

## ORIGINAL RESEARCH

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

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**Abstract**

**Aims:** To determine the accuracy of the forced expiratory volume ratio at one and six seconds (FEV<sub>1</sub>/FEV<sub>6</sub>) 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<sub>1</sub>/FEV<sub>6</sub> and post-BD FEV<sub>1</sub>/forced vital capacity (FVC) spirometry.

**Results:** The PiKo-6® FEV<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub> 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.

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**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](http://www.thepcrj.org)

**Introduction**

Chronic obstructive pulmonary disease (COPD) is a leading cause of mortality worldwide,<sup>1,2</sup> yet is typically not diagnosed until its advanced stages, causing a considerable burden to patients and health care resources.<sup>3</sup> Early case identification may enable better use of effective management interventions and hence a reduced disease burden.<sup>4</sup> However, it is accepted

that the onset of COPD is insidious, leading to under-diagnosis and misdiagnosis.<sup>5-12</sup>

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.<sup>13</sup> Among the tools currently available to primary care practitioners, spirometry is recognised as the 'gold standard' diagnostic test to demonstrate fixed airway obstruction.<sup>14,15</sup> However, spirometry is underutilised in clinical practice<sup>16,17</sup> as many practitioners do not own a spirometer, undergo little training, or lack confidence in its use or in the interpretation of results.<sup>18-21</sup> Symptom-based questionnaires may help practitioners identify individuals with

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COPD in at-risk populations.<sup>22</sup> However, the time required to conduct and analyse these questionnaires<sup>23</sup> 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<sub>6</sub>) is emerging as a valid alternative to forced vital capacity (FVC) for detection of COPD.<sup>24-27</sup> 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<sub>1</sub>/FEV<sub>6</sub> ratio, potentially provide a practical method for early screening for COPD in at-risk patient populations.<sup>26</sup> The current study examined the diagnostic accuracy of FEV<sub>1</sub>/FEV<sub>6</sub> using the PiKo-6® compared with post-bronchodilator (BD) FEV<sub>1</sub>/FVC spirometry conducted by trained operators using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometry COPD criteria<sup>14</sup> 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.<sup>22,23,28</sup>

## 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<sub>1</sub>/FEV<sub>6</sub> 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.<sup>14</sup>

### 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  $\geq 50$  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  $\geq 50$  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<sub>1</sub>/FEV<sub>6</sub> 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](http://www.thepcrj.org)). Development of these questionnaires for use in primary practice has been described previously.<sup>22,23,28</sup>

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

FEV<sub>1</sub>, FEV<sub>6</sub> 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<sub>1</sub> within 0.2 L) were taken. The measurement of acceptable quality with the highest summed value (FEV<sub>1</sub> + FEV<sub>6</sub>) was used.

### Spirometry

Spirometry testing with bronchodilator reversibility was performed independently by trained operators according to American Thoracic Society / European Respiratory Society guidelines.<sup>29</sup> 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<sub>1</sub> + 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<sup>14</sup> spirometry criteria. The reference criterion for COPD was a post-BD FEV<sub>1</sub>/FVC of < 0.70, which is consistent with the diagnosis used during development and validation of the COPD diagnostic questionnaires<sup>22,28</sup> and with reversibility ≤ 200 mL and ≤ 12% from baseline pre-BD FEV<sub>1</sub>. The post-BD FEV<sub>1</sub> percentage of predicted values was calculated<sup>30</sup> 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).<sup>23</sup>

