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The Burden of Community-Acquired Pneumonia Requiring Admission to ICU in the United States

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BACKGROUND: A paucity of studies have assessed the epidemiology of community-acquired pneumonia (CAP) that require ICU admission. We conducted a study on this group of patients with the primary objective of defining the incidence, epidemiology, and mortality rate of CAP in the ICUs in Louisville, Kentucky. The secondary objective was to estimate the number of patients who were hospitalized and the number of deaths that were associated with CAP in ICU in the United States.

RESEARCH QUESTIONS: What is epidemiology of CAP in the ICU in Louisville, Kentucky, and the projected incidence in the United States?

STUDY DESIGN AND METHODS: This was a secondary analysis of a prospective population-based cohort study. The setting was all nine adult hospitals in Louisville, Kentucky. The annual incidence of CAP in the ICU per 100,000 adults was calculated for the whole adult population of Louisville. The number of patients who were hospitalized because of CAP in ICU in the United States was estimated by multiplying the Louisville incidence rate of CAP in ICU by the 2014 US adult population.

RESULTS: From a total of 7,449 unique patients who were hospitalized with CAP, 1,707 patients (23%) were admitted to the ICU. The incidence of CAP in the ICU was 145 cases per 100,000 population of adults. Cases of CAP in the ICU were clustered in patients from areas of the city with high poverty. The mortality rate of patients with CAP in ICU was 27% at 30 days and 47% at one year. In the United States, the estimated number of patients who were hospitalized with CAP requiring the ICU was 356,326 per year, and the estimated number of deaths at 30 days and one year were 96,206 and 167,474, respectively.

INTERPRETATION: Almost one in five patients who are hospitalized with CAP requires intensive care. Poverty is associated with CAP in the ICU. Nearly one-half of patients with CAP in the ICU will die within one year. Because of its significant burden, CAP in the ICU should be a high priority in research agenda and health policy.   CHEST 2020; 158(3):1008-1016

KEY WORDS: epidemiology; incidence; pneumonia

Community-acquired pneumonia (CAP) that requires admission to the ICU represents 9% to 14% of all cases of CAP that require hospitalization.[1-4] Although CAP is associated with a mortality rate of <1% in the outpatient setting[1] and between 8% and 10.6% in different cohorts of hospitalized patients,[1,5,6] a mortality rate of 24% was recently reported for those who require the ICU.[7] Even if patients with CAP in the ICU survive to discharge from the hospital, they experience lasting consequences from the pneumonia and have a higher long-term mortality rate compared with other groups of patients who required hospitalization.[8]

To fully understand the impact of CAP in the ICU, estimates of its incidence and characterization of epidemiology are important. Recently, our group conducted a population-based study over 2 years of all cases of CAP that required admission to all adult hospitals in Louisville, Kentucky. Data were obtained by research staff who reviewed every record and gathered clinical information. This allowed us to define the incidence of hospitalizations because of CAP in Louisville, to estimate the number of hospitalizations because of CAP in the United States, and to epidemiologically and clinically characterize this patient population.[9] Recognizing the knowledge gap regarding incidence and epidemiology of CAP in the ICU in the United States, we focused on the subgroup of patients with CAP in the ICU from that cohort.

The primary objective was to define the incidence, epidemiology, and mortality rate of patients with CAP in ICUs in Louisville, Kentucky. The secondary objective was to estimate the number of patients who are hospitalized with CAP in the ICU and the number of deaths because of CAP in ICUs in the United States.

Methods

Study Design

This was an ancillary study to the University of Louisville Pneumonia Study, which was a population-based cohort study that included residents in Louisville, who experienced CAP and required hospitalization from June 1, 2014, to May 31, 2016. Details of the study were published previously.[9-11] All nine adult hospitals in Louisville were sites for this study. This study was approved by the University of Louisville Institutional Review Board (IRB number 11.0613) and each hospital's research department. Informed consent was waived.

