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Prediction of Readmission Following Sepsis Using Social Determinants of Health

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OBJECTIVES: To determine the predictive value of social determinants of health (SDoH) variables on 30-day readmission following a sepsis hospitalization as compared with traditional clinical variables.

DESIGN: Multicenter retrospective cohort study using patient-level data, including demographic, clinical, and survey data.

SETTINGS: Thirty-five hospitals across the United States from 2017 to 2021.

PATIENTS: Two hundred seventy-one thousand four hundred twenty-eight individuals in the AllofUs initiative, of which 8909 had an index sepsis hospitalization.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Unplanned 30-day readmission to the hospital. Multinomial logistic regression models were constructed to account for survival in determination of variables associate with 30-day readmission and are presented as adjusted odds rations (aORs). Of the 8909 sepsis patients in our cohort, 21% had an unplanned hospital readmission within 30 days. Median age (interquartile range) was 54 years (41–65 yr), 4762 (53.4%) were female, and there were self-reported 1612 (18.09%) Black, 2271 (25.49%) Hispanic, and 4642 (52.1%) White individuals. In multinomial logistic regression models accounting for survival, we identified that change to nonphysician provider type due to economic reasons (aOR, 2.55 [2.35–2.74]), delay of receiving medical care due to lack of transportation (aOR, 1.68 [1.62–1.74]), and inability to afford flow-up care (aOR, 1.59 [1.52–1.66]) were strongly and independently associated with a 30-day readmission when adjusting for survival. Patients who lived in a ZIP code with a high percentage of patients in poverty and without health insurance were also more likely to be readmitted within 30 days (aOR, 1.26 [1.22–1.29] and aOR, 1.28 [1.26–1.29], respectively). Finally, we found that having a primary care provider and health insurance were associated with low odds of an unplanned 30-day readmission.

CONCLUSIONS: In this multicenter retrospective cohort, several SDoH variables were strongly associated with unplanned 30-day readmission. Models predicting readmission following sepsis hospitalization may benefit from the addition of SDoH factors to traditional clinical variables.

KEYWORDS: readmission; sepsis; social determinants of health

IMPORTANCE

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection (1). In addition to high mortality, 17–27% of sepsis survivors are readmitted to the hospital within 30 days of discharge from hospitalization (2–4). Sepsis notably constitutes a significantly higher risk of readmission compared with patients with other conditions such as heart failure or chronic obstructive pulmonary disease (5). Besides being unfavorable to patients, readmission within 30 days has been identified by the

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KEY POINTS

Question: Are the social determinants of health important in identifying patients at high risk of 30-day readmission following a sepsis hospitalization?

Findings: Using patient-level data from 35 institutions and 8909 index sepsis hospitalization in the All of Us research program, we identified that several social determinants of health, and in particular, access and ability to pay for healthcare, including lack of transportation to follow-up and switching care to a nonphysician provider to save money, were strongly associated with unplanned 30 days readmissions following sepsis hospitalization.

Meaning: The social determinants of health are critical components in predicting 30-day readmission following sepsis hospitalization.

Centers for Medicare and Medicaid Services as a quality metric and has important financial implication for health systems (6). Predicting which patients are at risk for readmission following hospital admission for sepsis remains a challenge (7, 8). To date, several studies have identified at risk sepsis patients based on clinical and demographic data (2–4, 7, 9, 10). However, such studies have thus far relied mainly on administrative databases, which have well recognized methodological weaknesses due to the use of billing codes, among others (11, 12).

The social determinants of health (SDoH) are the environmental variables that affect health, functioning, and quality-of-life outcomes, including financial, educational, healthcare, built environment, and social/community contexts (13). The SDoH can predict readmission in conditions other than sepsis (14, 15) and that intervening on such factors can reduce the readmission risk (16). However, few studies have systematically assessed the influence of the SDoH on the risk of sepsis readmission. A recent scoping review on this topic found that most studies analyzed included race and ethnicity alone and many did not evaluate any other SDoH components (17).

OBJECTIVES

We sought to identify SDoH that are associated with an unplanned 30-day readmission to the hospital after an index sepsis hospitalization. We tested the hypothesis that the SDoH would demonstrate significance when included with traditional clinical risk factors for predicting the risk of unplanned readmission among hospitalized patients with sepsis. We also aimed to identify other actionable risk factors for readmission to allow prioritization of patients at risk who may benefit from close post-discharge follow-up.

