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Capacity strain and risk of ICU-onset bloodstream infection

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Capacity strain and risk of ICU-onset bloodstream infection

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An abstract of
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I. Abstract

Capacity strain and risk of ICU-onset bloodstream infection
By: Emily Niehaus

Background:
Capacity strain refers to the concept of a mismatch between medical workload and patient care resources, which leads to variability in the ability to provide high-quality care. Capacity strain in the intensive care unit (ICU) has been associated with increased odds of mortality and changes in patient-care processes. Less is known about the impact of capacity strain on healthcare-associated infections, especially hospital-onset bloodstream infections (BSI), which occur in 4.4-10% of all ICU admissions and are associated with increased mortality rate, longer length of stay, and higher hospital costs.

Methods:
Using a retrospective cohort of all adult patient encounters admitted to any critical care unit for more than three days at four university-affiliated hospitals between 01/01/2014 and 12/29/2018, we classified all ICU onset-BSI, occurring after ICU day 3, as true pathogen or contaminant. We used multivariable logistic regression to evaluate the relationship between capacity strain at the ICU level and patient-level risk factors for ICU-onset BSI. Capacity strain, the primary exposure, was defined as the number of days within the first three days of the patient's ICU stay that fell above the 90^{th} percentile for the unit's daily census in that year.

Results:
There were 24,786 patients included in the cohort, 387(1.6%) of which experienced a non-contaminant ICU-onset BSI. At the patient level, encounters that had ICU-onset BSI had higher SOFA scores at time of ICU admission (7 vs .5), were more likely to have a central line (83% vs. 57%) and require mechanical ventilation (62% vs. 39%), and had longer lengths of stay in ICU (18 vs. 6 days) than those who did not have ICU-onset BSI ($p<0.0001$ for all). While increased exposure to a strained unit was associated with risk of developing ICU-onset BSI when adjusting for patient risk factors (3 vs. 0 days of strain OR=1.53, 95% CI 1.11-2.11), there was no observed association after adjusting for unit characteristics.

Conclusion:
ICU-onset BSIs were infrequent (2%), but associated with higher acuity of illness and device utilization. ICU admission on a day with a census at $>90^{th}$ percentile was not associated with subsequently developing an ICU-onset bloodstream infection after adjusting for patient and unit level risk factors. Future studies should evaluate capacity strain and infection prevention processes of care in the ICU.

Capacity strain and risk of ICU-onset bloodstream infection

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Chapter I: Background

Healthcare-associated infections (HAIs) are associated with significant impact at both the patient and public health levels, including increased mortality, morbidity and healthcare costs. The Centers for Disease Control and Prevention (CDC) estimates that there were 721,800 HAIs in U.S. hospitals in 2011, including approximately 35% in intensive care units (ICU) [1]. Between 102,000 and 120,000 episodes of hospital-onset bloodstream infections (BSI) occur every year, while among ICU admissions, the incidence rate for ICU-onset BSI ranges from 4.4 - 10% [2-6]. BSIs associated with an ICU stay remain common, and are associated with substantial mortality, including a two- to four-fold increased odds of ICU mortality, and an estimated attributable mortality of 25% [5, 7, 8]. Hospital-onset BSIs have also been found to be associated with longer hospital stays and higher hospital costs [6, 9].

Hospital-onset bloodstream infection surveillance

The CDC's National Healthcare Safety Network (NHSN), which performs national HAI surveillance, delineates hospital-onset BSI into either primary or secondary infections [10]. The NHSN defines a primary BSI as any "recognized bacterial or fungal pathogen not included in the common commensal list, identified from one or more blood specimens by a culture or non-culture based microbiologic testing methods, and is not related to an infection at another site." This definition also includes blood culture results that are common oral or skin organisms, as long as the result was found in two unique cultures and there were signs and symptoms of infection. Currently, most states only require surveillance and mandatory reporting for central line-associated BSIs (CLABSI,

defined as primary BSIs occurring with the presence of a central line). However, some have argued that the CLABSI definition does not adequately reflect healthcare quality because the definition is not specific, determination of the primary or secondary relies on the application of additional criteria that can be variably interpreted, is not externally validated outside the institution, and risk adjustment is insufficient [11-13].

Hospital-onset BSIs have been an alternative, recently proposed infection metric to CLABSI. Total hospital-onset BSI may be a more objective and inclusive measure of HAI-related quality because it incorporates severe adverse outcomes from multiple types of HAIs, such as urinary tract infections and surgical site infections, and potential lapses in catheter care leading to blood culture contamination [14, 15]. In one multi-center study, only 6% of hospital-onset BSIs met definition for CLABSI, and the outcome of hospital-onset BSI had higher power to discriminate between infection rates among 80 ICUs [15]. With higher numbers of events and an objective culture-based definition, this broad category of infection may be more useful and reliable at distinguishing top performers in infection prevention [14-16]. In addition, the rates of both primary and secondary BSIs parallel changes in the rate of CLABSIs, and track closely with institutional infection prevention efforts [14, 15, 17]. Since publicly reported HAI rates such as CLABSI are available on hospital "report cards" to inform patient care decisions, and by the Centers for Medicare/Medicaid Services (CMS) to determine financial penalties, improving these quality measures have major implications for public health and patient safety.

Risk factors for healthcare-associated infections

To improve patient safety within the ICU and the whole hospital, prior research focused on identifying the risk factors and possible intervention strategies for reducing HAI rate [18-20]. The risk of hospital-onset infections depends on three main elements, related to the organism, the host, and the healthcare system.

First, in healthcare, patients are exposed to a wide range of potentially pathogenic microorganisms. These include the patient's endogenous microbiome, and exogenous organisms acquired from the environment including medical devices and equipment and patient room surfaces. Daily chlorhexidine bathing can remove potential pathogens from the patient's skin and reduces BSIs in the ICU by approximately 29% [21]. Disinfection of surfaces and terminal room cleaning can limit patients' exposure to microorganisms while in the hospital [19, 22].

