The Development of the Early Morning Symptoms of COPD Instrument (EMSCI)

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Introduction

- The morning hours are a difficult time for patients with chronic obstructive pulmonary disease (COPD).
  - COPD symptoms are commonly experienced in the morning.
  - Patients have reported that morning is the time of day when their symptoms are the most troublesome.[1-3]
  - Morning symptoms have been reported to limit morning activities of daily living[3] which, in turn, may have a negative impact on quality of life.[4]
- Two patient reported outcome (PRO) instruments have been used in clinical trials[4,7] to collect data about early morning symptoms. However, the published literature about these instruments suggests that they may not have been developed with sufficient evidence of content validity in order to make their development consistent with the US Food and Drug Administration's requirements[6] of a patient-reported outcome (PRO) instrument to collect data to support label claims. The two instruments were:
  - The Global Chest Symptoms Questionnaire (GCSQ)[4,5]
    - Used to assess COPD symptoms in the morning (pre- and post-morning dose)
  - The Capacity of Daily Living during the Morning (CDLM)[4,5]
    - Used to capture the effect of medications on morning activities.

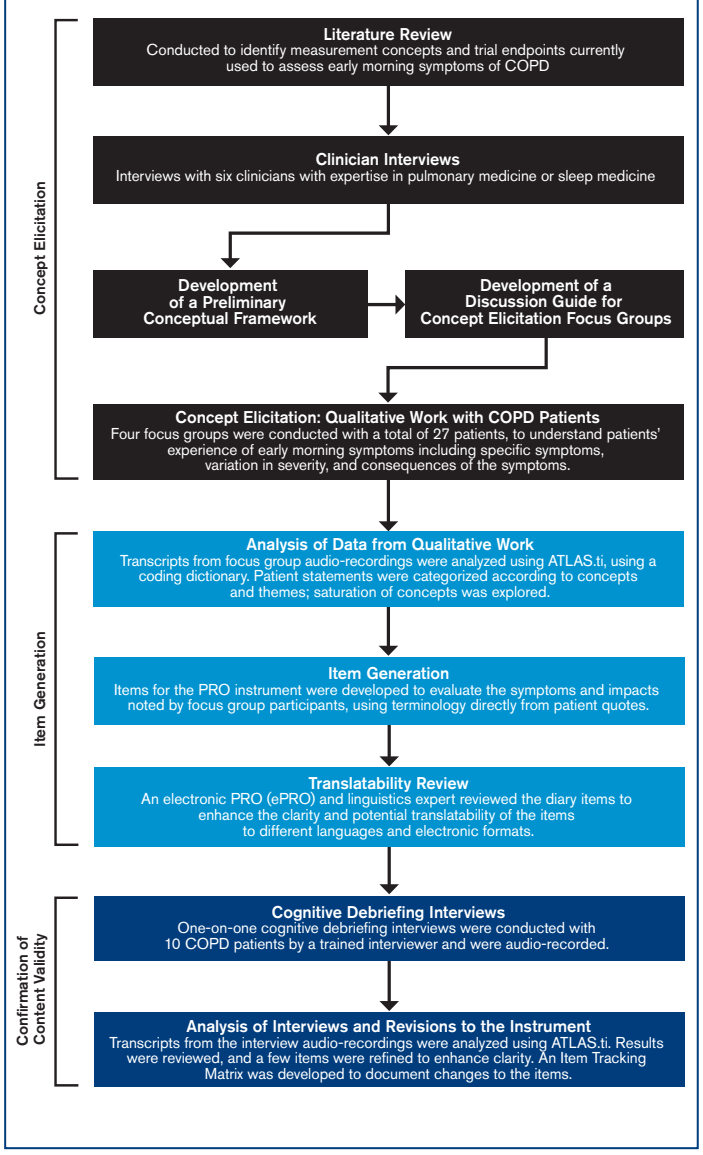
Objectives

- The objective of this study was to develop and test a PRO instrument that:
  - assesses patients' experience of COPD symptoms during the early morning
  - meets the evidence requirements for content validity, as described in the FDA PRO Guidance
  - can be used to collect data in clinical trials to support treatment benefit claims

Methods

- This study used the methods recommended for concept elicitation, item generation, and cognitive debriefing interviews as described in the FDA Guidance for Industry on Patient Reported Outcome Measures.[6]
- The methods used are described in Figure 1.

Figure 1. Overview of methods



Results

Literature Review

- Core symptoms of COPD in the early morning were identified:
  - Cough
  - Breathlessness
  - Tightness in chest
  - Increased phlegm
- Consequences of early morning symptoms of COPD were also identified:
  - Waking up too early
  - Morning and daytime tiredness
  - Restrictions or impacts on morning activities
  - Impaired daytime concentration
  - Rescue medication use

Clinician Interviews

- The clinicians indicated that:
  - Early morning symptoms of COPD are underreported by patients.
  - Morning symptoms of COPD are likely to be more bothersome than nighttime symptoms.
  - Many patients experience both nighttime and early morning symptoms.
  - Morning symptoms are tied to the ability of patients to perform activities.
- Results of the literature review and clinician interviews informed the development of the focus group discussion guide. This ensured comprehensive concept elicitation from the patient.

Description of Sample

- Four focus groups were conducted with 27 patients in Long Island, NY, Hampton Roads, VA, San Antonio, TX, and Raleigh, NC.
- After focus group data were analyzed and items generated, ten cognitive debriefing interviews were conducted in Richmond, VA.

