Prompt Recognition & Resuscitation in Pediatric Sepsis:

Hurry Up and Improve Outcomes!

Scott L. Weiss, MD MSCE FCCM

Assistant Professor of Critical Care and Pediatrics

Co-Fonder, Pediatric Sepsis Program

Children's Hospital of Philadelphia

University of Pennsylvania Perelman School of Medicine

Pediatric Sepsis Symposium

Morristown Medical Center

September 20, 2018

Conflict of Interest Disclosures for

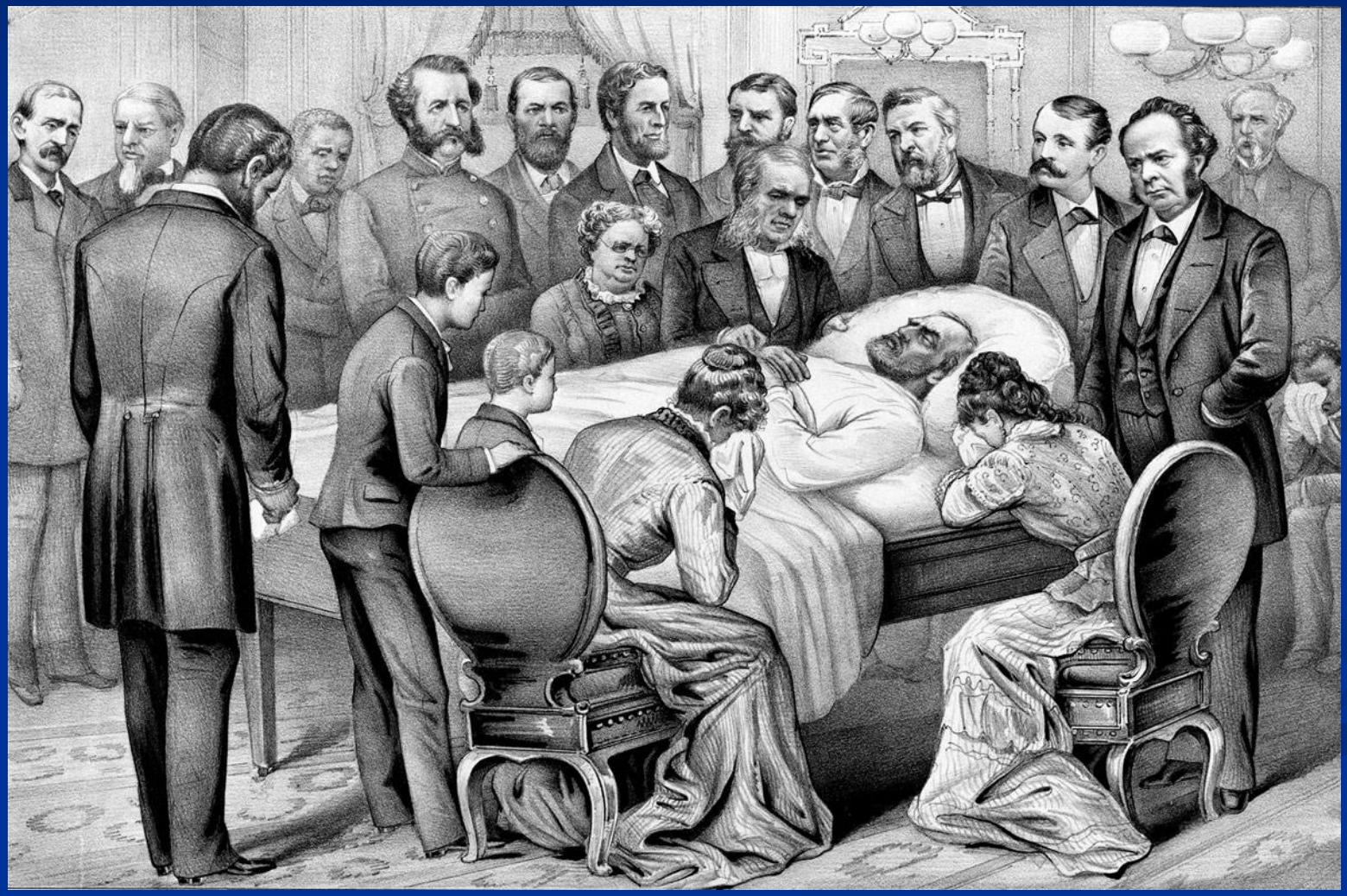
Scott L. Weiss, MD MSCE FCCM

Grant/Research Support	**National Institutes of Health** **Society of Critical Care Medicine** **Children's Hospital of Philadelphia**
Consultant	**Bristol-Meyers Squibb**
Speakers Bureau	Nothing to disclose
Stock Shareholder	Nothing to disclose
Other (identify)	**Royalties – Up-To-Date** **Honoraria – Thermo Fisher Scientific (Procalcitonin)** **Medscape/Roche**

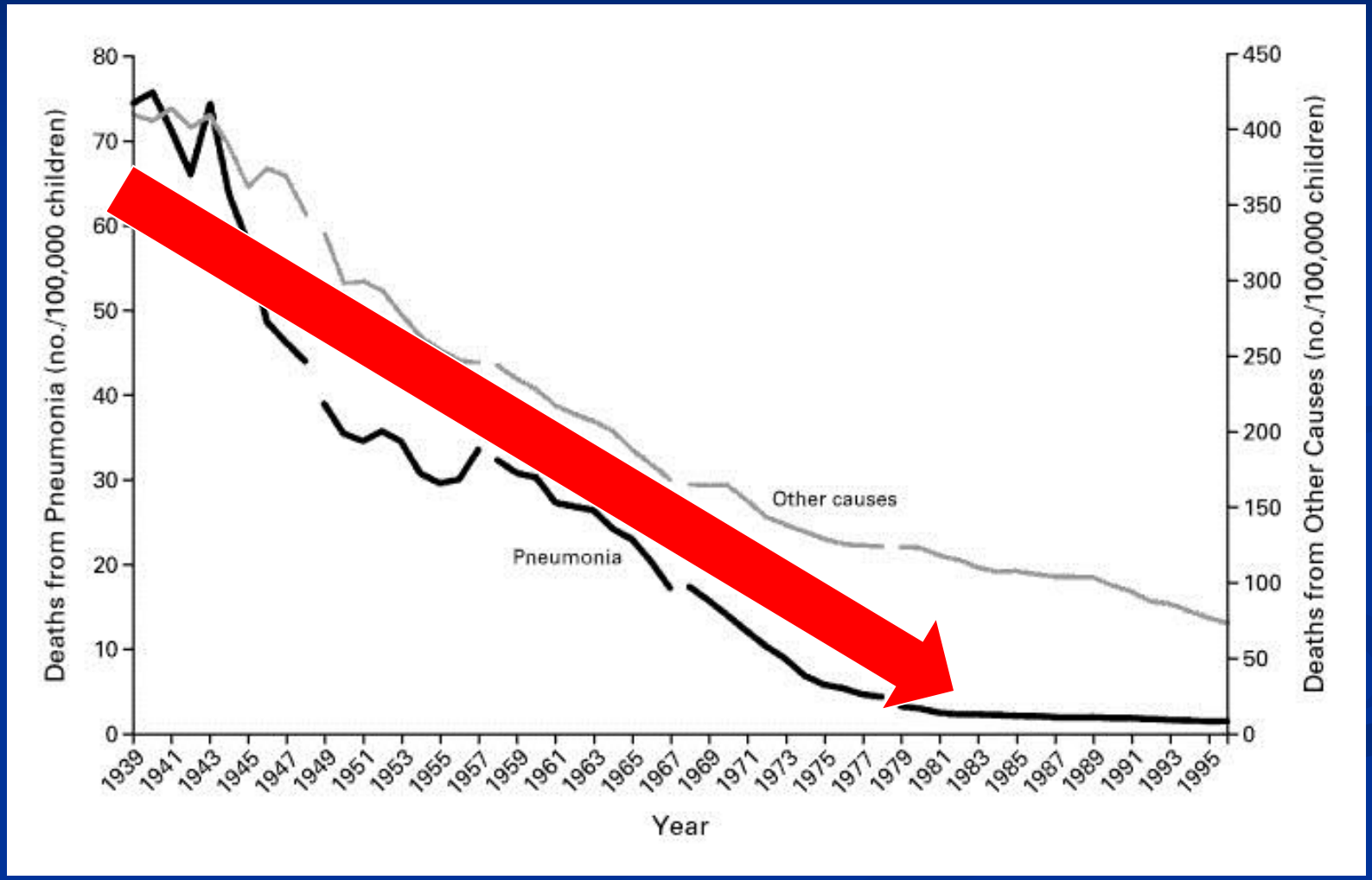
Objectives

1. Role for screening to enhance sepsis recognition
2. Approach to optimize pediatric sepsis resuscitation
3. Leveraging of multidisciplinary collaboration and national programs to improve outcomes

σ΄ηψις



Mortality in Sepsis:
A Medical Success Story!



Dowell et al *NEJM* 2000

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

- Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection
- Septic shock is subset with
  - *Circulatory* (hypotension despite vasoactives) ***AND***
  - *Cellular/metabolic* abnormalities (lactate >2 mmol/L)

JAMA Feb 2016

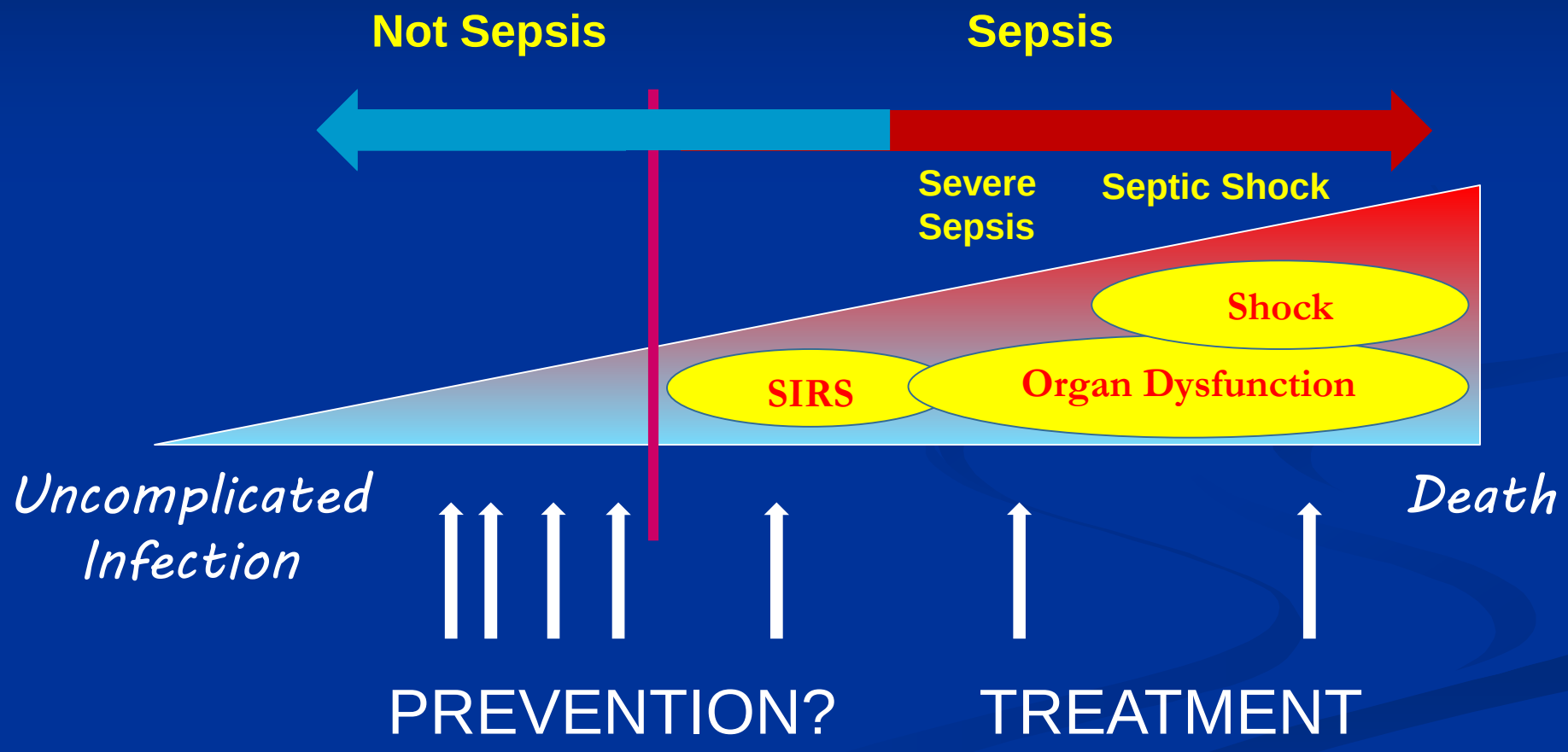
International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics*

Brahm Goldstein, MD; Brett Giroir, MD; Adrienne Randolph, MD; and the Members of the International Consensus Conference on Pediatric Sepsis

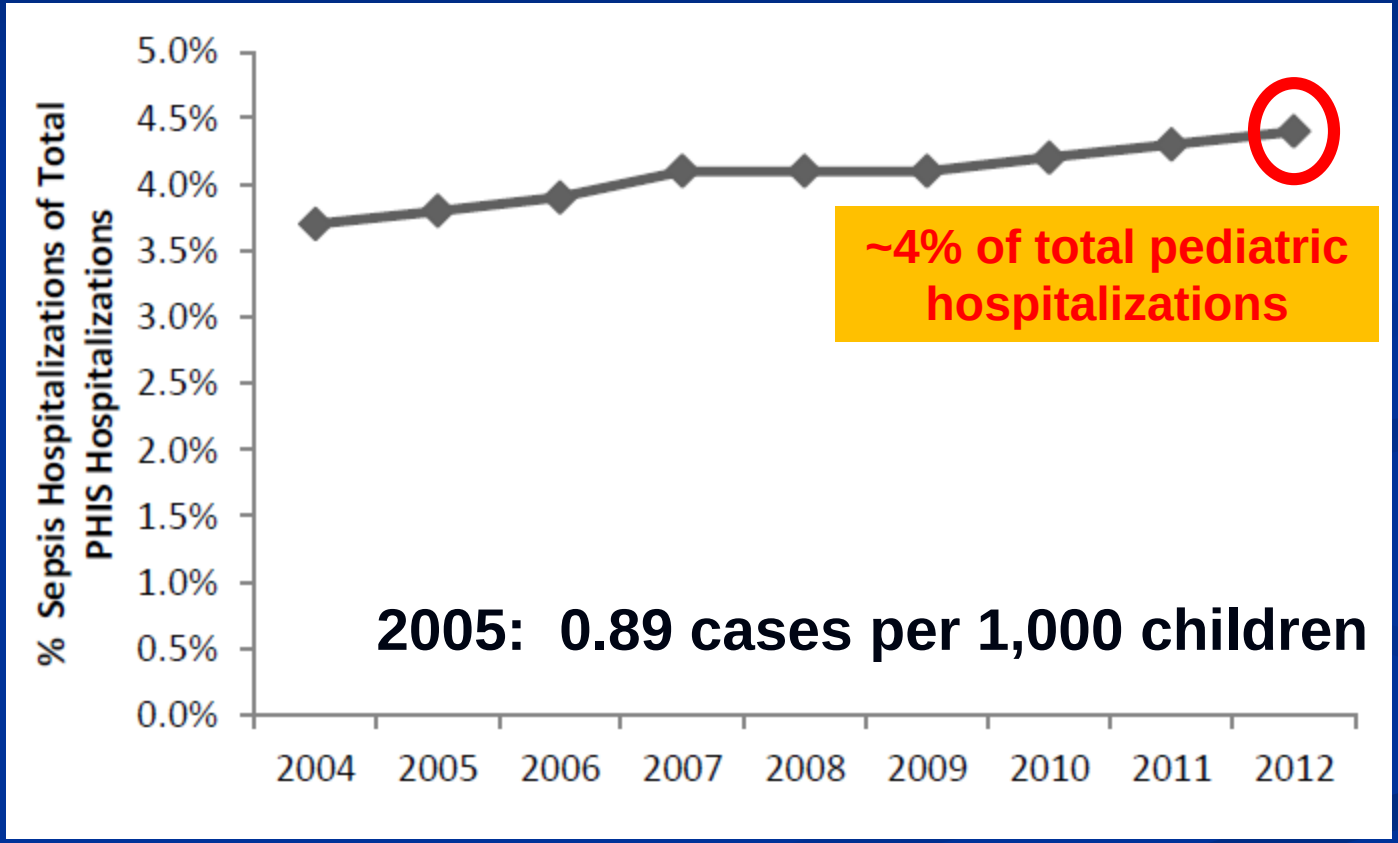
- SIRS: ≥ 2 abnormalities of temp, HR, RR, WBC
- Sepsis: SIRS, *plus* suspected or proven infection
- Severe sepsis: Sepsis, *plus* organ dysfunction
- Septic shock: Sepsis, *plus* CV dysfunction
  - CV dysfunction ≠ hypotension
  - Abnormal perfusion: ↑lactate, acidosis, oliguria, delayed CR

Pediatr Crit Care Med 2005

Defining Sepsis is Inherently Arbitrary

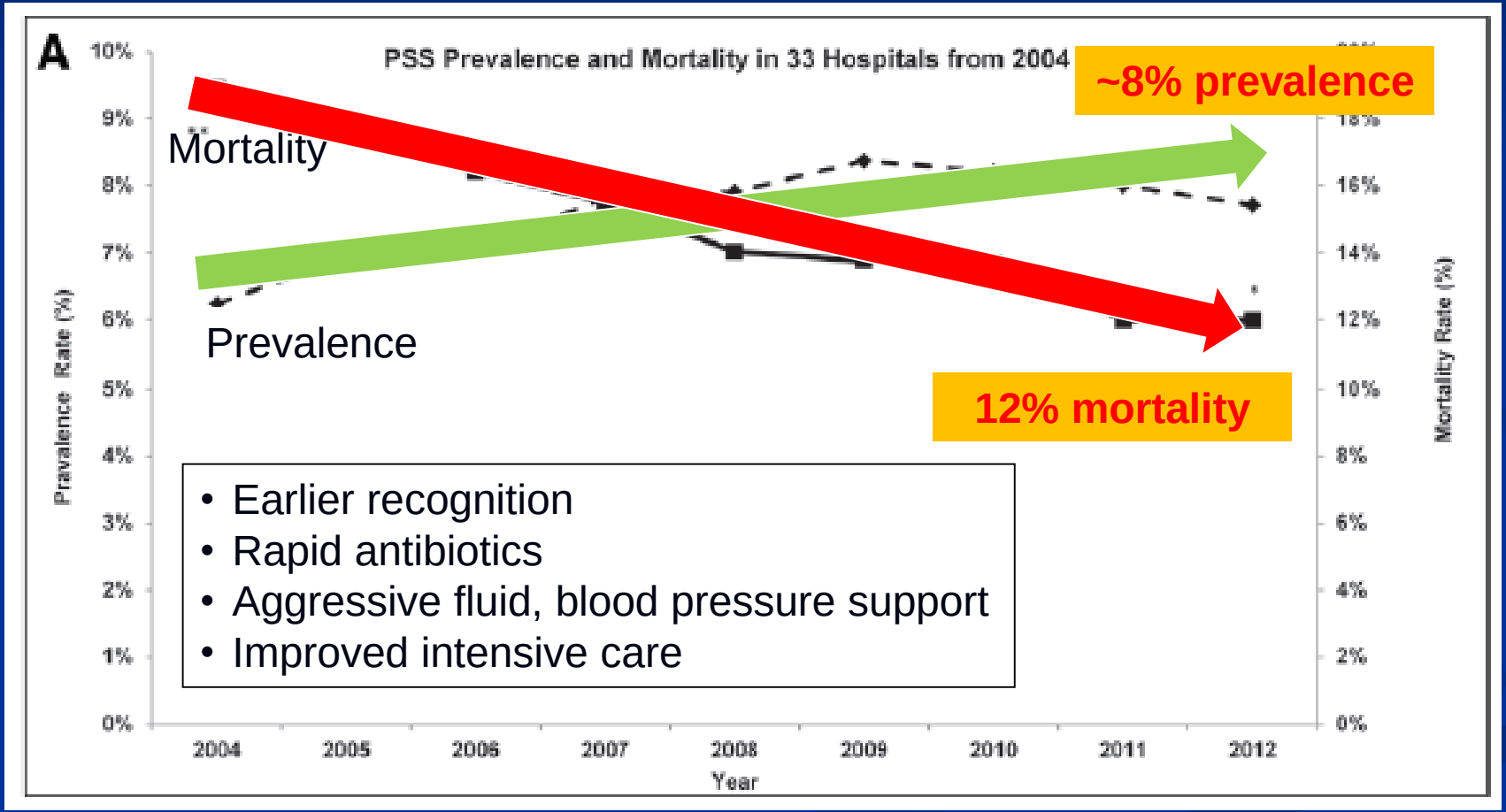


Increasing Prevalence of Pediatric Severe Sepsis



Balamuth et al *Pediatr Crit Care Med* 2014
Hartman et al *Pediatr Crit Care Med* 2013

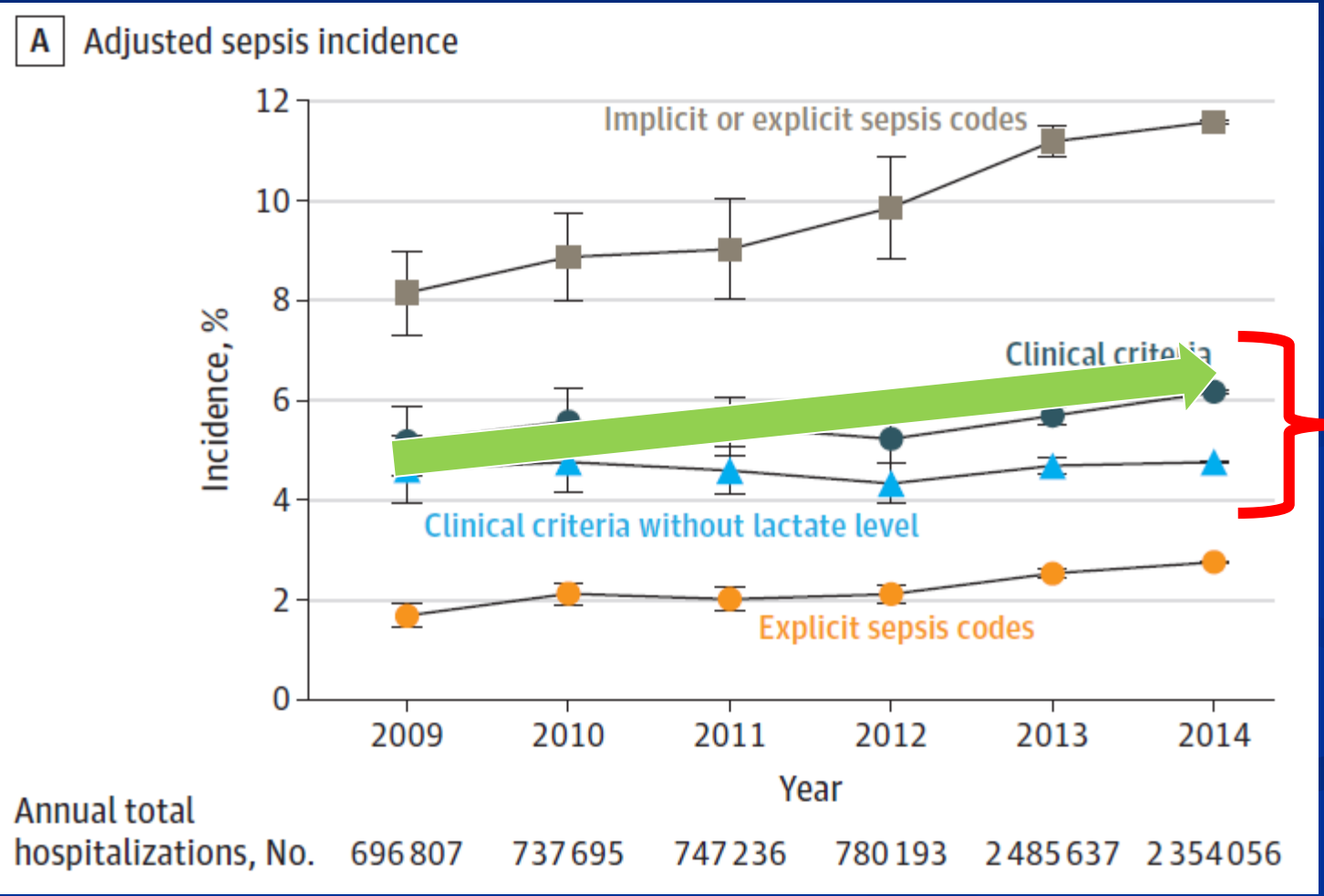
Increasing Prevalence, Decreasing Mortality



