

The Relationship Between Neighborhood Deprivation and Mortality in a Sepsis Cohort in England

A Retrospective Observational Study

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BACKGROUND: Worse health outcomes have been described for patients with sepsis from more deprived neighborhoods, but it is unclear if this disparity gap has narrowed. Moreover, the mechanisms by which neighborhood disadvantage influences sepsis outcomes are not understood fully.

RESEARCH QUESTION: What is the trajectory of mortality among patients with sepsis in England across varying levels of neighborhood deprivation, and to what extent do patterns of ICU admission and treatment explain observed differences?

STUDY DESIGN AND METHODS: This retrospective observational study using multivariable logistic regression included 519,789 patients older than 16 years admitted to the ICU with sepsis between April 1, 2009, and December 31, 2023, from 304 ICUs of 207 acute hospitals in England. The primary outcome was hospital mortality. The secondary outcomes were direct ICU admission from the emergency department; use of mechanical ventilation, renal replacement therapy, and vasopressor therapy; and decisions to limit life-sustaining therapy.

RESULTS: Mortality improved across all groups of neighborhood deprivation from the

RESULTS: Mortality improved across all groups of neighborhood deprivation from the baseline period from 2009 through 2011, and was 4.5% lower from 2022 through 2023 in the most deprived and 4.4% lower in the least deprived quartile, with no significant narrowing of the disparity gap over time (P=.833). Direct ICU admission from the emergency department was similar for patients across groups of neighborhood deprivation at baseline and increased similarly over time with no significant between-group difference. The gap in mechanical ventilation, renal placement therapy, and vasopressor use narrowed over time. Mortality trends were driven primarily by within-hospital improvements in care, and only a minor component was attributable to shift of patients from lower-quality to higher-quality hospitals.

INTERPRETATION: Although sepsis mortality has improved across England, a persistent disparity associated with neighborhood deprivation exists. Further investigation is required to evaluate other potential contributory factors to help understand better how living in deprived areas contributes to the mortality gap.

CHEST Critical Care 2025; 3(3):100165

KEY WORDS: mortality; neighborhood deprivation; sepsis

ABBREVIATIONS: DWLST = decision to limit (withdraw or withhold) life-sustaining therapy; ICNARC = Intensive Care National Audit and Research Centre; IMD = Index of Multiple Deprivation; IQR = interquartile range; MV = mechanical ventilation; NHS = National Health Service; RRT = renal replacement therapy

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DOI: https://doi.org/10.1016/j.chstcc.2025.100165

Take-Home Points

Study Question: What is the trajectory of mortality improvements in patients with sepsis in England across different levels of neighborhood deprivation, and to what extent do the patterns of ICU admission and treatments contribute to these differences? Results: Mortality resulting from sepsis has declined over time. However, the gap between patients from the most and least deprived neighborhoods has persisted. Our empirical approach suggests that overall improvements in sepsis care are responsible for this trend, rather than patients moving to higherperforming hospitals. Patients from more deprived neighborhoods received equitable access to critical care and received similar interventions in the ICU. Interpretation: Our findings suggest that the primary driver of health disparities may be the detrimental health effects of living in disadvantaged neighborhoods.

The World Health Organization has recognized sepsis as a global health concern, accounting for 1 in 5 of all deaths worldwide. ^{1,2} In the United Kingdom alone, deaths resulting from sepsis are estimated to exceed deaths resulting from breast, bowel, and prostate cancer combined. ³ Current efforts to improve sepsis outcomes in the National Health Service (NHS) have focused on early identification and protocolizing care. ⁴ Yet, several studies suggest that large variations remain across England in how these improvements have been operationalized, potentially resulting in disparities in access, treatment, and outcomes. ⁵⁻⁷

Large-scale studies on sepsis disparities often highlight an array of patient-level factors contributing to poorer outcomes in socioeconomically deprived populations. These factors include a higher burden of comorbidities, insufficient insurance coverage, and the characteristics of hospitals located in more deprived neighborhoods.8 However, the impact of broader contextual determinants—linked to structural and systematic inequalities such as neighborhood disadvantage—remains poorly understood, particularly for acute conditions managed within hospital settings, rather than in the community.^{9,10} Neighborhood disadvantage itself is a multifaceted concept that incorporates indicators like educational attainment, employment opportunities, housing quality, and poverty.¹¹ Residing in disadvantaged neighborhoods has been associated with reduced life

expectancy, higher hospital readmission, increased mortality, and higher rates of Alzheimer disease neuropathologic characteristics. 12-14 Moreover, much of our current understanding of sepsis-related health disparities originates from studies in the United States, where the effects of neighborhood deprivation often are confounded by insurance status and reimbursement incentives that can lead to limited access to care and lower-quality services. Exploring how neighborhood disparities in sepsis operate in the UK NHS, where patients receive free care from the point of use, would inform US policymakers seeking to reduce health inequity by isolating the effect of neighborhood deprivation distinct from insurance coverage or ability to pay.

