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Identifying cases of undiagnosed, clinically significant COPD in primary care: qualitative insight from patients in the target population

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BACKGROUND: Many cases of chronic obstructive pulmonary disease (COPD) are diagnosed only after significant loss of lung function or during exacerbations.

AIMS: This study is part of a multi-method approach to develop a new screening instrument for identifying undiagnosed, clinically significant COPD in primary care.

METHODS: Subjects with varied histories of COPD diagnosis, risk factors and history of exacerbations were recruited through five US clinics (four pulmonary, one primary care). Phase I: Eight focus groups and six telephone interviews were conducted to elicit descriptions of risk factors for COPD, recent or historical acute respiratory events, and symptoms to inform the development of candidate items for the new questionnaire. Phase II: A new cohort of subjects participated in cognitive interviews to assess and modify candidate items. Two peak expiratory flow (PEF) devices (electronic, manual) were assessed for use in screening.

RESULTS: Of 77 subjects, 50 participated in Phase I and 27 in Phase II. Six themes informed item development: exposure (smoking, second-hand smoke); health history (family history of lung problems, recurrent chest infections); recent history of respiratory events (clinic visits, hospitalisations); symptoms (respiratory, non-respiratory); impact (activity limitations); and attribution (age, obesity). PEF devices were rated easy to use; electronic values were significantly higher than manual ($P < 0.0001$). Revisions were made to the draft items on the basis of cognitive interviews.

CONCLUSIONS: Forty-eight candidate items are ready for quantitative testing to select the best, smallest set of questions that, together with PEF, can efficiently identify patients in need of diagnostic evaluation for clinically significant COPD.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the most common lung conditions seen in clinical practice and the fourth leading cause of death worldwide.¹ Internationally, data suggest that only a fraction of those with COPD (9 to 22%) have been diagnosed.² In the United States, analyses of data from the Third National Health and Nutrition Examination Survey (NHANES 2007–2010) found that fewer than 50% of adults with airflow obstruction have been told they have COPD.³

Goals of COPD management include relieving symptoms, improving exercise capacity and reducing the risk of acute exacerbations of COPD.^{4–6} Long-acting inhaled therapies, supplemental oxygen and pulmonary rehabilitation are particularly beneficial to symptomatic patients and to those with a forced expiratory volume in one second (FEV₁) less than 60% predicted.⁶ Exacerbations are common and costly events associated with decline in lung function,^{7–9} impaired health-related quality of life^{10,11} and death.¹² A history of acute exacerbations of COPD represents the most important risk factor for subsequent events,¹³ with treatments available to decrease frequency and improve outcomes.^{4,12}

There is evidence suggesting that many patients are first diagnosed with COPD when their airway obstruction has progressed substantially or during an acute respiratory illness.^{14–19} Studies in primary care suggest that the proportion of newly diagnosed COPD patients with moderate-to-severe airway obstruction in primary care ranges from 43% (Scotland, Colorado)¹⁵ to 70% (Greece).¹⁶ A United States managed care database analysis suggested that 31% were GOLD III or IV,¹⁷ whereas a study in China found that 86% were moderate to severe and 34% had ≥ 2 exacerbations the prior year.¹⁸ Exacerbation history is further exemplified by a study in France where investigators found that 96% of patients with newly diagnosed chronic bronchitis had been treated with antibiotics for similar episodes in the past year and 41% had at least two such episodes.¹⁹ Identifying individuals with undiagnosed clinically significant COPD (FEV₁ < 60% predicted or exacerbation risk) should set in motion effective medical treatment and improve short- and long-term health outcomes.

Several instruments have been proposed for COPD case identification, defined by airflow limitation (FEV₁/FVC (forced vital capacity) < 0.70) without reference to exacerbation risk.^{20–32}

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Table 1. Sample diagnostic and risk status classification (N = 50)

Group	Subgroup	Description	Number (N)
COPD, recently diagnosed	Group 1	COPD—GOLD II ^a Diagnosed ≤ 6 months No history of respiratory events in the past year ^b	7
	Group 2	COPD—GOLD II–IV ^a ≥ 1 respiratory event in the past year ^a Diagnosed ≤ 6 months	13
At-risk, no COPD	Group 3	2–3 risk factors ^c No COPD diagnosis	20
	Group 4	≥ 4 risk factors ^c No COPD diagnosis	10

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in one second; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

^aGOLD Stage II (FEV₁% predicted 50–80%), Stages II–IV (FEV₁% predicted < 50%), pre-bronchodilator.

