OBSERVATIONAL STUDY

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Sociodemographic Factors are Associated with Care Delivery and Outcomes in Pediatric Severe Sepsis

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IMPORTANCE: Sepsis is a leading cause of morbidity and mortality in the United States and disparate outcomes exist between racial/ethnic groups despite improvements in sepsis management. These observed differences are often related to social determinants of health (SDoH). Little is known about the role of SDoH on outcomes in pediatric sepsis.

OBJECTIVE: This study examined the differences in care delivery and outcomes in children with severe sepsis based on race/ethnicity and neighborhood context (as measured by the social vulnerability index).

DESIGN, SETTING, AND PARTICIPANTS: This retrospective, cross-sectional study was completed in a quaternary care children's hospital. Patients 18 years old or younger who were admitted between May 1, 2018, and February 28, 2022, met the improving pediatric sepsis outcomes (IPSO) collaborative definition for severe sepsis. Composite measures of social vulnerability, care delivery, and clinical outcomes were stratified by race/ethnicity.

MAIN OUTCOMES AND MEASURES: The primary outcome of interest was admission to the PICU. Secondary outcomes were sepsis recognition and early goal-directed therapy (EGDT).

RESULTS: A total of 967 children met the criteria for IPSO-defined severe sepsis, of whom 53.4% were White/non-Hispanic. Nearly half of the cohort (48.7%) required PICU admission. There was no difference in illness severity at PICU admission by race (1.01 vs. 1.1, $p = 0.18$). Non-White race/Hispanic ethnicity was independently associated with PICU admission (odds ratio [OR] 1.35 [1.01–1.8], $p = 0.04$). Although social vulnerability was not independently associated with PICU admission (OR 0.95 [0.59–1.53], $p = 0.83$), non-White children were significantly more likely to reside in vulnerable neighborhoods (0.66 vs. 0.38, $p < 0.001$). Non-White race was associated with lower sepsis recognition (87.8% vs. 93.6%, $p = 0.002$) and less EGDT compliance (35.7% vs. 42.8%, $p = 0.024$).

CONCLUSIONS AND RELEVANCE: Non-White race/ethnicity was independently associated with PICU admission. Differences in care delivery were also identified. Prospective studies are needed to further investigate these findings.

DOI: 10.1097/CCE.0000000000001056

Sepsis is a leading cause of morbidity, mortality, and healthcare utilization in the United States (1). Sepsis prevalence ranges from 1% to 26% with 10–20% mortality among hospitalized children (1, 2). The result is an estimated 4–7 billion dollars in annual healthcare expenditures (3, 4). Despite management advances, disparate outcomes related to sociodemographic characteristics persist. Black adults have a higher incidence of sepsis, longer hospital length of stay, higher hospital readmission rates, and higher sepsis-related mortality rates compared with White adults (5–8). Social determinants of health (SDoH) (9) often contribute to disparties in health outcomes. However, few

KEY POINTS

Question: Are there differences in care delivery and outcomes based on race/ethnicity or social determinants of health (as measured by the social vulnerability index) for patients with severe sepsis in a Southeastern United States freestanding children's hospital?

Findings: Non-White Race/Hispanic ethnicity is independently associated with PICU admission in patients with severe sepsis while social vulnerability index was not. Non-White race/Hispanic ethnicity was associated with lower sepsis recognition ($p = 0.002$) and less early goal-directed therapy compliance ($p = 0.024$).

Meaning: Further studies are necessary to explore the underlying causes for these differences in care delivery and outcomes.

studies have focused on pediatric sepsis outcomes and SDoH.

Multidimensional composite measures of the neighborhood context have been used to quantify SDoH and study their association with pediatric diseases and outcomes (10–13). One such measure is the social vulnerability index (SVI) developed by the Centers for Disease Control and Prevention (14). Constructed from 15 variables in the U.S. Census American Community Survey grouped into four themes (socioeconomic status, household composition, and disability, minority status and language, and housing and transportation), the SVI assigns national and state percentile rankings to each Census tract from 0 to 1, with values closer to 1 indicating greater vulnerability.