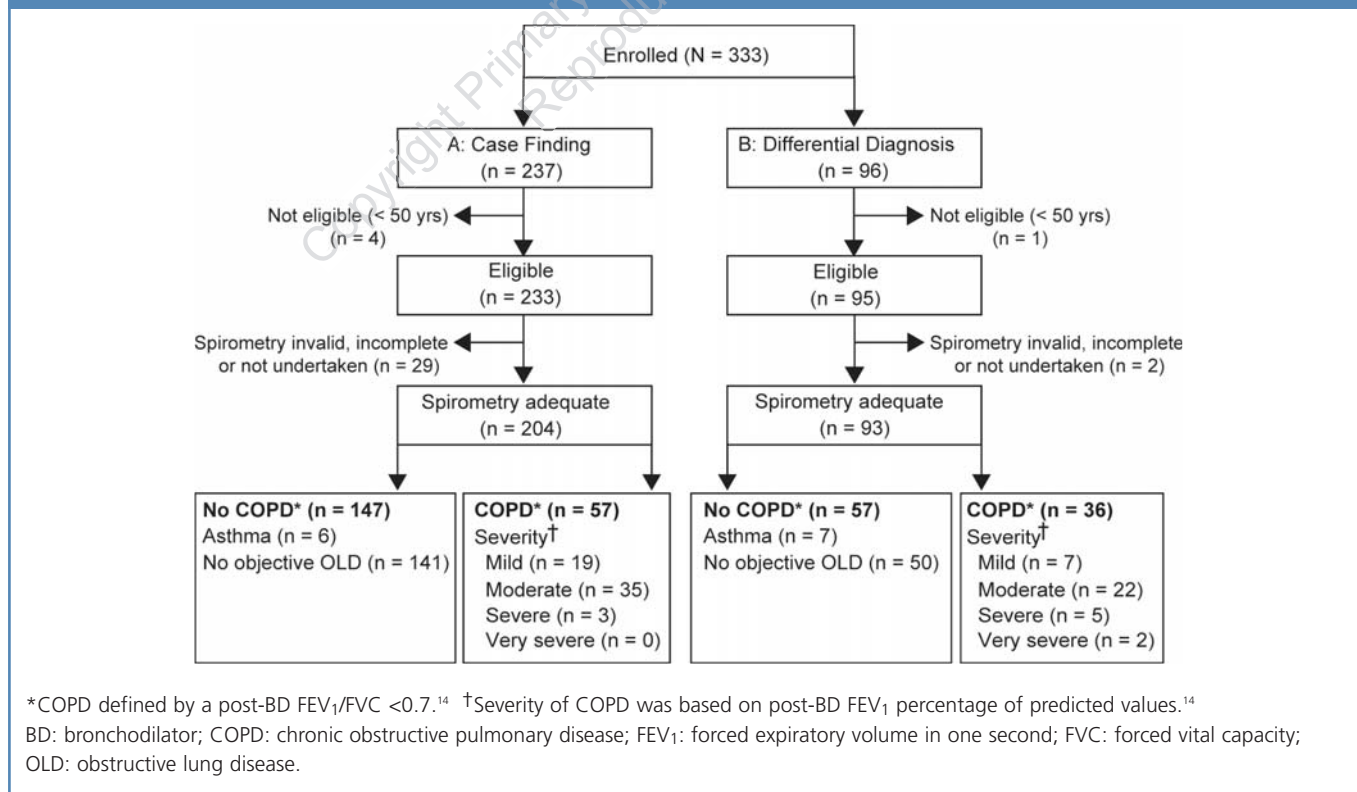
Diagnostic accuracies of the PiKo-6® FEV<sub>1</sub>/FEV<sub>6</sub> and COPD diagnostic questionnaires were summarised by calculating the area under the receiver operating characteristic (ROC) curve (ROCAUC; *roctab* procedure; STATA v9, StataCorp, TX, USA) and the kappa statistic for agreement between 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<sup>23</sup> and at FEV<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub> 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.**



**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 Strait 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<sub>1</sub>/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<sub>1</sub> ≥ 80% predicted) or ‘moderate’ (50% ≤ FEV<sub>1</sub> < 80% predicted) in severity on the basis of post-BD FEV<sub>1</sub> (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<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub> < 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<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub> ratio ≤ 0.6.

There were no statistically significant differences between the mean FEV<sub>1</sub>/FEV<sub>6</sub> determined using the simple flow meter or the spirometer. Mean pre-BD FEV<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub>. 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.\***