^bRespiratory event defined by colds, upper respiratory infection, missed work, clinic visit/ER visit/hospitalisation.

^cSymptoms (shortness of breath with activity; cough; phlegm (sputum) in the absence of a cold, wheezing); exposure (cigarette smoking; second-hand tobacco or other kinds of smoke at home or work; dust, gases or dirty air at work); health history (asthma; serious childhood breathing conditions; colds settling in the chest); recent history (≥ 1 respiratory event in the past year with missed work; clinic or emergency room visit or hospitalisation).

Methods used to develop these instruments vary widely. Target and test populations range from those with a history of cigarette smoking only^{21,25,29} to populations of smokers and non-smokers,^{20,22,26,27,30,32} and settings that include primary care, specialty clinics^{20–22,26,28,30} and general population screening.^{25,29,32} A few of these development studies have utilised qualitative research methods to inform and refine instrument structure and content^{22,27,28} or tested the use of peak expiratory flow (PEF) along with a questionnaire to enhance precision.^{29–32}

A 2008 National Institutes of Health (NIH)-COPD Foundation workshop suggested a three-stage approach for identifying undiagnosed individuals with moderate-to-severe airflow obstruction (FEV₁ < 60%): a questionnaire to eliminate those unlikely to have severe disease, a simple measure of expiratory airflow to exclude those with normal or near-normal pulmonary function, and diagnostic evaluation, including clinical assessment and spirometry.³³ Nelson *et al.*³² tested the effectiveness of this approach, by screening 5,638 diagnosed and undiagnosed individuals from the general population attending public events. In this setting, 6.3% of 3,791 with ≥ 2 risk factors had abnormal PEF, suggesting that a more sensitive questionnaire is needed.

We are developing a new screening method for identifying cases of clinically significant COPD (FEV₁ < 60% and/or at risk for acute exacerbations of COPD) in primary care settings. The two-step process will include a questionnaire and pre-bronchodilator peak flow (PEF) to identify patients in need of further diagnostic evaluation. PEF will be measured using a familiar, inexpensive and widely available device for estimating the presence of airflow obstruction.^{31–33} Development methods for the questionnaire included a review of the literature,³⁴ analyses of three existing COPD data sets using random forests methodology³⁵ and qualitative research with individuals from the target population.

This paper presents the qualitative research used to inform thematic content, format, instructions and candidate items for the screening questionnaire. The intent was to develop a comprehensive pool of items for empirical testing, maximising content validity by using words and phrases easily understood by men and

women in the target population. Ease of use and equivalence of two PEF metres were also assessed.

MATERIALS AND METHODS

Study design

This was a two-phase qualitative study: Phase I (elicitation) included focus groups and interviews, and Phase II involved cognitive interviews (see Online Supplementary).

Sample

The Phase I sample included participants from one of four categories (see Table 1). COPD severity was based on airflow obstruction, defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD),³⁶ and risk factors based on the literature and data mining. Subjects in categories (groups) 1 and 2 provided information on symptoms, risk factors, history and other breathing-related issues from the perspective of people recently diagnosed with clinically significant COPD—the target population. Groups 3 and 4 were designed to provide insight into how experienced (risk factor) but non-COPD (diagnosis naive) subjects describe their respiratory symptoms, risk factors, history and other breathing-related issues.

Inclusion criteria were as follows: ≥ 40 years old; stable state spirometry (FEV₁, FEV₁% predicted, FEV₁/FVC) in the past 12 months (on file or willing to undergo spirometry at the time of data collection); and able to attend a focus group or telephone interview, read and speak English and to provide written informed consent. Individuals were not eligible if they had physical or psychological impairments precluding participation or were hospitalised for a respiratory infection within the past 30 days. Current smokers (≥ 10 pack-years), ex-smokers (history of ≥ 10 pack-years) and never smokers (≤ 100 cigarettes/pipes/cigars in a lifetime) were included.

Procedures

Participants were recruited from four pulmonary clinics and one primary care clinic in the United States. Convenience sampling was used; clinical members of the Study Group approached potential participants by phone or during clinic visits. Efforts were made to recruit a diverse sample in terms of age, smoking status and history, gender, race/ethnicity and educational level. The protocol was approved by a central Institutional Review Board and local Institutional Review Board at each site; written informed consent was obtained from all the participants.

