

# Identifying and Measuring the Core Symptoms Reported by Persons with Asthma: A Review of the Existing Qualitative Literature and Patient-Reported Outcome Measures

L.M. Nelsen<sup>1</sup>, A. Gater<sup>2</sup>, R. Hall<sup>2</sup>, S.J. Coons<sup>3</sup> on behalf of the Patient-Reported Outcome Consortium's Asthma Working Group (Asthma WG)

<sup>1</sup>GlaxoSmithKline – King of Prussia, PA USA, <sup>2</sup>Adelphi Values – Cheshire, UK, <sup>3</sup>Critical Path Institute – Tucson, AZ, USA

## Background

- International guidelines issued by the Global Initiative for Asthma (GINA) and the National Institutes of Health (NIH, USA) state that the therapeutic aim of asthma management should be to achieve and maintain overall asthma control without treatment side effects.
- A recent NIH review indicated that “asthma clinical research will highly benefit from standardization of major outcomes in terms of definition and assessment methodology.”
- The FDA's PRO Guidance recommends that PRO instrument development should be based on direct patient input.

## Objectives

To support the content of an asthma symptom diary for assessing treatment benefit in adults and adolescents with a diagnosis of mild to severe persistent asthma, the objectives of this stage of the Asthma WG's research were to conduct systematic literature reviews to:

- identify the most relevant asthma-related symptoms reported in the published qualitative literature and;
- evaluate existing patient-reported outcome (PRO) instruments used to assess asthma symptoms in adults and adolescents

## Methods

### Literature Review to Identify Qualitative Research in Asthma

- Search of MEDLINE, Embase, and PsycINFO databases to identify key publications presenting results of qualitative research studies
- Pre-specified search terms, and inclusion and exclusion criteria were developed using disease (asthma), concept (symptom, control or quality of life) and qualitative research terms (e.g., interview, grounded theory, focus groups)
- Articles were ranked to identify articles of most relevance to the objectives with review. Full text articles were abstracted to collect study aim, sample demographics, methodology and results including key concepts relating to asthma symptoms

### Literature Review to Identify Instruments

- A previous literature review conducted in 2008/09 by one of the Sponsors of the Asthma WG was used as the basis for the current review and supplemented by new searches to identify PRO instruments focused specifically on symptoms
- Search Strategies included disease (i.e. asthma), concept (e.g. symptoms, quality of life) and measurement (e.g. questionnaire) terms
- A review of asthma symptom measures conducted by NIH (2012) was reviewed to ensure completeness of instrument identification