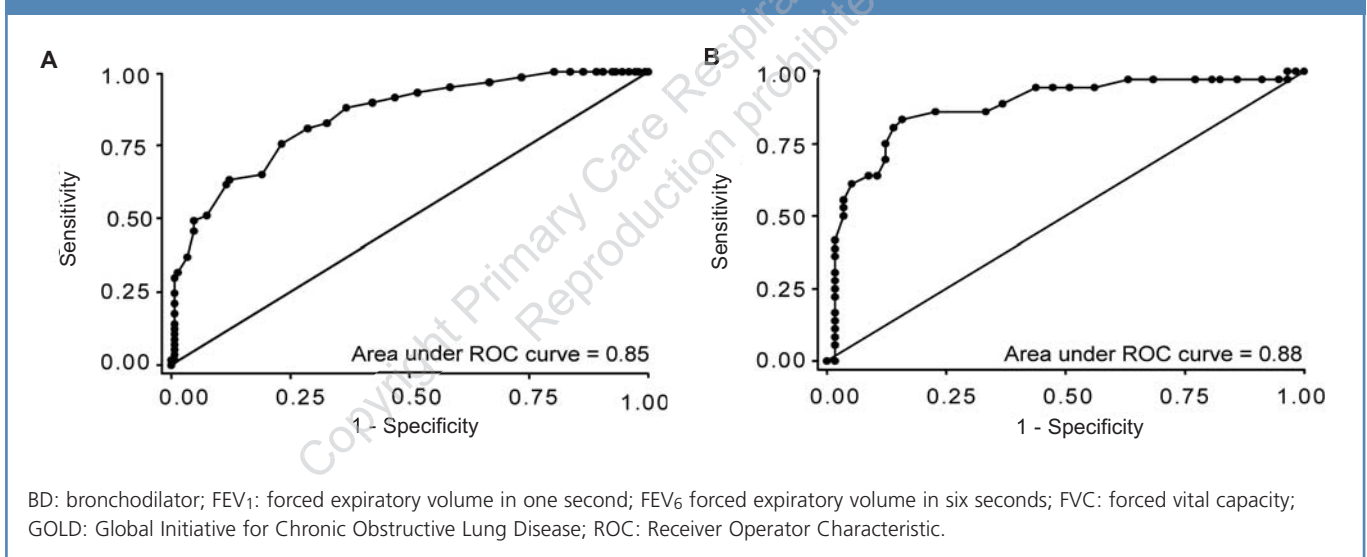
Study Group	Device cut-off ratio (FEV <sub>1</sub> /FEV <sub>6</sub> )			
	< 0.66	< 0.70	< 0.75	< 0.80
<b>Case Finding Group (n=204)</b>				
Sensitivity (%)	32 (20, 45)	51 (37, 64)	81 (68, 90)	93 (83, 98)
Specificity (%)	99 (95, 100)	93 (87, 96)	71 (63, 79)	48 (40, 57)
PPV (%)	90 (68, 99)	73 (56, 85)	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)
<b>Differential Diagnosis Group (n=93)</b>				
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<sub>1</sub>: forced expiratory volume in one second; FEV<sub>6</sub>: 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<sub>1</sub>/FEV<sub>6</sub>) against the GOLD spirometry criteria for obstruction (post-BD FEV<sub>1</sub>/FVC < 0.70) as the reference standard.<sup>14</sup> A: Case Finding group (n=204); B: Differential Diagnosis group (n=93).**



BD: bronchodilator; FEV<sub>1</sub>: forced expiratory volume in one second; FEV<sub>6</sub> 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<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FVC against the PiKo-6<sup>®</sup>-measured FEV<sub>1</sub>/FEV<sub>6</sub> 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<sub>1</sub>/FVC < 0.70)<sup>14</sup> and the PiKo-6<sup>®</sup> FEV<sub>1</sub>/FEV<sub>6</sub> that yielded optimal performance characteristics (FEV<sub>1</sub>/FEV<sub>6</sub> < 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.