We examine a national cohort of patients in the NHS admitted to the ICU to understand whether neighborhood disparities for sepsis outcomes in England improve during the care standardization period and to what extent any improvements in disparities are driven by better care within hospitals or by shifting patients with higher deprivation from lower-quality to higher-quality hospitals. Our inquiry is based on 3 specific hypotheses:

- Mortality trends hypothesis: We hypothesized that hospital mortality among patients with sepsis has declined over time across all neighborhoods, with a disproportionately larger reduction among patients from more deprived areas, thereby narrowing the mortality gap.
- 2. ICU admission and intervention gypothesis: We proposed that significant disparities in ICU admission patterns and the delivery of ICU interventions exist, with patients from more disadvantaged neighborhoods receiving different care compared with those from less deprived areas.
- 3. Mechanism of improvement hypothesis: We hypothesized that the overall improvement in sepsis outcomes is driven primarily by better quality of care within ICUs over time, rather than by the transfer of patients from more deprived hospitals to higher-quality hospitals. Therefore, we explored the following 3 questions: (1) What are the trends in hospital mortality for patients across neighborhoods of different deprivation, and has this gap narrowed over time? (2) Do disparities exist in patterns of ICU admission and interventions in the ICU? and (3) Are improvements driven by better care within ICUs over time or by shifts of patients who are more socioeconomically deprived to higher-quality hospitals?

Study Design and Methods

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (London School of Economics approval number 265486).¹⁵ Institutional review board exemption was obtained from the London School of Economics. Approval for use of patient data in the Case Mix Programme was obtained under section 251 of the National Health Service Act of 2006.

Data

We used data from the Intensive Care National Audit and Research Centre (ICNARC) Case-Mix Programme Database, which records all adult admissions to general ICUs in the United Kingdom. Our data set included all adult patients with sepsis admitted to ICUs in England from April 1, 2009, through December 31, 2023. Case-Mix Programme Database validation details have been published previously. ¹⁶⁻¹⁹

Patient Cohort

We identified patients with sepsis using the consensus definition for sepsis (the Third International Consensus Definitions for Sepsis and Septic Shock). We considered the index critical care admission for sepsis to be admission for an infection with a Sequential Organ Failure Assessment score of ≥ 2 and excluded patients younger than 16 years and patients with an ICU stay of < 16 h.

Study Variables

We used acute hospital mortality as the main outcome. The patterns of care we explored were timely access, measured as direct transfer to the ICU from the emergency department without any days in the ward, and in the ICU, namely, mechanical ventilation (MV), renal replacement therapy (RRT), and vasopressors, and a decision to limit (withdraw or withhold) life-sustaining therapy (DWLST). Direct ICU access may be related to increased awareness of sepsis and increased availability of ICU resources. Espsis causes organ dysfunction frequently requiring MV, RRT, and vasopressors. The receipt of these therapies therefore is a good indicator of the patterns of care provided.

Our main exposure variable was neighborhood deprivation, measured as the patient's Index of Multiple Deprivation (IMD), which is a composite measure of a neighborhood's disadvantage including income, living environment, education, and crime levels (e-Table 1).²² Each IMD represents a small geographic area of approximately 1,500 residents and ranges from 1 (most

deprived) to 32,844 (least deprived). This allows us to categorize neighborhood deprivation into quartiles, with the lowest quartile (quartile I) representing the most deprived neighborhoods and quartile IV representing the least deprived neighborhoods.

The analysis controlled for several variables: patient age, sex (male or female based on Case Mix Programme reporting), comorbidities (coded individually as severe dysfunction of the 7 organ systems), and functional status (determined by the degree of assistance in daily living). Race and ethnicity were considered as a single construct reported as White, Asian, Black, and other (multiracial [included mixed: White and Black Caribbean, mixed: White and Black African, mixed: White and Black Asian, and mixed: any other] and unknown [race not stated]). We include race and ethnicity because the neighborhood environment is 1 social determinant that is racially patterned, with racial and ethnic minority populations more likely to reside in disadvantaged neighborhoods.^{23,24} Therefore, we controlled for race and ethnicity to allow for a clearer assessment of how much neighborhood conditions, independent of individual racial or ethnic background, contribute to the outcomes of interest. We measured the severity of acute illness by the ICNARC 2023 model.²⁵ The ICNARC 2023 model uses physiologic measurements in the first 24 h of ICU admission as well as comorbidities, reason for ICU admission, and type of admission (medical or surgical) to estimate the probability of acute hospital death.²⁵ We included the distance from the patient's residence to the nearest hospital. The included ICUlevel and hospital-level characteristics were number of ICU beds and hospital type (nonuniversity, university, and university affiliated). We included a measure of racial and ethnic minority population-serving and high-deprivation-serving ICUs to control for ICU characteristics previously associated with poor sepsis outcomes.^{26,27} We measured ICU diversity as the proportion of non-White patients in the ICU by year and ICU deprivation as the proportion of patients in the ICU from quartile I by year.

Statistical Analysis

To better understand changes in the patient cohort across time, we computed baseline characteristics and unadjusted outcomes. Next, we used multivariable regression models to assess the patient-level primary outcomes of mortality, access to care, and processes of care. The model covariates included all patient variables, distance to nearest hospital as a continuous

measure of patient rurality, ICU bed number, hospital academic affiliation, ICU diversity, and ICU deprivation. We treated year as a categorical variable, using 2009 through 2011 as the reference period and grouping subsequent years into 2-year intervals. Additionally, we modelled the interaction between neighborhood deprivation and year category to assess how the outcome evolved over time. More details are provided in e-Appendix 1. We clustered SEs at the ICU level to account for the similarity of treatment within the same ICU. We then examined patterns of ICU admissions and interventions through annual trends in direct ICU access from the emergency department and the receipt of MV, RRT, and vasopressors; DWLST; and use of long-term care after ICU care.

