

Impact of Serum Glucose on Clinical Outcomes in Patients Hospitalized with Community-Acquired Pneumonia

**Desiree Godar BS, David Kumar BS,
John Schmelzer PhD, Kate Schmelzer BA
and Steven Yale MD**

Marshfield Clinic Research Foundation
Clinical Research Center

Overview

- Significance of community acquired pneumonia (CAP)
- Role of hyperglycemia in disease outcomes
- Study Objectives
- Methodology
- Results and Conclusions

Community Acquired Pneumonia: The Burden of Disease

- Most common reason for hospitalization other than for childbirth in 2006¹
- 8th leading cause of death in the U.S. in 2005²
- CAP-associated hospitalization costs were approximately \$11 billion in 2005³
- Improving outcomes and decreasing resource utilization in CAP patients should be a priority

¹Pneumonia Most Common Reason for Hospitalization. AHRQ News and Numbers, July 2, 2008. Agency for Health care Research and Quality, Rockville MD. <http://www.ahrq.gov/news/nn/nn070208.htm>

²Kung HC, Hoyert DL, Jiaquan X, Murphy SL. Deaths: Final Data for 2005. National Vital Statistics Reports; 56:1-22

³HCUPnet, Healthcare Cost and Utilization Project. Agency for Healthcare Research and Quality, Rockville, MD. <http://hcupnet.ahrq.gov/>

Impact of Hyperglycemia

- There are several immunological, metabolic and vascular consequences of chronic high blood glucose
- Hyperglycemia is associated with:
 - Prolonged hospitalization
 - Higher mortality rates
 - Higher rates of infections
 - Hospital costs 2.1 times higher than for non-diabetics⁴

⁴Campbell KR. Etiology and effect on outcomes of hyperglycemia in hospitalized patients. AM J Health-Syst Pharm. 2007;64: S4-S8

Hyperglycemia and CAP

- Lack of research on the impact of glucose control on outcomes in patients hospitalized with CAP
 - McAlister et al.⁵
 - Prospective cohort of 2,471 patients admitted to 6 Canadian hospitals
 - Concluded hyperglycemia at presentation is independently associated with worse outcomes in CAP patients
- Better control of blood sugar levels in patients with CAP may improve outcomes and decrease costs

⁵McAlister FA, Majumdar SR, Blitz S, Rowe BH, Romney J, Marrie TJ. The relation between hyperglycemic and outcomes in 2,471 patients admitted to the hospital with community-acquired pneumonia. *Diabetes Care* 2005; 28: 810-15.

Important Influences on CAP Outcomes

- Appropriate and timely antibiotic treatment
- Severity of illness
 - Pneumonia Severity Index (PSI)
- Co-morbid conditions
 - Charlson Co-morbidity Index
- Door to antibiotic time
- Adherence to IDSA guidelines

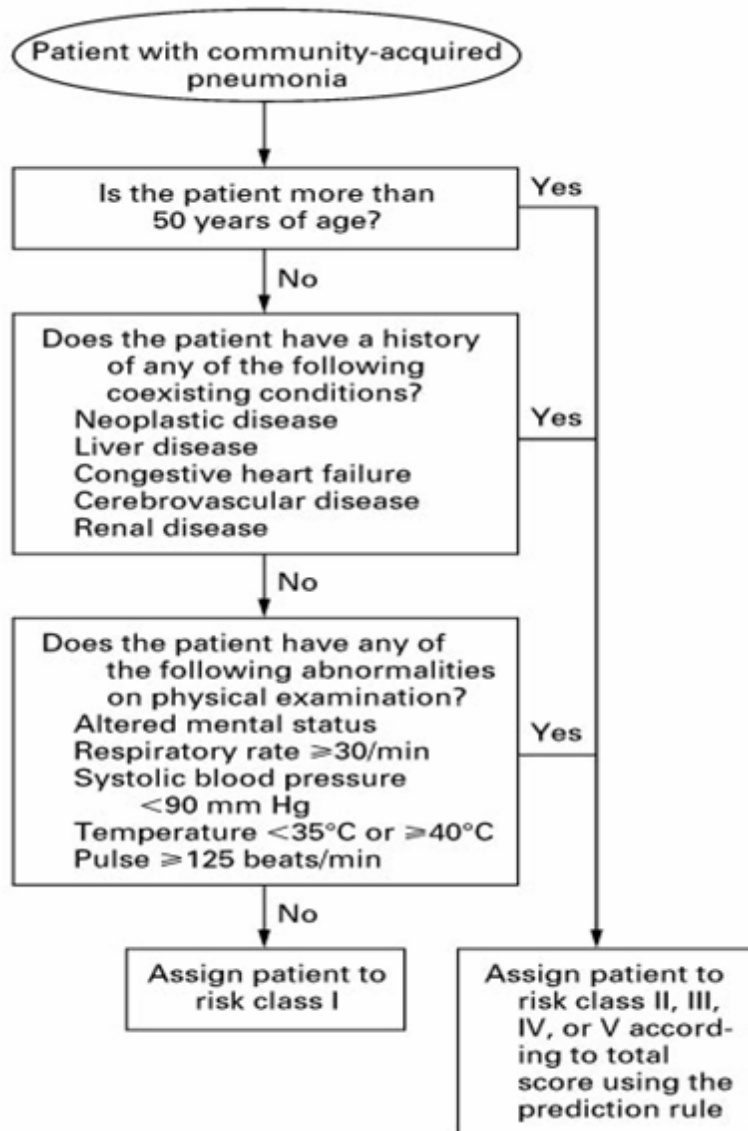
Assessing Pneumonia Severity: Pneumonia Severity Index