The goal of this study was to explore differences in care delivery and outcomes based on race/ethnicity and SVI for patients with severe sepsis in a Southeastern United States freestanding children's hospital. The first objective was to evaluate the association of race/ethnicity with the primary outcome of PICU requirement. We hypothesized that non-White race/Hispanic ethnicity and higher SVI scores would be independently associated with PICU admission requirements among pediatric patients with severe sepsis. The second objective was to explore differences in care delivery associated with race/ethnicity as measured by sepsis recognition and early goal-directed therapy (EGDT) compliance. We hypothesized that care delivery would not be associated with race/ethnicity or SVI.

MATERIALS AND METHODS

Setting and Study Design

This was a retrospective cross-sectional study of patients with severe sepsis at a quaternary care children's hospital. This children's hospital has a 24-bed PICU and a separate 26-bed step-down unit. Patients were admitted between May 1, 2018, and February 28, 2022, and met the improving pediatric sepsis outcomes (IPSO) collaborative definition for severe sepsis (15, 16). The cohort was identified using the quality improvement database maintained for IPSO collaborative participation. The institutional review board (IRB) at the University of Alabama at Birmingham reviewed the study protocol and granted an exemption of informed consent (IRB 300009426).

Data Collection

The majority of data elements were already available in the database. For new or missing data elements, manual abstraction from the electronic medical record was performed by three reviewers (E.P., V.S., J.T.). Accuracy was independently confirmed and adjudication was performed as needed among three physicians (J.E., J.L., L.W.). Self-reported patient addresses collected at the time of hospital admission were geocoded in ArcGIS (ESRI Inc., Redlands, CA) and linked to 2018 SVI scores for the state of Alabama obtained from the Centers for Disease Control and Prevention. Individuals with out-of-state residency, missing address data, or postoffice box addresses were excluded from SVI determination.

Definitions and Measures

The definition of a complex chronic condition (CCC) was adapted from Feudtner et al (17) and included any condition reasonably expected to last more than 12 months and require subspecialty care. CCC categories included respiratory, gastrointestinal, cardiovascular, genetic/syndromic, hematologic/immunologic, neurologic/neuromuscular, neoplastic (receiving therapy), prematurity (only subjects ≤ 2 yr old), metabolic, renal, transplantation history, and chronic invasive device/technology dependence.

Sepsis process measures were defined by the IPSO collaborative and were already recorded in the quality improvement database. The key process measures included screening, huddling, order set usage, time to first antibiotic, and time to first fluid bolus (15, 16). No standard screening or huddle process existed during the study period in the PICU. As such, events occurring in those environments were excluded from those process measures. In all other care environments, a nurse-driven sepsis screening and huddling process coupled with timing of vital signs checks was in place throughout the study period. Time to first antibiotic and fluid bolus were determined starting with IPSO-defined functional time zero (**Supplemental Fig. 1**, http://links.lww.com/CCX/B316). Therefore, events where the first antibiotic or bolus was functional time zero were excluded from those process measures. For the purposes of this study, two new process measures were defined a priori including recognition compliance and EGDT compliance. Recognition compliance was defined as presence of a positive sepsis screen, huddle completion, or order set utilization. EGDT compliance was defined as the first antibiotic within 1 hour and/or first fluid bolus within 20 minutes.

Invasive mechanical ventilation and vasopressor days were recorded as exposure calendar days. Subjects requiring invasive ventilation via a tracheostomy at baseline were excluded from the invasive mechanical ventilation metrics. Hospital readmission and emergency department visits only included those occurring at this institution within 12 months of hospital discharge. Sepsis-attributable mortality was already present in the ISPO database and was determined through monthly physician sepsis champion review (J.L.).

Race and ethnicity, either self-reported or provider-assigned at the time of admission to the hospital, were stratified as a dichotomous variable (White and non-Hispanic [White] vs. non-White or Hispanic [non-White]). Health insurance was also reported dichotomously (private vs. nonprivate/self-pay). The 2018 SVI overall and theme scores (socioeconomic status, household composition, and disability, minority status and language, and housing and transportation) for the state of Alabama were analyzed as continuous variables (10).

