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Validation of a Respiratory Symptoms Questionnaire for Chronic Obstructive Pulmonary Disease Detection

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ABSTRACT

Background: This paper proposes the use of a questionnaire on respiratory symptoms to timely detect excessive decline in lung function, a key feature in Chronic Obstructive Pulmonary Disease (COPD) among women exposed to firewood smoke.

Objective: To validate the respiratory symptoms questionnaire applied to women with cross-sectional and longitudinal lung function assessed by spirometry.

Methods: A total of 522 women from the Purepecha region of Michoacan completed a respiratory symptoms questionnaire and the spirometric maneuvers. Individual questions were selected based on the odds ratio and *p* value from logistic regression model and the area under curve (AUC) using the post-bronchodilator FEV_1/FVC baseline ratio and the excessive lung function decline (value below the LLD) as gold standards. Several simplified scoring systems were developed and proven by reliability tests and logistic regression.

Results: The initial questionnaire was reduced from 110 to 13 items after a bivariate analysis that included logistic regression and reliability tests. The final questionnaire included: daily cough, cough ≥3 months, cough during the day, phlegm during the morning, phlegm during the day, no allergies, cough during the morning, wheezing, wheezing without cold, chest tightness, stopped working due to cold, exposure time to biomass fuel >12 years and age >30 years. One combination of items raised an AUC=0.559 for the post-bronchodilator FEV_1/FVC ratio and another combination raised an AUC=0.556 for the excessive lung function decline.

Conclusions: The proposed items are useful to determine risk but not enough to predict the presence of the disease.

MAIN TEXT

The household use of solid fuels is the major source of indoor air pollution worldwide.(Romieu et al. 2009) Solid fuels are coal and biomass; the latter defined as those fuels derived from plants and animals intentionally burned by humans. Approximately 50% of households in the world and 90% of rural households use biomass fuels as their primary energy source.(Hu et al. 2010) There is strong evidence of chronic obstructive pulmonary disease (COPD) associated with exposure to biomass fuel smoke, and the risk tends to increase with longer exposure time.(Hu et al. 2010) Women, whether young or adult, and young children present the highest exposure to smoke from biomass fuels as they stay longer in the kitchen. In developing countries, women start cooking on average at age 15 and spend an average of 4-6 hours a day in the kitchen, usually an enclosed space with poor ventilation. Therefore, women are exposed for about 30 or 40 years to biomass fuel smoke, about 60,000 hours of exposure, about 25 million liters of contaminated air inhaled.(Salvi and Barnes 2010) The World Health Organization (WHO) considers indoor air pollution as the tenth preventable risk factor worldwide,(Salvi and Barnes 2010) estimating that 38.5 million of disability-adjusted life years are attributable these exposure, accounting for three percent of the global burden of disease.(Zuk et al. 2007)

In Mexico, 25% of households (about 27 million people) use wood as a primary energy source, either exclusively or combining it with LP gas stoves. Most of these households are in rural areas or indigenous communities.(Masera et al. 2005) Rural Mexican women spent on average 75% of their daily time indoors.(Perez-Padilla et al. 2010)

Chronic Obstructive Pulmonary Disease (COPD) is a disease characterized by chronic airflow limitation, marked extra-pulmonary effects and long-term decline in lung function. Although the terms emphysema and chronic bronchitis are often used as synonyms for COPD, these have not been included in the Global Initiative for Chronic Obstructive Lung Disease (GOLD).(Rabe et al. 2007)

The specific features of COPD are:(Rabe et al. 2007)

• Chronic airflow limitation, which is usually progressive and not fully reversible.

• Histopathological changes in the lungs, including the small airways and parenchyma.

• Extrapulmonary effects and co-morbidities that influence the degree of severity of the disease.

• The key feature is the long-term decline in lung function.

Lung or respiratory function is measured, using different tests that evaluate the various processes involved in the act of respiration: inspiration, expiration, exchange of oxygen and carbon dioxide, as well as volume and lung distension.(Carballo Cruz et al. 1996) The spirometry is an easy, reliable and accessible way to measure the mechanics of respiration; it serves to measure the lungs size and the bronchial caliber.(Vázquez Garcia and Pérez Padilla 2007) With the spirometry, we can obtain the following parameters: the forced expiratory volume that is a measure of the maximum amount of air that can be expelled in a given number of seconds during a determination of the vital capacity. It is usually expressed as FEV (for its acronym in English) followed by a subscript indicating the number of seconds in which the measurement is made, although sometimes given as the percentage of forced vital capacity; eg, forced expiratory volume in one second FEV_1 abbreviated. Forced vital capacity is the volume of air that is exhaled by a maximal expiration after a maximal inspiration.(Carballo Cruz et al. 1996)

The severity of COPD is classified into four stages based on both FEV_1 and FVC after giving a bronchodilator:(Rabe et al. 2007)

I. Mild. The quotient obtained by dividing the FEV_1 over FVC is less than 0.7 and FEV_1 equal to or greater than 80% predicted.

