Do Symptoms Predict COPD in Smokers?

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Background: The US Preventive Services Task Force recommends against spirometry in the absence of symptoms. However, as much as 50% of COPD cases in the United States remain undiagnosed.

Methods: Report of symptoms, smoking history, and spirometric data were collected from subjects screened for a work-related medical evaluation (N = 3,955). Prevalence of airflow obstruction and respiratory symptoms were assessed. Sensitivity, specificity, positive and negative predictive values, and relative risks of predicting symptoms and smoking history for COPD were calculated.

Results: Forty-four percent of smokers in our sample had airways obstruction (AO). Of these, 36% reported a diagnosis of or treatment for COPD. Odds ratio (95% CI) for AO with smoking (≥ 20 pack-years) was 3.73 (3.12-4.45), 1.98 (1.73-2.27) for cough, 1.79 (1.55-2.08) for dyspnea, 1.95 (1.70-2.34) for sputum, and 2.59 (2.26-2.97) for wheeze. Respiratory symptoms were reported by 92% of smokers with AO, 86% smokers with restriction, 76% smokers with normal spirometry, and 73% of nonsmokers. Sensitivity (92% vs 90%), specificity (19% vs 22%), positive (47% vs 40%) and negative (75% vs 80%) predictive values for the presence of one or more symptoms were similar between smokers and all subjects.

Conclusions: COPD is underdiagnosed in the United States. Symptoms are frequent in subjects with AO and increase their risk for COPD, but add little beyond age and smoking history to the predictive value of spirometry. In view of the high prevalence of symptoms and their poor predictive value, a simpler and more effective approach would be to screen older smokers.

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Abbreviations: AO = airways obstruction; GOLD = Global Initiative for Chronic Obstructive Lung Disease; LLN = lower limit of normal; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; RR = relative risk; USPSTF = US Preventive Services Task Force

COPD is a major public health issue,¹ but recent national survey data revealed that 50% of cases are not diagnosed.² Spirometry is the accepted standard for the diagnosis and classification of severity for COPD,³ but it is underused by most health-care

practitioners.⁴⁻¹⁰ The US Preventive Services Task Force (USPSTF) recently recommended against spirometric testing for COPD in the absence of symptoms, despite an admission that respiratory symptom status is not a reliable indicator of the presence of airways obstruction (AO).¹¹ However, the USPSTF further stated that spirometry may be beneficial in symptomatic adults who have an FEV₁ > 60% predicted for determining when to initiate therapy.

In this study, respiratory symptoms and spirometric data from a large cohort were evaluated to determine whether COPD is underdiagnosed and to

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Table 1—Subject Demographics Using Fixed Ratio To Define Airway Obstruction

Demographic	Total	Nonsmokers or < 20 Pack-y Smokers	Smokers ≥ 20 Pack-Years			
			Undiagnosed COPD	Diagnosed COPD/ Asthma	Restricted Spirometry	Normal Spirometry
No. subjects	3,955	1,038	744	525	856	792
Age, y	64.1 ± 9.6	63.2 ± 10.2	65.7 ± 8.9	67.2 ± 8.6	64.0 ± 9.4	61.9 ± 9.5
FEV ₁ , % predicted	74.9 ± 20.6	84.5 ± 17.4	65.3 ± 16.3	48.4 ± 18.4	71.0 ± 11.6	93.2 ± 8.9
Pack-y	39.4 ± 31.7	4.6 ± 6.4	53.4 ± 27.0	59.8 ± 30.1	51.2 ± 27.4	45.5 ± 25.4
BMI	29.2 ± 4.8	29.9 ± 4.9	27.8 ± 4.5	27.8 ± 5.0	30.4 ± 4.9	29.1 ± 4.2

Data are presented as mean ± SD. COPD is defined as FEV₁/FVC < 70% (aged ≥ 40 years and ≥ 20 pack-years of smoking). Unaffected smokers are defined as having a normal spirometry of FEV₁/FVC ≥ 70% and percent-predicted FVC > 80% (aged ≥ 40 years and ≥ 20 pack-years of smoking). Restricted smokers are defined as having an FEV₁/FVC ≥ 70% and percent-predicted FVC ≤ 80% (aged ≥ 40 years and ≥ 20 pack-years of smoking).

answer three questions: (1) Is there an association of symptoms with the presence of AO? (2) If there is such an association, are symptoms sensitive and specific for the presence of AO? (3) Does the absence of symptoms exclude AO (ie, is there underdiagnosis of COPD if only symptomatic smokers are tested)? We confirm that COPD is underdiagnosed and that most patients with AO are symptomatic. Symptoms increase the risk for COPD but add little beyond age and smoking history to positive predictive value of spirometry.