METHODS

Study Design and Cohort

We conducted a retrospective observational study using data from the National Institutes of Health's AllofUs (AoU) Research Program (C2021Q3R6). Institutional Review Board (IRB) approval with waiver of informed consent was obtained via AoU Research Program (IRB Protocol Number: 2016-05, approved March 17, 2021) with exemption provided by our local IRB. Research procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975. The AoU dataset is a multicenter cohort that currently contains patient-level data of 331,382 individuals from 35 hospitals in the United States. The AoU research program reflects the diverse population in the United States, with an emphasis to include minorities historically underrepresented in prior biomedical research. The dataset contains detailed survey information regarding patients' social and behavioral information, as well as medical history and data from the electronic health records, including vital signs and laboratory results. Gender, race and ethnicity data were self-reported by participants. Further details regarding the AoU dataset are described in the AoU Research Program special report (18). Our study was completed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (19).

We included all patients 18 years old or older who developed sepsis as defined by the Third International Consensus Definition of Sepsis ("Sepsis 3") (1) during their first ("index") sepsis hospitalization from the 35 hospitals in the AoU Research Program between 2017 and 2021 (**Fig. 1**). We identified patients with two-point or more increase in Sequential Organ Failure Assessment score and clinical suspicion of infection, defined as at least 1 day of antibiotic therapy

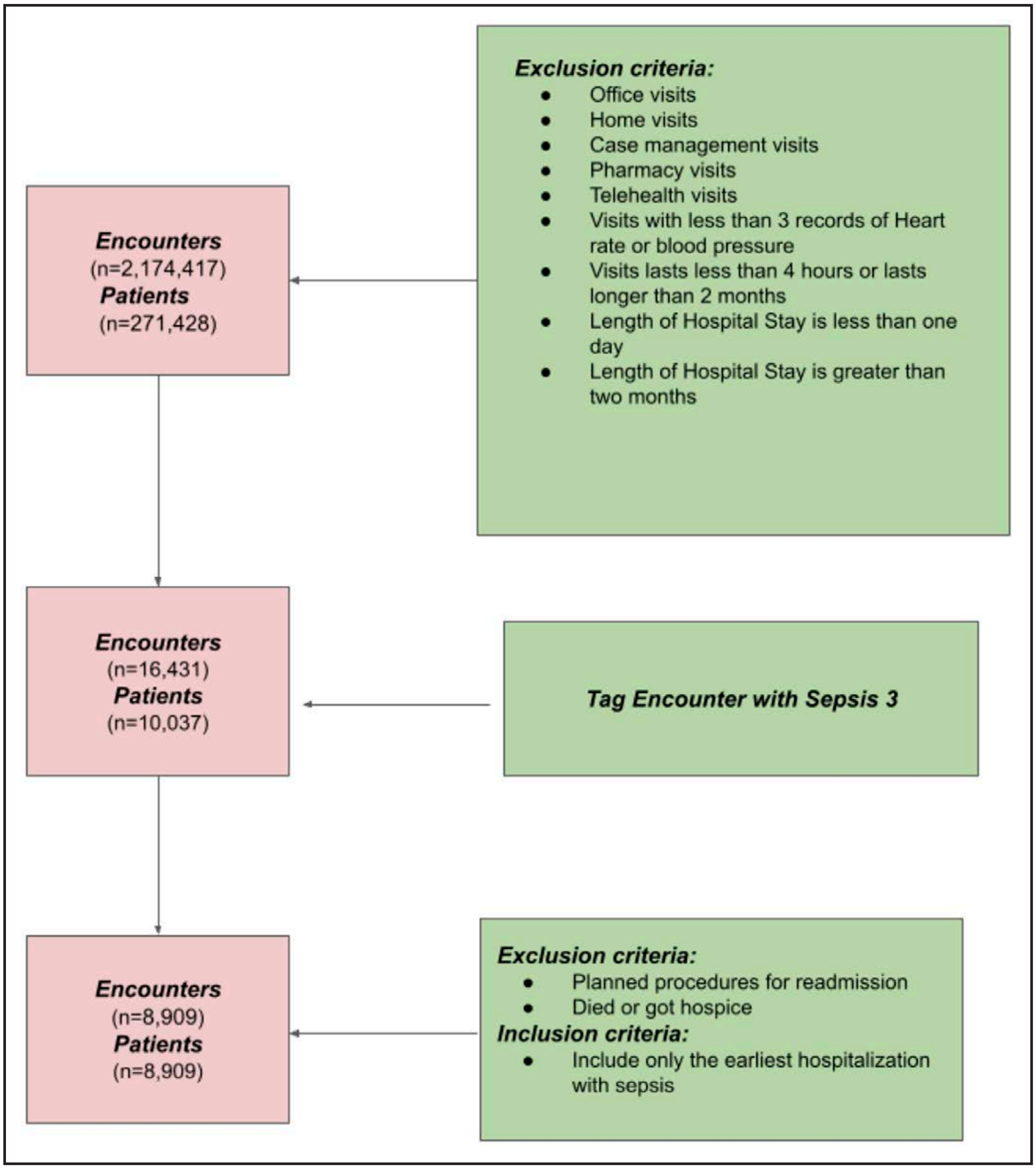

Figure 1. List of inclusion and exclusion criteria used to identify our patient population.