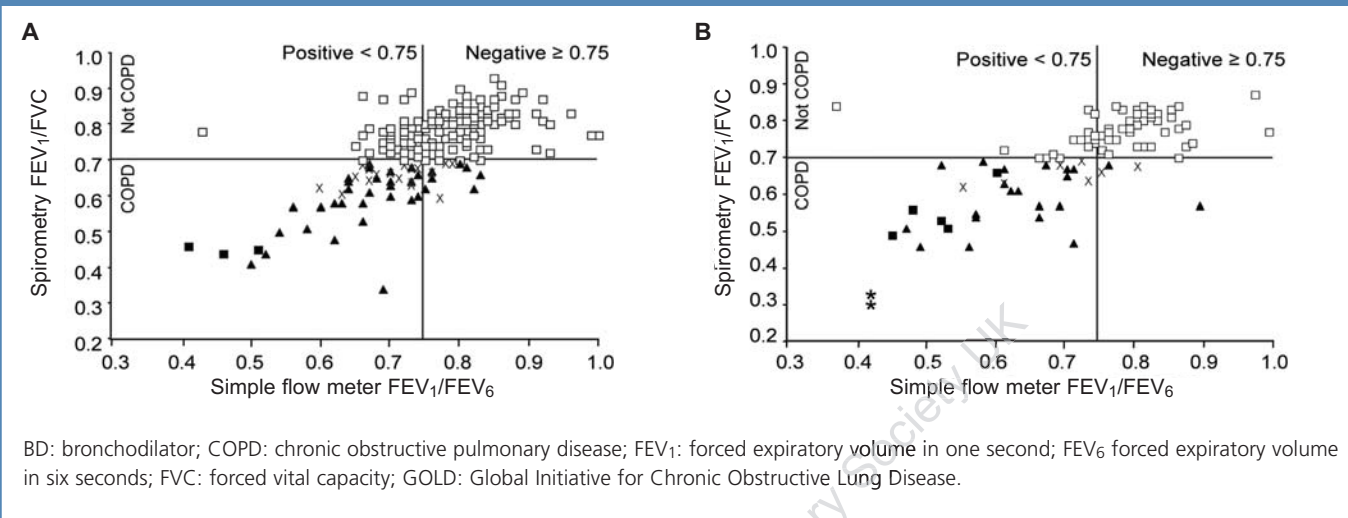
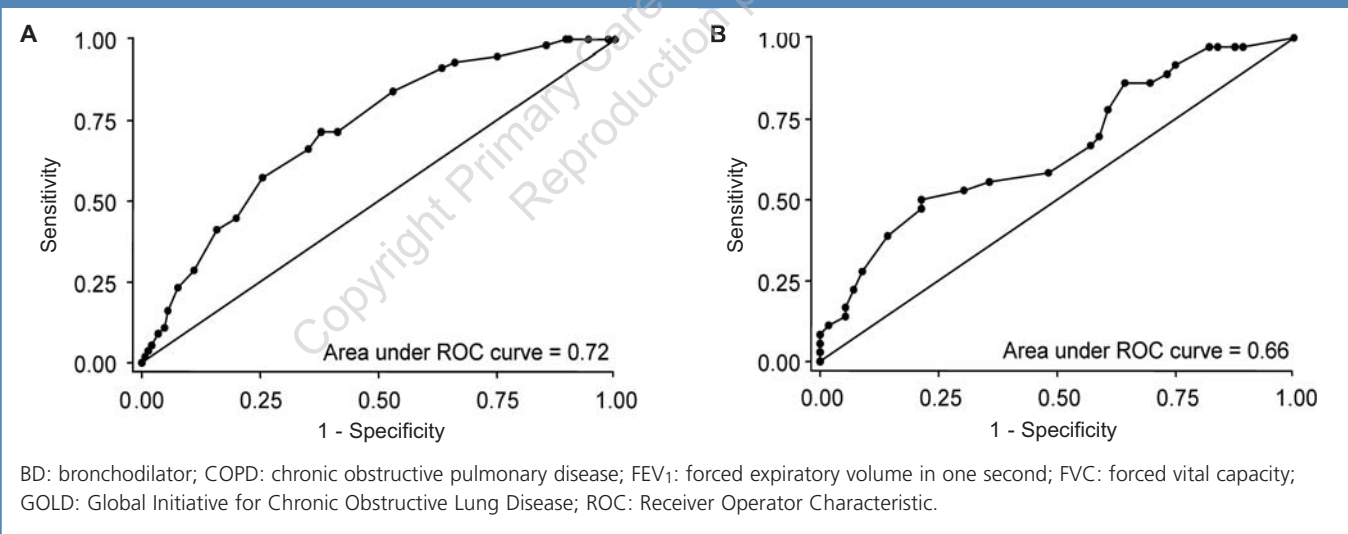


Figure 4. ROC curves for the COPD diagnostic questionnaires against the GOLD spirometry criteria for obstruction (post-BD FEV<sub>1</sub>/FVC < 0.70) as the reference standard.<sup>14</sup> A: COPD Diagnosis Questionnaire (Case Finding group, n=201); B: Differential Diagnosis Questionnaire (Differential Diagnosis group, n=92).



meter (in this case the PiKo-6<sup>®</sup>) using FEV<sub>1</sub>/FEV<sub>6</sub> in a primary care setting. The ROCAUC showed a strong correlation between the pre-BD FEV<sub>1</sub>/FEV<sub>6</sub> measured using the flow meter and the reference diagnosis of COPD (a post-BD FEV<sub>1</sub>/FEV<sub>6</sub> 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<sup>®</sup> is a simple and reliable screening tool that could facilitate early identification of airflow limitation.

