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Case-finding options for COPD: results from the Burden of Obstructive Lung Disease Study

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ABSTRACT: This study aimed to compare strategies for chronic obstructive pulmonary disease (COPD) case finding using data from the Burden of Obstructive Lung Disease study.

Population-based samples of adults aged ⩾40 yrs (n=9,390) from 14 countries completed a questionnaire and spirometry. We compared the screening efficiency of differently staged algorithms that used questionnaire data and/or peak expiratory flow (PEF) data to identify persons at risk for COPD and, hence, needing confirmatory spirometry. Separate algorithms were fitted for moderate/severe COPD and for severe COPD. We estimated the cost of each algorithm in 1,000 people.

For moderate/severe COPD, use of questionnaire data alone permitted high sensitivity (97%) but required confirmatory spirometry in 80% of participants. Use of PEF necessitated confirmatory spirometry in only 19–22% of subjects, with 83–84% sensitivity. For severe COPD, use of PEF achieved 91–93% sensitivity, requiring confirmatory spirometry in <9% of participants. Cost analysis suggested that a staged screening algorithm using only PEF initially, followed by confirmatory spirometry as needed, was the most cost-effective case-finding strategy.

Our results support the use of PEF as a simple, cost-effective initial screening tool for conducting COPD case-finding in adults aged ⩾40 yrs. These findings should be validated in real-world settings such as the primary care environment.

KEYWORDS: Adult, chronic obstructive pulmonary disease, epidemiology, peak expiratory flow, questionnaire, screening

Although chronic obstructive pulmonary disease (COPD) is an important cause of morbidity and mortality worldwide and is increasing in prevalence, it is often underdiagnosed [1–4]. This underdiagnosis has important policy implications since appropriate management of COPD is known to decrease the risk of future exacerbations and hospitalisations and to improve health status, including symptoms and even exercise tolerance [5]. Increased interest has therefore been focused on the development of cost-effective strategies for case finding [3, 6].

Post-bronchodilator spirometry is the current gold standard for diagnosing COPD [7]. However, even in countries with developed health services it is not feasible to perform high-quality spirometry on all at-risk patients in the context of short office visits. Also, in many parts of the world, spirometers may simply not be available in the primary care setting, or the cost of spirometry may restrict its use. Alternative case-finding strategies for use in the primary care setting are therefore needed. A recent workshop convened by the US National Institutes of Health (National Heart, Lung, and Blood Institute Division of Lung Diseases (DLD)) concluded in its executive summary that there is an ''urgent need'' to develop and test a strategy for COPD case finding that targets those with clinically significant COPD (specifically those with a forced expiratory volume in 1 s (FEV_1) <60% predicted) [8]. The executive summary suggested that this approach would probably include some combination of initial risk assessment (*via* a questionnaire) followed by a simple measurement of peak expiratory flow (PEF) and, as appropriate, full diagnostic pre-bronchodilator (BD) and post-BD spirometry.

For editorial comments see page 503.

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Simple validated questionnaires have been developed to identify those at risk for COPD [9, 10]. Additionally, PEREZ-PADILLA *et al*. [11] have shown that a pre-BD PEF measurement can successfully identify severe and very severe COPD (Global Initiative for Chronic Obstructive Lung Disease stages III and IV) >90% of the time, and that PEF still adds considerable predictive value, even in those at high risk based on self-reported symptoms and risk factors [11].

This study uses data from the international Burden of Obstructive Lung Disease (BOLD) study [1] to extend this earlier work by comparing the performance and cost effectiveness of a variety of algorithms for detecting moderate/severe and severe COPD. Our findings may be of use in informing the selection of case-finding methods in different countries.

METHODS

BOLD is an ongoing, international study of the prevalence and burden of COPD. It was approved by the relevant local ethics committees of each participating site, and all participants provided written informed consent. A description of the BOLD study's design and standardised methods has been published elsewhere [12].

We report data from 14 BOLD sites comprising 10,712 participants aged ⩾40 yrs. From this group, we excluded 711 (6.6%) due to poor-quality spirometry and 611 (5.7%) due to missing data, leaving a total of 9,390 individuals for the final analysis.

Questionnaire data were collected through face-to-face interviews in participants' native languages. The BOLD questionnaire included data about respiratory health and symptoms, comorbidities and risk factors for COPD, and includes sections taken from the 1978 American Thoracic Society (ATS)/DLD Respiratory Symptom Questionnaire [13] as well as the questionnaires used in the European Community Respiratory Health Study [14], the Italian National Research Council study [15] and the Obstructive Lung Disease in Northern Sweden study [16].