II. Moderate. The quotient obtained by dividing the FEV_1 over FVC is less than 0.7 and FEV_1 equal to or greater than 50% but less than 80% predicted.

III. Severe. The quotient obtained by dividing the FEV_1 over FVC is less than 0.7 and FEV_1 is equal or greater than 30% but less than 50% predicted.

IV. Very severe. The quotient obtained by dividing the FEV_1 over FVC is less than 0.7 and FEV1 is less than 30% predicted or FEV_1 is less than 50% predicted plus the presence of chronic respiratory failure.

Use of the lower limit of normal (LLN) forced expiratory volume in 1s (FEV_1) to forced vital capacity (FVC) compared to the fixed ratio criterion (FEV_1/FVC, 0.7) recommended by the Global Initiative for Chronic Obstructive Lung Disease, reduces the age-related increases in COPD prevalence that are seen among healthy never-smokers. The added requirement of an FEV_1 either, 80% predicted or below the LLN further reduced age-related increases and also led to the least site-to-site variability in prevalence estimates after adjusting for potential confounders. So, the use of the FEV_1/FVC LLN criterion instead of the FEV_1/FVC, 0.7 should minimize known age biases and better reflect clinically significant irreversible airflow limitation. (Vollmer et al. 2009)

The longitudinal limit for an annual decline (LLD) predicts the 95th percentile cut-off point for observed annual changes in lung function and thereby identifies 5% of individuals with excessive declines for FEV_1. This approach facilitates quality control on an individual basis, as it helps to identify individuals for whom spirometry quality control and/or respiratory conditions may need further investigation, or those who should have more frequent testing.(C)

Questionnaires to identify patients with COPD

The underdiagnosis of COPD is a worldwide problem. Generally, patients come to medical consultation when symptoms are severe or incapacitating; in addition, this disease is very commonly confused with other diseases. Among doctors, lack of clinical suspicion, and therefore screening for COPD, leads to the possibility of failure in the diagnosis and treatment.(van Schayck et al. 2005)

Although spirometry is considered the gold standard for the diagnosis of COPD, it should be noted that patients have their first contact with primary health care providers, rather than with the pulmonologist who performs spirometry; adding to this costs, availability of equipment and trained personnel, and the time required to perform the spirometry.(Price et al. 2006a)

Clinical practice guidelines published by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) are useful to enhance early detection of COPD. These guidelines recommend that when spirometry is not available, the diagnosis of COPD should be performed using all the tools available. The symptom-based questionnaires can help identify patients at the primary care that are more likely to have airflow obstruction.(Tinkelman et al. 2006) The Working Group of the U.S. Preventive Services does not support the practice use of spirometry as a routine screening.(Mintz et al. 2011)

A literature review found ten such instruments.(van Schayck et al. 2005) Of these questionnaires, only two have been validated in some way, with the limitations of being validated for people over 40 years of age and personal history of smoking.

Price, D.B. et al. (2006) developed a self-administered questionnaire for timely detection purposes of people at risk for COPD, using spirometry as a gold standard. One of these questionnaires(Price et al. 2006b) had a sensitivity of 80.4% and a specificity of 72%, for the 52 items result. The items were reduced to 17 by multiple regression, with eight of them significantly associated with the diagnosis of COPD: age, packs- year, body mass index (BMI), cough affected by weather, phlegm without the presence of cold, morning phlegm, frequent wheezing, and history of any allergies. The 52 items had an odds ratio between 0.23 and 12; including nine items with statistical significance at the 0.05 level. The same authors reported the application of this questionnaire in two groups, one for case finding and another for differential diagnosis.(Price et al. 2006a) The investigators constructed a point scale based on the results of the questionnaire classifying subjects into three risk groups (low, intermediate and high) for COPD, obtaining values of sensitivity 54-88%, specificity 58-88%, positive predictive values of 30-78% and negative 71-93%.

A summary of questionnaires for the detection of COPD is presented in the Supplemental Table 1.

Currently, we found one validated questionnaire in Spanish for early detection of chronic obstructive pulmonary disease; this tool was applied in a primary care service to people over 35 years old, and they were asked about respiratory symptoms, impact of disease, smoke history and socio-demographics; they obtained 93.4% of sensitivity and 65.45 of specificity using .(Miravitlles et al. 2012)

Taking into account the above data on the use of biomass, risk groups and intensity of exposure, it would be useful to have an instrument like this, in order to identify women in risk to further perform spirometry confirming the diagnosis, thus increasing the efficiency in the diagnosis and management opportunity in these patients. We did not found a validated questionnaire for Mexican population exposed to biomass fuel smoke.

Our general objective was to evaluate the agreement of a respiratory symptom questionnaire applied to women as part of the *Health impact assessment due the introduction of improved stoves in Michoacan* Study with the results for cross-sectional and longitudinal spirometry.