- Developed using data on 14,199 adult inpatients with CAP in the 1989 MedisGroups Comparative Hospital Database, which contains information on patients discharged from 78 hospitals in 23 states⁶
- Used to determine need for hospitalization in patients with CAP
- Determines overall risk of death within 30 days



⁶Fine MJ, Auble TE, Yearly DM, Hanusa BH, Weissfeld LA, Singer DE, Coley CM, Marrie TJ, Kapoor WN. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997; 336:243-50

Pneumonia Severity Index



CHARACTERISTIC	No. OF POINTS ASSIGNED
Demographic factors	
Age	
Men	Age (in yr)
Women	Age (in yr) - 10
Nursing home resident	+10
Coexisting illnesses	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Findings on physical examination	
Altered mental status	+20
Respiratory rate ≥ 30 /min	+20
Systolic blood pressure < 90 mm Hg	+20
Temperature $< 35^\circ\text{C}$ or $\geq 40^\circ\text{C}$	+15
Pulse ≥ 125 beats/min	+10
Laboratory and radiographic findings	
Arterial pH < 7.35	+30
Blood urea nitrogen ≥ 30 mg/dl (11 mmol/liter)	+20
Sodium < 130 mmol/liter	+20
Glucose ≥ 250 mg/dl (14 mmol/liter)	+10
Hematocrit $< 30\%$	+10
Partial pressure of arterial oxygen < 60 mm Hg or oxygen saturation $< 90\%$	+10
Pleural effusion	+10

Stratification of Risk Score

RISK	RISK CLASS	SCORE	MORTALITY
Low	I	Based on algorithm	0.1%
Low	II	≤ 70	0.6%
Low	III	71-90	0.9%
Moderate	IV	91-130	9.3%
High	V	> 130	27.0%

Charlson Co-morbidity Index

- Empirically based on the 1-yr mortality of a cohort of 604 patients admitted to New York Hospital during one month in 1984⁷
- Developed as a weighted scale for risk adjustment
- Alternative to the use of very restrictive inclusion criteria that would exclude individuals with co-morbidities⁷

⁷Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis.1987; 40:373-383

Charlson Co-morbidity Index

Assigned Weights	Conditions
1	Myocardial infarct Congestive Heart Failure Peripheral Vascular Disease Dementia Chronic Pulmonary Disease Connective Tissue Disease Ulcer Disease Mild Liver Disease Diabetes
2	Hemiplegia or Paraplegia Moderate or Severe Renal Disease Diabetes with Chronic Complications Any malignancy including lymphoma and leukemia
3	Moderate or Severe Liver Disease
6	Metastatic Solid Tumor AIDS

Study Aims

- Evaluate the impact of admission glucose levels on:
 - Length of Stay (LOS)
 - Development of medical complications
 - Hospital readmission within 30 days
 - 30, 60, 90 day and 1 year mortality
 - ICU transfer at any time during hospitalization