Statistical Analysis

Descriptive analyses included means with standard deviations (SD), medians with interquartile ranges (IQR), and frequency distributions as appropriate. Comparisons employed the Chi-square, Fisher exact, and Kruskal-Wallis tests. All hypothesis tests were two-tailed with a p value of less than 0.05 used to indicate statistical significance. Adjustments for multiple comparisons (e.g., Bonferroni correction) were not performed. Given the retrospective design, no sample size calculation was performed for the primary outcome. The primary outcome was all-cause PICU admission requirement. Secondary outcomes included sepsis recognition compliance and EGDT compliance. All other outcomes were considered exploratory and hypothesis-generating. A multivariate logistic regression analysis was performed for the primary outcome and included variables with a univariate p value of less than or equal to 0.1 when comparing White and non-White subjects. To assess for possible colinearity between covariates included in the multivariate logistic regression model, each was also individually evaluated in univariate logistic regression. The odds ratios (OR) estimates and significance were compared between the models. All analyses were performed using SPSS, Version 25, (IBM Inc., Armonk, NY).

RESULTS

During the study period, 967 subjects met IPSO-defined severe sepsis criteria which are described in **Table 1**. Approximately half (53.4%) were White. In the non-White cohort, the majority identified as Black, non-Hispanic (76.3%) followed by Hispanic (20.6%), and other race (3.1%). Although mean total CCCs were similar between the two race/ethnicity groups ($p = 0.18$), White patients had more renal (11.8% vs. 5.1%, $p < 0.001$) and neoplastic CCC (14% vs. 8.2%, $p = 0.005$). Non-White patients had disproportionately higher rates of public or self-pay payer sources (82% vs. 51.7%, $p < 0.001$). The median overall SVI score was higher for non-White individuals, indicating higher overall vulnerability (0.66, IQR 0.35–0.86 vs. 0.38, IQR 0.17n0.62, $p < 0.001$). Likewise, the median of all four SVI-themed scores was higher in the non-White group (all $p < 0.001$). Among all subjects, functional time zero most commonly occurred in the emergency department (58.6%) followed by non-PICU inpatient (20.8%), Unknown (13.1%), and PICU locations (7.4%) (**Fig. 1**).

TABLE 1.
Descriptive Statistics for Subjects With Sepsis Stratified by Race (White Versus Non-White)

Variable	White	Non-White	*p*
Subjects, *n* (%)	516 (53.4)	451 (46.6)	
Age (yr)	6 (2–14)	5 (1–13)	0.099
Male sex at birth, *n* (%)	280 (54.3)	249 (55.2)	0.77
Insurance payer source, *n* (%)			
Private	249 (48.3)	81 (18)	< 0.001
Nonprivate/self-pay	267 (51.7)	370 (82)	
Complex chronic condition category, *n* (%)			
Respiratory	146 (28.3)	128 (28.4)	0.98
Gastrointestinal	123 (23.8)	113 (25.1)	0.66
Cardiovascular	78 (15.1)	54 (12)	0.16
Genetic or syndromic	91 (17.6)	59 (13.1)	0.051
Hematologic or immunologic	42 (8.1)	42 (9.3)	0.51
Neurologic or neuromuscular	187 (36.2)	168 (37.3)	0.75
Neoplastic (receiving therapy)	72 (14)	37 (8.2)	0.005
Prematurity[a]	33 (20.4)	48 (28.7)	0.078
Metabolic	23 (4.5)	29 (6.4)	0.18
Renal	61 (11.8)	23 (5.1)	< 0.001
Transplantation history	39 (7.6)	28 (6.2)	0.41
Chronic invasive device/technology dependence	247 (47.9)	199 (44.1)	0.24
Mean total complex chronic conditions (SD)	2 (1.8)	1.9 (1.7)	0.18
Median social vulnerability index (interquartile range)	0.38 (0.17–0.61)	0.66 (0.35–0.86)	< 0.001
Theme 1—socioeconomic status	0.37 (0.17–0.62)	0.57 (0.29–0.83)	< 0.001
Theme 2—household and disability	0.44 (0.21–0.71)	0.58 (0.31–0.84)	< 0.001
Theme 3—minority status and language	0.37 (0.18-0.64)	0.72 (0.51–0.89)	< 0.001
Theme 4—housing type and transportation	0.47 (0.19–0.67)	0.56 (0.29–0.81)	< 0.001

[a]Including only those ≤ 2 yr old at the time of sepsis event.