Second, host-level factors refer to a patient's intrinsic and extrinsic risk factors for developing infection. Intrinsic risk factors include age, medical comorbidities, immunosuppression, and poor nutrition, which reduce the body's ability to combat a pathogenic organism after exposure and are generally non-modifiable. Extrinsic risk factors are often related to treatment strategies that occur in the healthcare setting, such as the need for invasive devices or invasive procedures, and can be important intervention targets. For example, a central venous catheter provides a direct pathway from the skin (insertion site) to the bloodstream, leading to increased risk of CLABSI. Management of these extrinsic risk factors, such as device use and maintenance, potentially reduce HAI in the ICU [6].

Lastly, HAI risk can be seen as a failure of a complex healthcare system, which encompasses individual healthcare worker behaviors, the utilization of numerous tools

and technologies, and the organizational structure of the hospital environment. The study of human factor engineering (HFE) can address these factors comprehensively and systematically in order to prevent hospital infections [23-25]. Understanding patient care workflow can lead to the creation of an environment where it is easier to perform a task correctly than it is to perform it incorrectly or not perform it at all, removing the fallibility of human behavior [19]. For example, placement of hand hygiene dispensers in locations with high visibility and along the typical workflow path has led to improved hand hygiene adherence in the hospital. The development of a central line maintenance kit that incorporated HFE principles demonstrated improved adherence to central line maintenance and reduction in the CLABSI rate [26]. These strategies are crucial in leading to the adherence of best practice guidelines for infection prevention. However, just as humans are prone to error, healthcare systems and structures can also break down. High levels of workload and system-level stress or capacity strain, may lead to failure at multiple places in the prevention of hospital-onset infections.

Definition of capacity strain in the ICU

Capacity strain represents a mismatch between medical workload and patient care resources, leading to undesired variability in a hospital unit's ability to provide high-quality care [27]. Capacity strain has been well studied in the emergency department, where overcrowding and high patient volumes are associated with increased mortality and delays in appropriate care delivery [28]. In the ICU, capacity strain may refer to a discrepancy between the availability of ICU resources, including beds, ventilators, staff, and time, and the mental, technical, and psychological demand of caring for medically

complex patients. ICU capacity strain has been defined by Halpern et. al as "a set of temporally varying influences on the ability of an ICU to provide high-quality care for everyone who is or could become a patient in that ICU on that day" [27].

A framework for the key contributors of ICU strain can help assess how these time-varying factors may impact patient care and patient outcomes. A qualitative study using focus groups across nine Canadian ICUs found four major themes of contributors to strain in the ICU setting: patient/family related (high patient acuity, communication issues, advance care planning, end-of-life care planning), provider related (nurse attrition, inexperienced workforce, high patient-to-nurse ratios), resource related (reduced capability after hours, physical bed shortage), and health-system related (high ward bed occupancy, preferential priority for certain services), but these are difficult to consistently and accurately measure [29]. Others have attempted to find objective markers that most closely represent the perceived strain by those responsible for patient care within the ICU. In a survey of nurses and physicians in a medical ICU, average patient acuity, ICU census, number of ICU admissions, and general ward census best modeled the nurse perception of strain [30]. Among physicians, only ICU census was associated with perceived strain. Despite no clear consensus on how to quantify capacity strain within the ICU, different measures of strain are associated with adverse patient outcomes, as summarized below.

Staffing ratios

The concept of capacity strain in the ICU has been indirectly studied for decades using nurse staffing levels. In observational studies, nurse-to-patient (staffing) ratios in

the ICU have been associated with numerous patient outcomes, including mortality, failure to rescue, quality of care, costs, length of stay, and infectious complications [31-34]. Low nurse to patient ratios have also been associated with hospital infection outbreaks [35-37] and increased risk of HAI at both the ICU unit level and at the individual level [38-45]. In a study that evaluated excessive nursing workload, excessive workload was independently associated with increased risk of CDC-defined HAIs when adjusting for age, clinical condition, and presence of invasive devices [46]. Yet, when mechanical ventilation was included in the multivariate model, excessive nursing workload was no longer associated with risk of HAI. A prospective study in Switzerland estimated that 26.7% of infections in the ICU could have been avoided if nurse-to-patient ratio was maintained above 2.2 [44].

Despite these findings, interventions to increase nurse to patient ratios have not led to a significant decrease in patient mortality or adverse events [47-49]. Massachusetts was the first state to implement a mandate for 1:1 or 1:2 nurse-to-patient ratio in ICUs. In a retrospective study of claims data comparing Massachusetts to other states, there was no significant increase in nurse staffing in the ICU and no change to patient outcomes after implementation of the mandate [49]. Scruth argues that the inconsistencies in observational and implementation studies are not surprising, as nurse staffing levels should reflect patient acuity and dependency, patient throughput, nursing competency, and availability of ancillary staff [50]. Staffing ratios may in fact represent a proxy measurement for ICU capacity strain, where times of high patient volume and high workload coincide with lower nurse to patient ratios. Therefore, ICU capacity strain may

be better understood in a framework that focuses instead on the variability in patient volume and needs.

Bed occupancy

Bed occupancy is a metric that captures variability in patient volume, and therefore an attractive candidate to model ICU capacity strain. Crowded units, where bed occupancy is high, seem to place patients at increase risk of developing a HAI. In a UK hospital, wards at 80-90% occupancy had 56% higher rates of *Clostrioides difficile* infection than patients on wards with 0-70% occupancy rates [51]. In the ICU, elevated monthly bed occupancy rate was associated with higher incidence rate of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in both single-institution and multi-center studies[52-54]. Overall the relationship between bed occupancy and HAI rate has primarily been studied in time-series analyses using month-level data. No studies have evaluated how daily variations in ICU census or bed occupancy may influence HAI risk at the patient level.