Inclusion and Exclusion Criteria

We defined CAP as the presence of a new pulmonary infiltrate and at least one of the following: (1) a new cough or increased sputum or sputum production, (2) fever or hypothermia, and (3) leukocytosis or leukopenia. Patients were excluded if an alternative diagnosis at discharge could justify the presence of the aforementioned criteria.[9] The intent was to enroll patients with CAP who lived in Louisville and who were counted in the 2010 US Census. Thus, patients were excluded if they (1) did not have a permanent or valid Louisville address based on US Census Bureau data, (2) did not have a valid social security number, and (3) were in a correctional system. Exclusions were not based on immune status, nursing home residence, or recent hospitalization. Patients who experienced pneumonia >48 hours after admission were considered to have nosocomial pneumonia and were excluded. A recent prior hospitalization was not an exclusion criterion.

ICU admission was characterized as early and late depending on the day of hospital admission. Early ICU admission was characterized as ICU admission on the day of hospital admission. ICU admission after the day of hospital admission was characterized as late ICU admission.

Data Collection

On a daily basis, research associates screened patients for CAP in the participating sites. We collected data on demographics, comorbidities, physical examination findings, and laboratory test results. To evaluate severity of disease, we obtained data to calculate Pneumonia Severity Index risk class, CURB (confusion, urea, respiratory rate, and BP)-65 score, qSOFA (sepsis-related organ failure assessment) score, and American Thoracic Society criteria for severe CAP. Data were entered into a Health Insurance Portability and Accountability Act of 1996-protected online platform, and data quality assessment was performed.

Incidence Calculations and Statistical Analyses

The annual incidence of CAP in the ICU per 100,000 adults was calculated for the whole adult population of Louisville and subpopulations according to age brackets and comorbidities. The number of patients hospitalized because of CAP in the ICU in the United States was estimated by multiplying the Louisville incidence rate of CAP in the ICU by the 2014 US adult population extrapolated from the 2010 US Census. The annual incidence of CAP in the ICU by comorbidities was obtained by dividing the average annual number of patients who were hospitalized with CAP in the ICU by the number of patients with each comorbidity in Louisville. The denominators for comorbidities were obtained by multiplying the estimated prevalence of each comorbidity by the 2014 estimated adult Louisville population. The Louisville 2014 Behavioral Risk Factor Surveillance System generated the prevalence multipliers for each comorbidity. For COPD, data from the 2014 National Health Interview Survey were also used to obtain the multiplier. Baseline categoric data are presented as frequency and percentage, while continuous data are presented as median and interquartile range. Categoric and continuous data were analyzed with Binomial and Gaussian family Generalized Estimating Equations, respectively, to account for patient within hospital correlation. Probability values that were reported are adjusted for family-wise error rate by Holm's method. Time-to-death analysis, up to one year, was performed for all unique patients. Kaplan-Meier curves were plotted to compare early and late ICU admission for survival estimates. A stratified, multivariable Cox proportional hazards regression was performed to assess the impact of demographics, risk factors, and comorbidities simultaneously. Strata correspond to the hospital. A probability value <.05 was considered statistically significant. Analysis was performed with R statistical software.

Geospatial Epidemiology

A description of the geospatial analyses was previously provided.[9] Briefly, heatmaps of unique patients with CAP in the ICU in

Louisville were created by obtaining the geomasked location of the home address of each patient through the US Census Bureau website.[12] Areas of significant risk for CAP in the ICU were identified via spatial scan statistic proposed by Kulldorff.[13] Associations between CAP in the ICU and other variables were assessed by choropleth maps. These variables, at the census tract level, were taken from the American Community Survey 2014 5-year estimates.[14] All geospatial analyses were done with ArcGIS 10.4 (Environmental Systems Research Institute. Redlands, CA) and SaTScan (version 9.5; Information Management Services, Inc).

