Copyright GPIAG - reproduction prohibited

Primary Care Respiratory Journal (2009); **18**(3): 198-207

Primary Care RESPIRATORY JOURNAL
www.thepcrj.org

ORIGINAL RESEARCH

Development and validation of the Chronic Obstructive Pulmonary Disease Assessment Questionnaire (COPD-AQ)

***William C Bailey[a], Frank C Sciurba[b], Nicola A Hanania[c], James F Donohue[d], Gary T Ferguson[e], Joseph D Zibrak[f], Amir Sharafkhaneh[c,g], Philip Marcus[h,i], Kathleen Rosa[j], Elisabeth C Piault[j], Fernando J Martinez[k]**

[a] University of Alabama Lung Health Center, University of Alabama, Birmingham, AL, USA.
[b] Emphysema/COPD Research Center, Division of Pulmonary and Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA.
[c] Section of Pulmonary, Critical Care and Sleep Medicine, Baylor College of Medicine, Houston, TX, USA.
[d] Division of Pulmonary and Critical Care Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.
[e] Pulmonary Research Institute of Southeast Michigan, Livonia, MI, USA.
[f] Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA.
[g] Michael E. Debakey VA Medical Center, Houston, TX, USA.
[h] Division of Pulmonary Medicine, St Francis Hospital, Roslyn, NY, USA.
[i] New York College of Osteopathic Medicine, Old Westbury, NY, USA
[j] Mapi Values, Boston, MA, USA.
[k] Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, MI, USA.

Received 27th February 2009; revised version received 20th April 2009; accepted 25th April 2009; online 3rd June 2009

Copyright General Practice Airways Group
Reproduction prohibited

Abstract

Aims: To develop a practical patient-completed chronic obstructive pulmonary disease assessment questionnaire (COPD-AQ) to improve COPD assessment and management in primary care, based on the concept of COPD stability.

Methods: An Expert Working Group defined parameters of COPD stability and a 10-item Physician's Global Assessment was established. A 21-item COPD-AQ was developed and validated in a cross-sectional, non-randomised study of patients with COPD (n=395). Items most discriminative of stability status (stable/unstable) were selected to produce a 5-item COPD-AQ, which was then validated.

Results: In the development sample, internal consistency reliability of the 5-item COPD-AQ was 0.74 (n=296). The COPD-AQ discriminated between stability groups based on physician assessment (F=44.26; p<0.0001) and post-bronchodilator spirometry measures (F=2.92; p<0.05). A questionnaire score >20 (range: 5.0–25.0) had a specificity of 82.9% and sensitivity of 64.7%.

Conclusions: The 5-item COPD-AQ proved a practical tool for assessing COPD status and was sufficiently simple for routine clinical use. However, overall validation was limited by small numbers of patients in the validation sample. Difficulties also existed over using the term 'stability' to define COPD status. COPD-AQ was not progressed further, but this work will prove valuable in the future development of a global questionnaire to improve COPD management in primary care.

© 2009 General Practice Airways Group. All rights reserved.
WC Bailey, *et al. Prim Care Resp J* 2009; **18**(3): 198-207.
doi:10.4104/pcrj.2009.00032

Keywords chronic obstructive pulmonary disease (COPD), patient-reported questionnaire, chronic bronchitis, symptom, predictive validity.

Introduction

Chronic obstructive pulmonary disease (COPD), the fourth leading cause of chronic morbidity and mortality in the United States, is predicted to become the fifth greatest burden of disease worldwide by 2020.[1-4] Unfortunately, COPD symptoms often go under-reported thus producing suboptimal management.[5-8]

In general, within the literature, patients' COPD status is

*** Corresponding author:** Dr William C Bailey, Professor of Medicine and Director, Lung Health Center, University of Alabama at Birmingham, 620 South 20th Street, Suite NHB 104, Birmingham, AL 35249, USA. Tel: +1 205-934-3915 Fax: +1 205-996-6340 and +1 205-975-0456
E-mail: wcbailey@uab.edu

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

described using two categories, 'stable' versus 'exacerbation', as per the American Thoracic Society (ATS)/European Respiratory Society (ERS) consensus statement,[9] both defined by a myriad of variables.[10-13] Guidelines for COPD have emphasised the use of spirometric assessment, which is more representative of disease severity than stability. Little work has been done to define 'stability' in COPD, whereas variable definitions of exacerbation exist.

Several of the current instruments[14-16] used to assess COPD status in clinical trials are not appropriate for use in a busy primary care setting. Whilst management of COPD may be more complex than other respiratory conditions – a result of the chronic and progressive nature of the disease – the development of a brief easy-to-use questionnaire for COPD assessment could improve patient care in a similar way to that seen following the wide adoption of the Asthma Control Test (ACT)[17] in the primary care management of asthma.

We report the initial development of a new disease-specific COPD assessment questionnaire (COPD-AQ) intended for use in primary care, in order to define COPD status objectively and improve the management of patients diagnosed with COPD. We discuss issues encountered in the development of this tool, and highlight additional developmental needs for the successful development of a new clinical tool for COPD management in primary care.

Materials and methods

The COPD-AQ was developed using published information relevant to COPD and pulmonary dysfunction, and physician and patient input. It involved the following steps: development of a conceptual framework; identification of items from existing COPD-specific self-completed questionnaires; selection of items based on their clinical validity; development of a draft questionnaire (alpha version); face and content validity testing (beta version); item selection based on their predictive validity (final version); and validation of the questionnaire (Figure 1).