Ruth et al *Pediatr Crit Care Med* 2014

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

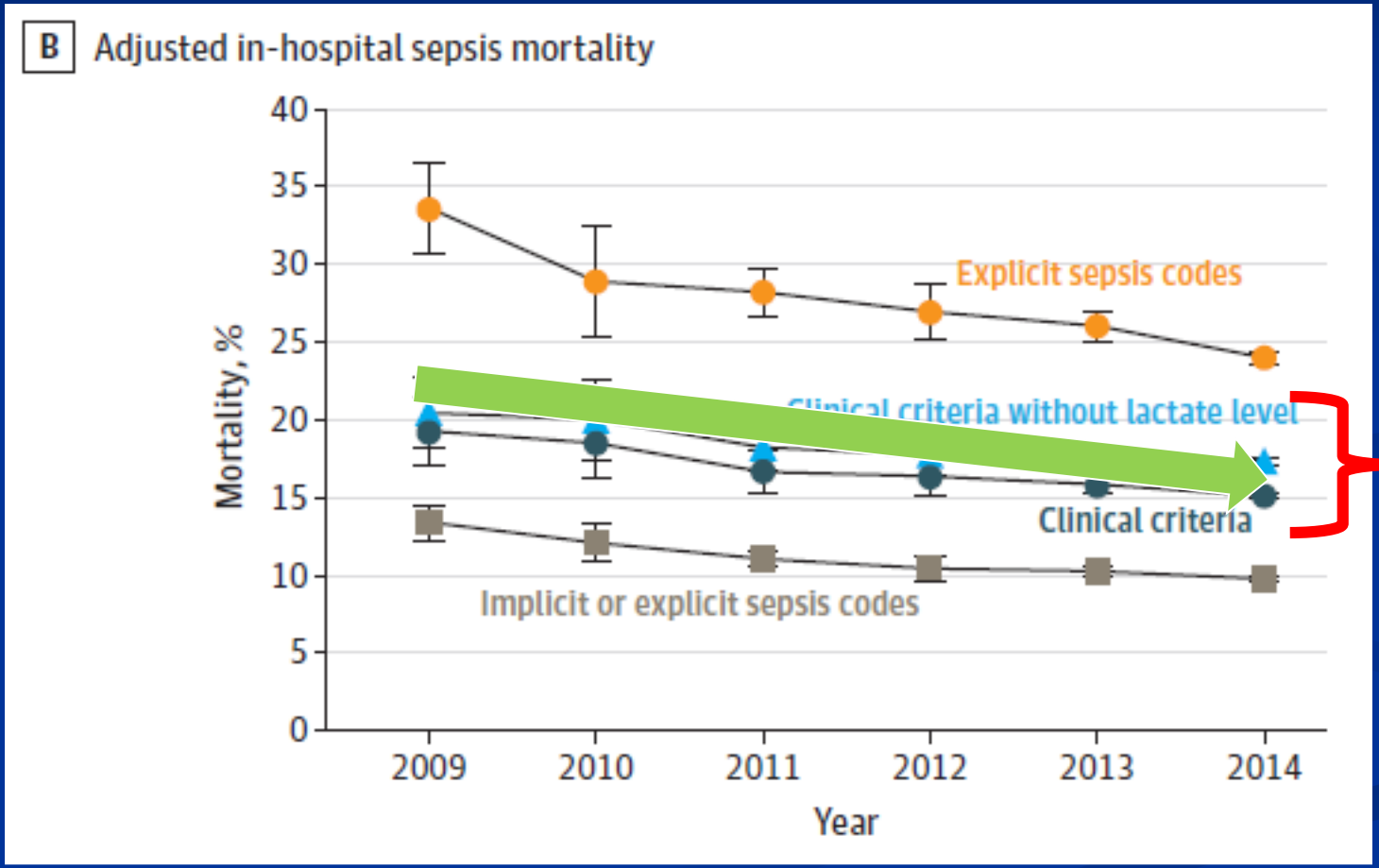
Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014



Rhee et al JAMA 2017

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

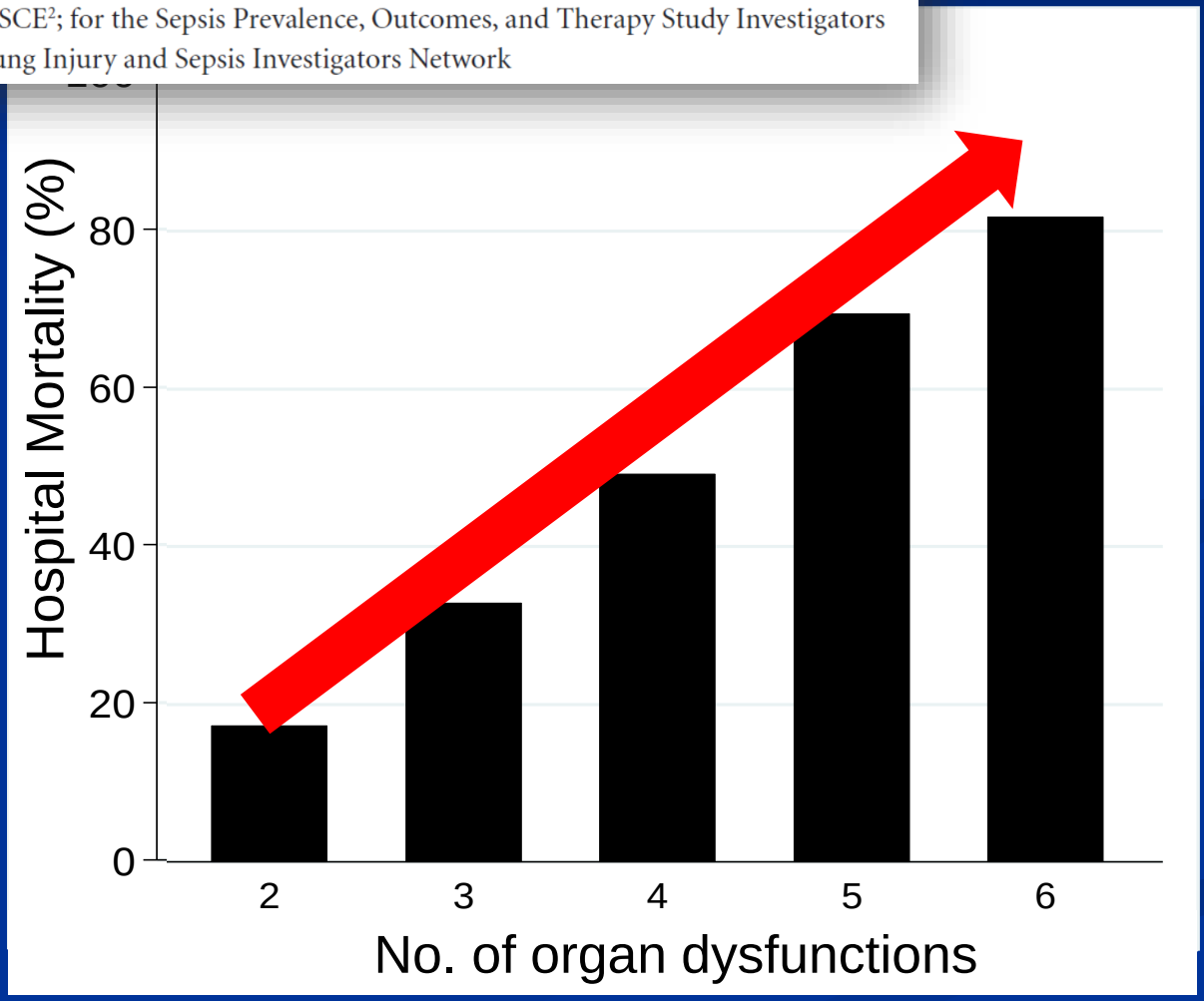
Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014



Rhee et al JAMA 2017

New or Progressive Multiple Organ Dysfunction Syndrome in Pediatric Severe Sepsis: A Sepsis Phenotype With Higher Morbidity and Mortality*

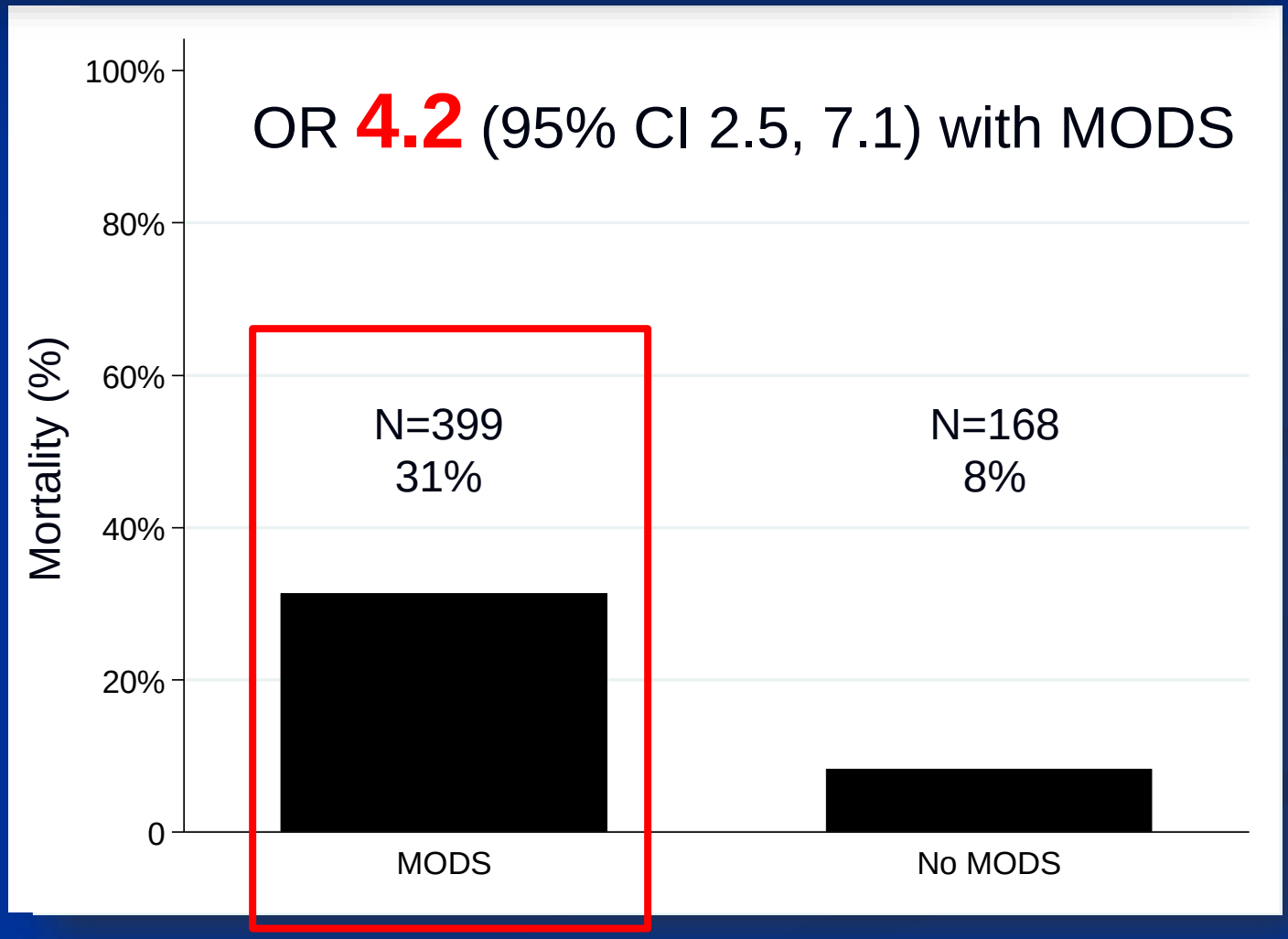
John C. Lin, MD[1]; Philip C. Spinella, MD, FCCM[1]; Julie C. Fitzgerald, MD, PhD[2]; Marisa Tucci, MD[3]; Jenny L. Bush, RN, BSN[2]; Vinay M. Nadkarni, MD[2]; Neal J. Thomas, MD, MSc[4]; Scott L. Weiss, MD, MSCE[2]; for the Sepsis Prevalence, Outcomes, and Therapy Study Investigators and Pediatric Acute Lung Injury and Sepsis Investigators Network



Lin et al *Peds Crit Care Med* 2017

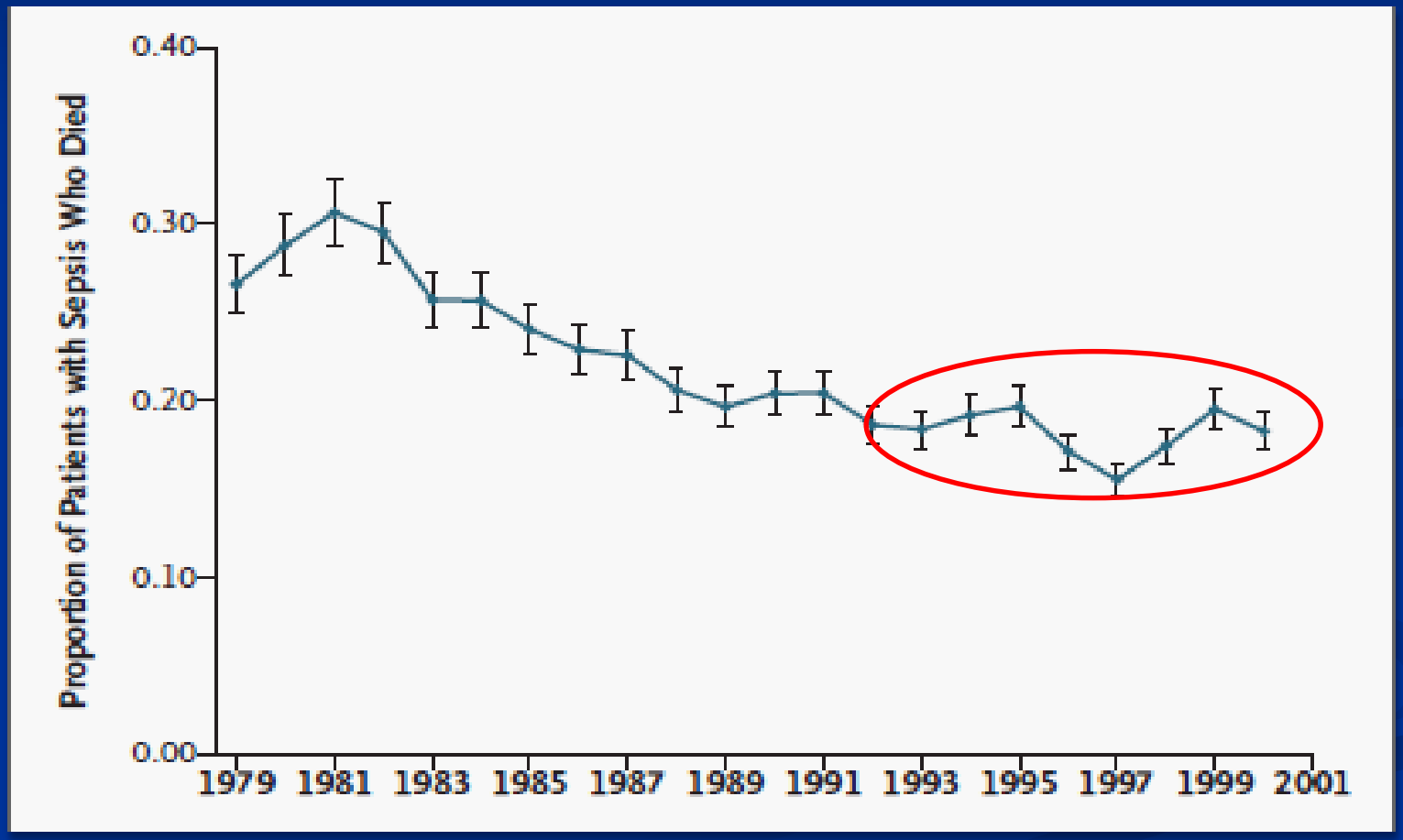
Global Epidemiology of Pediatric Severe Sepsis: The Sepsis Prevalence, Outcomes, and Therapies Study

Scott L. Weiss[1*], Julie C. Fitzgerald[1*], John Pappachan[2,3], Derek Wheeler[4,5], Juan C. Jaramillo-Bustamante[6], Asma Salloo[7], Sunit C. Singhi[8], Simon Erickson[9], Jason A. Roy[10], Jenny L. Bush[1], Vinay M. Nadkarni[1], and Neal J. Thomas[1,11]; for the Sepsis Prevalence, Outcomes, and Therapies (SPROUT) Study Investigators and the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network