Results

A total of 7,449 unique patients with CAP who required hospitalization were included in the cohort. During the 2 years of the study, a total of 1,946 ICU admissions because of CAP were documented. We identified 239 patients with CAP who were admitted to the ICU during an episode of rehospitalization. After excluding patients who were readmitted to the hospital with CAP in the ICU, the cases for a total of 1,707 unique patients (23%) with CAP who required ICU admission were analyzed. The study flowchart is shown in Figure 1. The baseline characteristics of the population of hospitalized patients with CAP who were admitted to the ICU on the day of hospital admission, the patients who were admitted to the ICU after the day of hospital admission, and the patients who were never admitted to the ICU are given in Table 1. The median age was 67 years (interquartile range, 56, 78), and slightly less than one-half of them were women. ICU admission on the day of hospitalization occurred in 1,275 (75%) of the patients who were admitted to the ICU. A total of 414 patients (24%) required invasive mechanical ventilation, and 346 patients (20%) required noninvasive ventilation. From a total of 4,538 patients who did not meet Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) criteria for ICU admission, 431 patients (9%) were admitted to the ICU. From a total of 2,911 patients who met IDSA/ATS criteria for ICU admission, 1,276 patients (44%) were admitted to the ICU. Table 2 shows severity scores on the day of hospital. e-Tables 1 and 2 display the characteristics of the population with CAP in the ICU according to whether they were dead or alive in different time frames.

Incidence of Patients With CAP in the ICU

The annual incidence of adult patients with CAP in the ICU in Louisville was 145 persons per 100,000 adult population. The incidence increased with age (e-Fig 1). Underlying chronic diseases have an important impact on the incidence of CAP in the ICU. COPD and congestive heart failure are the comorbidities associated with the highest incidence of CAP in the ICU (e-Fig 2).The estimated number of patients hospitalized with CAP in an ICU in the United States was 356,326 per year.

Geospatial Epidemiology

There was a clustering of CAP in ICU cases in the west side of Louisville. The population living in this section of the city had 1.83 times higher risk of experiencing CAP that required ICU care than elsewhere in the city (Fig 2A). The map of Louisville with the geomasked address of each patient who was hospitalized with CAP in the ICU with the area of the city with a relative risk of 1.83 was overlaid on 3 choropleth maps with the use of census tract-level data in relation to (1) percent poverty (Fig 2B), (2) percent black race (Fig 2C), and (3) percent ≥65 years of age (Fig 2D). Within the area of increased relative risk of CAP in the ICU, 82 census tracts (75%) were above the median percent poverty; 70 census tracts (64%) were above the median percent of black individuals, and only 40 census tracts (36%) were above the median percent ≥65 years of age.

