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Critical Care [ALERT]

Authoritative, evidence-based summaries for the critical care clinician

SPECIAL FEATURE

Post-intensive Care Syndrome: What Happens After the ICU?

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Dr. Radigan reports no financial relationships relevant to this field of study.

The number of ICU patients admitted annually continues to grow, with most recent estimates reaching 5.7 million.[1] As there are growing numbers of critically ill patients, sepsis survivorship also has grown as a substantial public health concern, with a significant number of survivors diagnosed with post-intensive care syndrome (PICS).[2] PICS is defined as a new or worsening impairment in mental, cognitive, or physical health status after critical illness and lasting beyond hospitalization for acute care.[3] It is important to go beyond saving lives in the ICU and devote additional time and attention to preventing and treating the psychiatric, cognitive, and physical sequalae of ICU illness in the follow-up setting.

Epidemiology. Although the exact prevalence of PICS among survivors of critical illness is unknown, it is estimated that one-quarter to one-half or more will suffer from some form of PICS.[3] Psychiatric illness after critical illness is widely underdiagnosed, with a national database registry reporting that only 1% of survivors of critical illness had a new psychiatric diagnosis of anxiety or depression but almost 20% were receiving one or more psychoactive medications.[4] Four times more common than PTSD, depression has been reported in one-third of patients 12 months after their ICU stay.[5] Cognitive impairment, including difficulty with executive function, memory, attention, and mental processing speed, is reported to occur in one-fourth of survivors, with some studies reporting an incidence up to 78%.[6] Physical limitations can vary quite substantially, but it is estimated that almost half of patients who are admitted with sepsis, multi-organ failure, or prolonged mechanical ventilation will suffer from ICU-acquired weakness.[7] Herridge et al revealed that 100% of acute respiratory distress survivors complained of weakness even five years after their hospitalization.[8]

Risk Factors. Common risk factors for the development of PICS include pre-existing illnesses such as neuromuscular disorders, dementia, psychiatric illness, and lower pre-ICU intelligence. Furthermore, ICU-specific factors also can contribute and may include length of mechanical ventilation, delirium,

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[INSIDE]

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sepsis, ARDS, use of corticosteroids, hyperglycemia, immobility, sedation, or hypoxia.[3] Additional risk factors include traumatic or delusional memories in the ICU, physical restraints, younger age, less education, female gender, personality type, and pre-ICU psychiatric symptoms.

Diagnostic Approaches in ICU, Follow-up Clinics. Every patient who is critically ill should undergo a thorough history and examination for the signs and symptoms of PICS. Addressing whether a patient has symptoms should not be the responsibility of the patient. Instead, the clinician should take ownership of recognizing when new or worsening cognitive, psychiatric, and physical signs and symptoms are found. Cognitive complaints often include difficulties in accomplishing executive tasks and hardships with attention, concentration, memory, mental processing speed, and executive function. Psychiatric complaints can vary substantially and include anxiety, depression, or PTSD. Physical complaints include weakness that ranges from generalized poor mobility and multiple falls to quadriparesis and tetraparesis. The identification of each component should occur as an inpatient and/or outpatient and rely on the elucidation of specific findings for each domain corroborated by examination and confirmatory testing when needed. As ICU clinics are not common practice, many ICU physicians will see patients in pulmonary follow-up clinics. There is no standard testing available for PICS, but applying a testing scheme used by the most experienced post-ICU clinics is the best option for diagnosis. For cognitive evaluation, the Montreal Cognitive Assessment and the Trail Making Test A and B are appropriate options. For depression, anxiety, and PTSD, the best options include the Beck Depression Inventory II, Hospital Anxiety and Depression Scale, and the PTSD checklist. If any patient complains of weakness, it is best for a medical professional trained in the diagnosis of ICU-acquired weakness to evaluate the individual. This medical professional should use a formal assessment. Formal electromyography and nerve conduction studies can confirm the diagnosis, if needed. Generally, there should be an extremely low threshold to consult and involve a multidisciplinary team that includes staff such as neurologists or neuropsychologists, psychiatrists, physical therapists, occupational therapists, and speech therapists.