Weiss, Fitzgerald et al, *AJRCCM*, 2015

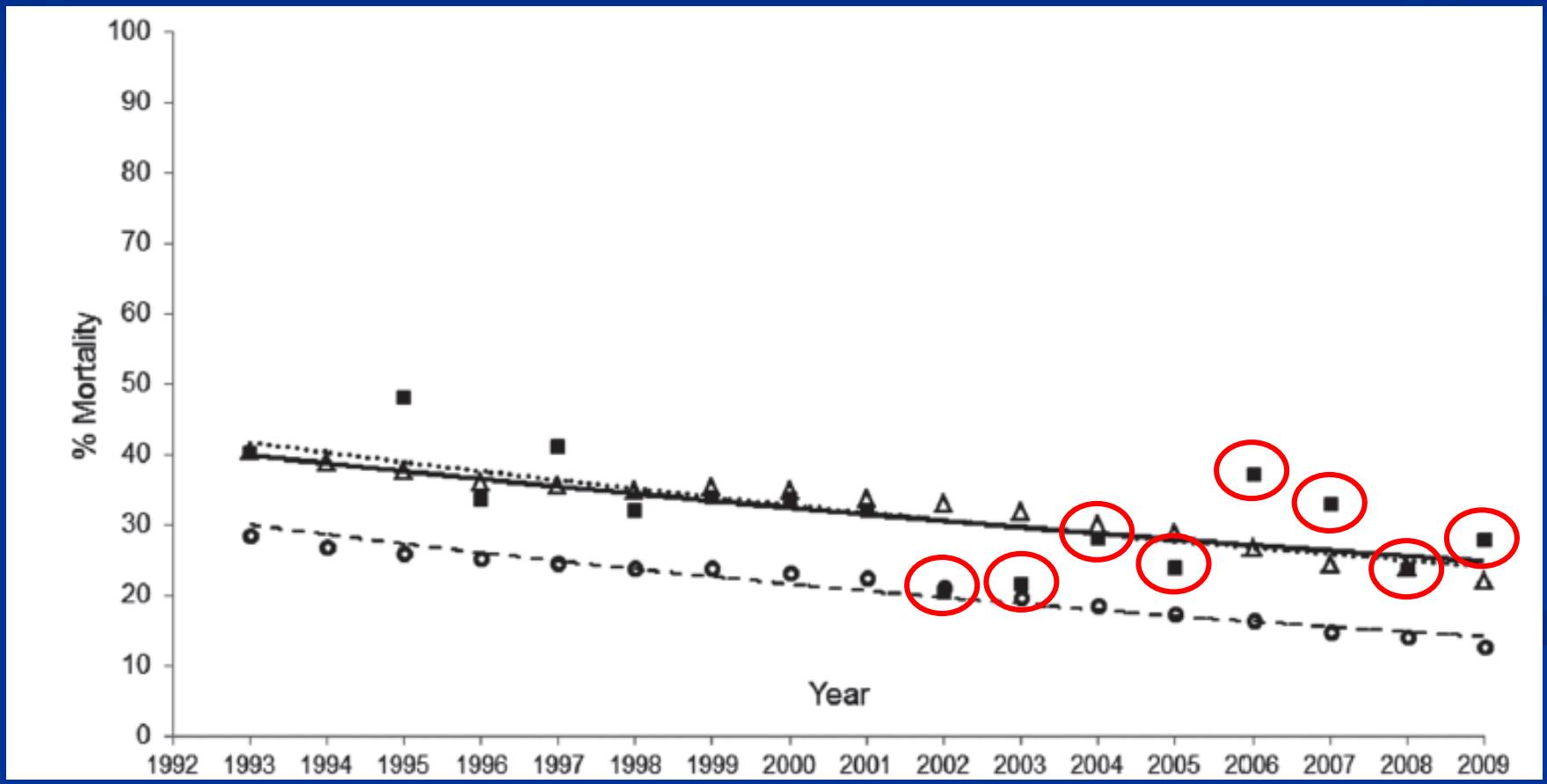
Outcome Improvement has *Stalled!*



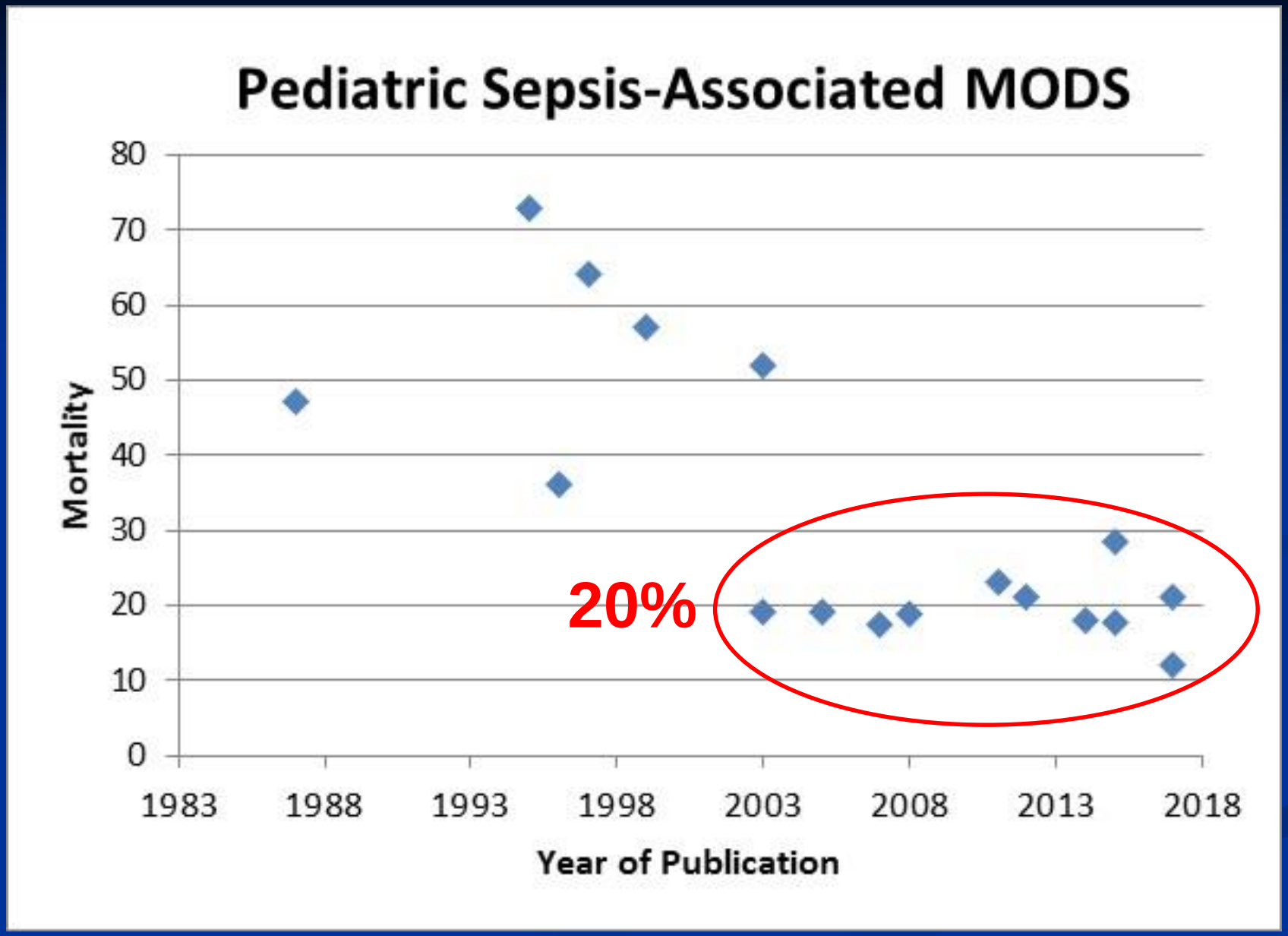
Martin et al. *NEJM*, 2003

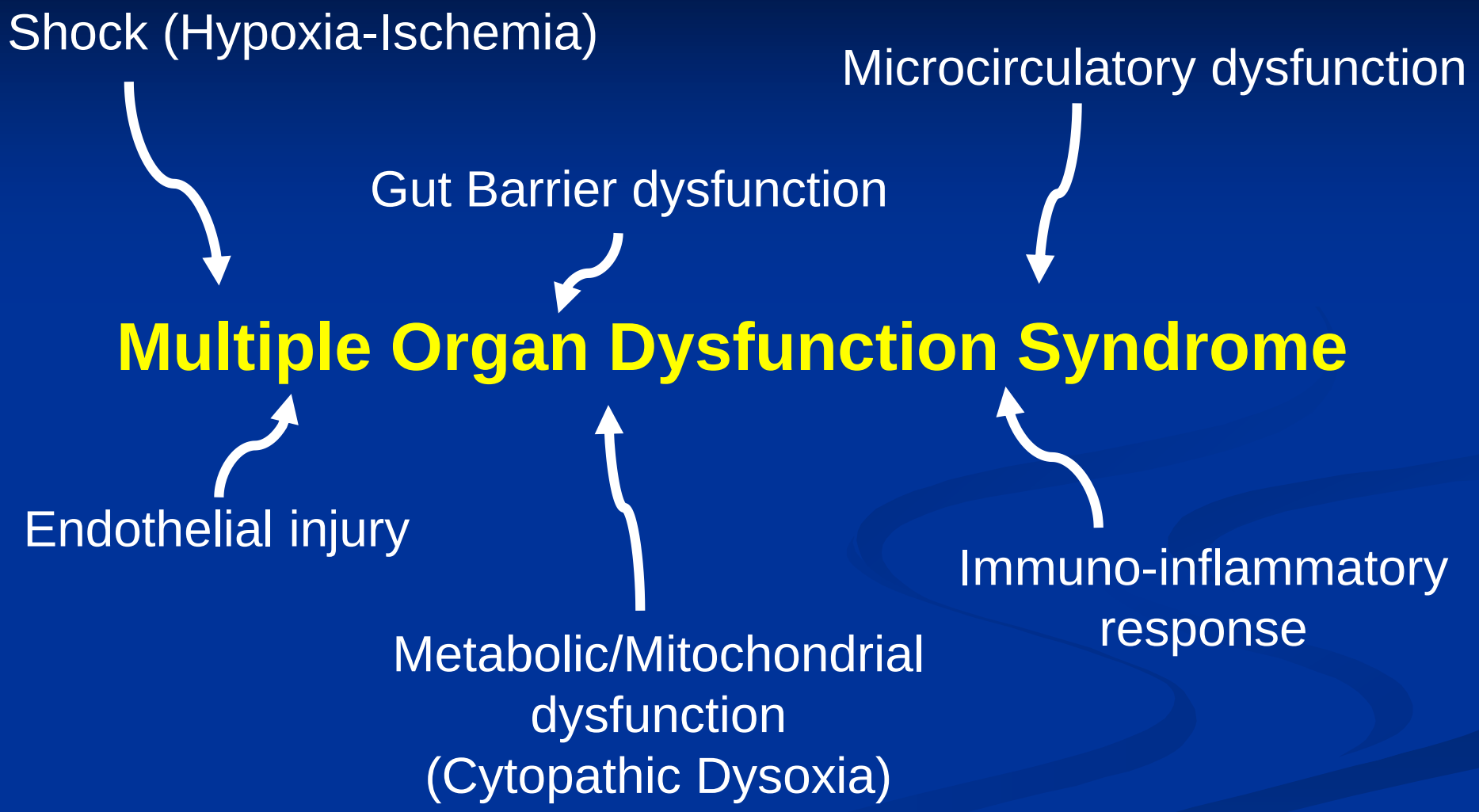
Two Decades of Mortality Trends Among Patients With Severe Sepsis: A Comparative Meta-Analysis*

Elizabeth K. Stevenson, MD, MS[1,2]; Amanda R. Rubenstein, MD[3]; Gregory T. Radin, MD[3]; Renda Soylemez Wiener, MD, MPH[1,2,4,5]; Allan J. Walkey, MD, MSc[1,2]

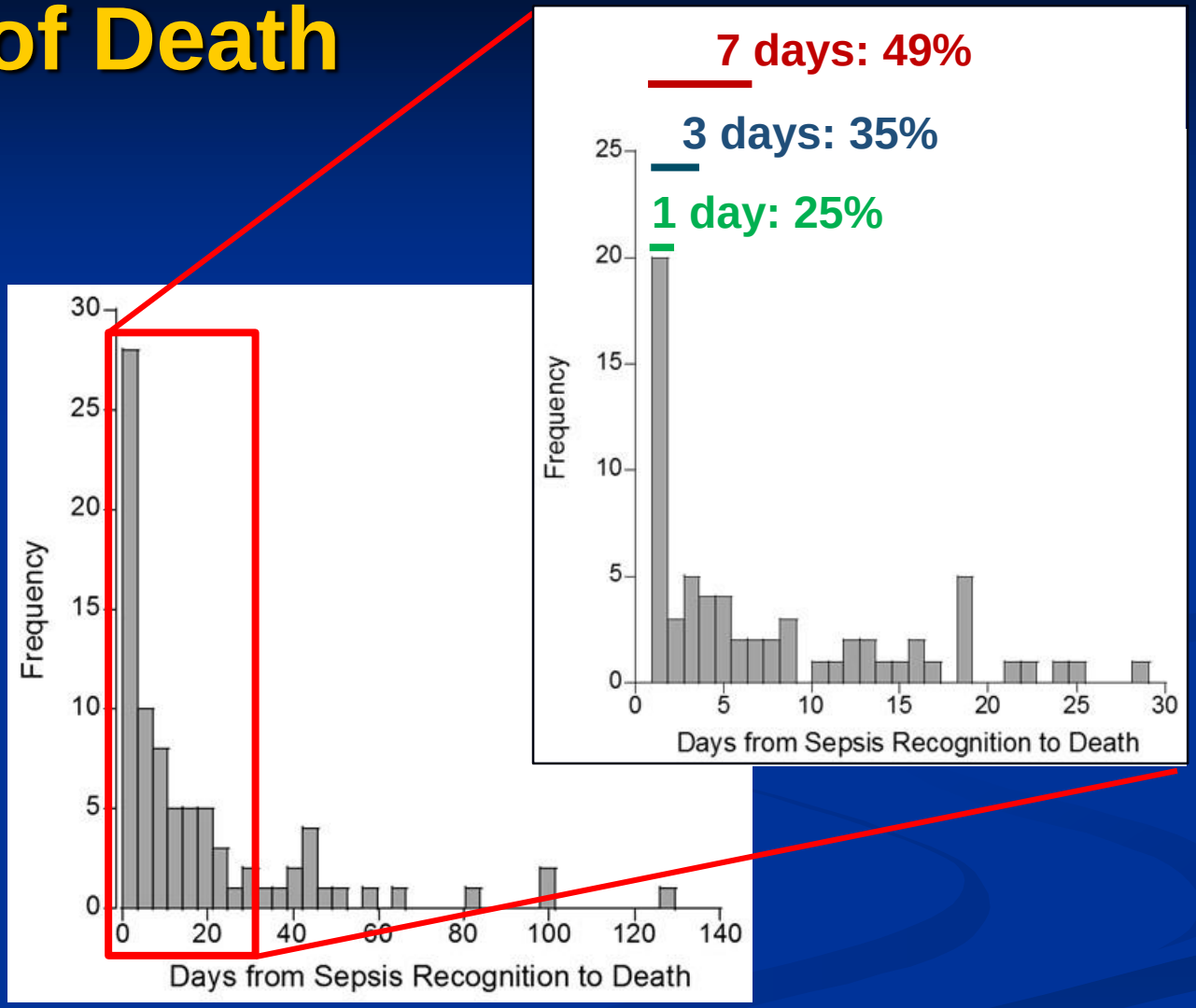


Crit Care Med 2014


Pediatric Sepsis-Associated MODS
Mortality
80
70
60
50
40
30
20
10
0
1983
1988
1993
1998
2003
2008
2013
2018
Year of Publication
20%


Shock (Hypoxia-Ischemia)
Microcirculatory dysfunction
Gut Barrier dysfunction
Multiple Organ Dysfunction Syndrome
Endothelial injury
Metabolic/Mitochondrial dysfunction (Cytopathic Dysoxia)
Immuno-inflammatory response

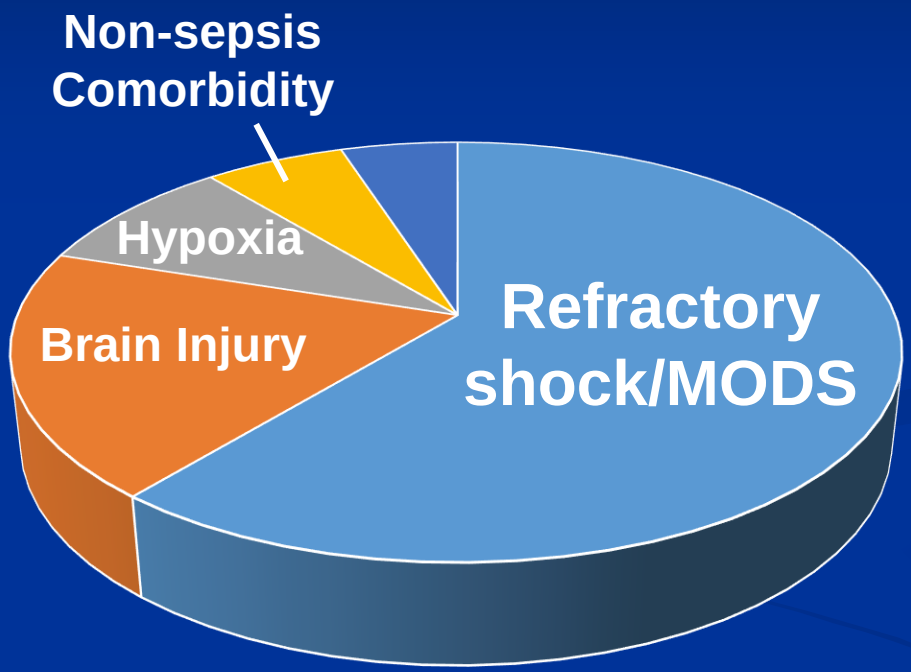
Timing of Death



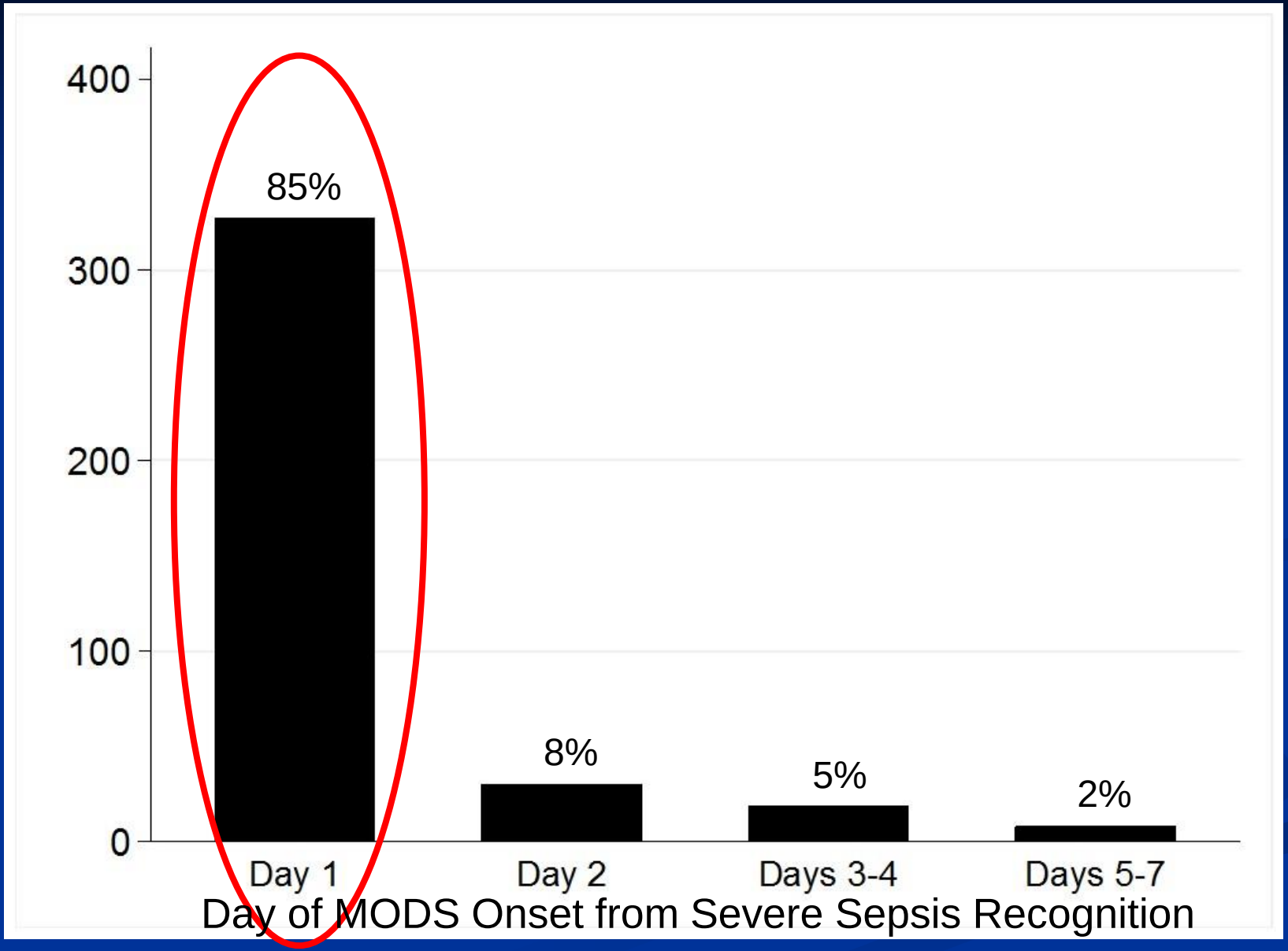
N=79 sepsis deaths at CHOP, Nationwide Children's

Weiss et al *Pediatric Crit Care Med* 2017

Cause of Death in Sepsis



Weiss et al *PCCM* 2017

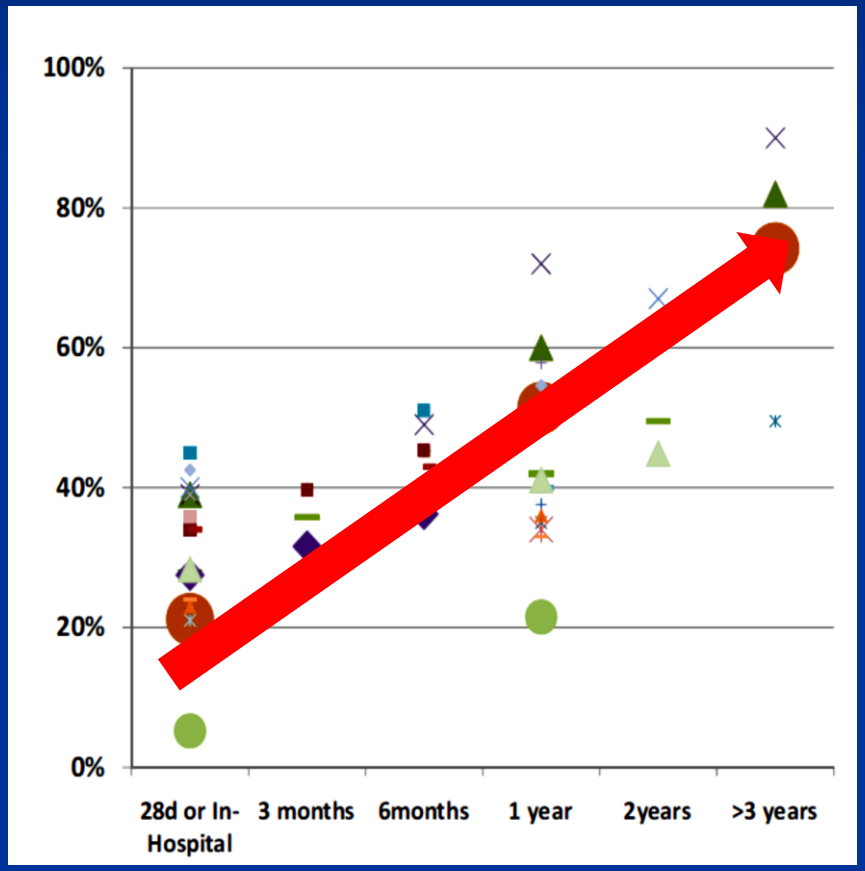


N=567 PICU patients

SPROUT study *Peds Crit Care Med* 2017

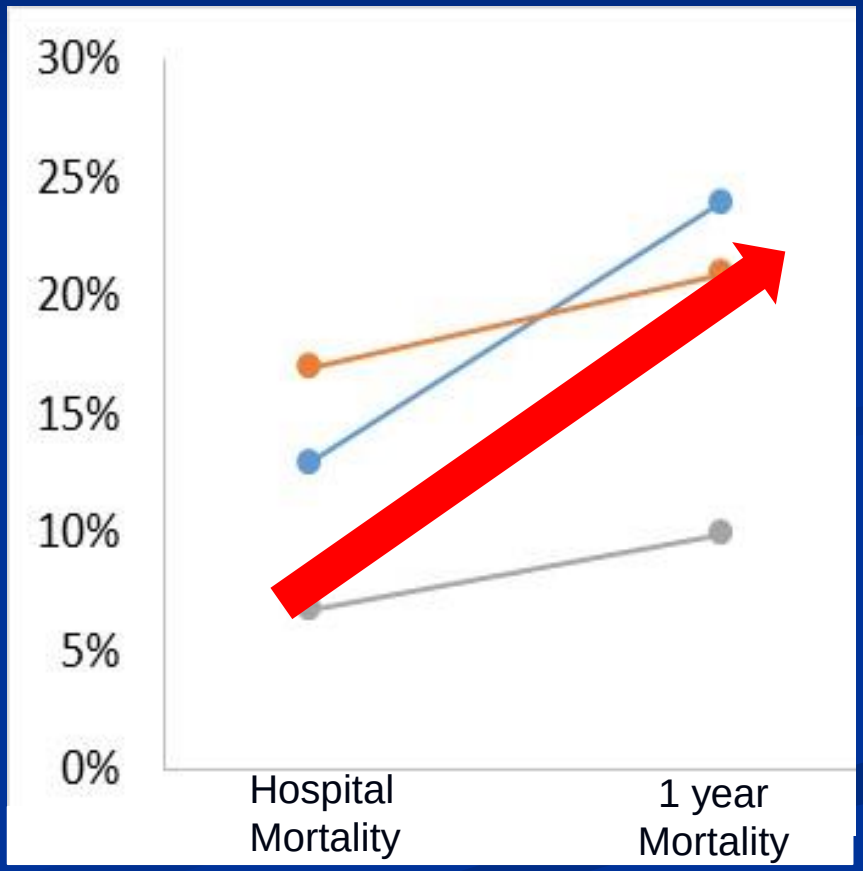
Long-Term Mortality After Sepsis

Adult Sepsis



Winters et al *Crit Care Med* 2010

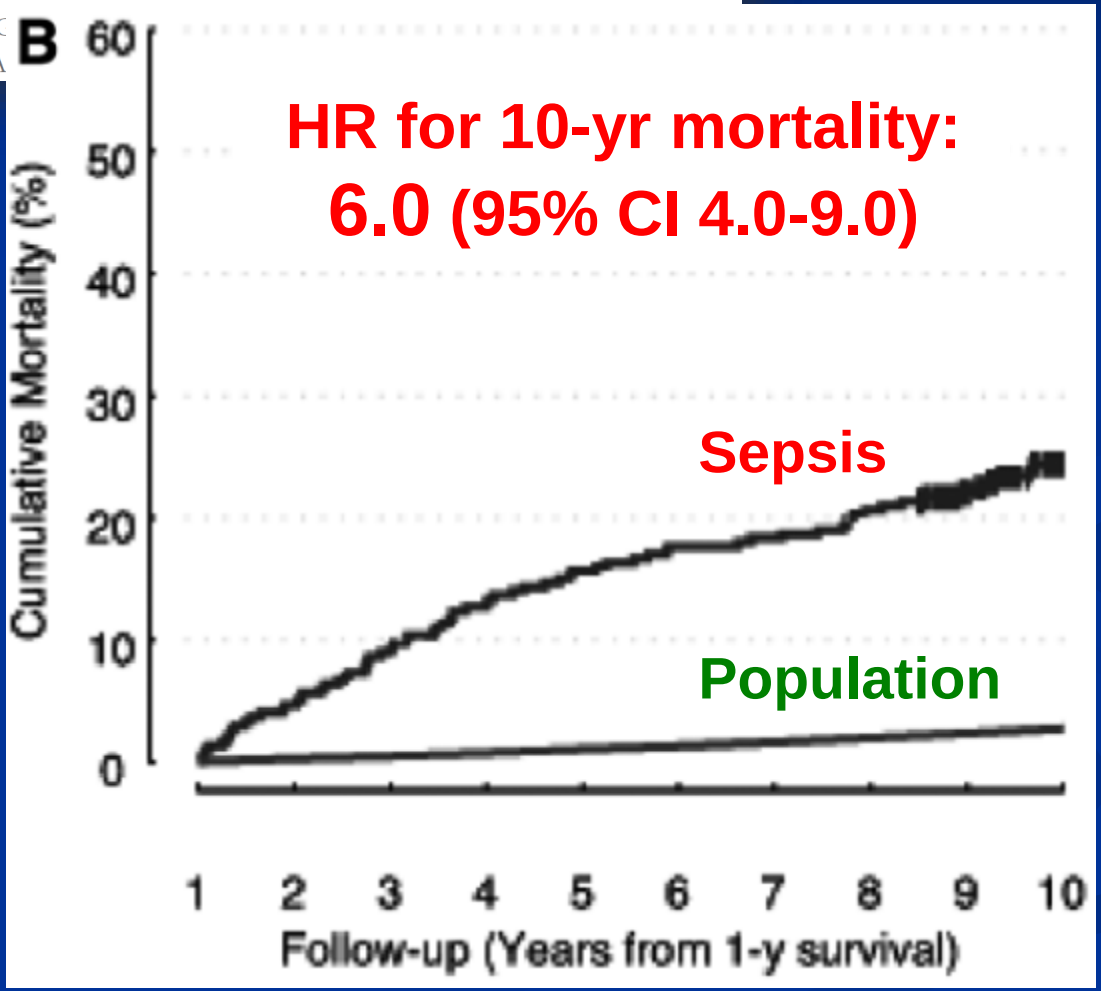
Pediatric Sepsis



CHOP Data
Cvetkovic et al *PCCM* 2015
Czaja et al *Pediatrics* 2009

Long-Term (10-Year) Mortality of Younger Previously Healthy Patients With Severe Sepsis/ Septic Shock Is Worse Than That of Patients With Nonseptic Critical Illness and of the General Population