Focus groups and interviews

Focus groups were held in a private room in the clinic; interviews were conducted by telephone. Experienced, trained research staff used a semi-structured interview guide to facilitate discussion. The guide included open-ended questions asking participants to describe their breathing-related symptoms and COPD risk-related experiences; COPD patients were also asked to consider these issues relative to their recent diagnosis. Sample questions for the COPD Groups (1 and 2) included the following: 'Looking back, were there any 'signals' that suggested you might have a breathing condition?' and 'What symptoms or experiences did you have that led you to believe you might have a breathing problem?' Sample questions for those without COPD (3 and 4) included the following: 'Describe your breathing for us. Are there any other symptoms you associate with your breathing?' and 'Can you think of any other experiences related to the symptoms we just discussed?'

Two researchers were present during focus groups: one served as moderator (LTM), while the second observed and took field notes (KK or AWS). Groups lasted 1.5–2 h, with breaks taken as needed. Telephone interviews were 1:1 (LTM, KK or AWS), with the interviewer taking notes, and they lasted for 20–50 min. Focus groups and interviews were audio-recorded and transcribed verbatim, with the data cleaned and de-identified for analyses.

Peak expiratory flow

Following each focus group or interview, clinical staff performed PEF on each participant using electronic (Vitalograph Asma-1 USB, Lenexa, KS, USA) and manual (Vitalograph AsmaPlan mech PFM) devices. Order of administration was randomised; SafeTway disposable mouthpieces were used. Upon completion, participants and staff completed ease-of-use

Table 2. Sample demographic characteristics

Characteristic	Total (N = 50)	COPD (Groups 1 & 2) (N = 20)	Risk, no COPD (Groups 3 & 4) (N = 30)
Age, Mean (s.d.)	60 (12)	62 (14)	58 (11)
Gender, n (%) Male	24 (48%)	7 (35%)	17 (57%)
Ethnicity, n (%)			
Hispanic or Latino	4/48 (8%)	2 (10%)	2/28 (7%)
Not Hispanic or Latino	44/48 (92%)	18 (90%)	26/28 (93%)
Racial background, n (%) ^a			
White	36 (72%)	17 (85%)	19 (63%)
Black or African American	13 (26%)	2 (10%)	11 (37%)
American Indian or Alaska Native	1 (2%)	1 (5%)	0 (0%)
Marital status, n (%)			
Married	16 (32%)	8 (40%)	8 (27%)
Other (single, divorced, separated, widowed)	34 (68%)	12 (60%)	22 (73%)
Employment status, n (%) ^a			
Employed	17 (34%)	6 (30%)	11 (37%)
Retired	13 (26%)	8 (40%)	5 (17%)
Disabled	14 (28%)	6 (30%)	8 (27%)
Other (student, unemployed, other)	9 (18%)	3 (15%)	6 (20%)
Education level, n (%)			
High school or less	16 (32%)	8 (40%)	8 (27%)
Some college, vocational training	22 (44%)	6 (30%)	16 (53%)
College degree or more	12 (24%)	6 (30%)	6 (20%)

Abbreviation: COPD, chronic obstructive pulmonary disease.

^aCategories are not mutually exclusive.

ratings (very easy, easy, neither difficult nor easy, difficult or very difficult to use).

Demographic and clinical measures

Participants also completed a sociodemographic and clinical history form, the RAND 36-Item Short Form Health Survey (SF-36)³⁷ and the COPD Assessment Tool,³⁸ a 10- to 15-min activity following the focus group or interview. Spirometric values (FEV₁, FEV₁% predicted, FEV₁/FVC) were obtained for all subjects, either from clinical charts (COPD groups) or by clinical site staff, at the time of the focus group or interview (no bronchodilation).

Data analysis

Using a content analysis approach, data (transcripts) were examined for key themes and constructs. A coding dictionary was developed and ATLAS.ti (version 7.1) was used to organise data. Two analysts independently coded the first transcript, and codes were compared and reconciled with senior scientific oversight. Terms and definitions in the coding dictionary were then refined for clarity. The remaining transcripts were coded thematically by one analyst and reviewed by a second analyst, with discrepancies resolved through discussion with the senior analyst. Saturation was defined by consistency of themes, construct descriptions or terms across groups and interviews.

Descriptive statistics were used to summarise sample characteristics, PEF values and PEF ease of use. A two-way analysis of variance was used to determine whether there was a significant difference between electronic and manual PEF values for participants with and without COPD. Paired-sample t-tests were used to compare PEF values between the electronic and manual devices within groups.

