



# **Community-Acquired Bacterial Pneumonia Patient-Reported Outcome Instrument Development: Concept Elicitation and Cognitive Debrief Interviews Final Report**

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## Introduction

### 1.1 Background

Despite the availability of antimicrobial therapies, community-acquired pneumonia

(CAP)/community-acquired bacterial pneumonia (CABP) remains a major cause of morbidity and mortality worldwide, particularly in elderly patients and in those with significant comorbidities. CABP affects over 5.5 million people each year in the United States, and *Streptococcus pneumoniae* is the most commonly identified pathogen in typical pneumonia.<sup>1</sup> The clinical presentations of pneumonia are usually very similar and several symptoms commonly present in patients across different etiological pneumonia types.<sup>1,2,3</sup> Historically, studies have evaluated treatment efficacy based on clinical outcomes such as mortality, bacteriologic response, stabilization of respiratory and heart rate, clinical cure/ response, adverse events/ safety, and hospitalization, and more recently on the basis of the health-care costs associated with outpatient visits, inpatient hospitalizations, the use of antibiotics/antimicrobials, and return to work or usual activities.<sup>4</sup>

Although there is agreement that patient-reported data are vital in assessing health outcomes, there is minimal literature examining the effect of treatment on CABP symptoms and health-related quality of life. No patient-reported outcomes (PRO) instrument has been developed to assess CABP-related symptoms specifically in accordance with the FDA Guidance for PRO measures (2009).<sup>5</sup> Beyond assessing clinical efficacy in registrational trials, understanding patient-reported outcomes in the newly defined regulatory CABP entity could more broadly and significantly influence decision-making about the optimal choice of antimicrobial agents.

At the request of the Food and Drug Administration (FDA), the Foundation for the National Institutes of Health (FNIH) Biomarkers Consortium (BC) assembled a Project Team, including members from the National Institutes of Health (NIH), FDA and other key academic and industry infectious diseases experts and leaders, to review historical and current data related to CABP clinical trials. This review identified CABP as a priority indication, and resulted in the development of a candidate list of endpoints for use in clinical trials. The review also highlighted that reliable, well-defined and clinically relevant PRO instruments are needed to assess endpoints that measure tangible benefits for patients in clinical trials of antibacterial drugs.<sup>6</sup>

The goal of the work is to elicit concepts of CABP from the patients' perspective in order to develop

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<sup>1</sup> Lutfiyya, M.N., Henley, E., & Chang, L.F. (2006). Diagnosis and treatment of community-acquired pneumonia. *American Academy of Family Physicians*, 73, 442-50.

<sup>2</sup> Fang, G-D, et al. (1990). New and emerging etiologies for community-acquired pneumonia with implications for therapy. *Medicine*, 69 (5), 307-316.

<sup>3</sup> Farr, B.M., Kaiser, D.L., Harrison, B.D.W., Connolly, C.K. (1989). Prediction of microbial aetiology at admission to hospital for pneumonia from the presenting clinical features. *Thorax*, 44, 1031-1035.

<sup>4</sup> Lamping, D.L., Schroter, S., Marquis, P., Marrel, A., Duprat-Lomon, I., Sagnier, P.P. (2002). The Community Acquired Pneumonia Questionnaire. A new, patient-based outcome measure to evaluate symptoms in patients with community-acquired pneumonia. *Chest*, 122, 920-929.

<sup>5</sup> Food and Drug Administration. (2009). Guidance for Industry on Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. *Federal Register*, 74(235),65132-65133

<sup>6</sup> Talbot GH, Powers JH, Fleming T, et al. (2012). Progress on Developing Endpoints for Registrational Clinical Trials of Community-acquired Bacterial Pneumonia and Acute Bacterial Skin and Skin Structure Infections: Update from the Biomarkers Consortium of the Foundation for the National Institutes of Health. *Clinical Infectious Disease*, 55(8), 1114-1121.

a PRO with established qualitative content validity; accordingly, an attempt will be made to interview as broad a patient population as possible. The PRO instrument was developed in accordance with the FDA Guidance for PRO measures used to support labeling claims (2009) for use in clinical trials of antibacterial interventions.

To date, a significant gap in the literature concerns the utilization of PROs to measure treatment effects in CABP. A review of the literature confirmed that no PRO instrument assessing CAP/CABP symptoms had been developed in accordance with the FDA PRO Guidance (2009). Generic PRO instruments (e.g., SF-36) have been used in CAP studies<sup>7</sup> and at least four CAP-specific instruments and two interviewer-administered measures including the presence/absence of 10 CABP symptoms,<sup>8</sup> plus the assessment of severity and both of five CAP symptoms, were developed to assess patient-reported symptoms prior to issuance of the draft FDA PRO Guidance (2006). These instruments could potentially be used as resources to help inform the development of the proposed CABP-specific PRO for use in clinical trials of antimicrobial drugs; however, the FNIH BC team decided that establishing content validity according to the FDA PRO Guidance (2009) within the specific CABP patient population of interest (patients enrolled in registrational trials) was warranted, and the team recommends that future studies in CABP assess outcomes that are most important to CABP patients.

The overall project team was comprised of members from the Biomarkers Consortium. A smaller research sub-team, with members having experience treating or conducting research with CABP patients and/or having experience developing and evaluating PRO measures, was also assembled to implement the core research activities for this study.

## 1.2 Literature Review

Prior to commencing the current study, the research team reviewed the CAP literature and interviewed several clinical experts in the field to collect information about CAP signs, symptoms, impacts, and treatment to help inform the development of a new PRO measure. The literature review identified a total of 34 articles that met inclusion criteria. Generally, the most frequently reported symptoms by CAP patients in the studies reviewed included cough, chest pain, dyspnea, sputum production and fatigue. Symptom resolution was the characteristic endpoint in studies as defined by the absence of symptoms at a specified time point. Older patients with CAP typically reported a lower number of respiratory and non-respiratory symptoms compared to younger patients. The overall evidence from the literature suggested that although CAP can be classified as typical or atypical, the clinical presentations are often similar. The literature also showed that generic PRO instruments (e.g., SF-36), and interviewer-administered measures including CAP-specific symptoms have been used in CAP studies. Despite some evidence of acceptable psychometric properties, the CAP-specific instruments showed notable methodological limitations, and all were developed prior to the draft FDA PRO Guidance (2006). Overall, the literature confirmed that there

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<sup>7</sup> Gleason PP, Kapoor WN, Stone RA, et al. Medical outcomes and antimicrobial costs with the use of the American Thoracic Society guidelines for outpatients with community-acquired pneumonia. *JAMA* 1997; 278:32–39.

<sup>8</sup> Marrie TJ, Lau CY, Wheeler SL, et al. Predictors of Symptom Resolution in Patients with Community-Acquired Pneumonia. *Clinical Infectious Diseases* 2000; 31:1362-7.

is a paucity of evidence on the most well-defined, reliable, reproducible, and feasible methods for measuring efficacy outcomes in future CABP trials for targeted patient populations. Despite the existence of previous CAP-specific measures, a new PRO instrument for CABP that is developed in accordance with the FDA Guidance for PRO measures (2009), addresses the limitations of existing tools, and accurately captures data on concepts and outcomes most important to patients with CABP is still needed.

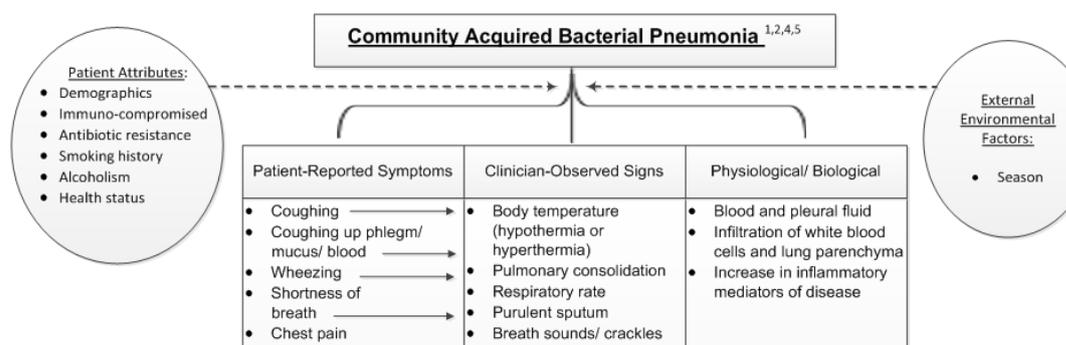
### 1.3 Clinical Expert Interviews

As part of the development process, six clinicians with expertise in the field of CAP/CABP were interviewed to assess their views on the common signs of CABP and frequently reported symptoms experienced by CABP patients. Numerous clinical signs for CABP were reported by the experts and the most frequently cited included: tachypnea, white blood cell count, elevated heart rate, and dyspnea. The experts also cited several patient-reported symptoms including cough, fever, chest discomfort/pain, sputum production, sleeplessness, fatigue, chills, and difficulty breathing/shortness of breath. A variety of examples were cited related to the effect of CABP symptoms on patients’ lives and functioning such as the inability to cook, make the bed, vacuum or walk, a loss of appetite, sleeplessness, and an effect on daily grooming. Experts also noted that patients often miss work due to lingering symptoms such as malaise, low energy or non-productive cough which can go on for weeks. Examples of effects on patients’ emotional functioning included feelings of distress, disappointment and anxiety about their health.

### 1.4 Conceptual Model

As a result of the literature review and clinical expert interviews, a conceptual model (Figure 1) was developed to illustrate CABP symptoms and the impact of CABP symptoms on functioning. Arrows linking the concepts show the direction of influence.

Figure 1: CABP Conceptual Model



This report describes the development of a new CABP-specific instrument building on the work previously described and aligned with regulatory guidance. The purpose of this study was to learn about patients' experience with CABP and the associated symptoms, plus how these symptoms affect their lives and functioning. The information gathered in the initial concept elicitation (CE) interviews was used to develop a conceptual framework, which formed the basis of a new CABP-specific PRO instrument. Draft items were developed to match the key concepts that arose from the CE interviews and items were grounded in language used by patients. After the draft measure was reviewed by experts, the instructions, items, response options and recall period were assessed for clarity, relevance, comprehensiveness, and meaningfulness through patient cognitive debriefing (CD) interviews. With completion of CD interviews and required changes made to the instrument, it is now ready for psychometric evaluation. This report summarizes the objectives, methods, results, and item development from both the CE and CD stages of the current qualitative study with the end result being a content-valid PRO for patients diagnosed with CABP.

## 2. Objectives

The purpose of the CABP PRO instrument development process was to conduct qualitative research on which to base the draft PRO items and to establish content validity of the new instrument. The objectives of the qualitative interviews were two-fold:

- (1) To elicit feedback from patients regarding their experience with CABP and related symptomatology using CE interviews, and
- (2) To determine whether the newly developed draft items were understandable and meaningful to CABP patients using CD interviews.

## 3. Methods

The cross-sectional, qualitative study was designed to gather information directly from patients about symptoms associated with CABP, and to ensure that a newly developed PRO measure in CABP would be understandable and meaningful to patients. The interviews were conducted by trained and experienced researchers.

### 3.1 Patient Selection and Recruitment

Twenty patients with CABP as defined by the recent FDA Guidance on Developing Drugs for Treatment of CABP in the U.S. were recruited for the CE stage of this study, and 9 were recruited for the CD stage. Patients were identified by six clinical sites (Ohio, Florida, California (2), Massachusetts, and Washington, D.C.). Institutional Review Board (IRB) approval was obtained prior to commencing recruitment. The sites identified consecutively eligible and interested adult patients with a confirmed diagnosis of CABP. Study enrollment was open to all people in terms of gender, ethnicity, and educational level. In order to document eligibility, the sites completed a Screening and Medical History Form for each individual. Those patients who fulfilled the study selection criteria were then included in the study. Written informed consent was obtained from all participants before interviews were scheduled. Specific inclusion/exclusion criteria were chosen to reflect CABP populations that are typically used in clinical trial studies, in order for the new measure to be relevant to that patient population. The criteria for both the CE and CD interviews are listed below:

#### 3.1.1 Inclusion Criteria

##### Signs and Symptoms (at least 3)

- Fever [defined as body temperature greater than 38°C (100.4°F) taken orally; greater than 38.5°C (101.2°F) tympanically; or greater than 39°C (102.2°F) rectally]; **or** hypothermia [defined as body temperature less than 35°C / 95°F]
- Cough
- Production of sputum
- Chest pain
- Dyspnea or tachypnea
- Clinical signs of pulmonary consolidation (e.g., dullness on percussion, bronchial breath sounds, or egophony)
- Elevated peripheral WBC count (>10 x 10<sup>9</sup>/L)
- >15% immature neutrophils

##### Radiographic

- The chest radiograph or other imaging (e.g., CT scan) should show the presence of a new infiltrate in a lobar or multilobar distribution characteristic of bacterial pneumonia

##### Other

- Patient has been diagnosed with CABP within the past 10 calendar days
- Patient is 18 years of age or older; at least 50% of patients should be 50 years of age or older

- Patient is willing to provide written informed consent, participate in a telephone interview for approximately 60 minutes and have the interview audio recorded
- Patient is able to read and speak English

### 3.1.2 Exclusion Criteria

- Confirmed or suspected respiratory tract infection attributable to etiologies other than bacterial pneumonia (e.g., visible/ gross aspiration pneumonia; suspected viral, fungal, or mycobacterial infection of the lung)
- Neoplastic lung disease, cystic fibrosis, progressively fatal pulmonary or extra-pulmonary disease, chronic neurological disorder preventing clearance of pulmonary secretions, or life expectancy of less than or equal to 3 months
- Medical or psychiatric illness that could, in the investigator's opinion, potentially interfere with the patient's ability to participate in this interview study

## 3.2 Study Interview Procedures

For both the CE and CD phases of the qualitative research, telephone interviews were conducted by an experienced qualitative interviewer. Before patient participation in the telephone interview, the informed consent procedure was carried out by the clinical site coordinator. The telephone interviews took place when the patient was either at the clinical site or at their home, depending on patient preference. Although in-person interviews are generally the preferred method of data collection, telephone interviews were the only feasible method due to the timeframe within which to interview the patient. Before audio recording was begun, patients were given the opportunity to ask questions about the study and also answered demographic and background questions. Interviews lasted between 30 and 70 minutes. The interviews were audio-recorded and transcribed verbatim. The patients received \$100 as compensation for their participation.

