

**ABSTRACT**

**Introduction:** Infections are classified according to the duration of signs and symptoms (S&S) as acute, subacute, or chronic. CAP is primarily an acute infection with patients presenting with less than 10 days of S&S. It is unclear why some patients with CAP seek medical attention soon after illness onset (within 72 hours) meanwhile others wait 4-10 days to seek medical care. We hypothesize that severity of disease may play a role in the duration of S&S before seeking medical attention, with patients having more severe disease. The objective of this study was to evaluate the association between severity of CAP and the duration of S&S prior to seeking medical attention.

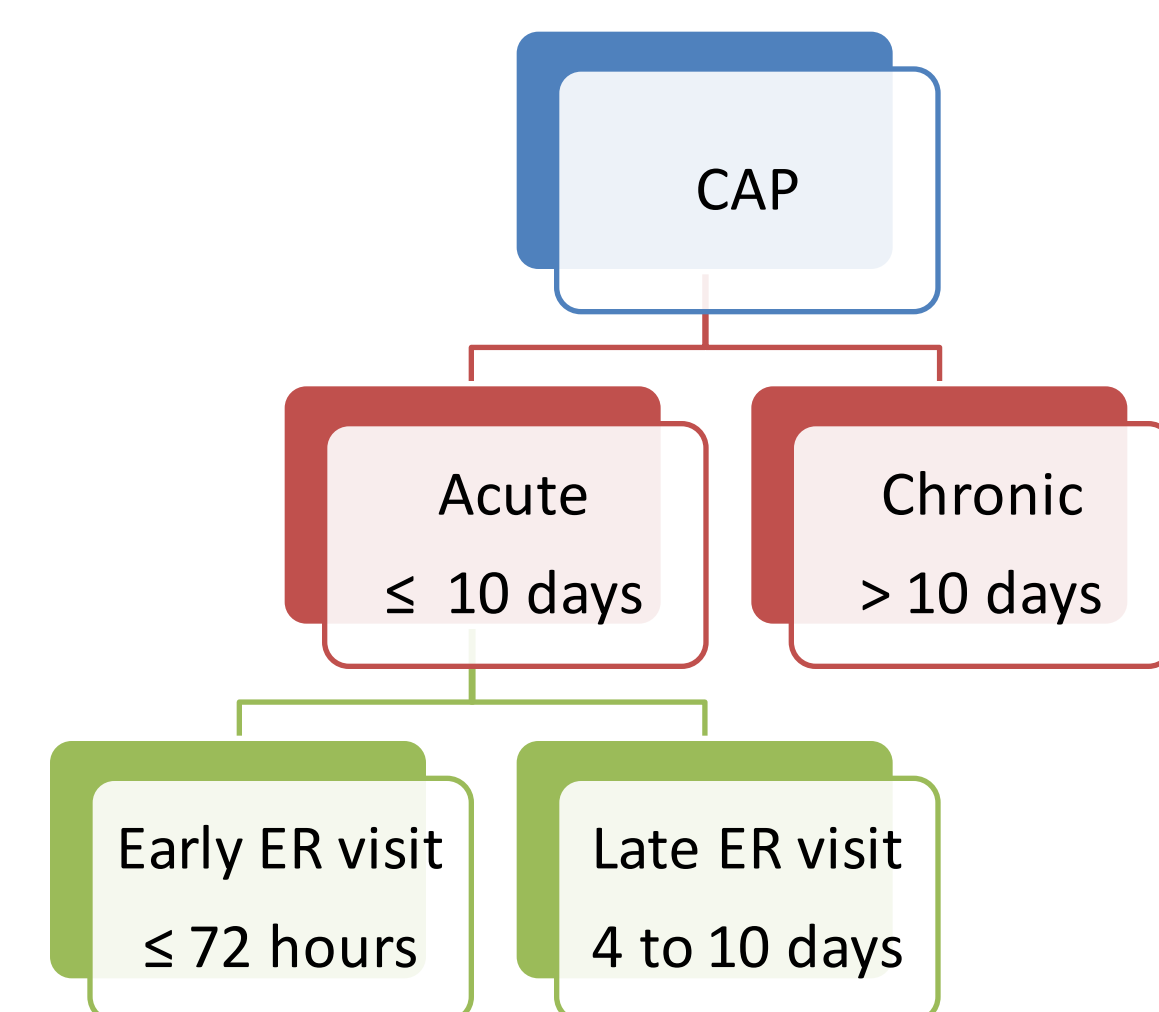
**Methods:** This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPO) International Cohort Study database. Severity of disease was evaluated using the Pneumonia Severity Index (PSI). Onset of S&S was self-reported by the patient at the time of admission to the hospital. Linear regression was used to define the adjusted association between duration of S&S and the PSI.

**Results:** A total of 4251 patients were included in the analysis. For every day increase in S&S prior to seeking care, the PSI decreased by approximately 2 points (P<0.001).

