

# CHALLENGES IN IMPLEMENTING SEPSIS CORE MEASURE IN CANCER CARE

Brenda K. Shelton DNP, RN, APRN-CNS, CCRN, AOCN,  
Clinical Nurse Specialist,

Sidney Kimmel Cancer Center at Johns Hopkins; Faculty,  
Johns Hopkins University Graduate School of Nursing;  
Baltimore, MD

[sheltbr@jhmi.edu](mailto:sheltbr@jhmi.edu)

Moffitt  
2/11/17



THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER



# Disclosures

- I have no financial or professional disclosures related to this topic
- There are no discussions that include non-FDA indications for therapeutics



# Learning Objectives

- Outline the current and proposed revised CMS core measure sepsis bundle guidelines.
- Describe how the sepsis core measure criteria are problematic for patients with cancer.
- Apply essential best practices in sepsis management to a hypothetical case study.



# Sepsis Statistics

- 3rd leading cause of death in world, most common cause nonmalignant death in oncology
- Severe sepsis occurs in 14% oncology patients
- Mortality from severe sepsis and/or septic shock in cancer is 30-40%, higher than other populations
- Early recognition saves lives
- Sepsis can present with atypical signs and symptoms in patients with cancer.
- Early and astute care by bedside clinicians can make the greatest difference in patient outcome

<http://www.bing.com/videos/search?q=sepsis+alliance+video&FORM=VIRE2#view=detail&mid=D1B58A028C89F931111CD1B58A028C89F931111C>



JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER

MAGNET  
RECOGNIZED  
AMERICAN NURSES  
CREDENTIALING CENTER

# Definitions

## SIRS

- Systemic Inflammatory Response Syndrome (SIRS) is two or more of the following: Temp  $>38.3^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ , Heart Rate (HR)  $>90$ , Respiratory Rate (RR)  $>20$ , WBC  $>12$  K/cu mm or  $<4$  K/cu mm or  $>10\%$  bands

## SEPSIS

- Two SIRS criteria PLUS a known or suspected bacterial, viral, or fungal infection

## SEVERE SEPSIS

- Sepsis + at least one sign of end organ dysfunction, such as altered mental status, decreased urinary output, thrombocytopenia, lactate  $> 2.0$ , systolic blood pressure (SBP)  $<90$  or mean arterial pressure (MAP)  $<65$ , prior to fluid resuscitation

## SEPTIC SHOCK

- Hypotension and elevated lactate  $\geq 4$  may be signs of hypoperfusion/ septic shock
- Septic shock is persistent hypotension despite adequate fluid resuscitation (30 mL/kg)

Dellinger et al, 2013



# Where does febrile neutropenia fit?

Even though this uses 38.3°C, oncology resources<sup>1,2</sup> recommend 38.0°C X 2 within one hour

## SIRS

- Temp >38.3°C or <36°C, HR >90, RR >20, WBC >12 or <4 K/cu mm or >10% bands

## SEPSIS

- SIRS + Infection



## SEVERE SEPSIS

- Sepsis + End Organ Damage or SBP <90 or MAP <65, prior to fluid resuscitation



## SEPTIC SHOCK

- Severe Sepsis → Hypotension refractory to fluids

Patients with neutropenia are escalated to at least sepsis

<sup>1</sup> Baden, Bensinger, Angarone,... Wilson, 2016

<sup>2</sup> Flowers, Seidenfeld, Bow, Karten, Gleason, Hawley, ...Ramsey, 2013



# Organ Dysfunction<sup>1</sup>

*(new onset)*

- Signs/ Symptoms
  - Altered mental status
  - Low urine output
  - Capillary refill > 3 seconds
  - Mottling
  - Weight gain > 20 mL/kg- ~ 2 kg previous 2 days
- Laboratory Abnormalities
  - Bilirubin > 2 mg/dl
  - Creatinine > 2.0 mg/dl
  - Glucose > 140 mg/dl  
absence diabetes
  - Hypoxemia requiring BiPAP
  - INR ≥ 1.5
  - Lactate > 2 mmol
  - Platelets < 100,000/mm<sup>3</sup>

<sup>1</sup> Dellinger et al, 2013

# Surviving Sepsis Campaign<sup>1</sup>

- Initial EBP recommendations 2001 United Kingdom
  - Endorsed by organizations internationally
  - Goal- reduce sepsis mortality 25% in 5 years
- Published sepsis guideline bundles- 2004
- Revised; separation of bundled interventions (2008)
  - Early goal directed therapy [EGDT] (3 and 6 hr interventions)
  - First 24 hrs
- Revised; performance measures, emphasis on continuous screening, establishment of “time zero”- 2012
- Endorsed by 135 organizations, 38 countries

<sup>1</sup> Dellinger et al, 2013





# Sepsis Core Measure

- Began Oct 1, 2015
- Reporting slated Fall 2016, delayed indefinitely
- Mirror Surviving Sepsis recommendations; slight variations
- Impacts all clinical areas across the hospital managing 18 years or older
- Not applicable:
  - Outside transfers
  - End of life/ comfort care
  - LOS > 120 days
- Goal to perform **all** recommended interventions as indicated for patients with severe sepsis or septic shock within defined timeframes
  - Pass or fail based on completeness and timeliness
  - No clear medical exceptions (e.g. fluids and heart failure)



# Surviving Sepsis Recommendations<sup>1</sup>: 1<sup>st</sup> 6 hours

## 3 hours

- Screen for sepsis at first encounter or defined intervals
- Obtain blood cultures and lactate if positive screen (core measure if severe sepsis)
- Assessment of organ function
- First antimicrobial dose within 60 min of triage (core measure accepts 3 hr)
- Oxygen if O<sub>2</sub> sat < 90%
- Initial fluid bolus *at least* 30 mL/kg if hypotensive (+/- 10%)

## 6 hours

- Assessment of infection source
- CVP line- goal 8-12 mm Hg (not in core measure)
- MAP ≥ 65 mm Hg
- Central venous oxygen saturation (ScvO<sub>2</sub>) ≥ 70 (not in core measure)
- Perfusion assessment by provider before vasopressor therapy that is given if refractory to fluids
- Urine output ≥ 0.5 mL/kg/hr



# Surviving Sepsis Recommendations<sup>1</sup>: 1<sup>st</sup> 24 hours

- Indications:
  - Severe sepsis or septic shock OR
  - Persistent hypotension OR
  - Hyperlactemia ( $\geq 4.0$  mmol/L)
- Low volume ventilation or maintain plateau pressures  $< 30$  mm
- Glucose goal  $< 180$  mg/dl
- Gastric Ulcer prophylaxis
- Venous thromboembolism (VTE) prophylaxis
- Low dose steroids for patients with hypotension\*



\* Exact methodology/ indications/ length of therapy is variable

<sup>1</sup>Dellinger et al, 2013



JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER

MAGNET  
RECOGNIZED  
AMERICAN NURSES  
CREDENTIALING CENTER

# Implementing Sepsis Bundle Interventions: Challenges in Evaluation of Cancer Patients

- Excluded from most studies<sup>1</sup>:
  - Congestive Heart Failure (35%)
  - Cancer patients (30%)
- Bundle variability among Quality Measurement Organizations<sup>2</sup>
- Alternative etiology of hyperlactemia<sup>3</sup>
  - Malignancy
  - Dehydration/ hypoperfusion

<sup>1</sup> Claessens, Aegerter, Boubaker, Guidet, Cariou, & Cub, 2013

<sup>2</sup> Fong, Cercere, Unterborn, Garpstad, Klee, & Devlin, 2007

<sup>3</sup> Casserley, Phillips, Schorr, Dellinger, Townsend, Osborn, ... Levy, 2015



# Generalizability of Sepsis Bundle Interventions

- Initial landmark study showed 7% mortality reduction if bundle elements completed 37% of time<sup>1</sup>
  - Unclear which interventions most important
- Mortality reduction with implementation of formalized process 7-15% across all studies
- Patients do not receive same care in all settings
  - “Time zero” recently revised- problematic since many interventions are time sensitive
  - Variables affecting timely antimicrobials- initially a different diagnosis, waiting for cultures to be obtained, younger patients, women, care by non-ED physician<sup>2,3</sup>
  - Prompt sepsis management activation systems not consistently available

<sup>1</sup> Rivers et al, 2001

<sup>2</sup> Cullen, Fogg, Delaney, 2013

<sup>3</sup> Madsen & Napoli, 2014



# Key Take Home Message...

*Probably not all interventions confer the same value, but research clarifying the most beneficial interventions is still in progress*



JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER

MAGNET  
RECOGNIZED  
AMERICAN NURSES  
CREDENTIALING CENTER

# Evidence: How to Implement Sepsis Bundle Interventions

Strategy	Pro	Con
Focused Education	Easy answer Easy to perform	Knowledge retention inconsistent Staff turnover
Protocols, policies, algorithms	Summarization complex literature Familiar structure	Accessibility when and where needed Complexity
Structured pre-printed or electronic orders	Guide prescribers to choose correct EBP interventions	Requires recognition of need to activate May lead to over-treatment
Unit based Champions/ super-users	Solutions within the unit culture Peer to peer influence	Labor-intensive Champions may not always be present/available
Rapid Response activation with protocols	High activation rates (crying wolf) Standardization/frequent usage	Resource intensive
Combined interventions	Proven most effective Targets different learning styles/ locus of motivation	Resource intensive for integration

- Multiple methods to reinforce information is better than a single one.
- Multidisciplinary interventions more effective than single profession.
- Electronic forced templated actions without “opt out” options are highly effective to drive interventions.
- Documenting decisions in real-time not the current workflow for most providers.