Prevention and Treatment in ICU and Follow-up. To minimize risk of developing PICS, the ABCDE bundle approach has been advocated, especially in those critically ill patients receiving mechanical ventilation. It includes the following strategies: **A**wakening and **B**reathing **C**oordination with daily sedative interruption and ventilator liberation practices, **D**elirium monitoring and management, and **E**arly ambulation in the ICU.

ICU physicians naturally spend most of their time on the medical concerns of critically ill patients. Some of this time is spent trying to mitigate PICS from the ABCDE aspect in the above model. Additional effort needs to be applied in preparing patients for the transition out of the ICU with the FGHI elements of the model. **F**amily presence, engagement, and empowerment; **G**ood handoff communication; **H**and the patient/family written information; and **I**CU diaries. This aspect of the bundle stresses the importance of patient-centered care, which is delivering care that is respectful of and responsive to specific patient preferences, needs, and values, and ensuring that patient values guide clinical decisions.[9] These areas are reviewed in detail below.

Family Presence, Engagement, and Empowerment. Family presence starts with encouraging family members to be present in the ICU. Adapting an environment that encourages family presence also may include a more open ICU without restrictions. Ninety percent of ICUs surveyed in 2008 maintained a restrictive visitation policy.[10] Previous research has shown that flexible visitation in the ICU may decrease a patient's anxiety, confusion, agitation, cardiovascular complications, and ICU length of stay while increasing feelings of security, patient satisfaction, and safety without an increased risk of infection.[11,12] To foster the idea of family presence, it also may be helpful to redesign units to improve family comfort.

The engagement of family members includes keeping patients and family actively involved in the decision-making process by ensuring daily updates are given and

making efforts for regularly scheduled meetings. It is also important for family members to feel like they are helping their loved one. For instance, family members can help by reorienting patients and talking about family and friends. They may also bring in sensory aids (hearing aid, glasses, etc.), decorate the room with the patients' belongings to enhance comfort and familiarity, participate in mobilization, and assist with ICU diaries. Family participation on rounds also may be an option for further engagement.

Family empowerment starts with education. It is important to stress to patients and families that survivors of critical illness may suffer from unusual thoughts, mental illness, cognitive losses, and functional losses. It is empowering for both patients and families to know other ICU patients are suffering from similar problems and that they are not alone, abnormal, or unusual. Also, it is important to educate families regarding these complications so they can be proactive in terms of knowing what to look for and advocating for their loved ones when they notice concerning patterns of behavior or physical function. Unfortunately, most ICU survivors do not have the advantage of following up with a physician who is both aware of PICS and knows how to best take care of these patients outside an ICU survivor clinic. Family knowledge is especially important in this setting.

Good Handoff Communication. Good handoffs may include medication reconciliation at the end of the ICU stay, functional reconciliation by nurses, and a comprehensive physician sign-out. A handoff occurs when a departing caregiver transfers primary authority and responsibility for providing clinical care to an oncoming caregiver.[13] It would be ideal for both physicians and pharmacists to perform medication reconciliation prior to transition of care. Recently, investigators found that medication reconciliation by pharmacists at the time of ICU transfer is an effective safety intervention, which can lead to a significant decrease in medication transfer errors and a cost-effective reduction in potential harm.[14] Nurses should be encouraged to provide functional reconciliation in which the nurse compares the current functional status with pre-hospitalization status and discusses the therapies the patient is receiving at the current time. Ideally, physicians should not be limited by the basic physician sign-out but also address the cognitive, mental health, and physical status of the patient. Floor referrals for patients who may need to be reordered immediately should be discussed and may include respiratory, physical, occupational, and speech therapists. It is also important to involve physiatrists as early as possible, and consider spiritual, financial, social work, psychological, or psychiatric referrals. If sign-offs from the ICU do not include a plan of care detailing referrals that are necessary, the patient may suffer from delay of care or no care at all. Taking proactive measures can ensure all aspects of the patient's care are addressed fully and without delay.

Additional transitional aspects of care that ICU physicians may want to highlight include letters to follow-up physicians. Letters that update the physicians regarding events of hospitalization but also educate physicians about PICS are ideal. It is helpful to list references and websites for the follow-up physicians to discover more information and provide as a reference for family. An example of a letter is included on the Society of Critical Care Medicine (SCCM) website under ICU liberation, titled "Physician letter (Adult)" (Available online at: https://bit.ly/2KLqmGn).

