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Incorporating the Patient's Voice into Instrument Development: How Do Patients Describe the Impact of Non-Small Cell Lung Cancer (NSCLC) on their Breathing?

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Background

- Lung cancer is among the most common cancers in terms of incidence. More than 220,000 new cases of lung cancer are projected to be diagnosed in the United States in 2015, with non-small cell lung cancer (NSCLC) representing approximately 83% of those cases. [1]
- Patients diagnosed with NSCLC often present with and/or develop significant breathing problems proximal to their disease.
- By exploring the patient experience with NSCLC through qualitative interviews, it is possible to better understand and document the specific lung cancer-related breathing concepts that are relevant to the patient as well as understand the patient's assessment of improvement in his or her condition.
- Once documented through this concept elicitation process, identified concepts can be considered for inclusion in NSCLC-specific clinical outcome assessments (COAs).

Aim

To identify the different expressions that patients with NSCLC use to describe their breathing-related symptoms in order to facilitate the incorporation of the patient's voice and perspective into new patient-reported outcome (PRO) measures.

Methods

Study Population

Recruitment was designed to enroll a diverse sample of patients similar to those who would be completing PRO instruments in future clinical trials of NSCLC treatments

- Recruitment quotas were employed to ensure appropriate representation of key subgroups within the NSCLC patient population, such as patients with early stage (I and II) tumors as well as those with comorbid chronic obstructive pulmonary disease (COPD).
- Beyond these specific recruitment quotas, each site targeted recruitment of a mix of patients with varying NSCLC-treatment histories, as well as broad representation across demographic characteristics such as age, sex, race/ethnicity and educational attainment.
- Subjects were recruited from 6 U.S. clinical sites in 6 states (AL, ID, IL, MT, ND, and NY).

References

[1] American Cancer Society. Cancer Facts and Figures, 2015. Available at http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2015/index

[2] Patrick DL, Burke LB, Gwaltney CJ, Leidy NK, Martin ML, Molsen E, Ring L. Content Validity—Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 1—Eliciting Concepts for a New PRO Instrument. *Value Health* 2011; 14:967-977

Methods, cont.

The eligibility criteria for the interview sample were designed to reflect common entry criteria for clinical trials in NSCLC:

Inclusion Criteria: Subjects were male or female and ≥18 years of age; had diagnoses of NSCLC; had an ECOG Performance Status of 0-2; were diagnosed with Stage I or II cancer and naive to treatment for NSCLC –or– diagnosed with Stage III or IV cancer and either naive to treatment for NSCLC or had recovered from any prior treatment-related toxicity/adverse events to Common Terminology Criteria for Adverse Events (CTCAE) v4.03 grade 1 (mild) or better; and were able to read, write, and speak English.

Exclusion Criteria: Subjects were excluded for severe clinically-significant mental health disorders or cognitive impairment; recent (12-month) history of clinically significant drug or alcohol abuse or dependence, excluding nicotine; current or recent (30 days) enrollment in any investigational device, drug, or biologics product study; or having any medical condition or disorder that could compromise his/her ability to give written informed consent and/or prevent or interfere with the patient's ability to successfully participate in a face-to-face interview and provide meaningful and non-confounded information about their lung cancer experience.

Concept Elicitation Interviews

Semi-structured qualitative interviews[2] were conducted by trained research staff with a non-random purposive sample of adult patients in the US diagnosed with Stage I-IV NSCLC.

- Interviews followed a pre-approved interview guide and used open-ended questions and day-reconstruction exercises to elicit spontaneous reports of symptom/impact concepts.
- Subsequent probing was used to assess concepts not spontaneously reported by subjects.
- Subjects were asked to rate the severity and level of bother or difficulty for reported symptoms and impacts using 0-10 numerical rating scale exercises.
- To guide item development, subjects were also asked about appropriateness of measuring the severity, frequency, or duration of each concept.

Content Analysis

- All interview sessions were audio recorded and transcribed.
- The concept elicitation interview transcripts were coded and analyzed by trained qualitative coders using Atlas.ti, and were summarized by like-content using an iterative coding framework.
- Coded concepts were grouped by similarity of content and analyzed to identify the most relevant expressions and most common language used by patients.
- A Saturation Grid was used to track symptoms and impacts expressed during the interviews and assess saturation of concept.
- Transcripts were ordered chronologically in groups of 8 transcripts. Codes from each group were compared with previous group to determine whether any new additional unique concepts emerged.

Results

Fifty-one interviews were conducted. Participants had a mean age of 65 years; 51% were female, 75% were white (non-Hispanic), and 35% had comorbid COPD (see Tables 1 and 2).

