Prim Care Respir J 2011; **20**(2): 190-198

Primary Care RESPIRATORY JOURNAL
www.thepcrj.org

ORIGINAL RESEARCH

Simplified COPD screening: validation of the PiKo-6® in primary care

***Peter Frith[a], Alan Crockett[b], Justin Beilby[c], David Marshall[d], Robyn Attewell[e], Avnesh Ratnanesan[f], Guy Gavagna[d]**

[a] Southern Respiratory Services, Repatriation General Hospital, Adelaide, South Australia
[b] Primary Care Respiratory Research Unit, School of Population Health & Clinical Practice, The University of Adelaide, South Australia
[c] Department of Health Sciences, University of Adelaide, South Australia
[d] Boehringer Ingelheim Pty Limited, North Ryde, New South Wales, Australia
[e] Covance Pty Limited, Braddon, Australian Capital Territory, Australia
[f] Pfizer Australia, West Ryde, New South Wales, Australia

Received 3rd February 2011; revised 17th March 2011; accepted 25th March 2011; online 20th May 2011

Abstract

Aims: To determine the accuracy of the forced expiratory volume ratio at one and six seconds (FEV_1/FEV_6) using a hand-held, expiratory flow meter (PiKo-6®, nSpire Health, Inc.) to screen for chronic obstructive pulmonary disease (COPD) in primary care settings.

Methods: Current and former smokers (≥ 50 years old) with no previous respiratory diagnosis (case finding [CF] = 204 subjects) or with an asthma diagnosis (differential diagnosis [DD] = 93 subjects) were evaluated using validated questionnaires, pre-bronchodilator (BD) FEV_1/FEV_6 and post-BD FEV_1/forced vital capacity (FVC) spirometry.

Results: The PiKo-6® FEV_1/FEV_6 showed good sensitivity and specificity (areas under the Receiver Operating Characteristic curves [95% confidence intervals]: CF = 0.85 [0.79, 0.90]; DD = 0.88 [0.80, 0.96]) and exceeded the accuracy of the questionnaires. An FEV_1/FEV_6 cut-off < 0.75 provided optimal sensitivity (CF = 81%; DD = 86%) and specificity (CF = 71%; DD = 67%) for COPD screening.

Conclusions: The PiKo-6® allows simple and reliable screening for COPD which could optimise early referral for spirometry and early, targeted interventions for COPD.

P Frith *et al*. *Prim Care Respir J* 2011; **20**(2): 190-198
doi: 10.4104/pcrj.2011.00040

Keywords COPD, primary care, spirometry, diagnostic questionnaire, early diagnosis, PiKo-6® mini-spirometer

See linked editorial by Kotz and van Schayck on pg 113

The full version of this paper, with online Appendix, is available at www.thepcrj.org

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of mortality worldwide,[1,2] yet is typically not diagnosed until its advanced stages, causing a considerable burden to patients and health care resources.[3] Early case identification may enable better use of effective management interventions and hence a reduced disease burden.[4] However, it is accepted that the onset of COPD is insidious, leading to under-diagnosis and misdiagnosis.[5-12]

There have been calls for greater awareness of COPD among primary care practitioners so that diagnosis is not delayed and patients can receive early and appropriate interventions.[13] Among the tools currently available to primary care practitioners, spirometry is recognised as the 'gold standard' diagnostic test to demonstrate fixed airway obstruction.[14,15] However, spirometry is underutilised in clinical practice[16,17] as many practitioners do not own a spirometer, undergo little training, or lack confidence in its use or in the interpretation of results.[18-21] Symptom-based questionnaires may help practitioners identify individuals with

*** Corresponding author:** Professor Peter Frith, Respiratory Allergy & Sleep Services, Adelaide Health Service, Southern Area, Repatriation General Hospital, Daw Park, Adelaide, South Australia 5041 Australia. Tel: +61 8 82751738 E-mail: Peter.Frith@health.sa.gov.au

COPD in at-risk populations.[22] However, the time required to conduct and analyse these questionnaires[23] may limit their usefulness in a busy primary care practice. Therefore, in contrast to the diagnosis of hypertension, simple and reliable tools have not been readily available for primary care practitioners to diagnose COPD during routine surgery visits.

In this study we sought to develop a simple yet reliable and practical solution to COPD screening within the busy workload in primary care. We projected that if our aims were realised, such an approach would achieve greater implementation than traditional spirometry initiatives. Forced expiratory volume at six seconds of exhalation (FEV_6) is emerging as a valid alternative to forced vital capacity (FVC) for detection of COPD.[24-27] Simple hand-held expiratory flow meters such as the PiKo-6® (nSpire Health, Inc. Longmont, CO, USA [formerly Ferraris Respiratory; Louisville, CO, USA]), that measure FEV at one and six seconds of exhalation as well as the FEV_1/FEV_6 ratio, potentially provide a practical method for early screening for COPD in at-risk patient populations.[26] The current study examined the diagnostic accuracy of FEV_1/FEV_6 using the PiKo-6® compared with post-bronchodilator (BD) FEV_1/FVC spirometry conducted by trained operators using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometry COPD criteria[14] in at-risk patients in a primary care setting. In addition, the diagnostic accuracy of the PiKo-6® was compared with symptom-based COPD diagnostic questionnaires that have been validated in primary care settings.[22,23,28]

Methods

Study design

This prospective, multicentre validation study was conducted between August and December 2006, was approved by the Royal Australian College of General Practitioners National Research and Evaluation Ethics Committee, and was undertaken in accordance with the Declaration of Helsinki and Australian regulatory requirements. Subjects were recruited from four Australian primary care practices during routine practice visits, by invitation to prescheduled study days, or through a local newspaper advertisement (one site). Two screening tests (FEV_1/FEV_6 measured using the PiKo-6® and one of two diagnostic questionnaires) were compared with the GOLD reference criteria for COPD, based on post-BD spirometry.[14]

Study groups

Subjects were grouped into a case finding (CF) or a differential diagnosis (DD) group. Case finding group inclusion criteria were current or former smokers aged ≥ 50 years, no previous diagnosis of obstructive lung disease (including COPD, chronic bronchitis, emphysema and/or asthma), and no treatment for obstructive lung disease in the past year. Differential diagnosis group inclusion criteria were current and former smokers aged ≥ 50 years, a previous diagnosis of or treatment for asthma, and no previous diagnosis of COPD. Treatment for obstructive lung disease or asthma included use of inhaled or oral bronchodilators, corticosteroids, theophyllines or leukotriene inhibitors in the past year.