**Conclusions:** This study indicates that patients with more severe disease tend to seek medical care earlier compared to patients with less severe disease. Clinicians may use duration of S&S prior to medical care as another index of disease severity.

**INTRODUCTION**

Community Acquired Pneumonia (CAP) is a serious infectious cause of morbidity and mortality around the world. Pneumonia and influenza combined are the eighth most common cause of death in the United States.<sup>1,2</sup> Most cases of CAP are managed in the outpatient setting and the mortality is low (approximately 1%), but pneumonia requiring hospitalization is associated with a higher mortality rate (approximately 15%).<sup>3</sup> Pneumonia is classified according to the duration of signs and symptoms (S&S) as acute, subacute or chronic. This is represented in Figure 1. CAP is primarily an acute infection with patients presenting with less than 10 days of S&S.



**Figure 1: Classification of CAP based on duration of signs and symptoms**

**INTRODUCTION (cont'd)**

Common S&S of CAP include productive cough, fever, tachycardia, crackles, dyspnea and pleuritic chest pain. It is unclear why some patients with CAP seek medical attention soon after illness onset (within 72 hours) meanwhile others wait longer to seek medical care. There is scarce information regarding the association between S&S of CAP with severity of disease. We hypothesize that severity of disease may play a role in the duration of S&S before seeking medical attention, with patients having more severe disease seeking care sooner.

The objective of this study was to evaluate the association between severity of CAP and the duration of S&S prior to seeking medical attention.

**METHODS**

This was a secondary analysis of patients enrolled in the Community-Acquired Pneumonia Organization (CAPO) international cohort study. Data was collected from 2006 to 2015. In each participating center, non-consecutive medical records of hospitalized patients with the diagnosis of CAP were reviewed. A sample of the data collection form is available at the study website ([www.caposite.com](http://www.caposite.com)). Validation of data quality was performed at the study center before the case was entered in to the CAPO database. Institutional Review Board approval was obtained by each participating center.

**Study definitions**

- CAP:** Diagnosis of CAP required the presence of criterion A, B, and C:
- New pulmonary infiltrate on imaging (CT scan or chest x-ray) at the time of admission to the hospital.
  - Signs and Symptoms of CAP (at least one of the following)
    - New or increased cough (per the patient)
    - Fever >37.8°C (100.0°F) or hypothermia <35.6°C (96.0°F).
    - Changes in WBC (leukocytosis >11,000 cells/mm<sup>3</sup>, left shift > 10% band forms/microliter, or leukopenia < 4,000 cells/mm<sup>3</sup>)
  - Working diagnosis of CAP at the time of hospital admission with antimicrobial therapy given within 24 hours of admission.

**Statistical Analysis**

Baseline categorical explanatory variables were summarized as frequencies and percentages. Continuous variables were summarized as frequencies and interquartile range. We used a linear regression model to evaluate PSI scores in patients hospitalized with CAP, while controlling for the number of days with respiratory symptoms prior to admission, and history of COPD. All data were analyzed in R v.3.1.1 (R Foundation for Statistical Computing, Vienna, Austria). For the purposes of our research a P-value of ≤ 0.05 was considered statistically significant.

**RESULTS**

- A total of 4,251 patients were included in the analysis.
- Patients' characteristics are shown in Table 1.
- The correlation between severity of CAP upon admission and duration of S&S is shown in Figure 2. For every day increase in S&S prior to seeking care, the PSI decreased by approximately 2 points (P<0.001).

Table 1: Patients' characteristics

Variables	
<b>Demographics</b>	
Age, Median(IQR)	68 (29)
Nursing Home, n(%)	414 (5.3)
Sex, n(%)	4724 (60.3)
<b>Comorbidities</b>	
Acute Myocardial Infarction, n(%)	63 (0.8)
Cancer, n(%)	775 (9.9)
Cardiac Arrhythmia, n(%)	203 (2.6)
Cardio-pulmonary Edema, n(%)	130 (1.7)
Cardiovascular Meds, n(%)	639 (8.2)
CHF, n(%)	1310 (16.7)
COPD, n(%)	1871 (23.9)
CVA, n(%)	15 (0.2)
Diabetes Mellitus, n(%)	1364 (17.4)
HIV, n(%)	480 (6.1)
Liver Disease, n(%)	418 (5.3)
Long-term Arrhythmia, n(%)	85 (1.1)
Pulmonary Embolism, n(%)	25 (0.3)
Renal Disease, n(%)	779 (9.9)
<b>Physical Examination</b>	
Altered Mental Status, n(%)	1020 (13)
Respiratory Rate, Median(IQR)	22 (10)
Systolic Blood Pressure, Median(IQR)	125 (30)
Temperature, Median(IQR)	37.8 (1.6)
<b>Labs / Radiography</b>	
BUN, Median(IQR)	32 (32)
Glucose, Median(IQR)	120 (51)
Hematocrit, Median(IQR)	38 (8)
PAO2 (ABG), Median(IQR)	62 (19.5)
Ph (ABG), Median(IQR)	7.5 (0.1)
Pleural Effusion, n(%)	117 (1.5)
Sodium, Median(IQR)	137 (6)
<b>Severity of Disease</b>	
Admitted to ICU, n(%)	1009 (12.9)
Pneumonia Severity Index, Median(IQR)	99 (50)