Table 1. Participant demographics and clinical characteristics – focus groups and cognitive debriefings

Characteristics	Focus groups N=27	Cognitive debriefings N=10
Demographic		
Age, mean (SD)	68.1 (8.7)	68.1 (6.4)
Female, n (%)	14 (51.9)	7 (70)
Race/ethnicity, n (%)		
White	24 (88.9)	5 (50)
Black or African American	2 (7.4)	5 (50)
Native American or Alaska Native	1 (3.7)	0 (0)
Hispanic or Latino (not exclusive of race)	2 (7.4)	0 (0)
Clinical information (as reported by clinicians at recruiting sites)		
GOLD stage, n (%)		
I	2 (7.4)	2 (20)
II	15 (55.6)	2 (20)
III	4 (14.8)	4 (40)
IV	6 (22.2)	2 (20)
Current smoker, n (%)	9 (33.3)	2 (20)

Concept Elicitation

- Concepts that reflect patients' experience of early morning symptoms of COPD and impacts of those symptoms on patients' daily activities were identified through the analyses of focus groups' transcripts.
- Key concepts were confirmed by participants in subsequent discussions and no new emerging concepts were mentioned, thus saturation of concepts was reached.
- A saturation grid depicting emergent early morning symptoms of COPD and the impact of these symptoms are shown in Table 2.
- The focus groups uncovered all relevant patient experiences of early morning symptoms of COPD.

Saturation Grids

Table 2. Symptoms and impacts as experienced by focus group participants

Symptom	FG1 (Virginia) n=8	FG2 (New York) n=7	FG3 (Texas) n=4	FG4 (North Carolina) n=8
Wheezing	X			
Coughing	X	X	X	X
Mucus or phlegm	X	X	X	X
Congestion		X	X	
Shortness of breath	X	X	X	X
Tightness in chest		X	X	
Impact (Limitations to activities)				
Moving slowed down or difficult	X	X		X
Can't do anything	X	X	X	
Difficulty showering/ bathing		X		X
Difficulty brushing teeth		X		

Item Generation

- A draft questionnaire, the Early Morning Symptoms of COPD Instrument (EMSCI) was developed.
- Items were generated to cover concepts in the framework using patient terminology. A few examples of item generation are given in Table 3.

Table 3. Examples of concepts, quotes from the focus groups, and the resulting ESMCI item

Concept	Quotes	EMSCI item
Coughing	107: I cough in the morning. And after I clear myself, then I hack all day. 408: When I first get up—coughing.	Did you experience any of the following this morning? ▪ Cough
Phlegm	401: Usually, when I wake after sleeping all night, I will have phlegm that will-I'll need to clear airways so I-I'll cough. Sometimes it'll bring up phlegm, sometimes not.	Did you experience any of the following this morning? ▪ Difficulty bringing up phlegm
Congestion	[I]s there anything that sort of triggers that mucus in the morning or that coughing? 207: It's congested, tight, just normal nasty feeling.	Did you experience any of the following this morning? ▪ Chest congestion
Limitation to activity	107: Um-hmm [yes]. I can't do anything for awhile. I can sit and drink my coffee, and that's about it.	How much have you limited your activities his morning because of your COPD symptoms?

Cognitive Debriefing

- Cognitive debriefing interviews with patients demonstrated that the items were understandable, relevant, and interpreted as intended.

Table 4. Examples of probes used by interviewer, and patient responses

	Trigger	*Probe* Patient Response
Item Clarity	How much have you limited your activities this morning because of your COPD symptoms?	***[W]hat does 'limit your activities' mean?*** 102: What were you doing. How-you know, I was cooking-getting ready to cook breakfast. And I did eat
Response Options	Response options categorized as: ☐ I did not experience any symptoms ☐ Mild ☐ Moderate ☐ Severe ☐ Very Severe	***Why did you choose that one?*** 109: Because I did on that one because that's what it was. It was mild. I mean I don't let it get any worse
Timeframe	In regards to the first 6 questions on the EMSCI	***What time period […] were you thinking?*** 101: Um, this morning it would have been, um, 6:40 when I-when I got out of bed. 'Cause I had to get out of bed early. So, it was 6:00-about 6:00-between 6:30-I'd say 6:40

- Participant feedback from cognitive debriefing interviews were used to revise the measure. One example of this modification is shown in Table 5.

Table 5. Sample feedback from cognitive debriefing interviews and instrument revision

Participant feedback	Revisions to the measure
Are 'coughing' in the morning and 'coughing up phlegm' in the morning different? 108: *Oh yeah. […] It's involuntarily I cough it. You know where you don't have to, it just comes. Is coughing up phlegm a voluntary thing? Yeah.*	The related item was revised to query 'difficulty bringing up phlegm' to distinguish this concept from 'cough.'

Conclusions

- A new PRO measure has been developed to evaluate early morning symptoms of COPD.
- The measure was developed using the methodology outlined in the FDA requirements for use in clinical trials to support label claims.
- Evidence of content validity of the measure has been documented.

Future Directions

- The sample was limited in terms of ethnic diversity. The relevance of concepts will be tested in a more diverse sample during additional patient testing (e.g. usability testing).
- An electronic version of the measure is being developed and tested for use in clinical trials.
- Psychometric testing, including item reduction and evaluation of measurement properties, is planned for the current EMSCI.

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