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Predicting risk of airflow obstruction in primary care: Validation of the lung function questionnaire (LFQ)

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Summary
The Lung Function Questionnaire (LFQ) is being developed as a case finding tool to identify patients who are appropriate for spirometry testing to confirm the diagnosis of chronic obstructive pulmonary disease (COPD). The cross-sectional study reported herein was conducted to validate the LFQ, to identify item-response scales associated with the best accuracy, and to determine the impact on accuracy of the addition of another item on activity limitations (AL). Patients $\geq$ 40 years old seen at 2 primary care offices completed the LFQ, a demographic questionnaire followed by spirometry. Of the 837 evaluable patients, 18.6% had airflow obstruction (forced expiratory volume in 1 s/forced vital capacity [FEV_1/FVC] $<$ 0.70). The 5 items (age, wheeze, dyspnea, smoking, and cough) previously identified in initial LFQ development predicted airflow obstruction and showed good evidence of screening accuracy. Screening accuracy was significantly better with 5-point ordinal item-response scales (78%)

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than binary (yes/no) item-response scales (74%)($p < 0.05$). Screening accuracy was good regardless of whether airflow obstruction was defined as $FEV_1/FVC < 0.70$ or $FEV_1/FVC < 0.70$ and $FEV_1 < 80\%$ of predicted. Based on ≤ 18 was selected to suggest presence of airflow obstruction with area under the receiver operating characteristic curve 0.652; sensitivity 82.6%; specificity 47.8%; 54.3% correctly classified. While the specificity of LFQ is low, its high sensitivity suggests that it can serve to identify patients who should be further assessed using spirometry. Our results confirm the screening accuracy of the LFQ, a simple and effective tool to facilitate early recognition and diagnosis of COPD.

Introduction

Chronic obstructive pulmonary disease (COPD) is a global health problem that by 2020 is projected to rank fifth in burden of disease worldwide.[1] Although damage to lung tissue in COPD appears to be irreversible, evidence suggests the course of COPD can be altered through measures such as smoking cessation, pulmonary rehabilitation, oxygen, and use of pharmacotherapy.[2–6] Demonstrations of intervention-associated reductions in symptoms and frequency of exacerbations and improvement in exercise capacity in studies such as the TORCH trial[7] and other large, randomized trials[8,9] have shifted the focus of COPD management from symptomatic and supportive care to disease-modifying interventions.[3,4] In this new paradigm for managing COPD, early identification of the disease is regarded as integral to optimizing outcomes.[5] To this end, the multinational ECLIPSE trial (Evaluation of COPD Longitudinally to Identify Predictive surrogate Endpoints) is designed to identify parameters and biomarkers that predict progression in COPD and that can ultimately be used to optimize treatment.[10–12] Likewise, multinational trials such as UPLIFT (Understanding the Potential Long-Term Impacts on Function with Tiotropium) are helping to increase understanding of the natural history of COPD in a global population and to shed light on potentially disease-modifying approaches to therapy.[13]

COPD remains undiagnosed in almost 50% of those patients who suffer from this disease.[14] Early recognition of COPD can be challenging because patients and health care professionals often fail to recognize early manifestations of the disease.[2] According to both the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines[1] and the American Thoracic Society/European Respiratory Society (ATS/ERS) Standards for the Diagnosis and Management of Patients with COPD,[15] spirometry is crucial to confirm the diagnosis of COPD. The ATS/ERS Standards for the Diagnosis and Management of Patients with COPD state that case finding is a simple and effective means of enhancing the diagnosis of COPD in primary care and recommend spirometry by primary care providers to detect airway obstruction and facilitate smoking cessation.[15] However, primary care health professionals often lack spirometry equipment and have no practical tools to help identify COPD at an early stage when symptoms and activity restrictions may be subtle.[2]

The Lung Function Questionnaire (LFQ) is a simple, brief, self-administered instrument, being developed to address the need for a screening tool to identify patients appropriate for COPD spirometry-confirmed diagnostic evaluation. The questionnaire[16] is based on data obtained from a sample of adults who self-reported chronic bronchitis during the Third National Health and Nutrition Examination Survey (NHANES III). Items from the NHANES III that could discriminate between patients with and without spirometry-based airflow obstruction, the primary manifestation of COPD, were identified for possible inclusion in the LFQ. Item reduction phases of development resulted in a set of five questions that had very good screening accuracy, specificity, and sensitivity. The final step in the development phase is the need to validate the LFQ and to identify item-response scales (yes/no versus five-point scale) associated with the greatest accuracy. Since activity limitation is believed to be an important outcome of COPD, this study also assessed the impact of adding an activity limitations (AL) item to the LFQ screening accuracy. Because primary care physicians are thought to provide care for the majority of patients with early or mild COPD and are crucial in efforts to diagnose COPD earlier,[2] this study was conducted in two primary care practices.

Methods

Design and sample

This cross-sectional study was conducted from March to May 2008 in two family physician group offices—one in a rural Kentucky (Hazard) and one in a large Kentucky metropolitan area (Lexington). The University of Kentucky institutional review board (IRB) approved the protocol for both study sites. Men and women 40 years and older visiting the practices were eligible. No other inclusion or exclusion criteria were applied.

