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Factors associated with abnormal spirometry among HIV-infected individuals

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Abstract

Objective—HIV-infected individuals are susceptible to development of chronic lung diseases but little is known regarding prevalence and risk factors associated with different spirometric abnormalities in this population. We sought to determine the prevalence, risk factors and performance characteristics of risk factors for spirometric abnormalities among HIV-infected individuals.

Design—Cross-sectional cohort study

Methods—We analyzed cross-sectional US data from the NHLBI-funded Lung-HIV consortium, a multi-center observational study of heterogeneous groups of HIV-infected participants in diverse geographic sites. Logistic regression analysis was performed to determine factors statistically significantly associated with spirometry patterns.

Results—A total of 908 HIV-infected individuals were included. The median age of the cohort was 50 years, 78% were male and 68% current smokers. An abnormal spirometry pattern was present in 37% of the cohort: 27% had obstructed and 10% had restricted spirometry patterns. Overall, age, smoking status and intensity, history of *Pneumocystis* infection, asthma diagnosis and presence of respiratory symptoms were independently associated with an abnormal spirometry pattern. Regardless of presence of respiratory symptoms, five HIV-infected participants would need to be screened with spirometry to diagnose two individuals with any abnormal spirometry pattern.

Conclusions—Nearly 40% of a diverse US cohort of HIV-infected individuals had an abnormal spirometry pattern. Specific characteristics including age, smoking status, respiratory infection history and respiratory symptoms can identify those at risk for abnormal spirometry. The high prevalence of abnormal spirometry and the poor predictive capability of respiratory symptoms to identify abnormal spirometry should prompt clinicians to consider screening spirometry in HIV-infected populations.

Keywords

HIV; lung disease, obstructive; respiratory tract disease; lung function; spirometry

INTRODUCTION

Human immunodeficiency virus (HIV) infection has become a controllable chronic disease in the current era of effective anti-retroviral therapy (ART).[1–3] As morbidity and mortality from opportunistic infections has decreased, it has become evident that HIV-infected individuals are susceptible to chronic diseases at greater rates than those observed in HIV-uninfected persons.[4–7] A large body of literature has described an association between HIV infection and chronic lung diseases such as asthma and chronic obstructive pulmonary disease (COPD).[8–15] While risk factors such as smoking, opportunistic infections and injection drug use contribute to the increased risk for chronic lung disease, HIV infection and markers of HIV disease severity also have been associated with increased risk.[16]

Chronic lung diseases can be categorized by the patterns of abnormalities detected with spirometry testing. An obstructive airflow pattern, as can be seen in asthma, bronchiectasis and COPD, is characterized by a disproportional reduction in the forced expiratory volume in 1 second (FEV1) compared to the forced vital capacity (FVC), generally with a reduction in the $FEV1/FVC < 0.70$ used to define disease.[17]. Restrictive patterns of airflow, seen in interstitial lung disease and respiratory muscle insufficiency, are defined by a normal $FEV1/FVC$ (> 0.70), but an $FVC < 80\%$ of predicted value. Both obstructive and restrictive spirometry patterns are associated with increased mortality in the general population.[18–20] The prevalence and clinical risk factors for these spirometric patterns are under-explored in HIV-infected populations despite the increased frequency of chronic lung disease in this population.[13, 21]

The multi-center Lung-HIV consortium has collected spirometric and clinical data from heterogeneous groups of HIV-infected participants in diverse geographic sites,[22] providing a unique opportunity to define patterns of lung function abnormalities among HIV-infected individuals. Using cross-sectional spirometric and clinical data from United States sites, we determine the prevalence and risk factors for any abnormal pattern as well as for obstructed and restricted spirometry patterns. To help inform clinical evaluation, we also characterize the performance characteristics [i.e., sensitivity, specificity and area under the curve (AUC)] of different risk factors for abnormal spirometry, and determine the number of HIV-infected individuals needed to screen with spirometry to detect one abnormal result. Some of these results have been previously reported in abstract form.[23]

METHODS

Study Cohort

The Lung-HIV Study was a NHLBI-sponsored consortium that collected data on HIV-associated lung diseases from 2008 to 2013. The consortium included eight clinical centers and a data coordinating center. Clinical centers enrolled different risk groups of HIV-infected and HIV-uninfected individuals. While each site had unique research initiatives, site investigators collaborated to create common data collection forms and standardized pulmonary testing procedures, permitting harmonized clinical and spirometric datasets. Five US clinical centers collected spirometry measurements along with demographic and clinical data, at clinical enrollment sites that included Atlanta GA, Baltimore MD, Columbus OH,