### 3.2.1 Concept Elicitation Interviews

During the CE interviews, the interviewer used the Concept Elicitation Interview Guide to ask patients about their CABP symptoms and how these symptoms affected their lives and functioning. The interview guide was semi-structured and contained open-ended questions, as well as specific probes. For each symptom that patients mentioned, the interviewer probed for further details (i.e. frequency, intensity, duration). The concept elicitation interview data was used to develop a conceptual framework and to draft the CABP-specific instrument, including instructions, items, and responses.

### 3.2.3 Cognitive Debriefing Interviews

During the CD interviews, the Cognitive Debriefing Interview Guide was used to ascertain each patient's interpretation, understanding and assessment of the ease of use of the newly developed CABP-specific instrument. During the interview, patients were asked to read the instructions, each question, and the associated response options. The interviewer then used the questions and probes in the interview guide to ask patients whether the text was clear, easy to understand, and relevant to them. A "think-aloud" approach was used, which involved the patient thinking aloud about what they think each question is asking them. The patient was asked to suggest alternative wording in cases where they thought the question was unclear or could be improved.

### 3.3 Analysis

The methodology and analysis were conducted in line with the FDA's final Guidance on PRO instrument development (2009).<sup>9</sup>

#### 3.3.1 Concept Elicitation Interview Data Analysis

Thematic analysis was conducted to evaluate the information gathered during the CE interviews, according to the methodology described by Joffe and Yardley (2004).<sup>10</sup> This analysis consisted of an initial reading and re-reading of the data to identify themes and concepts emerging from the data. The analysis distinguished between symptoms and impacts that were elicited spontaneously versus those that had been endorsed after probing. A qualitative analysis software tool, MaxQDA, was used to facilitate the analysis process. The themes/concepts emerging from the analysis were recorded in a saturation grid, and saturation was monitored in accordance with the methods described by Kerr et al. (2010),<sup>11</sup> in line with the FDA PRO guidance (2009). Saturation was achieved within the number of interviews completed for this study and is described further in the results section.

#### 3.3.2 Conceptual Framework Development and Item Generation

The draft conceptual framework presented in the DDT Briefing Document was used as a framework in the analysis of the CE data. Its purpose was to demonstrate the relationship of items to domains and domains to total score of a PRO instrument. The qualitative interviews focused on CABP symptoms and their impact. Concepts that emerged from the CE interviews were then used to generate draft items for the new PRO instrument. The conceptual framework was further modified to represent the areas/concepts of importance to patients as demonstrated in the qualitative data analysis.

#### 3.3.3 Expert Review

To check the validity of the items in the draft new instrument, 3 experts in CABP were consulted: Dr. Thomas File (Summa Health System), Dr. Mihaela Stefan (Baystate Medical Center), and Dr. Andrew Auerbach (University of California, San Francisco). Two of the 3 experts (Drs. Stefan and Auerbach) did not overlap with the prior expert interviews described in the introduction. The 3 experts were asked to complete a survey that included questions about each item in the instrument. The purpose of this survey was to obtain information from the experts regarding which symptoms would be most important to include in the final instrument. The experts were asked to identify which symptom and functioning aspects are most relevant or most likely to be reported by patients, to comment about whether or not the items were easy to understand, and to assess if the symptoms mentioned are sensitive to change.

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<sup>9</sup> Food and Drug Administration. (2009). Guidance for Industry on Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Federal Register, 74(235), 65132-65133.

<sup>10</sup> Joffe, H., & Yardley, L. (2004). Content and thematic analysis. In: Research methods for clinical and health psychology. 1<sup>st</sup> ed. London: SAGE.

<sup>11</sup> Cicely Kerr. Saturation in qualitative PRO research. Oxford Outcomes Webinar, November 2010

### 3.3.4 Cognitive Debriefing Interview Data Analysis

Analysis of the cognitive debrief interviews was performed on an item-by-item basis, as outlined by Willis (2005)<sup>12</sup> with the goal of identifying items that presented cognitive challenges and performing an assessment of content validity. The cognitive debriefing data were analyzed using a combined approach of thematic and content analysis (Joffe & Yardley, 2004). Thematic analysis is particularly well-suited to the identification of themes and concepts which emerge from conversational data; content analysis provides a more detailed examination of participants' responses to particular questions.

An item tracking matrix was used to record patients' comments regarding each item, the response options, instructions and recall period. This matrix provided a record of any modifications occurring throughout the CD process and a transparent history of the development process overall. The item tracking matrix showed the point at which no further comments were generated in relation to each item of the new instrument.

## 4. Results

### 4.1 Concept Elicitation

#### 4.1.1 Patient Characteristics

A total of 20 CE interviews were conducted to identify symptoms associated with CABP and what areas of patients' lives were affected by the condition. The patients' demographic and clinical characteristics are summarized in Table 1 below. The mean age of patients was 59.5 (SD=18.8) years old with a range of 29-90, and the majority were male. Patients were primarily Caucasian (60%) or Black/African American (30%), and the highest level of education attained was primarily high school/GED, some college, or a bachelor's degree. The employment status of the sample participants varied, with many participants who reported being retired or semi-retired (30%), some temporarily or permanently unable to work (30%), others in full-time or part-time employment (25%), others who were self-employed (10%), and others who were unemployed or seeking work (5%). All patients were hospitalized as a result of CABP and they spent a mean of 3.5 days (SD=1.9) in the hospital. Only one patient experienced recent trauma. The majority (83%) of patients had one or more co-morbidities and 30% had a previous diagnosis of CAP. The majority (60%) of patients were past or current smokers and only one patient had a history of alcoholism. Only two patients showed a positive microbiological culture.

*Table 1: Demographic and Clinical Characteristics*

Characteristic	Distribution (N=20)
<b>Age</b>	
Mean (SD)	59.5 (18.8)
Range	29-90

<sup>12</sup> Willis, G. (2005). Cognitive Interviewing: A Tool for Improving Questionnaire Design. London: SAGE.

Characteristic	Distribution (N=20)
<b>Sex: Female</b>	9 (45%)
<b>Race/Ethnicity</b>	
Caucasian	12 (60%)
Hispanic	-
Black/ African American	6 (30%)
Asian	1 (5%)
American Indian/Alaskan Native	1 (5%)
<b>Education</b>	
High School/GED	6 (30%)
Some college	5 (25%)
Associate's degree	1 (5%)
Did not complete high school	3 (15%)
Bachelor's degree	5 (25%)
<b>Employment Status</b>	
Student	-
Employed full-time	4 (20%)
Employed part-time	1 (5%)
Retired	5 (25%)
Semi-Retired	1 (5%)
Unemployed/seeking work	1 (5%)
Temporarily unable to work	2 (10%)
Permanently unable to work	4 (20%)
Other (e.g. self-employed)	2 (10%)
<b>Other Characteristics</b>	
Patient was hospitalized	20 (100%)
Mean days in hospital (SD) <sup>1</sup>	3.5 (1.9)
Recent trauma <sup>2</sup>	1 (5%)
Comorbidity <sup>3</sup>	14 (70%)
Previous CAP	7 (35%)
Smoking (past or current) <sup>4</sup>	12 (60%)
History of alcoholism	1 (5%)
Positive microbiological culture <sup>5</sup>	2 (10%)

<sup>1</sup> Data only available for 11 patients <sup>2</sup> & <sup>3</sup> Data only available for 17 patients <sup>4</sup> Data only available for 19 patients. <sup>5</sup> Culture not taken for 7 patients; unknown result for 1 patient

#### 4.1.2 Symptoms of CABP

The CE interviews resulted in the spontaneous report of a wide range of symptoms (N=27) linked to CABP. Report of symptoms reached saturation at interview sixteen. A saturation grid for symptoms is shown in Table 2 below. The seven most frequently reported symptoms were: tiredness/lack of energy (N=18 of 20 patients, 90%), problems with breathing (N=16 patients, 80%), cough (N=16 patients, 80%), mucus/phlegm production, (N=11 patients, 55%), chest hurt/pain (N=9 patients, 45%), fever/elevated body temperature (N=9 patients, 45%), and aches/pains (N=9 patients, 45%). A further 22 symptoms were reported by participants, with varying degrees of frequency. Table 3 below shows the frequency of all spontaneously reported symptoms. A summary of findings for each of the symptoms is provided below.

Table 2: Saturation Grid-Symptoms

Symptoms	Patient ID's (Age)									
	201-001 (47)	201-002 (34)	201-004 (43)	203-001 (67)	203-002 (63)	201-006 (76)	203-004 (36)	203-005 (52)	203-008 (51)	203-011 (59)
Fever/elevated body temp	X		X	X	X		X		X	
Headache	X		X	X			X		X	
Vomiting	X	X		X				X		
Weakness	X	X	X	X				X		
Mucus/phlegm production	X			X		X	X		X	
Nasal congestion	X						X			
Dizziness	X			X				X	X	
Cough	X		X	X		X	X	X	X	
Chest hurt/pain	X					X	X			X
Problems with breathing		X	X	X	X	X	X	X	X	X
Loss of appetite		X		X			X		X	X
Tiredness/lack of energy		X	X		X	X	X	X	X	X
Sweating/night sweats		X		X	X		X	X	X	X
Pressure in Chest		X			X			X		
Sore/aching throat			X	X					X	
Aches and pains			X				X		X	
Wheezing				X		X				X
Chills				X			X		X	
Nausea								X		
Diarrhea	X									
Seeing spots/visual impairment		X		X						
Stomach hurt/pain				X						X
Fainting/loss of consciousness				X						
Elevated heart rate										X
Difficulty concentrating/focusing										
Runny Nose										
Sneezing										

**Key**

First time code applied

**Patient ID's (Age)**

<b>Symptoms</b>	<b>203-015 (63)</b>	<b>203-016 (31)</b>	<b>202-001 (90)</b>	<b>205-001 (70)</b>	<b>205-003 (77)</b>	<b>206-014 (29)</b>	<b>206-020 (83)</b>	<b>206-052 (85)</b>	<b>205-004 (77)</b>	<b>205-007 (58)</b>
Fever/elevated body temp	X	X					X			
Headache	X	X		X						
Vomiting		X	X			X				
Weakness		X		X	X					
Mucus/phlegm production	X	X	X	X		X		X		X
Nasal congestion										
Dizziness		X				X				X
Cough	X	X	X	X	X	X	X	X		X
Chest hurt/pain		X		X		X	X			X
Problems with breathing	X	X	X	X	X	X				X
Loss of appetite		X						X		
Tiredness/lack of energy	X	X	X	X	X	X	X	X	X	X
Sweating/night sweats		X								
Pressure in chest	X	X	X			X				
Sore/aching throat										
Aches and pains	X	X		X		X	X			X
Wheezing										
Chills	X	X					X			
Nausea						X				
Diarrhea		X								
Seeing spots/visual impairment										
Stomach hurt/pain		X				X				
Fainting/loss of consciousness		X								X
Elevated heart rate							X			
Difficulty concentrating/focusing				X					X	
Runny nose		X								
Sneezing						X				

**Key**

**First time code applied**

*Table 3: Frequency of Spontaneously Reported Symptoms\**

Symptom	Frequency (%), (N=20 patients)
Tiredness/lack of energy	18 (90%)
Problems with breathing	16 (80%)
Cough	16 (80%)
Mucus/phlegm production	12 (60%)
Fever/elevated body temp	9 (45%)
Chest pain/hurt	9 (45%)
Aches and pains	9 (45%)
Headache	8 (40%)
Weakness	8 (40%)
Sweating/night sweats	8 (40%)
Pressure in chest	7 (35%)
Dizziness	7 (35%)
Vomiting	7 (35%)
Loss of appetite	7 (35%)
Chills	6 (30%)
Stomach pain/hurt	4 (20%)
Fainting/loss of consciousness	3 (15%)
Sore/aching throat	3 (15%)
Wheezing	3 (15%)

\*The following symptoms were each mentioned by fewer than 3 patients: elevated heart rate (n=2), difficulty concentrating/ confusion (n=2), seeing spots/visual impairment (n=2) diarrhea (n=2), nausea (n=2), nasal congestion (n=2), runny nose (n=1), and sneezing (n=1).