and the presence of blood cultures drawn within 72 hours of each other during a hospitalization (20). Time of sepsis was defined the earliest time of clinical suspicion of infection (either initiation of IV antibiotics or checking blood cultures) (21). Thirty-day unplanned readmissions were defined as hospitalization of at least a midnight within 30 days from the index hospitalization discharge date. We excluded patients readmitted for a planned procedure within 30 days, encounters where a patient had an observation admission (< 2 midnights admission), or were evaluated only in the emergency department (22). For patients with multiple hospitalizations, we only included the index sepsis admission and first corresponding 30-day readmission.

Outcomes

We assessed the SDoH factors that were significantly associated with 30-day hospital readmission before and after adjusting for sepsis survival bias, as well as traditional clinical factors associated with readmission. Our investigation aimed to determine whether there were significant SDoH factors associated with an unplanned 30-day readmission. Additionally, we included readmission diagnosis within 30 days from index hospital discharge.

Data Abstraction

Clinical and SDoH variables were obtained via automated Observational Medical Outcomes Partnership (OMOP) common data model queries provided by Amrollahi et al (20). The SDoH features were extracted from survey questions available in the AoU dataset. The survey questions were optional for participants; however, 97.7% of individuals in the AoU repository elected to share patient-level data (23). All survey instruments in the AoU have previously been validated by an external group and demonstrate an ability to capture participant-provided information, including race and ethnicity and are available at the AoU survey explorer webpage (https://www.researchallofus.org/data-tools/survey-explorer/) (24). We had access to the following surveys at the time of our initial analysis: Basic, Overall Health, Personal Medical History, Lifestyle, and Healthcare Access and Utilization. Each of these were reviewed by a panel of study authors (F.A., A.M., G.W.) who determined relevance of survey questions and ultimately, inclusion into the article. Of the included patients in this article, 95.4% completed these surveys during their index hospitalization with sepsis, whereas 1.6% of the surveys were filled out before admission, and 3.0% were completed post-discharge. *International Classification of Diseases*, 10th Edition codes were used to extract etiologies for patients who were readmitted within 30 days based on previously published methodology (3). All clinical variables were extracted from the AoU database using OMOP concepts codes. For variables with multiple concept codes with distinct measurement units, we applied appropriate conversion rates. A complete list of all clinical and SDoH variables used in this investigation can be found in **Supplemental Tables 1** and **2** (http://links.lww.com/CCX/B344), including variable type (e.g., categorical, numeric, etc.), which were taken directly from the AoU data repository. The closest survey to hospital stay (either admission or discharge) was used for extracting SDoH features. Median imputation was used for laboratory measurements, and K-nearest neighbor search was used to impute demographics and SDoH features to account for the likelihood of nonrandom missingness. All numerical variables have been standardized. Missingness of variables is reported throughout tables in the main text and supplement.

Statistical Methods

A two-sided alpha of less than $1e^{-3}$ was considered significant for all statistical analyses. We used the Wilcoxon rank-sum test and the two-sided chi-square test to assess differences in populations as appropriate. We used a threshold p value of less than 0.001 in univariate analysis or biologic plausibility to determine the threshold for inclusion into our multivariate model. To assess the association between SDoH factors and risk of readmission, we used a multivariate regression with SDoH and other confounders as the independent factors and the risk of 30 days readmission among index septic patients as the dependent variable. Odds ratios were extracted from this multivariate logistic regression model for readmission. A complete list of variables included in this analysis is provided in **Supplemental Table 3** (http://links.lww.com/CCX/B344). A considerable degree of missing data in the Healthcare Access survey (of the 8909 surviving hospitalized patients with sepsis, 2040 [22.9%] participated in the Healthcare Access survey). To address this issue, we carried out a sensitivity analysis including only patients who completed this survey to validate our findings (**Supplemental Table 4**, http://links.lww.com/CCX/B344). This sensitivity analysis followed a methodology similar to that employed in our multivariate analysis, whenever those variables were applicable to this subset of our patient population.

To address the mediating effect of hospital survival on the risk of readmission, we used a directed acyclic graph (DAG) to explicitly address potential confounding relationships. **Figure 2** depicts a DAG representation that shows how survival (S) influences the relationship between SDoH, as well as other confounders (C), and the likelihood of being readmitted (R) to the hospital. As an example, wealth may be positively correlated with both survival and a reduced risk of readmission; however, those who survive hospitalization are at risk for readmission and vice versa. To account for the confounding effect of survival, we first constructed a separate multivariate regression with SDoH and other confounders as the independent factors and the likelihood of survival (S) as the dependent factor. Next, we included predictions from this model (S') as an additional variable into the readmission model to adjust for the confounding effect of survival on readmission. A list of clinical variables used in this study and their unit of measurement is provided in **Supplemental Table 5** (http://links.lww.com/CCX/B344). After this adjustment, the readmission regression coefficients and the corresponding odds ratios are more likely to capture the direct effect of SDoH factors on the risk of readmission. Unless otherwise specified, we present adjusted odds ratios (aORs) adjusted for survival in the article.