Houston TX, Los Angeles CA, New York (including Manhattan and the Bronx) NY, Pittsburgh PA, and San Francisco CA (see Crothers[22] for details of individual site enrollment criteria and consortium integration). For this analysis, all HIV-infected Lung-HIV participants from the United States sites who contributed clinical and demographic data, spirometric measures, and HIV-related laboratory testing were included (see Supplemental Digital Content 1 for contributing centers and participant selection). While individual sites have previously included data on lung function in subsets of participants included in this analytical cohort,[10, 21, 24–27] prior analyses included spirometry measurements obtained at different time points during follow-up or in the context of different research objectives. Prior publications have not published on restrictive physiology patterns or compared risk factors for obstruction and restriction versus normal spirometry pattern among HIV-infected individuals. The Lung-HIV study protocol was approved by the Institutional Review Boards (IRB) at each clinical site and the data coordinating center. All participants provided written, informed consent to participate in both their local site's research study as well as in Lung-HIV group studies.

Data Collection

Demographic and clinical data was collected using standardized Lung-HIV forms. History of cigarette smoking, injection drug use, and ART use were obtained through self-report. History of asthma, COPD, and respiratory infections (bacterial, *Pneumocystis*, tuberculosis) were determined through self-report of physician diagnosis rather than medical records abstraction because self-reported data could be standardized and collected across the diverse Lung-HIV clinical centers. Respiratory symptoms were assessed using a modified version of the American Thoracic Society respiratory questionnaire,[28] which included the following questions: "Do you usually have a cough?", "Do you usually bring up phlegm from your chest?" and "Have you ever had an attack of wheezing or whistling in your chest that made you feel short of breath?". Dyspnea was assessed using the modified Medical Research Council (mMRC) questionnaire with a validated 0–4 scale, with a higher score indicating worse dyspnea.[29, 30] CD4 cell counts and HIV viral load were obtained from participant records obtained in the context of research or clinical visits closest to the date of pulmonary function testing based on individual site protocols.

Categories of Spirometric Patterns

Pre-bronchodilator spirometry FEV1 and FVC measurement was performed in accordance with American Thoracic Society guidelines.[31] Percent predicted values were calculated using standard formulas.[32] Separate categories of spirometric patterns were defined using prior published definitions[33, 34] as follows: obstructed ($FEV1/FVC < 0.70$), restricted ($FEV1/FVC \geq 0.70$ and $FVC < 80\%$ predicted and any FEV1 value), undefined ($FEV1/FVC \geq 0.70$ and $FVC \geq 80\%$ predicted and $FEV1 < 80\%$ predicted) and normal ($FEV1/FVC \geq 0.70$ and $FVC \geq 80\%$ predicted and $FEV1 \geq 80\%$ predicted). In separate analyses, lower limit of normal (LLN) criterion to define an obstructive ventilatory defect were calculated using reference equations.[35] All spirometry testing was done when patients were in stable condition free of recent respiratory infections.

Statistical Analysis

For comparisons of demographic and clinical characteristics across different spirometry patterns, Kruskal-Wallis tests and chi-square tests were used. Logistic regression analysis was performed to determine factors associated with three separate spirometry groups: any abnormal spirometry versus normal pattern, obstructed versus normal spirometry pattern, and restricted versus normal spirometry pattern. Respiratory symptoms were examined individually and also with a combined variable “any respiratory symptoms” defined as present if participant answered yes to any of the questions regarding cough, phlegm, wheeze or had an mMRC score >2 . Predictors identified as significant in univariable analyses (i.e., $p < 0.20$) were included in multivariable models. Parsimonious models were generated to determine characteristics independently associated with abnormal spirometric patterns. The AUC and performance characteristics (sensitivity, specificity) of covariates included in multivariable models were calculated. A p -value of <0.05 was used to infer statistical significance. Stata 13.0 (College Station, Texas) software was used for statistical analyses.

