BRIEF REPORT

OPEN

# Hospital Strain and Variation in Sepsis ICU Admission Practices and Associated Outcomes

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**OBJECTIVES:** To understand how strain-process-outcome relationships in patients with sepsis may vary among hospitals.

**DESIGN:** Retrospective cohort study using a validated hospital capacity strain index as a within-hospital instrumental variable governing ICU versus ward admission, stratified by hospital.

**SETTING:** Twenty-seven U.S. hospitals from 2013 to 2018.

**PATIENTS:** High-acuity emergency department patients with sepsis who do not require life support therapies.

**INTERVENTIONS:** None.

**MEASUREMENTS AND MAIN RESULTS:** The mean predicted probability of ICU admission across strain deciles ranged from 4.9% (lowest ICU-utilizing hospital for sepsis without life support) to 61.2% (highest ICU-utilizing hospital for sepsis without life support). The difference in the predicted probabilities of ICU admission between the lowest and highest strain deciles ranged from 9.0% (least strain-sensitive hospital) to 45.2% (most strain-sensitive hospital). In pooled analyses, emergency department patients with sepsis ($n = 90,150$) experienced a 1.3-day longer median hospital length of stay (LOS) if admitted initially to the ICU compared with the ward, but across the 27 study hospitals ($n = 517$-$6,564$), this effect varied from 9.0 days shorter (95% CI, −10.8 to −7.2; $p < 0.001$) to 19.0 days longer (95% CI, 16.7–21.3; $p < 0.001$). Corresponding ranges for inhospital mortality with ICU compared with ward admission revealed odds ratios (ORs) from 0.16 (95% CI, 0.03–0.99; $p = 0.04$) to 4.62 (95% CI, 1.16–18.22; $p = 0.02$) among patients with sepsis (pooled OR = 1.48).

**CONCLUSIONS:** There is significant among-hospital variation in ICU admission rates for patients with sepsis not requiring life support therapies, how sensitive those ICU admission decisions are to hospital capacity strain, and the association of ICU admission with hospital LOS and hospital mortality. Hospital-level heterogeneity should be considered alongside patient-level heterogeneity in critical and acute care study design and interpretation.

**KEYWORDS:** hospital strain; hospital variation; intensive care unit; processes of care; sepsis

Recent evidence suggests that many patients with sepsis have discretionary hospital admission patterns such that they may be admitted to ICUs or wards depending on hospital strain (1, 2). Among these patients—of high acuity but who do not require life support therapies—admission to ICUs may confer longer length of stay (LOS) and higher mortality on average (3). However, because hospitals are known to vary significantly in many processes or outcomes of care (4), these overall effects may not be useful for guiding individual hospitals on how to improve their triage of patients with sepsis. We,

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## KEY POINTS

**Question:** Among high-acuity patients with sepsis, is there variation between hospitals in the association between ICU admission, compared with ward admission, and clinical outcomes?

**Findings:** In this retrospective cohort study, emergency department patients with sepsis experienced a 1.3-day longer median hospital length of stay if admitted initially to the ICU compared with the ward, but across hospitals, this effect varied from 9 days shorter to 19 days longer.

**Meaning:** More research is needed to identify hospital-level care processes that are most impactful on triage and outcomes, and hospital-level differences should be taken into account when designing and interpreting acute care studies.

therefore, sought to understand among-hospital variation in ICU admission rates, how sensitive those ICU admission decisions are to hospital capacity strain, and the association of ICU admission with clinical outcomes among high-acuity patients with sepsis who do not require life support therapies.

## MATERIALS AND METHODS

Details about the construction of this sepsis cohort using data from 27 hospitals across Penn Medicine and Kaiser Permanente Northern California have been reported previously (1, 3). For this analysis, we studied patients who: met criteria for sepsis in the emergency department (ED), based on an adaptation of the Sepsis-3 consensus definition (5, 6) (Sepsis-related Organ Failure Assessment [SOFA] score or quick SOFA score ≥ 2; serum lactate ≥ 4 mmol/L; oxygen saturation [$Spo_2$] ≤ 85%; or receipt of a $Fio_2$ ≥ 60% or noninvasive ventilation [1, 3]); had high acuity based on a Laboratory-based Acute Physiology Score v2 (LAPS2) (7, 8) greater than or equal to 100 (previously validated as a cutoff below which patients are rarely admitted to the ICU (1) and above which inhospital mortality increases notably (3)); and were admitted to a medical or medical-surgical ward, step-down unit, or ICU. We excluded patients who required mechanical ventilation or vasopressors in the ED or who had a care limitation beyond a simple do-not-resuscitate/do-no-intubate order at admission. Patients requiring other organ support therapies, such as dialysis, were eligible for inclusion.

