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Publication Date

2023-03-01

DOI

10.1016/j.rmed.2023.107126

Peer reviewed

HHS Public Access

Author manuscript

Respir Med. Author manuscript; available in PMC 2024 March 01.

Published in final edited form as:

Respir Med. 2023 March ; 208: 107126. doi:10.1016/j.rmed.2023.107126.

Prevalence of Abnormal Spirometry in Individuals with a Smoking History and No Known Obstructive Lung Disease

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T.T and S.F. had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the analysis. They both contributed equally to the conception and design of the study. All authors including G.K., A.C., K.H., A.B., A.J.M., J.L.C., N.H., R.C., K.A.Y., V.K., B.M., E.S.W., A.A.D., J.H., J.D.C., E.K.S., S.P.B., and E.R. contributed to drafting and revising the article.

Conflicts of Interests

Alejandro Comellas has consulted for GSK and VIDA Diagnostics. Arianne K. Baldomero is supported by the NIH National Center for Advancing Translational Sciences Grants KL2TR002492 and UL1TR002494. Jeffrey L. Curtis is supported by R01 HL144718, R01 HL144849, U01 HL137880, and I01 CX001969 and has consulted for AstraZeneca PLC, Novartis AG, and CSL Behring LLC. Richard Casaburi has received consultant fees or honoraria from Boehringer Ingelheim, Glaxo Smith Kline and Inogen. Victor Kim has consulted for Boehringer Ingelheim, Gala Therapeutics and AstraZeneca and received personal fees from American Board of Internal Medicine. Alejandro A. Diaz is supported by NIH grants R01-HL133137, R01-HL14986; has reported speaker fees from Boehringer Ingelheim, outside the submitted work. Edwin K. Silverman has received grant support from GlaxoSmithKline and Bayer.

Surya P. Bhatt is supported by NIH Grants R01HL151421, R21EB027891, and UG3HL155806 and he has served on advisory boards for Boehringer Ingelheim and Sanofi/Regeneron. Spyridon Fortis has received grants from American Thoracic Society and Fisher &Paykel and served as a consultant for Genentech. The rest of the authors have no relevant conflicts to disclose.

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Abstract

Introduction—Recent evidence suggests a high prevalence of undiagnosed chronic obstructive pulmonary disease (COPD). These individuals are at risk of exacerbations and delayed treatment. We analyzed an at-risk population for the prevalence of abnormal spirometry to provide clarity into who should undergo early spirometry.

Methods—We analyzed data from the COPDGene study. Participants with ≥10 pack-years of smoking were included. Individuals with self-reported or physician-diagnosed COPD, asthma, chronic bronchitis, emphysema and/or were on inhalers were excluded. Parsimonious multivariable logistic regression models identified factors associated with abnormal spirometry, defined as either airflow obstruction (AFO) or preserved ratio impaired spirometry. Variables were selected for the final model using a stepwise backward variable elimination process which minimized Akaike information criterion (AIC). Similarly, during the 5-year follow-up period, we assessed factors associated with incident diagnosis of COPD.

Results—Of 5,055 individuals, 1,064 (21%) had undiagnosed AFO. Age, pack-years, current smoking and a history of acute bronchitis were associated with AFO while body mass index, female sex, and Black race were inversely associated. Among 2,800 participants with 5-year follow-up, 532 (19%) had an incident diagnosis of COPD. Associated risk factors included mMRC

≥2, chronic productive cough, respiratory exacerbations during the follow-up period, and abnormal spirometry. Age was inversely associated.

Conclusions—The prevalence of undiagnosed COPD is high in at-risk populations. We found multiple factors associated with undiagnosed COPD and incident diagnosis of COPD at follow up. These results can be used to identify those at risk for undiagnosed COPD to facilitate earlier diagnosis and treatment.

Keywords

Chronic Obstructive Pulmonary disease; Diagnosis

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of death and exerts a large burden on the healthcare system [1]. The course of COPD is often worsened by exacerbations, defined as acute deterioration of respiratory symptoms, which can become more frequent as the disease progresses. COPD exacerbations are associated with increased mortality and lung function decline [2].

Pharmacotherapy has been shown to reduce exacerbations, hospital admission rates, and improve quality of life [3]. Despite this, there is often a delay in starting medications because of an underdiagnosis of COPD [4]. Recent studies have suggested that up to 3% of the general population could be unaware that they have COPD, while 71% of those eventually diagnosed already had chronic respiratory symptoms [5]. A study using administrative data in the United Kingdom showed that up to 85% of patients with COPD had missed an opportunity to be diagnosed within the previous five years [6].