RESULTS

Study Participants

After excluding 22 participants with an undefined spirometry pattern, 908 HIV-infected individuals contributed clinical and spirometric data to analysis (Table 1). The median age of the cohort was 50 years, 78% were male and 64% self-identified as black race. Cigarette smoking was common, with 68% reporting current smoking and 19% reporting former tobacco use. The median smoking exposure was 18 pack-years (IQR 8–33). Overall, 382 (44%) participants reported a history of injection drug use. The median CD4 cell count for the cohort was 425 cells/ μ l (IQR 262–627) with 16% having a CD4 cell count less than 200 cells/ μ l. The median log HIV viral load was 3.87 copies/ml (IQR 3.69–7.58). A total of 69% had an undetectable HIV viral load and 73% reported current ART use. Of the cohort, 21% self-reported a physician-diagnosis of asthma while 14% self-reported a physician-diagnosis of COPD. There was a weak, but statistically significant correlation between self-report of asthma and COPD diagnoses ($r=0.234$; $p<0.001$). Prior respiratory infections were frequent in the cohort, with 26% reporting bacterial pneumonia, 11% *Pneumocystis* pneumonia and 4% pulmonary tuberculosis.

Spirometric Pattern

Overall, the median FEV1 and FVC measures were near normal, with median FEV1 and FVC 92.0 and 97.8 percent predicted, respectively. The median FEV1/FVC was 0.76 (IQR 0.69–0.80). Despite the overall preserved mean values of spirometry measures, 37% of the cohort had an abnormal spirometry pattern, with 27% having an obstructed and 10% having a restricted spirometry pattern (Figure 1).

Compared to participants with a normal spirometry pattern, those with an obstructed pattern were older, more likely to be current smokers and had higher pack-years smoked (Table 2). Participants with airflow obstruction were also more likely to report a diagnosis of asthma, COPD, respiratory symptoms and have a history of more bacterial pneumonia and *Pneumocystis* infection. Notably, among participants with spirometry-confirmed airflow

obstruction, only 21% reported a diagnosis of COPD, 29% asthma and 10% both asthma and COPD. A total of 60% of participants with airflow obstruction had no prior diagnosis of either asthma or COPD. Of those reporting a diagnosis of asthma, 43% met spirometric criteria for airflow obstruction while 46% of participants reporting a diagnosis of COPD also met spirometric criteria for airflow obstruction. When defining obstructive ventilatory pattern using LLN rather than fixed ratio criterion, 95% of participants had similar designation of diseased or normal airflow patterns.

Compared to participants with a normal spirometry pattern, those with a restricted pattern of airflow were older, more likely to be African-American and report a diagnosis of COPD (Table 2). Wheeze, dyspnea and history of tuberculosis were more frequent in restricted compared with normal spirometry patterns. Across the different spirometry patterns, there were no differences in CD4 count, viral load or ART use.

Univariable and Multivariable Predictors of Specific Spirometric Patterns

Univariable logistic regression determined demographic and clinical characteristics associated with any abnormal spirometry pattern, an obstructed pattern, or a restricted spirometry pattern (Supplemental Digital Content 2). Several covariates were associated with any abnormal spirometry pattern. These included increasing age, current smoking status, history of asthma, history of COPD, history of *Pneumocystis* and presence of any respiratory symptoms. Greater smoking intensity, measured by pack-years smoked, was linearly associated with abnormal spirometry using thresholds of 10, 20, 30 and 40 pack-years, with the highest odds ratio for abnormal spirometry comparing >40 to 40 pack-years. A similar cluster of covariates were associated with an obstructed ventilatory pattern. These included increasing age, current smoking, history of asthma, history of COPD, history of *Pneumocystis* infection and presence of any respiratory symptoms. Also similar to the analysis of any abnormal spirometry pattern, greater smoking intensity was associated with an increased odds of an obstructed pattern, with the greatest association in those who smoked more than 20 pack-years. Unlike any abnormal pattern, a history of bacterial pneumonia was also associated with an obstructed ventilatory pattern. Slightly different characteristics were associated with a restrictive ventilatory pattern. These included increasing age, African-American race, >40 pack-year smoking history, history of COPD, history of tuberculosis and presence of any respiratory symptoms.

Multivariable modeling incorporating factors identified from the univariable analyses are summarized in Table 3. Several factors remained statistically associated with the presence of any abnormal spirometry: age (per 10 years, OR 1.75; 95% CI 1.45–2.13), current smoking status (OR 1.42 compared to non-smokers; 95% CI 1.02–1.98), history of *Pneumocystis* (OR 1.72; 95% CI 1.10–2.67) and presence of any respiratory symptoms (OR 1.95; 95% CI 1.40–2.73). While both self-report of asthma and COPD were associated with abnormal spirometry pattern in univariable analysis, inclusion of both asthma and COPD in multivariable analysis resulted in statistical significance only for self-report of asthma diagnosis (OR 1.69; 95% CI 1.17–2.44). Incorporation of different thresholds for pack-years smoked into multivariable models demonstrated that a history of smoking >30 pack-years

was the lowest level associated with abnormal spirometry (OR 1.52; 95% CI 1.12–2.08). The overall AUC for this multivariable model was 0.690.