Between-Hospital vs Within-Hospital Effects: One of the issues that we explored is whether the improvement in mortality over time reflects improvements in practice generally or differences in hospital quality. To determine whether mortality trends between patients facing different levels of neighborhood deprivation were driven by within-hospital effects (reductions in differential care within the same institution) vs between-hospital effects (patient with higher neighborhood deprivation moving to higher-quality hospitals), we ran a logistic regression model with added hospital fixed effects. The model with hospital fixed effect gives us the within-hospital effect on mortality. The model without hospital fixed effects gives us the total effect. The difference between these models is the between-hospital effect.

Because we observed the same hospital over time, this longitudinal data could be exploited to account for differences in quality between hospitals using hospital-specific fixed effects. Model 2 estimated the relationship between variation in neighborhood deprivation and mortality within hospitals. This approach estimated the relationship between neighborhood disparity and mortality, purged of any between-hospital difference in quality.

Subgroup Analysis: We considered the possibility that the patients who are more socioeconomically deprived and high risk might experience less improvement in mortality over time, resulting in widening disparities for this subgroup. To explore the potential for differential improvements in mortality, we undertook a subgroup analysis of high-risk patients. We considered high-risk patients as those patients older than 65 years or with a > 20% predicted risk of death at ICU admission.

Sensitivity Analysis: A key limitation of using in-hospital mortality, rather than a time-restricted outcome, is that differences in discharge practices—such as the use of hospice care—across patient groups might explain the observed variations in in-hospital mortality.³² To address this, we conducted a sensitivity analysis using a composite outcome of death and discharge to hospice. We undertook a sensitivity analysis to isolate hospital effects from neighborhood effects by exploring the consistency of the primary findings across different types of institutional characteristics. We considered academic affiliation, the proportion of patients from racial and ethnic minority groups, and the proportion of patients treated from the most deprived quartile as center characteristics. Academic affiliation has been associated with better outcomes for patients with higher disparity.³³ Racial and ethnic minority population-serving institutions and institutions serving higher proportion of patients who socioeconomically deprived were shown previously to operate with fewer resources relative to demand, to have less quality improvement infrastructure, and to be more likely to have emergency department overcrowding and lower ratios of nurses to patients. 26,34,35 Therefore, hospitals that treat higher concentrations of patients from racial and ethnic minority groups or who are socioeconomically deprived have tended to show less improvement in mortality.36

Results

A total of 519,789 patients admitted to the ICU met the Third International Consensus Definitions for Sepsis and Septic Shock criteria (excluding readmissions and transfers) (e-Fig 1). Patients in quartile I (most deprived) were younger on average (59.3 years) as compared with those in quartile IV (least deprived; 66.1 years; P < .001) (Table 1, e-Table 2). Compared with patients in quartile IV, patients in quartile I were less likely to be categorized

as White (82.8% vs 90.3%; P < .001) and were marginally sicker, having a higher ICNARC predicted risk of death (26.9 vs 29.9; P < .001) at admission. Patients in quartile I were more likely to be treated in university hospitals compared with patients in quartile IV (39.9% vs 32.5%; P < .001) and patients in quartile I were more likely to be treated in ICUs with a higher percentage of patients from racial and ethnic minority groups in the ICU (mean, 14.2% vs 12.3%; P < .001.