## Implementing Sepsis Best Practices





# SCREENING AND ASSESSMENT



JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER



# Variations In Screening Criteria

*Invented Interpretations  
I have heard*



- We decided that neutropenia should be omitted since most patients are neutropenic, therefore two other criteria must be met.
- Many of our patients have baseline heart rates greater than 90/min, so we changed the criteria to “complex tachycardia”.
- Patients are often beta blocked and so heart rate is not a reliable indicator.
- Since so many people meet criteria, we just call the RRT and tell them not to come because we have the situation in hand.
- Subnormal temperatures are common therefore can't be reliable as a trigger criteria.



# Largest Threat to Effective Implementation

Recognizing the  
septic patient early

**BUT...**

Oncology may require  
revised screening processes  
OR anticipate many false  
positive alerts



# Johns Hopkins Baltimore: *Revised Sepsis Criteria*

Parameter	Surviving sepsis	JHH
Temperature (T)	T < 36.0C or > 38.3C	T < 35.5C (without symptoms) or >38.0C <sup>1,2,3</sup>
Heart rate (HR)	HR > 90/min	HR > 100/min <sup>3,4</sup>
Respirations (RR)	RR > 20/min	RR > 20/min
Blood pressure (BP)	Systolic BP < 90 mm or > 40 mm drop from baseline, OR MAP < 65 mm	Systolic BP < 90 mm or > 40 mm drop from baseline, OR MAP < 65 mm
WBC	< 4000/mm <sup>3</sup> or > 12,000/mm <sup>3</sup> , or > 10% bands	< 4000/mm <sup>3</sup> or > 12,000/mm <sup>3</sup> , or > 10% bands, neutropenia <sup>1,4</sup>
Other	None	Glucose > 140 mg/dl in absence of diabetes <sup>2,5</sup> Altered mental status <sup>2,4,5,6</sup> Mottling <sup>4,5,6</sup>

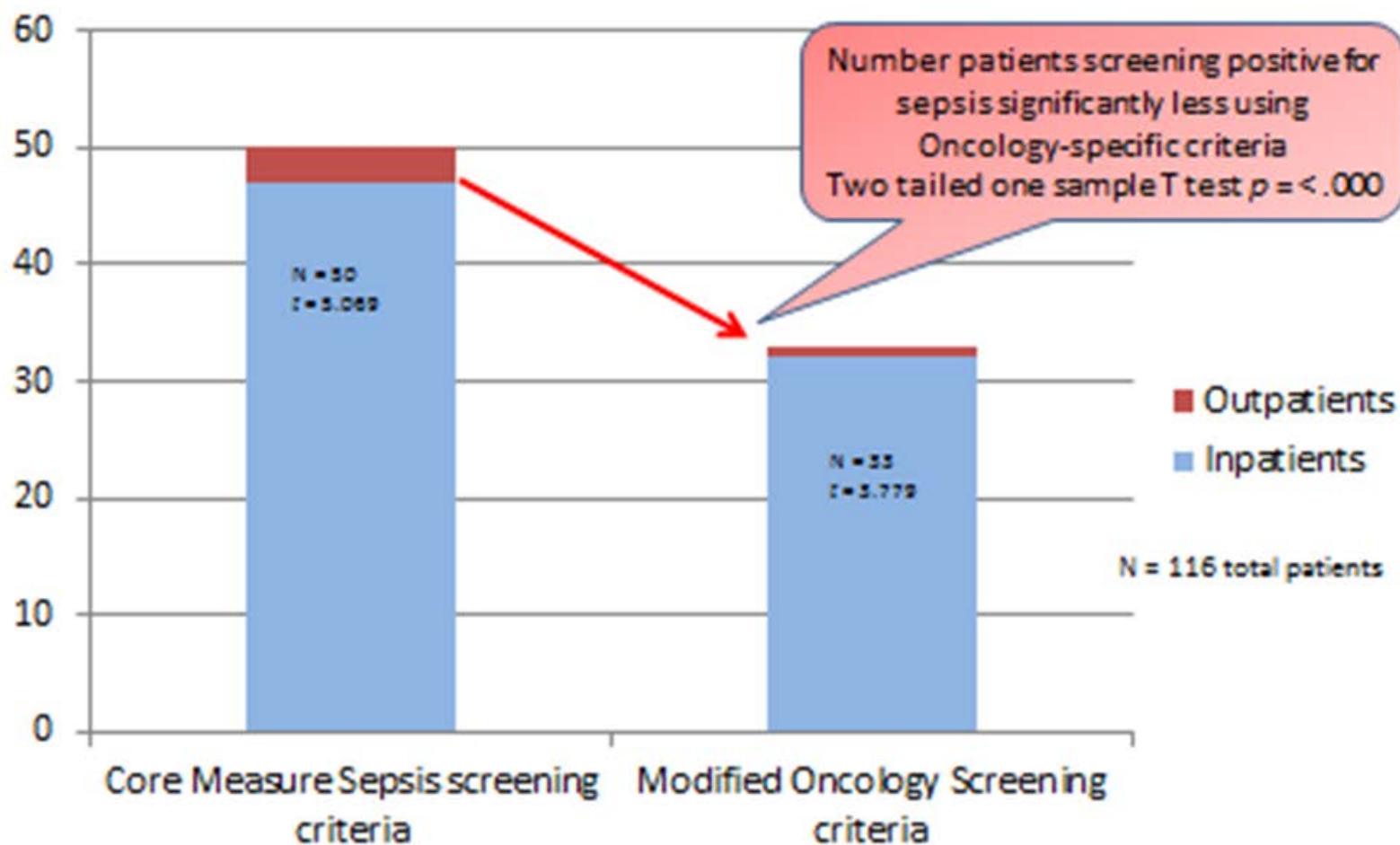
<sup>1</sup> Baden et al, 2016  
<sup>2</sup> Shelton et al, 2016  
<sup>3</sup> Hanzelka et al, 2013

<sup>4</sup> Cooksley et al, 2012  
<sup>5</sup> Dellinger, 2012  
<sup>6</sup> Singer et al, 2016



# Differences in Screen Positive Patients

*No missed cases true sepsis*



# Blood Lactate as Predictor for Severe Sepsis/ Shock in Oncology

- Options
  - Whole blood lactate
  - Serum lactic acid
- Not universally available
- Rapid results variable
- Alternative reasons high lactate
  - Dehydration
  - Renal impairment
  - Hepatic clearance problems
  - Increased metabolic rate
  - Type B lactic acidosis of malignancy
- Surviving Sepsis 2016<sup>1,2</sup>
  - Lactate + hypotension or vasopressors predict poor outcomes
  - Elevated lactate may precede other signs/symptoms
- Multisite database<sup>3</sup>
- Cancer patients<sup>4,5</sup>
  - High sensitivity, low specificity

<sup>1</sup>Singer et al, 2016

<sup>2</sup>Seymour et al, 2016

<sup>3</sup>Cooksley et al, 2015

<sup>4</sup>Hanzelka et al, 2013

<sup>5</sup>Kece et al, 2016



# Common Findings in Sepsis: Mottling



Picture reproduced with permission  
for educational purposes



**JOHNS HOPKINS**  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER

MAGNET  
RECOGNIZED  
AMERICAN NURSES  
CREDENTIALING CENTER

# TIME-SENSITIVE INTERVENTIONS



JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER





# Johns Hopkins Baltimore

*Hematology-  
Oncology Clinic  
Nurse Driven  
Protocol and  
Conditional  
Orders*