As opposed to the general population, the prevalence of undiagnosed COPD among individuals with extensive smoking exposure is uncertain. We hypothesized that many of these individuals have COPD but are unaware of their diagnosis. This at-risk population is particularly important to recognize as continuing to smoke with COPD has been associated with faster rates of lung function decline, increased symptoms burden and mortality [7].

Using the Genetic Epidemiology of COPD (COPDGene) cohort, we retrospectively reviewed participants with at least 10 pack-years of smoking who did not self-report or carry a physician diagnosis of COPD, asthma, emphysema or chronic bronchitis at enrollment. We assessed the prevalence of airflow obstruction (AFO), preserved ratio impaired spirometry (PRISm), or abnormal spirometry (AFO or PRISm) among those individuals. We additionally assessed factors associated with AFO, PRISm, or abnormal spirometry, and factors associated with incident diagnosis of COPD at their 5-year follow-up visit.

Methods

We analyzed data from participants in COPDGene (ClinicalTrials.gov Identifier: NCT00608764), a prospective observational cohort study conducted at multiple clinical centers across the United States (http://www.copdgene.org/). The institutional review boards

at each participating center approved the study protocol (e-Appendix 1). Written informed consent was obtained from all participants. The study protocol has been previously published [8]. Briefly, participants had at least 10 pack-years of accumulative smoking history, were aged between 45 and 80 years at enrollment, and self-identified themselves as non-Hispanic Whites (NHW) or Black/African Americans (AA). All participants had an enrollment visit and a proportion of them had two follow-up visits approximately at 5 and 10 years afterwards. At the visits, they completed a modified American Thoracic Society Respiratory Epidemiology questionnaire which included a modified Medical Research Council (mMRC) scale to assess dyspnea, pre- and post-bronchodilator spirometry, and volumetric chest computed tomography (CT) scans. Spirometry was performed according to 2005 American Thoracic Society–European Respiratory Society (ATS-ERS) guidelines [9, 10]. Volumetric chest CT scans at total lung capacity (TLC) (maximal inspiration) and at functional residual capacity (FRC) (end-tidal expiration) were obtained. Data regarding respiratory exacerbations were collected prospectively after enrollment. Participants were contacted every 6 months and completed a standardized questionnaire regarding respiratory exacerbations through the longitudinal follow-up program.

For this analysis we excluded participants: i) with a current diagnosis of asthma, self-reported or physician diagnosed COPD, chronic bronchitis and/or emphysema diagnosis at study enrollment, ii) who receive treatments with inhaled/oral glucocorticosteroids and/or bronchodilators at study enrollment, and iii) with no available post-bronchodilator spirometry.

Definitions and Outcomes

Current asthma diagnosis was defined when a participant answered “Yes” to the question: “Have you ever had asthma?”, “At about what age did it start?”, and “Do you still have it?”. COPD diagnosis was defined when a participant answered “Yes” to at least one of these questions: “Have you ever had chronic bronchitis?”, “Have you ever had emphysema?” and “Have you ever had COPD?”. History of acute bronchitis was defined when a participant answered “Yes” to the questions: “Have you ever had an attack of bronchitis?”. History of pneumonias was defined when a participant answered “Yes” to the questions: “Have you ever had pneumonia or bronchopneumonia?”. Whether the participant was receiving respiratory medication was defined when a participant answered “Yes” to the question: “At present, do you use medications to treat your breathing problems?” Sleep apnea, coronary artery disease, and high blood pressure were also self-reported. Chronic productive cough was defined when participants reported that they coughed chronic cough and phlegm production for ≥3 months/year for at least 2 consecutive years.

Spirometry patterns were divided into 3 categories: i) Normal, defined as post-bronchodilator forced expiratory volume in one second divided by forced vital capacity (FEV_1/FVC) ≥0.7 and post-bronchodilator FEV_1 % predicted ≥80%, ii) AFO defined as a post-bronchodilator FEV_1/FVC <0.7, and iii) preserved ratio impaired spirometry (PRISm) defined as post-bronchodilator FEV_1/FVC ≥0.7 combined with a post-bronchodilator FEV_1 %predicted <80%.

CT Structural Abnormality was defined as ≥5% emphysema (low attenuation area [LAA] ≤−950 Hounsfield units [HU]) on inspiratory CT, and/or ≥15% gas-trapping (LAA ≤−856 HU) on expiratory CT, and/or Pi10 (Square root of airway wall area for a standardized airway of 10 mm internal perimeter) ≥2.5 mm [11].

