Supplemental Appendix for

Frequency and Types of Healthcare Encounters in the Week Preceding a Sepsis Hospitalization: A Systematic Review

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eTable 1. Database Search Strategies

Database	Search Strategies
PubMed (New)	(((((((sepsis[MeSH:NoExp]) OR (shock, septic[MeSH Terms])) OR (sepsis[Title/Abstract])) OR (septicemia*[Title/Abstract])) OR (severe sepsis[Title/Abstract])) OR (septic shock[Title/Abstract])) AND (((((((((hospitalization[MeSH Terms]) OR (hospitalization*[Title/Abstract])) OR (inpatient admission*[Title/Abstract])) OR (hospital admission*[Title/Abstract])) OR (length of stay[Title/Abstract])) OR (stay length[Title/Abstract])) OR (hospital stay*[Title/Abstract])) OR (patient admission*[Title/Abstract])) OR (patient handoff*[Title/Abstract])) OR (patient readmission*[Title/Abstract])) OR (patient transfer*[Title/Abstract]))) AND ((((((((((health services[MeSH:NoExp]) OR (health services for the aged[MeSH Terms])) OR (diagnostic errors[MeSH Terms])) OR (critical care[MeSH:NoExp])) OR (ambulatory care[MeSH Terms])) OR (delayed diagnoses[MeSH Terms])) OR (time-to-treatment[MeSH Terms])) OR (transitional care[MeSH Terms])) OR (primary health care[MeSH Terms])) OR ((health service*[Title/Abstract]) OR (health care service*[Title/Abstract]) OR (healthcare service*[Title/Abstract]) OR (healthcare exposure*[Title/Abstract]) OR (health care exposure*[Title/Abstract]) OR (health care utilization*[Title/Abstract]) OR (healthcare utilization*[Title/Abstract]) OR (primary care[Title/Abstract]) OR (primary health care[Title/Abstract]) OR (primary healthcare[Title/Abstract]) OR (ambulatory care[Title/Abstract]) OR (outpatient health service*[Title/Abstract]) OR (outpatient service*[Title/Abstract]) OR (urgent care*[Title/Abstract]) OR (clinic visit*[Title/Abstract]) OR (health services for the aged[Title/Abstract]) OR (geriatric health services[Title/Abstract]) OR (diagnostic errors[Title/Abstract]) OR (misdiagnosis*[Title/Abstract]) OR (critical care[Title/Abstract]) OR (delayed diagnos*[Title/Abstract]) OR (late diagnos*[Title/Abstract]) OR (time to treatment*[Title/Abstract]) OR (delayed treatment*[Title/Abstract]) OR (treatment delay*[Title/Abstract]) OR (transitional care[Title/Abstract]) OR (emergency department*[Title/Abstract]) OR (patient transfer*[Title/Abstract]) OR (continuum of care[Title/Abstract]) OR (continuity of care[Title/Abstract])))
Scopus	(((TITLE-ABS-KEY (sepsis) OR TITLE-ABS-KEY (septicemia) OR TITLE-ABS-KEY ({severe sepsis}) OR TITLE-ABS-KEY ({septic shock}))) AND ((TITLE-ABS-KEY ({health service}) OR TITLE-ABS-KEY ({health care service}) OR TITLE-ABS-KEY ({healthcare service}) OR TITLE-ABS-KEY ({healthcare exposure}) OR TITLE-ABS-KEY ({health care exposure}) OR TITLE-ABS-KEY ({health care utilization}) OR TITLE-ABS-KEY ({healthcare utilization}) OR TITLE-ABS-KEY ({primary care}) OR TITLE-ABS-KEY ({primary health care}) OR TITLE-ABS-KEY ({primary healthcare}) OR TITLE-ABS-KEY ({ambulatory care}]) OR TITLE-ABS-KEY ({outpatient health service}) OR TITLE-ABS-KEY ({outpatient service}) OR TITLE-ABS-KEY ({urgent care}) OR TITLE-ABS-KEY ({clinic visit}) OR TITLE-ABS-KEY ({health services for the aged}) OR TITLE-ABS-KEY ({geriatric health services}) OR TITLE-ABS-KEY ({diagnostic errors}) OR TITLE-ABS-KEY (misdiagnosis) OR TITLE-ABS-KEY ({critical care}) OR TITLE-ABS-KEY ({delayed diagnosis}) OR TITLE-ABS-KEY ({late