#### 4.1.2.1 Tiredness/lack of energy

Tiredness/lack of energy was the most frequently reported symptom of CABP, mentioned by 18 of the 20 (90%) patients who participated in the CE interviews. Patients typically described the tiredness/lack of energy as severely debilitating in terms of interfering with the ability to move around, work, drive, and cook. Sample patient descriptions are provided below:

201-004: *“Cough, dry cough, not having enough energy to do regular things, sleeping all day long, headaches. I was not myself.”*

203-004: *“You have no energy, period... I was at work and my whole body felt – I just felt tired at work. I felt like my legs was going to give out... It’s like a leech, it just sucks the life out of you... No energy at all to do anything like even there was a time I was hungry, I had no energy to get up and cook.”*

205-001: *You don't have energy. It kicks – it gradually saps all of your energy because you're not getting oxygen. I probably want to say that, but my legs were, I mean, my whole body, you know? Would, you know, you could hardly move. Get into a car, into my car and drive away, slowly get out. I would go into a store to get something and come back out. And it was all very slow and – and of course anybody seeing me would say you look like hell. It's basically – the energy is taken from me by the pneumonia."*

#### 4.1.2.2 Problems with breathing

A problem with breathing was a frequently reported symptom of CABP, mentioned by 16 of the 20 (80%) patients. Patients described the act of breathing as hard and requiring effort. Many referred to general difficulties with breathing (i.e. 'hard to breathe', difficulty "catching" a breath), while others used the term 'shortness of breath'. Sample patient descriptions are provided below:

203-004: *"It's hard to breathe. It's like you're trying to breathe through a straw. You are gasping for breath a lot."*

203-015: *"I could not get my breath. In order to just go to the restroom it would just take everything out of me and I would just be totally out of breath."*

203-008: *"It's hard to catch your breath. You have to gasp for air."*

2003-001: *"If I walk around in the house, I get short of breath."*

#### 4.1.2.3 Cough

Cough was a frequently reported symptom of CABP, mentioned by 16 of the 20 (80%) patients. Patients typically talked about this symptom in terms of severity and how it bothered them. They often described their coughing as persistent and painful. Sample patient descriptions are provided below:

203-005: *"You just keep coughing. You keep coughing... About three nights before I came in I started coughing and I was coughing all night. And it kept me up all night for the last three nights before I went to the hospital. And then, on Saturday I got up and I couldn't breathe. I was breathing okay, I was just coughing. Saturday I got up and I couldn't breathe...The coughing was bothering me. It was getting to where people was like, boy you sound like you're dying. You sound like you're dying. You need to go to the hospital. You need to go to the doctor."*

203-016: *"I had the cough maybe for about 2-3 days. Maybe 2-3 days. You know how you cough and your chest [Respondent demonstrates crackling sound]. You cough and you're like, I don't want to cough ever again. It hurts so bad. You can really hear it rattling."*

201-001: *"The cough is the worst...Yes. It hurts when you cough."*

Several patients talked about their cough being associated with trying to get rid of mucus or phlegm in their chests, which is described further in the next subsection.

#### 4.1.2.4 Mucus/phlegm production

Mucus/phlegm production was reported by 12 of the 20 (60%) patients. Patients typically described the mucus/phlegm production in terms of severity and as abundant and constant. Some patients talked about coughing up mucus/phlegm, i.e:

202-001: *"I had a lot of phlegm...I felt like I was choking."*

201-006: *"A lot of coughing, it's a lot of phlegm coming up."*

203-015: *“I was starting the real heavy coughing—and the phlegm, and just stuff coming up.*

Some patients also talked about having difficulty coughing up mucus/phlegm (i.e. they could feel the mucus/phlegm on their chest but often could not cough it up):

203-016: *“And I had phlegm coming up... Sometimes it was, and then sometimes I had to cough five times in a row to get it up, or I would go into a coughing fit and then it’ll come up after. And then, sometimes I’d cough and it’d just come right up. But a lot of times when the cough got worse it was me coughing to where my whole body moved. It would jerk my whole feet off the floor. I’m sitting down and my feet will come off the floor. That’s how hard the cough was.”*

201-001: *“The mucus [inaudible\10:50.0] coming up. I could feel it, but it just ain’t coming up. It has been coming up, some of it. I don’t want to try to force it, that will make me throw up because the mucus is right there in the chest. I try to make it, force it to come out and...”*

#### 4.1.2.5 Fever/elevated body temperature

Fever/elevated body temperature was reported by 9 of the 20 (45%) patients. When describing this symptom, patients spoke about how hot or warm they felt. When talking about their fever, patients often mentioned other symptoms such as sweating and aching. Sample patient descriptions are provided below:

203-002: *“I thought I had the flu is what I thought I had. Then I just – I was sweating and I was running a fever. That’s about it, just sweating and running a fever.”*

203-015: *“And I normally do not run a fever. But I started running a fever and aching.”*

203-001: *“It was serious because I woke up that Wednesday morning and my fever, I had had fever so bad like I was wringing wet with sweat when I woke up and I knew that was my fever was high because I could feel it, how hot I was.”*

#### 4.1.2.6 Chest pain/hurt

Chest pain or chest hurting was reported by 9 of the 20 (45%) patients. When describing this symptom, patients typically described their chest pain in terms of severity and as forceful. Sample patient descriptions are provided below:

203-011: *“And I was having chest pains and then I have having pain on my left side—of my upper chest.”*

206-014: *“Well, my doctor actually went to talk to them about it already. All I told them was that I was having a lot of chest pains and spitting up mucus. I just told them I was having chest pains and I was spitting up green—“*

206-020: *“I’ll tell you, it’s not good. You don’t feel good. You feel very bad and your chest hurts. Not all the time, but it hurts.”*

A couple of patients also talked about the chest pain/hurt being associated with their lungs or breathing, for example:

203-004: *“The lining of your lungs hurt. When you breathe, it hurts.”*

206-014: *“Everything I just said; sore, painful, hurts to lay down. You feel your lungs swelling up. It’s hard to breathe. You feel fatigued, sometimes nauseous, and then you might get a little dizzy.”*

#### 4.1.2.7 Aches and Pains

Aches and pains were mentioned by 9 of the 20 (45%) patients. Patients typically described the aches and pains as consuming their entire body. Sample patient descriptions are provided below:

201-004: *"My whole body was aching and I was so sorry I had this [Inaudible/0:04:53.2] I went to an emergency clinic."*

203-004: *"[Y]our whole body hurts, aches, pains..."*

203-016: *"It started around Sunday. I had a sharp pain underneath my right shoulder. My whole entire body, but especially my back right up underneath my shoulder on the right side was sharp. It hurt. I was moaning and crying, just feeling like something was happening to me."*

#### 4.1.2.8 Headache

Headache was mentioned by 8 of the 20 (40%) patients. Patients typically described this symptom as being severe and persistent. Sample patient descriptions are provided below:

203-004: *"I had headaches pretty much through the whole thing for two days."*

203-015: *"I had a really bad headache."*

203-008: *"I had a headache. Yeah, pretty bad. Well, I took Tylenol and that didn't even help."*

#### 4.1.2.9 Weakness

Weakness was reported by 8 of the 20 (40%) patients. Patients typically described their weakness as incapacitating, preventing them from standing up or walking independently. Sample patient descriptions are provided below:

201-001: *"It just makes you feel weak like, you feel kind of weak and it's like you try to stand up and you get a little like you're drunk."*

203-005: *"And I was weak and tired. I needed help myself, just to get ready to go to the hospital is what I felt like."*

203-001: *"When I stand up, I would stand up on the floor, I just fell down and couldn't get up and I just was weak. I lose all – in my body, I lose the whole feel of it..."*

#### 4.1.2.10 Sweating/night sweats

Sweating was mentioned by 8 of the 20 (40%) patients. Patients typically focused on the severity and volume of sweat produced and how it soaked through clothes and bedding. Sample patient descriptions are provided below:

203-004: *"I kept sweating through all my clothes. I had to wash all my sheets and cover and everything."*

203-008: *"I was constantly sweating, hot, dripping with sweat."*

201-002: *"I was seeing black spots and then after the black spots, like someone threw a bucket of water on me. I was just drenched in sweat."*

#### 4.1.2.11 Pressure in chest

Pressure or tightening in the chest was reported by 7 of the 20 (35%) patients. While some patients felt this symptom as a discomfort, others described it as unbearable. Some patients described feeling as if someone were sitting on their chest. Sample patient descriptions are provided below:

201-002: *"I couldn't take the pressure building up in my chest and the shortness of breath."*

203-015: *"Like I say, it just felt like somebody was sitting on my chest. So, there at the end it was discomfort. It wasn't hurting, but it was discomfort."*

205-001: *"Eventually – eventually – I don't know. The tightening of the chest was, got to a pretty – pretty constant situation."*

#### 4.1.2.12 Dizziness

Dizziness was reported by 7 of the 20 (35%) patients. Patients typically described dizziness as tremendously incapacitating, warranting assistance to stand or walk. Sample patient descriptions are provided below:

201-001: *"It hurt a little bit and then I got real dizzy. I could not walk. I could not stand."*

203-016: *"I was very dizzy. I've been dizzy the whole entire time. I have a little slight dizziness still, but it's nowhere compared to what I had during this. When I would sit up it felt like someone was spinning me around the whole time."*

203-005: *"Yeah. I had to grab a hold of something to get my balance and then I'd be okay. Well, it was pretty bad because I fell a couple of times."*

#### 4.1.2.13 Vomiting

Vomiting was mentioned by 7 of the 20 (35%) patients. Patients typically described this symptom as a direct effect of "being sick," and some patients focused on the frequency of this symptom. Sample patient descriptions are provided below:

203-005: *"I was just really sick to my stomach and just puked."*

201-002: *"That's when I started vomiting. From like a regular cough, but I'm about to vomit. I have been coughing seriously. The vomit comes."*

203-005: *"I got sick a couple of times. Threw up a couple of times, so that wasn't any fun."*

#### 4.1.2.14 Loss of appetite

Loss of appetite was mentioned by 7 of the 20 (35%) patients. Patients typically described a severe loss of appetite as not wanting to eat for extended periods of time but often forcing themselves to do so out of necessity. Sample patient descriptions are provided below:

203-001: *"I couldn't eat nothing. I could eat a bite of food, that's it. I'd eat because I'm a diabetic and I'd try to eat, and I couldn't. I'd eat a bite, I'd try to eat enough to keep me going. I try to eat something to keep me going, keep me going so I can take my medicine."*

203-011: *"You feel awful...You don't want anything to eat and the only thing you want to do is drink something because you're so thirsty."*

203-004: *"There were days I didn't feel like eating. I didn't eat anything for two days. Like I said, I felt like I should eat, I mean, I know I didn't eat. The second day I knew I should eat, that's when I wanted to cook something and that's when I turned off the stove. I didn't have enough energy to even finish cooking it. I wasn't hungry at all, I just knew I didn't eat for a day or two."*

#### 4.1.2.15 Chills

Having chills was mentioned by 6 of the 20 (30%) patients. Patients described their chills as a significant indicator of their illness. Sample patient descriptions are provided below:

203-001: *"I went in the hospital, I was having chills. I knew something was wrong when I started having chills."*

203-011: *"Just you feel achy, tired, achy, your head hurts. You get cold chills like you are sweating but you're, it's like when you go out and shovel snow and you are shoveling the driveway and you don't really pay attention and you're sweaty but you're cold at the same time. You get cold chills and everything."*

203-016: *"I was sweating, and freezing, and I had chill bumps everywhere too."*

#### 4.1.2.16 Stomach pain/hurt

Stomach pain or hurt was mentioned by 4 of the 20 (20%) patients. Patients typically described their stomach pain in terms of severity and as a forceful physical sensation. Sample patient descriptions are provided below:

203-001: *"I thought I was getting better, but my daughter said you need to go to the hospital and I said no. I said I'd lay down while my stomach was hurting. After I laid down for a while with my stomach hurting, I had chills. I would try to go to the bathroom but I couldn't because I thought I had diarrhea or something, but I didn't."*

206-014: *"Yeah, because I would throw up a lot. So, it would cause my stomach to hurt. It would be so tight it hurts."*

#### 4.1.2.17 Fainting/loss of consciousness

Fainting or loss of consciousness was mentioned by 3 of the 20 (15%) patients. When describing this symptom, patients mentioned that this symptom caused them to collapse on the floor. Sample patient descriptions are provided below:

203-001: *"When I stand up, I would stand up on the floor, I just fell down and couldn't get up and I just was weak. I lose all – in my body, I lose the whole feel of it and I couldn't get up and then I know that I – first I had another chill and then when I went to get up, I just passed out."*

203-016: *"Which also, on Saturday I actually collapsed. I was brought in Saturday by the ambulance because I collapsed on the floor."*

#### 4.1.2.18 Sore/aching throat

Sore or aching throat was mentioned by 3 of the 20 (15%) patients. Patients described the symptom in association with other symptoms such as headaches and cough. Sample patient descriptions are provided below:

201-004: *"I was starting having headaches and cough and throat started aching and I started having fever."*

203-008: *"I felt like my throat was tightening up."*

203-001: *"I have this headache and my throat. My throat is bothering me now."*

#### 4.1.2.19 Wheezing

Wheezing was mentioned by 3 of the 20 (15%) patients. When describing this symptom, patients focused on its severe, immobilizing effect. Sample patient descriptions are provided below:

203-005: “Well, I had to lay down a couple of times and rest because of the wheezing.”

