

# Multicenter study of the COPD-6 screening device: feasible for early detection of chronic obstructive pulmonary disease in primary care?

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**Background and aim:** Early detection of COPD may reduce the future burden of the disease. We aimed to investigate whether prescreening with a COPD-6 screening device (measuring FEV<sub>1</sub> and FEV<sub>6</sub>) facilitates early detection of COPD in primary care.

**Methods:** In primary care, individuals at high risk of COPD (ie, age  $\geq 35$  years, relevant exposure, and at least one respiratory symptom) and no previous diagnosis of obstructive lung disease were examined with a COPD-6 screening device. In prioritized order, the criteria for proceeding to confirmatory spirometry were FEV<sub>1</sub>/FEV<sub>6</sub>  $< 0.7$ , FEV<sub>1</sub>  $< 80\%$ pred, or clinical suspicion of COPD regardless of test result (medical doctor's [MD] decision). Based on spirometry, including bronchodilator (BD) reversibility test, individuals were classified as COPD (post-BD FEV<sub>1</sub>/FVC  $< 0.70$ ), asthma ( $\Delta$ FEV<sub>1</sub>  $\geq 0.50$  L), or no obstructive lung disease.

**Results:** A total of 2,990 subjects (54% men, mean age 59 years, and mean 28 pack-years) were enrolled, of whom 949 (32%) proceeded from COPD-6 screening to confirmative spirometry based on the following criteria: 510 (54%) FEV<sub>1</sub>/FEV<sub>6</sub>  $< 0.70$ , 382 (40%) FEV<sub>1</sub>  $< 80\%$ pred, and 57 (6%) MD decision. Following confirmative spirometry, the 949 individuals were diagnosed as having COPD (51%), asthma (3%), and no obstructive lung disease (45%). COPD was diagnosed in 487 (16%) of the enrolled subjects in whom confirmative spirometry was performed in 69% based on FEV<sub>1</sub>/FEV<sub>6</sub>  $< 0.7$  and in 29% based on FEV<sub>1</sub>  $\leq 80\%$ pred.

**Conclusion:** Prescreening with the COPD-6 device showed acceptable specificity for the selection of subjects for diagnostic spirometry and is likely to be a useful alternative to current practice in primary care.

**Keywords:** early COPD, diagnosis, spirometry, general practice

## Introduction

Previous studies have shown that opportunistic screening in primary care enables early diagnosis of chronic obstructive pulmonary disease (COPD).<sup>1,2</sup> However, in general, this practice is sparsely implemented. In population-based registry studies, only one third of subjects or less with newly diagnosed COPD had spirometry performed.<sup>3-6</sup> Furthermore, the requirement of conventional spirometry has been identified as a barrier to early diagnosis.<sup>7</sup> Delayed diagnosis is a missed opportunity for early secondary prevention, most importantly smoking cessation, which could substantially alter the prognosis.<sup>8</sup> The demand for screening of an increasing number of subjects has further stressed the need for a feasible procedure.

More than a decade ago, Buffels et al suggested that hand-held spirometers should be made available in primary care.<sup>9</sup> FEV<sub>6</sub> is a measure of forced expiratory volume in

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6 seconds as opposed to a full forced vital capacity (FVC) maneuver. Studies have suggested  $FEV_1/FEV_6$  measured by spirometry as a valid alternative to  $FEV_1/FVC$  in screening a high-risk population for COPD.<sup>10,11</sup> A meta-analysis based on 11 studies found a sensitivity of 0.89 (95% CI 0.83–0.93) and specificity of 0.98 (95% CI 0.95–0.99) for  $FEV_1/FEV_6$  in recognition of airway obstruction.<sup>12</sup> Several studies have concluded that hand-held screening devices including the COPD-6 and PiKo-6 device are reliable in screening for airway obstruction and selecting subjects for further diagnostic workup.<sup>13–20</sup> A recent meta-analysis concluded that the accuracy of  $FEV_1/FEV_6$  measured by hand-held devices seems to be lower than spirometry, but sufficiently accurate to screen for airway obstruction.<sup>21</sup>

Existing studies of hand-held screening devices have called for studies conducted in a realistic screening setting. This study aimed to investigate whether prescreening with a COPD-6 device facilitates early detection of COPD in a primary care setting.

## Materials and methods

### Materials

Denmark has ~3,600 general practitioners (GPs), covering a population of 5.9 million. We aimed to include a representative sample, on a voluntary basis, comprising 180 GPs (corresponding to 5% of Danish GPs) from all over Denmark. Written information about the study as well as the invitation to participate was distributed to all interested GPs by the sponsor's local representative.