Exclusion criteria for both groups were refusal or inability to give consent, pre-existing or concomitant non-obstructive lung disease, symptoms suggestive of unstable heart disease, and contraindications to spirometry.

Study procedures

All tests were undertaken in a primary care setting and, with the exception of three subjects, were conducted on the same day. The test sequence comprised

(i) a COPD diagnostic questionnaire

(ii) measurement of pre-BD FEV_1/FEV_6 using the PiKo-6®, and

(iii) pre- and post-BD spirometry.

Adverse events were reported at each visit.

Questionnaires

The COPD Diagnosis Questionnaire (CDQ) and the Differential Diagnosis Questionnaire (DDQ) were administered to the CF group and DD group, respectively (see Appendix 1, available at www.thepcrj.org). Development of these questionnaires for use in primary practice has been described previously.[22,23,28]

Hand-held expiratory flow meter (PiKo-6®)

FEV_1, FEV_6 and the calculated ratio were measured to two decimal places. Each study nurse or general practitioner (GP) was given uniform, brief training on how to use the device according to the manufacturer's instructions. Subjects were required to inhale maximally, and then exhale as hard as possible into the mouthpiece for at least six seconds until an end-of-blow beep was heard. At least three reproducible measurements (FEV_1 within 0.2 L) were taken. The measurement of acceptable quality with the highest summed value ($FEV_1 + FEV_6$) was used.

Spirometry

Spirometry testing with bronchodilator reversibility was performed independently by trained operators according to American Thoracic Society / European Respiratory Society guidelines.[29] All study sites used the same model of spirometer (EasyOne®; ndd Medical Technologies, Andover, MA, USA). Spirometers were calibrated before each day's testing and were cross-calibrated across all sites at the beginning and end of the study. Operators were blinded to the questionnaire and PiKo-6® results. Lung function parameters were measured before, and 20 minutes after, administration of a bronchodilator (360 mcg salbutamol: a total of four inhalations of 90 mcg salbutamol, at two inhalations five minutes apart). At least three adequate baseline and post-BD FVC manoeuvres were performed, with the measurement of acceptable quality and highest summed value (FEV_1 + FVC) used. Subjects in the DD group were not asked to withhold any respiratory medications (including

corticosteroids or bronchodilators) before spirometry. Spirometry quality was monitored by one respiratory physiologist blinded to the questionnaire and PiKo-6® results.

Study diagnosis of COPD was based on GOLD[14] spirometry criteria. The reference criterion for COPD was a post-BD FEV_1/FVC of < 0.70, which is consistent with the diagnosis used during development and validation of the COPD diagnostic questionnaires[22,28] and with reversibility ≤ 200 mL and ≤ 12% from baseline pre-BD FEV_1. The post-BD FEV_1 percentage of predicted values was calculated[30] and the severity of COPD classified according to GOLD definitions.

Analysis

The sample size was chosen to yield a precision (width of 95% confidence interval [CI]) between ± 5% and ± 18% for the standard validation statistics. A small intra-cluster correlation was assumed (0.05) to account for multiple subjects per GP. Assuming a dropout rate of 15%, a sample size of 300 subjects was chosen to yield 255 subjects (165 in CF; 90 in DD). The underlying prevalence of undiagnosed COPD in each group (18% for CF; 50% for DD) was based on age-scaled Australian data (R. Attewell; unpublished data). Spirometry data were checked at 50% enrolment to confirm the prevalence of COPD in each group; no interim analyses of the device data or COPD diagnostic questionnaires were undertaken.

Questionnaires were scored by the study programmer at the completion of the trial according to the standard scoring algorithms. For each questionnaire, subjects were classified on their summed score into one of three categories (increased, intermediate or decreased likelihood of airways obstruction).[23]

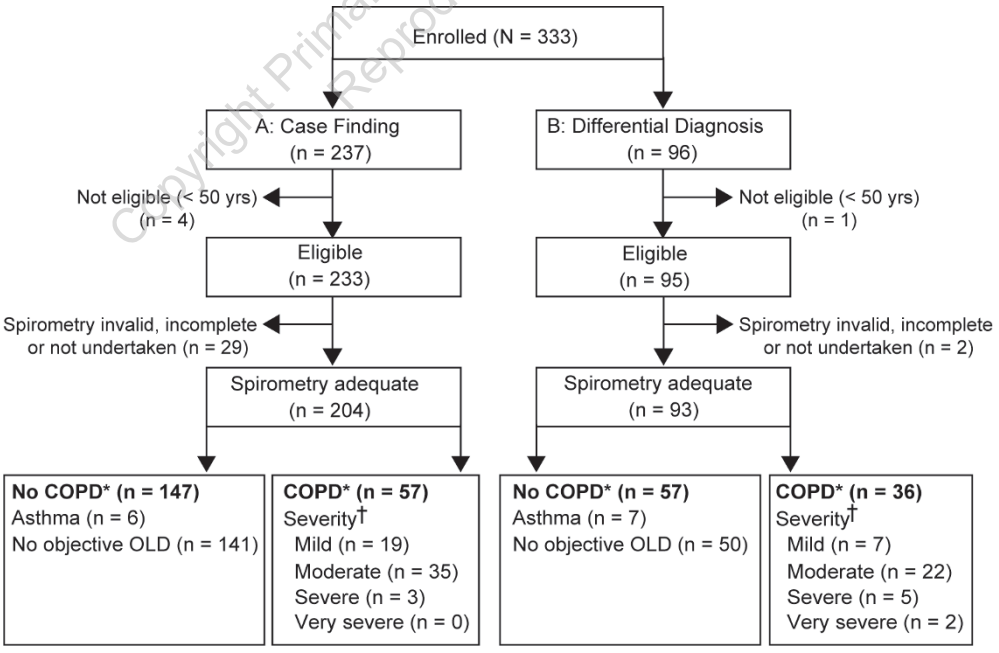
Diagnostic accuracies of the PiKo-6® FEV_1/FEV_6 and COPD diagnostic questionnaires were summarised by calculating the area under the receiver operating characteristic (ROC) curve (ROCAUC; *roctab* procedure; STATA v9, StataCorp, TX, USA) and the kappa statistic for agreement between classifications. Standard validation measures, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratio (for a positive test), were calculated at predefined cut-off points for the COPD diagnostic questionnaires[23] and at FEV_1/FEV_6 ratios of < 0.66, < 0.70, < 0.75 and < 0.80 for device measurements. Calculations were undertaken with and without adjustment for clustering by each centre using the Generalised Estimating Equation approach (STATA v9). A comparison of pre-BD FEV_1/FEV_6 measured using the device and spirometer was conducted using a two-sided, paired t-test. Differences were considered statistically significant at $P < 0.05$.