Respiratory exacerbation between enrollment and follow-up visit was defined as episodes of worsening respiratory symptoms requiring use of antibiotics and/or systemic steroids. Severe exacerbations were defined as those requiring emergency room visit or hospitalization.

Incident obstructive lung disease was defined when a participant with no known obstructive lung disease at enrollment received a diagnosis of COPD, asthma, chronic bronchitis or emphysema or were prescribed respiratory medication before their 5-year follow-up visit based on the questions described above.

Statistical analysis

We categorized participants by their spirometric pattern at enrollment. We compared baseline characteristics by lung function category (normal spirometry, AFO, and PRISm). We used a Student's t test or Wilcoxon rank sum for continuous variables and Chi-square or Fisher's exact test for categorical variables.

To identify factors associated with: i) AFO (AFO vs PRISm and normal spirometry), ii) abnormal spirometry (PRISm and AFO vs normal spirometry), and iii) abnormal spirometry and/or abnormal chest CT, we created parsimonious multivariable logistic regression models. The following variables were considered: age, body mass index (BMI), sex, race, smoking status (current or former smoking), pack-years of smoking, chronic productive cough, dyspnea (mMRC ≥2), history of acute bronchitis, history of pneumonia, history of sleep apnea, history of coronary artery disease, history of hypertension, highest educational degree earned, and whether the participant was currently employed or not. Variables were selected for the final model using a stepwise backward variable elimination process to minimize the Akaike information criterion (AIC) [12]. We assessed for variable multicollinearity using correlation matrices and variance inflation factors. Then we assessed factors associated with incident diagnosis of obstructive lung disease at 5-year follow-up visit using logistic regression models as above. The following variables were considered for the model: age, BMI, sex, race, smoking status (current or former smoking), pack-years of smoking, chronic productive cough, dyspnea (mMRC ≥2), history of coronary artery disease, history of hypertension, occurrence of at least once exacerbation between enrollment and follow-up, spirometric pattern at enrollment, highest educational degree earned, employment status, an increase in mMRC ≥1, and change in FEV_1 between visits. Variables were selected for the final model using a stepwise backward variable elimination process to minimize the Akaike information criterion (AIC) as above. Further, we employed interval-censored proportional hazard regression models to identify factors associated with incident diagnosis of obstructive lung disease during the entire follow-up time. In the sensitivity analysis, we repeated the analysis defining AFO as pre-bronchodilator FEV_1/FVC <lower limit of normal (LLN) and PRISm as pre-bronchodilator FEV_1/FVC ≥LLN and FEV_1 <LLN. We used Global Lung Function Initiative (GLI) reference values for the lower limit of normal and predicted FEV_1 and FVC provided by "rspiro" package

[13]. All statistical analyses were conducted using R statistical software (http://www.r-project.org/).

Results

Of 10,194 participants with at least 10 pack-years of smoking, we excluded 4,737 participants due to having a current diagnosis of asthma or a self-reported or physician diagnosed history of COPD, chronic bronchitis or emphysema, 312 due to already being prescribed any respiratory medications, and 90 because of an absence of post-bronchodilator spirometry, leaving 5,055 participants (Figure 1).

Baseline characteristics (n = 5,055)

Normal spirometry was found in 3,306 (65.4%) participants while 1,064 (21.0%) and 685 (13.6%) had AFO and PRISm, respectively. Table 1 shows the demographic features of the participants categorized by spirometry. Compared to participants with normal spirometry, those with AFO were more likely to be older, have a greater pack-years of smoking, and a history of coronary artery disease, acute bronchitis or a chronic productive cough. Similarly, when compared to those with normal spirometry, individuals with PRISm had a higher BMI, greater pack-years, mMRC ≥2 and a history of coronary artery disease or hypertension. The prevalence of undiagnosed AFO and of abnormal spirometry was higher in groups with greater pack-years of smoking history (Supplemental Figure 1). Although AFO was found only in 11% of participants with 10–19 pack-years of smoking, 37% of participants with >80 pack-years had AFO.

Factors associated with spirometry patterns in participants at enrollment

On multivariable analysis, AFO (AFO vs normal and PRISm) was associated with age, pack-years, current smoking, and a history of acute bronchitis. AFO was less common in those with greater BMI, female sex, and Black race (Table 2).

Factors associated with abnormal spirometry are shown in Supplemental Table 1. Age, pack-years, current smoking, mMRC ≥2 and a history of acute bronchitis were all associated with an increased odds ratio of having abnormal spirometry. Black race and having either a Master's degree or doctorate were associated with a decreased odds ratio.

