What Happens to our Septic Patients after Hospital Discharge?

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Ohio Hospital Association

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Disclosures

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- Key Funding
  - NIH/NIGMS
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- This talk does not necessarily represent the views of the U.S. Government or Department of Veterans Affairs

Outline

- A patient case
- Life after sepsis

In August:

- What can we do to help improve long-term outcomes

Case

49 year old female, mid-level manager at a large corporation.

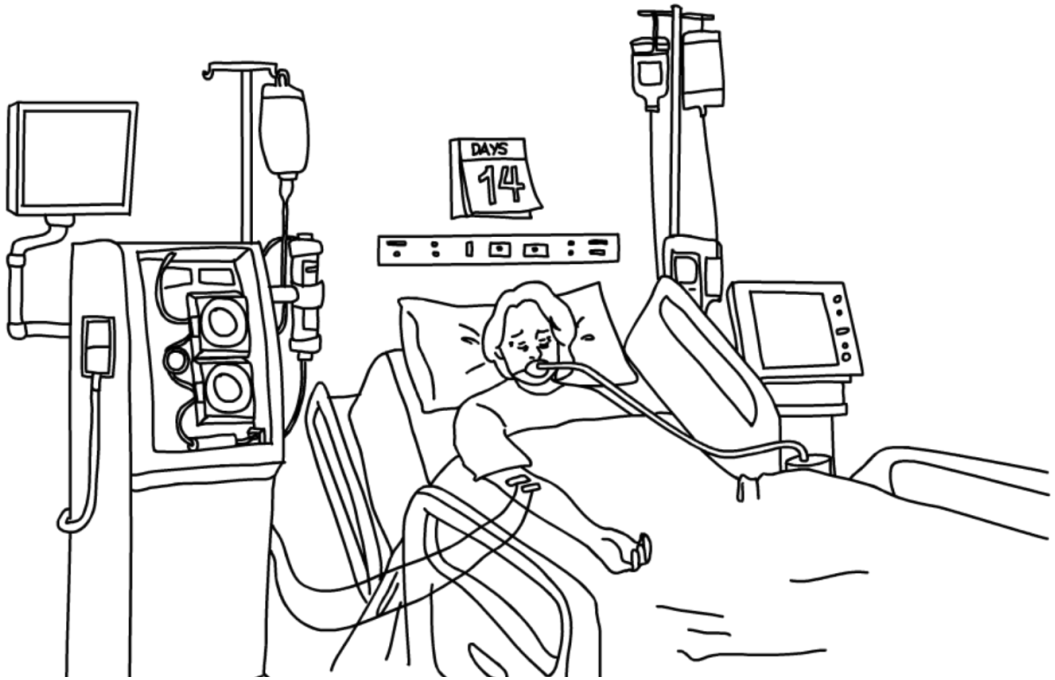
PMH: HTN, mild asthma

- Presented to ED with fevers, chills, sore throat, cough
- Admitted with community-acquired pneumonia
- Treated with IV antibiotics

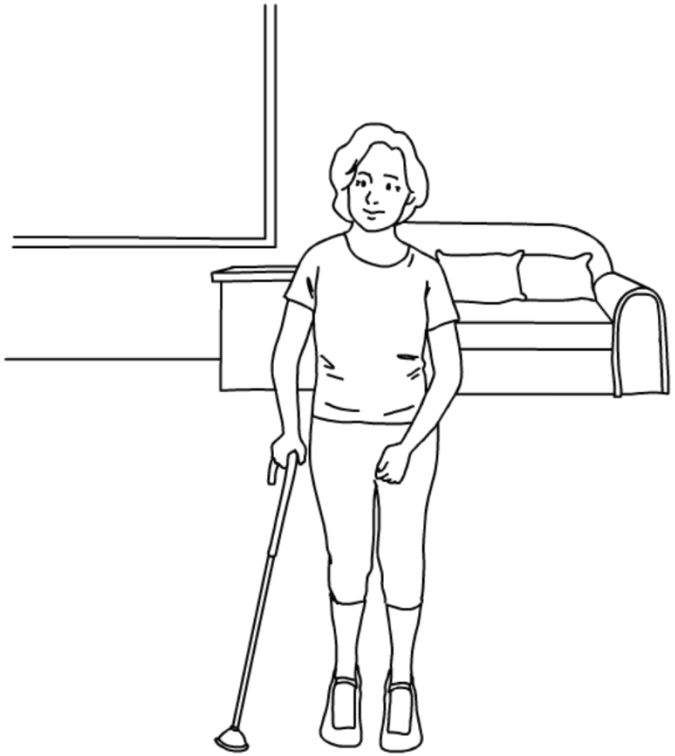
Situation

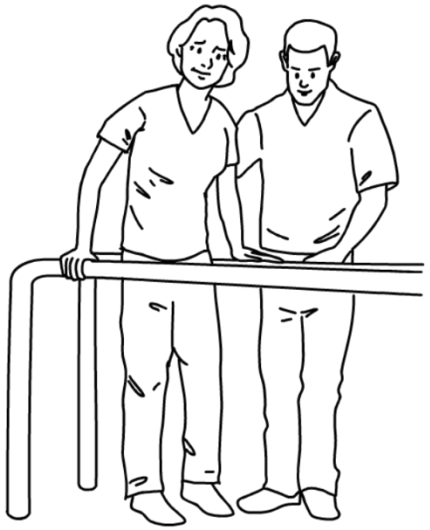
- ARDS
- Septic Shock

- Day #36: extubated
- Day #43: to rehab

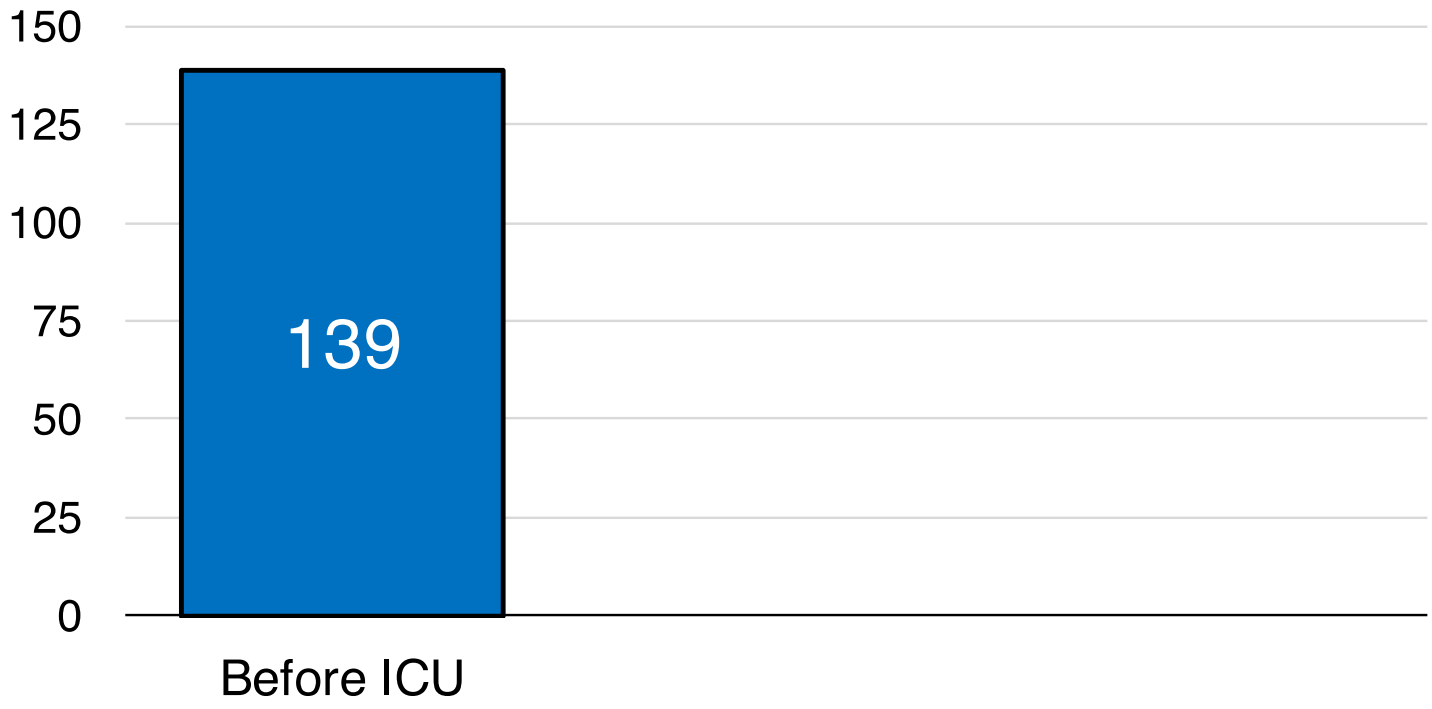


3 Weeks of Inpatient Rehab

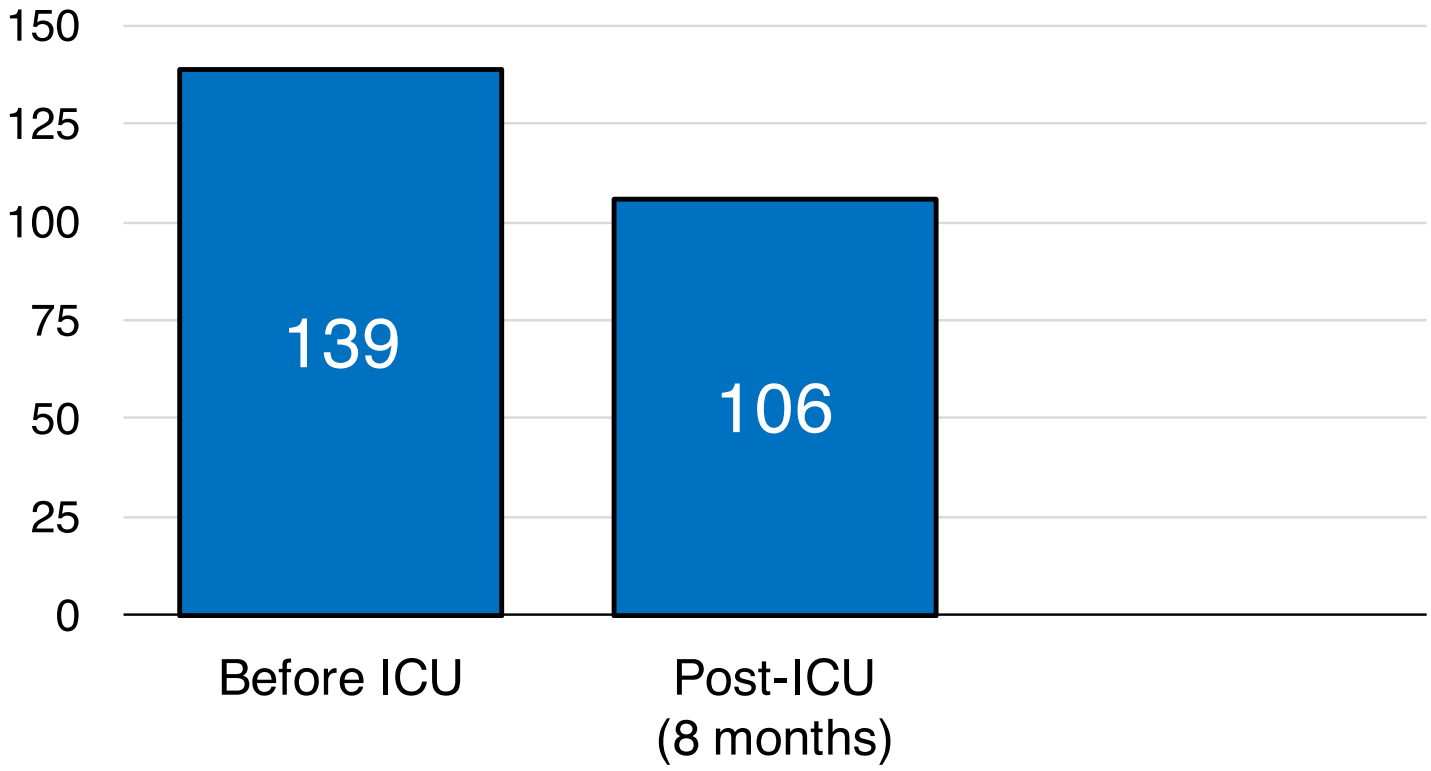




IQ Testing, [1]



IQ Testing, cont'd



Jackson *et al*. *Southern Med J*. 2009.

Interview with Gordon Bernard, 2004

Is there a residue in sepsis survivors who have had multi-organ failures or dysfunctions?

Interview with Gordon Bernard, 2004, cont'd

Is there a residue in sepsis survivors who have had multi-organ failures or dysfunctions?

"Most people return to normal or near-normal lives even if they have had severe organ failures…

Most surviving patients come back to being normal."

Our Patient

“I just don’t feel right…

Is this because of my sepsis?”

Symptoms

- Weight loss
- Muscle weakness
- Fatigue
- Reduced QOL
- Reduced walk distance
- Inability to return to work

The NEW ENGLAND JOURNAL of MEDICINE

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One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome

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ABSTRACT

BACKGROUND

As more patients survive the acute respiratory distress syndrome, an understanding of the long-term outcomes of this condition is needed.

METHODS

We evaluated 109 survivors of the acute respiratory distress syndrome 3, 6, and 12 months after discharge from the intensive care unit. At each visit, patients were interviewed and underwent a physical examination, pulmonary-function testing, a six-minute–walk test, and a quality-of-life evaluation.

RESULTS

Patients who survived the acute respiratory distress syndrome were young (median age, 45 years) and severely ill (median Acute Physiology, Age, and Chronic Health Evaluation score, 23) and had a long stay in the intensive care unit (median, 25 days). Patients had lost 18 percent of their base-line body weight by the time they were discharged from the intensive care unit and stated that muscle weakness and fatigue were the reasons for their functional limitation. Lung volume and spirometric measurements were normal by 6 months, but carbon monoxide diffusion capacity remained low throughout the 12-month follow-up. No patients required supplemental oxygen at 12 months, but 6 percent of patients had arterial oxygen saturation values below 88 percent during exercise. The median score for the physical role domain of the Medical Outcomes Study 36-item Short-Form General Health Survey (a health-related quality-of-life measure) increased from 0 at 3 months to 25 at 12 months (score in the normal population, 84). The distance walked in six minutes increased from a median of 281 m at 3 months to 422 m at 12 months; all values were lower than predicted. The absence of systemic corticosteroid treatment, the absence of illness acquired during the intensive care unit stay, and rapid resolution of lung injury and multiorgan dysfunction were associated with better functional status during the one-year follow-up.

CONCLUSIONS

Survivors of the acute respiratory distress syndrome have persistent functional disability one year after discharge from the intensive care unit. Most patients have extrapulmonary conditions, with muscle wasting and weakness being most prominent.

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N Engl J Med 2003;348:683-93.