Daily ICU capacity strain

ICU capacity strain, measured in terms of daily variability in patient care needs, resulted in poor patient outcomes, including mortality [55, 56]. A systematic review evaluating the role of capacity strain on inpatient outcomes found that there was a statistically significant increase in mortality at times of high daily capacity strain in 9 out of 12 studies in the ICU setting [28, 57]. Increased odds of mortality at times of high ICU capacity strain may be mediated by direct factors, such as increased workload and

inability to devote appropriate attention to all patient needs. Indirect factors also play an important role. For example, at times of high bed occupancy, the average patient has higher acuity and likely requires more advanced care, with resulting impact on patient outcome [58].

Daily capacity strain may alter patient care processes in the ICU, including treatment decisions, judgments about resuscitation appropriateness, and discharge preparation. High daily census and the proportion of new admissions was found to be associated with lower receipt of appropriate venous-thromboembolism prophylaxis [59]. Multiple measures of increased capacity strain were associated with shorter time to DNR order for ICU patients [60]. Additionally, ICU census is associated with higher rates of readmission or death after discharge, suggesting the ICU occupancy may affect physician decision-making about readiness for discharge [61, 62].

There have been no studies that investigate the relationship between capacity strain and infection prevention processes of care in the ICU. However, the relationship between hand hygiene compliance and daily patient volumes has been studied in the emergency department [63, 64]. When using a validated tool for overcrowding that factors in patient acuity and timeliness of care, higher levels of crowding were associated with reduced hand hygiene compliance [64].

Summary and Study Goals

Overall, the literature strongly suggests that ICU capacity strain may lead to suboptimal quality of care and adverse patient outcomes in the ICU, which may extend to increased risk for HAIs. Previous research related to HAI and strained ICUs have

focused on increased bed occupancy rates, suggesting that unit overcrowding leads to increased rates of hospital infections. Low nurse to patient ratios are also implicated as contributors to HAI rates in the ICU, though the problem of ICU strain extends beyond simply staffing variability. While there are many definitions used to measure ICU capacity strain, we will utilize a method for examining daily ICU strain through extreme variations from the normal unit census. Using patient-level data gives further insight into how capacity strain in the ICU, where workload and patient-care resources vary daily in a unit, may adversely impact individual patient outcomes.

Chapter II: Manuscript

Title: Capacity strain and risk of ICU-onset bloodstream infection

Emily D. Niehaus, Chad Robichaux, Jesse T. Jacob

Introduction

Hospital-onset infections in the intensive care unit (ICU) setting are associated with increased mortality, morbidity, and healthcare costs. [1]. While infection prevention programs have made significant progress in the reduction of healthcare-associated infections (HAIs) by changing healthcare worker behaviors and managing patient-level risk factors, these prevention efforts may be vulnerable at times of high capacity strain. Capacity strain can be defined as a mismatch between medical workload and patient care resources, leading to lapses in basic prevention efforts or undesirable variability in the ability to provide high-quality care [30, 65].

Capacity strain in the ICU, where patients have numerous complex medical needs, influences care delivery processes and contributes to adverse patient outcomes [28, 55-58]. Daily capacity strain, most frequently defined as high daily ICU census, has been associated with increased mortality, reduced receipt of appropriate venous-thromboembolism prophylaxis, shorter time to DNR order, and higher rates of readmission, suggesting that a strained ICU may affect both physician decision-making and healthcare worker behaviors [28, 59-62]. However, the relationship between ICU capacity strain and hospital-onset infection risk is less well established. High ICU bed occupancy rates are associated with increased rates of methicillin-resistant

Staphylococcus aureus infections and *Clostroides difficile* infections in the hospital, but these studies assessed overcrowding over a month-period rather than daily variations in strain [51-54]. Low nurse to patient ratios are associated with increased risk of HAI after adjusting for patient-level risk factors, but these studies do not account for strain on other healthcare workers, and ICU census may service as better predictor of perceived strain [30, 38, 41, 44, 45].

We sought to evaluate the association between high ICU census during the first three days of a patient's ICU stay and subsequent hospital-onset bloodstream infection (BSI). Hospital-onset bloodstream infections (BSI) affect between 4.4-10% of patients admitted to intensive care units (ICU) and are associated with increased risk of death, longer hospital stays, and higher hospital costs, and maybe a better indicator of quality of care than central line-associated bloodstream infections (CLABSI) [3-9].

Methods

Study Design & Setting:

We created a retrospective cohort of all adult patient encounters admitted to 22 ICUs (303 ICU beds) at four Atlanta-area university-affiliated hospitals between January 1, 2014 and December 29, 2018. Patient-level data was obtained from the Emory Healthcare Clinical Data Warehouse (CDW), which houses clinical, administrative, and laboratory data for four facilities. All patient encounters that included an admission to an ICU, according to date and time-stamped bedded location data, were included in the study. Patients were excluded from cohort if they were discharged to the floor, were

transferred between ICUs, or died prior to their fourth consecutive ICU day. Only the first ICU stay with 4 consecutive days was included for analysis.

Patient's age, gender, race, ethnicity, insurance status (private, public, and/or unknown), and admission and discharge dates to ICUs and the hospital were obtained from the CDW. Length of stay for the hospital and the ICU were determined using date and time-stamped bedded location data. The Charlson Comorbidity Index (CCI) and, where available, Sequential Organ Failure Assessment (SOFA) scores during day 1 or 2 of ICU admission, were obtained from the CDW using a previously validated method. Presence of mechanical ventilation and central lines in the first 3 days of ICU stay were determined through CDW documentation.