Procedures

Patients who agreed to participate in the study and who provided informed consent completed the LFQ and a demographic questionnaire in the waiting room. The LFQ comprised an age item, a smoking item, 3 symptom items (cough, dyspnea, wheeze), and, for some participants, an item on AL (Table 1). Symptom items were administered with both a binary response scale (yes or no) and an ordinal response scale (Table 1). After patients completed the questionnaires, pre-bronchodilator (pre-BD) spirometry was performed using EasyOne spirometers.

Data analysis

Data analyses were conducted in 3 phases. In the first phase, the degree to which the AL item could significantly predict airflow obstruction status was determined. Chi-

Table 1 Items used in the LFQ scale analyses.

Factor	Question	Response choices
Age	Age 50 or older (dichotomized answers to question above)	Yes/No
	What is your age range?	40—50, 50—60, 60—70, 70 + years
Cough	Do you frequently cough mucus?	Yes/No
	How often do you cough mucus?	Very often, often, sometimes, rarely, never
Wheeze	Does your chest often sound noisy (wheezy, whistling) when you breathe?	Yes/No
	How often does your chest sound noisy (wheezy, whistling) when you breathe?	Very often, often, sometimes, rarely, never
Dyspnea	Do you experience shortness of breath upon physical exertion?	Yes/No
	How often do you experience shortness of breath upon physical exertion	Very often, often, sometimes, rarely, never
Smoking	Smoked at least 20 years (dichotomized answers to question above)	Yes/No
	How many years did you or have you smoked?	Never, 10 or less, 11—20, 21—30, 31—40, 41—50, 50+ years
AL	Feels limited often or very often	Yes/No
	How often limited in daily activities by your breathing problems?	Very often, often, sometimes, rarely, never

square tests of statistical independence were used to determine whether obstructed respondents and non-obstructed respondents differed significantly on the AL item and each of the remaining LFQ items. Airflow obstruction was defined as a ratio of the forced expiratory volume in 1 s (FEV_1) to the forced vital capacity (FVC) < 0.70 ($FEV_1/FVC < 0.70$) (pre-BD). Investigators rated spirometry quality as Grade 1 (reliable and reproducible), Grade 2 (reliable but not reproducible), or Grade 3 (neither reliable nor reproducible). Only spirometries of Grades 1 and 2 were included in the analyses. Very few spirometries were Grade 3.

In the second phase of analysis, alternative LFQ scales comprising various combinations of the items with binary and ordinal response scales were compared. Binary multiple logistic regression was used to compare the scales in terms of sensitivity, specificity, and the area under the receiver operating characteristic (ROC) curve (AUC). The dependent variable was airflow obstruction (1 = yes, 0 = no). The estimated odds ratios were examined to confirm the expected relationship between each LFQ item and airflow obstruction (i.e., whether greater symptom severity, older age, and more years smoked were associated with greater risk of obstruction) and to study potential changes to each of the original item scales (caused by possibly redundant response choices). Wald chi-square tests were used to establish statistical significance. In addition to the AUC obtained using the full set of LFQ items as predictors of obstruction, a second scale-specific AUC value was derived from a binary logistic regression model in which the scale's summed score was the only independent variable predicting obstruction. Tests of statistical significance for the difference between the AUCs of 2 scales were conducted using the method of Delong and Delong.[17]

As part of the second phase of analyses, additional sensitivity analyses were conducted to evaluate the accuracy of the LFQ using FEV_1% predicted with the fixed ratio ($FEV_1/FVC < 70\%$). Airway obstruction was defined (regardless of age) as having both $FEV_1/FVC < 70\%$ and % predicted $FEV_1 < 80\%$ to resemble more closely GOLD stage 2 severity.

In the third phase of analyses, the best-performing scale was chosen based on measures of predictive accuracy (AUC, sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV], and percentage of correctly classified observations) as well as clinician input keeping in mind the intended purpose of the tool. For these analyses, a scale was obtained by simple summation of the LFQ items. Binary (0/1) cumulative summed score indicators were created for each value of the scale. Each of these variables was subsequently used as the predictor of airway obstruction using binary logistic regression. The predictor in the model with the highest AUC reflected the minimum score of the LFQ that most accurately predicted airway obstruction.

Discriminant validity was assessed via the method of known-groups validity[18] and using spirometry-defined severity stages among those who were obstructed. These analyses determined whether LFQ scores discriminated among patients of differing levels of severity. LFQ scores were also examined across levels of general health (using SF-1). One-way analysis of variance (ANOVA) was used to compare the performance of alternative LFQ scales.

Upon selection of the items and response options, the resulting questionnaire was tested via one-on-one cognitive interviews in 15 patients with confirmed chronic bronchitis, emphysema, or COPD. The interviews provided patient input and feedback on the readability of the instructions, questions, response options, and scoring. A key objective of these qualitative interviews was to explore the format and content of the AL question in an effort to define the concept of activity limitation more fully.

Results

Sample

937 patients participated in this study. Of these 937, 855 patients provided evaluable data for the main analysis variables. Of these 855 patients, 18 were excluded based

Table 2 Demographics of study population.