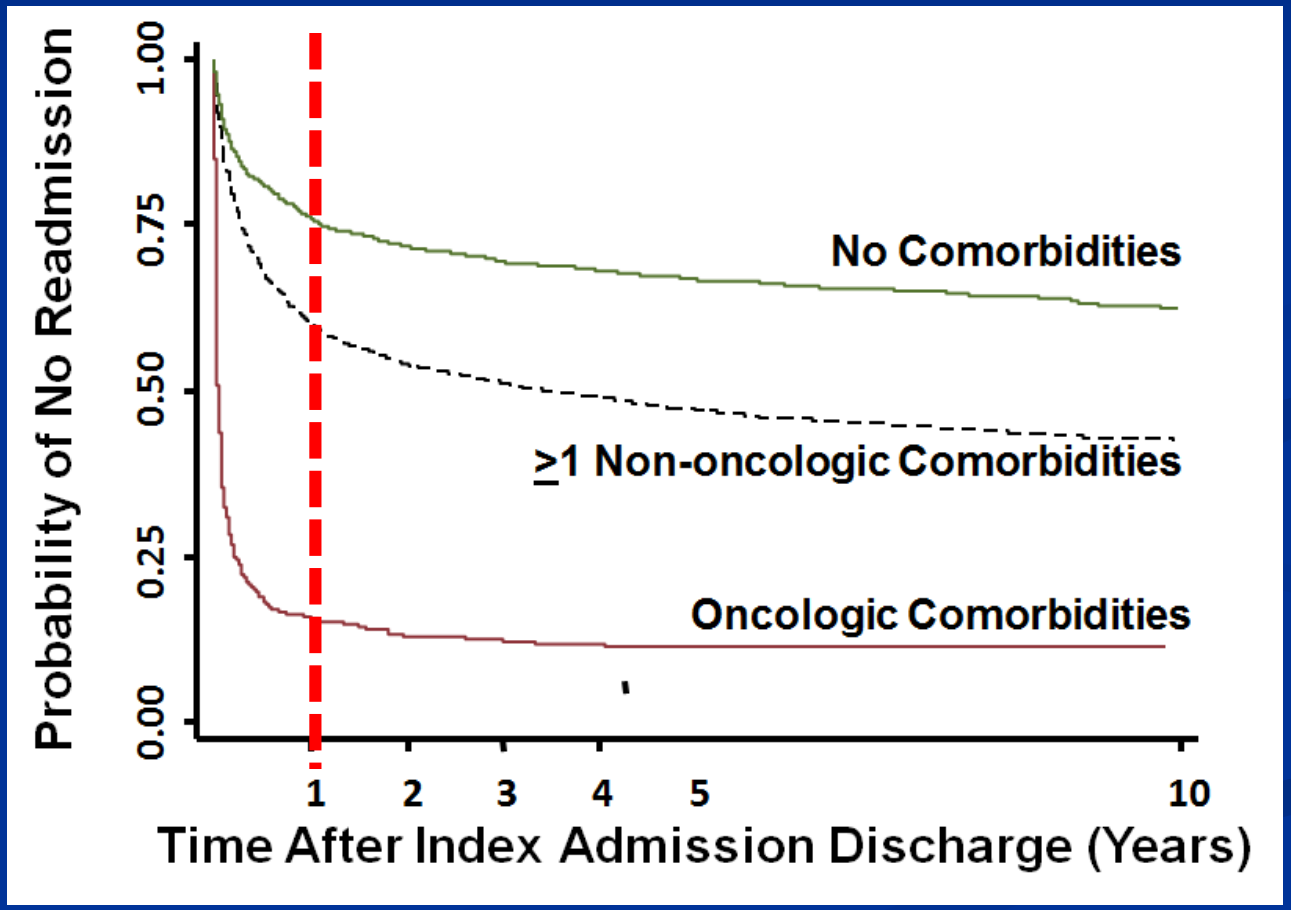
Adam Linder, MD[1,2]; Daphne C
Aslam H. Anis, PhD[3,4]; James A



Linder et al *Crit Care Med* 2014

Readmission After Pediatric Sepsis

47% of survivors had at least one readmission



Czaja et al *Pediatrics* 2009

How Can We Do Better?

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes, MB BS, MD(Res) (Co-chair)[1]; Laura E. Evans, MD, MSc, FCCM (Co-chair)[2]; Waleed Alhazzani, MD, MSc, FRCPC (methodology chair)[3]; Mitchell M. Levy, MD, MCCM[4]; Massimo Antonelli, MD[5]; Ricard Ferrer, MD, PhD[6]; Anand Kumar, MD, FCCM[7]; Jonathan E. Sevransky, MD, FCCM[8]; Charles L. Sprung, MD, JD, MCCM[9]; Mark E. Nunnally, MD, FCCM[2]; Bram Rochwerg, MD, MSc (Epi)[3]; Gordon D. Rubenfeld, MD (conflict of interest chair)[10]; Derek C. Angus, MD, MPH, MCCM[11]; Djillali Annane, MD[12]; Richard J. Beale, MD, MB BS[13];

A. INITIAL RESUSCITATION

1. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS).

B.SCREENING FOR SEPSIS AND PERFORMANCE IMPROVEMENT

1. We recommend that hospitals and hospital systems have a performance improvement program for sepsis, including sepsis screening for acutely ill, high-risk patients (BPS).

Crit Care Med 2017
Intensive Care Med 2017

Screening for Sepsis:
Easy to Say, Hard to do!

- Sepsis is a *syndrome*, not a disease
- Very heterogeneous
  - Patient factors
  - Microbiology
  - Host response
  - Onset, progression of symptoms
- Non-specific diagnostic criteria

"I shall not attempt to further define ~~***pornography***~~ ***sepsis,***

but I know it when I see it."

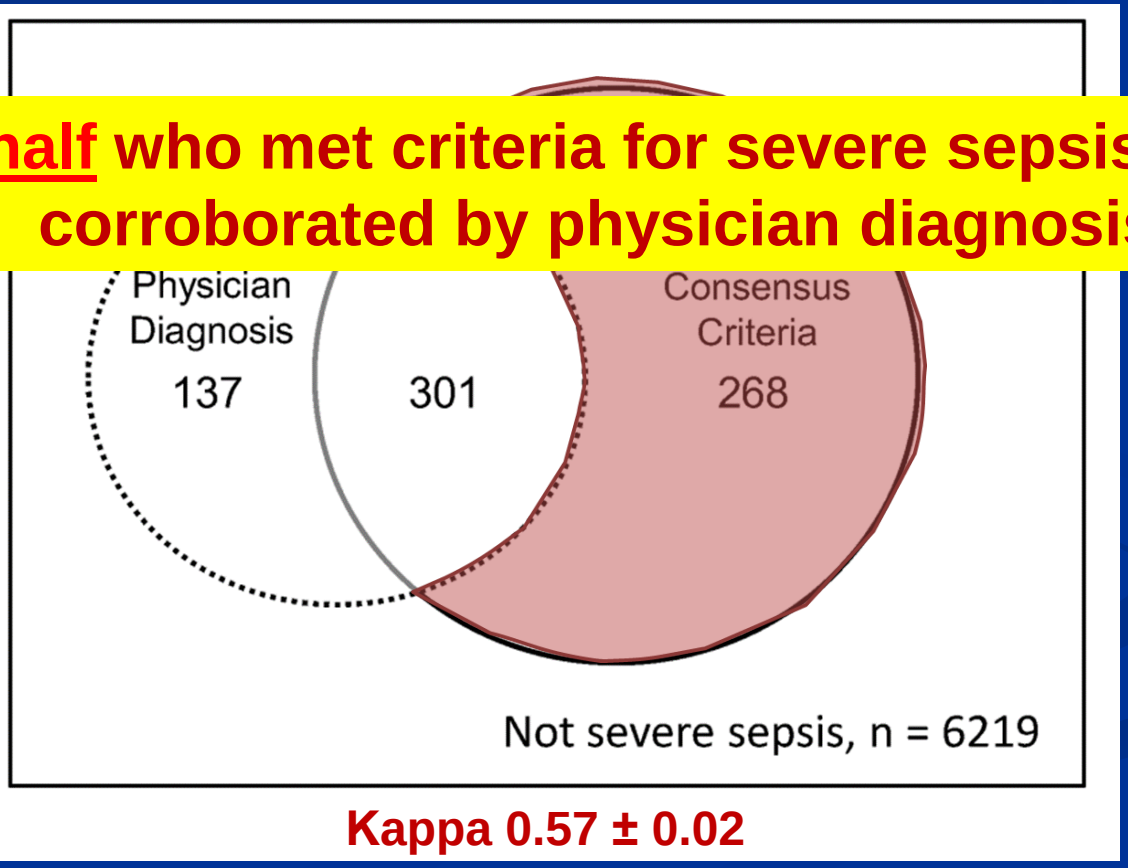
-U.S. Supreme Court Justice Potter Stewart
Jacobellis vs Ohio 1964

RESEARCH Open Access

Discordant identification of pediatric severe sepsis by research and clinical definitions in the SPROUT international point prevalence study

Scott L. Weiss[1*], Julie C. Fitzgerald[1], Frank A. Maffei[2], Jason M. Kane[3], Antonio Rodriguez-Nunez[4], Deyin D. Hsing[5], Deborah Franzon[6], Sze Ying Kee[7], Jenny L. Bush[1], Jason A. Roy[8], Neal J. Thomas[9], and Vinay M. Nadkarni[1], for the SPROUT Study Investigators and Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network

Nearly half who met criteria for severe sepsis were not corroborated by physician diagnosis



Kappa 0.57 ± 0.02

Crit Care, 2015

ABOUT NEW YORK

An Infection, Unnoticed, Turns Unstoppable

Rory Staunton taking his first flying lesson in 2011.

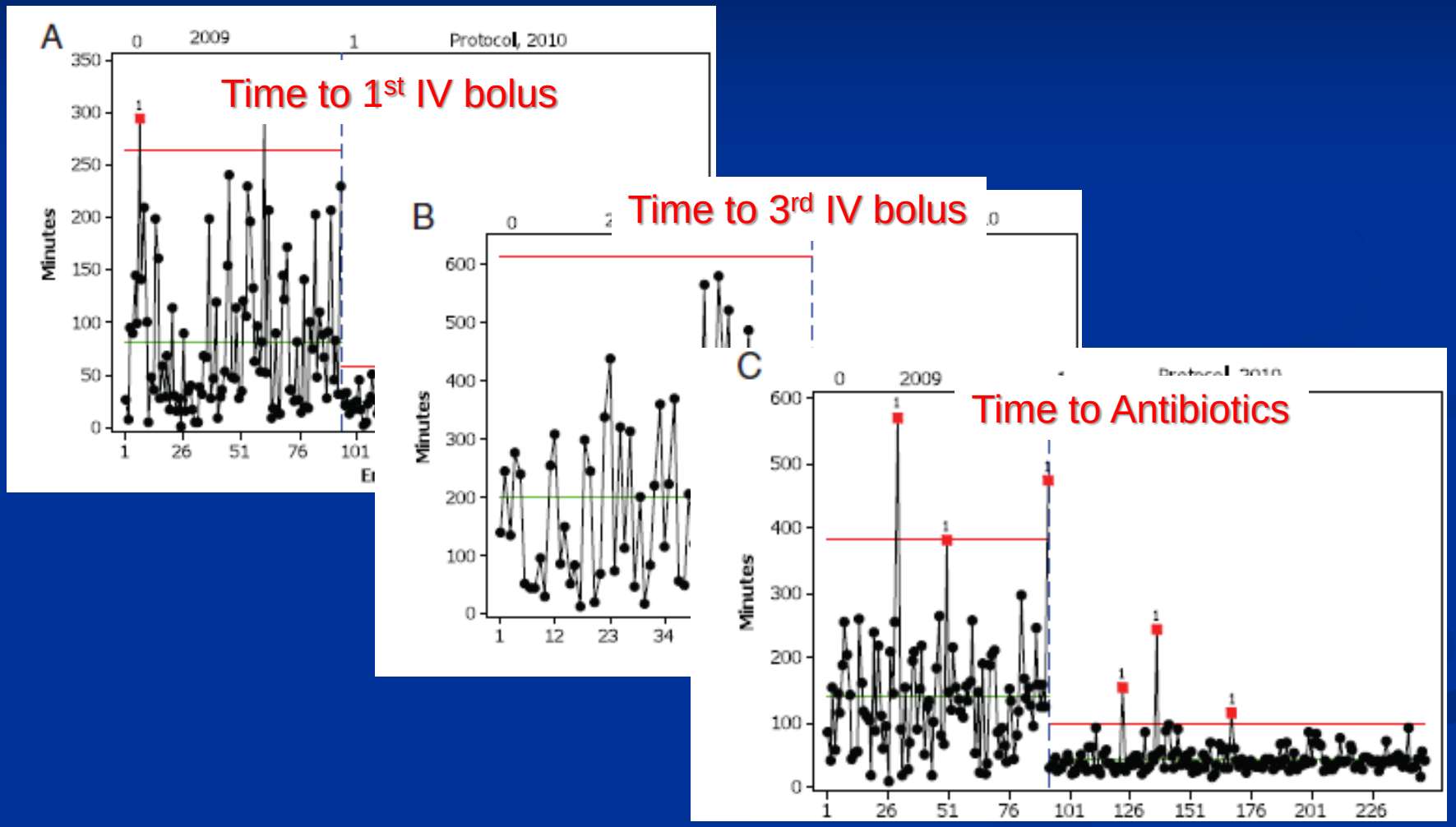
By JIM DWYER

Published: July 11, 2012

Screening for Sepsis

- Routine, systematic screening can facilitate:
  - Earlier sepsis recognition
  - More timely therapies
  - Improved patient outcomes

Texas Children's Experience



Cruz et al, *Pediatrics*, 2011

Development, Implementation, and Impact of an Automated Early Warning and Response System for Sepsis

Craig A. Umscheid, MD, MSCE[1,2,3,4,5,6*], Joel Betesh, MD[1], Christine VanZandbergen, PA, MPH[7], Asaf Hanish, MPH[1], Gordon Tait, BS[7], Mark E. Mikkelsen, MD, MSCE[2,3], Benjamin French, PhD[1,3,4,5], Barry D. Fuchs, MD, MS[2]

Sepsis Sniffer:

- 200% increase in rapid antibiotics
- 50% increase in rapid ICU transfer
- 50% increase in sepsis documentation

Required WBC, lactate → in pediatrics, often measured *after* sepsis recognized

Journal Hospital Medicine 2015

Definitions *vs* Diagnosis

Sepsis Definitions (2005)

- SIRS *plus*
- Low BP despite 40 ml/kg fluid
- Need for vasoactive
- Two of the following:
  - Base deficit < -5
  - Lactate > 4 mmol/L
  - UOP < 0.5 ml/kg/hr
  - CR > 5 seconds
  - Core-peripheral temp gap

Prognostic – Worse Outcomes

Shock Guidelines (2014)

- Fever/hypothermia *plus*
- Hypotension
- Altered mental status
- Bounding pulses, flash CR
- CR > 2 seconds
- UOP < 1 ml/kg/hr
- Cool or mottled extremities

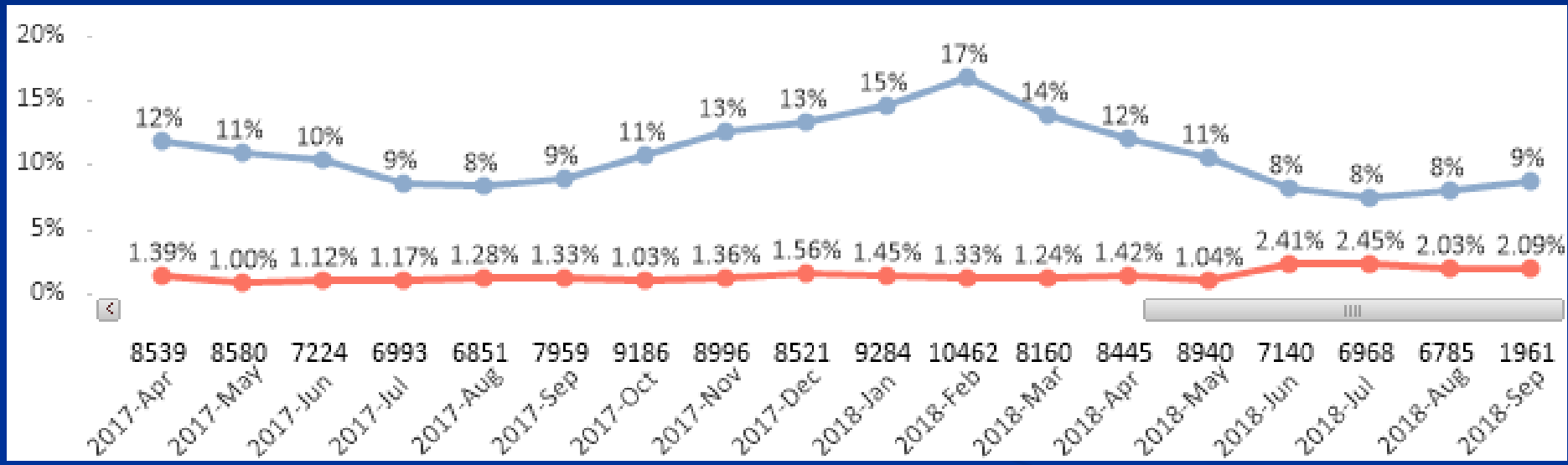
Operational – Early Recogntion, Tx

Goldstein et al *Ped Crit Care Med* 2005
ACCM *Ped Crit Care Med* 2017

CHOP ED Sepsis Screen

1. Fever (or concern for infection) w/ tachycardia or hypotension
2. Poor perfusion, altered MS, or high-risk condition
3. Rapid triage, “sepsis huddle”

CHOP ED: Sepsis Alert Burden

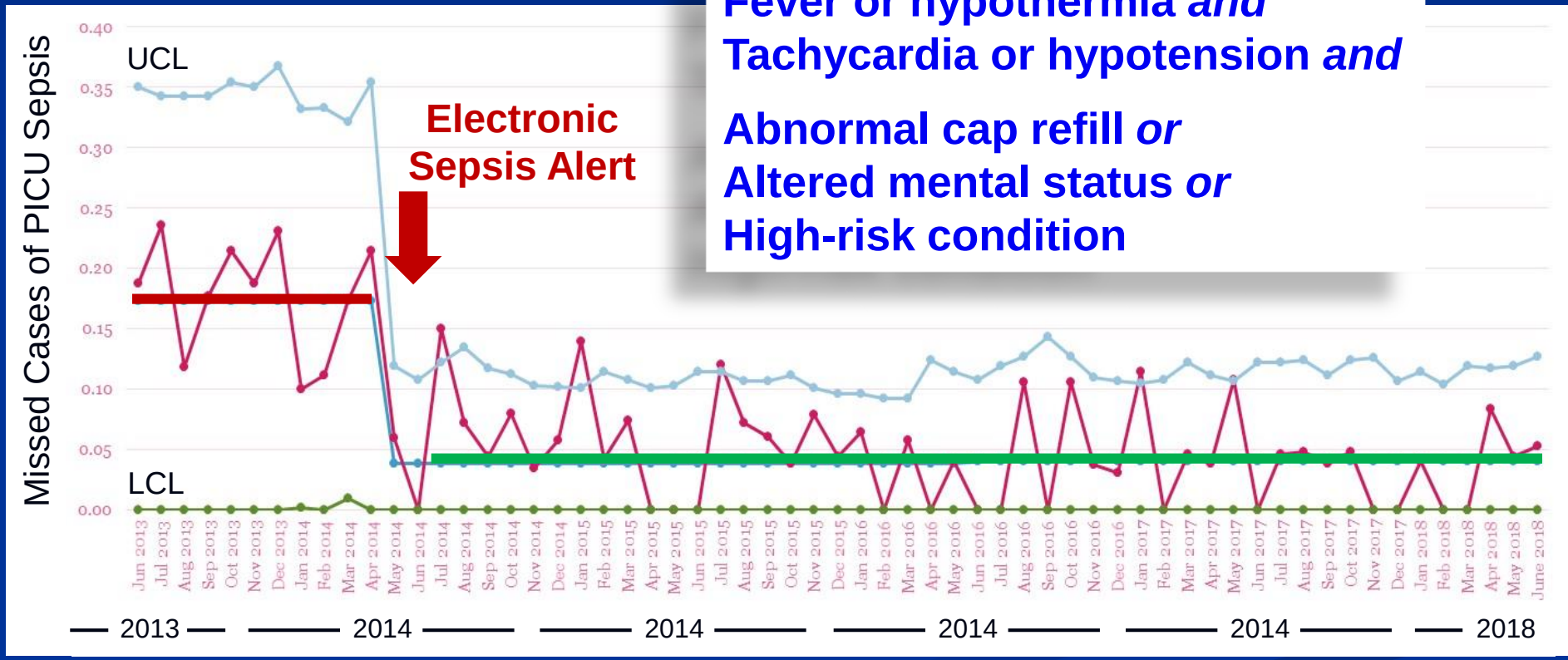


% ED patients with INITIAL alert

% ED patients with SECOND alert

EHR-Augmented Sepsis Recognition

(The CHOP ED Experience)



