Online Supplemental Files for: **Hilton RS, Hauschildt K, Shah M, Kowalkowski MA, Taylor SP.** Assessment of social determinants of health in post-sepsis mortality and readmission: a scoping review

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	supplement
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	6
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	6, appendix
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	6

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	tables
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	tables
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	tables
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	tables
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	tables
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	9
Limitations	20	Discuss the limitations of the scoping review process.	12
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	12
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	1

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

Online Supplement Table 1. Initial Search strategy used to identify eligible articles
(hospital readmission[MeSH Terms])) OR (hospital readmissions[MeSH Terms])) OR (patient readmission[MeSH Terms])) OR (readmission, hospital[MeSH Terms])) OR (patient readmissions[MeSH Terms])) OR (late mortality[Title/Abstract])) OR (long-term mortality[Title/Abstract])) AND ((((((((((((((((sepsis[MeSH Terms]) OR (sepsis, severe[MeSH Terms])) OR (sepsis syndrome[MeSH Terms])) OR (sepsis syndromes[MeSH Terms])) OR (septicemia[MeSH Terms])) OR (septicemia[Title/Abstract])) OR (septicaemia[Title/Abstract])) OR (sepsis[Title/Abstract])) OR (septic*[Title/Abstract]))) Filters: English, from 1992/1/1 - 2021/5/1

Online Supplement Table 2. Eligible studies that did not include social determinants of health

Study ID	Year of publication	Cohort size (n=?)	Multicenter (y/n)	Country of data source
Angus, 2004	2004	1,690	yes	Multiple
Bozza, 2007	2007	60	yes	Brazil
Brakenridge, 2019	2019	301	no	U.S.
Braun, 2004	2004	>10000	yes	US
Buendgens, 2017	2017	219	no	Germany
Burdick, 2020	2020	17,758	yes	U.S.
Chao, 2014	2014	15,535	yes	Taiwan
Contrin, 2013	2013	349	no	Brazil
Danese, 2006	2006	22,130	yes	U.S.
Dean, 2006	2006	17,728	yes	U.S.
Deb, 2019	2019	170,571	yes	U.S.
DeMerle & Royer, 2017	2017	472	yes	U.S.
DeMerle & Vincent, 2017	2017	26,561	yes	U.S.
Demiralp, 2017	2017	100-1000	yes	U.S.
Dick, 2012	2012	17,537	yes	U.S.
Dreiher, 2012	2012	5,155	yes	Israel
Drewry, 2014	2014	335	no	US
Flesishman, 2021	2021	116,507	yes	Germany
Gilmore, 2015	2015	98	no	U.S.
Guirgis, 2021	2021	104	no	U.S.
Haas, 2021	2021	532	yes	Multiple
Henriksen, 2017	2017	1,713	no	Denmark
Honselmann, 2015	2015	1,406	no	Germany
Jia, 2021	2021	4,370	no	U.S.
Jones, 2014	2014	120,943	yes	U.S.

Kaukonen, 2014	2014	101,064	yes	Australia and New Zealand
Khoury, 2017	2017	259	no	Israel
Kim, 2019	2019	274	no	South Korea
Kim, 2021	2021	4,625	yes	South Korea
Laupland, 2005	2005	4,845	yes	Canada
Lee, 2008	2008	525	no	U.S.
Li, 2018	2018	112	no	China
Lichtenauer, 2017	2017	348	no	Germany
Linder, 2014	2014	2,289	no	Canada
Liu, 2014	2014	6,344	yes	U.S.
Liu, 2021	2021	1,405	yes	U.S.
Meurer, 2010	2010	50	no	US
Nesseler, 2013	2013	96	no	france
Norman, 2017	2017	633,407	yes	U.S.
Ou, 2016	2016	>10000	yes	Taiwan
Perner, 2014	2014	804	yes	dutch
Prescott, 2015	2015	46,575	yes	U.S.
Prescott, 2015	2015	2,843	yes	U.S.
Prescott, 2016	2016	3,029	yes	U.S.
Prescott, 2017	2017	28,618	yes	U.S.
Quartin, 1997	1997	1,505	yes	U.S.
Rahmel, 2020	2020	83,974	yes	Germany
Ranzani, 2013	2013	229	no	Brazil
Rice Crescencio, 2012	2012	127	no	U.S.
Rice, 2013	2013	56,527	yes	U.S.
Rygård, 2016	2016	1,005	yes	Denmark
Sasse, 1995	1995	153	no	US
Scheer, 2017	2017	14,115	no	Germany