Item pool development and cognitive interviewing

Results were examined together with those from the literature review³⁴ and data mining³⁵ to inform the development of a pool of candidate questions for further evaluation and testing. Items were generated using an iterative process of development, review, revision, discussion and revision, with input from the High-Risk-COPD Screening Study Group.

Candidate questions with instructions were formatted in a questionnaire layout and evaluated by a new set of subjects from the target population using cognitive interviewing methodology (see Online Supplementary).

RESULTS

Eight focus groups ($n=44$) and six one-on-one telephone interviews ($n=6$) were conducted. Sample characteristics are summarised in Tables 2 and 3. For the COPD patients, mean post-bronchodilator FEV₁ was 68% predicted (s.d.=10) (mean FEV₁=2.21 (s.d.=0.8)), and time since diagnosis averaged three months.

Spirometric values for three cases in the non-COPD groups suggested possible airway obstruction; these participants were referred to their physician for follow-up. In two cases, spirometry was performed after their focus groups. The third case was uncovered after screening and enrolment, and the decision was made to have him participate in the originally assigned no-COPD group so that he could share his experiences in an environment of people without COPD experience. Data from these three cases were also examined separately, comparing their responses with others.

Six major themes were identified in the data: (1) exposure to smoke and other pollutants (e.g., chemicals, paint, gasoline), either through a friend/relative, work environment or living condition; (2) personal and family history of respiratory health conditions, such as emphysema, pneumonia, frequent colds and sinus infections; (3) recent history of respiratory events, including factors that may trigger an event (perfumes, cigarette smoke, exertion) and recent clinic visits or hospitalisations owing to respiratory symptoms such as shortness of breath, coughing and chest tightness that continued to worsen; (4) symptoms, including respiratory (e.g., shortness of breath with and without exertion, sputum and phlegm production, wheezing, chest tightness and congestion) and nonrespiratory (e.g., feeling tired after slight

Table 3. Sample clinical characteristics

Characteristic	Total (N = 50)	COPD (Groups 1 & 2) (N = 20)	Risk, no COPD (Groups 3 & 4) (N = 30)
<i>Smoking status and history</i>			
Never smoked, n (%)	17 (34%)	3 (15%)	14 (47%)
Smoked cigarettes, n (%)	32 (64%)	17 (85%)	15 (50%)
Former, n (%)	16/32 (50%)	6/17 (35%)	10/15 (67%)
Current, n (%)	16/32 (50%)	11/17 (65%)	5/15 (33%)
Age started smoking, mean (s.d.)	17 (4)	17 (5)	17 (4)
Duration of smoking (years)	33 (13)	37 (10)	29 (14)
Pack-years ^a	40 (32)	44 (34)	34 (30)
<i>Other risk factors, n (%) Yes</i>			
History of asthma	20 (40%)	9 (45%)	11 (37%)
Exposure (smoke, dust, gas, air)	41 (82%)	18 (90%)	23 (77%)
Colds move to chest	35 (70%)	16 (80%)	19 (63%)
Childhood breathing conditions	7/49 (14%)	3/19 (16%)	4 (13%)
Family history of breathing problems	22 (44%)	9 (45%)	13 (43%)
<i>Breathing-related symptoms^b, n (%)</i>			
None	3 (6%)	1 (5%)	2 (7%)
Chest symptoms ^c	26 (52%)	13 (65%)	13 (42%)
Cough	28 (56%)	15 (75%)	13 (43%)
Shortness of breath (overall)	42 (84%)	16 (80%)	26 (87%)
With strenuous activity	38 (76%)	15 (75%)	23 (77%)
With light activity	25 (50%)	13 (65%)	12 (40%)
At rest	9 (18%)	5 (25%)	4 (13%)
<i>Breathing events past year, n (%)</i>			
None	18 (36%)	3 (15%)	15 (50%)
Cold	18 (36%)	13 (65%)	5 (17%)
Chest infection or pneumonia	16 (32%)	10 (50%)	6 (20%)
<i>Breathing event impact, n (%)</i>			
Missed work or school	9 (18%)	5 (25%)	4 (13%)
Clinic visit	15 (30%)	5 (25%)	10 (33%)
Emergency room visit/urgent care	10 (20%)	6 (30%)	4 (13%)
Hospitalisation	3 (6%)	2 (10%)	1 (3%)
<i>Non-respiratory health conditions, n (%)</i>			
None	7 (14%)	0 (0%)	7 (23%)
Cardiovascular	20 (40%)	8 (40%)	12 (40%)
Metabolic	7 (14%)	0 (0%)	7 (23%)
Musculoskeletal	14 (28%)	9 (45%)	5 (17%)
Other (e.g., GI, cancer)	17 (34%)	5 (25%)	12 (40%)
<i>Health status, mean (s.d.), median</i>			
SF-36—Physical Component Summary (PCS)	38 (12); 37	36 (13) ^d ; 37	39 (12) ^d ; 37
SF-36—Mental Component Summary (MCS)	47 (13); 50	46 (11) ^e ; 46	47 (14) ^e ; 51
COPD Assessment Test (CAT)	17 (9); 18	19 (9) ^f ; 19	16 (8) ^f ; 17