Factors associated with abnormal spirometry or chest CT in participants at enrollment

Of 3,467 participants who had a chest CT at enrollment, 2,865 (82.6%) had an abnormal spirometry and/or chest CT at enrollment. Age and pack-years were all associated with an abnormal spirometry and/or abnormal chest CT. Female sex was inversely associated (Supplemental Table 2).

Five-year follow up analysis

A 5-year follow up visit was completed by 2,800 participants. Among them, 532 (19.0%) had an incident diagnosis of COPD or were on new treatment for obstructive lung disease and 183 (34.4%) reported at least one interval exacerbation (Figure 2). Of the remaining participants, 1,495 (53.4%) had normal spirometry, 490 (17.5%) had AFO, and 283 (10.1%)

had PRISm. At least one exacerbation was seen between enrollment and their follow-up visit in 14.5%, 16.1%, and 18.4% of those with normal spirometry, AFO, and PRISm, respectively. We observed similar findings regarding those participants who had severe exacerbations (Figure 2).

In the multivariable analysis, the composite outcome of incident COPD diagnosis or treatment with respiratory medications was associated with mMRC ≥2, chronic productive cough or having at least one exacerbation during the follow up period. Either AFO or PRISm at enrollment were associated with an incident diagnosis of COPD and/or treatment while age was associated with lower risk (Table 3).

Longitudinal analysis

Results from the interval-censored proportional hazard regression models are shown in Supplemental Figure 2 and Supplemental Table 7. Current or former smoking status were the only variables associated with an incident diagnosis of obstructive lung disease during follow up. By the 5-year mark, there was a less percentage of COPD-free individuals seen in those who were currently smoking as opposed to those who were former smokers. However, the difference between the two groups eventually diminished by the 8-year mark.

Sensitivity analysis using LLN and GLI criteria

A sensitivity analysis was performed using the same data but defining AFO as pre-bronchodilator FEV_1/FVC <LLN and PRISm as pre-bronchodilator FEV_1/FVC ≥LLN and FEV_1 <LLN while using the GLI reference data for establishing the LLN.

There was a difference between the number of individuals in each spirometric category at enrollment. More participants were diagnosed with normal spirometry (3,306 vs 3,565) while there were less diagnoses of AFO (1,064 vs 844) or PRIsm (685 vs 586). In the AFO group, age, history of acute bronchitis and CAD were no longer found to be statistically different when compared to the normal spirometry group. Additionally, in the PRISm group, current smoking status also no longer became statistically different (Supplemental Table 3).

When identifying factors associated with AFO at enrollment, age and female sex were not statistically significant (Supplemental Table 4). Age was also no longer a significant factor with abnormal spirometry at enrollment (Supplemental Table 5). Lastly, at the 5-year follow up period, PRISm diagnosis was not significant when evaluating factors associated with the development of COPD (Supplemental Table 6).

Discussion

By analyzing a well-phenotyped, geographically diverse group (n=5,055) with a smoking history (≥10 pack-years) without a current history of asthma or a baseline self-reported or physician diagnosed COPD, chronic bronchitis, emphysema, or respiratory medication treatment, we show that objective evidence of undiagnosed lung disease is common. Through post-bronchodilator spirometry alone, we found 34.6% total diagnoses of abnormal spirometry (21.0% and 13.6% for AFO and PRISm, respectively); if additionally considering abnormal CT imaging, baseline prevalence was 82.6%. Among our participants

who completed a five-year follow up visit, incident diagnosis of COPD or new respiratory therapy developed in a further 19.0%, and at least one interval healthcare utilization-defined exacerbation occurred in 34.4% of those participants. By providing additional evidence that the burden of COPD is grossly underappreciated and leads to inadequate provision of therapies that could reduce exacerbations, these results point to a significant opportunity to improve healthcare utilization.

Our estimates of the prevalence of COPD among those with smoking histories extend the existing literature on the underdiagnosis of this common condition. Unsurprisingly, our results greatly exceed the estimate of 6.4% for this diagnosis in the general US population [14]. The prevalence of undiagnosed COPD is almost doubled, with recent data suggesting a rate of 12.1–13.7% [15, 16]. In higher risk individuals, this statistic can reach as high as 70–80%, in line with our results when we included abnormal imaging consistent with COPD [5, 17, 18].