More than 95% of Danish GPs own a spirometer, which was a requirement to participate in this study. Subjects were eligible for enrollment in the study provided they fulfilled the inclusion criteria based on recommendations from the Danish National Board of Health on opportunistic screening for COPD: age  $\geq 35$  years, smoker/ex-smoker or other risk exposures for COPD, at least one respiratory symptom (dyspnea, cough, wheeze, sputum, or recurrent respiratory tract infections)<sup>31</sup> and had no previous diagnosis of obstructive lung disease or treatment with inhaler medication within the last 12 months. Exclusion criteria were absence of informed consent and inability to perform COPD-6- or spirometry procedure.

### Methods

This multicenter study was conducted from March to December 2015. Based on the spirometry guidelines from the Danish Respiratory Society,<sup>32</sup> participating GPs were educated in the functions of the COPD-6 (Vitalograph®, Buckingham, UK) and spirometry procedures. The COPD-6

test was repeated three times with the highest values recorded. The device automatically detected blows of poor quality (start too slow, coughing, or  $< 3$  seconds duration of blow). Spirometry was performed with at least three forced expiratory maneuvers (and at least two measurements of  $FEV_1$  and FVC, differing by  $< 5\%$ ). European Community of Steel and Coal reference values for lung function were used.<sup>33</sup>

The bronchodilator (BD) reversibility tests were performed with 0.4 mg inhaled salbutamol (or equivalent) followed by repeated spirometry 15 minutes later. All procedures were performed in general practice.

Subjects who fulfilled the criteria for inclusion were screened with the COPD-6 device (screening test) and proceeded to diagnostic spirometry with BD reversibility test, based on three criteria in prioritized order: 1) airway obstruction ( $FEV_1/FEV_6 < 0.70$ ), 2) lung function impairment, that is,  $FEV_1 < 80\%pred$ , or 3) medical doctor's (MD) decision ( $FEV_1/FEV_6$  close to 0.70 and sustained suspicion of COPD). The prioritized order meant that subjects presenting with both airway obstruction and decreased lung function were categorized into airway obstruction. Based on the findings at the diagnostic spirometry, subjects were categorized as asthma ( $\Delta FEV_1 \geq 0.50$  L), COPD (post-BD  $FEV_1/FVC$  ratio  $< 0.70$ ), or no obstructive lung disease (remaining individuals).

### Data handling and analysis

The aim was to identify at least 500 subjects with COPD and thereby allow for subgroup analyses. Recruitment of 180 GPs was estimated to be sufficient based on, 1) an expected inclusion of at least 30 subjects by each GP, 2) a 15% prevalence of COPD, and 3) an expected dropout rate of 10%.

Data on age, sex, height, body weight, smoking status and/or other risk exposure, pack-years, respiratory symptoms (described above), severity of dyspnea (Medical Research Council scale),<sup>34</sup> and results of COPD-6 ( $FEV_1$ ,  $FEV_6$ ) and spirometry ( $FEV_1$ , FVC, post-BD  $FEV_1$ , and FVC) were entered into a consolidated web-based database. Body mass index (BMI),  $FEV_1/FEV_6$ , and  $FEV_1/FVC$  were automatically calculated and recorded.

Statistical analyses were performed by using IBM SPSS version 21 (IBM Corporation, Armonk, NY, USA). Analyses were limited to subjects with complete data. Continuous data were tested for normality and paired *t*-test was applied if applicable. For continuous non-normal distributed data, Mann–Whitney *U* test was used. Categorical data were analyzed by Pearson's chi-squared test. A significance level of 0.05 was set in all analyses.

## Ethics

The study was endorsed by the Danish College of General Practitioners. According to the European Federation of Pharmaceutical Industries and Associations code and the Danish Association of the Pharmaceutical Industry, the present study was a non-drug, non-interventional study. Approval from the Danish Scientific Ethics Committee and The Danish Medicines Agency was not mandatory, but they were given all relevant study information. Data handling was approved by the Danish Data Protection Agency.

## Results

### Characteristics of enrolled subjects

A total of 149 GPs participated in the study, representing a nationwide sample of both large and small clinics. A total of 2,990 subjects were tested with the COPD-6 screening tool and had complete data (Figure 1). The study population had a mean age of 59 years (range 35–92 years), mean 28 pack-years of smoking, 54% current smokers, and a COPD-6 mean FEV<sub>1</sub> of 2.6 L (88%pred) (Table 1).

### Prevalence of COPD

According to the predefined criteria, confirmative spirometry was indicated in 949 cases (32% of study population) distributed as follows: 510 FEV<sub>1</sub>/FEV<sub>6</sub> <0.7 (with or without FEV<sub>1</sub> <80%pred), 382 FEV<sub>1</sub> <80%pred, and 57 MD decision. Of the 949 subjects tested with diagnostic spirometry, 487 (51%) fulfilled the criteria for COPD (corresponding to 16% of the study population), 31 (3%) were categorized

as having asthma ( $\Delta$ FEV<sub>1</sub> >0.5 L), and 431 (45%) as “no obstructive lung disease” (Figure 1).