	$FEV_1/FVC \geq 70\%$ ($n = 681$)	$FEV_1/FVC < 70\%$ ($n = 156$)	All ($N = 837$)
	% Respondents		
Age			
40–49	38.2	21.8	35.1
50–59	32.3	29.5	31.8
60–69	19.4	27.6	20.9
70+	10.0	20.5	11.9
NA	0.1	0.6	0.2
Sex			
Male	36.1	46.8	38.1
Female	63.7	52.6	61.6
NA	0.1	0.6	0.2
Race			
White	85.9	91.0	86.9
Black	10.9	7.1	10.2
Asian	1.9	0.6	1.7
American Indian/Alaskan native	0.7	0.0	0.6
Other	0.3	0.6	0.4
NA	0.3	0.6	0.4
Education			
No school	0.3	1.3	0.5
1–8	8.7	21.8	11.1
9–12	13.1	20.5	14.5
12 or General educational development	31.6	23.7	30.1
13–15	24.7	16.7	23.2
16+ Years	20.7	13.5	19.4
NA	1.0	2.6	1.3
Employment			
Employed	41.4	19.2	37.3
Self-employed	4.3	4.5	4.3
Disabled	27.9	45.5	31.2
Out of work >1 Year	2.2	0.6	1.9
Out of work <1 Year	1.2	1.3	1.2
Homemaker	6.9	6.4	6.8
Student	0.7	0.6	0.7
Retired	15.0	19.9	15.9
NA	0.4	1.9	0.7

on inconsistent responses on smoke-related questions to yield a total sample of 837 for all items. The AL question was given to 304 patients.

Demographics of the sample as a whole and the subgroups with and without airflow obstruction are shown in Table 2. FEV_1/FVC ratio was <0.70 in 156 respondents for a prevalence of airflow obstruction of 18.6%.

Impact of the AL item on accuracy

Table 3 shows the distribution of responses on LFQ items for the subsample ($n = 304$) that completed the AL item. The extent to which the respondent reported being limited in daily activities did not predict the presence of airflow obstruction ($P = 0.2003$) (Table 3). The majority of respondents indicated presence of some level of dyspnea but also reported not being limited in activities they performed. This pattern of results suggests that the wording of the AL question might not have been sufficiently explicit in eliciting appropriate responses from patients. This possibility was explored in subsequent patient interviews, results of which are described below. Given that the AL item was not significantly associated with obstruction status, this item was not considered in further analyses.

Comparison of scoring formats

Results of a comparison of the accuracy of the LFQ with all binary item-response scales versus the LFQ with all ordinal item-response scales suggest that the latter was more accurate as measured by AUC (binary AUC = 0.739 [95% confidence interval (CI) = 0.695–0.783]; ordinal AUC = 0.777 [95% CI = 0.736–0.818]; $P = 0.0049$). This result supports the use of ordinal response options or LFQ items.

The item on number of years smoked was collapsed from 7 response categories to 5 response categories based on

Table 3 Responses on LFQ items for the subsample completing the AL item.

Factor		$FEV_1/FVC \geq 70\%$ ($n = 258$)	$FEV_1/FVC < 70\%$ ($n = 46$)	All ($N = 304$)
		% respondents		
How often activities limited?	Never	47.3	32.6	45.1
$P = 0.2003$	Rarely	24.8	23.9	24.7
	Sometimes	17.4	23.9	18.4
	Often	5.8	8.7	6.3
	Very often	4.7	10.9	5.6
Age	40–49	36.4	23.9	34.5
$P = 0.401$	50–59	34.5	41.3	35.5
	60–69	20.2	26.1	21.1
	70+	8.9	8.7	8.9
Years smoked?	Never smoked	50.8	21.7	46.4
$P = 0.0001$	≤10 Years	13.6	8.7	12.8
	11–20 Years	12.8	13.0	12.8
	21–30 Years	11.6	23.9	13.5
	31–40 Years	7.8	19.6	9.5
	41–50 Years	3.1	8.7	3.9
	>50 Years	0.4	4.3	1.0
How often cough?	Never	27.1	13.0	25.0
$P = 0.0105$	Rarely	36.8	23.9	34.9
	Sometimes	23.3	43.5	26.3
	Often	8.1	15.2	9.2
	Very often	4.7	4.3	4.6
How often short of breath? (dyspnea)	Never	17.1	4.3	15.1
$P = 0.0650$	Rarely	23.3	23.9	23.4
	Sometimes	29.1	32.6	29.6
	Often	15.1	28.3	17.1
	Very often	15.5	10.9	14.8
How often noisy breathing? (wheeze)	Never	39.5	15.2	35.9
$P = 0.0002$	Rarely	33.7	26.1	32.6
	Sometimes	16.3	43.5	20.4
	Often	6.6	8.7	6.9
	Very often	3.9	6.5	4.3
Total (obstructed: 46/304 = 15.1%)		100.0	100.0	100.0

P-values are derived from chi-square significance tests of difference in the distribution of symptom categories across obstructed and non-obstructed groups.

odds ratios and distribution of responses as well as high standard errors in the extreme categories (*31–40 years*, *41–50 years*, and *more than 50 years*). The recoded smoke variable consisted of a 5-point ordinal scale including the categories of *never*, *10 or fewer years*, *11–20 years*, *21–30 years*, and *31+ years*. The recoded smoke variable was evaluated further in patient interviews. Table 4 shows the results of multivariate logistic regression analyses undertaken between the binary scale and the ordinal scale after recoding smoke into 5 categories. Given these results, data obtained from other models (not shown), and the input of LFQ Working Group, ordinal item-response scales including the 5-category scale for the item for the number of years smoked were chosen for further evaluation. Although cough and dyspnea did not achieve statistical significance in both response formats, they were included in the questionnaire based on clinical relevance (face validity).