MATERIALS AND METHODS

Study Population

Subjects were recruited from a cohort referred for a work-related medical evaluation from 1980 to 2008 that included a questionnaire, chest radiographs, and pulmonary function tests. The cohort originally was described in 2004.¹² Referrals were drawn from trade unions and television and newspaper advertisements. Cigarette smoking was quantified by pack-years. Subjects were queried about the presence and duration of symptoms, such as cough, sputum, dyspnea on exertion, and wheeze, on most days of the week for ≥ 1 year and asked to list all current medications. They were asked whether and when they had received a diagnosis from a health-care professional of asthma, COPD, chronic bronchitis, or emphysema. All responses were verified by the physician-examiner during face-to-face interviews. A chest radio-

graph was read by a certified B reader according to International Labor Organization standards to exclude subjects with significant pneumoconiosis.¹³ This protocol was reviewed and approved by the Saint Louis University and Wake Forest University institutional review boards.

Pulmonary Function Testing

Pulmonary function testing was performed according to American Thoracic Society guidelines.^{14,15} Spirometric data were expressed as percent predicted using National Health and Nutrition Examination Survey (NHANES) standards.^{15,16} COPD was defined in accordance with Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines,¹⁷ using a fixed FEV₁/FVC ratio < 70% in long-term smokers aged ≥ 40 years. Long-term smoking was defined as ≥ 20 pack-years. Never-smokers or those who smoked < 20 pack-years were considered nonsmokers. Severity of airway obstruction was quantified in accordance with GOLD guidelines.¹⁷ The fixed FEV₁/FVC ratio is known to underestimate the presence of obstruction in young patients and to overestimate it in older patients^{16,18–21}; therefore, a secondary analysis of the data using the lower limit of normal (LLN) definition for obstruction based on NHANES standards was performed.^{22,23}

Subject Groups and Variables Measured

Smokers were divided into three groups based on spirometry: subjects with COPD (FEV₁/FVC, < 70%) (n = 1,269), unaffected smokers with normal spirometry (FEV₁/FVC, ≥ 70%; percent-predicted FVC, > 80%) (n = 792), and restricted smokers (FEV₁/FVC, ≥ 70%; percent-predicted FVC, ≤ 80%) (n = 856). Exclusion

Table 2—Frequency of Symptoms^a Using Fixed Ratio To Define Obstruction

Symptom	Total	Nonsmokers or < 20-Pack-y Smokers	Smokers ≥ 20 Pack-y			
			Diagnosed COPD	Undiagnosed COPD	Restricted Spirometry	Normal Spirometry
Cough	58.3	46.1	78.4	65.4	60.5	51.8
Sputum	46.6	46.0	63.7	51.6	40.9	36.9
Wheeze	53.5	38.5	84.3	59.1	58.2	42.4
Dyspnea	67.6	63.1	90.1	66.9	70.8	55.5
No symptom	17.6	27.2	2.5	11.8	14.0	24.2
No. of symptoms, mean ± SD	2.1 ± 1.4	1.7 ± 1.4	3.1 ± 1.1	2.4 ± 1.4	2.3 ± 1.4	1.8 ± 1.4

^aPercentage of subjects experiencing symptoms.

Diagnosis of COPD in subjects with remote history of lung cancer

FIGURE 1. Long-term smokers with a remote history of lung cancer and spirometric evidence of airflow obstruction were more likely to have received a diagnosis of COPD than long-term smokers with airflow obstruction and no history of lung cancer. Dxed = diagnosed; Hx = history.

criteria were radiographic evidence of significant pneumoconiosis, the presence of mesothelioma, active lung cancer, and any disorder with an expected survival of <1 year. Study variables evaluated were age; pack-years smoked; and the presence of cough, sputum, wheeze, and dyspnea. A physician diagnosis of asthma, chronic bronchitis, emphysema, and COPD was based on patient report.