The prevalence of COPD in subjects selected for diagnostic spirometry by criteria FEV<sub>1</sub>/FEV<sub>6</sub> <0.70 was 352/510 (69%) and 110/382 (29%) based on the criteria FEV<sub>1</sub> <80% alone (Figures 2 and 3). The prevalence of airway obstruction at the COPD-6 test and at the pre- and post-BD spirometry are given in Table 2.

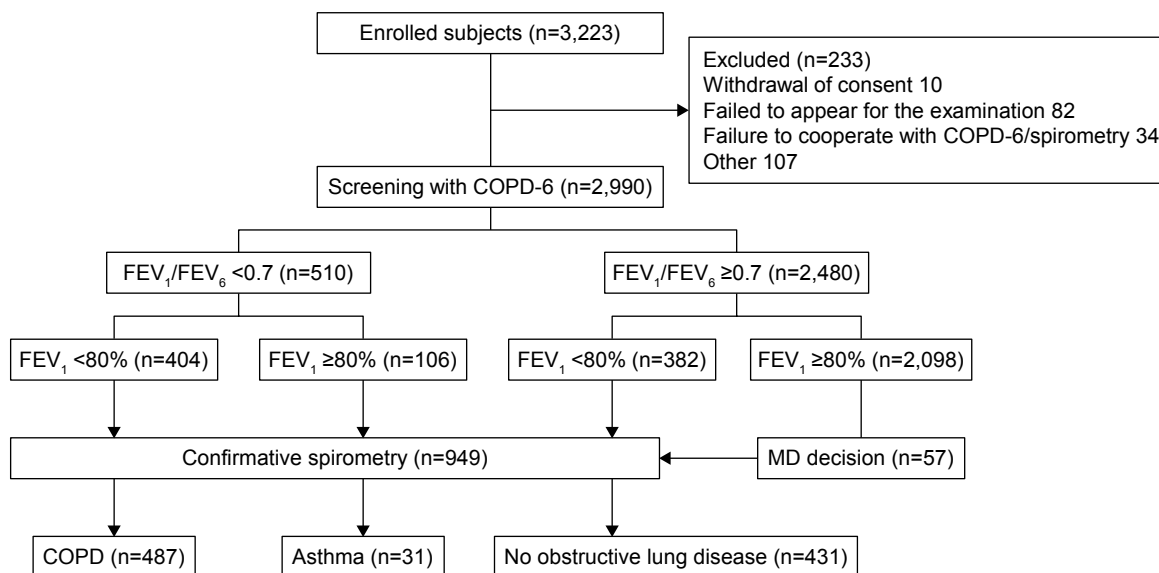
### Criteria for confirmative spirometry

Applying the single criteria FEV<sub>1</sub>/FEV<sub>6</sub> <0.70 for further diagnostic work-up, 17% of the screened population would have proceeded to confirmative spirometry. However, compared to the combined criteria used in the current study, a diagnosis of COPD would have been missed in 135 (487–352) subjects, corresponding to 27% of all subjects diagnosed with COPD in the study. In total, 439 subjects had an FEV<sub>1</sub>/FEV<sub>6</sub> ≥0.70 at the COPD-6 test, but proceeded to diagnostic spirometry based on FEV<sub>1</sub> <80%pred (382) or MD decision (57). Of these subjects, 137 had a post-BD <0.7 and 135 (31%) were diagnosed with COPD (Table 2).

For each subject diagnosed with COPD, six COPD-6 tests and two diagnostic spirometry procedures were performed.

### Characteristics of subjects screened only with COPD-6 test

Subjects who did not meet criteria for diagnostic spirometry were in comparison to subjects diagnosed with COPD, significantly younger, had less tobacco exposure, and had an overall



**Figure 1** CONSORT diagram of enrolled subjects.

**Notes:** The following diagnostic criteria were applied: 1) COPD: post-bronchodilator (BD) FEV<sub>1</sub>/FVC <0.7 and <0.5 L post-BD increase in FEV<sub>1</sub>, 2) asthma: post-BD FEV<sub>1</sub> increase ≥0.5 L, and 3) no obstructive lung disease, that is, not fulfilling any of these criteria.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; FEV, forced expiratory volume; FVC, forced vital capacity; MD, medical doctor's.