Schmidt, 2020	2020	1,975	no	Germany
Singh, 2019	2019	1,068	no	U.S.
Stenholt, 2021	2021	662	no	Denmark
Stiermaier, 2013	2013	139	yes	Multiple
Storgaard, 2013	2013	212	no	Denmark
Styrvoky, 2015	2015	230	no	U.S.
Styrvoky, 2016	2016	1,049	no	U.S.
Tacke, 2014	2014	299	no	Germany
Tacke, 2016	2016	311	no	Germany
Taylor, 2020	2020	189	yes	U.S.
Tsaganos, 2016	2016	200	yes	Greece
Tsen, 2015	2015	990	yes	non-US
Vashi, 2013	2013	4,028,555	yes	U.S.
Vasile, 2013	2013	926	no	U.S.
Wang, 2014	2014	29,644	yes	U.S.
Weinreich, 2017	2017	1,355	no	US
Weycker, 2003	2003	16,019	yes	U.S.
Whiles, 2016	2016	7,071	no	US
Yende, 2014	2014	823,462	yes	U.S.
Yende, 2019	2019	483	yes	U.S.
Zhao, 2021	2021	183	no	China
Zilberberg, 2015	2015	1,697	no	U.S.

Online Supplement Table 3. Additional data from eligible studies that did include social determinants of health

Study ID (Author, year)	Cohort data source (single/multi center, n =)	Cohort description	Follow-up method and outcome assessment	Social determinants included	Social determinant assessment method (EHR, survey, census)	Social determinant level (individual or neighborhood)	Missing data on social determinants (low, high)	Confounder assessment	SDOH independently associated with outcomes
Schnegelsberg, 2016	Aarhus University Hospital, Denmark, Nov 2008 - Dec 2010 sepsis cohort, SC, n= 387	Adult sepsis, severe sepsis, septic shock patients (ICU); definitions per Surviving Sepsis Campaign	30-day mortality post ICU admission **80-day mortality after hospital discharge** **First unplanned readmission within 180 days after hospital discharge**	1.Education level 2.Income 3.Cohabitation status	1.Database (Population's Education Register) 2.Database (Income Statistic Register) 3.Database (Population Statistics Register)	1.Individual 2.Individual 3.Individual	Low	Yes, Cox regression analysis	30-day mortality: income (low)

Leu, 2013 (abstract)	Lincoln Medical and Mental Health Center, Bronx, NY, 2009-2011, SC, n= 479	Survivors of severe sepsis and septic shock (medical-ICU)	Hospital mortality ICU/hospital LOS **30-day readmission** **180-day readmission**	1.Ethnicity	1.EHR	1.Individual	Not reported	Yes, logistics regression analysis, mutlivariate analysis	30-day readmission: Latino background 180-day readmission; Latino background
Ahmad, 2014 (abstract)	Healthcare Costs and Utilization Project State Inpatient Database (CA), 2006-2011, MC, n= 640,954	Patients hospitalized for severe sepsis; ICD-9-CM	In-hospital mortality **30-day readmission** Length of stay	1.Homelessness	1.Database	1.Individual	Not reported	Yes, multivariate logistic regression	None
Davis, 2014	Royal Darwin Hospital, Tiwi, Darwin, NT, May 6 2007-May 5 2008, SC, n= 1028	All patients hospitalized for sepsis between May 6 2007-May 5 2008; 1992 ACCP-SCCM criteria. Severe sepsis identified as per definitions in PROWESS study.	**5-year mortality**	1.Race	1.Not reported	1.Individual	Not reported	Kaplan-Meier Survival Rate estimates	Mortality: Race (higher risk if Indigenous (Aboriginal Australian))