When examining characteristics independently associated with an obstructed spirometry pattern, a similar list of factors was identified. These included increasing age (per 10 years, OR 1.92; 95% CI 1.54–2.39), current smoking status (OR 1.77 compared to non-smokers; 95% CI 1.20–2.62), history of *Pneumocystis* (OR 1.97; 95% CI 1.22–3.18) and presence of any respiratory symptoms (OR 1.88; 95% CI 1.28–2.76). Compared to analysis of any abnormal spirometry pattern, a lower pack-years threshold (>20 pack-years) was associated with the presence of an obstructed pattern (OR 1.68; 95% CI 1.20–2.36). As was observed with the analysis of any abnormal spirometry pattern, self-report of asthma, but not COPD, was statistically associated with an obstructed airflow pattern (OR 1.81; 95% CI 1.21–2.71). The overall AUC for this multivariable model was 0.717. Multivariable models using LLN criteria to define obstructed spirometry pattern demonstrated similar associations (Supplemental Digital Content 3).

Only three factors remained associated with a restricted spirometry pattern in multivariable analysis: increasing age (per 10 years, OR 1.46; 95% CI 1.11–1.93), African-American race (OR 1.75; 95% CI 1.05–2.94) and presence of any respiratory symptoms (OR 2.23; 95% CI 1.35–3.71). The overall AUC for this multivariable model was 0.648.

Performance Characteristics of Covariates

The sensitivity and specificity for individual characteristics incorporated into multivariable models of any abnormal spirometry are provided in Table 4. Age greater than 40 years had the highest sensitivity for predicting the presence of any abnormal spirometry, with a sensitivity of 93%. Current smoking status and smoking history exceeding 10 pack-years demonstrated lower sensitivities of 72% and 80%, respectively. While self-report of asthma diagnosis or prior *Pneumocystis* infection had good specificity for predicting any abnormal spirometry (84% and 91%, respectively), the sensitivity was relatively poor (28% and 16%, respectively). The presence of any respiratory symptom demonstrated 78% sensitivity and 41% specificity for predicting any abnormal spirometry patterns. Other performance characteristics are summarized in Supplemental Digital Content 4 and 5.

Given the clinical relevance, analysis restricted to participants with any respiratory symptoms was performed. Using the presence of respiratory symptoms to predict abnormal spirometry would result in 66% of the cohort being diagnosed with a chronic lung disease. However, of those with respiratory symptoms, only 261 (44%) had any abnormal spirometry pattern, resulting in a false positive rate of 59% when using respiratory symptoms alone to define chronic lung disease. Of the 44% of participants with respiratory symptoms and abnormal spirometry, 32% demonstrated an obstructive pattern and 11% a restrictive pattern. Compared to the 44% prevalence of abnormal spirometry pattern among those with respiratory symptoms, the prevalence of abnormal spirometry among those without symptoms was 24% ($p<0.001$). The performance characteristics of factors identified in the multivariable analysis of any abnormal spirometry pattern among those with respiratory symptoms were comparable to the entire cohort (Supplemental Digital Content 6).

DISCUSSION

In this analysis of 908 HIV-infected participants recruited from multiple US cities, we found that abnormal spirometry-defined airflow patterns are common, with nearly 40% of participants demonstrating abnormalities. An obstructed spirometry pattern was three times as common as a restrictive spirometry pattern. In this cohort, HIV-specific indices such as CD4 cell count and HIV viral load were not associated with specific patterns. The presence of specific risk factors among HIV-infected individuals should prompt an evaluation for undiagnosed lung impairment during the clinical care of HIV-infected patients. Regardless of respiratory symptoms, five HIV-infected participants would need to be screened with spirometry to diagnose two individuals with abnormal spirometry.