	diagnosis}) OR TITLE-ABS-KEY ({time to treatment}) OR TITLE-ABS-KEY ({delayed treatment}) OR TITLE-ABS-KEY ({treatment delay}) OR TITLE-ABS-KEY ({transitional care}) OR TITLE-ABS-KEY ({emergency department}) OR TITLE-ABS-KEY ({patient transfer}) OR TITLE-ABS-KEY ({prehospital}) OR TITLE-ABS-KEY ({continuum of care}) OR TITLE-ABS-KEY ({continuity of care}))) AND ((TITLE-ABS-KEY (hospitalization*) OR TITLE-ABS-KEY ({inpatient admission*}) OR TITLE-ABS-KEY ({hospital admission*}) OR TITLE-ABS-KEY ({length of stay}) OR TITLE-ABS-KEY ({stay length}) OR TITLE-ABS-KEY ({hospital stay*}) OR TITLE-ABS-KEY ({patient admission*}) OR TITLE-ABS-KEY ({patient handoff*}) OR TITLE-ABS-KEY ({patient readmission*}) OR TITLE-ABS-KEY ({patient transfer*}))))
CINAHL	TI sepsis OR TI septicemia* OR TI "severe sepsis" OR TI "septic shock" OR AB sepsis OR AB septicemia* OR AB "severe sepsis" OR AB "septic shock" OR (MH "Sepsis") OR (MH "Shock, Septic") AND (MH "Hospitalization") OR (MH "Aged, Hospitalized") OR TI hospitalization* OR AB hospitalization* OR TI "inpatient admission*" OR AB "inpatient admission*" OR TI hospital admission*" OR AB "hospital admission*" OR TI "length of stay" OR AB "length of stay" OR TI "stay length" OR AB "stay length" OR TI "hospital stay*" OR AB "hospital stay*" OR TI "patient admission*" OR AB "patient admission*" OR TI "patient handoff*" OR AB "patient handoff*" OR TI "patient readmission*" OR AB "patient readmission*" OR TI "patient transfer*" OR AB "patient transfer*" AND (MH "Health Services") OR (MH "Health Services for the Aged") OR (MH "Diagnostic Errors+") OR (MH "Critical Care") OR (MH "Rapid Response (Emergency Care)") OR (MH "Ambulatory Care") OR (MH "Diagnosis, Delayed") OR (MH "Treatment Delay") OR (MH "Transitional Care") OR (MH "Primary Health Care") OR TI "health service*" OR AB "health service*" OR TI "health care service*" OR AB "health care service*" OR TI "healthcare service*" OR AB "healthcare service*" OR TI "healthcare exposure*" OR AB "healthcare exposure*" OR TI "health care exposure*" OR AB "health care exposure*" OR TI "health care utilization*" OR AB "health care utilization*" OR TI ""healthcare utilization*" OR AB "healthcare utilization*" OR TI "primary care" OR AB "primary care" OR TI "primary health care" OR AB "primary health care" OR TI "primary healthcare" OR AB "primary healthcare" OR TI "ambulatory care" OR AB "ambulatory care" OR TI "outpatient health service*" OR AB "outpatient health service*" OR TI "outpatient service*" OR AB "outpatient service*" OR TI "urgent care*" OR AB "urgent care*" OR TI "clinic visit*" OR AB "clinic visit*" OR TI "health services for the aged" OR AB "health services for the aged" OR TI "geriatric health services" OR AB "geriatric health services" OR TI "diagnostic errors" OR AB "diagnostic errors" OR TI misdiagnosis* OR AB misdiagnosis* OR TI "critical care" OR AB "critical care" OR TI "delayed diagnos*" OR AB "delayed diagnos*" OR TI "late diagnos*" OR AB "late diagnos*" OR TI "time to treatment*" OR AB "time to treatment*" OR TI "delayed treatment*" OR AB "delayed treatment*" OR TI "treatment delay*" OR AB "treatment delay*" OR TI "transitional care" OR AB "transitional care" OR TI "emergency department*" OR AB "emergency department*" OR TI "patient transfer*" OR AB "patient transfer*" OR TI "continuum of care" OR AB "continuum of care" OR TI "continuity of care" OR AB "continuity of care"