Balamuth, Weiss et al *Ann Emerg Med* 2017

Community ED Pediatric Sepsis Screen

1. Tachycardia or hypotension (based on age – see Table)?
   - ☐ No – STOP
   - ☐ Yes – Proceed to #2

T: _____ HR: _____ RR: _____

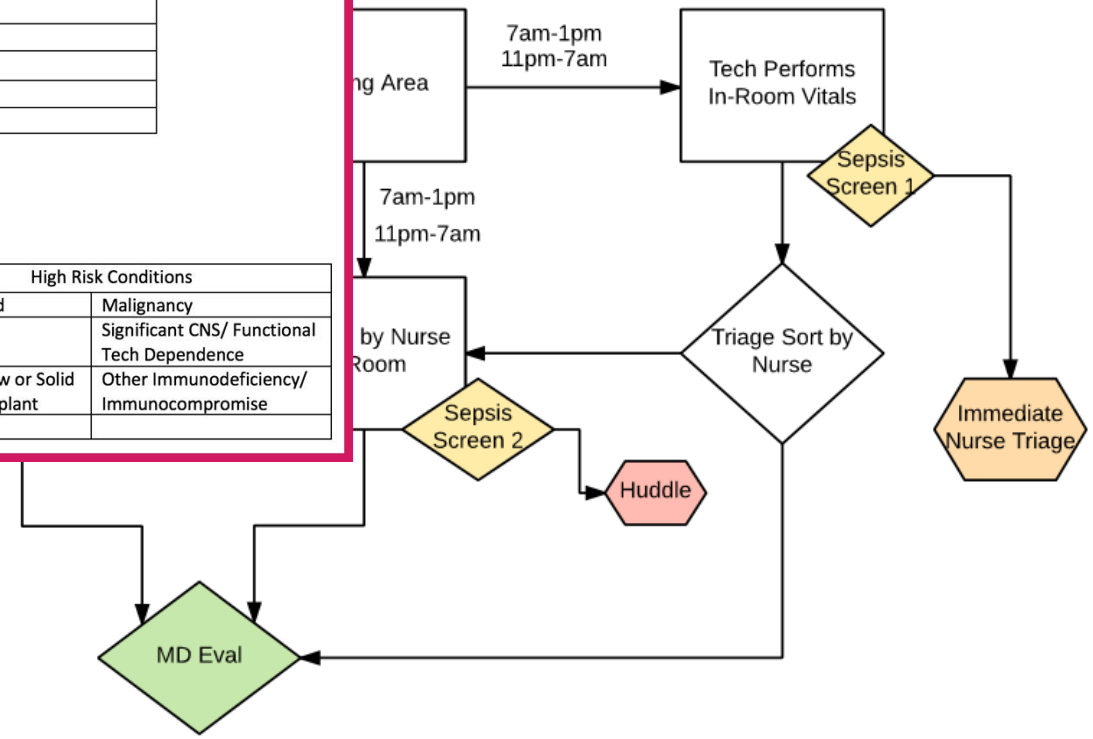
BP: _____ POx: _____

Age	Tachycardia (> 95th percentile)	Hypotension - Systolic (<5th percentile)
1 mon – 1 yr	>180	<75
>2 – 5 yrs	>140	<74
>6 – 12 yrs	>130	<83
>13 – 18 yrs	>110	<90

2. Is there fever, hypothermia or signs/symptoms of infection?
   - ☐ No – STOP
   - ☐ Yes – Proceed to #3

3. Is there a delay in capillary refill (>3 seconds), altered mental status, or existing high-risk condition (see Table)?
   - ☐ No – STOP
   - ☐ **Yes – Sepsis Huddle with ED Attending**

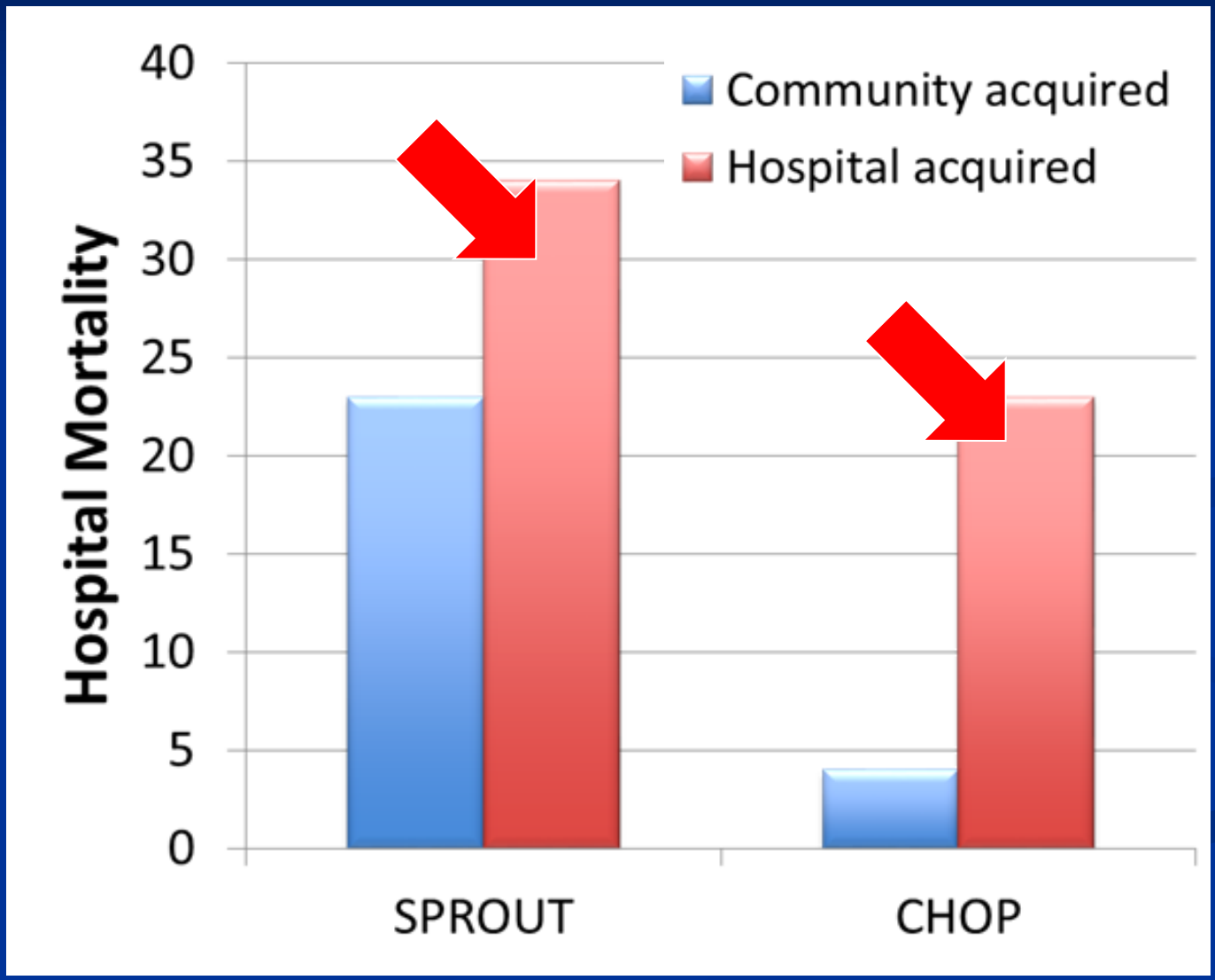
High Risk Conditions	
< 56 days old	Malignancy
Asplenia	Significant CNS/ Functional Tech Dependence
Bone Marrow or Solid Organ Transplant	Other Immunodeficiency/ Immunocompromise
Central Line	




HAP
The Hospital + Healthsystem
Association of Pennsylvania
Children's Hospital
of Philadelphia

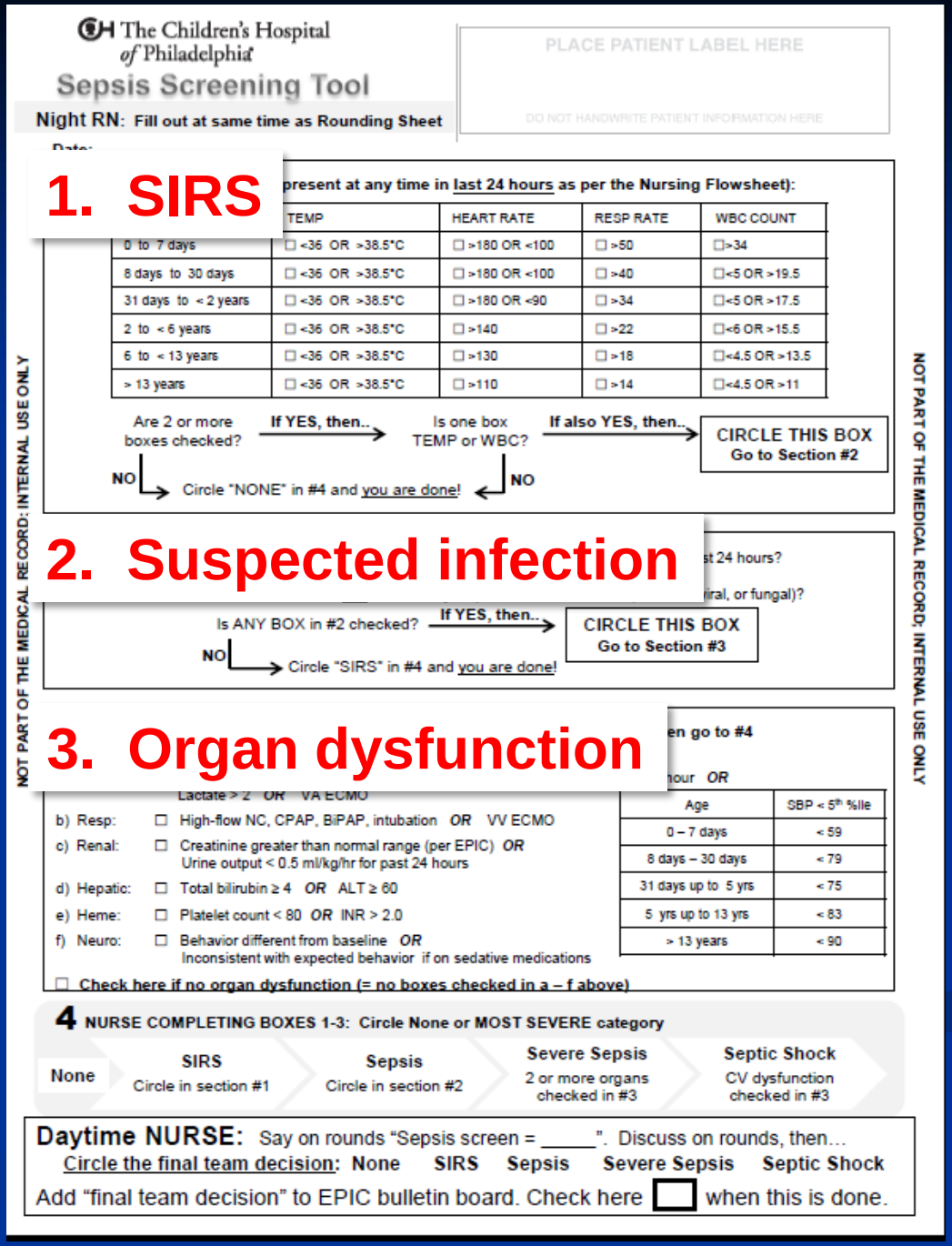

READING HEALTH
SYSTEM
Advancing Health. Transforming Lives.
Lehigh Valley
Health Network

Challenge of Hospital-Acquired Sepsis



Initial CHOP PICU screening tool

- Consensus criteria
- SIRS-based
- Laborious
- Inaccurate



The Children's Hospital of Philadelphia

Sepsis Screening Tool

PLACE PATIENT LABEL HERE

DO NOT HANDWRITE PATIENT INFORMATION HERE

Night RN: Fill out at same time as Rounding Sheet

Date:

1. SIRS

present at any time in last 24 hours as per the Nursing Flowsheet):

	TEMP	HEART RATE	RESP RATE	WBC COUNT
0 to 7 days	☐ <36 OR >38.5°C	☐ >180 OR <100	☐ >50	☐ >34
8 days to 30 days	☐ <36 OR >38.5°C	☐ >180 OR <100	☐ >40	☐ <5 OR >19.5
31 days to < 2 years	☐ <36 OR >38.5°C	☐ >180 OR <90	☐ >34	☐ <5 OR >17.5
2 to < 6 years	☐ <36 OR >38.5°C	☐ >140	☐ >22	☐ <6 OR >15.5
6 to < 13 years	☐ <36 OR >38.5°C	☐ >130	☐ >18	☐ <4.5 OR >13.5
> 13 years	☐ <36 OR >38.5°C	☐ >110	☐ >14	☐ <4.5 OR >11

Are 2 or more boxes checked? If YES, then.. Is one box TEMP or WBC? If also YES, then.. CIRCLE THIS BOX Go to Section #2

NO → Circle "NONE" in #4 and you are done! ← NO

2. Suspected infection

st 24 hours?

iral, or fungal)?

Is ANY BOX in #2 checked? If YES, then.. CIRCLE THIS BOX Go to Section #3

NO → Circle "SIRS" in #4 and you are done!

3. Organ dysfunction

en go to #4

hour *OR*

Age	SBP < 5th %ile
0 – 7 days	< 59
8 days – 30 days	< 79
31 days up to 5 yrs	< 75
5 yrs up to 13 yrs	< 83
> 13 years	< 90

Lactate > 2 *OR* VA ECMO

b) Resp: ☐ High-flow NC, CPAP, BiPAP, intubation *OR* VV ECMO

c) Renal: ☐ Creatinine greater than normal range (per EPIC) *OR* Urine output < 0.5 ml/kg/hr for past 24 hours

d) Hepatic: ☐ Total bilirubin ≥ 4 *OR* ALT ≥ 60

e) Heme: ☐ Platelet count < 80 *OR* INR > 2.0

f) Neuro: ☐ Behavior different from baseline *OR* Inconsistent with expected behavior if on sedative medications

☐ Check here if no organ dysfunction (= no boxes checked in a – f above)

4 NURSE COMPLETING BOXES 1-3: Circle None or MOST SEVERE category

None | SIRS: Circle in section #1 | Sepsis: Circle in section #2 | Severe Sepsis: 2 or more organs checked in #3 | Septic Shock: CV dysfunction checked in #3

Daytime NURSE: Say on rounds "Sepsis screen = _____". Discuss on rounds, then…

Circle the final team decision: None SIRS Sepsis Severe Sepsis Septic Shock

Add "final team decision" to EPIC bulletin board. Check here ☐ when this is done.

NOT PART OF THE MEDICAL RECORD; INTERNAL USE ONLY

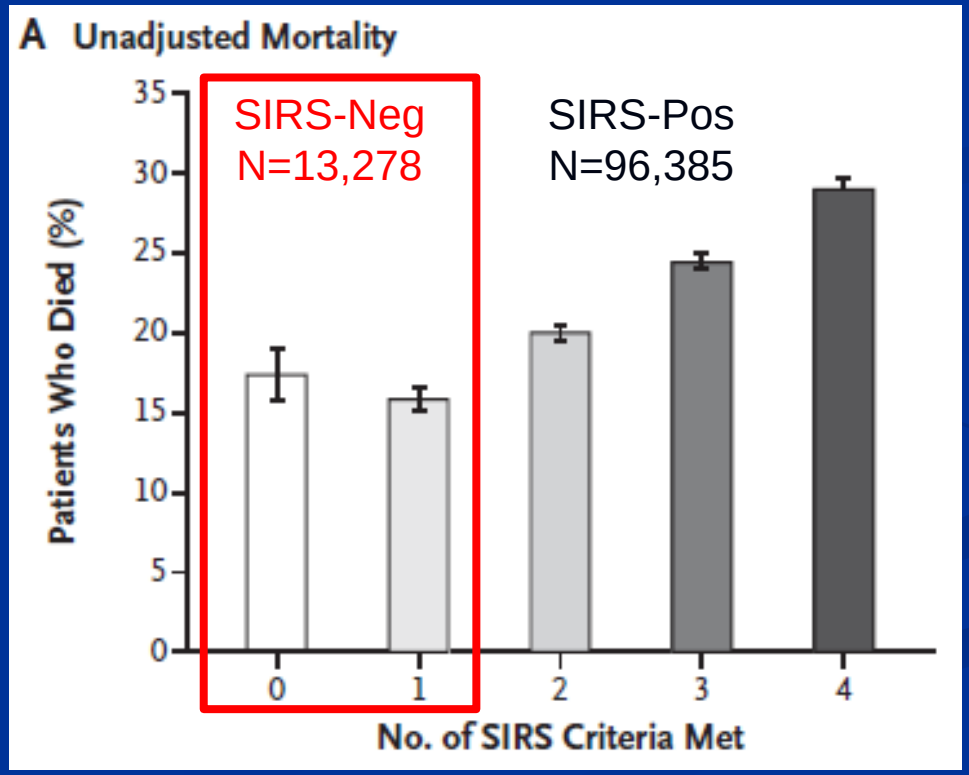
NOT PART OF THE MEDICAL RECORD; INTERNAL USE ONLY

ORIGINAL ARTICLE

Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis

Kirsi-Maija Kaukonen, M.D., Ph.D., Michael Bailey, Ph.D., David Pilcher, F.C.I.C.M., D. Jamie Cooper, M.D., Ph.D., and Rinaldo Bellomo, M.D., Ph.D.

N=109,663 adult pts in 172 Aust/NZ ICUs
Infection + organ failure



NEJM 2015

ORIGINAL CONTRIBUTION

CME

The Prevalence and Diagnostic Utility of Systemic Inflammatory Response Syndrome Vital Signs in a Pediatric Emergency Department

Halden F. Scott, MD, Sara J. Deakyne, MPH, Jason M. Woods, MD, and Lalit Bajaj, MD, MPH

N=40,356 pediatric pts in single US pediatric ED

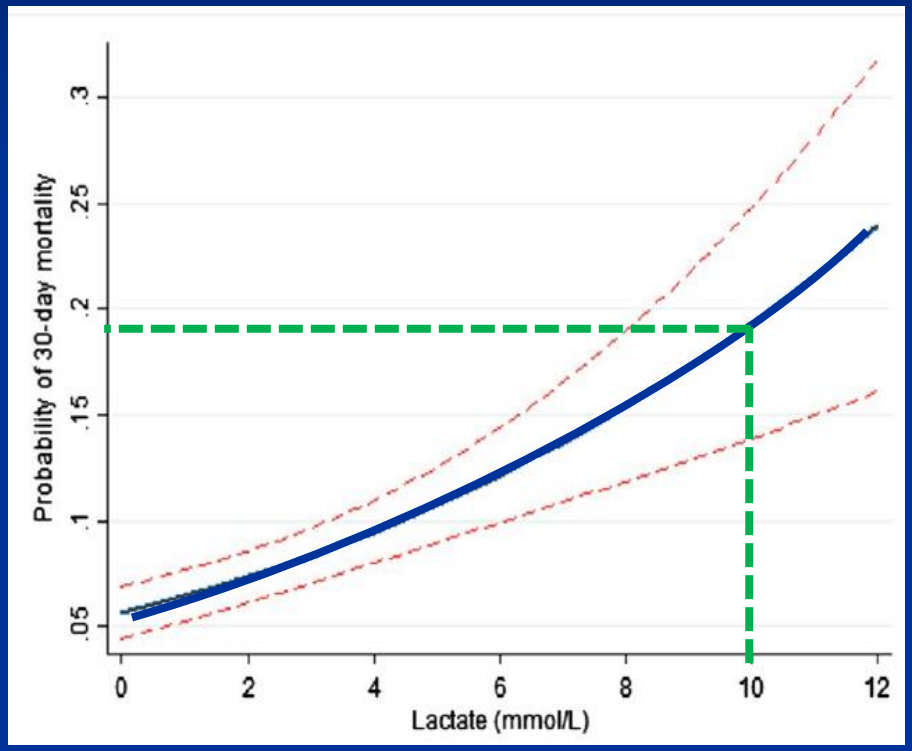
Who needs PICU admission?

Condition	Sensitivity	Specificity
Any SIRS pair	**23%** (15-33%)	**85%** (84-85%)

Value (95% confidence interval)

