

## Case-Finding for Persistent Airway Obstruction in Farmers: A Questionnaire With Optimal Diagnosis Criteria

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**Introduction:** Appropriate identification of subjects who are candidates for spirometry through case-finding questionnaires may help solve the problem of chronic obstructive pulmonary disease misdiagnosis. The performance of case-finding questionnaires depends at least partially on the characteristics of the population used for their development. The use of an accurate threshold for the forced expiratory volume in 1 second / forced vital capacity ratio to define persistent airway obstruction is also vital in ascertaining chronic obstructive pulmonary disease.

**Methods:** Using a population examined between October 2012 and May 2013 that included a large subset of agricultural workers both exposed and unexposed to tobacco smoking, the authors aimed to select a combination of items that would identify persons most likely to have persistent airway obstruction defined as forced expiratory volume in 1 second / forced vital capacity less than the lower limit of normal according to the Global Lung Initiative–2012 equations. Two thirds of the population ( $n=3,397$ ) were randomly selected to develop a questionnaire, and one third ( $n=1,698$ ) was reserved for questionnaire validation. Statistical analysis was performed in 2016.

**Results:** The selected items were sex, dyspnea, BMI, tobacco smoking habits, age, history of respiratory diseases, and history of occupation at risk. The C-index of the model was 0.84 (95% CI=0.80, 0.88) for the development population and 0.76 (95% CI=0.66, 0.86) for the validation population. Using the selected items in combination, the sensitivity and specificity in identifying persistent airway obstruction were 76% and 77%, respectively, in the development population (and 68% and 73%, respectively, in the validation population) for a threshold value of 2.50%.

**Conclusions:** This seven-item questionnaire is the first developed from a population comprising a large subset of agricultural workers and using the Global Lung Initiative–2012 equations.

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease that has become one of the leading causes of morbidity and mortality worldwide.<sup>1</sup> Diagnosis of COPD remains challenging, and as few as 20% of those who have COPD are actually identified, whereas more than half of patients who receive a diagnosis of COPD are in fact misdiagnosed.<sup>2,3</sup>

Although tobacco smoking is the single most important causal factor for COPD,<sup>4,5</sup> occupational exposures account for 15%–20% of all COPD cases.<sup>4,6–9</sup> When combined, smoking and occupational exposures may

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have either an additive or a synergistic effect on COPD.<sup>10</sup> Some farming jobs, presumably because they expose to organic and inorganic dusts and gases, are associated with higher prevalence of COPD than jobs from the service sector (tertiary jobs).<sup>9</sup> Most of these cases however are undiagnosed,<sup>11</sup> perhaps because prevalence of tobacco smoking is lower in farmers than in subjects with tertiary jobs.<sup>12</sup>

Several approaches have been proposed to improve COPD diagnosis. Systematic COPD screening by spirometry is currently not recommended, as global costs of such an approach would outweigh individual benefits.<sup>13</sup> A radically different approach, recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), is to perform spirometry only in subjects who report at least one COPD-related symptom in addition to exposure to at least one risk factor for the disease.<sup>4</sup> This strategy displays good specificity but is more likely to identify advanced forms of COPD. A third alternative, thought to optimize the cost/effectiveness ratio, is to use a case-finding approach that consists of performing spirometry only in at-risk subjects who are identified by questionnaires.<sup>14</sup>

The performance of case-finding questionnaires depends at least partially on the characteristics of the population used for their development, and on the criteria used to define persistent airway obstruction.<sup>15</sup> Most available questionnaires were constructed with populations of ever smokers, thus neglecting the fact that COPD may develop in never smokers with occupational exposures. Furthermore, there is increasing evidence that a post-bronchodilator forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) ratio below the statistically based, age-specific lower limit of normal (LLN) is a more appropriate criterion to define persistent airway obstruction than the fixed cut-off of 0.70.<sup>16</sup> Nevertheless, most questionnaires developed for COPD case-finding currently do not use this post-bronchodilator LLN cut-off.

A screening questionnaire and its associated nomogram were therefore developed and validated for the identification of persistent airway obstruction defined by a post-bronchodilator FEV1/FVC ratio below LLN among a population comprising a large subset of agricultural workers with various tobacco exposures and occupations. The performances of different diagnostic strategies are also compared, either by case-finding with the developed questionnaire, by systematic screening, or by case-finding with the GOLD diagnosis recommendations.

## METHODS

### Study Population

Data were collected from October 2012 to May 2013 in nine departments from three different French regions (Doubs, Haute-

Saône, Jura, Territoire de Belfort, Finistère, Ille-et-Vilaine, Côtes-d'Armor, Morbihan, and Gironde) among affiliated members of the French national social security system for agricultural workers (Mutualité Sociale Agricole). During this period, 17,213 subjects aged 40–75 years were invited to attend a free health checkup, according to a procedure described elsewhere (Figure 1).<sup>9</sup>

Ethical approval was received (Comité de Protection des Personnes Est; 13-682), and written consent was obtained from all subjects.

### Measures

Spirometry was performed using a calibrated pneumotachograph, as previously described.<sup>9</sup> A bronchodilator test was proposed to all subjects with a baseline FEV1/FVC ratio <LLN, according to the Global Lung Initiative (GLI)-2012 equations.<sup>17</sup> Persistent airway obstruction was defined by a post-bronchodilator FEV1/FVC ratio <LLN, according to the GLI-2012 equations.<sup>16,17</sup> COPD was defined as the presence of persistent airway obstruction associated with at least one symptom among dyspnea, chronic cough, and chronic sputum.<sup>5</sup>

Subjects filled out self-administered questionnaires assessing respiratory symptoms (dyspnea, chronic cough, and chronic sputum); past medical history (including asthma and cardiovascular diseases); atopy; and tobacco history. These questionnaires were adapted French versions of the European Community Respiratory Health Survey.<sup>18</sup> Dyspnea was defined according to the modified Medical Research Council scale. Chronic cough was defined as usual morning cough, being woken by an attack of cough, or both during the last past year. Chronic sputum was defined as usual morning sputum, usual sputum from the chest, or both. History of respiratory disease was defined as self-reported chronic bronchitis (defined as cough and expectoration for  $\geq 3$  months of the year for at least 2 consecutive years); emphysema; bronchiectasis; chronic farmer's lung disease; tuberculosis; asthma; or any combination of these.

The smoking history included the number of cigarettes/pipe/cigars smoked per day and the dates when smoking was taken up/given up. Never smokers were defined as those having smoked on average less than one cigarette, one cigar, or one pipe a day for a year. Current smokers smoked this amount or more, and former smokers had stopped smoking at least 1 month before the time at which they filled out the questionnaire.<sup>18</sup>

Data regarding professional history included the designation of the last five jobs held by the subjects, with the start and finish dates for each job. Subjects who declared having worked in non-agricultural jobs only without any exposure were included as "not at risk." Exclusive crop farmers were considered to be "not at risk" of COPD regardless of the duration of their activity.<sup>9,19</sup> Subjects with any other farming activity <10 years in duration were also considered as "not at risk." By contrast, all subjects with an agricultural activity >10 years—with the exception of crop farmers—were labeled as "at risk."<sup>9</sup>

### Statistical Analysis

Statistical analysis was performed in 2016. The population was divided in two subsamples: two thirds were randomly selected to contribute to the questionnaire development (development population) and the remaining third was reserved for questionnaire validation (validation population). To improve the reliability of the validation population, the bootstrap method was used to create

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