Cochrane Library	sepsis OR septic shock OR septicemia OR severe sepsis in Title Abstract Keyword AND hospitalization OR inpatient admission OR hospital admission OR length of stay OR stay length OR hospital stay OR patient admission OR patient handoff OR patient readmission OR patient transfer in Title Abstract Keyword AND health service OR health care service OR healthcare service OR healthcare exposure OR health care exposure OR health care utilization OR healthcare utilization OR primary care OR primary health care OR primary healthcare OR ambulatory care OR outpatient health service OR outpatient service OR urgent care OR clinic visit OR health services for the aged OR geriatric health services OR diagnostic errors OR misdiagnosis OR critical care OR delayed diagnosis OR late diagnosis OR time to treatment OR delayed treatment OR treatment delay OR transitional care OR emergency department OR patient transfer OR continuum of care OR continuity of care in Title Abstract Keyword

eTable 2. Risk of Bias Assessment†

Study	Selection				Comparability	Outcome			
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of the study	Comparability of cohorts	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up	Total
Liu 2018	*	*	*	*	*	*	*	*	8
Loots 2018	*	*	*	*	*	*	*	*	8
Buchman 2019	*	*	*	*	0	*	*	*	7
Fay 2020	*	*	*	*	0	*	*	*	7
Cecil 2021	*	*	*	*	*	*	*	*	8
Miller 2021	*	*	*	*	0	*	*	*	7

†In the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies, a maximum of one point (denoted by *) can be awarded for each item within the Selection and Outcome categories. A maximum of two stars may be given for Comparability assessment.

eTable 3. Characteristics of Included Studies

Reference	Study Period	Study Design	Study Population & Country	Pre-Sepsis Admission Healthcare Exposure Timeframe of Study	Patient Age	Comorbidities	Method of Identifying Sepsis	Classification of Pre-Sepsis Healthcare Encounter	Number of Patients
Liu 2018	Kaiser Permanente Northern California: 2010-2013 Veterans Affairs: 2009	Retrospective Cohort	21 Kaiser Permanente Northern California Hospitals 114 Veterans Affairs Hospitals Patients' first sepsis hospitalization with sepsis present on admission (United States)	On the day of sepsis hospitalization or 7 days prior	Kaiser Permanente Northern California: 74 (62-83) years[a] Veterans Affairs: 69 (61-80) years[a]	Charlson Comorbidity Index: Kaiser Permanente Northern California: 2 (1-3)[a] Veterans Affairs: 3 (1-5)[a]	ICD-9 codes for infection and acute organ dysfunction	Pre-sepsis admission encounter categorized as: hospitalization, SNF, ED, urgent care, primary care visit, specialty care visit	Kaiser Permanente Northern California: n =14,658 sepsis hospitalizations Veterans Affairs: n = 31,369 sepsis hospitalizations
Loots 2018	2011-2015	Retrospective Cohort	Patients admitted to ICU of single center (Netherlands)	Up to 72 hours before hospital admission	70 (58-78) years[a]	Cardiovascular disease: 32.3% Diabetes: 33.1% Chronic obstructive pulmonary disease: 25.2% Kidney disease: 13.4% Malignancy: 7.9% Immuno-suppression: 7.9% Multimorbidity 39.4%	Medical record review (sepsis diagnosis during ICU stay)	Assessment of healthcare exposures before sepsis hospitalization focused on general practitioner (typically located with hospital emergency departments and managed by large scale cooperatives)	263 ICU admissions with sepsis

Buchman 2019	2012-2017	Retrospective Cohort	Medicare Fee-For Service beneficiaries with sepsis inpatient admission and nonsepsis inpatient admission (United States)	7 days leading up to inpatient admission	Sepsis inpatient stay: <65=16.1% 65-74 =27.7% 75-84 =30.2% >85=26.1% Non-sepsis inpatient stay: <65=14.2% 65-74 =32.7% 75-84 =31.3% >85=21.9%	Hypertension: ~82% Dyslipidemia: ~70% Type II diabetes: ~40%	ICD-9 and ICD-10 code sets for sepsis (including septicemia, sepsis, severe sepsis, and septic shock)	Healthcare Common Procedure Coding System	23,032,730 inpatient admissions
Fay 2020	2014-2015	Retrospective Cohort	28 hospitals in Centers for Disease Control and Prevention Emerging Infections Program (United States)	Outpatient encounters in the 7 days before hospital admission Any pre-hospital medical treatment within 30 days of admission	64 (53-75) years[a]	Alcohol use: 10.9% Diabetes: 35.9% Immuno-suppression: 26.3% Pulmonary disease: 24.5% Vascular disease: 30.2% Chronic Kidney Disease: 18.7%	ICD-9 codes for severe sepsis or septic shock	Outpatient encounter recorded as medical/ pediatric specialty, ED or urgent care, or primary care Pre-hospital medical treatment defined as receipt of antimicrobial drug, chemotherapy, wound care, dialysis, or surgery within 30 days of admission	1,078 patients admitted with sepsis or septic shock