 TABLE 1] Patient and Hospital Characteristics From 2009 Through 2023

	Quantiles of Neighborhood Deprivation							
Variable	Quartile I	Quartile II	Quartile III	Quartile IV	Total	P Value		
No.	128,671	128,828	130,706	131,583	519,788	NA		
Age, y	59.3 (0.05)	61.8 (0.05)	64.1 (0.05)	66.1 (0.05)	62.9 (0.02)	< .001		
Male sex	71,191 (55.3%)	71,581 (55.6%)	73,697 (56.4%)	74,911 (56.9%)	291,380 (56.1%)	< .001		
Race or Ethnicity						< .001		
White	106,484 (82.8%)	105,570 (81.9%)	114,360 (87.5%)	118,884 (90.3%)	445,298 (85.7%)			
Asian	8,567 (6.7%)	8,408 (6.5%)	5,480 (4.2%)	3,763 (2.9%)	26,218 (5.0%)			
Black	5,319 (4.1%)	5,423 (4.2%)	2,536 (1.9%)	1,042 (0.8%)	14,320 (2.8%)			
Mixed/other ^{a37}	8,301 (6.5%)	9,427 (7.3%)	8,330 (6.4%)	7,894 (6.0%)	33,952 (6.5%)			
Level of dependency in daily activities						< .001		
No assistance	90,717 (70.9%)	91,689 (71.6%)	93,934 (72.2%)	97,178 (74.2%)	373,518 (72.2%)			
Some assistance	35,085 (27.4%)	34,214 (26.7%)	33,965 (26.1%)	31,729 (24.2%)	134,993 (26.1%)			
Total assistance	2,151 (1.7%)	2,238 (1.7%)	2,143 (1.6%)	2,092 (1.6%)	8,624 (1.7%)			
ICNARC risk model	26.9 (0.07)	27.8 (0.07)	29.0 (0.07)	29.9 (0.08)	28.4 (0.04)	< .001		
Miles to nearest hospital	4.5 (0.01)	5.9 (0.02)	7.1 (0.02)	6.9 (0.01)	6.1 (0.01)	< .001		
Comorbidities								
Severe cardiovascular disease	2,035 (1.6%)	1,836 (1.4%)	1,760 (1.4%)	1,631 (1.2%)	7,262 (1.4%)	< .001		
Severe respiratory disease	5,869 (4.6%)	4,567 (3.6%)	3,984 (3.1%)	3,228 (2.5%)	17,648 (3.4%)	< .001		
End-stage kidney disease	2,061 (1.6%)	1,906 (1.5%)	1,757 (1.4%)	1,550 (1.2%)	7,274 (1.4%)	< .001		
Severe liver disease	3,325 (2.6%)	2,798 (2.2%)	2,475 (1.9%)	2,168 (1.7%)	10,766 (2.1%)	< .001		
Metastatic disease	2,302 (1.8%)	2,884 (2.2%)	3,272 (2.5%)	3,850 (2.9%)	12,308 (2.4%)	< .001		
Hematologic malignancy	3,322 (2.6%)	3,922 (3.1%)	5,014 (3.9%)	5,916 (4.5%)	18,174 (3.5%)	< .001		
Immunocompromised	7,634 (6.0%)	8,874 (6.9%)	10,289 (7.9%)	11,735 (9.0%)	38,532 (7.4%)	< .001		
Hospital characteristics								
Academic affiliation						< .001		
Nonuniversity	53,942 (41.9%)	60,800 (47.2%)	67,873 (51.9%)	69,227 (52.6%)	251,843 (48.5%)			
University	50,491 (39.2%)	45,858 (35.6%)	39,968 (30.6%)	42,713 (32.5%)	179,030 (34.4%)			
University affiliated	24,238 (18.8%)	22,170 (17.2%)	22,865 (17.5%)	19,643 (14.9%)	88,916 (17.1%)			
ICU beds	17.3 (0.03)	16.5 (0.03)	15.6 (0.03)	15.3 (0.02)	16.2 (0.01)	< .001		
Hospital proportion non-White	0.142 (0.00)	0.164 (0.00)	0.135 (0.00)	0.123 (0.00)	0.141 (0.00)	< .001		
Hospital proportion most deprived	0.363 (0.00)	0.261 (0.00)	0.216 (0.00)	0.190 (0.000)	0.258 (0.000)	< .001		

(Continued)

TABLE 1 | (Continued)

			Quantiles of Neighborhood Deprivation	od Deprivation		
Variable	Quartile I	Quartile II	Quartile III	Quartile IV	Total	P Value
Treatment						
Mechanical ventilation	64,240 (49.9%)	63,287 (49.1%)	63,093 (48.3%)	63,222 (48.0%)	253,842 (48.8%)	< .001
Vasopressors	32,081 (24.9%)	35,321 (27.4%)	36,407 (27.9%)	37,361 (28.4%)	141,170 (27.2%)	< .001
RRT	19,275 (15.0%)	20,151 (15.6%)	19,969 (15.3%)	20,062 (15.2%)	79,457 (15.3%)	< .001
Outcomes						
ICU mortality	29,931 (23.3%)	29,976 (23.3%)	30,259 (23.2%)	31,032 (23.6%)	121,198 (23.4%)	.055
Hospital mortality n(%)	38,887 (30.3%)	39,491 (30.8%)	40,219 (30.9%)	41,283 (31.5%)	159,880 (30.9%)	< .001
Discharge to hospice	227 (0.2%)	302 (0.2%)	374 (0.3%)	413 (0.3%)	1,316 (0.3%)	< .001
Hospital LOS, d	15 (8-29)	15 (8-30)	15 (8-30)	15 (8-30)	15 (8-30)	.232
DWLST	19,479 (15.1%)	19,651 (15.3%)	19,794 (15.1%)	20,910 (15.9%)	79,834 (15.4%)	< .001

Data are presented as No. (%), mean (SE), or median (interquartile range) unless otherwise indicated. DWLST = decision to limit (withdraw or withhold) life-sustaining therapy; ICNARC = Intensive Care National Audit 'The classification of race is based on the NHS Data Dictionary ethnic codes. Multiracial includes mixed - White and Black Caribbean, mixed - White and Black African, mixed - White and Asian, mixed - any other mixed any other mixed and Research Centre; LOS = length of stay; NA = not applicable; RRT = renal replacement therapy. background; unknown includes race not stated.

Mortality

At baseline, a significant difference in mortality across quartiles was found, with slightly higher mortality in the most deprived neighborhood (32.2% in quartile I and 31.1 % in quartile IV; difference, 1.1%; P = .004) (Fig 1, Table 2). With the exception of the period affected by the COVID-19 pandemic (2020-2021), mortality rates decreased significantly for all groups over time, but no statistically significant narrowing of the mortality gap was noted (Figs 1, 2, Table 2). During the 2020 through 2021 COVID-19 pandemic, sepsis mortality increased from baseline by 7.6% in quartile I and 5.8% in quartile IV, with a between-group difference of 1.9% (P = .001).