Bath, 2019 (abstract)	Nationwide Inpatient Sample data, 2012-2014, MC, n= 3,082,888	All patients discharged with primary diagnosis of septicemia	**30-day readmission**	1.Payer type 2.Median income per zip code 3.Residential type (metro, etc.)	1.Database 2.Database 3.Database	1.Individual 2.Neighborhood 3.Neighborhood	Not reported	No	30-day readmission rate: payer type (under Medicare), residential type (Living in Metropolitan areas)
Davis, 2011	Royal Darwin Hospital, Tiwi, Darwin, NT, May 6 2007-May 5 2008, SC, n= 1090	Patients with probable or definite infection and meeting at least two or more SIRS criteria	Hospital mortality **28-day mortality**	1.Race	1.Not reported	1.Individual	Not reported	Yes, univariate and multivariate regression	None
Abu-Kaf, 2018	Israeli Sepsis Group (ISR-SEPSIS) database, 2003-2011, MC, n= 409	Sepsis survivors discharged from ICU; ICD-9-CM	Mortality **Long-term mortality (2 year)**	1.Marital status	1.Not reported	1.Individual	Not reported	Chi-square test or Fisher exact test	2-year mortality: marital status
Chao, 2016	Taiwan's National Health Insurance Research Database (NHIRD), 1995-2011, MC, n= 272,879	Patients, 20 years old or older, with first-time ICU hospitalization for sepsis; Septicemia defined with ICD-9-CM plus receipt of antimicrobial therapy	**1-year mortality** **2-year mortality** **5-year mortality**	1.Monthly income 2.Urbanization	1.Database 2.Database	1.Individual 2.Neighborhood	Not reported	Yes, univariate and multivariate analysis	None

		during hospitalization.							
Ortego, 2015	Hospital of the University of Pennsylvania, Dec 2007 - Jan 2010, SC, n= 997	Patients admitted from the ED with septic shock, defined as a serum lactate level ≥4 mmol/L or systolic blood pressure <90 mm Hg after volume resuscitation or use of a vasoactive agent.	ED visits (treat-and-release) **All-cause hospital readmission to any UPHS hospital within 30 days of discharge after the index hospitalization for septic shock**	1.Race	1.EHR	1.Individual	Low	Yes, multivariate logistic regression	None
Lopes, 2010	Centro Hospitalar Lisboa Norte, Infectious Disease Intensive Care Unit, July 2002 - June 2007, SC, n= 234	Sepsis survivors with AKI; sepsis classified in accordance with the American College of Chest Physicians and the Society of Critical Care	**2-year mortality**	1.Race	1.Unit database/EHR	1.Individual	Not reported	Yes, univariate and multivariate regression	None

		Medicine consensus.							
Shankar-Hari, 2019	Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme, April 1, 2009 - March 31, 2014, MC, n= 94,748	Adult patients sepsis survivors (ICU); Sepsis-3 criteria	**All-cause long-term mortality (up to 6 years)**	1.Race	1.Database	1.Individual	Low	Yes, Cox regression analysis	Mortality: some or total dependency, (from KH: race as well (Asian and other less likely than White, I believe) They only intermittently mention in the abstract/findings, which is a little odd?)
Gameiro, 2020	Division of Intensive Medicine of the Centro Hospitalar Universitário Lisboa Norte, Jan 2008 - Dec 2014, MC, n= 256	Patients 18 years or older with a diagnosis of sepsis at admission to the Division of Intensive Medicine who developed AKI within the first week of ICU hospitalization; Sepsis-3 criteria	**30-day mortality** **Long-term mortality (5 year)** Long-term adverse renal outcomes	1.Race	1.EHR	1.Individual	Low	Yes, multivariate and univariate regression analysis	None