## Screen for sepsis

- With vital signs
- With condition changes
- After labs resulted

## Activate conditional orders- blood cultures and lactate

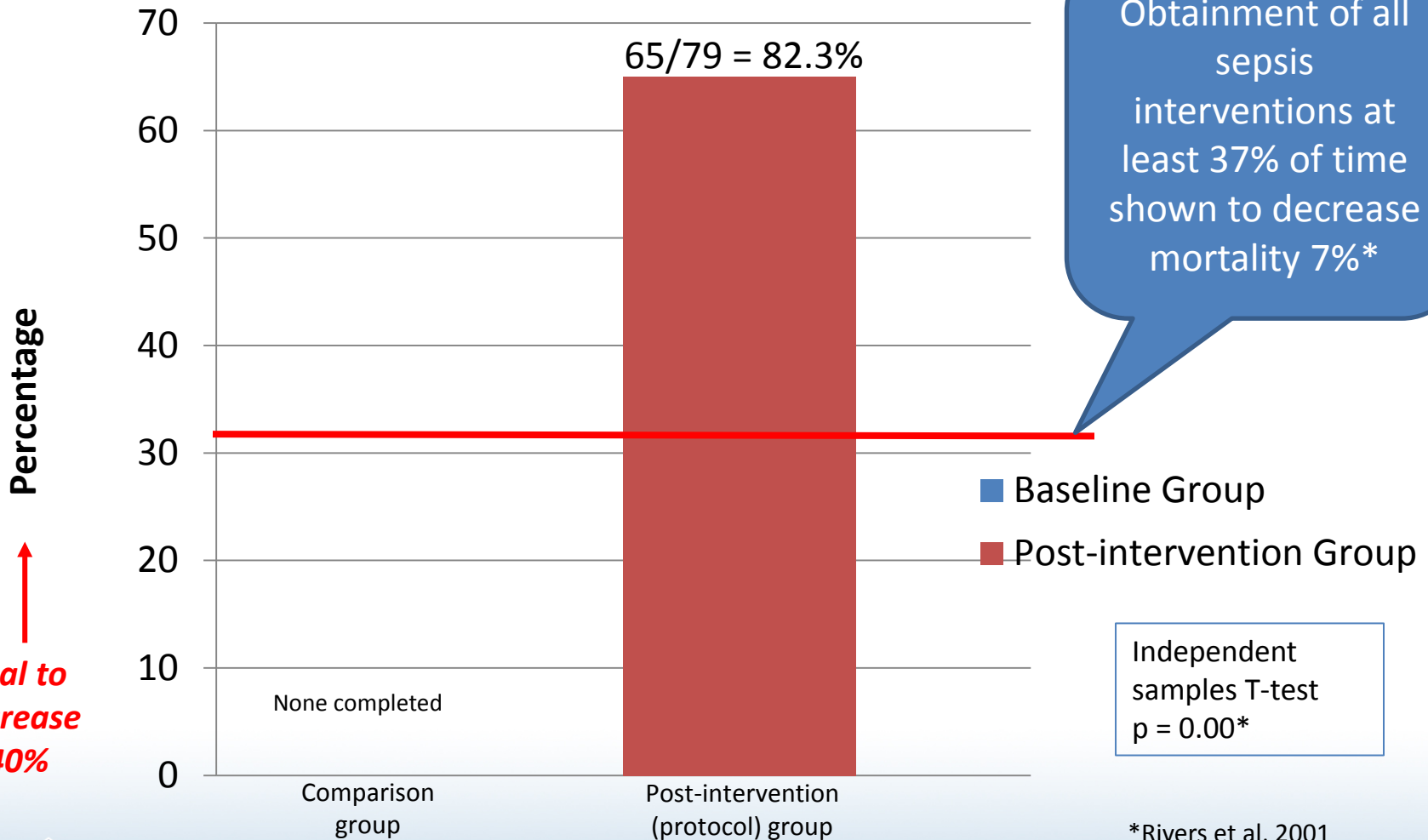
- Alert provider of sepsis screen positive, signs/ symptoms severe sepsis or shock
- Accept orders for diagnostic tests or antimicrobials

## Treat cardiorespiratory symptoms

- Initiate fluids for hypotension
- Initiate oxygen for hypoxemia



# Timely Completion of All Sepsis Interventions



\*Rivers et al, 2001

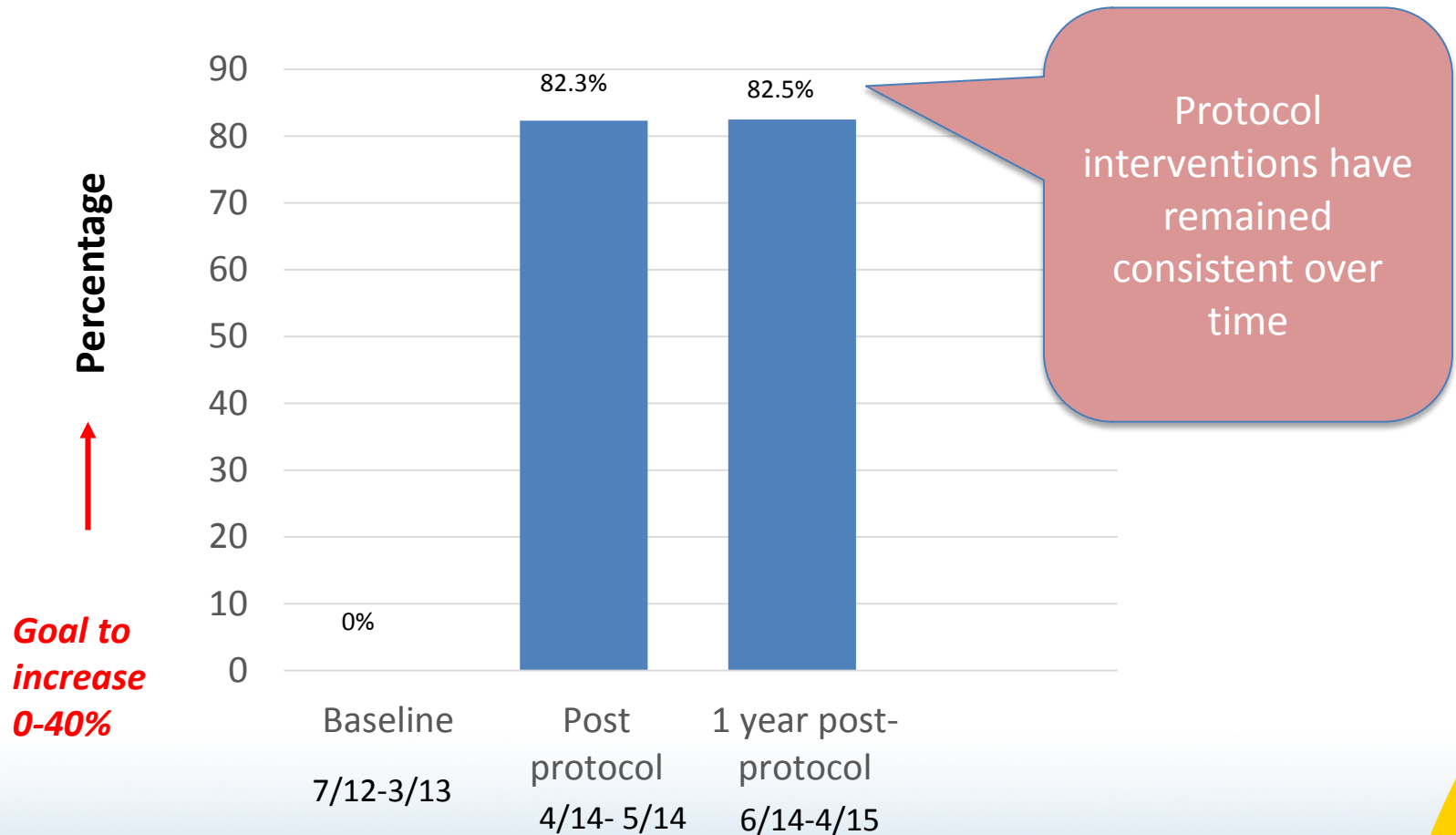


JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER



# Timely Completion of All Sepsis Interventions



# Follow-up Actions

- Nurse activated antibiotic orders
  - Provider identifies which antibiotic to activate with first fever
  - Nurse identifies presence of trigger criteria
  - Nurse calculates creatinine clearance and activates correct order
- Altered “best practice alerts” (BPAs) with new electronic record go-live
  - Based on pilot oncology-specific criteria
- Cancer-center wide sepsis protocol implementation



# CRITICAL SEPSIS INTERVENTION TRACKING

(For Quality Improvement Purposes Only)

(Not Part Of Medical Record)



Date: \_\_\_\_\_ Patient Name: \_\_\_\_\_ Medical Record #: \_\_\_\_\_

SIRS  
(Systemic Inflammatory  
Response Syndrome)

Temp > 100.9 (°F)  
Respiratory rate > 20 /min  
HR > 90 /min  
WBC > 12,000 /mm<sup>3</sup>

Cross-unit  
communication  
tool








Best estimate of **TIME ZERO** (clock start time):

Time Zero = when the patient meets the following:

- 2 or more SIRS criteria met **AND** Suspected infection **AND** Organ dysfunction noted in labs / Lactate > 2 mmol/L
- OR**
- Hypotension and/ or Lactate ≥4 mmol/L

