HOSPITAL-ACQUIRED BACTERIAL PNEUMONIA: DEVELOPMENT OF A NEW PATIENT-REPORTED OUTCOME INSTRUMENT.

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INTRODUCTION

- It is essential to develop reliable, well-defined and clinically relevant endpoints that measure tangible benefits for patients in clinical trials of antibacterial drugs in accordance with the FDA Guidance for patient-reported outcome (PRO) measures and hospital-acquired bacterial pneumonia (HABP).[1] Currently used endpoints in HABP clinical trials such as clinical response, clinical cure, and time to event, are only indirect measures of treatment benefit and have not been validated.
- Currently there is no HABP PRO instrument to capture additional symptoms of how patients feel, function, or survive.
- The Foundation for the National Institutes of Health (FNIH) Biomarkers Consortium and ICON plc are developing clinically relevant endpoints that measure tangible benefits for patients in clinical trials of antibacterial drugs.

PURPOSE

- The goal of this study was to explore HABP symptoms and impacts as reported by patients, and to develop a draft PRO symptom instrument using methods in-line with the FDA PRO Guidance (2009).[2]
- The information gathered in concept elicitation (CE) interviews, expert reviews, and cognitive debriefing (CD) interviews will be used to modify and expand the conceptual framework which will form the basis of a new HABP-specific PRO instrument.

METHODS

- CE was conducted by telephone interviews with patients within 10 days of HABP diagnosis. Data were analyzed on a rolling basis using an iterative process to identify themes and concepts and recorded in a saturation grid.
- After 8 interviews, a point of saturation was achieved as no new pneumonia concepts had emerged. Overall, concepts endorsed by HABP patients were similar to concepts reported by patients in our previous study to develop a symptom PRO measure for community-acquired bacterial pneumonia (CABP) (See PIN 84, ISPOR 2015).[3]
- A decision was made to begin combined CE and CD interviews using items from our previously developed CABP PRO measure due to the overlap of symptoms and impacts between the two patient populations. In addition to eliciting HABP related concepts, the combined CE/CD interviews are being conducted to assess item readability, relevance, comprehensiveness, and content validity of the original CABP PRO items with the HABP patient population.
- To date, 8 patients have participated in CE interviews and 3 patients have participated in combined CE/CD interviews. Demographics and patient characteristics are reported below in Table 1.

TABLE 1. Patient Characteristics and Demographics

Characteristic	Distribution (N=11)
Age	
Mean (SD)	60.8 (10.9)
Range	41-75
Sex	
Female	5 (45%)
Male	6 (55%)
Race/Ethnicity	
Caucasian	6 (55%)
Black/ African American	5 (45%)
Education	
Did not complete high school	1 (9%)
High School/GED	5 (45%)
Some college	3 (27%)
Bachelor's degree	1 (9%)
Graduate degree	1 (9%)
Employment Status	
Employed part-time	1 (9%)
Retired	4 (36%)
Temporarily unable to work	2 (18%)
Permanently unable to work	4 (36%)
Other Characteristics	**Distribution (N=11)**
Interview conducted while patient still in hospital	3 (27%)
Mean days in hospital (SD)	4 (.76)
Comorbidity	10 (91%)
Previous HABP	1 (9%)
Smoking (past or current)	6 (55%)
History of alcoholism	2 (18%)
Positive microbiological culture	2 (18%)*

*Culture not taken for 2 patients; unknown result for 5 patients; negative culture confirmed for 2 patients

RESULTS

- Among all 11 HABP patients, the most common spontaneously reported symptoms were problems with breathing (N=9), chest pain/hurt (N=7), warm/hot (N=7) and cough (N=6). Nearly half of the patients experienced tiredness/lack of energy, aches and pains, weakness, and chills. The most common spontaneously reported symptom impacts included physical functioning (e.g. walking) (N=10), emotional functioning (N=9) and activities of daily living (N=9). Figure 1 below shows the frequency of all spontaneously reported symptoms and impacts.
- Symptoms frequently reported by both the current HABP patient sample and CABP patients interviewed in our previous PRO study included problems with breathing, chest pain/hurt, warm/hot, and cough.[3,4] The impact frequently reported by both patient groups included physical functioning. Figure 2 shows a comprehensive list of spontaneously reported symptoms among both HABP and CABP patients.
- Three combined CE/CD interviews conducted with HABP patients to date demonstrated that the items in the draft PRO are understandable, relevant, and interpreted as intended. The Project Team will continue to revise the conceptual framework to represent the item numbers, specific domains, and total symptom score.