Primary Outcome—PICU Admission Requirement

In univariate analysis, non-White group was associated with greater odds of PICU admission requirement (OR 1.36; 95% CI, 1.05–1.75; $p = 0.018$). Pediatric Index of Mortality-3 scores at the time of PICU admission were similar when comparing White versus Non-White cohorts (1.01 vs. 1.1, $p = 0.117$). A multivariate logistic regression model was developed with PICU requirement as the primary outcome and race/ethnicity, SVI, renal CCC, neoplastic CCC, and health insurance type as covariates. Non-White race/ethnicity (OR 1.35; 95% CI, 1.01–1.80; $p = 0.041$) and neoplastic CCC (OR 0.55; 95% CI, 0.36–0.84; $p = 0.006$) were both independently associated with PICU admission requirement. Individual univariate logistic regression models for each covariate did not demonstrate evidence of significant colinearity (**Supplemental Table 1**, http://links.lww.com/CCX/B316).

Secondary Outcomes—Care Delivery Measures

Sepsis care delivery process measures stratified by race/ethnicity are shown in **Table 2**. The non-White group was associated with longer median time to first fluid bolus (absolute difference 6 min, $p = 0.012$). Similarly, the non-White race/ethnicity was associated with

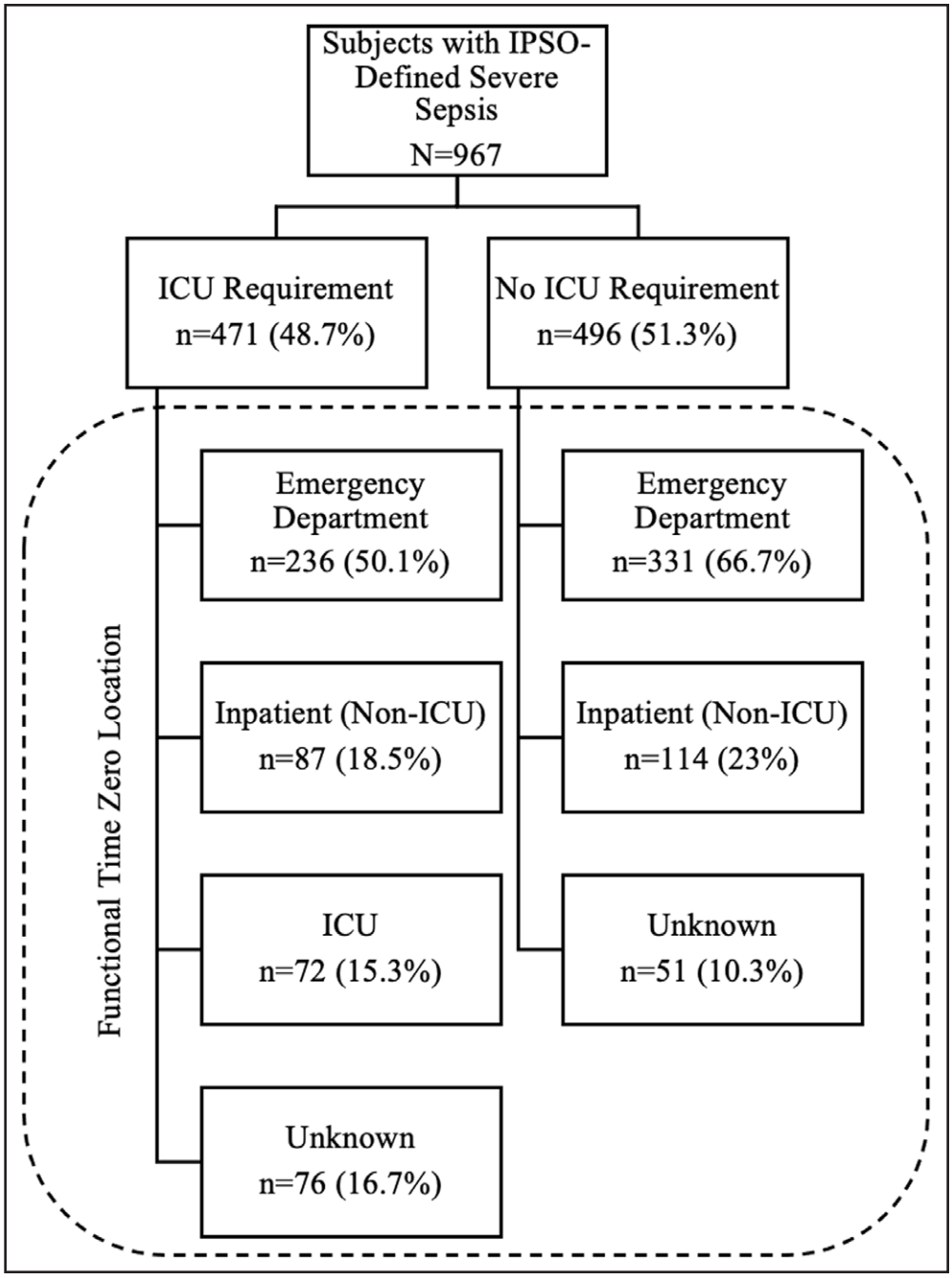

Figure 1. Consort diagram showing primary outcome and location of sepsis onset (functional time zero). IPSO = Improving Pediatric Sepsis Outcomes.

lower sepsis recognition (87.8% vs. 93.6%, $p = 0.002$), EGDT compliance (35.7% vs. 42.8%, $p = 0.024$), and total compliance (31.7% vs. 40.1%, $p = 0.007$).

Exploratory Clinical Outcome Measures

Additional exploratory clinical outcome measures are shown in **Table 3**. The non-White cohort was associated with both longer PICU and hospital length of stay (both $p = 0.044$). Non-White individuals demonstrated greater odds of any vasopressor requirement (OR 1.52; 95% CI, 1.04–2.24; $p = 0.031$) but similar median days on vasopressor support ($p = 0.58$). Odds of invasive mechanical ventilation requirement were greater in the non-White group (OR 1.96; 95% CI, 1.43–2.69; $p < 0.001$), whereas median ventilator days were not statistically different ($p = 