Although office spirometry has been widely promoted,<sup>12,24</sup> cost and benefit analysis does not support routine spirometric screening in primary care settings.<sup>31</sup> 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.<sup>18-21</sup>

**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.<sup>23</sup> 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<sup>®</sup>, 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.<sup>24,25,32</sup> Although concerns have been raised in relation to sensitivity<sup>33,34</sup> and specificity<sup>35</sup> of spirometric FEV<sub>1</sub>/FEV<sub>6</sub> 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<sup>®</sup> with a high cut-off point (FEV<sub>1</sub>/FEV<sub>6</sub> < 0.80) may improve detection of airflow limitation in primary care settings.<sup>26</sup> 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<sub>1</sub>/FEV<sub>6</sub> < 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<sub>1</sub>/FEV<sub>6</sub> 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<sup>20,36</sup> 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<sub>1</sub>/FEV<sub>6</sub> ≥ 0.75 with the PiKo-6<sup>®</sup> used in this study, do not have COPD. The proposed flow meter cut-off point is similar to the spirometry FEV<sub>1</sub>/FEV<sub>6</sub> cut-off point (< 0.73), which was previously shown to be a valid alternative to FEV<sub>1</sub>/FVC < 0.70 as a fixed cut-off point for the diagnosis of airway obstruction.<sup>37,38</sup>

Estimates of the prevalence of COPD in the general population vary from 5-21% of adults in developed countries.<sup>39</sup>

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%).<sup>22,28</sup>

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.<sup>22,23,28</sup> 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).<sup>40</sup> As in our study, specificity values were considerably lower than those reported by Price and co-workers.<sup>23</sup>

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.<sup>41</sup> 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<sub>1</sub>/FEV<sub>6</sub> 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.<sup>41</sup> 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<sup>®</sup> requires full patient cooperation, but training for both the operator and the patient is straightforward. Given the findings from this study, the PiKo-6<sup>®</sup> 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<sup>®</sup> could fit into the busy work schedule of a primary care practitioner, alongside screening for hypertension. Further, using FEV<sub>1</sub>/FEV<sub>6</sub> 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.

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### 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.

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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.*

<b><i>Please read the questions in this column...</i></b>	<b><i>...and mark a single answer in this column</i></b>
1. What is your age (in years)?	<input type="checkbox"/> 40 - 49 <input type="checkbox"/> 50 - 59 <input type="checkbox"/> 60 - 69 <input type="checkbox"/> 70 or older
2. What is the total number of years you have smoked cigarettes?	_____ years <input type="checkbox"/> 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 <input type="checkbox"/> 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?	<input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> I do not have a cough
7. Do you ever cough up phlegm (sputum) from your chest when you don't have a cold?	<input type="checkbox"/> YES <input type="checkbox"/> NO
8. Do you usually cough up phlegm (sputum) from your chest first thing in the morning?	<input type="checkbox"/> YES <input type="checkbox"/> NO
9. How frequently do you wheeze?	<input type="checkbox"/> Never <input type="checkbox"/> Occasionally or more often
10. Do you have or have you had any allergies?	<input type="checkbox"/> YES <input type="checkbox"/> 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 about how to answer a question, please give the best answer you can.*

<b>Please read the questions in this column...</b>	<b>...and mark a single answer in this column</b>
1. What is your age (in years)?	<input type="checkbox"/> 40 - 49 <input type="checkbox"/> 50 - 59 <input type="checkbox"/> 60 - 69 <input type="checkbox"/> 70 or older
2. What is the total number of years you have smoked cigarettes?	_____ years <input type="checkbox"/> 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 <input type="checkbox"/> I have never smoked cigarettes*
4. Have you coughed more in the past few years?	<input type="checkbox"/> YES <input type="checkbox"/> 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?	<input type="checkbox"/> YES <input type="checkbox"/> NO
6. Have you ever been admitted to hospital with breathing problems?	<input type="checkbox"/> YES <input type="checkbox"/> NO
7. Have you been short of breath more often in the past few years?	<input type="checkbox"/> YES <input type="checkbox"/> NO
8. On average, how much phlegm (sputum) do you cough up most days?	<input type="checkbox"/> Less than 1 tablespoon (15 ml) per day <input type="checkbox"/> 1 tablespoon (15 ml) per day or more
9. If you get a cold, does it usually go to your chest?	<input type="checkbox"/> YES <input type="checkbox"/> NO
10. Are you taking any treatment to help your breathing?	<input type="checkbox"/> YES <input type="checkbox"/> NO

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

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5.000	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7.500	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.000	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15.000	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
20.000	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
50.000	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Andere:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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