**RESULTS (cont'd)**

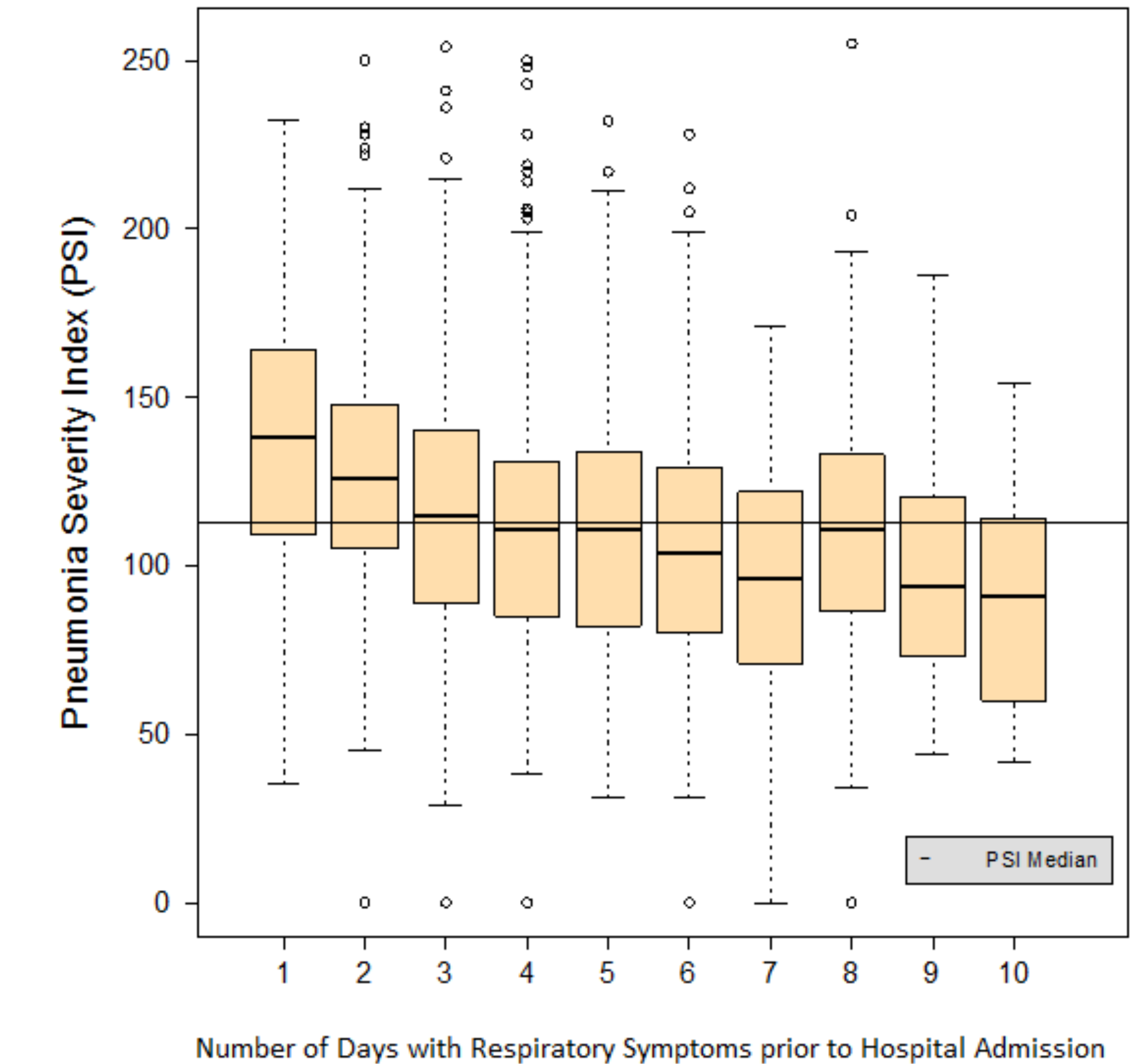


Figure 2: Association of Pre-hospital S&S and PSI

**CONCLUSIONS**

- This study indicates that patients with more severe disease tend to seek medical care earlier compared to patients with less severe disease.
- It is possible that those patients with a longer course present late to the hospital due to the lack of resolution of S&S and not necessarily because they feel severely sick.
- On the contrary, early presentation to the hospital may be due to more aggressive inflammatory response evidence by high fever and more symptomatology.
- Clinicians may use duration of S&S prior to medical care as another index of disease severity.

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