**Table 1** Baseline characteristics of all enrolled subjects (n=2,990) and classification according to whether participants were only screened with COPD-6 test (n=2,041) or proceeded to confirmative spirometry (n=949)<sup>a</sup>

	All (n=2,990)	COPD-6 test only (n=2,041)	Confirmative spirometry (n=949)	P-value <sup>b</sup>
Sex, male	1,624 (54%)	1,119 (55%)	505 (53%)	NS
Age (years)	59 (11.7)	58 (11.7)	62 (11.0)	<0.001
BMI (kg/m <sup>2</sup> )	28 (5.7)	27 (5.6)	27 (5.9)	NS
Pack-years	28 (20.0)	25 (18.8)	34 (22.2)	<0.001
FEV <sub>1</sub> (L)	2.6 (0.8)	2.9 (0.73)	2.0 (0.64)	
FEV <sub>1</sub> %pred	88 (18.9)	97 (12.8)	69 (15.1)	
FEV <sub>6</sub> (L)	3.4 (0.97)	3.7 (0.92)	2.9 (0.86)	<0.001
Symptoms				
Cough	1,825 (61%)	1,232 (60%)	593 (63%)	NS
Dyspnea	1,144 (38%)	724 (36%)	420 (44%)	<0.001
Wheezing	298 (10%)	151 (7%)	147 (16%)	<0.001
Sputum	544 (18%)	327 (16%)	217 (23%)	<0.001
Recurrent RTI	112 (4%)	65 (3%)	47 (5%)	0.018
MRC <sup>c</sup>				
1	NA	NA	176 (19%)	
2	NA	NA	234 (25%)	
3	NA	NA	83 (9%)	
4	NA	NA	13 (1%)	
5	NA	NA	2 (0.43%)	

**Notes:** <sup>a</sup>Numerical data presented as mean (SD) and categorical data as n (%).

<sup>b</sup>Subjects screened only with the COPD-6 test compared to subjects who proceeded to confirmative spirometry. <sup>c</sup>Medical Research Council dyspnea scale.

**Abbreviations:** BMI, body mass index; FEV, forced expiratory volume; MRC, Medical Research Council; NA, not applicable; NS, not significant; RTI, Respiratory tract infections.

lower occurrence of respiratory symptoms with significantly less dyspnea, wheezing, and sputum (Table 1). As expected, the FEV<sub>1</sub> was also on average significantly higher; 2.9 versus 2.0 L (97% vs 69% predicted), respectively.

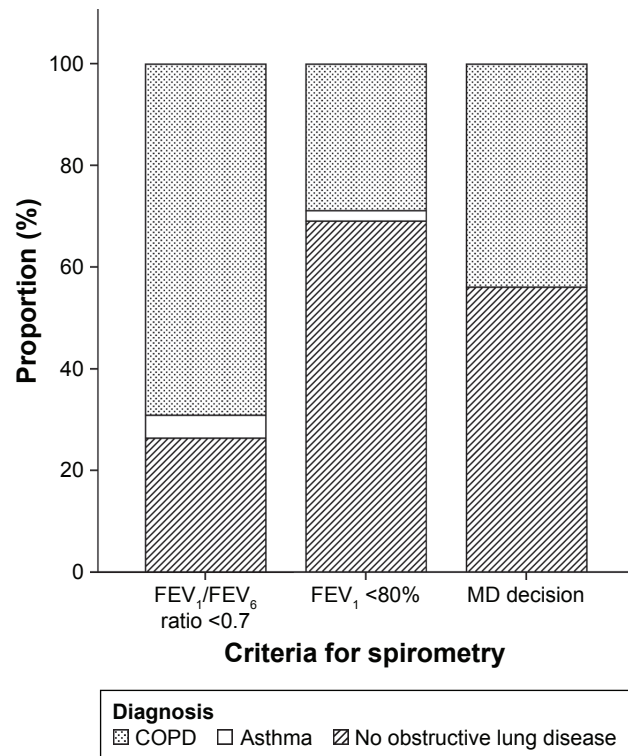
## Characteristics of subjects with COPD compared to other diagnostic groups

Compared to subjects categorized as having asthma, subjects with COPD had significantly more pack-years and lower FEV<sub>1</sub> and FVC (Table 3). There were no significant differences in symptoms between the two groups, although occurrence of sputum tended to be higher in subjects with COPD.

Subjects with COPD, compared to subjects categorized as having no obstructive lung disease, had significant higher age, lower BMI, and higher number of pack-years and had significantly higher occurrence of dyspnea and sputum (Table 3).

In the group with no obstructive lung disease, 215 (50%) subjects had FEV<sub>1</sub>>80%pred. For participants finally classified as having no obstructive lung disease, but having a confirmatory spirometry performed based on FEV<sub>1</sub>/FEV<sub>6</sub> ratio <0.70, 50% had a FEV<sub>1</sub>/FEV<sub>6</sub> ratio close to 0.7 (≥0.65). The mean increase in FEV<sub>1</sub> at the BD reversibility test was 0.14 L (0.10).

Detailed spirometry data according to the three criteria for diagnostic spirometry are presented in Table 4.



**Figure 2** Prevalence of final diagnosis, that is, COPD, asthma, or no obstructive lung disease, according to the three different criteria for proceeding to confirmative spirometry.