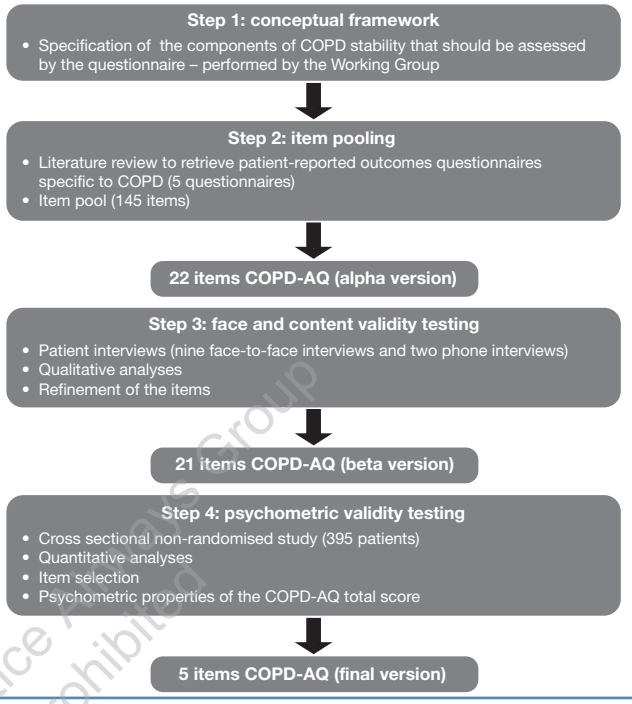
Development of a conceptual framework

A conceptual framework to define the need for a COPD assessment tool and to identify the different questionnaire components was developed by two Expert Working Groups, comprising eight primary care providers (PCPs) and five pulmonologists, all experts in COPD. The consensus was that a measure of COPD stability should account for objective factors (forced expired volume in one second – FEV1) and subjective factors, such as symptoms (including dyspnoea, cough and sputum), exacerbations, physical functioning and emotional wellbeing.

Identification of items and development of a draft questionnaire

A literature and questionnaire review was conducted, and 5 (of 12) existing questionnaires (Seattle Obstructive Lung Disease Questionnaire,[18] Clinical COPD Questionnaire,[19] St George's Respiratory Questionnaire,[15] Chronic Respiratory Disease Questionnaire,[20] and the Airways Questionnaire)[21] were selected to contribute to item generation. The items deemed most relevant to measuring COPD stability, as matched to the concepts listed in the conceptual framework, were then pooled (n=145) and short-listed to produce a 22-item questionnaire (alpha version).

Figure 1. Development and validation of the chronic obstructive pulmonary disease assessment questionnaire.



Face and content validity determination – alpha version

Eleven patients were interviewed to validate the alpha version to confirm that it measured what it was purported to measure (face validity) and that it addressed concepts relevant to patients with COPD (content validity). The clarity, relevance, applicability and acceptability of each item, and the appropriateness of response options, were also determined. A 21-item questionnaire (beta version) was then produced.

Item selection and validation of the questionnaire

The COPD-AQ beta version was included in a cross-sectional, observational, non-randomised study of 395 patients enrolled by seven pulmonologists (30–100 patients/site) and recruited through newsletters and flyers. The study protocol was reviewed and approved by local Institutional Review Boards. Patients with COPD who were naïve to the investigator were eligible if they were aged >40 years, capable of performing

Copyright General Practice Airways Group Reproduction prohibited

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

spirometry, had a smoking history of >10 pack-years and provided informed consent. Exclusion criteria were New York Heart Association heart failure class III and IV, asthma and concurrent respiratory disease. The total sample was used to document demographic and medical characteristics. Patients were divided randomly into development (75%) and validation (25%) samples: the development sample was used for item selection and documenting the reduced questionnaire's psychometric properties, including predictive validity (e.g. specificity and sensitivity); and the validation sample was used to evaluate the robustness of the validity of the reduced questionnaire in a sample of patients not used during the item selection process.

To standardise the clinical evaluation of COPD disease stability, pulmonologists adhered to the global assessment criteria, which included: assessment of COPD symptoms; pulmonary function test assessment; evaluation of activities of daily living; exacerbation assessments; assessments of psychosocial and emotional impacts associated with COPD; healthcare utilisation; smoking status; sputum; cough; and use of rescue medication. Following assessment, patients were classified into four stability states depending on the response of their physician to the question, 'How would you rate this patient's COPD stability status after your overall assessment?', using a four-point Likert scale (not at all stable, poor stability, somewhat stable, or completely stable). Incomplete assessments (COPD-AQ) were excluded from the analysis dataset. Both spirometric evaluation and the Physician's Global Assessment (PGA) of COPD stability were regarded as the gold standard for assessing COPD severity and COPD stability status, respectively.

Data analyses

Item selection: Items capable of discriminating patients' stability status were determined using stepwise logistic regression modeling and the Expert Working Group's clinical expertise. All 21 items in the COPD-AQ were entered into the model as independent variables; the dependent variable was COPD stability, dichotomised as stable (response: completely stable) and unstable (responses: somewhat stable, not at all stable, and poor stability). Items to be included in future versions of the COPD-AQ were those that remained within the model (using entry and staying criterion of 0.15) and those which the Expert Working Group identified as critical to assess stability. Logistic regression models evaluated the goodness-of-fit of the final model consisting of the most predictive items. The overall performance of the model was evaluated using area under the curve (AUC) statistics from the receiver operating characteristic (ROC) curves. The Hosmer and Lemeshow Goodness-of-Fit (H–L GoF) test was used to determine how well the data fit a logistic model.