RESULTS

Patient Cohort Demographics and Characteristics

There were 2,174,417 patient encounters in the AoU dataset during the study period. We identified 16,431 patients hospitalized with sepsis, of which 9,128 were index admissions (Fig. 1). Thirty-seven patients with a sepsis index admission were excluded from our cohort because their readmission was for a planned procedure (e.g., chemotherapy, surgical procedure, etc.) leaving

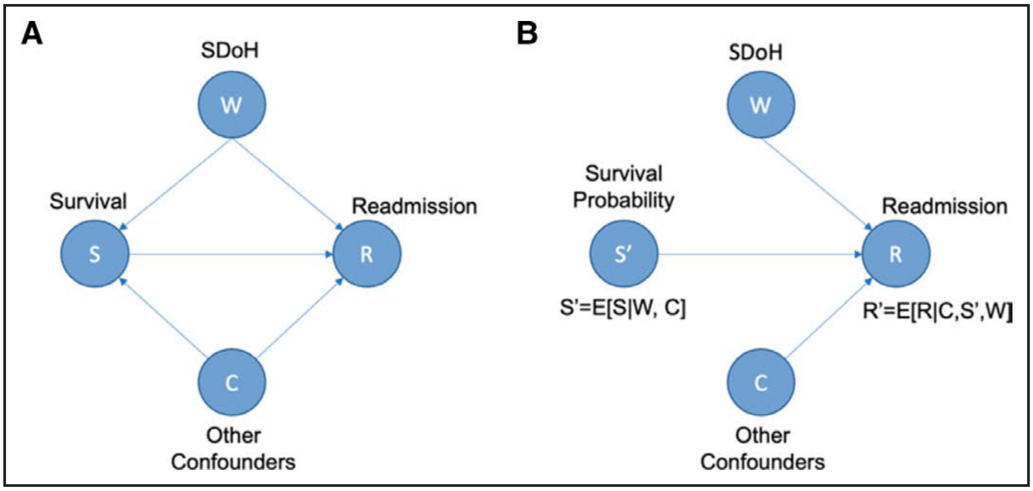

Figure 2. Directed acyclic graph representation showing how survival (S) influences the relationship between social determinants of health (SDoH) (W) and other confounders (C) and the likelihood of being readmitted (R) to hospital. Because survival can act as a confounder when determining factors associated with readmission, two multinomial logistic regression models were developed. The first model (**A**) serves for predicting the risk for survival and the second model (**B**) uses the risk of survival along with other variables to predict the risk of 30 d readmission among index septic patients. E = conditional expected value, R' = probability of readmission, S' = probability of survival.

a final cohort of 8909 unplanned sepsis readmission encounters. The median age of patients in the cohort was 54 years old (Supplementary Table 1, http://links.lww.com/CCX/B344). Female patients comprised 53.4% of patients in the dataset, 44.7% were male and 0.4% identified as transgender and nonbinary. Included patients had a median Charlson Comorbidity Index (CCI) of 2 (interquartile range, 0–4). Among septic patients who survived index admission with specified discharge disposition 69.5% were discharged home, 12.4% were discharged to nursing facility care, 0.7% discharged themselves against medical advice, 9.25% were discharged to home with home care, 1.1% were discharged to a rehabilitation facility, and 1% were transitioned to hospice (**Supplemental Table 6**, http://links.lww.com/CCX/B344). Approximately 21% of patients (n = 1903) had an unplanned 30-day readmission after their index hospital discharge. The highest percent of readmissions to the hospital following discharge after an index sepsis hospitalization occurred within the first 5–6 days (**Supplemental Fig. 1**, http://links.lww.com/CCX/B344).

Readmission Diagnoses at 30 Days Post-Hospitalization

The most common condition present at an unplanned readmission within 30 days after a sepsis index hospitalization (diagnoses not exclusive) was an infectious process, present in 33.4% of readmissions followed by cardiovascular, present in 23.3% of readmissions and hematologic diagnoses, and present in 12.9% of readmissions as shown in **Supplemental Table 7** (http://links.lww.com/CCX/B344). Of the most common category, an infectious process (present in 33.4% of readmitted patients), sepsis was the most common etiology by 30 days post-hospital discharge (19.2%) followed by pneumonia (8.0%), urinary tract infection or complication of genitourinary prosthetic devices implants and grafts (6.6%), bacteremia (5.7%), and central venous catheter related infection (1.3%). The most common causes of cardiovascular cause of readmission were related to cardiac arrhythmias and heart failure, whereas the most common hematologic causes were related to anemia and pancytopenia.