Results

Study groups

A total of 333 subjects were enrolled (see Figure 1). Following early review of spirometry, one site was closed because of poor

Figure 1. Disposition of subjects from enrolment through to analysis for the (A) Case Finding and (B) Differential Diagnosis groups.



*COPD defined by a post-BD FEV_1/FVC <0.7.[14] †Severity of COPD was based on post-BD FEV_1 percentage of predicted values.[14]
BD: bronchodilator; COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; OLD: obstructive lung disease.

Table 1. Baseline and clinical characteristics of subjects enrolled in Case Finding and Differential Diagnosis groups.

Characteristic	Case Finding (n=204)	Differential Diagnosis (n=93)
Age (years; mean ± SD)	61 ± 8.0	62 ± 8.8
Age Group (%)		
50 – 59 years	49	44
60 – 69 years	38	30
70 + years	13	26
Male (%)	69	54
Body Mass Index (mean ± SD)	28 ± 4.8	28 ± 4.6
Smoking Status (%)		
Current Smoker	45	31
Former Smoker	55	69
Smoker (Not Specified)	<1	0
Pack-Years (mean ± SD)	39 ± 29.9	32 ± 26.3
Pack-Year Categories (%)*		
1 – 14	22	27
15 – 24	17	13
25 – 49	28	37
50 +	32	23
Unknown	1	1
Ethnicity (%)*		
Caucasian	83	85
Aboriginal / Torres Straight Islander	2	0
Asian	3	5
Other	13	8
Unknown	0	2
Respiratory History (%)		
Asthma, no COPD	0†	98
No Asthma or COPD, but Respiratory Medication	0†	2
No Asthma, COPD or Respiratory Medication	100	0†

COPD: chronic obstructive pulmonary disease; SD: standard deviation.

* Percentages do not add up to 100% because of rounding of the data.

† Not eligible for this arm of the study.

Case finding group: no previous diagnosis or treatment for obstructive lung disease (including COPD, chronic bronchitis, emphysema and/or asthma) in the past year.

Differential diagnosis group: previous diagnosis or treatment for asthma and no previous diagnosis of COPD.

compliance with the spirometry protocol. Valid spirometry and simple flow meter data were obtained from a total of 297 eligible subjects. Of these, four failed to complete the questionnaires (DD group = 1, CF group = 3).

Of the 204 eligible subjects in the CF group, 28% (57/204) had a spirometry post-BD $FEV_1/FVC < 0.70$ ratio, and were assigned a study diagnosis of COPD (Figure 1). Within the DD group, 39% (36/93) of subjects had spirometry-confirmed COPD. Most subjects (DD group = 81%, 29/36; CF group = 95%, 54/57) with a new diagnosis of COPD were classified as either 'mild' ($FEV_1 \geq 80\%$ predicted) or 'moderate' ($50\% \leq FEV_1 < 80\%$ predicted) in severity on the basis of post-BD FEV_1 (Figure 1).

Reversible airflow limitation, consistent with asthma, was observed in 3% (6/204) of subjects in the CF group and 8% (7/93) of subjects in the DD group (Figure 1). In the DD group, 30% (28/93) of subjects were taking oral or inhaled corticosteroids at the time of the study, 20% (19/93) used bronchodilators before the flow meter measurements, and 27% (25/93) used bronchodilators before spirometry.

Mean age and body mass index were similar between each group, and the proportion of males and current smokers was slightly higher in the CF group than the DD group (see Table 1).

Diagnostic accuracy of the PiKo-6®

The validation estimates across cut-off points were similar between the CF groups (Table 2). As the cut-off point was lowered, FEV_1/FEV_6 became less sensitive but more specific, the PPV increased, the NPV decreased, and the likelihood ratio of a positive test increased. For both groups, a cut-off point corresponding to $FEV_1/FEV_6 < 0.75$ offered optimal sensitivity (CF group = 81%; DD group = 86%) and specificity (CF group = 71%; DD group = 67%). Estimates did not differ by more than one percentage point when adjustment for clustering by device operator was incorporated into the calculations; however, the intra-cluster correlations varied in the positive and negative ranges (data not shown).

The diagnostic accuracy of the PiKo-6® FEV_1/FEV_6 in discriminating between subjects with and without COPD (as summarised by the ROCAUC value) was 0.85 (95% CI 0.79, 0.90) for the CF group and 0.88 (95% CI 0.80, 0.96) for the DD group (Figure 2).

The diagnostic performance at the optimum FEV_1/FEV_6 cut-off (< 0.75) by COPD severity is illustrated in Figure 3. The low PPV estimates (52% and 62% for the CF and DD groups, respectively) were due to the proportion of subjects without COPD who recorded 'false positive' FEV_1/FEV_6 ratios between 0.6 and 0.74. The high NPV estimates (CF group = 91%; DD group = 88%) resulted from relatively few subjects recording 'false negative' results (Figure 3). All subjects who blew a false negative result had either mild or moderate COPD, and all subjects with severe or very severe COPD recorded an FEV_1/FEV_6 ratio ≤ 0.6.

There were no statistically significant differences between the mean FEV_1/FEV_6 determined using the simple flow meter or the spirometer. Mean pre-BD FEV_1/FEV_6 for the CF group were 0.754 (simple flow meter) and 0.762 (spirometer), P = 0.14. The corresponding values for the DD group were 0.717 (simple flow meter) and 0.721 (spirometer), P = 0.64.

Few adverse events were reported. There was one case each of dizziness, chest pain and shortness of breath.