The New England Journal of Medicine

Herridge *et al. NEJM.* 2003.

ICU Patients

Neurologic Critical Care

Six-month neuropsychological outcome of medical intensive care unit patients

James C. Jackson, PsyD; Robert P. Hart, PhD; Sharon M. Gordon, PsyD; Ayumi Shintani, PhD; Brenda Truman, MSN; Lisa May, BSN; E. Wesley Ely, MD, MPH

Objective: To examine neuropsychological function, depression, and quality of life 6 months after discharge in patients who received mechanical ventilation in the intensive care unit.

Design: Prospective cohort study.

Setting: Tertiary care, medical and coronary intensive care unit of a university-based medical center.

Study Population: A total of 275 consecutive, mechanically ventilated patients from a medical intensive care unit were prospectively followed. At 6 months, 157 were alive, of whom 41 (26%) returned for extensive follow-up testing.

Measurement and Main Results: Neuropsychological testing and assessment of depression and quality of life were performed at 6-month follow-up. Seven of 41 patients were excluded from further analysis due to preexisting cognitive impairment determined via surrogate interviews using the Modified Blessed Dementia Rating Scale and a review of medical records. On the basis of strict criteria derived from normative data, we found that 11 of 34 patients (32%) were neuropsychologically impaired. Impairment was generally diffuse but occurred primarily in areas of psychomotor speed, visual and working memory, verbal fluency, and visuo-construction. The rate of neuropsychological deficits in the study population was markedly higher than population norms for mild dementia. Scores on the Geriatric Depression Scale–Short Form were significantly more abnormal in the neuropsychologically impaired group than in the nonimpaired group at hospital discharge ($p = .04$) and at 6-month follow-up ($p = .02$), and clinically significant depression was found in 27% of impaired subjects at hospital discharge and in 36% at 6-month follow-up. No differences were observed between groups in quality of life as measured with the Short Form Health Survey-12 at discharge or 6-month follow-up.

Conclusions: Prolonged neuropsychological impairment is common among survivors of the medical intensive care unit and occurs with greater than anticipated frequency when compared with relevant normative data. Future investigations are warranted to elucidate the nature of the association between critical illness, neuropsychological impairment, depression, and decreased quality of life. (Crit Care Med 2003; 31:1226–1234)

Key Words: cognitive impairment; critical illness; delirium; depression; encephalopathy; mechanical ventilation; neuropsychological assessment; psychoactive medications; quality of life; respiratory disease

Rapid technological and medical advances have combined to facilitate the treatment of critically ill patients. Indeed, many patients recover from critical illness they may not have survived a decade ago (1–5). Those who survive often fail to return to baseline levels of health and report diminished quality of life (6–8). In addition, the psychiatric consequences of critical illness are being studied with heightened scrutiny (9–13).

In the last decade, researchers have become increasingly interested in the relationship between critical illness and cognitive outcomes, and a small but impressive body of evidence is emerging that documents pervasive neuropsychological impairment among patients after critical illness (14). Among patients with sepsis, encephalopathy has been reported to occur acutely in as many as 70% of cases (15, 16), and diffuse neuropsychological deficits have been documented in individuals with toxic shock syndrome (17), yet few data exist regarding the long-term neuropsychological consequences of sepsis. In the acute respiratory distress syndrome, 80% of survivors in one cohort were found to have impaired memory, attention, concentration, or decreased processing speed a year after hospital discharge (18), and in another report, nearly 25% had mild cognitive impairment even 6 yrs after their intensive care unit (ICU) stay (19). However, there are no prospective reports describing neuropsychological impairment in the general medical ICU population. In addition, no information is currently available on the prognostic significance of delirium during an ICU stay in regard to long-term neuropsychological outcome. The few data that exist for general medical patients in studies that take into account preexisting cognitive impairment suggest that long-term mental status is worse in patients with a history of delirium (20–22).

We therefore undertook the current investigation to study the prevalence and types of neuropsychological impairment among medical ICU patients who had developed respiratory failure necessitating

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Dr. Ely was supported, in part, by the AFAR Pharmacology in Aging Grant, the Paul Beeson Faculty Scholar Award from the Alliance for Aging Research, and a K23 from the National Institutes of Health (AG01023-01A1).

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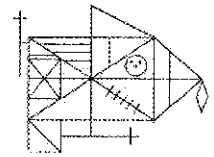
- Depression
- Cognitive Impairment



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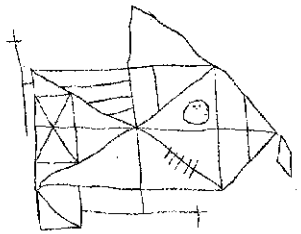
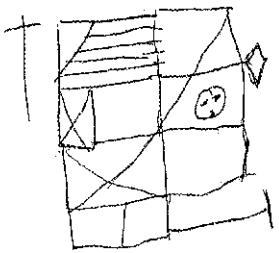


Near normal rendition by unimpaired 69 y/o pulmonary embolus survivor

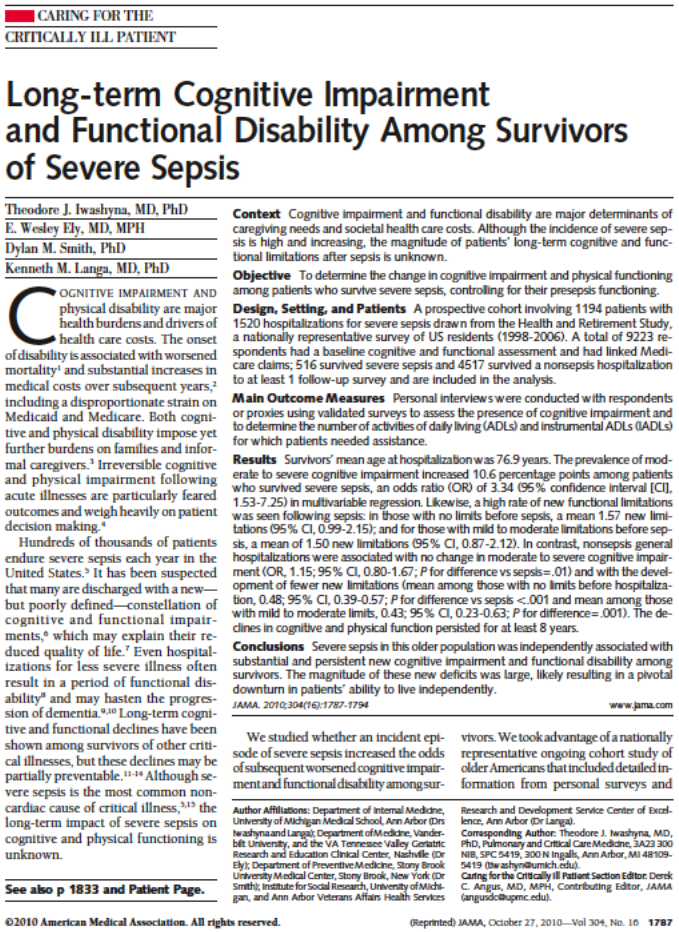


Moderate to severely impaired 89 y/o Pneumonia survivor

Severely impaired 72 y/o ARDS survivor

Jackson *et al. Crit Care Med.* 2003.

Disability



CARING FOR THE CRITICALLY ILL PATIENT

Long-term Cognitive Impairment and Functional Disability Among Survivors of Severe Sepsis

Theodore J. Iwashyna, MD, PhD
E. Wesley Ely, MD, MPH
Dylan M. Smith, PhD
Kenneth M. Langa, MD, PhD

Context Cognitive impairment and functional disability are major determinants of caregiving needs and societal health care costs. Although the incidence of severe sepsis is high and increasing, the magnitude of patients' long-term cognitive and functional limitations after sepsis is unknown.

Objective To determine the change in cognitive impairment and physical functioning among patients who survive severe sepsis, controlling for their presepsis functioning.

Design, Setting, and Patients A prospective cohort involving 1194 patients with 1520 hospitalizations for severe sepsis drawn from the Health and Retirement Study, a nationally representative survey of US residents (1998-2006). A total of 9223 respondents had a baseline cognitive and functional assessment and had linked Medicare claims; 516 survived severe sepsis and 4517 survived a nonsepsis hospitalization to at least 1 follow-up survey and are included in the analysis.

Main Outcome Measures Personal interviews were conducted with respondents or proxies using validated surveys to assess the presence of cognitive impairment and to determine the number of activities of daily living (ADLs) and instrumental ADLs (IADLs) for which patients needed assistance.

Results Survivors' mean age at hospitalization was 76.9 years. The prevalence of moderate to severe cognitive impairment increased 10.6 percentage points among patients who survived severe sepsis, an odds ratio (OR) of 3.34 (95% confidence interval [CI], 1.53-7.25) in multivariable regression. Likewise, a high rate of new functional limitations was seen following sepsis: in those with no limits before sepsis, a mean 1.57 new limitations (95% CI, 0.99-2.15); and for those with mild to moderate limitations before sepsis, a mean of 1.50 new limitations (95% CI, 0.87-2.12). In contrast, nonsepsis general hospitalizations were associated with no change in moderate to severe cognitive impairment (OR, 1.15; 95% CI, 0.80-1.67; *P* for difference vs sepsis=.01) and with the development of fewer new limitations (mean among those with no limits before hospitalization, 0.48; 95% CI, 0.39-0.57; *P* for difference vs sepsis <.001 and mean among those with mild to moderate limits, 0.43; 95% CI, 0.23-0.63; *P* for difference=.001). The declines in cognitive and physical function persisted for at least 8 years.

Conclusions Severe sepsis in this older population was independently associated with substantial and persistent new cognitive impairment and functional disability among survivors. The magnitude of these new deficits was large, likely resulting in a pivotal downturn in patients' ability to live independently.

JAMA. 2010;304(16):1787-1794 www.jama.com

COGNITIVE IMPAIRMENT AND physical disability are major health burdens and drivers of health care costs. The onset of disability is associated with worsened mortality[1] and substantial increases in medical costs over subsequent years,[2] including a disproportionate strain on Medicaid and Medicare. Both cognitive and physical disability impose yet further burdens on families and informal caregivers.[3] Irreversible cognitive and physical impairment following acute illnesses are particularly feared outcomes and weigh heavily on patient decision making.[4]

Hundreds of thousands of patients endure severe sepsis each year in the United States.[5] It has been suspected that many are discharged with a new—but poorly defined—constellation of cognitive and functional impairments,[6] which may explain their reduced quality of life.[7] Even hospitalizations for less severe illness often result in a period of functional disability[8] and may hasten the progression of dementia.[9,10] Long-term cognitive and functional declines have been shown among survivors of other critical illnesses, but these declines may be partially preventable.[11-14] Although severe sepsis is the most common noncardiac cause of critical illness,[3,15] the long-term impact of severe sepsis on cognitive and physical functioning is unknown.

See also p 1833 and Patient Page.

We studied whether an incident episode of severe sepsis increased the odds of subsequent worsened cognitive impairment and functional disability among survivors. We took advantage of a nationally representative ongoing cohort study of older Americans that included detailed information from personal surveys and

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Caring for the Critically Ill Patient Section Editor: Derek C. Angus, MD, MPH, Contributing Editor, *JAMA* (angusdc@upmc.edu).

- In national sample with baseline measurement, new and persistent disability is common after sepsis

Iwashyna, *et al*. *JAMA*. 2010.

Post-Intensive Care Syndrome

Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference*

Dale M. Needham, MD, PhD; Judy Davidson, DNP, RN; Henry Cohen, PharmD; Ramona O. Hopkins, PhD; Craig Weinert, MD, MPH; Hannah Wunsch, MD, MSc; Christine Zawistowski, MD; Anita Bemis-Dougherty, PT, DPT; Susan C. Berney, PT, PhD; O. Joseph Bienvenu, MD, PhD; Susan L. Brady, MS; Martin B. Brodsky, PhD; Linda Denehy, PT, PhD; Doug Elliott, RN, PhD; Carl Flatley, DDS; Andrea L. Harabin, PhD; Christina Jones, RN, PhD; Deborah Louis, RN; Wendy Meltzer, JD; Sean R. Muldoon, MD, MPH, MS; Jeffrey B. Palmer, MD; Christiane Perme, PT, CCS; Marla Robinson, OTR/L, MSc, BCPR; David M. Schmidt, MD, PhD; Elizabeth Scruth, RN; Gayle R. Spill, MD; C. Porter Storey, MD; Marta Render, MD; John Votto, DO; Maurene A. Harvey, RN, MPH, FCCM

Background: **Millions of patients are discharged from intensive care units annually. These intensive care survivors and their families frequently report a wide range of impairments in their health status which may last for months and years after hospital discharge.**

Objectives: **To report on a 2-day Society of Critical Care Medicine conference aimed at improving the long-term outcomes after critical illness for patients and their families.**

Participants: **Thirty-one invited stakeholders participated in the conference. Stakeholders represented key professional organizations and groups, predominantly from North America, which are involved in the care of intensive care survivors after hospital discharge.**

Design: **Invited experts and Society of Critical Care Medicine members presented a summary of existing data regarding the potential long-term physical, cognitive and mental health problems after intensive care and the results from studies of postintensive care unit interventions to address these problems. Stakeholders provided reactions, perspectives, concerns and strategies aimed at improving care and mitigating these long-term health problems.**

Measurements and Main Results: **Three major themes emerged from the conference regarding: (1) raising awareness and education, (2) understanding and addressing barriers to practice, and (3) identifying research gaps and resources. Postintensive care syndrome was agreed upon as the recommended term to describe new or worsening problems in physical, cognitive, or mental health status arising after a critical illness and persisting beyond acute care hospitalization. The term could be applied to either a survivor or family member.**

Conclusions: **Improving care for intensive care survivors and their families requires collaboration between practitioners and researchers in both the inpatient and outpatient settings. Strategies were developed to address the major themes arising from the conference to improve outcomes for survivors and families. (Crit Care Med 2012; 40:502–509)**

Key Words: aftercare; caregivers; continuity of patient care; critical care; follow-up studies; intensive care units; outcome assessment; patient care planning; patient care team; postintensive care syndrome; stress disorders, post-traumatic; survivors

*See also p. 681.

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Dr. Needham has received grant support from the National Institutes of Health. Dr. Bienvenu has received funding from the National Institutes of Health. Ms. Louis is employed by Kaiser Permanente. Dr. Muldoon is employed by and has stock ownership in Kindred Healthcare. The remaining authors have not disclosed any potential conflicts of interest.