203-006: “That lasted – after that day in the hospital, the day after I got to the hospital. He was telling me – he said my wheezing was really bad.”

#### 4.1.2.20 Other Symptoms

Symptoms among CABP patients mentioned fewer than 3 times (n=8) are included below. Symptoms mentioned include the following:

- Elevated heart rate (n=2)
- Difficulty concentrating/focusing (n=2)
- Seeing spots/visual impairment (n=2)
- Diarrhea (n=2)
- Nausea (n=2)
- Congestion (n=2)
- Runny nose (n=1)
- Sneezing (n=1)

#### 4.1.3 Impact of Symptoms

In addition to identifying symptoms associated with CABP, the CE interviews resulted in the spontaneous report of how these symptoms impacted functioning. Symptoms negatively affected physical functioning, social functioning/relationships, activities of daily living, emotions, and sleep (difficulty sleeping and increased sleep). Table 4 below shows the frequency of all spontaneously reported impacts. Reports of the impacts on functioning reached saturation at interview four. A saturation grid for impacts is shown in Table 5. A summary of findings for each of the six impacts is also provided below.

*Table 3: Frequency of Spontaneously Reported Symptom Impacts*

<b>Impact</b>	<b>Frequency (%) (N=20 patients)</b>
Physical functioning	17 (85%)
Social/relationships	10 (50%)
Activities of daily living	9 (45%)
Difficulty sleeping	7 (30%)
Increased sleep	6 (30%)
Emotions	5 (25%)

Table 4: Saturation Grid-Symptom Impacts

Impacts	Patient ID's (Age)									
	201-001 (47)	201-002 (34)	201-004 (43)	203-001 (67)	203-002 (63)	201-006 (76)	203-004 (36)	203-005 (52)	203-008 (51)	203-011 (59)
Emotions				X	X		X	X		
Activities of daily living			X	X			X	X		
Physical functioning	X	X	X	X	X	X		X		X
Social/Relationships			X			X	X	X		
Difficulty Sleeping		X	X	X			X	X	X	
Increased Sleep		X	X	X				X		

Impacts	Patient ID's (Age)									
	203-015 (63)	203-016 (31)	202-001 (90)	205-001 (70)	205-003 (77)	206-014 (29)	206-020 (83)	206-052 (85)	205-004 (77)	205-007 (58)
Emotions			X							
Activities of daily living	X		X	X	X	X				
Physical functioning	X	X	X	X	X	X	X	X		X
Social/Relationships	X	X	X		X	X	X			
Difficulty Sleeping								X		
Increased Sleep					X		X			

**Key**

First time code applied

#### 4.1.3.1 Physical Functioning

Impairment in physical functioning was experienced by 17 of the 20 (85%) patients. Patients described impairment as limitations in walking/movement, inability to drive, and difficulty working/performing labor. Sample patient descriptions are provided below:

201-001: *"It hurt a little bit and then I got real dizzy. I could not walk. I could not stand."*

205-003: *"I was not able to focus. I don't want to take a chance driving. I don't think I was myself, so I stayed away from driving. So that did affect my normal routine."*

203-016: *"Like I said, I'm an artist and I'm supposedly going on tour. And I can't exercise and do the things I have to do to keep up with my body. There's everything--photo shoots, music videos, recording. Those things you have to do I can't do because I'm in the bed."*

#### 4.1.3.2 Social/Relationships

Social impact of symptoms was felt by 10 of the 20 (50%) patients who participated in the CE interviews. When describing the impact, many patients reported its negative effects on their relationships with family and friends, as well as, dating life. Sample patient descriptions are provided below:

206-014: *"Yeah, because it's hard to try to date somebody and then you date them, and then a week, month, or two later you're in the hospital. Some people can't deal with that. I do find myself alone a lot. And then, when you have pneumonia you don't want to pass it to people. So, a lot of people that would usually help me can't. So, I feel like I'm kind of really on my own, just by myself."*

205-003: *"Yes. I just didn't want to talk to them. That was nasty to my sister which I regret now. You tend to be nasty when you don't feel good, even though you try hard not to."*

203-004: *"I have a baby I take care of. I didn't talk to my fiancé. I didn't pay attention to my fiancé, I didn't pay attention to my kid. I didn't talk to any of my friends. It was like you dropped off a bridge completely."*

#### 4.1.3.3 Activities of Daily Living

Impairment in performing activities of daily living was experienced by 9 of the 20 (45%) patients. When describing activities of daily living, patients reported difficulty with cooking, eating, cleaning, and showering. Sample patient descriptions are provided below:

205-007: *"Nothing. There is nothing you can do. You can't eat, you can't sleep, you can't walk next door, you can't read the paper. There is nothing you can do until you are hooked up for days and days and they get this thing – get antibiotics pumped into you and get you on your way. There is nothing."*

203-001: *"Right now I can't do the things I used to do around the house. I can't do too much of cooking, I can't stand up to cook too much. I can't do none of that right now."*

201-004: *"Once I take the medicine, again, it's kind of—I do some—sometimes I skip shower because [Inaudible/0:20:06.7] sat in the shower and so on, so forth because I can't really do it."*

#### 4.1.3.4 Difficulty Sleeping

Difficulty sleeping was mentioned by 7 of the 20 (35%) patients. Patients described difficulty sleeping to be caused by coughing and having to use the bathroom frequently. Sample patient descriptions are provided below:

203-005: *"About three nights before I came in I started coughing and I was coughing all night. And it kept me up all night for the last three nights before I went to the hospital."*

203-008: “[M]ainly sleep because I’m constantly up and down coughing and everything, using the bathroom, and everything.”

203-004: “I felt like crap and I couldn’t sleep.”

#### 4.1.3.5 Increased Sleep

Increased sleep was mentioned by 6 out of 20 (30%) patients. When describing this symptom, patients focused on how they were sleeping more frequently and longer than usual. Sample patient descriptions are provided below:

201-002: “My appetite just was going away and started feeling shortness of breath and my walking, my legs got weak. I just started sleeping longer hours.”

201-004: “Deep inside I'm feeling that I'm not okay. I was sleeping all day long and all night long and then coughing in the night, basically.”

#### 4.1.3.6 Emotions

Emotional impact of symptoms was experienced by 5 of the 20 (25%) patients. When describing the impact of their symptoms, patients reported feeling upset, for example:

**Interviewer:** What was that like for you other than what you told me?

203-002: “Excuse me. It made me sick to my stomach because I never had anything like that.”

**Interviewer:** Oh, so you were sick to your stomach?

203-002: “Well, no, I mean upset.”

Others reported feeling irritable, for example:

204-004: “I had to wash all my sheets and cover and everything and I was just getting – I told my girlfriend with her working, I tried to help her and screamed at her for no reason at all. I was like screw it, just take me to the hospital.”

#### 4.1.4 Most Bothersome and Important to Treat Symptoms

Each patient was also asked to report his/her most bothersome symptoms, and the symptoms they felt were the most important to treat. Impacts of symptoms and signs of CABP were also spontaneously reported. A detailed description of the results is presented in Tables 6 and 7. Overall, cough (N=5) and problems with breathing (N=5) were the most bothersome symptoms mentioned by patients. Problems with breathing (N=10), cough (N=7), and fever (N=5) were mentioned as the most important symptoms/signs to treat.

*Table 5: Patients’ Self-Reported Most Bothersome Symptoms/Signs/Impacts\**

Symptom	Frequency (%) (N=20 patients)
Cough	5 (25%)
Problems with breathing	5 (25%)
Impaired physical functioning	2 (10%)
Tiredness	2 (10%)
Headache	2 (10%)
Phlegm	2 (10%)
Weakness	1 (5%)

Chest pain	1 (5%)
Chest Tightness	1 (5%)
Low Energy	1 (5%)
Chest pressure	1 (5%)
Sleeping all day long	1 (5%)
Throat hurting	1 (5%)
Fever	1 (5%)
Stomach hurting	1 (5%)
Swollen lungs	1 (5%)

*Table 6: Patients' Self-Reported Most Important Symptoms/Signs/Impacts to Treat\**

<b>Symptom</b>	<b>Frequency (%) (N=20 patients)</b>
Problems with breathing	10 (50%)
Cough	7 (35%)
Fever	5 (25%)
Body aches/pain	3 (15%)
Chest pain	3 (15%)
No energy	2 (10%)
Tiredness	2 (10%)
Wheezing	1 (5%)
Dizziness	1 (5%)
Wheezing	1 (5%)
Impaired physical functioning	1 (5%)
Headache	1 (5%)
Sweating	1 (5%)
Elevated heart rate	1 (5%)
Confusion/difficulty concentrating/focusing	1 (5%)
Painful lungs	1 (5%)
Stomach hurts	1 (5%)
Leg hurts	1 (5%)
Swollen lungs	1 (5%)
Hard time swallowing	1 (5%)
Nausea	1 (5%)
Vomiting	1 (5%)
Chills	1 (5%)
Loss of appetite	1 (5%)

## 4.2 Development of the Draft Instrument Items

### 4.2.1 Identification of Relevant Symptoms and Impacts: CE Interviews

Following the CE interviews with patients, the wider project team was consulted to review all patient-reported symptoms and impacts, and to generate the first draft of the daily symptom diary. After close review of the

symptom concepts that emerged from the CE interview data, it was decided that 21 of the 27 symptoms should be included as draft items in the symptom diary. Most of these 21 symptoms were also mentioned by patients as either most bothersome (i.e. cough, problems with breathing, phlegm, chest hurt/pain, pressure in the chest, tiredness, headache, weakness, low energy, fever, and stomach pain) or most important to treat (cough, fever, body aches/pain, chest hurting/pain, no energy, tiredness, dizziness, headache, sweating, elevated heart rate, confusion/difficulty concentrating/focusing, stomach pain, nausea, vomiting, chills, and loss of appetite). Overall, the symptoms were classified as either respiratory-specific or systemic, as detailed below.

#### Respiratory-specific symptoms

- Cough
- Problems with breathing
- Coughing up mucus or phlegm
- Chest hurt/pain
- Pressure in the chest

#### Systemic Symptoms

- Tiredness/lack of energy
- Weakness
- Warm/hot<sup>13</sup>
- Body aches/pain
- Headache
- Sweating
- Dizziness
- Loss of appetite
- Cold/chills
- Sore/aching throat
- Stomach hurt/pain
- Nausea
- Diarrhea
- Difficulty concentrating/focusing
- Elevated heart rate
- Vomiting

It was suggested that the remaining 6 symptoms be eliminated as they were deemed by the team to be relatively uncommon or unrelated to CABP (wheezing, seeing spots/visual impairment, fainting/loss of consciousness, runny nose, nasal congestion, and sneezing). Wheezing was removed because although the concept was cited in the literature, only 1 of 6 experts mentioned the symptom during their interviews and only 3 of 20 patients reported the symptom spontaneously during CE. Seeing spots/visual impairment and fainting/loss of consciousness were removed

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<sup>13</sup> Although the concept of fever/change in body temperature was mentioned by 45% of CABP patients, the actual manifestations of these concepts varied across patients. Since fever produces an array of distinct and unique symptoms, the experts suggested the need to distinguish each of these symptoms in the diary, such as the experience of heat/warmth and cold/chills. Therefore, the broad symptom of fever/change in body temperature was removed.

because these symptoms were only mentioned by 2 patients during CE and were not cited in the literature or by clinical experts. Runny nose was removed because this symptom was only mentioned by 1 patient during CE and was not cited in the literature or by clinical experts. Nasal congestion was removed because this symptom was only mentioned by 2 patients during CE and was not cited in the literature or by clinical experts. Lastly, sneezing was removed because this symptom was only mentioned by 1 patient during CE and was not cited in the literature or by clinical experts.

For the majority of the 21 symptoms, one item was developed for each symptom. For some symptoms, two items were generated, based on patient and/or expert explanations of those symptoms. For example, tiredness/lack of energy was separated into two items as this symptom was considered two distinct concepts. Tiredness was reported by 13 of 20 patients and lack of energy was reported by 6 of 20 patients. Two patients mentioned both tiredness and lack of energy. Five patients also described these symptoms in terms of “fatigue” and one patient mentioned “malaise.” Two items were used to capture the “mucus/phlegm” symptom as patient quotes, and expert feedback, highlighted that it is not only the presence of mucus but the patient having trouble coughing up the mucus/phlegm which is also a separate and clinically important concept. Although descriptions of chest “hurt” and “pain” were reported by patients, only chest hurt was included as an item to help avoid any potential confusion with chest pain being associated with cardiovascular symptoms. Although “difficulty breathing” and “shortness of breath” were mentioned synonymously during the interviews, patients’ descriptions suggested both terms were used to describe problems with breathing. Only an item for difficulty breathing was initially included in the diary because, based on expert input, “difficulty breathing” was deemed more patient-friendly language whereas “shortness of breath” was considered more of a clinical /medical term. Although “difficulty concentrating/focusing” and “nausea” were only reported by 2 patients each, these symptoms were considered for inclusion as draft items because “difficulty concentrating/focusing” was also mentioned in the literature and by clinical experts, and “nausea” was also mentioned in the literature.