Hypothesis

- Even after controlling for previously-documented diabetes status, pneumonia severity, co-morbidities, and timing of antibiotic administration, patients with hyperglycemia and CAP will have:
 - Longer Length of Stay
 - Higher rate of intensive care (ICU) admission
 - Higher 30-day readmission
 - Higher 30-day mortality

Methods



- Retrospective observational cohort study of patients hospitalized at St. Joseph's Hospital, Marshfield WI for CAP
- January 1, 1992 and June 23, 2007
- *International Classification of Disease (ICD-9)* codes 480.0-487.9
- Screened 4,546 individuals, resulting in a pool of 1641 potential cases
- Chart abstraction validated 969 qualifying cases of CAP

Inclusion Criteria

- Age > 17 years at diagnosis
- Radiologic evidence of CAP within 6 hours of presentation, including pulmonary infiltration, air space disease, consolidation, interstitial, density, infiltrate, opacity, or overt pneumonitis
- One or more symptom(s) of acute lower respiratory tract infection, including:
 - Fever ($\geq 38^{\circ}\text{C}$ or 100.4°F) or hypothermia ($\leq 36^{\circ}\text{C}$ or 96.8°F)
 - Rigors or chills
 - Sweats or diaphoresis
 - New cough with or without sputum production, or the worsening of a chronic cough (frequent/more intense)
 - Increase in the quantity of respiratory secretions
 - Appearance of new secretions, or change in color of respiratory secretions associated with a chronic cough, chest discomfort or chest pain (included “chest pressure”)
 - Onset of new or worsening dyspnea or shortness of breath
- At least one fasting glucose measure within 6 hours of presentation

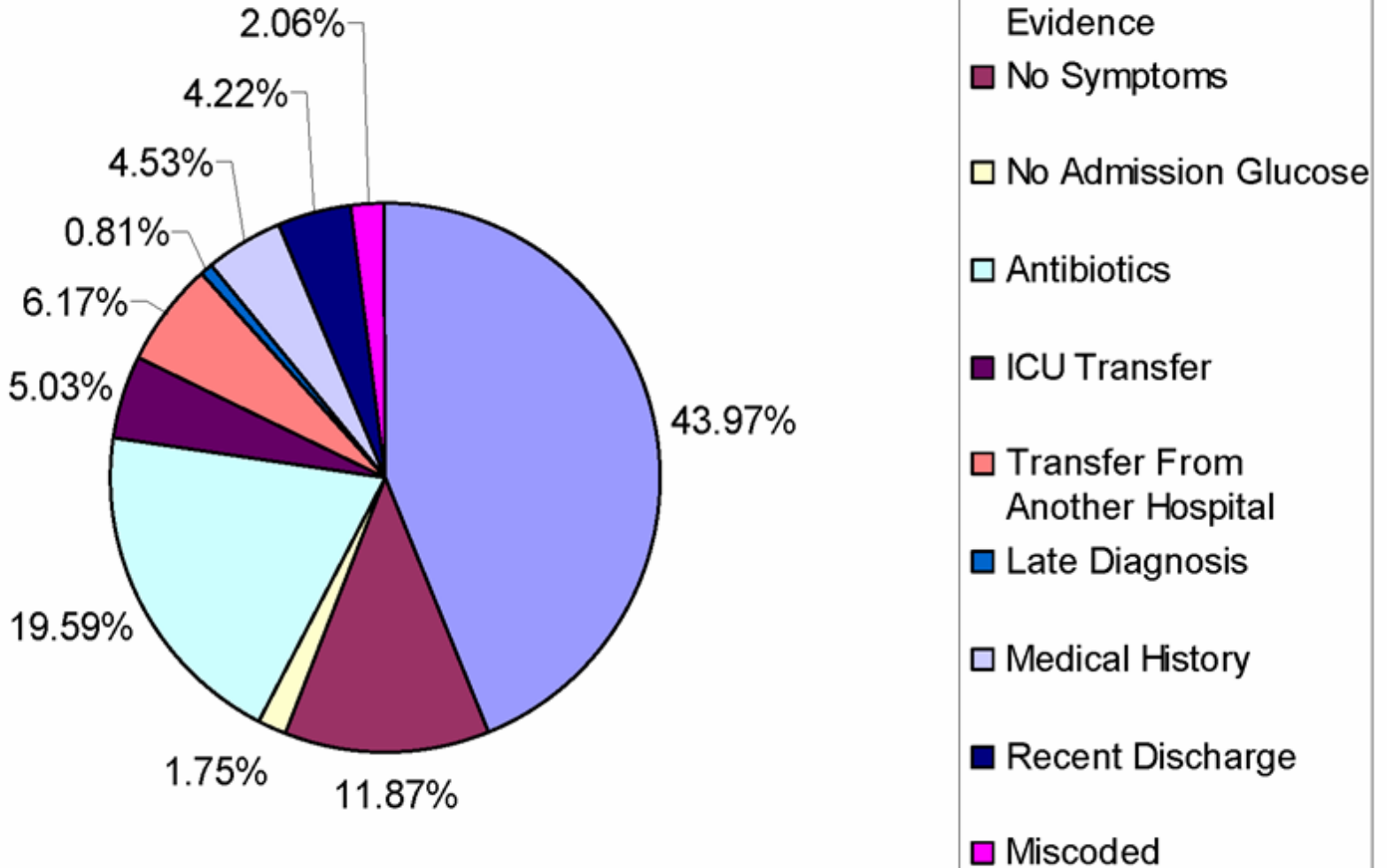
Case Definition of Community Acquired Pneumonia