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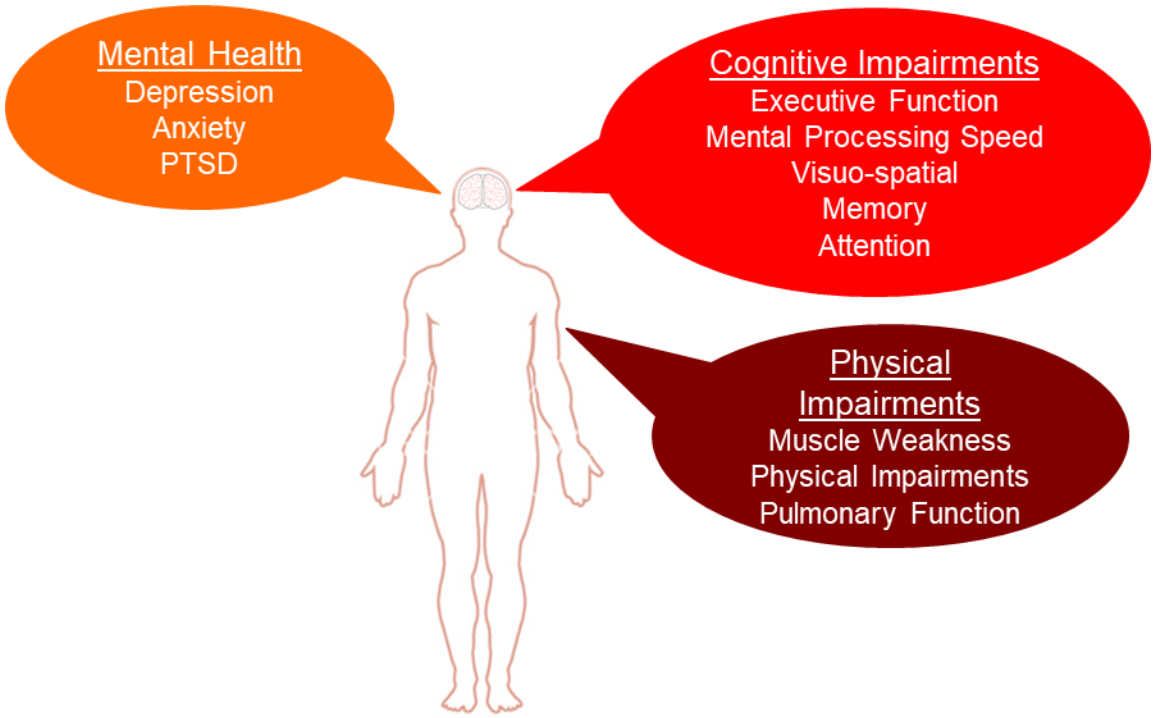
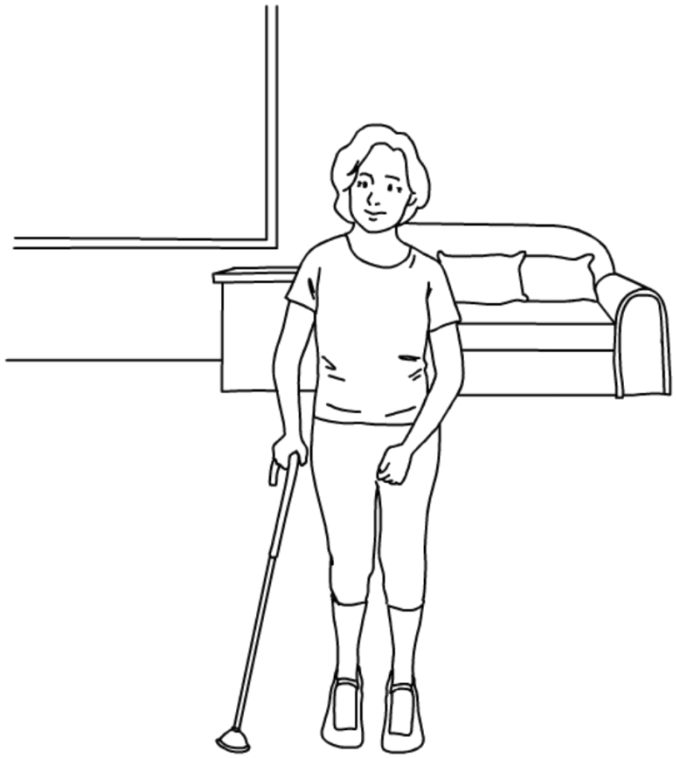


Needham, *et al*. *Crit Care Med*. 2012.

Our Patient, 2



“Am I going to die from this?”

More Resarch Needed

RESEARCH Open Access

Evidence for a causal link between sepsis and long-term mortality: a systematic review of epidemiologic studies

Manu Shankar-Hari[1,2*†], Michael Ambler[1†], Viyaasan Mahalingasivam[1], Andrew Jones[1,2], Kathryn Rowan[3] and Gordon D. Rubenfeld[4]

Conclusions: Epidemiologic criteria for a causal relationship between sepsis and post-acute mortality were not consistently observed. Additional epidemiologic studies with recent patient level data that address the pre-illness trajectory, confounding, and varying control groups are needed to estimate sepsis-attributable additional risk and modifiable risk factors to design interventional trials.

Shankar-Hari, *et al*. *Crit Care*. 2016.

Mortality Link

RESEARCH

Late mortality after sepsis: propensity matched cohort study

Hallie C Prescott,[1, 2, 3, 4] John J Osterholzer,[1, 4] Kenneth M Langa,[1, 2, 3, 5] Derek C Angus,[6] Theodore J Iwashyna[1, 2, 3, 4, 5, 7]

Hypothesis:

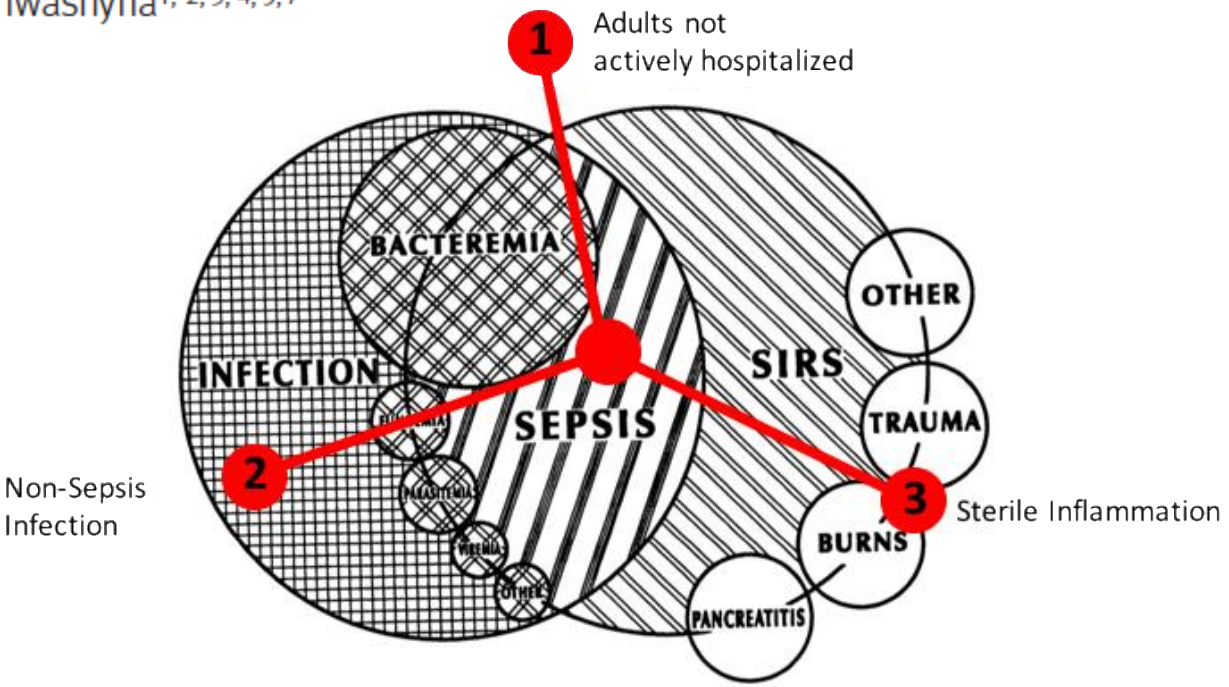
Sepsis itself is associated with excess late mortality.

Late Mortality

RESEARCH

Late mortality after sepsis: propensity matched cohort study

Hallie C Prescott,[1, 2, 3, 4] John J Osterholzer,[1, 4] Kenneth M Langa,[1, 2, 3, 5] Derek C Angus,[6] Theodore J Iwashyna[1, 2, 3, 4, 5, 7]



Bone, *et al. Chest*. 1992.
Prescott, *et al*. *BMJ.* 2016.

37,000 Older Americans Studied

RESEARCH

Late mortality after sepsis: propensity matched cohort study

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- NIA-funded cohort
- 1992 - ongoing
- 37,000 older Americans
- Detailed survey data
- Linked Medicare records

Prescott, *et al*. *BMJ*. 2016.

Study Cohort

RESEARCH

Late mortality after sepsis: propensity matched cohort study

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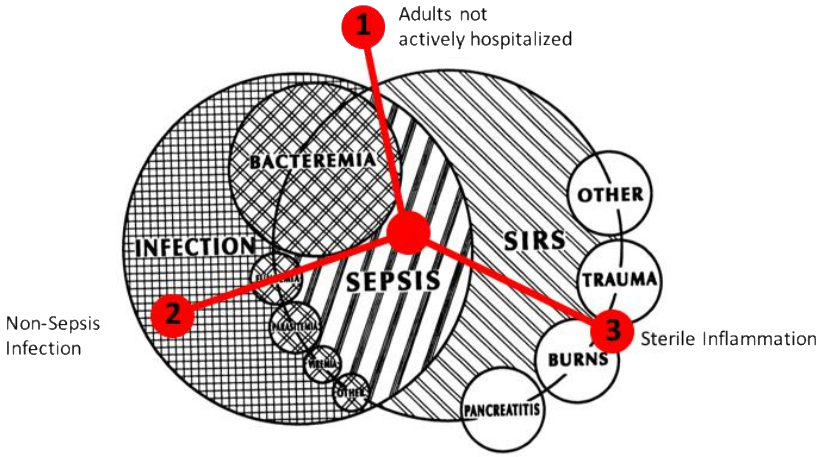

Demographics	Healthcare Utilization	Economic Status	Health Status	Comorbidity Burden
Age	Hospitalization	Total Wealth	Functional Limitations	Charlson Index
Gender	Sepsis Hospitalization	Government Assistance	Self-Rating of Health	CHF
Race	Residence in Nursing Facility		Body Mass Index	Cancer
Ethnicity				Connective Tissue Disease
Married/ partnered				Dementia
				Liver Disease
				Renal Disease

Hospitalization Variable

RESEARCH

Late mortality after sepsis: propensity matched cohort study

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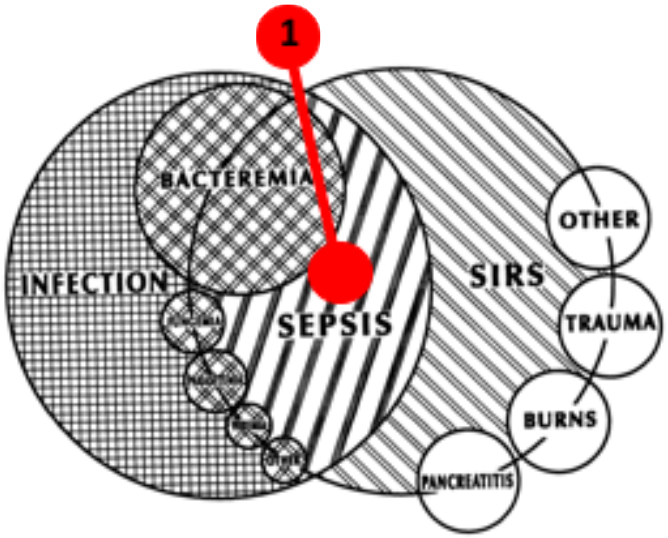


1. Sepsis versus Non-hospitalized

Adjusted Odds Ratio
for Late* Mortality:

Absolute Increase
in Late Mortality:

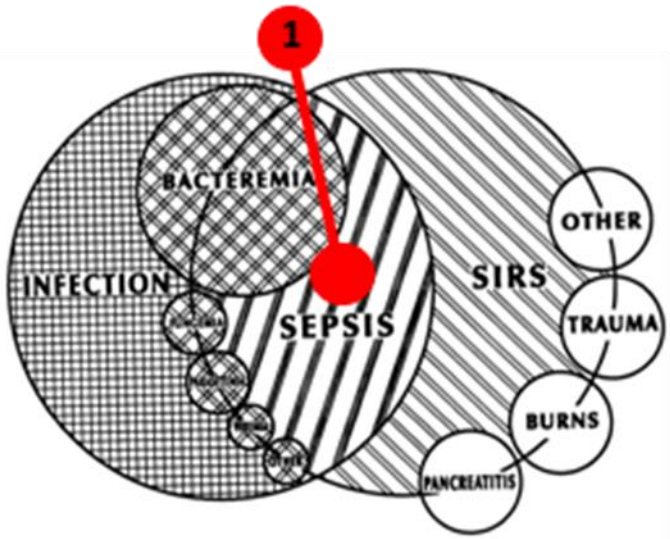
*Late mortality = mortality in the 31 days – 2 years post-sepsis

Late Mortality Increase

RESEARCH

Late mortality after sepsis: propensity matched cohort study

Hallie C Prescott,[1, 2, 3, 4] John J Osterholzer,[1, 4] Kenneth M Langa,[1, 2, 3, 5] Derek C Angus,[6] Theodore J Iwashyna[1, 2, 3, 4, 5, 7]



1. Sepsis versus Non-hospitalized

Adjusted Odds Ratio
for Late* Mortality:
3.5 ($p < 0.001$)

Absolute Increase
in Late Mortality:
22%

*Late mortality = mortality in the 31 days – 2 years post-sepsis

Sepsis vs Non-Sepsis Infection

RESEARCH

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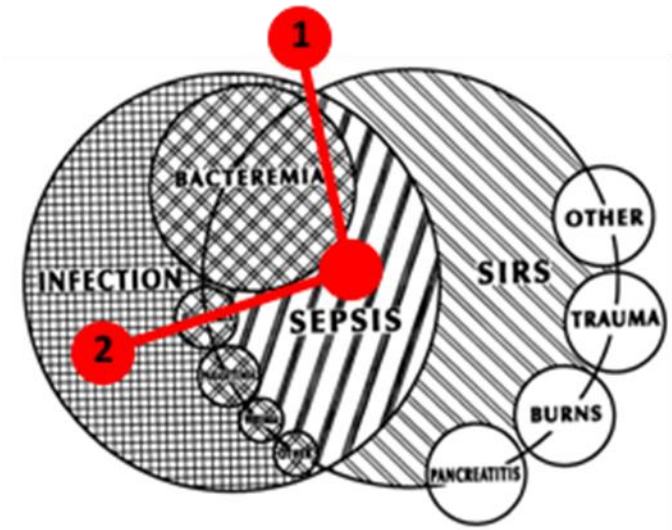

2 Sepsis versus Non-sepsis Infection

Adjusted Odds Ratio
for Late* Mortality:
1.6 (p = 0.01)