Acad Emerg Med 2015

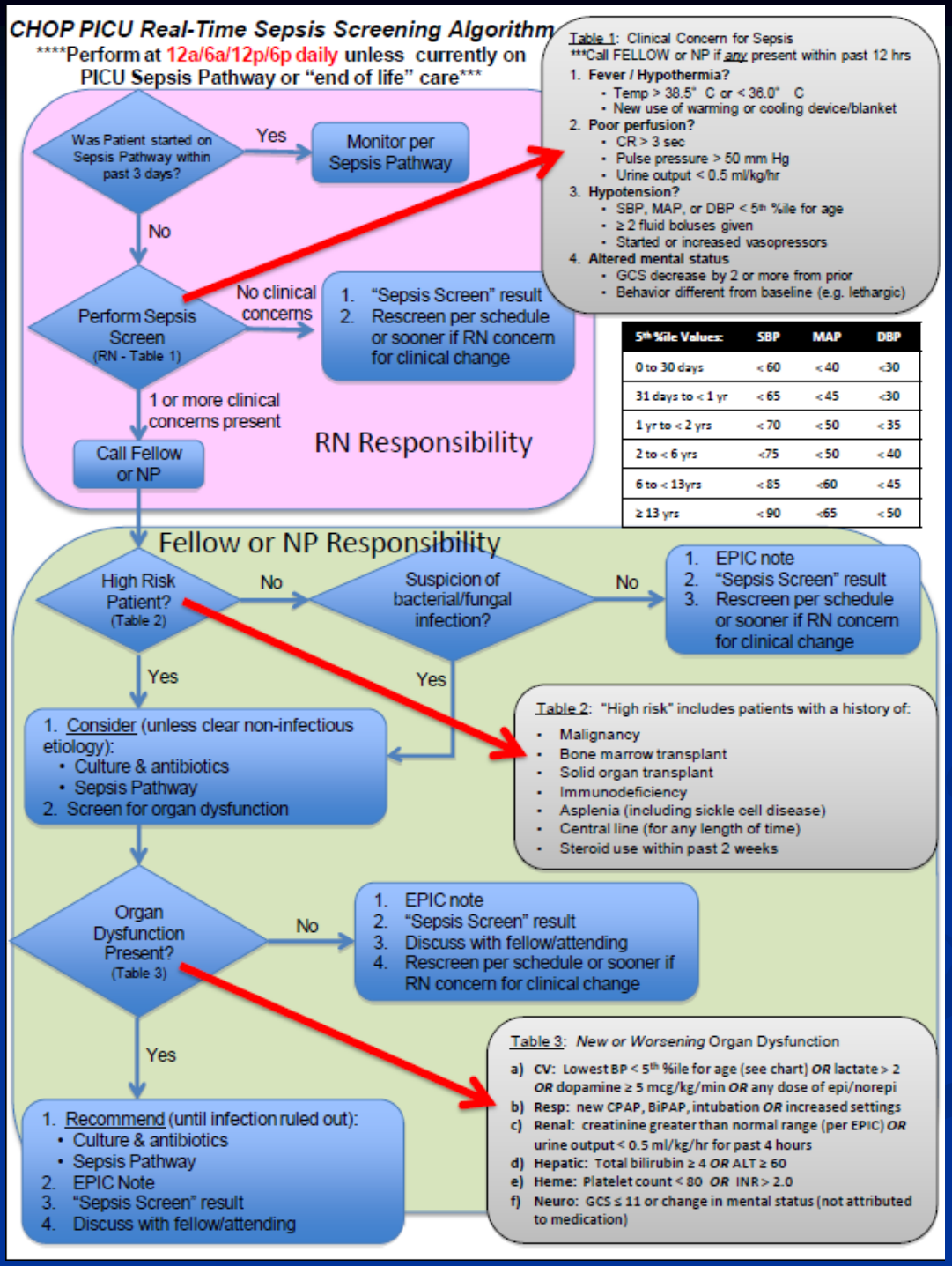
Lactate in Pediatric Septic Shock



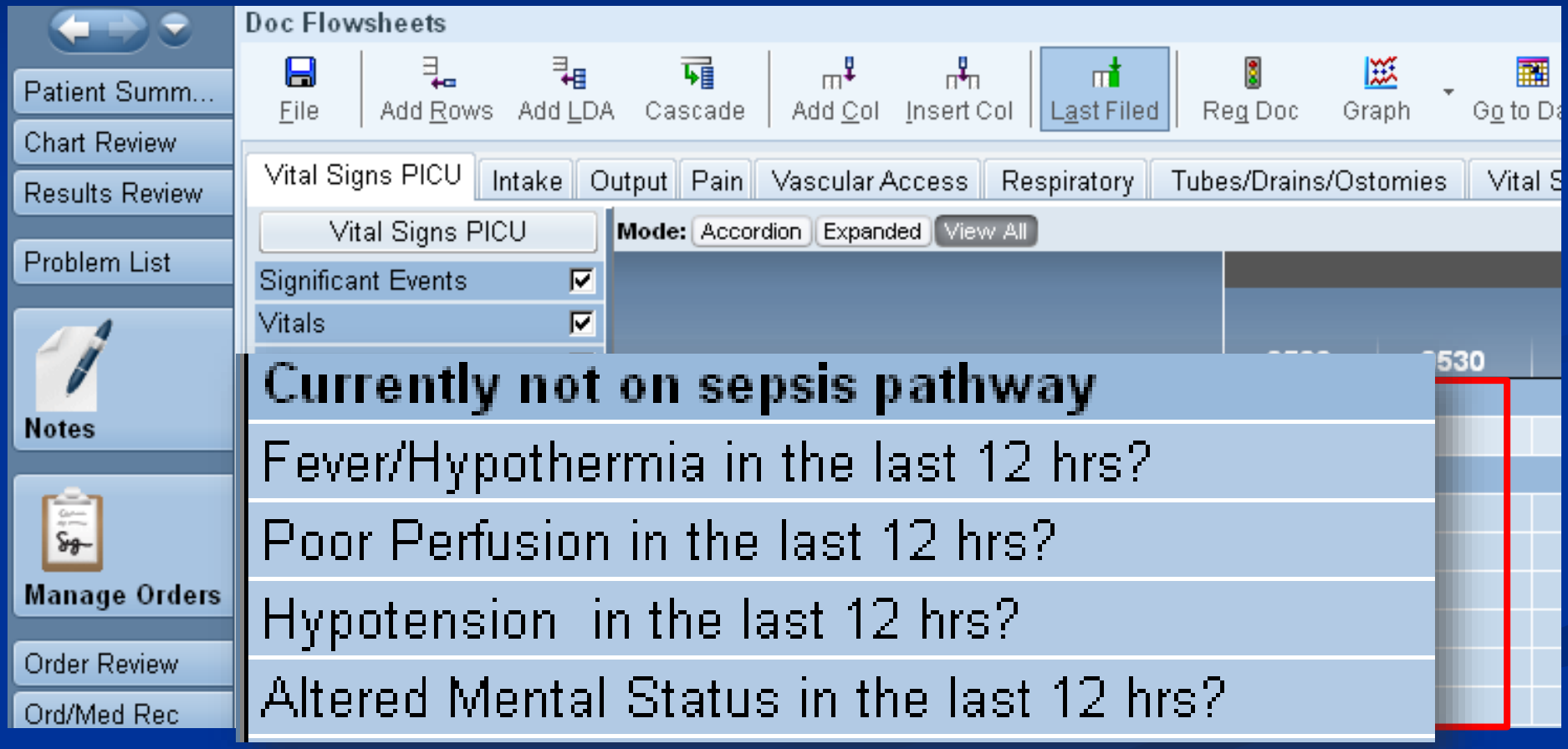
Schlapbach et al *Intensive Care Med* 2017

To consider:

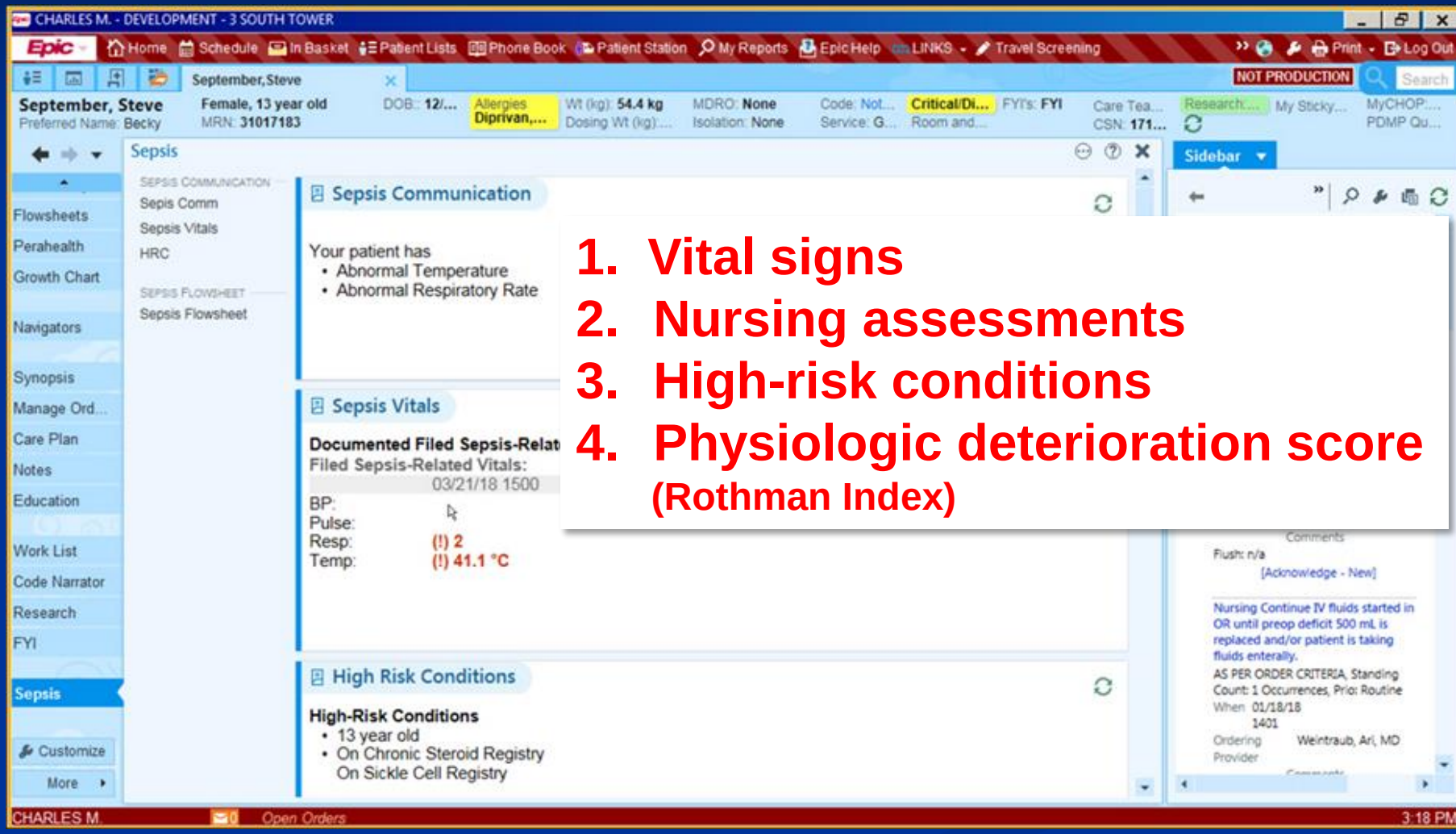
- Most high lactate do well
- Low lactate not always reassuring
- Current emphasis (correctly!) on perfusion


CHOP PICU Real-Time Sepsis Screening Algorithm
****Perform at 12a/6a/12p/6p daily unless currently on PICU Sepsis Pathway or "end of life" care***
Was Patient started on Sepsis Pathway within past 3 days?
Yes
Monitor per Sepsis Pathway
No
Perform Sepsis Screen (RN - Table 1)
No clinical concerns
1. "Sepsis Screen" result
2. Rescreen per schedule or sooner if RN concern for clinical change
1 or more clinical concerns present
Call Fellow or NP
RN Responsibility
Table 1: Clinical Concern for Sepsis
***Call FELLOW or NP if any present within past 12 hrs
1. Fever / Hypothermia?
• Temp > 38.5° C or < 36.0° C
• New use of warming or cooling device/blanket
2. Poor perfusion?
• CR > 3 sec
• Pulse pressure > 50 mm Hg
• Urine output < 0.5 ml/kg/hr
3. Hypotension?
• SBP, MAP, or DBP < 5th %ile for age
• ≥ 2 fluid boluses given
• Started or increased vasopressors
4. Altered mental status
• GCS decrease by 2 or more from prior
• Behavior different from baseline (e.g. lethargic)
5th %ile Values: SBP MAP DBP
0 to 30 days < 60 < 40 <30
31 days to < 1 yr < 65 < 45 <30
1 yr to < 2 yrs < 70 < 50 < 35
2 to < 6 yrs <75 < 50 < 40
6 to < 13yrs < 85 <60 < 45
≥ 13 yrs < 90 <65 < 50
Fellow or NP Responsibility
High Risk Patient? (Table 2)
No
Suspicion of bacterial/fungal infection?
No
1. EPIC note
2. "Sepsis Screen" result
3. Rescreen per schedule or sooner if RN concern for clinical change
Yes
Yes
1. Consider (unless clear non-infectious etiology):
• Culture & antibiotics
• Sepsis Pathway
2. Screen for organ dysfunction
Table 2: "High risk" includes patients with a history of:
• Malignancy
• Bone marrow transplant
• Solid organ transplant
• Immunodeficiency
• Asplenia (including sickle cell disease)
• Central line (for any length of time)
• Steroid use within past 2 weeks
Organ Dysfunction Present? (Table 3)
No
1. EPIC note
2. "Sepsis Screen" result
3. Discuss with fellow/attending
4. Rescreen per schedule or sooner if RN concern for clinical change
Yes
1. Recommend (until infection ruled out):
• Culture & antibiotics
• Sepsis Pathway
2. EPIC Note
3. "Sepsis Screen" result
4. Discuss with fellow/attending
Table 3: New or Worsening Organ Dysfunction
a) CV: Lowest BP < 5th %ile for age (see chart) OR lactate > 2 OR dopamine ≥ 5 mcg/kg/min OR any dose of epi/norepi
b) Resp: new CPAP, BiPAP, intubation OR increased settings
c) Renal: creatinine greater than normal range (per EPIC) OR urine output < 0.5 ml/kg/hr for past 4 hours
d) Hepatic: Total bilirubin ≥ 4 OR ALT ≥ 60
e) Heme: Platelet count < 80 OR INR > 2.0
f) Neuro: GCS ≤ 11 or change in mental status (not attributed to medication)

CHOP PICU Sepsis Screen



CHOP Hospital-Wide Sepsis Screen

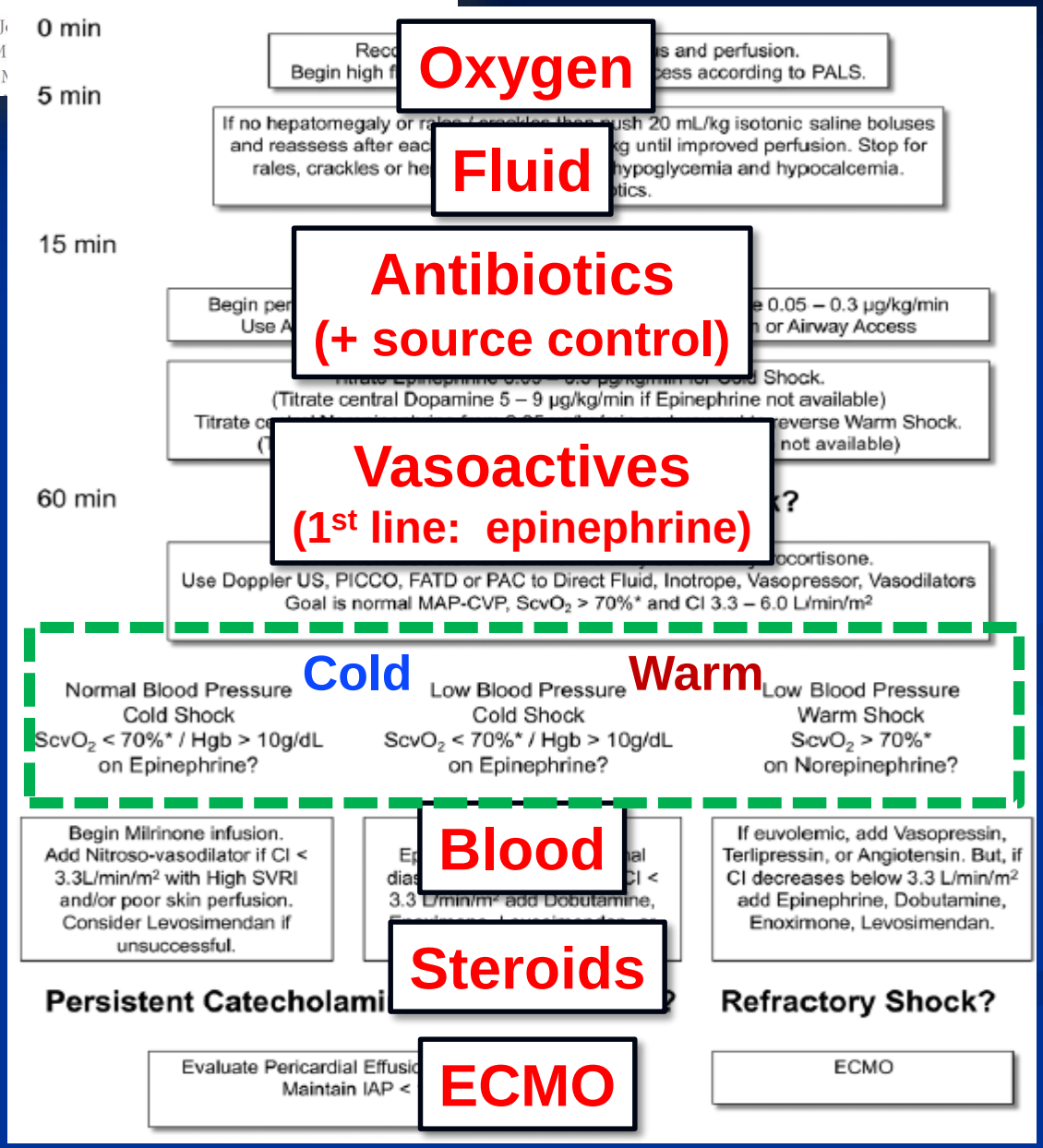


1. **Vital signs**
2. **Nursing assessments**
3. **High-risk conditions**
4. **Physiologic deterioration score (Rothman Index)**

How Can We Use Guidelines to Optimize Resuscitation?

American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock

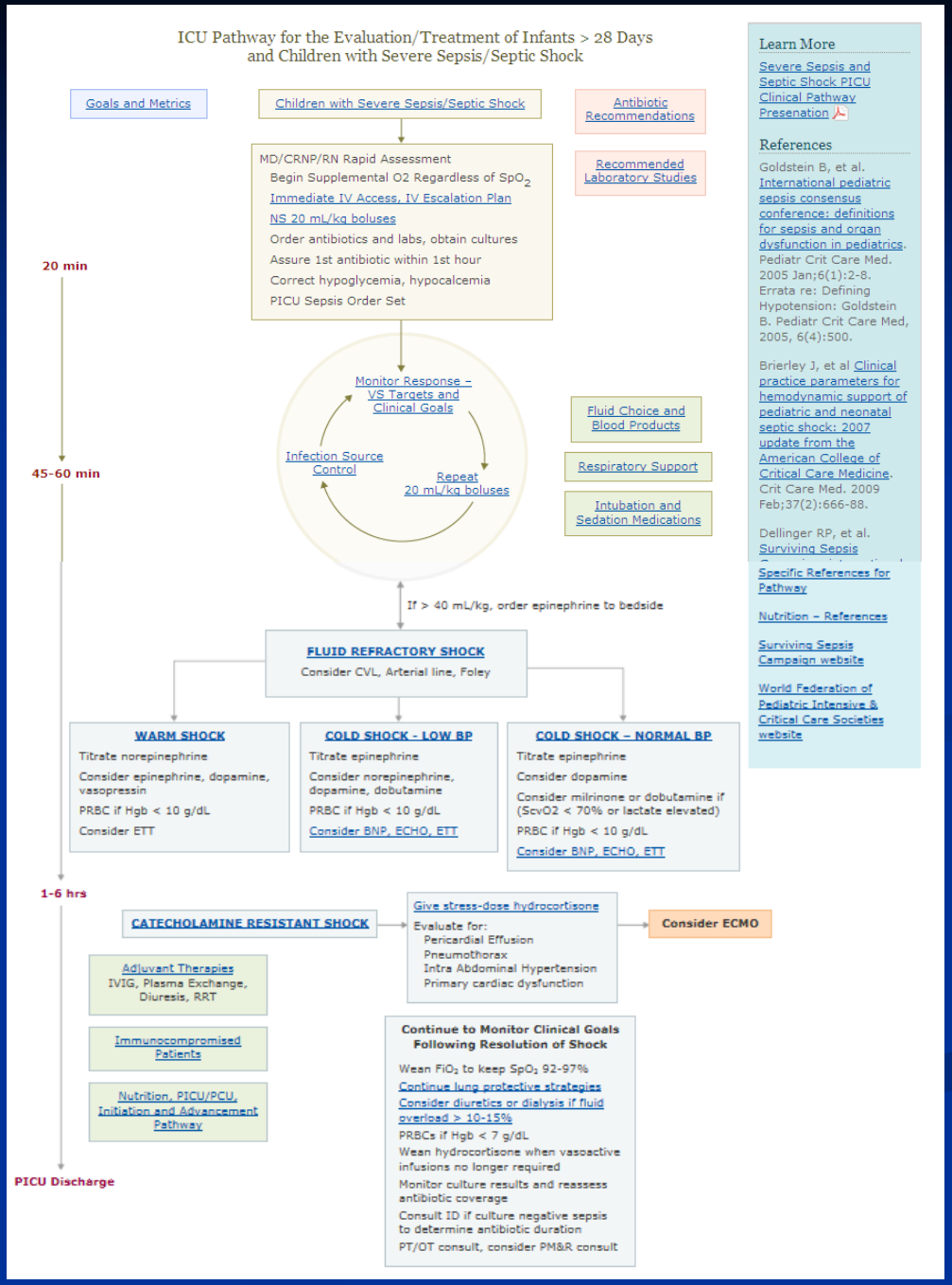
Alan L. Davis, MD, MPH, FAAP, FCCM[1]; J
Andreas J. Deymann, MD[3]; John C. Lin, M
Regina S. Okhuysen-Cawley, MD, FAAP[5]; N



PCCM 2017
CCM 2017

CHOP Sepsis Pathway

(www.chop.edu)



How do we use guidelines to improve patient outcomes?

- Implement what we know works
- Determine what may work better

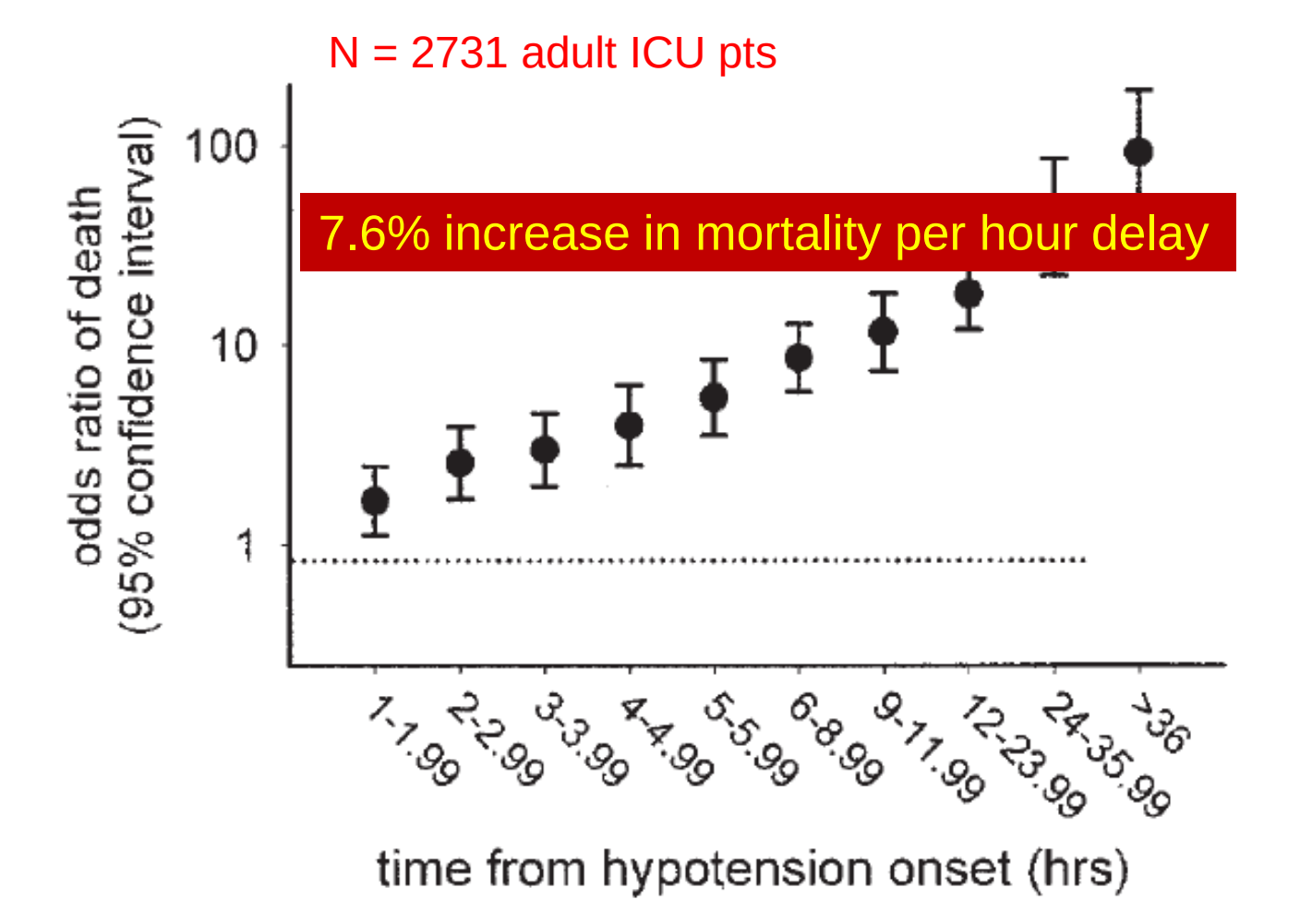
How to Optimize Sepsis Resuscitation

- What do we know that works for sepsis?
  - Early antibiotics
  - Goal-directed shock reversal
  - “Bundled” care

How to Optimize Sepsis Resuscitation

- What do we know that works for sepsis?
  - **Early antibiotics**
  - Goal-directed shock reversal
  - “Bundled” care