In the sensitivity analysis that defined airflow obstruction as $FEV_1/FVC < 70\%$ and $FEV_1 < 80\%$ of predicted, 19 respondents who had previously been classified as obstructed were reclassified for a change in the prevalence from 18.6% to 16.4%. With this definition of obstruction I compared with the fixed ratio of FEV_1/FVC, a slightly higher AUC was observed (0.765 versus 0.743 for the summed score scale) (Table 5). However, the relationship between individual items and airflow obstruction status was generally similar between the approaches (Table 5).

Predictive accuracy and classification threshold of the LFQ

Table 6 shows several measures of accuracy for various cutpoints of the LFQ scale that included ordinal item-response scales with the 5-category scale for the item for the number of years smoked. A score of ≤18, which yielded an AUC of 0.652, sensitivity of 82.6%, and specificity of 47.8%, was selected as appropriate cut point for the LFQ as

Table 4 Results of multiple logistic regression analyses for binary item-response scales versus ordinal item-response scales.

	Binary item-response scales		Ordinal item-response scales		
	Odds ratio	(95% CI)	Response choices	Odds ratio	(95% CI)
Age[a]	2.146	(1.39–3.32)	70+ y	4.733	(0.53–8.85)
			60–70 y	3.219	(1.82–5.70)
			50–60 y	1.571	(0.93–2.65)
Smoke[a]	3.232	(2.21–4.74)	31+ y	3.601	(2.04–6.35)
			21–30 y	4.260	(2.40–7.57)
			11–20 y	1.990	(1.03–3.85)
			≤10 y	1.253	(0.58–2.70)
Cough	1.959	(1.26–3.04)	Very often	1.159	(0.37–3.65)
			Often	0.999	(0.40–2.51)
			Sometimes	0.903	(0.42–1.96)
			Rarely	0.572	(0.27–1.23)
Dyspnea	0.872	(0.54–1.40)	Very often	1.359	(0.48–3.84)
			Often	1.653	(0.61–4.50)
			Sometimes	1.445	(0.55–3.78)
			Rarely	1.887	(0.71–5.04)
Wheeze[a]	1.755	(1.12–2.76)	Very often	3.364	(1.06–10.71)
			Often	4.888	(1.97–12.15)
			Sometimes	2.619	(1.23–5.58)
			Rarely	1.688	(0.84–3.41)
Model AUC (95% CI)	0.739	(0.695–0.783)	na	0.777	(0.736–0.818)
Sum score AUC (95% CI)	0.718	(0.673–0.763)	na	0.742	(0.699–0.786)

For binary (yes/no) symptom items, the reference category is 'no' (i.e., symptom absent). For dichotomized age and smoke, *<50* and *<20* were the reference categories, respectively. For ordinal (5-point scale) items, the first category was taken as the reference (*'never'* for symptom and smoke items, *40–50* for age).
Model AUC refers to the area under curve for a model in which the LFQ items are the 5 predictors of obstruction while the sum score AUC indicates the AUC for a model in which the sum of the 5 items forms a single predictor of obstruction.
For yes/no option, only dyspnea did not reach statistical significance.
[a] Age, smoking and wheeze $P < 0.05$ and therefore statistically significant for 5-point scale.

a case finding tool. Using an LFQ score of 18 or lower as consistent with failed screening, 54.3% of the sample were correctly classified as either obstructed or not (Table 6). A negative predictive value of 92% shows that the instrument was extremely accurate in not missing many cases with potential COPD, a vital characteristic for a case finding tool. LFQ showed good discriminant validity across spirometry-defined severity groups as well as general health. LFQ is scored such that lower scores indicate higher risk of obstruction. In addition, LFQ scores discriminated among patients of differing levels of severity as defined in on the GOLD guidelines although FEV_1 measurement was based on pre-bronchodilator values (Table 7).

Results of cognitive debriefing interviews

Overall, patients preferred the 5-point scoring to the yes/no responses. Some changes were made to the instructions at the beginning to clarify the intent of the questionnaire (Fig. 1) as well as instructions at the end. Other major changes included replacement of the word ''exertion'' by the word ''activity'' in question 3; inclusion of the term ''rattling'' in question 2; and simplification of the smoking and age questions. This phase ensured that readability and understandability of patients with the LFQ were good. Two versions of the AL item were explored: 1) How often are you limited in your daily activities by your breathing problems?; 2) Thinking about your health BEFORE you had breathing problems, how often are you limited in your daily activities (such as household chores, social activities, going to work) by your breathing problems? Patients could not agree on 1 of these items, and items could not be sufficiently refined to obtain saturation. Therefore, this question was not included in the LFQ but will continue to be explored in future studies.

Discussion

The diagnosis of COPD requires objective evidence of airflow limitation in patients with risk factors such as smoking and/or symptoms of chronic sputum production, wheezing, and dyspnea.[1] However, spirometry has not been shown to be a practical screening tool in every patient with smoking history. Spirometry is also very rarely utilized in primary care for identifying risk of airflow obstruction because of its lack of practicality and some practitioners' lack of awareness of its application. In addition, health care professionals and patients often miss the subtle early-stage symptoms leaving COPD to be underdiagnosed.[19–21] Simple, valid, sensitive yet specific case finding tools are needed to identify COPD when the attempts at disease modification remain feasible. In this study, the brief, self-administered LFQ containing items on age, smoking, cough, dyspnea, and wheeze predicted airflow obstruction and showed

Table 5 Results of multiple logistic regression analyses for the criterion measure of airflow obstruction defined as $FEV_1/FVC < 0.7$ versus $FEV_1/FVC < 0.7$ and $FEV_1 < 80\%$.