A total of 281 breathing-related sign and symptom expressions were identified in the transcripts and grouped into three distinct sub-concepts based on the language used by patients:

- **Shortness of Breath**, describing limited air intake (example patient language: *Breathing a little off, Breathless, Winded more easily, Limited airway, Short breathing, Short of breath, Shortness of breath, Slight shortness of breath*);
- **Difficulty Breathing** (*Breathing difficulties, Difficult breathing, Difficulty breathing, Harder to breathe, Trouble breathing, When it's cold hard to breathe*); and
- **Wheezing** (*Coughing with wheezy feeling, Loud breathing-wheezing night, Wheezing*).

Saturation of novel respiratory symptom/sign expressions was achieved within the first 27 interviews.

Table 1: Demographic Characteristics of Participants

		Total Subjects N=51 (100%)
Age (Years):	- Mean (SD)	64.9 (11.2)
	- Median	66
	- Range	46-86
Gender:	- Female	26 (51%)
Ethnicity	- Hispanic, Latino or Spanish Origin	5 (10%)
	- Non-Hispanic or Latino	46 (90%)
Race:	- Asian	2 (4%)
	- Black or African American	8 (16%)
	- White	38 (74%)
	- Other Race / Multiple Races†	3 (6%)
Highest Level of Education Completed:	- Less than High School	3 (6%)
	- High School	25 (49%)
	- Some College	13 (25%)
	- Bachelor's Degree	3 (6%)
	- Graduate or Professional School	7 (14%)

†Note: The three participants electing "Other" race self-identified as: "Hispanic," "Mexican American," and "White + American Indian/Alaska Native"

Table 2: Clinical Characteristics of Participants

		Total Subjects N=51 (100%)
NSCLC Stage (at time of screening/ interview)	- I	6 (12%)
	- III	19 (37%)
	- IV	26 (51%)
ECOG performance status	- 0	17 (33%)
	- 1	24 (47%)
	- 2	10 (20%)
Current line of NSCLC treatment	- Early stage (treatment-naïve)	19 (37%)
	- 1st line advanced/metastatic	18 (35%)
	- 2nd line advanced/metastatic	9 (18%)
	- 3rd line advanced/metastatic	3 (6%)
	- Other: Observation, Subsequent	2 (4%)
Comorbid COPD	- Diagnosis present	18 (35%)
Smoking history	- Current smoker	7 (14%)
	- Ex-smoker	36 (70%)
	- Never a regular smoker	8 (16%)
	Mean (SD) number of pack years smoked	32.5 (22.0)

Table 3: Predominance of Breathing Concepts

Concept	# Patient Language Expressions within Concept	% of Total Breathing-Related Symptom Expressions (N=281)	# Transcripts Contributing to Concept Expression	% of Transcripts Contributing (N=51)
Shortness of Breath	152	54.1%	35	68.6%
Difficulty Breathing	94	33.4%	21	41.2%
Wheezing	35	12.5%	12	23.5%

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Table 4: Ratings of Breathing Concepts

	Symptom Severity Ratings			Symptom Bother Ratings		
Concept	N Rating	Mean	SD	N Rating	Mean	Median
Shortness of Breath	29	6.7	2.0	29	6.9	2.5
Difficulty Breathing	11	6.1	2.5	10	6.0	2.5
Wheezing	9	6.2	2.5	10	6.4	3.2

Results, cont.

The most frequently reported breathing-related symptom concept was **Shortness of Breath** (N=152 total expressions; see Table 3). This represents 54.1% of the total number of coded breathing-related symptoms (N=281). Expressions about Shortness of Breath were contributed by 35 subjects in the dataset, and spontaneously reported by 27 subjects.

After Shortness of Breath, the two other predominant symptom concepts expressed in interviews were **Difficulty Breathing** (94 expressions by 21 different interview transcripts) and **Wheezing** (35 expressions by 12 different interview transcripts). Eleven subjects spontaneously reported **Difficulty Breathing** during the concept elicitation interviews, and 9 subjects spontaneously reported **Wheezing**.

Although patient severity ratings had large standard deviations, **Shortness of Breath** had the highest observed mean severity and bothersome ratings (6.7 [SD=2.0] and 6.9 [2.5], respectively; see Table 4), followed by **Wheezing** (6.2 [2.5] and 6.4 [3.2]; and **Difficulty Breathing** (6.1 [2.5] and 6.0 [2.5]).

Conclusions

While a range of patient language was used to describe breathing-related signs and symptoms, "shortness of breath" was the most frequently-reported sub-concept and had the highest observed mean severity and bothersomeness ratings among elicited sub-concepts. These findings provide support for the expression "shortness of breath" as relevant patient language for assessing breathing-related problems within a PRO instrument for NSCLC.

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