New Radiographic evidence dictated on an x-ray report containing any of the following terms:	Symptoms of acute respiratory infection including one or more of the following:
▪ Infiltrate	▪ Documented evidence of fever ($\geq 38^{\circ}\text{C}/104^{\circ}\text{F}$) or hypothermia ($\leq 36^{\circ}\text{C}/96.8^{\circ}\text{F}$)
▪ Air bronchogram	▪ Rigors or chills
▪ Interstitial	▪ Sweats or diaphoresis
▪ Air space disease	▪ New cough with or without sputum production
▪ Consolidation	▪ Change in color of respiratory secretions in a patient with a chronic cough
▪ Opacity	▪ Chest discomfort or chest pain
▪ Pneumonitis	▪ Onset of dyspnea or shortness of breath
▪ Density	

Exclusion Criteria

- Antibiotics initiated for respiratory symptoms within 3 weeks prior to reference hospitalization
- Intensive care unit admission or transfer within 12 hours following reference hospital admission
- Transferred from another hospital
- Hospital admission to a short-term general stay hospital/facility
- Left the hospital against medical advice during reference hospitalization
- Hospital discharge < 30 days preceding reference hospital admission date (to rule out nosocomial pneumonia)
- Pneumonia diagnosed \geq 48 hours after reference hospital admission date
- History of or suspected:
 - Aspiration, fungal, or viral pneumonia at reference hospitalization (i.e. influenza pneumonia, RSV, adenoviruses, aspergillosis, histoplasmosis, coccidioidomycosis, blastomycosis, sporotrichosis)
 - Pulmonary tuberculosis or pneumocystis carinii pneumonia within one year prior to admission
 - Acquired immune deficiency syndrome or human immunodeficiency virus infection
 - Tracheostomy

Reasons for Exclusion



Appropriate Antibiotic Treatment

- IDSA Guideline:
 - Developed 1998
 - Revised 2000 and 2003
- 1998 Guidelines: 1999-2000
- 2000 Guidelines: 2001-2003
- 2003 Guidelines: 2004-2007