To our knowledge, this report describes the largest analysis of US HIV-infected individuals in the post-ART era using spirometric testing to define airflow abnormalities. We found that abnormal spirometry results were common in this population, with 27% and 10% having obstructed and restricted airflow patterns, respectively. These rates are higher than reported in studies of general US populations of HIV-uninfected individuals, with obstructed and restricted spirometry prevalence of 7–14% and 7%, respectively.[36–38] A portion of the increased prevalence of spirometric abnormalities in our cohort likely reflects increased risk factors for airflow obstruction such as smoking and respiratory infections. However, among the general population, only 13% of current smokers and 9% of former smokers have obstructive airflow patterns on spirometry.[36] Prior publications from individual Lung-HIV sites focusing on other research questions have demonstrated prevalence of airflow obstruction ranging from 16–18%.[10, 26, 27] The analysis presented here includes a larger, more diverse cohort of HIV-infected individuals, reinforcing the importance of recognizing the risk for lung disease among HIV-infected individuals.

Our results suggest that the use of screening spirometry among at-risk HIV infected individuals will likely increase estimates of disease prevalence in this population. However, compared to Centers for Disease Control data on US HIV-infected individuals,[39] current tobacco and ever drug use are over-represented in Lung-HIV. Thus, we may have observed a higher prevalence of spirometry abnormalities than a cohort with lower rates of smoking and drug use. The benefits of screening spirometry may differ in HIV-infected groups with different risk profiles and studies are needed.

In this analysis, several characteristics were identified which were independently associated with an abnormal spirometry pattern. These characteristics included older age, current smoking, greater smoking history, prior diagnosis of asthma, history of *Pneumocystis* infection and presence of any respiratory symptoms. Many of these characteristics are similar to established risk factors for abnormal spirometry in HIV-uninfected individuals. [33, 36, 38] Respiratory infections are known to contribute to the development of chronic lung diseases in general populations[40] as well as HIV-infected populations.[41] In our analysis, we observed that *Pneumocystis* infection, but not bacterial respiratory infections were associated with obstructed physiology. *Pneumocystis* has been implicated as a causative agent for the development of COPD in both HIV-infected and uninfected individuals.[42–44] The detection of prior pneumonia may represent a proxy for severe

immunodeficiency, which can be associated with late access to health care as well as end-organ harms of uncontrolled HIV. Nadir CD4 and duration of HIV illness were not available from all Lung-HIV sites, thus this analysis is not able to determine the independent effects of respiratory infections from severe immunodeficiency and access to care. Studies in the pre-ART era have shown pneumonia to be a primary risk factor for lung abnormalities among HIV-infected individuals independent of CD4 count[41] as well as in persons without underlying HIV [40, 45], but these data may not be applicable to patients with less severe immunodeficiency. Prior studies have described an association between tuberculosis infection and lung function impairment,[45–47] an association not observed in this analysis, likely reflecting the low occurrence of tuberculosis in this cohort (4%).

Our analysis did not reveal an association between markers of HIV infection and presence of abnormal spirometry. Several studies have observed that increased HIV viral load or reduced CD4 cell count are associated with an increased prevalence of obstructed spirometry pattern,[10] diagnosis of COPD[48] and more rapid lung function decline over time.[16] These studies included a substantial number of individuals with poorly controlled disease. Nearly 69% of this cohort had an undetectable HIV viral load, attenuating the ability to detect impact of uncontrolled HIV on lung manifestations. However, our findings highlight that even in the era of effective ART, spirometry-defined lung function abnormalities remain a substantial burden.

Studies have highlighted the burden of respiratory symptoms among HIV-infected individuals.[49–52] In this analysis, the presence of any respiratory symptom approximately doubles the likelihood of abnormal spirometry testing. Therefore, clinicians caring for HIV-infected individuals should inquire about the presence of non-specific respiratory symptoms, and when present should consider spirometric testing. However, it is important to note that the presence of respiratory symptoms alone was a relatively poor predictor of abnormal airflow patterns, and should not substitute for spirometry when diagnosing lung disease among HIV-infected individuals. While current guidelines do not specifically address the role of screening spirometry in all HIV-infected individuals, the high prevalence of abnormal spirometry and the poor predictive capability of respiratory symptoms alone suggest this may be warranted.