Validation: The COPD-AQ total score was described using the mean and the proportion of responses at the maximum and minimum response categories (i.e. ceiling and floor effects). Internal consistency reliability was evaluated using Cronbach's coefficient alpha; additionally, multitrait analysis was run to evaluate the item level convergent validity. The capacity of the COPD-AQ to discriminate among clinically diverse groups was assessed in patients categorised into stable versus unstable groups and four severity groups (mild, moderate, severe, and very severe, based on GOLD guidelines[4]). Analysis of variance (ANOVA) was used to evaluate the ability of the COPD-AQ total score to discriminate between these groups.

To determine the scores at which a patient's COPD may not be stable, ROC analyses were performed to predict those with unstable versus stable disease from their COPD-AQ total scores. The odds ratios, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), percentage correctly classified and AUC were estimated at each cut-point score. The selection of a cut-point score was based on: (1) balance between sensitivity and specificity, (2) relatively high specificity for adequate accuracy in identifying those patients that were unstable, and (3) high AUC and percentage correctly classified. The validation sample (n=99) was used to confirm the results from the development sample (n=296) and to validate the cut-point score selected, by performing clinical validity and ROC analyses. A p-value of 0.05 was selected a priori and was used for all analyses of the reduced instrument. All tests of significance were two-sided. Ad hoc analyses were conducted on the total sample to investigate whether the cut-point performed adequately in the mild/moderate patients, and whether it performed as well in these patients – who are more likely to be untreated or under-treated for their COPD – as it did in the severe/very severe patients.

Copyright General Practice Airways Group
Reproduction prohibited

Results

Population characteristics

The characteristics of the patients (n=395) in the total sample are presented in Table 1. Patients were classified according to their stability (using the PGA of COPD stability) and severity status (Tables 1 and 2).

Item selection and face-validity of the COPD Assessment Questionnaire

Five items were selected based on the Expert Working Group's judgment and the items' ability to predict COPD stability according to the physician's dichotomised assessment of COPD stability (0=unstable and 1=stable). The COPD-AQ total score reflects the sum of all five item scores (lowest score 5.0 [worst possible outcome]; highest score 25.0 [best possible outcome]; Table 3). Weighting was not necessary for this algorithm because all items have the same number of

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

Table 1. Clinical characteristics of the cross-sectional validation study (total sample, continuous and categorical variables, n=395).

Variables	Results
Age – mean (years; SD)	64.8 (9.24)
Pre-bronchodilator spirometry – mean (SD)	
FEV_1 (L)	1.3 (0.56)
FEV_1 % predicted	44.1 (16.07)
FVC (L)	2.6 (0.85)
FEV_1/FVC	49.98 (13.32)
Post-bronchodilator spirometry – mean (SD)	
FEV_1 (L)	1.5 (0.61)
FEV_1 % predicted	48.7 (16.99)
FVC (L)	2.9 (0.94)
FEV_1/FVC	50.45 (13.18)
COPD severity* (post-bronchodilator spirometry results) – n (%)	
1. Mild	7 (1.77)
2. Moderate	165 (41.77)
3. Severe	141 (35.70)
4. Very severe	58 (14.68)
5. Missing†	24 (6.07)
Specialist's assessment of COPD stability – n (%)	
Not stable at all (1)	10 (2.53)
Poor stability status (2)	102 (25.82)
Somewhat stable (3)	215 (54.43)
Completely stable (4)	62 (15.70)
Missing	6 (1.52)

*COPD severity: mild COPD=mild airflow limitation (actual FEV_1/FVC <70% and FEV_1 ≥80% predicted); moderate COPD=worsening airflow limitation (actual FEV_1/FVC <70% and FEV_1 >50% <80% predicted); severe COPD= further worsening of airflow limitation (actual FEV_1/FVC <70% and FEV_1 <50% >30% predicted <50%); very severe COPD=actual FEV_1/FVC <70% and FEV_1 <30% predicted).

†Patients with missing data were excluded from any analyses.

COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; SD, standard deviation.

Table 2. Frequency distribution of physician assessment of stability by chronic obstructive pulmonary disease severity as defined by post-bronchodilator spirometry results (total sample, n=395)

Upper number= frequency Lower number= percentage		COPD severity** (post-bronchodilator spirometry)				
		Mild	Moderate	Severe	Very Severe	Total
COPD stability* (Specialist's assessment)	Not stable	0 0.00	1 0.27	4 1.09	5 1.36	10 2.72
	Poor stability	1 0.27	30 8.17	41 11.17	24 6.54	96 26.16
	Somewhat stable	4 1.09	91 24.80	83 22.62	25 6.81	203 55.3
	Completely stable	2 0.54	39 10.63	13 3.54	4 1.09	58 15.80
	Total	7 1.91	161 43.87	141 38.42	58 15.80	367 100.00

*COPD severity (using post-bronchodilator spirometry results): mild COPD=FEV_1/FVC <70% and FEV_1 % ≥80% predicted; moderate COPD=FEV_1/FVC <70% and FEV_1 >50% <80% predicted; severe COPD=FEV_1/FVC <70% and FEV_1 <50% >30% predicted <50%; very severe COPD= FEV_1/FVC <70% and FEV_1 <30% predicted.

**Note: Missing data from 28 patients.

COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

response options (i.e. a five-point Likert scale [range: 1–5]). Maximum likelihood estimates are provided for a model with the selected predictive items of COPD stability (Table 4). The model showed good statistical fit with an AUC of 0.832 and percentage concordant and percentage tied results of 82.80 and 0.90. The H–L GoF test indicated good fit (H–L GoF=0.9775) to the logistic model.