Absolute Increase
in Late Mortality:
10%

*Late mortality = mortality in the 31 days – 2 years post-sepsis

Sterile Inflammation

RESEARCH

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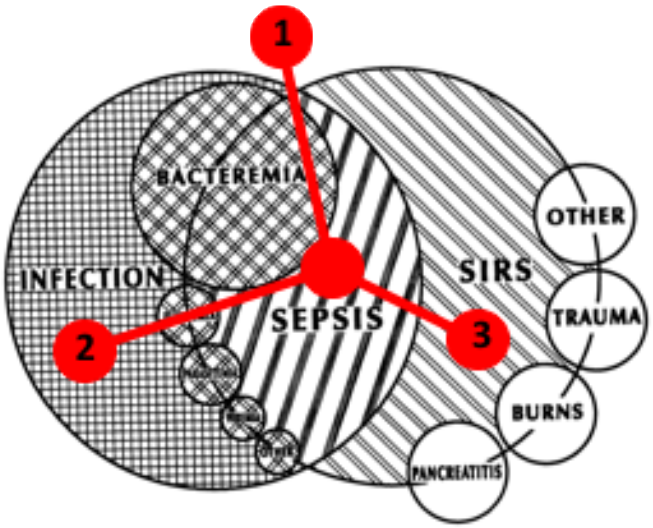

Sepsis versus Sterile Inflammation

Adjusted Odds Ratio
for Late* Mortality:
2.3 ($p < 0.001$)

Absolute Increase
in Late Mortality:
16%

*Late mortality = mortality in the 31 days – 2 years post-sepsis

Overall Factors Studied

RESEARCH

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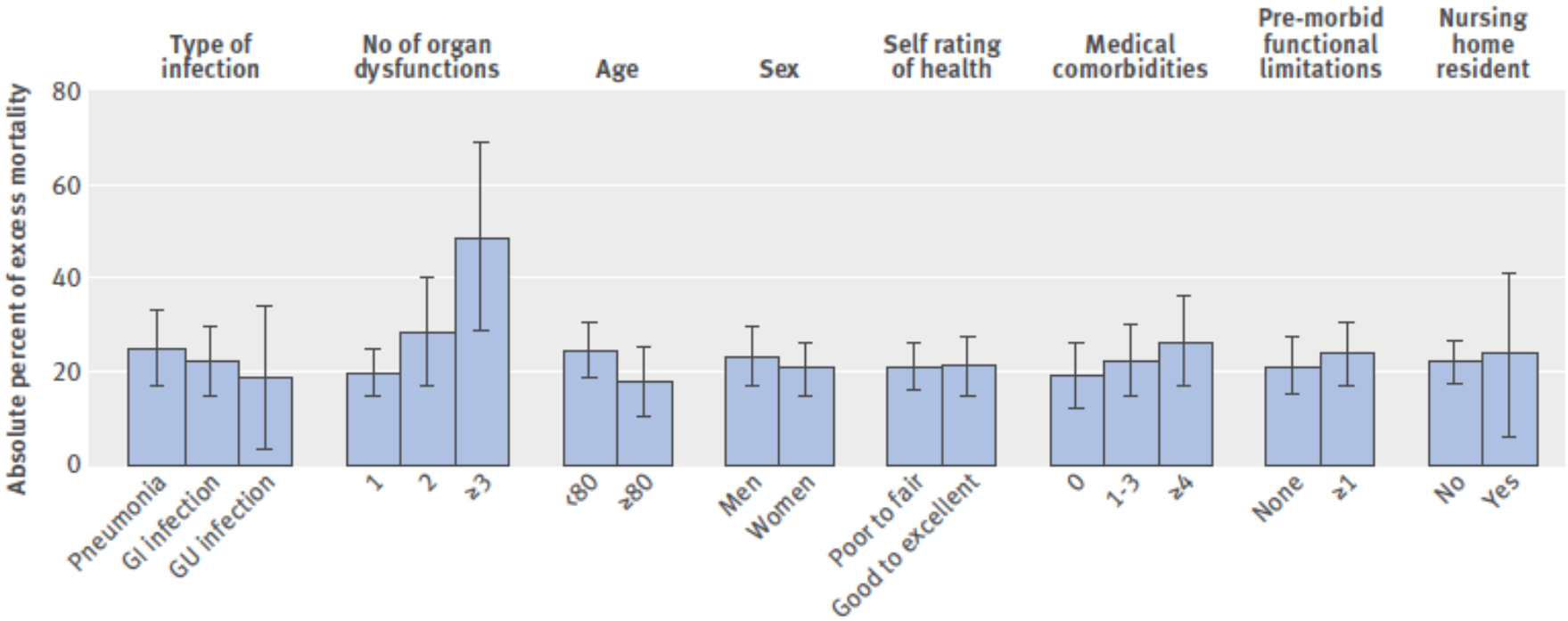

Mortality Conclusions

RESEARCH

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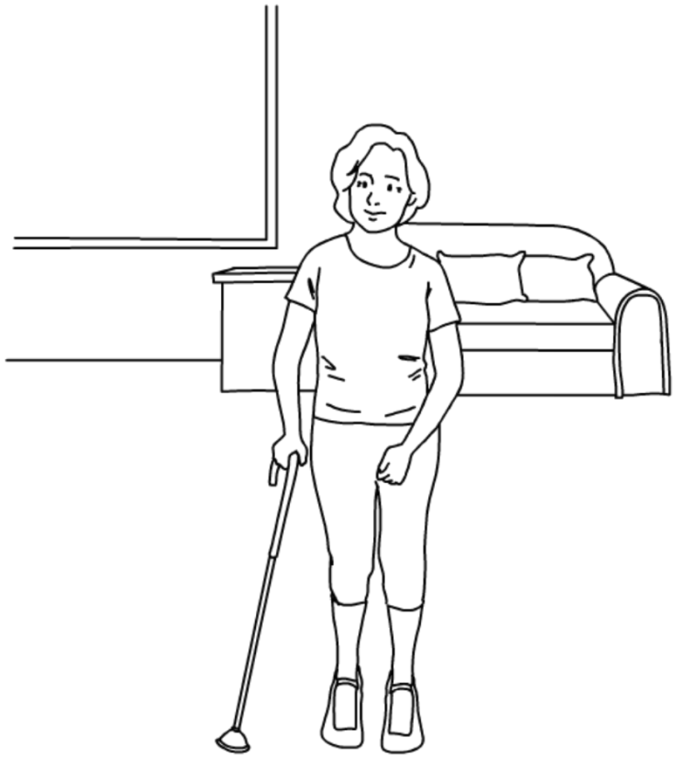
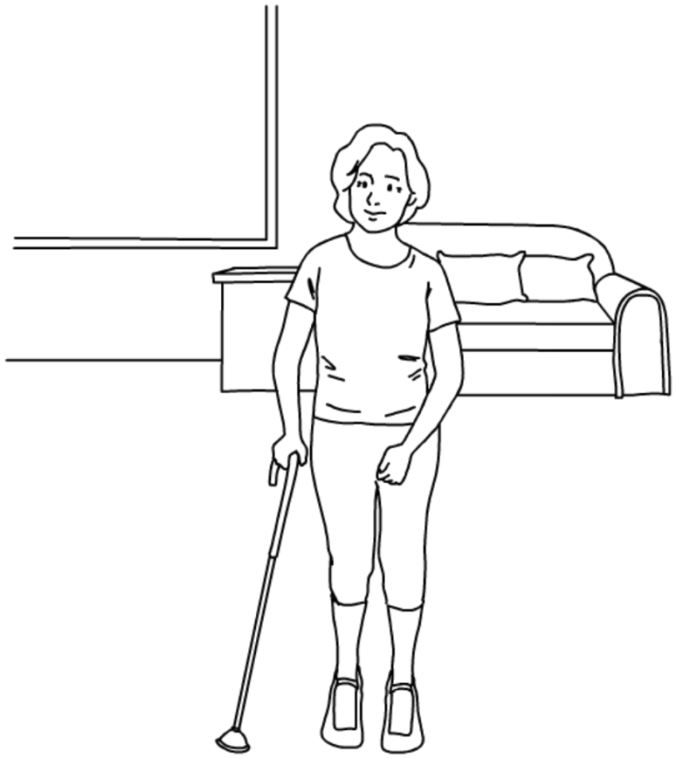
- Conclusions:
- More than 1 in 5 sepsis survivors with a late death not explained by pre-sepsis health status
- Amenable to intervention?

Our Patient, 3



“If I do survive,
what will the next year look like?”

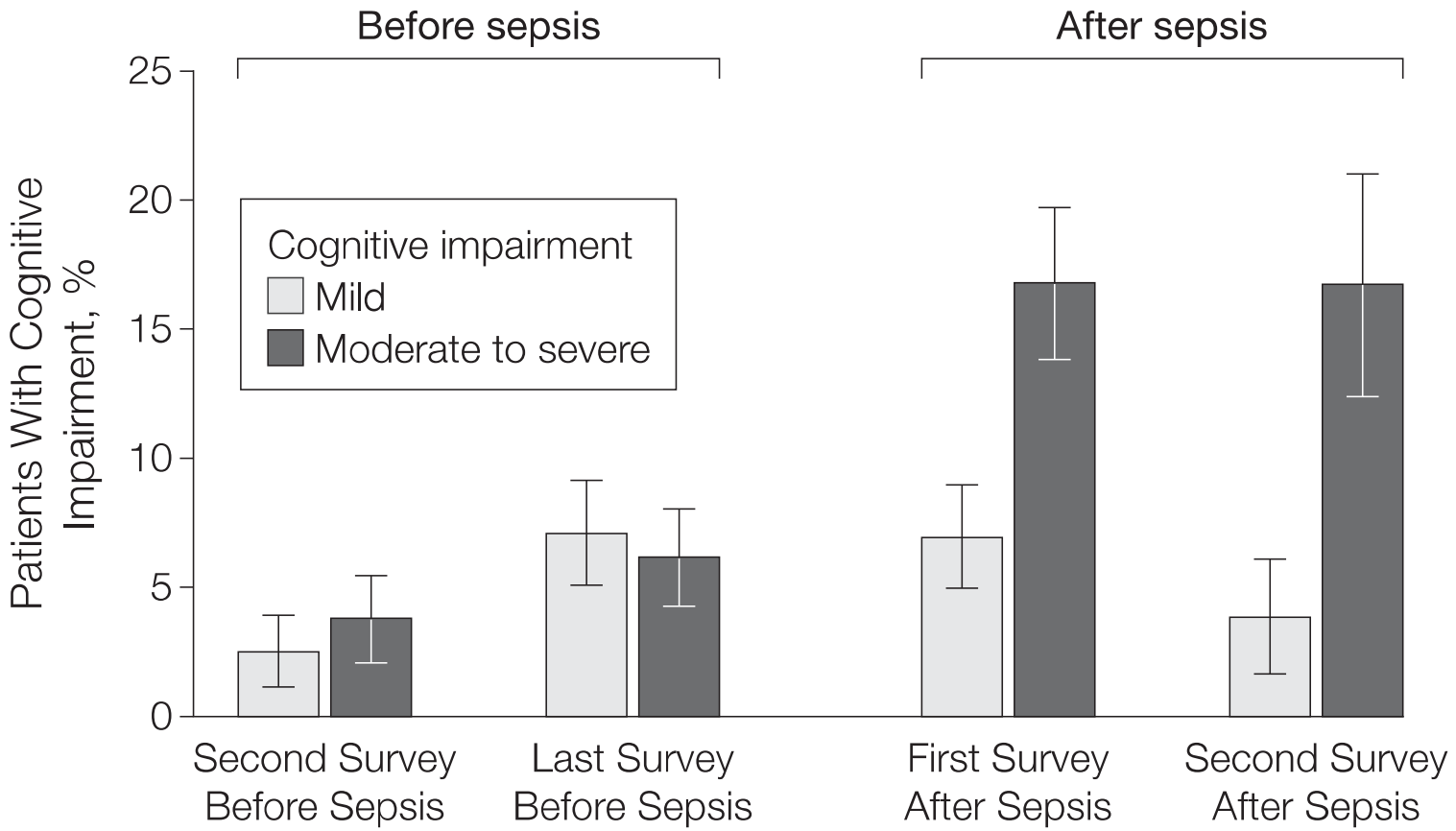
Our Patient, 4



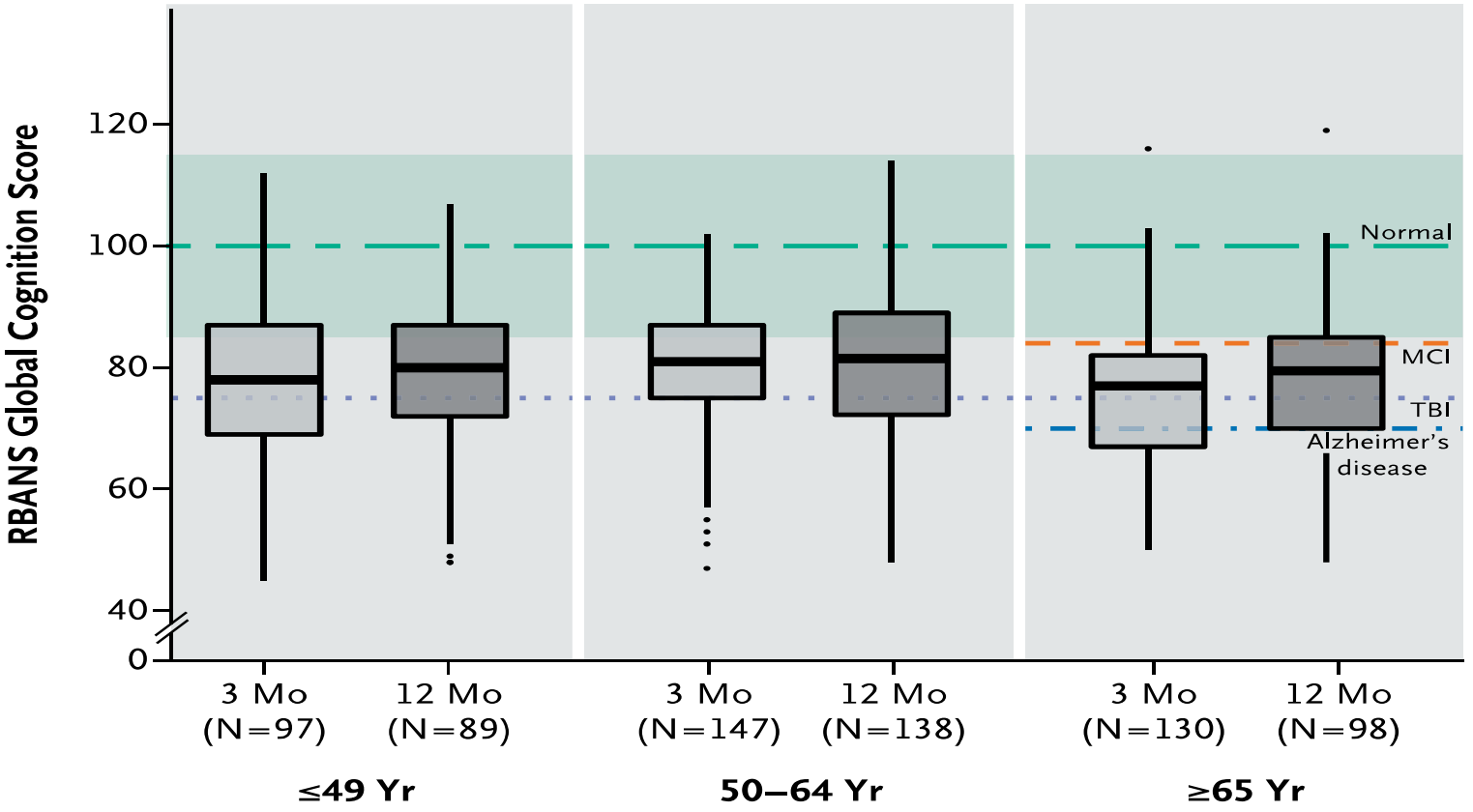
“If I do survive,
what will the next year look like?”