Results

Demographic and Risk/Severity Factors

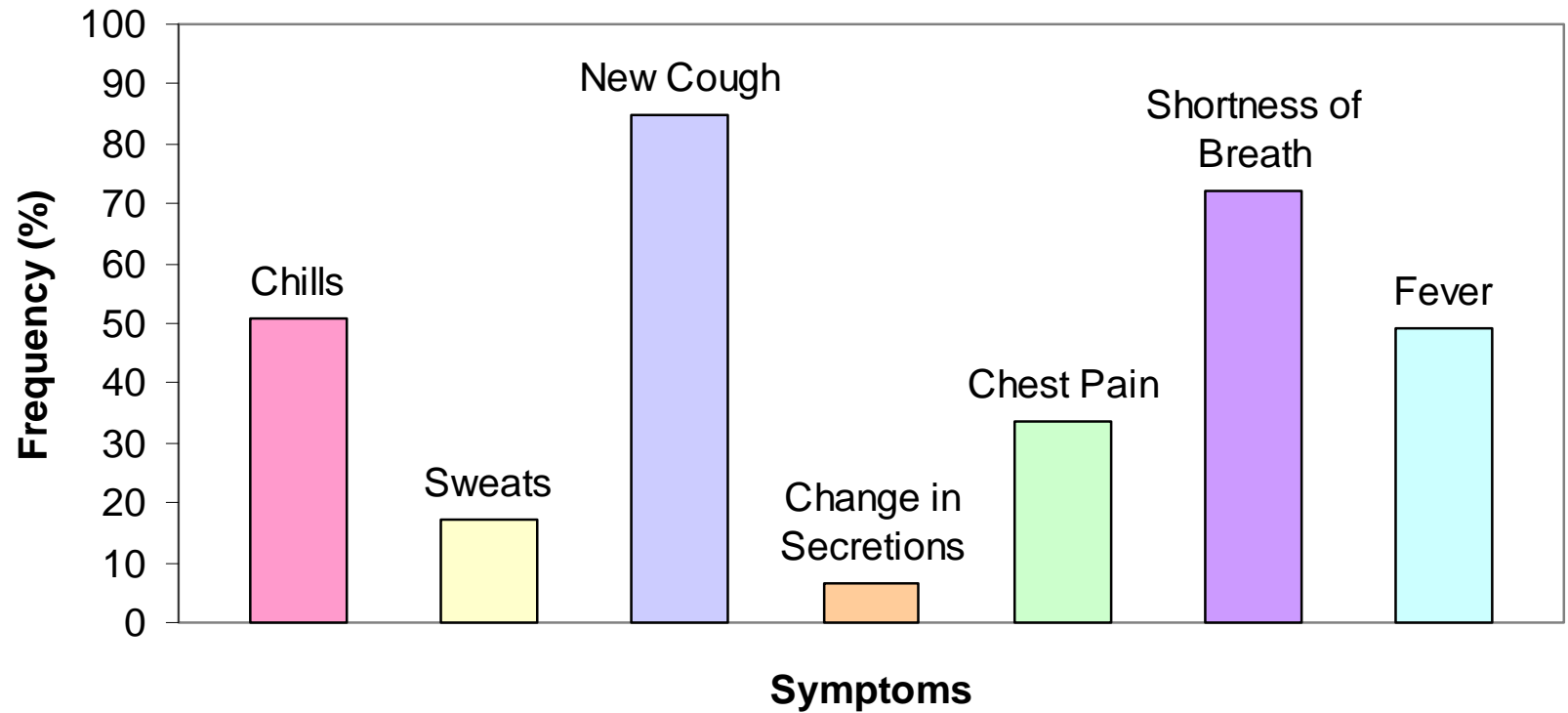
Factor	N/Measure	%
Study subjects (N)	969	100.0
Age (mean)	73.8 yrs	--
Gender:		
Male	544	56.1 (544/969)
Female	425	43.9 (425/969)
Diabetes Diagnosis	212	21.9 (212/969)
PSI Risk Class:		
1	39	4.0 (39/969)
2	834	86.1 (834/969)
3	61	6.3 (61/969)
4	34	3.5 (34/969)
5	1	0.1 (1/969)
CCI Class:		
0	185	19.1 (185/969)
1-2	437	45.1 (437/969)
3-9	334	34.5 (334/969)
≥10	13	1.3 (13/969)

Demographic and Risk/Severity Factors (cont'd)

Factor	N/Measure	%
Glucose @ Admission (mg/dL):		
<90		2.3 (22/969)
90-139		59.5 (577/969)
≥140		38.2 (370/969)
One Year Mortality	205	21.16 (205/969)
Admission Symptoms:		
Fever		49.22 (473/961)
Chills		51.30 (494/963)
Sweats		16.91 (161/952)
New cough		84.78 (819/966)
Change in secretions		6.57 (63/959)
Chest pain		34.06 (327/960)
Shortness of Breath		72.29 (699/967)
PSI = Pneumonia Severity Index ; CCI = Charleston Comorbidity Index		