Diagnostic accuracy of the COPD diagnostic questionnaires

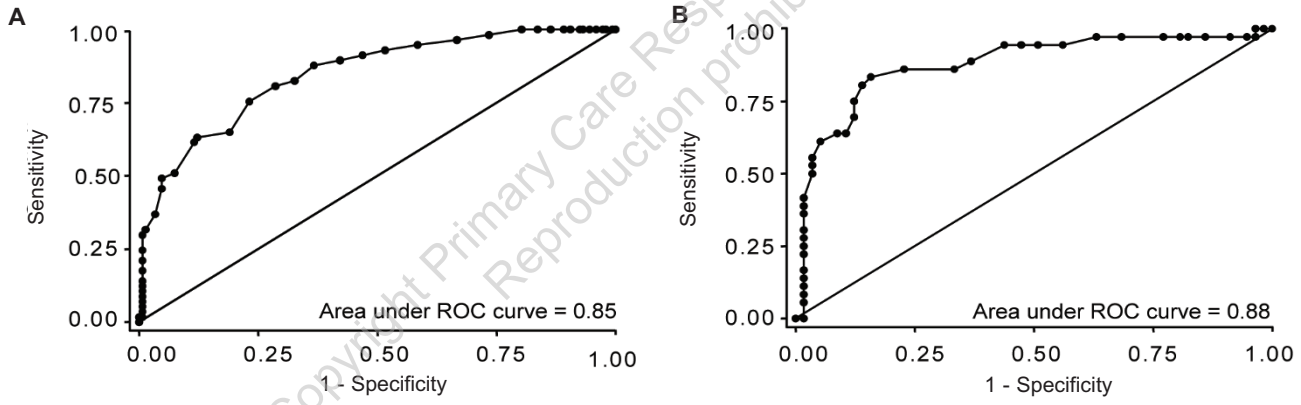
The diagnostic accuracy of the questionnaires was lower than the PiKo-6® FEV_1/FEV_6. The diagnostic accuracy of the

Table 2. Diagnostic accuracy of the simple flow meter across different cut-off points in the Case Finding and Differential Diagnosis groups.*

Study Group	Device cut-off ratio (FEV_1/FEV_6)			
	< 0.66	< 0.70	< 0.75	< 0.80
Case Finding Group (n=204)				
Sensitivity (%)	32 (20, 45)	51 (37, 64)	81 (68, 90)	93 (83, 98)
Specificity (%)	99 (95, 100)	93 (87, 96)	71 (63, 79)	48 (40, 57)
PPV (%)	90 (68, 99)	73 (56, 85)	52 (41, 63)	41 (33, 50)
NPV (%)	79 (72, 84)	83 (76, 88)	91 (84, 95)	95 (87, 99)
Likelihood Ratio (positive)	23.2 (5.6, 96.8)	6.8 (3.7, 12.7)	2.8 (2.1, 3.8)	1.8 (1.5, 2.1)
Differential Diagnosis Group (n=93)				
Sensitivity (%)	56 (38, 72)	69 (52, 84)	86 (71, 95)	94 (81, 99)
Specificity (%)	96 (88, 100)	88 (76, 95)	67 (53, 79)	44 (31, 58)
PPV (%)	91 (71, 99)	78 (60, 91)	62 (47, 75)	52 (39, 64)
NPV (%)	77 (66, 87)	82 (70, 91)	88 (75, 96)	93 (76, 99)
Likelihood Ratio (positive)	15.8 (3.9, 63.7)	5.7 (2.7, 11.7)	2.6 (1.8, 3.8)	1.7 (1.3, 2.1)

FEV_1: forced expiratory volume in one second; FEV_6: forced expiratory volume in six seconds; NPV: negative predictive value; PPV: positive predictive value.
* Data unadjusted for clustering by device operator.
Estimates are shown with 95% confidence limits in parentheses.

Figure 2. ROC curves for the PiKo-6® (FEV_1/FEV_6) against the GOLD spirometry criteria for obstruction (post-BD FEV_1/FVC < 0.70) as the reference standard.[14] A: Case Finding group (n=204); B: Differential Diagnosis group (n=93).



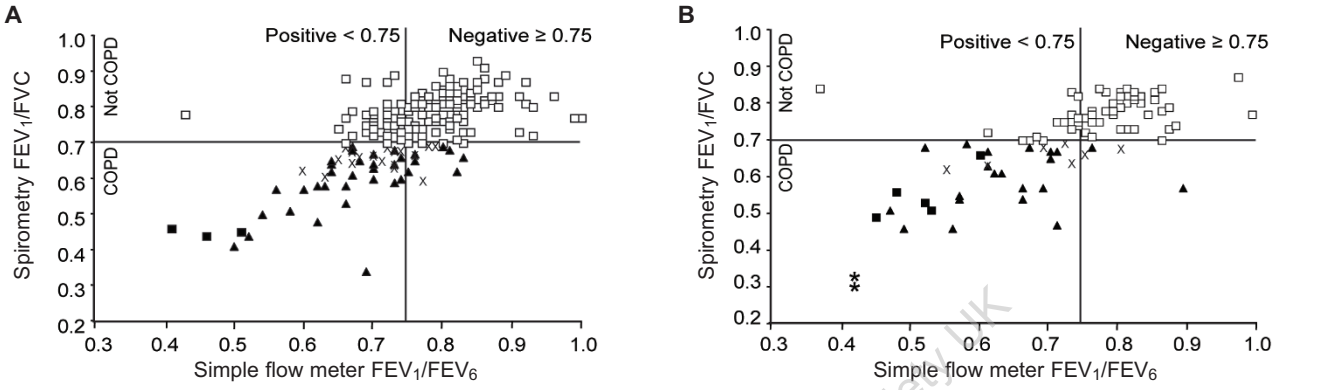
BD: bronchodilator; FEV_1: forced expiratory volume in one second; FEV_6 forced expiratory volume in six seconds; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; ROC: Receiver Operator Characteristic.

questionnaires in discriminating between subjects with and without COPD (as summarised by the ROCAUC value) was 0.72 (95% CI 0.64, 0.79) for the CDQ score and 0.66 (95% CI 0.54, 0.77) for the DDQ score (Figure 4). Although the lower cut-off point provided high sensitivity and NPV in the CF group, neither cut-off provided high specificity or PPV for either group (see Table 3). The PPV estimates for both questionnaires at either cut-off point were relatively low (between 36% and 44%) because of the high proportion of subjects without COPD who recorded scores in the 'increased' and 'intermediate' risk zones (false positives). Estimates of NPV were considerably higher owing to the low number of subjects with COPD scoring false negative values (< cut-off point 2; Table 3). The effect of adjustment for clustering depended on the size and sign of the estimated intra-cluster variation and was much more variable within the DD group (data not shown). The level of agreement between the classification of subjects based on the PiKo-6® FEV_1/FEV_6 cut-off ratio < 0.75 and the questionnaire scores at cut-off point 1 was fair (kappa overall = 0.22, kappa CF group = 0.21, kappa DD group = 0.23).