What is the patient transfer hand-off report time? \_\_\_\_\_

What is the 3 hour goal time? (Time Zero + 3 hours): \_\_\_\_\_

To be done within <b>3 hours</b> of Time Zero				To be done within <b>6 hours</b> of Time Zero		
Vitals: Increase frequency of VS to Q2hrs x 3, unless ordered more frequently				Vitals: Increase frequency for level of care		
						
Lactate level collected within 3 hours of start time  Time collected:	Cultures obtained before giving antibiotics	Fluid bolus (30 mL/kg) given as ordered if hypotensive or lactate ≥ 4 mmol/L  Within 1 Hour After infusion: BP#1 _____ Time: _____ BP#2 _____ Time: _____	Antibiotics infused Abx name: _____ Time hung: _____ Abx name: _____ Time hung: _____	Repeat lactate within 5 hours of Time Zero, if first lactate is > 2	If hypotensive after fluid bolus, remind provider to complete <b>Septic Shock Reassessment Note</b>	Vasopressors if persistent hypotension
Check if done <input type="checkbox"/>	Check if done <input type="checkbox"/>	Check if done <input type="checkbox"/>	Check if done <input type="checkbox"/>	Check if done <input type="checkbox"/>	Check if done <input type="checkbox"/>	Check if done <input type="checkbox"/>

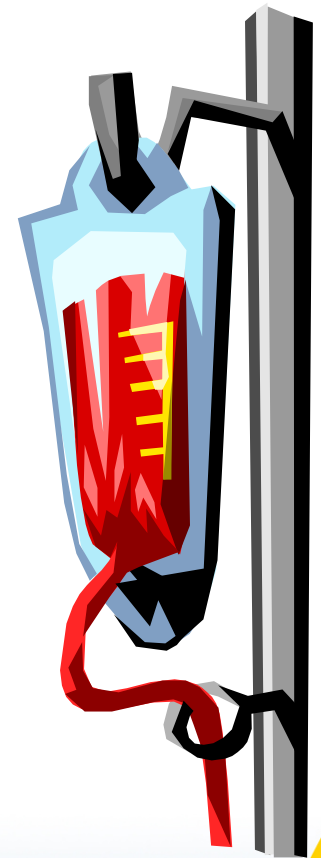
**FLUID BOLUS, BP AFTER INFUSION, AND ANTIBIOTIC TIME HUNG MUST BE DOCUMENTED IN PATIENT CHART**

Any delays or issues (document here)? \_\_\_\_\_

Updated on  
01/19/16

# Fluid Administration

- Crystalloids recommended in guidelines
- Crystalloids may not be ideal for oncology patients with disease or chemotherapy-related capillary permeability.
  - Traditional resuscitation fluid- 0.9% normal saline
  - Newer recommendations for large volume-lactated ringers
  - Must be “wide open” or timed less than 1 hr
  - Required amount 30 mL/kg actual wgt (+/- 10%)
- Blood is time-consuming to obtain and has risks
- Albumin/ plasma is costly



# After Fluids and before Vasopressors...



- Two consecutive vital signs assessments within 60 minutes completion of fluid showing hypotension
- Focused physical exam (date/ time) includes:
  - Heart & Lungs
  - Skin- temperature, color
  - Capillary refill
  - Peripheral pulses
- Before 3 hours and before start of vasopressors
- Provider may “attest” to review vital signs only
- Alternate to focused exam (any 2)
  - Central venous pressure (CVP)
  - Central venous oxygen saturation
  - Bedside CV ultrasound
  - Passive Leg raise test

# ANTIMICROBIALS

- Broad spectrum unless known organism documented
- Start before 3 hours from time zero
- Oral vancomycin acceptable with C-difficile infection





# Evidence: Antimicrobials within One Hour

Citation	Methods	Results
Gaieski, Pines, Band, Mikkelsen, Massone, Furia, Shofer, Goyal, 2010	Single center, retrospective cohort, 161 pts with severe sepsis and septic shock from 2005-2006	Median time to antimicrobials was 119 min Significant association between antimicrobial administration > 1 hr to increased mortality <u>Mortality increased 7.6% for every hour delay in antimicrobial administration</u>
Fletcher, Hodgkiss, Zhang, Browning, Hadden, Hoffman, Winick, McCavit, 2013	Single center, retrospective cohort, 1628 pediatric febrile neutropenia admissions (653 pts) from 2001-2009	Adverse outcomes 11.1%, 0.7% mortality, 4.7% PICU admission, 10.1% fluid resuscitation Time to antibiotics associated with adverse outcomes as composite <u>Two times greater risk adverse outcomes &gt; 60 minutes until first antimicrobial</u>
Ali, Baqir, Hamid, Khurshid, 2013	Single center, retrospective cohort, 81 adult and pediatric cancer pts (mostly heme malignancy pts 64%) with FN in ED after PI intervention to improve time to antimicrobial	Mean time to antimicrobials was 45 min <u>Nine patients longer than 60 min, and included the only three that developed severe sepsis</u>
Ko, Ahn, Lee, Kim, Lim, Lee, 2015	1001 FN episodes mostly solid tumor pts (80%) from 2011-2014	Mean time to antimicrobials was 140 min <u>Time to antimicrobial did NOT influence incidence of severe sepsis, septic shock or mortality</u>
Mokart, Saillard, Sannini, Chow-Chine, Brun, Faucher, Blache, Blaise, Leone, 2014	Single center, retrospective cohort, 118 pts admitted to ICU with severe sepsis or septic shock from 2008-2010	<u>Multivariate analysis showed most important predictor for mortality was time to antibiotic greater than 1 hr</u>

# Antimicrobials

Every hour delay  
beyond the first 60  
minutes, increases  
mortality about  
7.6%





(for Fevers that are unrelated to blood product transfusion)

Goal: Administration of a broad-spectrum antibiotic within 60 minutes.

"New" fever - a patient that has been previously treated for a fever and remains afebrile for 48 hours but later develops fever. This is to be treated as a "new" fever.

If patient has a NEW temperature $\geq 38^{\circ}\text{C}$ then proceed with the following:		
<b>NURSING INTERVENTIONS</b>	Time Done	Initial (RN)
<input type="checkbox"/> Inform a medical officer or consultant to assess the patient immediately		
<input type="checkbox"/> IV access (if not already initiated)		
<input type="checkbox"/> FBC, SP1 and 2 sets of blood cultures (2 peripheral or 1 peripheral and 1 via central line if in place). <i>If obtaining 2 sets of blood cultures will delay administration of antibiotic by <math>\geq 60</math> minutes, initiate antibiotic after 1st set of blood cultures and then proceed to obtain second set</i>		
<input type="checkbox"/> Urine FEME and culture		
<input type="checkbox"/> Monitor vital signs every hour for 4 hours or until stable then per routine		
<input type="checkbox"/> If patient is hypotensive (systolic blood pressure less than 90) or tachycardic (heart rate greater than 125), then monitor vital signs every 15 minutes for 1 hour until stable and then as above		
<input type="checkbox"/> Place Intra nasal O <sub>2</sub> at 2L/min if O <sub>2</sub> saturation is less than 93% or in respiratory distress		
<b>PHYSICIAN ORDERS</b>		
<input type="checkbox"/> Portable Chest X-ray		
<b>IV fluids (if required)</b>	<i>(Continuous infusions order on MAR)</i>	
<input type="checkbox"/> Normal Saline bolus 500ml		
<input type="checkbox"/> Normal Saline bolus 1000ml		
<input type="checkbox"/> Other: _____		
<b>Antibiotics (to be administered within 60 minutes)</b>		
<i>(All orders are one-time orders - routine antibiotics should be ordered on MAR)</i>		
Allergies: <input type="checkbox"/> NKA Other: _____		
	Reaction Type: _____	
<i>*For hemodynamically unstable or suspected neutropenic patients, consider antibiotics in bold</i>		
<input type="checkbox"/> <b>*Piperacillin/Tazobactam 4.5g IV</b>		
<input type="checkbox"/> <b>*Cefepime 1 or 2 (circle) gram IV</b>		
<input type="checkbox"/> <b>*Meropenem 1 gram IV</b>		
<input type="checkbox"/> <b>*Imipenem 750 mg IV</b>		
<input type="checkbox"/> Cefazidime 1 gram IV		
<input type="checkbox"/> If Penicillin allergy, Aztreonam 1 gram IV & Amikacin 15 mg/kg IV		
<input type="checkbox"/> Other: _____		
<b>Other Laboratory Tests</b>		
<input type="checkbox"/> PT/PTT		
<input type="checkbox"/> D-dimer		
<input type="checkbox"/> Sputum Gram Stain and culture		
<input type="checkbox"/> Other: _____		

# Sample Fever Orders

- Cross-over communication between inpatient and outpatient
- Increase cultures before antibiotics
- Pre-approved antibiotics for more rapid administration
- Template nursing assessment and vital signs



