Don't Stop Believing: Barriers and Facilitators to Achieving High Reliable Sepsis Care

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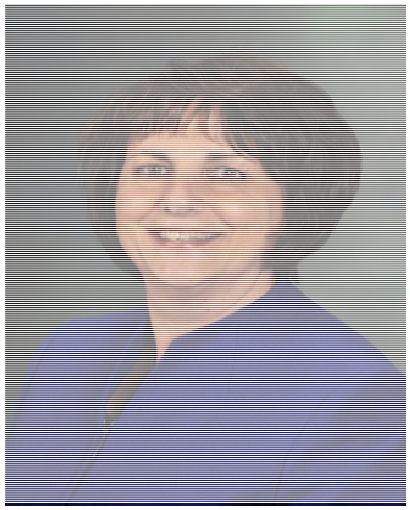
Our Speakers



Pat Posa *RN, BSN, MSA, CCRN-K, FAAN*

- Quality and Patient Safety Program Manager at Michigan Medicine-University of Michigan
- Prior Sepsis coordinator
- Sepsis Coordinator Advisory Committee for Sepsis Alliance
- Lectured extensively for numerous conferences and webinars on sepsis, care of the critically ill-ICU Liberation
- Published on topics of sepsis, patient safety and ICU Liberation

Our Speakers

Angela Craig *MS, RN, APN, CCNS*

- Clinical Nurse Specialist for the ICU at Cookeville Regional Medical Center in Cookeville, TN
- Sepsis coordinator
- Sepsis Coordinator Advisory Committee for Sepsis Alliance
- Lectured extensively for numerous conferences and webinars on sepsis and hemodynamic topics
- Published the topics of sepsis and heart failure

Our Speakers

Kathleen Vollman, *MSN, RN, CCNS, FCCM, FCNS, FAAN*

- Clinical Nurse Specialist, educator and consultant
- Published and lectured nationally and internationally on a variety of pulmonary, critical care, prevention of health care acquired injuries, work culture and sepsis recognition and management
- Subject matter expert for prevention of CAUTI, CLABSI and HAPI as well as sepsis recognition/management and the culture of safety for HRET and the Michigan Hospital Association
- Appointed to serve as an honorary ambassador to the World Federation of Critical Care Nurses

Disclosures

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- Consultant-Tennessee Hospital Association
- Nurse Consultant with Edwards Lifesciences, speakers bureau
- Baxter – Key opinion leader (KOL) & speakers bureau

Pat Posa

- Consultant-Michigan Hospital Association Keystone Center
- Consultant-HRET Hospital Improvement Innovation Network (HIIN) Subject matter expert: CAUTI, CLABSI, HAPU, Sepsis, Safety culture

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- Consultant and speaker bureau:
  - Sage Products LLC
  - Eloquest
  - Baxter

Overview-Objectives

- Identify barriers preventing consistent application of evidenced based sepsis care and strategies to resolve through case-based learning
- Outline different approaches to use data to drive improvement in sepsis care
- Examine new evidence related to sepsis care and future research and prevent long-term sequelae

Sepsis is a Public Health Problem

- Affects >1.7 million Americans per year
- 3rd leading cause of death in the US
- 1-week mortality for Medicare beneficiaries with sepsis is 18% vs 4.1% with no sepsis
- Sepsis occurs in just 10% of U.S. hospital patients, but it contributes to as many as half of all hospital deaths
- $41.5 billion spent on sepsis inpatient care and skilled nursing for Medicare beneficiaries in 2018
- 87% of all adult sepsis cases begin outside the hospital

> 700 people die each day from sepsis in the U.S.

Rhee C, et al. *JAMA*. 2017;318(13):1241-1249.
Angus DC, et al.. *Crit Care Med* 2001;29:1303-10.
Buchman TG, et al. Crit Care Med. 2020;48(3):276-288.
Novosad SA, et al. CDC Morbidity and Mortality Weekly Report., 2016;65(33):864-869
Buchman TG, et al. Crit Care Med. 2020;48(3):276-288

Common Causes of Hospitalization Adults aged 85 and over: U.S.

First-listed diagnosis	2000	2005	2010	Percent change[1] (2000 to 2010)
	Rate of hospitalization per 1,000 population			
Congestive heart failure	48	47	43	-9.5
Pneumonia	51	52	34	-32.8
Urinary tract infection	19	24	30	+55.9
Septicemia	15	18	28	+84.8
Stroke	37	27	28	-25.0
Hip fracture	28	23	21	-25.4

[1]Percent change for each diagnosis is significant from 2000 through 2010 ($p < 0.05$).

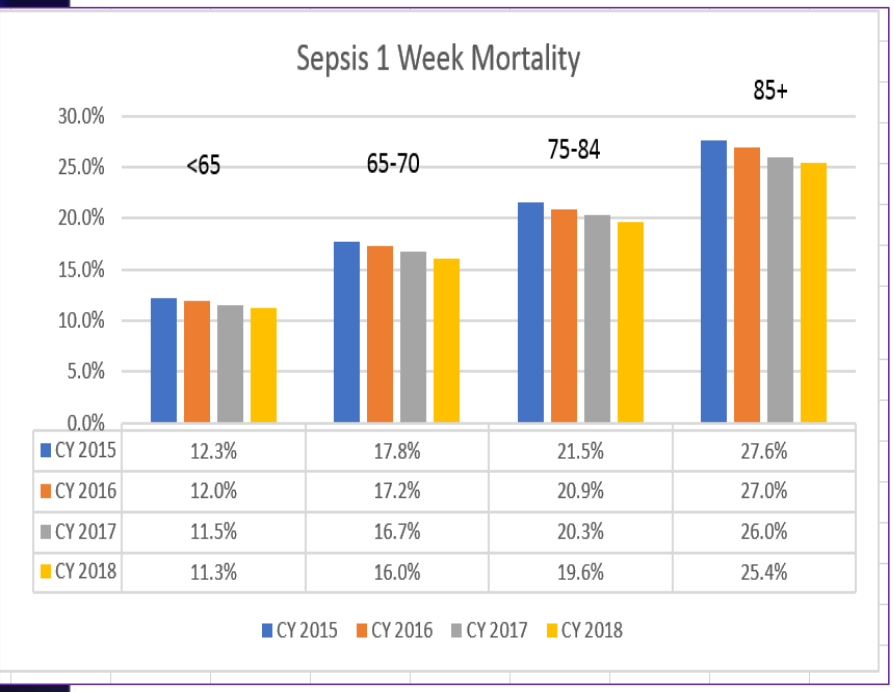
NOTE: First-listed diagnosis is considered to be the main cause or reason for the hospitalization. The diagnoses were chosen because they were the top six first-listed diagnoses in 2010.

SOURCE: CDC/NCHS, National Hospital Discharge Survey, 2000–2010.

Levant S, Chari K, DeFrances CJ. Hospitalizations for patients aged 85 and over in the United States, 2000–2010. NCHS data brief, no 182. Hyattsville, MD: National Center for Health Statistics. 2015.

Sepsis Admissions and Mortality for Medicare Beneficiaries

Over the 7-year study interval, the rate of sepsis admissions increased by 50%.

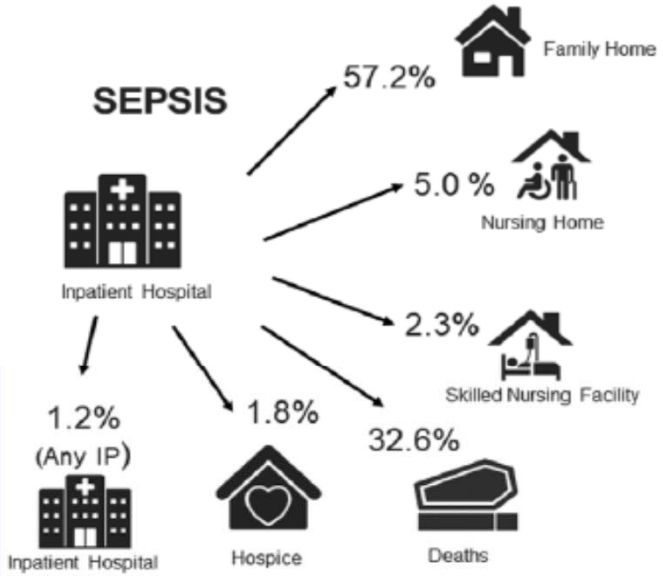


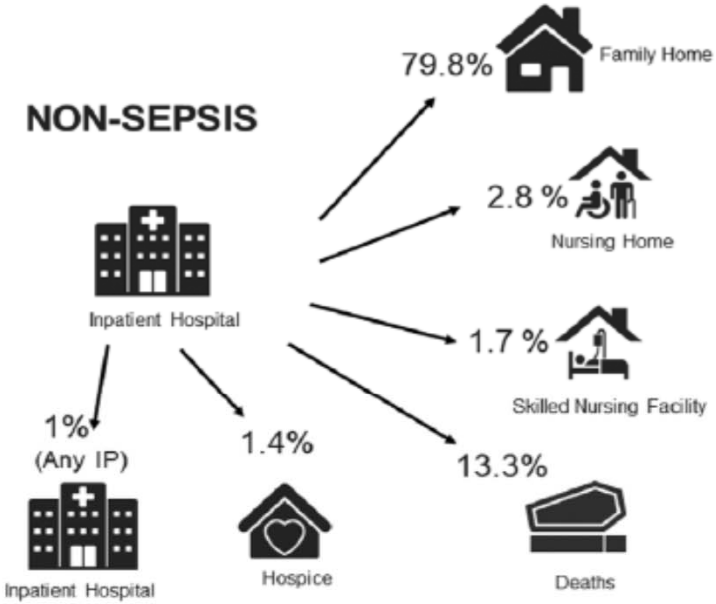
Mortality after hospital discharge is high

- The one-week mortality after discharge among Medicare beneficiaries for
  - Septic shock 40.6%
  - Severe sepsis 15.3%
  - Unspecified sepsis is 11%.
- 6-month after discharge (CY 2018), Medicare beneficiaries mortality rate;
  - septic shock 60%
  - severe sepsis 36%
  - unspecified sepsis 30.9%.
- This high mortality rate continues at 1 and 3 years post initial sepsis hospitalization.

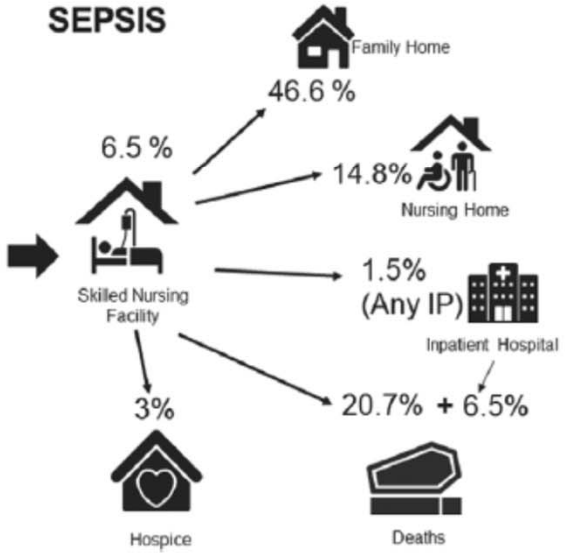
Buchman TG, et al. Crit Care Med. 2020;48(3):276-288, Supplement

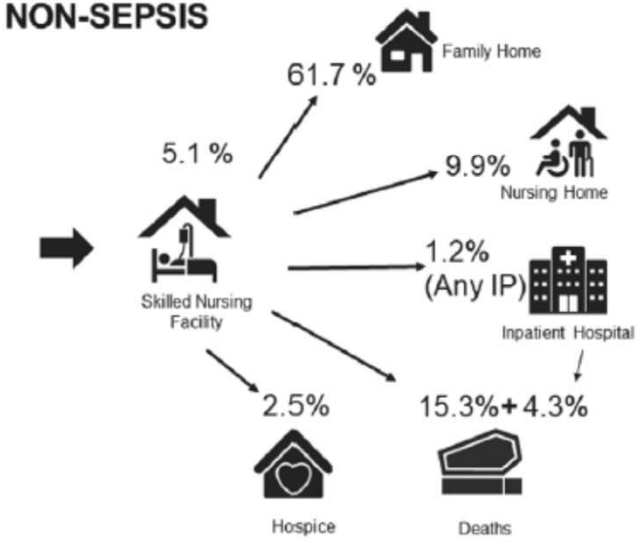
Medicare Beneficences





Initial Sepsis sent to Skilled Facility from Hospital





Hospital Readmission is Common

- Sepsis survivors have an increased risk for readmission (40% within 90 days for Medicare patients) related to
  - infection/sepsis
  - heart failure
  - renal failure.
- Reconciling medications, infection prevention, management of chronic conditions, and cognitive and functional rehabilitation will aid in preventing readmissions.

Table. Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis

	Severe Sepsis (n = 2617)	
Diagnosis[a]	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;313(10):1055-1057.
- Prescott HC and Angus DC. JAMA. 2018;319(1):62-75.

Sepsis and COVID 19

- Sepsis and COVID-19 overlap and are more similar than different
  - There are semantic in real differences between subsystem COVID-19
  - In both the early and later phases of the disease sepsis in COVID-19 are nearly indistinguishable in clinical treatment goals are the same
- Both conditions require timely and accurate diagnosis in order to provide appropriate treatment
  - Phenotyping an endo typing may be valuable for directing therapy
- SSG for COVID:
  - For severe & critical
    - Systemic Corticosteroids
    - Venous thromboprophylaxis
  - Non-ventilated patients/severe
    - Remdesivir
  - For the acute resuscitation of adults with COVID-19 and shock, we suggest using a conservative over a liberal fluid strategy.

Alhazzani W, et al. Critical Care Medicine: March 2021 - Volume 49 - Issue 3

A Sepsis Patient's Journey

Patient goes to a busy ED (100,000 visits a year)

Patient arrives to ED: 58-year-old 89kg woman with productive cough and malaise, PMH of HTN and COPD

Triaged within 20 minutes, Initial vitals : HR 95/min, RR 22 min, Temp 97, BP: 100/48 SaO2 97% RA

Sent back to the waiting room for 2hrs/then placed in a room/Re-triaged: Vitals HR 100/min, RR 22min, BP, 96/48 Temp 98 and SaO2 94% RA

sepsis screen completed/screened negative because felt no infection presence because of normal temp

Move to the back: routine labs drawn WBC 14,000, with 10% bands, Hgb 14, Hct 30, Electrolytes WNL, BUN 20, create 0.9,

chest x-ray ordered/shows pneumonia orders received for blood cultures, antibiotic and a lactate. Lactate is 2.3 so clinician does another set of vitals

Vitals: HR 110/min, RR 24/min, BP 89/50, Temp 99, order received for 1 liter fluid bolus

1/liter given over 1 hr, and vitals stable

BP alarm rings: 75/48 and HR 120/min, RR 26/min Sat 90% on RA

Additional liter given over 1hr/VS: 65/40, HR 124/min, RR 26/min, Sat 88%

3/L of boluses under pressure given, with BP finally responding at 110/60 and HR 95/min, RR 30/min, Sat 86% on 5/L

Barriers/Facilitators

Identification

- Screening: EMR, BPA, Routine Screening, Machine Learning
- Sepsis 2 and Sep 3 definitions

Time sensitive interventions

- Antibiotics
- Fluids—early fluids and later fluids and vasopressors
- Repeat lactate
- Reassessment

Inadequate program resources

- Lack of sepsis coordinator
- Lack of physician lead/champion

Timely Data

- Timely feedback

TO SAVE LIVES.....

Early identification

Early antibiotics

Early fluid resuscitation

Screening for Severe Sepsis

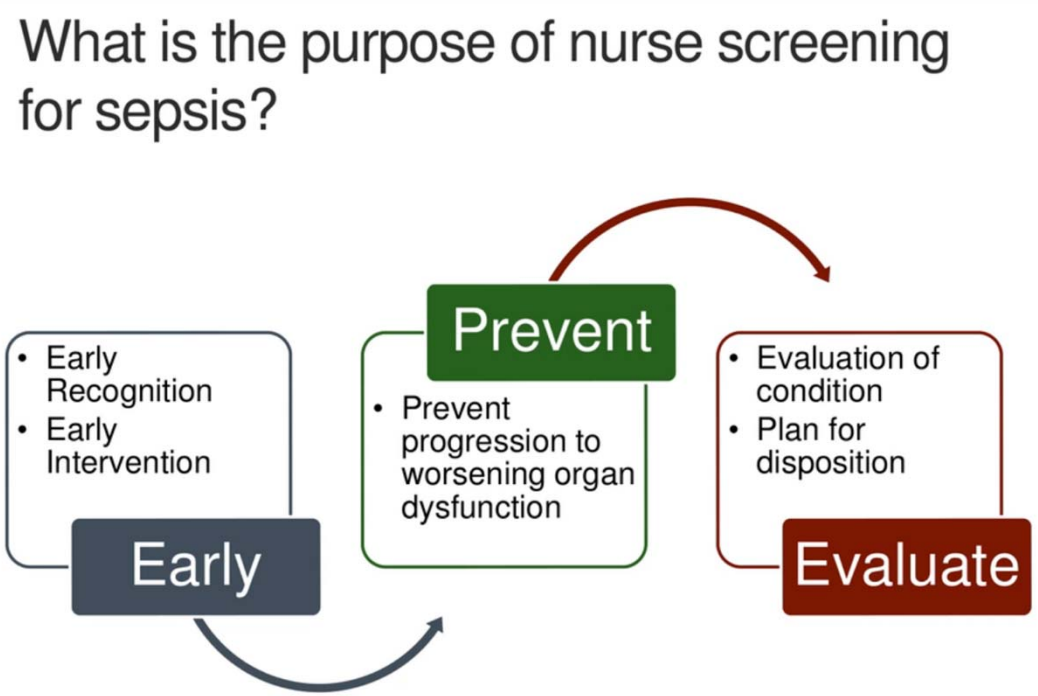
- **Develop screening process for ED, rapid response team, ICU and house wide**

  (To screen effectively, it must be part of the nurses' daily routines— i.e., part of admission and shift assessment)
- Education beyond PowerPoint…case studies
- Develop audit process to evaluate compliance and effectiveness
- Ensure screening process has clear "next steps" defined for nursing staff

If you don't screen you will miss patients
that may have benefited from the interventions

Dellinger RP, Levy MM, Carlet JM, et al. 2008. Crit Care Med. 2008;36:296-327.
Schorr C. et al Journal of Hospital Medicine, 2016;11:S32-S39

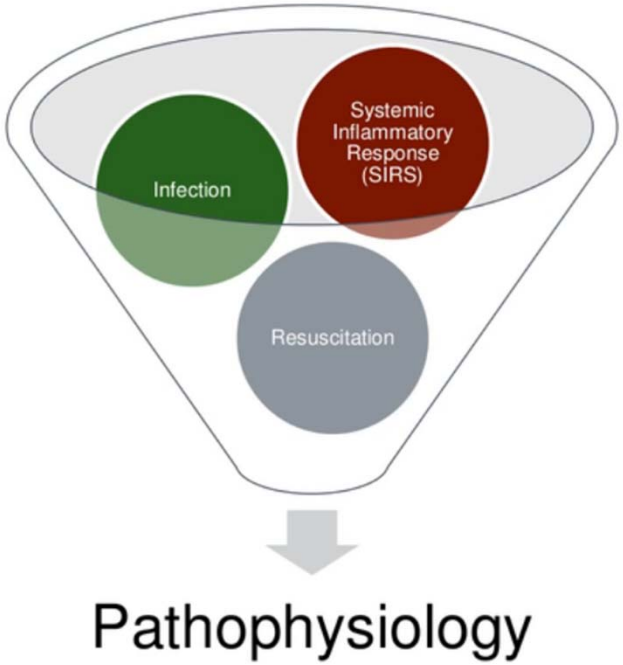
What is the Purpose of Nurse Screening



Empowering Nurses for Early Sepsis Recognition accessed on https://www.youtube.com/watch?v=s687VMj6iwo

Understanding the Why: Sepsis Screening Not Just Another Task

- Pathophysiology connected to screening components
- Bundle elements
- Educational tools and reminders to help remember over time

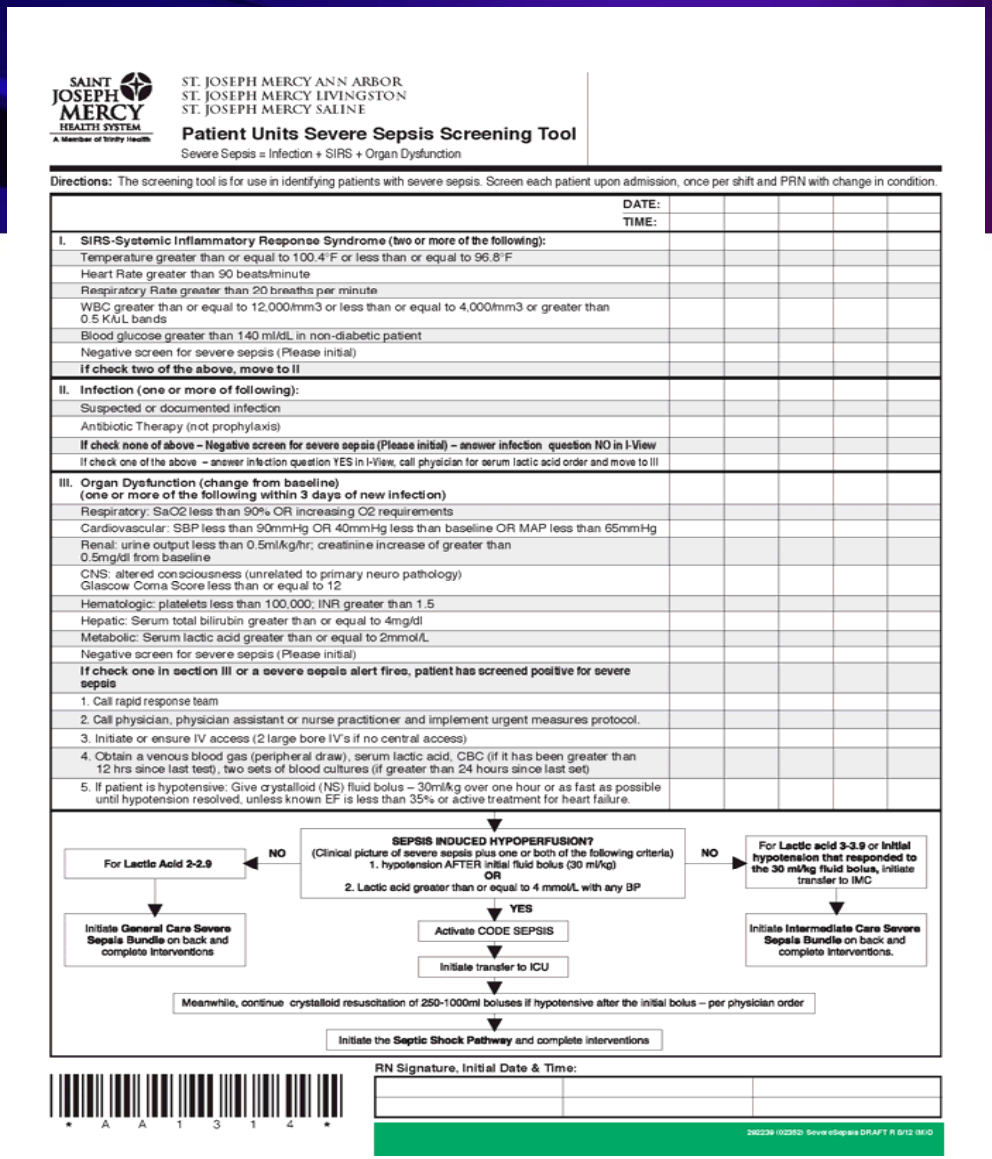


Schorr C. et al. Journal of Hospital Medicine. 2016;11;S1: s32-s39

SEP-2 Definitions (used by CMS and coders)

- **Infection**
- **Sepsis:** infection plus 2 or more SIRS
- **Severe Sepsis:** infection plus 2 or more SIRS plus new organ dysfunction
- **Septic Shock:** severe sepsis with a lactic acid greater than or equal to 4mmol/L OR continued hypotension (systolic BP<90 or 40mmHg decrease from their baseline) after initial fluid bolus (30ml/kg)

PATIENT CARE UNIT SEVERE SEPSIS SCREENING TOOL



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Patient Units Severe Sepsis Screening Tool

Severe Sepsis = Infection + SIRS + Organ Dysfunction

Directions: The screening tool is for use in identifying patients with severe sepsis. Screen each patient upon admission, once per shift and PRN with change in condition.

	DATE:					
	TIME:					
I. SIRS-Systemic Inflammatory Response Syndrome (two or more of the following):						
Temperature greater than or equal to 100.4°F or less than or equal to 96.8°F						
Heart Rate greater than 90 beats/minute						
Respiratory Rate greater than 20 breaths per minute						
WBC greater than or equal to 12,000/mm3 or less than or equal to 4,000/mm3 or greater than 0.5 K/uL bands						
Blood glucose greater than 140 ml/dL in non-diabetic patient						
Negative screen for severe sepsis (Please initial)						
If check two of the above, move to II						
II. Infection (one or more of following):						
Suspected or documented infection						
Antibiotic Therapy (not prophylaxis)						
If check none of above – Negative screen for severe sepsis (Please initial) – answer infection question NO in I-View						
If check one of the above – answer infection question YES in I-View, call physician for serum lactic acid order and move to III						
III. Organ Dysfunction (change from baseline) (one or more of the following within 3 days of new infection)						
Respiratory: SaO2 less than 90% OR increasing O2 requirements						
Cardiovascular: SBP less than 90mmHg OR 40mmHg less than baseline OR MAP less than 65mmHg						
Renal: urine output less than 0.5ml/kg/hr; creatinine increase of greater than 0.5mg/dl from baseline						
CNS: altered consciousness (unrelated to primary neuro pathology) Glascow Coma Score less than or equal to 12						
Hematologic: platelets less than 100,000; INR greater than 1.5						
Hepatic: Serum total bilirubin greater than or equal to 4mg/dl						
Metabolic: Serum lactic acid greater than or equal to 2mmol/L						
Negative screen for severe sepsis (Please initial)						
If check one in section III or a severe sepsis alert fires, patient has screened positive for severe sepsis						
1. Call rapid response team						
2. Call physician, physician assistant or nurse practitioner and implement urgent measures protocol.						
3. Initiate or ensure IV access (2 large bore IV's if no central access)						
4. Obtain a venous blood gas (peripheral draw), serum lactic acid, CBC (if it has been greater than 12 hrs since last test), two sets of blood cultures (if greater than 24 hours since last set)						
5. If patient is hypotensive: Give crystalloid (NS) fluid bolus – 30ml/kg over one hour or as fast as possible until hypotension resolved, unless known EF is less than 35% or active treatment for heart failure.						

SEPSIS INDUCED HYPOPERFUSION?
(Clinical picture of severe sepsis plus one or both of the following criteria)
1. hypotension AFTER initial fluid bolus (30 ml/kg)
OR
2. Lactic acid greater than or equal to 4 mmol/L with any BP

NO → **For Lactic Acid 2-2.9** → Initiate **General Care Severe Sepsis Bundle** on back and complete interventions

NO → For **Lactic acid 3-3.9** or **initial hypotension that responded to the 30 ml/kg fluid bolus,** initiate transfer to IMC → Initiate **Intermediate Care Severe Sepsis Bundle** on back and complete interventions.

YES → Activate CODE SEPSIS → Initiate transfer to ICU

Meanwhile, continue crystalloid resuscitation of 250-1000ml boluses if hypotensive after the initial bolus – per physician order

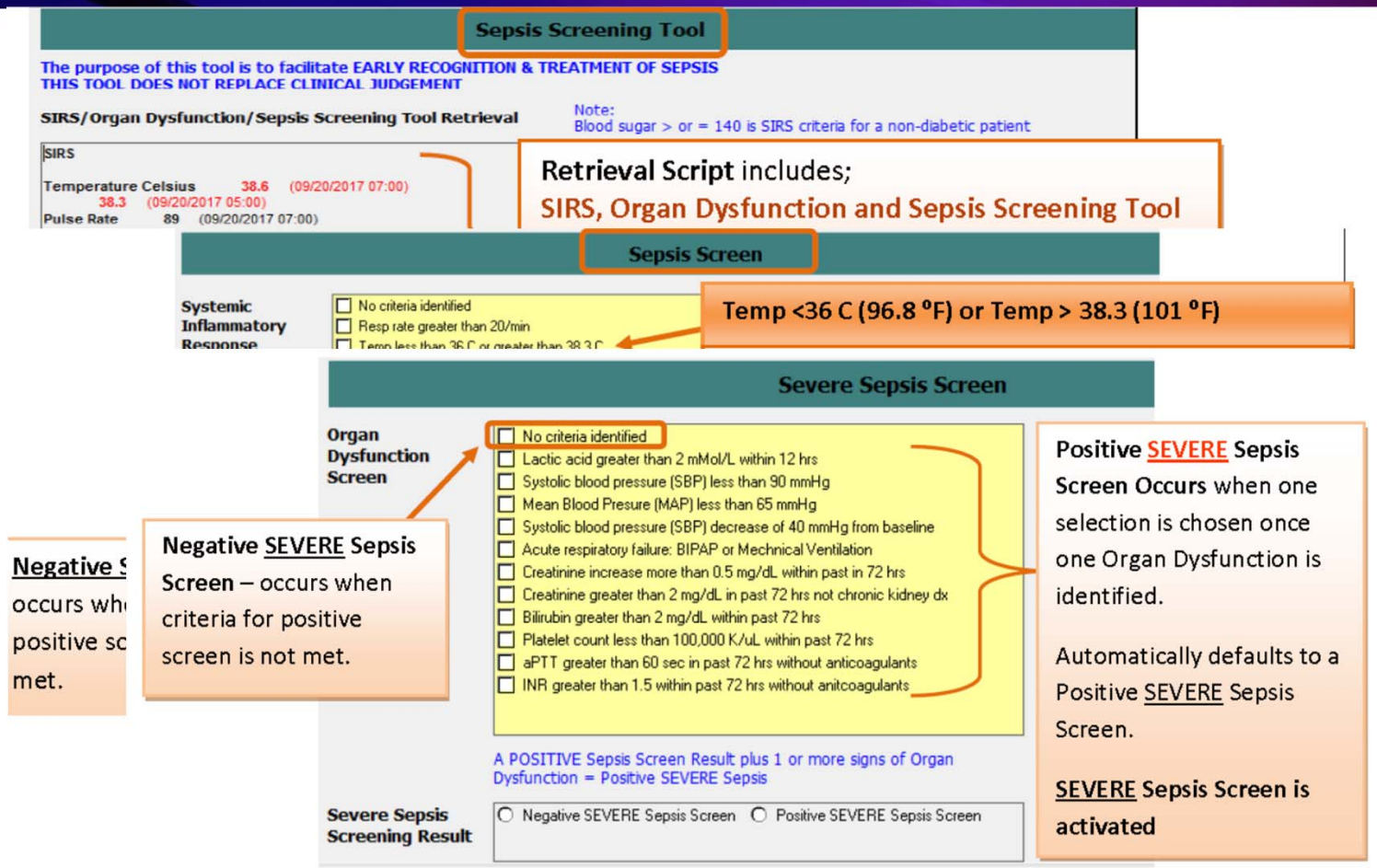
Initiate the **Septic Shock Pathway** and complete interventions

RN Signature, Initial Date & Time:

* A A 1 3 1 4 *

292239 (02/12) SevereSepsis DRAFT R 0/12 IM/O

Electronic Routine Screening



Sepsis 3:

- **Sepsis is:** 'life-threatening organ dysfunction caused by a dysregulated host response to infection'
  - Sepsis-3 does away with:
    - SIRS criteria (sepsis is pro- and anti-inflammatory)
    - Severe sepsis (sepsis = the old severe sepsis)
    - Antiquated concepts: sepsis syndrome; septicemia
- **Sepsis:** infection plus 2 or more SOFA (Sequential Organ Failure Assessment) points
- **Septic shock:** vasopressor-dependent hypotension + lactate >2

Sepsis-3 includes clinical criteria to predict life-threatening disease

Singer et al, JAMA 2016. PMID: 26903338

SOFA

qSOFA: (have 2 or more of these, then evaluate for SOFA)

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score*

System	Score 0	1	2	3	4
Respiration					
PaO_2/FIO_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: FIO_2, fraction of inspired oxygen; MAP, mean arterial pressure; PaO_2, partial pressure of oxygen.

* Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

Respiratory Rate ≥ 22
Altered Mental Status
Systolic BP ≤ 100mmHg

- 13% to 50% of patients with infections who died within 30 days had a q SOFA score of ≥ 2 at ED presentation
- Predictors of mortality, not designed to predict an etiology of illness

Uffen JW et al. Clinical Microbiology and Infection. 2020 in press

Challenges with New Sep-3 Definitions

- SIRS not part of the definition:
  - the most appropriate use for SIRS is that its presence prompts an immediate search for both infection, as its possible source, and organ dysfunction, as its possible companion
- Doesn't recognize 'cryptic shock'
- People will begin to use qSOFA as a screening tool
  - qSOFA and SOFA are predictors of mortality; they are not test of early sepsis at risk to progress to organ failure
- Only their predictive ability for morality and prolonged ICU stay have been evaluated, not their utility in reducing mortality

Simpson, S. Chest. January 2018 SIRS in the Time of Sepsis-3

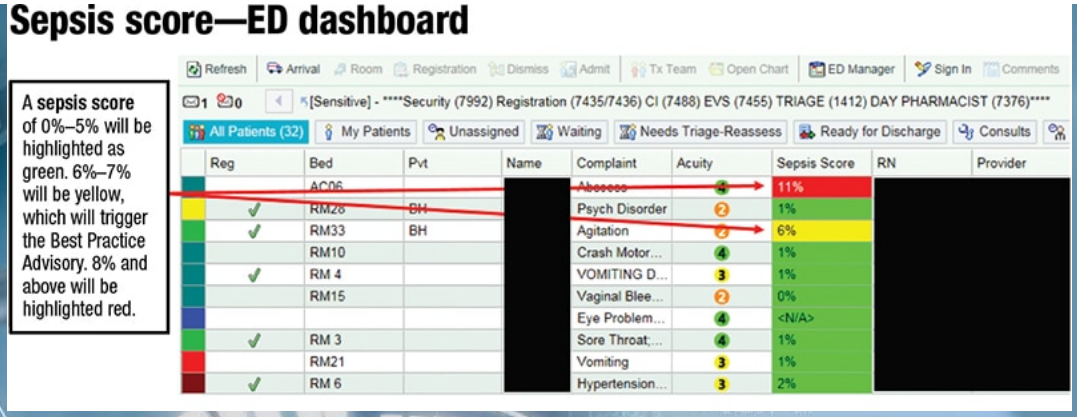
Table 3. Tradeoffs among Tools for Screening for Abnormal Physiology

	Accuracy	Timeliness	Feasibility	Comments
SIRS	★	★★	★★★	With high sensitivity but very low specificity, SIRS can be expected to generate many false positives. It is incorporated into CMS's Sep-1 approach and is familiar to many providers.
qSOFA	★★	★	★★★	qSOFA is incorporated into Sepsis 3 as a prompt for clinicians to consider sepsis. It has better specificity than SIRS, but sacrifices some sensitivity.
Early Warning Scores	★★	★★	★★	Early warning scores such as MEWS, NEWS, and PEWS have been incorporated by many hospitals as part of rapid response system deployments. They require the computation of a score at bedside, which may limit feasibility.
Computerized algorithms	★★★	★★★	★	Computerized algorithms use many parameters to enhance sensitivity and specificity of detecting patients at risk of poor outcomes, but their complexity may require specialized informatics support for practical implementation. They have not been widely disseminated or adopted; therefore, their wide application has yet to be confirmed.

- SCCM Early Identification of Sepsis on the floors 2019

Machine Learning

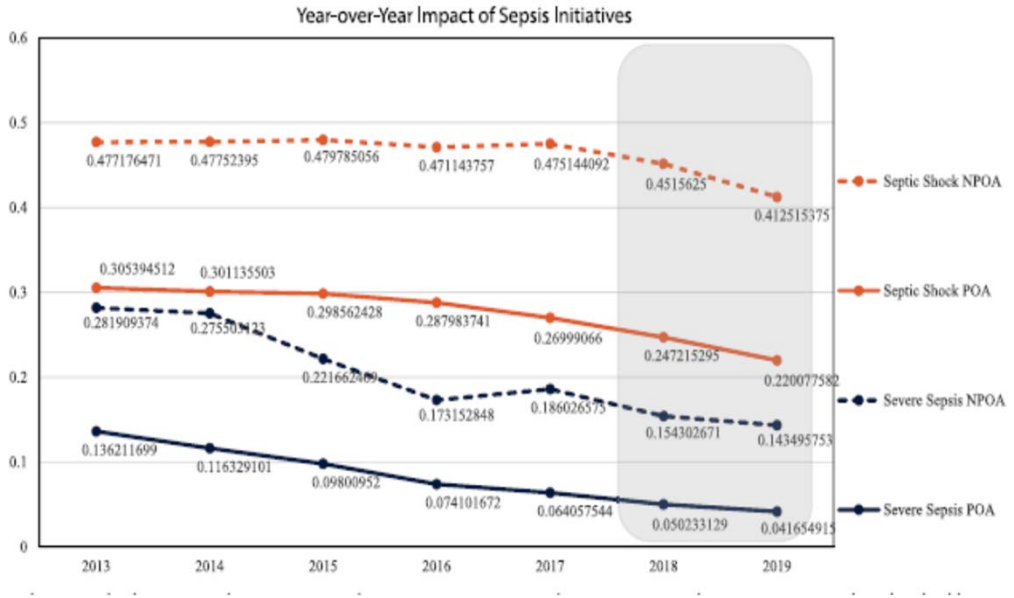
- EPIC's ESPM: Predictive model /scan data q 15 min. When it reach a threshold, a BPA is fired for the nurse to screen the patient for severe sepsis (AUC .73)[1]
- Deterioration Index—to recognize patient who is significantly changing (not specific for sepsis)
- Early Warning scores/not specific for sepsis
- SPOTting: HCA tool for sepsis



1.Bennett T, 2019 accessed at https://arxiv.org/abs/1902.07276

SPOTting Sepsis to Save Lives: HCA Computer Algorithm to Detect Sepsis

- SPOT Algorithm designed as rules-based detection of defined criteria in near real time
- Defines sepsis as presence of SIRS, documented suspected infection (BC or therapeutic antibiotic within 24hrs of SIRS)
- Transmitted alert through telemetry techs-relays to the nurse
- Nurse preforms a sepsis screen
- Near real time data for the sepsis coordinator
- Can be reproduced by any health system or EHR company



Perlin JB, et al. The Joint Commission Journal on Quality & Patient Safety. 2020;46:381-391

Early Recognition Challenges & Solutions

SCCM Early Identification of Sepsis on the floors

- Barriers/Contributing Factors
  - Time for nurses to do it (perception vs. reality)
  - Screening is not sensitive only for severe sepsis
  - Positive screen is not a diagnosis of severe sepsis
  - Nursing staff does not recognize when the patient is met sepsis criteria
  - Hesitant to call physician regarding possible sepsis patients or hesitant to question or recommend treatment

Targeted Education/Solutions

- Must assign responsibility and enforce accountability
- Develop enhanced education to improve knowledge of risk and sepsis recognition
- Develop and implement standardized sepsis screening tools and treatment protocols
- Perform audits to measure compliance and identify problems
- Round on unit and ask nurses how it is going and discuss issues
- Implement scepsis tool/positive sepsis screen form to communicate with charge nurse

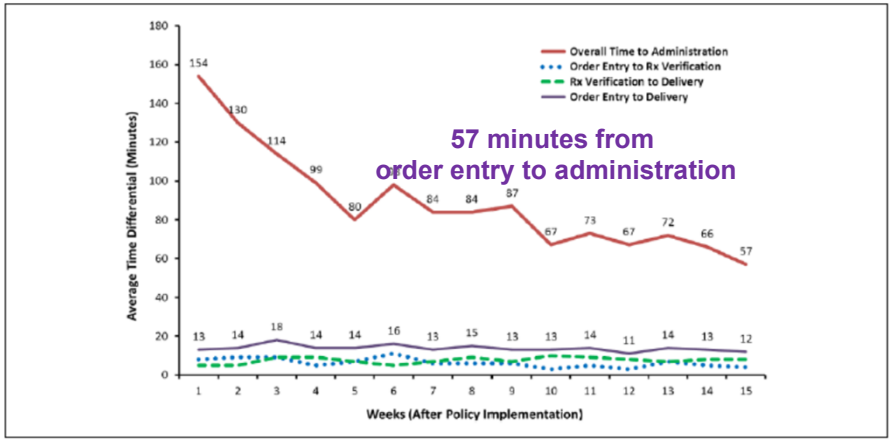
Strategies: Establish Trigger for Rapid Implementation of SSC Bundles

- Clearly define next steps for patients with positive screen for severe sepsis
  - Alert RRT/Med Team
  - Notify Physician
  - Begin 3-hour bundle: lactate, blood cultures, antibiotics, fluid

SBAR
Situation:
Screened Positive for Severe Sepsis
Background:
1. Positive Systemic Response to Infection
2. Known or suspected infection
3. Organ dysfunction: share which organs
Assessment:
Share any other clinical changes?
Recommendations:
1. I need you to come and evaluate the patient to confirm if they have severe sepsis
2. It is recommended that I get an ABG, lactate, blood cultures and a CBC (if > 12 hrs since last one). Can I proceed and get these?
3. Any other labs you would like me to obtain? Do you want to order antibiotics?
4. If patient is hypotensive: Can I start an IV and give a bolus of NS—30ml/kg
Date/time of call: _____
RRT called: Yes No

Clinical & Economic Impact of a QI to Improve Early Recognition/Treatment

- 433 bed tertiary Medical Center
- Retrospective observational study
- 181 pre/216 post
- Interventions;
  - 1st-dose stat antibiotic policy
  - electronic sepsis screening per shift
- Measurement:
  - ICU & hospital LOS
  - Mortality



Combined Septicemia DRGS	Historical Group N=181	Intervention Group n =216	P value
ICU LOS	5.9 (4.4)	4.2 (3.6)	0.003
Total cost per case	$14,377.89	$12,310.99	0.03

Judd WR, et al. Annals of Pharmacotherapy. 2014;48(10):1269-1275

Nurse Driven Screening Tool: Impact

- Academic medical center IMU
- Introduce screening every q shift
- 245 pts, 2143 screens
- 39 pts + screen
- Sensitivity/specificity 95%/92%
- Negative predictive value 99%
- Positive predictive value 54%

Gyang E, et al. Journal of Hospital Medicine. 2015;10:97-103

Screening in the ED: The Impact

- 310 bed acute care hospital
- Development of an ER based screening tool
- Pre and post measurement
- Education and next steps provided

Table. Bundle Completion Time, Antibiotic Completion Time, LOS, and Mortality

Variable	Preintervention (n = 165) Mean (SD)	Postintervention (n = 145) Mean (SD)	*P*
Time to bundle complete	593 (1388)	135 (236)	<.001
Time to antibiotic administration	185 (337)	84 (150)	<.001
LOS	9.15 (10.77)	9.17 (8.97)	.663
Mortality	12.1%	6.2%	.074

Threatt DL. J Nurs Care Quality, 2019;35(2):135-139

"As the physician say of hectic fever, that in the beginning of the malady it is difficult to detect but easy to treat, but in the course of time, having been neither detected nor treated in the beginning, it becomes easy to detect but difficult to treat"

Niccolo Machiavelli, 14th Century

Simpson, S. Chest. January 2018 SIRS in the Time of Sepsis-3

Sepsis Management

SEP-1

TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION † :

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L

† *"time of presentation" is defined as the time of earliest chart annotation consistent with all elements severe sepsis or septic shock ascertained through chart review.*

Time Zero

- Will always be when the chart annotation suggests signs and symptoms are all present.
- May be from **nursing charting/screens**, lab flow sheets, physician documentation, order sets, anything with a time stamp.
- Will = triage time if all signs and symptoms are present at triage.
- ***It does not require MD documentation of the clock starting and relying on this alone in the ED would likely result in late clock starts.***

Slides courtesy of Sean Townsend

SEP-1

TO BE COMPLETED WITHIN 6 HOURS OF TIME OF PRESENTATION:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65mmHg
6. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion and document findings according to table 1.
7. Re-measure lactate if initial lactate elevated.

SEP-1

TABLE 1

DOCUMENT REASSESSMENT OF VOLUME STATUS AND TISSUE PERFUSION WITH:

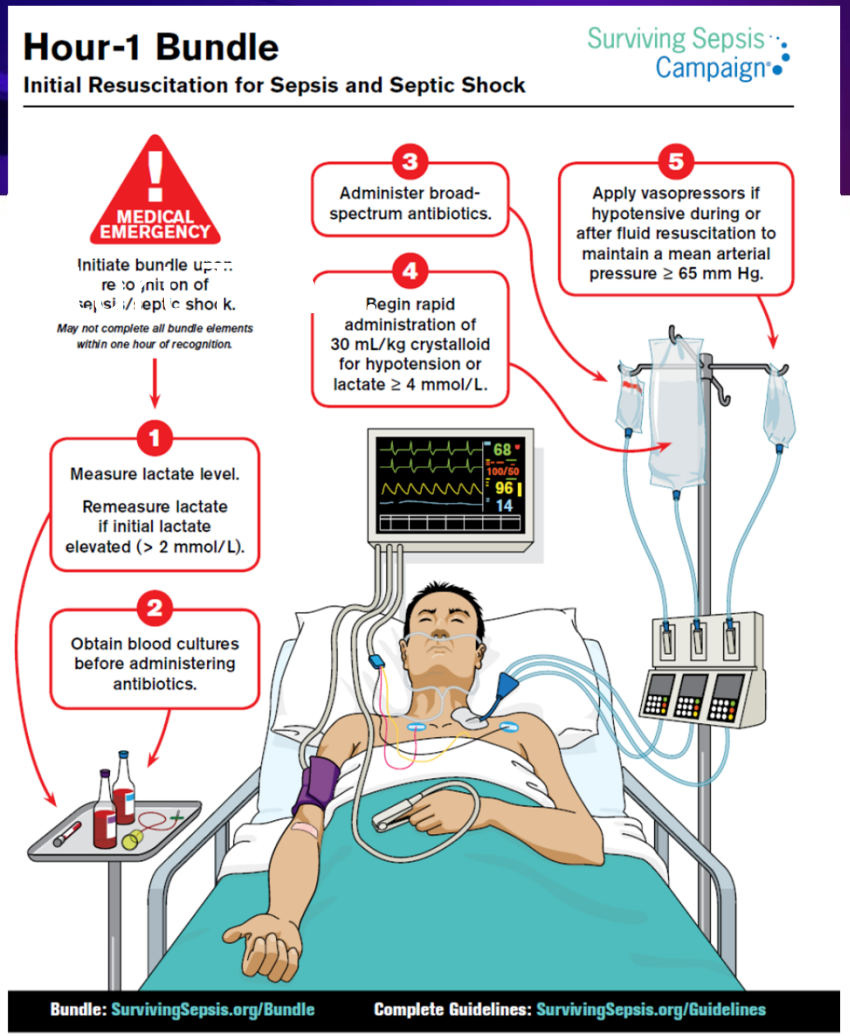
Either

- Repeat focused exam(after initial fluid resuscitation) by licensed independent practitioner including vital signs, cardiopulmonary, capillary refill, pulse and skin findings.

Or one of the following:

- Measure CVP
- Measure ScvO2
- Bedside cardiovascular ultrasound
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

Launched with Controversy



http://www.survivingsepsis.org/Bundles/Pages/default.aspx

Challenges with the Bundles

- Timely antibiotics
- 30ml/kg fluid bolus
- Repeat lactate
- Sepsis reassessment

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early, Goal-Directed Therapy for Septic Shock — A Patient-Level Meta-Analysis

The PRISM Investigators*

- 3723 patients at 138 hospitals in seven countries (all patients from the PROCESS, PROMIS and ARISE trials)
- **Prior to randomization >92% of patients were identified early, and provided the 3 hour bundle (including 2L of fluid and antibiotics- given within 70 minutes of presentation to ED)**
- No difference in 90 day mortality between EGDT and Usual Care groups
- Authors stated: "It remains possible that general advances in the provision of care for sepsis and septic shock, to the benefit of all patients, explain part or all of the difference in findings between the trial by Rivers et al. and the more recent trials"

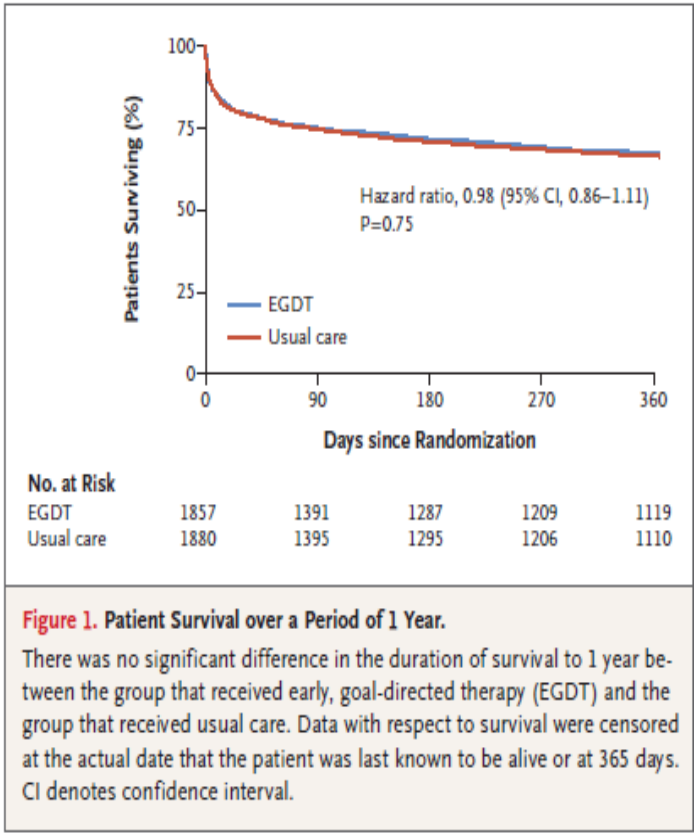


Figure 1. Patient Survival over a Period of 1 Year.
There was no significant difference in the duration of survival to 1 year between the group that received early, goal-directed therapy (EGDT) and the group that received usual care. Data with respect to survival were censored at the actual date that the patient was last known to be alive or at 365 days. CI denotes confidence interval.

NEJM , March 21, 2017

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

Christopher W. Seymour, M.D., Foster Gesten, M.D., Hallie C. Prescott, M.D., Marcus E. Friedrich, M.D., Theodore J. Iwashyna, M.D., Ph.D., Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H., Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M

- In 2013, New York began requiring hospitals to follow protocols for the early identification
- April 2014 to June 30, 2016
- 49,331 patients at 149 hospitals
- 82.5% had the 3-hour bundle completed within 3 hours (median time was 1.3 hrs)
- Longer time to completion of the 3-hour bundle was associated with higher risk-adjusted in-hospital mortality as well as longer time to administration of antibiotics (14% higher for both)

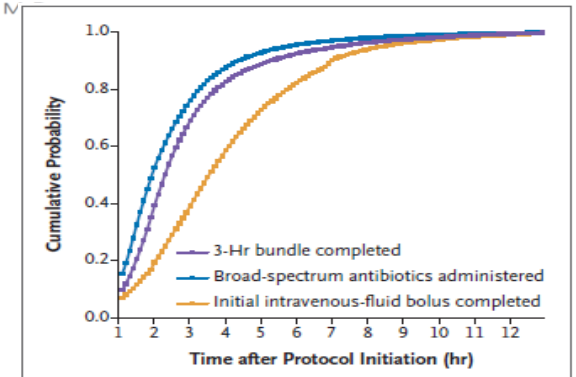


Figure 1. Cumulative Probability of Completion of the 3-Hour Bundle, Administration of Broad-Spectrum Antibiotics, and Completion of the Initial Intravenous-Fluid Bolus after the Time That the Sepsis Protocol Was Initiated.

- Risk adjusted mortality decreased from 28.8% to 24.4% ($p<0.001$)
- Risk adjusted mortality decreased by 5% for every 10% increase in compliance with the 3- and 6-hour bundle Levy, M. AJRCC. Dec. 2018

Antibiotics are Key

ORIGINAL ARTICLE

The Timing of Early Antibiotics and Hospital Mortality in Sepsis

Vincent X. Liu[1], Vikram Fielding-Singh[2], John D. Greene[1], Jennifer M. Baker[1], Theodore J. Iwashyna[3,4], Jay Bhattacharya[5], and Gabriel J. Escobar[1]

[1]Kaiser Permanente Division of Research, Oakland, California; [2]Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, California; [3]Center for Clinical Management Research, VA Ann Arbor Health System, Ann Arbor, Michigan; [4]Division of Pulmonary and Critical Care, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan; and [5]Primary Care and Outcomes Research, Stanford University, Stanford, California

American Journal of Respiratory and Critical Care Medicine Volume 196 Number 7 | October 1 2017

- Each elapsed hour between presentation and antibiotic administration was associated with a 9% increase in the odds of mortality with sepsis of all severity strata

Increased Time to Initial Antimicrobial Administration Is Associated With Progression to Septic Shock in Severe Sepsis Patients

Bristol B. Whiles, BS1; Amanda S. Deis, MS1; Steven Q. Simpson, MD2
Critical Care Medicine. April 2017. Vol 45. Number 4

- Each hour until initial antimicrobial administration was associated with a 8% increase in progression to septic shock.
- Patients who progressed to shock had significant increase in hospital LOS (18.7 days vs 9.66 days) and mortality (30.1% vs 7%)

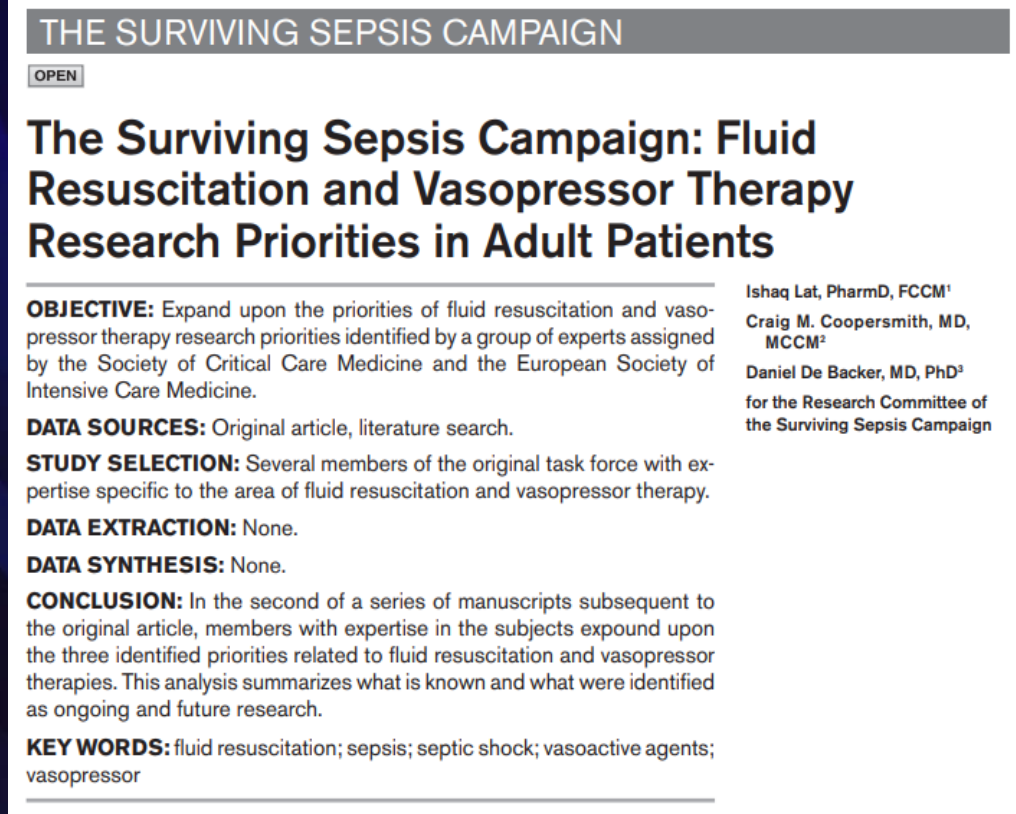
Antibiotics

- Appropriate initial antibiotics
  - Guide for providers recommending the appropriate antibiotic based on whether hospital or community acquired, source and your hospitals antibiogram
- Turnaround time---from indication to hanging
  - ED vs ICU vs Floor
- Understand your current process and where the gaps are
- Make antibiotics rapidly available
- Factors that showed delay administration
  - Higher APACHE, older, presence of co-morbidities, HLOS before hypotension, dx of pneumonia, admin to academic hospitals & transfer from medical wards

Amaral ACKB, et al. Crit Care Med;2016;44:2145-2153

Challenge with Fluids and Sepsis Patient

SCCM April 2021



THE SURVIVING SEPSIS CAMPAIGN

OPEN

The Surviving Sepsis Campaign: Fluid Resuscitation and Vasopressor Therapy Research Priorities in Adult Patients

Ishaq Lat, PharmD, FCCM[1]
Craig M. Coopersmith, MD, MCCM[2]
Daniel De Backer, MD, PhD[3]
for the Research Committee of the Surviving Sepsis Campaign

OBJECTIVE: Expand upon the priorities of fluid resuscitation and vasopressor therapy research priorities identified by a group of experts assigned by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine.

DATA SOURCES: Original article, literature search.

STUDY SELECTION: Several members of the original task force with expertise specific to the area of fluid resuscitation and vasopressor therapy.

DATA EXTRACTION: None.

DATA SYNTHESIS: None.

CONCLUSION: In the second of a series of manuscripts subsequent to the original article, members with expertise in the subjects expound upon the three identified priorities related to fluid resuscitation and vasopressor therapies. This analysis summarizes what is known and what were identified as ongoing and future research.

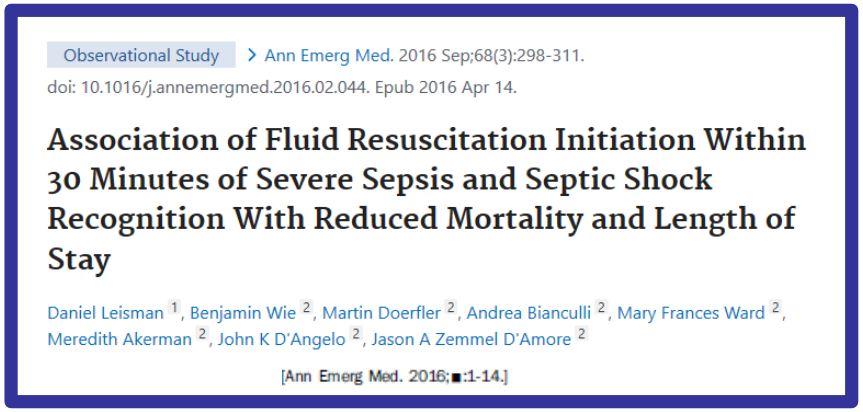
KEY WORDS: fluid resuscitation; sepsis; septic shock; vasoactive agents; vasopressor

Ishaq Lat, etal, Critical Care Medicine April 2021 Volume 49, Number 4

The three fluid and vasopressor questions identified by the Task Force as a whole are as follows:

1. What are ideal endpoints for volume resuscitation and how should volume resuscitation be titrated?
2. What is the optimal fluid for sepsis resuscitation
3. What is the optimal approach to selection, dose titration, and escalation of vasopressor therapy?