Discussion

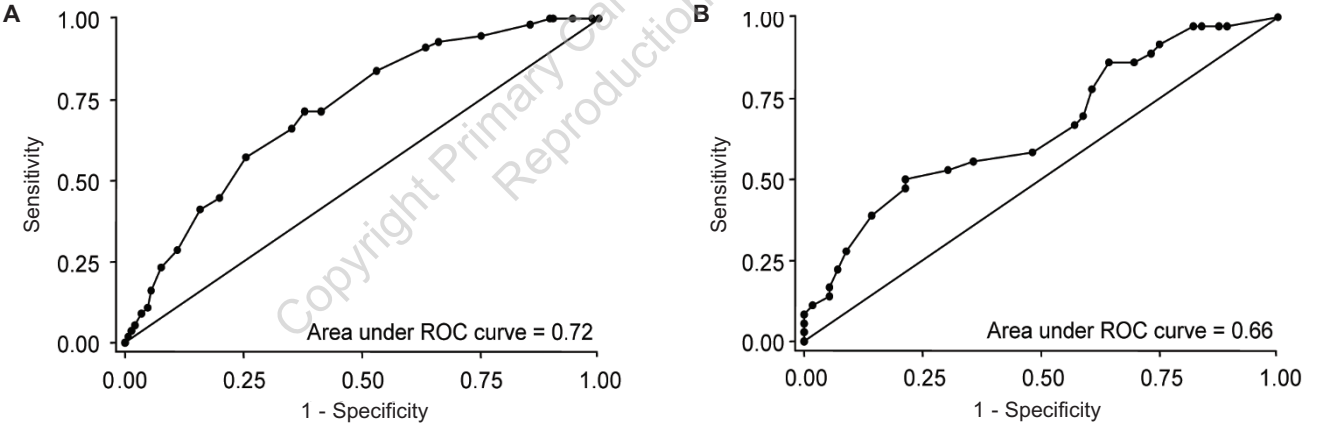
To our knowledge, this is the first validation study of the diagnostic accuracy of a simple, hand-held, expiratory flow

Figure 3. Scatter plots of the spirometry post-BD FEV_1/FVC against the PiKo-6®-measured FEV_1/FEV_6 for the A: Case Finding group (n=204), and B: Differential Diagnosis group (n=93). The quadrants are defined by the GOLD spirometry criteria for obstruction (post-BD $FEV_1/FVC < 0.70$)[14] and the PiKo-6® FEV_1/FEV_6 that yielded optimal performance characteristics ($FEV_1/FEV_6 < 0.75$). The symbols indicate the severity of COPD according to GOLD criteria as follows: □ no COPD; x mild COPD; ▲ moderate COPD; ■ severe COPD; * very severe COPD.



BD: bronchodilator; COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in one second; FEV_6 forced expiratory volume in six seconds; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease.

Figure 4. ROC curves for the COPD diagnostic questionnaires against the GOLD spirometry criteria for obstruction (post-BD $FEV_1/FVC < 0.70$) as the reference standard.[14] A: COPD Diagnosis Questionnaire (Case Finding group, n=201); B: Differential Diagnosis Questionnaire (Differential Diagnosis group, n=92).



BD: bronchodilator; COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; ROC: Receiver Operator Characteristic.

meter (in this case the PiKo-6®) using FEV_1/FEV_6 in a primary care setting. The ROCAUC showed a strong correlation between the pre-BD FEV_1/FEV_6 measured using the flow meter and the reference diagnosis of COPD (a post-BD FEV_1/FEV of < 0.7). Equally high ROCAUC values were obtained in current and former smokers aged ≥ 50 years old with no previous respiratory diagnosis (CF group; ROCAUC = 0.85) or previous asthma diagnosis (DD group; ROCAUC = 0.88). These values exceeded the ROCAUC estimates obtained in each group using COPD diagnostic questionnaires. Results indicated that the PiKo-6® is a simple and reliable screening tool that could facilitate early identification of airflow limitation.

Although office spirometry has been widely promoted,[12,24] cost and benefit analysis does not support routine spirometric screening in primary care settings.[31] Significant barriers to spirometry in primary care include equipment and training costs, low reimbursement, low confidence with use and interpretation of results, perceived lack of utility, and quality assurance issues.[18-21]

Table 3. Diagnostic accuracy of the COPD Diagnostic Questionnaires at different cut-off points.*

Characteristic	COPD Diagnosis Questionnaire (n=201)		Differential Diagnosis Questionnaire (n=92)	
	Cut-off Point 1 (19.5)	Cut-off Point 2 (16.5)	Cut-off Point 1 (24.5)	Cut-off Point 2 (18.5)
Sensitivity (%)	71 (58, 83)	91 (80, 97)	58 (41, 74)	89 (74, 97)
Specificity (%)	62 (54, 70)	37 (29, 45)	52 (38, 65)	27 (16, 40)
PPV (%)	42 (32, 53)	36 (28, 44)	44 (29, 59)	44 (32, 56)
NPV (%)	85 (77, 91)	91 (81, 97)	66 (50, 80)	79 (54, 94)
Likelihood Ratio (positive)	1.88 (1.4, 2.5)	1.44 (1.2, 1.7)	1.21 (0.8, 1.8)	1.21 (1.0, 1.5)

COPD: chronic obstructive pulmonary disease; NPV: negative predictive value; PPV: positive predictive value.

* Data unadjusted for clustering; Cut-off points as described by Price and co-workers.[23] Estimates are shown with 95% confidence limits in parentheses.

A key finding from this study was that despite the brief training provided to health care workers, a low-cost expiratory flow meter had remarkably high accuracy and reliability in the detection of airflow limitation. These findings suggest that simple, low-cost flow meters that require minimal training, such as the PiKo-6®, could facilitate the identification of patients who are likely to benefit from quality-assured spirometric evaluation.