All 5 symptom impacts reported by CABP patients were considered relevant and meaningful, and were included as items in the diary. Based on patient responses and input from the project team, only “difficulty sleeping” was considered for inclusion as a separate item in the draft diary as it was judged to be a more relevant concept than “increased sleep.” For example, “difficulty sleeping” was mentioned as an important concept during both patient and clinical expert interviews. “Increased sleeping” was only mentioned during patient interviews and the clinical team considered this concept related to and potentially captured by concepts already included such as “tired” and “lack of energy.” Based on expert and patient feedback, emotional functioning was divided into 2 items, “upset” and “worried,” to fully capture the emotional impact of the disease. Notably, one of the 5 symptom-related impacts (physical functioning) was also mentioned by patients as most bothersome and most important to treat.

#### Symptom-related Impacts

- Emotional functioning (2 items – upset, and worried)
- Social functioning
- Activities of daily living
- Physical functioning
- Difficulty sleeping

In total, 29 items were developed from the 21 symptoms and 5 symptom impacts mentioned in the CE interviews with CABP patients. Items on the instrument were grouped and ordered based on category (i.e. respiratory symptoms, systemic symptoms, and symptom related impacts).

## 4.2.2 Identification of Response Options and Recall period

A 24-hour recall period was chosen due to the variability and frequency of symptoms represented by patients during the CE interviews. Likert scale response options of “not at all, a little bit, somewhat, quite a bit, and very much” were chosen because CABP symptoms and impact were typically described in terms of varying levels of severity or degree as illustrated in the below examples:

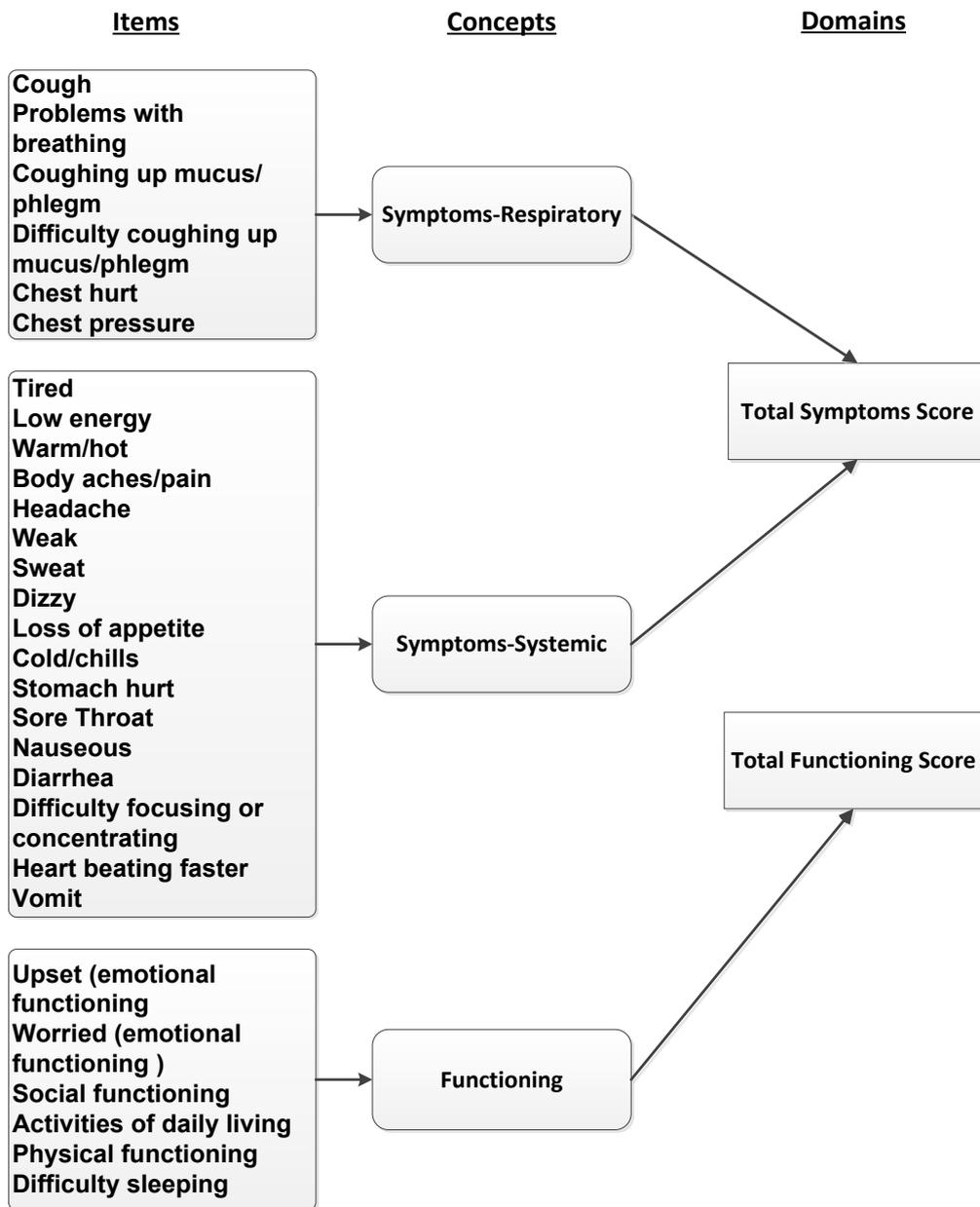
**Interviewer:** And let’s see. How serious were your chills before you came to the hospital?

206-020: *“Not very serious. You just notice it’s abnormal because a normal person has no chills. When you have a chill that’s not too cold for me.”*

203-001: *“Mm-hmm [yes]. It just kept on just getting worser and worser, getting badder and badder. Each day it was getting badder and badder. I’d be sitting up, I’d get up and walk from the house, from one room to the bathroom and I was out of breath. I said I’m going to have to sit down and rest, it’s getting bad. My breathing was real bad. I – how hard it was coming. I could hear myself breathing coming from the inside. I could hear myself breathing.”*

A daily diary mode of administration for the new PRO instrument was chosen to also capture frequency of symptoms. A draft conceptual framework model for the new PRO instrument is shown in Figure 2.

Figure 2: Draft Conceptual Framework Model



### 4.2.3 Section Summary

Following a carefully documented process of concept elicitation and item generation, a 29-item CABP symptom and functioning diary, with each item comprised of 5 response options, was developed. In order to comply with the FDA final guidance on instrument development the draft instrument required further evaluation by patients using a cognitive debrief methodology; this process is detailed in Section 4.4, following Section 4.3 on expert review of draft items.

### 4.3 Expert Review

Three clinical CABP experts were independently surveyed about the draft PRO instrument. They completed a survey electronically or by phone with an ICON researcher. The purpose of the survey was to gather information about which symptom and functioning aspects were most relevant or most likely to be reported by patients. The experts also evaluated the extent to which the items were easy to understand and if the symptoms mentioned were sensitive to change.

At least 1 expert agreed or strongly agreed that 25 of the 29 concepts (20 symptoms- tired, low energy, chest hurt, cough, cough up mucus or phlegm, difficulty coughing up mucus or phlegm, difficulty breathing, headache, loss of appetite, weakness, sweating, pressure in the chest, cold/chills, difficulty focusing/concentrating, sore throat, nausea, elevated heart rate, vomiting, warm/hot, diarrhea and 5 impacts- physical functioning, activities of daily living, social functioning, difficulty sleeping, worried) were either relevant to patients with CABP or likely to be reported by CABP patients. Regarding relevance or likelihood of report for the remaining 4 concepts, all 3 experts were either neutral or disagreed (body aches/pain, dizziness, stomach hurt, upset). The experts noted that several of the concepts were either too similar or hard to distinguish (i.e. cough versus difficulty coughing up mucus/phlegm, weakness versus low energy) or uncommon (i.e. aches/pain, headache, stomach pain). One expert noted that patients may have difficulty interpreting the concept of pressure in the chest as it can be associated with cardiac problems. Two experts also mentioned that patient report of diarrhea may be confounded by antibiotic treatment. Another expert noted that the concept of “nausea” may not be understood by all patients. However, as these concepts were reliably identified as important to the patients during CE and subsequently endorsed by the cognitive interviews, the items were left in the diary and will be further reviewed during the psychometric phase of the study.

Experts were also asked whether the symptoms and impacts were likely to show change over the course of a clinical trial of a new treatment for CABP. At least 1 expert agreed or strongly agreed that 26 of the 29 symptoms or impacts were likely to show this change (21 symptoms- tired, low energy, chest hurt, cough, cough up mucus or phlegm, difficulty coughing up mucus or phlegm, difficulty breathing, headache, body aches/pain, loss of appetite, weakness, sweating, pressure in the chest, cold/chills, difficulty focusing/concentrating, sore throat, nausea, elevated heart rate, vomiting, warm/hot, diarrhea and 5 impacts- physical functioning, activities of daily living, social functioning, difficulty sleeping, worried). All 3 experts were either neutral or disagreed that the remaining 3 symptoms and impacts would show change. Some of the experts reported that some symptoms may take longer to improve (e.g. tired) and other symptoms were too general and not CABP specific (e.g. difficulty sleeping) to demonstrate valid change.

Although the above observations are important to document, all symptoms and impacts were left in the diary because they were still considered to be important to the patients during the CE interviews and then further acknowledged by patients as important during the cognitive interviews. These and other similarities between items in the draft instrument will be fully explored in the psychometric validation stage of research. Any item redundancy will be identified in the item-level analysis.

Lastly, the experts were asked to list if there were any other relevant symptoms or functions relevant to patients with CABP that were not included in the diary. Two of the 3 experts reported that all of the relevant concepts were covered. One expert stated that the concept of “depression” should be considered for the instrument as it’s often a symptom of cognitive problems or delirium that accompanies pneumonia.

Although suggestions from the experts were considered, no items were removed or added at this stage following expert review of the diary. Symptoms that were not seen as particularly common by experts, were deemed relevant by patients. It is also unlikely that any clinical experts would be able to articulate the entire spectrum of the CABP patient experience compared to patients themselves. Comments from experts were taken into consideration during the cognitive debriefing phase, where interviewers used additional probes during the cognitive interviews with patients to confirm relevance and interpretation of concepts, and ability of patients to distinguish between similar symptoms. Interviewers also documented when and if any new concepts were used by patients during the cognitive interviews. The results of these cognitive interviews are presented in the next section.

## 4.4 Cognitive Debrief Interviews

### 4.4.1 Patient Characteristics

Cognitive debrief interviews were conducted with 9 additional CABP patients who had not participated in the original concept elicitation interviews. The demographic information and clinical characteristics of the sample are provided in Table 8. The mean age of patients was 62.4 (SD=13.1) years with a range of 34-79, and the majority were female. Patients were primarily Caucasian (67%) or Black/African American (33%), and the highest level of education attained was primarily some college, bachelor's degree, or did not complete high school. The employment status of the sample participants varied, with many participants reporting retirement (56%), full time/part-time employment (22%), or temporarily/permanently unable to work (22%). All patients were hospitalized as a result of CABP and they spent a mean of 3.3 days (SD=1.7) in the hospital. Two patients had experienced recent trauma. The majority (78%) of patients had co-morbidities and 33% had a previous diagnosis of CABP. The majority (78%) of patients were past or current smokers, and no patient had a history of alcoholism.

*Table 7: Demographic and Clinical Characteristics-Cognitive Debriefing*

Characteristic	Distribution (N=9)*
<b>Age</b>	
Mean (SD)	62.4 (13.1)
Range	34-79
<b>Sex: Female</b>	7 (78%)
<b>Race/Ethnicity</b>	
Caucasian	6 (67%)
Black/ African American	3 (33%)
<b>Education</b>	
High School/GED	1 (11%)
Some college	3 (33%)
Associate's degree	1 (11%)
Did not complete high school	2 (22%)
Bachelor's degree	2 (22%)
<b>Employment Status</b>	
Employed full-time	1 (11%)
Employed part-time	1 (11%)
Retired	5 (56%)
Temporarily unable to work	1 (11%)
Permanently unable to work	1 (11%)

Other Characteristics	Distribution (N=9)
Patient was hospitalized	9 (100%)
Mean days in hospital (SD) <sup>1</sup>	3.3 (1.7)
Recent trauma	2 (22%)
Comorbidity	7 (78%)
Previous CABP	3 (33%)
Smoking (past or current)	7 (78%)
History of alcoholism	-
Positive microbiological culture <sup>2</sup>	-

<sup>1</sup> Data only available for 4 patients <sup>2</sup> Culture not taken for 4 patients; unknown results for 5 patients

\* Percentages may not add up to 100% due to rounding

## 4.4.2 Instructions

The instructions on the CABP PRO ask respondents to complete the diary at the same time every day, choose one response number for each statement, record the date and time at which the respondent completes the diary, and think about how they have felt in the past week with respect to their pneumonia. Patients were asked how they interpreted the instructions and if the instructions were clear and easy to understand. All of the interviewed patients (N=9) were able to correctly interpret the CABP PRO instructions, for example:

205-003: *“Keep track of everything that has happened or happening...And you know they want it filled out at the same time. And they want me to answer every question--each and every question.”*

203-017: *“Okay, it’s telling me to do this on a daily basis, and to only give one answer per question.”*

Patients were also asked if they felt that the instructions were understandable and all patients indicated that the instructions were clear and easy to understand:

**Interviewer: Okay. And were these instructions clear?**

205-101: *“Very clear. Very clear. I think it wants to be clear.”*

**Interviewer: Did you understand what you had to do?**

203-017: *“Yes.”*

**Interviewer: Was there anything that could be changed?**

203-017: *“No, not as far as the instructions.”*

**Interviewer: Did you find them [instructions] clear and easy to understand?**

203-018: *“...I just got started looking at them, just going down through it, so, yes, it’s easy to understand.”*