**Notes:** Criteria for, 1) COPD: post-bronchodilator (BD) FEV<sub>1</sub>/FVC <0.7 and ΔFEV<sub>1</sub> <0.5 L at BD reversibility test; 2) asthma: ΔFEV<sub>1</sub> ≥0.5 L at BD reversibility test; Non-OLD: not fulfilling criteria 1) or 2). MD decision: MD decision to perform confirmative spirometry based on suspicion of COPD and an FEV<sub>1</sub>/FVC ratio close to 0.7. Subjects with both FEV<sub>1</sub>/FEV<sub>6</sub> ratio <0.7 and FEV<sub>1</sub> <80% were counted in the group "FEV<sub>1</sub>/FEV<sub>6</sub> ratio <0.7".

**Abbreviations:** FEV, forced expiratory volume; FVC, forced vital capacity; MD, medical doctor's; OLD, obstructive lung disease.

## Discussion

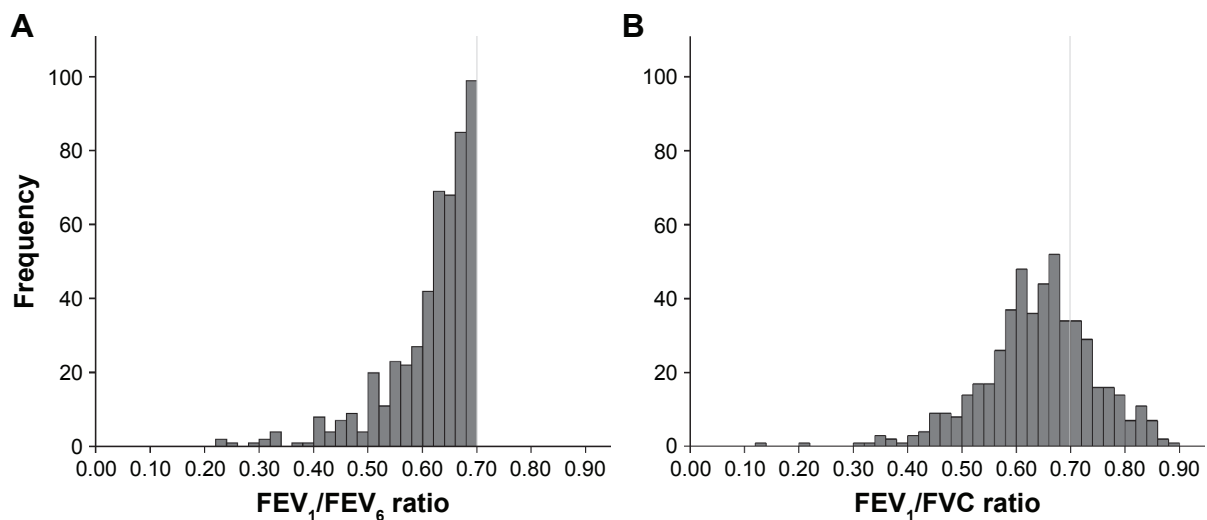
### Main findings

The study demonstrates that, in a real-life setting, prescreening of high-risk subjects with the COPD-6 device followed by spirometry in selected cases can identify COPD in a high percentage of subjects (16%). Selection of subjects for confirmatory spirometry based on a single criteria FEV<sub>1</sub>/FEV<sub>6</sub> <0.70 was found to be insufficient, and the sensitivity was markedly increased primarily by adding the criterion FEV<sub>1</sub> <80%pred, and to a lesser extent the criterion MD decision.

Screening with the COPD-6 device showed acceptable specificity for the selection of subjects for diagnostic spirometry.

### Interpretation of findings in relation to previously published work

A COPD prevalence of 16% was comparable to findings (17%) reported from a previous study with similar study design, but screening performed only by conventional spirometry.<sup>2</sup>



**Figure 3** Comparison of the  $FEV_1/FEV_6$  ratio for subjects with airway obstruction (defined as  $FEV_1/FEV_6 < 0.70$ ) at the COPD-6 test (**A**) ( $n=510$ ) with the  $FEV_1/FVC$  ratio at the subsequent post-BD spirometry (**B**).

**Abbreviations:** BD, bronchodilator; FEV, forced expiratory volume; FVC, forced vital capacity.

A post hoc analysis of data from that study showed that six screening spirometry and 1.4 confirmative spirometry procedures had to be performed per diagnosed subject with COPD.<sup>22</sup> Compared to the current study, the COPD-6 device as expected did not reduce the total number of procedures (screening tests plus diagnostic tests), but worked as a replacement for the conventional spirometry screening test.

Six other GP multicenter studies of screening with a COPD-6 device for early detection of COPD were identified. In accordance with the other studies, the vast majority of subjects in the current study had mild to moderate disease. For subjects with available data also on exacerbations, two-thirds belonged to GOLD group A.