Mortality Rate

The mortality rate of patients with CAP in the ICU during hospitalization was 17% (or 25 people per 100,000), at 30 days was 27% (or 40 people per 100,000), at 6 months was 39% (57 people per 100,000), and at one year was 47% (or 67 people per 100,000). The estimated number of in-hospital deaths yearly in patients with CAP in the ICU in the United States is 60,576. Among patients in the ICU, the in-hospital mortality rate was 11% for patients who did not meet IDSA/ATS criteria and 19% for patients who met the criteria. Table 3 shows the mortality rates in patients with CAP in different time frames according to whether they had early (day 0) or late (after day 0) ICU
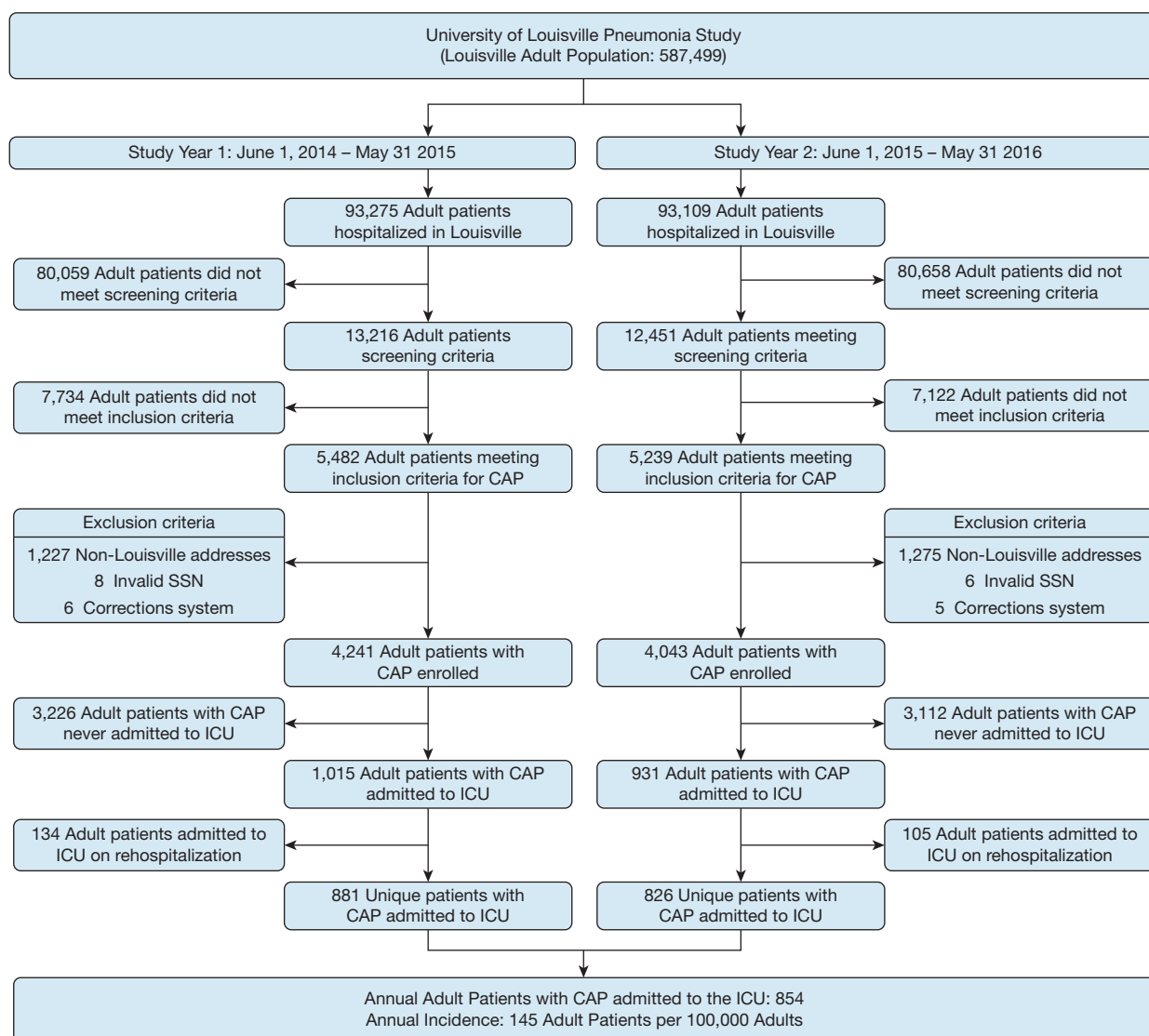
Figure 1 – *Study flowchart. CAP = community-acquired pneumonia; SSN = social security number.*

admission. Day 0 represents the day of hospital admission.

e-Figure 3 demonstrates Kaplan-Meier curves comparing early and late ICU admission for survival estimates up to one year. e-Figure 4 provides a stratified, multivariable Cox proportional hazards regression analysis that assesses the impact of demographics, risk factors, and comorbidities on mortality rates.

Discussion

We demonstrated that CAP in the ICU is common, with an incidence of 145 cases per 100,000 adults per year. The incidence increases with aging and the presence of comorbidities, of which congestive heart failure and COPD have the highest impact. An ecologic association suggests that adults living in impoverished areas are at increased risk for hospitalization because of CAP requiring admission to the ICU. Patients with CAP in the ICU are at high risk of death, as demonstrated by an in-hospital mortality rate of 17% and a one-year mortality rate approaching 50%. When the Louisville data are extrapolated to the United States, the estimated number of patients with CAP in the ICU is 356,326 per year, and the total number of deaths at one year is 167,474 patients per year.