Characteristics Associated With Readmission Within 30 Days in Multivariate Analysis With Adjustment for Survival

Table 1 shows the major findings of our multivariate analysis. Supplemental Table 3 (http://links.lww.com/CCX/B344) contains all variables in the multivariate analysis.

Gender Race and Ethnicity. Characteristics associated with readmission within 30 days of hospital discharge from index hospitalization, after adjustment for survival, were male gender (as compared with being female gender; aOR, 1.39 [1.36–1.42]) and Hispanic ethnicity (as compared with not Hispanic; aOR, 1.21 [1.17–1.25]), whereas Asian race (as compared with being White) was protective (aOR, 0.71 [0.68–0.74]) as shown in Table 1. Black race (as compared with White) did not significantly change the odds for readmission (aOR, 1.00 [0.99–1.03]) after adjustment for likelihood

TABLE 1.
Major Findings of Multivariate Analysis of 30-Day Unplanned Readmission From Index Hospitalization

Characteristic	OR (95% CI) Without Adjustment for Survival	OR (95% CI) With Adjustment for Survival
Demographic data		
Female	Reference	Reference
Male	1.38 (1.35–1.41)	1.39 (1.36–1.42)
Ethnicity		
Not Hispanic	Reference	Reference
Hispanic	1.20 (1.16–1.23)	1.21 (1.17–1.25)
Race		
White	Reference	Reference
Black	0.99 (0.97–1.01)	1.00 (0.99–1.03)
Asian	0.67 (0.64–0.70)	0.71 (0.68–0.74)
Insurance type		
None	Reference	Reference
Government	0.55 (0.04–1.00)	0.54 (0.02–1.00)
Sponsored	0.75 (0.13–1.32)	0.72 (0.10–1.29)
Social determinants of health variables		
Highest level of education (ordinal)	1.00 (0.99–1.01)	0.99 (0.98–1.00)
Income (ordinal)	0.96 (0.96–0.97)	0.97 (0.96–0.97)
Lower quality of life (ordinal)	0.99 (0.98–1.00)	1.00 (0.99–1.01)
Lower physical activity (ordinal)	1.11 (1.10–1.12)	1.09 (1.08–1.10)
Lower social activity (ordinal)	1.05 (1.04–1.06)	1.04 (1.03–1.05)
Relationship satisfaction	0.91 (0.90–0.91)	0.91 (0.91–0.92)
Has primary care	0.35 (0.33–0.37)	0.35 (0.33–0.38)
Delayed pay out of pocket	1.27 (1.20–1.34)	1.27 (1.19–1.33)
Able to afford follow-up care	1.64 (1.57–1.71)	1.59 (1.52–1.66)
Therapies change due to economic reasons[a]	2.67 (2.46–2.86)	2.55 (2.35–2.74)
Delayed care due to transportation	1.71 (1.66–1.76)	1.68 (1.62–1.74)
Socioeconomic factors by ZIP code		
% of population in ZIP code below poverty level	1.28 (1.25–1.31)	1.26 (1.22–1.29)
% of population in ZIP code without health insurance	1.23 (1.22–1.25)	1.28 (1.26–1.29)
Clinical variables		
Charlson Comorbidity Index	1.16 (1.15–1.16)	1.28 (1.27–1.29)
Median hospital length of stay, d	1.20 (1.19–1.20)	1.21 (1.20–1.22)
Required vasopressors	1.27 (1.24–1.29)	1.19 (1.17–1.21)
Organ transplant	1.34 (1.32–1.36)	1.24 (1.22–1.26)
Difficulty concentrating	1.63 (1.60–1.71)	1.65 (1.59–1.72)

(*Continued*)

TABLE 1. (*Continued*)
Major Findings of Multivariate Analysis of 30-Day Unplanned Readmission From Index Hospitalization

Characteristic	OR (95% CI) Without Adjustment for Survival	OR (95% CI) With Adjustment for Survival
Laboratory variables		
Discharge hemoglobin	0.89 (0.88–0.90)	0.85 (0.83–0.85)
Discharge platelets	1.11 (1.10–1.12)	1.08 (1.08–1.09)

OR = odds ratio.
[a]Selected "Yes" to: "To save money, patients preferred to use naturopathy, traditional medicine, homeopathy, meditation, progressive relaxation, yoga, etc."

of survival. The sensitivity analysis revealed no significant variation in the association between race and ethnicity and the 30-day readmission rate (Supplemental Table 5, http://links.lww.com/CCX/B344).