Kaplan, 2017 (abstract)	University of Florida Hospital, August 2013 - December 2015, SC, n= 4,711	Patients 18 years or older admitted to university hospital with sepsis	**Recidivism (multiple admissions for sepsis)**	1.Race	1.EHR	1.Individual	Not reported	Uses univariate and bivariate chi-square analysis	Race
Chang, 2015	Healthcare Costs and Utilization Project's - California State Inpatient Database, 2009-2011, MC, n= 240,198 (Sepsis hospitalizations)	Adult patients hospitalized for sepsis; ICD-9 CM	**All-cause 30-day readmission rate**	1.Race 2.Medican income by ZIP Code 3.Urbanicity 4.Payer Category	1.Database 2.Database 3.Database 4.Database	1.Individual 2.Neighborhood 3.Neighborhood 4.Individual	Not reported	Yes, logistic regression analysis	Higher odds of 20-day readmission; Race (Black, Native American), lower income, and residence in metropolitan areas
Donnelly, 2015	UHC clinical database, MC, n= 345,657	Severe sepsis, Angus definition	**7-day readmissions 30-day readmissions**	1.Race 2. Payer type 3. Population setting (metro)4. Census region	1.EHR, linkage 2.EHR, linkage 3.EHR, linkage 4.EHR, linkage	1.Individual 2.Individual 3.Neighborhood 4.Neighborhood	Not reported	Yes, mixed effects logistic regression	Readmission: Medicaid

Goodwin, 2015	Health Care Cost and Utilization Project State Inpatient Databases (CA, FL, NY), Q1 + Q2 of 2011, MC, n= 43,452	Patients ≥ age 20 who experienced severe sepsis and/or septic shock; ICD-9 CM	**30-day readmissions**	1.Race 2.Payer type	1.Database 2.Database	1.Individual 2.Individual	Not reported	Yes, multivariate logistic regression	30-day readmission; Race (Black), insurance type (Medicare and/or Medicaid)
Galiatsatos, 2020	Johns Hopkins Bayview Medical Center, 2017, SC, n= 647	Patients ≥ age 18 who were discharged with sepsis, severe sepsis, or septic shock; ICD-10 CM, Sepsis-3 criteria	**30-day readmissions**	1.Race 2.Insurance type 3.Area deprivation index (neighborhood disadvantage)	1.Database 2.Database 3.Database; census	1.Individual 2.Individual 3.Neighborhood	Not reported	Yes, multivariable logistic regression	30-day readmission; Area Deprivation Index (Neighborhood disadvantage)
Rice, 2014 (abstract)	Healthcare Cost and Utilization Project database (FL), 2010, MC, n= not reported	Patients who survived index admission for sepsis, severe sepsis, or septic shock; ICD-9 CM	**30-day readmissions**	1.Race 2.Income 3.Insurance	1.Database 2.Database 3.Database	1.Individual 2.Individual 3.Individual	Not reported	Yes, multivariable logistic regression	30-day readmission; race (Hispanic, black) Protective - Insurance (commercial or no insurance), discharge location (discharge to hospice)

Lemay, 2014	Department of Veterans' Affairs Health Care databases, Oct 2001 - Sept 2007, MC, n= 2,727	Patients ≥ age 65 discharged with sepsis diagnosis plus at least 1 code for acute organ dysfunction; ICD-9 CM	**90-365-day mortality** **>365 day mortality**	1.Race 2.Married 3.VA Priority Group	1.Database 2.Database 3.Database	1.Individual 2.Individual 3.Individual	Not reported	Yes, cox proportional hazard regression	None
Sun, 2016	University of Pennsylvania Health System, May 2012 - July 2012, MC, n= 444	Adult sepsis survivors; ICD- 9 CM	**30-day readmission**	1.Race 2.Marital Status 3.Insurance status	1.Not reported 2.Not reported 3.Not reported	1.Individual 2.Individual 3.Individual	Not reported	Yes, multivariate logistic regression	None
Jones, 2015	University of Pennsylvania Health System, July 10 - July 2012, MC, n= 3,620	Adult sepsis survivors; ICD- 9 CM	**30-day readmission**	1.Race 2.Marital status 3.Insurance status	1.Database; EHR 2.Database; EHR 3.Database; EHR	1.Individual 2.Individual 3.Individual	Not reported	Yes, multivariate logistic regression	None