Convergence and reliability validity of the COPD Assessment Questionnaire

In the development sample, the observed COPD-AQ total score was 7.0–25.0. No patients had scores at the floor of the scale (5.0) and only 3.4% of 292 patients had a score at the ceiling of the scale (25.0). Multitrait analysis showed good item convergent validity of the COPD-AQ total score (Pearson item-scale correlation corrected for overlap range: 0.38–0.64), with one item not achieving the threshold of 0.40 (Table 5). The Cronbach's coefficient alpha for the COPD-AQ total score was 0.74 and satisfied the minimum recommended level of 0.70.

COPD Assessment Questionnaire's clinical validity using known-group methodology

For the surrogate endpoint of COPD stability, mean COPD-AQ total scores were higher for the stable group(s) than the unstable group(s), as defined by the PGA. Furthermore, statistically significant group differences tested by a one-way ANOVA (p-value <0.0001) were found for each of the surrogate endpoints (Table 6). COPD-AQ total score means were lower for the groups rated as severe or very severe and were in the expected order. The group differences were not statistically significant (except for the PGA of COPD stability) in the validation sample, probably because of the smaller sample sizes (Table 6).

COPD Assessment Questionnaire score cut-points

A logistic regression underlying the ROC analysis using the

Copyright General Practice Airways Group Reproduction prohibited

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

Table 3. Scoring algorithm of the Chronic Obstructive Pulmonary Disease Assessment Questionnaire.

COPD-AQ items		Response values	Item score
COPD-AQ 4	During the past 4 weeks, how often have you had **shortness of breath while at rest**?	1=almost all of the time to 5=none of the time	Actual score
COPD-AQ 12	During the past 4 weeks, how often have you felt **frightened** because you had difficulty breathing?	1=almost all of the time to 5=none of the time	Actual score
COPD-AQ 14	During the past 4 weeks, how often have you felt that you were **in control** of your lung disease?	1=almost all of the time to 5=none of the time	Reverse score: 6 – initial response value
COPD-AQ 18	During the past 4 weeks, how often have you felt **tired** because of your lung disease?	1=almost all of the time to 5=none of the time	Actual score
COPD-AQ 21	During the past year, how many times have you visited **a doctor, an urgent care facility or a hospital emergency room** because your lung symptoms got worse?	1=not at all to 5=more than 7 times per year	Reverse score: 6 – initial response value

COPD-AQ, Chronic Obstructive Pulmonary Disease Assessment Questionnaire.

Table 4. Analysis of maximum likelihood estimates (development sample, n=296).

Chronic Obstructive Pulmonary Disease Assessment Questionnaire items		Estimate	SE
COPD-AQ 4	During the past 4 weeks, how often have you had **shortness of breath while at rest**?	0.15	0.21
COPD-AQ 12	During the past 4 weeks, how often have you felt **frightened** because you had difficulty breathing?	0.46	0.24
COPD-AQ 14 (rev)*	During the past 4 weeks, how often have you felt that you were **in control** of your lung disease?	0.24	0.14
COPD-AQ 18	During the past 4 weeks, how often have you felt **tired** because of your lung disease?	0.55	0.20
COPD-AQ 21 (rev)*	During the past year, how many times have you visited a **doctor, an urgent care facility or a hospital emergency room** because your lung symptoms got worse?	0.55	0.27

*Rev: the item score was reversed so that a higher score (5) is a better outcome.

COPD-AQ, Chronic Obstructive Pulmonary Disease Assessment Questionnaire; SE, standard error.

Table 5. Convergent validity of the Chronic Obstructive Pulmonary Disease Assessment Questionnaire (development sample, n=296).

Chronic Obstructive Pulmonary Disease Assessment Questionnaire items		N	Pearson item-scale correlation
COPD-AQ 4	During the past 4 weeks, how often have you had **shortness of breath while at rest**?	295	0.54
COPD-AQ 12	During the past 4 weeks, how often have you felt **frightened** because you had difficulty breathing?	294	0.59
COPD-AQ 14 (rev)*	During the past 4 weeks, how often have you felt that you were **in control** of your lung disease?	293	0.40
COPD-AQ 18	During the past 4 weeks, how often have you felt **tired** because of your lung disease?	294	0.64
COPD-AQ 21 (rev)*	During the past year, how many times have you visited **a doctor, an urgent care facility or a hospital emergency room** because your lung symptoms got worse?	294	0.38

*Rev: the item score was reversed so that a higher score (5) is a better outcome.

COPD-AQ, Chronic Obstructive Pulmonary Disease Assessment Questionnaire.

Copyright General Practice Airways Group Reproduction prohibited

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

Table 6. Known-groups validity of Chronic Obstructive Pulmonary Disease Assessment Questionnaire total score (development sample [n=296] and validation sample [n=99]).

Clinical parameter	Category	Development sample				Validation sample			
		n	Mean (SD)	Statistic*	p-value†	n	Mean (SD)	Statistic*	p-value†
Physician's assessment of COPD stability	Not stable at all	8	12.75 (3.65)	44.26	<0.0001	2	11.00	10.20	<0.0001
	Poor stability status	75	14.44 (3.39)			24	15.21		
	Somewhat stable	156	17.81 (3.71)			56	19.00		
	Completely stable	51	21.24 (2.79)			11	20.00		
Physician's assessment of COPD stability (dichotomised)‡	Unstable	239	16.58 (3.98)	–7.94	<0.0001	82	17.70	–1.80	0.0758
	Stable	51	21.24 (2.79)			11	20.00		
COPD severity (post-bronchodilator)§	Mild	5	17.60 (4.28)	2.92	0.0343	38	18.87	2.63	0.0778
	Moderate	127	17.99 (4.28)						
	Severe	103	17.52 (3.97)			36	17.92		
	Very severe	42	15.83 (3.81)			16	16.19		

*F-ratios are portrayed for ANOVA results; t-statistics for t-tests.