We have previously reported on the development, validation, and deployment of a novel composite hospital capacity strain index as a within-hospital instrumental variable governing ICU admission for this sepsis cohort (1, 3). This hospital-specific strain index, derived from 22 strain metrics standardized to bed capacity, fulfills the required instrumental variable assumptions in this patient population in that it is: 1) highly associated with the exposure of interest (i.e., ICU vs ward admission), 2) not associated with the outcomes of interest (i.e., hospital LOS and hospital mortality specifically in this sepsis cohort), except via the exposure of interest, and 3) not meaningfully associated with other confounders in the exposure-outcome relationship (1).

For this study, we first conducted a retrospective cohort analysis using multivariable logistic regression to assess the association of hospital strain and ICU (vs ward) admission, adjusted for age, gender, race, ethnicity, insurance status, LAPS2, and Comorbidity Point Score v2 (9), and stratified by hospital. We next conducted second retrospective cohort analyses using two-stage instrumental variable quantile regression and residual inclusion regression similarly adjusted and stratified by hospital to assess the association between ICU admission and hospital LOS and hospital mortality, respectively (3, 4, 10–14). For the LOS outcome, death was ranked as equivalent to the 99th percentile of hospital LOS in the cohort by hospital (13–16).

Using the results from a previously described and published survey of study hospital characteristics (4), we then assessed the correlation between individual hospital characteristics and four hospital-level outcomes: mean predicted probability of ICU admission across hospital strain deciles (i.e., ICU utilization), the range of predicated probability of ICU admission between the lowest and highest hospital strain deciles (i.e., strain sensitivity), change in hospital LOS with ICU admission, and odds ratio (OR) of hospital mortality with ICU admission. Continuous variables were assessed by Pearson correlation coefficient ($R$), and categorical and binary variables were assessed by analysis of variance ($F$). Finally, we used the hospital

variables found to have univariate correlations with the outcomes of interest (based on $p < 0.05$) to construct multivariable linear regression models to assess the association between hospital characteristics and the above hospital-level outcomes of interest.

The study protocol was reviewed and approved with a waiver of informed consent by the Institutional Review Boards of Kaiser Permanente Northern California (Protocol CN-16-2816, "Assessing the Needs and Net Benefits of Critical Care," approved January 09, 2017) and the University of Pennsylvania (Protocol 827541, "Benefits of ICU Admission for Patients With Acute Respiratory Failure or Sepsis: A Mixed-Methods Study Across 26 Hospitals," approved May 24, 2017). The procedures followed were in accordance with the ethical standards of the Institutional Review Boards and with the Helsinki Declaration of 1975.

## RESULTS

Patient characteristics for this sepsis cohort have been reported previously (1, 3). In summary, among 90,150 patients with sepsis, mean age was 73.6 years, 12.4% were of Black race, 79.5% were admitted directly to a ward or step-down unit, observed median hospital LOS was 3.9 days (interquartile range, 2.4–6.7 d), and observed hospital mortality was 17.2%.

Hospitals ($n = 27$) varied in the proportion of sepsis patients they admitted to the ICU and in the strength of the association between hospital strain and ICU admission. The mean predicted probability of ICU admission across strain deciles ranged from 4.9% (lowest ICU-utilizing hospital) to 61.2% (highest ICU-utilizing hospital). The difference in the predicted probabilities of ICU admission between the lowest and highest strain deciles ranged from 9.0% (least strain-sensitive hospital) to 45.2% (most strain-sensitive hospital). ICU utilization and strain sensitivity were moderately positively correlated (Spearman $\rho = 0.68$, $p = 0.0001$), such that higher overall ICU-utilizing hospitals are likely to have a wider range of utilization across the spectrum of strain.