Daily unit census was determined by bed occupancy every midnight for all units and summarized to give the 90^{th} percentile for the daily census in each individual unit for each year. If an ICU was open for <90 days in a given year because of construction or renovation, the daily census data for this year was combined with the previous year's or following year's data to give a valid assessment of census variability over this time frame. National Healthcare Surveillance Network (NHSN) annual survey data were used to determine ICU type (medical, surgical, combined medical-surgical, medical cardiac, surgical cardiothoracic, or neurosurgical) and bed capacity. If unit census exceeded the maximum occupancy of the unit, the census was corrected to represent 100% occupancy. To assess baseline patient volume in the units included, the units' median bed occupancy was calculated for each year under study. Additionally, the number of admissions to each ICU was summed and divided by the unit bed size to calculate the number of admissions/bed/year for each unit and year.

For each patient encounter in the cohort, daily unit census was matched to date of ICU admission (day 1) and the two following calendar days, to the give the unit census for the first 3 days of patient's ICU stay. A "high strain day" was defined as census being above the 90th percentile for daily census for the unit during the year in question. For each of the first three days of the patient's ICU stay, the number of days that the patient was exposed to capacity strain was counted, so that patients could be exposed to zero, one, two, or three days of high strain.

The primary outcome, ICU-onset BSI, was defined as any positive blood culture with new isolate that was obtained on or after day 4 of ICU stay and before ICU discharge. Organism names, and for *Staphylococcus aureus*, susceptibility to methicillin, as well as blood culture dates were obtained from the CDW. Organisms listed by NHSN as common commensals were considered pathogenic only if present in two or more cultures from the same date. We did not use the presence of symptoms such as fever for commensals, and nor attribute any positive culture to a secondary source. Only the first positive blood culture for a given organism and the first episode of ICU-onset BSI were included as an event. Time from ICU admission to date of ICU-onset BSI was calculated using the admission date as day 1. Time at risk for ICU-onset BSI was determined using ICU length of stay, or days from ICU admission to ICU-onset BSI for patients who experienced an event. We assessed ICU death as a secondary outcome. If patient death occurred on date of last bedded date in ICU, the death was attributed to the ICU and the time to death was calculated from ICU admission.

We used the chi-square or Wilcoxon rank sum tests to compare patients who experienced ICU-onset BSI to those who did not. Multivariate logistic regression was

performed to determine the association between ICU-onset BSI and main exposure of interest: the number of days that encounter experienced high capacity strain in the ICU. Subgroup analyses were performed by hospital location, central line utilization, and mechanical ventilation utilization. All p-values < 0.05 were considered significant. SAS 9.4 (Cary, NC) was used for statistical analysis. The study was approved by the Emory University Institutional Review Board.

Results

Over the five-year study period, there were 67,947 encounters with an admission to an ICU, with 28,531 encounters admitted to an ICU for at least three days, representing a cohort of 24,786 unique patients. The median age of the patient cohort was 63 years, 51% were white, and the median Charlson Comorbidity Index was 4 (Table 1). The median Sequential Organ Failure Assessment (SOFA) score at ICU admission was 5, with high use of central line (57%,) and mechanical ventilation (39%) during the first three days of ICU stay. No SOFA scores were available for patients admitted to Hospital D (6% of overall cohort). ICUs had high variability in baseline patient volume across included units (median: 23.8; range: 11.8 to 42.1 admissions per bed per year).

Among the 24,786 patients with an ICU length of stay > 3 days, 552 had at least one positive blood culture, including 165 contaminated blood cultures and 387 (70%) ICU-onset BSIs, for an incidence of 16 ICU-onset BSIs per 1000 patient encounters. For ICU-onset BSIs, blood cultures grew gram-negative rods in 142 (37%), gram-positive cocci in 127 (33%), fungi in 78 (20%), and were polymicrobial in 19 (5%) (Table 2). Most gram negative BSIs were caused by Enterobacteriaceae (95/142) or Pseudomonads (38/142), while most gram positive BSIs were caused by enterococci (54/127), *S. aureus*

(28/127), or coagulase negative staphylococci (26/127). The most common organism of all ICU-onset BSIs was *Candida albicans* (32/387). The median time from ICU admission to ICU-onset BSI was 9 days, with no differences by organism type.

Patients with ICU-onset BSI were younger, were more likely to be admitted to a surgical ICU, and had higher rates of mechanical ventilation and central line utilization compared to the 28,061 patients without ICU-onset BSI (Table 1). One hospital accounted for 65% of ICU-onset BSIs, despite accounting for only 45% of the patient encounters in the cohort. Overall, ICU death was higher in patients with (20.4%) compared to those without (3.5%) ICU-onset BSI.

More than a third (36%) of the total observed days over the five-year study period had a census above the 90^{th} percentile for the unit, as some units remained at maximum capacity for close to half of the days in the year, though this varied by facility (Figure 1). Only 18% of patient encounters at Hospital A experienced no days of high ICU strain, while approximately 60% of patients at Hospitals B, C, and D had zero days of capacity strain. Encounters with three days of high capacity strain were less likely to be admitted from the Emergency Department and more likely to be admitted to a neurosurgical or surgical ICU than encounters with lower levels of capacity strain. There were no differences in mechanical ventilation, central line utilization, SOFA scores, or CCI in groups with zero, one, two, or three days of high strain.