Factor	Standard definition (Fixed ratio < 0.7)		Modified definition	
	Odds ratio	(95% CI)	Odds ratio	(95% CI)
Age				
70+ y	4.733	(2.53–8.85)	4.700	(2.42–9.14)
60–70 y	3.219	(1.82–5.70)	3.054	(1.65–5.65)
50–60 y	1.571	(0.93–2.65)	1.729	(1.00–3.01)
Smoke				
31+ y	3.601	(2.04–6.35)	4.575	(2.47–8.47)
21–30 y	4.260	(2.40–7.57)	4.828	(2.57–9.05)
11–20 y	1.990	(1.03–3.85)	2.215	(1.07–4.57)
≤10 y	1.253	(0.58–2.70)	1.404	(0.60–3.29)
Cough				
Very often	1.159	(0.37–3.65)	0.950	(0.28–3.18)
Often	0.999	(0.40–2.51)	0.878	(0.33–2.36)
Sometimes	0.903	(0.42–1.96)	0.775	(0.33–1.81)
Rarely	0.572	(0.27–1.23)	0.522	(0.22–1.21)
Dyspnea				
Very Often	1.359	(0.48–3.84)	1.457	(0.45–4.72)
Often	1.653	(0.61–4.50)	2.220	(0.71–6.90)
Sometimes	1.445	(0.55–3.78)	1.381	(0.45–4.20)
Rarely	1.887	(0.71–5.04)	2.191	(0.71–6.75)
Wheeze				
Very often	3.364	(1.06–10.71)	4.783	(1.41–16.21)
Often	4.888	(1.97–12.15)	5.280	(1.97–14.15)
Sometimes	2.619	(1.23–5.58)	3.369	(1.46–7.77)
Rarely	1.688	(0.84–3.41)	1.718	(0.78–3.79)
AUC	0.776		0.794	
Sum score AUC	0.743		0.765	

Note: GOLD Stage II Definition of Airflow Obstruction is $FEV_1/FVC < 70\%$ and $FEV_1 < 80\%$ of predicted. Fixed ratio refers to $FEV_1/FVC < 70\%$ only. Applied only to patients with obstruction (by definition). Pre-BD spirometry used in this study.

strong evidence of screening accuracy in a primary care population. The summed score of the LFQ scale containing the age, smoking, cough, dyspnea, and wheeze items ranged between 5 and 25 points. The LFQ is intended to identify patients at risk for obstruction who are candidates for further evaluation via spirometry to confirm diagnosis of COPD wherever applicable. Cut point selection is typically amenable to adaptation for specific purposes. An expert panel of clinicians felt that a cut point with higher sensitivity would be more appropriate (not missing many ''cases'') keeping in mind the high prevalence of undiagnosed COPD in primary care. Accordingly, a high NPV means that of those who test negative for risk of COPD, the LFQ correctly identifies 92% of patients who do not have COPD. The LFQ therefore captures the majority of patients who may have potential COPD. Underdiagnosis is a troublesome problem in COPD and the focus for a screening test is therefore upon not missing undiagnosed patients who may progress onto a severe stage before being diagnosed. Therefore, a cut point score of ≤18 was selected to identify patients at risk of obstruction despite the fact that a score of ≤16 yielded the highest AUC. This tool focuses on capturing early COPD. Although it does not address other respiratory conditions, it does facilitate patient-physician

Table 6 Performance of LFQ items in screening for airflow obstruction: sensitivity and specificity.

Cut point	Sensitivity	Specificity	PPV	NPV	% Correct	AUC
≤8	5.2	98.8	50.0	82.1	81.4	0.520
≤9	8.4	98.5	56.5	82.5	81.8	0.535
≤10	13.5	97.1	51.2	83.1	81.6	0.553
≤11	21.3	94.3	45.8	84.0	80.7	0.578
≤12	32.9	91.8	47.7	85.7	80.8	0.623
≤13	43.9	87.9	45.3	87.3	79.8	0.659
≤14	53.5	82.9	41.7	88.7	77.5	0.682
≤15	61.9	74.1	35.3	89.5	71.9	0.680
≤16	71.0	66.5	32.5	90.9	67.3	0.687
≤17	76.8	56.9	28.9	91.5	60.6	0.668
≤18	82.6	47.8	26.5	92.3	54.3	0.652
≤19	88.4	36.8	24.2	93.3	46.3	0.626
≤20	93.5	26.6	22.5	94.8	39.0	0.601
≤21	95.5	18.8	21.1	94.8	33.1	0.572
≤22	98.1	11.6	20.2	96.3	27.7	0.548
≤23	98.7	5.6	19.2	95.0	22.9	0.521
≤24	99.4	1.9	18.8	92.9	20.0	0.506