This study has limitations. The selection of subsets of individuals from larger study cohorts introduces the potential for selection bias. The cross-sectional nature of the analysis limits the determination of causal relationships between participant characteristics, spirometric abnormalities and long-term clinical outcomes. Historical data obtained via self-report are susceptible to recall bias. Post-bronchodilator testing was not performed at all Lung-HIV sites; thus, a subset of individuals may have partially or fully reversible airflow obstruction. Our analysis was limited to spirometry data only. Performance of lung volume testing is required to confirm restrictive lung disease. Because not all sites within the Lung-HIV consortium enrolled HIV-uninfected individuals, this analysis is not able to provide estimates of background prevalence of abnormal spirometry patterns. The prevalence of obstructed spirometry pattern among HIV-uninfected individuals from published cohorts of smoking-injection drug users and MACS/WIHS ranged from 16–20%. [10, 26] These estimates were lower than the 27% observed in this analysis of HIV-infected individuals.

In conclusion, using data from multiple US cohorts of HIV-infected individuals, we have found that abnormal spirometry patterns are common, with nearly 40% of HIV-infected individuals having physiologic lung impairment. Specific risk factors are associated with obstructive lung disease, including older age, tobacco use, history of asthma and *Pneumocystis* infection. Restrictive lung impairments were less common, and associated with older age and black race. The presence of respiratory symptoms was strongly associated with abnormal airflow patterns, and should prompt formal spirometry testing when encountered in the clinical care of HIV-infected individuals. However, the use of respiratory symptoms in the absence of spirometry testing is inadequate to ascertain the presence of airflow abnormalities. Screening five HIV-infected participants would lead to diagnose of abnormal spirometry in two individuals. These findings highlight the importance of recognizing and diagnosing chronic lung diseases in HIV-infected populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Prevalence of abnormal, obstructed and restricted spirometry patterns among 908 Lung-HIV cohort participants. See methods section for definitions of spirometric categories.

Table 1

Clinical characteristics of participants (N=908)

Age, years	50 (44–55)
African-American race	581 (64)
Male	709 (78)
Smoking status	
Current	614 (68)
Former	169 (19)
Never	125 (14)
Pack-years smoking	17.8 (7.8–33.0)
History of injection drug use	382 (44)
CD4 count, cells/mm ³	425 (262–627)
CD4 category, cells/μl	
<100	53 (6)
100–199	96 (11)
200–349	202 (23)
350+	554 (61)
Viral load, log ₁₀ (copies/ml)	3.87 (3.69–7.58)
Viral load undetectable	555 (69)
Current ART use	571 (73)
History of asthma	185 (21)
History of COPD	128 (14)
History of pneumonia	229 (26)
History of <i>Pneumocystis</i>	101 (11)
History of tuberculosis	39 (4)
Cough present	289 (32)
Phlegm present	312 (35)
Wheeze present	322 (36)
MRC score	0 (0–1)
FEV1, Absolute (L)	2.96 (2.37–3.56)
FEV1, % predicted	92.0 (80.6–103.5)
FVC, Absolute (L)	3.98 (3.31–4.71)

FVC, % predicted	97.8 (87.9–107.5)
FEV1/FVC ratio	0.76 (0.69–0.80)
FEV1 severity category	
>70% predicted	788 (87)
50–69% predicted	95 (10)
<50% predicted	25 (3)
Category of impairment	
Restricted	92 (10)
Obstructed	244 (27)
Normal	572 (63)

All values median (IQR) or n (%). ART= antiretroviral therapy; COPD= chronic obstructive pulmonary disease

Table 2

Clinical characteristics of HIV-infected participants by Spirometry Pattern

	Obstructed Spirometry	Restricted Spirometry	Normal Spirometry	P –Obstructed vs. Normal	P –Restricted vs. Normal
N	244	92	572		
Age, years	52 (47–57)	51 (44–56)	48 (43–53)	<0.001	0.011
African-American race	142 (58)	70 (76)	369 (65)	0.23	0.027
Male	196 (80)	70 (76)	443 (77)	0.36	0.77
Smoking status					
Current	186 (76)	57 (62)	371 (65)		
Former	36 (15)	23 (25)	110 (19)		
Never	22 (9)	12 (13)	91 (16)	0.004	0.40
Pack-years smoking	37 (13–40)	18 (8–32)	17 (8–37)	<0.001	0.18
Prior injection drug use	104 (46)	44 (49)	234 (43)	0.52	0.30
CD4 count, cells/mm ³	408 (255–611)	419 (242–600)	429 (269–636)	0.47	0.45
CD4 category, cells/ μ l					
<100	16 (7)	4 (4)	33 (6)		
100–199	24 (10)	9 (8)	63 (11)		
200–349	56 (23)	26 (28)	123 (22)		
350+	148 (61)	53 (58)	353 (62)	0.90	0.53
Viral load, log ₁₀ (copies/ml)	3.87 (3.69–6.11)	3.87 (3.69–7.93)	3.87 (3.69–7.90)	0.082	0.88
Viral load undetectable	159 (74)	58 (67)	338 (68)	0.091	0.98
Current ART use	159 (74)	58 (72)	354 (72)	0.70	0.91
History of asthma	71 (29)	21 (23)	93 (16)	<0.001	0.13
History of COPD	51 (21)	17 (19)	60 (11)	<0.001	0.021