# Challenging Value of Selected Interventions

*(ProCESS Investigators, 2014)*

- Randomized controlled trial
- Compared three arms management of severe sepsis/ septic shock
  - bundled Early Goal-Directed Therapy
  - protocol-based care without central venous catheter, ScvO<sub>2</sub>, inotropes or transfusions
  - usual care in a practice setting trained in bundle interventions
- Setting: 1341 patients, 31 Emergency departments
- Outcome measurement: 90 day mortality, 1 year mortality, need for organ support
- Results: No mortality differences at 90 days/ 1 year, no differences in organ support



# Central Venous Pressures (CVP)

Unclear if CVP  
measurements or  
CVP guided therapy  
enhances outcomes



# Corticosteroids in Sepsis

*Volbeda, Wetterslev, Gluud, Zijlstra, van der Horst & Keus, 2015, Int Care Med, 41, 1220-1234*

- Cochrane methodology
- Randomized clinical trials evaluating corticosteroids for sepsis in adults
- 35 trials; 4682 patients
- Outcomes:
  - Mortality
  - Serious adverse effects (SAE)
- All trials except two had high risk of bias
- Findings:
  - No statistically significant effect of any dose steroids versus placebo on mortality or SAE
  - Low risk bias trials confirmed findings
  - No difference in steroid dose on outcomes
  - No difference in days of treatment on outcomes



# Corticosteroids

No established best practice  
for steroid use in sepsis  
despite recommendations  
from Surviving Resuscitation



# Implementation in Resource-limited settings

Concern	Response
Screening criteria sensitive, many false positives	New recommended qSOFA criteria are simpler with better predictability for poor outcomes <sup>1,2</sup> qSOFA = $\geq 2$ - altered mental status, SBP < 100 mm, RR > 20
Time sensitivity of recommendations	Studies show benefit even with less than optimal implementation <sup>3,4,5</sup>
Availability of lactate measurement	Hypotension paired with other clinical signs of hypoperfusion (urine out, mottling) may be equally predictive <sup>6,7</sup>
Perfusion evaluation requiring technology	Latest recommendations no longer suggest central venous catheter or central venous oxygen saturation. Physical evaluation of perfusion acceptable <sup>7,8</sup>

<sup>1</sup> Seymour et al, 2015

<sup>5</sup> Wang et al, 2012

<sup>2</sup> Dellinger et al, 2012

<sup>6</sup> Casserly et al, 2015

<sup>3</sup> Mahavanakul et al, 2012

<sup>7</sup> Singer et al, 2016

<sup>4</sup> Kuan et al, 2012

<sup>8</sup> The ProCess Investigators, 2014



# Sepsis Interventions *CAN* be implemented in resource-limited settings

China

Thailand

Singapore

Inner city

Community Hospitals

Portugal

Brazil

Rural settings

- Escalate screening for highest risk
- Broaden screen positive triggers
- Protocolize care for efficiency
- Any effort to standardize has reduced mortality in all settings
- Use biomarkers if available
- Don't expect perfection



JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER



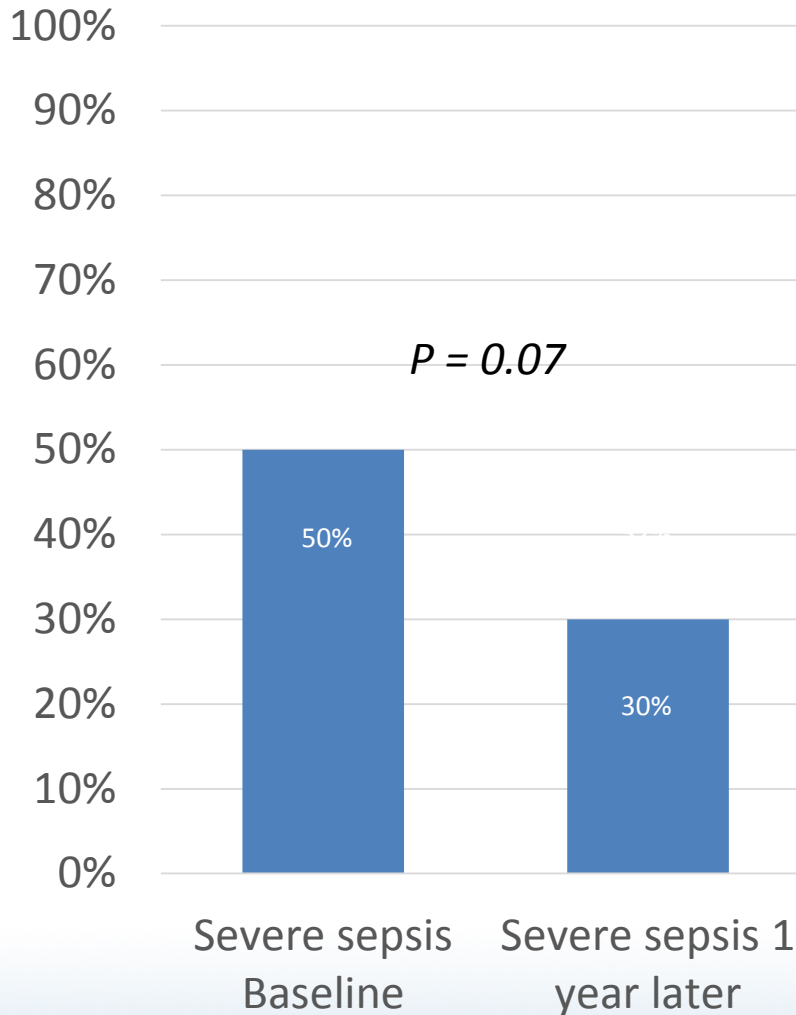
# The MD Anderson Experience

Hanzelka, Yeung, Chisholm, Merriman, Gaeta, Malik, Rice, 2013; Support Care Cancer 21: 727-734.

- Purpose: Compare baseline and post-protocol (orders, algorithm) for Early Goal-Directed Therapy sepsis management
- Setting: Emergency setting, single center, NCI Designated comprehensive Cancer Center
- Methods:
  - Sample (n= 355): 100 pts severe sepsis or septic shock prior to intervention, and at least 100 randomly selected severe sepsis or septic shock post intervention
  - Modified screening criteria:
    - Fever and/or hypotension plus another SIRS
    - Neutropenia NOT included
    - Heart rate modified to 100/min
  - No measurement of central venous pressure related interventions
- Outcome measures:
  - 28 day mortality
  - ICU length of stay (LOS) / hospital LOS
  - Goal mean arterial pressure and urine output at 6 hours
  - Time to lactic acid measure
  - Appropriateness and timeliness of antimicrobials
- Significant Results:
  - Mortality significantly reduced (20% vs 38%)
  - Patients reaching goal BP (74% vs 90%)
  - Patients reaching goal urine output (79% vs 96%)



# Incidence of Severe Sepsis



## Definition of severe sepsis (SIRS + any one):

- Lactate > 2.0 mmol
- Hypotension
- New onset organ failure
- Altered mental status