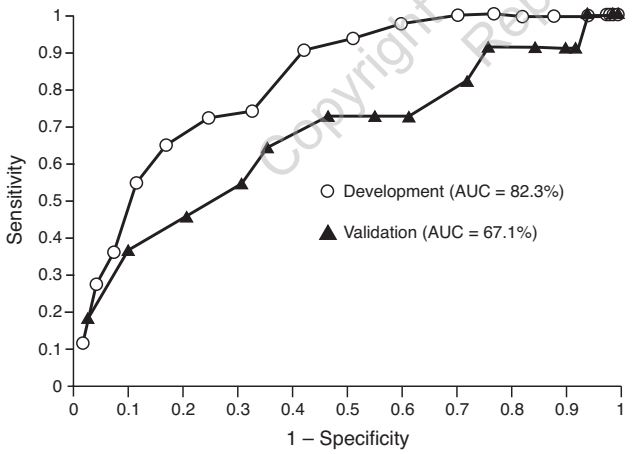
†p-values are derived from one-way ANOVA (or tests) testing mean differences between defined groups.

‡COPD stability definition is based on the physician's total assessment of COPD stability: stable=completely stable.

§COPD severity: mild COPD=FEV_1/FVC <70% and FEV_1 % ≥80% predicted; moderate COPD=FEV_1/FVC <70% and FEV_1 >50% <80% predicted; severe COPD= FEV1/FVC <70% and FEV_1 <50% >30% predicted <50%; very severe COPD= FEV_1/FVC <70% and FEV_1 <30% predicted.

ANOVA, analysis of variance; COPD-AQ, Chronic Obstructive Pulmonary Disease Assessment Questionnaire; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; NA, not applicable; SD, standard deviation.

Figure 2. Chronic obstructive pulmonary disease assessment questionnaire receiver operational characteristic curve.



COPD-AQ total score was able to predict the outcome of the physician's assessment of COPD stability as unstable versus stable. Cut-points of 17, 19 and 20 demonstrated the highest area under the ROC curve (0.740, 0.739 and 0.738, respectively; Figure 2). A cut-point of 19 showed a balance between sensitivity (72.55) and specificity (75.31), whereas a cut-point of 20 exhibited acceptable sensitivity (64.71) but improved specificity (82.85). This cut-point demonstrated a PPV of 44.6% (to be considered against the prevalence of stability in this sample of only 17%) and an NPV of 91.7%. The overall percentage correctly classified was 79.7% (Table 7). The ROC analyses were re-run using the validation sample (n=99); however, imbalanced numbers in the stable (n=11) and unstable groups (n=82) limit the ROC analyses. Thus, the results are likely to be unreliable because the impact of one stable subject being misclassified has a profound effect on sensitivity (1/11*100=9.1 point impact per stable subject classified). However, the overall pattern of results still supported a cut-point of 20.

Ad hoc analyses conducted on the total sample confirmed the good performance of a cut-point higher than 20 on the COPD-AQ total score for the mild/moderate subgroup. The cut-point performed comparably in the mild/moderate subgroup and the severe/very severe subgroup with a specificity of 76.0% vs 80.6%, and a percentage of patients correctly classified of 75.3% vs 77.2%. The mild/moderate subgroup showed a sensitivity of 73.17, a PPV of 50.0%, an NPV of 89.6% and an odds ratio of 8.64. The severe/very severe subgroup had corresponding values of 41.18, 16.7%, 93.5%, and 2.90, respectively. Patients included in this analysis had to have a total score, a stability rating and a severity rating, which resulted in 186 patients in the

Copyright General Practice Airways Group Reproduction prohibited

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

Table 7. Summary of the performance of the Chronic Obstructive Pulmonary Disease Assessment Questionnaire total score at various cut-points predicting physician's assessment of COPD stability (development sample, n=296).

Cut-point	Odds ratio	Sensitivity	Specificity	Positive predictive value (%)	Negative predictive value (%)	% Correctly classified	c-statistic
>17	12.57	90.20	57.74	31.3	96.5	63.4	0.740
>18	6.03	74.51	67.36	32.8	92.5	68.6	0.709
>19	8.06	72.55	75.31	38.5	92.8	74.8	0.739
>20	8.85	64.71	82.85	44.6	91.7	79.7	0.738

moderate/mild subgroup and 197 in the severe/very severe subgroup. Small numbers of stable patients in the severe/very severe subgroup make the estimates unreliable for this subgroup.

Discussion

In most countries primary care providers (PCPs), rather than specialists, treat the majority of patients with COPD, and accordingly assessment of disease status is often based solely on clinical judgment.[2] Traditionally, patients have been classified into those with stable disease and those who experience an exacerbation; however, this is complicated by the known variability in symptoms and disease expression normally experienced by patients with COPD.[10] Validated measures of disease status have taken a prominent role in asthma management,[22] but have not been well documented in COPD. We describe the development process for a COPD assessment tool for use in primary care, which uses patient-reported features that strongly correlate with a physician's impression of clinical stability. The COPD-AQ takes into consideration the multi-component nature of COPD and assesses a range of criteria potentially indicating disease status.