Early Fluid Resuscitation is Key



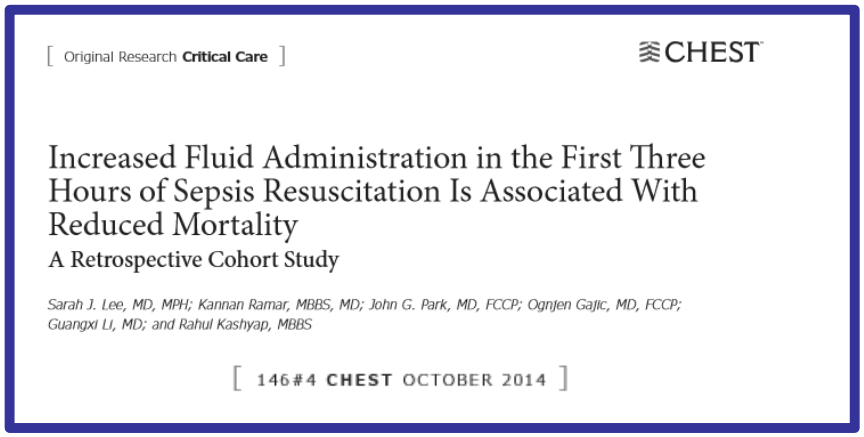
Observational Study > Ann Emerg Med. 2016 Sep;68(3):298-311.

doi: 10.1016/j.annemergmed.2016.02.044. Epub 2016 Apr 14.

Association of Fluid Resuscitation Initiation Within 30 Minutes of Severe Sepsis and Septic Shock Recognition With Reduced Mortality and Length of Stay

Daniel Leisman [1], Benjamin Wie [2], Martin Doerfler [2], Andrea Bianculli [2], Mary Frances Ward [2], Meredith Akerman [2], John K D'Angelo [2], Jason A Zemmel D'Amore [2]

[Ann Emerg Med. 2016;■:1-14.]



[Original Research **Critical Care**]

CHEST

Increased Fluid Administration in the First Three Hours of Sepsis Resuscitation Is Associated With Reduced Mortality

A Retrospective Cohort Study

Sarah J. Lee, MD, MPH; Kannan Ramar, MBBS, MD; John G. Park, MD, FCCP; Ognjen Gajic, MD, FCCP; Guangxi Li, MD; and Rahul Kashyap, MBBS

[146#4 **CHEST** OCTOBER 2014]

↑ mortality with later fluid administration 13.3% (30 minutes) versus 16.0% (31 to 60 minutes) versus 16.9% (61 to 180 minutes) versus 19.7% (>180 minutes)

After adjusting for confounders, the higher proportion of total fluid received within the first 3 hrs was associated with decreased hospital mortality

Early Fluid Resuscitation is Key

Multicenter Implementation of a Treatment Bundle for Patients with Sepsis and Intermediate Lactate Values

Vincent X. Liu[1,2], John W. Morehouse[2], Gregory P. Marelich[2], Jay Soule[2], Thomas Russell[2], Melinda Skeath[3], Carmen Adams[3], Gabriel J. Escobar[1,2], and Alan Whippy[2]

[1]Kaiser Permanente Division of Research, Oakland, California; [2]The Permanente Medical Group, Oakland, California; and [3]Kaiser Foundation Hospitals and Health Plan, Oakland, California

American Journal of Respiratory and Critical Care Medicine Volume 193 Number 11 | June 1 2016

Patterns and Outcomes Associated With Timeliness of Initial Crystalloid Resuscitation in a Prospective Sepsis and Septic Shock Cohort*

Daniel E. Leisman, BS[1,2,3]; Chananya Goldman, MD[4]; Martin E. Doerfler, MD[4,5]; Kevin D. Masick, PhD[6]; Susan Dries, RN, PhD[6]; Eric Hamilton, BA[6]; Mangala Narasimhan, DO[7]; Gulrukh Zaidi, MD[7]; Jason A. D'Amore, MD[1]; John K. D'Angelo, MD[1,2]

Critical Care Med October 2017 • Volume 45 • Number 10

Decrease in hospital mortality was observed primarily in patients with heart and/or kidney failure ($p<0.04$) who received at least 2 Liters fluid resuscitation for severe sepsis with lactate between 2.1-3.9

Early fluid initiation (30-120 minutes) was associated with significantly lower hospital mortality, mechanical ventilation, ICU admission, LOS and ICU days & no harm seen to the patients

Heart Failure—Going to Flood My Patient Not Based in Evidence

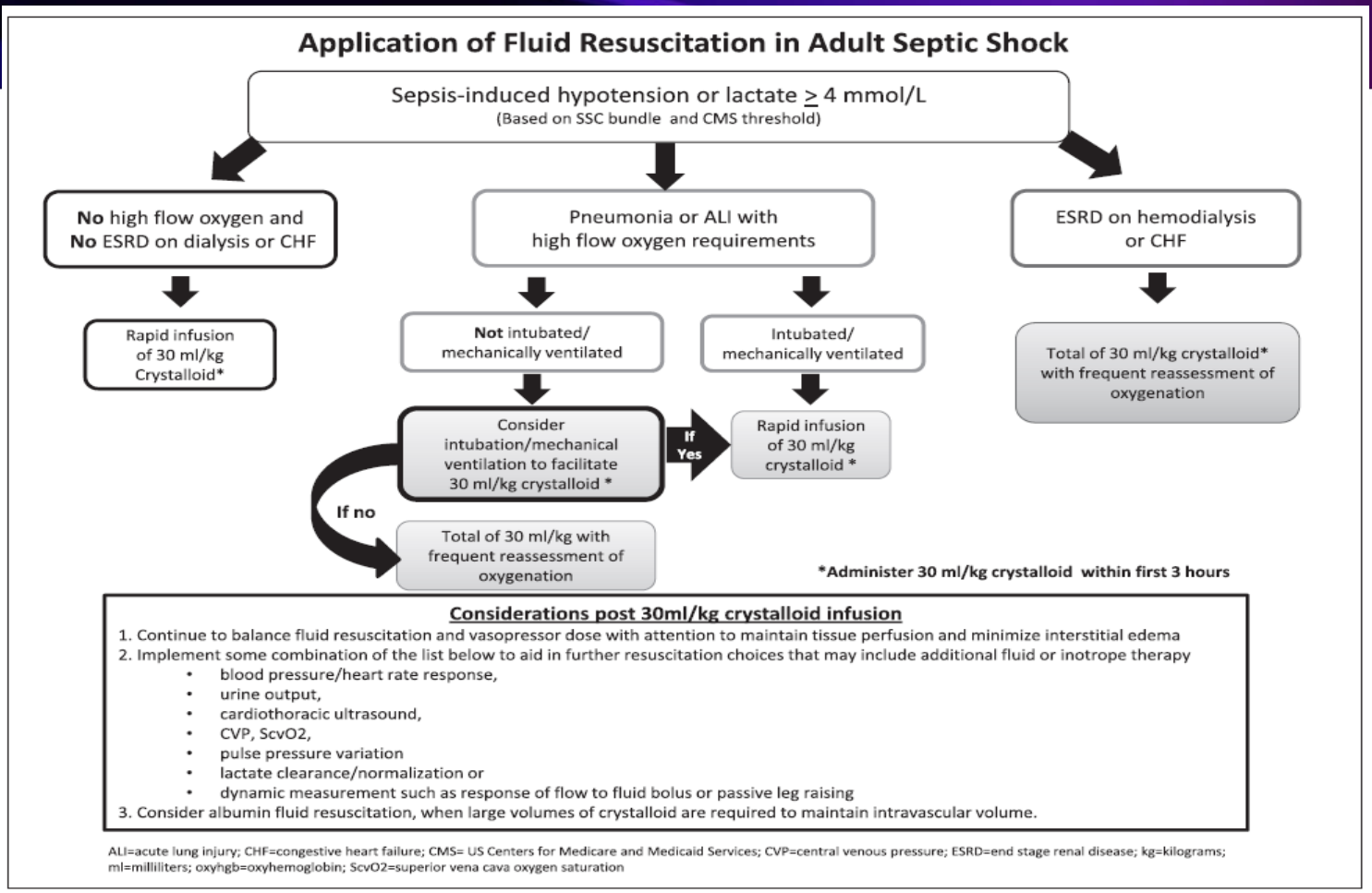
- Rivers et al Study: % Ventilated Patients

	Hours after start of Therapy		
	0-6	7-72	0-72
Standard Therapy	53.8%	16.8%	70.6%
Early Goal Directed Therapy	53%	2.6%	55.6%
P Value		<.001	0.02

Chronic coexisting conditions-CHF:
Control 30.2%
EGDT 36.7%

N Engl J Med 2001;345:1368-1377

Application of Fluid Resuscitation in Adult Septic Shock



User's Guide to the 2016 Surviving Sepsis Guidelines Dellinger, CCM published ahead of print 1-2017

Why Do All Severe Sepsis Patients Need Some Volume?

- Vascular volume is lost into interstitial space do to diffuse capillary leaking from cytokine release
- Both venous and arteriolar tone is reduced & blood volume occupies a larger intravascular space than normal
- Many patients also have GI and Skin losses
- Only 40% of NS stays intravascular the rest goes into the interstitial space. An initial BP response is not an indication to not give full bolus

Resuscitation fluid is different than long term fluids

Why Do All Severe Sepsis Patients Need Volume?

- Large trial before and after bundle implementation for patients with intermediate lactate values >2 < 4.
- ↓ in hospital mortality in the bundle implementation group was observed in the patient with CHF and kidney disease compared with patients without
- Received more fluid with the bundle approach

Liy VX, et al Am J of Respir and Crit Care Med, 2016;193:1264-1297

The Risks of Under-Resuscitation vs Over Resuscitation

Under-Resuscitation

- Altered tissue perfusion
- Renal failure
- Confusion, risk of CVA
- Splanchnic ischemia
- Multi-System Organ Failure (MSOF)
- Circulatory collapse

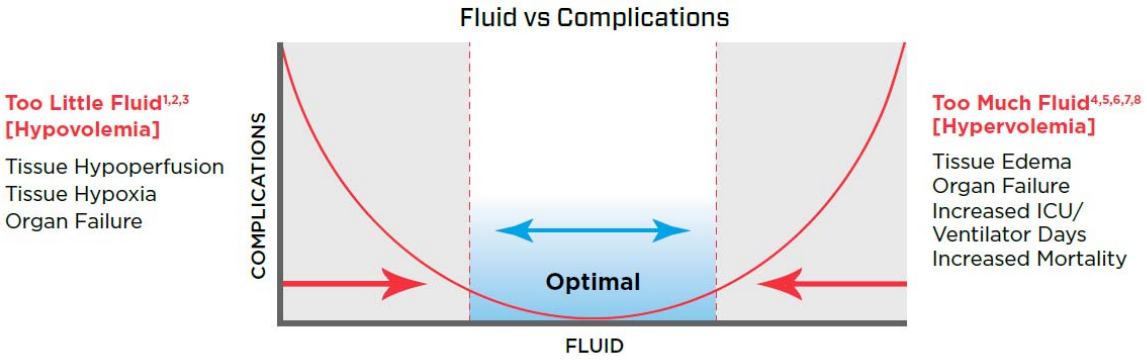
Over-Resuscitation

- Lung water (ARDS)
- Peripheral edema
- Delirium
- Abdominal Hypertension
- Abdominal Compartment Syndrome
- Acute Kidney Injury
- Increased ICU and Hospital LOS
- Increased ventilator days

Vincent JL, *Kidney International*, 2019;96:52-57

We Need to Get the Fluids Just Right

FLUID IMBALANCE can lead to SERIOUS CONSEQUENCES



SEPSIS/SHOCK	VOLUME OVERLOAD IN SEPTIC PATIENTS IS ASSOCIATED WITH AN INCREASED RISK OF MORTALITY.[6,7]
SURGERY (ERAS)	CAREFUL MANAGEMENT OF INTRAOPERATIVE FLUIDS CAN GREATLY ENHANCE PATIENT OUTCOMES.[5]

References:

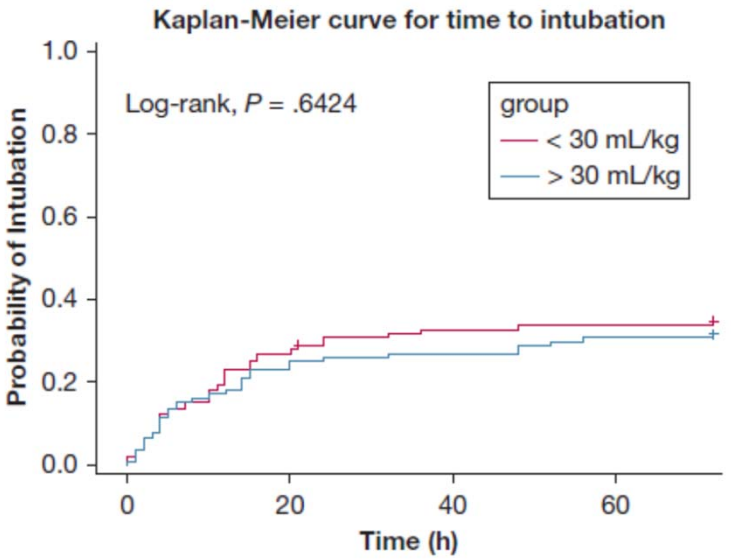
1. Shoemaker W et al. Tissue oxygen debt as a determinant of lethal and nonlethal postoperative organ failure. Crit Care Med 1988; 16:1117-1120.
2. Vermeulen H et al. Intravenous fluid restriction after major abdominal surgery: A randomized blinded clinical trial. Trials 2009; 10:50.
3. Rivers E et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. NEJM 2001; 345:1368-1377.
4. Gustafsson UO et al. Enhanced Recovery after Surgery Society. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations. Clin Nutr. 2012; 31:783-800.
5. Corcoran T et al. Perioperative Fluid Management Strategies in Major Surgery: A stratified meta-analysis. Anesth Analg 2012; 114:640-651.
6. Boyd J et al. Vasopressin in Septic Shock Trial (VASST). Critical Care Medicine 2011; 39:259-265.
7. Vincent JL et al. Sepsis in European ICU: Results of the SOAP Study. Critical Care Med 2006; 34:344-353.
8. Kelm D et al. Fluid overload in patients with severe sepsis and septic shock treated with early goal directed therapy is associated with increased acute need for fluid-related medical interventions and hospital death. Shock 2015; 43:680-73.

Association Volume Resuscitation & Intubation

- Propensity score matched retrospective cohort study
- Severe sepsis or septic shock admitted to MICU (high risk cirrhosis, CHF & renal failure pts in both groups)
- IV fluid volume 1st 6 hours after sepsis diagnosis
  - ≥ 30 ml/kg (104 pts) -3386cc ± 1069cc
  - < 30 ml/kg (104 pts)-1390cc ± 700cc

TABLE 2] Primary and Secondary Outcomes

Outcome	Restricted Group (< 30 mL/kg) (n = 104)	Standardized Group (> 30 mL/kg) (n = 104)	*P* Value
Intubation within 72 h	36 (35%)	33 (32%)	.64
Change in F_{IO_2}, %	6 ± 14	7 ± 12	.89
Time to intubation, h	14 ± 15	16 ± 19	.55
Alive ICU-free days at day 28	17 ± 10	17 ± 11	.64
Hospital mortality	19 (18%)	26 (25%)	.21
Ventilator days	11 ± 16	10 ± 12	.96



Khan RA, et al Chest. 2020;157(2):286-292

Evaluation of Fluid Resuscitation in Severe Sepsis & Septic Shock

- Retrospective cohort study
- All outcome analysis controlled for sex and stage renal disease, heart failure , sepsis severity and obesity
- Urban tertiary care center 01/2014-05/2017
- 1032 ED patients
  - 49% 30/by 3hrs
  - Failure to meet 30by3 irrespective of comorbidities increase odds
    - Mortality
    - Delay hypotension
    - Increase LOS

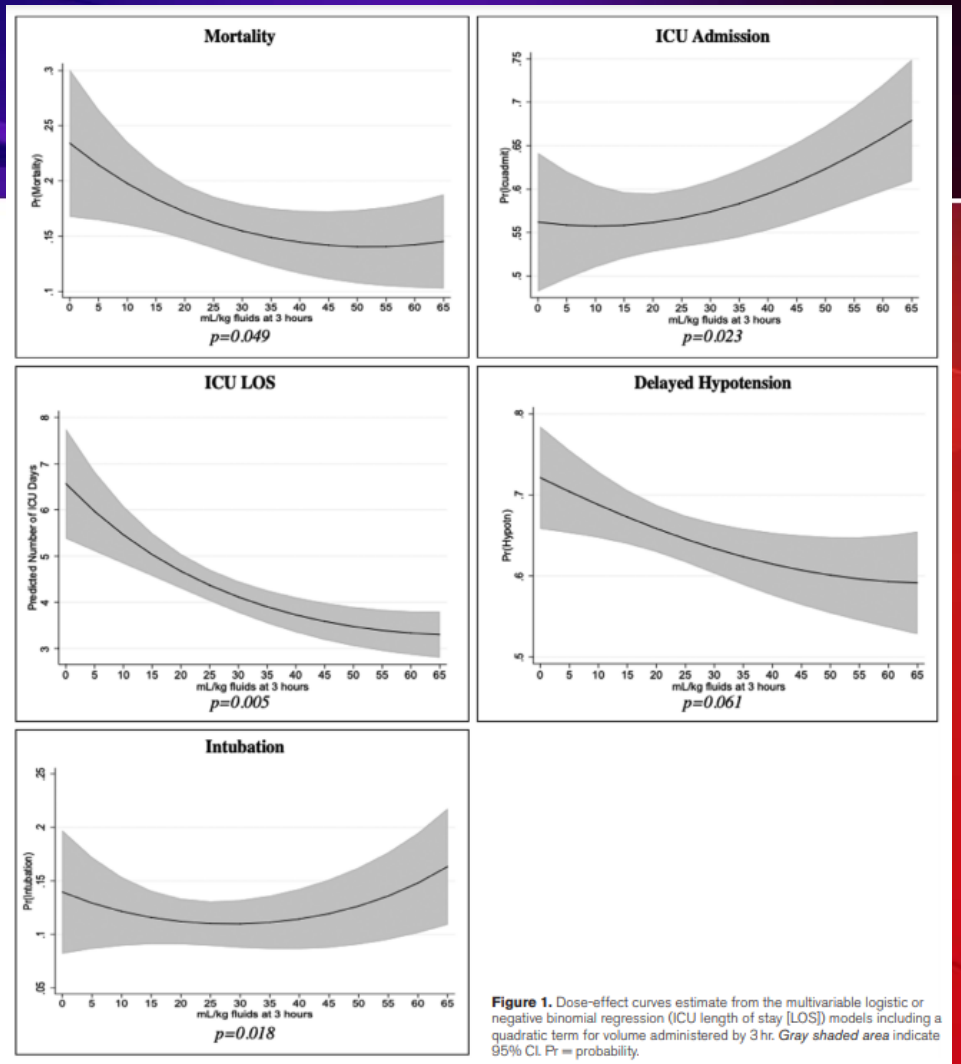


Figure 1. Dose-effect curves estimate from the multivariable logistic or negative binomial regression (ICU length of stay [LOS]) models including a quadratic term for volume administered by 3 hr. *Gray shaded area* indicate 95% CI. Pr = probability.

Kuttab HI, et al. Crit Car Med 2019;47:1582-1590

What is Associated with Early vs Late Fluid Initiation?

- Early fluid Initiation
  - Presented in the Ed versus the wards
  - Had urinary or soft tissue infections
  - Febrile
  - Hypotensive
  - Higher initial lactate
- Later Fluid Initiation
  - Heart failure
  - Renal failure
  - Baseline altered gas exchange treated at a tertiary center

Leismean D, et al. *Crit Care Med*. 2017;45(10):1596-1606

Type of Fluid

SALT-ED and SMART Studies - RCT

SALT-ED

- 13,347 patients
- Saline vs. LR/Plasma-Lyte in non-critically ill
- Median fluids administered 1079 ml

Saline led to a higher incidence of acute kidney injury (AKI)
Saline Challenges:
High Sodium and Chloride Content
Hyperchloremia
Acidosis

SMART

- 15,802 patients
- Saline vs. LR/Plasma-Lyte in critically ill
- Median fluids administered ~ 2.5 L
  - ~ 33% mechanical ventilation
  - ~ 25% vasopressors

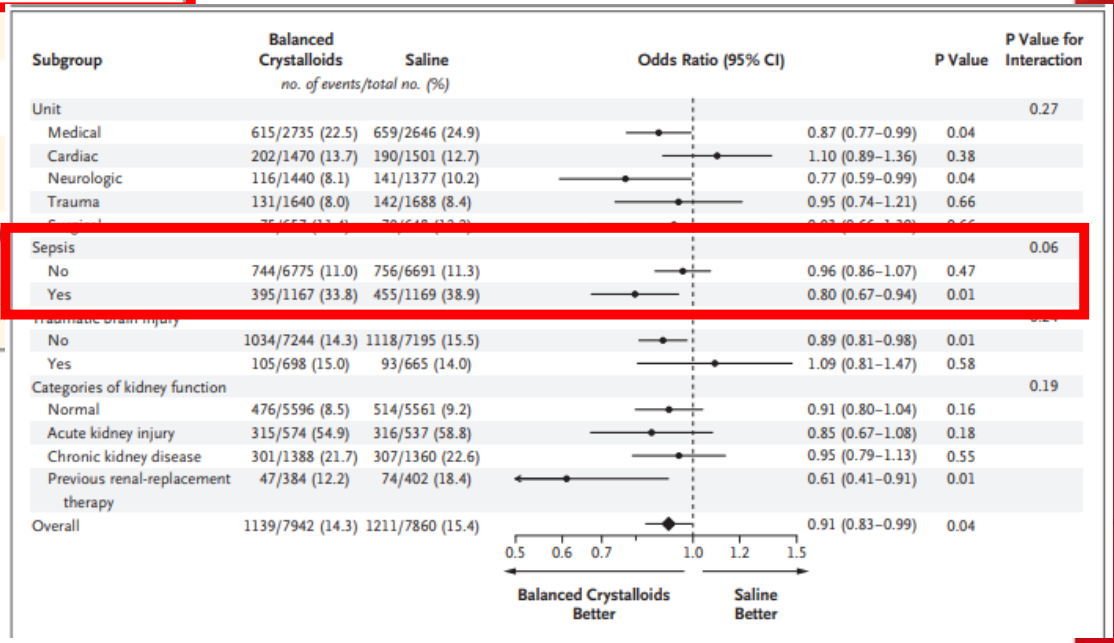
Self et al *NEJM 2018;* 378;9
Semler et al *NEJM 2018*; 378;9

Results: SALT ED SMART

Table 3. Clinical Outcomes According to Assigned Treatment Group in the Intention-to-Treat Analysis.

Outcome	Balanced Crystalloids (N=6708)	Saline (N=6639)	Adjusted Odds Ratio (95% CI)*	Adjusted P Value
Median hospital-free days to day 28 (IQR)	25 (22–26)	25 (22–26)	0.98 (0.92–1.04)	0.41
Major adverse kidney event within 30 days — no. (%)	315 (4.7)	370 (5.6)	0.82 (0.70–0.95)	0.01
Death — no. (%)	94 (1.4)	102 (1.5)	0.89	
New renal-replacement therapy — no./total no. (%)†	18/6582 (0.3)	31/6530 (0.5)	0.56	
Final serum creatinine ≥200% of baseline — no./total no. (%)†	253/6582 (3.8)	293/6530 (4.5)	0.84	
Stage 2 or higher acute kidney injury — no./total no. (%)†	528/6582 (8.0)	560/6530 (8.6)	0.91 (0.80–1.0	
In-hospital death — no. (%)	95 (1.4)	105 (1.6)	0.88 (0.66–1.1	

KIDNEY Injury Events!



Semler, Self et al *NEJM*. 2018:378;9,

Secondary Analysis of SMART

- 15,802 patients enrolled in SMART
- 1,641 patients were admitted to the medical intensive care unit with a diagnosis of **sepsis**
- 217 patients **(26.3%)** in the balanced crystalloids group experienced 30-day in-hospital morality, compared with,
- 255 patients **(31.2%)** in the saline group
  - (adjusted odds ratio, 0.74; 95% confidence interval, 0.59 – 0.93; p = 0.01)

Secondary Outcomes

- Patients in the balanced group experienced a lower incidence of major adverse kidney events within 30 days
  - (35.4% vs 40.1%; OR 0.78; 95% CI 0.63 – 0.97)
- Greater number of vasopressor-free days
  - (20 ± 12 vs 19 ± 13; OR 1.25; 95% CI 1.02 – 1.54)
- Renal replacement therapy-free days
  - (20 ± 12 vs 19 ± 13; OR 1.35 [1.08 – 1.69])

Brown, Wang, Coston et al *Am J Respir Crit Care Med*. 2019;200(12):1487-1495

Septic Shock: Vasopressors and Precision Driven Fluid Resuscitation

Pt to the ICU after 6 hours in the ED
Post 5L Fluid Resuscitation

Patient sent to the ICU to be evaluated due to the hypoxia.

Vitals on arrival to ICU:

- HR 110
- BP 92/44 (60)
- RR 26
- SpO_2 sat 88%
- Placed on 50% mask
- Temp 38.6˚C (101.4˚F)

- Lactate redrawn and is 3.8 mmol/L
  - up from 2.3 mmol/L on presentation in the ED
- Weight 89 kg
- Patient is lethargic

Clinical Question

What would you recommend?

1. Give another liter of fluid
2. Start a vasopressor
3. Both fluid and pressor
4. I don’t really have enough information to decide

Can too Much Fluid be Deadly?

- When 5 to > 9 liters of fluid is given in the 1st 24 hours:
  - Mortality ↑ by 2.3% for each additional liter > 5 L (p = 0.0003)
  - Total hospital costs ↑ by $999 for each Liter > 5 (p = 0.005)

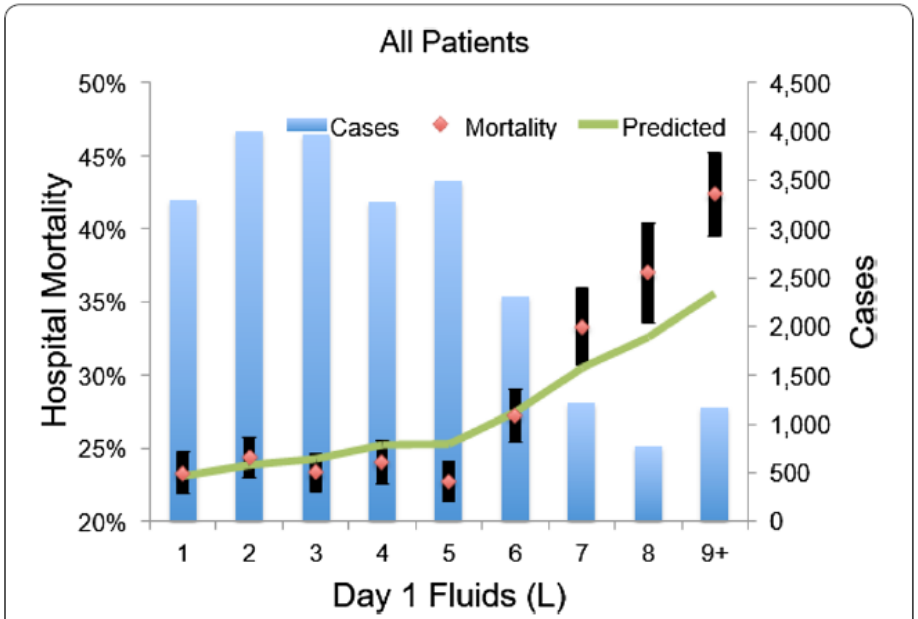


Fig. 2 Actual and expected hospital mortality, by day 1 fluid groups

Marik, Linde-Zwirble, Bittner et al. *Int Care Med* 2017 43:625-32

How do you Know if your Hypotensive Patient is a Fluid Responder?

OR

2016 SSC Recommendations

If the shock is not resolving…

- Suggest dynamic over static variable be used to guide/predict fluid responsiveness where available (weak recommendation; low quality of evidence)

You need a stroke volume measure!!

- Suggest using Dobutamine in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents (weak recommendation; low quality of evidence)

Surviving Sepsis Campaign: International Guidelines for the Management of Sepsis and Septic Shock: 2016. Rhodes, Evans, Alhazzani et al. *Crit Care Med 2017*;45(3)

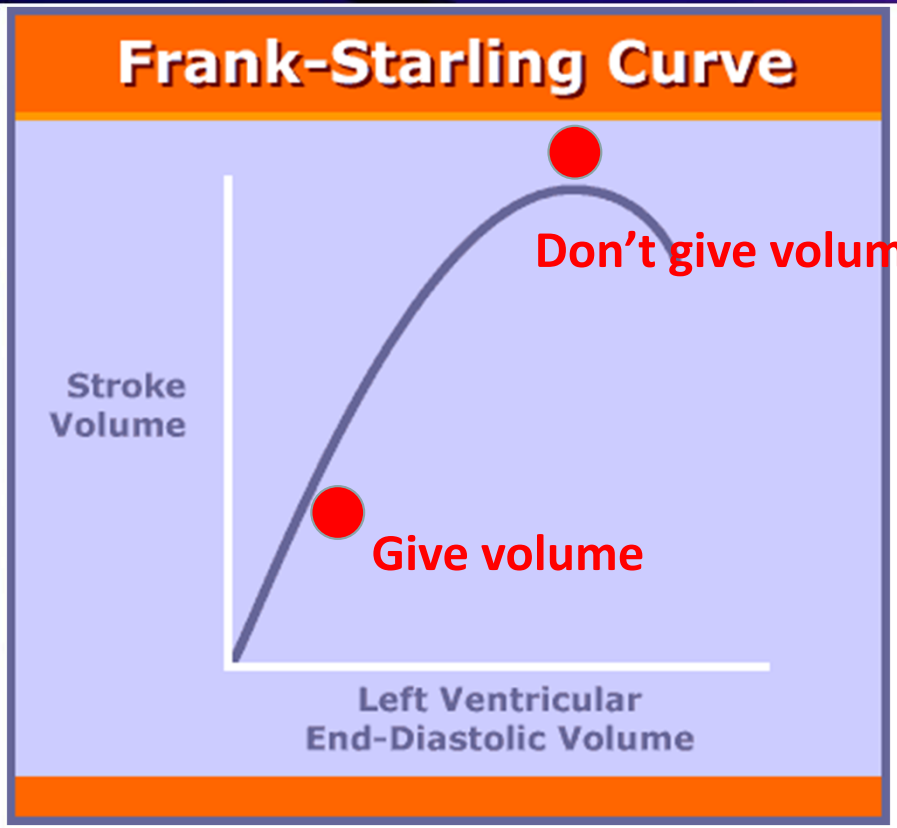
Is There a Practice Change Over Time: What Drives Administration a Fluid Bolus?