Statistical Analysis

Sensitivity, specificity, and negative and positive predictive values of variables for the presence of obstruction were calculated. Logistic regression was used to estimate the odds ratios (OR) of both individual and combinations of respiratory symptoms, age, and smoking history of ≥ 20 pack-years for AO. To do so, we saturated the model with all the variables and their two-way interactions. We next eliminated the terms that appeared to be statistically insignificant based on likelihood test ($-2 \cdot \log$ likelihood ratio) and a significance threshold P value of .05. We also used logistic regression to generate a predictive model that estimates the relative risk (RR) for the different combinations of variables. The outcome was the presence or absence of COPD defined based on FEV_1 and FEV_1/FVC ratio. We included the presence or absence of four discrete variables (wheeze, dyspnea, cough, and sputum), two continuous variables (age and smoking), and two-way interactions of all variables. We applied the backward elimination strategy to obtain the final predictive model. Every term that had a $P < .1$ or had an interaction term with a $P < .1$ was kept in the model. This model generated a logit function for calculating the RRs (approximations based on ORs) of COPD for combinations of symptoms.

Table 3—Number of Symptoms in Long-Term Smokers ($n = 2,917$) by Pack-Year and FEV_1

No. Symptoms	Pack-y	FEV_1 , % Predicted
0	45.1 $\pm$ 23.5	83.1 $\pm$ 15.5
1	48.4 $\pm$ 25.3	77.1 $\pm$ 17.8
2	51.7 $\pm$ 28.2	73.1 $\pm$ 19.0
3	53.5 $\pm$ 27.5	69.5 $\pm$ 19.9
4	55.8 $\pm$ 29.7	62.9 $\pm$ 21.9

Data are presented as mean $\pm$ SD.

For wheeze and shortness of breath, the RR was calculated. Because cough showed a significant interaction ($P < .1$) with both age and pack-years, the next step in calculation of RRs was based on the presence or absence of cough. Because having sputum depends on having cough, the RRs for sputum is offered only when cough is present. Based on the presence or absence of cough, the RR for the difference in age and the difference in pack-years smoked was calculated.

We used a t test to evaluate the significance of differences between groups for continuous variables. Statistical analysis was performed using SAS version 9.1 (SAS Institute; Cary, NC). Values are expressed as mean $\pm$ SD.

RESULTS

Study Population Demographics

Smokers with obstruction were older, smoked more, and experienced more symptoms than smokers with restrictive or normal spirometry ($P < .001$) (Tables 1, 2). Few smokers had a remote history of lung cancer (Fig 1). In the 1,269 subjects with obstructed spirometry, 86% were GOLD stages II to IV. BMI was significantly greater in restricted smokers compared with all other smoking groups and lower in smokers with obstruction compared with smokers with normal spirometry ($P < .05$) (Table 1). Only fixed-ratio comparisons are presented because there were marginal differences in results between these and LLN.

Prevalence of Respiratory Symptoms, AO, and COPD

Symptoms were present in 92% of the smokers with obstruction and were linearly related ($P < .001$) to pack-years smoked and FEV_1 (Tables 3, 4). Symptoms also were present in 76% of smokers with normal and 86% of smokers with restricted spirometry. Most of the asymptomatic smokers with obstruction had GOLD stage II COPD (62%), and 10% had GOLD stage III or IV COPD.

There was a 17% prevalence of obstruction in subjects who never smoked ($n = 178$) or smoked <20 pack-years ($n = 1,038$). Of these subjects, 79% had symptoms. The mean FEV_1 for the nonsmokers with obstruction was $66.6 \pm 18.2\%$, and their average age was 68.2 ± 9.7 years. Of the 178 nonsmokers

Table 4—Percentage of Long-Term Smokers ($n = 2,917$) With Symptoms by FEV_1

Symptom	$FEV_1 > 80\%$ Predicted, %	$FEV_1 < 30\%$ Predicted, %
Cough	54	86
Dyspnea	58	95
Sputum	39	73
Wheeze	43	93

FIGURE 2. COPD was frequently underdiagnosed in long-term smokers. Dx = diagnosis. See Figure 1 legend for expansion of the other abbreviation.

with obstruction, 78 never smoked, and the 100 who did smoke had a 10.5 ± 5.9 -pack-year history of smoking.