In developing the COPD-AQ, we aimed to produce a brief, practical, patient-completed tool for the assessment of COPD stability that would be simple to use, would improve patient–physician communication, and would raise patients' awareness of COPD and changes in their disease status. Unsurprisingly, evaluations of breathlessness were prominent in the questionnaire.[23] The process of developing the COPD-AQ provided an important step towards adopting a more patient-focused approach to assessing the impact of COPD on patients and aiding optimal management. It also highlighted previously-overlooked criteria, including parameters of emotional wellbeing – such as 'feeling in control', 'frightened' and 'tired', which prove to be some of the most predictive criteria from the patient perspective. These data emphasise the need for physicians to discuss with the patient the emotional impact of COPD, in addition to symptom frequency and severity, and highlight the increasing recognition of the psychological impact of COPD.[24-26]

In common with most other disease-specific patient instruments, the COPD-AQ was designed to complement, rather than replace, other physician measures by providing valuable additional information to guide clinical decision-making. While co-morbidities (e.g. heart failure, bronchiectasis and osteoporosis[9]) are often present in patients with COPD and may worsen symptoms,[27] the COPD-AQ was designed to assess only the symptoms of COPD itself, as is the standard with disease-specific tools. Attempting to design a questionnaire which also assesses the impact of co-morbidities would significantly complicate the simplicity of disease-specific questionnaires such as the COPD-AQ.

Although the concept of assessing COPD stability status and the initial development of a COPD questionnaire proved feasible, and confirmed a need for such an approach to facilitate improved management of COPD, this study also highlighted additional areas that need to be considered in order to develop and validate successfully a brief COPD questionnaire for routine use in clinical practice.

We have identified the following limitations in our development work that require consideration in the successful development of such a tool in the future.

1. Conceptual framework

In the development of the COPD-AQ the term 'stable' was used because within the current literature patients with COPD are described as 'stable' or 'exacerbating'. Nonetheless, 'stability', although a feature of the ATS/ERS consensus statement,[9] has not been adequately or universally defined and may not be the most appropriate concept in the assessment of a patient's status in a progressive disease such as COPD. Given the complexity involved in defining COPD stability, other measurement concepts have been discussed subsequently by an expanded global group of leading

Copyright General Practice Airways Group Reproduction prohibited

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

physicians. The concept of an 'optimised state', whereby the health status of a patient with COPD is the best it can be relative to the severity of their lung damage, might have more clinical utility than 'stability' in assessing the impact of COPD on the patient and in determining optimal management to minimise disease impact. Validation of this concept is currently ongoing.

2. Patient input

We aimed to use data obtained from the patient's perspective (e.g. emotional wellbeing) to evaluate COPD status. However, the original 21 items comprising the draft questionnaire were derived from searches of the literature and thus might not reflect what patients feel to be the most relevant aspects of their COPD status. The development of a new questionnaire would need to incorporate greater involvement of patients during item development combined with additional face- and content-validity to help ensure that questions are relevant to the patient.

3. Validation comparator: Physicians Global Assessment (PGA)

In the absence of a traditional gold standard by which COPD stability can be assessed, PGA was the criterion measure chosen to determine stability for the COPD-AQ because it was considered the most complete and clinically meaningful assessment for establishing a patient's stability status. Although the COPD-AQ in this format strongly correlated with this definition of clinical stability, this approach does not eliminate all subjectivity. Without a universally accepted definition of COPD stability and because of the variable nature of this progressive disease, the use of the term 'stability' to determine COPD health status has been questioned. Previous approaches to assess COPD stability have been defined generally within the context of clinical trials. One group defined patients with stable COPD as patients presenting with an FEV_1 <1.5 L, FEV_1/forced vital capacity (FVC) <50%, partial pressure of oxygen in arterial blood (PaO_2) <75 mmHg, partial pressure of carbon dioxide ($PaCO_2$) >45 mmHg, and no acute exacerbation in the three months prior to study entry.[28] However, FEV_1 and FVC provide a measure of COPD severity rather than stability.[2] Other studies have defined stability based on medication change, treatments in the emergency department, or hospitalisation for disease exacerbation for arbitrary time periods.[18,29-31] Thus, multiple definitions of COPD stability exist within the literature but all have limited use in the daily management of patients.

Both the PGA of COPD stability and spirometric evaluation were regarded as the gold standard for assessing COPD stability and severity, respectively, in the context of this study. However, spirometry might not be available in many primary care practices and PCPs might encounter problems interpreting spirometry data;[2] therefore, these results may not be easily replicated in the primary care setting.

4. Validation study

For methods attempting to assess surrogate markers, such as symptoms, quality of life or, in this case, disease stability, it is crucial to conduct sufficient psychometric validation.[32,33] In this study, cross validation was compromised by small sample numbers in some subgroups resulting in the validation analyses being underpowered. It would have been desirable to have interviewed a larger sample covering a range of COPD severity, especially since the development of the conceptual framework did not include any direct patient input at all. When the validation study was designed, it was predicted that there would be equal proportions of patients classified as stable versus unstable. However, in practice, recruitment leaned heavily towards the unstable class, mainly as a result of the more conservative *post hoc* definitions selected to dichotomise patients into stable and unstable groups. Under these criteria, patients deemed somewhat stable were grouped as unstable and only patients identified as completely stable were classified as stable. Recruitment of patients and assessment by pulmonary specialists might also have had some influence.

The current study was designed to exclude patients with mild disease (the seven patients with mild COPD representing protocol violators); thus, the COPD-AQ validation included mostly moderate-to-severe patients. The generalisability of these results in a primary care setting where disease severity may be milder cannot therefore be verified.

Although the small subgroup sizes in the validation sample impact the p-values in the analyses, the overall patterns of results appear supportive of the validity of the measure. However, in the validation of tools developed in the future, a larger sample and a longitudinal design would be needed to confirm validity and to evaluate the responsiveness of the tool over time. Additionally, inclusion and exclusion criteria should reflect more closely the distribution of disease severity seen in the primary care setting.