Six-second expiratory manoeuvres offer several advantages over measurements of FVC in the elderly and in primary care.[24,25,32] Although concerns have been raised in relation to sensitivity[33,34] and specificity[35] of spirometric FEV_1/FEV_6 for diagnosing airways obstruction, our findings show that this parameter may be a useful screening tool for COPD in at-risk primary care populations. Previous findings have suggested that the PiKo-6® with a high cut-off point ($FEV_1/FEV_6 < 0.80$) may improve detection of airflow limitation in primary care settings.[26] However, this cut-off point was based on personal experience of the authors and was selected to maximise specificity, albeit with a high rate of false-positive findings. The proposed cut-off point ($FEV_1/FEV_6 < 0.75$) in our study was derived using standard validation statistics and identified patient groups with a high 'pre-spirometry likelihood' of COPD. The PPVs from our study suggest that about one out of every two patients who record a value below this cut-off point will exhibit a post-BD FEV_1/FEV of < 0.7 with spirometry. We would regard this as an efficient use of diagnostic resources. Following referral, diagnostic spirometry could be conducted within the primary care practice, an intermediate or community facility[20,36] or specialist lung function laboratory. Conversely, the NPV estimates provide practitioners with a high degree of confidence that most (nine out of ten) patients who record a $FEV_1/FEV_6 \geq 0.75$ with the PiKo-6® used in this study, do not have COPD. The proposed flow meter cut-off point is similar to the spirometry FEV_1/FEV_6 cut-off point (< 0.73), which was previously shown to be a valid alternative to FEV_1/FVC < 0.70 as a fixed cut-off point for the diagnosis of airway obstruction.[37,38]

Estimates of the prevalence of COPD in the general population vary from 5-21% of adults in developed countries.[39] However, in this study, we assessed COPD in a selected population comprising adults attending primary care practices. Therefore, the prevalence of COPD in the CF and DD groups was higher than the prevalence of COPD that has been estimated from more general populations. The prevalence of spirometry-confirmed COPD in the CF (28%) and DD (39%) groups in this study was similar to findings from equivalent populations in the UK (CF = 21.9%, DD = 45%) and the US (CF = 16.0%, DD = 36%).[22,28]

In our study, the diagnostic accuracy of the COPD diagnostic questionnaires was different from Price and co-workers, who reported ROCAUC values of 0.82 and 0.84 for the CDQ and DDQ, respectively.[22,23,28] The reasons for this discrepancy in performance are not readily apparent. There were slight differences in the demographics of the study populations (the original study groups were, on average, slightly younger and had lower cumulative cigarette consumption). However, a more plausible explanation is that the COPD diagnostic questionnaires are of limited utility outside the development and validation populations. A recent external validation study found the CDQ to be a poor discriminator of those with and without COPD in a population of current smokers (ROCAUC = 0.65).[40] As in our study, specificity values were considerably lower than those reported by Price and co-workers.[23]

In the present study, subjects were representative of individuals likely to be screened for COPD in primary care practices. Although the study diagnosis was made on the basis of spirometry at one visit and was not conducted in a lung function laboratory, the spirometers were calibrated, the operators were trained and blinded to previous test results, and the quality of spirometry was monitored. As there was no warning to withhold bronchodilator medication, there is a possibility that the 'no objective obstructive lung disease group' included subjects with well-controlled or inactive asthma, subjects with only minor obstructive changes, or subjects with asthma who had taken their bronchodilator before the visit.[41] Withholding of medication was not enforced because the study aimed to approximate the 'real-life' use of the device for

Difficulties encountered: Compliance with spirometry protocol at one site.
Alternative methodologies: Inclusion of a no obstructive lung disease group, diagnosis via gold standard spirometry based on more than one visit.
New questions arising: Results should be validated in randomised controlled studies, conducted in specialist lung function laboratories.
Lessons for clinical practice: Use of FEV_1/FEV_6 from a simple flow meter provides a simple, reliable and practical screening tool for COPD and could facilitate early referral for spirometry and early, targeted interventions.

opportunistic targeted screening. An alternative possibility would be an unsuspected restrictive respiratory disorder.[41] More studies in specialist lung function laboratories and randomised enrolment of patients would be required to confirm the findings from this study.

This is the first validation study to determine the diagnostic accuracy of an easy-use expiratory flow meter in a primary care setting. Similar to spirometry, the PiKo-6® requires full patient cooperation, but training for both the operator and the patient is straightforward. Given the findings from this study, the PiKo-6® should provide health care workers with a simple, reliable and practical method for targeted screening of patients at high risk of COPD. The simplicity and reliability of this case-finding tool, and the importance of COPD in adults, means that the PiKo-6® could fit into the busy work schedule of a primary care practitioner, alongside screening for hypertension. Further, using FEV_1/FEV_6 from a simple flow meter could optimise early referral for spirometry and improve provision of early, targeted interventions aimed at reducing the burden of COPD.

Funding

The salary of the research coordinator, together with costs of spirometry and questionnaire administration, data collection and analysis were met by Boehringer Ingelheim Pty Ltd Australia and Pfizer Australia.

Conflicts of interest

PF, AC and JB have received past or present funding support for research or education from one or more pharmaceutical or other health technology companies. None of the three has any direct or family financial interests in either of the sponsor companies.

GG and DM are employees of Boehringer Ingelheim Pty Limited, manufacturer of SPIRIVA (tiotropium) and AR is an employee of Pfizer Australia Pty Limited [alliance partner of Boehringer Ingelheim Pty Limited on SPIRIVA (tiotropium)].

At the time this study was conducted, RA was an employee of Covance Pty Limited, a contract research organization that has received funding from several pharmaceutical or other health technology companies. The study was conducted independently from commercial interests. No drug manufactured or marketed by the sponsors was tested or used in this study.

