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Qualitative Development and Content Validity of the Non–Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ), A Patient-Reported Outcome Instrument

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ABSTRACT

Purpose: The purpose of this article was to describe the process and results of the preliminary qualitative development of a new symptoms-based patient-reported outcome (PRO) measure intended for assessing treatment benefit in clinical trials of advanced non–small cell lung cancer (NSCLC).

Methods: Individual qualitative interviews were conducted in adults with NSCLC (Stages I–IV) in the United States. Experienced interviewers conducted concept-elicitation (CE) and cognitive interviews using semistructured interview guides. The CE interview guide was used for eliciting spontaneous reports of symptom experiences along with probing to further explore and confirm concepts. Interview transcripts were coded and analyzed by professional qualitative coders, and were summarized by like content using an iterative coding framework. Data from the CE interviews were considered alongside existing literature and clinical expert opinion during an item-generation process, leading to the development of a preliminary version of the NSCLC Symptom Assessment Questionnaire (SAQ). Three waves of cognitive interviews were conducted to evaluate concept relevance, item interpretability, and structure of the draft items and to facilitate further instrument refinement.

Findings: Fifty-one subjects (mean [SD] age, 64.9 [11.2] years; 51.0% women) participated in the CE interviews. A total of 1897 expressions of NSCLC-related symptoms were identified and coded in interview transcripts, representing ~42 distinct symptom concepts. A 9-item initial-draft instrument was developed for testing in 3 waves of cognitive interviews with additional subjects with NSCLC (n = 20), during which both paper and electronic versions of the instrument were evaluated and refined. Participant responses and feedback during cognitive interviews led to the removal of 2 items and substantial modifications to others.

Implications: The NSCLC-SAQ is a 7-item PRO measure intended for use in advanced NSCLC clinical trials to support medical product labelling. The NSCLC-SAQ uses a 7-day recall period and verbal rating scales. It was developed in accordance with the US Food and Drug Administration's PRO Guidance and scientific best practices, and the resulting

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qualitative interview data provide evidence of content validity. The NSCLC-SAQ has been prepared in both paper and electronic administration formats and a tablet computer–based version is currently undergoing quantitative testing to confirm its measurement properties and support US Food and Drug Administration qualification. (*Clin Ther*. 2016;▮:▮▮▮–▮▮▮)

Key words: NSCLC, patient-reported outcome (PRO), content validity, qualitative research, scale development.

INTRODUCTION

Lung cancer is the leading cause of cancer-related mortality in the United States, with ~180,000 deaths expected to have occurred in 2015.[1] Non–small cell lung cancer (NSCLC) is the most prevalent form of the disease and accounts for 85% of all lung cancers in the United States.[2] Early-stage NSCLC is often asymptomatic or undetected due to similar symptoms experienced by those with comorbid diseases (eg, asthma, chronic obstructive pulmonary disease [COPD]).[3] However, the degree of impairment experienced by patients with NSCLC is often affected by the severity of disease-related symptoms. Therefore, accurate assessment and monitoring of these symptoms is an essential component of evaluating NSCLC treatment benefit in clinical studies.[4]

Patient-reported outcomes (PROs), defined as symptoms or health status reported unfiltered and subjectively by a patient, have been established as the "gold standard" of the capture of the patients' symptom experience.[5–7] An increase in the assessment of PROs in clinical trials led the US Food and Drug Administration (FDA) to release regulatory recommendations in its 2009 Guidance for Industry titled Patient-Reported Outcome Measures: Use in Medical Product Development To Support Labeling Claims (hereafter referred to as *FDA PRO Guidance*).[8] The FDA PRO Guidance contains specific expectations for a given measure's psychometric properties, including conceptual framework, reliability, construct validity, and ability to detect clinically relevant score changes.[8] Most importantly, the FDA PRO Guidance recommends that content validity be established through the comprehensive qualitative elicitation of concepts from patients in the targeted disease population, as well as through cognitive interviewing to confirm respondents' understanding of the PRO items assessing each measured concept.

In addition, in 2014, the FDA released the Guidance for Industry and FDA Staff: Qualification Process for Drug Development Tools (hereafter referred to as FDA Qualification Guidance).[9] Qualification, as defined by the FDA's Center for Drug Evaluation and Research, is a formal conclusion that the results obtained from the PRO instrument within a stated context of use can be relied upon to have a specific interpretation and application in drug development and regulatory review.[9]

For NSCLC, a number of condition-specific PRO measures exist that capture disease-related symptoms, including the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire—Lung Cancer,[10] Functional Assessment of Cancer Therapy—Lung,[11] Lung Cancer Symptom Scale,[12] and MD Anderson Symptom Assessment Inventory—Lung Cancer.[13] Despite each of these measures being rigorously tested and widely used, the development history, content, and comprehensiveness of these tools with respect to documenting symptom concepts that have been specifically elicited from first-hand accounts of a patient's experience with NSCLC may not necessarily satisfy the expectations of the FDA PRO Guidance. As such, the Critical Path Institute's PRO Consortium, with consultation from FDA advisors, identified the need for a well-defined and reliable PRO instrument for measuring NSCLC symptoms and providing evidence for US drug labeling.

To address this gap, the PRO Consortium established the NSCLC Working Group, with the objective of qualifying a PRO instrument to be used for assessing clinical benefit in advanced NSCLC clinical trials.[14] The NSCLC Working Group comprises pharmaceutical-firm representatives and personnel from the Critical Path Institute. As part of a competitive bidding process, Health Research Associates was awarded a contract to provide research services for the working group.

The development team for the NSCLC Symptom Assessment Questionnaire (NSCLC-SAQ) included members of the NSCLC Working Group and PRO measurement scientists from Health Research Associates, who employed rigorous methodologic approaches similar to those used in the Depression Working Group's PRO instrument development efforts.[15] In addition, an advisory panel of clinical