In conclusion, based on the results of this study and the limitations identified, we have now ceased the development of the COPD-AQ. Although the five-item COPD-AQ provided a practical, patient-completed instrument for the assessment of COPD stability, it was limited by the level of validation and the subjective definition of disease stability. Its ease of use and operating characteristics suggested that it could significantly foster communication between patients and physicians when targeting ongoing, accurate assessment of the condition. A validated tool, therefore, has the potential to improve COPD management.

On the basis of the complexity encountered in defining COPD stability, a global group of leading physicians has been convened to debate the most appropriate concept

Copyright General Practice Airways Group
Reproduction prohibited

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

terminology and concept definition for a clinically-useful COPD assessment tool. Research is ongoing to address these limitations and to build upon the strengths of the COPD-AQ work to produce a simple, easy-to-use questionnaire – the COPD Assessment Test (CAT) – which is currently undergoing extensive validation in order to provide a well-validated tool for primary care use, which, with local adaptation, could be used worldwide.

Acknowledgements

We would like to thank Glen Crater, MD, Priti Jhingran, PhD, Christopher Kalberg, MS, Gretchen Marcucci, MS, Somali M. Burgess, PhD, William Buie, BA, and Jacqueline Carranza Rosenzweig, PharmD, MS, for their contributions to this manuscript.

Conflict of interest declarations

William C. Bailey, MD, has received National Institutes of Health and pharmaceutical company grant monies and has carried out pharmaceutical consultancy. He has also participated in speaking activities and industry advisory committees. Some of the companies Professor Bailey has been involved with are: GlaxoSmithKline (GSK), Schering-Plough, Merck, Inspire, Rhone Poulenc Rorer, Pfizer, Aventis, Boehringer Ingelheim, Altana and Novartis.

Frank C. Sciurba, MD, has received National Institutes of Health grant monies and has received pharmaceutical company grant monies from Emphasys Medical, Inc. He has received pharmaceutical company grant monies from, and acts as a consultant for, GSK, Pfizer, Boehringer Ingelheim, AstraZeneca, Novartis, and Sepracor. Additionally, he works as a consultant for Schering-Plough, Respironics, PNeumRX and DEY.

Nicola A. Hanania, MD, has received research grant support and has served as a consultant for GSK, Sepracor, DEY, Boehringer Ingelheim and Novartis.

James F. Donohue, MD, has received pharmaceutical company grant monies from, and acts as a consultant for, GSK, Boehringer Ingelheim and Sepracor. He also conducts lectures and serves as a consultant advisor to GSK.

Gary T. Ferguson, MD, has received pharmaceutical company grant monies from GSK, Boehringer Ingelheim, Emphasys, Novartis and DEY. He is a consultant for GSK and serves on advisory boards for GSK, Boehringer Ingelheim and Novartis. Dr Ferguson has participated in industry activities for both GSK and Boehringer Ingelheim.

Joseph D. Zibrak, MD, acts as a consultant for GSK, and serves on advisory boards and presents for GSK, Pfizer and Boehringer Ingelheim

Amir Sharafkhaneh, MD, serves on advisory boards and presents for GSK, Pfizer and DEY. He also speaks for Boehringer Ingelheim

Philip Marcus, MD, MPH, receives honoraria for speaking on behalf of several pharmaceutical companies, including GSK, Sepracor, Boehringer Ingelheim, Altana, AstraZeneca, Pfizer, Schering, Teva, Genentech and Novartis. He also participates in several clinical trials.

Kathleen Rosa, MS, PhD, is employed at MAPI values, a CRO contracted to work on this project. As part of her employment, Dr Rosa consults and presents at conferences.

Elisabeth C. Piault, PharmD, MA, is employed at MAPI values, a CRO contracted to work on this project.

Fernando J. Martinez, MD, has received honoraria for serving on advisory boards with several pharmaceutical companies, including GSK, Schering-Plough, Novartis, Altana/Nycomed, AstraZeneca, Mpex, Genzyme and Forest/Almirall. He has participated in speaker bureaus for several companies, including Boehringer Ingelheim, GSK, Schering-Plough, AstraZeneca and Sepracor. He has participated in industry sponsored studies with Actelion, Altana/Nycomed, Boehringer Ingleheim, Johnson & Johnson and Gilead.