Access

Controlling for patient and hospital characteristics, no significant difference was found in direct ICU admission from the emergency department between quartile I and IV (35.3% vs 34.7%, respectively; difference, 0.7%; P = .173) (Fig 1). Over time, a higher proportion of patients in all groups were admitted to the ICU directly (Fig 1). The trend favored the most deprived group (Fig 2, e-Table 3).

Interventions in the ICU

A significantly higher percentage of patients received MV at baseline in quartile I compared with those in quartile IV (57.8% vs 56.1%, respectively; difference, -1.7%; P < .001) (Fig 1, e-Table 4). The percentage of patients receiving MV decreased significantly over the study period for all groups of disparity (Figs 1, 2). The gap between quartile I and quartile IV groups narrowed significantly over time (Fig 1). The use of RRT at baseline was 15.9% in quartile I and 16.6% in quartile IV (P = .038) (Fig 1, e-Table 5). The percentage of patients receiving RRT decreased over time for all groups, although with no significant between-group differences (Figs 1, 2). At baseline, patients in the most deprived quartile were more likely to receive vasopressors than those patients in the least deprived quartile (33.6% vs 32.5%, respectively; difference, -1.1%; P = .014) (Fig 1, e-Table 6). Vasopressor use decreased significantly for all groups over time, with a significant narrowing of the gap between quartiles I and IV for the periods until 2018 through 2019. For the periods from 2020 through 2021 and from 2022 through 2023, the gap remained unchanged (Fig 2). At baseline, no significant difference in DWLST was found for patients in

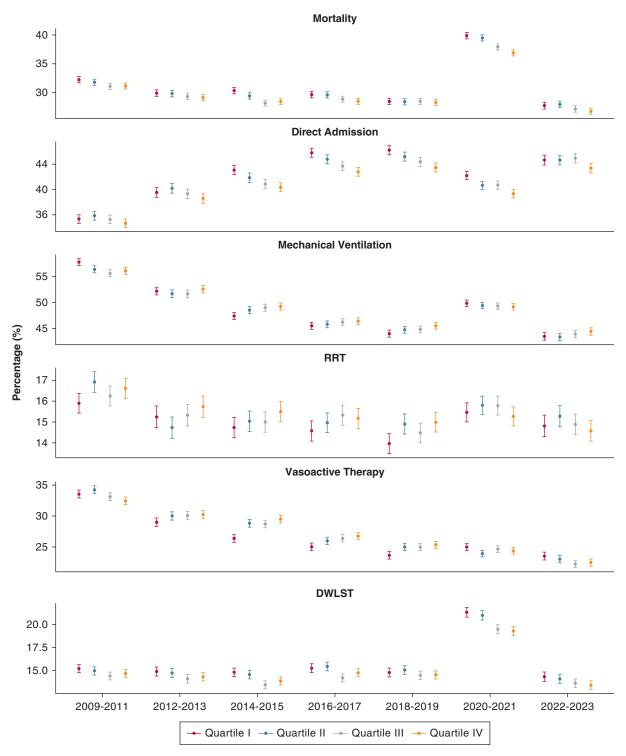


Figure 1 – A-F, Graphs showing temporal trends in hospital mortality among patients admitted to an ICU with sepsis across quartiles of neighborhood: mortality (A), direct admission (B), mechanical ventilation (C), RRT (D), vasopressor use (E), and DWLST (F). Quartile I is the most deprived, and quartile IV is the least deprived. Dots represent point estimates in percent for each outcome, and the whisker plot represents the 95% CI for each quartile. DWLST = decision to limit (withdraw or withhold) life-sustaining therapy; RRT = renal replacement therapy.

quartiles I and IV (15.2% vs 14.7%; difference, -0.5%; P = .087) (Fig 1). No significant change was found in the trend in within-group or between-group

differences in DWLST over the study period, except for the period from 2020 through 2021 (Fig 2, e-Table 7). From 2020 through 2021, the percentage of

TABLE 2 Average Annual Change in Mortality Rates for Patients With Differing Levels of Neighborhood Deprivation From 2009 Through 2023