Using the same COPDGene data but including those who self-reported a physician diagnosis of asthma or were on respiratory therapy medications, Mamary et al showed that of 4,484 individuals with AFO, only 1,450 (32%) had prior physician diagnosis of COPD [19]. The present study excluded that population, which may help to explain why the prevalence of AFO in our cohort was lower. A recent prospective study that included participants with a prior COPD diagnosis or on respiratory therapy medications assessed the prevalence of undiagnosed COPD in a Danish population [5]. Based on pre-bronchodilator spirometry, 3,699 participants had AFO; of those, 2,903 (78%) were undiagnosed at enrollment, and of those, 2,052 (70.7%) were already symptomatic. Globally, Lamprecht and colleagues used data from multiple epidemiological surveys (n=30,874) that included respiratory questionnaires and post-bronchodilator spirometry [17]. Although 26.4% already had a diagnosis of COPD, they estimated worldwide underdiagnosis of COPD to be 81.4%. In contrast to these studies which examined patients with known obstructive lung disease diagnoses, we examined patients without any diagnoses or ongoing treatment, and showed that even these seemingly healthy patients have increased risk of an ultimate diagnosis of AFO.

There are several reasons theorized to explain this high prevalence of COPD underdiagnosis, including failure to identify symptoms, attributing symptoms to other causes, and the absence of efficacious screening tools [18]. As such, the US Preventive Services Task Force recommends against screening in asymptomatic individuals, but they acknowledge that further research is needed regarding screening in high-risk asymptomatic individuals [20, 21]. Global Initiative for Chronic Obstructive Lung Disease guidelines refer to screening the general population for COPD as controversial and recommends screening if someone has a greater than 10 pack-year history of smoking [2]. A recent general population study created a scoring system to identify subclinical AFO and found that fewer than four individuals need to be screened to identify one case of AFO [22]. Our study provides additional insight into whom should be screened. Among individuals with ≥45 years of age and ≥10 pack-year smoking exposure, we found multiple factors to be associated with undiagnosed AFO, including age, higher pack-years, current smoking status and a history of acute bronchitis.

Conversely, misclassification of COPD is a real clinical issue. A recent study by Farooqi et al showed that in a Canadian population of 21,142 participants, 973 (4.6%) self-reported a physician diagnosis of COPD [23]. However, after spirometry was completed, only 217 of the entire cohort (1%) had results consistent with AFO. Misattributing patient symptoms can lead to false diagnoses and hence ineffective or potentially harmful therapies. Indeed, Josephs and colleagues found that a large amount of their participants without AFO by spirometry had comorbid conditions such as cardiovascular disease that could explain their respiratory symptoms [24].

Importantly, during our longitudinal analysis, the percentage of participants sustaining interval exacerbations, whether defined by medication change or requiring hospital care, was more than twice as high among those with an incident COPD diagnosis as those with abnormal spirometry still not meeting diagnostic criteria for COPD. Recently, Bhatt et al. examined 14,204 asymptomatic adults also without previously known respiratory disease. The prevalence of AFO in their cohort was 14.2%. Similar to our study, the rate of respiratory exacerbations in the individuals with subclinical AFO was 3–5 times higher than the individuals without AFO [22].

Using a fixed ratio to diagnose AFO ($FEV_1/FVC < 0.7$) is also thought to be controversial and instead there has been more recent interest in using $FEV_1/FVC <$LLN [25]. Our analysis does show that by using LLN, more individuals were categorized with normal spirometry at enrollment and less with AFO or PRISm. Additionally, age no longer became a significant factor associated with either AFO or abnormal spirometry. However, the remainder of factors retained their significance while using the LLN cut-off.

Exacerbations of COPD have been known to cause both an increase in mortality and a reduction in quality of life [26]. Thus, prevention of exacerbations has been a mainstay of COPD treatment. Multiple recent meta-analyses have shown that respiratory inhaler medications can reduce the incidence of COPD exacerbations [27, 28]. Our data provides insight into at risk patients that should be screened for COPD, potentially leading to earlier treatment and reducing risk for exacerbations and long-term complications. Future studies could focus on assessing the potential benefits of diagnosing COPD earlier, including rates of tobacco cessation or lung cancer screening.

This study has several limitations. First, COPDGene is not a population-based study, but instead recruited primarily from university medical centers. Second, there are demographic disparities in our population. We focused only on participants with significant smoking exposure and thus do not have information regarding other causes of COPD which include exposure to biomass combustion or other environmental factors. Additionally, although we had a large proportion of female participants, we recruited only Black and non-Hispanic white individuals. Our analysis was also reliant on participant’s self-reported physician diagnosis of obstructive lung diseases and medication usage. Nevertheless, data was collected prospectively using questionnaires that had undergone strict quality control. The above limitations cannot undermine our strength which are the wealth of spirometry and epidemiological data.