Courtright, 2020	Medicare Beneficiary Summary file, Medicare Inpatient Standard Analytic File (SAF), Outpatient SAF, Home Health SAF, Hospice SAF, Part B SAF, Chronic Conditions Warehouse, US Census data, Outcome and Assessment Information Set, 2013 - 2014, MC, n= 87,581	Adult sepsis survivors who have received at least 1 home health care visit within 1 week of discharge; ICD-9 CM	**1-year mortality** Hospitalization in the last 30 days of life Death in an acute care hospital Hospice use among decedents	1.Race/ethnicity 2.Medicaid eligibility	1.Database; census 2.Database; census	1.Individual 2.Individual	Low	Yes, multivariate logistic regression	None
Oh, 2021	National Health Insurance database, South Korea, 2011 - 2014, MC, n= 45,826	Sepsis survivors admitted for sepsis or septic shock and survived for over 365 days; ICD-10 CM	**5-year all cause mortality**	1.Residence at diagnosis of sepsis (Seoul, other metro city, or other area) 2.Income level	1.Database 2.Database	1.Neighborhood 2.Individual	Not reported	Yes, multivariable Cox regression model	5-year all cause mortality; residence at diagnosis of sepsis (other metropolitan city [than Seoul], other area), follow-up after discharge (follow-up in the same hospital).

Shankar-Hari, 2020	Intensive Care National Audit & Research Centre Case Mix Programme database & Hospital Episode Statistics database and Office for National Statistics death registrations, April 1 2009 - March 31 2014, MC, n= 94,748	Adult sepsis survivors; Sepsis-3 criteria	**Unplanned readmission (1 year)** **1-year mortality**	1.Race/ethnicity 2.IMD2015 in England quintiles	1.Database 2.Database	1.Individual 2.Neighborhood	Not reported	Yes, multivariable logistic regression	Unplanned readmission & 1-year mortality; IMD2015 in England quintiles (Most deprived)
Gadre, 2019	Healthcare Cost and Utilization Project National Readmission Data, 2013 - 2014, MC, n= 1,030,335	Sepsis survivors; ICD-9 CM	**30-day readmission**	1.Payer information 2.Median household income category for patient's ZIP code, percentile	1.Database 2.Database	1.Individual 2.Neighborhood	Low	Yes, multivariable regression model	30-day readmission; payer information (decreased risk for private insurance and self-pay), decreased risk for higher SES
Bowles, 2020	Medicare beneficiaries national dataset, July 1 2013 - June 30 2014, MC, n= 165,228	Sepsis, severe sepsis, or septic shock survivors discharged to HHC;	**Readmissions (Out to 30-day)**	1.Race/ethnicity	1.Database	1.Individual	Low	Yes, multivariate logistic regression	None

		ICD-9 CM, Angus							
Lizza, 2021	Barnes Jewish Hospital, SC, n= 3390	ED patients with ICD-9 Clinical Modification code for either severe sepsis (995.92) or septic shock (785.52). Beginning in 2015, using ICD-10 Clinical Modification codes R65.20 (severe sepsis) and R65.21 (septic shock)	**Mortality** **Readmission (1-year)**	1. Race 2. Insurance 3. Income using zip code	1. EHR 2. Linkage to Census database	1. individual 2. individual 3. neighborhood	Low	Yes, regression but no causal	Increased readmission for Black race, decreased for uninsured, no differences for mortality
Farrah, 2021	National Dataset in Canada, MC, n= 196,922	ICD-10 Revision-coded algorithm (Sepsis-2 definition), including cases with organ dysfunction (severe	**Mortality** **Readmission (1-year)**	1. Rural/urban 2. Neighborhood income 3. Ontario marginalization index (composite of	1. EHR with linkage to national database	1. Neighborhood 2. Neighborhood 3.Neighborhood/Individual	Not Reported	Propensity score	None

		sepsis) and without (nonsevere)		race, other social factors)					