## 4.4.3 Recall Period

The recall period for the CABP PRO is 24 hours. When patients were asked what time period they were considering when responding to each item overall, 6 of 9 patients who were asked this question reported that they had followed the instructions to think about the past 24 hours and the remaining 3 patients were thinking about the time since their pneumonia was diagnosed or the time since the infection started:

**Interviewer: So, the time period, what time period were you thinking about for these questions?**

203-018: *“Let me see here—I’d say 24 hours, definitely.”*

**Interviewer: Okay, 24 hours. Did you find it easy or difficult to think about the 24 hours?**

203-018: *“Easy.”*

**Interviewer: So for questions 1 through 24, what time period were you thinking of when answering those questions?**

205-003: *“Yesterday and today.”*

203-020: *“The last 24 hours—early on it was a different story.”*

Although patients thought the 24-hour recall period was easy to think about overall, 8 of 9 patients were thinking about the time since their pneumonia was diagnosed or the time since the infection started, for at least one item in the diary. Some patients preferred to recall their experience over the past few days or week, for example:

203-021: *“I was thinking about the time when I was getting sick, and I didn’t know what was wrong with me.”*

203-020: *“The question asks if I was thinking of it over the last 24 hours, but I was comparing my experience from when I was first diagnosed with pneumonia, when I was having chills, so I know the difference.”*

203-018: *“Overall I was thinking, like I said, more like 72 hours.”*

**Interviewer: So how long has that been?**

205-102: *“Since Wednesday, and this is Friday.”* **Interviewer: What time period were you thinking about when you answered the question?** 205-102: *“Last week when I was home.”*

Although this recall differential is important to consider, this instrument will be administered as a daily diary; therefore, the tendency for patients to consider the entire length of their infection will be reduced and the 24-hour recall will most likely be reflected. Prior to the clinical trial, a training session for clinical sites responsible for administering the instrument will also ensure a 24-hour recall period is considered. Because this cognitive interview was completed with the patient at one time only, patients were inclined to consider the entire time in which they had had pneumonia.

Patients were also asked if their responses to the questions would change if they were asked how they felt “right now”. For nearly all questions in the diary, one or more patients reported their answer would have changed if they were asked how they felt right now. Many patients reported a decrease in severity in their response option when asked how they felt right now due to perceptions that their pneumonia was improving compared to the previous 24 hours. For example:

203-020: *“Yes, because I would say, probably, not at all [if asked about right now] but looking at it over the last 24 hours, last night was a bad night.”*

203-018: *“If it was now, not at all, but yesterday I did have that at the beginning of the day.”*

#### 4.4.4 Response Options

The response options for each item on the CABP PRO consist of a 5-point Likert scale ranging from “Not at all” to “Very much”. When patients were asked if they thought the response options allowed them to choose an accurate response to each item, most patients stated that they were able to choose an accurate response:

**Interviewer: In other words, how were these response options for you, were you able to answer the questions given the response options provided?**

203-018: *“Yes.”*

**Interviewer: Anything about these specific questions that you would change or add?**

203-018: *“No, they’re pretty straightforward and to the point, I mean I’ve never had it before, but that’s the way it affects, that’s what happens.”*

**Interviewer: And overall any difficulty picking any of the answers for the questions?**

203-018: *“No.”*

**Interviewer:** Did you have difficulty picking an answer to any of the questions that I asked you so far?

203-017: *“No—no, not at all.”*

**Interviewer:** Was it helpful to have the instructions, select only one response, included after each of these items?

205-102: *“Yeah, it was helpful. It was helpful.”*

**Interviewer:** Did you have any difficulty picking an answer to this question?

203-020: *“No, I didn’t, not at all—I did not.”*

#### 4.4.5 Items – Summary of Responses

An in-depth summary of the results for each item of the draft CABP instrument is presented in the item tracking matrix in Table 9. This table also shows the changes made to the diary after analysis of the cognitive interviews. As shown in Table 9, 24 items were left unchanged because all participants interpreted the concept correctly, reported it as easy to understand, and found it relevant to their CABP experience. These were:

- Item 2 (low energy)
- Item 3 (cough)
- Item 4 (problems with breathing)
- Item 5 (cough up mucus/phlegm)
- Item 6 (difficulty coughing up mucus/phlegm)
- Item 7 (warm/hot)
- Item 8 (chest hurt)
- Item 9 (body aches/pain)
- Item 10 (headache)
- Item 11 (weak)
- Item 13 (dizzy)
- Item 14 (eating)
- Item 15 (pressure in the chest)
- Item 16 (difficulty sleeping)
- Item 18 (stomach hurt)
- Item 12 (diarrhea)
- Item 22 (difficulty focusing/concentrating)
- Item 23 (heart beating faster)
- Item 24 (vomit)
- Item 25 (physical functioning)
- Item 26 (social functioning)
- Item 27 (activities of daily living)
- Item 28 (upset)
- Item 29 (worried)

Four items were revised, one item was added, and one item was removed based on feedback from the patient and expert reviews. Details of these revisions are presented below:

1. Item 1, “During the past 24 hours, did you feel tired?” was changed to “During the past 24 hours, did you feel tired more than usual?” because the phrase “more than usual” can help distinguish from how one would normally feel tired in a 24 hour time period. Both experts and patients preferred this question to include a “more than usual” qualifier, and it was consistent with item #12 (e.g. “sweat more than usual”). For example:

**Interviewer:** Okay and so would you have answered this question differently if I had asked, 'during the past 24 hours did you feel tired more than usual?'

205-003: *“I would have answered the same way.”*

**Interviewer:** You would have answered the same way. So what do you think is more relevant to you? During the past 24 hours did you feel tired? Or would you prefer for us to ask during the past 24 hours did you feel tired more than usual? What do you think is more relevant or meaningful to you in this context?

205-003: *“More than usual.”*

**Interviewer:** More than usual yeah okay. Why?

205-003: *“Because the way I feel right now, it could be different than the way that I normally feel.”*

Including a “more than usual” qualifier is also supported by patient reports during initial concept elicitation with tiredness being described as “unusual or not normal.” For example:

205-003: *“Now that I think back, I was tired. I slept a lot, which I don’t usually. You know, I’d nap for three hours and get up for two or three hours. I was going to go see my grandchildren and I couldn’t even run around with them because I was just too tired and I couldn’t breathe.”*

206-020: *“It hurts. Your chest doesn’t hurt all the time, but you’re very tired all the time. You’re very tired and it takes a long time to cure. It takes a while to feel better, but pneumonia doesn’t heal overnight. It didn’t happen overnight probably...Normal people when they get tired go to sleep. When they wake up they’re not tired.”*

**Interviewer:** And the tiredness you mentioned, How about that?

201-006: *“Well, that all came about at around the same time. Always tired, if I walked a little bit, I got tired, short winded, and that’s normally not like me.”*

2. Despite the initial decision to only include “difficulty breathing” to describe breathing problems that patients mentioned in the concept elicitation phase, “shortness of breath” was added to the diary as a separate item based on patient and expert feedback during the cognitive debriefing process. Although “difficulty breathing” was seen as more patient-friendly language, “shortness of breath” was reported to also be a relevant term/concept during the cognitive debriefing interviews. The majority (N=6) asserted that “shortness of breath” was a distinct symptom, for example:

205-003: *“Because--it's just--difficulty breathing could be I don't know how to word it--I'll rephrase that. Shortness of breath is when you feel you can't get your breath. And difficulty breathing is when you're literally almost hyperventilating.”*

203-020: *“I think shortness of breath is more of a gasping, panting, where you really can’t catch your breath, whereas difficulty breathing is you’re really laboring over the in and out process.”*

204-102: *"Yes, because 'short of breath' I couldn't talk long. I could only say a couple of words. I've got to breathe and rest before I could complete a sentence. So, it is a big difference to me. So, I became more short of breath than difficult breathing."*

A separate item for "shortness of breath" was also supported by evidence from patients who reported that this concept was equally relevant to "difficulty breathing:"

**Interviewer: And so which one did you experience or have you experienced both?**

205-102: *"I have experienced both of them."*

**Interviewer: Okay. So they are equally relevant to you?**

205-102: *"Yeah."*

- Item 12, "During the past 24 hours, did you sweat?" was changed to "During the past 24 hours, did you sweat more than usual?" because the phrase "more than usual" can help distinguish how one would normally feel tired in a 24 hour time period. Both experts and patients preferred this question to include a "more than usual" qualifier and it was consistent with language in item #1 (e.g. "tired more than usual"). Patients thought adding "more than usual" to the item would make the question and underlying concept clearer as well as make more relevant to their experience:

**Interviewer: What about if I asked you during the past 24 hours did you sweat more than usual?**

203-018: *"That's where I kind of interpreted it myself."*

**Interviewer: You did, okay, so when you read this question you thought it was more than usual?**

203-018: *"That's what I thought to myself, did you sweat more than usual...Definitely more than usual."*

**Interviewer: Okay. And how about if I asked you though 'during the past 24 hours did you sweat more than usual'? Would you have answered differently?**

205-003: *"No."*

**Interviewer: What's more relevant or meaningful to you, though? During the past 24 hours did you sweat? Or during the past 24 hours did you sweat more than usual?**

205-003: *"More than usual."*

- Item 17 was changed from "During the past 24 hours, did you feel cold or have chills?" to "During the past 24 hours, did you have chills" because feeling cold and having chills were different concepts to the majority of patients (N=8), and this eliminated any potential double barreled confusion. It was decided to remove "feel cold" completely and keep "chills" because this concept was more relevant to patients in terms of severity of their condition and it better captured the concept's original definition:

205-003: *"Well cold could be you don't feel yourself. You know you're--you just don't feel like yourself. Where chills is I take it more like with me when I first had the chills, I was literally shaking. I don't feel they're--that they should be in the same sentence."*

203-020: *"Well, cold is just the temperature, cover me up and I'm going to feel fine. When you have chills, cover me up and I'm still chilling, I'm still shaking."*

205-101: *"I think it's (chills) – it's more serious than being cold. Shiver. Sweating."*

**Interviewer:** What's more relevant to you, feeling cold or having chills in terms of your pneumonia?

203-017: *"I would say having chills, because it was like even though I felt cold, when I had the chills it was like they just wouldn't go away, just come and go, come and go, I guess like a hot flash, it's constant."*

5. Item 20, "During the past 24 hours, were you nauseous?" was changed to "During the past 24 hours, did you feel nauseated," to clarify the difference the clinical experts from the wider project team pointed out between "nauseous," referring to something that actually causes a feeling of sickness, and "nauseated," referring to the actual sensation of sickness. These experts suggested the use of "nauseated" to be consistent with the original definition of this concept as it applies to pneumonia patients. Support for this item change was also illustrated by patients in the cognitive debriefing interviews as they either understood the difference between the concepts or felt the word "nauseated" was equally relevant to "nauseous:"

203-017: *"Because I mean if you can feel nauseous, it could be periodically, but when you're constantly throwing up mucus and phlegm [patient describing "nauseated"], then you know that these toxins are working their way out of your body, but just it's going just as fast to get them out."*

**Interviewer:** What do you think is more relevant to you? Feeling nauseous or feeling nauseated?

205-101: *"I think they are both pretty relevant."*

**Interviewer:** They are both pretty relevant?

205-101: *"Yeah."*

Although most of the participants felt that the overall symptoms included in the diary were relevant, 1 item was removed at this stage due to lack of relevancy reported by the patient and expert review panel.

6. The original item #19, "During the past 24 hours, did you have a sore throat?" was removed because nearly half of patients in the cognitive debriefing interviews (4 of 9) felt this question was not relevant to their experience. Additionally, only 3 of 20 patients reported this symptom during CE, none of the 6 clinical experts mentioned this symptom when interviewed at the beginning of the study, and 2 of 3 clinical experts who were surveyed about the item in the draft instrument, were either neutral or disagreed that sore throat was relevant to patients with CABP or likely to be reported by CABP patients.

**Interviewer:** Was it relevant to you?

205-003: *"No."*

**Interviewer:** Yeah why not?

205-003: *"Because I didn't have a sore throat."*

**Interviewer:** Was it relevant to you?

203-020: *"No, because it doesn't hurt."*

205-102: *"During the past 24 hours, did you have a sore throat? No, not at all."*

**Interviewer:** Not at all? All right. So what is this question asking you then?

205-102: *"I guess it is referring to pneumonia, I guess. Maybe some people have sore throats. I don't know, but I—I didn't. I didn't have one. I don't have one."*

Interviewer: Okay. So [it is] not relevant to you then? Or is it relevant to you?

205-102: *"No."*

#### 4.4.6 General Comments on Draft instrument

Patients completed one-on-one telephone interviews while going through their responses with the interviewer. Patients were able to understand and interpret the CABP PRO instrument instructions, items, response options, and recall period without any problem. When asked whether any CABP symptoms and impacts they experienced were missing from the diary, most patients who were asked this question mentioned that the diary captured their experience and did not have anything to add:

Interviewer: Are there any other symptoms of your pneumonia that were not covered in this diary?

203-018: *"No, actually, everything was."*

Interviewer: ...Are there any aspects of your pneumonia that impacted you that were not covered in the diary?