- Cognitive Impairment
- Physical Disability
- Mental Health Impairment

Cognitive Impairment



Not Just Older Patients



Paripande, *et al*. *NEJM.* 2013.

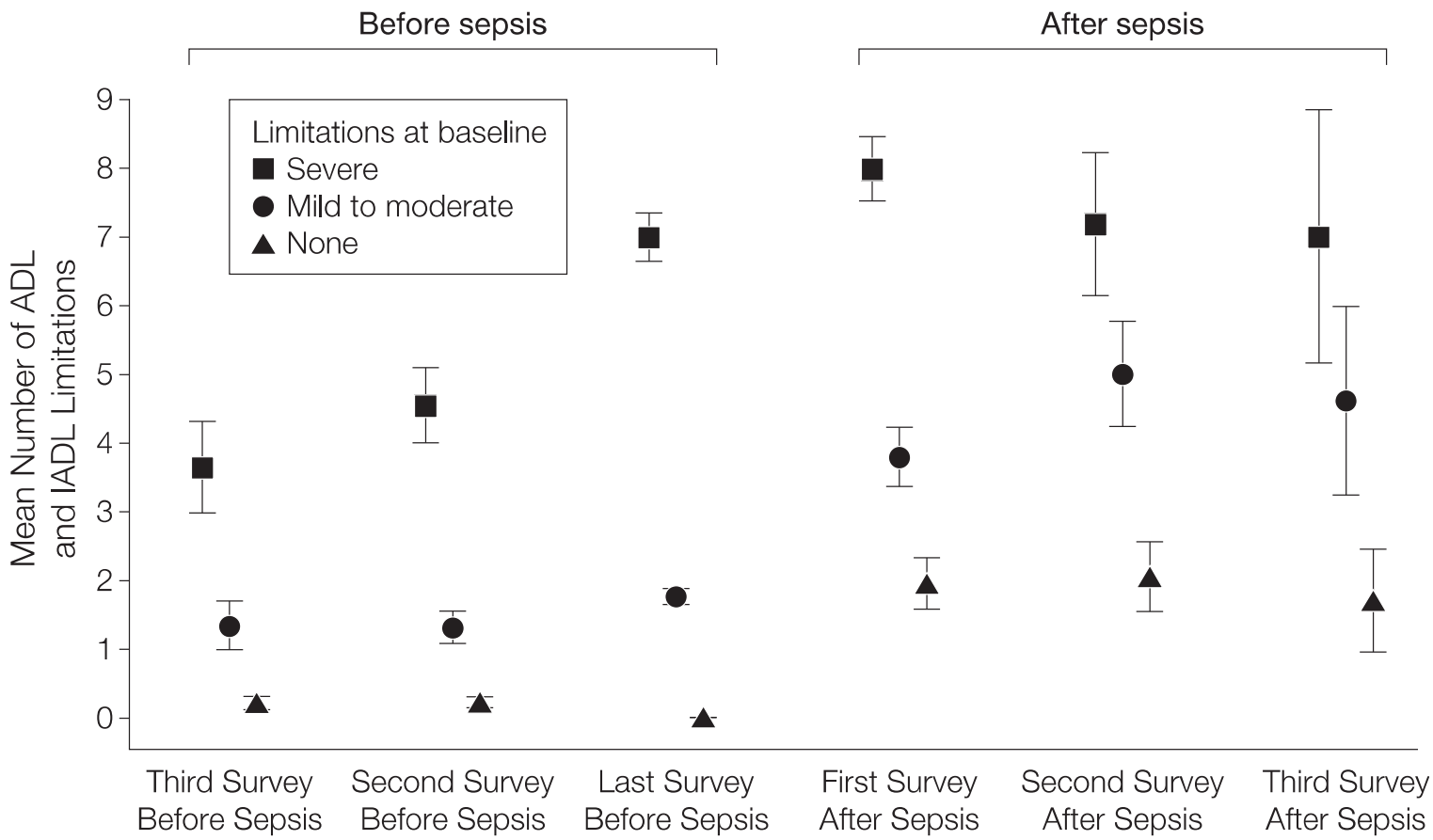
Not Just Sickest Patients

TABLE 2. RISK OF DEMENTIA DID NOT VARY BASED ON SEVERITY OF INFECTION*

Variable	Number of Cases	Hazard Ratio	95% Confidence Interval	*P* Value
Pneumonia	320	2.24	1.62–3.11	<0.0001
Pneumonia with organ dysfunction†	82	2.06	0.92–4.61	0.07
Pneumonia without organ dysfunction	240	2.19	1.52–3.16	<0.0001
Severe sepsis	198‡	2.28	1.38–3.77	0.001
Other infections	1,049§	1.98	1.61–2.43	<0.0001

Shah, *et al*. *AJRCCM*. 2013.

Physical Disability



Iwashyna, *et al*. *JAMA*. 2010.

Physical Disability, 2

RESEARCH ARTICLE Open Access

Functional outcomes of general medical patients with severe sepsis

Andrew J Odden[1*], Jeffrey M Rohde[1], Catherine Bonham[2], Latoya Kuhn[3], Preeti N Malani[1,4], Lena M Chen[1,5], Scott A Flanders[1] and Theodore J Iwashyna[1,3]

New physical disability was common in general ward patients with sepsis, even in those with good baseline function.

Back of Envelope

for every 100 patients with severe sepsis:

Back of Envelope, 2

for every 100 patients with severe sepsis:

18 patients die in the hospital

Back of Envelope, [3]

for every 100 patients with severe sepsis:

18 die in days 1-90 after discharge

Back of Envelope, [4]

for every 100 patients with severe sepsis:

8 patients die in days 91-365 after discharge

Back of Envelope, [5]

for every 100 patients with severe sepsis:

11 have moderate-severe cognitive impairment

Back of Envelope, [6]

for every 100 patients with severe sepsis:

37 have ≥1 ADL limitation

Mental Health

Mental Health, 2

Review Article

Anxiety symptoms in survivors of critical illness: a systematic review and meta-analysis☆

Sina Nikayin, M.D. [a,b], Anahita Rabiee, M.D. [a,b], Mohamed D. Hashem, M.D. [a,b], Minxuan Huang, Sc.M. [a,b], O. Joseph Bienvenu, M.D., Ph.D. [a,c], Alison E. Turnbull, D.V.M., M.P.H., Ph.D. [a,b,d], Dale M. Needham, F.C.P.A., M.D., Ph.D. [a,b,e,*]

In Meta-Analysis of 22 Studies, Prevalence of Anxiety:

- 32% at 2-3 months
- 40% at 6 months
- 34% at 12-14 months
- did not differ by ICU admission diagnosis in 4 of 4 studies.

Nikayin, *et al*. *Gen Hosp Psych*. 2016.

Mental Health, 3

Depressive Symptoms After Critical Illness: A Systematic Review and Meta-Analysis

Anahita Rabiee, MD[1,2]; Sina Nikayin, MD[1,2]; Mohamed D. Hashem, MD[1,2]; Minxuan Huang, ScM[1,2]; Victor D. Dinglas, MPH[1,2]; O. Joseph Bienvenu, MD, PhD[1,3]; Alison E. Turnbull, DVM, MPH, PhD[1,2,4]; Dale M. Needham, FCPA, MD, PhD[1,2,5]

In Meta-Analysis of 22 Studies, Prevalence of Depression:

- 29% at 2-3 months
- 34% at 6 months
- 29% at 12-14 months
- Did not differ by ICU admission diagnosis in 5 of 6 studies.

Mental Health, 4

Posttraumatic Stress Disorder in Critical Illness Survivors: A Metaanalysis*

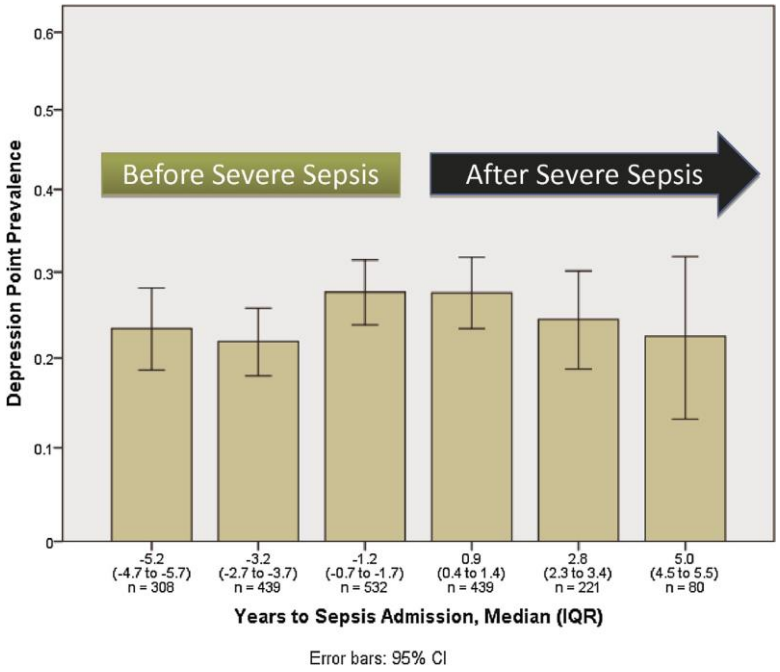
Ann M. Parker, MD[1,2]; Thiti Sricharoenchai, MD[3]; Sandeep Raparla, MD[4]; Kyle W. Schneck, BA[5]; O. Joseph Bienvenu, MD, PhD[2,6]; Dale M. Needham, FCA, MD, PhD[1,2,7]

In Meta-Analysis of 22 Studies, Prevalence of PTSD:

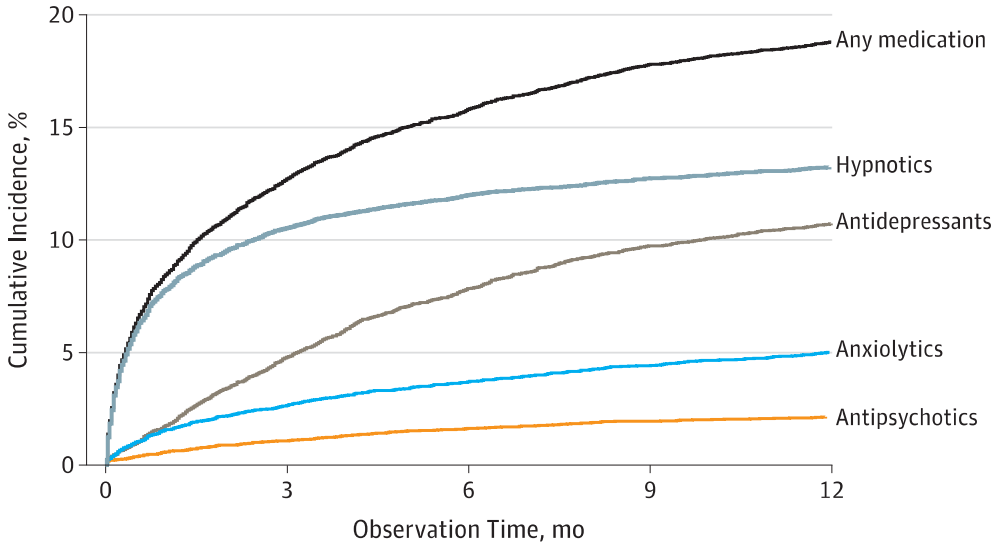
- 44% at 1-6 months
- 34% at 7-12 months.
- did not differ by ICU admission diagnosis in 7 of 7 studies.

Is Critical Illness a Marker or Mediator of Mental Health Impairments?

Depressive symptoms



New Psychoactive prescriptions



Survivors

ORIGINAL ARTICLE

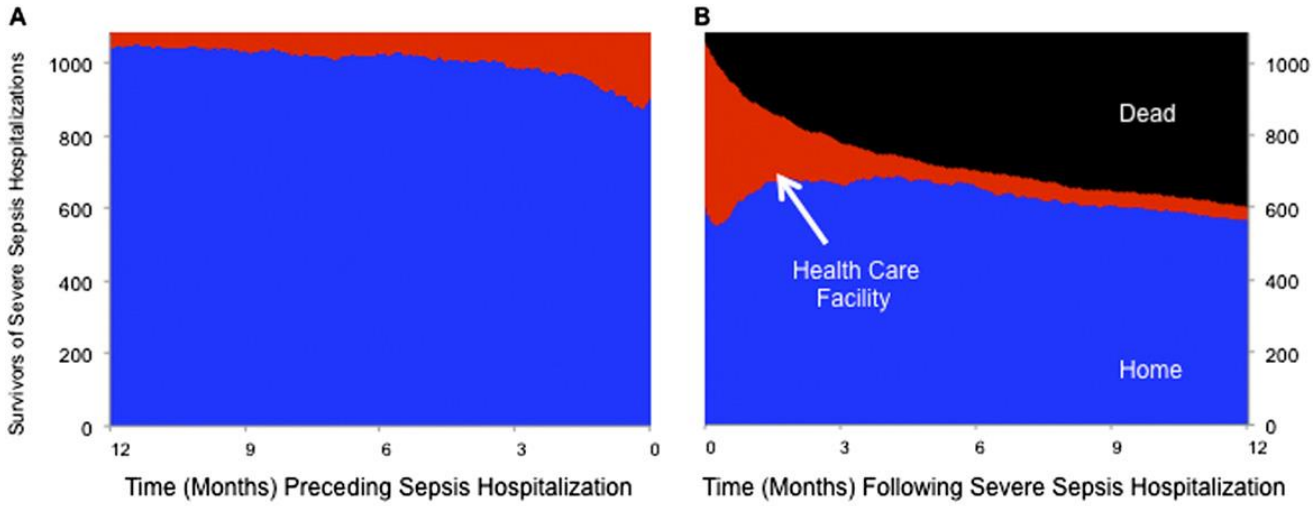
Increased 1-Year Healthcare Use in Survivors of Severe Sepsis

Hallie C. Prescott[1], Kenneth M. Langa[1,2,3], Vincent Liu[4], Gabriel J. Escobar[4], and Theodore J. Iwashyna[1,2,3]

[1]Department of Medicine, University of Michigan, Ann Arbor, Michigan; [2]VA Center for Clinical Management Research, HSR&D Center for Excellence, Ann Arbor, Michigan; [3]Institute for Social Research, Ann Arbor, Michigan; and [4]Kaiser Permanente Division of Research, Oakland, California

Before Sepsis

After Sepsis



Prescott, *et al*. *AJRCCM*. 2014.