Bas	Baseline Mortality (2009-2011)			Difference at Baseline (2009-11)			
Quartile		Percent			Comparison	Percent	P Value
Quartile I		32.2			NA	NA	NA
Quartile II		31.8			Quartile II vs I	-0.5	.238
Quartile III		31.1			Quartile III vs I	-1.2	.002
Quartile IV		31.1			Quartile IV vs I	-1.1	.004
Difference in Mortality From Baseline	Total	<i>P</i> Value	Within	Between	Difference-in-Difference From Baseline		
2012-2013							
Quartile I	-2.3	< .001	-2.4	-0.1	NA	NA	NA
Quartile II	-1.9	< .001	-1.9	0.0	Quartile II vs IW	0.4	.498
Quartile III	-1.7	< .001	-1.7	0.0	Quartile III vs I	0.6	.281
Quartile IV	-2.0	< .001	-2.1	0.1	Quartile IV vs I	0.4	.525
2014-2015							
Quartile I	-1.9	< .001	-2.1	0.2	NA	NA	NA
Quartile II	-2.4	< .001	-2.4	0.1	Quartile II vs I	-0.4	.414
Quartile III	-2.9	< .001	-3.0	0.1	Quartile III vs I	-1.0	.065
Quartile IV	-2.7	< .001	-2.9	0.2	Quartile IV vs I	-0.8	.139
2016-2017							
Quartile I	-2.6	< .001	-2.8	0.2	NA	NA	NA
Quartile II	-2.2	< .001	-2.4	0.2	Quartile II vs I	0.4	.438
Quartile III	-2.2	< .001	-2.4	0.2	Quartile III vs I	0.4	.492
Quartile IV	-2.7	< .001	-2.8	0.2	Quartile IV vs I	-0.1	.902
2018-2019							
Quartile I	-3.8	< .001	-4.0	0.3	NA	NA	NA
Quartile II	-3.4	< .001	-3.6	0.2	Quartile II vs I	0.4	.485
Quartile III	-2.6	< .001	-2.8	0.2	Quartile III vs I	1.2	.029
Quartile IV	-2.8	< .001	-3.1	0.2	Quartile IV vs I	0.9	.086
2020-2021							
Quartile I	7.6	< .001	7.3	0.3	NA	NA	NA
Quartile II	7.7	< .001	7.4	0.3	Quartile II vs I	0.1	.888
Quartile III	6.8	< .001	6.6	0.2	Quartile III vs I	-0.8	.146
Quartile IV	5.8	< .001	5.5	0.3	Quartile IV vs I	-1.9	.001
2022-2023							
Quartile I	-4.5	< .001	-4.8	0.3	NA	NA	NA
Quartile II	-3.8	< .001	-4.1	0.2	Quartile II vs I	0.7	.234
Quartile III	-3.9	< .001	-4.1	0.2	Quartile III vs I	0.6	.288
Quartile IV	-4.4	< .001	-4.6	0.2	Quartile IV vs I	0.1	.833

Data are presented as percentage unless otherwise indicated. Quartile I is the most deprived and quartile IV is the least deprived. Control variables include: assistance in daily activities before ICU admission, race, age, sex, Intensive Care National Audit and Research Centre 2018 risk of death at ICU admission, severe respiratory disease, severe cardiac disease, end-stage renal disease, severe liver disease, metastatic disease, hematologic malignancy, immunocompromization, ICU beds, hospital academic affiliation, miles to the nearest hospital, ICU racial and ethnic minority population serving proportion, and ICU proportion of highest deprivation quartile. NA = not applicable.

patients receiving a DWLST increased significantly compared with baseline (6.1% in quartile I vs 4.6% in quartile IV; difference, -1.5%; P = .001).

Within-Hospital and Between-Hospital Effects

Almost all the reduction in mortality over time across quartiles of neighborhood deprivation

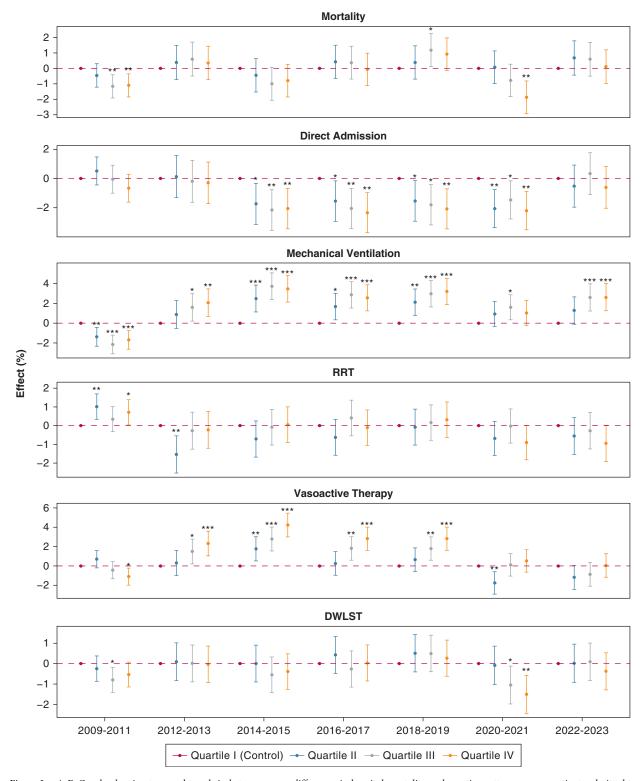


Figure 2 – A-F, Graphs showing temporal trends in between-group differences in hospital mortality and practice patterns among patients admitted to an ICU with sepsis across quartiles of neighborhood: mortality (A), direct admission (B), mechanical ventilation (C), RRT (D), vasopressor use (E), and DWLST (F). Quartile I is the most deprived, and quartile IV is the least deprived. Dots represent the difference in point estimates in percent for each outcome, and the whisker plot represents the 95% CI compared with quartile I. If the CI overlaps with the horizontal dotted line, then the quartile is not statistically significant compared with quartile I. $^{a}P < .05$. $^{b}P < .01$. $^{c}P < .001$. DWLST = decision to limit (withdraw or withhold) life-sustaining therapy; RRT = renal replacement therapy.

was driven by within-hospital effects (improvements in mortality within the same institution), and only a minor component was attributable to between-hospital factors (shifts of patients from low-quality to high-quality hospitals) (Table 2). A similar within-hospital effect was noted for patterns of direct admission to the ICU; the percentage of MV, RRT, and vasopressor use; and DWLST (e-Tables 3-7).