References

1. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J* 2006;**28**(3):523-32. http://dx.doi.org/10.1183/09031936.06.00124605
2. Vermeire P. The burden of chronic obstructive pulmonary disease. *Respir Med* 2002;**96**(Suppl C):S3-10. http://dx.doi.org/10.1016/S0954-6111(02)80028-2
3. Buist AS. Guidelines for the management of chronic obstructive pulmonary disease. *Respir Med* 2002;**96**(Suppl C):S11-6. http://dx.doi.org/10.1016/S0954-6111(02)80029-4
4. van der Molen T, Ostrem A, Stallberg B, Ostergaard MS, Singh RB. International Primary Care Respiratory Group (IPCRG) Guidelines: management of asthma. *Prim Care Respir J* 2006;**15**(1):35-47. http://dx.doi.org/10.1016/j.pcrj.2005.11.001
5. Bednarek M, Maciejewski J, Wozniak M, Kuca P, Zielinski J. Prevalence, severity and underdiagnosis of COPD in the primary care setting. *Thorax* 2008;**63**(5):402-07. http://dx.doi.org/10.1136/thx.2007.085456
6. Griffiths C, Feder G, Wedzicha J, Foster G, Livingstone A, Marlowe GS. Feasibility of spirometry and reversibility testing for the identification of patients with chronic obstructive pulmonary disease on asthma registers in general practice. *Respir Med* 1999;**93**(12):903-08. http://dx.doi.org/10.1016/S0954-6111(99)90057-4
7. Hill K, Goldstein RS, Guyatt GH, *et al*. Prevalence and underdiagnosis of chronic obstructive pulmonary disease among patients at risk in primary care. *CMAJ* 2010;**182**(7):673-8. http://dx.doi.org/10.1503/cmaj.091784
8. Lindberg A, Bjerg-Backlund A, Ronmark E, Larsson LG, Lundback B. Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking Report from the Obstructive Lung Disease in Northern Sweden Studies. *Respir Med* 2006;**100**(2):264-72. http://dx.doi.org/10.1016/j.rmed.2005.04.029
9. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance - United States, 1971-2000. *MMWR Surveill Summ* 2002;**51**(6):1-16.
10. Matheson MC, Abeysena C, Raven JM, *et al*. How have we been managing chronic obstructive pulmonary disease in Australia? *Intern Med J* 2006;**36**(2):92-9. http://dx.doi.org/10.1111/j.1445-5994.2006.01011.x
11. Vandevoorde J, Verbanck S, Gijssels L, *et al*. Early detection of COPD: a case finding study in general practice. *Respir Med* 2007;**101**(3):525-30. http://dx.doi.org/10.1016/j.rmed.2006.06.027
12. Walker PP, Mitchell P, Diamantea F, Warburton CJ, Davies L. Effect of primary-care spirometry on the diagnosis and management of COPD. *Eur Respir J* 2006;**28**(5):945-52. http://dx.doi.org/10.1183/09031936.06.00019306
13. Kaplan A, Rodriguez M. Early diagnosis of COPD does help! IPCRG Opinion Sheet 5; International Primary Care Respiratory Group. 17 November 2009. [Accessed 22 December 2010]: Available from: http://www.theipcrg.org/resources/ipcrg_copd_opinion_5.pdf.
14. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. 2009 update. [Accessed August 2010]; Available from: www.goldcopd.org.
15. Levy ML, Quanjer PH, Booker R, Cooper BG, Holmes S, Small I. Diagnostic spirometry in primary care: Proposed standards for general practice compliant with American Thoracic Society and European Respiratory Society recommendations. *Prim Care Respir J* 2009;**18**(3):130-47. http://dx.doi.org/10.4104/pcrj.2009.00054
16. Han MK, Kim MG, Mardon R, *et al*. Spirometry utilization for COPD: how do we measure up? *Chest* 2007;**132**(2):403-09. http://dx.doi.org/10.1378/chest.06-2846
17. Joo MJ, Lee TA, Weiss KB. Geographic variation of spirometry use in newly diagnosed COPD. *Chest* 2008;**134**(1):38-45. http://dx.doi.org/10.1378/chest.08-0013
18. Bolton CE, Ionescu AA, Edwards PH, Faulkner TA, Edwards SM, Shale DJ. Attaining a correct diagnosis of COPD in general practice. *Respir Med* 2005;**99**(4):493-500. http://dx.doi.org/10.1016/j.rmed.2004.09.015
19. Johns DP, Burton D, Walters JA, Wood-Baker R. National survey of spirometer ownership and usage in general practice in Australia. *Respirology* 2006;**11**(3):292-8. http://dx.doi.org/10.1111/j.1440-1843.2006.00851.x
20. Lwin AM, McKinley RK. Management of COPD in primary care in Leicestershire.

Prim Care Respir J 2005;**14**(1):38-41. http://dx.doi.org/10.1016/j.pcrj.2004.06.011