Post-Acute Care Increase

ORIGINAL ARTICLE

Increased 1-Year Healthcare Use in Survivors of Severe Sepsis

Hallie C. Prescott[1], Kenneth M. Langa[1,2,3], Vincent Liu[4], Gabriel J. Escobar[4], and Theodore J. Iwashyna[1,2,3]

[1]Department of Medicine, University of Michigan, Ann Arbor, Michigan; [2]VA Center for Clinical Management Research, HSR&D Center for Excellence, Ann Arbor, Michigan; [3]Institute for Social Research, Ann Arbor, Michigan; and [4]Kaiser Permanente Division of Research, Oakland, California

- Conclusion: Sepsis is followed by significant increases in healthcare use.

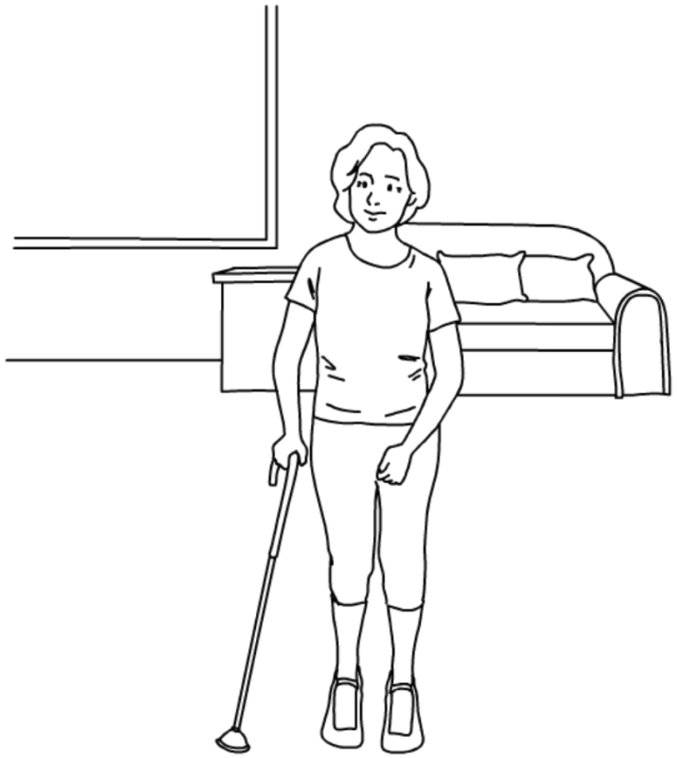
- Median: 10% of days alive in healthcare facility.
- Most is increase is post-acute care use.

Most Common Index Diagnosis & Most Costly Cause of Readmission

Table 1. High-volume conditions ranked by rate of readmission for all causes within 30 days, 2013

Rank	Principal diagnosis for index hospital stay	Number of index admissions	Number of all-cause readmissions	Aggregate cost of readmissions, $ millions	Rate of all-cause readmission
Total index admissions for any cause		**28,124,869**	**3,900,556**	**52,398**	**13.9**
1	Congestive heart failure, non-hypertensive	782,079	183,534	2,728	23.5
2	Schizophrenia and other psychotic disorders	366,256	83,245	772	22.7
3	Respiratory failure, insufficiency, arrest (adult)	290,892	62,684	961	21.5
4	Diabetes mellitus with complications	486,886	99,108	1,204	20.4
5	Acute renal failure	431,452	87,537	1,190	20.3
6	Chronic obstructive pulmonary disease and bronchiectasis	570,077	114,067	1,384	20.0
7	Complication of device, implant or graft	581,289	111,838	1,973	19.2
8	Alcohol-related disorders	261,072	50,081	366	19.2
9	Septicemia	1,011,496	191,156	3,154	18.9
10	Fluid and electrolyte disorders	358,640	65,704	839	18.3

Our Patient, [5]



“What might I be hospitalized for?

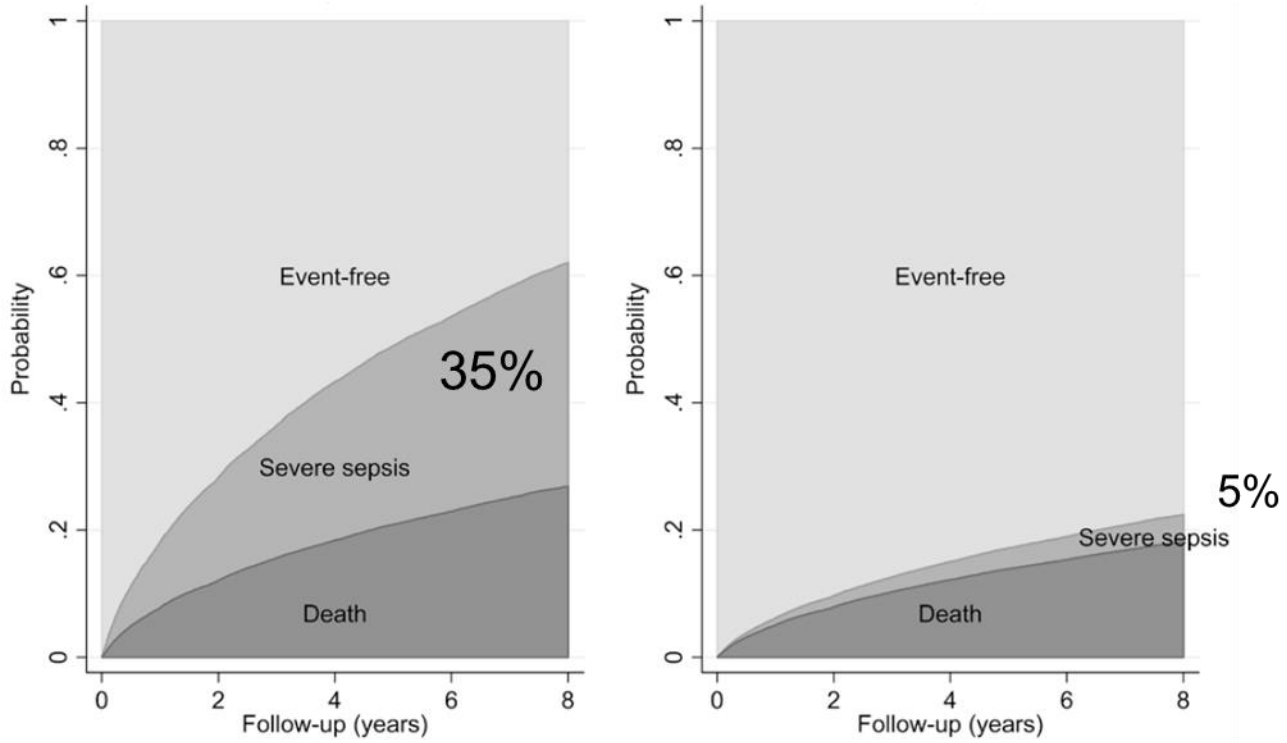
Will my sepsis come back?”

Risk of Recurrence: After Surviving Sepsis

A Matched Cohort Study

Hsiu-Nien Shen, MD, PhD[1]; Chin-Li Lu, MS[2]; Hsi-Hsing Yang, MD[1]

Cumulative incidence of sepsis and death in sepsis survivors (left) and matched controls (right)



How Common is Recurrent Sepsis? New or Relapsed Infection?

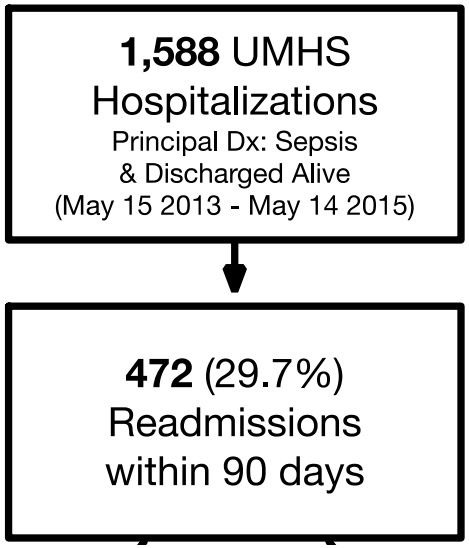
Hypothesis:

Recurrent sepsis is common and most commonly due to new infections.

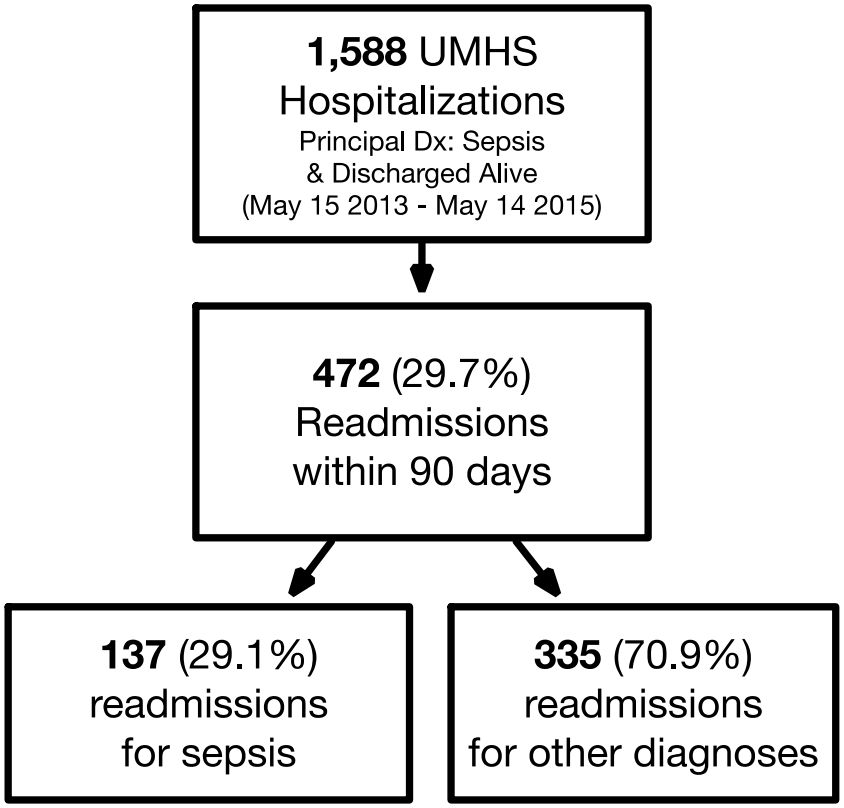
How Common is Recurrent Sepsis?

1,588 UMHS Hospitalizations
Principal Dx: Sepsis
& Discharged Alive
(May 15 2013 - May 14 2015)

How Common is Recurrent Sepsis?, [2]



How Common is Recurrent Sepsis? [3]



New or Relapsed Infection?

Organism Concordance	Site Concordance		
	Different Site	Same Site	Unknown
Different Organism			
Same Organism			
Culture Negative			

New or Relapsed Infection? [2]

Organism Concordance	Site Concordance		
	Different Site	Same Site	Unknown
Different Organism	14 (10%)	30 (22%)	3 (2%)
Same Organism	0 (0%)		
Culture Negative	17 (12%)		

- 64 (47%) are new infections (new site and/or new organism).

New or Relapsed Infection? [3]

Organism Concordance	Site Concordance		
	Different Site	Same Site	Unknown
Different Organism	14 (10%)	30 (22%)	3 (2%)
Same Organism	0 (0%)	26 (19%)	
Culture Negative	17 (12%)		

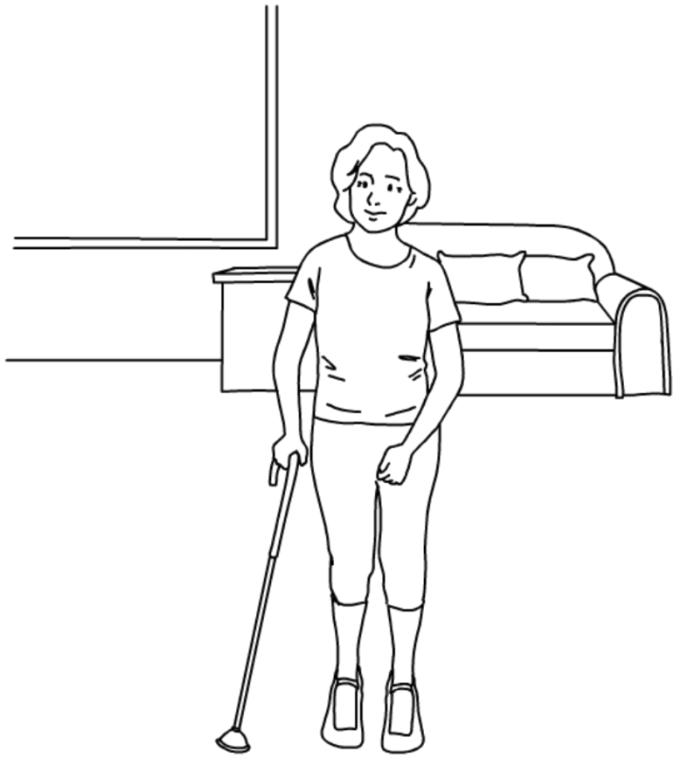
- 64 (47%) are new infections (new site and/or new organism).
- 26 (19%) are relapsed infections (same site and same organism).

New or Relapsed Infection? [4]

Organism Concordance	Site Concordance		
	Different Site	Same Site	Unknown
Different Organism	14 (10%)	30 (22%)	3 (2%)
Same Organism	0 (0%)	26 (19%)	1 (1%)
Culture Negative	17 (12%)	38 (28%)	8 (6%)

- 64 (47%) are new infections (new site and/or new organism).
- 26 (19%) are relapsed infections (same site and same organism).
- 47 (34%) are unclear (culture negative or unknown site).

Our Patient, 6



“What other types of medical set-backs am I at risk for?”

Readmission Diagnoses

RESEARCH LETTER

Readmission Diagnoses After Hospitalization for Severe Sepsis and Other Acute Medical Conditions

Q1: What are the most common readmission diagnoses after sepsis?

Q2: To what extent are readmissions after sepsis potentially preventable?

Hypothesis: A limited number of diagnoses will explain the bulk of post-sepsis readmissions.