Spirometry was performed using the ndd EasyOne Spirometer (ndd Medical Technologies, Andover, MA, USA) before and 15 min after administration of 200 μg albuterol/salbutamol *via* a spacer. We used 200 μg rather than 400 μg primarily for reasons of safety, since not all testing was performed in the clinic setting and a physician was not always present. Spirometry data were reviewed centrally and assigned a quality score based on ATS/European Respiratory Society 2005 acceptability and repeatability criteria [17, 18].

Spirometry outcomes included FEV_1, forced vital capacity (FVC) and PEF. All were defined as the maximum value from the best three acceptable manoeuvres. We used post-BD measurements of FEV_1 and FVC to define COPD. To control for their association with height, PEF measurements were divided by height squared (Ht^2) and are expressed in units of $L \cdot s^{-1} \cdot m^{-2}$.

Although international guidelines define COPD on the basis of a post-BD FEV_1/FVC <0.70, this measure is known to vary with age [19, 20]. For this analysis we defined moderate/severe COPD as post-BD FEV_1/FVC below the lower limit of normal (LLN) and FEV_1 <80% pred; and severe COPD as post-BD FEV_1/FVC <LLN and FEV_1 <60% pred because this is the level at which COPD is considered clinically significant [21]. We used the prediction equations for Caucasian males and females derived from the third US National Health and Nutrition Examination Survey (NHANES) III to calculate the LLN and the FEV_1 % pred [22].

Statistical methods

We randomly divided each site's population into separate test and validation samples using a 7:3 ratio. We then conducted initial model building using the test sample and validated the prediction results using the validation sample. Only validation sample results are presented here.

For both moderate/severe COPD and severe COPD, we developed case identification algorithms using questionnaire data alone, questionnaire data plus pre-BD PEF data, and questionnaire data plus both pre- and post-BD PEF data. In each case we used classification and regression tree (CART) analysis to arrive at a best-fitting model [23]. CART uses a successive splitting algorithm in which it considers, at each stage, all possible dichotomisations of each predictor variable and finds the one that best separates individuals with the identified outcome from those without the outcome. This process is then independently repeated for each of the new branches of the tree, stopping when the degree of separation between subsequent branches does not pass a user-defined threshold. We ''pruned'' the tree structures so as to maximise both sensitivity and specificity, since one of the purposes of the case-finding method is to reduce the number of spirometry tests that would be needed while still maximising overall case detection. We strove for parsimonious models that could be easily described and implemented in the clinical setting.

We also fitted a staged model to reflect the potential clinical scenario in which pre-BD PEF testing would only be conducted on patients at *a priori* ''high risk'' based on symptoms and risk factor profile, and post-BD PEF would only be performed on the subset that was still at high risk, based on the pre-BD PEF results. For these analyses we adopted the approach used by PEREZ-PADILLA *et al.* [11] and defined an *a priori* high-risk group as anyone who met any of the following criteria: ''usual'' cough/phlegm; wheeze in the last year; dyspnoea on exertion (Medical Research Council (MRC) score >1); >10 pack-yrs of smoking; >200 h-yrs of exposure to biomass smoke (1 h-yr exposure = exposed for 1 h per day for 1 yr); >5 yrs occupational dust/smoke exposure; or a previous medical diagnosis of COPD, emphysema, chronic bronchitis or asthma. In these models, the CART methodology was used only to define the PEF cut-offs.

To simplify interpretation of our models, in all of the above analyses we grouped continuous variables into categorical variables as follows: age (40–49, 50–59, 60–69 and ⩾70 yrs); body mass index (⩽20, 20–25, 25–30 and >30 $kg \cdot m^{-2}$); years smoked (never-smoker and 0–10, 10–20 and >20 yrs); and PEF per Ht^2 (⩽1.3, >1.3–1.8, >1.8–2.2, >2.2 $L \cdot s^{-1} \cdot m^{-2}$).

In order to assess the extent to which our final models gave consistent results across the various sites, we fitted logistic regression models to the full cohort (test and validation samples combined), with indicators for risk status (high *versus* low), study site and a site-by-risk status interaction. CART models were constructed using SPSS Answer Tree 3.0 (Aspire Software,

Ashburn, VA, USA) and all other analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC, USA).