0.89$). Furthermore, renal replacement therapy requirement was also associated with non-White group (OR 2.49; 95% CI, 1.01–6.17; $p = 0.041$). No discharge outcomes analyzed were associated with race/ethnicity. However, observed 30-day all-cause mortality was higher among non-White individuals (OR 2.28; 95% CI, 1.18–4.41; $p = 0.012$).

DISCUSSION

We conducted a cross-sectional study with data from a quaternary children's hospital in the Southeastern United States to evaluate the role of race/ethnicity and neighborhood context in health disparities among children with severe sepsis. Non-White descent ($p = 0.041$) and neoplastic CCC ($p = 0.006$) were both independently associated with PICU admission, but not neighborhood vulnerability as measured by the SVI. There were statistically significant differences in care delivery—sepsis recognition, EGDT, and total compliance. However, observed differences were small and of questionable clinical significance.

TABLE 2.
Sepsis Recognition and Early Goal-Directed Therapy Metrics Stratified by Race (White Versus Non-White)

Process Metric	White	Non-White	*p*
Screen performed (%)[a]	370 (94.9)	465 (97.1)	0.095
Screen sensitivity for severe sepsis[b]	280 (60.2)	232 (62.7)	0.46
Huddle performed (%)[c]	288 (61.3)	247 (64.8)	0.29
Sepsis order set used (%)	291 (56.4)	252 (55.9)	0.87
Median minutes to first antibiotic (IQR)[d]	40 (21–80)	49 (25–88)	0.057
Median minutes to first fluid bolus (IQR)[e]	20 (0–36.3)	26 (0–46)	0.012
Recognition compliant[f]	483 (93.6)	396 (87.8)	0.002
EGDT compliant[g]	221 (42.8)	161 (35.7)	0.024
Recognition and EGDT-compliant	207 (40.1)	143 (31.7)	0.007

EGDT = early goal-directed therapy, IQR = interquartile range.
[a]Exclude *n* = 98 no screening process (ICUs).
[b]Including only those with a screen performed.
[c]Exclude *n* = 116 no screening process (ICUs) or no screen performed.
[d]Exclude *n* = 162 where the first antibiotic dose was functional time zero.
[e]Exclude *n* = 1202 where functional time zero was fluid bolus or no fluid bolus given.
[f]Defined as positive screen OR huddle performed OR order set used.
[g]Defined as first antibiotic < 1 hr AND/OR first fluid bolus < 20 min.