One study (Miravittles et al) had to be disregarded as it was published only in Spanish.<sup>18</sup> The two studies by Muller et al and Represas-Represas et al only included subjects if they had respiratory symptoms and exposure to tobacco smoke.<sup>14,19</sup>

**Table 2** Prevalence of airway obstruction ( $FEV_1/FVC < 0.70$ ) at the COPD-6 test and at pre- and post-bronchodilator spirometry according to criteria for performing confirmative spirometry

Criteria for spirometry	COPD-6	Spirometry pre-BD <sup>a</sup>	Spirometry post-BD <sup>b</sup>
(A) $FEV_1/FEV_6 < 0.7$ ( $n=510$ )	510	402 (79%)	368 (72%)
(B) $FEV_1 < 80\%pred^c$ ( $n=382$ )	NA	139 (36%)	112 (29%)
(C) MD <sup>d</sup> ( $n=57$ )	NA	31 (54%)	25 (44%)
All ( $n=949$ )	510	572 (60%)	505 (53%)

**Notes:** <sup>a</sup>Pre-BD values. <sup>b</sup>Post-BD values. <sup>c</sup>Subjects with both  $FEV_1/FEV_6 < 0.7$  and  $FEV_1 < 80\%pred$  included in A. <sup>d</sup>MD decision (continued clinical suspicion of COPD and  $FEV_1/FEV_6$  close to 0.70).

**Abbreviations:** BD, bronchodilator; FEV, forced expiratory volume; FVC, forced vital capacity; MD, medical doctor's; NA, not applicable.

Muller et al<sup>19</sup> included 17,856 subjects and found airway obstruction ( $FEV_1/FEV_6 < 0.7$ ) in 17% of the subjects, and interestingly, a diagnosis of COPD was independently suspected by the MD three times more than indicated by the COPD-6 device. No data from confirmative spirometry was included in the study, thus, direct comparison with our study is not possible. A recent smaller study by Represas-Represas et al included a mixed cohort of 362 subjects from general practice, emergency services, and community pharmacies and found a COPD prevalence of 40% in the general practice cohort ( $n=167$ ).<sup>23</sup> The high prevalence of COPD most likely reflects a much higher tobacco exposure compared to the current study (75% active smokers, mean pack-years 39). An optimal cutoff of  $FEV_1/FEV_6$  of 0.8 was proposed corresponding to a sensitivity of 92% and specificity of 53%.

Llordes et al included 407 subjects and found a COPD prevalence of 26%.<sup>24</sup> The study was similar to our study with regard to smoking exposure and age, and no obvious explanation for the difference in prevalence can be identified based on the available information. Different screening strategies including screening questionnaires and the COPD-6 device were tested, and the latter was found significantly superior with an  $FEV_1/FEV_6$  cutoff of 0.78 (sensitivity 88% and specificity 72%).

Another multicenter study by Thorn et al including 305 subjects found a COPD prevalence of 25%.<sup>17</sup> The higher prevalence of COPD in that study was likely due to inclusion criteria with a minimum smoking exposure of  $\geq 15$  pack-years. An  $FEV_1/FEV_6$  cutoff of 0.73 was suggested, which corresponds to a sensitivity and specificity of 79% and 80%,

**Table 3** Characteristics of subjects diagnosed with COPD compared to subjects diagnosed with asthma and no obstructive lung disease (no OLD)<sup>a,b</sup>

	<b>COPD (n=487)</b>	<b>Asthma (n=31)</b>	<b>P-value (COPD vs asthma)</b>	<b>No OLD (n=431)</b>	<b>P-value (COPD vs no OLD)</b>
Sex, male	259 (53%)	22 (71%)	0.054	224 (52%)	0.714
Age (years)	64 (10.5)	63 (12.5)	0.433	61 (11.2)	<0.001
BMI (kg/m <sup>2</sup> )	26 (5.1)	28 (5.8)	0.061	28 (6.5)	<0.001
Pack-years	37 (21.4)	27 (17.6)	0.005	30 (22.8)	<0.001
FEV <sub>1</sub> (L)	2.0 (0.65)	3.0 (0.92)	<0.001	2.4 (0.73)	<0.001
FEV <sub>1</sub> %pred	72 (16.9)	87 (21.1)	<0.001	80 (14.8)	<0.001
FVC (L)	3.3 (0.98)	4.5 (1.3)	<0.001	3.1 (0.93)	<0.001
FEV <sub>1</sub> /FVC	0.61 (0.08)	0.69 (0.14)	0.005	0.77 (0.06)	<0.001
ΔFEV <sub>1</sub> (L)	0.08 (0.18)	0.74 (0.30)	<0.001	0.05 (0.18)	<0.001
<b>Symptoms</b>					
Cough	309 (63%)	18 (58%)	0.547	266 (62%)	0.588
Dyspnea	242 (50%)	15 (48%)	0.888	163 (38%)	<0.001
Wheezing	77 (16%)	6 (19%)	0.602	64 (15%)	0.687
Sputum	129 (27%)	6 (19%)	0.380	82 (19%)	0.007
Recurrent RTI	22 (5%)	1 (3%)	0.735	24 (6%)	0.466
<b>MRC<sup>c</sup></b>					
1	142 (34%)	8 (50%)		26 (6%)	
2	194 (47%)	7 (44%)		33 (8%)	
3	64 (15%)	7 (44%)		18 (4%)	
4	13 (3%)	0 (0%)		0 (0%)	
5	2 (0.5%)	0 (0%)		0 (0%)	
<b>GOLD stage<sup>d</sup></b>					
I	152 (31%)				
II	294 (60%)				
III	38 (8%)				
IV	3 (1%)				
<b>GOLD group<sup>d,e</sup></b>					
A	303 (62%)				
B	57 (12%)				
C	33 (7%)				
D	22 (5%)				

