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Assessing Asthma Symptoms in Adolescents and Adults: Qualitative Research Supporting Development of the Asthma Daily Symptom Diary

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ABSTRACT

Background: Despite the widespread availability of patient-reported asthma questionnaires, instruments developed in accordance with present regulatory expectations are lacking. To address this gap, the Patient-Reported Outcome (PRO) Consortium's Asthma Working Group has developed a patient-reported asthma daily symptom diary (ADSD) for use in clinical research to assess outcomes and support medical product labeling claims in adults and adolescents with asthma. **Objectives:** To summarize the qualitative research conducted to inform the initial development of the ADSD and to provide evidence for content validity of the instrument in accordance with the Food and Drug Administration's PRO Guidance. **Methods:** Research informing the initial development and confirming the content validity of the ADSD is summarized. This comprised a review of published qualitative research, semi-structured concept elicitation interviews (n = 55), and cognitive interviews (n = 65) with a diverse and representative sample of adults and adolescents with a clinician-confirmed diagnosis of asthma in the United States to understand the asthma symptom experience and to assess the relevance and understanding of the newly developed ADSD. **Results:** From the qualitative literature review and concept elicitation interviews, eight core asthma symptoms emerged. These were broadly categorized as breathing symptoms (difficulty breathing, shortness of breath, and wheezing), chest symptoms (chest tightness, chest pain, and pressure/weight on chest), and cough symptoms (cough and the presence of mucus/phlegm). Conceptual saturation was achieved and differences in the experience of participants according to socio-demographic or clinical characteristics were not observed. Subsequent testing of the ADSD confirmed participant relevance and understanding. **Conclusions:** The ADSD is a new patient-reported asthma symptom diary developed in accordance with the Food and Drug Administration's PRO Guidance. Evidence to date supports the content validity of the instrument. Item performance, reliability, and construct validity will be assessed in future quantitative research.

Keywords: asthma, content validity, patient-reported outcomes, symptoms.

Introduction

Asthma is a chronic inflammatory disorder of the airways that causes recurrent episodes of coughing, wheezing, breathlessness, and chest tightness [1]. These episodes are usually associated with variable airflow obstruction that is often reversible, either spontaneously or with treatment [2]. The worldwide prevalence of asthma is estimated to be approximately 300 million, and it is expected to increase by 33% to 400 million by 2025 [3]. Despite advances in the understanding of asthma and broader availability of disease management guidelines, the proportion of patients with uncontrolled asthma remains high [4,5].

A number of objective methods for determining asthma disease severity exist. Forced expiratory volume in 1 second and peak expiratory flow, for example, typically serve as standard measurements of airway function in clinical studies. There is also increasing evidence to support the value of various biomarkers (including fractional exhaled nitric oxide, total Immunoglobin E,

Conflicts of interest: At the time this research was conducted, J. Jason Lundy was associate director of the Critical Path Institute's Patient-Reported Outcome Consortium.

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and blood eosinophils) [6]. Among the goals of asthma management (as highlighted in clinical guidelines), and an indicator of overall asthma control, is the eradication of or reduction in asthma symptoms [7–9]. Nevertheless, there is a poor correlation between the aforementioned objective measures of disease severity and patients' experience of asthma symptoms [10–12]. To provide a holistic understanding of patient disease severity and asthma control in clinical research, there is a need for standardized ways of assessing patients' experience of asthma symptoms.

Many symptoms of asthma can be known only to patients themselves and are therefore best reported via patient-reported outcome (PRO) instruments. Nevertheless, although there is no shortage of PRO instruments used in asthma studies, no instrument has been identified for the assessment of asthma symptoms that has been developed according to the regulatory expectations described by the US Food and Drug Administration (FDA) in its guidance for industry titled "Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims" (PRO Guidance) [13]. Indeed, a recent asthma outcomes workshop by the National Institutes of Health stated that "asthma clinical research will highly benefit from standardization of major outcomes in terms of definition and assessment methodology" [14] and concluded that no published asthma symptom diary had sufficient validation information to be chosen as a core asthma outcome for use in clinical research sponsored by the National Institutes of Health [15]. In particular, strong evidence supporting the content validity (the extent to which the PRO measures the concept of interest, i.e., asthma symptoms) of existing instruments in adolescents and adults with asthma is lacking.