Most subjects who reported symptoms had multiple complaints (Table 2). Among the 3,955 subjects evaluated, 3,261 (83%) reported at least one symptom, and 2,579 (65%) reported multiple symptoms. This finding also was true of the subset of long-term smokers ($n = 2,917$), where 2,504 (86%) reported at least one symptom, and 2,054 (70%) reported multiple symptoms. The most common combination was cough and sputum production either alone or in combination with wheeze or dyspnea. Only 13 of 3,261 symptomatic subjects and 10 of 2,504 symptomatic long-term smokers reported sputum without cough; therefore, the complaint of sputum in the absence of cough was not analyzed further.

Underdiagnosis of COPD

COPD was underdiagnosed in the entire cohort (Fig 2) and the subset limited to long-term smokers (Fig 3). Smokers with spirometric criteria for COPD who received medications for or reported a having received a diagnosis of COPD tended to have a lower percent-predicted FEV₁ ($P < .001$) (Table 1) and were more symptomatic than those who had not received a diagnosis of or medication for COPD ($P < .001$) (Table 2). They also were slightly older ($P = .003$) and smoked marginally more ($P < .001$) than those without COPD (Table 1). Of the 744 long-term smokers with AO who were neither given a diagnosis of nor medicated for COPD, 80% were GOLD stage II or greater, and 87% had one or more symptoms (Table 5). Conversely, 4% of smokers with normal spirometry and 11% with restricted spirometry were misclassified as having COPD. Additionally,

FIGURE 3. COPD was missed more frequently in the cohort of smokers and nonsmokers than in the subset of long-term smokers alone. See Figure 1 legend for expansion of abbreviation.

3% of smokers with normal and 4% of smokers with restricted spirometry reported having been given a diagnosis of asthma.

Association of Symptoms With AO

On univariate analysis, smoking history, cough, dyspnea, sputum, and wheeze all were significantly associated with AO (Table 6). Smoking showed the highest OR for association with COPD at 3.73 (95% CI, 3.12-4.45) and was significantly greater than the unadjusted OR for any one of the four respiratory symptoms evaluated.

Sensitivity, Specificity, Negative and Positive Predictive Values, and RRs of Smoking History and Respiratory Symptoms

Although the absence of symptoms predicted the absence of COPD, the presence of symptoms poorly predicted the presence of AO in smokers at risk for COPD. Sensitivity, specificity, predictive values and

Table 5—Smokers With Airways Obstruction Not Diagnosed as COPD or Asthma ($n = 744$)

Symptom	Value
FEV ₁ , % predicted	65.3 $\pm$ 16.3
Pack-y	53.4 $\pm$ 26.9
Age, y	65.7 $\pm$ 8.9
FEV ₁ 50%-80% predicted	466 (63)
FEV ₁ 30%-50% predicted	117 (16)
FEV ₁ <30% predicted	12 (2)
Presence of ≥ 1 symptom	656 (88)
Cough	485 (65)
Sputum	382 (52)
Wheeze	427 (59)
Dyspnea	486 (67)

Data are presented as mean $\pm$ SD or No. (%).

Table 6—Odds Ratios (95% CIs) for Having Airway Obstruction

Symptom	All Subjects		Smokers	
	Unadjusted	Adjusted ^a	Unadjusted	Adjusted ^a
Cough	1.98 (1.73-2.27)	NA ^b	1.85 (1.58-2.17)	NA ^b
SOB	1.79 (1.55-2.08)	1.23 (1.03-1.47)	1.91 (1.62-2.26)	1.29 (1.07-1.56)
Sputum	1.95 (1.70-2.34)	1.74 (1.42-2.13)	2.01 (1.73-2.34)	1.63 (1.31-2.04)
Wheeze	2.59 (2.26-2.97)	1.90 (1.61-2.25)	2.28 (1.94-2.66)	1.85 (1.54-2.21)
Smoking ^c	3.73 (3.12-4.45)	3.59 (2.80-4.61)	Adjusted for smoking	Adjusted for smoking

NA = not applicable; SOB = shortness of breath.