Indicator	SAFE 2000 (n = %)	SAFE TRIPS 2007 (n = %)	Fluids TRIPS 2014 (n = %)
BP	67.9	63.7	71.8
CVP	54.8	19.5	11.2
HR	59.8	52.3	30
UOP	54.8	30	41
Cap refill	55.2	12.4	20.1

BP is still most commonly used to make fluid decisions

Bihari S, et. al. *Int.Care Med* 2020; published online April 24th

Is Your Patient Fluid Responsive?



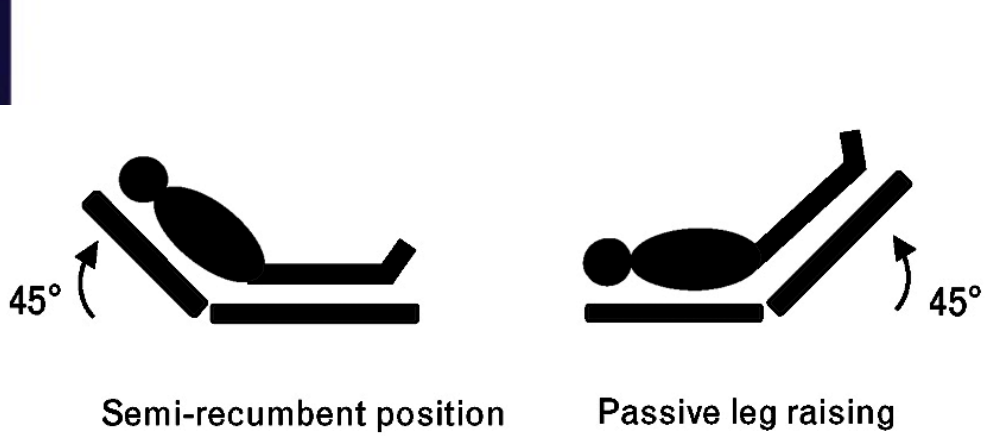
- When fluid is administered, does the **SV** increase?
- An increase in stroke volume (SV) of ≥ 10% after the patient receives:
  - 500 ml of crystalloid over 10-15 minutes **or**
  - A shift in fluids (physiologic bolus) by Passive Leg Raise (PLR) test

Interestingly, numerous studies have demonstrated only ~50% of unstable patients are NOT fluid responsive

Marik PE et al. *Current Opinion Crit Care*.2019;25(3):246-251

Passive leg raise test (PLR)

Transfer of blood from legs and abdominal compartment toward the heart



Limitations to the PLR

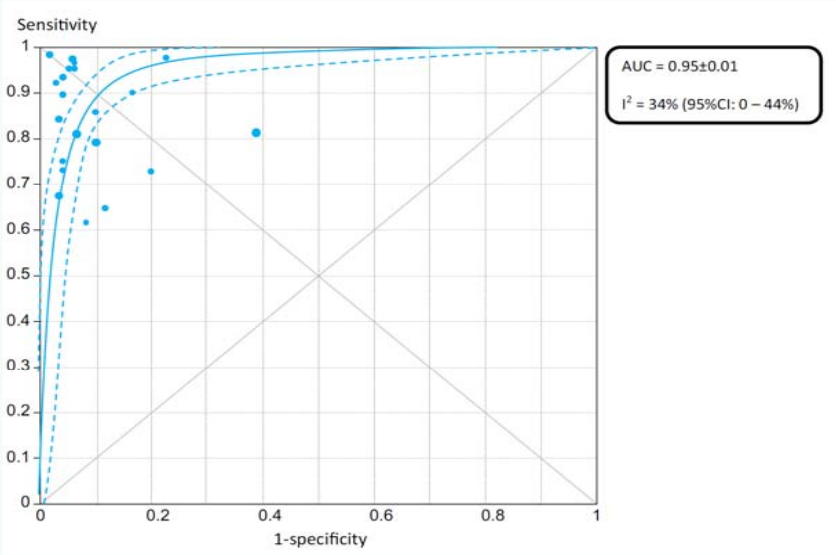
- Intra-abdominal hypertension
- Head trauma/ICP issues
- Lower Extremity DVT
- Venous compression stockings
- Amputated leg
- SEVERE Hypovolemia/Hemorrhage

Legs elevated for 1 - 2 minutes
Re-evaluate – requires stroke volume measure

PLR Meta-analysis

- 21 studies assessing PLR with SV/CO measurement and PP
  - ECHO (6)
  - Pulse Contour Analysis (6)
  - Bioreactance (4)
  - Esophageal doppler (3)
  - PA Cath (1)
  - Suprasternal Doppler (1)

PLR used with CO/SV measure to predict fluid responsiveness = **AUC 0.95**



PLR induced changes in pulse pressure **= AUC 0.77**

Monnet, Marik and Teboul. *Int.Care Med 2016*;42:1935-47

FRESH Trial

- 13 US and UK Hospitals
- Non-blinded RCT
- n = 124 patients
  - 83 treatment vs. 41 Usual Care
  - 2:1 enrollment
- Enrolled in the ER
  - Refractory septic shock
  - < 3L of fluid administered

- PLR with dynamic measure of SV change using Bioreactance
  - Used to guide decision of fluid vs. vasopressors for clinical hypoperfusion
  - Over the next 72 hours of care, or ICU discharge
- Hypoperfusion defined as:
  - MAP < 65
  - Persistent hyperlactemia
  - Cryptic shock – lactate > 4 without hypotension

Douglas I et al, *CHEST* 2020

Primary Endpoint

- **Decreased 72-hour Fluid Balance** (p=0.02)
  - Treatment Group: 0.65 L +/- 2.85 L
  - Control Group: 2.02 L +/- 3.44 L
- Favoring Treatment Group: -1.37 L

- 43% fluid responsive on initial PLR
- 33% fluid responsive between 48 – 72 hours
- 18% never fluid responsive

Douglas I et al, *CHEST* 2020

Secondary Endpoints

- **Renal Replacement Therapy (RRT)** p = 0.04
  - Treatment Group 5.1%
  - Control Group 17.5 %
- **Mechanical Ventilation** p = 0.04
  - Treatment Group 17.7%
  - Control Group 34.1%
- **ICU LOS** p = 0.11
  - Treatment Group 3.31
  - Control Group 6.22
- **Discharge Home** p = 0.035
  - Treatment Group 63.9%
  - Control Group 43.9 %

Douglas I et al., *CHEST* 2020

Back to Our Patient…

Pre-Passive leg raise (PLR) Test:

- HR 110
- BP 92/44 (60)
- CI 3.9 L/min/m^2
- SV 122 ml/beat
- SVI 68 ml/beat/m^2
- SVR/TPR 522 dynes/sec/cm^{-5}
- SVRI/TPRI 1008 dynes/sec/cm^{-5}/m^2

Post-Passive leg raise (PLR) Test:

- HR 106
- BP 92/44 (60)
- CI 4.0 L/min/m^2
- SV 126 ml/beat
- SVI 70 ml/beat/m^2
- SVR/TPR 524 dynes/sec/cm^{-5}
- SVRI/TPRI 1015 dynes/sec/cm^{-5}/m^2

What would you like to do?

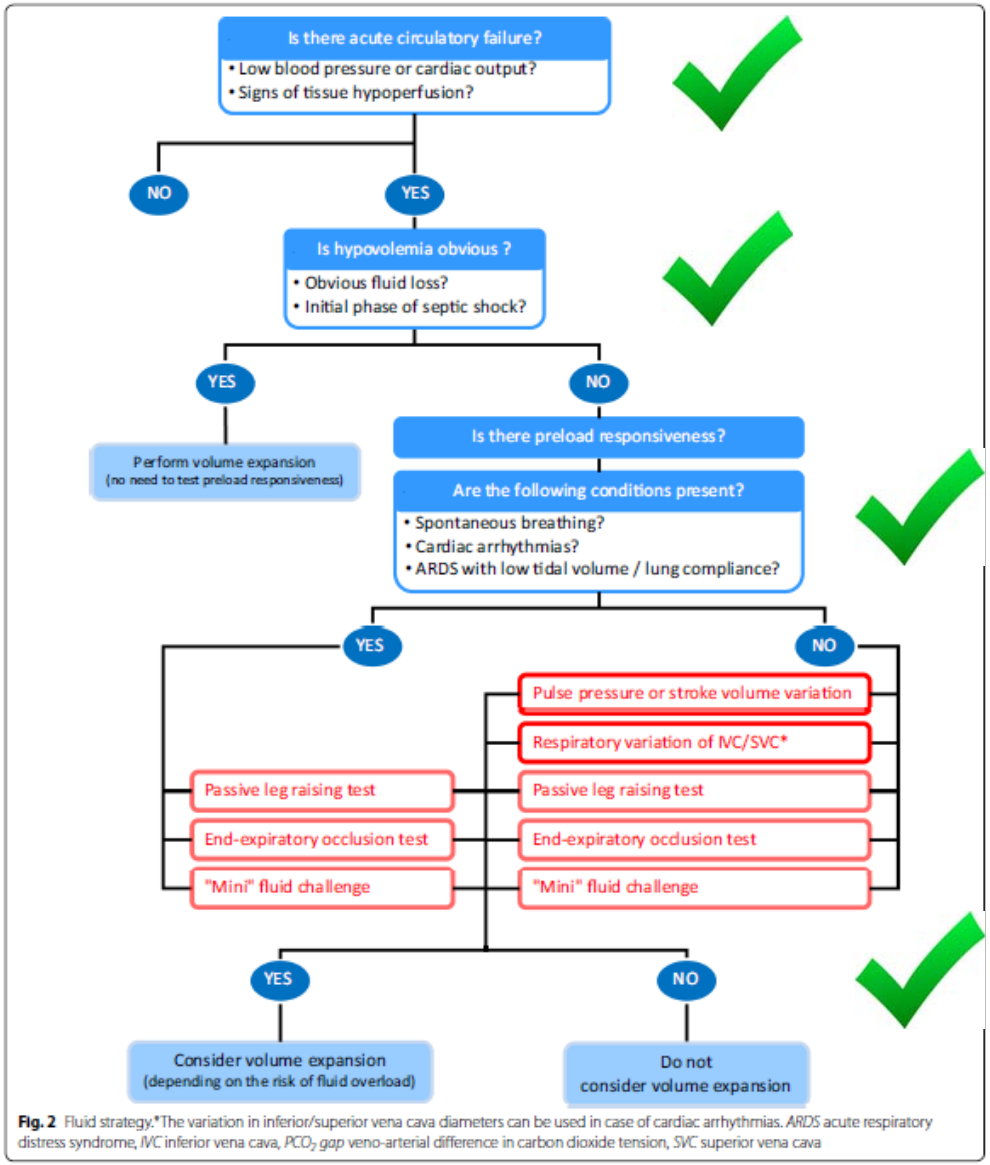


Fig. 2 Fluid strategy.*The variation in inferior/superior vena cava diameters can be used in case of cardiac arrhythmias. *ARDS* acute respiratory distress syndrome, *IVC* inferior vena cava, PCO_2 *gap* veno-arterial difference in carbon dioxide tension, *SVC* superior vena cava

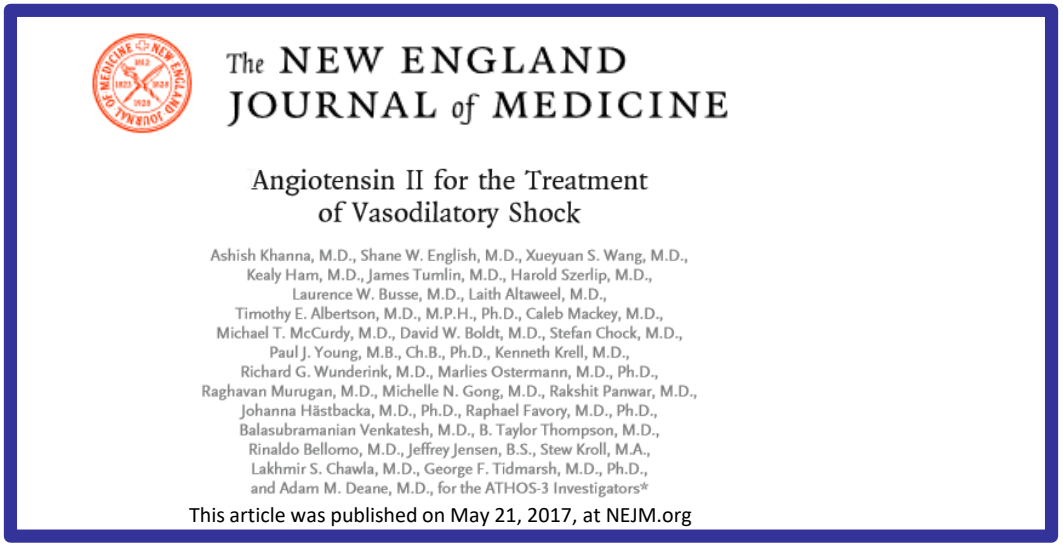
It's time to start a vasopressor!

Vasopressor of choice for Sepsis?

Norepinephrine!

Monnet X, et al. *Ann, Int. Care*.2016;6:11

Recent Studies: Vasopressor Type & Timing



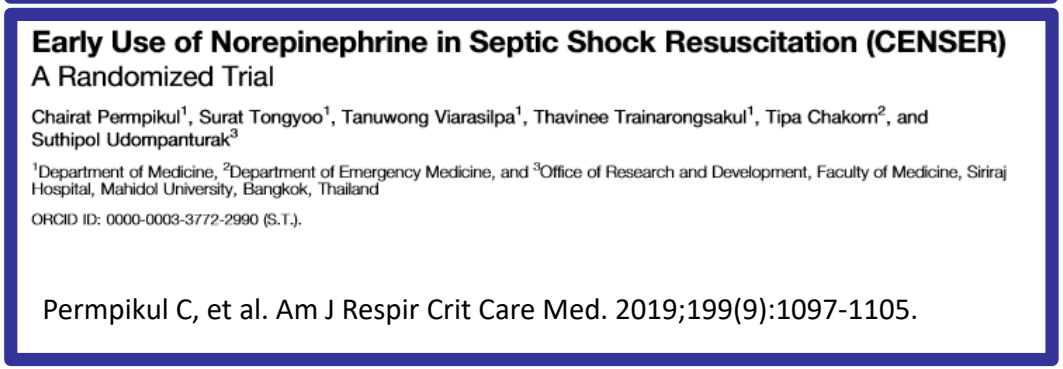
The NEW ENGLAND JOURNAL of MEDICINE

Angiotensin II for the Treatment of Vasodilatory Shock

Ashish Khanna, M.D., Shane W. English, M.D., Xueyuan S. Wang, M.D., Kealy Ham, M.D., James Tumlin, M.D., Harold Szerlip, M.D., Laurence W. Busse, M.D., Laith Altaweel, M.D., Timothy E. Albertson, M.D., M.P.H., Ph.D., Caleb Mackey, M.D., Michael T. McCurdy, M.D., David W. Boldt, M.D., Stefan Chock, M.D., Paul J. Young, M.B., Ch.B., Ph.D., Kenneth Krell, M.D., Richard G. Wunderink, M.D., Marlies Ostermann, M.D., Ph.D., Raghavan Murugan, M.D., Michelle N. Gong, M.D., Rakshit Panwar, M.D., Johanna Hästbacka, M.D., Ph.D., Raphael Favory, M.D., Ph.D., Balasubramanian Venkatesh, M.D., B. Taylor Thompson, M.D., Rinaldo Bellomo, M.D., Jeffrey Jensen, B.S., Stew Kroll, M.A., Lakhmir S. Chawla, M.D., George F. Tidmarsh, M.D., Ph.D., and Adam M. Deane, M.D., for the ATHOS-3 Investigators*

This article was published on May 21, 2017, at NEJM.org

Angiotension II effectively increases blood pressure in patients with vasodilatory shock that did not respond to high doses of conventional vasopressors



Early Use of Norepinephrine in Septic Shock Resuscitation (CENSER)
A Randomized Trial

Chairat Permpikul[1], Surat Tongyoo[1], Tanuwong Viarasilpa[1], Thavinee Trainarongsakul[1], Tipa Chakorn[2], and Suthipol Udompanturak[3]

[1]Department of Medicine, [2]Department of Emergency Medicine, and [3]Office of Research and Development, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

ORCID ID: 0000-0003-3772-2990 (S.T.).

Permpikul C, et al. Am J Respir Crit Care Med. 2019;199(9):1097-1105.

- Single center study, 310 patients evaluating early norepinephrine in septic shock.
- Early norepinephrine was significantly associated with increased shock control by 6 hours along with fluid therapy
- Early vasopressor associated with less cardiogenic pulmonary edema

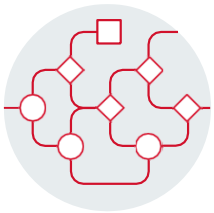
Predictive Analytics
Hypotension Prediction Index software algorithm

Past Events

Machine learning based on arterial blood pressure waveform from development dataset

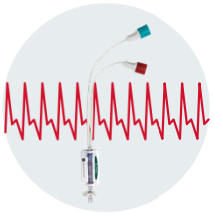
Analyzed 200,000 hypotensive and non-hypotensive events*

+130M cardiac cycles



Algorithm with 23 predictive features

Real Time Input



Patient waveform from sensor

Predictive Output

HPI parameter value

*A hypotensive event is defined as MAP <65 mmHg for a duration of at least one minute. A non-hypotensive event is calculated by identifying segments of data points such that the segment is at least 20 minutes away from any hypotensive events and all data points in that segment have MAP>75 mmHg. One non-event (negative) data point is taken for each of the non-hypotensive event segments.

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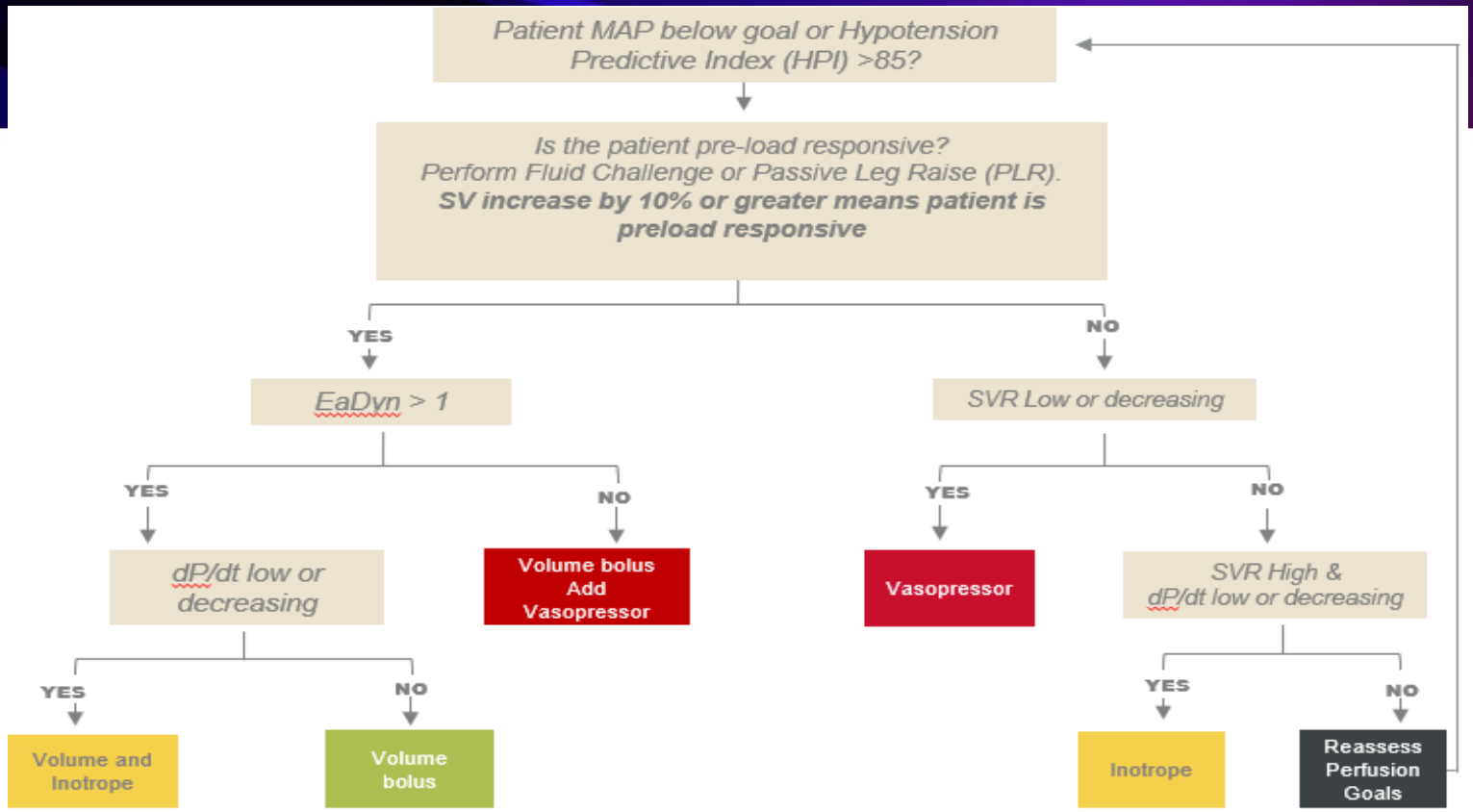
Hemodynamic Optimization



HPI parameter

- The HPI parameter displays as a value ranging from 0 to 100, with higher values indicating higher likelihood of a hypotensive event*
- The HPI value is updated every 20 seconds

Source: Hypotension Prediction Index software for management of hypotension during moderate-to-high-risk noncardiac surgery: protocol for a randomized trial. Trial.gov (2019)

Systolic slope (dP/dt)

- Arterial dP/dt is the maximum upslope of the arterial pressure waveform measured from a peripheral artery
- The "trend" values of dP/dt may be an indicator of increasing or decreasing contractility

Dynamic elastance (Ea_{dyn})

- Ea_{dyn} is simply the ratio of PPV: SVV
- Ea_{dyn} is a measure of the afterload to the left ventricle by the arterial system, relative to the left ventricular elastance
- In the same way that we consider dynamic parameters like SVV to predict "fluid responsiveness," Ea_{dyn} has been shown to be an indicator of "pressure responsiveness" – predicting if blood pressure will increase in response to fluid administration (in preload responders)

Facilitators for Fluid

- Journal club-use the evidence
- Use your own data to show difference with and without fluid
- Precision driven fluid using dynamic measures

CMS Fluid Changes in July

Impacts:
Crystalloid Fluid Administration

Rationale: The *Crystalloid Fluid Administration* data element was updated with clarifying guidance for determining the target ordered volume, determining if the target ordered volume was completely infused, and clarification of an authorized patient advocate.

Description of Changes:
Notes for Abstraction
Add new 3rd bullet point:

Specifications Manual for Hospital Inpatient Quality Measures
Discharges 07-01-21 (3Q21) through 12-31-21 (4Q21)

Release Notes Version 5.10

- Select value "1" if less than 30 mL/kg were ordered and given, and if all the following criteria were met:
  - The ordering physician/APN/PA must have documented within a single note in the medical record:
    - that administration of 30 mL/kg of crystalloid fluids would be detrimental or harmful for the patient despite having hypotension, a lactate >= 4 mmol/L, or documentation of septic shock;
    - AND that the patient has one of the following conditions, OR that a portion of the crystalloid fluid volume was administered as colloids (if a portion consisted of colloids, there must be an order and documentation that colloids were started or noted as given);
      - advanced or end-stage heart failure (with documentation of NYHA class III or symptoms with minimal exertion, OR NYHA class IV or symptoms at rest or with any activity)
      - advanced or end-stage chronic renal disease (with documentation of stage IV or GFR 15-29 mL/min, OR stage V or GFR < 15 mL/min or ESRD)
    - AND the volume of crystalloid fluids in place of 30 mL/kg the patient was to receive;
    - AND an order for the volume of fluids in place of 30 mL/kg to be administered;
  - All other applicable requirements for the Crystalloid Fluid Administration data element are met.

Specifications manual for hospital Inpatient Quality Measures
Discharges 07-01-21 (3Q21) Through 12-31-21 (4Q21)

Repeat Lactate Strategies

- Repeat lactate can be drawn anytime after fluid bolus
  - Reflex lactate for any initial lactate greater than 2
  - 2nd lactate order included when first one is ordered

Focused Examination

- Vital Signs
  - Temp, HR, BP, RR
- Cardiopulmonary
  - Rhythm, S1/2/3/4, presence of murmur and lung sounds
- Peripheral Pulses
  - 1+, 2+ or absent
- Capillary Refill
  - Brisk, <2 sec, >2 sec
- Skin
  - Mottled vs no mottling, to what level. Warm vs cold, etc

Study compared physical findings of ineffective circulation (cap refill >2, skin mottling and cool extremities) to PA catheter- Physical findings not useful predictor of low cardiac index or low mixed venous

Grissom CK, et al. Crit Care Med, 2009;37:2720-2726

Recent Studies: Perfusion Assessment

Randomized Controlled Trial > JAMA. 2019 Feb 19;321(7):654-664. doi: 10.1001/jama.2019.0071.

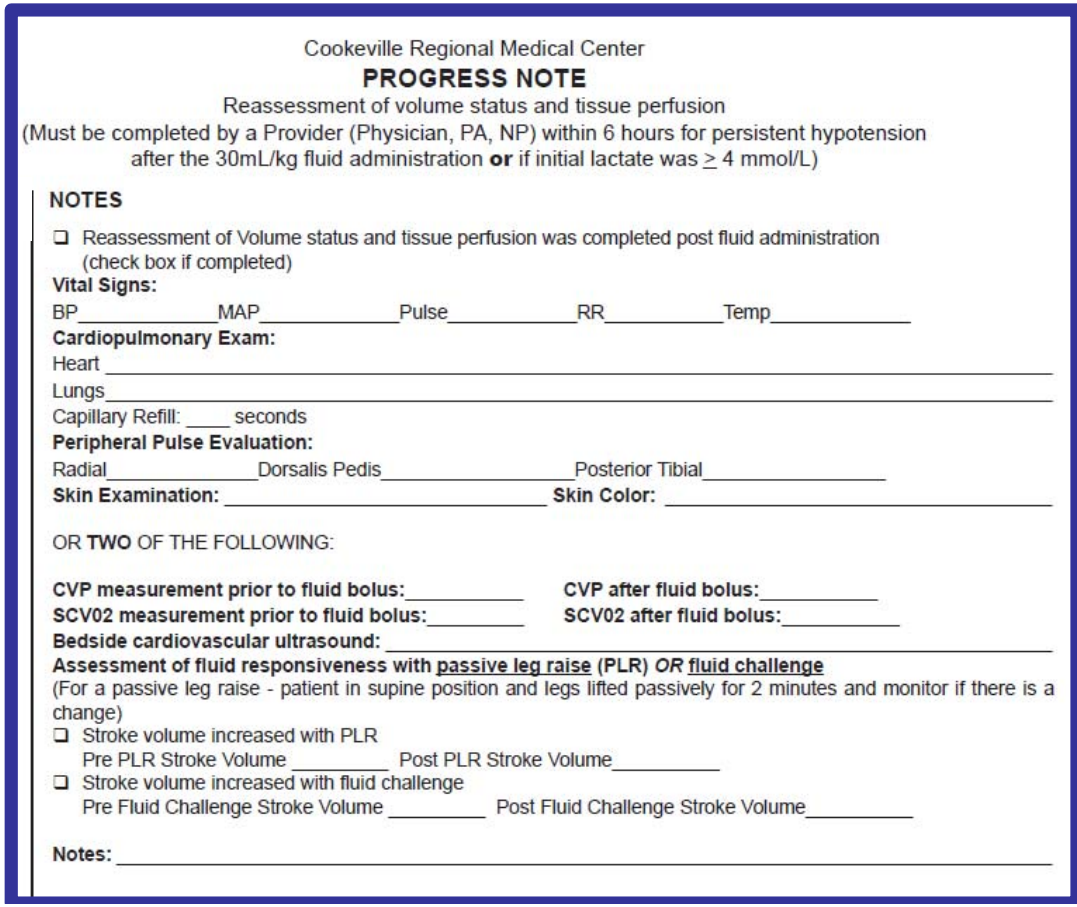
Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28-Day Mortality Among Patients With Septic Shock: The ANDROMEDA-SHOCK Randomized Clinical Trial

- 28 ICU's in 5 countries, 424 patients
- Objective was to determine if a peripheral perfusion–targeted resuscitation during early septic shock in adults is more effective than a lactate level–targeted resuscitation for reducing mortality.
- 28-day mortality was not reduced targeting peripheral perfusion versus lactate normalization (p=.06)
- Was associated with less organ dysfunction at 72hrs

Hernández G, et al.. *JAMA*. 2019;321(7):654–664

Reassessment

- Requirement changes in July, 2018 for CMS
  - Still a requirement for physician/APP to reassess volume status and tissue perfusion, just no requirement to state how that reassessment occurred or what the outcome of the assessment was
  - IE: " perfusion reassessed; "sepsis reassessment done"
  - Only need to do one out of 2 of the reassessment measurement (CVP, ScvO2, Echo, dynamic responsiveness)
- Strategies to comply with documentation requirements
  - Standard provider note or dot phrase
  - Expect that whoever orders the 30ml/kg fluid bolus is responsible for the reassessment documentation
  - Part of a sepsis checklist



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PROGRESS NOTE

Reassessment of volume status and tissue perfusion

(Must be completed by a Provider (Physician, PA, NP) within 6 hours for persistent hypotension after the 30mL/kg fluid administration **or** if initial lactate was ≥ 4 mmol/L)

NOTES

❑ Reassessment of Volume status and tissue perfusion was completed post fluid administration (check box if completed)

Vital Signs:

BP_____MAP_____Pulse_____RR_____Temp_____

Cardiopulmonary Exam:

Heart _____

Lungs_____

Capillary Refill: ____ seconds

Peripheral Pulse Evaluation:

Radial_____Dorsalis Pedis_____Posterior Tibial_____

Skin Examination: _____ **Skin Color:** _____

OR **TWO** OF THE FOLLOWING:

CVP measurement prior to fluid bolus:_____ **CVP after fluid bolus:**_____

SCV02 measurement prior to fluid bolus:_____ **SCV02 after fluid bolus:**_____

Bedside cardiovascular ultrasound: _____

Assessment of fluid responsiveness with passive leg raise (PLR) *OR* fluid challenge

(For a passive leg raise - patient in supine position and legs lifted passively for 2 minutes and monitor if there is a change)

❑ Stroke volume increased with PLR

Pre PLR Stroke Volume _____ Post PLR Stroke Volume_____

❑ Stroke volume increased with fluid challenge

Pre Fluid Challenge Stroke Volume _____ Post Fluid Challenge Stroke Volume_____

Notes: _____

Inadequate Program Resources

Impact of Sepsis Coordinator

HCA added sepsis coordinators to all facilities (FTE was based upon sepsis volume)

- Severe sepsis/septic shock mortality dropped from 22% to 15%
- Bundle compliance improved to 61%
- Other key elements initiated were order sets, sepsis alerts, routine screening, sepsis champions and community outreach

Sepsis Coordinator Network

- 1,682 members
- 1,448 hospitals and facilities

www.sepsisalliance.org

Presentation at Colorado Hospital association Sepsis Program

The role of nursing best practice champions in diffusing practice guidelines: a mixed methods study

Worldviews EvidBased Nurs.2010 Dec;7(4):238-51. doi: 10.1111/j.1741-6787.2010.00202.x. Epub2010 Sep 28.