Online Supplement Table 4. Characteristics of studies including (**N = 28**) versus not including (**N = 75**) social determinants of health in evaluation			
Study feature	No SDH n (%)	Included SDH, n (%)	Included SDH other than race (**N = 19**), n (%)
Year			
1990-2000	2 (3%)	0 (0%)	0 (0%)
2000-2010	9 (12%)	1 (4%)	0 (0%)
2010-present	64 (85%)	27 (96%)	19 (100%)
Cohort size			
<100	4 (5%)	0 (0%)	0 (0%)
100-<1000	29 (39%)	8 (29%)	4 (21%)
1,000-10,000	20 (27%)	6 (21%)	3 (16%)
>10,000	22 (29%)	14 (50%)	12 (63)
Multicenter	41 (55%)	19 (68%)	5 (26%)
Country of data source			
United States	41 (55%)	17 (61%)	14 (74%)
Non-U.S.	34 (45%)	11 (39%)	7 (37%)

Online Supplement Appendix 1. References for eligible studies that did not include social determinants of health

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PROTOCOL FOR SYSTEMATIC REVIEW OF THE ASSESSMENT OF SOCIAL DETERMINANTS OF HEALTH IN STUDIES OF POST-SEPSIS OUTCOMES

Rationale

Sepsis, life-threatening organ dysfunction caused by a dysregulated host response to infection, is responsible for significant acute and chronic morbidity and mortality.[refs] Two commonly studied adverse outcomes for sepsis survivors are i) rehospitalization and of ii) long-term mortality. Systematic reviews have reported a mean 1-year rehospitalization rate of 39.0% (95% CI, 22.0%-59.4%) and a mean 1-year mortality rate of 16.1% (95% CI, 14.1%-18.1%) among adult sepsis survivors. A systematic review of rehospitalization risk factors (predictors) for sepsis survivors that included 56 studies highlighted characteristics that were predictors of increased risk of readmission across studies, categorized as generic, sepsis-specific, and hospital-level factors.

Despite the increased attention to recovery after sepsis, an important topic that remains unknown is the association of social determinants of health (SDH) with adverse outcomes. The clinical significance of SDH has been demonstrated in numerous other settings, and SDH may be a particularly salient contributor to the risk of hospital readmission. Indeed, a number of studies have demonstrated the relationship between SDH and hospital readmission. We found no systematic reviews to date that explore the relationship between SDH and risk for rehospitalization or mortality after sepsis in adults. Understanding the social determinants that impact adverse outcomes after sepsis is important to inform interventions that adequately address the whole-person needs of sepsis survivors.

Purpose and objectives

The proposed review aims to summarize knowledge and identify gaps in evidence about the relationship between social determinants and post-sepsis outcomes.

Research question

Is there evidence to support the association between social determinants of health and mortality or rehospitalization after sepsis in adults?

Methods

This study will conform to the PRISMA guidelines for systematic reviews, and is registered with the International prospective register of systematic reviews (PROSPERO CRD pending).

Inclusion criteria

We will search for both randomized clinical trials (RCTs) and observational studies published since 1992 in the following databases: MEDLINE (including in-process and non-indexed citations), Cochrane Library and its associated databases (including Database of Abstracts of Reviews of Effects (DARE), Web of Science, and EMBASE. The search strategy will use controlled vocabulary terms and text words for sepsis and post-sepsis mortality or hospital readmission, and the search set will be limited to humans and English language. Subject headings will be exploded and mapped to the appropriate controlled vocabulary terms. The year 1992 was chosen to coincide with the year of publication of the first consensus sepsis definitions. The full electronic search strategy for MEDLINE is presented in Appendix 1 and modified for other databases. The initial literature search was on XX and was updated on YY.

Study Selection

Two reviewers will independently screen citations for those reporting either of the primary outcomes after index sepsis discharge i) all-cause mortality or ii) hospital readmission in the title or abstract. The full text of any citation considered potentially relevant by either reviewer will be retrieved. Eligible studies have a cohort, case–control, or Randomized-Controlled Trial (RCT) design; enrolled hospital survivors of an admission for sepsis; and reported all-cause

readmission or late mortality as a primary outcome. For inclusion into the review, sepsis was defined as infection-related organ dysfunction managed in hospital setting and includes studies that used the equivalent terminology of sepsis, severe sepsis, and septic shock. We will exclude studies restricted to children and to special populations such as those with HIV, cancer, and other immunocompromised states. We will also exclude studies enrolling survivors of uncomplicated infections, such as pneumonia, without referring to organ dysfunction or to International Classification of Diseases (ICD) codes for sepsis, severe sepsis, or septic shock in their index sepsis case definitions. We will screen reference lists of included studies, related review articles, and editorials.