^aAdjusted for age, sex, and pack-years smoked in a model including all four symptoms.

^bThe odds ratio (OR) for cough depended on the amount of smoking (interaction $P = .008$), and it followed the formula $OR = e^{0.015 \times \text{pack-years smoked}}$, where $e = 2.7183$. Therefore, the ORs were 1.35 for 20 pack-years; 1.820 for 40 pack-years; 2.46 for 60 pack-years; 3.32 for 80 pack-years; 4.48 for 100 pack-years, and 6.05 for 120 pack-years.

^c ≥ 20 pack-years.

RRs of specific respiratory symptoms for COPD compared with the absence of these symptoms were modest (Tables 7, 8).

DISCUSSION

This study shows that AO is common in long-term smokers aged > 40 years but is infrequently recognized by health-care workers. The prevalence of symptoms is high among smokers with AO, but they are not sensitive, specific, or predictive of AO. There is a statistically significant association of both symptoms and smoking history with the presence of AO. The addition of symptoms to smoking history improves diagnostic yield marginally in a complicated statistical model but not enough to make them clinically relevant.

Our study showed that only 42% of long-term smokers with AO were given a diagnosis of COPD, confirming NHANES III data.² Others have reported underdiagnosis of COPD.^{24,25} In a spirometry-based screening study of subjects aged > 40 years, only 35.1% with AO reported receiving a previous diagnosis of chronic bronchitis, emphysema, or COPD.²⁵ Similarly, in a study of subjects hospitalized for a COPD exacerbation, 56% were receiving respiratory

medications, and 36% had not been given a prior diagnosis of COPD at admission.²⁴

Data from this study suggest one possible cause for the underdiagnosis of COPD, namely confusion with asthma. Asthma and COPD share common susceptibility genes,^{26,27} common pathophysiologies such as bronchial hyperreactivity,²⁸ and accelerated annual decline in FEV₁.^{29,30} and remodeled asthma is a cause of COPD.³¹ The reported asthma prevalence (12%) in our population is significantly higher than Centers for Disease Control and Prevention estimates for asthma prevalence in men aged > 35 years (5.5%-5.8%),³² which supports the premise that diagnostic overlap between asthma and COPD is a cause of COPD underdiagnosis. Conversely, 4% of subjects with normal and 11% with restricted spirometry were misdiagnosed as COPD.²² The fixed-ratio definition of COPD leads to underdiagnosis in younger patients and misdiagnosis in the elderly patients.³³ The population evaluated in this study showed little difference between fixed-ratio and LLN values for obstruction, thus limiting the misdiagnosis rate.

This study adds to NHANES in providing prevalence and specific data on type of respiratory symptoms. We show that smokers with AO frequently report symptoms that are linked to FEV₁. The frequency of symptoms in smoking populations is

Table 7—Sensitivity, Specificity, and Positive and Negative Predictive Values of Symptoms for Airway Obstruction

Symptom	All Subjects (N = 3,955)				Smokers ≥ 20 Pack-y (n = 2,917)			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
Cough	69	48	43	72	71	44	49	66
Dyspnea	75	37	41	72	76	37	48	67
Sputum	56	60	48	68	57	61	53	65
Wheeze	68	55	47	75	70	49	52	68
≥ 1 symptom	90	22	40	80	92	19	47	75
Smoking ≥ 20 pack-y	88	34	43	83	...	...	...	...

NPV = negative predictive value; PPV = positive predictive value.