In exploratory analysis, non-White race/ethnicity was associated with worse outcomes such as vasopressor exposure, invasive ventilation requirement, and all-cause mortality despite similar illness severity scores at PICU admission. These findings should be considered hypothesis-generating.

Although data are mixed, there are several studies that have linked neighborhood disadvantage to adverse child health outcomes, including increased PICU admission, but studies in pediatric sepsis are limited (12, 18–20). We used the SVI to explore the association between neighborhood social vulnerability and ICU admission for pediatric sepsis. Although neighborhood vulnerability was not independently associated with PICU admission, non-White individuals were significantly more likely to reside in vulnerable neighborhoods than White counterparts ($p < 0.001$), and race/ethnicity was associated with PICU admission. It is possible that our study was underpowered to detect associations between neighborhood vulnerability and PICU admission. Another explanation may concern measurement. The SVI provides relative rankings of census tracts (neighborhoods) in the entire state of Alabama, whereas our hospital's catchment area is mostly limited to a seven-county area in the north-central part of the state, which may have resulted in a different SVI variability within our sample. These findings exemplify the ongoing challenge in area-level measurements and the need to compare the relative precision of different metrics (21, 22). Additionally, Alabama is a predominantly rural state, and a measure of rurality may have been a useful measure in our population (23).

Sepsis can be challenging to recognize in children. Common vital sign changes such as fever and tachycardia are relatively nonspecific. Other objective signs, such as hypotension and lactic acidosis, are often late findings. Standardized sepsis processes can improve care and outcomes by decreasing variability of practice among providers (24–27). However, we found that non-White race/Hispanic ethnicity was associated with a longer time to fluid bolus ($p = 0.012$) as well as lower sepsis recognition ($p = 0.002$), EGDT ($p = 0.024$), and total compliance ($p = 0.007$). Although the observed differences were of questionable clinical significance, their existence should not be ignored. There was nearly a 10% difference in the frequency of the combined measure of recognition compliance and EGDT between the two cohorts. There are various possible explanations for these differences in care delivery. First, it can be challenging to detect common clinical

TABLE 3.
Clinical Outcomes Stratified by Race (White Versus Non-White)

Clinical Outcomes	White	Non-White	*p*
Length of stay measures			
ICU admission, *n* (%)	235 (45.2)	238 (52.8)	0.02
Median ICU length of stay, d (IQR)[a]	2 (1–5)	3 (1–8)	0.044
Median hospital length of stay, d (IQR)	5 (3–11)	5 (3–14)	0.044
Intervention exposure measures			
Any vasopressor required (%)	53 (10.3)	67 (14.9)	0.031
Median vasopressor days (IQR)	2 (1–3)	2 (1–3)	0.58
Invasive mechanical ventilation required (%)[b]	83 (16.8)	122 (28.4)	< 0.001
Median invasive mechanical ventilation days (IQR)[b,c]	4 (2–9)	5 (2–8.2)	0.83
Extracorporeal membrane oxygenation required (%)	6 (1.2)	12 (2.7)	0.086
New renal replacement therapy required (%)[d]	7 (1.4)	15 (3.3)	0.041
Discharge Outcome Measures			
Any new invasive device at discharge (%)[e]	61 (12.2)	54 (12.7)	0.79
Higher respiratory support at discharge (%)[f]	45 (9.1)	35 (8)	0.56
New tracheostomy at discharge (%)[f]	24 (4.8)	21 (4.8)	0.98
Hospital readmission ≤ 12 mo (%)[e]	221 (44)	193 (45.5)	0.65
Repeat emergency department visit ≤ 12 mo (%)[e]	246 (49)	229 (54)	0.13
Total emergency department visits ≤ 12 mo (%)[g]	2 (1–4)	2 (1–4)	0.22
Mortality measures			
30 d All-cause mortality (%)	14 (2.7)	27 (6)	0.012
30 d Sepsis-attributable mortality (%)	3 (0.6)	8 (1.8)	0.081