As the number of days at capacity strain increased from zero to three days, the crude odds ratio (OR) of developing an ICU-onset BSI increased in a stepwise fashion (Table 3). When adjusting for patient level covariates that were also associated with ICU-onset BSI, experiencing one day of high capacity strain was associated with an OR

of 1.38 (95% CI 1.06-1.80) for developing a BSI in the ICU and increased to 1.53 (95% CI 1.11-2.11) for three days of strain. However, after controlling for unit-level covariates, including hospital, unit type, and median bed occupancy of unit, the number of days that the patient experienced high capacity strain was no longer associated with increased risk of ICU-onset BSI (3 vs. 0 days of strain OR=1.00 95% CI=0.71-1.43). Additionally, when adjusting for both patient-level and unit-level covariates, risk of ICU-onset BSI was not associated with experiencing at least one day of strain among the first three days of ICU stay (OR=1.06, 95% CI=0.84-1.35), or with high strain on day of admission (OR=0.99, 95% CI=0.80-1.24).

When stratifying by hospital site, the number of high strain days was not associated with risk of developing a BSI in the ICU for any of the four hospital sites. There was also not a significant association between capacity strain and ICU-onset BSI among the subset of patients who had a central line in place or required mechanical ventilation in the first three days of their ICU stay. Admission from the Emergency Department, CCI ≥3, use of mechanical ventilation, central line placement, time at risk for ICU-onset BSI, and hospital site remained significant predictors of ICU-onset BSI.

Discussion

In this retrospective study of 24,786 patients admitted to an ICU for more than three days, we found that patient-level risk factors, including device utilization, but not the unit-level risk factor of daily high ICU census, was associated with increased risk of ICU-onset BSIs. While much infection prevention research has been devoted to CLABSIs in the ICU, there has been relatively little attention to the inclusive category of

hospital-onset BSIs. With higher number of events and an objective culture-based definition, this broad category is attractive for evaluating infection-based quality of care [14-16]. At 16 infections per 1000 admissions, the incidence of hospital-onset BSIs observed in this cohort was lower than previously described in the ICU setting [5, 6, 8, 16]. However, the high case-fatality rate and substantially longer lengths of stay among patients experiencing ICU-onset BSI in our cohort demonstrates the importance of this HAI measure.

The distribution of organisms causing ICU-onset BSIs in our cohort was similar to isolates found in other studies [16, 66, 67]. However, our study found that 19% of ICU-onset BSIs were caused by yeast, in contrast to 5 – 8% of infections in other ICU reports. Few studies have evaluated patient risk factors for ICU-onset BSI specifically, though risk factors for hospital-onset infections, as a broad category and as disease-specific entities, are well described in the literature [18, 20, 68, 69]. In our cohort, patients who were admitted directly from the Emergency Department were at a decreased risk of ICU-onset BSI, which may be reflective of increased risk among patients who required surgical procedures prior to ICU admission or among patients in the hospital for several days before requiring ICU admission. As expected, illness severity and the use of invasive devices were associated with increased risk of ICU-onset BSI.

Our study did not find an association between daily capacity strain early in the patient's ICU stay and risk of ICU-onset BSI. This finding may indicate that daily variation in ICU census does not impact healthcare delivery, care quality, and patient outcomes in our healthcare system. Previous multicenter studies have described significant heterogeneity in the effect that capacity strain can have on patient outcomes,

which may be reflected in our study findings. Hospital sites included in this study all have comprehensive infection prevention programs, as well as an institutional emphasis on healthcare quality, which may dampen the role that system-level strain plays on infection risk.

Another possibility is that our study did not adequately measure variations in capacity strain. Given the complexity and multidimensionality of ICU patient care, capacity strain in the ICU has been studied from several different perspectives, and there is no agreed-upon definition in the literature [27, 70]. Some metrics used to connect system-level strain to patient outcomes include standardized unit census, admission-adjusted census, and severity-adjusted census [27]. The measure for capacity strain used in this study, while obtainable from administrative records, has significant limitations. Some units in our study cohort, particularly at Hospital A, had a median ICU census that represented 100% occupancy. Therefore, capturing a higher level of strain above the baseline would require the incorporation of a metric for patient acuity or patient transfers rather than simply patient number. This limitation of our exposure variable likely contributed to the lack of association observed in multivariate analysis, when both unit and hospital characteristics were included in the model. In addition to limitations in the exposure definition, our study may not have captured all BSI outcomes that could have been affected by strain, as we did not include BSIs that were discovered after the patient left the ICU.

Measures of baseline strain at the unit-level were also evaluated in this study, including the number of admissions per bed per year and the median bed occupancy of the unit. In multivariate analysis, these unit metrics were not associated with an

increased risk of developing ICU-onset BSI in our cohort, despite previous studies demonstrating that crowded units and high patient turnover were associated with increased infection rates [16, 53].

Additional limitations of this study are a result of the retrospective nature of the data retrieval and analysis. Without available data for signs and symptoms of infection, there may have been misclassification of ICU-onset BSIs, with over-inclusion of contaminated blood culture results. We were also not able to assess whether patients had recent surgeries or if they were transferred from an outside hospital, which may have confounded the relationship under study. Also, changes in leadership, ICU culture, teaching environment, and hospital infection prevention practices could have contributed to variability in daily strain metrics, as well as our primary infection endpoint.

Overall, this study innovatively evaluated the role of daily variations in ICU census on patient's risk for developing a hospital-onset infection. Given the increasing recognition and evidence suggesting that capacity strain impacts ICU quality of care and patient outcomes, it seems plausible that there is also an association with infection, but this requires capturing the appropriate discrete measurements of capacity strain, as well as defining the appropriate outcome. Because infections remain relatively uncommon, it may be easier to demonstrate impact on infection prevention processes of care metrics. This data supports current infection prevention priorities on device utilization, and suggests that measurement of capacity strain warrants further exploration.