**Notes:** <sup>a</sup>1) Criteria for COPD: post-BD FEV<sub>1</sub>/FVC <0.7 and ΔFEV<sub>1</sub> <0.5 L at BD reversibility test; 2) Asthma: ΔFEV<sub>1</sub> ≥0.5 L at BD reversibility test; No OLD: not fulfilling criteria 1) or 2). <sup>b</sup>Numerical data presented as mean (SD) and categorical data as n (%). <sup>c</sup>Medical Research Council dyspnea scale. <sup>d</sup>Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for Diagnosis, Management and Prevention of COPD; 2016. <sup>e</sup>In 72 (15%) cases, the number of exacerbations was not recorded, thus the GOLD group could not be specified.

**Abbreviations:** BD, bronchodilator; BMI, body mass index; FEV, forced expiratory volume; FVC, forced vital capacity; MRC, Medical Research Council; OLD, obstructive lung disease; RTI, Respiratory tract infections.

respectively and at a cutoff of 0.7, the numbers were 53% and 90%, respectively. They concluded that the COPD-6 device may reduce the number of unnecessary spirometry tests, and the results were similar to two other studies, in which an almost similar device (Piko-6, measuring FEV<sub>1</sub>/FEV<sub>6</sub>) was validated for the prediction of COPD.<sup>15,16</sup> None of the described studies accounted for the occurrence of asthma in the cohort. The present study also differed in the use of a combined criteria for confirmatory spirometry including both FEV<sub>1</sub>/FEV<sub>6</sub> ratio <0.7 and FEV<sub>1</sub> <80%pred.

While general screening of all individuals with smoking exposure is not recommended, US Preventive Services

Task Force (USPSTF) recently recommended screening of all exposed individuals with respiratory symptoms, which is in concordance with the latest recommendations from GOLD.<sup>25,26</sup>

Studies of spirometry and the correlation between FEV<sub>1</sub>/FEV<sub>6</sub> ratio and FEV<sub>1</sub>/FVC have suggested that the cutoff for airway obstruction when using FEV<sub>6</sub> should be set at a significantly higher level.<sup>11,12,27,28</sup> Accordingly studies of the COPD-6 device show that the best correlation to an FEV<sub>1</sub>/FVC ratio of 0.7 is an FEV<sub>1</sub>/FEV<sub>6</sub> ratio of 0.73–0.75.<sup>14,17,18</sup> However, our COPD-6 device was technically limited to a cutoff value for airway obstruction of 0.7. Thus, the combined

**Table 4** Spirometry data grouped by selection criteria for confirmative spirometry

	Criteria A <sup>a</sup> (n=510)	Criteria B <sup>b</sup> (n=382)	Criteria C <sup>c</sup> (n=57)
COPD-6			
FEV <sub>1</sub> (L)	1.9 (0.65)	2.06 (0.52)	2.72 (0.63)
FEV <sub>1</sub> <80%pred	65% (17.6)	70% (7.5)	91% (8.4)
FEV <sub>6</sub> (L)	3.0 (0.93)	2.68 (0.67)	3.57 (0.87)
FEV <sub>1</sub> /FEV <sub>6</sub> ratio	0.62 (0.08)	0.77 (0.05)	0.77 (0.06)
Confirmative spirometry <sup>d</sup>			
FEV <sub>1</sub> (L)	2.18 (0.76)	2.24 (0.64)	2.73 (0.68)
FEV <sub>1</sub> <80%pred	75% (19.2)	77% (13.4)	88% (15.4)
FVC (L)	3.39 (1.10)	3.06 (0.85)	3.81 (0.94)
FEV <sub>1</sub> /FVC ratio	0.64 (0.11)	0.73 (0.08)	0.72 (0.07)
ΔFEV <sub>1</sub> (L)	0.11 (0.31)	0.07 (0.17)	0.03 (0.15)
ΔFEV <sub>1</sub> >0.2 L and 12%	88 (17%)	40 (10.5%)	1 (1.8%)

**Notes:** <sup>a</sup>FEV<sub>1</sub>/FEV<sub>6</sub> <0.7. <sup>b</sup>FEV<sub>1</sub> <80% predicted. Subjects with both FEV<sub>1</sub>/FEV<sub>6</sub> <0.7 and FEV<sub>1</sub> <80% predicted are counted as A. <sup>c</sup>Medical Doctor's decision (continued suspicion of COPD and FEV<sub>1</sub>/FEV<sub>6</sub> ~0.7). <sup>d</sup>Post-bronchodilator values.