203-018: *"No, it was all covered."*

Interviewer: And you told me about the things that you would change—anything missing or could be included that you feel is important?

203-018: *"No, I think everything in here is most important."*

Interviewer: Now like I asked you in the beginning during my opening statement regarding any other symptoms of your pneumonia that were not covered in the diary, do you have any examples or do you think it's pretty comprehensive?

203-020: *"I think it's pretty comprehensive, I just—I was surprised, I keep thinking with pneumonia you should be having a cold and coughing at the onset, and it was just all the aches and pain and the constant headache that you're kind of unprepared for—and I never really felt like I had chest pain before I was diagnosed."*

Interviewer: Okay. How about, are there any other aspects of how your pneumonia impacts you that were not covered in the diary?

205-101: *No.*

Interviewer: Are there any aspects of how your pneumonia impacts you that were not covered in this diary?

203-019: *"How it impacts me?"*

Interviewer: Yeah.

203-019: *"No, not really."*

Interviewer: Anything else about this questionnaire that you would change?

203-019: *"No."*

Table 8: Item Tracking Matrix

Item #	Original Item and Response Options	Intended Meaning/Concept Definition	Concept <sup>14</sup> (General Domain)	Expert Review (n=3) <sup>15</sup>	Comments	Potential Actions	Final Item #, Final item, and Response Options
Instructions 1	Please fill out this diary at the same time each day. Please give only one answer for each question and answer every question. Thank you for your time.	The intention for this instruction is for participants to complete the diary at the same time each day when answering each question.	N/A	<ul style="list-style-type: none"> <li>Question not asked in guide</li> </ul>	<ul style="list-style-type: none"> <li>No Change</li> <li>Time period correct=9/9</li> <li>Interpretation (Yes=9/9)</li> <li>Clear (Yes=9/9)</li> </ul>	N/A	Please fill out this diary at the same time each day. Please give only one answer for each question and answer every question. Thank you for your time.
	<p>Please record the current date (MM/DD/YY):</p> <p>Please record the current time: AM / PM (circle one)</p> <p>While answering the following questions, please think about your pneumonia and how you felt during the past 24 hours.</p>	The intention for this instruction is for participants to focus on the previous 24 hours only when answering each question.	N/A	<ul style="list-style-type: none"> <li>Question not asked in guide</li> </ul>	<ul style="list-style-type: none"> <li>No Change</li> <li>Time period correct=9/9</li> <li>Interpretation (Yes=9/9)</li> <li>Clear (Yes=9/9)</li> </ul>	N/A	<p>Please record the current date (MM/DD/YY):</p> <p>Please record the current time: AM / PM (circle one)</p> <p>While answering the following questions, please think about your pneumonia and how you felt during the past 24 hours.</p>
#1	<p>During the past 24 hours, did you feel tired? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p>	Feeling fatigued or tired.	Tired (fatigue-systemic symptom)	<ul style="list-style-type: none"> <li>Takes a long time to improve (n=1)</li> <li><b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>Interpretation (Yes=9/9)</li> <li>Clear (Yes=9/9)</li> <li>Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li><b>Leave as is</b></li> <li><b>OR</b></li> <li>A possible suggestion was to add "more than usual" to be consistent with the 'sweat more than usual' question</li> </ul>	<p>8. During the past 24 hours, did you feel tired more than usual? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p>

<sup>14</sup> These are overall general concepts of the item. Domains and sub domains will be illustrated in the conceptual framework

<sup>15</sup> These comments will be further explained and addressed in the expert review section of the final report

	4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much					(#12): During the past 24 hours, did you feel tired more than usual? Also this would incorporate the expert review feedback and patient input about including a qualifier. To help distinguish how one would normally feel tired in a 24 hour time period.	4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much
						<b>FINAL DECISION: add "more than usual"</b>	
<b>#2</b>	During the past 24 hours, did you have low energy? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much	Having low energy or a lack of energy.	Low energy (fatigue-systemic symptom)	• Leave as is (n=2)	• Interpretation (Yes=9/9) • Clear (Yes=9/9) • Relevant (Yes=9/9)	• Leave as is	9. During the past 24 hours, did you have low energy? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much
<b>#3</b>	During the past 24 hours, did you have a cough? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much	Having a cough or coughing.	Cough (respiratory- localized symptom)	• Leave as is (n=2)	• Interpretation (Yes=9/9) • Clear (Yes=9/9) • Relevant (Yes=9/9)	• Leave as is	1. During the past 24 hours, did you have a cough? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much
<b>#4</b>	During the <u>past 24 hours</u> , did you have difficulty breathing?	Problems with breathing	Problems with breathing (respiratory- localized)	• Leave as is (n=2)	• Interpretation (Yes=9/9) • Clear (Yes=9/9) • Relevant (Yes=9/9)	• Leave as is  <b>AND add an item for "shortness of breath" as a</b>	2. During the <u>past 24 hours</u> , did you have difficulty breathing? (Select only one

	(Select only one response.)		symptom)		separate item based on patient and expert feedback during the cognitive debriefing process.	response.)	
	<p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p> <p>4 <input type="checkbox"/> Quite a bit</p> <p>5 <input type="checkbox"/> Very much</p>					<p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p> <p>4 <input type="checkbox"/> Quite a bit</p> <p>5 <input type="checkbox"/> Very much</p>	
	During the past 24 hours, did you have shortness of breath? (Select only one response.)	Problems with breathing	Problems with breathing (respiratory- localized symptom)	N/A	N/A	• Leave as is	3. During the past 24 hours, did you have shortness of breath? (Select only one response.)
	<p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p> <p>4 <input type="checkbox"/> Quite a bit</p> <p>5 <input type="checkbox"/> Very much</p>						<p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p> <p>4 <input type="checkbox"/> Quite a bit</p> <p>5 <input type="checkbox"/> Very much</p>
#5	During the past 24 hours, did you cough up mucus or phlegm? (Select only one response.)	Experiencing congestion/excess mucus or phlegm production.	Mucus/phlegm Production (respiratory- localized symptom)	<ul style="list-style-type: none"> <li>• Neither agree or disagree that the item expresses the concept as noted, is relevant/likely to be reported by patients with CABP, or is likely to show change (n=1)</li> <li>• PRO team response: Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=8/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	• Leave as is	4. During the past 24 hours, did you cough up mucus or phlegm? (Select only one response.)
	<p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p> <p>4 <input type="checkbox"/> Quite a bit</p> <p>5 <input type="checkbox"/> Very much</p>						<p>1 <input type="checkbox"/> Not at all</p> <p>2 <input type="checkbox"/> A little bit</p> <p>3 <input type="checkbox"/> Somewhat</p> <p>4 <input type="checkbox"/> Quite a bit</p> <p>5 <input type="checkbox"/> Very much</p>
#6	During the past 24 hours, did you have difficulty coughing up mucus or phlegm? (Select only one response.)	Experiencing difficulty coughing up excess mucus or phlegm.	Mucus/phlegm production (respiratory- localized symptom)	<ul style="list-style-type: none"> <li>• Neither agree or disagree that the item expresses the concept as noted, is relevant/likely to be reported by patients with CABP, or is likely to</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=8/8)</li> <li>• Clear (Yes=6/8)</li> <li>• Relevant (Yes=8/8)</li> </ul>	• Leave as is	5. During the past 24 hours, did you have difficulty coughing up mucus or phlegm? (Select only one response.)
							<p>1 <input type="checkbox"/> Not at all</p>

			show change (n=1)				<input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much
				<b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.			
<b>#7</b>	During the <u>past 24 hours</u> , did you feel warm or hot? (Select only one response.)	Feeling warm or hot in reference to general body temperature.	Fever/elevated body temp (body temperature-systemic symptom)	<ul style="list-style-type: none"> <li>• Leave as is (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	11. During the <u>past 24 hours</u> , did you feel warm or hot? (Select only one response.)
	<input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much						<input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much
<b>#8</b>	During the <u>past 24 hours</u> , did your chest hurt? (Select only one response.)	Feeling chest pain or chest hurting.	Chest hurt/pain (respiratory- localized symptom)	<ul style="list-style-type: none"> <li>• Leave as is (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=8/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	6. During the <u>past 24 hours</u> , did your chest hurt? (Select only one response.)
	<input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much						<input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much
<b>#9</b>	During the <u>past 24 hours</u> , did you have body aches and pain? (Select only one response.)	Having bodily aches and pains.	Body aches/pain (systemic symptom)	<ul style="list-style-type: none"> <li>• Uncommon, more associated with breathing pain (n=2)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=8/9)</li> <li>• Clear (Yes=8/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	14. During the <u>past 24 hours</u> , did you have body aches and pain? (Select only one response.)
	<input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit						<input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit

	5 <input type="checkbox"/> Very much						5 <input type="checkbox"/> Very much
<b>#10</b>	During the <u>past 24 hours</u> , did you have a headache? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much	Experiencing a headache/pain in the head.	Headache (systemic symptom)	<ul style="list-style-type: none"> <li>• Uncommon (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=7/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	15. During the <u>past 24 hours</u> , did you have a headache? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much
<b>#11</b>	During the <u>past 24 hours</u> , did you feel weak? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much	Feeling overall body weakness; a general feeling of reduced body strength.	Weak (fatigue-systemic symptom)	<ul style="list-style-type: none"> <li>• Too similar to low energy (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD. Will be reviewed during psychometric validation phase.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	10. During the <u>past 24 hours</u> , did you feel weak? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much
<b>#12</b>	During the <u>past 24 hours</u> , did you sweat? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much	Experiencing sweating, perspiring more than usual and not due to another cause like exercise or external temperature.	Sweating/night sweats (systemic symptom)	<ul style="list-style-type: none"> <li>• Prefers chills as better word to capture concept (n=1)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=8/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• A possible suggestion was to add "more than usual" to be consistent with the 'tired more than usual' question (#1): During the past 24 hours, did you sweat more than usual? Also this would incorporate the expert review feedback and patient input about including a qualifier. To help distinguish how one would normally feel tired in a 24 hour time period.</li> </ul>	13. During the <u>past 24 hours</u> , did you sweat more than usual? (Select only one response.)  1 <input type="checkbox"/> Not at all 2 <input type="checkbox"/> A little bit 3 <input type="checkbox"/> Somewhat 4 <input type="checkbox"/> Quite a bit 5 <input type="checkbox"/> Very much

FINAL DECISION: add "more than usual"							
#13	During the <u>past 24 hours</u> , did you feel dizzy? (Select only one response.)	Feeling dizzy.	Dizziness (systemic symptom)	<ul style="list-style-type: none"> <li>• Uncommon, difficult for patient to differentiate between this and weak, and low energy as they express same thing (n=2)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD. Will be reviewed during psychometric validation phase</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=6/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	16. During the <u>past 24 hours</u> , did you feel dizzy? (Select only one response.)
	<input type="checkbox"/> 1 Not at all <input type="checkbox"/> 2 A little bit <input type="checkbox"/> 3 Somewhat <input type="checkbox"/> 4 Quite a bit <input type="checkbox"/> 5 Very much						<input type="checkbox"/> 1 Not at all <input type="checkbox"/> 2 A little bit <input type="checkbox"/> 3 Somewhat <input type="checkbox"/> 4 Quite a bit <input type="checkbox"/> 5 Very much
#14	During the <u>past 24 hours</u> , did you feel like eating? (Select only one response.)	Having a loss of appetite.	Loss of appetite (systemic symptom)	<ul style="list-style-type: none"> <li>• Suggested, "Did you have an appetite?" (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=8/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	17. During the <u>past 24 hours</u> , did you feel like eating? (Select only one response.)
	<input type="checkbox"/> 1 Not at all <input type="checkbox"/> 2 A little bit <input type="checkbox"/> 3 Somewhat <input type="checkbox"/> 4 Quite a bit <input type="checkbox"/> 5 Very much						<input type="checkbox"/> 1 Not at all <input type="checkbox"/> 2 A little bit <input type="checkbox"/> 3 Somewhat <input type="checkbox"/> 4 Quite a bit <input type="checkbox"/> 5 Very much
#15	During the <u>past 24 hours</u> , did you feel pressure in your chest? (Select only one response.)	Feeling pressure in chest area.	Pressure in chest (respiratory- localized symptom)	<ul style="list-style-type: none"> <li>• Too likely interpreted as cardiac origin, suggested to combine with chest pain (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD. Will be further reviewed during psychometric validation phase.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=8/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	7. During the <u>past 24 hours</u> , did you feel pressure in your chest? (Select only one response.)
	<input type="checkbox"/> 1 Not at all <input type="checkbox"/> 2 A little bit <input type="checkbox"/> 3 Somewhat <input type="checkbox"/> 4 Quite a bit <input type="checkbox"/> 5 Very much						<input type="checkbox"/> 1 Not at all <input type="checkbox"/> 2 A little bit <input type="checkbox"/> 3 Somewhat <input type="checkbox"/> 4 Quite a bit <input type="checkbox"/> 5 Very much