Method

Design

This is a validation study of a questionnaire from the original study *Improved biomass stove intervention in rural Mexico: Impact on the respiratory health of women.*

Participants

Women using biomass fuels mostly in open fires in rural Purepecha of Michoacan were selected. The original study was a randomized community intervention to evaluate the health impact of efficient biomass stoves Patsari.(Romieu et al. 2009) From 668 selected participants, 522 concluded the study with information for questionnaires and the spirometric maneuvers, as shown in Figure 1.

Procedures

For the original study 668 homes were selected in six communities that met the inclusion criteria: 1) the source of domestic energy is fuel wood and 2) that there was a mother and a child less than five years of age. The localities selected for study were Comachuén, Mojonera and Turícuaro in Nahuatzén Township; Tanaco and Casimiro Leco in the town of Cherán, and Quinceo in the town of Paracho. A questionnaire including 102 items administered by interviewers was asked to each participant woman at baseline. The interview lasted about 30 minutes on average for the respiratory symptoms section.

Before applying this baseline questionnaire in the original study, a pilot study was conducted in Cucuchucho and Ihuatzío; communities with similar characteristics to the study communities and finally in Comachuén, a community selected for the study. Some of the interviewers spoke

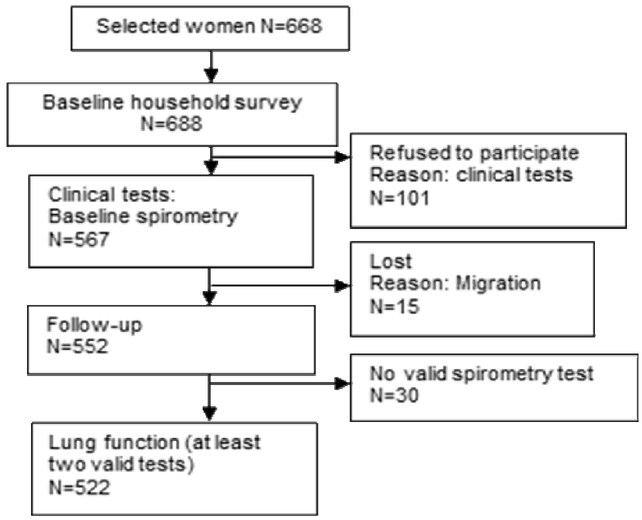
Purepecha and had the ability to do the translation when necessary. These pilot tests showed that women comprised the questions and knew the differences between symptoms.

As part of the baseline questionnaire, the time each woman has been cooking with fuelwood was asked.

Spirometry was conducted using portable battery-operated ultrasonic spirometer (Easy-One from NDD, Zurich, Switzerland) in accordance with the ATS/ERS recommendation,(Miller et al. 2005) with subjects in a sitting position and wearing nose clips. Technicians had standardized training and were certified as spirometrists before starting the study. We performed a maximum of eight forced expirations maneuvers in order to obtain three acceptable maneuvers according to the criteria of ATS/ERS. The test was repeated on average every three months during the follow up period. The spirometry test was reviewed for quality control and assurance by Dr. Rogelio Perez-Padilla, expert pulmonologist. If a spirometry was considered inadequate, the test was repeated in the following weeks. Daily, the spirometer was checked with a three-liter syringe, with a range of error of less than 3% (from 2.91 to 3.09 liters).

200 mg of salbutamol were applied with a spacer and after 20 minutes spirometry was performed again.

Figure 1. Flowchart showing the sample of the original study



Outcome definitions

- We used the lower limit of normal (LLN) cutoffs for FEV_1/FVC, and FEV_1 from the Hankinson, JL equations (Hankinson et al. 1999) in place of the fixed ratio and the FEV_1 80% predicted criteria from the GOLD definitions to define obstruction during the baseline post-bronchodilator test.
- Excessive lung function decline was defined as a value below the approximate one-sided 95% confidence limit for absolute longitudinal decline (LLD_a) obtained by the (Hnizdo et al. 2007), with a referent slope of 30 ml/year, including at least two valid tests during baseline and follow up.
- Acute bronchodilator responsiveness for the baseline test was defined as: a) FVC and/or FEV_1 increment ≥12% plus ≥200mL over baseline; or b) FEV_1≥15%increase over baseline; or c) FEV_1 increase ≥10% predicted value.(Montes de Oca et al. 2010)