Finally, we conducted a cost analysis to calculate the comparative costs of each of the three different case-finding scenarios and the costs of missed cases in each scenario. First, we assumed that all three tests (PEF, questionnaire and spirometry) could be undertaken by staff of a similar grade. Secondly, we estimated the time for undertaking and recording the test as 10 min for the PEF or the questionnaire and 40 min for the pre- and post-BD spirometry. We fixed the costs at one unit of cost each for questionnaires and PEF, and four units of cost for spirometry. We ignored capital and consumable costs as probably being relatively small in most places and ignored the time commitment of the patients. By adding the time taken for the tests in each strategy, we could estimate the cost in time units for each strategy. This gave us a cost for each strategy, a cost per case identified, and a marginal cost of identifying further cases if a more sensitive strategy was followed.

RESULTS

Of the 9,390 individuals, 756 (8.1%) met the criteria for moderate/severe COPD (532 in the test sample and 224 in the validation sample). Mean age was 56.1 yrs, 52% were females, 37% reported having ever worked in a dusty job and 57% reported having ever smoked (table 1). Male ever-smokers had greater exposure to cigarette smoke than did female ever-smokers (26.6 *versus* 19.3 pack-yrs; $p<0.0001$). 12% of the cohort reported MRC dyspnoea scores of $\geqslant 2$, and 7.4% reported a doctor diagnosis of chronic bronchitis, emphysema or COPD. While the prevalence of doctor diagnosis of chronic bronchitis, emphysema or COPD increased with increasing COPD severity, only 19% of those with moderate COPD and 38% of those with severe COPD reported having this diagnosis. More than two-thirds of those reporting one of these diagnoses were in the ''no or mild'' COPD group.

Models for predicting moderate/severe COPD

Using questionnaire data only, the general CART modelling identified a high-risk subgroup comprising 55% of the sample and consisting of individuals who had ever been told they had COPD/emphysema or else were long-term smokers ($\geqslant$20 pack-yrs) or reported any dyspnoea (table 2). These people had a 12.6% risk (positive predictive value (PPV)) of having moderate/severe COPD. The remaining low-risk group comprised 45% of the sample and had only a 2.2% probability of having moderate/severe COPD. This classification rule identified 87.5% of the cases (sensitivity). The much broader *a priori* high-risk classification yielded a much better sensitivity (97.3%), but at the cost of a lower PPV (7.3%) and a much larger high-risk group (80% of the sample) requiring confirmatory spirometry.

When pre-BD PEF was also available, both the staged and unstaged models identified high-risk groups comprising only ~20% of the population, but still with reasonably high sensitivity (~83%) and much better PPVs (31–37%). The unstaged model used only PEF because CART did not select any of the risk factors from the questionnaire, and hence had slightly higher sensitivity than the corresponding staged model. For both the staged and unstaged models, the additional inclusion of post-BD PEF data in the pool of predictors did not change the prediction model.

Models for predicting severe COPD

Table 3 summarises the models for predicting severe COPD. Using the *a priori* ''high-risk'' cohort and ignoring PEF yielded excellent sensitivity (98%) for identifying cases of severe COPD, but had very low PPV and resulted in a very large ''high-risk'' group (74% of the sample) requiring confirmatory spirometry. By contrast, including the PEF measurements resulted in sensitivities of 91–93% while reducing the need for confirmatory spirometry to only 8–9% of the sample, a distinct improvement on the results obtained for moderate/severe COPD and in marked contrast to the results obtained using questionnaire data alone. Use of post-BD PEF measurements did further improve prediction in the unstaged model, but only very marginally.

Logistic regression models using the full cohort did not show evidence of significant differences in risk factor effects between sites.

Economic implications of different case-finding algorithms

Table 4 shows the relative costs of five different strategies of case finding. Costs were measured in units of 10 min of technician time. In Algorithm 1, the whole population of 1,000 participants would be tested directly with spirometry, which resulted in 1,000 spirometry tests at four ''cost units'', which gave a total cost of 4,000 units. This method identified all 80 cases of moderate/severe COPD at a cost of 50 units per case.

In Algorithm 2, the CART questions were used to screen for high-risk individuals, who then proceeded directly to spirometry; 1,000 questionnaires would be administered at a cost of 1,000 units and 554 positives referred for spirometry at a cost of 2,216 units, giving a total cost of 3,216 units for the programme. In this algorithm, 70 cases were identified, giving a cost per case identified of 45.9 units.