Hand the Patient/Family Written Information. It is also important not only to provide verbal education but also to hand the patient and/or family written information addressing PICS. If available, additional information regarding post-ICU support groups for patients and families also may be helpful. Providers might find more useful tools at the SCCM website (Available at: https://bit.ly/2uflQVq) and the website for ICUsteps (Available at: https://bit.ly/2L4bM94).

ICU Diaries. Keeping ICU diaries for patients is a new approach to help patients understand what happened in the ICU. In one specific study, nursing staff maintained diaries for the duration of the patients' ICU stay. The diaries contained specific information about the patients' physical condition, procedures and treatments, events that occurred on the unit, and significant events that occurred outside the unit.[15] These diaries were found to affect both anxiety and depression positively, even after the ICU admission for the individual patients.

Post-ICU Clinic. ICU clinics designed specifically with the ICU survivor in mind have been developed in recognition of the need to care for patients and families after the sequelae of critical illness. The goal is to specifically address the medical, mental health, social support, and counseling needs after critical illness, with the overall goal to improve quality of life and reduce readmission rates. Although the data regarding their benefit are controversial, it is hopeful that after further development of the ideal model and additional research asking the correct questions, clinic interventions such as these may definitively improve outcomes for PICS survivors and/or their families.

One such clinic that has substantial experience is the Vanderbilt ICU Recovery Center. Although the Vanderbilt model uses a medical ICU's nurse practitioner, clinical pharmacist, neurocognitive psychologist, and a caseworker, many of these roles can be provided by the critical care physician with the already

established support within the clinic. See Table 1 to see a list of suggested roles that are helpful to fulfill in the follow up setting. If the physician has minimal support within the clinic setting, it is also helpful to ask patients to complete electronic questionnaires prior to the ICU follow-up visit to reduce workload of post-ICU care providers and ask a physiotherapist to perform comprehensive physical screening. Additional stakeholders that may be involved include a dietitian, palliative care specialist, rehabilitation medicine specialist, speech language pathologist, primary care provider, occupational therapist, and geriatrician.[16] The Vanderbilt ICU Recovery Center takes referrals from all ICUs. Once the referral is made, the MICU nurse practitioners review the chart for inclusion and exclusion criteria. Adapted criteria from the Vanderbilt group can be seen in Table 2. To assist with follow-up rate, the providers have found that following the patient while inpatient has improved familiarity with the ICU Recovery Center's function and subsequent follow-up. Even if this model cannot be emulated, it is helpful to learn from what is addressed within this setting and adapt to the resources available within the specific clinic setting. Some centers specialize in goal management training, a program that targets attention and executive dysfunction, which also may be helpful.[17] Although Vanderbilt University Medical Center has been working on their program since 2012, they still stress the barriers to effective post-ICU care remain evident. Two of the most prominent obstacles remain the logistics of recruiting and scheduling patients and the availability of adequate resources. The ICU Recovery Clinic at Vanderbilt University Medical Center is one example of how critical care providers can use a PICS clinic to improve the care of patients. As already mentioned, the model may be adapted to

Table 1. Roles in Constructing Patients' Plan of Care

- Manage recommendations from each specialist and clinician, review final plan with patient/family
- Review and interpret six-minute walk and spirometry results
- Screen for anxiety, depression, and PTSD
- Provide therapeutic dialogue with referrals to assist with ongoing therapy
- Medication reconciliation
- Review and address vaccine status
- Address employment status
- Provide support for individuals involved in care
- Tracheostomy, wound care, and nutritional education as indicated
- Review level of independence for activities of daily living
- Access durable medical equipment and follow up with home health services as indicated
- Ensure services planned at discharge are received

Adapted from: Huggins EL, et al. A clinic model: Post-intensive care syndrome and post-intensive care syndrome-family. *AACN Adv Crit Care* 2016;27:204-211.