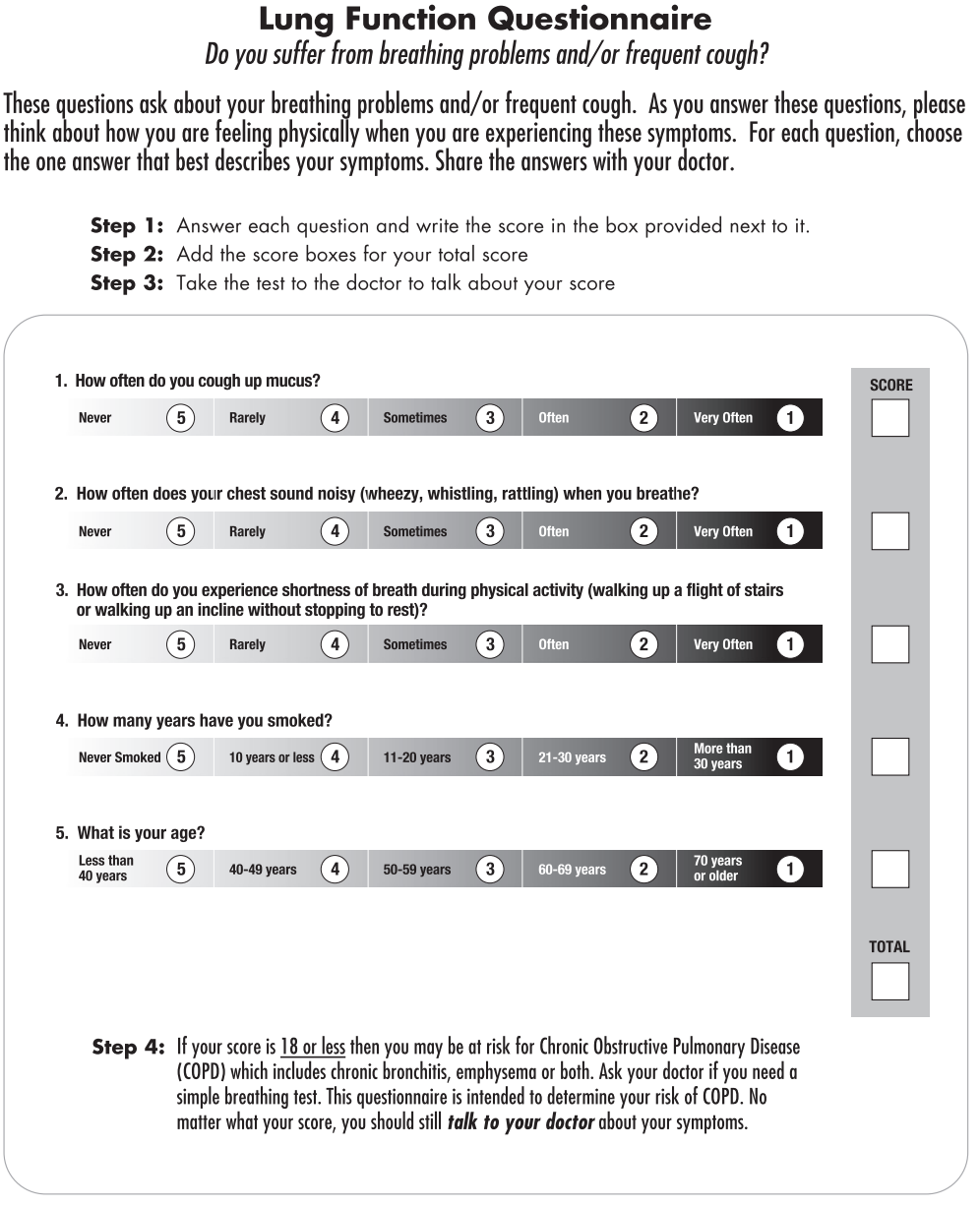
Table 7 Known-groups discriminant validity of LFQ using gold stage, FEV_1% predicted, general health, and FEV_1/FVC fixed ratio.

GOLD stage[a]	**I mild (17)**	**II moderate (76)**	**III severe (44)**	**IV Very severe (11)**	***F*-statistic**
Mean (SD) LFQ score	16.76 (3.7)	15.01 (3.7)	13.25 (3.3)	11.55 (2.8)	7.12*
FEV_1% predicted (*n*)	≥100% (132)	80 to <100% (327)	60 to <80% (256)	<60% (122)	
Mean (SD) LFQ score	19.13 (3.2)	18.60 (3.5)	16.65 (3.6)	13.43 (3.4)	79.18*
General health (*n*)	Excellent/Very good (29)	Good (52)	Fair (46)	Poor (19)	
Mean (SD) LFQ score	17.69 (2.7)	14.00 (3.9)	14.17 (3.2)	11.32 (2.4)	68.23*
FEV_1/FVC (*n*)	≥70% (681)	<70% (156)			
Mean (SD) LFQ score	17.97 (3.7)	14.54 (3.8)			106.63*
p-value < *0.0001*					

Note. The categories in ''Excellent'' and ''Very good'' were collapsed into 1 since only 3 responses were present in both. SF-1 consists of a single question asking, ''In general how would you rate your health?''

[a] pre-BD spirometry.

* $p < 0.05$.



Lung Function Questionnaire

Do you suffer from breathing problems and/or frequent cough?

These questions ask about your breathing problems and/or frequent cough. As you answer these questions, please think about how you are feeling physically when you are experiencing these symptoms. For each question, choose the one answer that best describes your symptoms. Share the answers with your doctor.