Role of the Sepsis Coordinator

- Facilitates implementation/evaluation of the Sepsis program including all systems necessary for the multidisciplinary approach throughout the continuum of care.
- Makes regular rounds on sepsis patients to evaluate appropriateness of orders, treatment plans, nursing intervention, physician documentation and compliance with the Sepsis bundle
- Utilizes currently available reports to identify sepsis cases and facilitates data collection process and assesses and analyzes outcomes.
- Collaborates with frontline staff to identify on-going care concerns related to sepsis care
- Collaborates with leadership and colleagues in identifying sepsis quality of care issues

Role of the Sepsis Coordinator

- Determines baseline compliance with physician documentation and compliance with the Sepsis bundle.
- Provides real time/detailed feedback to all clinical providers and departments and scheduled updates to the Sepsis Collaborative Team and work groups.
- Assist the rapid response team and other hospital staff, when necessary, if dealing with a patient situation
- Conducts sepsis organizational tracers to identify quality and safety issues.
- Analyze data to identify trends and issues, also use improvement tools to assist with problem solving and action planning.
- Provides formal and informal education to medical and clinical staff.
- Maintains knowledge of current trends and developments in the sepsis management, fields of quality, and safety.

Challenges with Physician Buy In

- Cook book medicine
- “I know I can treat them better” or “I have been treating this patient my whole career”
- “ I don’t have enough time”

Strategies to Address Buy In

- Use hospital sepsis mortality data and nationally data to show it makes up the majority of deaths
- Strong informal leaders connect individually
- Identify who's opinion they would respect and provide discussion or feedback
- Individual physician data on patients treated including bundle compliance
- Quick turn around time on data to change behavior

Barriers/Facilitators

Identification

- Screening: EMR, BPA, Routine Screening, Machine Learning
- Sepsis 2 and Sep 3 definitions

Time sensitive interventions

- Antibiotics
- Fluids—early fluids and later fluids and vasopressors
- Repeat lactate
- Reassessment

Inadequate program resources

- Lack of sepsis coordinator
- Lack of physician lead/champion

Timely Data

- Timely feedback

Data, Data, Data !!!

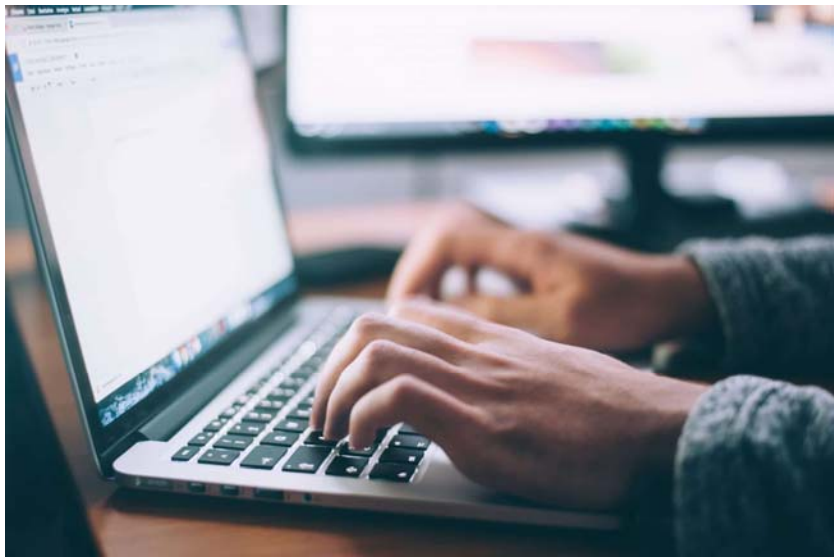
What data do you need to evaluate your program?

Data sharing—who, what and how often?

How to use the data to drive improvement?

What Outcome and Process Data Should be Collected & Reviewed?

- Understand your volume of sepsis, severe sepsis and septic shock—look at mortality, LOS, cost, readmission
- Stratify your data by:
  - POA, non-POA
  - Medical vs surgical
  - Discharge disposition
  - Admission source
  - Sepsis severity
- Process Metrics
  - Overall SEP-1 compliance
  - 3 hour bundle compliance
  - Each individual element compliance



CRMC Sepsis Data Sample

Indicator	Oct 2020	Nov 2020	Dec 2020	Jan 2021
Total Severe Sepsis Patients	58	56	66	70
Core Septic Shock Patients	14	10	19	14
Septic Shock Patients Rate %	24.14	17.86	28.79	20
Ethnicity of Total Severe Sepsis/Septic Shock Patients	58	56	66	70
White	58	55	64	69
Black or African American	0	1	2	1
UTD	0	0	0	0
Avg Elapsed Time 1st Antibiotic Hung - minutes	22.5	88.8	63.3	77.5
Core Focus Severe Sepsis Pt. 30 Day Readmit	0	2	4	1
Core Sepsis 30 Day Readmit %	0	3.4	5.9	1.4
Core Sepsis Total Patient Expired	14	15	9	19
Total Sepsis Expired Rate %	23.7	25.9	13.2	27.1
Severe Sepsis Patients Expired w/o Shock	10	12	5	15
Severe Sepsis Expired Rate No Shock %	16.9	20.7	7.4	21.5
Septic Shock Patients Expired	4	3	4	4
Septic Shock Expired Rate %	28.6	30	21.1	28.6
Sepsis Avg Age Dx R65.21 w/Shock & R65.20 w/o	74	68	69	65
Sepsis ALOS Dx R65.21 w/Shock & R65.20 w/o	11	11	12	9
Sepsis 2 to PNA with lace >/= 10 and educated on sepsis	0	2	6	
sepsis 2 to PNA with lace >/= 10	0	2	6	
readmit with index of sepsis due to PNA	0	1	1	

Severe Sepsis/Septic Shock Summary	Oct'20	Nov'20	Dec'20	Jan'21
Early Mgt Bundle Compliance Rate:	50.00%	48.00%	62.00%	56.00%
Severe Sepsis Bundle:				
# of patients that met criteria	58	56	66	70
Initial Lactate w/in 3 hrs	95.00%	98.00%	97.00%	100.00%
Bld C/S prior to ATB and w/in 3 hrs	83.00%	93.00%	89.00%	90.00%
ATB w/in 3 hrs	97.00%	86.00%	89.00%	87.00%
Repeat lactate w/in 6 hrs (if initial >2)	97.00%	88.00%	97.00%	100.00%
Septic Shock Bundle:				
# of patients that met criteria	14	10	19	14
Resuscitation W/crystalloid fluid w/in 3 hrs for pt w/initial hypot	50.00%	82.00%	73.00%	63.00%
Resuscitation w/crystalloid fluid w/in 3hrs for pt w/septic shock	57.00%	90.00%	84.00%	79.00%
Vasopressors for persist. Hypotension w/in 6 hrs	100.00%	66.00%	100.00%	50.00%
Repeat volume status/ tissue perfusion assessment w/in 6 hrs	100.00%	90.00%	95.00%	93.00%
Other:				
Survival rate for severe sepsis and septic shock patients	76.00%	73.00%	86.00%	72.00%
Readmission Rate	0	3.00%	4.00%	1.00%
sepsis worksheet	22.00%	27.00%	24.00%	30.00%

Bundle Compliance

SEP-1 Bundle Compliance

Discharge Month	SEP1 Num	SEP1 Denom	SEP-1
Oct-15	173	500	34.6%
Nov-15	209	517	40.4%
Dec-15	216	496	43.5%
Jan-16	155	361	42.9%
Feb-16	73	170	42.9%
Mar-16	7	11	63.6%
Total	**833**	**2055**	**40.5%**

Severe Sepsis - 3-Hour Bundle Compliance

Discharge Month	Lactate Num	Lactate Denom	Initial Lactate	Admin. Num	Admin. Denom	ABX Admin.	Cultures	Cultures	Cultures
Oct-15	464	520	89.2%	421	503	83.7%	387	450	86.0%
Nov-15	483	534	90.4%	448	519	86.3%	398	480	82.9%
Dec-15	474	517	91.7%	435	499	87.2%	396	464	85.3%
Jan-16	344	377	91.2%	330	367	89.9%	293	343	85.4%
Feb-16	163	175	93.1%	146	170	85.9%	138	152	90.8%
Mar-16	10	11	90.9%	11	11	100.0%	11	11	100.0%
Total	**1938**	**2134**	**###**	**1791**	**2069**	**###**	**1623**	**1900**	**85.4%**

Severe Sepsis - 6-Hour Repeat Lactate Level

Discharge Month	Repeat Lactate Num	Repeat Lactate Denom	at Lactate
Oct-15	182	321	56.7%
Nov-15	209	327	63.9%
Dec-15	190	303	62.7%
Jan-16	140	231	60.6%
Feb-16	77	108	71.3%
Mar-16	4	7	57.1%
Total	**802**	**1237**	**61.8%**

Septic Shock - 6-Hour Bundle Compliance

Discharge Month	Resus. Num	Resus. Denom	Fluid Resus.	Vaso pr Num	pr Denom	Vaso pr	/ Asses	/ Asses	/ Asses
Oct-15	87	168	51.8%	34	50	68.0%	18	59	30.5%
Nov-15	95	149	63.8%	31	44	70.5%	17	61	27.9%
Dec-15	95	139	68.3%	29	34	85.3%	21	63	33.3%
Jan-16	70	106	66.0%	19	31	61.3%	23	51	45.1%
Feb-16	31	51	60.8%	8	11	72.7%	7	21	33.3%
Mar-16	2	3	66.7%	1	1	100.0%	2	2	100.0%
Total	**380**	**616**	**61.7%**	**122**	**171**	**71.3%**	**88**	**257**	**###**

Discharge Month

Oct-15 | Nov-15 | Dec-15 | Jan-16 | Feb-16 | Mar-16

Also want to evaluate screening compliance

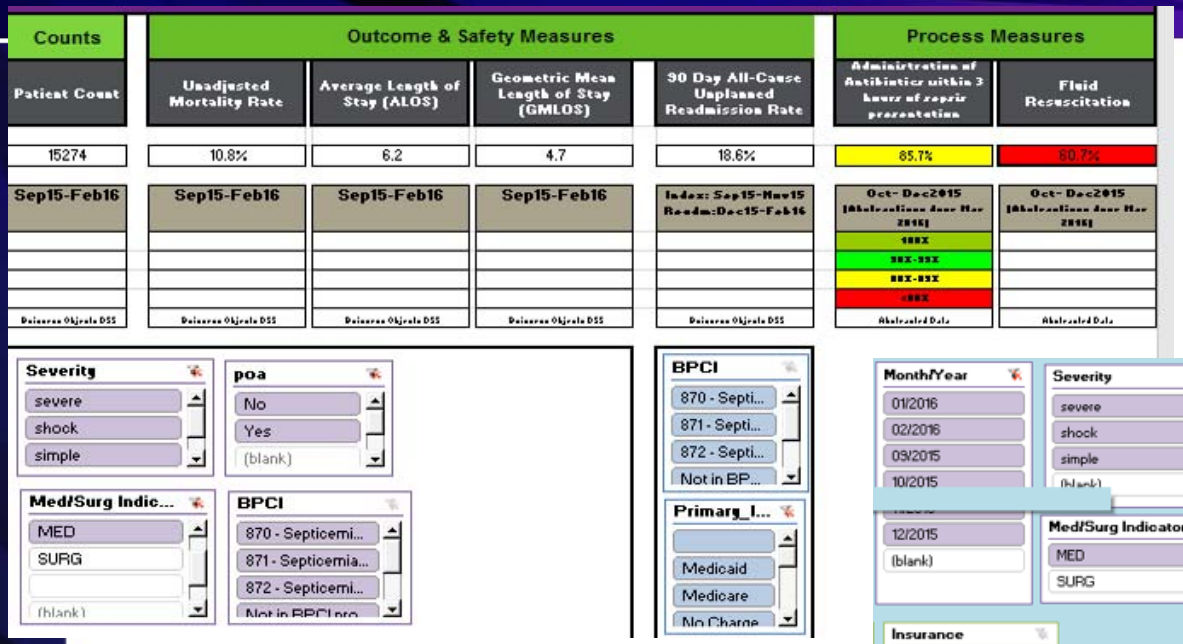
Adult Sepsis Shift Screen Completion by Unit

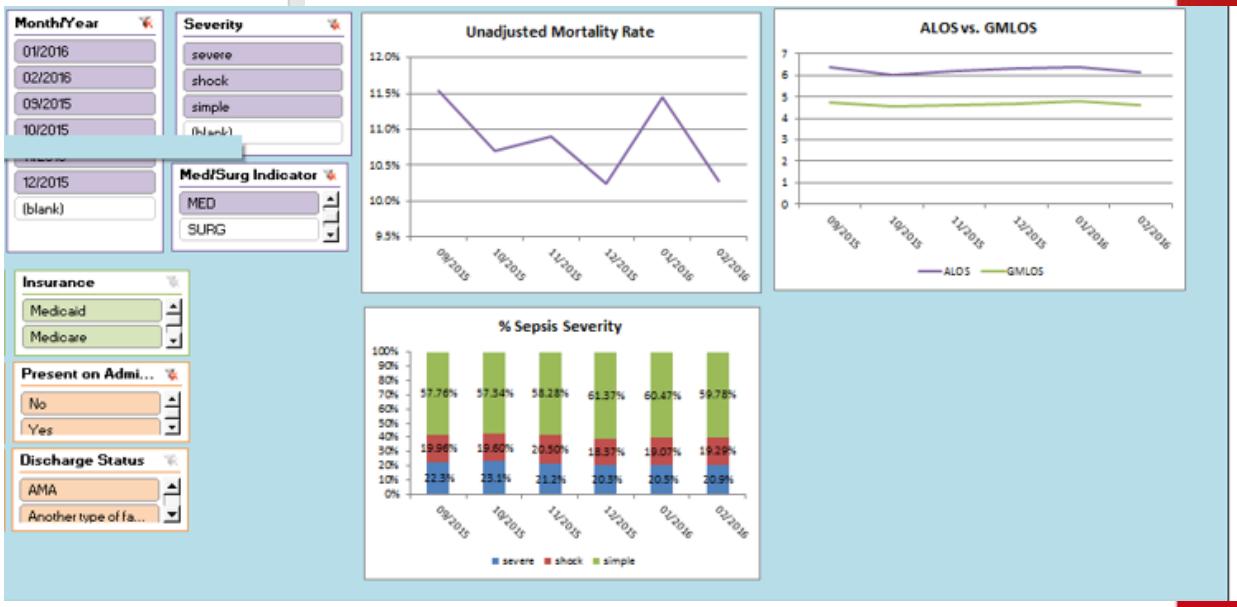
Shift Screen Start Time / Shift

January 2021		February 2021		Grand Total
day	night	day	night	
75%	87%	84%	93%	84%
86%	79%	87%	85%	84%
96%	83%	96%	84%	90%
92%	61%	92%	75%	80%
81%	88%	79%	91%	85%
78%	78%	77%	88%	80%
83%	82%	84%	78%	82%
93%	93%	93%	93%	93%

Make sure to review SEP 1 cases all the way through—even if failed any early step in the process, to understand performance on all elements

Sepsis Dashboards





Score Cards

Clinical Measures - June 2020

Measure	Compliance	Previous Year	Nat'l	Trend	Item/Action
ED - DTA to ED departure	170	148	101 min.		Data depicted is Medicare patients only; actual LOS for June 2020 for all payors - 195 minutes
Sepsis : Early Mgmt Bundle Compliance Rate	50%	56%	60%	Top 10% - 82%	Severe Sepsis Bundle:(81 patients qualified) Septic Shock Bundle: (14/81 patients qualified) Previous Month Bundle Compliance Rate: 48%
Severe Sepsis Bundle - Blood C/S prior to ATB and w/in 3 hrs	94%	92%	N/A		5 patients failed to have blood cultures drawn prior to the initial dose of abx (see attachment for details)
Severe Sepsis Bundle - Initial Lactate drawn w/I 3 hrs of Time ZERO	98%	88%	N/A		2 patients failed to have lactate drawn w/I 3 hrs of time zero.(see attachment for details)
Severe Sepsis Bundle- Broad Spectrum antibiotic w/I 3 hrs of TIME ZERO	91%	91%	N/A		7 patients failed to receive abx w/I 3 hr time frame (please see attachment for details)
Severe Sepsis Bundle - Repeat Lactate w/I 6 hrs (if initial >2)	77%	93%	N/A		10 patients with lactic acid >2 failed to have a repeat lactic acid drawn w/I 6 hrs of presentation of severe sepsis (please see attachment for details)
Septic Shock Bundle- crystalloid fluid w/I 3 hrs.	55%	69%	N/A		9 patients failed this measure because they did not receive the recommended fluid bolus amount or did not receive w/I the 3 hr window (please see attachement for details)
Septic Shock Bundle - Vasopressors for persistent hypotension w/I 6 hrs	100%	100%	N/A		0 patients failed to receive vasopressors w/I 6 hours for persistent hypotension(please see attachment for details)
Septic Shock Bundle - Repeat Volume Status/ tissue perfusion assessment w/I 6 hrs	93%	91%	N/A		1 patient failed to have repeat volume status and tissue perfusion assessment (see attachment for details)
SEPSIS - Readmission Rate	5%	9%	N/A		4 patients were readmitted w/I 30 days
SEPSIS - Survival Rate	95%	89%	N/A		77/81 patients survived

Performance Graphs

Role of Data

Outcome data

- Share with staff and administration to keep momentum going
- Helps convince/move skeptics

Process data

- Celebrate small successes
- Helps identify where opportunities for improvement still exist

Data Sharing—Who, What and How Often?

Sepsis Team (core group)

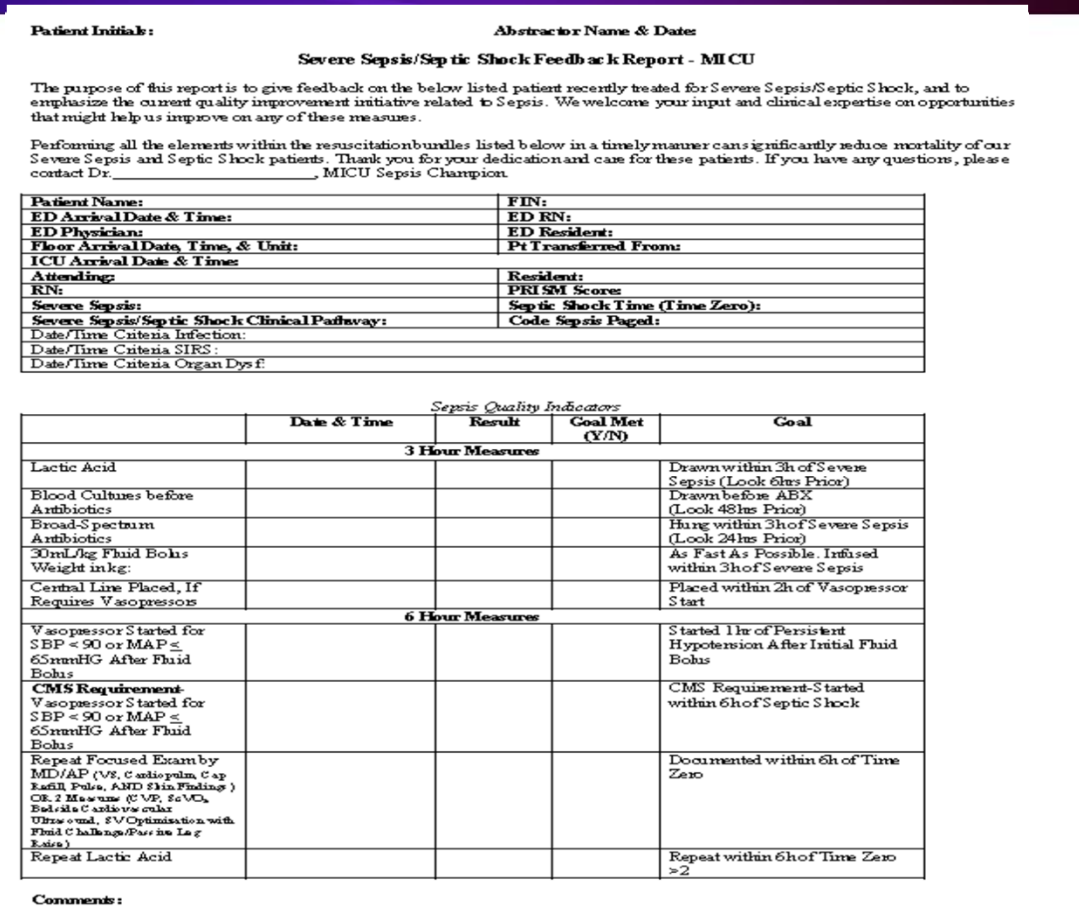
- Monthly multidisciplinary sepsis team meeting with consistent attendance
  - nursing and physician champions
  - lab, pharmacy, and radiology as needed
- Accountable executive understands the role, holds team accountable and assists with problem-solving and removing barriers
  - Timely feedback (data) to the team providing care to the sepsis patients

Review data at:

- Sepsis team meeting
- Quality meeting
- Patient safety meeting
- Unit based meetings
- Medical staff/department meetings
- Board meeting

Data Sharing—Who, What and How Often?

- Use examples of hospital patients in case studies for education of staff (good outcomes and bad)
- Provider specific data on compliance with bundle elements *and* patient outcomes, compared to the goal
- Individual case feedback based on case reviews



Patient Initials: **Abstractor Name & Date:**

Severe Sepsis/Septic Shock Feedback Report - MICU

The purpose of this report is to give feedback on the below listed patient recently treated for Severe Sepsis/Septic Shock, and to emphasize the current quality improvement initiative related to Sepsis. We welcome your input and clinical expertise on opportunities that might help us improve on any of these measures.

Performing all the elements within the resuscitation bundles listed below in a timely manner can significantly reduce mortality of our Severe Sepsis and Septic Shock patients. Thank you for your dedication and care for these patients. If you have any questions, please contact Dr. _____, MICU Sepsis Champion.

Patient Name:	**FIN:**
ED Arrival Date & Time:	**ED RN:**
ED Physician:	**ED Resident:**
Floor Arrival Date, Time, & Unit:	**Pt Transferred From:**
ICU Arrival Date & Time:	
Attending:	**Resident:**
RN:	**PRISM Score:**
Severe Sepsis:	**Septic Shock Time (Time Zero):**
Severe Sepsis/Septic Shock Clinical Pathway:	**Code Sepsis Paged:**
Date/Time Criteria Infection:	
Date/Time Criteria SIRS:	
Date/Time Criteria Organ Dysf:	

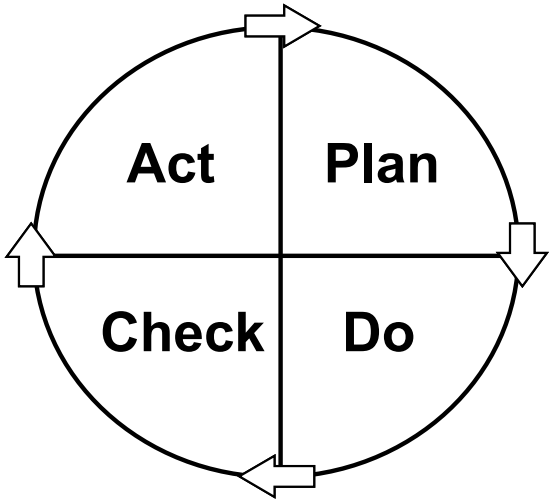
Sepsis Quality Indicators

	Date & Time	Result	Goal Met (Y/N)	Goal
3 Hour Measures				
Lactic Acid				Drawn within 3h of Severe Sepsis (Look 6hrs Prior)
Blood Cultures before Antibiotics				Drawn before ABX (Look 48hrs Prior)
Broad-Spectrum Antibiotics				Hung within 3h of Severe Sepsis (Look 24hrs Prior)
30mL/kg Fluid Bolus Weight in kg:				As Fast As Possible. Infused within 3h of Severe Sepsis
Central Line Placed, If Requires Vasopressors				Placed within 2h of Vasopressor Start
6 Hour Measures				
Vasopressor Started for SBP < 90 or MAP ≤ 65mmHG After Fluid Bolus				Started 1hr of Persistent Hypotension After Initial Fluid Bolus
CMS Requirement- Vasopressor Started for SBP < 90 or MAP ≤ 65mmHG After Fluid Bolus				CMS Requirement-Started within 6h of Septic Shock
Repeat Focused Exam by MD/AP (VS, Cardiopulm, Cap Refill, Pulse, AND Skin Findings) OR 2 Measure (CVP, ScVO2, Bedside Cardiovascular Ultrasound, SVOptimization with Fluid Challenge/Passive Leg Raise)				Documented within 6h of Time Zero
Repeat Lactic Acid				Repeat within 6h of Time Zero >2

Comments:

How to Use the Data to Drive Improvement? Identify Gaps in Application of Evidence

- Set performance targets
  - IE: 90% compliance with obtaining lactates in 3 hours
- Prioritize area to work on first
  - Focus on screening and the 3-hour bundle first then move to the 6-hour bundle
- Understand the 'why' there are gaps
  - "go and see"—walk the process, talk with front line staff
  - Cause and effect—Fishbone
- Define action plan—
  - Can use IHI Model for Improvement
  - PDCA—tests of change



Determining the Gaps: Understanding Why

Success relies on a complex set of tasks being completed in a limited amount of time

Requires data collection and analysis to determine the bottleneck(s)

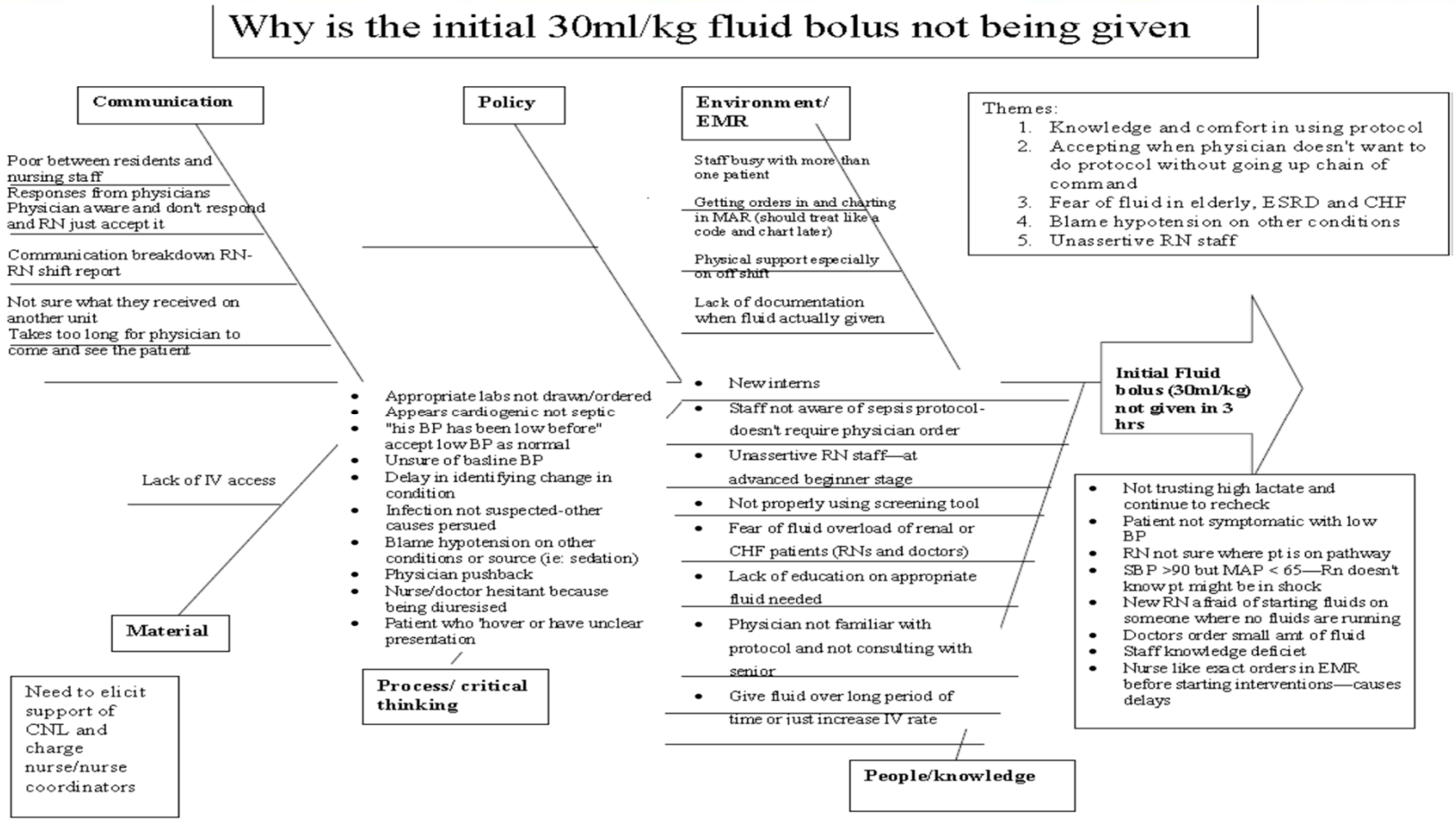
Must analyze the workflow for patients arriving in the ED as well as those who become septic after hospitalization