Recently, Storms et al[15] conducted a study that included 6 medical sites in the United States and calculated the rate of pneumonia hospitalization with ICU admission in adults as 76 per 100,000 population/year. Their figure is approximately one-half of what was obtained in our

TABLE 1] Patient Characteristics on Day of Hospitalization

Characteristics	ICU Admission			P Value
	Early	Late	None	
Total study population, No.	1,275	432	5,742	
Demographics				
Age, median [interquartile range], y	67 [56, 77]	67 [56, 78]	68 [56, 81]	.703
Male sex, No. (%)	659 (52)	222 (51)	2,562 (45)	.001
Black race, No. (%)	243 (19)	93 (22)	1,139 (20)	.671
Social and medical history, frequency (%)				
COPD	657 (52)	197 (46)	2,621 (46)	< .001
Renal disease	523 (41)	168 (39)	1,494 (26)	< .001
Diabetes mellitus	473 (37)	163 (38)	1,797 (31)	< .001
Congestive heart failure	462 (36)	173 (40)	1,489 (26)	< .001
Obese	455 (36)	149 (34)	2,011 (35)	.703
Current smoker	459 (36)	138 (32)	1,746 (30)	.073
Stroke	184 (14)	59 (14)	713 (12)	.671
Neoplastic disease	164 (13)	66 (15)	760 (13)	.703
Chronic renal failure	131 (10)	35 (8)	362 (6)	.143
HIV disease	14 (1)	6 (1)	90 (2)	< .001
Physical examination findings				
Altered mental status, No. (%)	541 (42)	80 (19)	786 (14)	< .001
Heart rate, median [interquartile range], beats/min	115 [99, 131]	110 [94, 124]	103 [90, 116]	< .001
Respiratory rate, median [interquartile range], breaths/min)	29 [24, 35]	24 [21, 28]	22 [20, 24]	< .001
Systolic BP, median [interquartile range], mm Hg	97 [84, 118]	112 [96, 133]	119 [104, 137]	< .001
Diastolic BP, median [interquartile range], mm Hg	48 [40, 58]	56 [46, 67]	59 [51, 69]	< .001
Temperature, median [interquartile range], degrees Celsius	37 [37, 38]	37 [37, 38]	37 [37, 38]	.703
Laboratory & radiographic findings, median [interquartile range]				
Hematocrit level, %	35 [30, 40]	34 [30, 39]	36 [32, 40]	< .001
Serum bicarbonate, mEq/L	25 [21, 29]	26 [22, 29]	26 [24, 29]	.186
BUN, mg/dL	26 [16, 41]	24 [15, 36]	18 [12, 26]	< .001
Serum glucose, mg/dL	166 [131, 228]	150 [118, 204]	137 [111, 185]	< .001
Serum sodium, mEq/L	137 [133, 140]	137 [133, 140]	137 [134, 140]	.466
Pleural effusion, frequency (%)	480 (38)	189 (44)	1,738 (30)	< .001
Ventilatory support and vasopressors, No. (%)				
Invasive mechanical ventilatory support	394 (31)	20 (5)	15 (0)	< .001
Noninvasive mechanical ventilatory support	305 (24)	41 (9)	209 (4)	< .001
Vasopressors	186 (15)	6 (1)	21 (0)	< .001

study. Important distinctions of their study to ours are that they relied on administrative data for the diagnosis of pneumonia and the underlying population consisted of enrollees into an insurance plan.