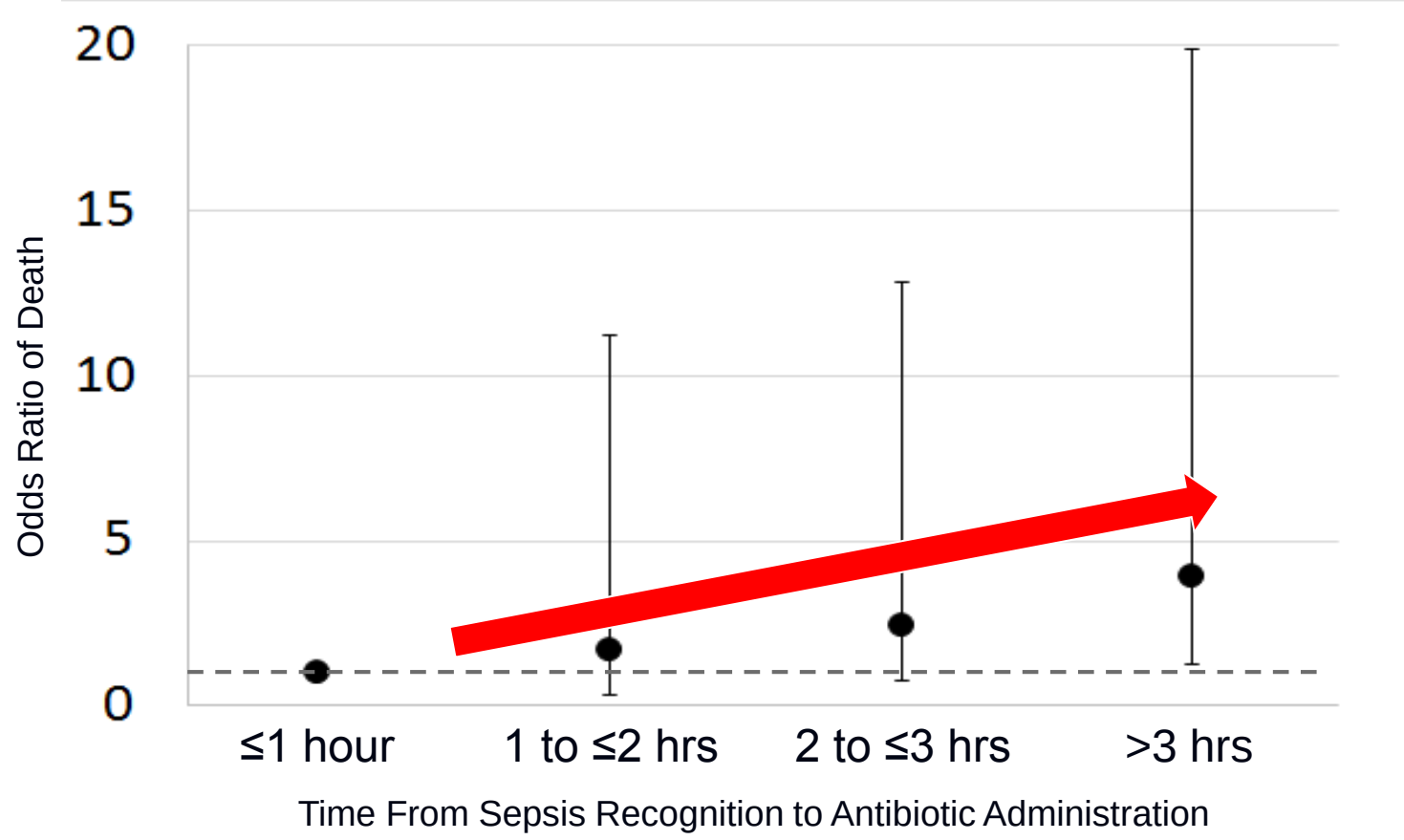
Delayed Antibiotics Worsens Mortality



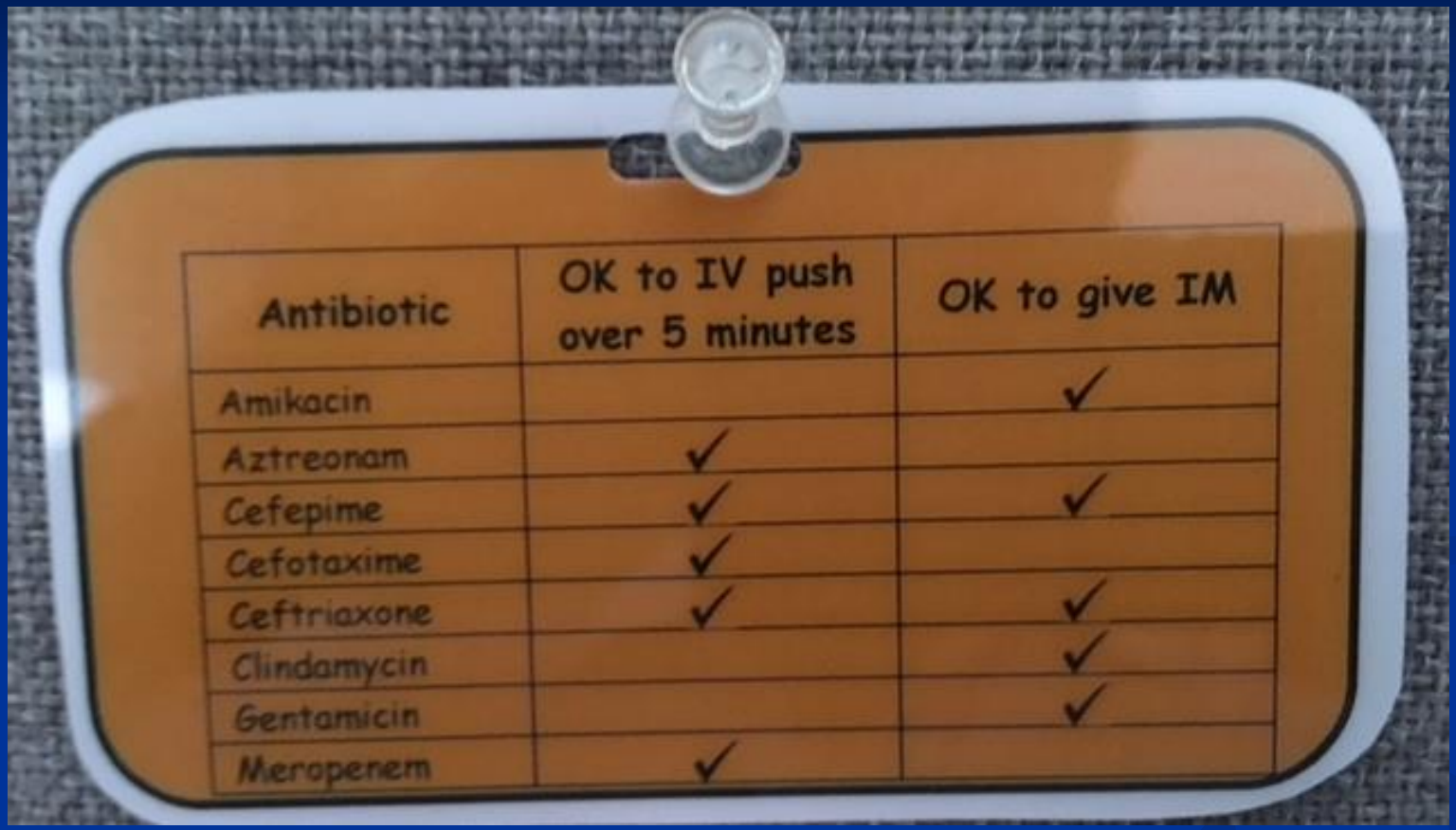
Kumar et al, *Crit Care Med*, 2006

Delayed Antimicrobial Therapy Increases Mortality and Organ Dysfunction Duration in Pediatric Sepsis

Scott L. Weiss, MD[1]; Julie C. Fitzgerald, MD, PhD[1]; Fran Balamuth, MD, PhD[2]; Elizabeth R. Alpern, MD, MSCE[3]; Jane Lavelle, MD[2]; Marianne Chilutti, MS[4]; Robert Grundmeier, MD[4,5]; Vinay M. Nadkarni, MD, MS[1]; Neal J. Thomas, MD, MSc[6]



Crit Care Med 2014



Antibiotic	OK to IV push over 5 minutes	OK to give IM
Amikacin		✓
Aztreonam	✓	
Cefepime	✓	✓
Cefotaxime	✓	
Ceftriaxone	✓	✓
Clindamycin		✓
Gentamicin		✓
Meropenem	✓	

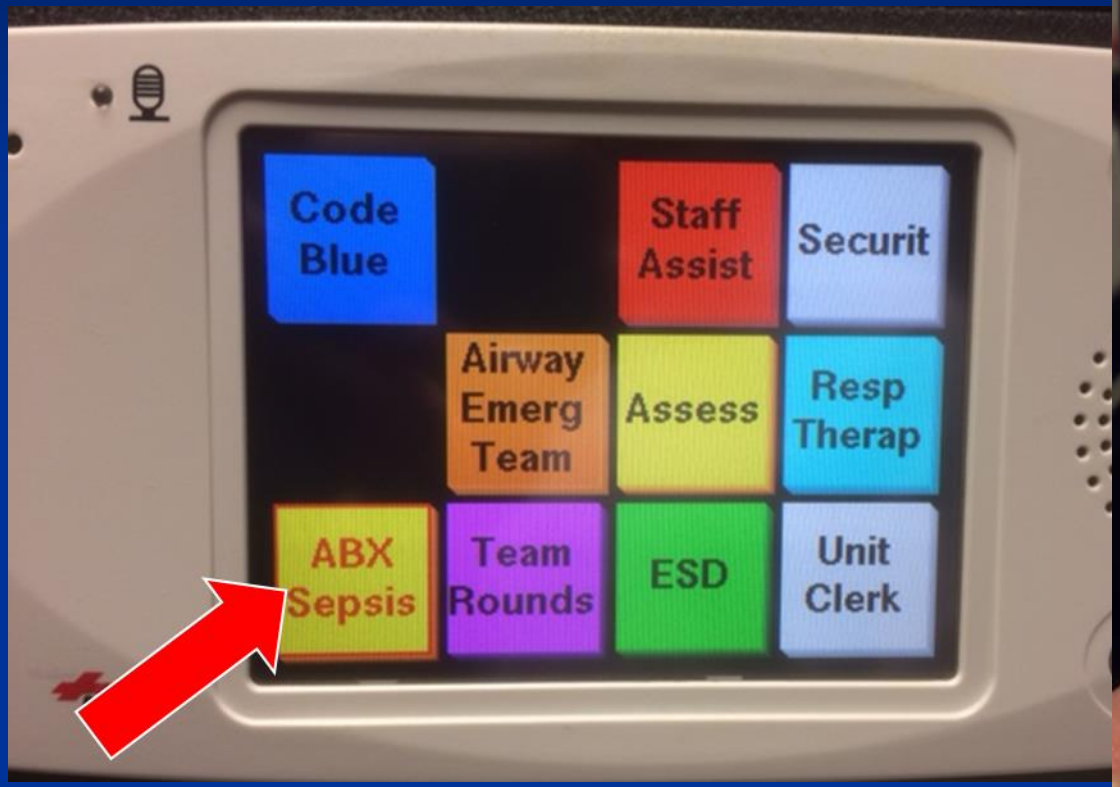
The Children's Hospital of Philadelphia Antimicrobial Stewardship Program Guidelines:
Antibiotic Recommendations for Patients with Severe Sepsis/Septic Shock

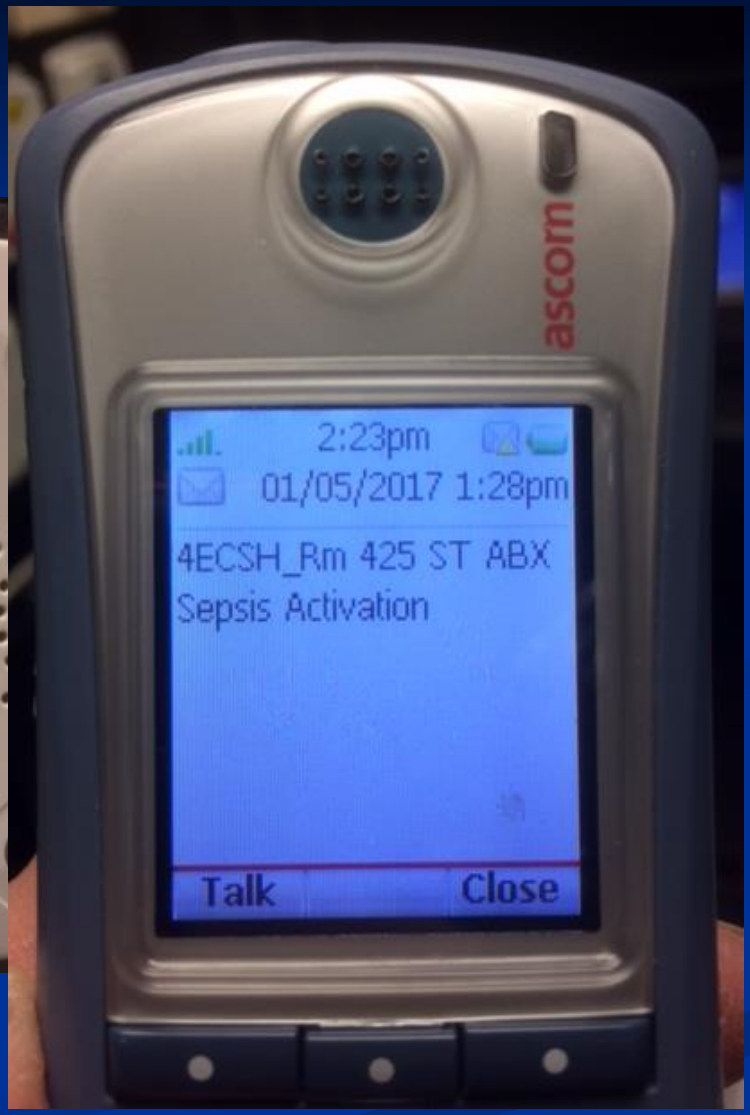
Use Sepsis Order Set – administer antibiotics in the order listed
1st antibiotic within 1 hour
Remaining antibiotics within 3 hours

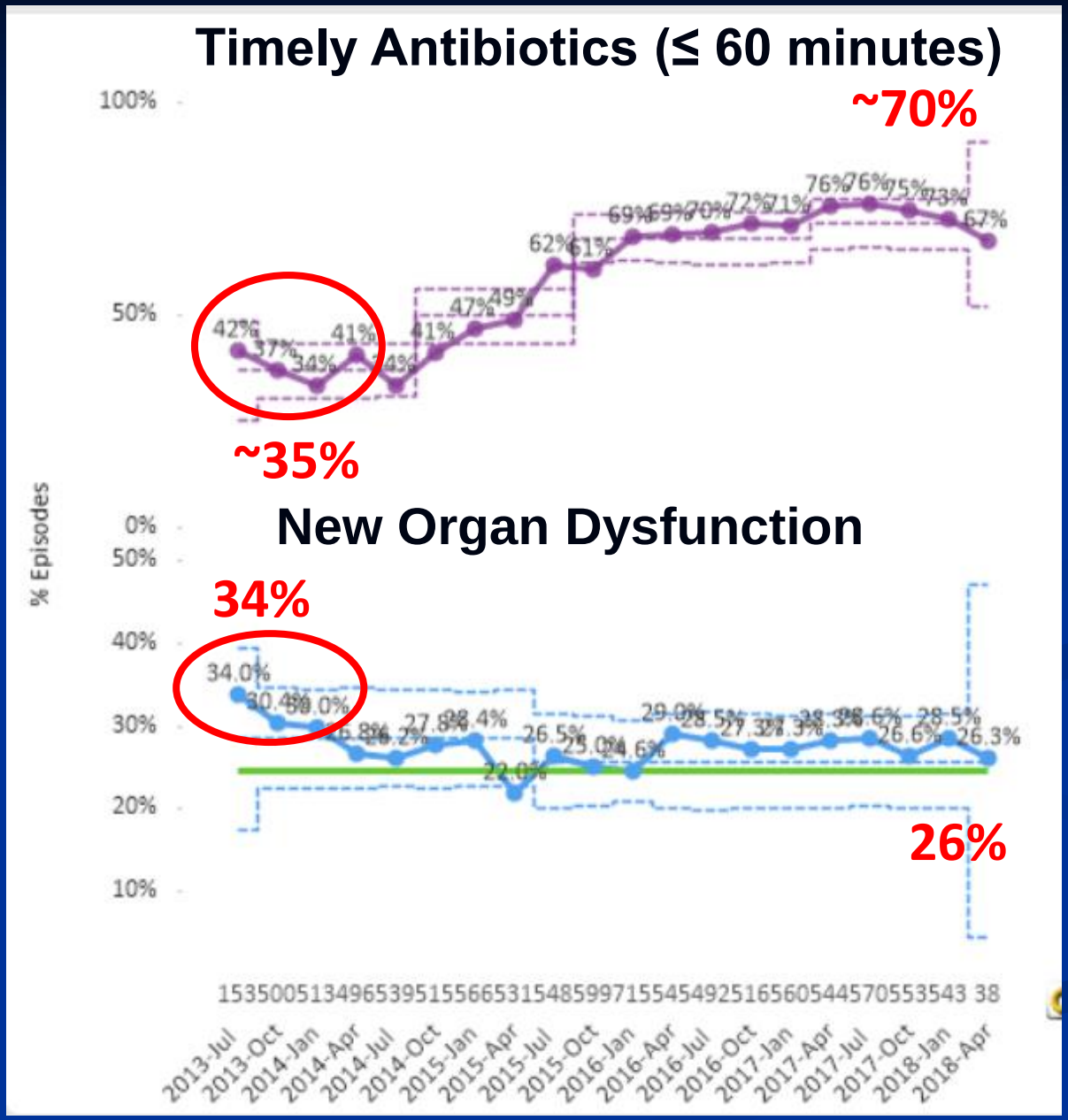
Healthy Patient No Central Line	Patient with any of the following: - Central line - Chronic medical condition - Immunocompromised - Oncologic process - Receiving immunosuppressive medications[1] - Recent hospitalization (> 4 days within 2 months)	In	
1. Ceftriaxone[3] 2. Vancomycin 3. Gentamicin	1. Cefepime[3] 2. Vancomycin 3. Gentamicin	1. Piperacillin/tazobactam[3,4] 2. Vancomycin 3. Gentamicin	1. Imipenem 2. Vancomycin 3. Amikacin

Give beta-lactam or cephalosporin FIRST as "push"

CONSIDER ADDITIONAL ANTIMCIROBIALS WITH THE FOLLOWING CLINCIAL SCENERIOS	
Toxin Medicated Syndromes	Clindamycin
Risk for Fungemia[4]	Caspofungin
Suspicion of Influenza	Oseltamivir

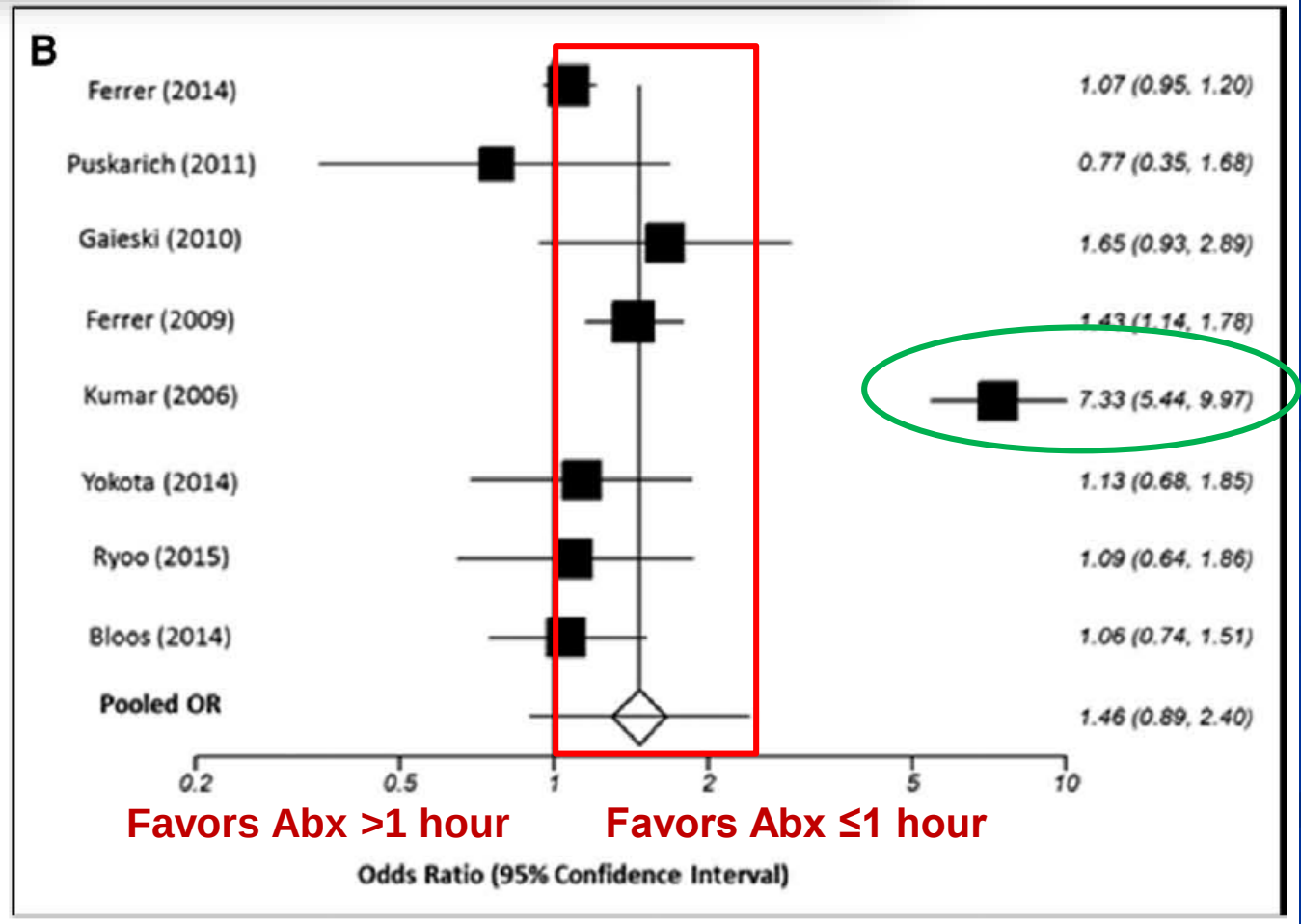

Code Blue
Staff Assist
Securit
Airway Emerg Team
Assess
Resp Therap
ABX Sepsis
Team Rounds
ESD
Unit Clerk


ascom
2:23pm
01/05/2017 1:28pm
4ECSH_Rm 425 ST ABX Sepsis Activation
Talk
Close


Timely Antibiotics (≤ 60 minutes)
~70%
~35%
New Organ Dysfunction
34%
26%
% Episodes
100%
50%
0%
40%
30%
20%
10%
2013-Jul
2013-Oct
2014-Jan
2014-Apr
2014-Jul
2014-Oct
2015-Jan
2015-Apr
2015-Jul
2015-Oct
2016-Jan
2016-Apr
2016-Jul
2016-Oct
2017-Jan
2017-Apr
2017-Jul
2017-Oct
2018-Jan
2018-Apr

The Impact of Timing of Antibiotics on Outcomes in Severe Sepsis and Septic Shock: A Systematic Review and Meta-Analysis*

Sarah A. Sterling, MD; W. Ryan Miller, MD; Jason Pryor, MD; Michael A. Puskarich, MD; Alan E. Jones, MD