FIGURE 1: Frequency of Symptoms and Impacts in HABP (N=11)

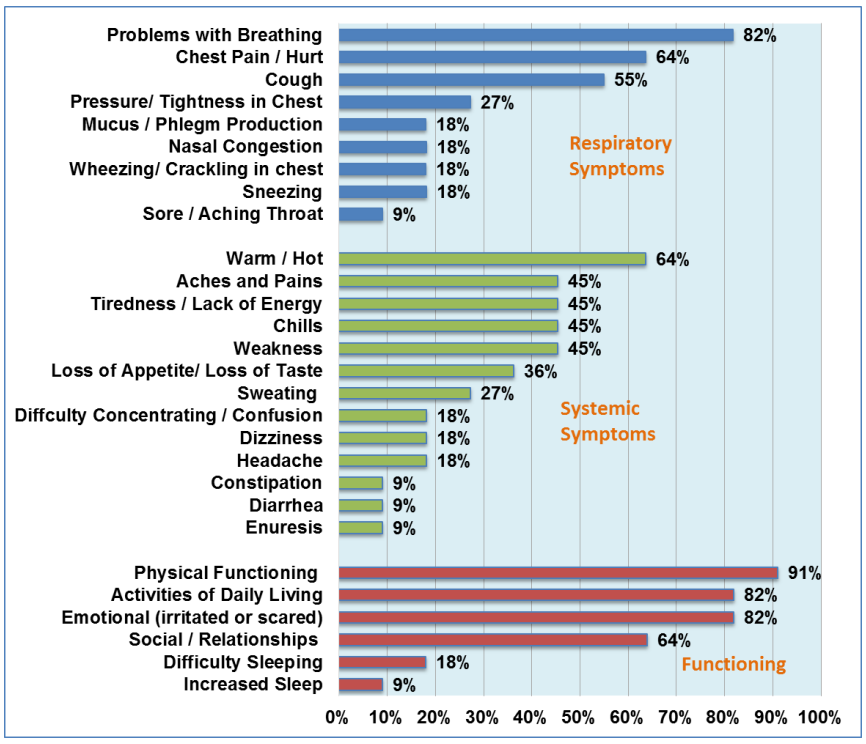
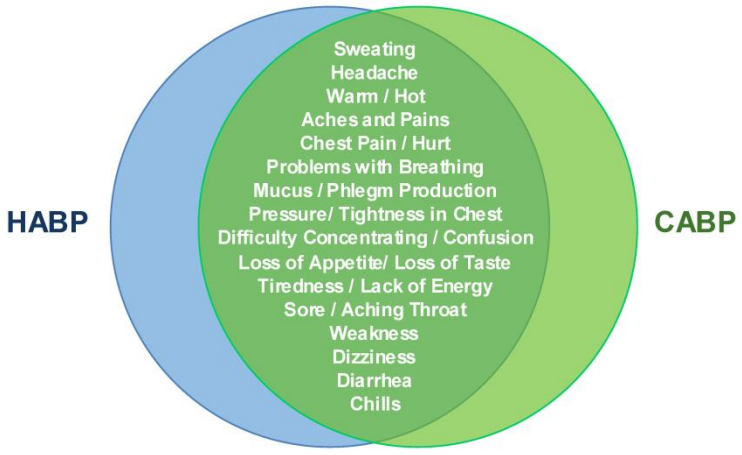


FIGURE 2: Symptoms reported by both HABP (N=11) and CABP patients (N=20)



CONCLUSIONS

- Qualitative data gathered in the CE and joint CE/CD interviews will be combined with input from experts to form the basis of a final HABP PRO structure and item pool.
- Results from the initial CE/CD interviews support the use of items from the CABP PRO measure as HABP patients have found the original CABP items to be relevant and meaningful to their disease experience.
- Preliminary evidence may suggest the use of a unified PRO instrument that can be used to aid the evaluation of new bacterial treatments for both HABP and CABP.
- After completion of the PRO instrument development work described above, a daily symptom diary with established content validity will be ready for psychometric validation.

AFFILIATIONS AND ACKNOWLEDGEMENTS

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