Our study showed a clustering of cases of CAP in the ICU in an area of Louisville that was affected by a higher proportion of poverty. In children, there is a large body of literature that shows an association between poverty

TABLE 2] Severity of Pneumonia on Day of Hospitalization

Severity	ICU Admission, No. (%)			P Value
	Early	Late	None	
Total study population, No.	1,275	432	5,742	
Pneumonia Severity Index risk class				
I	9 (1)	13 (3)	423 (7)	< .001
II	37 (3)	31 (7)	1,097 (19)	< .001
III	93 (7)	67 (16)	1,163 (20)	< .001
IV	395 (31)	174 (40)	2,090 (36)	< .001
V	741 (58)	147 (34)	969 (17)	< .001
CURB-65 score				
0	28 (2)	40 (9)	837 (15)	< .001
1	136 (11)	79 (18)	1,529 (27)	< .001
2	283 (22)	130 (30)	1,691 (29)	.040
3	409 (32)	119 (28)	1,254 (22)	< .001
4	325 (25)	55 (13)	390 (7)	< .001
5	94 (7)	9 (2)	41 (1)	< .001
qSOFA score				
0	7 (1)	7 (2)	245 (4)	< .001
1	388 (30)	249 (58)	3,818 (66)	< .001
2	542 (43)	145 (34)	1,475 (26)	< .001
3	338 (27)	31 (7)	204 (4)	< .001
American Thoracic Society major and minor criteria				
Multilobar infiltrates	540 (42)	199 (46)	2,374 (41)	.230
PaO_2/FIO_2 ratio ≤250	800 (63)	157 (36)	891 (16)	< .001
Respiratory rate ≥30 breaths/min	583 (46)	101 (23)	572 (10)	< .001
Confusion/disorientation	541 (42)	80 (19)	786 (14)	< .001
Uremia	836 (66)	259 (60)	2,537 (44)	< .001
Leukopenia	69 (5)	21 (5)	253 (4)	.230
Thrombocytopenia	124 (10)	30 (7)	265 (5)	< .001
Hypothermia	65 (5)	3 (1)	61 (1)	< .001
Hypotension	840 (66)	258 (60)	3,046 (53)	< .001
Invasive mechanical ventilation	394 (31)	20 (5)	15 (0)	< .001
Vasopressors	186 (15)	6 (1)	21 (0)	< .001

CURB = confusion, urea, respiratory rate, and BP; qSOFA = sepsis-related organ failure assessment.

and pneumonia.[16-20] The number of articles on the topic in adults is lower, but the available literature points in the same direction.[21,22] The association between poverty and incidence of CAP in the ICU, or any disease for that matter, is complex. A number of factors may play a role and may include lack of access to basic preventative health care such as vaccination, higher exposure to pollution,[23] lack of home utilities such as air conditioning,[24] and illiteracy.[19] The role of race on the incidence of pneumonia is not as straightforward and could be confounded by other factors. Our ecologic analysis did not show a relation between race and incidence of pneumonia. Conversely, Burton et al[21] have found that black individuals are at a higher risk of pneumonia after data are adjusted for poverty. We also failed to demonstrate an increased risk for CAP in the ICU in census tracts with a high percentage of elderly individuals.