Table 2. Recommended Inclusion and Exclusion Criteria for an Appointment in the Post-Intensive Care Syndrome Clinic

Inclusion

Primary: Critically ill adults, especially those with diagnosis of acute respiratory distress syndrome or sepsis

Secondary (one or more of the following):

- Shock > 6 hours
- Delirium > 2 days
- Neuromuscular blockade or high-dose steroids > 3 days
- Bed rest > 3 days
- Intensive care unit course > 7 days
- New organ dysfunction slow to recover
- Multiple new deficits anticipated at discharge

Exclusion

- Preexisting cognitive deficit
- Life expectancy < 6 months
- Managed primarily by a subspecialty service (i.e., transplant)
- Organized program such as stroke or cardiac rehabilitation after hospitalization
- Long-term resident of skilled nursing facility or long-term acute care facility

Adapted from: Huggins EL, et al. A clinic model: Post-intensive care syndrome and post-intensive care syndrome-family. *AACN Adv Crit Care* 2016;27:204-211.

the specific resources within a hospital, but the goal is to optimally manage the transition of the patient's care to a general practitioner.

Summary. As there are growing numbers of critically ill patients, the number of patients diagnosed with PICS also has grown substantially. Critical care physicians can improve long-term functioning and quality of life for survivors. It is paramount to prevent and treat PICS with the ABCDE/FGHI Bundle and ensure that all patients and families are educated and empowered. Furthermore, taking the initiative to develop an ICU clinic designed specifically with the ICU survivor in mind and adapted to the specific resources within the particular clinic setting may be the next best step in fostering the recovery process following an ICU admission. ■

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ABSTRACT & COMMENTARY

Neighborhood Socioeconomic Status Associated With Infection Risk, But Not Sepsis

By Betty Tran, MD, MSc, Editor

SYNOPSIS: Based on a large, national, prospective cohort study, lower neighborhood socioeconomic status was associated with a higher incidence of hospitalizations for infection (but not sepsis) at presentation.

SOURCE: Donnelly JP, et al. Association of neighborhood socioeconomic status with risk of infection and sepsis. *Clin Infect Dis* 2018;66:1940-1947.

Community or neighborhood factors play a key role in determining outcomes in many diseases and overall health.[1-3] In addition, other investigators have reported that lower neighborhood socioeconomic status (nSES) is associated with increased sepsis hospitalizations and sepsis-related mortality, although these studies were localized to a specific city/state or used imprecise measures of nSES.[4-6] Using prospectively gathered data from a study called the REasons for Geographic and Racial Differences in Stroke (REGARDS), a national cohort of more than 30,000 community-dwelling adults > 45 years

of age with intentional oversampling of blacks and individuals from the southeast United States, Donnelly et al sought to examine further the association between nSES and hospitalization for infection and sepsis. nSES was summarized by a score comprised of several factors including: percentage of adults who completed high school and college; percentage of participants who work in professional, executive, or managerial jobs; median household incomes; median home value; and percentage of households receiving rental fees, interest, or dividends.

Regarding outcomes, ED visits and hospital admissions for serious infection were identified by trained abstractors. These abstractors reviewed medical records to confirm the existence of infection on first presentation as one reason for admission, with additional adjudication with physician review (if needed). There was excellent interrater agreement for presence of serious infection (Kappa = 0.92).

Hospitalizations for sepsis were defined as infection with two or more sepsis-related organ failure assessment (SOFA) score points. Additionally, hospitalizations for infection with two or more systemic inflammatory response syndrome (SIRS) criteria and two or more "quick" SOFA (qSOFA) criteria also were identified.

Ten-year infection incidence per 1,000 person-years was examined across quartiles of nSES, with adjustment for several confounding factors (chronic kidney disease, age, race, education, sex, chronic lung disease geographic region, stroke, hypertension, alcohol use, smoking, myocardial infarction, and high-sensitivity C-reactive protein). The effects of potential mediators on the associations also were evaluated, including: individual income, physical weakness (based on the physical composite score on the 12-Item Short-Form Health Survey), self-reported exhaustion and physical activity, obesity, and diabetes.

The authors included 26,604 participants in the analysis. They observed significant variation among the nSES components across nSES quartiles. Participants in the lowest nSES quartile were disproportionately smokers, female, black, and nonusers of alcohol. Additionally, such subjects were disproportionately from the Stroke Belt, earned less annual income than others, had attained less education, and were more likely to present with comorbidities, abnormal biomarker labs, and reduced functional status.