### Instrument Review Criteria

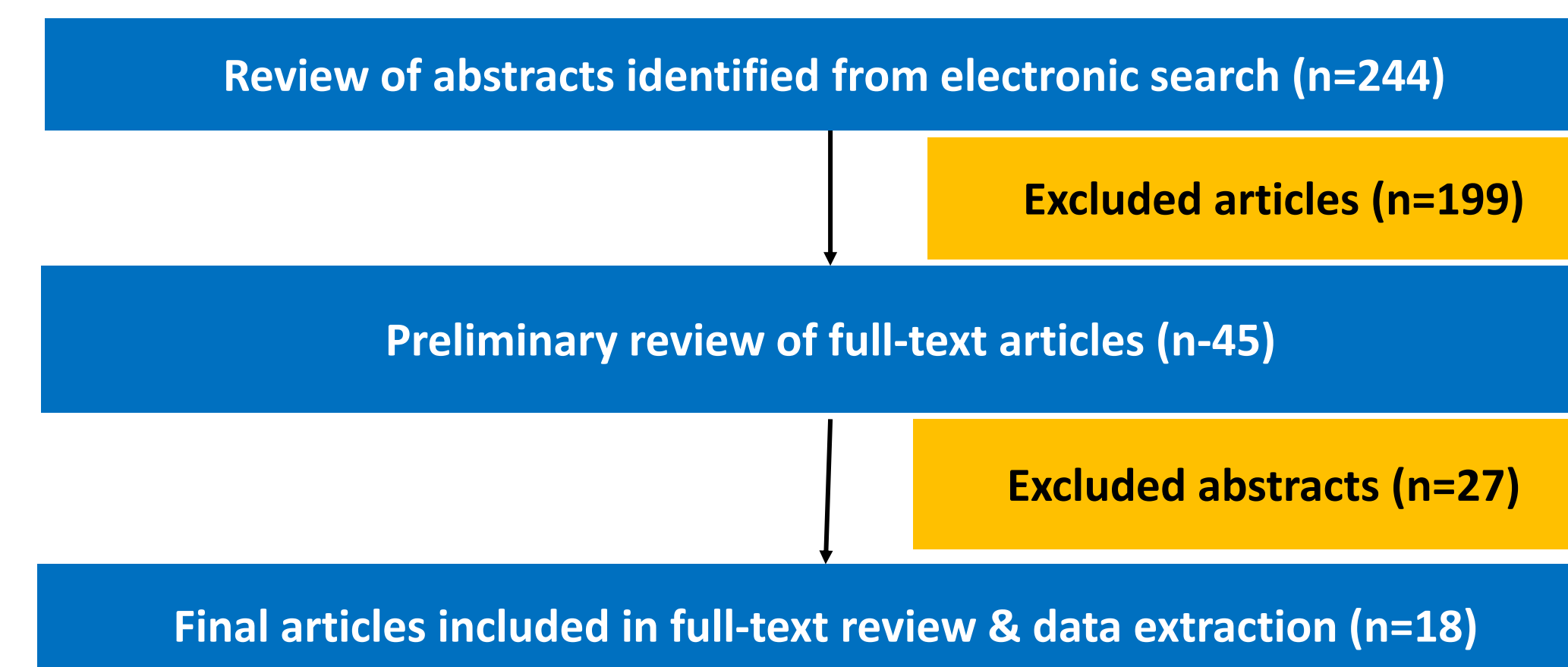
- Instruments focusing on the assessment of the patient experience of asthma symptoms or impact were reviewed for content validity;
  - Measures concepts of key importance to patients
  - Easily understood and interpreted by respondents
  - Evidence that the content of the instrument was developed directly from input from patients in the target population