At one year, the mortality rate in our cohort was approximately 50%. The reason that patients with CAP in the ICU who were discharged from the hospital had
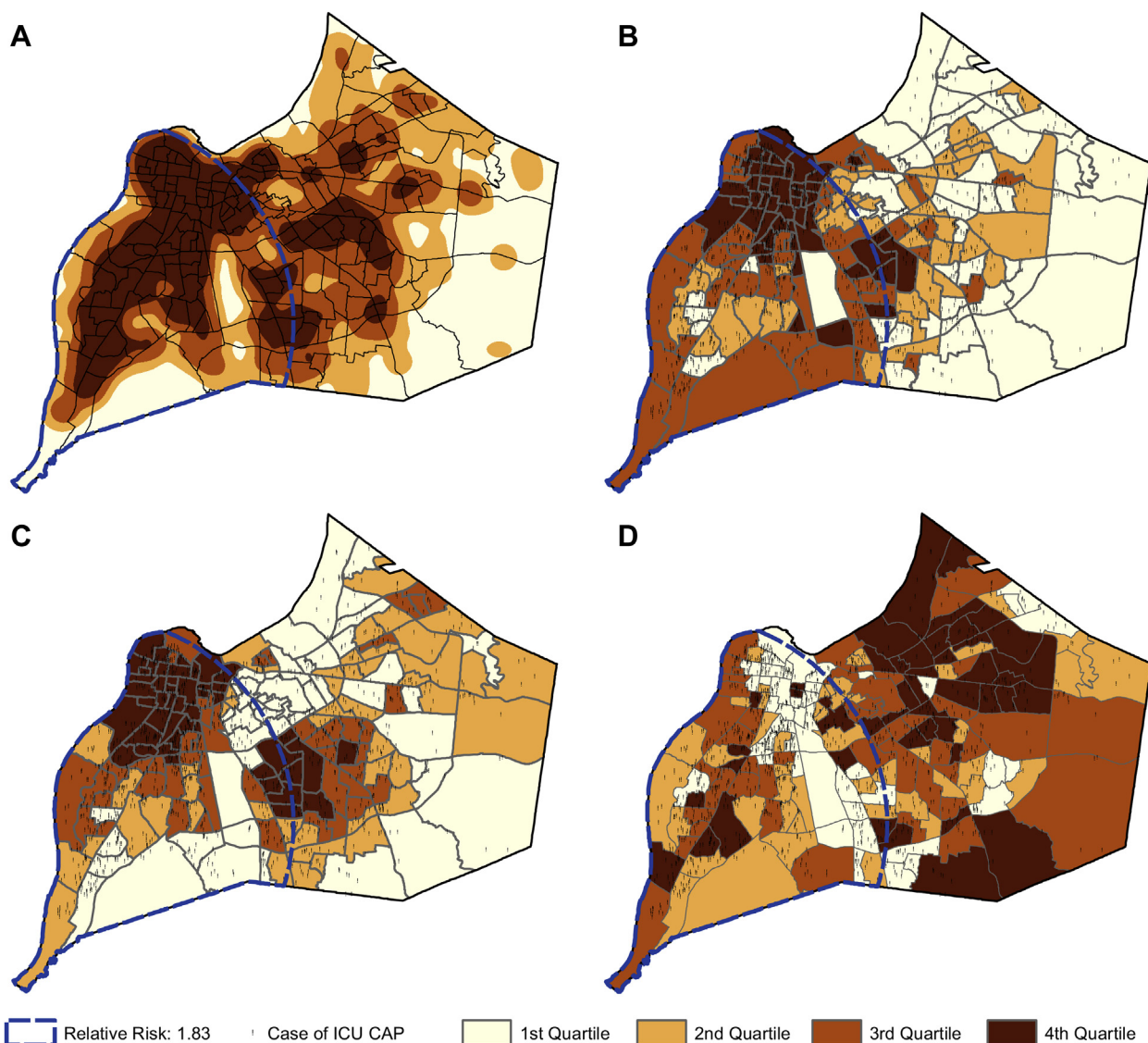
Figure 2 – A-D, Heatmap shows unique hospitalized patients with severe community-acquired pneumonia (A) and their ecologic association with poverty (B), black race (C), and age (D).

such a high mortality rate after their pneumonia was long cured is unclear. The answer may be that these patients have a number of comorbidities that place them both at risk for the development of pneumonia and unfavorable long-term outcomes. But the presence of comorbidities does not seem to fully explain this finding. In a retrospective cohort study that included 6971 patients who were admitted to a tertiary Veterans Affairs Hospital, those who had CAP on admission had a 40% increase in death on long-term follow up as compared with those who were admitted for other reasons. This increased risk of death was independent of comorbidities.[8] In a prospective cohort study that enrolled 1895 patients who were hospitalized for CAP,

higher levels of inflammatory markers close to or on discharge were associated with higher risk of death over one year after there was adjustment for comorbidities.[25] This study highlights the important role that inflammation plays in determining long-term prognosis in patients with CAP.