Abbreviations: COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; NS, not significant.

^aPack-years = (cigarettes per day/20 cigarettes per pack) × duration of smoking (years).

^bCategories are not mutually exclusive.

^cChest congestion, discomfort, tightness, pain or wheeze.

^dScale: 0–100; higher scores are better; $t = 0.91$: COPD versus non-COPD, NS, $P = 0.37$.

^eScale: 0–100; higher scores are better $t = 0.28$: COPD versus non-COPD, NS, $P = 0.78$.

^fScale: 0–100; higher scores are worse $t = 1.49$: COPD versus non-COPD, NS, $P = 1.4$.

exertion, low energy, sleeping problems such as waking up at night feeling short of breath); (5) impact of breathing-related problems on daily life (e.g., slowing down or stopping owing to breathlessness, unable to complete daily chores, unable to keep up with others); and (6) the attribution of symptoms or experiences (e.g., breathless, being tired or slowing down attributed to age or weight; cough attributed to smoking or smoke exposure).

Themes were consistent across COPD and non-COPD participants, with some cross-group variation in emphasis within each theme. Spontaneous symptom reporting rates were generally lowest for Group 3 (non-COPD ≤ 2 risk factors); rates for Group 4 (non-COPD, ≥ 4 risk factors) were similar to the COPD groups on

sputum/phlegm (100%); tight, wheezy or noisy chest (90%); slowing down (40%); fatigue (50%); and sleep problems (40%). No qualitative differences were found between data provided by the three subjects with evidence of airway obstruction and other participants. Sample quotes for each theme are shown in Table 4. Candidate item content is shown in Table 5.

Electronic and manual PEF devices were rated as 'easy' or 'very easy' to use by participants (96%; 94%) and clinical site staff (80%; 84%). PEF values by device and group are shown in Table 6.

With the data analysed, a draft questionnaire with 48 candidate items was constructed and subjected to cognitive interviewing in a separate sample of 27 subjects. The instructions and item pool were easily understood and appropriately interpreted by the