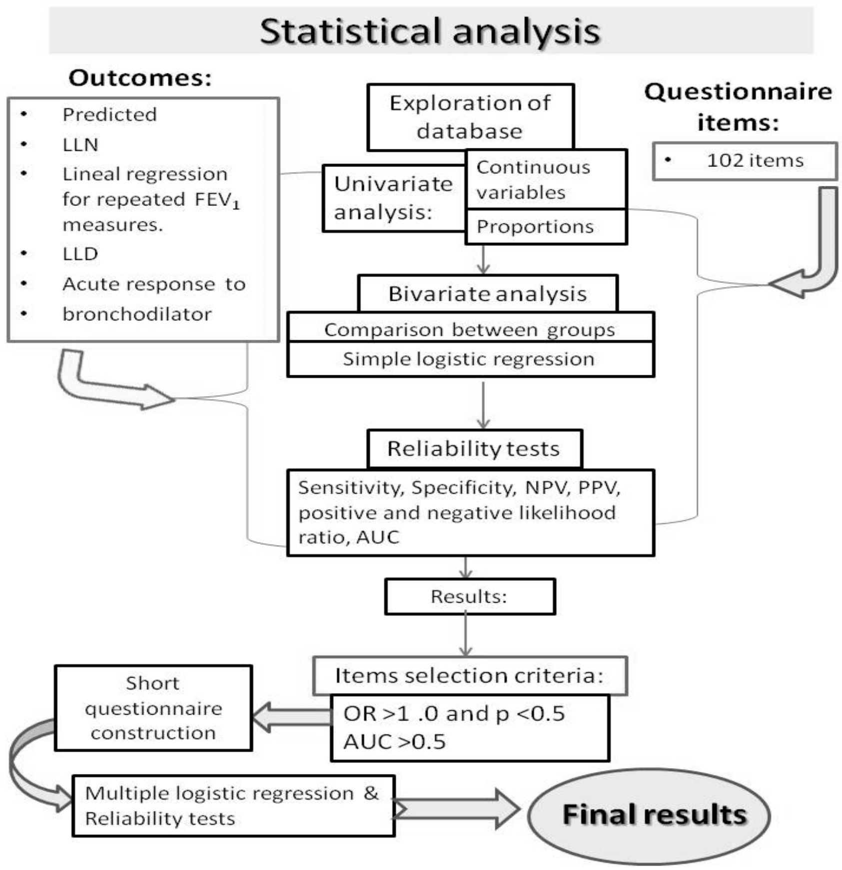
Statistical analysis

After the initial exploration of the database, univariate analysis was performed obtaining frequency for the categorical variables and mean, standard deviation and variance (measures of central tendency and dispersion) for continuous variables. Subsequently, we did a bivariate analysis to assess possible relationships between individual characteristics against the dependent variables and selected those that were significantly related to the outcome variables.

Bivariate analysis included the comparison between groups using chi-squared test or Fisher exact test for categorical variables and t-test for the continuous variables, as well as simple logistic regression.

We obtained the specificity, sensitivity, positive and negative likelihood ratios of the proposal questionnaire according to the level of agreement using the excessive lung function decline and the cross-sectional definition of obstruction as the gold standards.(Ruiz de Adana Pérez 2009) The statistical packages used were *Stata 11.0* and *Spirola 3.0.1.*

Figure 2. Flowchart of the statistical analysis of the study.



Results

The Table 1 displays selected characteristics of the study population; a total of 522 women had complete data for this analyses. The distribution of the variables was similar between sites. The most of the population was young with 30 years or less. A little more of a half presented overweight or obesity (52 %). The mean wood smoke exposure time was of 13.1 years. The frequencies of symptoms report included in the baseline questionnaire are shown in Table 2 and the lung function results are shown in Table 3. The percentage predicted of FEV_1 pre-bronchodilator mean was of 104.3 (S.D. ±10.8) and post-bronchodilator 106.28 (S.D. ±11.63). The FEV_1/FVC pre-bronchodilator mean was 0.83 (±0.06) and 0.86 (±0.06) post-bronchodilator. Proportions of women with spirometric values under the LLN were: 2.11% and 13.4% for pre-bronchodilator FEV_1 and FEV_1/FVC, respectively; 1.55% and 6.43% for post-bronchodilator FEV_1 and FEV_1/FVC, respectively.

During baseline questionnaire, 102 items were asked. An item reduction was performed by logistic regression using post-bronchodilator $FEV_1/FVC<LLN$ and FEV_1 annual decline$<LLD_a$ as the outcome variables, considering OR>1.0, *p*=<0.500 and AUC>0.50 as the selection criteria. The final questionnaire was reduced to 13 items displayed in Table 4. This proposal was analyzed by ROC (Receiver Operator Characteristic) and reliability tests, and the results are showed for both outcomes (post-bronchodilator FEV_1/FVC and excessive lung function decline) in Table 4 and Figure 3. The final questionnaire included: daily cough, cough ≥3 months, cough during the day, phlegm during the morning, phlegm during the day, no allergies, cough during the morning, wheezing, wheezing without cold, chest tightness, stopped working due to cold, exposure time to biomass fuel >12 years and age >30 years.

Table 1. Characteristics of the study population in Michoacan, 2005.