QI/PI teams are a great resource when available

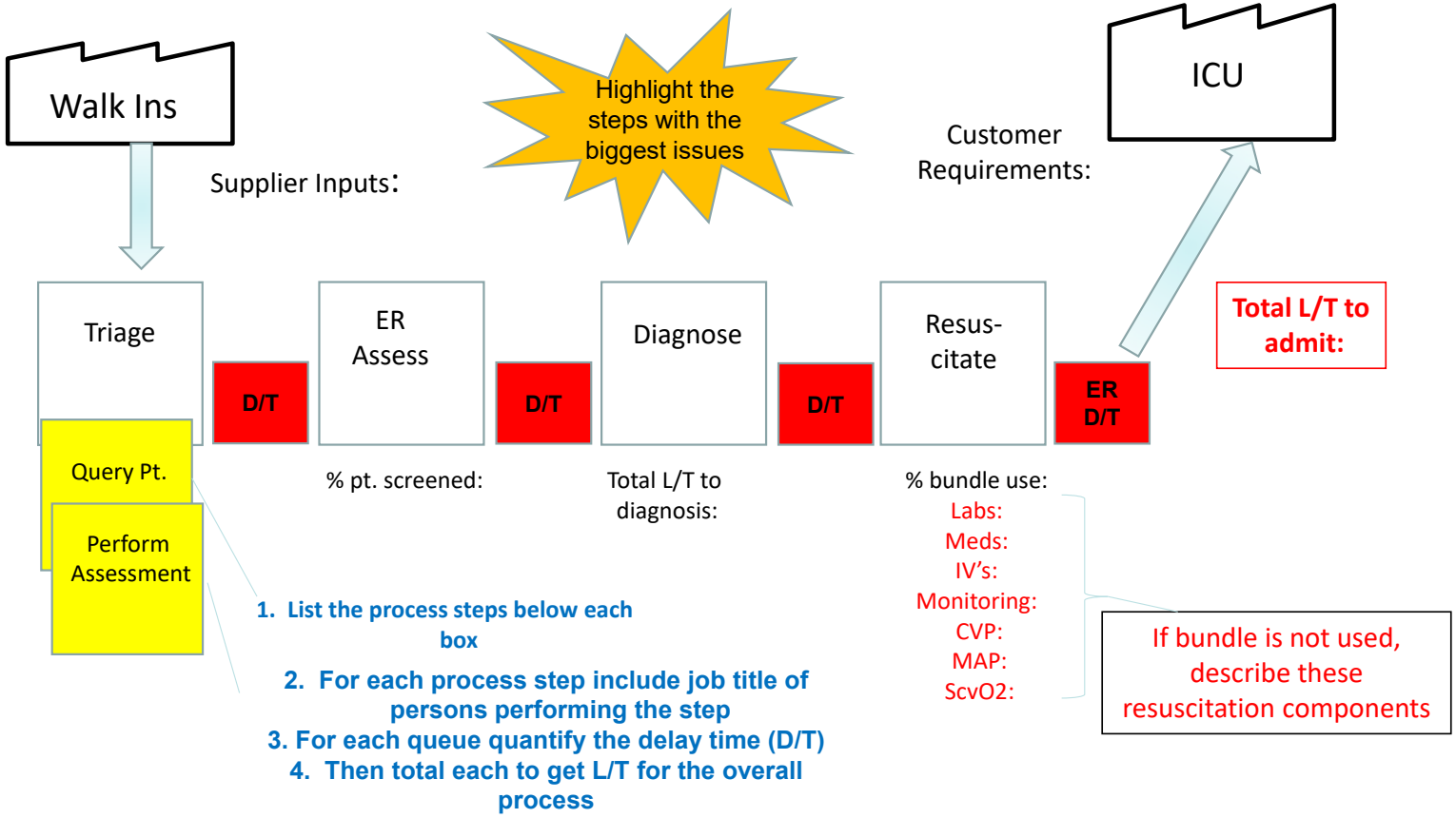
Multiple tools have proven successful

Some examples of diagnostic tools used for analysis, and the “therapeutic” tools developed out of the analysis

Cause and Effect Diagram



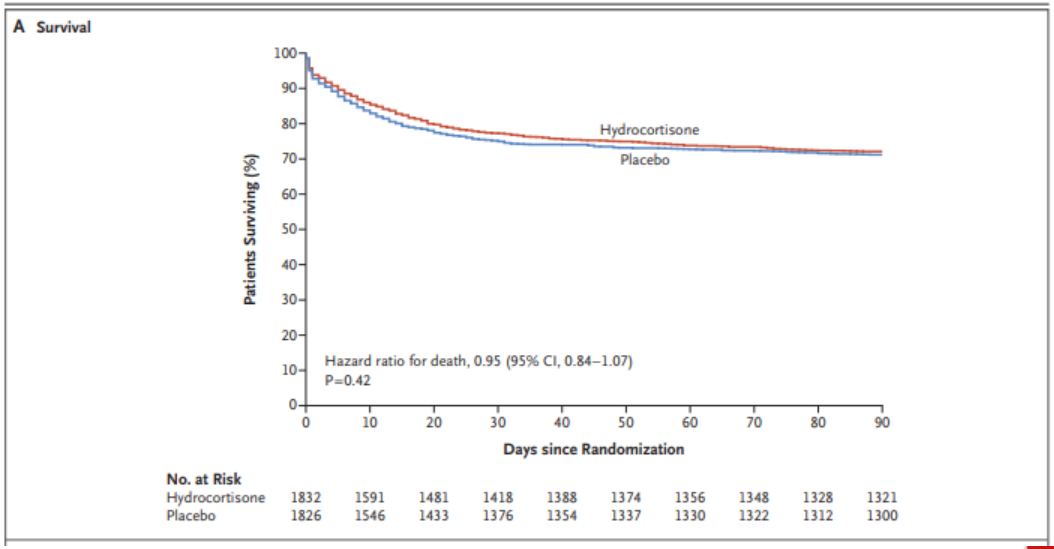
Sepsis Patient Flow Template: Emergency Department



Recent Studies

Adjunctive Corticosteroid Treatment in Critically Ill Patients With Septic Shock-ADRENAL Trial

- RCT-3800 patients
  - 5 countries (Australia, NZ, Saudi Arabia, UK & Denmark
  - Tx: 200mg infusion hydrocortisone vs placebo
  - No tapering done/no stim test
    - Inclusion:
      - > 18 years
  - Proven or strong suspicion of infection
    - Shock or pressors for a minimum of 4 hours
      - > 2 SIRS criteria
  - Mechanical ventilation
    - Etomidate native



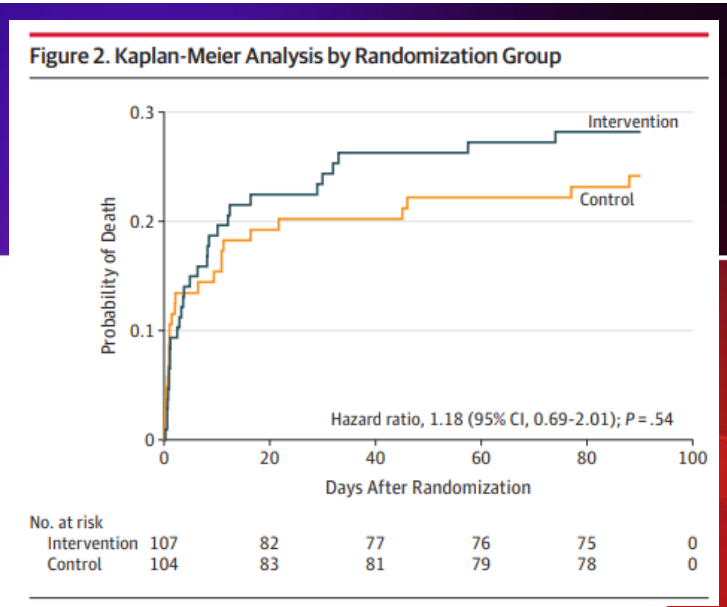
Secondary Benefits

- Faster time to shock reversal
  - D/C from ICU faster
    - Less PRBC's
- Faster time to extubation

Venkatesh B, et al. N Engl J Med 2018 Mar 1;378(9):797-808

Vitamins RCT: Vitamin C, Hydrocortisone and Thiamine vs. Hydrocortisone Alone

- RCT 10 ICU's in Australia, New Zealand and Brazil
- 216 patients/Sepsis 3 definition for Septic Shock
  - Intervention group-109
    - IV vitamin C (1.5g q 6 hrs), IV hydrocortisone (50mg q 6 hrs) & thiamine (200 mg every 12 hrs)
  - Control group-107
    - IV hydrocortisone (50 mg q 6 hrs) until shock resolution or 10 days



Results

Time alive and vasopressor free up to day 7

- Intervention group 122.1 hrs
- Control group 124.6 hrs p=.83

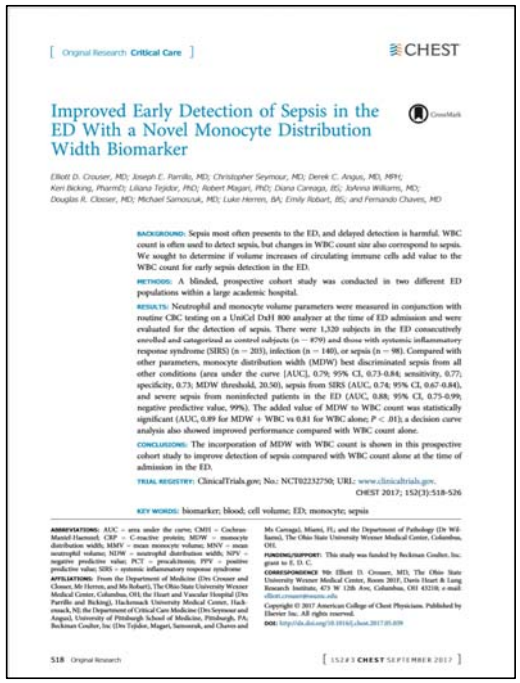
No difference in any secondary outcomes

Limitations:

- Open label
- Under powered to detect difference in mortality
- 24 hrs must meet SEP 3 criteria
- **Median time to first dose of Vitamin C was 12.1 hrs from ICU admission**

Fujii T et al. JAMA 2020;323(5):423-431

Monocyte Distribution Width (MDW)



[Original Research Critical Care]

CHEST

Improved Early Detection of Sepsis in the ED With a Novel Monocyte Distribution Width Biomarker

Elliott D. Crouser, MD; Joseph E. Parrillo, MD; Christopher Seymour, MD; Derek C. Angus, MD, MPH; Keri Bicking, PharmD; Liliana Tejidor, PhD; Robert Magari, PhD; Diana Careaga, BS; JoAnna Williams, MD; Douglas R. Closser, MD; Michael Samoszuk, MD; Luke Herren, BA; Emily Robart, BS; and Fernando Chaves, MD

BACKGROUND: Sepsis most often presents to the ED, and delayed detection is harmful. WBC count is often used to detect sepsis, but changes in WBC count size also correspond to sepsis. We sought to determine if volume increases of circulating immune cells add value to the WBC count for early sepsis detection in the ED.

METHODS: A blinded, prospective cohort study was conducted in two different ED populations within a large academic hospital.

RESULTS: Neutrophil and monocyte volume parameters were measured in conjunction with routine CBC testing on a UniCel DxH 800 analyzer at the time of ED admission and were evaluated for the detection of sepsis. There were 1,320 subjects in the ED consecutively enrolled and categorized as control subjects (n = 879) and those with systemic inflammatory response syndrome (SIRS) (n = 203), infection (n = 140), or sepsis (n = 98). Compared with other parameters, monocyte distribution width (MDW) best discriminated sepsis from all other conditions (area under the curve [AUC], 0.79; 95% CI, 0.73-0.84; sensitivity, 0.77; specificity, 0.73; MDW threshold, 20.50), sepsis from SIRS (AUC, 0.74; 95% CI, 0.67-0.84), and severe sepsis from noninfected patients in the ED (AUC, 0.88; 95% CI, 0.75-0.99; negative predictive value, 99%). The added value of MDW to WBC count was statistically significant (AUC, 0.89 for MDW + WBC vs 0.81 for WBC alone; $P < .01$); a decision curve analysis also showed improved performance compared with WBC count alone.

CONCLUSIONS: The incorporation of MDW with WBC count is shown in this prospective cohort study to improve detection of sepsis compared with WBC count alone at the time of admission in the ED.

TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT02232750; URL: www.clinicaltrials.gov.

CHEST 2017; 152(3):518-526

KEY WORDS: biomarker; blood; cell volume; ED; monocyte; sepsis

ABBREVIATIONS: AUC = area under the curve; CM10 = Cochran-Mantel-Haenszel; CRP = C-reactive protein; MDW = monocyte distribution width; MMV = mean monocyte volume; MNV = mean neutrophil volume; NDW = neutrophil distribution width; NPV = negative predictive value; PCT = procalcitonin; PPV = positive predictive value; SIRS = systemic inflammatory response syndrome

AFFILIATIONS: From the Department of Medicine (Drs Crouser and Closser, Mr Herren, and Ms Robart), The Ohio State University Wexner Medical Center, Columbus, OH; the Heart and Vascular Hospital (Drs Parrillo and Bicking), Hackensack University Medical Center, Hackensack, NJ; the Department of Critical Care Medicine (Drs Seymour and Angus), University of Pittsburgh School of Medicine, Pittsburgh, PA; Beckman Coulter, Inc (Drs Tejidor, Magari, Samoszuk, and Chaves and Ms Careaga), Miami, FL; and the Department of Pathology (Dr Williams), The Ohio State University Wexner Medical Center, Columbus, OH.

FUNDING/SUPPORT: This study was funded by Beckman Coulter, Inc. grant to E. D. C.

CORRESPONDENCE: Dr Elliott D. Crouser, MD, The Ohio State University Wexner Medical Center, Room 201F, Davis Heart & Lung Research Institute, 473 W 12th Ave, Columbus, OH 43210; e-mail: Elliott.Crouser@osumc.edu

DOI: http://dx.doi.org/10.1016/j.chest.2017.05.039

Monocyte Distribution Width: A Novel Indicator of Sepsis-2 and Sepsis-3 in High-Risk Emergency Department Patients*

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*See also p. 1152.

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[5]Beckman Coulter, Inc., Miami, FL.

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

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DOI: 10.1097/CCM.0000000000003799

Objectives: Most septic patients are initially encountered in the emergency department where sepsis recognition is often delayed, in part due to the lack of effective biomarkers. This study evaluated the diagnostic accuracy of peripheral blood monocyte distribution width alone and in combination with WBC count for early sepsis detection in the emergency department.

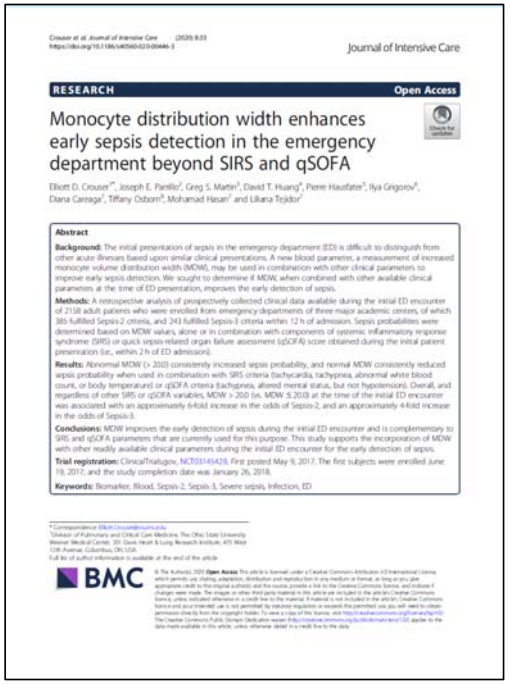
Design: An Institutional Review Board approved, blinded, observational, prospective cohort study conducted between April 2017 and January 2018.

Setting: Subjects were enrolled from emergency departments at three U.S. academic centers.

Patients: Adult patients, 18–89 years, with complete blood count performed upon presentation to the emergency department, and who remained hospitalized for at least 12 hours. A total of 2,212 patients were screened, of whom 2,158 subjects were enrolled and categorized per Sepsis-2 criteria, such as controls ($n = 1,088$), systemic inflammatory response syndrome ($n = 441$), infection ($n = 244$), and sepsis ($n = 385$), and Sepsis-3 criteria, such as control ($n = 1,529$), infection ($n = 386$), and sepsis ($n = 243$).

Interventions: The primary outcome determined whether an monocyte distribution width of greater than 20.0 U, alone or in combination with WBC, improves early sepsis detection by Sepsis-2 criteria. Secondary endpoints determined monocyte distribution width performance for Sepsis-3 detection.

Measurements and Main Results: Monocyte distribution width greater than 20.0 U distinguished sepsis from all other conditions based on either Sepsis-2 criteria (area under the curve, 0.79; 95% CI, 0.76–0.82) or Sepsis-3 criteria (area under the curve, 0.73; 95% CI, 0.69–0.76). The negative predictive values for monocyte distribution width less than or equal to 20 U for Sepsis-2 and Sepsis-3 were 93% and 94%, respectively. Monocyte distribution width greater than 20.0 U combined with an abnormal WBC further improved Sepsis-2 detection (area under the curves, 0.85; 95% CI, 0.83–0.88) and as reflected by likelihood ratio and



Crouser et al. Journal of Intensive Care (2020) 8:33
https://doi.org/10.1186/s40560-020-00446-3

Journal of Intensive Care

RESEARCH Open Access

Monocyte distribution width enhances early sepsis detection in the emergency department beyond SIRS and qSOFA

Elliott D. Crouser[1*], Joseph E. Parrillo[2], Greg S. Martin[3], David T. Huang[4], Pierre Hausfater[5], Ilya Grigorov[6], Diana Careaga[7], Tiffany Osborn[8], Mohamad Hasan[1] and Liliana Tejidor[7]

Abstract

Background: The initial presentation of sepsis in the emergency department (ED) is difficult to distinguish from other acute illnesses based upon similar clinical presentations. A new blood parameter, a measurement of increased monocyte volume distribution width (MDW), may be used in combination with other clinical parameters to improve early sepsis detection. We sought to determine if MDW, when combined with other available clinical parameters at the time of ED presentation, improves the early detection of sepsis.

Methods: A retrospective analysis of prospectively collected clinical data available during the initial ED encounter of 2158 adult patients who were enrolled from emergency departments of three major academic centers, of which 385 fulfilled Sepsis-2 criteria, and 243 fulfilled Sepsis-3 criteria within 12 h of admission. Sepsis probabilities were determined based on MDW values, alone or in combination with components of systemic inflammatory response syndrome (SIRS) or quick sepsis-related organ failure assessment (qSOFA) score obtained during the initial patient presentation (i.e., within 2 h of ED admission).

Results: Abnormal MDW (> 20.0) consistently increased sepsis probability, and normal MDW consistently reduced sepsis probability when used in combination with SIRS criteria (tachycardia, tachypnea, abnormal white blood count, or body temperature) or qSOFA criteria (tachypnea, altered mental status, but not hypotension). Overall, and regardless of other SIRS or qSOFA variables, MDW > 20.0 (vs. MDW ≤ 20.0) at the time of the initial ED encounter was associated with an approximately 6-fold increase in the odds of Sepsis-2, and an approximately 4-fold increase in the odds of Sepsis-3.

Conclusions: MDW improves the early detection of sepsis during the initial ED encounter and is complementary to SIRS and qSOFA parameters that are currently used for this purpose. This study supports the incorporation of MDW with other readily available clinical parameters during the initial ED encounter for the early detection of sepsis.

Trial registration: ClinicalTrials.gov, NCT03145428. First posted May 9, 2017. The first subjects were enrolled June 19, 2017, and the study completion date was January 26, 2018.

Keywords: Biomarker, Blood, Sepsis-2, Sepsis-3, Severe sepsis, Infection, ED

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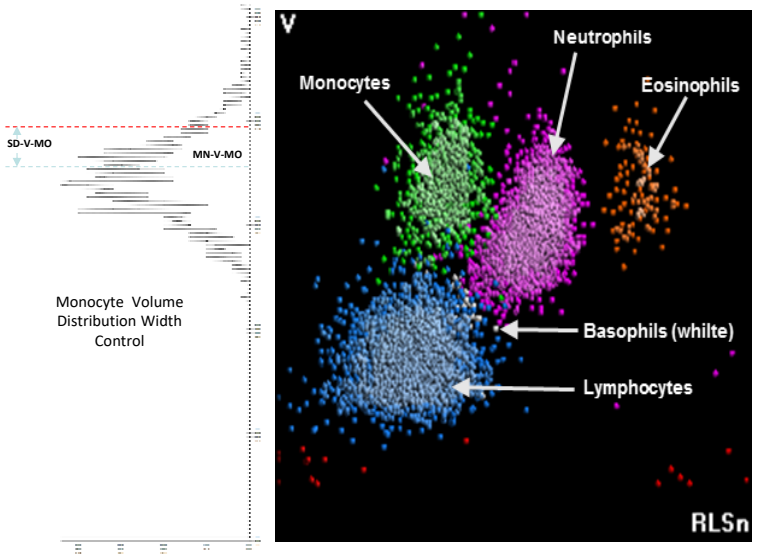
Full list of author information is available at the end of the article

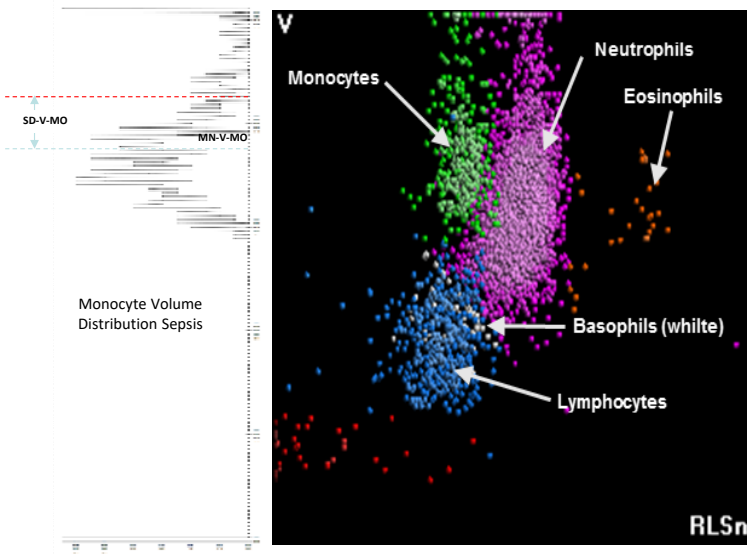
BMC

Monocyte Distribution Width (MDW)
Histograms of CBC Diff and Measurement of MDW



Non-septic

MDW = 19.1
WBC cells x10^3 = 4.73



Septic

MDW = 24.3
WBC cells x10^3 = 10.27

VICTAS Trial: Vitamin C, Thiamine and Steroid in Treatment of Sepsis

- 43 Hospitals
  - ED or ICU enrollment
  - Patients with sepsis induced cardiac or respiratory dysfunction
  - 500 patients funding withheld (study stopped)/Prior to COVID
  - Vasopressors
    - HFNC, NIV, IMV
  - Vit C 1.5 gm, thiamine (100mg) & steroids (50mg) q 6 vs. placebo
  - Infusion 96hrs, d/c ICU or death
- Outcome Measurements
  - Vasopressor free days
  - Ventilator free days
  - 30-day mortality

Results

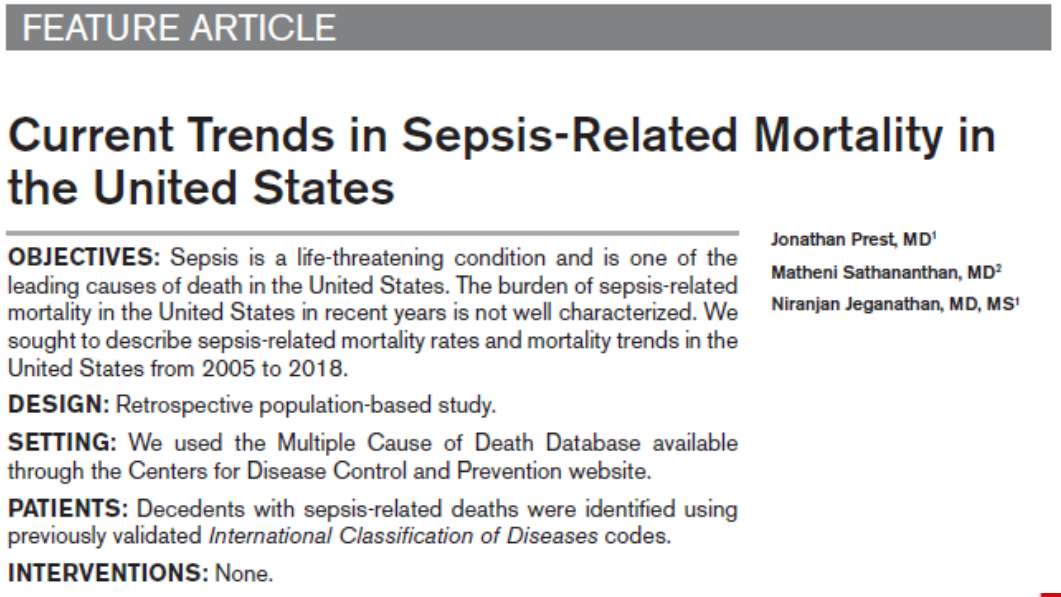
- Open label steroids administration 32% in both groups
- No difference in VFD or vasopressor free days
- No difference in 30-day mortality

Sevransky LE, et al. JAMA. 2021;325(8):742-750

Sepsis Mortality Trends in the United States

Conclusions:

- 2005-2018 overall sepsis-related mortality rates were stable but there were significant racial and gender disparities in mortality trends
- 6.7% of the deaths in the US were sepsis related from 2005-2018
- Increased mortality in females 45-65 years old and males 55-65 years old
- Sepsis-related mortality trends decreased significantly in Blacks, Hispanics, and Asians and increased in Whites and Native Americans



FEATURE ARTICLE

Current Trends in Sepsis-Related Mortality in the United States

Jonathan Prest, MD[1]
Matheni Sathananthan, MD[2]
Niranjan Jeganathan, MD, MS[1]

OBJECTIVES: Sepsis is a life-threatening condition and is one of the leading causes of death in the United States. The burden of sepsis-related mortality in the United States in recent years is not well characterized. We sought to describe sepsis-related mortality rates and mortality trends in the United States from 2005 to 2018.

DESIGN: Retrospective population-based study.

SETTING: We used the Multiple Cause of Death Database available through the Centers for Disease Control and Prevention website.

PATIENTS: Decedents with sepsis-related deaths were identified using previously validated *International Classification of Diseases* codes.

INTERVENTIONS: None.

Prest, Jonathan MD1; Sathananthan, Matheni MD2; Jeganathan, Niranjan MD, MS1 Current Trends in Sepsis-Related Mortality in the United States, Critical Care Medicine: April 6, 2021 - Volume Latest Articles - Issue - doi: 10.1097/CCM.0000000000005017

Coming Attractions!!