Table 4. Key themes and representative quotes^a

<p>Exposure:</p> <ul style="list-style-type: none"> ○ All my family smokes.^{3: 004-102} ○ I worked in a tobacco warehouse for about a year...I was a...dancer for 13 years, barroom smoke.^{2: 002-110} ○ Working with material, fuzzy material and breathing it in.^{2: 001-101} ○ Around different chemicals, paint, plastic, you name it and we did it all.^{1: 002-101} <p>Personal and family history:</p> <ul style="list-style-type: none"> ○ My parents were both smokers...my mother was 92 when she was diagnosed with COPD and my father died of emphysema.^{2: 001-139} ○ When it takes that long to recover from 1, when you have like 2 or 3 in the course of a 3 or 4-month winter...it ends up you're feeling—you're feeling crummy for 75% of the time.^{1: 001-145} ○ I've gotten sinus infections in the spring and the fall, I bet, for the last 10 years...and I think like 5 times it has ended up as pneumonia.^{2: 006-104}; I've had pneumonia ... maybe 7, 8 times in my life.^{3: 004-125} <p>Recent history:</p> <ul style="list-style-type: none"> ○ The smell of—of detergents and, uh, lovely perfumes do affect, um, my deep breathing.^{2: 001-123} ○ If I'm going to be around dust or chemicals or cigarette smoke...I have to wear a mask because if not, it will be like, uh, I will, uh, start feeling the tightness in midst of—at first sign, it's like my chest will start tightening up.^{3: 004-127} ○ You're trying to breathe and it hurts, and it hurts and you have pain and then it hurts and ...then go to the hospital for it—it's the lungs.^{4: 003-131} <p>Symptoms—respiratory and non-respiratory:</p> <ul style="list-style-type: none"> ○ Just feels like you've got like something like a ton of bricks just sitting on your chest.^{2: 002-110} ○ I wouldn't have any trouble breathing hardly, but I'd just be running short on breath. Like I could walk a country mile, like a stroll, but I can't go up a flight of stairs if I get in a hurry.^{1: 002-103} ○ I walk up the driveway to my car, and—I'm really tired after that. I feel me [panting] breathing...you kind of feel tired all the time.^{2: 002-106} <p>Impact:</p> <ul style="list-style-type: none"> ○ I'd go out to lunch with...people from my office... I'd really have to kind of push myself to keep up with them ...had to work to keep up.^{2: 001-141} ○ I have a hard time...climbing stairs, and I've got to take it slow. I have to walk slowly.^{1: 002-113} ○ Walk up and down them halls, and sometimes I just feel like okay, wait, and I stop for a minute.^{4: 002-113} <p>Attribution:</p> <ul style="list-style-type: none"> ○ I've got a smoker's cough because I smoke.^{2: 002-109} ○ I noticed I was starting to slow down with my breathing, but it actually got worse after I started having all this other health issues.^{1: 002-101} 	
<p>Abbreviation: COPD, chronic obstructive pulmonary disease. ^aSuperscripts show subgroup membership and patient ID.</p>	

Table 5. Key themes and candidate content

Theme	Candidate content
Exposure	<ul style="list-style-type: none"> ● Smoking (current, history) ● Second-hand smoke ● 'Dirty' air
Personal and family history	<ul style="list-style-type: none"> ● Family smoking history ● Relatives with COPD, lung cancer, asthma ● Personal history of recurrent chest infections/colds
Recent history	<ul style="list-style-type: none"> ● Environmental triggers affect breathing ● Colds, acute bronchitis ● Clinic visits for or with breathing-related problems ● Hospitalisations for or with breathing-related problems ● Missed school or work days owing to breathing-related problems
Symptoms	<ul style="list-style-type: none"> ● Respiratory: dyspnoea, cough, sputum, chest congestion, wheezy/noisy breathing, chest tightness, chest heavy ● Non-respiratory: fatigue, feeling tired, lack of energy, sleep difficulties, slowing down
Impact	<ul style="list-style-type: none"> ● Activity limitations—stairs, steps, walking quickly ● Frequent stopping, keeping up with others
Attribution	<ul style="list-style-type: none"> ● Symptom attribution to smoking, age, weight or other health conditions

Abbreviation: COPD, chronic obstructive pulmonary disease.

Table 6. Mean (s.d.) peak flow by device type and group

Device	Total (N = 50)	COPD (Groups 1 & 2) (N = 20)	Risk, no COPD (Groups 3 & 4) (N = 30)
Electronic	362 (158)	274 (124)	424 (151)
Manual	315 (131)	249 (104)	358 (130)
Difference	43.79 (60.76) <i>t</i> = 4.89 ^b	24.89 (38.69) ^a <i>t</i> = 2.80 ^c	57.09 (70.05) ^a <i>t</i> = 4.23 ^d

Abbreviation: ANOVA, analysis of variance; COPD, chronic obstructive pulmonary disease.
^aANOVA testing group effects showed no difference ($F = 3.29$, $P = 0.076$).
^bPaired *t*-test, $P < 0.0001$.
^cPaired *t*-test, $P < 0.05$.
^dPaired *t*-test, $P < 0.001$.

subjects; several adjustments were made to enhance clarity. PEF results were similar to those found in the elicitation sample (see Online Supplementary).

DISCUSSION

Main findings

This qualitative study is part of a larger multi-method approach to develop a screening method for identifying patients with undiagnosed, clinically significant COPD in primary care. Six key themes were identified; candidate items were developed, using words and phrases easily understood by people in the target population. Although participants and clinical staff rated the two PEF devices easy to use, values produced by the electronic device were significantly higher than those provided by the manual device.