To fill this gap, the PRO Consortium's Asthma Working Group (WG) at the Critical Path (C-Path) Institute [16] embarked on the development and qualification of the asthma daily symptom diary (ADSD) in collaboration with the FDA. The intent is for the ADSD to be used as a co-primary or secondary end-point in clinical trials to establish treatment outcomes and to support medical product labeling claims. This article summarizes the qualitative research conducted to inform the initial development of the ADSD and to provide evidence for content validity of the instrument in accordance with the FDA PRO Guidance.

Methods

Figure 1 summarizes the methods involved in the development of the ADSD. At each stage of this process, input was obtained from the Asthma WG, C-Path scientists, the expert panel (J.K., S.S., M.S., and J.H.), and representatives of the FDA Center for Drug Evaluation and Research via the formal Drug Development Tool qualification process [17].

Qualitative interviews during the development of the ADSD were conducted in accordance with the Declaration of Helsinki and approval was obtained from the Copernicus Group Independent Review Board (approval code ADE2-12-282).

Review of Existing Qualitative Literature

A targeted review of published qualitative research studies was conducted to identify the symptoms and effects experienced by adults and adolescents with asthma. Published peer-reviewed articles were identified via title and abstract searches in electronic bibliographic databases: MEDLINE, Embase, and PsycNFO. Disease (i.e., asthma), symptom and impact (i.e., symptom, control, health-related quality of life), and qualitative research (i.e., qualitative, phenomenology, thematic analysis, grounded theory, interview, focus group) medical subject headings (MeSH) terms or keywords were combined using Boolean logic commands. Searches were conducted in May 2012 and limited to articles published in English, concerning human subjects and published between 1997 and 2012.

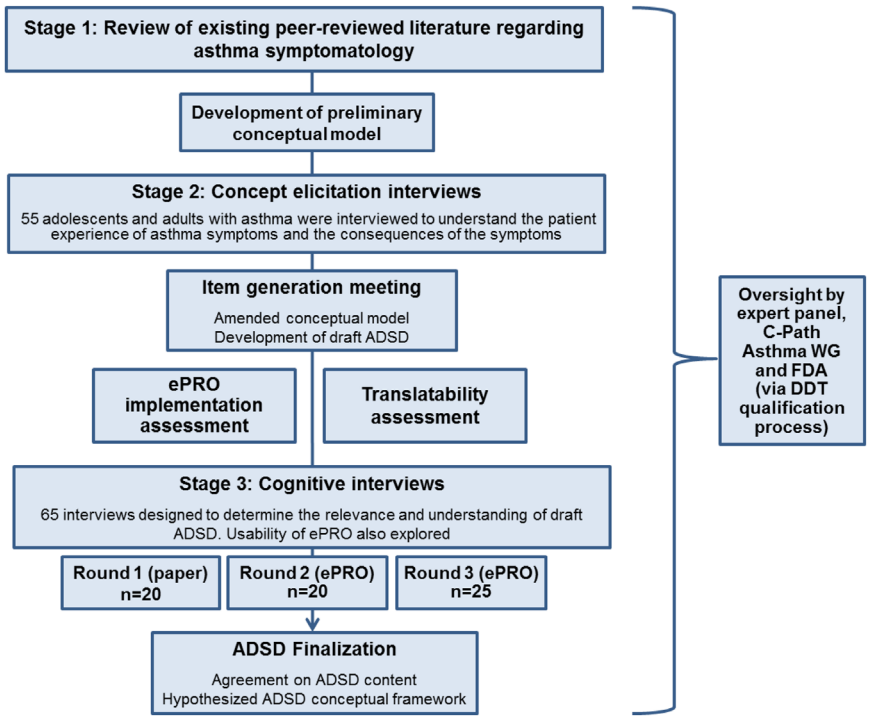

Fig. 1 – Overview of study methods. ADSD, asthma daily symptom diary; C-Path, Critical Path; DDT, drug development tool; ePRO, electronic patient-reported outcome; FDA, Food and Drug Administration; WG, Working Group.