In prior published pooled analyses, this cohort of ED patients with sepsis experienced a 1.3-day longer median hospital LOS if admitted initially to the ICU compared with the ward (3), but in the new present analyses, across the 27 study hospitals ($n = 517$-$6{,}564$). this effect varied from 9.0 days shorter (95% CI, –10.8 to –7.2; $p < 0.001$) to 19.0 days longer (95% CI, 16.7–21.3; $p < 0.001$) (**Fig. 1**). Corresponding ranges for inhospital mortality revealed ORs from 0.16 (95% CI, 0.03–0.99; $p = 0.04$) to 4.62 (95% CI, 1.16–18.22; $p = 0.02$) among patients with sepsis (pooled OR 1.48 [3]) who were admitted to the ICU as compared with those admitted to the ward (**Fig. 2**).

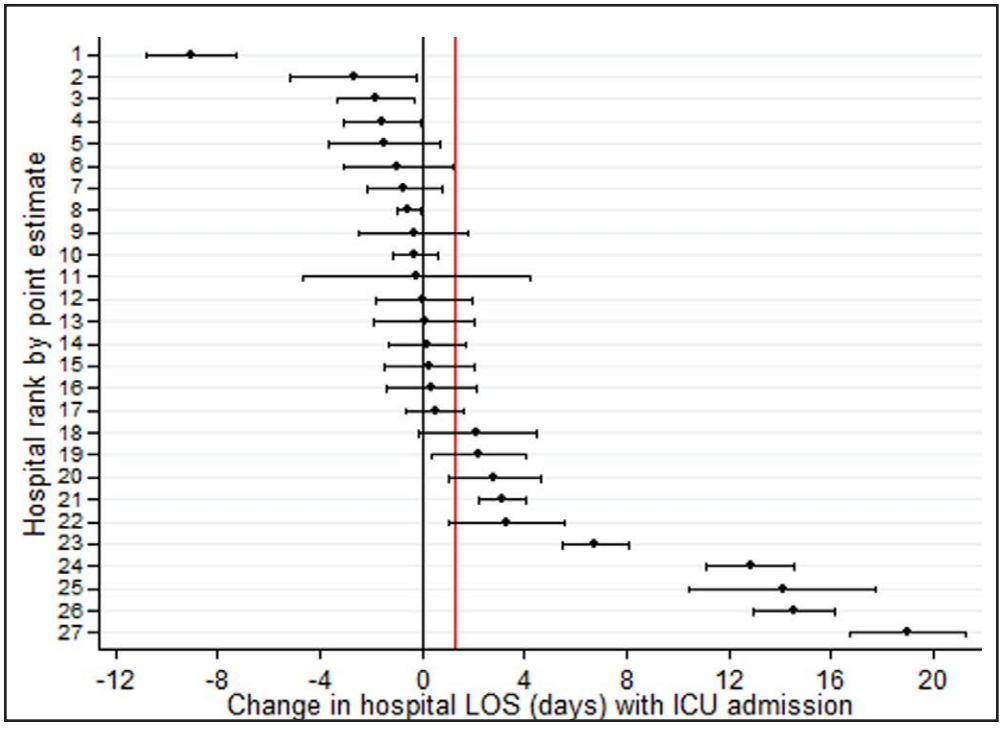


**Figure 1.** Among-hospital variation in the association between ICU admission and hospital length of stay in patients with sepsis. In pooled analyses, emergency department patients with sepsis ($n =$ 90,150) experienced a 1.3-d longer median hospital length of stay (LOS) if admitted initially to the ICU compared with the ward, but across the 27 study hospitals ($n = 517$–$6{,}564$), this effect varied from 9.0 d shorter (95% CI, −10.8 to −7.2; $p < 0.001$) to 19.0 d longer (95% CI, 16.7–21.3; $p <$ 0.001). Hospitals are ranked on the *y*-axis by their change in hospital LOS point estimate. *Vertical black line* displays no change in LOS, and *vertical red line* displays the pooled point estimate of 1.3 d. *Horizontal black bars* represent 95% CIs.