Strengths and limitations of this study

This is among the first known uses of qualitative data to inform the development of a screening tool for COPD case identification in a clinical setting. The study included men and women with varied COPD experiences, risk factors and education. The fact that all subjects were from the United States and most were white (70%) and not Hispanic or Latino (92%) is a limitation of the study. In addition, although a larger number of subjects with undiagnosed COPD would have been ideal, a study design that explicitly included screening and identifying subjects with undiagnosed clinically significant COPD (using methods not designed for this purpose) would have been cost-prohibitive. The fact that all moderators and interviewers were female may have influenced participant responses, although staff were experienced and trained to encourage discussion and minimise bias.

Interpretation of findings in relation to previously published work

The attribution theme offers insight into why certain symptoms are not reported or recognised as indicators of COPD. Participants who smoked often attributed their cough to smoking; others attributed slowing down, feeling tired or becoming breathless with exertion to ageing, weight or other health issues. These findings are consistent with descriptions of barriers to diagnosis;³⁹ quantitative evidence that symptom-based diagnosis of COPD in primary care settings is unreliable, particularly if patients are overweight;⁴⁰ and qualitative research suggesting that people minimise and negotiate the importance of symptoms and need to acknowledge 'there must be something wrong' as part of the diagnostic process.⁴¹

Most of the respiratory symptoms identified in this study were consistent with existing, symptom-based questionnaires for

identifying undiagnosed COPD. Cough, phlegm, dyspnoea and wheeze,^{21–23} as well as history of chest infections, breathing-related disability or hospitalisations,^{23,24} for example, were broached and characterised by these participants. In addition, however, subjects described chest symptoms, including congestion, noisy or tight, as well as feelings of fatigue and sleep difficulties. Participant descriptions of family history of respiratory-related problems, symptoms, activity limitations and acute respiratory illnesses offer new insight into candidate items for identifying undiagnosed cases of clinically significant COPD.

Smokers and non-smokers were included to facilitate the use of the questionnaire in both groups. There is evidence to suggest that one-fourth to one-third of all COPD cases are non-smokers, with country-to-country variability.⁴² The international study of Lamprecht *et al.*⁴² found that 81% of never smokers with moderate-to-severe airway obstruction were undiagnosed. The study of Bednarek *et al.*² in Poland suggested that detection of COPD is reduced by 26% when a 'smokers only' criterion is used, whereas in the Third US NHANES database, 'never smokers' accounted for 23% of airway obstruction cases, 69% of whom had no prior respiratory diagnosis.⁴³

Sample clinical characteristics provide further qualitative insight into the challenges associated with variable selection for case identification. Descriptively, the frequency of breathing-related symptoms (e.g., cough, shortness of breath) and other risk factors (e.g., history of asthma, family history of breathing problems) were similar across groups. The COPD group reported more breathing events over the past year (e.g., cold, chest infection). Although there were no significant differences in health status between the two groups, the descriptively higher COPD Assessment Test scores for COPD subjects suggest a trend toward poorer health in areas specific to COPD, with the mean between-group difference exceeding the proposed two-point minimum clinically important difference.⁴⁴ These exploratory results suggest that a small set of targeted questions may be more effective than a large number of general health questions for identifying people with COPD.

Implications for future research, policy and practice

As part of our screening tool development, we will be testing the added value of including PEF to increase sensitivity and specificity. To facilitate and optimise utilisation of PEF as part of the screening process, we evaluated the usability and comparability of electronic and manual devices. Most patients and clinic staff rated the devices easy or very easy to use, suggesting that either might be suitable. However, differences in PEF values indicate a need for standardisation to simplify the process by providing a single threshold for interpretation. With cost and availability in mind, the manual PEF device will be tested further during the next phase of screening tool development. The questionnaire's sensitivity and specificity will be optimised independently of PEF, and thus those preferring to use FEV₁ or PEF captured through an electronic/digital device would be free to do so, applying their preferred threshold for follow-up evaluation.

Conclusions

This qualitative study is part of a multi-method approach for developing a new screening method for identifying primary care patients who may have undiagnosed, clinically significant COPD. Six themes were identified: exposure, personal and family health, recent history of respiratory events, respiratory and non-respiratory symptoms, impact, and attribution. A pool of 48 candidate items was developed and revised based on cognitive interview results. Items will be tested and eliminated during the next phase of instrument development, with the intent of finding the best, smallest set of questions that, together with PEF, can identify patients in need of diagnostic evaluation for COPD.