Potentially Preventable Readmissions

- “can potentially be avoided if ambulatory care is provided in a timely and effective manner”[1]

- “[diagnoses] for which timely and effective outpatient care can help reduce the risks of hospitalization by either preventing the onset of an illness or condition, controlling an acute episodic illness or condition, or managing a chronic disease or condition”[2]

[1]Weissman, *et al*. *JAMA*. 1992.
[2]Billings, *et al. Health Affairs*. 1993.

Potentially Preventable Readmissions, cont'd

1. Pneumonia
2. Dehydration
3. UTI
4. CHF
5. Asthma
6. COPD exacerbation
7. Uncontrolled diabetes
8. Diabetes w/ complication
9. LE amputation in diabetics
10. Perforated appendix
11. Angina without procedure
12. HTN
13. Sepsis
14. Skin/soft tissue infection
15. Acute renal failure
16. Aspiration pneumonitis

Post-Sepsis Readmission Diagnoses

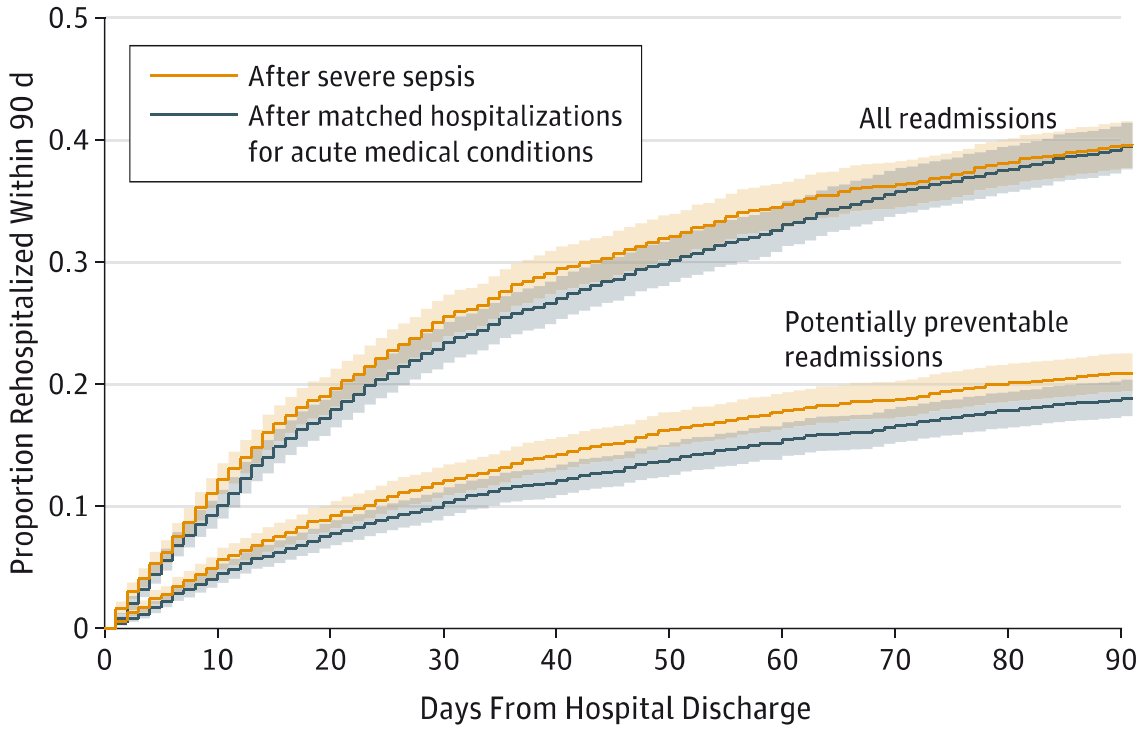
Table. Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis

Diagnosis[a]	Severe Sepsis (n = 2617)	
	No. of Survivors	% (95% CI)
Sepsis	167	6.4 (5.4-7.3)
Congestive heart failure	144	5.5 (4.6-6.4)
Pneumonia	92	3.5 (2.8-4.2)
Acute renal failure	87	3.3 (2.6-4.0)
Rehabilitation	74	2.8 (2.2-3.5)
Respiratory failure	65	2.5 (1.9-3.1)
Complication of device, implant, or graft	52	2.0 (1.5-2.5)
COPD exacerbation	49	1.9 (1.4-2.4)
Aspiration pneumonitis	47	1.8 (1.3-2.3)
Urinary tract infection	44	1.7 (1.2-2.2)

Prescott, *et al*. *JAMA*. 2015.

Preventable Readmissions Among Survivors

Figure. Total and Potentially Preventable 90-Day Readmissions Among Survivors of Severe Sepsis and Matched Hospitalizations for Acute Medical Conditions



Prescott, *et al*. *JAMA*. 2015.

Readmission Conclusions

RESEARCH LETTER

Readmission Diagnoses After Hospitalization for Severe Sepsis and Other Acute Medical Conditions

Patients are frequently rehospitalized within 90 days after having severe sepsis.[1] Little is known, however, about the reasons for readmission and whether they can be reduced. We sought to determine the most common readmission diagnoses after hospitalization for severe sepsis, the extent to which readmissions may be potentially preventable by posthospitalization ambulatory care, and whether the pattern of readmission diagnoses differs compared with that of other acute medical conditions.

Methods | We studied participants in the nationally representative US Health and Retirement Study,[2] a multistage probability sample of households with adults aged 50 years or older, that is linked to Medicare claims (1998-2010). We identified hospitalizations with severe sepsis using a validated approach that requires *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for both infection and acute organ dysfunction.[3,4] We matched hospitalizations for severe sepsis to hospitalizations for 15 common acute medical conditions (**Table**) 1:1 by age, sex, postdischarge comorbidity burden (Charlson Comorbidity Index), prehospitalization functional disability (limitations of activities and instrumental activities of daily living), and length of hospitalization using coarsened exact matching.[5]

We measured the rate and 95% confidence interval of 90-day readmissions. Using the Healthcare Cost and Utilization Project's Clinical Classification Software, we determined the most common readmission diagnoses. To gauge what proportion of rehospitalizations may be potentially preventable, we measured ambulatory care sensitive conditions (ACSCs), which are diagnoses for which effective outpatient care may reduce hospitalization rates.[6] We used ACSCs identified by the Agency for Healthcare Research and Quality,[6] and an expanded definition also including sepsis, skin or soft tissue infection, acute renal failure, and aspiration pneumonitis, all of which could plausibly be prevented or treated early to avoid rehospitalization.

We compared readmission rates using McNemar χ^2 tests with significance at $P < .001$ (2-sided) given multiple comparisons. The University of Michigan institutional review board approved this study; patients provided oral informed consent at enrollment and for Medicare linkage.

Results | We identified 3494 hospitalizations for severe sepsis, of which 2843 (81.4%) survived to discharge. Of these, 2617 (92.1%) were matched to hospitalizations for other acute medical conditions. The cohort's mean age was 78.9 years (SD, 8.9 years), 57.3% were female, and they had some preexisting functional disability (median, 1 limitation; interquartile range [IQR], 0-4 limitations). At discharge, patients had moderate comorbidity burden (median Charlson Index, 6; IQR, 3-8). Median hospitalization length was 7 days (IQR, 4-11 days). Age, sex, co-

Table. Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis

	Severe Sepsis (n = 2617)		Matched Hospitalizations for Other Acute Medical Conditions (n = 2617)[b]		
Diagnosis[a]	No. of Survivors	% (95% CI)	No. of Survivors	% (95% CI)	*P* Value[c]
Sepsis	167	6.4 (5.4-7.3)	73	2.8 (2.2-3.4)	<.001
Congestive heart failure	144	5.5 (4.6-6.4)	204	7.8 (6.8-8.8)	.001
Pneumonia	92	3.5 (2.8-4.2)	85	3.3 (2.6-3.9)	.58
Acute renal failure	87	3.3 (2.6-4.0)	30	1.2 (0.7-1.6)	<.001
Rehabilitation	74	2.8 (2.2-3.5)	120	4.6 (3.8-5.4)	.001
Respiratory failure	65	2.5 (1.9-3.1)	38	1.5 (1.0-1.9)	.007
Complication of device, implant, or graft	52	2.0 (1.5-2.5)	59	2.3 (1.7-2.8)	.50
COPD exacerbation	49	1.9 (1.4-2.4)	41	1.6 (1.1-2.0)	.40
Aspiration pneumonitis	47	1.8 (1.3-2.3)	31	1.2 (0.8-1.6)	.06
Urinary tract infection	44	1.7 (1.2-2.2)	47	1.8 (1.3-2.3)	.75

Abbreviation: COPD, chronic obstructive pulmonary disease.

[a] Listed from most frequent to least frequent. The most frequent readmission diagnoses accounted for 51.5% of all readmissions within 90 days after hospitalization for severe sepsis.

[b] Principal diagnoses were heart failure, pneumonia, cardiac arrhythmia, COPD exacerbation, acute myocardial infarction, acute cerebrovascular disease, complication of a device, implant, or graft, chest pain, fluid or electrolyte disorder, urinary tract infection, hip fracture, gastrointestinal hemorrhage, complication of surgical or medical care, syncope, and diabetes with complication.

[c] Calculated using McNemar χ^2 tests.

Conclusions

Readmissions are common.
Many potentially preventable.

A small number of conditions account for the bulk of the problem:

Prescott, *et al*. *JAMA*. 2015.

Problem Conditions

RESEARCH LETTER

Readmission Diagnoses After Hospitalization for Severe Sepsis and Other Acute Medical Conditions

Patients are frequently rehospitalized within 90 days after having severe sepsis.[1] Little is known, however, about the reasons for readmission and whether they can be reduced. We sought to determine the most common readmission diagnoses after hospitalization for severe sepsis, the extent to which readmissions may be potentially preventable by posthospitalization ambulatory care, and whether the pattern of readmission diagnoses differs compared with that of other acute medical conditions.

Methods | We studied participants in the nationally representative US Health and Retirement Study,[2] a multistage probability sample of households with adults aged 50 years or older, that is linked to Medicare claims (1998-2010). We identified hospitalizations with severe sepsis using a validated approach that requires *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for both infection and acute organ dysfunction.[3,4] We matched hospitalizations for severe sepsis to hospitalizations for 15 common acute medical conditions (**Table**) 1:1 by age, sex, postdischarge comorbidity burden (Charlson Comorbidity Index), prehospitalization functional disability (limitations of activities and instrumental activities of daily living), and length of hospitalization using coarsened exact matching.[5]

We measured the rate and 95% confidence interval of 90-day readmissions. Using the Healthcare Cost and Utilization Project's Clinical Classification Software, we determined the most common readmission diagnoses. To gauge what proportion of rehospitalizations may be potentially preventable, we measured ambulatory care sensitive conditions (ACSCs), which are diagnoses for which effective outpatient care may reduce hospitalization rates.[6] We used ACSCs identified by the Agency for Healthcare Research and Quality,[6] and an expanded definition also including sepsis, skin or soft tissue infection, acute renal failure, and aspiration pneumonitis, all of which could plausibly be prevented or treated early to avoid rehospitalization.

We compared readmission rates using McNemar χ^2 tests with significance at $P < .001$ (2-sided) given multiple comparisons. The University of Michigan institutional review board approved this study; patients provided oral informed consent at enrollment and for Medicare linkage.

Results | We identified 3494 hospitalizations for severe sepsis, of which 2843 (81.4%) survived to discharge. Of these, 2617 (92.1%) were matched to hospitalizations for other acute medical conditions. The cohort's mean age was 78.9 years (SD, 8.9 years), 57.3% were female, and they had some preexisting functional disability (median, 1 limitation; interquartile range [IQR], 0-4 limitations). At discharge, patients had moderate comorbidity burden (median Charlson Index, 6; IQR, 3-8). Median hospitalization length was 7 days (IQR, 4-11 days). Age, sex, co-

Table. Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis

	Severe Sepsis (n = 2617)		Matched Hospitalizations for Other Acute Medical Conditions (n = 2617)[b]		
Diagnosis[a]	No. of Survivors	% (95% CI)	No. of Survivors	% (95% CI)	*P* Value[c]
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COPD exacerbation	49	1.9 (1.4-2.4)	41	1.6 (1.1-2.0)	.40
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Abbreviation: COPD, chronic obstructive pulmonary disease.

[a] Listed from most frequent to least frequent. The most frequent readmission diagnoses accounted for 51.5% of all readmissions within 90 days after hospitalization for severe sepsis.

[b] Principal diagnoses were heart failure, pneumonia, cardiac arrhythmia, COPD exacerbation, acute myocardial infarction, acute cerebrovascular disease, complication of a device, implant, or graft, chest pain, fluid or electrolyte disorder, urinary tract infection, hip fracture, gastrointestinal hemorrhage, complication of surgical or medical care, syncope, and diabetes with complication.

[c] Calculated using McNemar χ^2 tests.

Conclusions

Readmissions are common.
Many potentially preventable.

A small number of conditions account for the bulk of the problem:

- Infection (particularly recurrent sepsis)
- CHF exacerbation
- COPD exacerbation
- Acute renal failure
- Aspiration pneumonitis.

Prescott, *et al*. *JAMA*. 2015.

Prevention

Letters

RESEARCH LETTER

Readmission Diagnoses After Hospitalization for Severe Sepsis and Other Acute Medical Conditions

Patients are frequently rehospitalized within 90 days after having severe sepsis.[1] Little is known, however, about the reasons for readmission and whether they can be reduced. We sought to determine the most common readmission diagnoses after hospitalization for severe sepsis, the extent to which readmissions may be potentially preventable by posthospitalization ambulatory care, and whether the pattern of readmission diagnoses differs compared with that of other acute medical conditions.

Methods | We studied participants in the nationally representative US Health and Retirement Study,[2] a multistage probability sample of households with adults aged 50 years or older, that is linked to Medicare claims (1998-2010). We identified hospitalizations with severe sepsis using a validated approach that requires *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for both infection and acute organ dysfunction.[3,4] We matched hospitalizations for severe sepsis to hospitalizations for 15 common acute medical conditions (**Table**) 1:1 by age, sex, postdischarge comorbidity burden (Charlson Comorbidity Index), prehospitalization functional disability (limitations of activities and instrumental activities of daily living), and length of hospitalization using coarsened exact matching.[5]

We measured the rate and 95% confidence interval of 90-day readmissions. Using the Healthcare Cost and Utilization Project's Clinical Classification Software, we determined the most common readmission diagnoses. To gauge what proportion of rehospitalizations may be potentially preventable, we measured ambulatory care sensitive conditions (ACSCs), which are diagnoses for which effective outpatient care may reduce hospitalization rates.[6] We used ACSCs identified by the Agency for Healthcare Research and Quality,[6] and an expanded definition also including sepsis, skin or soft tissue infection, acute renal failure, and aspiration pneumonitis, all of which could plausibly be prevented or treated early to avoid rehospitalization.

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Different Readmission Diagnoses?

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Prescott, *et al*. *JAMA*. 2015.