Variables	Value (n=522)	FEV_1/FVC postBD <LLN	FEV_1/FVC postBD>LLN
Demographics			
Age (years)	25.67 (±6.77)	24.9 (±5.5)	25.8 (±6.7)
Age %			
<30 years	73.37	72.7	73.3
≥30 years	26.63	27.3	26.7
Location %			
Casimiro Leco	6.51	0	7.10
Comachuén	21.84	24.24	21.50
Mojonera	11.88	9.10	12.10
Quinceo	20.88	21.21	20.80
Tanaco	20.31	18.18	20.40
Turícuaro	18.58	27.27	18.10
BMI	25.83 (±4.05)	24.77(±4.45)	25.96(±4.02)
BMI %			
Low weight	1.15	0	1.25
Normal	46.36	60.61	44.58
Overweight	36.21	27.27	37.29
Obesity	16.28	12.12	16.88
Wood smoke exposure time (years)	13.10 (±7.72)	14.23(±7.8)	12.96(±7.7)
Wood smoke exposure time %			
≤7 years	26.63	18.18	27.29
From 7 to 12 years	25.29	24.24	25.83
> 12 and ≤ 18 years	24.90	36.36	23.75
>18 years	23.18	21.21	23.13
Medical history %			
Active tobacco smoking	1.73	0	1.88
Passive tobacco smoking	20.23	12.12	21.14
Asthma	0.57	0	0.63
Chronic bronchitis	0.58	0	0.63

Note: Values are expressed in percentage (%) or mean (±SD).

Table 2. Baseline report of respiratory symptoms in Michoacan, 2005

Respiratory symptoms %	Value % (n=522)	FEV_1/FVC postBD <LLN	FEV_1/FVC postBD>LLN
Cough everyday	5.56	12.12	5.21
Cough every morning	7.10	9.09	7.10
Cough during the day	3.64	9.09	3.33
Overnight coughs	5.56*	15.5	5.0
Cough for three months or more	4.08	9.38	3.80
Phlegm	14.20	15.15	14.41
Phlegm every morning	12.45	18.18	12.29
Phlegm during the day	6.15	9.09	6.07
Overnight phlegm	3.83	3.03	3.96
Phlegm for three months or more	4.87	6.06	4.88
Worsening period of cough or phlegm	5.43	0	5.91
Wheezing	5.36	3.03	5.63
Wheezing with shortness of breath	1.92	0	2.08
Wheezing without cold	2.87	0	3.13
Chest tightness	10.15	6.06	10.21
Episode of breathlessness	5.66	0	6.16
Waking up short of breath in the last 12 months	5.17	0	5.63
Waking up short of breath in the last 3 months	3.11	0	3.39
Shortness of breath when walking on level ground	11.65	3.23	12.42
Shortness of breath when walking at her own pace	11.13	3.33	11.85
Has stopped working because of cold	15.56	18.75	15.64
History of allergy	45.21	39.39	45.83

* $p<0.05$

Also, women performed up to six spirometries for which we obtained slopes for annual decline. An excessive decline and the possible associations with the items of the questionnaire were analyzed. A total of 408 women completed a minimum of two spirometries and 50 (12.25%) of them had an excessive decline defined as a result greater than LLD_a, as shown in Table 3. Of all women with FEV_1/FVC<LLN, only one (3%) had an excessive lung function decline that represents 3% of all cases with a pre-bronchodilator FEV_1 value>LLD_a.