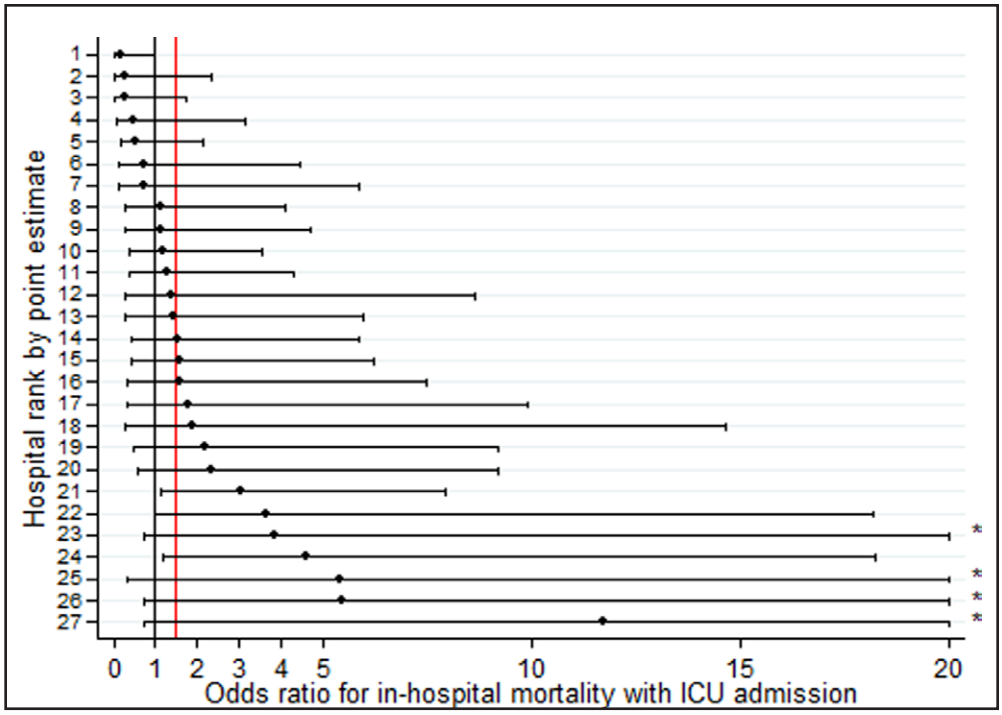


**Figure 2.** Among-hospital variation in the association between ICU admission and hospital mortality in patients with sepsis. In pooled analyses, emergency department (ED) patients with sepsis experienced an odds ratio (OR) of 1.48 for inhospital mortality if admitted initially to the ICU compared with the ward, but across the 27 study hospitals, this effect varied from OR 0.16 (95% CI, 0.03–0.99; $p = 0.04$) to 4.62 (95% CI, 1.16–18.22; $p = 0.02$). Hospitals are ranked on the *y*-axis by their inhospital morality OR point estimate. *Vertical black line* displays no change in mortality (OR = 1), and *vertical red line* displays the pooled point estimate of OR = 1.48. *Horizontal black bars* represent 95% CIs. *Upper bound beyond figure range.

Among hospital characteristics, maximum ED patient capacity ($R = {}^{-}0.43$; $p = 0.03$) and daytime ICU staffing model ($F = 6.61$; $p = 0.01$) were correlated with the range of predicated probability of ICU admission between the lowest and highest hospital strain deciles (i.e., strain sensitivity), and nighttime primarily responsible clinician for ED disposition decisions was correlated with the OR of hospital mortality with ICU admission ($F = 3.67$; $p = 0.03$). No other hospital characteristic-outcome pairings had statistically significant correlations, including with hospital LOS.

We then constructed two multivariable linear regression models: No hospital characteristics were associated with the range of predicated probability of ICU admission across strain deciles (i.e., strain sensitivity). The nighttime primarily responsible clinician for ED disposition decisions being a hospitalist ($\beta = -3.53$; $p = 0.02$) or a combination of clinicians (i.e., among hospital medicine, ICU, and ED physicians) ($\beta = -4.41$; $p = 0.01$), compared with the ED physician alone, was associated with a reduced OR of hospital mortality with ICU admission; there was no mortality difference if the triaging clinician was the ICU physician alone.

## DISCUSSION

This study used a stratified hospital-level analysis of a retrospective cohort study and a paired hospital characteristic survey to shed new light on among-hospital differences in critical care practices and outcomes for high-acuity patients with sepsis who do not require life support therapies. The key findings of these analyses are that for high-acuity patients with sepsis not requiring life support therapies: 1) there is significant among-hospital variation in ICU admission rates and in how sensitive those ICU admission decisions are to hospital capacity strain and 2) there is significant among-hospital variation in the association of ICU admission with hospital LOS and hospital mortality.