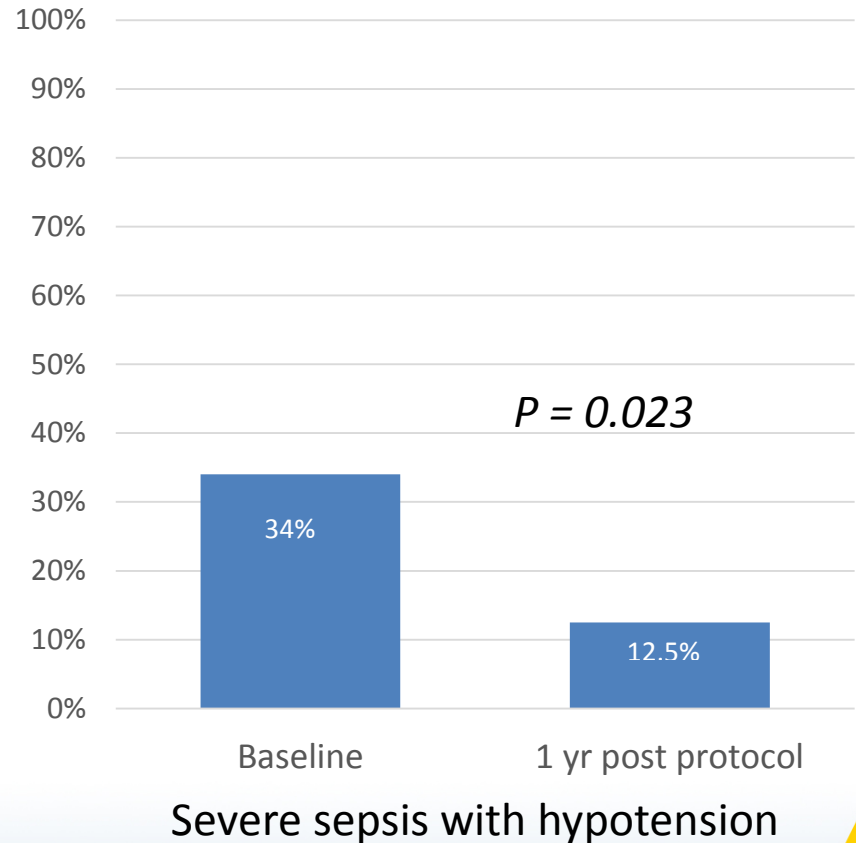
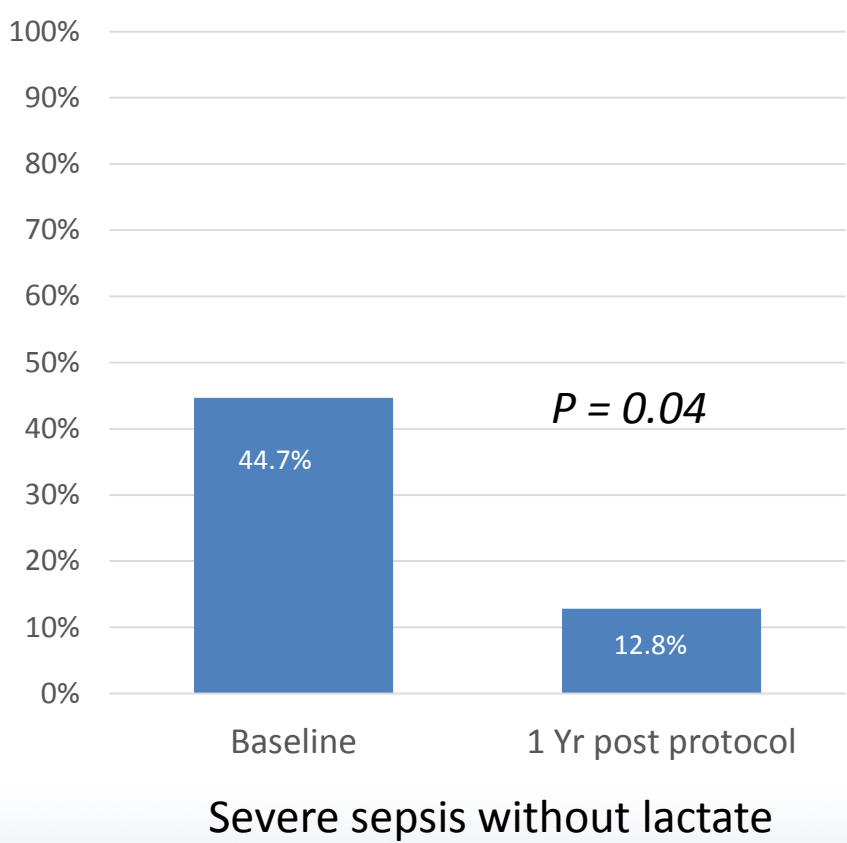
## Baseline and post-protocol group comparisons:

- Similar demographic variables
- Similar incidence of confirmed infection and culture positivity
- Lactate obtained for 1/38 baseline patients, 33/40 1 yr post-protocol
- Criteria meeting severe sepsis different between groups
- Post-protocol group met severe sepsis

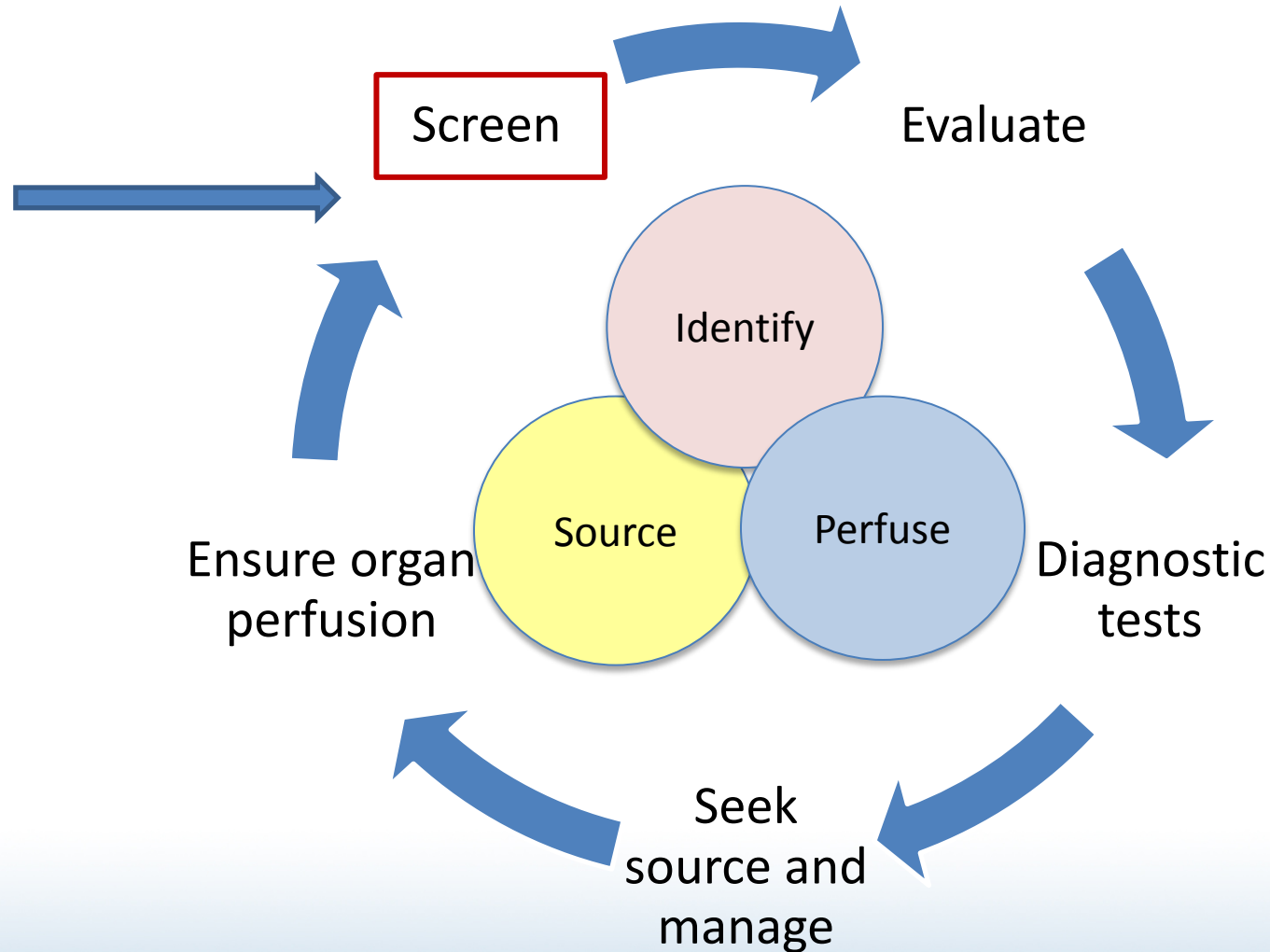


# Comparison of Groups

(Excluding lactate)



# Sepsis Management Algorithm



# Clock Start Times



## ➤ **Severe Sepsis (if both, earliest time used)**

- Prescriber documents “severe sepsis”,

**OR**

- Prescriber documents suspected new infection (removed from core measure if provider note redefines to non-sepsis diagnosis)
- $\geq 2$  SIRS
- New onset organ dysfunction (list of clinical and lab criteria)
- Lactate  $> 2.0$  mmol

## ➤ **Septic Shock**

- Hypotension (SBP  $< 90$ , SBP decreased by  $> 40$  mmHg prior recorded SBP, or MAP  $< 65$ )

**OR**

- Lactate  $\geq 4$



# Sepsis Core Measure Requirements (Interventions and Documentation)



## Severe Sepsis

(Time Zero = ↓ BP, new organ failure or lactate > 2.0)

- |  |  |  |
|--|--|--|
| <input type="checkbox"/> Lactate       | <input type="checkbox"/> Bolus* 30 ml/kg crystalloid fluid if ↓BP or lactate > 2.0 | <input type="checkbox"/> Repeat lactate if > 2.0 and after fluid bolus—consider more fluid |
| <input type="checkbox"/> BCx           |  |  |
| <input type="checkbox"/> Antibiotic(s) |  |  |

0                      1                      2                      3                      4                      5                      6

## Septic Shock

(Time Zero = ↓BP despite fluids or lactate > 4.0)

- |  |  |   |
|--|--|---|
| <input type="checkbox"/> Lactate       | <input type="checkbox"/> Bolus 30ml/kg crystalloid fluid | <input type="checkbox"/> Two BP measurements**    |
| <input type="checkbox"/> BCx           |  | <input type="checkbox"/> Vasopressors if MAP < 65 |
| <input type="checkbox"/> Antibiotic(s) |  | <input type="checkbox"/> Document response***     |

0                      1                      2                      3                      4                      5                      6