After adjusting for participant characteristics, Donnelly et al noted that infection incidence was 0.84-fold lower for the highest quartile vs. lowest quartile of nSES. However, after adjustment, the authors noted no association between quartiles of nSES and sepsis incidence as defined by SOFA or qSOFA scores. Donnelly et al found that comorbid diabetes, physical weakness, and participant income produced modest (at least 10%) indirect effects on the association between nSES and infection risk.

Overall, infection type was similar across nSES quartiles, with respiratory infections listed as the most common. Median length of stay was longer for participants in the lowest nSES quartile, but the authors found no significant differences in SOFA scores or percentages of in-hospital death among nSES quartiles.

■ COMMENTARY

Donnelly et al have expanded on prior efforts to explore the complex association between social determinants of health and risk of hospitalization for infection and sepsis. Compared to prior studies, the Donnelly et al investigation features several strengths. First, data were collected prospectively as part of a national cohort. Second, the definition of nSES used was much more granular, based on census block groups and incorporating multiple domains as opposed to a single proxy such as insurance status.[6] Outcomes were measured more accurately based on medical abstraction and published criteria for sepsis (e.g., SOFA scores) as opposed to ICD-9 codes.[4] Third, follow-up was fairly extensive at 10 years. Finally, the mediating role of several factors was examined, providing hypotheses for further explorative and intervention-based studies. For example, individual income was found to mediate the association between nSES and infection risk, suggesting factors such as social isolation, reduced food availability, and lack of transportation may be targeted areas that could reduce hospitalizations for infection.

Overall, no association was found between nSES and sepsis incidence, to the extent that hospitalizations for infection may portend future hospitalizations for sepsis. However, the findings from this study support the premise that improving sepsis outcomes might be achieved outside of focusing exclusively on inpatient care by way of improvements in decreasing healthcare disparities that result in infection hospitalizations. This could include social interventions such as improving safe transportation options as well as improved aggressive medical management of chronic diseases such as diabetes. As such, findings from this study are a helpful reminder for us to think outside the box in our attempts to improve sepsis outcomes. ■

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ABSTRACT & COMMENTARY

Are In-hospital Deaths Related to Community-acquired Pneumonia Preventable?

By Betty Tran, MD, MSc, Editor

SYNOPSIS: This secondary analysis of data from five tertiary care centers found that among patients hospitalized for community-acquired pneumonia, very few deaths potentially were related to a lapse in in-hospital quality of pneumonia care.

SOURCE: Waterer GW, et al. In-hospital deaths among adults with community-acquired pneumonia. *Chest* 2018 May 30. pii: S0012-3692(18)30801-8. doi: 10.1016/j.chest.2018.05.021. [Epub ahead of print].

Although hospitalization for and subsequent mortality related to community-acquired pneumonia (CAP) is common, it is unclear whether improvements in inpatient pneumonia-related care can affect pneumonia-related mortality. A prior study showed that only about half of all deaths in patients with CAP were attributable to their acute illness.[1]

Waterer et el conducted a secondary analysis of the Etiology of Pneumonia in the Community (EPIC) study of adults hospitalized for CAP at five tertiary care hospitals (three in Chicago, two in Nashville). Notably, patients with recent prior hospitalizations, tracheotomies/gastric tubes, cystic fibrosis, neutropenic cancer, transplant, and HIV with CD4 counts < 200/mm^3 were excluded. Treating physicians made management decisions for each patient. For patients who died during their index CAP hospitalization, a five-physician panel at each study city (with expertise in emergency medicine, infectious diseases, pulmonary, and critical care) made several determinations. These included: cause of death based on *a priori* criteria; whether the cause of death was directly, indirectly (major or minor contribution), or not related to CAP; whether management was consistent with current recommendations in care quality metrics (antibiotics administered per Infectious Diseases Society of America and American Thoracic Society guidelines, antibiotics delivered within six hours of presentation or one hour [if shock present], using arterial blood gas or pulse oximetry to assess oxygenation); and whether end-of-life limitations in care existed. All five panelists discussed the cases, with complete medical records available for review until the physicians reached a consensus (four out of five or five out of five in agreement).