	Obstructed Spirometry	Restricted Spirometry	Normal Spirometry	P – Obstructed vs. Normal	P – Restricted vs. Normal
History of pneumonia	75 (32)	21 (23)	133 (24)	0.020	0.89
History of <i>Pneumocystis</i>	41 (17)	10 (11)	50 (9)	0.001	0.50
History of tuberculosis	9 (4)	8 (9)	22 (4)	0.94	0.04
Cough present	106 (43)	33 (36)	150 (26)	<0.001	0.06
Phlegm present	121 (50)	28 (31)	163 (29)	<0.001	0.69
Wheeze present	118 (48)	37 (41)	167 (29)	<0.001	0.03
MRC score	1 (0–3)	0 (0–3)	0 (0–1)	<0.001	0.01
FEV1, Absolute (L)	2.39 (2.01–2.89)	2.31 (1.92–2.59)	3.28 (2.80–3.82)	<0.001	<0.001
FEV1, % predicted	77.6 (64.5–87.3)	71.8 (70.0–77.6)	99.4 (90.9–108)	<0.001	<0.001
FVC, Absolute (L)	3.93 (3.32–4.64)	2.85 (2.40–3.23)	4.21 (3.59–4.86)	<0.001	<0.001
FVC, % predicted	96.4 (86.6–107)	72.9 (67.0–77.0)	101 (92.9–109)	<0.001	<0.001
FEV1/FVC ratio	0.64 (0.58–0.68)	0.79 (0.74–0.83)	0.80 (0.75–0.83)	<0.001	0.05

All values median (IQR) or n (%). ART= antiretroviral therapy; COPD= chronic obstructive pulmonary disease; P-value via Kruskal-Wallis or χ^2 test

Table 3

Multivariable models of factors associated with spirometry patterns

	Odds Ratio (95% CI)	P-value
Any Abnormal Spirometry		
Age (per 10 years)	1.75 (1.45–2.13)	<0.001
Current smoking	1.42 (1.02–1.98)	0.037
>30 pack-years smoking	1.52 (1.12–2.08)	0.008
History of asthma	1.69 (1.17–2.44)	0.005
History of <i>Pneumocystis</i>	1.72 (1.10–2.67)	0.017
Respiratory symptoms*	1.95 (1.40–2.73)	<0.001
Obstructed Spirometry Pattern		
Age (per 10 years)	1.92 (1.54–2.39)	<0.001
Current smoking	1.77 (1.20–2.62)	0.004
>20 pack-years smoking	1.68 (1.20–2.36)	0.003
History of asthma	1.81 (1.21–2.71)	0.004
History of <i>Pneumocystis</i>	1.97 (1.22–3.18)	0.005
Respiratory symptoms*	1.88 (1.28–2.76)	0.001
Restricted Spirometry Pattern		
Age (per 10 years)	1.46 (1.11–1.93)	0.007
African-American race	1.75 (1.05–2.94)	0.032
Respiratory symptoms*	2.23 (1.35–3.71)	0.002

* Answers yes to any of the following: cough, phlegm, wheeze, mMRC 2; Only variables from univariable models with $p < 0.2$ included in multivariable model (see supplementary table 2 for univariate model results)

Table 4

Performance characteristics of factors associated with presence of any abnormal spirometry pattern

Variable	Sensitivity	Specificity	AUC
Age			
>40 years	93	15	0.543
>50 years	63	56	0.594
> 60 years	14	92	0.527
Current smoker	72	35	0.537
Pack-years smoked			
>10	80	31	0.554
>20	57	58	0.578
>30	42	73	0.575
>40	27	85	0.561
History of asthma	28	84	0.556
History of <i>Pneumocystis</i>	16	91	0.534
Respiratory symptoms*	78	41	0.592

* Answers yes to any of the following: cough, phlegm, wheeze, mMRC 2