## Hours

\*Bolus is 30 mL/kg in less than 1 hr

\*\* After fluid bolus for ↓BP, check two BP measurements within one hour of completion

\*\*\* Document peripheral pulses, skin color and warmth



# Case Study Application

- Mr C, 68 year old male, pancreatic cancer, treatment cycle 2/ 17 days ago- gemcitabine, abraxane.
- Biliary stent revision yesterday, sent home
- Return to oncology clinic nurse with chills, aches, malaise, no fever
- VS: T-35.4, HR-118 (irreg), R-22, BP-92/50, O2 sat 90% room air
- Provider orders- CBC/chem/blood and urine cultures, chest x-ray
- Key lab results- WBC 12.8, Platelets 79,000, BUN 30, Creat 1.8
- X-ray- lobular infiltrates, pneumonia
- Registration time- 1000
- First encounter (vital signs) time- 1015
- Diagnostic orders- 1040
- Lab draw done- 1050
- Completed X-ray- 1110
- Resulted labs- 1130
- Resulted x-ray- 1200
- Does this patient have: sepsis, severe sepsis, septic shock
- What is time zero? 1000, 1015, 1040, 1130, 1200





# Discussion

- Sepsis core measure has a clinical impact upon workload.
  - Organizations should consider resources needed to implement the core measure in specific populations and adjust workflow.
- Hospital-wide efforts to detect and intervene in sepsis should be tailored to the population
  - Cancer-specific sepsis triggers missed with universal screening criteria.
  - Oncology-specific criteria require more robust evaluation.
  - Pilot data suggest that modified screening criteria reduces workload without sacrificing sensitivity of screening.
- Accurate and streamlined early screening for sepsis permits more time for recommended three-hour interventions.



# Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

*Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, ...  
Angus DC. JAMA, 2016 315(8), 801-810. doi: 10.1001/jama.2016.0287*

- Process
  - Task force of experts
  - Meetings
  - Delphi processes
  - Analysis of records
  - 31 organization endorsement
- Screening change
  - SOFA score increase 2 points in ICU
  - Quick SOFA (qSOFA) in non-ICU (any two)
    - RR > 22/min
    - Altered mentation
    - SBP < 100 mm Hg
- Sepsis and septic shock
  - Sepsis: life-threatening organ dysfunction
  - Septic shock: subset of sepsis patients requiring vasopressors to maintain a MAP > 65 mm Hg OR serum lactate > 2.0mmol/L in absence of hypovolemia



# Revised CMS Core Measure 2017

- Identification
  - Removed if provider documents sepsis R/O
- Diagnostic tests
  - Unable to obtain
  - Refusal
- Antimicrobials
  - Targeted antimicrobials with known organism
- Fluids
  - Estimated weight
  - Within 10% expected
- Reperfusion assessment
  - Provider can attest to others' assessment VS





# Questions?



JOHNS HOPKINS  
NURSING

THE SIDNEY KIMMEL  
COMPREHENSIVE CANCER CENTER



# References

- Aitken, L.M., Williams, G., Harvey, M., Blot, S., Kleinpell, R., Labeau, S., Ahrens, T. (2011). Nursing considerations to complement the Surviving Sepsis Campaign guidelines. *Critical Care Medicine*, 39(7), 1800-1818.
- Ali, N., Baqir, M., Hamid, A., & Khurshid, M. (2015). Febrile neutropenia: Door to needle time-Results of an initial audit. *Hematology*, 20(1). 26-30.
- ARISE Investigators, ANZIC's Clinical Trials Group, Peake, SL, Delaney, A, Bailey, M, Bellomo, R, Williams, P. (2014). Goal-directed resuscitation for patients with early septic shock. *N Engl J Med*, 371(16), 1496-1506.
- Baden, L.R., Bensinger, W., Angarone, M., Blouin, G., Camins, B.C., Casper, C., ... Wilson, J.W. (2015). Prevention and treatment of cancer-related infections. Version 2-2015 National Comprehensive Cancer Network (NCCN) clinical practice guidelines. <http://www.nccn.org> . Accessed March 1, 2015.
- Barochia, A.V., Cui, X., Vitburg, D., Suffredini, A.F., O'Grady, N.P., Bauks, S.M., et al. (2010). Bundled care for septic shock: an analysis of clinical trials. *Critical Care Medicine*, 38, 668-678.
- Berg, G.M., Vasquez, D.G., Hale, L.S., Nyberg, S.M., Moran, D.A. (2011). Evaluation of process variations in noncompliance in the implementation of evidence-based sepsis care. *Journal Healthcare Quality*, Oct 12. Doi:10.1111/j.1945-1474.2011.00168.x
- Bion, J. (2012). Surviving sepsis: a systems issue. *The Lancet*, 12, 898-899.
- Campbell, J. (2008). The effect of nurse champions on compliance with keystone intensive care unit sepsis=screening protocol. *Critical Care Nursing Quarterly*, 31(3), 251-269.
- Cannon, C.M., Holthaus, C.V., Zubrow, M.T., Posa, P., Gunaga, S., Kella, V., Rivers, E.P. (2012). The GENESIS Project (GENeralized Early Sepsis Intervention Strategies): a multicenter quality improvement collaborative. *Journal of Intensive Care Medicine*, epub ahead of print. Doi: 10.1177/0885066612453025

- Capuzzo, M., Rambaldi, M., Pinelli, G., Campesato, M., Pigna, A., Zanello, M., Toschi, E. (2012). Hospital staff education on severe sepsis/ septic shock and hospital mortality: an original hypothesis. *BMC Anesthesiology*, 12, 28. Doi: 10.1086/1471-2253-12-28.
- Carlom, D.J., Rubenfield, G.D. (2007). Barriers to implementing protocol-based sepsis resuscitation in the emergency department- results of a national survey. *Crit Care Med*, 35, 25-32.
- Chamberlain, D.J., Willis, E.M., Bersten, A.B. (2011). The severe sepsis bundles as processes of care: a meta-analysis. *Australian Critical Care*, 24, 229-243.
- Claessens, Y.E., Aegerter, P., Boubaker, H., Guidet, B., Cariou, A., Cyb-Rea Network (2013). Are clinical trials dealing with severe infection fitting routine practices? Insights from a large registry. *Crit Care*, 17(3), R89. Doi: 1186/cc12734
- Cooksley, T., Kitlowski, E., Hajii, M.P. (2012). Effectiveness of modified early warning score in predicting outcomes in oncology patients. *QJM*, 105(11), 1083-1088.
- Cullen, M., Fogg, T., Delaney, A. (2013). Timing of appropriate antibiotics in patients with septic shock: a retrospective cohort study. *Emerg Med Australas*, 25(4), 308-315. Doi: 10.1111/1742-6723
- Daniels, R., Nutbeam, I., McNamara, G., et al. (2010). The sepsis six and the severe sepsis resuscitation bundle: a prospective observational cohort study. *Emerg Med J*, doi:10.1136/emj.2010.095067.
- Dellinger, R.P., Carlet, J.M., Masur, H., et al. (2004). Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med*, 32, 858-873.
- Dellinger, R.P., Levy, M.M., Carlet, J.M., et al. (2008). Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock. Special Article. *Crit Care Med*, 36, 296-327.



- Dellinger, R.P., Levy, M.M., Rhodes, A., Annane, D., Gerlach, H., Opal, S.M..... The Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. (2013). Surviving Sepsis Campaign: International Guidelines for management of severe sepsis and septic shock, 2012. *Int Care Med*, 39, 165-228.
- Fletcher, M., Hodgkiss, H., Zhang, S., Browning, R., Hadden, C., Hoffman, T., Winick, N., & McCavit, T.L. (2013). Prompt administration of antibiotics is associated with improved outcomes in febrile neutropenia in children with cancer. *Pediatric blood cancer*.
- Flowers, C.R., Seidenfeld, J., Bow, E.J., Karten, C., Gleason, C., Hawley, D.K., ... Ramsey, S.D. (2013). Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol*. 31,794-810.
- Fong, J.J., Cecere, K., Urerborn, J., Garpstad, E., Klee, M., Devlin, J.W. (2007). Factors influencing variability in compliance rates and clinical outcomes among three different severe sepsis bundles. *Ann Pharmacother*, 41(6), 929-936.
- Gaieski, D.F., Mikkelsen, M.E., Bond, R.A., et al. (2010). Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. *Crit Care Med*, 38, 1045-1053.
- Gyang, E., Shieh, L., Forsey, L., & Maggio, P. (2014). A nurse-driven screening tool for the early identification of sepsis in an intermediate care unit setting. *Journal of Hospital Medicine*, 10(2), 97-103.
- Hanzelka, K., Yeung, S., Chisholm, G., Merriman, K.W., Gaeta, S., Malik, I., & Rice, T.E. (2012). Implementation of modified early-goal directed therapy for sepsis in an emergency center of a comprehensive cancer center. *Support Cancer Care*, 21. 727-734.