Subgroup Analysis

In high-risk patients, defined here as those with a > 20% probability of death at ICU admission or patients 65 years of age or older, the pattern of mortality differences across quartiles of neighborhood deprivation was similar to the primary analysis and is described in detail in e-Appendix 1 (e-Tables 8, 9). These results suggest that no differential effect occurred in reductions in mortality for high-deprivation, high-risk patients.

Sensitivity Analysis

First, we used a composite of death and discharge to hospice to determine whether shifts in attribution from index hospitalization to hospice could explain any of the observed differences in the association between neighborhood deprivation and mortality. The composite outcome was similar to the primary analysis and is included in e-Table 10. Second, in terms of academic affiliation, significant differences were found in mortality at baseline for quartile I compared with quartile IV for patients cared for in nonacademic hospitals (33.6% vs 32.0%, respectively; difference, -1.5%; P = .005). Mortality differences in university hospitals were not significant across groups of deprivation (Fig 3). Finally, we did not observe any widening of the mortality disparity gap for hospitals treating a higher proportion of patients from racial and ethnic minority groups or who are economically deprived (e-Figs 2, 3).

Discussion

In this national cohort study conducted in England, we found that patients from more deprived neighborhoods showed significantly higher baseline mortality. Despite significant improvements in mortality, this disparity gap has not narrowed. We explored the potential mechanisms underlying this persistent gap. Our analysis revealed an increase in the proportion of patients from all levels of neighborhood deprivation being directly admitted to the ICU from the emergency department, indicating overall progress in earlier critical care treatment.³⁸ Patients from

more deprived areas were admitted directly to the ICU more frequently, suggesting that timely access to care is unlikely to explain the mortality disparity. Additionally, we found no significant differences in practices patterns in ICU care related to MV, RRT, or vasopressor use, as well as DWLST across levels of deprivation. This suggests that the patterns of ICU admission and interventions in the ICU are unlikely to explain the mortality gap. These findings support the hypothesis that the ongoing mortality disparity may be attributed to the adverse health effects associated with living in disadvantaged neighborhoods. For example, current guidelines for pneumococcal vaccination, 1 of the largest and most effective strategies to prevent sepsis, target patients older than 65 years with no consideration for the higher burden of sepsis in younger people living in deprived neighborhoods. Our findings have several important implications for policymakers concerned with the impact of neighborhood deprivation on disparities in acute care. First, despite the increasing financial pressures, decreasing real funding, and rising demand faced by the English NHS during the study period, we observed improvements in the quality of care without widening the disparity gap. 39,40 This suggests that the centralized structure and coordination of care (ie, the introduction of a Cross System Sepsis Programme Board and NHS National Action Plan to improve diagnosis and treatment of sepsis), and not only total investment, may produce care improvements without widening disparities in outcomes. 41-43 This juxtaposes US statewide initiatives to improve sepsis care, which improved care overall, but seemingly widened disparities.5

Second, our results indicate that mortality reductions are driven primarily by improvements within institutions, and only a minor component of the variation was explained by the movement of patients from lowerquality to higher-quality hospitals. This trend was consistent across all other measures of access and patterns of acute care, suggesting that a broad-based quality improvement program is equally effective across different types of hospitals. Much of the literature on health disparities in sepsis is from the United States and describes widening gaps across several domains of disadvantage, including by sex, race, ethnicity, and socioeconomic status.⁵ Although socioeconomic differences in life expectancy and health have been described in England and the United States, 44,45 the level of income and wealth inequality is substantially higher in the United States, with a relatively limited government safety net. 44,46 Adults with the most