Table 8—Relative Risk for Developing COPD Calculated Based on a Logistic Regression Predictive Model

Variable	Cough + Age in Years				No Cough + Age in Years			
	40	50	60	70	40	50	60	70
0 pack-y								
No other symptom	1.64	2.23	3.05	4.15	1	1.61	2.58	4.14
Wheeze	3.13	4.26	5.82	7.92	1.91	3.08	4.93	7.91
SOB	2.05	2.79	3.81	5.19	1.25	2.01	3.23	5.18
Cough	1.64	2.23	3.05	4.15	...	...	...	...
Sputum	2.92	3.97	5.43	7.39	...	...	...	...
Wheeze + SOB	3.92	5.33	7.29	9.92	2.39	3.85	6.17	9.89
Wheeze + sputum	5.57	7.58	10.36	14.09	...	...	...	...
SOB + sputum	3.65	4.96	6.79	9.23	...	...	...	...
Wheeze + SOB + sputum	6.96	9.47	12.95	17.61	...	...	...	...
10 pack-y								
No other symptom	1.90	2.59	3.54	4.81	1.07	1.72	2.76	4.43
Wheeze	3.63	4.94	6.75	9.19	2.04	3.30	5.28	8.46
SOB	2.38	3.24	4.42	6.02	1.34	2.15	3.46	5.54
Cough	1.90	2.59	3.54	4.81	...	...	...	...
Sputum	3.39	4.61	6.30	8.57	...	...	...	...
Wheeze + SOB	4.55	6.18	8.46	11.51	2.56	4.12	6.60	10.58
Wheeze + sputum	6.46	8.79	12.02	16.34	...	...	...	...
SOB + sputum	4.23	5.75	7.88	10.71	...	...	...	...
Wheeze + SOB + sputum	8.07	10.99	15.02	20.43	...	...	...	...
20 pack-y								
No other symptom	2.20	2.99	4.09	5.56	1.15	1.85	2.96	4.75
Wheeze	4.19	5.71	7.80	10.61	2.19	3.53	5.65	9.07
SOB	2.75	3.74	5.11	6.95	1.43	2.31	3.70	5.94
Cough	2.20	2.99	4.09	5.56	...	...	...	...
Sputum	3.91	5.32	7.28	9.90	...	...	...	...
Wheeze + SOB	5.25	7.14	9.77	13.29	2.74	4.42	7.08	11.34
Wheeze + sputum	7.46	10.16	13.88	18.88	...	...	...	...
SOB + sputum	4.89	6.65	9.10	12.37	...	...	...	...
Wheeze + SOB + sputum	9.33	12.69	17.35	23.60	...	...	...	...
40 pack-y								
No other symptom	2.95	4.01	5.49	7.47	1.32	2.12	3.39	5.44
Wheeze	5.63	7.67	10.48	14.26	2.51	4.05	6.48	10.40
SOB	3.69	5.02	6.86	9.34	1.64	2.64	4.25	6.81
Cough	2.95	4.01	5.49	7.47	...	...	...	...
Sputum	5.26	7.15	9.77	13.30	...	...	...	...
Wheeze + SOB	7.06	9.59	13.12	17.86	3.14	5.06	8.11	13.01
Wheeze + sputum	10.03	13.64	18.65	25.36	...	...	...	...
SOB + sputum	6.57	8.93	12.22	16.61	...	...	...	...
Wheeze + SOB + sputum	12.53	17.05	23.31	31.70	...	...	...	...
70 pack-y								
No other symptom	4.59	6.24	8.54	11.62	1.61	2.60	4.16	6.68
Wheeze	8.76	11.93	16.30	22.18	3.08	4.97	7.96	12.77
SOB	5.74	7.81	10.67	14.53	2.02	3.24	5.21	8.36
Cough	4.59	6.24	8.54	11.62	...	...	...	...
Sputum	8.18	11.12	15.20	20.69	...	...	...	...
Wheeze + SOB	10.98	14.92	20.41	27.78	3.86	6.21	9.96	15.96
Wheeze + sputum	15.60	21.22	29.01	39.45	...	...	...	...
SOB + sputum	10.22	13.89	19.01	25.84	...	...	...	...
Wheeze + SOB + sputum	19.49	26.52	36.26	49.31	...	...	...	...

Logistic regression predictive model derived from backward elimination (threshold $P = .10$) of statistical terms that included symptoms, age, pack-years smoked, and their two-way interactions. The final model was as follows: $\text{logit (probability of COPD)} = -4.4646 + 0.6463 \times \text{wheeze} + 0.2223 \times \text{SOB} + 0.4949 \times \text{cough} + 0.5782 \times \text{sputum} + 0.0474 \times \text{age} - 0.0164 \times \text{age} \times \text{cough} + 0.0068 \times \text{pack-years} + 0.0079 \times \text{pack-years} \times \text{cough}$.