Social Determinants of Health. In our multivariable analysis of SDoH factors, after adjustment for survival, switching care to a nonphysician/alternative therapies (e.g., naturopathy, traditional medicine, homeopathy) to save money (aOR, 2.55 [2.35–2.74]), delay of receiving medical care due to lack of transportation (aOR, 1.68 [1.62–1.74]), and inability to afford flow-up care (reported by subjects in the surveys as any type of follow-up care; aOR, 1.59 [1.52–1.66]) were associated with higher rates of readmission (Table 1). Having a primary care physician was protective from readmission (aOR, 0.35 [0.33–0.38]) after survival adjustment.

The inability to seek care because of out-of-pocket expenses also increased readmission risks (aOR, 1.27 [1.19–1.33]). Other SDoH such as physical health at baseline or lower physical activity was also associated with increased odds for readmission, while relationship satisfaction was protective. Lack of health insurance or poverty by ZIP code was significantly associated with readmission after sepsis index hospitalization in multivariable analysis (aOR, 1.26 [1.22–1.29]) and no health insurance by ZIP code (aOR, 1.28 [1.26–1.29]), respectively, after adjustment for mortality. The sensitivity analysis we conducted on patients who filled the Healthcare Access SDoH survey was largely similar to our multivariate analysis with the entire population with the exception of a single ZIP code variable (Supplemental Table 5, http://links.lww.com/CCX/B344).

Clinical Variables. In the multivariable analysis, we found that the median hospital length of stay was significantly associated with readmission (aOR, 1.21 [1.20–1.22]). The CCI also showed a significant association (aOR, 1.28 [1.27–1.29]).

DISCUSSION

Our study makes several major contributions to the existing literature. In contrast to prior work in which SDoH are often limited to race and ethnicity, our study evaluates specific patient reported SDoH linked to health outcomes after sepsis. By illuminating not only the importance of the SDoH but the specific factors associated with rehospitalization after sepsis, we have generated potentially modifiable factors contributing to readmission after sepsis hospitalizations. We observed that access to care for patients following sepsis hospitalization was associated with a significant decrease in chance of an unplanned 30-day readmission. Furthermore, patients with financial concerns who sought care from nonphysicians were much more likely to be readmitted. In addition, patients unable to afford transportation were also at risk of readmission. Further, we observed several associations between race and ethnicity and readmission. Specifically, Hispanic individuals were at increased risk of readmission following sepsis hospitalization as compared with non-Hispanic people. The reason for the increased risk of Hispanic people being readmitted is likely complex but may include biological differences, possible language barriers, and/or social/cultural issues. However, Asian persons had lower associations of readmission as compared with Whites. Black persons were at minimally different risk as compared with the White reference control group, in contrast to some prior studies (25). Finally, although ZIP code had some predictive value consistent with prior studies, our findings suggest that patient-level information may be more predictive (26).

Based on our study design we are unable to isolate underlying mechanisms but offer some speculation to guide subsequent research. Lack of access to care post-discharge may be problematic with increased odds for readmission, consistent with a recent randomized trial conducted by Taylor et al (8). We speculate that the visit to the primary care physician post-discharge may be helpful in early identification of potential deterioration, reconciling medications that may have been changed during hospitalization, provision of other preventative measures (diet, exercise, risk factor stratification, glucose control in diabetes etc.) and/or facilitating subspecialty referral (27). Seeking care from alternative medicine providers may delay appropriate medical care, although mechanisms underlying this deleterious association are beyond the scope of this study. Although cost-effectiveness analyses were not the focus of this article, one might hypothesize that provision of primary care visits and/or transportation to healthcare providers may be economical compared with rehospitalization. We are optimistic that targeted approaches to reducing readmission may allow reductions in healthcare spending.

Self-reported cognitive impairment was associated with risk of readmission. The etiology of the impairment is unclear as it may be preexisting or could be a result of the sepsis hospitalization. Because the survey question could be filled before (patients can choose to be part of AoU at any time), during, or after their visits and because we selected the survey with closest time to the hospital stay (either admission or discharge), we are unable to discern preexisting from acquired cognitive impairment in our study. Considerable literature has shown that delirium during hospitalization is predictive of longer-term neurocognitive impairment (28). Although on the other hand, preexisting cognitive impairment puts patients at increased risk for delirium. Given the risk of cognitive impairment for readmission after sepsis hospitalization (as identified via concentration disability) observed in the present study, further efforts to prevent delirium and/or support these individuals who are suffering may well be beneficial in preventing readmissions following sepsis hospitalization. Prospective studies would be required to confirm these findings.