References

1. World Health Organisation, Colin D.Mathers, Claudia Stein, Doris Ma Fat, Chalapati Rao, Mie Inoue, *et al*. Global Burden of Disease 2000: Version 2 methods and results:1-108.
2. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease, 2007:1-30.
3. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 1997;**349**(9064):1498-504. http://dx.doi.org/10.1016/S0140-6736(96)07492-2
4. Sin DD, McAlister FA, Man SF, Anthonisen NR. Contemporary management of chronic obstructive pulmonary disease: scientific review. *JAMA* 2003;**290**(17):2301-12. http://dx.doi.org/10.1001/jama.290.17.2301
5. American Association for Respiratory Care. Confronting COPD in America: Executive Summary. http://www aarc org/resources/confronting_copd/exesum pdf (last accessed 19 September 2008).
6. Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;**157**(5 Pt 1):1418-22.
7. Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;**169**(12):1298-303. http://dx.doi.org/10.1164/rccm.200310-1443OC
8. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic Obstructive Pulmonary Disease Surveillance - United States, 1971-2000. In: Surveillance Summaries, August 2, 2002. *MMWR* 2002;**51**(No. SS-6):1-16.
9. Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 2004;**23**(6):932-46. http://dx.doi.org/10.1183/09031936.04.00014304
10. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. *Chest* 2000;**117**(5 Suppl 2):398S-401S. http://dx.doi.org/10.1378/chest.117.5_suppl_2.398S
11. Celli BR, Cote CG, Marin JM, *et al*. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med* 2004;**350**(10):1005-12. http://dx.doi.org/10.1056/NEJMoa021322
12. Celli BR, Calverley PM, Rennard SI, *et al*. Proposal for a multidimensional staging system for chronic obstructive pulmonary disease. *Respir Med* 2005;**99**(12):1546-54. http://dx.doi.org/10.1016/j.rmed.2005.03.019
13. Jones PW. Health status measurement in chronic obstructive pulmonary disease. *Thorax* 2001;**56**(11):880-7. http://dx.doi.org/10.1136/thorax.56.11.880
14. Selim AJ, Ren XS, Fincke G, Rogers W, Lee A, Kazis L. A symptom-based measure of the severity of chronic lung disease: results from the Veterans Health Study. *Chest* 1997;**111**(6):1607-14. http://dx.doi.org/10.1378/chest.111.6.1607
15. Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. *Respir Med* 1991;**85** Suppl B:25-31.
16. Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea. Contents, interobserver agreement, and physiologic correlates of two new clinical indexes. *Chest* 1984;**85**(6):751-8. http://dx.doi.org/10.1378/chest.85.6.751
17. Nathan RA, Sorkness CA, Kosinski M, *et al*. Development of the asthma control test: a survey for assessing asthma control. J Allergy Clin Immunol 2004;**113**(1):59-65. http://dx.doi.org/10.1016/j.jaci.2003.09.008
18. Tu SP, McDonell MB, Spertus JA, Steele BG, Fihn SD. A new self-administered questionnaire to monitor health-related quality of life in patients with COPD. Ambulatory Care Quality Improvement Project (ACQUIP) Investigators. *Chest* 1997;**112**(3):614-22. http://dx.doi.org/10.1378/chest.112.3.614
19. van der Molen T, Willemse BW, Schokker S, ten Hacken NH, Postma DS, Juniper EF. Development, validity and responsiveness of the Clinical COPD Questionnaire. *Health Qual Life Outcomes* 2003;**1**:13. http://dx.doi.org/10.1186/1477-7525-1-13
20. Wijkstra PJ, TenVergert EM, Van Altena R, *et al*. Reliability and validity of the

Copyright General Practice Airways Group
Reproduction prohibited

http://www.thepcrj.org

Copyright GPIAG - reproduction prohibited

chronic respiratory questionnaire (CRQ). *Thorax* 1994;**49**(5):465-7. http://dx.doi.org10.1136/thx.49.5.465

21. Barley EA, Quirk FH, Jones PW. Asthma health status measurement in clinical practice: validity of a new short and simple instrument. *Respir Med* 1998;**92**(10):1207-14. http://dx.doi.org/10.1016/S0954-6111(98)90423-1
22. National Asthma Education and Prevention Program (NAEPP). Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (2007).
23. Mahler DA. Mechanisms and measurement of dyspnea in chronic obstructive pulmonary disease. *Proc Am Thorac Soc* 2006;**3**(3):234-8. http://dx.doi.org/10.1513/pats.200509-103SF
24. Norwood R. Prevalence and impact of depression in chronic obstructive pulmonary disease patients. *Curr Opin Pulm Med* 2006;**12**(2):113-17. http://dx.doi.org/10.1097/01.mcp.0000208450.50231.c6
25. Wagena EJ, Arrindell WA, Wouters EF, van Schayck CP. Are patients with COPD psychologically distressed? *Eur Respir J* 2005;**26**(2):242-8. http://dx.doi.org/10.1183/09031936.05.00010604
26. Di Marco F, Verga M, Reggente M, *et al*. Anxiety and depression in COPD patients: The roles of gender and disease severity. Respir Med 2006;100(10):1767-74.http://dx.doi.org/10.1016/j.rmed.2006.01.026
27. Fabbri LM, Luppi F, Beghe B, Rabe KF. Complex chronic comorbidities of COPD. *Eur Respir J* 2008;**31**(1):204-12. http://dx.doi.org/10.1183/09031936.00114307
28. Girault C, Muir JF, Mihaltan F, *et al*. Effects of repeated administration of zolpidem on sleep, diurnal and nocturnal respiratory function, vigilance, and physical performance in patients with COPD. *Chest* 1996;**110**(5):1203-11. http://dx.doi.org/10.1378/chest.110.5.1203
29. van Noord JA, Aumann JL, Janssens E, *et al*. Effects of tiotropium with and without formoterol on airflow obstruction and resting hyperinflation in patients with COPD. *Chest* 2006;**129**(3):509-17. http://dx.doi.org/10.1378/chest.129.3.509
30. Calverley P, Pauwels R, Vestbo J, *et al*. Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. *Lancet* 2003;**361**(9356):449-56. http://dx.doi.org/10.1016/S0140-6736(03)12459-2
31. Mahler DA, Wire P, Horstman D, *et al*. Effectiveness of fluticasone propionate and salmeterol combination delivered via the Diskus device in the treatment of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2002;**166**(8):1084-91. http://dx.doi.org/10.1164/rccm.2112055
32. European Agency for the Evaluation of Medicinal Products. Human Medicines Evaluation Unit. CPMP/ICH/363/96. ICH Topic E9. Statistical Principles for Clinical Trials. Step 4, Consensus guideline, 1998.
33. European Agency for the Evaluation of Medicinal Products. Human Medicines Evaluation Unit. CPMP/ICH/364/96. ICH Topic E 10. Choice of Control Group in Clinical Trials. Step 4, Consensus guideline, 2000.

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

Copyright General Practice Airways Group
Reproduction prohibited

http://www.thepcrj.org