  - Evaluates primary symptoms of asthma as identified in the literature review and GINA guidelines.
- Attributes of face validity (item wording, recall period, response options, scoring) were evaluated

## Results

### Qualitative Literature Search

244 abstracts (1997-2012) were identified and 18 articles included in the full text review (Figure 1)

Figure 1: Flowchart of abstract review



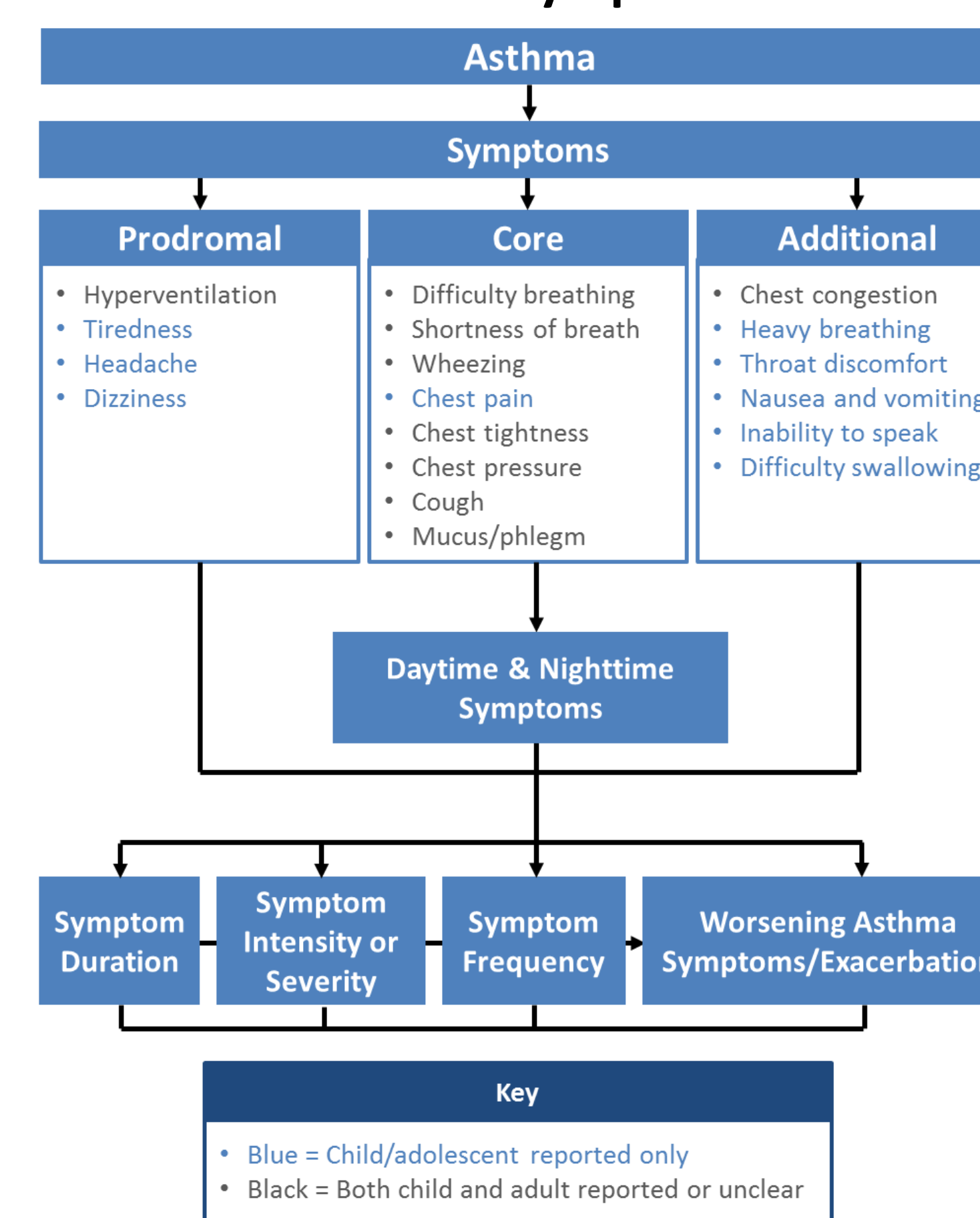
Key aspects of study methodologies and demographics were noted