IQR = interquartile range.
[a]Including only those admitted to the ICU.
[b]Excluding *n* = 143 requiring home invasive mechanical ventilation.
[c]Including only those requiring invasive mechanical ventilation.
[d]Excluding *n* = 18 with chronic dialysis requirement.
[e]Excluding *n* = 141 mortalities.
[f]Excluding *n* = 132 on home ventilation via trach at baseline.
[g]Including only those with repeat emergency department visits.

signs of sepsis, such as delayed capillary refill and hypoxemia, in patients with darker skin tones. Polfer et al (28) found that Black patients with limb ischemia were significantly less commonly identified compared with White patients (23.3% vs. 92.9%). Conventional pulse oximetry is also less sensitive to hypoxemia in Black individuals (29–32). Neoplastic CCC was more common in the White cohort. This may have triggered earlier recognition and treatment in this high-risk population. Provider implicit bias may also play a role in the observed racial differences in sepsis recognition. Some providers indeed demonstrate an implicit preference for White patients over Black patients in various clinical settings (33, 34). Patients may be more susceptible to implicit bias when clinical judgement primarily drives decision-making.

This study has several limitations. The single-center setting prevented us from generalizing the results to other geographic areas or institutions. Second, the study design introduces documentation bias and prevents us from exploring other important variables at the patient level, such parental income or educational attainment. Neighborhood vulnerability is not perfectly correlated with individual socioeconomic status, especially for racial/ethnic minorities (35). Additionally, applying a statewide ranking of neighborhood vulnerability to a

localized sample with a different racial/ethnic distribution may have skewed or masked otherwise important associations. Third, it is common to use race descriptors in clinical medicine and these are often provider-assigned instead of self-reported. Subjectively assigned race tends to be much less accurate (36). Although the policy at our institution is to obtain self-reported race on intake, we acknowledge that this cannot be verified. Additionally, although we did not explore primary language in this study, limited English proficiency has been associated with disparate access to care, healthcare utilization, and worse outcomes (37–39). Finally, there may be unmeasured confounders that influenced the observed differences in care delivery and subsequent outcomes.

This study has important implications for research and clinical practice. Race/ethnicity remained independently associated with PICU admission for pediatric sepsis. Given that race is a social rather than biological construct (40), future studies should explore these disparities with a multilevel approach incorporating both individual and community factors. These data can be particularly useful to inform targeted interventions for high-risk populations. Finally, exploratory analysis demonstrated significantly increased odds of mortality among non-White patients. This finding merits close evaluation in appropriately powered, ideally multicenter, studies.

CONCLUSIONS

In individuals with severe sepsis at a Southeastern quaternary children's hospital, non-White descent was independently associated with all-cause PICU admission. Differences in care delivery were likewise identified. These findings along with exploratory analyses suggestive of worse outcomes, particularly all-cause mortality, mandate appropriately powered, prospective studies to further explore these racial/ethnic disparities.

ACKNOWLEDGMENTS

Special thanks to Dr. Gabriela Oates for her review of this article and Dr. Inmaculada Aban for her aid in statistical analysis.

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Dr. Webb designed the study, supervised data collection, analyzed the data, drafted the initial article, and reviewed and revised the article. Dr. Evans supervised data collection and reviewed and revised the article. Ms. Pettibone, Ms. Smith, Mr. Tofil, Ms. Hicks, and Ms. Green collected the data and reviewed and revised the article. Ms. Nassel conducted geospatial analysis and reviewed and revised the article. Dr. Loberger designed the study, supervised data collection, analyzed the data, drafted the initial article, critically reviewed the article for important intellectual content, and was the final editor of the article. All authors approved the final article as submitted and agreed to be accountable for all aspects of the work.

The authors have disclosed that they do not have any potential conflicts of interest.

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