100,000 (OR, 1.28; 95% CI, 1.26–1.30). White individuals had the next highest rate at 20.76 per 100,000 persons. This group was used as the reference rate because it accounted for the most deaths overall. Black/African American individuals (OR, 0.56; 95% CI, 0.55–0.57) and