Different Readmission Diagnoses? cont'd

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Different Readmission Diagnoses? **Yes**

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Prescott, *et al*. *JAMA*. 2015.

Cardiovascular Risks

Long-Term Mortality and Major Adverse Cardiovascular Events in Sepsis Survivors

A Nationwide Population-based Study

Shuo-Ming Ou[1,2,3*], Hsi Chu[2,4*], Pei-Wen Chao[5,6], Yi-Jung Lee[2,7], Shu-Chen Kuo[2,8,9], Tzeng-Ji Chen[10], Ching-Min Tseng[2,11], Chia-Jen Shih[2,12,13‡], and Yung-Tai Chen[2,14‡]

- 1.4-fold increase over population controls
- 1.3-fold increase over hospitalized controls

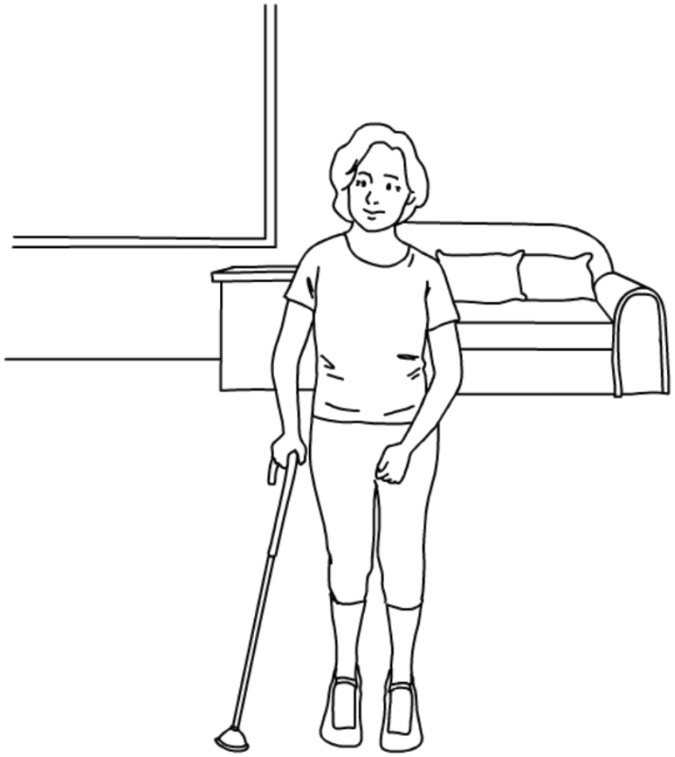
Risk of Cardiovascular Events in Survivors of Severe Sepsis

Sachin Yende[1,2], Walter Linde-Zwirble[3], Florian Mayr[4], Lisa A. Weissfeld[5], Steven Reis[6], and Derek C. Angus[1,2]

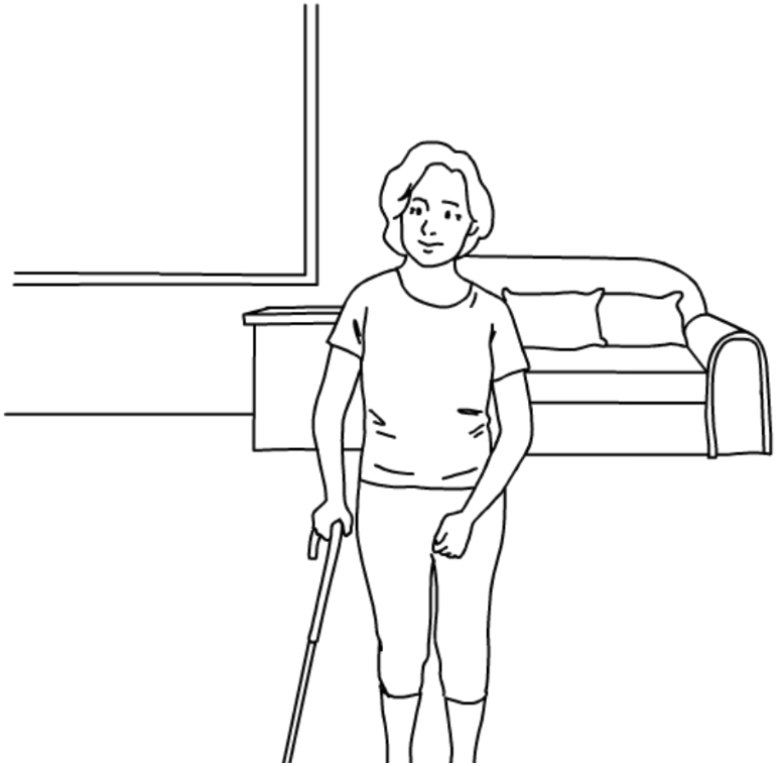
- 1.9-fold increase over population controls
- 1.1-fold increase over hospitalization controls
- Equivalent to ICU controls

Ou, *et al. AJRCCM.* 2016.
Yende, *et al. AJRCCM.* 2014.

Our Patient, 7

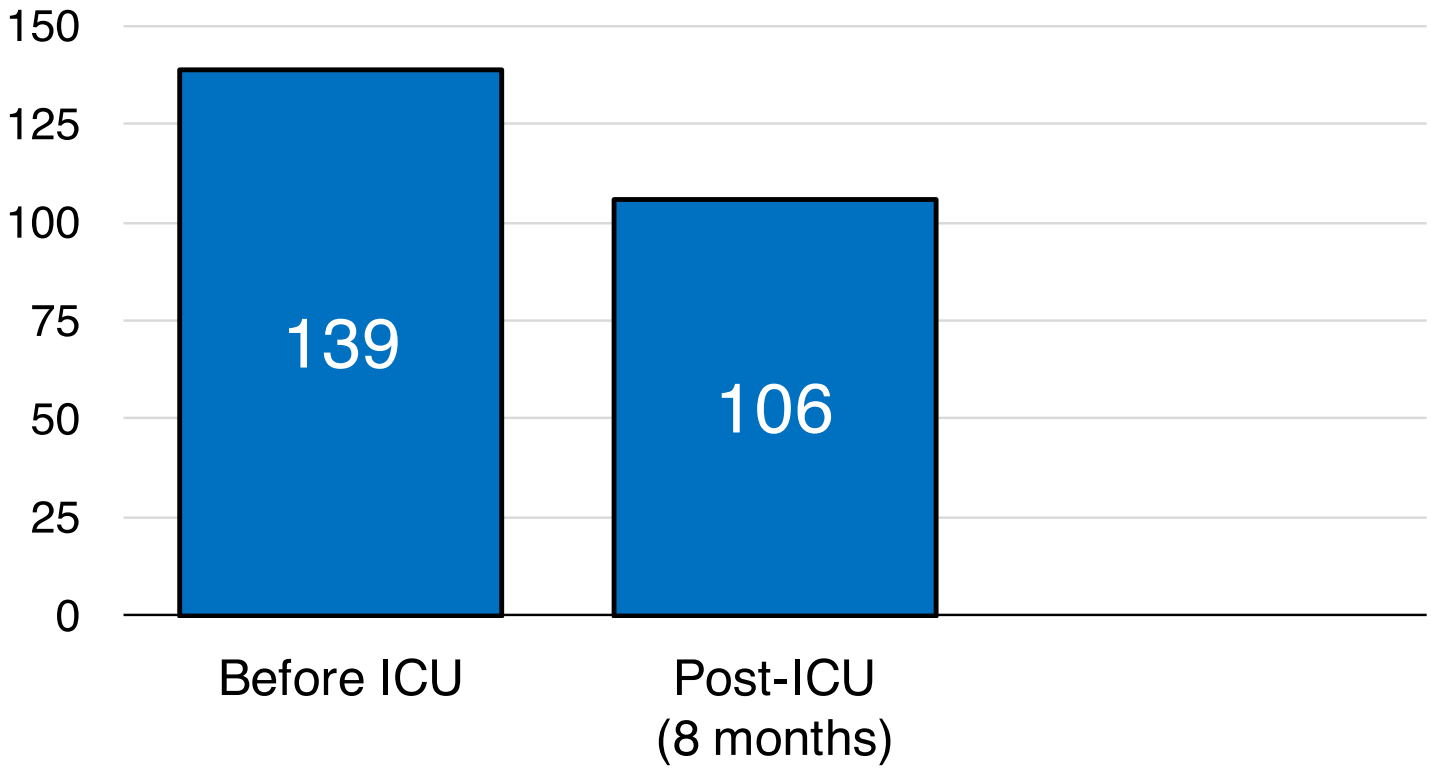


Our Patient, 8

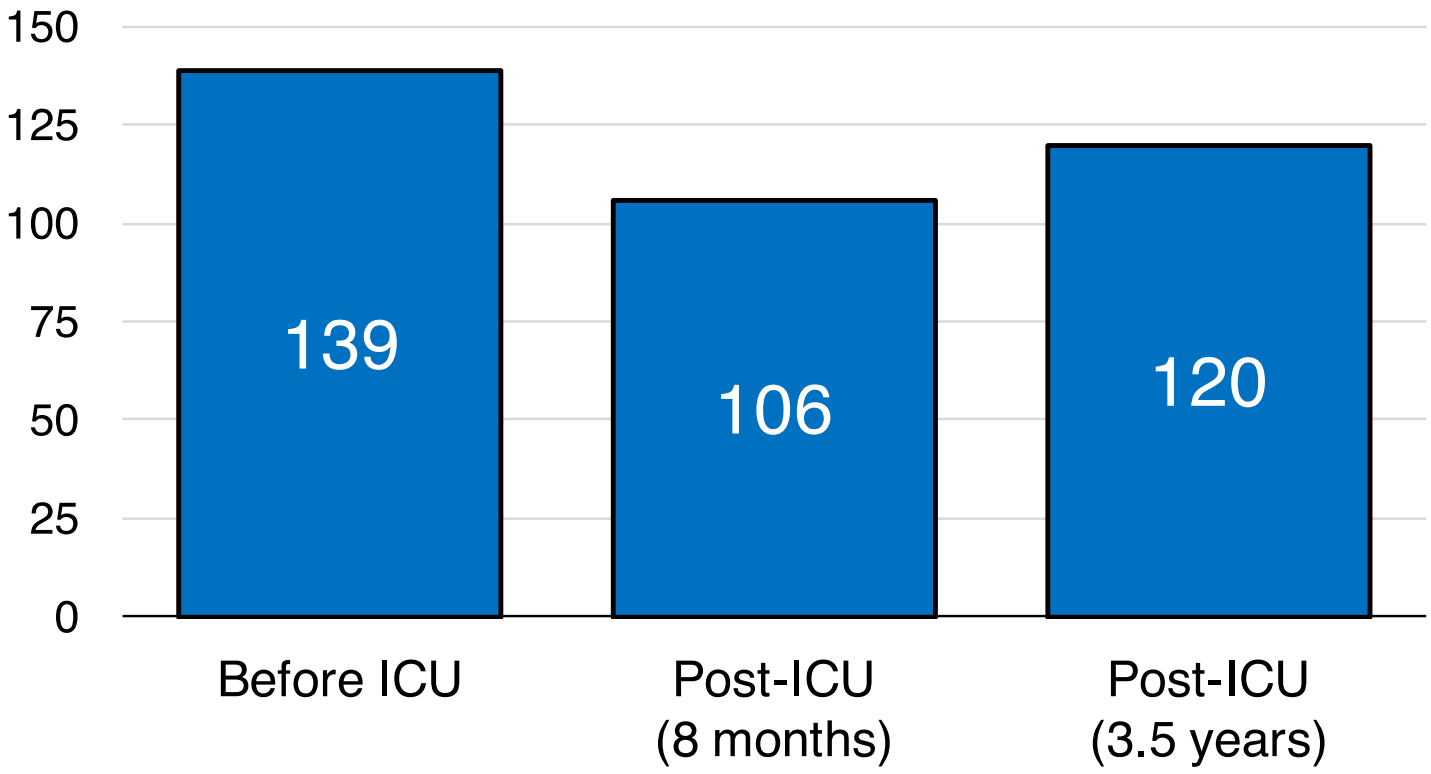


- Multiple readmissions for infection
- Returned to work, but never 100%
- Retired early
- Participates in peer-to-peer support group
- Mentor to new sepsis survivors

IQ Testing

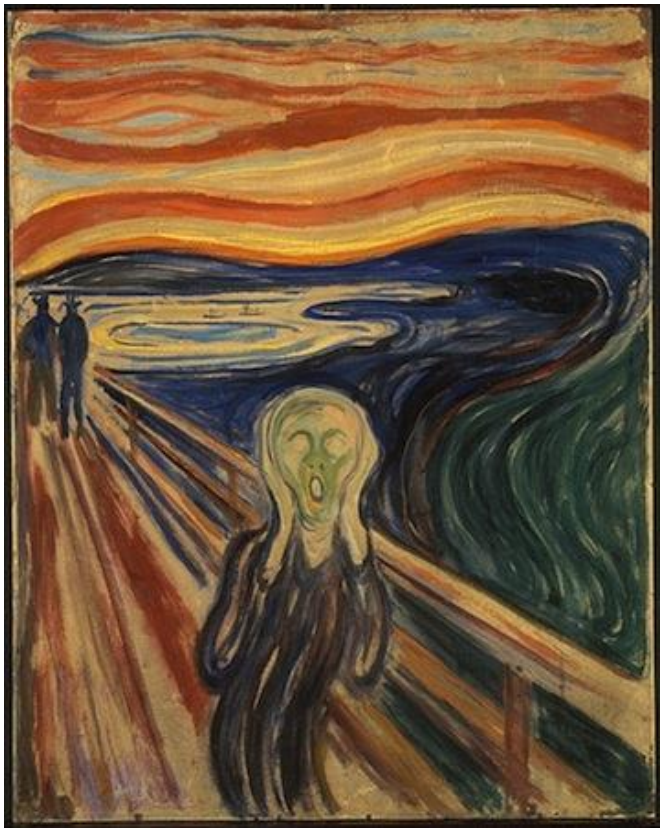


IQ Testing, [2]



Jackson, *et al*. *Southern Med J.* 2009.

Conclusions



Life after sepsis is scary.

- New morbidity
- Increased risk for death
- Discharge to post-acute care
- Frequent re-hospitalization

Conclusions, cont'd

- Sepsis survivors face heightened risk for death. 1 in 5 sepsis survivors with a late death due to lasting effects of sepsis.
- Over half of patients acquire new physical disability
- Cognitive decline common; ~15% with mod-severe impairment
- Anxiety, depression, PTSD each affect ~1/3 of survivors
- Healthcare use and readmission are common. Often due to the same "usual suspects"—that we know how to treat: infection, CHF, AKI, COPD, aspiration.
- Risk for Infection, AKI, aspiration, and ?CV events are increased in sepsis survivors.

In August….

We will discuss strategies to:

- reduce re-admissions
- improve long-term outcomes in sepsis survivors

Questions

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