From this model, we calculated the relative risk (an approximation from the odds ratio) for different combinations as appear in the table. In this model, the relative risk for age and pack-years smoked depended on the presence or absence of cough (a reflection of significant interaction between these two variables and cough). See the Table 6 legend for expansion of abbreviation.

between 66% and 92%, with higher symptom frequencies reported in populations with a lower FEV₁.³⁴⁻³⁶ We show that the OR for smoking history

was greater than that for respiratory symptoms, which is consistent with other studies where age (OR, 2.2-23.8) and smoking status (OR, 2.5-5.8)

have been reported to be associated with COPD and tend to be greater than OR values reported for respiratory symptoms (cough OR, 1.15-8.3; dyspnea OR, 1.6-1.68; wheeze OR, 1.49-3.1; sputum OR, 1.6-2.58).³⁷⁻⁴⁵

Symptoms have been shown to be nonspecific and poor predictors of COPD.^{37,46-49} More than one-third of the US population reports respiratory symptoms.³⁵ This study shows that the presence of symptoms is not sensitive, specific, or predictive of AO, with values similar to other reports³⁹⁻⁴⁵ of sensitivity (54%-92%), specificity (24%-89%), and positive (30%-92%) and negative (79%-96%) predictive values. Sensitivity, specificity, and positive and negative predictive values for the presence of at least one symptom in this study were nearly identical to analogous values for smoking history alone. Therefore, at the population level, assessment of symptoms did not add to the value of smoking history in finding COPD cases. This observation underpins the idea that smokers at risk for COPD should undergo pulmonary function testing.

Establishing a diagnosis of COPD is important because exacerbations of this condition are linked to accelerated rate of decline in FEV₁, quality of life, and 50% to 75% of all COPD costs,⁵⁰⁻⁵² and initiation of maintenance therapy has been shown to reduce exacerbation frequency.⁵³⁻⁵⁴ Maintenance therapy for COPD also may affect mortality and rate of decline of FEV₁. *Post hoc* analysis of the TORCH (Towards a Revolution in COPD Health)⁵⁵ and UPLIFT (Understanding Potential Long-term Impacts on Function with Tiotropium)⁵⁰ data sets show a positive effect of therapy on rate of decline of FEV₁^{56,57} and mortality⁵⁸; however, these conclusions should be drawn with caution because they were not the predetermined end points of these technically negative studies.

This study is limited by the use of prebronchodilator spirometry. Reversibility is common in patients with COPD.^{59,60} Diagnosis and staging of COPD based on postbronchodilator spirometry is the gold standard.¹⁷ Therefore, prebronchodilator spirometry may have led to an overestimation of the prevalence and severity of COPD in this population.^{61,62} However, not all guidelines recommend postbronchodilator spirometry because the added burden of reversibility testing is considered impractical.⁶³

This study shows that most male smokers aged > 40 years with AO are symptomatic, but only slightly more than one-third report having been given a diagnosis of COPD, emphysema, or chronic bronchitis. Our data show that the OR for a smoking history of > 20 pack-years for AO is approximately threefold higher than that of wheeze, cough, sputum, or dyspnea. Underdiagnosis of COPD in clinical practice appears not to result from failure to report symptoms

but more likely from failure to follow up the report of symptoms with spirometry. Use of COPD symptom questionnaires should improve symptom assessment; however, in view of the near-universal presence of symptoms in persons with AO, the poor sensitivity and specificity of symptoms, the strong predictive value of a smoking history of ≥ 20 pack-years, and emerging data that therapy might modify the course of COPD, perhaps a simpler and more effective approach would be to screen smokers aged ≥ 40 years and with a history of ≥ 20 pack-years smoking with spirometry.

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Dr Ohar: contributed the idea of the paper and was the primary writer.

Dr Sadeghnejad: contributed to methods and statistical analysis.

Dr Meyers: contributed to supervision of statistical analysis.

Dr Donohue: contributed to supervision of clinical methods and assessments.

Dr Bleecker: contributed to supervision of clinical methods and assessments.

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