In Algorithm 3 the *a priori* questions alone were used, so 1,000 questionnaires and 802 spirometry tests would be administered with total cost of 4,208 units, and 53.9 units per case. This was actually more costly than performing spirometry on everyone.

In Algorithm 4, peak flow alone was used, with 1,000 peak flow measurements with a total cost of 1,000 units, and only 218 participants would be referred for spirometry at a cost of 872 units. The total cost would be 1,872 units. Slightly fewer cases were identified (67 out of the 80 possible), but the cost per case identified was still much lower at 27.9 units.

Algorithm 5 shows the staged screening using the *a priori* questionnaire; 1,000 questionnaires followed by 802 peak flows and 178 spirometry tests at a total cost of 2,514 units. This approach identified one fewer case than the peak flow-only model and at the same time cost 37% more (38.1 *versus* 27.9 units) per case identified. The results were qualitatively similar when applied to identification of severe COPD.

DISCUSSION

Case finding for COPD is becoming an important global health issue as healthcare systems gear up to tackle high-burden noncommunicable diseases such as COPD [6]. Our findings

TABLE 1 Characteristics of the sample

	COPD status			Total[+]	p-value[§]
	Absent/mild	Moderate[#]	Severe[¶]		
Subjects	8634	425	331	9390	
Age yrs	55.6±11.1	61.1±11.7	62.4±11.8	56.1±11.3	0.0001
Female	4547 (52.7)	192 (45.2)	169 (51.1)	4908 (52.3)	0.0095
Ever worked in dusty job	3132 (36.3)	184 (43.3)	173 (52.3)	3489 (37.2)	0.0001
Doctor-diagnosed COPD[ƒ]	490 (5.7)	81 (19.1)	127 (38.4)	698 (7.4)	0.0001
Doctor-diagnosed asthma[##]	935 (10.8)	100 (23.5)	116 (35.0)	1151 (12.3)	0.0001
Doctor-diagnosed TB	282 (3.3)	33 (7.8)	53 (16.0)	368 (3.9)	0.0001
Pre-BD PEF per Ht^2 L·s^{-1}·m^{-2}					0.0001
⩽1.3	47 (0.5)	39 (9.2)	196 (59.2)	282 (3.0)	
>1.3–1.8	352 (4.1)	139 (32.7)	108 (32.7)	599 (6.4)	
>1.8–2.2	1000 (11.6)	131 (30.8)	21 (6.3)	1152 (12.3)	
>2.2	7235 (83.8)	116 (27.3)	6 (1.8)	7357 (78.3)	
Smoking history					0.0001
Never	3873 (44.9)	96 (22.6)	54 (16.3)	4023 (42.8)	
0–10 pack-yrs	612 (7.1)	9 (2.1)	6 (1.8)	627 (6.7)	
10–20 pack-yrs	848 (9.8)	20 (4.7)	15 (4.5)	883 (9.4)	
>20 pack-yrs	3301 (38.2)	300 (70.6)	256 (77.3)	3857 (41.1)	
Biomass exposure h-yrs[¶¶]	16.9±56.2	16.7±52.9	26.1±61.4	17.3±56.3	0.0034
Cough/phlegm in last yr	967 (11.2)	88 (20.7)	118 (35.7)	1173 (12.5)	<0.0001
Wheeze in last yr	1843 (21.4)	194 (45.7)	192 (58.0)	2229 (23.7)	<0.0001
MRC dyspnoea score					0.0001
0	5964 (75.8)	192 (52.0)	86 (31.0)	6242 (73.3)	
1	1077 (13.7)	84 (22.8)	53 (19.1)	1214 (14.2)	
2	316 (4.0)	40 (10.8)	31 (11.2)	387 (4.5)	
⩾3	515 (6.5)	53 (14.4)	107 (38.6)	675 (7.9)	