The authors included 2,320 adults hospitalized for CAP in the final study population. Fifty-two patients died during their CAP hospitalization. The most common causes of death were hypoxemic respiratory failure (25.0%) and septic shock (23.1%). Compared with patients who survived hospitalization, those who died were older and exhibited more comorbidities.

The physician panel attributed 27 deaths directly to CAP. Panelists attributed 10 deaths to situations in which CAP played an indirect role with major contribution. Further, physicians found that nine deaths occurred when CAP played a minor role. Finally, the physicians ruled that CAP was unrelated to the other six deaths. There were DNR orders for a significant number of patients who died (21 of 52 patients). Ten had DNR orders in place prior to admission, eight after admission but > 48 hours prior to death, and three within 48 hours of death. Sixty-seven percent of in-hospital deaths occurred within the first 10 days of admission.

Among the 52 patients who died in the hospital, the physician panel identified nine who had a lapse in quality of in-hospital CAP care. However, the physicians judged five of these nine deaths to be unrelated to the lapse in care quality. Further, the physicians judged two of the nine deaths were patients who had end-of-life care limitations in which decisions were made not to pursue ICU care at the time of admission. Therefore, only two patients who were not DNR were identified to have a lapse in quality in-hospital pneumonia care, potentially contributing to in-hospital death. In one patient, there was difficulty finding intravenous access, with a subsequent delay in antibiotics.

For the other patient, medical staff thought there was an intra-abdominal infection, based on an admit chest X-ray that did not show signs of pneumonia, and administered ciprofloxacin only; however, a CT scan the next day was consistent with pneumonia.

■ COMMENTARY

This authors of this prospective, multicenter study of more than 2,000 adults hospitalized for CAP found a low in-hospital mortality rate of 2.2% (52 patients) and identified only two patients for whom a lapse in in-hospital pneumonia care potentially contributed to death. As such, the authors concluded that most in-hospital deaths among adults with CAP would not have been preventable with improved quality of in-hospital care.

The study has several strengths, including review of patient cases by multiple physicians with clinical expertise. These physicians paid careful attention to whether CAP could be an indirect contributor (minor or major) to death based on a broad view of how acute pneumonia could lead to extrapulmonary complications (e.g., new cardiovascular disease, stroke, renal failure, secondary infection after initial stabilization of CAP). Also, the authors captured end-of-life limitations on care, which affects whether patients die in the hospital.

The most important limitation to this study is its generalizability. The five hospitals were academic, urban, U.S. facilities that maintain extensive training programs and employ clinician scientists who are dedicated to studying CAP and providing high-quality care. The relatively low mortality rate and high compliance with quality pneumonia care are reflective of this. Thus, the study's findings likely are not generalizable to other institutions, where in-hospital deaths due to CAP may be reduced by following recommended guidelines for CAP and sepsis management. This study and its case report template (available in Appendix 1 in the online supplement) would be a helpful starting point for individual hospitals to evaluate their own outcomes and guide quality improvement initiatives related to CAP hospitalizations. ■

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CME/CE QUESTIONS

1. **The Vanderbilt ICU Recovery Center has set up a post-ICU clinic, modeled after that which is seen in the ICU, with an outpatient team that includes which of the following:**
   a. Medical ICU nurse practitioner
   b. Pharmacist
   c. Pulmonary intensivist
   d. All of the above

2. **Based on the study by Donnelly et al, neighborhood socioeconomic status is associated with which of the following?**
   a. Hospitalization for infection
   b. Hospitalization for sepsis
   c. Hospitalization for septic shock
   d. All of the above

3. **In the Donnelly et al study, which of the following was *not* found to be a modest (at least 10%) mediator in the association between neighborhood socioeconomic status and infection risk?**
   a. Diabetes mellitus
   b. Income level
   c. Obesity
   d. Physical weakness

4. **Which statement is *true* based on the findings in the Waterer et al study regarding community-acquired pneumonia (CAP)?**
   a. Adults hospitalized with CAP have a mortality rate of 23%.
   b. Most in-hospital deaths among patients admitted for CAP do not appear preventable with improvements in inpatient care.
   c. Most inpatient CAP deaths are among adults < 65 years of age.
   d. Most inpatient CAP deaths occurred after 14 days.