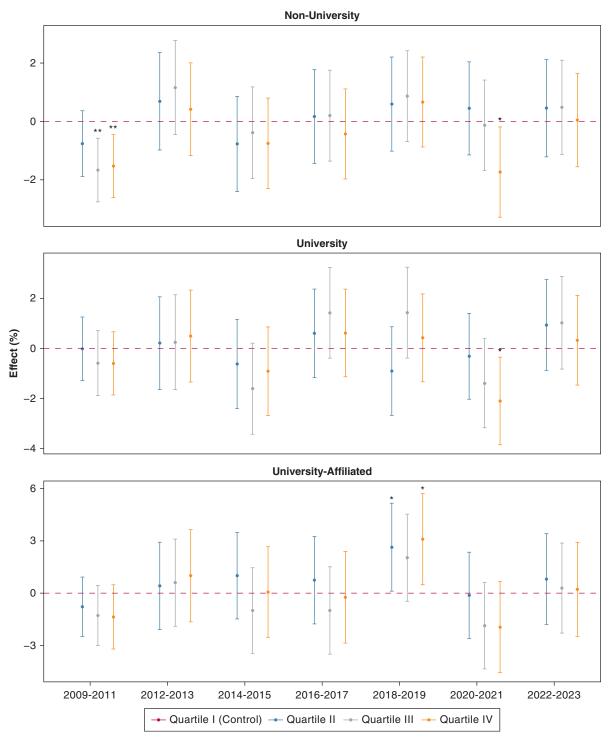


Figure 3 – A-C, Graphs showing sensitivity analysis of the average annual change in hospital mortality for patients with differing levels of neighborhood deprivation. Academic affiliation is categorized into nonuniversity (A), university (B), and university affiliated (C). Quartile I is the most deprived, and quartile IV is the least deprived. Dots represent the difference in point estimates in percent for mortality, and the whisker plot represents the 95% CI compared with quartile I. If the CI overlaps with the horizontal dotted line, then the quartile is not statistically significant compared with quartile I. $^{a}P < .05$. $^{b}P < .01$. $^{c}P < .001$.

socioeconomic disadvantage in the United States tend to have worse health than the comparable group in England. 45

Recent work using more granular US data suggests unequal access to high-quality care and to life-sustaining therapies for higher deprivation groups contributes to

health disparities in sepsis, despite efforts to standardize care. Our study, examining similar processes of care in England, found improvements in all groups of neighborhood deprivation and a trend toward more equitable processes of care, which may suggest more equal availability of high-quality care to patients of different socioeconomic deprivation as compared with those in the United States. Our study finds improvements across all levels of neighborhood deprivation and a trend toward more equitable care practices, which may suggest more equal access to care for patients of different socioeconomic backgrounds compared with those in the United States. Prior research in the United States suggested that patients with sepsis from more deprived neighborhoods are more likely to seek care in underperforming hospitals. 26,27,47 In contrast, we did not find hospitals serving patients with high neighborhood deprivation or hospitals serving populations from racial and ethnic minority groups to have worse mortality. This may be because of the more entrenched residential segregation in the United States that significantly affects the quality of hospital services that patients receive. In the United States, patients from highly deprived neighborhoods are more likely to be treated in hospitals facing resource constraints, limiting quality improvement interventions and widening disparities.⁴⁸ In England, quality improvements seem to be achieved more equitably. Additionally, the centralized structure of health financing and the absence of financial barriers to treatment within the hospital also may contribute to more equitable acute care in England.

Third, our study extended previous research by describing the trajectory of disparities across different levels of neighborhood deprivation and considered the patterns of mechanisms of access and quality of care. We found that despite equitable patterns of ICU admission and interventions in the ICU, the mortality gap persisted. This suggests that the negative social conditions associated with high levels of neighborhood deprivation continue to affect sepsis outcomes even when patients receive high-quality acute care. We highlighted persistent disparities in outcomes for patients in a country with universal health coverage, indicating that without addressing neighborhood deprivation, universal health coverage alone will not resolve health inequities fully.

Study Limitations

A major strength of this work is the completeness and coverage of 100% of all ICUs in England, using a clinical registry of granular data. However, our study also has

limitations. First, we used the IMD, a composite of several dimensions of deprivation, to classify neighborhoods. The construction of this composite requires the inclusion and weighting of unavoidably subjective components. We argue that the IMD can be seen as advantageous to single measures of deprivation and, in the absence of a gold standard, is the official measure of neighborhood deprivation used to allocate public funds. Second, the data do not include details of some care processes, such as time to antibiotic and fluid administration, or the care delivered in the emergency department before ICU admission, which may explain some of the underlying mechanisms of disparity. Third, our study described the patterns of use of MV, RRT, vasopressors, and DWLST, but did not have the granularity to describe the physiologic thresholds to inform the appropriateness of these interventions. We argue that by using a well-defined cohort and a detailed list of controls, much of the observed variation in use is driven by system-level inequalities. However, it is possible that some of the observed variation in use is related to unmeasured severity of illness. Finally, although the analysis of DWLST does account for many associated factors such as illness severity, age, and severe comorbidities, the data set does not include patient preferences for life-sustaining therapy. Therefore, this outcome may be prone to omitted variable bias.

Interpretation

Over the study period, sepsis mortality improved, although the disparity gap persists. Some improvements likely are driven by better ICU access, evident from lower acuity scores over time and higher proportions of patients directly admitted to the ICU. The disparity gap seems to narrow in terms of patterns of ICU interventions, suggesting that care received in the hospital does not completely explain the disparity gap's persistence. The persistence of the mortality gap might be explained by the detrimental effects of neighborhood deprivation before hospitalization. Therefore, strategies that target neighborhood deprivation are necessary to achieve health parity in patients with sepsis. However, further investigation is required to address some of the limitations of this study.

Funding/Support

The authors have reported to CHEST Critical Care that no funding was received for this study.

Financial/Nonfinancial Disclosures

None declared.

Acknowledgments

Author contributions: All authors contributed to the methodology, interpretation of data, and preparation of the manuscript. Additionally, R. M. undertook data analysis, wrote the original draft manuscript, and produced the figures. R. M. and I. P. conceptualized the study. I. P. supervised the study and provided critical feedback throughout. All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Additional information: The e-Appendix, e-Figures, and e-Tables are available online under "Supplementary Data."

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