Poverty by ZIP code did not have as strong an association to 30-day hospital readmission as anticipated when compared with prior publications comparing geographical markers. In particular, Galiatsatos et al (26) demonstrated a marked risk for 30-day readmission following sepsis hospitalization based on Area Deprivation Index (ADI). The distinction with this prior study may result from the use of ADI, a more granular geographical marker utilizing relative socioeconomic conditions of neighborhoods, compared with the boundaries of ZIP codes. Although ZIP codes are more easily accessed this may support the utility of more specific contextual factors, such as ADI when predicting healthcare outcomes. Still our findings do suggest the importance of geographic context.

Our data suggest that the addition of certain SDoH factors may augment ability to identify which sepsis patients may have a 30-day unplanned readmission. Current scoring systems used to identify patients at high risk of readmission, such as the LACE+ index or HOSPITAL score were not specifically developed or validated for sepsis patients (29, 30). These scores ignore the SDoH and focus on more traditional predictors of readmission, such as preceding hospitalizations, comorbidity burden, and index admission type. The few studies investigating how current readmission scores perform in sepsis patients have found that the predictive abilities of the LACE+ index was significantly lower for sepsis patients than what was reported in the initial development and validation cohorts (7, 20). Recent data suggest that programs designed to prevent post-discharge readmission and mortality for sepsis survivors can result in significant reductions in morbidity, with effects up to 1 year (8, 31). The inclusion of the SDoH into scoring systems that determine which patients receive these services may help appropriately allocate resources potentially to prevent readmissions in high-risk sepsis patients. Importantly, even SDoH factors considered nonmodifiable may assist in determining or benchmarking risk of readmission.

Despite our study's strengths, we acknowledge several limitations. First, based on our study design, we cannot rigorously separate correlation from causation. However, a large sample size allowed for multivariable regression analysis of several important variables allowing for robust independent associations. Second, as with most survey data, the AoU database is susceptible to misreporting, missingness, and participation bias. Although the AoU database is more comprehensive and granular than most other datasets, the data missingness may impact findings since we are uncertain if missingness is at random or not. The high degree of missingness of data from one survey we accessed in particular may limit generalizability, although we conducted a sensitivity analysis to ensure key findings were robust. Thus, our conclusions are limited to the population studied and we are highly supportive of additional research to confirm or refute our findings. Third, despite our identification of potentially "actionable" factors predicting readmission, we did not perform an interventional study. Thus, although we speculate that provision of follow-up care and adequate access to care and transportation may well reduce the risk of readmission, interventional studies would be required to draw rigorous conclusions. Finally, AoU is an evolving collaborative initiative with frequent updates as subjects are added. Our analysis shows data with 331,382 subjects. Updates made by AoU since our initial submission have not been included in this article. The ultimate goal by AoU is to enroll 1,000,000 subjects and our results will have to be confirmed in the final version of AoU, once available. Despite these limitations, we view our findings as an important addition to the literature that may guide clinical decision-making until more definitive data are available.

CONCLUSIONS

Various SDoH variables, particularly those related to access and ability to pay for healthcare, were associated with an unplanned 30-day readmission following hospitalization with sepsis. Future studies should include these into risk prediction tools and models to identify better patients at high risk of readmission.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

Drs. Wardi, Nemati, Malhotra, and Amrollahi conceived the research question. Drs. Amrollahi and Nemati performed data acquisition, analysis, and provided the results. Drs. Kennis, Malhotra, Taylor, Wardi, and Meier drafted the article. Drs. Amrollahi, Wardi, and Meier had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors provided critical revisions to the article.

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Drs. Wardi and Meier contributed equally and are joint senior authors.

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All data used in this investigation is readily available from the AllofUs research initiative available at: https://www.researchallofus.org/. Request for data used specifically in this investigation may be provided upon reasonable request.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al: The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016; 315:801–810
2. Jones TK, Fuchs BD, Small DS, et al: Post-acute care use and hospital readmission after sepsis. *Ann Am Thorac Soc* 2015; 12:904–913
3. Gadre SK, Shah M, Mireles-Cabodevila E, et al: Epidemiology and predictors of 30-day readmission in patients with sepsis. *Chest* 2019; 155:483–490
4. Goodwin AJ, Rice DA, Simpson KN, et al: Frequency, cost, and risk factors of readmissions among severe sepsis survivors. *Crit Care Med* 2015; 43:738–746
5. Mayr FB, Talisa VB, Balakumar V, et al: Proportion and cost of unplanned 30-day readmissions after sepsis compared with other medical conditions. *JAMA* 2017; 317:530–531