Cecil 2021	2014-2017	Retrospective Cohort	Patients from the Clinical Practice Research Datalink data base (a national primary care database) with an emergency hospital admission (United Kingdom)	Within 3 days of the emergency hospital admission	66 (41-81) years[a]	≥ 2 comorbidities: 59.5% 1 comorbidity: 21.4% No comorbidity: 19.1%	ICD-10 codes for sepsis	Primary care consultation with general practitioner (consultations with other healthcare professionals excluded)	405,878 emergency admissions, 5,383 of which were for sepsis
Miller 2021	2017	Retrospective Cohort	Patients admitted to a single center, with an established outpatient provider within the center's health system (United States)	Within 1 calendar day of admission	58 (49-70) years[a]	Diabetes: 47.5% Chronic kidney disease: 27.1% Chronic pulmonary disease: 23.7% Metastatic cancer: 21.2% Liver disease: 18.6%	ICD-10 codes for severe sepsis or septic shock	Clinic types included primary care, specialty care, and urgent care. Visits classified as routine or acute.	1150 patients admitted with severe sepsis or septic shock and established outpatient provider

[a]Median (interquartile range)

ICD= International Classification of Diseases; SNF=subacute nursing facility; ED=emergency department; ICU=intensive care unit

eTable 4. Study Outcomes

Reference	Percent of Patients with Prehospital Encounter		Requirement for ICU care		Hospital Mortality		Hospital Length of Stay[a]	
Liu 2018	Kaiser Permanente Northern California: Pre-sepsis healthcare visit: 7,747/14,658 (52.9%)	Veterans Affairs: Pre-sepsis healthcare visit: 14,280/31,369 (45.5%)	Kaiser Permanente Northern California: Pre-sepsis healthcare visit: Yes: n=3,838 (49.5%) No: n=3,272 (47.3%) p=0.10 for comparison	Veterans Affairs: Pre-sepsis healthcare visit: Yes: n=5,638 (39.5%) No: 7,143 (41.8%) p <0.01 for comparison	Kaiser Permanente Northern California: Pre-sepsis healthcare visit: Yes: n = 1,374 (17.7%) No: n = 953 (13.8%) p<0.01 for comparison	Veterans Affairs: Pre-sepsis healthcare visit: Yes: n = 1,974 (13.8%) No: n = 2,219 (13%) p=0.03 for comparison	Kaiser Permanente Northern California: Pre-sepsis healthcare visit: Yes: 5 (3-9) days No: 5 (3-8) days p<0.01 for comparison	Veterans Affairs: Pre-sepsis healthcare visit: Yes: 7 (4-14) days No: 7 (4-14) days p=0.57 for comparison
Loots 2018	127/263 (48.3%) Breakdown of general practitioner encounters: Home visit following telephone triage: 59.8% Clinic visit: 18.9% Telephone consultation: 8.7% Directly via ambulance following telephone triage: 12.6%		All patients admitted to ICU per study design		General practitioner encounter before sepsis hospitalization: Yes: 32/127 (25.2%) No: 31/136 (22.8%)		General practitioner encounter before sepsis hospitalization: Yes: 13.6 (9.6-22.5) days No: 13.4 (7.8-22.6) days	
Buchman 2019	Sepsis stay: 1,279,564/ 6,731,827 (19.0%) with office/outpatient visit		Not reported		Sepsis stay: 32.6%		Not reported	

Fay 2020	Outpatient medical encounter within 7 days: 260/1078 (24.1%) Pre-hospital medical treatment within 30 days: 447/1078 (41.5%)	68.6% of entire cohort	285/1078 (26.4%) within 30 days of sepsis diagnosis	7 (4-14) days
Cecil 2021	1,546/5383 (28.7%) patients admitted with sepsis had contact with general practitioner in the 3 days prior to admission	Not reported	Not reported	Not reported
Miller 2021	118/1150 (10.3%) seen in clinic: 74.6% day of admission and 25.4% the day prior to admission 73.7% of visits were routine vs. 26.3% acute	37/118 (31.4%)	10/118 (8.5%)	6 days

[a]Median (interquartile range)
ICU=intensive care unit