Symptoms

Frequency of Reported Symptoms



Association Between Risk Factors and LOS, Univariate Analysis

Factor	LOS median days (N)	P-value
PSI (≥ 4 vs. ≤ 3)	6.95 (35) vs. 4.02 (934)	0.0016
CCI (≥ 5 vs. ≤ 4)	4.19 (107) vs. 4.02 (862)	0.1856
Complication* (at least 1 vs. none)	7.52 (124) vs. 3.84 (845)	<0.0001
Smoking (current/previous smoker vs. never smoked)	3.78 (507) vs. 4.10 (462)	0.0064
Alcohol (current/previous abuse vs. never abuse)	4.89 (71) vs. 4.02 (898)	0.0109
Corticosteroids use (yes vs. no)	4.69 (121) vs. 3.97 (848)	0.0098
Treatment for Malignancy (yes vs. no)	5.82 (41) vs. 4.02 (928)	0.0193
Transfer to ICU (yes vs. no)	13.26 (29) vs. 4.00 (937)	< 0.0001
Admission glucose ($90 < \text{Glu} < 140$ vs. ≤ 90 & ≥ 140)	3.99 (572) vs. 4.16 (397)	0.0398

*Complication includes diagnosis of sepsis, neurological, cardiac, renal, and pulmonary.

PSI = Pneumonia Severity Index ; CCI = Charleston Comorbidity Index

30- Day Hospital Readmission

- Hospital readmission: 8% (77/969)
- No relationship between demographic and clinical factors (glycemic control, timeliness and quality of antibiotic therapy) and hospital readmission
- Age was associated with 30 day readmission (80.6 vs. 76.9; $P=.0071$)

Treatment with Hyperglycemic Agents and Corticosteroids

- Serum glucose declined during hospitalization
- Antihyperglycemic medications (N=212) experienced a large decrease in serum glucose levels (median= 37.7 mg/dl; P<.0001)
- No corticosteroids 3 weeks prior to hospital admission (N=839) also experienced a decrease in serum glucose (median 5.6 mg/dl; P=.0009)
- PSI \leq 3 decrease in serum glucose compared to PSI \geq 4 (median difference 4.5 mg/dl; P=.0156)

ICU Transfer/Medical Complication

- High glucose levels not associated with ICU admission
- More likely admitted to ICU
 - Not treated according to IDSA guidelines (OR=3.2; P=.0176)
 - Developed a complication (sepsis, neurological, cardiac renal or pulmonary) (OR=8.224; P<.0001)

Univariate Analysis of Potential Risk Factors Associated with Development of Complications

Risk Factor	Odds Ratio	<i>P</i>
High Pneumonia Severity Index Score*	3.033	0.0067
High Charlson Comorbidity Index Score*	1.853	0.0269

PSI = Pneumonia Severity Index ; CCI = Charleston Comorbidity Index
* High PSI Score \geq Category 4
* High CCI Score \geq 5

Multivariate Logistic Regression Results for Mortality Risks at Various Time Periods

Mortality Risk Factor	30-Day Odds Ratio	P-value	60-Day Odds Ratio	P-value	90-Day Odds Ratio	P-value	1-Year Odds Ratio	P-value
PSI \geq 4	6.97	<0.0001	6.63	<0.0001	8.85	<.0001	4.62	< 0.0001
CCI \geq 5	---	---	---	---	---	---	1.70	0.0264
Complication	2.48	0.0052	2.09	0.0137	---	---	1.74	0.0138
Comorbidities	4.93	0.0290	6.93	0.0078	5.44	0.0045	3.85	0.0002
Transfer to ICU	3.56	0.0122	4.13	0.0021	4.23	0.0011	---	---
Corticosteroid	---	---	---	---	---	---	1.80	0.0091
Alcohol Abuse	---	---	---	---	2.10	0.0351	1.94	0.0191
Malignancy Treatment	---	---	---	---	---	0.0218	2.23	---
Concordant (%)	54.1		51.3		45.3		58.3	
AUC	0.724		0.711		0.682		0.691	

PSI = Pneumonia Severity Index ; CCI = Charleston Comorbidity Index; ICU = Intensive Care Unit; AUC = Area under curve

Glucose

- Admission glucose values (> 140 mg/dl) as well as glucose values <90 mg/dl experience a longer LOS
- Serum glucose values not predictive of:
 - ICU admission
 - 30-day readmission
 - Mortality (30, 60, 90 or 1 year)
 - Discharge disposition

Time to Administer Antibiotics

- No association between time to antibiotic treatment:
 - LOS
 - Medical complications
 - 30 day readmission
 - Mortality
- Applied a continuous measurement of time to antibiotics using presentation time as the index time

Questions