Data collection and validity assessment

When two or more studies are identified that reported data from the same patient cohort, the most relevant article will be identified as the most recent full manuscript. Three authors will extract data from the included studies and issues of uncertainty will be resolved by consensus. We will include full manuscripts and conference abstracts for assessing the count of studies assessing social determinants but only the full manuscripts for assessing social determinants as independent risk factors. From each of the included studies, we will extract data on study design, number of patients, duration of follow-up, description of index sepsis admission, rehospitalization events, mortality events, and social determinants assessed as independent risk factors for rehospitalization (see Data Abstraction form, Appendix 2).

Assessment of methodological quality

For studies reported as full-text manuscripts, study quality will be assessed using domains from the modified Newcastle Ottawa Score (NOS) checklist. These include patient selection (cohort data source for representativeness of exposed cohort, selection of nonexposed cohort, exposure ascertainment using sepsis definitions or International Classification of Diseases

codes), minimum duration of follow-up for outcome to occur of 30 days, assessment of confounding (use of comparator populations, matching, restriction, stratification, and regression), and outcome (outcome assessment, length, and adequacy of follow-up). The SDH reported as independent risk factors for mortality and rehospitalization will be identified from studies that used regression models to account for confounders.

Ethics and Dissemination

Approval from a research ethics board will not be required for this review. Once completed, the review will be submitted for publication in a peer-reviewed journal, and findings will be presented in local and national forums.

Data analysis

The co-primary outcomes are all-cause rehospitalization and all-cause mortality occurring after index hospitalization among sepsis survivors, at follow-up time points as reported in studies. We will provide a descriptive comparison of social determinants included among studies, the methodological quality of SDH data, and those social determinants identified as increasing the risk of rehospitalization or mortality in sepsis survivors between studies.

Discussion

This review will be the first review to focus on social determinants of health in the context of post-sepsis adverse outcomes. Most current research focuses on biologic or illness-related risk factors for adverse outcomes after sepsis. Such risk factors include age, gender, comorbidities, and severity of illness. Although understanding biologic risk factors is important to addressing post-sepsis outcomes, social factors have been implicated in the progression and development of many health conditions and are likely important contributors to post-sepsis outcomes as well. The discovery of which social determinants affect recovery after sepsis is pivotal to advancing knowledge to further guide support and management approaches in this vulnerable population.

Table 1. Description of studies assessing SDH and post-sepsis outcomes

Study ID (Author, year)	Cohort data source (single/ multi center, n =)	Cohort description	Follow-up method and outcome assessment	Social determinants included	Social determinant assessment method (HER, survey, census)	Social determinant level (individual or neighborhood)	Missing data on social determinants (low, high)	Confounder assessment	Non-sepsis comparisons

Table 2. Summary of full manuscripts included in the review and SDOH associated with increased risk of rehospitalization or mortality in studies reporting regression models

Study ID	Study characteristics (Data source and sample size)	Regression model for the outcome	SDOH with independent association with rehospitalization	SDOH with independent association with mortality

Appendix

Search strategy

(("sepsis"[MeSH Terms] OR "shock, septic"[MeSH Terms] OR "sepsis"[Text Word] OR "severe sepsis"[Text Word] OR "sepsis syndrome*"[Text Word] OR "septic*"[Text Word]) AND (1992/01/01:2021/05/01[Date - Publication] AND "english"[Language]) AND ((("patient readmission"[MeSH Terms] OR "patient readmission"[MeSH Terms] OR "readmission*"[Text Word] OR "rehospitalization*"[Text Word] OR "rehospitalisation*"[Text Word]) AND (1992/01/01:2021/05/01[Date - Publication] AND "english"[Language])) OR (("late mortality"[Text Word] OR "long-term mortality"[Text Word] OR ("post-discharge"[Text Word] OR "after discharge"[Text Word])) AND (1992/01/01:2021/05/01[Date - Publication] AND "english"[Language])))) AND ((1992/1/1:2021/5/1[pdat]) AND (english[Filter])