Data are presented as n, mean±SD or n (%), unless otherwise stated. COPD: chronic obstructive pulmonary disease; TB: tuberculosis; BD: bronchodilator; PEF: peak expiratory flow; Ht: height; MRC: Medical Research Council. [#]: post-BD forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) below the lower limit of normal (LLN) and FEV_1 <80% predicted. [¶]: post-BD FEV_1/FVC<LLN and FEV_1 <60% predicted. [+]: sites included Guangzhou, China; Adana, Turkey; Salzburg, Austria; Reykjavik, Iceland; Cape Town, South Africa; Krakow, Poland; Hannover, Germany; Bergen, Norway; Vancouver, Canada; Manila, Philippines; Lexington, KY, USA; Sydney, Australia; London, UK; Uppsala, Sweden. [§]: two-tailed p-value based on Pearson's Chi-squared test for categorical data or t-test for continuous data. [ƒ]: patient ever told by a healthcare provider that they have chronic bronchitis, emphysema or COPD. [##]: patient ever told by a healthcare provider that they have asthma, asthmatic bronchitis or allergic bronchitis. [¶¶]: highly skewed, so p-value is based on transformed biomass exposure variable.

show that use of a simple pre-BD peak flow measurement has the potential to serve as a cost-effective way to screen for those individuals most likely to benefit from confirmatory spirometry. Use of a screening questionnaire, either alone or in combination with peak flow measurement, appears to increase the costs of screening for COPD and may reduce the number of cases ultimately identified.

Our results build on previous work by PEREZ-PADILLA *et al*. [11], showing that a simple pre-BD PEF measurement could be used to rule out severe COPD, by addressing the epidemiological question of what might be an optimal COPD screening algorithm. We also conducted an economic analysis, albeit a crude one, comparing the cost implications of various case-finding algorithms.

We focused on the detection of moderate/severe COPD, since the clinical management of those with milder disease primarily consists of smoking cessation, which should be offered to all smokers. No evidence exists to support the cost effectiveness of more aggressive management, including treatment with pharmacotherapy, in those with milder disease if they are asymptomatic [24–26]. The biggest escalation in costs for COPD-related morbidity and mortality occurs primarily in those with severe disease. A growing body of evidence suggests that appropriate management of these individuals can improve quality of life, reduce exacerbations [5], possibly reduce decline in FEV_1 [27, 28] and also reduce the burden on family/caregivers and decrease demands on public resources related to hospitalisation costs [29]. Our definition of moderate/severe disease is intended to overcome the limitations of the fixed ratio criterion [20], and is consistent with that suggested by a recent clinical efficacy assessment study [21].

Although post-BD spirometry is the current gold standard for diagnosing and staging COPD, the cost of performing spirometry on all individuals with risk factors for COPD (the majority of the population in some countries) makes this an inefficient tool for population-based case finding. The challenge is to develop a screening algorithm that efficiently rules out moderate/severe COPD in a large number of individuals

TABLE 2 Summary of models for detecting moderate/severe chronic obstructive pulmonary disease (COPD): validation sample

Prediction variables used in model	Definition of group	Population %	Cases %#	Risk
General (unstaged) CART modelling				
Questionnaire data only				
High risk	Reports doctor-diagnosed COPD/emphysema or any dyspnoea or smoking ⩾20 pack-yrs	55.4	87.5	12.6
Low risk	Everyone else	44.6	12.5	2.2
Pre-BD peak flow and questionnaire data				
High risk	PEF per Ht^2 ⩽2.2 $L \cdot s^{-1} \cdot m^{-2}$	21.8	83.9	30.7
Low risk	PEF per Ht^2 >2.2 $L \cdot s^{-1} \cdot m^{-2}$	78.2	16.1	1.6
Pre- and post-BD peak flow and questionnaire data				
High risk	Pre-BD PEF per Ht^2 ⩽2.2 $L \cdot s^{-1} \cdot m^{-2}$	21.8	83.9	30.7
Low risk	Pre-BD PEF per Ht^2 >2.2 $L \cdot s^{-1} \cdot m^{-2}$	78.2	16.1	1.6
Staged screening models				
Questionnaire data only				
High risk	*A priori* ''high risk''	80.2	97.3	7.3
Low risk	*A priori* ''low risk''	19.8	2.7	0.8
Pre-BD peak flow and questionnaire data				
High risk	*A priori* ''high risk'' and PEF per Ht^2 ⩽2.2 $L \cdot s^{-1} \cdot m^{-2}$	17.8	82.6	36.9
Low risk	*A priori* ''low risk'' or PEF per Ht^2 >2.2 $L \cdot s^{-1} \cdot m^{-2}$	82.2	17.4	1.7
Pre and post-BD peak flow and questionnaire data				
High	*A priori* ''high risk'' and pre-BD PEF per Ht^2 ⩽2.2 $L \cdot s^{-1} \cdot m^{-2}$	17.8	82.6	36.9
Low	*A priori* low risk or pre-BD PEFper Ht^2 >2.2 $L \cdot s^{-1} \cdot m^{-2}$	82.2	17.4	1.7

Data for risk are presented as positive predictive value. CART: classification and regression tree; BD: bronchodilator; PEF: peak expiratory flow; Ht: height. #: sensitivity.

while retaining high sensitivity. Such an algorithm would require confirmatory spirometry for only the segment of the population at highest risk. Our analysis is intended to guide the selection of such an algorithm.