**Abbreviations:** FEV, forced expiratory volume; FVC, forced vital capacity.

criterion for diagnostic spirometry was decided in order to compensate for the risk of insufficient sensitivity. Our results confirmed the issue by showing that although 439 diagnostic spirometry procedures could be spared, 27% of the subjects with COPD in the study would have been missed by the single criterion diagnostic algorithm. Accordingly, of the 439 subjects with a normal COPD-6 test who proceeded to diagnostic spirometry based on the other two criteria, 31% was diagnosed with COPD.

GOLD recommends a simple and operational definition of airway obstruction in primary care (post-BD FEV<sub>1</sub>/FVC <0.70) and points out the risk of over-diagnosis in the elder- and under-diagnosis of the younger population.<sup>26</sup> The MD decision criterion, by which the GP was allowed to perform diagnostic spirometry in subjects with FEV<sub>1</sub>/FEV<sub>6</sub> close to 0.7, was in accordance with GOLD recommendations.

Significant BD reversibility is not uncommon in COPD.<sup>29</sup> In the current study, a strict definition of asthma (FEV<sub>1</sub> change >0.5 L) was chosen not only to exclude this group of subjects but also because some of these participants may have asthma-COPD overlap.<sup>30</sup> As a result, the group of subjects diagnosed as having asthma was small (n=31). As expected, compared to the asthma group, the COPD group had significantly higher tobacco exposure, lower FEV<sub>1</sub>, and a trend toward a higher occurrence of sputum.

Subjects in the category “no obstructive lung disease” were overall a little younger with less tobacco exposure and less dyspnea and sputum. Half the subjects had normal FEV<sub>1</sub> at confirmative spirometry and the majority of the group

were overweight or obese, most likely representing subjects without clinically significant lung disease, although some individuals may have asthma despite an only moderate, or no, response to a BD.

## Strengths and limitations of this study

The number of GPs enrolled was less than the planned 180 GPs. Nevertheless, the aim of identifying 500 subjects with COPD was largely met (n=487). An acceptable number of potentially eligible subjects (n=233) were excluded for various reasons; further details are given in Figure 1. The study sample was large and included 149 GPs with a wide geographical representation from across the nation including large and small GP clinics. Thus, the results are very likely to be representative for GP clinics in general, at least in Denmark. The study group had a wide representation of age and an even distribution of sex. A large proportion (more than half) of the study population were current smokers. With regard to the subjects who did not proceed to diagnostic spirometry, the characteristics seem to justify exclusion: younger, less tobacco exposure, less symptoms, and a mean FEV<sub>1</sub> predicted of 97%. Furthermore, in order to improve the quality of the COPD-6 and spirometry test, experienced personnel visited the clinics and gave training in performing the procedures.

It limits the study that confirmative spirometry was not conducted on all included patients. Thus, the extent of false-negative COPD-6 procedures could not be examined. However, the number of COPD patients found in the study equals what was expected based on a prior spirometry screening study also in Danish primary care, which indicates few false negatives.<sup>22</sup> Furthermore, the possibility of a false-negative COPD-6 test and missed COPD diagnosis was limited to subjects with mild disease (FEV<sub>1</sub> >80%). Conducting both COPD-6 and conventional spirometry on all included patients would have conflicted with the secondary aim of the study to test whether the GPs found the COPD-6 device feasible in everyday work. However, by leaving it out, a direct comparison of COPD-6 and conventional spirometry in COPD screening could not be done.

## Implications for future research, policy, and practice

As the COPD-6 screening test seems to be less time consuming and easier to perform, our results support the procedure as a favorable alternative which can facilitate the detection of COPD in primary care. The important aspect of the

participating GPs' experience with the COPD-6 screening tool is, therefore, currently being studied.

With focus on the COPD-6 device as a possible quick and handy screening tool, quality of the procedure must not be neglected. Standardization of the procedure is important to ensure reliability and reproducibility, as done in the present study.

## Conclusion

The COPD-6 device seems to be a feasible alternative to conventional spirometry for early detection of COPD in general practice. Qualitative evaluation is necessary to fully assess the potential of the device in overcoming current barriers in screening for COPD in high-risk populations. Consensus on the exact criteria for performing confirmative spirometry including the optimal cutoff value for FEV<sub>1</sub>/FEV<sub>6</sub> ratio is needed.

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## Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

## Disclosure

All the authors are members of the TOPTrack steering committee. The authors report no other conflicts of interest in this work.

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