- Research was conducted worldwide (North America, Europe and China) with an ethnically and racially diverse sample of asthma participants
- Ages included older adolescents (16+) to elderly patients (90) with several papers included proxy reports from parents about their children
- Standard qualitative methodologies were used including semi-structured qualitative individual interviews and focus groups with systemic identification and coding of relevant concepts to build an understanding of patient experience

### Provisional Conceptual Model from the Qualitative Research

- Model incorporates patient experience of prodromal (early symptoms of asthma attack), core asthma and additional symptoms (co-occur but not disease defining) (Figure 2)
- Symptoms are characterized occurring during the day or night and mediated by factors such as duration, intensity/severity, frequency and worsening/exacerbation of symptoms

Figure 2: Conceptual model of asthma symptoms

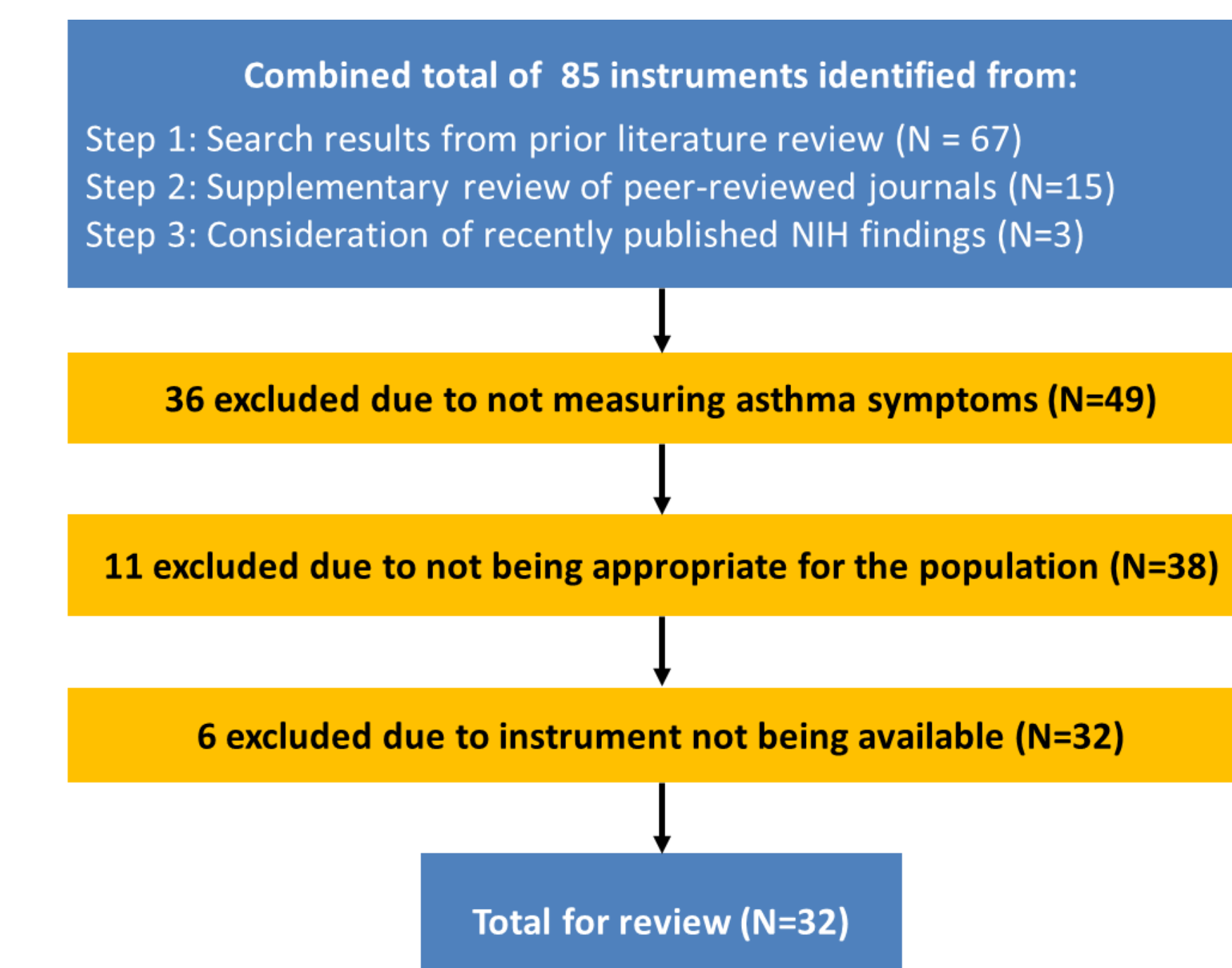


### Instrument Review

- 85 instruments were identified from the Sponsor search, NIH review, and the search conducted for this research; 32 were included for final review (Figure 3)
- Of the 32 instruments, 14 instruments were identified that assess the three categories of core symptoms (i.e., breathing symptoms, chest symptoms, cough symptoms) of asthma
- No instrument that assessed all 8 of the core symptoms was identified

## Results (cont)

Figure 3: Flowchart of instrument identification



The attributes of the 14 instruments were evaluated (Table 1)

Table 1: Instrument attributes

PRO Aspect	Findings from review
Recall period	9 of 10 instruments had recall periods of past week rather than asking respondents to focus on current or recent state
Item wording	Generally items were well worded although items measuring multiple concepts were noted in several of the 10 instruments
Response options	5- and 7-point verbal rating scales were most commonly used to measure the frequency of occurrence of asthma symptoms. Several instruments were identified with yes/no and 3-point scales, which may restrict the ability of the measure to distinguish between asthma states and to demonstrate changes in symptoms over time
Scoring	All measures had domains which did not clearly reflect defined symptom concepts
Development history	Limited information was presented regarding the level of patient involvement, attainment of “conceptual saturation,” or details of the patient characteristics

## Conclusions

- Consistent with current guidelines for the diagnosis and management of asthma, findings from the qualitative literature review indicate that asthma can be characterized by 3 major categories of core symptoms:
  - Breathing symptoms (difficulty breathing, shortness of breath, wheezing),
  - Chest symptoms (chest pain, chest tightness, chest pressure, mucus/phlegm)
  - Cough
- Existing qualitative research is limited with very little evidence on the experience of asthma by adults
- Despite a large number of PRO instruments (n=85) designed to monitor and evaluate asthma outcomes, few have adequate evidence of content validity to support FDA product labeling requirements
- Based on these findings and limitations, the Asthma WG engaged expert clinical advisors and undertook an extensive qualitative research effort in adolescents and adults with asthma in the US to support development of a novel asthma symptom measure suitable for measuring asthma symptom burden in the context of clinical trials (Abstract 51552<sup>1</sup>)

## Reference

<sup>1</sup> MocarSKI M, Gater A, Fleming S, Nelsen LM, Coons SJ. Development of the Initial Version of the Asthma Daily Symptom Diary (ADSD). Poster 51552 at: American Thoracic Society International Conference, May 16-21, 2014, San Diego, California.

Disclosures: Conflicts of Interest and Financial - None to declare