Table 3. Main results of the lung function tests in Michoacan, 2005

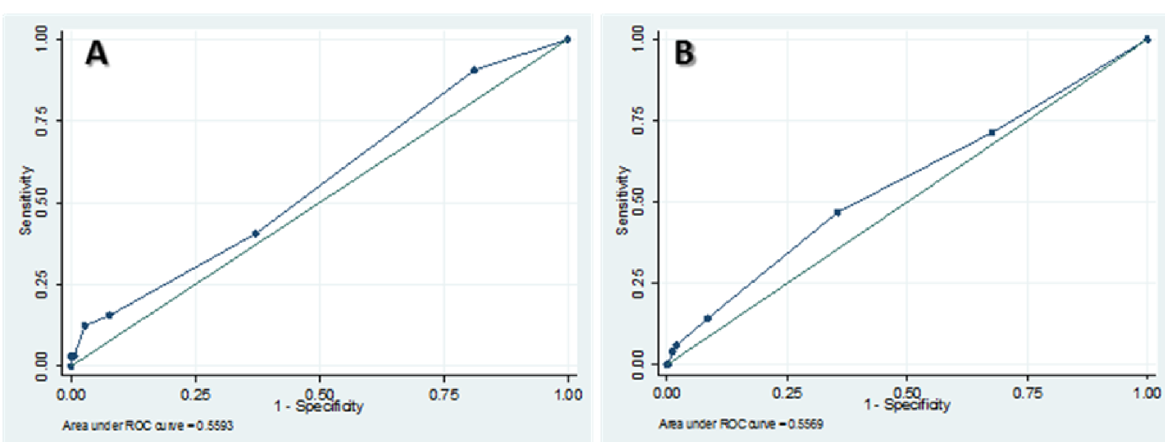
Lung Function Tests	Value (n=522)
Baseline pre-bronchodilator spirometry	
FEV_1(L)	2.93 (±0.35)
FEV_1 % predicted *	104.3 (±10.8)
FEV_1 <80 % predicted	1.15
FEV_1 < LLN	2.11
FEV_1/FVC	0.83(±0.06)
FEV_1/FVC <0.7	4.21
FEV_1/FVC < LLN	13.4
Baseline post-bronchodilator spirometry	
FEV_1 (L)	2.99 (±0.37)
FEV_1 % predicted*	106.28 (±11.63)
FEV_1 < 80% predicted	1.15
FEV_1 < LLN	1.55
FEV_1/FVC	0.86 (±0.06)
FEV_1/FVC < 0.7	2.30
FEV_1/FVC < LLN	6.43
Post-bronchodilator FEV_1 changes	
Absolute change (mL)	54 (±0.19)
Percentage change	1.50 (±6.72)
Acute bronchodilator responsiveness	
FVC and/or FEV_1 increment ≥12% plus ≥200mL over baseline	8.25
FEV_1≥15%increase over baseline	2.52
FEV_1 increase ≥10% predicted value	6.98
Lung function decline FEV_1 pre-bronchodilator (mL per year)	52.6 (± 192)
Lung function decline FEV_1 post-bronchodilator (mL per year)	124.6 (±245)
Excessive lung function decline: FEV_1 pre-bronchodilator > LLD_a, %	12.25

Note: Values are expressed in percentage (%) or mean (±SD). *NHANES III predicted value. LLN: Low Limit Normal obtained by the equation from Hankinson JL et al (Hankinson JL, Odencrantz JR, Fedan KB. *Spirometric reference values from a sample of the general U.S. population.* Am J Respir Crit Care Med 1999;159:179-187).

Table 4. Analysis of the items from the reduced questionnaire

Item (n=522)	Post-BD FEV_1/FVC <LLN				AUC
	OR	*p*	CI		
Cough everyday	2.5103	0.107	0.8188	7.6956	0.534
Cough ≥3 months	2.6200	0.140	0.7296	9.4123	0.527
Cough during the day	2.9000	0.105	0.800	10.5057	0.528
Phlegm during the morning	1.5862	0.329	0.6281	4.0054	0.529
Phlegm during the day	1.5482	0.491	0.4458	5.3760	0.515
Exposure time >12 years	1.0207	0.361	0.9767	1.0666	0.550
No allergies	1.3017	0.473	0.6330	2.6770	0.523
Sum of items	1.4076	0.032	1.0304	1.9230	0.559
Item (n=522)	**Excessive lung function decline**				**AUC**
	OR	*p*	CI		
Cough during the morning	1.6551	0.331	0.5986	4.5758	0.518
Wheezing	1.8777	0.230	0.6716	5.2500	0.522
Wheezing without cold	1.8404	0.358	0.5009	6.7620	0.513
Chest tightness	1.4384	0.443	0.5680	3.6423	0.516
Stopped working due to cold	2.4791	0.010	1.2456	4.9340	0.572
Exposure time>12 years	1.0196	0.323	0.9810	1.0597	0.522
Age>30 years	1.0205	0.388	0.9745	1.0686	0.501
Sum of items	1.2423	0.104	0.9611	1.6059	0.556

Figure 3. Area under curve of the reduced questionnaire for the outcomes



The second cutoff was the best for sensitivity and specificity in both outcomes. *A*: Area under curve (AUC) for FEV_1/FVC post-bronchodilator, Sensitivity=40.6% and Specificity=62.8%; *B*: AUC for excessive lung function decline, Sensitivity=46.9% and Specificity=64.4%.

Finally, we did an age stratified analysis using the age of 30 years (third quartile) as cutoff to create two groups and we found several differences between groups, as shown in Table 5.

Table 5. Age stratified analysis of the reduced questionnaire by outcome

Sum of items (n=522)	Prevalence of Post-BD FEV_1/FVC <LLN	OR	*p*	CI		AUC
<30 years	6.38	1.4243	0.053	0.9947	2.0394	0.552
≥ 30 years	6.57	1.3884	0.337	0.7106	2.7127	0.576
	p=0.939					
Correctly classified (cutpoint <=2)	61.37					
All	6.43	1.4076	0.032	1.0304	1.9230	0.559
Sum of items (n=522)	**Prevalence of Excessive lung function decline**	**OR**	***p***	**CI**		**AUC**
<30 years	11.60	1.1731	0.376	0.8238	1.6706	0.532
≥ 30 years	13.91	1.6834	0.073	0.9521	2.9764	0.628
	p=0.522					
Correctly classified (cutpoint <=2)	62.28					
All	12.25	1.2423	0.104	0.9611	1.6059	0.556