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Tables

Table 1: Characteristics of patients in cohort, with and without ICU-onset BSI

Patient Characteristics	Entire cohort (N=24,786)	Non-contaminant ICU-onset BSI (n=387)	No ICU-onset BSI (n=24,399)	p-value
Age	63 (21)	59 (21)	63 (21)	<0.0001
Gender, male	13,400 (54%)	216 (56%)	13,184 (54%)	0.49
Race				
Caucasian or White	12,956 (52%)	194 (55%)	12,762 (55%)	0.95
African American or Black	9,575 (39%)	147 (42%)	9,428 (41%)	
Other	851 (3%)	12 (3%)	839 (4%)	
Unknown / Unreported	1,404 (6%)	37	1,414	
Ethnic group				
Hispanic or Latino	564 (2%)	11 (3%)	553 (3%)	0.33
Non-hispanic or Latino	21,130 (85%)	307 (97%)	20,823 (97%)	
Unknown / Unreported	3,092 (12%)	69	3,023	
Insurance status				
Private insurance only	7,063 (29%)	126 (33%)	6,937 (28%)	0.01
Medicare + other insurer	5,071 (20%)	85 (22%)	4,986 (20%)	
Medicare only	9,126 (37%)	112 (29%)	9,014 (37%)	
Medicaid only	2,072 (8%)	43 (11%)	2,029 (8%)	
Self-pay	1,454 (6%)	21 (5%)	1,433 (6%)	
Admitted from Emergency Department	7,653 (31%)	66 (17%)	7,587 (31%)	<0.0001
Admitted to ICU on same day as hospital admission	17,766 (72%)	255 (66%)	17,511 (72%)	0.01
Charlson Comorbidity Index (CCI)				
< 3	7075 (29%)	48 (12%)	7,027 (29%)	<0.0001
≥ 3	17,711 (71%)	339 (88%)	17,372 (71%)	
SOFA score at time of ICU admission	5 (6)	7 (7)	5 (6)	<0.0001
Mechanical ventilation (day 1-3 of ICU admission)	9,754 (39%)	240 (62%)	9,514 (39%)	<0.0001

Central line (day 1-3 of ICU admission)	14,173 (57%)	321 (83%)	13,852 (57%)	<0.0001
Capacity strain measure				
Number of days at high capacity				
0 days	9,914 (40%)	118 (30%)	9,796 (40%)	0.001
1 day	6,673 (27%)	112 (29%)	6,561 (27%)	
2 days	5,256 (21%)	101 (26%)	5,155 (21%)	
3 days	2,943 (12%)	56 (15%)	2,887 (12%)	
Unit Characteristics				
Hospital				
A	11,034 (45%)	253 (65%)	10,781 (44%)	<0.0001
B	8,121 (33%)	93 (24%)	8,028 (33%)	
C	4,200 (17%)	33 (9%)	4,167 (17%)	
D	1,431 (6%)	8 (2%)	1,423 (6%)	
Unit Type				
Surgical Cardiothoracic	5,296 (21%)	71 (18%)	5,225 (21%)	<0.0001
Medical Cardiac	2,909 (12%)	50 (13%)	2,859 (12%)	
Medical	4,019 (16%)	54 (14%)	3,965 (16%)	
Medical-Surgical	4,273 (17%)	38 (10%)	4,235 (17%)	
Neurosurgical	4,936 (20%)	76 (20%)	4,860 (20%)	
Surgical	3,353 (14%)	98 (25%)	3,255 (13%)	
Number of ICU admissions per unit bed per year	23.8 (9.5)	23.8 (9.5)	23.1 (9.8)	0.25
Median bed occupancy of unit (%)	83 (27)	91 (25)	83 (27)	<0.0001
Outcomes				
Length of stay in ICU, days	6 (5)	18 (17)	6 (5)	<0.0001
Length of stay in hospital, days	12 (11)	25 (38)	11 (10)	<0.0001
Died in ICU	936 (4%)	83 (21%)	853 (4%)	<0.0001

Table 2: Distribution of microorganisms present in non-contaminant ICU-onset bloodstream infections (N=387)

Group	Organism		N
Monomicrobial aerobic gram-positive cocci (N=127)			
Staphylococcus aureus		28	
	Methicillin-sensitive		12
	Methicillin-resistant		16
Coagulase-negative staphylococcus		26	
Streptococcus		18	
	Streptococcus pneumoniae		1
	Streptococcus viridans group		5
	Streptococcus anginosus		4
	Streptococcus agalactiae		1
	Nutritionally-variant streptococcus		1
	Streptococcus species, unspecified		6
Enterococcus		54	
	Enterococcus faecalis		25
	Enterococcus faecium		18
	Enterococcus species, unspecified		11
Other		1	
	Dolosigranulum pigrum		1
Monomicrobial aerobic gram-negative rods (N=142)			
Enterobacteriaceae		95	
	Citrobacter fruendii		4
	Citrobacter koseri		1
	Citrobacter species, unspecified		1
	Escherichia coli		25
	Enterobacter asburiae		1
	Enterobacter cloacae		11
	Enterobacter species, unspecified		
	Klebsiella pneumoniae		22
	Klebsiella oxytoca		3
	Klebsiella aerogenes		7
	Klebsiella species, unspecified		1
	Morganella morganii		1
	Pantoea agglomerans		3
	Pantoea species, unspecified		2
	Proteus mirabilis		1
	Serratia marcescens		12
Pseudomonads		38	
	Psuedomonas aeruginosa		29
	Other pseudomonas species, unspecified		1