Even though many of the case-finding algorithms currently being proposed suggest a staged screening approach in which peak flow measurement is only performed in symptomatic or high-risk individuals, our findings suggest that such an approach, while more cost-effective than performing spirometry on everyone, is actually less efficient than simply measuring PEF in everyone. In the context of a healthcare delivery system, this would suggest use of PEF as a standard vital sign much like blood pressure and weight, without completion of an accompanying questionnaire. Because lung function impairment generally occurs at a gradual pace, such a measurement might only need to be carried out every few years as a further cost saving. Asking about prior exposure history is valuable from a clinical perspective, but from a purely screening perspective it is less efficient and may lead to greater costs and fewer identified cases. Given that PEF per Ht^2 is highly correlated with the FEV1/FVC ratio, and the variable level of correlation between symptoms and severity of COPD, it is perhaps not too surprising that a simple measure involving only PEF provided our best screening algorithm.

A potential criticism of a case-finding algorithm for severe COPD is that the individuals who are identified would all already have the diagnosis. However, the facts suggest otherwise. Our own data show that, even among individuals meeting our criteria for severe COPD, only 38% report a doctor diagnosis of chronic bronchitis, emphysema or COPD. Furthermore, in the USA, only 25% of patients with a diagnosis of COPD in their medical records have ever had a spirometry test [30] and we suspect this percentage is even lower in low- and middle-income countries. Therefore, there is certainly plenty of opportunity to uncover new cases of previously undiagnosed and/or not spirometrically confirmed COPD that are clinically significant. Conversely, 6% of individuals with no or mild COPD report a doctor diagnosis of chronic bronchitis, emphysema or COPD and may benefit from confirmatory spirometry to address a possible misdiagnosis. We believe these observations support the need for COPD case finding for both adult smokers lacking the diagnosis and for patients with the diagnosis but who have never had spirometry.

A strength of our study is that it was based on population samples from 14 different sites around the world and was not restricted only to smokers. This latter point is of particular importance since occupational and biomass exposures are increasingly being recognised as important potential risk factors for COPD [31]. Additionally, our split-sample analysis enabled us to independently validate the results of our prediction models.

An important limitation of the study is that PEF measurements were taken during a forced expiratory manoeuvre using an

TABLE 3 Summary of models for detecting severe chronic obstructive pulmonary disease (COPD): validation sample

Prediction variables used in the model	Definition of group	Population %	Cases# %	Risk
General (unstaged) CART modelling				
Questionnaire data only				
High risk	Patient reports doctor-diagnosed COPD/emphysema or dyspnoea ⩾grade 3 or BMI <20 kg·m^{-2} or wheeze with shortness of breath	19.6	70.0	11.4
Low risk	Everyone else	80.4	30.0	1.2
Pre-BD peak flow and questionnaire data				
High	PEF per Ht^2 ⩽1.8 L·s^{-1}·m^{-2}	9.0	93.3	33.3
Low	PEF per Ht^2 >1.8 L·s^{-1}·m^{-2}	91.0	6.7	0.2
Pre- and post-BD peak flow and questionnaire data				
High	Pre-BD PEF per Ht^2 ⩽1.3 L·s^{-1}·m^{-2} or post-BD PEF per Ht^2 ⩽1.8 L·s^{-1}·m^{-2}	7.5	92.2	39.3
Low	Pre-BD PEF per Ht^2 >1.3 L·s^{-1}·m^{-2} and post-BD PEF per Ht^2 >1.8 L·s^{-1}·m^{-2}	92.5	7.8	0.3
Staged screening models				
Questionnaire data only				
High risk	Symptomatic	73.8	97.8	4.2
Low risk	Asymptomatic	26.2	2.2	0.3
Pre-BD peak flow and questionnaire data				
High risk	Symptomatic and PEF per Ht^2 ⩽1.8 L·s^{-1}·m^{-2}	8.1	91.1	36.0
Low risk	Asymptomatic or PEF per Ht^2 >1.8 L·s^{-1}·m^{-2}	91.9	8.9	0.3
Pre- and post-BD peak flow and questionnaire data				
High risk	Symptomatic and pre-BD PEF per Ht^2 ⩽1.8 L·s^{-1}·m^{-2}	8.1	91.1	36.0
Low risk	Asymptomatic or pre-BD PEF per Ht^2 >1.8 L·s^{-1}·m^{-2}	91.9	8.9	0.3