Clover Study
Crystalloid Liberal or Vasopressors Early Resuscitation in Sepsis

Hypothesis

- Restrictive (vs liberal) fluid treatment strategy during the 1st 24hr of resuscitation for sepsis-induced hypotension will reduce 90-day in hospital mortality
  - Conservative (vasopressor first followed by rescue fluids)
  - liberal (fluids followed by rescue vasopressors)

Enrollment to be completed by June 2021

Method

- Multicenter, randomized prospective phase 3 trial
- Intervention: protocolized fluid titration strategies for up to 24 hours
- Sample: 2,320 patients planned to enrollment
- Primary outcome: 90 day inpatient mortality
- 50 Hospitals—acute and critical care (part of Petal Network)

Numerous Trials on Resuscitation in Sepsis and Fluid Type

Showing: 1-10 of **77** studies 10 studies per page

Show/Hide Columns

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Not yet recruiting	**Fluid Resuscitation** in **Septic Shock** Patients With BMI Elevation	• Sepsis • **Septic Shock** • Obesity	• Procedure: Actual Body Weight Dosing • Procedure: Adjusted Body Weight Dosing • Procedure: Ideal Body Weight Dosing	• Carolinas Medical Center Charlotte, North Carolina, United States
2	☐	Unknown ᵀ	Peripheral Perfusion Versus Lactate Targeted **Fluid Resuscitation** in **Septic Shock**	• **Septic Shock** • Hyperlactatemia • Peripheral Perfusion	• Other: CRT guided **resuscitation** • Other: Lactate guided **resuscitation**	• Pontificia Universidad Catolica de Chile Santiago, Metropolitana, Chile
3	☐	Completed	Echo vs. EGDT in Severe Sepsis and **Septic Shock**	• Severe Sepsis • **Septic Shock**	• Other: Echo guided **fluid resuscitation** • Other: EGDT **fluid resuscitation**	• Intermountain Medical Center Murray, Utah, United States
4	☐	Not yet recruiting	Bicarbonated Ringer's Solution Versus Lactated Ringer's Solution in Patients With **Septic Shock**	• **Septic Shock** • **Fluid Resuscitation** • Crystalloid Solution • Intensive Care Unit	• Drug: Bicarbonated Ringer's solution • Drug: Lactated Ringer's solution	• Zhongnan Hospital of Wuhan University Wuhan, Hubei, China
5	☐	Completed	Balanced Salt Solutions vs. Normal Saline in Children With **Septic Shock**	• **Septic Shock** • **Shock**	• Drug: Balanced salt solution • Drug: Normal saline	• All India Institute of Medical Sciences New Delhi, Delhi, India • PGIMER Chandigarh, India • JIPMER Puducherry, India
6	☐	Not yet recruiting	Acetated Ringer's Solution Versus Saline in Patients With **Septic Shock**	• **Septic Shock** Hyperdynamic	• Drug: **Fluid resuscitation**	
7	☐	Completed	**Fluid Resuscitation** in Early **Septic Shock**	• **Septic Shock** • Sepsis • Severe Sepsis	• Drug: 5% albumin • Drug: Normal Saline	• University of Alberta Hospital Edmonton, Alberta, Canada • Winnipeg Health Sciences Center Winnipeg, Manitoba, Canada • Halifax Capital Health Center Halifax, Nova Scotia, Canada • (and 3 more...)
8	☐	Not yet recruiting	**Septic Shock** Management Guided by Ultrasound: SEPTICUS Trial	• **Septic Shock**	• Procedure: USSM protocol • Procedure: ACCM protocol	• RSUD dr. Saiful Anwar Malang, Jawa Timur, Indonesia
9	☐	Completed	Restrictive Intravenous **Fluids** Trial in Sepsis	• **Septic Shock** • Severe Sepsis	• Other: Intravenous **Fluid** Cap	• Rhode Island Hosptial Providence, Rhode Island, United States

https://www.clinicaltrials.gov/ct2/results?cond=Septic+shock&term=fluid+resuscitation&cntry=&state=&city=&dist=&Search=Search

10 Current Vitamin C Trials

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	**Vitamin C**, Thiamine and Hydrocortisone for the Treatment of **Septic Shock**	• **Septic Shock**	• Drug: **Vitamin C**,thiamine,hydrocortisone • Drug: Placebo	• Northern Jiangsu Province people's hospital Yangzhou, Jiangsu, China
2	☐	Recruiting	Modulation of Endothelial Dysfonction Using **Vitamin C** in **Septic Shock** Patients	• **Septic Shock**		• Intensive care department- Hôpital saint Antoine Paris, France
3	☐	Recruiting	**Vitamin C**, Steroids, and Thiamine, and Cerebral Autoregulation and Functional Outcome in **Septic Shock**	• **Septic Shock**	• Drug: Stress-dose Hydrocortisone plus **Vitamin C** • Drug: isotonic sodium chloride solution placebo plus isotonic sodium chloride solution placebo	• Evaggelismos General Hospital Athens, Attica, Greece
4	☐	Active, not recruiting	Outcomes of **Septic Shock** Patients Treated With a Metabolic Resuscitation Bundle Consisting of Intravenous Hydrocortisone, **Ascorbic Acid** and Thiamine.	• **Septic Shock** • **Ascorbic Acid** Deficiency	• Drug: Intravenous **Ascorbic Acid**	• University of Wisconsin Hospital and Clinics Madison, Wisconsin, United States
5	☐	Active, not recruiting	**Vitamin C** to Reduce Vasopressor Dose in **Septic Shock**	• **Septic Shock** • Sepsis	• Drug: **Vitamin C** • Drug: Placebos	• Hospital Español Mexico City, Mexico
6	☐	Recruiting	Pilot Study on the Use of Hydrocortisone, **Vitamin c** and Tiamine in Patient With Sepsis and **Septic Shock**	• Sepsis • **Septic Shock**	• Drug: red blood cells transfusion, tranexamic acid (TXA) and fibrinogen concentrate • Drug: on crystalloid fluid and Tranexamic acid	• Hospital Dr Josep Trueta Girona, Spain
7	☐	Recruiting	**Vitamin C**, Hydrocortisone and Thiamine for **Septic Shock**	• **Shock, Septic**	• Drug: Combined **Vitamin C** and Stress-Dose Hydrocortisone • Drug: Placebo plus placebo	• Evaggelismos General Hospital Athens, Attica, Greece • General Hospital of Nikaia Saint Panteleimon Piraeus, Attica, Greece
8	☐	Recruiting	**Vitamin C** & Thiamine in Sepsis	• Sepsis • **Septic Shock**	• Drug: **Vitamin C** • Drug: **Vitamin** B1	• Saint Francis Hospital and Medical Center Hartford, Connecticut, United States
9	☐	Recruiting	Clinical Trial of Antioxidant Therapy in Patients With **Septic Shock**	• Oxidative Stress • **Septic Shock**	• Drug: Melatonin 5 mg • Drug: **Vitamin C** 1 GM Oral Tablet • Drug: **Vitamin** E 400 UNT • Drug: N-acetylcysteine	• Centro Médico ABC Mexico City, Mexico
10	☐	Active, not recruiting	Antioxidants as Adjuvant Therapy to Standard Therapy in Patients With COVID-19	• Pneumonia, Viral • Covid19 • ARDS • Oxidative Stress	• Drug: **Vitamin C** • Drug: **Vitamin** E • Drug: Melatonin • (and 2 more...)	• Unidad Temporal COVID-19 en Centro Citibanamex Mexico City, Mexico

https://www.clinicaltrials.gov/ct2/results?cond=Septic+Shock&term=vitamin+C&type=&rslt=&recrs=a&recrs=f&recrs=d&age_v=&age=1&age=2&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=

Sepsis Emerging Drugs

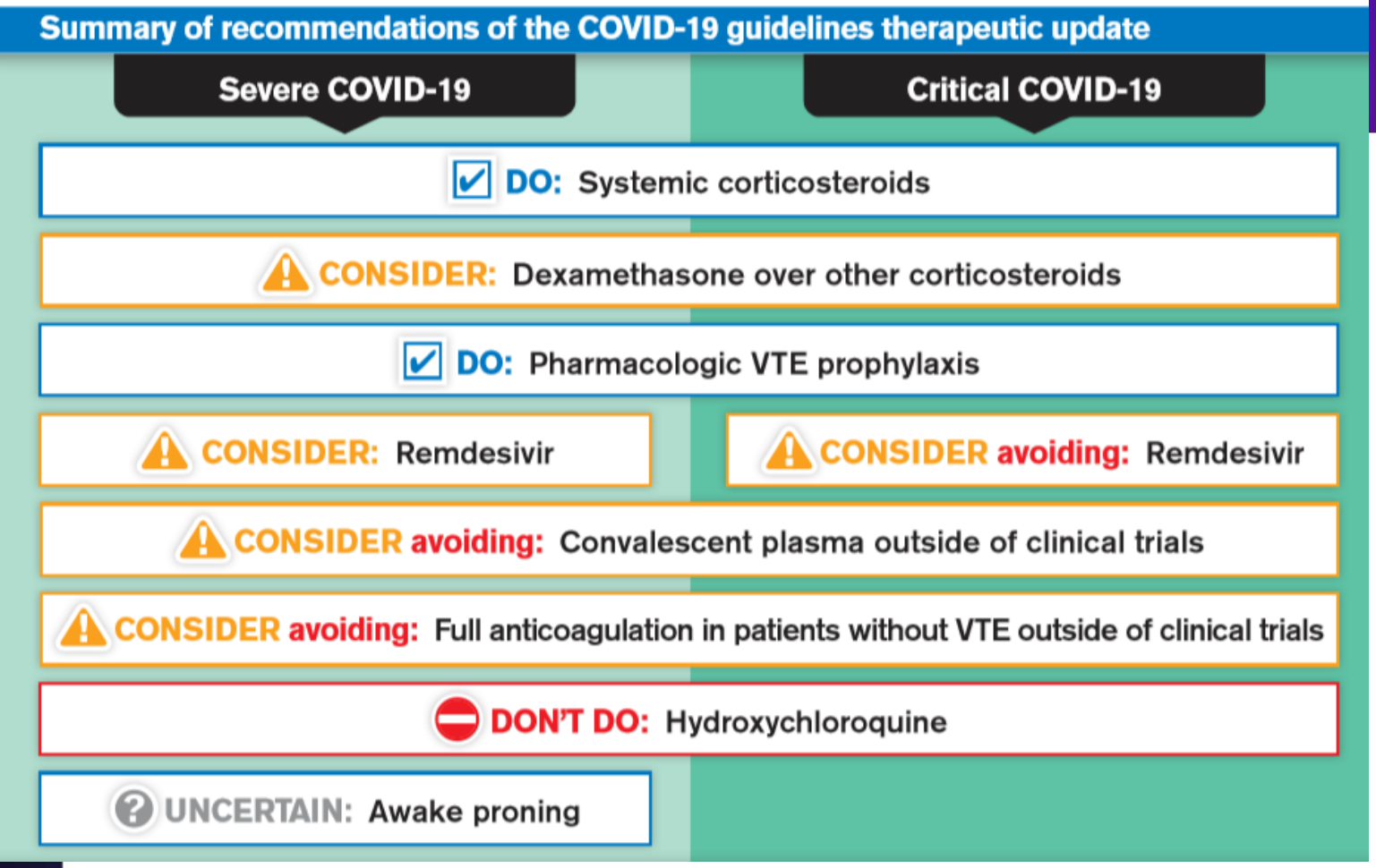
Rezafungin is a novel, once-weekly antifungal being developed for the treatment and prevention of serious fungal infections. Rezafungin (formerly CD101) is an echinocandin drug, currently in Phase III clinical development for candidemia, invasive candidiasis and for prophylaxis of invasive fungal infections due to Candida, Aspergillus, and Pneumocystis. The U.S. Food and Drug Administration (FDA) has granted Qualified Infectious Disease Product (QIDP) and fast track designations for rezafungin.

VBI-S is made of small particles of specific lipid called micelles and liposomes for the treatment of hypotension. VBI-S is an intravenously injectable fluid comprised of phospholipid nanoparticles that were specifically designed to shift the biophysical properties of the body's fluid volume in hypovolemic shock, due to sepsis, from non-survival to survival. The therapy is currently under phase II clinical evaluation for the treatment of hypovolemia due to sepsis/septic shock.

https://www.businesswire.com/news/home/20210209005785/en/World-Sepsis-Pipeline-Insight-2021-Pipeline-Product-Profiles-Therapeutic-Assessment-Pipeline-Assessment-Inactive-Drugs-Assessment-Unmet-Needs---ResearchAndMarkets.com

COVID-19 Resources

SCCM Sepsis/
COVID Resources



Post Sepsis Syndrome
What is it and How to Prevent it?

Post Sepsis Syndrome

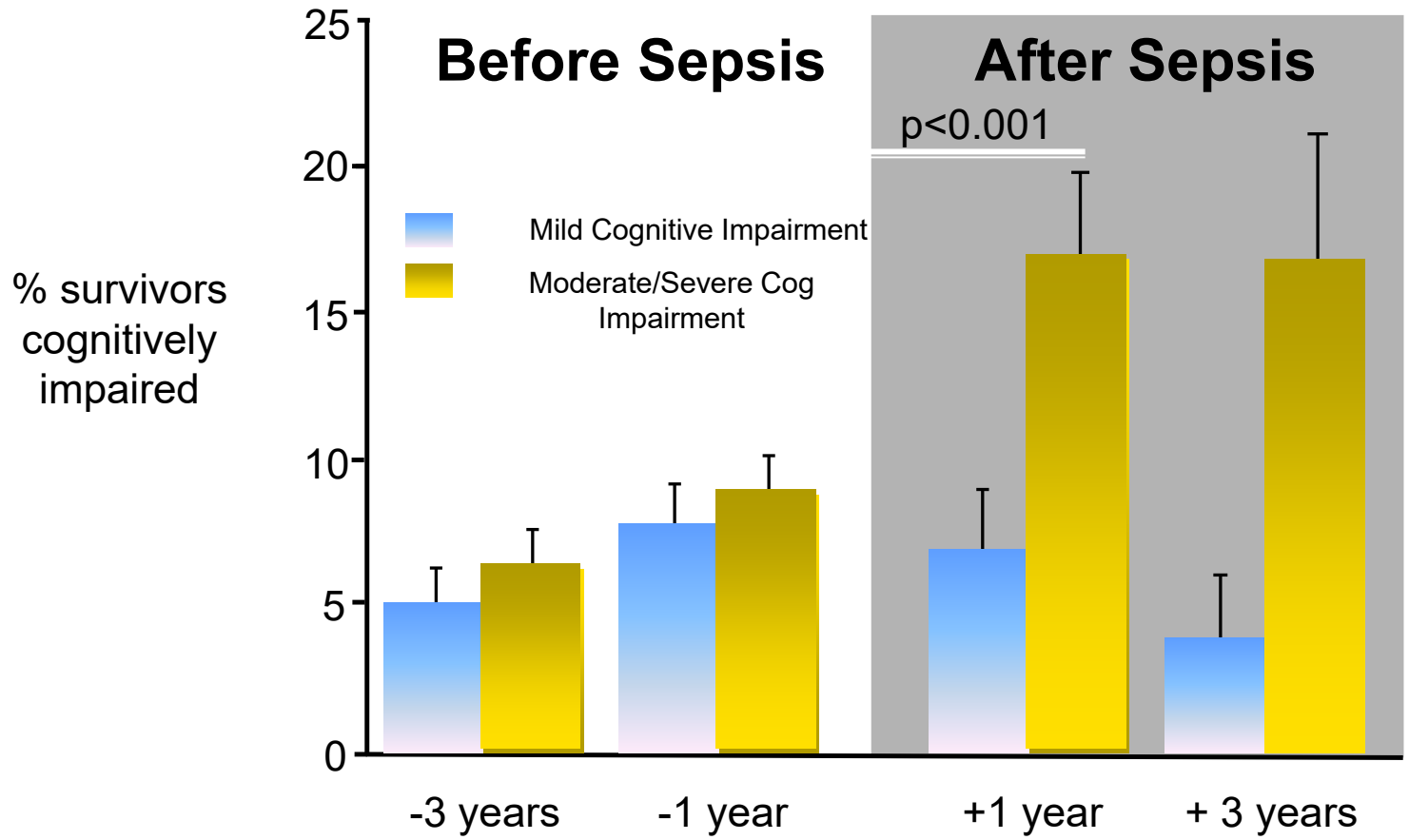
People who have suffered from severe sepsis and especially those treated in an intensive care unit are at greatest risk of suffering post-sepsis syndrome.

"60 percent of hospitalizations for severe sepsis were associated with worsened cognitive and physical function among surviving older adults. The odds of acquiring moderate to severe cognitive impairment were 3.3 times higher following an episode of sepsis than for other hospitalizations."

Sepsis survivors may be more at risk for developing other infections both viral and bacterial

Iwashyna, T. JAMA 2010;
Mukherjee, S SHOCK 2012

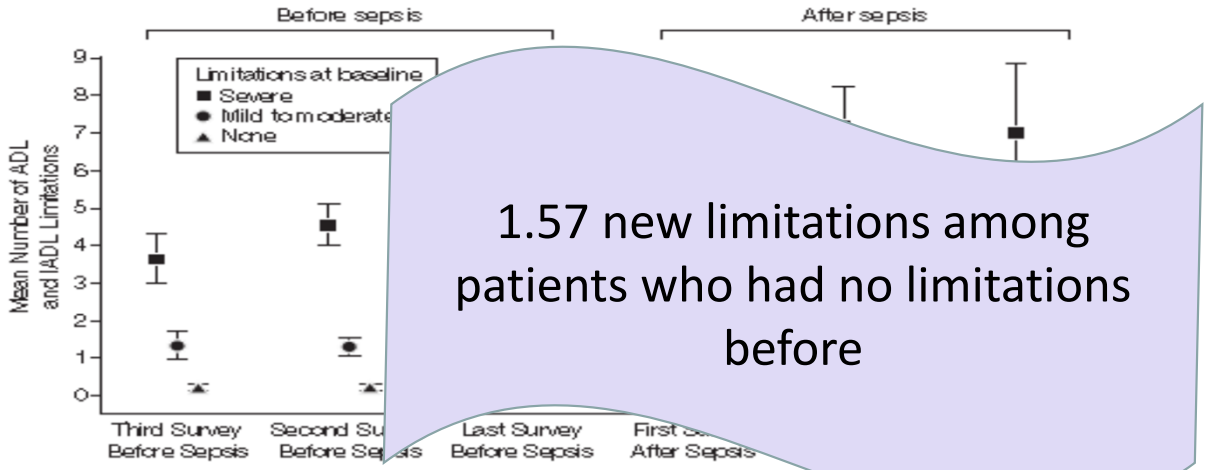
Cognitive Impairment: Sepsis



Iwashyna T, JAMA 2010;304:1787-1794

Functional Trajectories by Baseline Functioning

Figure 3. Functional Trajectories by Baseline Functioning



Time to sepsis admission, median (IQR), y	−5.2 (−5.6 to −4.7)	−3.1 (−3.7 to −2.7)	−1.1 (−1.7 to −0.7)	0.9 (0.4 to 1.4)	(2.3 to 3.4)	
No. of patients, by baseline physical functioning						
Severe limits	87	127	159	159	42	14
Mild to moderate limits	105	151	195	195	93	28
No limits	142	206	269	269	153	56

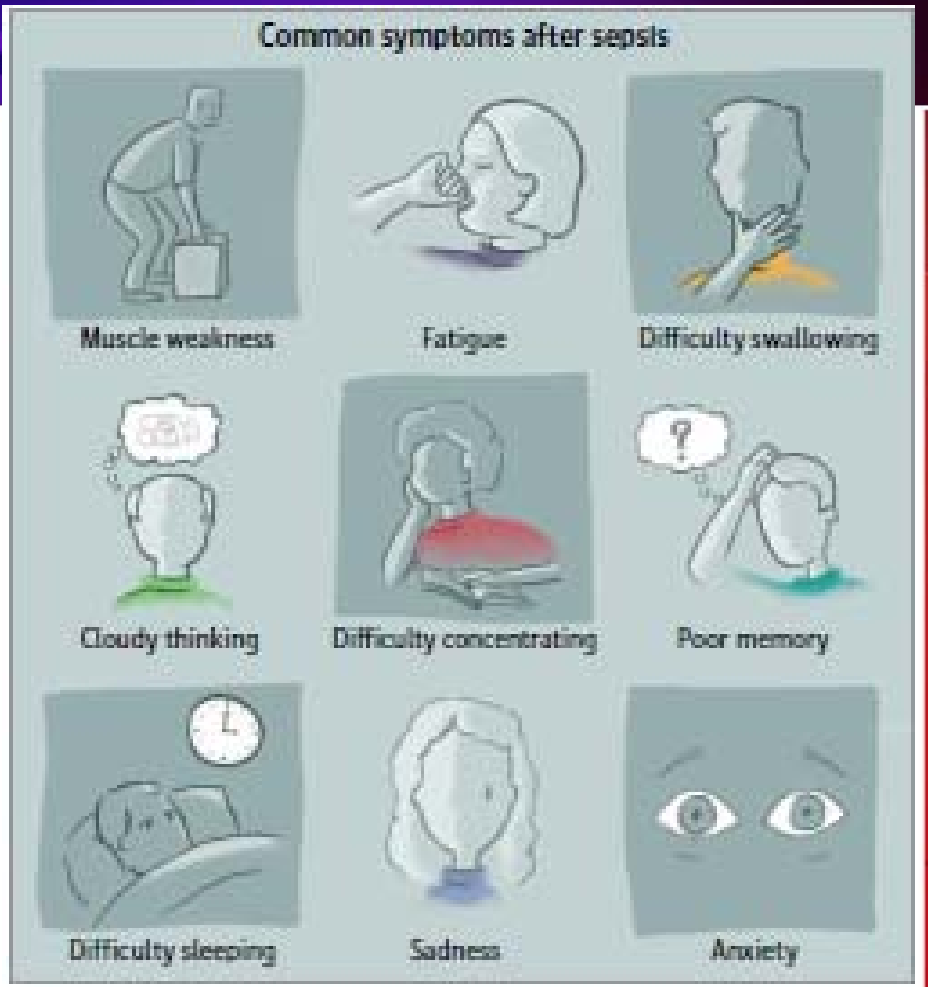
1.57 new limitations among patients who had no limitations before

ADL: walking, dressing, bathing, eating, getting into and out of bed and toileting
IADL: preparing a hot meal, shopping for groceries, making telephone calls, taking medicines, and managing money

Iwashyna T, JAMA 2010;304:1787-1794

Post-Sepsis Syndrome

- Describes physical and/or long-term effects that affects up to 50% of people who survive sepsis.
- Longer term effects of sepsis include:
  - Sleep disturbance including insomnia
  - Experiencing nightmares, hallucinations, flashbacks and panic attacks
  - Muscle and joint pains which can be severe and disabling
  - Extreme tiredness and fatigue
  - Inability to concentrate
  - Impaired mental (cognitive) functioning
  - Loss of confidence and self-belief



JAMA. Jan. 2, 2018 Patient Page, Postsepsis Morbidity

Cause of Post Sepsis Syndrome

- Response to systemic inflammation
- Brain, muscle and nerve injury from inflammation, ischemia and ischemia-reperfusion
- Poor perfusion, blood clots
- End organ damage

Post-Intensive Care Syndrome

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

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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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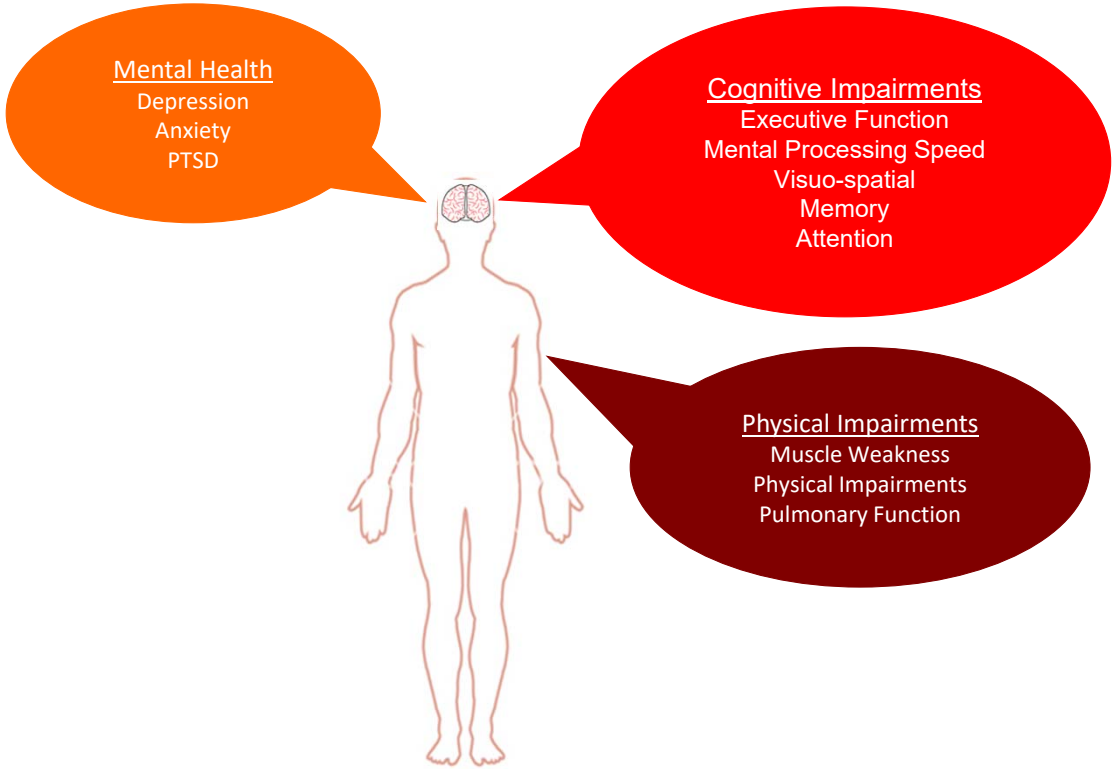
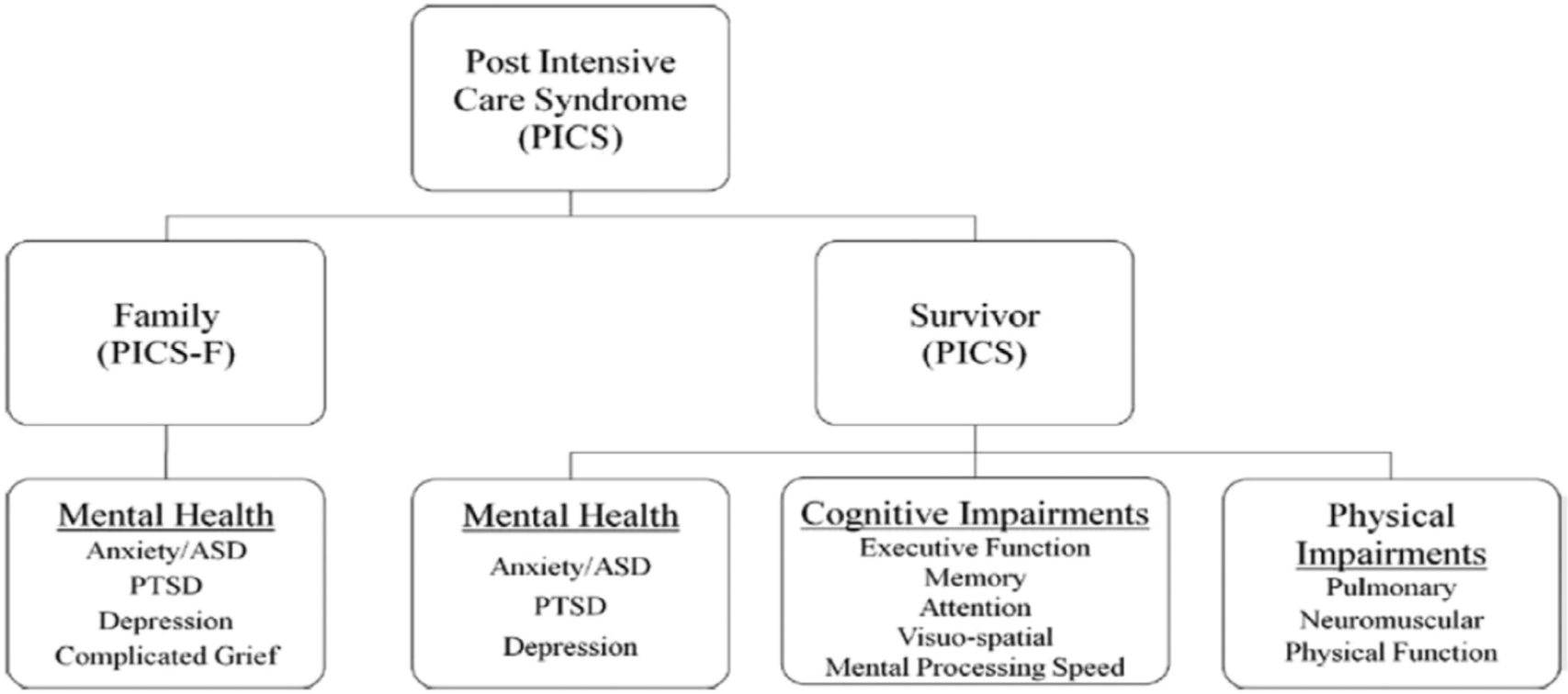
DOI: 10.1097/CCM.0b013e318232da75



Needham, et al. Crit Care Med. 2012.