- Hird, C. (2012). Editorial: How nurses can support the surviving sepsis campaign. *Journal of Clinical Nursing*, doi: 10.1111/j.1365-2702.2010.03323.x
- Hitti, E.A., Lewin, J.J., Lopez, J., Hansen, J., Pipkin, M., Itani, T., Gurny, P. (2012). Improving door-to-antibiotic time in severely septic emergency department patients. *The Journal of Emergency Medicine*, 42(4), 462-469.
- Jones, A.E., Focht, A., Horton, J.M. (2007). Prospective external validation of an emergency department-based early goal-directed therapy protocol for severe sepsis and septic shock. (2007). *Chest*, 132, 425-432.
- Kang, M.J., Shin, T.G., Jo, I.J., Jeon, K., Suh, G.Y., Sim, M.S., Lim, S.Y., Song, K.J., & Jeong, Y.K. (2012). Factors influencing compliance with early resuscitation bundle in the management of severe sepsis and septic shock. *Shock*, 38(5), 474-479.
- Kece E., Yaka, E., Yilmaz, S., Dogan, N.O., Alyesil, C., Pekdemir, M. (2016). Comparison of diagnostic and prognostic utility of lactate and procalcitonin for sepsis in adult cancer patients presenting to emergency department with systemic infection. *Turk J Emerg Med*, 16(1), 1-7.
- Kleinpell, R., Aitken, L, Schorr, C.A. (2013). Implications of the new international sepsis guidelines for nursing care. *American Journal of Critical Care*, 22(3), 212-222.
- Ko, B.S., Ahn, S., Lee, Y.S., Kim, W.Y., Lim, K.S., & Lee, J.L. (2015). Impact of time to antibiotics on outcomes of chemotherapy-induced febrile neutropenia. *Support Cancer Care*, 23, 2799-2804.
- Kuan, W.S., Mahadevan, M., Tan, J.H., Guo, J., Ibrahim, I. (2012). Feasibility of introduction and implementation of the Surviving Sepsis Campaign bundle in a Singaporean Emergency department. *Eur J Emerg Med*, online 1-7
- Kuo, Y.W., Chang, H.T., Wu, P.C., Chen, Y.F., Lin, C.K., Wen, Y.F., Jerng, J.S. (2012). Compliance and barriers to implementing the sepsis resuscitation bundle for patients developing septic shock in the general medical wards. *Journal Formos Medical Association*, 111(2), 77-82.





- Lam, S.W., Bauer, S., R., Guzman, J.A. (2013). Septic shock: the initial moments and beyond. *Cleveland Clinic Journal of Medicine*, 80(3), 175-184.
- Levy, M.M., Artigas, A., Phillips, G.S., Rhodes, A., Beale, R., Osborn, T., Vincent, J.L., Townsend, S., Lemeshaw, S., & Dellinger, R.P. (2012). Outcomes of the surviving sepsis campaign in intensive care units in the USA and Europe: a prospective cohort study. *The Lancet*, 12, 919-924.
- Levy, M.M., Dellinger, R.P., Townsend, S.R., et al. (2010). The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. *Crit Care Med*, 38, 1-8
- Madsen, T.E., Napoli, A.M. (2014). The DISPARITY-II study: delays to antibiotic administration in women with severe sepsis or septic shock. *Acad Emerg Med*, 21(12), 1499-1502
- Mahavanakul, W., Nickerson, E.K., Srisomang, P., Teparrukkul, P., Lorvinitnum, P. Wongyingsinn, M., ... Peacock, S.J. (2012). Feasibility of modified surviving sepsis campaign guidelines in a resource-restricted setting based on a cohort study of severe s-aureus sepsis. *PLoS*, 7(2), e29858
- Mariotte, E., Canet, E., Debrumetz, A., Lemiale, V., Seguin, A., Darmon, M., Schlemmer, B., & Azoulay, E. (2012). Survival in neutropenic patients with severe sepsis or septic shock. *Critical Care Medicine*, 40(1). 43-49.
- McKinley, B.A., Moore, L.J., Sucher, J.F., Todd, S.R., Turner, K.L., Valdivia, A., Sailors, R.M., Moore, F.A. (2011). Computer protocol facilitates evidence-based care of sepsis in the surgical intensive care unit. *Journal of TRAUMA*, 70(5), 1153-1167.
- Mokart, D., Saillard, C., Sannini, A., Chow-Chine, L., Brun, J.P., Faucher, M., Blache, J.L., Blaise, D., Leone, M. (2014). Neutropenic cancer patients with severe sepsis: need for antibiotics in the first hour. *Intensive Care Med*, 40(8), 1173-1174.



- Nguyen, H.M., Schiavoni, A., Scott, K.D., Tanios, M.A. (2012). Implementation of sepsis management guideline in a community-based teaching hospital- can education be potentially beneficial for septic patients? *Int J Clin Pract*, 66(7), 705-710. Doi: 10.1111/j.1742-1241.2012.02939.
- Phua, J., Ho, B.C., Tee, A., Chan, K.P., Johan, A., Loo, S., So, C.R., Chia, N., Tan, A.Y., Tham, H.M., Chan, Y.H., Koh, Y. (2012). The impact of clinical protocols in the management of severe sepsis: a prospective cohort study. *Anaesthesia Intensive Care*, 40(4), 663-674.
- ProCESS Investigators, Yealy, D.M., Kellum, J.A., Huang, D.T., Barnato, A.E., Weissfeld, L.A.,... Angus, D.C. (2014). A randomized trial of protocol-based care for early septic shock. *N Engl J Med*, 370(18), 1683-1693. Doi: 10.1056/NEJMoa1401602
- Raghunathan, K, Shaw, A., Nathanson, B., Sturmer T., Brookhart, A., Stefan, M.S., Lindenauer, P.K. (2014). Association between the choice of IC crystalloid and in-hospital mortality among critically ill adults with sepsis. *Crit Care Med*, 42, 1585-1591.
- Reade, M.C., Huang, D.T., Bell, D., Coats, T.J., Cross, A.M., Moran, J.L.,... for the British Association for Emergency Medicine, the UK Intensive Care Society, the UK Society for Acute Medicine, the Australasian Resuscitation in Sepsis Evaluation (ARISE) Investigators and the Protocolized Care for Early Septic Shock (ProCESS) Investigators. (2010). Variability in management of early severe sepsis. *Emergency Medicine Journal*, 27, 110-115.
- Rivers, E., Nguyen, B., Haystad, S., et al. (2001). Early goal-directed therapy in the treatment of severe sepsis and septic shock. *New Eng J Med*, 345, 1368-1377.
- Schorr, CA, Dellinger, RP. (2014).The surviving sepsis campaign: past, present, and future. *Trends Mol Med*, 20(4), 192-194.
- Seymour, C.W., Liu, V.X., Brunkhorst, F.M., Rea, T.D., Scherag, A., ... Angus, D.C. (2016). Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*, 315(8), 762-774.



- Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, ... Angus DC. The Third International consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*, 2016 315(8), 801-810. doi: 10.1001/jama.2016.0287
- Van den Bosch, CM, Hulscher, ME, Natsch, S, Gyssens, IC, Prins, JM, Geerlings, SE, Dutch QI expert panel. (2014). Development of quality indicators for antimicrobial treatment in adults with sepsis. *BMC Infect Dis*, 14, 345.
- Venkatesh, A.K., Avula, U., Bartimus, H., Reif, J., Schmidt, M.J., Powell, E.S. (2013). Time to antibiotics for septic shock: evaluating a proposed performance measure. *American Journal Emergency Medicine*, 31, 680-683.
- Volbeda, M., Wetterslev, J., Gluud, C., Zijlstra, J.G., van der Horst, I.C.C., Keus, F. (2015). Glucocorticoids for sepsis: systematic review with meta-analysis and trial sequential analysis. *Int Care Med*, 41, 1220-1234
- Wang, Z., Schorr, C., Hunter, K., Dellinger, R.P. (2010). Contrasting treatment and outcomes of septic shock: presentation on hospital floors versus emergency department. *Chinese Medicine Journal*, 123(24), 3550-3553.
- Wang, Z., Xiong, X., Schorr, C., Dellinger, R.P. (2013). Impact of sepsis bundle strategy on outcomes of patients suffering from severe sepsis and septic shock in China. *J Emerg Med*, online, 1-7.
- Westphal, G.A., Kornig, A., Filho, M.C., Feijo, J., Trindade de Oliveira, L., Nunes, F., Fujiwara, K., Martins, S.F., Goncalves, A.R.R. (2011). Reduced mortality after the implementation of a protocol for the early detection of severe sepsis. *Journal of Critical Care*, 26, 76-81.
- Young, R.S., Gobel, B.H., Schumacher, M., Lee, J., Weaver, C., Weitzman, S. (2014). Use of the modified early warning score and serum lactate to prevent cardiopulmonary arrest in hematology-oncology patients: a quality improvement study. *Am J Med Qual*, 29(6), 530-537.