6. Centers for Medicare & Medicaid Services: Hospital Readmissions Reduction Program (HRRP). 2023. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program. Accessed March 18, 2022
7. Wardi G, Shashikumar S, Allen T, et al: 1233: Development and validation of a novel machine learning algorithm to predict sepsis readmissions. *Crit Care Med* 2021; 49:620–620
8. Taylor SP, Murphy S, Rios A, et al: Effect of a multicomponent sepsis transition and recovery program on mortality and readmissions after sepsis: The improving morbidity during post-acute care transitions for sepsis randomized clinical trial. *Crit Care Med* 2021; 50:469–479
9. McCoy A, Das R: Reducing patient mortality, length of stay and readmissions through machine learning-based sepsis prediction in the emergency department, intensive care unit and hospital floor units. *BMJ Open Qual* 2017; 6:e000158
10. Liu V, Lei X, Prescott HC, et al: Hospital readmission and healthcare utilization following sepsis in community settings. *J Hosp Med* 2014; 9:502–507
11. Memtsoudis SG: Limitations associated with the analysis of data from administrative databases. *Anesthesiology* 2009; 111:449; author reply 450–451
12. Haut ER, Pronovost PJ, Schneider EB: Limitations of administrative databases. *JAMA* 2012; 307:2589; author reply 2589–2590
13. Healthy People 2030, U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion: Social Determinants of Health. Available at: https://health.gov/healthypeople/objectives-and-data/social-determinants-health. Accessed March 18, 2022
14. Chin MH, Goldman L: Correlates of early hospital readmission or death in patients with congestive heart failure. *Am J Cardiol* 1997; 79:1640–1644
15. Meddings J, Reichert H, Smith SN, et al: The impact of disability and social determinants of health on condition-specific readmissions beyond medicare risk adjustments: A cohort study. *J Gen Intern Med* 2017; 32:71–80
16. Evans WN, Kroeger S, Munnich EL, et al: Reducing readmissions by addressing the social determinants of health. *Am J Health Econ* 2021; 7:1–40
17. Hilton RS, Hauschildt K, Shah M, et al: The assessment of social determinants of health in postsepsis mortality and readmission: A scoping review. *Crit Care Explor* 2022; 4:e0722
18. Denny JC, Rutter JL, Goldstein DB, et al; All of Us Research Program Investigators: The "All of Us" research program. *N Engl J Med* 2019; 381:668–676
19. von Elm E, Altman DG, Egger M, et al; STROBE Initiative: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *BMJ* 2007; 335:806–808
20. Amrollahi F, Shashikumar SP, Meier A, et al: Inclusion of social determinants of health improves sepsis readmission prediction models. *J Am Med Inform Assoc* 2022; 29:1263–1270
21. Lauritsen SM, Kristensen M, Olsen MV, et al: Explainable artificial intelligence model to predict acute critical illness from electronic health records. *Nat Commun* 2020; 11:3852
22. Centers for Medicare & Medicaid Services: 2024 National Impact Assessment of the Centers for Medicare & Medicaid Services (CMS) Quality Measures Report. Baltimore, MD, U.S. Department of Health and Human Services. 2024. Available at: https://www.cms.gov/Medicare/Quality-Initiatives-Patient-AssessmentInstruments/QualityMeasures/National-Impact-Assessment-of-the-Centers-for-Medicare-andMedicaid-Services-CMS-Quality-Measures-Reports. Accessed May 21, 2024
23. Joseph CLM, Tang A, Chesla DW, et al: Demographic differences in willingness to share electronic health records in the all of us research program. *J Am Med Inform Assoc* 2022; 29:1271–1278
24. Cronin RM, Jerome RN, Mapes B, et al: Development of the initial surveys for the all of us research program. *Epidemiol Camb Mass* 2019; 30:597–608
25. Lizza BD, Betthauser KD, Juang PH, et al: Racial disparities in readmissions following initial hospitalization for sepsis. *Crit Care Med* 2021; 49:e258–e268
26. Galiatsatos P, Follin A, Alghanim F, et al: The association between neighborhood socioeconomic disadvantage and readmissions for patients hospitalized with sepsis. *Crit Care Med* 2020; 48:808–814
27. Wardi G, Pearce A, DeMaria A, et al: Describing sepsis as a risk factor for cardiovascular disease. *J Am Heart Assoc* 2023; 12:e028882
28. Girard TD, Jackson JC, Pandharipande PP, et al: Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Crit Care Med* 2010; 38:1513–1520
29. van Walraven C, Wong J, Forster AJ: LACE+ index: Extension of a validated index to predict early death or urgent readmission after hospital discharge using administrative data. *Open Med* 2012; 6:e80–e90
30. Donzé J, Aujesky D, Williams D, et al: Potentially avoidable 30-day hospital readmissions in medical patients: Derivation and validation of a prediction model. *JAMA Intern Med* 2013; 173:632–638
31. Kowalkowski MA, Rios A, McSweeney J, et al: Effect of a transitional care intervention on rehospitalization and mortality after sepsis: A 12-month follow-up of a randomized clinical trial. *Am J Respir Crit Care Med* 2022; 206:783–786