	Stenotrophomonas maltophilia		5
	Burkholderia cepacia		2
	Burkholderia gladioli		1
Other		9	
	Acinetobacter braumannii		4
	Aeromonas hydrophila		1
	Haemophilus influenzae		3
	Pasteurella multocida		1
Monomicrobial fungi (N=78)			
Yeast		74	
	Candida albicans		32
	Candida dubliniensis		2
	Candida glabrata		17
	Candida krusei		1
	Candida lusitaniae		4
	Candida parapsilosis		8
	Candida tropicalis		7
	Yeast, unspecified		3
Other		4	
	Cryptococcus species		1
	Cryptococcus neoformans		1
	Fusarium species		1
	Mucor cirinelloides		1
Monomicrobial anaerobes (N=15)			
	Actinomyces odontolyticus		1
	Bacteroides caccae		1
	Bacteroides eggerthii		1
	Bacteroides thetaiotaomicron		1
	Bifidobaterium species		1
	Clostridiodes species		1
	Fusobacterium necrophorum		1
	Fusobcaterium mortiferum		1
	Paenibacillus species		1
	Parivmonas micra		1
	Prevotella buccae		1
	Prevotella melaninogenica		2
	Prevotella oralis		1
	Veillonella species		1
Monomicrobial other organisms (n=9)			
Mycobacteria		1	1
Gram-positive bacilli		4	
	Bacillus species, not *B. anthracis*		2
	Lactobacillus species		1

	Coryneform bacteria, unspecified	1
Gram-negative cocci	1	
	Neisseria elongata	1
Polymicrobial (N=19)		
Polymicrobial, bacterial	12	
	Bacteroides thetaiotaomicron, Enterobacter cloacae	1
	Bacteroides vulgatus, Escherichia coli	1
	Citrobacter freundii, Enterococcus avium, Enterococcus faecalis, Pseudomonas aeruginosa	1
	Enterobacter cloacae, Pseudomonas aeruginosa	1
	Enterococcus faecium, Klebsiella pneumoniae	1
	Citrobacter fruendii, Klebsiella oxytoca	1
	Enterobacter cloacae, Psuedomonas aeruginosa	
	Klebsiella pneumoniae, Proteus mirabilis	1
	Escherichia coli, Klebsiella pneumoniae	2
	Klebsiella pneumoniae, Coagulase-negative staphylococcus	1
	Neisseria species (not N. gonorrhoeae or N. meningitidis), Nutritionally-variant streptococcus	1
	Streptococcus anginosus group, Coagulase-negative staphylococcus	1
Polymicrobial, fungal	3	
	Candida glabrata, Candida albicans	2
	Candida glabrata, Saccharomyces cerevisiae	1
Polymicrobial, mixed	4	
	Candida albicans, Corynebacterium striatum	1
	Candida parapsilosis, *Proteus mirabilis*	1
	C. albicans, Coagulase-negative staphylococcus	1
	Enterococcus faecalis, Yeast with pseudohyphae	1

Table 3: Logistic regression evaluating capacity strain and risk of ICU-onset BSI

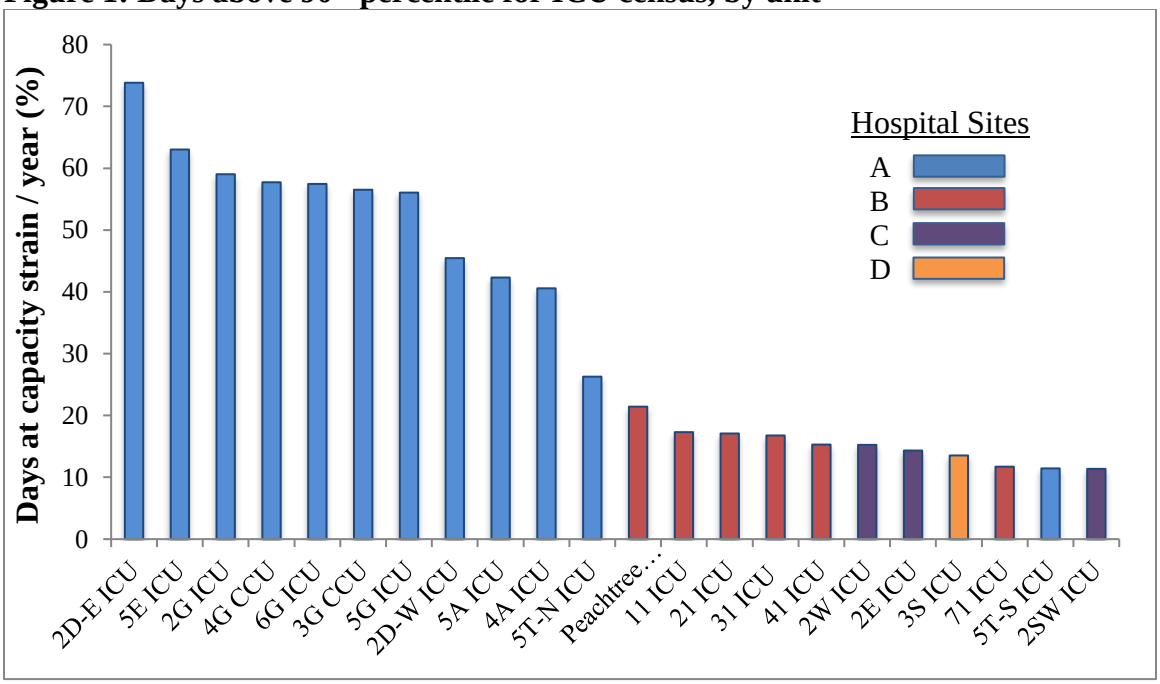
Variable	Odds Ratio (95% CI)		
	Univariate Analysis	**Model 1: Adjusting for patient covariates**	**Model 2: Adjusting for patient and unit covariates**
ICU Capacity Strain			
Number of days at high capacity strain			
0 days	ref	ref	ref
1 day	1.42 (1.09-1.84)	1.38 (1.06-1.80)	1.11 (0.84-1.45)
2 days	1.63 (1.24-2.13)	1.50 (1.14-1.96)	1.03 (0.77-1.38)
3 days	1.61 (1.17-2.22)	1.53 (1.11-2.11)	1.00 (0.71-1.43)
Patient Characteristics			
Admitted from ED	0.46 (0.35-0.60)	0.59 (0.45-0.77)	0.62 (0.47-0.83)
CCI ≥ 3	2.86 (2.11-3.87)	2.83 (2.09-3.85)	2.54 (1.86-3.46)
SOFA score	1.17 (1.14-1.20)	-	-
Mechanical ventilation	2.55 (2.08-3.14)	1.76 (1.41-2.20)	1.98 (1.57-2.48)
Central line	3.70 (2.84-4.83)	2.50 (1.88-3.32)	2.52 (1.89-3.37)
Time at risk for ICU-onset BSI (days)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
Unit Characteristics			
Hospital			
A	ref		ref
B	0.49 (0.39-0.63)		0.66 (0.49-0.91)
C	0.34 (0.23-0.49)		0.45 (0.25-0.82)
D	0.24 (0.12-0.49)		0.39 (0.16-0.95)
Unit Type			
Medical	ref		ref
Surgical Cardiothoracic	1.00 (0.70-1.43)		0.77 (0.52-1.15)
Medical Cardiac	1.28 (0.87-1.89)		1.43 (0.85-2.39)
Medical-Surgical	0.66 (0.43-1.00)		1.43 (0.85-2.39)
Neurosurgical	1.15 (0.81-1.63)		1.05 (0.71-1.54)