Step 1: Answer each question and write the score in the box provided next to it.
Step 2: Add the score boxes for your total score
Step 3: Take the test to the doctor to talk about your score

					SCORE
1. How often do you cough up mucus?	Never (5)	Rarely (4)	Sometimes (3)	Often (2)	Very Often (1)	
2. How often does your chest sound noisy (wheezy, whistling, rattling) when you breathe?	Never (5)	Rarely (4)	Sometimes (3)	Often (2)	Very Often (1)	
3. How often do you experience shortness of breath during physical activity (walking up a flight of stairs or walking up an incline without stopping to rest)?	Never (5)	Rarely (4)	Sometimes (3)	Often (2)	Very Often (1)	
4. How many years have you smoked?	Never Smoked (5)	10 years or less (4)	11-20 years (3)	21-30 years (2)	More than 30 years (1)	
5. What is your age?	Less than 40 years (5)	40-49 years (4)	50-59 years (3)	60-69 years (2)	70 years or older (1)	
					TOTAL	

Step 4: If your score is 18 or less then you may be at risk for Chronic Obstructive Pulmonary Disease (COPD) which includes chronic bronchitis, emphysema or both. Ask your doctor if you need a simple breathing test. This questionnaire is intended to determine your risk of COPD. No matter what your score, you should still ***talk to your doctor*** about your symptoms.

Figure 1 The lung function questionnaire. Copyright (c) 2008 GlaxoSmithKline. All rights reserved.

dialogue that can aid in addressing patients' respiratory symptoms. There is potential for a screening tool to further stratify likely cases with obstruction using a more severe criterion measure ($FEV_1/FVC < 0.7$ and % predicted $FEV_1 < 65\%$, for example) and consequently a lower cut point for the LFQ. These possibilities will be investigated further in subsequent studies conducted using the LFQ. When the criterion measure was redefined in the current study to $FEV_1/FVC < 0.7$ and % predicted $FEV_1 < 65\%$, screening characteristics still indicated a negative predictive value of 96% at a lower cut point of 14 (data not shown). These results suggest that while targeting a more severe group the LFQ may miss only 4% of possible cases (majority of this 4% possibly milder) and thus affirms its status as a case finding tool.

The screening accuracy of the LFQ was significantly better with ordinal item-response scales than with binary (yes/no) item-response scales. The screening accuracy of the questionnaire was 78% with items having 5-point response scales compared with 74% with items having yes/no response scales. These findings are consistent with previous evidence suggesting that continuum-based scales have better psychometric properties than dichotomous yes/no scales.[22] The failure of the AL to add any value to the LFQ was surprising based on clinical experience and work on previous COPD and Asthma questionnaires.[23,24] However the lack of concordance between reported dyspnea and activity limitation suggests that the questions for these 2 areas are measuring different concepts. The hope that an AL item could identify patients that considered themselves asymptomatic due to modification of activities was not realized. It was difficult to obtain consensus among physicians and patients on the exact wording of the AL question to make a question that was both sufficiently general as well as specific. It appears that many patients with COPD learn to cope with their impairment but do not perceive those modifications as AL. The group agreed that this question would be best asked within the context of patient-physician introductory verbal dialog as opposed to part of a questionnaire. Cough and dyspnea did not reach statistical significance in the combined model. Both these variables were strong independent predictors of airflow obstruction within a bivariate model. Within a multivariate regression framework, with independent variables competing for variance in the dependent model, these variables lost statistical significance (multicollinearity). Excluding these variables from the model did not significantly improve screening accuracy. Moreover, model performance was not adversely impacted when cough and dyspnea were retained. Also, in view of the face/clinical validity of cough and dyspnea, these 2 important concepts were retained in the final LFQ. Other studies of similar tools have identified cough and dyspnea as being important predictors of airflow obstruction as well.

LFQ demonstrated very good screening accuracy regardless of whether airflow obstruction was defined as $FEV_1/FVC < 0.70$ or according to the more stringent criterion of $FEV_1/FVC < 0.70$ and $FEV_1 < 80\%$ of predicted.[1] In fact, the screening accuracy of the LFQ increased, as reflected by an increase in the AUC, with the more stringent criterion for definition of airflow obstruction. This pattern of results suggests that the questionnaire is not vulnerable to misclassification of natural, age-related diminishment in lung capacity as the presence of airflow obstruction. A classification scheme relying on FEV_1/FVC alone potentially introduces a large false-positive rate among elderly respondents who have age-related diminishment in lung capacity (''aging'' lung). Both the GOLD guidelines and the ATS/ERS guidelines use a similar spirometry-based diagnosis paradigm as well as similar severity staging.[1,15]

The development phase of the LFQ has been described elsewhere.[16] In this study, body mass index (BMI) (specifically, $BMI < 25$) was also statistically significant in stepwise analyses, it was only weakly related to pre-bronchodilator FEV_1/FVC in linear regression analyses. This variable was eliminated from consideration for the reduced subset because of low discriminatory power and the difficulty of easily and reliably assessing it in a patient-reported questionnaire (as calculation involves computation). Smoking was captured in terms of both number of cigarettes smoked and duration of smoking in the validation study. Both of these variables were highly collinear because they captured related information. Smoking duration was used in the final model based on the results of stepwise selection procedures.