A substantial proportion of patients with CAP in the ICU were treated with noninvasive ventilation. The value of noninvasive ventilation for CAP is debatable. Observational cohort studies have reported a high rate of failure of noninvasive ventilation in patients with CAP.[26,27] The failure of noninvasive ventilation in patients with CAP may represent a marker of the severity

TABLE 3] Number of Deaths in Patients With Community-Acquired Pneumonia Admitted to the ICU in Louisville and the United States

ICU Admissions and Mortality	Louisville, Kentucky[a]			United States of America[b]
	ICU Admission			
	Early	Late	Total	
Adult patients in the ICU with community-acquired pneumonia, No. (%)	1,275	432	1,707	356,326[c]
In-hospital deaths[d]	200 (16)	87 (20)	287 (17)	60,576[c]
15-Day deaths	233 (18)	84 (19)	317 (19)	66,172[c]
30-Day deaths[d]	319 (25)	140 (33)	459 (27)	96,209[c]
6-Month deaths[d]	471 (38)	189 (44)	660 (39)	138,968[c]
1-Year deaths	563 (45)	216 (51)	779 (47)	167,474[c]

[a]Estimated adult population, 587,499.
[b]Estimated adult population, 245,273,438.
[c]Yearly estimates from percentage totals from Louisville, Kentucky.
[d]Indicates a significant difference in deaths between Early and Late ICU admission ($P < .05$).

of their illness. Here, we see an opportunity for research addressing the proper implementation of noninvasive ventilation in these patients.

Patients with late ICU admission had higher 6-month mortality rate as compared with those with early ICU admission. Yet, patients with late ICU admission had lower severity of illness scores on admission to the hospital. A few potential explanations for these findings can be pondered. First, severity of illness scores may not have captured fully the gravity of pneumonia in patients with late ICU admission. Second, treatments or interventions may not have been implemented as early in patients with late admission, who seemed less ill on admission to the hospital. Third, factors other than severity of illness, such as frailty, may have played a greater role in patients with late admission.

A number of patients who were admitted to the ICU did not have severe CAP as determined by the Pneumonia Severity Index or CURB-65. It is known that clinicians overestimate the risk of death in patients with pneumonia, which conceivably could explain this finding.[28] Conversely, factors not contemplated by clinical prediction rules can play a role in the decision-making by the clinician. A previous study showed that 19% of patients with CAP and a Pneumonia Severity Index risk score I or II who were seen in the ED required hospitalization. These patients experienced complications such as a need for mechanical ventilation (2.4%), the development of empyema (1.4%), and death

(0.9%).[29] Patients in risk class I and II in our study had a mean age of 44 years, which indicates that the Pneumonia Severity Index may not predict ICU admission well in patients who are not elderly.

The estimated number of CAP in the ICU and associated mortality rates for the United States is based on the assumption that Louisville has social and demographic features that are representative of the United States. Although no major city in the United States perfectly represents the US population, Louisville has more similarities than differences. Similarities include median household income of $55,775 for the United States vs $51,259 for Louisville; poverty rate of 14.7% for the United States vs 15.1% for Louisville; median age of 37.8 years for the United States vs 38.1 years for Louisville; and proportion of white residents of 61.5% for the United States vs 68.8% for Louisville. But a few differences are worthy of note: Hispanic individuals represent 17.6% of US population but only 4.9% of the Louisville population. Black individuals represent 12.3% of the US population but 20.7% in Louisville.[30]

In conclusion, our study sheds light on the epidemiology of CAP in the ICU in the United States. We demonstrated that CAP in the ICU is common and that patients have an extremely high mortality rate at one year, which highlights the importance of future research in long-term outcomes. We also demonstrated that CAP in ICU cases cluster in areas with higher poverty. This is

actionable information that provides the opportunity to tackle factors related to health disparity in these areas, such as better access to health care and vaccination programs. This analysis may have important implications for health-care resources allocation and policy.

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