Although the interpretation of the prior reported pooled result would suggest that more high-acuity patients with sepsis may be admitted to the ward with the same or improved outcomes (3), the results of this study reveal a more complex relationship between ICU admission and outcomes that varies on the hospital level, similar to that found in partner analyses of a related acute respiratory failure cohort (4). Variation among hospitals across these domains—how ICUs and wards are utilized, how that utilization changes in relation to strain, and the risk or benefit gleaned from ICU relative to ward admission—suggests most fundamentally that critical care (and/or ward care) is heterogeneous in both use and impact. This theorized and now further documented phenomenon has implications for interpreting pooled analyses of prospective or observational studies of clinical and organizational interventions across the inpatient setting. This is true

for our prior work in the present sepsis population as above and, more broadly, has been a growing focus on the greater critical care literature dominated by null interventional studies among heterogeneous, multihospital cohorts. There is notable commentary on potentially missing efficacious interventions due to heterogeneity of treatment effects based on patient-level clinical heterogeneity (17). Our study suggests that a similar phenomenon may be occurring due to hospital-level heterogeneity. Our interventions, clinical or organizational, that aim to move the outcomes needle and the studies that evaluate them may, therefore, need to be carried out in a more nuanced way that takes into account both hospital-level and patient-level heterogeneities.

In hypothesis-generating analyses, we found that hospital medicine leadership or input on the nighttime ED disposition decisions to ICU versus ward was associated with reduced hospital mortality with ICU admission. That might suggest that hospitalists provide added insight, compared with ED and ICU physicians, into more optimal ICU versus ward sepsis patient selection that better aligns patients with an appropriate level of care. It is plausible that among patients likely or potentially admitted to ICUs (i.e., above a certain acuity threshold and not almost always admitted to wards), those with relatively lower acuity might be most susceptible to a net risk from ICU admission. This may occur because such patients are exposed to ICU-specific potentially harm-inducing phenomena (such as aggressive care and procedures [18], reduced sleep quality [19, 20], and reduced mobility and strength [21]) and at the same time have less to gain from that aggressive care based on their comparatively lower acuity. The potentially appropriate preferential triage of these patients to ward-level care may be best facilitated by involvement or leadership by hospitalists, which would, in turn, reduce the measured higher hospital mortality with ICU admission, the above observed finding.

Overall, only a small number of the hospital characteristics measured in our survey were correlated or associated with process and clinical outcomes. This all likely suggests that more nuanced qualitative and quantitative methods are required to identify aspects of the ED-ward-ICU hospital organizational structure that are most impactful on triage and outcomes, before the results of this, and related preceding studies should routinely guide clinical decisions.

The results of this study should be interpreted with known limitations. First, hospital-level stratified analyses of original larger pooled analyses have smaller size and wider CIs. Second, instrumental variable analyses have notable limitations in comparison with prospective randomization: if the instrumental variable compliers—patients whose ED disposition decision differed as a result of hospital strain—were different across hospitals, the comparison of among-hospital instrumental variable results may be of different types of patients and of less utility. A total of 26,404 (29.3%) patients also had acute respiratory failure and were included in a previously published partner study (3, 4). Although similar among-hospital variation was found in both cohorts, the pooled treatment effect estimates and the range of hospital-stratified treatment effect estimates remain divergent between the two patient groups despite partial cohort overlap. Because the results of these instrumental variable analyses only apply to instrumental variable compliers, the least strain-sensitive hospitals would have the fewest such applicable patients. The nuanced role of prolonged care in the ED during periods of high hospital capacity strain is not fully treated in this report, but in the preceding pooled analysis, adjustment for ED LOS only attenuated a still-significant hospital LOS outcome and did not alter the hospital mortality results (3). Although the strain index inputs are standardized to local bed capacity, the ratio of ICU-to-ward beds is not included and may be influential.

In conclusion, there is significant among-hospital variation in ICU admission rates for high-acuity patients with sepsis not requiring life support therapies, how sensitive those ICU admission decisions are to hospital capacity strain, and the association of ICU admission with hospital LOS and hospital mortality. More nuanced qualitative and quantitative data are needed to better identify aspects of the ED-ward-ICU hospital organizational structure that are most impactful on triage and outcomes, and critical care and acute care study design should take into account both patient-level and hospital-level heterogeneities.

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