#16	<p>During the past 24 hours, did you have difficulty sleeping? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Inability or increased difficulty sleeping due to pneumonia, i.e. difficulty falling asleep or remaining asleep.</p>	<p>Difficulty sleeping (functioning/impact-physical)</p>	<ul style="list-style-type: none"> <li>• Uncommon, prefer way to capture item as it relates to respiratory and not generalized sleeping problems (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is.</b></li> </ul>	<p>24. During the past 24 hours, did you have difficulty sleeping? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>
#17	<p>During the past 24 hours, did you feel cold or have chills? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Feeling cold in reference to general body temperature or experiencing chills (in relation to transitioning from hot to cold or during or after sweating).</p>	<p>Chills (body temperature- systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Leave as it (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=8/9)</li> <li>• Relevant (Yes=7/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Cold and having chills were perceived as different concepts for the majority of patients (N=8)</li> </ul> <p>Final decision: Remove "feel cold" completely and keep "chills" because this concept was more relevant to patients in terms of severity of their condition and "chills" better captures the concept's original definition</p>	<p>12. During the past 24 hours, did you have chills? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>
#18	<p>During the past 24 hours, did your stomach hurt? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Having stomach pain or hurting.</p>	<p>Stomach Pain (systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Uncommon (n=1).</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=6/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	<p>18. During the past 24 hours, did your stomach hurt? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>

#19	<p>During the past 24 hours, did you have a sore throat? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Having a sore or aching throat.</p>	<p>Sore/Aching Throat (systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Neither agree or disagree that the item expresses the concept as noted, is relevant/likely to be reported by patients with CABP, or is likely to show change (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=4/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Nearly half of patients (4 of 9) felt this question was not relevant to their experience and lack of relevance was corroborated by experts.</li> </ul> <p><b>Final decision: Remove item</b></p>	<p><b>REMOVE</b></p> <p>During the past 24 hours, did you have a sore throat? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>
#20	<p>During the past 24 hours, were you nauseous? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Feeling nausea, i.e. a queasy feeling, or the need to puke, vomit, or throw-up.</p>	<p>Nausea (GI- systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Neither agree or disagree that the item expresses the concept as noted, is relevant/likely to be reported by patients with CABP, or is likely to show change (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by some patients during CD</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=8/9)</li> <li>• Relevant (Yes=6/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Experts suggested the use of "nauseated" to be consistent with the original definition of this concept as it applies to pneumonia patients in order to clarify the difference between "nauseous," referring to something that actually causes a feeling of sickness, and "nauseated," referring to the actual sensation of sickness.</li> </ul> <p><b>Final decision: Change "nauseated"</b></p>	<p>19. During the past 24 hours, did you feel nauseated? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>
#21	<p>During the past 24 hours, did you have diarrhea? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Having diarrhea.</p>	<p>Diarrhea (GI- systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Leave as it (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=6/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	<p>20. During the past 24 hours, did you have diarrhea? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>

#22	<p>During the past 24 hours, did you have difficulty focusing or concentrating? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Experiencing difficulty with focusing or concentrating.</p>	<p>Focusing/concentrating (systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Leave as is (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=8/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	<p>23. During the past 24 hours, did you have difficulty focusing or concentrating? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>
#23	<p>During the past 24 hours did you feel your heart beating faster? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>	<p>Experiencing an increase in heart rate.</p>	<p>Elevated heart rate (systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Neither agree or disagree that the item expresses the concept as noted, is relevant/likely to be reported by patients with CABP, or is likely to show change (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by some patients during CD</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	<p>22. During the past 24 hours did you feel your heart beating faster? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much</p>
#24	<p>During the past 24 hours, how many times did you vomit? (Select only one response.)</p> <p>1 <input type="checkbox"/> 0 times  2 <input type="checkbox"/> 1 time  3 <input type="checkbox"/> 2 times  4 <input type="checkbox"/> 3 times  5 <input type="checkbox"/> 4 or more times</p>	<p>Frequency of vomiting.</p>	<p>Vomiting (GI- systemic symptom)</p>	<ul style="list-style-type: none"> <li>• Neither agree or disagree that the item expresses the concept as noted, is relevant/likely to be reported by patients with CABP, or is likely to show change (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by some patients during CD</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=6/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	<p>21. During the past 24 hours, how many times did you vomit? (Select only one response.)</p> <p>1 <input type="checkbox"/> 0 times  2 <input type="checkbox"/> 1 time  3 <input type="checkbox"/> 2 times  4 <input type="checkbox"/> 3 times  5 <input type="checkbox"/> 4 or more times</p>
#25	<p>During the past 24 hours, did you have difficulty doing your usual activities or getting around? (Select only one</p>	<p>Reporting of effects on physical functioning.</p>	<p>Physical Functioning (functioning/impact-physical)</p>	<ul style="list-style-type: none"> <li>• Leave as is (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	<p>25. During the past 24 hours, did you have difficulty doing your usual activities or getting around? (Select only one response.)</p>

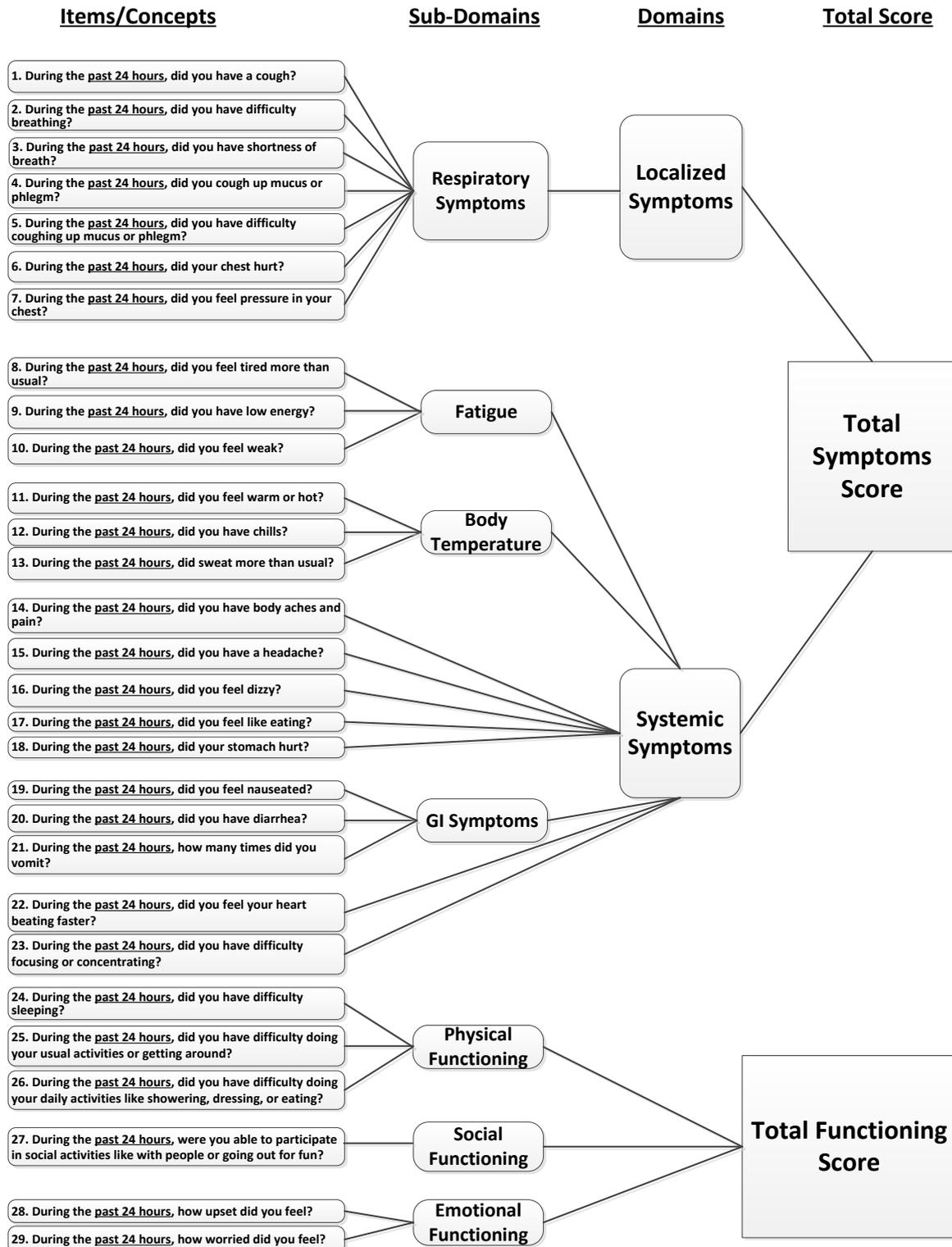
	response.)						<input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much <input type="checkbox"/> Not applicable
#26	<p>During the past 24 hours, were you able to participate in social activities like visiting with people or going out for fun? (Select only one response.)</p> <input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much <input type="checkbox"/> Not applicable	<p>Reporting that illness interferes with their interpersonal and social relationships. Avoiding or not wanting to do activities with friends and family.</p>	<p>Social/Relationships (functioning/impact-social)</p>	<ul style="list-style-type: none"> <li>• Not relevant for elder population (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=8/9)</li> <li>• Relevant (Yes=8/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	<p>27. During the past 24 hours, were you able to participate in social activities like visiting with people or going out for fun? (Select only one response.)</p> <input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much <input type="checkbox"/> Not applicable
#27	<p>During the past 24 hours, did you have difficulty doing your daily activities like showering, dressing, or eating? (Select only one response.)</p> <input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much <input type="checkbox"/> Not applicable	<p>Difficulty with usual daily activities, such as showering, dressing or eating.</p>	<p>Activities of daily living (functioning/impact-physical)</p>	<ul style="list-style-type: none"> <li>• Leave as is (n=2)</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=8/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• Leave as is</li> </ul>	<p>26. During the past 24 hours, did you have difficulty doing your daily activities like showering, dressing, or eating? (Select only one response.)</p> <input type="checkbox"/> Not at all <input type="checkbox"/> A little bit <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite a bit <input type="checkbox"/> Very much <input type="checkbox"/> Not applicable

#28	<p>During the past 24 hours, how upset did you feel? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much  6 <input type="checkbox"/> Not applicable</p>	<p>Reporting that illness causes them to feel a certain emotion.</p>	<p>Emotion (functioning/impact-emotion)</p> <ul style="list-style-type: none"> <li>• Not a good question (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by the CD.</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	<p>28. During the past 24 hours, how upset did you feel? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much  6 <input type="checkbox"/> Not applicable</p>
#29	<p>During the past 24 hours, how worried did you feel? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much  6 <input type="checkbox"/> Not applicable</p>	<p>Reporting that illness causes them to feel a certain emotion.</p>	<p>Emotion (functioning/impact-emotion)</p> <ul style="list-style-type: none"> <li>• Neither agree or disagree that the item expresses the concept as noted, is relevant/likely to be reported by patients with CABP, or is likely to show change (n=1)</li> <li>• <b>PRO team response:</b> Left in as it was important to the patients during CE and subsequently endorsed by some patients during CD</li> </ul>	<ul style="list-style-type: none"> <li>• Interpretation (Yes=9/9)</li> <li>• Clear (Yes=9/9)</li> <li>• Relevant (Yes=9/9)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b></li> </ul>	<p>29. During the past 24 hours, how worried did you feel? (Select only one response.)</p> <p>1 <input type="checkbox"/> Not at all  2 <input type="checkbox"/> A little bit  3 <input type="checkbox"/> Somewhat  4 <input type="checkbox"/> Quite a bit  5 <input type="checkbox"/> Very much  6 <input type="checkbox"/> Not applicable</p>
24-Hour Recall Period			<ul style="list-style-type: none"> <li>• Question not asked in guide</li> </ul>	<ul style="list-style-type: none"> <li>• Most patients thought the recall period was easy to think about</li> <li>• Some patients thought about since the beginning of the infection</li> <li>• Some patients thought about since they were seen in the clinic</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Leave as is</b> because this is a daily diary, patients may not think about their infection as broadly as they did for these interviews</li> </ul>	

## 5. Final Conceptual Framework Model

Following cognitive debriefing, the conceptual framework was revised to represent the item numbers, specific domains, and total symptom score. The draft conceptual framework is shown in Figure 3 below and illustrates how the draft items are related to the symptom and functioning concepts that emerged from the qualitative concept elicitation and cognitive debriefing interviews.

Figure 3: Final Conceptual Framework Model



## 6. Conclusion

The purpose of this report was to summarize the development and evaluative work conducted to establish the content validity of the new CABP PRO measure. To explore content validity, 20 concept elicitation interviews were conducted to elicit key symptoms and impacts of CABP. Using patients' own words from their description of their symptoms, a draft pool of items was developed and evaluated by an expert panel. Although there are apparent similarities between several of these items (e.g. tired, low energy, and weak, etc.), any potential redundancy will be evaluated in the psychometric analysis and the data from that quantitative stage of the research will allow any necessary item reduction to occur.

These draft items were then assessed in cognitive debriefing interviews with a new sample of 9 patients with CABP. The results illustrate that the new CABP PRO instrument is relevant and understandable to the target patient population. Some minor revisions were made to the final set of items in order to maximize consistency, relevance and ease of understanding. All edits are documented in the item tracking matrix. These interviews underscored the relevance and importance of the 29 concepts as well as established that the CABP PRO measure is interpretable and meaningful to this patient population. Patients were able to correctly interpret the instructions and items, and felt that the response options allowed them to select an accurate response to each of the statements on the CABP PRO. In addition, patients felt that the 24-hour recall period was an appropriate timeframe to consider when selecting a response.

In sum, the results of the concept elicitation and cognitive debrief interviews support the content validity of the CABP PRO measure. The conceptual framework has been updated and the draft instrument is now ready for psychometric testing.