Surgical	2.21 (1.58-3.09)	1.37 (0.96-1.96)
Median bed occupancy of unit	1.02 (1.02-1.03)	1.01 (0.99-1.01)

*ED=Emergency Department. CCI= Charlson Comorbidity Index. SOFA= Sequential Organ Failure Assessment

Figures

Figure 1: Days above 90th percentile for ICU census, by unit



Chapter III: Public Health Implications

Clarifying the relationship between systematic strain and hospital-onset infections requires a better understanding of how to best protect and care for patients while they are in the hospital. While we did not observe a significant association between extremes of daily unit census and hospital-onset risk, other measures of capacity strain may demonstrate a relationship. An improved understanding of which metrics are associated with patient safety outcomes may clarify how ICU workflow breaks down at times of stress, and lead to the development of potential safeguards. Developing these measures may be important to reduce HAIs further, especially in busy ICUs with competing priorities and fixed resources. Such measures may need to be more widely implemented to assess the impact on HAIs.

Elucidating the relationship between capacity strain and hospital-onset infections also may have several indirect implications for both HAI outcome research and surveillance efforts. If metrics of capacity strain are found to have a significant effect on risk for hospital-onset infections, these factors likely contribute to the observed intra- and inter-ICU variability in infection risk. From the research perspective, including such time-varying factors in future models may reduce unexplained variance and help identify more effective infection prevention interventions in the critical care setting. For surveillance purposes, inclusion of capacity strain metrics may allow for a more appropriately adjusted model for comparison across ICUs, providing for a more representative picture of healthcare quality.

Finally, while not directly evaluated in this study, capacity strain likely affects not only patients, but also healthcare providers who work under those conditions. Capacity strain in the ICU may contribute to high staff turnover and burnout that is observed in this

setting. Therefore, increased attention to this topic may help create a healthcare environment that is more beneficial to both patients and healthcare workers alike.

Chapter IV: Appendix

Appendix Table 1: Logistic regression evaluating capacity strain and risk of ICU-onset BSI, with exclusion of Hospital D patient encounters because no SOFA scores were available.

Variable	**Odds Ratio (95% CI)**		
	Univariate Analysis	**Model 1: Adjusting for patient covariates**	**Model 2: Adjusting for patient and units covariates**
ICU Capacity Strain			
Number of days at high capacity strain			
0 days	ref	ref	ref
1 day	1.42 (1.09-1.84)	1.39 (1.06-1.83)	1.16 (0.87-1.54)
2 days	1.63 (1.24-2.13)	1.50 (1.14-2.01)	1.09 (0.80-1.49)
3 days	1.61 (1.17-2.22)	1.49 (1.06-2.10)	1.02 (0.70-1.48)
Patient Characteristics			
Admitted from ED	0.46 (0.35-0.60)	0.59 (0.45-0.77)	0.66 (0.49-0.89)
CCI ≥ 3	2.86 (2.11-3.87)	2.53 (1.82-3.52)	2.39 (1.71-3.34)
SOFA score	1.17 (1.14-1.20)	1.10 (1.07-1.13)	1.10 (1.06-1.13)
Mechanical ventilation	2.55 (2.08-3.14)	1.23 (0.95-1.60)	1.37 (1.04-1.80)
Central line	3.70 (2.84-4.83)	2.18 (1.59-3.01)	2.29 (1.65-3.16)
Time at risk for ICU-onset BSI (days)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
Unit Characteristics			
Hospital			
A	ref		ref
B	0.49 (0.39-0.63)		0.67 (0.49-0.92)
C	0.34 (0.23-0.49)		0.56 (0.30-1.03)
Unit Type			
Medical	ref		ref
Surgical Cardiothoracic	1.00 (0.70-1.43)		0.90 (0.59-1.35)
Medical Cardiac	1.28 (0.87-1.89)		1.40 (0.92-2.14)
Medical-Surgical	0.66 (0.43-1.00)		1.61 (0.94-2.76)
Neurosurgical	1.15 (0.81-1.63)		1.36 (0.91-2.05)
Surgical	2.21 (1.58-3.09)		1.36 (0.94-1.98)
Median bed occupancy of unit	1.02 (1.02-1.03)		1.01 (0.99-1.01)

ED=Emergency Department. CCI= Charlson Comorbidity Index. SOFA= Sequential Organ Failure Assessment