In summary, we show that one-third of our participants without known obstructive lung disease despite at least 10 pack-year smoking exposure had abnormal spirometry and over two-thirds had abnormal chest imaging indicative of emphysema or small airway disease. We identified multiple risk factors for prevalent lung disease, most of which also predict incident disease development within five years. Healthcare providers should lower their thresholds to interrogate this group for COPD. Investigating the mechanisms underlying these diagnostic delays may expedite patients receiving appropriate care and improve outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Grant Support and Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States Government.

COPD Foundation Funding

COPDGene is also supported by the COPD Foundation through contributions made to an Industry Advisory Board that has included AstraZeneca, Bayer Pharmaceuticals, Boehringer Ingelheim, Genentech, GlaxoSmithKline, Novartis, Pfizer, and Sunovion.

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University of Texas Health, San Antonio, San Antonio, TX: Antonio Anzueto, MD; Sandra Adams, MD; Diego Maselli-Caceres, MD; Mario E. Ruiz, MD; Harjinder Singh

Funding:

This work was supported by NHLBI U01 HL089897 and U01 HL089856. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute or the National Institutes of Health. The COPDGene study (NCT00608764) is also supported by the COPD

Foundation through contributions made to an Industry Advisory Committee comprised of AstraZeneca, Bayer Pharmaceuticals, Boehringer-Ingelheim, Genentech, GlaxoSmithKline, Novartis, Pfizer and Sunovion.

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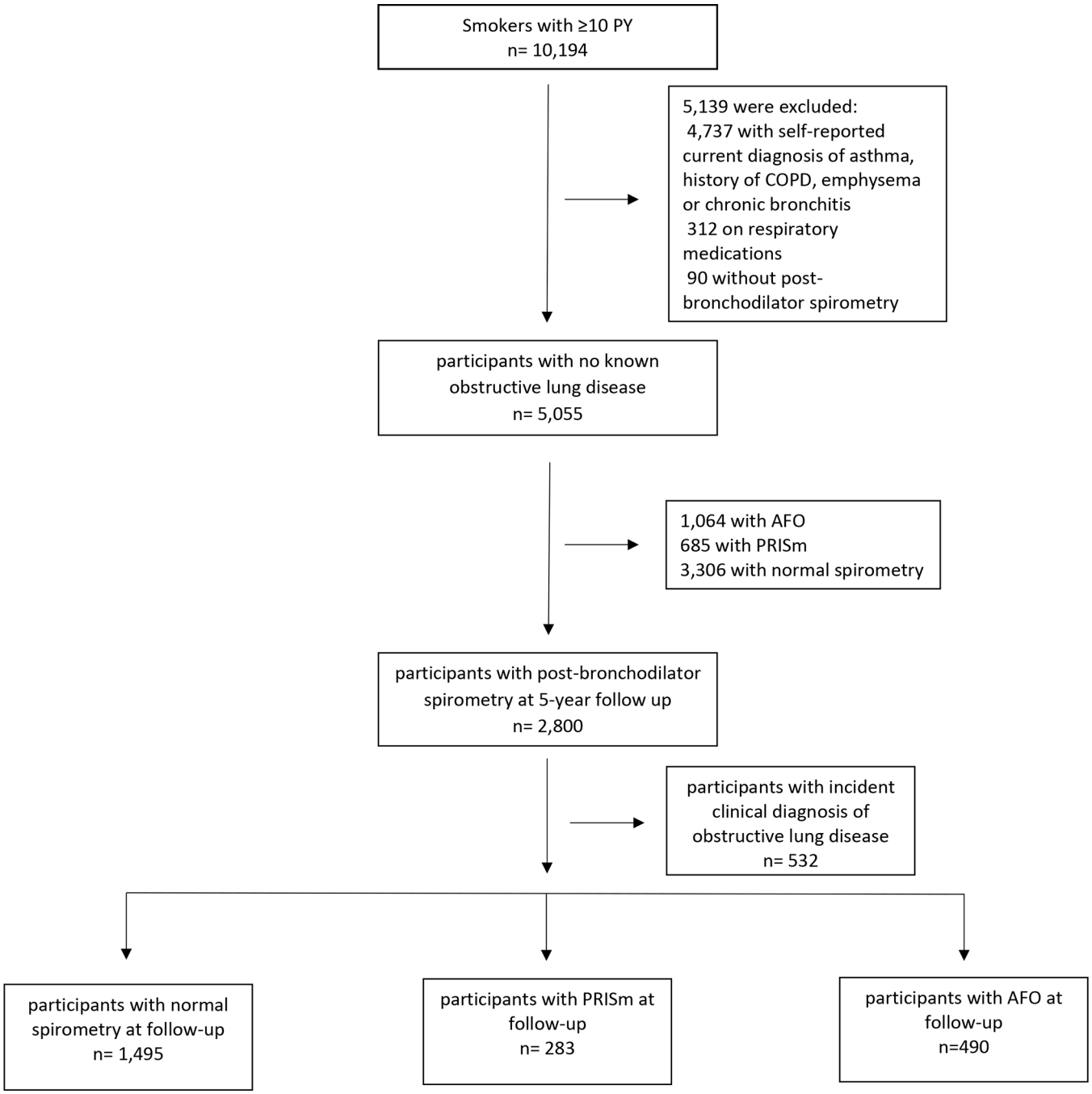

Figure 1.