Post Intensive Care Syndrome



Harvey M, Davidson J. Crit Care Med, 2016;44(2):381-385

Key Components of Sepsis Care

- Infection prevention
- Early identification
- Early and aggressive management (bundles)
- Avoid iatrogenic harm
  - Understand post sepsis syndrome and how to minimize its impact
  - Prevent sepsis readmissions

ALL of these must be provided across the continuum of care

ICU Liberation Bundle: A to F

- **A** ASSESS, PREVENT & MANAGE PAIN
- **B** BOTH SAT & SBT
- **C** CHOICE OF ANALEGISA or SEDATION
- **D** DELIRIUM
- **E** EARLY MOBILITY
- **F** FAMILY/PATIENT ENGAGEMENT

Assessments and Monitoring

PAD SYMPTOMS	ASSESSMENT & MONITORING TOOLS	CARE IMPROVEMENT ABCDEF BUNDLE
PAIN	**NRS:** Numeric Rating Scale **BPS:** Behavioral Pain Scale **CPOT:** Critical Care Pain Observation Tool	**A**ssess, Prevent, and Manage Pain **B**oth Spontaneous Awakening Trials and Spontaneous Breathing Trials **C**hoice of Sedation **D**elirium: Assess, Prevent and Manage **E**arly Mobility and **E**xercise **F**amily Engagement and Empowerment
AGITATION	**RASS:** Richmond Agitation Sedation Scale **SAS:** Sedation Agitation Scale	
DELIRIUM	**CAM-ICU:** Confusion Assessment Method for ICU **ICDSC:** Intensive Care Delirium Screening Checklist	

http://www.iculiberation.org/SiteCollectionDocuments/ICU-Liberation-ABCDEF-Bundle-Implementation-Assess-Prevent-Manage-Pain.pdf

A Assess, Prevent and Manage Pain

Assess

- Assess pain ≥ 4x/shift & PRN
- **Significant pain with NRS >3, BPS >5, or CPOT ≥3**

Treat

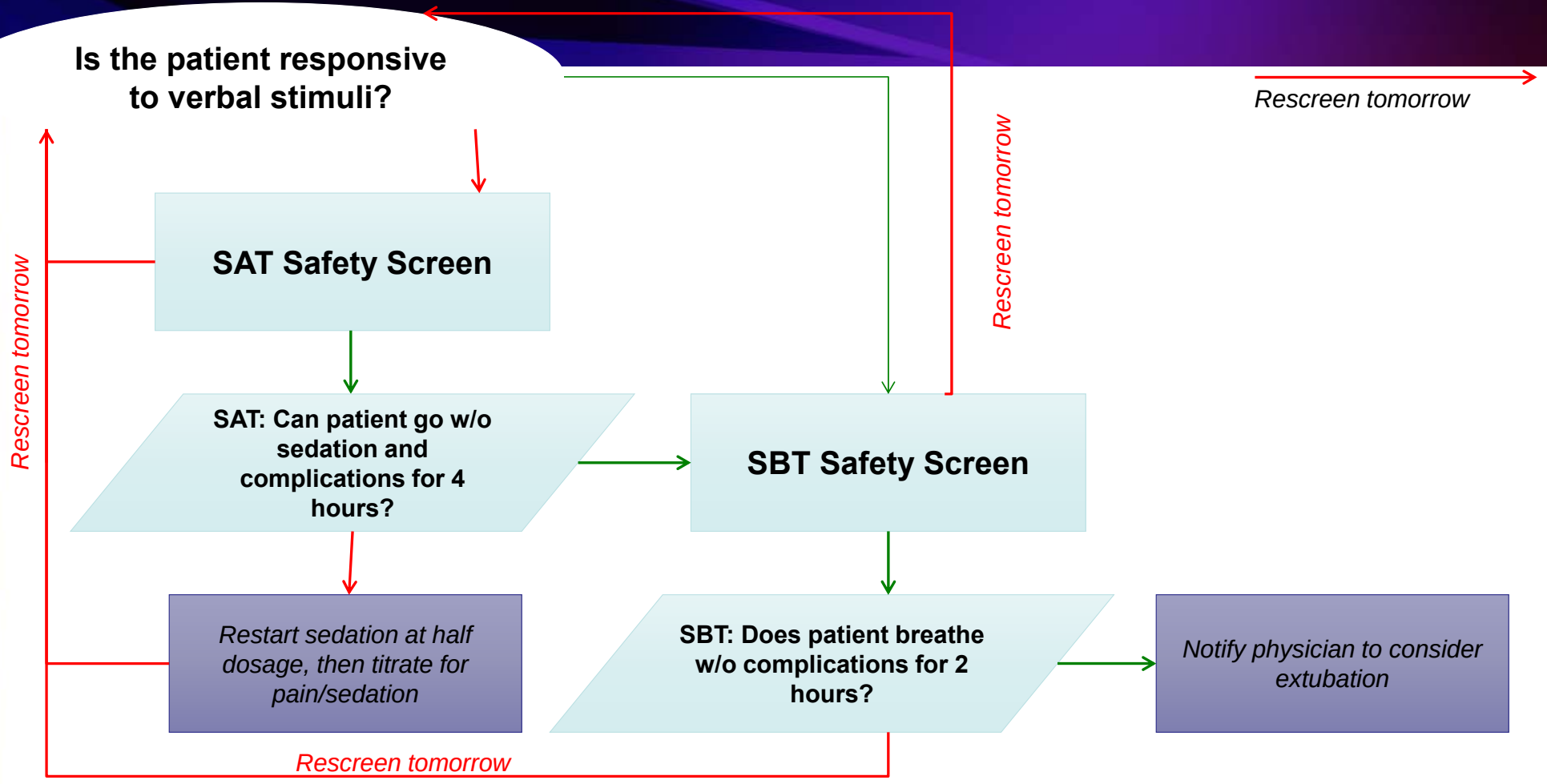
- **Treat pain within 30 minutes** of detecting significant pain & REASSESS:
- Non-pharmacological treatment (e.g. relaxation)
- Pharmacological treatment

Prevent

- Administer pre-procedural analgesia and/or non-pharmacological interventions
- **Treat pain first, then sedate**

Barr. J Crit Care Med 2013;41(1):263-306

B SAT & SBT Protocol



ABC Trial (RCT Paired Sedation & Vent Weaning Protocols)

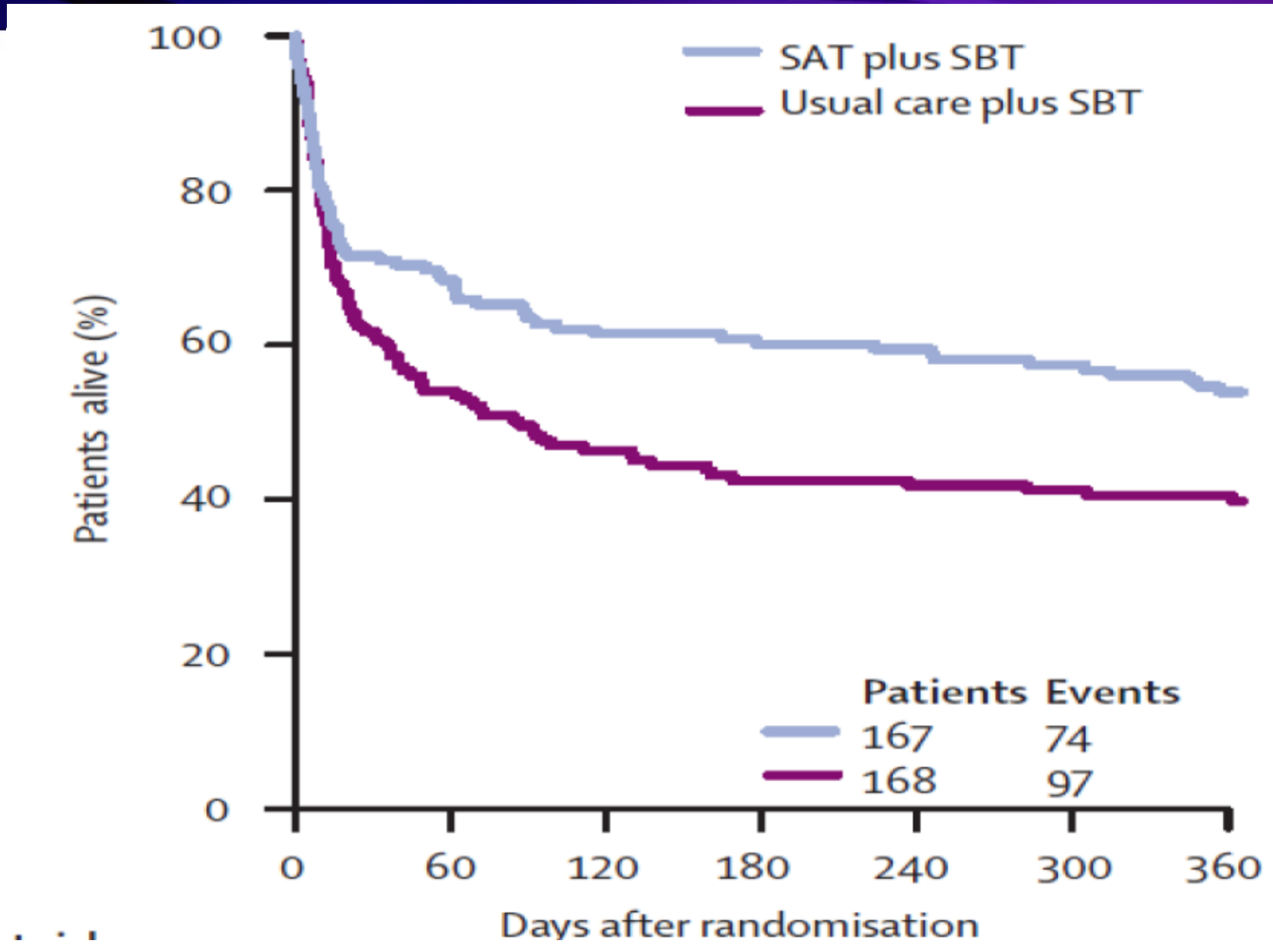
- To determine the efficacy and safety of a protocol combining daily interruption of sedatives and spontaneous breathing trials (SBTs)
  - Ventilator-free days
  - ICU and hospital length of stay
  - Survival
  - Duration of coma and delirium
  - Long-term neuropsychological outcomes

Outcome*	SBT	SAT+SBT	*P* value
Ventilator-free days	12	15	0.02
Time-to-event, days			
Successful extubation, days	7.0	5	0.05
ICU discharge, days	13	9	0.02
Hospital discharge, days	19	15	0.04
Death at 1 year, n (%)	97 (58%)	74 (44%)	0.01
Days of brain dysfunction			
Coma	3.0	2.0	0.002
Delirium	2.0	2.0	0.50

*Median, except as noted

Girard, et al, Lancet. 2008;371:126-34

ABC Trail: Mortality at 1 Year



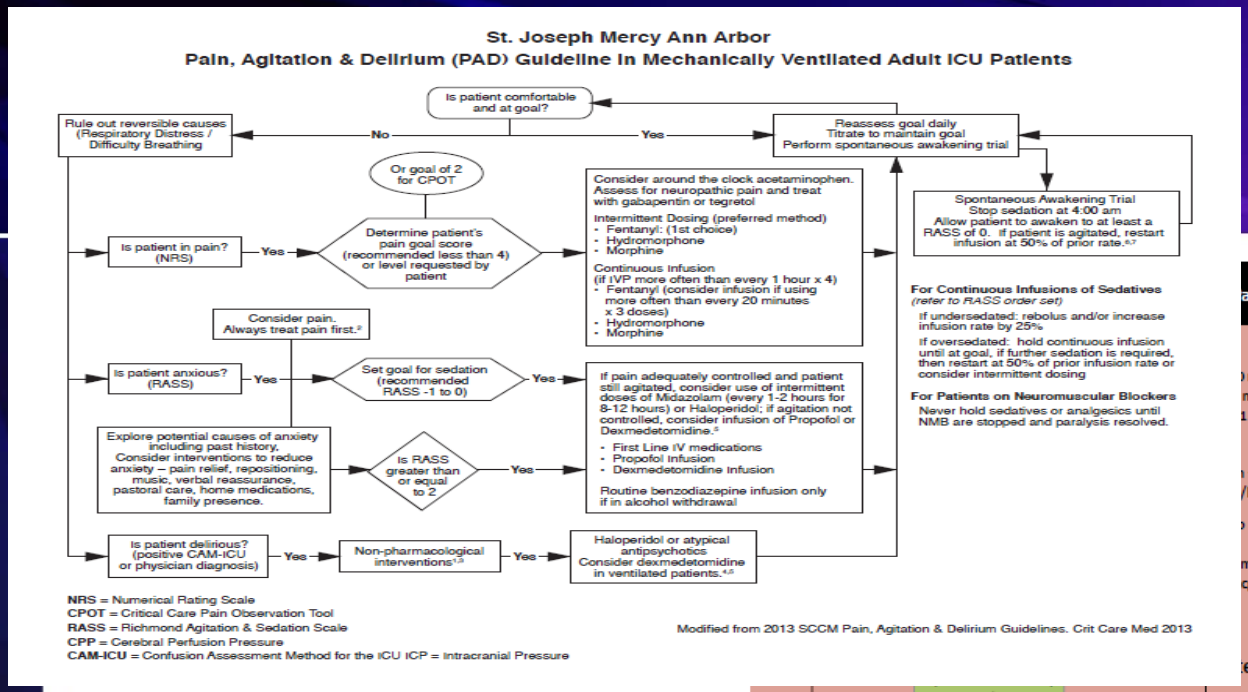
Girard, et al, Lancet. 2008;371:126-34

C Choice of Analgesia and Sedation

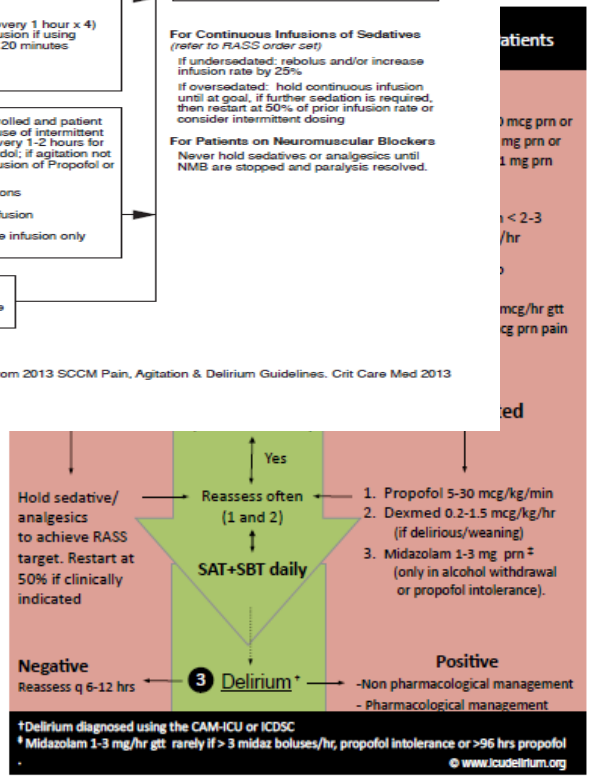
- All ICU patients should be routinely assessed for:
  - **Pain** (Likert self-report, or BPS/CPOT non-self-report)
  - **Agitation/depth of sedation** (RASS/SAS)
  - **Delirium** (CAM-ICU/ICDSC)
- Important factors influence the choice and dose of analgesia and sedative medications
- Non-pharmacologic strategies play an important role when managing pain and agitation

- Goals of Sedation
  - Calm
  - Comfortable
  - Cooperative
  - Reduce anxiety and agitation
  - Facilitate mechanical ventilation
  - Decrease traumatic memory of ICU stay and procedures

Barr. J Crit Care Med 2013;41:263-306
Devlin, Crit Care Med, 2018;46:1532-1548



Targeted Sedation/P
Example



D Delirium: Assess, Prevent and Manage

What is delirium:

- Disturbance in attention and awareness
- Disturbance in cognition: e.g., memory, disorientation, language, perception
- Develops over a short period of time and tends to fluctuate during the course of the day

Routinely assess for delirium using:

- Confusion Assessment Method for ICU (CAM-ICU)
- Intensive Care Delirium Screening Checklist (ICDSC)

- Independently associated with increased risk of death:
  - Each day of delirium increase 1 yr mortality by 10%
- Duration assoc. with short & long term cognitive impairment
- 1 out of 4 patients had cognitive impairment at 12 months
- ↑ Mech Vent duration
- ↑ ICU & Hospital Length of Stay
- Estimated national costs $4 to $16 **Billion**
- Post-d/c anxiety/ PTSD symptom from delirious memory

Klouwenberg *BMJ* 2014;349:g6652; Ely. ICM 2001; 27, 1892-1900 Ely, JAMA 2004; 291: 1753-1762 ; Lin, SM CCM 2004; 32: 2254-2259; Girard CCM 38(7):1513-1520; Milbrandt E.,CCM 2004; 32:955-962. Jackson. Neuropsychology Review 2004; 14: 87-98. Oimet ICM 2007; 33:1007-1013; Davydow Gen. Hosp. Psych 2008;30:421-434 Pandharipande, PP. et al. N Engl J Med;369:1306:1316

Delirium Assessment

STEP 1 — RICHMOND AGITATION-SEDATION SCALE (RASS)

Sedation Assessment

Scale	Label	Description	
+4	COMBATIVE	Combative, violent, immediate danger to staff	VOICE
+3	VERY AGITATED	Pulls to remove tubes or catheters; aggressive	
+2	AGITATED	Frequent non-purposeful movement, fights ventilator	
+1	RESTLESS	Anxious, apprehensive, movements not aggressive	
0	ALERT & CALM	Spontaneously pays attention to caregiver	
-1	DROWSY	Not fully alert, but has sustained awakening to voice (eye opening & contact >10 sec)	
-2	LIGHT SEDATION	Briefly awakens to voice (eyes open & contact <10 sec)	
-3	MODERATE SEDATION	Movement or eye opening to voice (no eye contact)	

If RASS is ≥ -3 proceed to CAM-ICU (Is patient CAM-ICU positive or negative?)

-4	DEEP SEDATION	No response to voice, but movement or eye opening to physical stimulation	TOUCH
-5	UNAROUSEABLE	No response to voice or physical stimulation	

If RASS is -4 or -5 → STOP (patient unconscious), RECHECK later

Sessler, et al., Am J Repir Crit Care Med 2002; 166: 1338-1344 Ely, et al., JAMA 2003; 286, 2983-2991

STEP 2 — Confusion Assessment Method for the ICU (CAM-ICU)

DELIRIUM ASSESSMENT

1. Acute Change or Fluctuating Course of Mental Status:
- Is there an acute change from mental status baseline? OR
- Has the patient's mental status fluctuated during the past 24 hours?

NO → CAM-ICU negative NO DELIRIUM

YES

2. Inattention:
- *"Squeeze my hand when I say the letter 'A'."*
  Read the following sequence of letters: S A V E A H A A R T
  ERRORS: No squeeze with 'A' & Squeeze on letter other than 'A'
- If unable to complete Letters → Pictures

0 - 2 Errors → CAM-ICU negative NO DELIRIUM

> 2 Errors

3. Altered Level of Consciousness
Current RASS level (think back to sedation assessment in Step 1)

RASS other than zero → CAM-ICU positive DELIRIUM Present

RASS = zero

4. Disorganized Thinking:
1. Will a stone float on water?
2. Are there fish in the sea?
3. Does one pound weigh more than two?
4. Can you use a hammer to pound a nail?

Command: "Hold up this many fingers" (Hold up 2 fingers)
"Now do the same thing with the other hand" (Do not demonstrate)
OR "Add one more finger" (If patient unable to move both arms)

> 1 Error → CAM-ICU positive DELIRIUM Present

0 - 1 Error → CAM-ICU negative NO DELIRIUM

D Interventions for Delirium

- Analgesia and Sedative Algorithm
  - Control pain first, then anxiety
  - Use intermittent meds first before continuous
- Target RASS + 1 to -1
- Daily SAT (spontaneous awakening trial)
- Daily SBT (spontaneous breathing trial)
- Early mobility and rehabilitation
- Sleep enhancement (via nonpharm and hygiene)
- Reducing unnecessary and deliriogenic medications
- Structured reorientation
- Adequate oxygenation

American Geriatric Society 2014 Guidelines. J Am Geriat Soc. 2016;63:142-150
Inouye. N Engl J Med. 1999;340:669-676
McNamara. Am J Crit Care. 2008;17:576

E Early Mobility

- Evidence that early mobility:
  - Reduces duration of ventilation and ICU LOS
  - May help reduce atelectasis and delirium
- Less time on ventilator should reduce risk for VAE

- Lord. Crit Care Med 2010;41:717-724
- Schweickert. Lancet 2009;373:1874-1882
- Needham. Arch Phys Med Rehabil 2010;91: 536-542
- Dammeyer. Crit Care Nurs Q 2013;36:37-49
- Drolet. Phys Therapy 2013;93:197-207

Mobility Program

Early Progressive Mobility Program | ICU Safety Screen*

M **Myocardial Stability (except CTS)**
- ☐ Active chest pain and/or dynamic EKG changes

O **Oxygenation Stability**
- ☐ Chest tube
- ☐ PEEP >10 cm H_2O
- ☐ FiO2 > 0.70
- ☐ Unstable airway

V **VTE**
- ☐ Iliac Clot
- ☐ PE with documented or suspected Mod to Severe RV dysfunction
- ☐ PE with RV dysfunction and residual femoral clot

V **Vasopressor**
- ☐ Vasopressor use or new/unstable cardiac arrhythmia

E **Engages to Voice**
- ☐ RASS less than -2 or greater than +2

N **Neuro Stability**
- ☐ Abdominal solid organ injury
- ☐ Acute or uncontrolled intracranial event
- ☐ Stroke less than 24 hrs

If **any of the above criteria** checked, discuss mobility progression with attending physician.

If **no criteria** checked above go to **Step 2** and progress as outlined in BMAT tool.

Mandatory Contraindications
- ☐ Open chest without wound vac; IABP; hypothermia protocol; Impella; femoral temp pacer/sheathe
- ☐ Open abdomen without wound vac
- ☐ Unstable/uncleared spine or orthopedic injury, open lumbar drain
- ☐ Femoral arterial/venous sheath

If any criteria checked, stay at bed mobility and re-evaluate PRN.

**Complete only for patients in the ICU.*
Document reason if decision made not to mobilize.

B.M.A.T. | Bedside Mobility Assessment Tool for Nurses

*Functional Assessment	Pass	Fail
Sit and Shake (trunk strength and seated balance) Instructions: Obtain necessary assistive device, cane or walker. 1) From a semi-reclined position, ask patient to sit or assist the patient to the side of the bed. May use bed rail. 2) Note patient's ability to sit for more than two minutes without caregiver assistance. 3) Ask patient to reach out and grab your hand and shake making sure patient reaches across midline	If patient can sit unassisted, reach across midline and shake your hand, continue to Stretch and Point Assessment *May assist patient to side of bed, but must then sit unassisted continue to Stretch and Point Assessment	If patient cannot sit unassisted, reach across midline and shake your hand, he/she is a mobility **Bed**. Follow mobility **Bed** interventions and equipment below.
Stretch and Point (lower extremity strength and stability) Instructions: 1) With patient seated, have patient place both feet on floor and knees no higher than hips. 2) Ask patient to stretch one leg and straighten knee, then bend the ankle/flex and point toes. If appropriate, repeat with other leg. May test with only one leg (i.e., ankle cast, stroke).	If patient can stretch and point both legs (or one, if appropriate) continue to Stand Assessment	If patient cannot stretch and point both legs (or one, if appropriate), he/she is a mobility **Dangle**. Follow mobility **Dangle** interventions and equipment below.
Stand (lower extremity strength for standing) Instructions: Consider patient's cognitive ability, orientation and presence of delirium. 1) Ask patient to elevate off the bed or chair (seated to standing). May use assistive device (cane, bedrail). 2) Patient should be able to raise buttocks off of bed and hold for count of five. May repeat once. May test with only one leg (i.e., ankle cast, stroke).	If patient can hover his/her buttocks off the bed for a count of five, continue to Walk Assessment.	If patient cannot hover his/her buttocks off the bed for a count of five, he/she is a mobility **Chair**. Follow mobility **Chair** interventions and equipment below.
Walk (standing balance and gait) Instructions: Use assistive device if needed. 1) Ask patient to march in place at bedside. 2) Then ask patient to advance step and return each foot. 3) Assess patient's balance, stability and safety awareness.	If patient can advance a step (ie., put one foot in front of the other) he/she is a mobility **Ambulation**. Follow mobility **Ambulation** interventions and equipment below.	If patient cannot advance a step (ie., put one foot in front of the other) he/she is a mobility **Chair**. Follow mobility **Chair** interventions and equipment below.

*The BMAT is a functional assessment, if patient has cognitive limitations (unable to follow commands) proceed through functional assessment using appropriate equipment. Always default to the safest patient equipment if there is any doubt in patient's ability to perform task. Consider notifying provider to place PT/OT consult for patient not at baseline or who demonstrates declining mobility/ADL.

Early Progressive Mobility Program | Implement Progressive Mobility

Bed
- Passive/Active ROM TID
- Turn Q2 hours
- Active-resistance exercises
- Sitting position 20 min TID
- Mechanical lift to chair
- Consult PT/OT if can't progress to **Dangle**

Goal: Clinical stability and able to move arm against gravity

Dangle
- Bed mobility interventions
- Dangle edge of bed w/feet on floor
- Mechanical lift to chair
- Consult PT/OT if can't progress to **Chair**

Goal: Sitting upright and able to move leg against gravity

Chair
- Dangle mobility interventions
- Active transfer to chair ≥20 min 2x/day
- Consult PT/OT if require assistive device to get to chair

Goal: Increased strength, stands w/min to mod assist

Ambulation
- Chair mobility interventions
- Active transfer to chair ≥20 min 3x/day)
- Ambulation (marching in place, walking in halls). 3x/day with increasing distance.
- Consult PT/OT, if patient is not at baseline

Goal: Strength and distance walk

F Family Engagement and Empowerment

Good communication with the family is critical at every step of a patient's clinical course, and empowering the family to be part of the team to ensure best care is adhered to diligently will improve many aspects of the patient's experience

Strategies:

- Part of interdisciplinary rounds
- Shared decision making
- Open visiting hours—promoting family presence
- Family involvement menu
- Education on delirium and post ICU syndrome
- ICU diaries

Minnesota Star Tribune

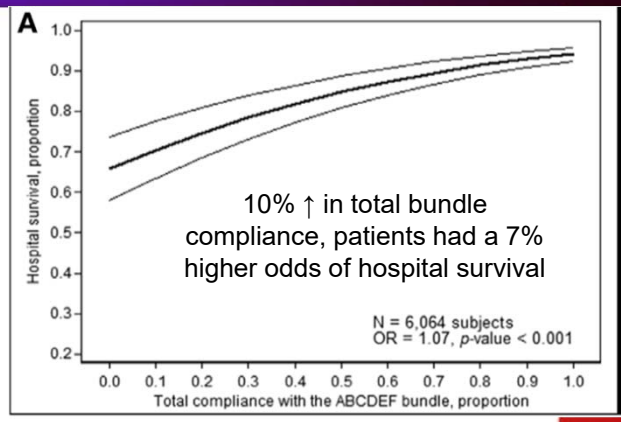
Guidelines for Family-Centered Care in the Neonatal, Pediatric, and Adult ICU. Davidson et al CCM 2016
www.icudelirium.org

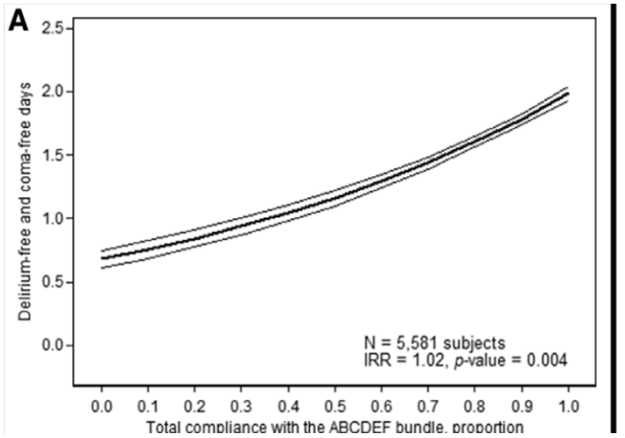
ABCDEF Bundle: Improving Survival & Reducing Brain Dysfunction

Ventilated and non-ventilated medical and surgical ICU patients enrolled between January 1, 2014, and December 31, 2014

Determine association between ABCDEF bundle compliance/total & partial & outcomes of hospital survival and delirium-free and coma-free days/ adjusting for age, severity of illness, and presence of mechanical ventilation

Patients experienced more days alive and free of delirium and coma with both total bundle compliance (incident rate ratio, 1.02; 95% CI, 1.01–1.04; $p = 0.004$) and partial bundle compliance (incident rate ratio, 1.15; 95% CI, 1.09–1.22; $p < 0.001$).





Barnes-Daly, CCM 2017

Caring for Critically Ill Patients with the ABCDEF Bundle: Results of the ICU Liberation Collaborative in Over 15,000 Adults

- **Objective:** Evaluate the relationship between ABCDEF bundle performance and patient-centered outcomes in critical care
- **Design:** Prospective, multicenter, cohort study from a national quality improvement collaborative.
- **Setting:** 68 academic, community, and federal ICUs collected data during a 20-month period.
- **Patients:** 15,226 adults with at least one ICU day.
- **Interventions:**
  - We defined ABCDEF bundle performance (our main exposure) in two ways: 1) complete performance (patient received every eligible bundle element on any given day) and 2) proportional performance (percentage of eligible bundle elements performed on any given day).
  - We explored the association between complete and proportional ABCDEF bundle performance and three sets of outcomes: patient-related (mortality, ICU and hospital discharge), symptom-related (mechanical ventilation, coma, delirium, pain, restraint use), and system-related (ICU readmission, discharge destination).

Pun B et al. CCM 2019;143

Caring for Critically Ill Patients with the ABCDEF Bundle: Results of the ICU Liberation Collaborative in Over 15,000 Adults

Measurements and Results: Complete ABCDEF bundle performance was associated with lower likelihood of seven outcomes:

- Hospital death within 7 days (adjusted hazard ratio, 0.32; CI, 0.17–0.62),
- Next-day mechanical ventilation (adjusted odds ratio [AOR], 0.28; CI, 0.22–0.36),
- Coma (AOR, 0.35; CI, 0.22–0.56),
- Delirium (AOR, 0.60; CI, 0.49–0.72),
- Physical restraint use (AOR,0.37; CI, 0.30–0.46),
- ICU readmission (AOR, 0.54; CI, 0.37–0.79), and
- Discharge to a facility other than home (AOR, 0.64; CI,0.51–0.80).

There was a consistent dose-response relationship between higher proportional bundle performance and improvements in each of the above-mentioned clinical outcomes ($p < 0.002$)

Pun B et al. CCM 2019;144

Educate Patient and Families on Post Sepsis/Post ICU Syndrome

https://www.youtube.com/watch?v=LmTMrdrKMjU

Peer Support

- Adaptation to new limitations
- Coping
- Empathy
- Giving back

Applications will re-open in fall 2018:
http://www.myicucare.org/Thrive/Healthcare-Provider/Pages/THRIVE-Peer-Support-Collaborative.aspx

Society of Critical Care Medicine
The Intensive Care Professionals

thrive

COVID Long Haulers

Long haulers are people who have not fully recovered from COVID-19 weeks or even months after first experiencing symptoms. Some long haulers experience continuous symptoms for weeks or months, while others feel better for weeks, then relapse with old or new symptoms. The constellation of symptoms long haulers experience, sometimes called post-COVID-19 syndrome or post-acute sequelae of SARS-CoV-2 infection (PASC), is not unique to this infection.

The most commonly reported long-term symptoms include:

- Fatigue
- Shortness of breath
- Cough
- Joint pain
- Chest pain

Other reported long-term symptoms include:

- Difficulty with thinking and concentration (sometimes referred to as “brain fog”)
- Depression
- Muscle pain
- Headache
- Intermittent fever
- Heart palpitations

COVID Long Haulers

CDC MMWR Report in July 2020

April 15–June 25, 2020, telephone interviews were conducted with a random sample of adults aged ≥18 years 14-21 days after a first positive COVID 19 test at an outpatient visit at one of 14 U.S. academic health care systems in 13 states

- Of the 292 responders to this survey, a vast majority (94%) reported one or more symptoms at testing, and of these, more than one-third (35%) stated that they had not returned to their usual state of health by the survey date (a median 16 days post testing)

Table 1: Characteristics Associated With Not Returning to Usual Health

Factor	Adjusted Odds Ratio	95% Confidence Interval
Age (≥50 years vs. 18-34 years)	2.29	1.14-4.58
Chronic Medical Conditions (≥3 vs. 0)	2.29	1.07-4.90
Obesity (BMI ≥30 kg/m^2)	2.31	1.21-4.42
Reported a Psychiatric Condition	2.32	1.17-4.58

- Impacts people that did not need to be hospitalized
- In the study of Italian patients, the most common symptoms reported at follow up were fatigue, shortness of breath, joint pain, and chest pain, in that order. None of the patients had a fever or other sign or symptom of acute illness, but about 44% of them had a worsened quality of life. Pts with CAP can also have persistent symptoms
- Fauci noted that some long haulers' symptoms lke brain fog and fatigue are "highly suggestive of myalgic encephalomyelitis/chronic fatigue syndrome

STILL LOTS TO LEARN AND UNDERSTAND

MMWR Morb Mortal Wkly Rep.2020;69:993-8).
JAMA. 2020;324(14):1381-1383

The Journey to High Reliable Sepsis Care and Amazing Outcomes

Don’t Stop Believing