Data for risk are presented as positive predictive value. CART: classification and regression tree; BD: bronchodilator; BMI: body mass index; PEF: peak expiratory flow; Ht: height. #: sensitivity.

electronic spirometer. In addition, the measurements were conducted as part of a formal research study that required standardised methods across participating sites and strict attention to quality control. As a consequence, the predictive value and sensitivity of the PEF-based algorithms developed here might be better than might be expected if using ordinary peak flow meters in clinic settings or as a part of general community-based screening programmes [32, 33]. However, a recent study found results similar to ours in health screening settings other than medical offices [34]. Additionally, our economic analysis considered only one set of costing assumptions and assumed these held in a uniform manner across the countries and settings undertaking the screening. Nonetheless, we did not find evidence of significant differences in risk factor effects between sites. A final limitation is that our gold standard for defining COPD is based only on spirometry. We recognise that in clinical practice the diagnosis should also be based on signs and symptoms and a relevant exposure history [7], but for the purposes of a screening programme, spirometry is a logical first step that might then trigger a more detailed clinical consultation.

Although there is as yet no cure for COPD, we can reduce symptoms and exacerbations, improve quality of life and provide supportive management. This paper strongly suggests that focused case finding using a simple peak flow assessment would best help us to identify those who would benefit most from spirometry and justify the resources used. Many national and international groups have been considering the issue of how best to screen for COPD, and our results provide valuable information for recommendations that are currently being considered. Nonetheless, further studies need to be performed to see to what extent our findings hold up when peak flow measurements are done in primary care settings by clinic staff and using peak flow meters in place of spirometers and without the rigorous quality control that was a part of the BOLD protocol. In this regard, we view the current study as an important first step that highlights the potential usefulness of such a screening programme.

SUPPORT STATEMENT

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TABLE 4 Financial implications of the three testing schedules based on 1,000 patients being selected for testing

	Tests performed			Cost resource units[#]				Cases identified	Cases missed	Cost/case identified	Marginal cost per case identified relative to base
	Questionnaires	PEFs	Spirometries	Questionnaires	PEFs	Spirometries	Total cost				
Moderate/severe											
1. Spirometry only			1000	0	0	4000	4000	80	0	50.0	163.7
2. CART questions only	1000	0	554	1000	0	2216	3216	70	10	45.9	448.0
3. *A priori* questions only	1000	0	802	1000	0	3208	4208	78	2	53.9	212.4
4. PEF only	0	1000	218	0	1000	872	1872	67	13	27.9	
5. Staged: *a priori* questions, then PEF in subgroup	1000	802	178	1000	802	712	2514	66	14	38.1	-642.0[¶]
Severe											
1. Spirometry only			1000	0	0	4000	4000	35	0	114.3	1320.0
2. CART questions only	1000	0	196	1000	0	784	1784	25	10	71.4	-53.0[¶]
3. *A priori* questions only	1000	0	738	1000	0	2952	3952	34	1	116.2	2592.0
4. PEF only	0	1000	90	0	1000	360	1360	33	2	41.2	
5. Staged: *a priori* questions, then PEF in subgroup	1000	738	81	1000	738	324	2062	32	3	64.4	-702.0[¶]

Data are presented as n. PEF: peak expiratory flow; CART: classification and regression tree. [#]: resource unit = 10 min of nurse/technician time; [¶]: marginal costs per case are negative for algorithms that identify fewer cases than PEF only.

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STATEMENT OF INTEREST

Statement of interest for A. Jithoo, P.L. Enright, P. Burney, A.S. Buist, W.C. Tan, M. Studnicka and W.M. Vollmer, and for the study itself can be found at www.erj.ersjournals.com/site/misc/statements.xhtml

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