Flowchart of study population

Abbreviations: AFO = airflow obstruction, COPD = chronic obstructive pulmonary disease, PY = pack-years, PRISm = preserved ratio impaired spirometry

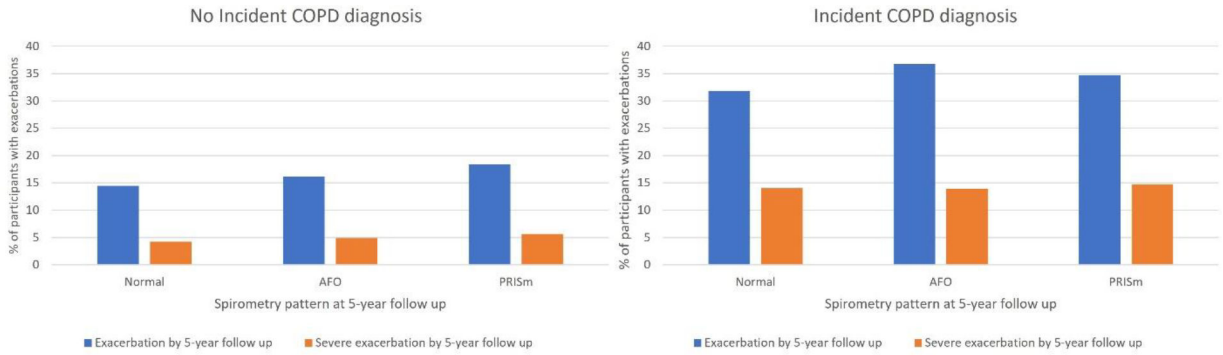

Figure 2.

Participants with and without an incident diagnosis of COPD but at least one exacerbation between enrollment and 5-year follow-up stratified by spirometry at 5-year follow-up.

Abbreviations: AFO = airflow obstruction, PRISm = preserved ratio impaired spirometry

Table 1.

Characteristics of participants with no known obstructive lung disease categorized by spirometrie pattern at enrollment (n= 5,055).

Variable	Normal	AFO	PRISm
n	3306	1064	685
Age, y ± SD	56.6 ± 8.4	61.1 ± 8.9 *	57.1 ± 8.1
Female sex, n (%)	1409 (42.6%)	405 (38.1%)	312 (45.5%)
Black race, n (%)	1359 (41.1%)	274 (25.8%) *	297 (43.4%)
BMI± SD	28.7 ± 5.6	27.6 ± 5.2 *	30.8 ± 7.0 *
Current smoking, n (%)	1965 (59.4%)	662 (62.2%)	443 (64.7%)
PY ± SD	36.3 ± 19.4	45.7 ± 22.7 *	41.0 ± 21.4 *
mMRC ≥2, n (%)	547 (16.6%)	203 (19.1%)	187 (27.3%) *
History of acute bronchitis, n (%)	741 (22.4%)	304 (28.6%) *	172 (25.1%)
Chronic productive coughf, n (%)	319 (9.6%)	160 (15.0%) *	67 (9.8%)
History of pneumonia, n (%)	721 (21.8%)	275 (25.8%)	178 (26.0%)
History of coronary artery disease, n (%)	148 (4.5%)	95 (8.9%) *	57 (8.3%) *
History of hypertension, n (%)	1102 (33.3%)	414 (38.9%)	298 (43.5%) *
History of obstructive sleep apnea, n (%)	307 (9.3%)	93 (8.7%)	90 (13.1%)
History of childhood asthma, n (%)	69 (2.1%)	29 (2.7%)	19 (2.8%)
Currently employed, n (%)	1296 (39.2%)	381 (35.8%)	221 (32.3%) *
Post-bronchodilator FEV_1 categories, n (%)			
>80% predicted	3306 (100%)	464 (43.6%)	0 (0%)
50–80% predicted	0 (0%)	543 (51.0%)	677 (98.8%)
35–50% predicted	0 (0%)	50 (4.7%)	8 (1.2%)
<35% predicted	0 (0%)	7 (0.7%)	0 (0%)
Post-bronchodilator FEV_1% predicted ± SD	98.0% ± 11.6%	77.3% ± 16.0%	71.8% ± 7.1%
Chest CT findings			
>5% Chest CT emphysema, n (%)	337 (17.5%)	319 (58.1%) *	34 (8.0%) *
≥ 15% gas-trapping, n (%)	584 (22.1%)	554 (61.7%) *	88 (17.3%)
≥ 2.5 mm Pi10, n (%)	381 (12.3%)	346 (34.1%) *	222 (35.4%) *
Highest educational degree earned			
Highschool degree or lower, n (%)	1198 (36.2%)	373 (35.1%)	308 (45.0%)
College degree, n (%)	1772 (53.6%)	592 (55.6%)	328 (47.9%)
Master's degree or doctorate, n (%)	336 (10.2%)	99 (9.3%)	49 (7.2%)