Discussion

Previously other authors have reported results for questionnaires to detect COPD in risk groups, for example smokers,(Price et al. 2006a; Price et al. 2006b; Van Schayck et al. 2002; Kotz et al. 2008; Calverley et al. 2005; Frith et al. 2011; Miravitlles et al. 2011) with persons over 40 years specially.(Price et al. 2006a; Tinkelman et al. 2006; Price et al. 2006b; Kotz et al. 2008; Calverley et al. 2005; Frith et al. 2011; Yawn et al. 2009; Müllerová et al. 2004; Mahesh et al. 2009) In this work, we have investigated the accuracy and reliability of a list of questions to identify outcomes related to COPD of predominantly young women (95.4% < 40 years old) using biomass fuel, and presenting a very small prevalence of active smoking (1.73%).

After an item reduction, we obtained a short questionnaire with a medium capacity to detect an excessive decline in lung function (AUC=0.556, 46.9% Sensitivity and 64.4% Specificity) and to determine the risk of having an abnormally low baseline pulmonary function (AUC=0.559, 40.6% Sensitivity and 62.8% Specificity). These results are lower than those found in other studies,(Price et al. 2006a; Tinkelman et al. 2006; Price et al. 2006b; Kotz et al. 2008; Calverley et al. 2005; Frith et al. 2011; Yawn et al. 2009; Frank et al. 2003; Martínez et al. 2008; Miravitlles et al. 2011; Mintz et al. 2011; Müllerová et al. 2004; Mahesh et al. 2009) but these differences can be due to younger age and the use of alternative definitions of the outcome of interest (FEV_1<80% predicted or FEV_1/FVC<0.7 or pre-bronchodilator FEV_1/FVC_6 or Expert Clinical Review). None of these reports used post BD FEV_1/FVC<LLN as the gold standard.

The mean annual loss of FEV_1 was 52.6 mL (± 192), a lower average decline compared to a study in elderly people (62 mL)(Mannino et al. 2007) but greater than the results reported for young smoker women (23.9 mL) (Kohansal et al. 2009).

The predictive values of the short questionnaire (sum of items) was not significant for the post BD $FEV_1/FVC<LLN$ as gold standard (OR=1.24, p=0.104) and this can be due to age too, because the vital capacity increases with age until it plateaus in female at about 40 years of age.(Kohansal et al. 2009) The wide variability of spirometry results can explain the large standard deviation in the annual lung function decline.

We obtained results for the acute bronchodilator responsiveness with all available data. Currently, there is no clear consensus about the application of this results because of the overlapping values for differential diagnosis between COPD and asthma.(Chhabra 2013) Different criteria are used to determine the acute response to bronchodilator, so that test results vary widely, as shown in this work.

Limitations: should explore the validity of this questionnaire in populations with other demographic profile although the questions are simple (External Validity). Quality of spirometric maneuvers should be more strictly observed in the follow up.

Strengths: We made efforts to reduce potential biases such as no performance of spirometry. Sub-groups were compared (performance versus no performance) through Xi2 and t-tests, no differences were found between the two groups using variables such age, location and education. The population was relatively young and was not expected to show obvious acute exacerbations (COPD diagnosed), the used reference value were a post-bronchodilator FEV_1/FVC < Low Limit Normal that is more appropriate for this population in the COPD diagnosis. We used the gold standard for measuring respiratory function and diagnose obstructive pulmonary disease, unlike other studies that have used other standards (such as Expert Reviews, for example).(Frank et al. 2003; Martinez et al. 2008)

A contribution of this work is that a questionnaire in Spanish for COPD case finding was used because there are only a few reports about validated questionnaires in this language for Mexican young woman, who does not belong to a specific occupational group, e.g. miners.

Conclusions

Other studies with similar population characteristics and the same spirometric reference values are necessary to confirm the present results for in risk for COPD screening. The proposed items are useful to determine risk but not enough to predict the presence of the disease.

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Supplemental table 1. Summary of questionnaires for COPD detection