The objective of the LFQ is to include questions that are easily completed by patients with information readily known to them without any computations. Content of items was both driven and confirmed by patients and physicians, and question and response options were refined based on patient and physician feedback in order to maximize their relevance to patients and to the disease of interest.[16] This tool was part of a rigorous scientific process and guided by a scientific committee comprising expert pulmonologists and primary care physicians in academic settings. The LFQ is unique among existing COPD screening/case finding tools[25–35] in having demonstrated both content validity and face validity, which are critical to utility in clinical practice. A recent questionnaire, the COPD-PS, was developed to explore similar objectives.[26] The LFQ has several advantages over the COPD-PS as well as other similarly developed screening questionnaires. Feedback from both patients and physicians (primary care as well as specialists) drove the item development as well as validation process for the LFQ. Patient feedback is important to developing a patient-reported outcomes measure. LFQ incorporated patient feedback at various stages in development as well as validation process. Spirometry performed in the LFQ validation study had a high degree of acceptance to American Thoracic Society spirometric standards (very few unusable/irreproducible spirometries) unlike the study reported by Martinez et al.[26] Also, in the development sample for the COPD-PS, initial models constructed based on usable spirometries ($n = 295$) were applied to the entire sample ($n = 697$) to conduct psychometric analyses, a practice that is not optimal.

Several characteristics render the LFQ particularly appropriate for use in the busy primary care setting: the LFQ is easy to self-administer, does not require interviewer administration or information from medical records, and is broadly useful across patient types. Other potential applications of the LFQ include use as an initial case finder in epidemiological studies, disease management programs,

and clinical research. While the LFQ can help health care providers identify patients in need of further evaluation for possible COPD, it is not intended to be used as a diagnostic tool. Patients whose LFQ score suggests the presence of airflow obstruction require clinical evaluation and spirometric testing to assess for and confirm diagnosis of COPD.

The results of this study should be interpreted with the knowledge that pre-BD spirometry was used as the criterion measure. Post-bronchodilator spirometry, after accounting for reversibility, is generally regarded as a more accepted measure of lung function than pre-BD spirometry. Also, GOLD stages have been defined (albeit pre-BD) as sensitivity analyses that show minimal changes to screening accuracy and performance of individual questions. In subsequent studies of the LFQ, post-bronchodilator spirometry will be explored as a criterion measure. This change is not expected to result in any major changes in the characteristics or performance of questionnaire. Also, data were collected from the state of Kentucky, which may not be representative of the United States population. However, the inclusion of both rural and urban locations might render the data representative in this regard. The degree to which the results generalize to countries other than the United States is not known although the authors are aware of no reason to suggest that the results would differ in other countries. One limitation of the tool may be asymptomatic older patients with a significant smoking history may turn out to score $\leq$18 on LFQ and thus classified as ''at risk''. For example, an aymptomatic 72-year old with a 20 pack year history of smoking would score 18 on the LFQ. While this person may not have symptoms, one might argue that this is the patient who may need further questioning as to whether they are minimizing symptoms. By definition, they are at risk and this tool points out that further workup may be necessary. Another limitation of this case-finding tool is the potential of finding cases of potential obstruction that are not confirmed by spirometry (false positives). LFQ does have a higher rate of false positives. With any patient reported tool, a good blend of sensitivity and specificity aims to reach a fair balance in that the tool doesn't find too many false positives but at the same time doesn't miss too many cases (true positives). Considering the high prevalence of undiagnosed COPD, the LFQ WG felt that a cut point targeted to not miss too many cases was needed for the LFQ. A factor to consider in certain segments of primary care is also the cost of spirometry which rules out its use as a population screener. Therefore, the LFQ can serve as a conduit to reduce performing spirometry in every symptomatic at risk patient with a smoking history and result in conducting further evaluation in smaller subset of patients with the knowledge that the tool will not miss too many potential cases, a key objective in COPD care. Of course, the LFQ false positive rate is also associated with cost concerns but in the current environment health plans and insurance companies do vest heavily in disease management programs as well as prevention (of exacerbations) initiatives for a chronic progressive disease like COPD.

In summary, the LFQ is a simple, 5 item COPD case finding tool with good screening accuracy in a primary care patient population. This research extends previous findings establishing the instrument's content validity and face validity according to primary care physicians and patients.[16] The LFQ is an appropriate case finding tool to facilitate early recognition and diagnosis of COPD in primary care.

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Conflict of interest

This study was funded by GlaxoSmithKline (GSK). Dr. Hanania has received research grant support and served as a consultant or speaker for GSK, Dey, Sepracor, Novartis, and Boehringer Ingelheim. Dr. Mapel has received research grants from and served as a consultant for GlaxoSmithKline, Pfizer Pharmaceuticals, and Boehringer Ingelheim, Inc. Dr. Mintz has been a speaker and advisor for GSK, AstraZeneca, and Sepracor. Dr. Mannino serves on advisory boards for Boehringer Ingelheim, Pfizer, GSK, and Ortho Biotech; is on the speakers bureau for Boehringer Ingelheim, Pfizer, GSK, and Dey; and has received research grants from GSK, Novartis, and Pfizer. Dr Samuels has served as a consultant for GSK. Dr. Yawn has received research grants from and served as a consultant to GlaxoSmithKline, Pfizer Pharmaceuticals and the American Lung Association. Dr. Jim F. Donohue has received honoraria for consulting, speaking, advising from GSK and has been an investigator on clinical trials. Dr. Martinez is a consultant for Altana and has also served on advisory boards for Genzyme, GSK, Novartis, Schering Plough, AstraZeneca, and Forrest/Almirall. Dr. Martinez is a member of the speakers bureau for GSK, AstraZeneca, Schering Plough, and Boehringer Ingelheim.Drs. Dalal and Jhingran are employees of GlaxoSmithKline.

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