We characterized the participants with at least 10 pack-years of smoking by their spirometric pattern.

* indicates $p < 0.001$ vs normal.

Abbreviations: AFO = airflow obstruction, BMI = body mass index, COPD = chronic obstructive pulmonary disease, FEV_1 = forced expiratory volume in 1 second, mMRC = modified medical research council, PY = pack-years, PRISm = preserved ratio impaired spirometry, SD = standard deviation

Table 2.

Factors associated with AFO at enrollment.

Variable	OR (95% CI)	P value
Age (for every 10 years)	1.99 (1.79 – 2.20)	< 0.001
Female sex	0.75 (0.64 – 0.87)	< 0.001
Black race	0.57 (0.47 – 0.69)	< 0.001
BMI (for every 1 point)	0.95 (0.94 – 0.96)	< 0.001
Current smoking	2.01 (1.67 – 2.42)	< 0.001
PY (for every 10 pack-years)	1.12 (1.08 – 1.16)	< 0.001
mMRC ≥2	1.30 (1.07 – 1.58)	0.009
History of acute bronchitis	1.36 (1.15 – 1.62)	< 0.001
Chronic productive cough	1.42 (1.14 – 1.76)	0.002
Currently employed	1.13 (0.96 – 1.32)	0.141
Highest educational degree earned		
High school or lower	ref	ref
College degree	0.94 (0.80 – 1.11)	0.483
Master’s degree or doctorate	0.66 (0.50 – 0.88)	0.004

We used logistic regression model to determine the odds ratio and corresponding p values for each adjusted variable. We created parsimonious multivariable logistic regression models. Variables considered for the model but not retained: history of pneumonia, coronary artery disease, hypertension, and obstructive sleep apnea. Variables were selected for the final model using a stepwise backward variable elimination process to minimize the Akaike information criterion (AIC).

Abbreviations: AFO = airflow obstruction, BMI = body mass index, CAD = coronary artery disease, mMRC = modified medical research council, PY = pack-years

Table 3.

Factors associated with an incident diagnosis of obstructive lung disease at 5-year follow up visit.

Variable	OR (95% CI)	P value
Age (for every 10 years)	0.96 (0.94 – 0.99)	0.003
Female sex	1.03 (0.99 – 1.07)	0.101
Black race	1.04 (0.99 – 1.08)	0.120
PY (for every 10 pack-years)	1.01 (1.00 – 1.02)	0.017
mMRC ≥2	1.22 (1.16 – 1.29)	< 0.001
Chronic productive cough	1.15 (1.08 – 1.23)	< 0.001
History of hypertension	1.04 (1.00 – 1.08)	0.039
At least one exacerbation during follow-up period	1.13 (1.08 – 1.18)	< 0.001
Currently employed	0.97 (0.94 – 1.01)	0.159
Spirometric pattern at enrollment		
Normal	ref	ref
AFO	1.22 (1.17 – 1.27)	< 0.001
PRISm	1.10 (1.04 – 1.16)	< 0.001

We used logistic regression model to determine the odds ratio and corresponding p values for each adjusted variable. We created parsimonious multivariable logistic regression models. Variables considered for the model but not retained: BMI, smoking status (current or former smoking), history of sleep apnea, coronary artery disease, and highest educational degree earned. Variables were selected for the final model using a stepwise backward variable elimination process to minimize the Akaike information criterion (AIC). Incident obstructive lung disease was defined when a participant with no known obstructive lung disease at enrollment received a diagnosis of asthma, COPD or were prescribed respiratory medication before their 5-year follow-up visit based on the questions described above.

Abbreviations: AFO = airflow obstruction, mMRC = modified medical research council, PY = pack-years, PRISm = preserved ratio impaired spirometry