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HIGH-RISK-COPD SCREENING STUDY GROUP

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CONTRIBUTIONS

Each named author participated in the study design and data analyses and interpretation. BPY, DMM, BMT, RGB, SIR, JFH, MKH, CAM, RPB and FM also participated in subject recruitment and data collection activities; LTM, KK and AWS served as focus group moderators, field note takers and interviewers. NKL, EDB, KK, AWS and LTM contributed to data management, analyses and interpretation. All the authors participated in manuscript development, review and/or editing. NKL, DMM and FM serve as co-investigators of the grant and, together with the co-authors, attest to the accuracy of the information contained in this manuscript.

COMPETING INTERESTS

NKL, EDB, KK, AWS and LTM are employees of Evidera, a health care research firm that provides consulting and other research services to pharmaceutical, device, government and non-government organisations. In this salaried position, they work with a variety of companies and organisations and receive no payment or honoraria directly from these organisations for services rendered. BPY has received research funding from NIH, AHRQ, CDC and from BI for research on COPD. BPY has received compensation from Merck and Forrest for COPD advisory boards on COPD, and Grifols for advisory board on Alpha-1 antitrypsin deficiency states. DMM has received honoraria/consulting fees and served on speaker bureaus for GlaxoSmithKline PLC, Novartis Pharmaceuticals, Pfizer Inc., Boehringer-Ingelheim, AstraZeneca PLC, Forest Laboratories Inc., Merck, Amgen and Creative Educational Concepts. Furthermore, he has received royalties from UpToDate and is on the Board of Directors of the COPD Foundation. BMT has consulted for Boehringer-Ingelheim and has been on advisory boards for GlaxoSmithKline PLC, Novartis, AstraZeneca PLC and Forest. RGB received grant support from NIH, US-EPA and the Alpha1 Foundation; he has received royalties from UpToDate. SIR has had or currently has a number of relationships with companies who provide products and/or services relevant to outpatient management of chronic obstructive pulmonary disease, including AARC, American Board of Internal Medicine, Able Associates, Align2 Acton, Almirall, APT, AstraZeneca, American Thoracic Society, Beilenson, Boehringer Ingelheim, Chiesi, CIPLA, Clarus Acuity, CME Incite, COPD Foundation, Cory Paeth, CSA, CSL Behring, CTS Carmel, Daiichi Sankyo, Decision Resources, Dunn Group, Easton Associates, Elevation Pharma, FirstWord, Forest, GLG Research, Gilead, Globe Life Sciences, GlaxoSmithKline, Guidepoint, Health Advance, HealthStar, HSC Medical Education, Johnson and Johnson, Leerink Swan, LEK, McKinsey, Medical Knowledge, Medimmune, Merck, Navigator, Novartis, Nycomed, Osterman, Pearl, PeerVoice, Penn Technology, Penside, Pfizer, Prescott, Pro Ed Communications, PriMed, Pulmatrix, Quadrant, Regeneron, Saatchi and Saatchi, Sankyo, Schering, Schlesinger Associates, Shaw Science, Strategic North, Summer Street Research, Synapse, Takeda, Telecon SC, ThinkEquity; these relationships include serving as a consultant, advising regarding clinical trials, speaking at continuing medical education programmes and performing funded research both at basic and clinical levels. SIR does not own any stock in any pharmaceutical companies. JFH declares no conflict of interest. MKH has consulted for GSK, Boehringer-Ingelheim and Regeneron. She has served on speaker bureaus for GSK, Novartis, Boehringer-Ingelheim, Forest and Grifols. CAM declares no conflict of interest. BJM has participated in research studies and/or served on medical advisory boards for AstraZeneca, Boehringer-Ingelheim, CSL Bering, GlaxoSmithKline, Forest, Novartis, Spiration and Sunovion. The work of RPB has been funded by the NIH, FAMRI, Butcher Foundation and John W. Carson Foundation. He participates in AstraZeneca- and GSK-sponsored clinical trials. He has received compensation as a member of scientific advisory boards of Boehringer Ingelheim Pharmaceutical. JWW declares no conflict of interest. FM has participated in Steering Committee in COPD or IPF sponsored by Bayer, Centocor, Forest, Gilead, Janssens, GSK, Nycomed/Takeda and Promedior. He has participated in advisory boards for COPD or IPF for Actelion, Amgen, AstraZeneca, Boehringer Ingelheim, Carden Jennings, CSA Medixal, Ikaria, Forest, Genentech, GSK, Janssens, Merck, Pearl, Nycomed/Takeda, Pfizer, Roche, Sudler & Hennessey, Veracety and Vertex. He has prepared or presented continuing

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