21. Walters JA, Hansen E, Mudge P, Johns DP, Walters EH, Wood-Baker R. Barriers to the use of spirometry in general practice. *Aust Fam Physician* 2005;**34**(3):201-03.
22. Price DB, Tinkelman DG, Halbert RJ, *et al*. Symptom-based questionnaire for identifying COPD in smokers. *Respiration* 2006;**73**(3):285-95. http://dx.doi.org/10.1159/000090142
23. Price DB, Tinkelman DG, Nordyke RJ, Isonaka S, Halbert RJ. Scoring system and clinical application of COPD diagnostic questionnaires. *Chest* 2006;**129**(6):1531-9. http://dx.doi.org/10.1378/chest.129.6.1531
24. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: A consensus statement from the National Lung Health Education Program. *Chest* 2000;**117**(4):1146-61. http://dx.doi.org/10.1378/chest.117.4.1146
25. Jing JY, Huang TC, Cui W, Xu F, Shen HH. Should FEV1/FEV6 replace FEV1/FVC ratio to detect airway obstruction? A metaanalysis. *Chest* 2009;**135**(4):991-8. http://dx.doi.org/10.1378/chest.08-0723
26. Kaufmann M, Hartl S, Geyer K, Breyer MK, Burghuber OC. Measuring FEV(6) for detecting early airway obstruction in the primary care setting. Quality and utility of the new PiKo-6 device. *Respiration* 2009;**78**(2):161-7. http://dx.doi.org/10.1159/000197466
27. Vollmer WM, Gislason T, Burney P, *et al*. Comparison of spirometry criteria for the diagnosis of COPD: results from the BOLD study. *Eur Respir J* 2009;**34**(3):588-97. http://dx.doi.org/10.1183/09031936.00164608
28. Tinkelman DG, Price DB, Nordyke RJ, *et al.* Symptom-based questionnaire for differentiating COPD and asthma. *Respiration* 2006;**73**(3):296-305. http://dx.doi.org/10.1159/000090141
29. Miller MR, Hankinson J, Brusasco V, *et al.* Standardisation of spirometry. *Eur Respir J* 2005;**26**(2):319-38. http://dx.doi.org/10.1183/09031936.05.00034805
30. Gore CJ, Crockett AJ, Pederson DG, Booth ML, Bauman A, Owen N. Spirometric standards for healthy adult lifetime nonsmokers in Australia. *Eur Respir J* 1995;8(5):773-82.
31. Wilt TJ, Niewoehner D, Kim C, *et al.* Use of Spirometry for Case Finding, Diagnosis and Management of Chronic Obstructive Pulmonary Disease (COPD). Summary, Evidence Report/Technology Assessment No. 12. Rockville, MD: Agency for Healthcare Research and Quality (prepared by the Minnesota Evidence-based Practice Center) 2005. Report No.: AHRQ Publication No.: 05-E017-1, Contract No.: 290-02-0009
32. Bellia V, Sorino C, Catalano F, *et al.* Validation of FEV6 in the elderly: correlates of performance and repeatability. *Thorax* 2008;**63**(1):60-6. http://dx.doi.org/10.1136/thx.2007.080572
33. Demir T, Ikitimur HD, Koc N, Yildirim N. The role of FEV6 in the detection of airway obstruction. *Respir Med* 2005;**99**(1):103-06. http://dx.doi.org/10.1016/j.rmed.2004.05.016
34. Hansen JE, Sun XG, Wasserman K. Should forced expiratory volume in six seconds replace forced vital capacity to detect airway obstruction? *Eur Respir J* 2006;**27**(6):1244-50. http://dx.doi.org/10.1183/09031936.06.00136905
35. Gleeson S, Mitchell B, Pasquarella C, Reardon E, Falsone J, Berman L. Comparison of FEV6 and FVC for detection of airway obstruction in a community hospital pulmonary function laboratory. *Respir Med* 2006;**100**(8):1397-401. http://dx.doi.org/10.1016/j.rmed.2005.11.012
36. Enright P. Does screening for COPD by primary care physicians have the potential to cause more harm than good? *Chest* 2006;**129**(4):833-5. http://dx.doi.org/10.1378/chest.129.4.833
37. Melbye H, Medbo A, Crockett A. The FEV1/FEV6 ratio is a good substitute for the FEV1/FVC ratio in the elderly. *Prim Care Respir J* 2006;**15**(5):294-8. http://dx.doi.org/10.1016/j.pcrj.2006.07.002
38. Vandevoorde J, Verbanck S, Schuermans D, Kartounian J, Vincken W. Obstructive and restrictive spirometric patterns: fixed cut-offs for FEV1/FEV6 and FEV6. *Eur Respir J* 2006;**27**(2):378-83. http://dx.doi.org/10.1183/09031936.06.00036005
39. Soriano JB, Zielinski J, Price D. Screening for and early detection of chronic obstructive pulmonary disease. *Lancet* 2009;**374**(9691):721-32. http://dx.doi.org/10.1016/S0140-6736(09)61290-3
40. Kotz D, Nelemans P, van Schayck CP, Wesseling GJ. External validation of a COPD diagnostic questionnaire. *Eur Respir J* 2008;**31**(2):298-303. http://dx.doi.org/10.1183/09031936.00074307
41. Mannino DM, Ford ES, Redd SC. Obstructive and restrictive lung disease and markers of inflammation: data from the Third National Health and Nutrition Examination. *Am J Med* 2003;**114**(9):758-62. http://dx.doi.org/10.1016/S0002-9343(03)00185-2

Available online at **http://www.thepcrj.org**

Appendix 1

COPD Diagnostic Questionnaire (CDQ)

This questionnaire is to be completed by smokers or non-smokers with no prior respiratory diagnosis or treatment.

Please answer every question by selecting the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

Please read the questions in this column…	***…and mark a single answer in this column***
1. What is your age (in years)?	☐ 40 - 49 ☐ 50 - 59 ☐ 60 - 69 ☐ 70 or older
2. What is the total number of years you have smoked cigarettes?	_____ years ☐ I have never smoked cigarettes*
3. How many cigarettes do you currently smoke each day? (If you are an ex-smoker, how many did you smoke each day?)	_____ cigarettes ☐ I have never smoked cigarettes*
4. What is your height ?	_____cm or _____ft ____inches
5. What is your weight?	_____kg or _____stone
6. Does the weather affect your cough?	☐ YES ☐ NO ☐ I do not have a cough
7. Do you ever cough up phlegm (sputum) from your chest when you don't have a cold?	☐ YES ☐ NO
8. Do you usually cough up phlegm (sputum) from your chest first thing in the morning?	☐ YES ☐ NO
9. How frequently do you wheeze?	☐ Never ☐ Occasionally or more often
10. Do you have or have you had any allergies?	☐ YES ☐ NO

*** If never smoked, this patient is ineligible for this study.**

Appendix 1

Differential Diagnosis Questionnaire (DDQ)

This questionnaire is to be completed by smokers or non-smokers with a prior diagnosis or treatment for asthma, but not COPD.

Please answer every question by selecting the answer as indicated. If you are unsure bout how to answer a question, please give the best answer you can.

Please read the questions in this column…	***…and mark a single answer in this column***
1. What is your age (in years)?	☐ 40 - 49 ☐ 50 - 59 ☐ 60 - 69 ☐ 70 or older
2. What is the total number of years you have smoked cigarettes?	_____ years ☐ I have never smoked cigarettes*
3. How many cigarettes do you currently smoke each day? (If you are an ex-smoker, how many did you smoke each day?)	_____ cigarettes ☐ I have never smoked cigarettes*
4. Have you coughed more in the past few years?	☐ YES ☐ NO
5. During the past 3 years have you had any breathing problems that have kept you off work, indoors, at home, or in bed?	☐ YES ☐ NO
6. Have you ever been admitted to hospital with breathing problems?	☐ YES ☐ NO
7. Have you been short of breath more often in the past few years?	☐ YES ☐ NO
8. On average, how much phlegm (sputum) do you cough up most days?	☐ Less than 1 tablespoon (15 ml) per day ☐ 1 tablespoon (15 ml) per day or more
9. If you get a cold, does it usually go to your chest?	☐ YES ☐ NO
10. Are you taking any treatment to help your breathing?	☐ YES ☐ NO

* If never smoked, this patient is ineligible for this study.