Authors/Year	Type of study	*n*	Population characteristics	Instrument	Application	Reference values	Results
van Schayck CP et al. 2002	Sub-sample of a cross-sectional	169	Age: 35-70 y.o. Smokers. No COPD diagnosis. Netherlands.	9 items	Auto-applied	FEV_1<80% predicted	NPV:82-87 1-6 individual items NPV:85-89 1-3 item combinations
Price DB et al. 2005	Prospective concordance	818	49.3% men ≥40 y.o. Smokers. No COPD diagnosis USA & UK	52 items	Postal	FEV_1/FVC<0.7	Sens: 80.4 Spec: 72.0
van Schayck CP et al. 2005	Literature review	--	10 several questionnaires: for detection or diagnosis or differential diagnosis or finding case	Only 2 significative questionnaires for pre-diagnosis	1. Auto-applied 2. Applied by nursing	Several	Several
Tinkelman DG et al. 2006	Prospective concordance	597	≥40 y.o. Previous COPD diagnosis	52 items reduced to 19. (9 significative)	Postal	FEV_1/FVC<0.7	OR: 0.33-20.7 individual items. Short questionnaire (9 items): Sens:72.0 y Spec:82.7
Price DB et al.2006	Prospective concordance	818 for detection 597 for differential diagnosis	Group 1. ≥40 y.o. Smoke history No COPD diagnosis	8 items for detection 9 items for differential diagnosis	Applied by health personnel. Score system: 3 subgroups by risk of obstruction (higher risk, no changes or reduced risk).	FEV1/FVC<0.7	Group 1. Higher risk: (ROC) PPV 30.3,NPV:92.7 Sens:80.4 Spec:57.5. Reduced risk: (ROC) PPV:37,NPV:89, Sens:58.7 y Spec:77.
			Group 2: ≥40 y.o. COPD diagnosis Scotland & USA				Group 2. Higher risk: (ROC) PPV:63.4, NPV:82.3, Sens:82.1, Spec:63.7 Reduced risk PPV:77.8, NPV:71.4, Sens:53.8, Spec:88.2
Kotz et al. 2008	External validation	676	40-70 y.o. Smoke history No COPD diagnosis	Score questionnaire by Price, DB	Applied by health personnel	FEV1/FVC<0.7	AUC= 0.65
Yawn BP et al. 2009	Retrospective concordance	387	≥40 y.o. Chronic bronchitis diagnosis referred in a USA survey	*Lung Function Questionnaire*: 8 items in 8 several combinations	Items selected from a National Survey. Lung function values were compared between individual with and without chronic bronchitis referred diagnosis using Xi^2 and *t*.	FEV1/FVC<0.7	Proposed model (5 items): AUC= 0.72, Sens:73.2 Spec:58.2.

Supplemental table 1. Summary of questionnaires for COPD detection *(Continuation)*

Authors/Year	Type of study	*n*	Population characteristics	Instrument	Application	Reference values	Results
Calverley PMA et al. 2005	Internal validation	7,701	General population 35-75 y.o. USA	7 items	Retrospective analysis from NHANES III	$FEV_1/FVC<0.7$	For smokers and ≥ 40 y.o. Sens: 85%, Spec:45%, NPV: 88%, PPV: 38%.
Frank TL et al. 2003	Internal validation	202	General population. UK	7 items in 2 scoring systems	Postal	Expert clinical review	First scoring system: PPV 75.1% Sens: 50.2% Spec: 95.3% Second scoring system: PPV: 82.3% Sens: 46.9% Spec: 97.1%
Frith P et al 2011	Prospective comparison of tests	204 case finding 93 differential diagnosis	Smokers ≥50 y.o. UK	COPD Diagnosis Questionnaire (CDQ) Differential diagnosis questionnaire (DDQ)	Auto-applied	Pre BD FEV_1/FV_6 $FEV_1/FVC<0.7$	CDQ: AUC=0.72 DDQ: AUC=0.66
Martínez FJ et al. 2008	Internal validation	697	Patients from pulmonary care services. USA	COPD-PS : 45 items in 7 domains. An expert clinical review determined patients to perform spirometry.	Auto-applied	$FEV_1/FVC<0.7$ Expert clinical review	For ratio: AUC=0.81, Sens:59.6%, Spec: 83.2% For clinical diagnosis: AUC=0.89, Sens:66% Spec:89%
Miravitlles M et al. 2011	External validation	173	Patients from Primary Care Service ≥ 35 y.o. Smokers Spain	COPD-PS Spanish translation (5 items)	Auto-applied	Pre-BD FEV_1 %	AUC: 0.79 Correctly classified: 78.1% Sens:93.6% Spec:64.8% PPV: 69.5% NPV: 92.2%
Mintz et al. 2011	External validation	1,575	Patients from Primary Care Service ≥ 30 y.o. Smokers. USA	LFQ: 5 items.	Auto-applied	$FEV_1/FVC<0.7$	Sens: 88% Spec: 25% PPV:21% NPV:90%
Müllerová H et al. 2004	Internal Validation	104	Outpatient respiratory clinic 65.5 (±10.3) mean age. USA	3 items: one directly asked previous diagnosis of COPD.	Administered by one single person	$FEV_1/FVC<0.7$	Correctly classified: 86.5% Sens: 92% Spec: 72.4%
Mahesh PA et al. 2009	Pilot study of validation and prevalence	105: pilot 900: prevalence	≥ 40 y.o. Men 71.9% smokers Women no smokers Women exposed to biomass fuel the prevalence of COPD was: 3.9% India	3 domains: exposure risk factors, age and respiratory symptoms.	Administered by a trained respiratory nurse	Golden criteria	Correctly classified: 83.8% Sens: 62.5% Spec: 87.6% PPV: 47.6% NPV: 92.85%