Critical Care Med 2015

How to Optimize Sepsis Resuscitation

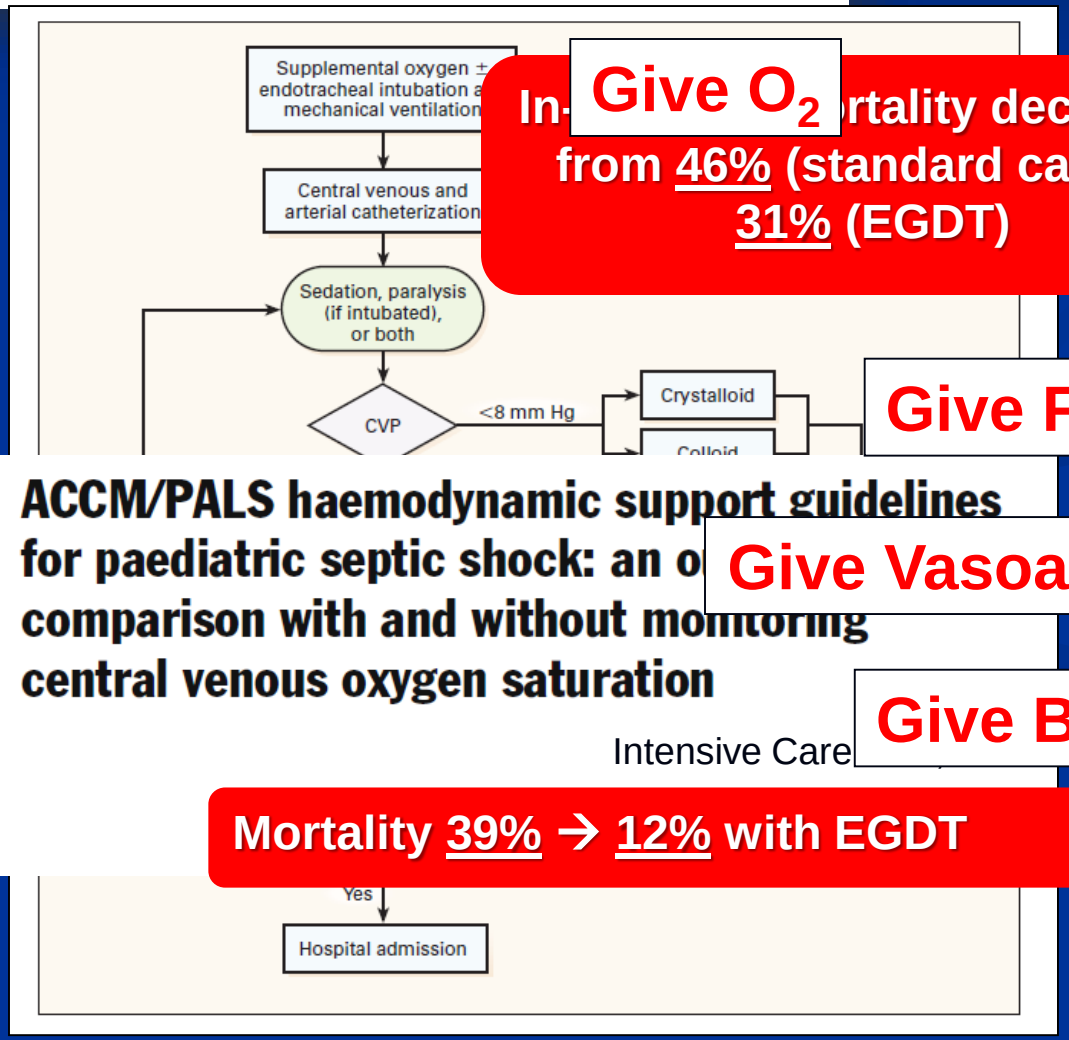
- What do we know that works for sepsis?
  - Early antibiotics
  - **Goal-directed shock reversal**
  - “Bundled” care

The New England Journal of Medicine

NEJM, 2001

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*



In- rtality decreased from 46% (standard care) to 31% (EGDT)

Give O_2

Give Fluid

Give Vasoactives

Give Blood

Mortality 39% → 12% with EGDT

Cláudio F. de Oliveira
Débora S. F. de Oliveira
Adriana F. C. Gottschald
Juliana D. G. Moura
Graziela A. Costa
Andréa C. Ventura
José Carlos Fernandes
Flávio A. C. Vaz
Joseph A. Carcillo
Emanuel P. Rivers
Eduardo J. Troster

ACCM/PALS haemodynamic support guidelines for paediatric septic shock: an o comparison with and without mo central venous oxygen saturation

Intensive Care

Is "Early Goal-Directed Therapy" Still Important?


ORIGINAL ARTICLE

A Randomized Trial of Protocol-Based Care for Early Septic Shock

ProCESS (2014)


ORIGINAL ARTICLE

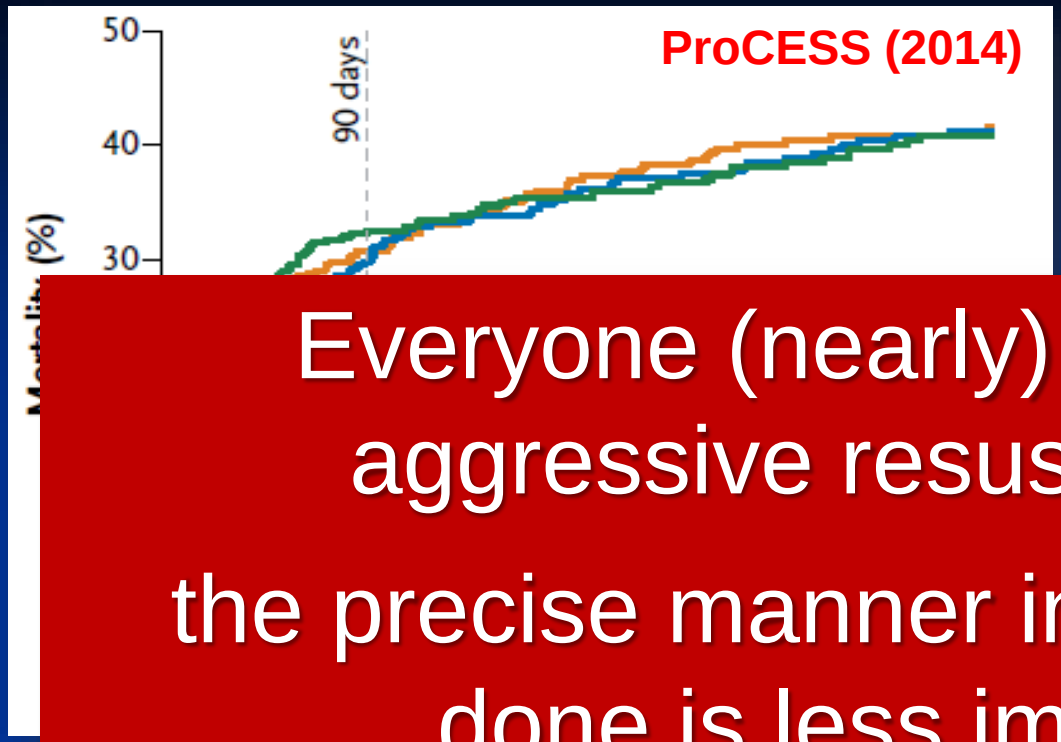
Goal-Directed Resuscitation for Patients with Early Septic Shock

ARISE (2014)


ORIGINAL ARTICLE

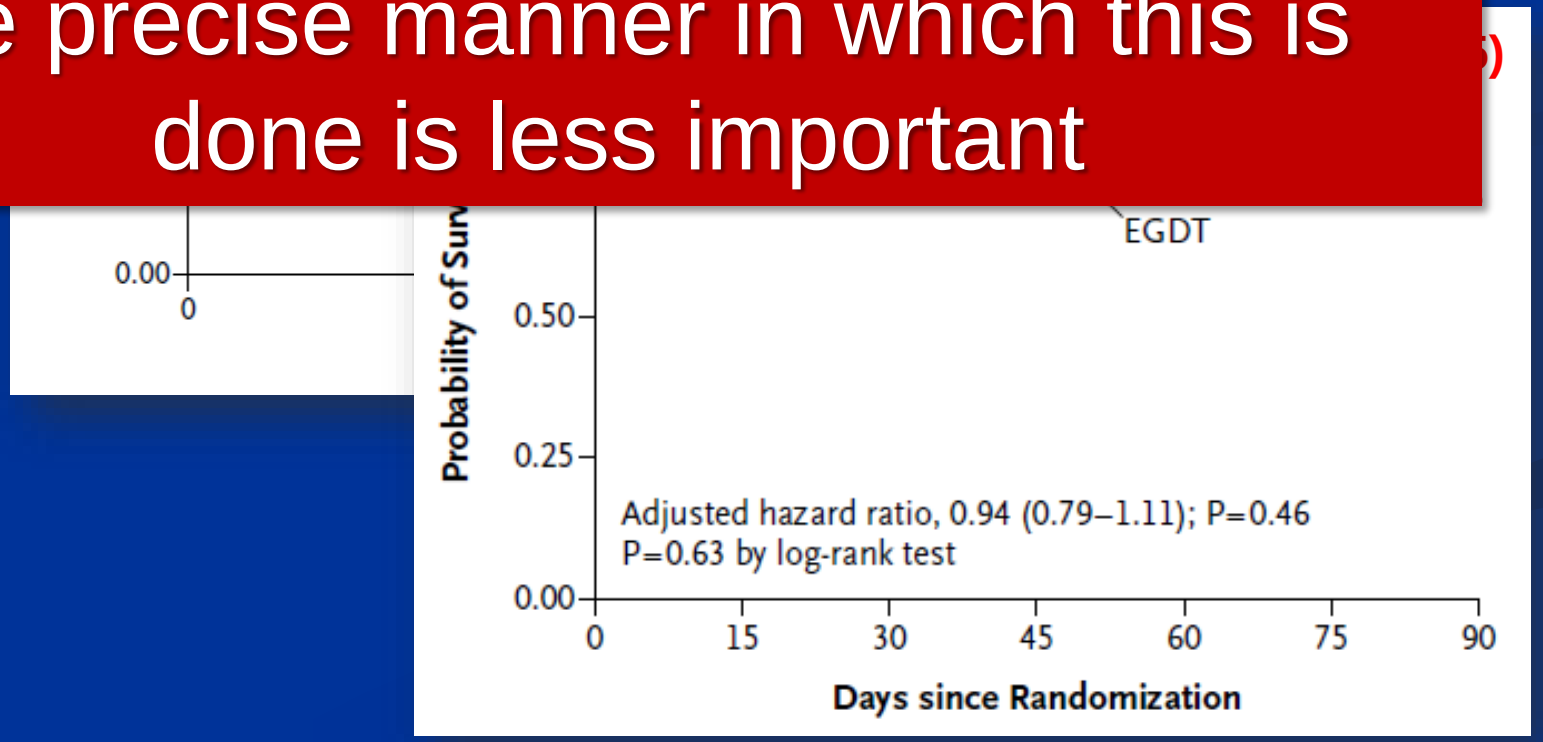
Trial of Early, Goal-Directed Resuscitation for Septic Shock

ProMISe (2015)



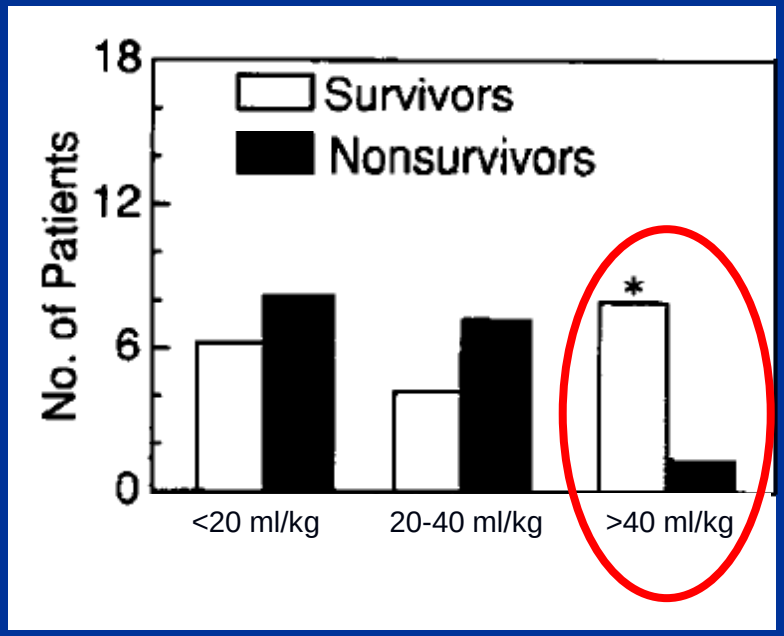
Everyone (nearly) gets early, aggressive resuscitation –

the precise manner in which this is done is less important



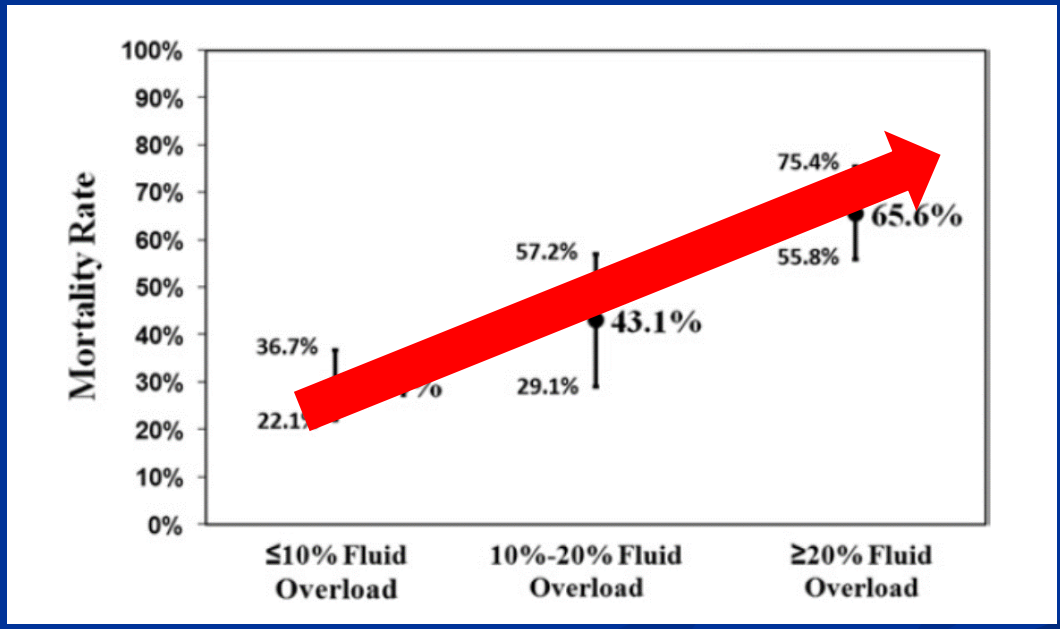
How Much Fluid to Give?

Then…



Carcillo et al *JAMA* 1991

Now…



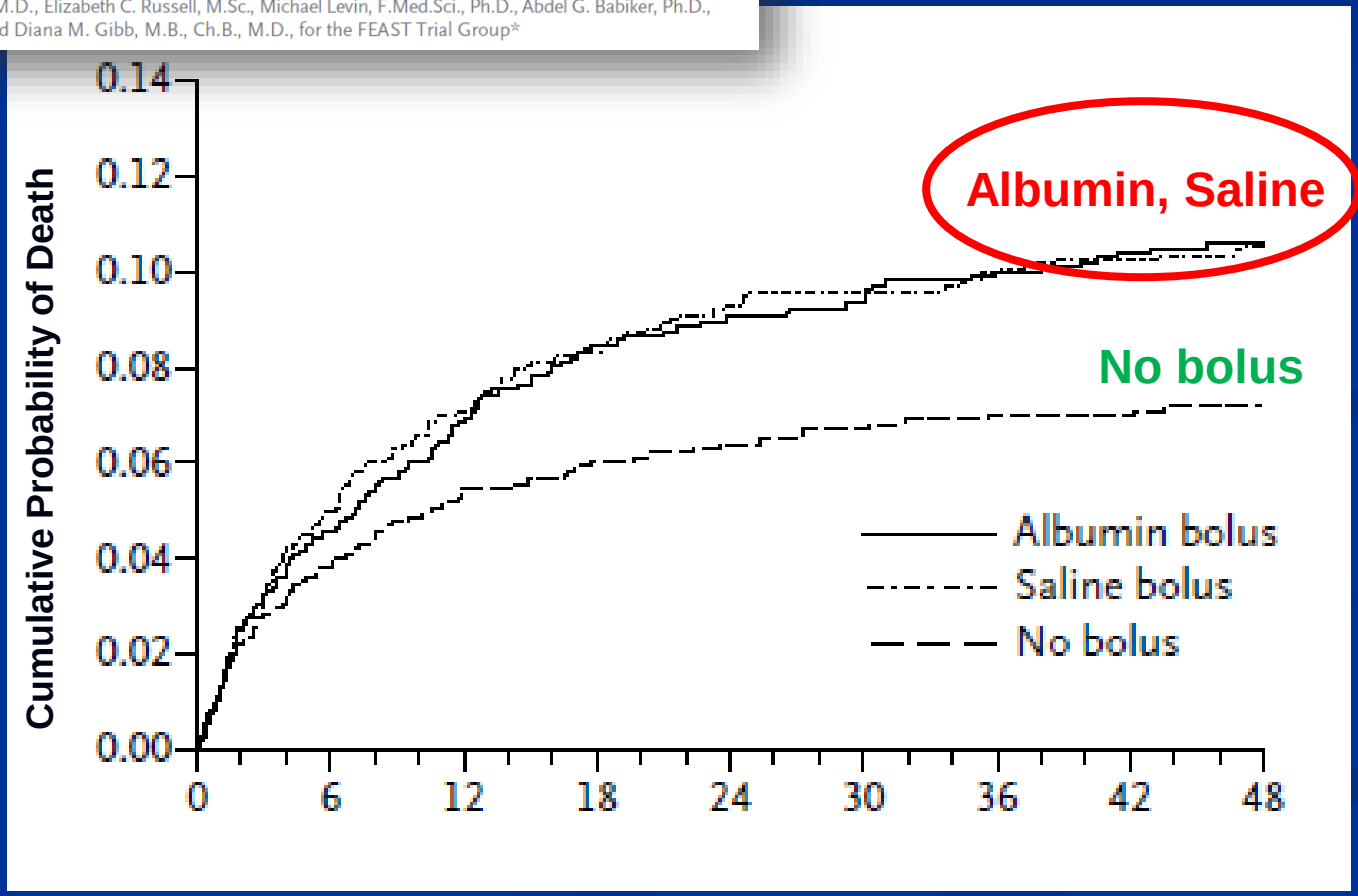
Sutherland et al *AJKD* 2010

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 30, 2011 VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*



FEAST Trial *NEJM* 2011

Optimize Fluid Resuscitation

Optimal volume?

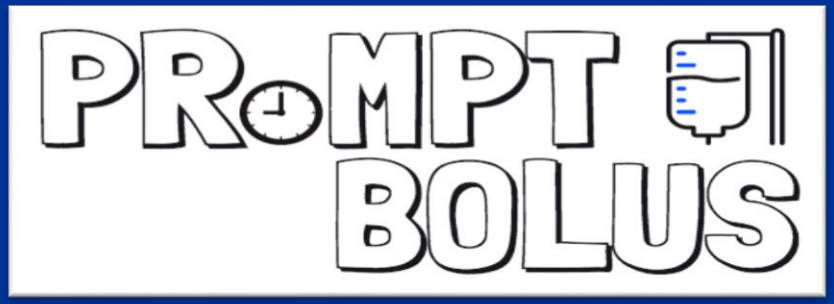
10 mL/kg vs 20 mL/kg boluses

United Kingdom *(Dr. David Inwald)*

Optimal duration?

Usual care vs early norepinephrine

Canada *(Dr. Melissa Parker)*



Optimal type?

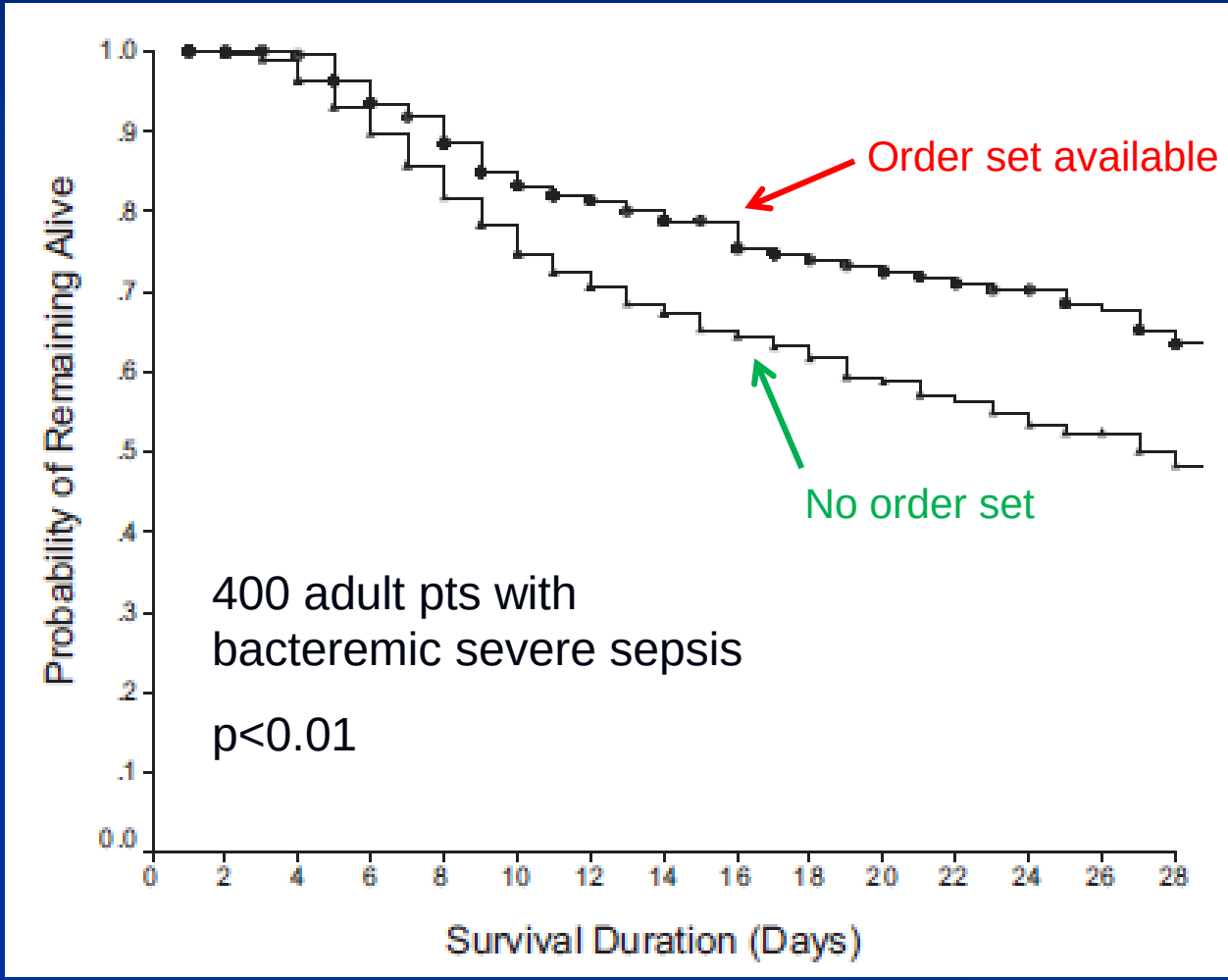
Normal saline vs lactated Ringer's

United States *(Drs. F Balamuth, S. Weiss)*

How to Optimize Sepsis Resuscitation

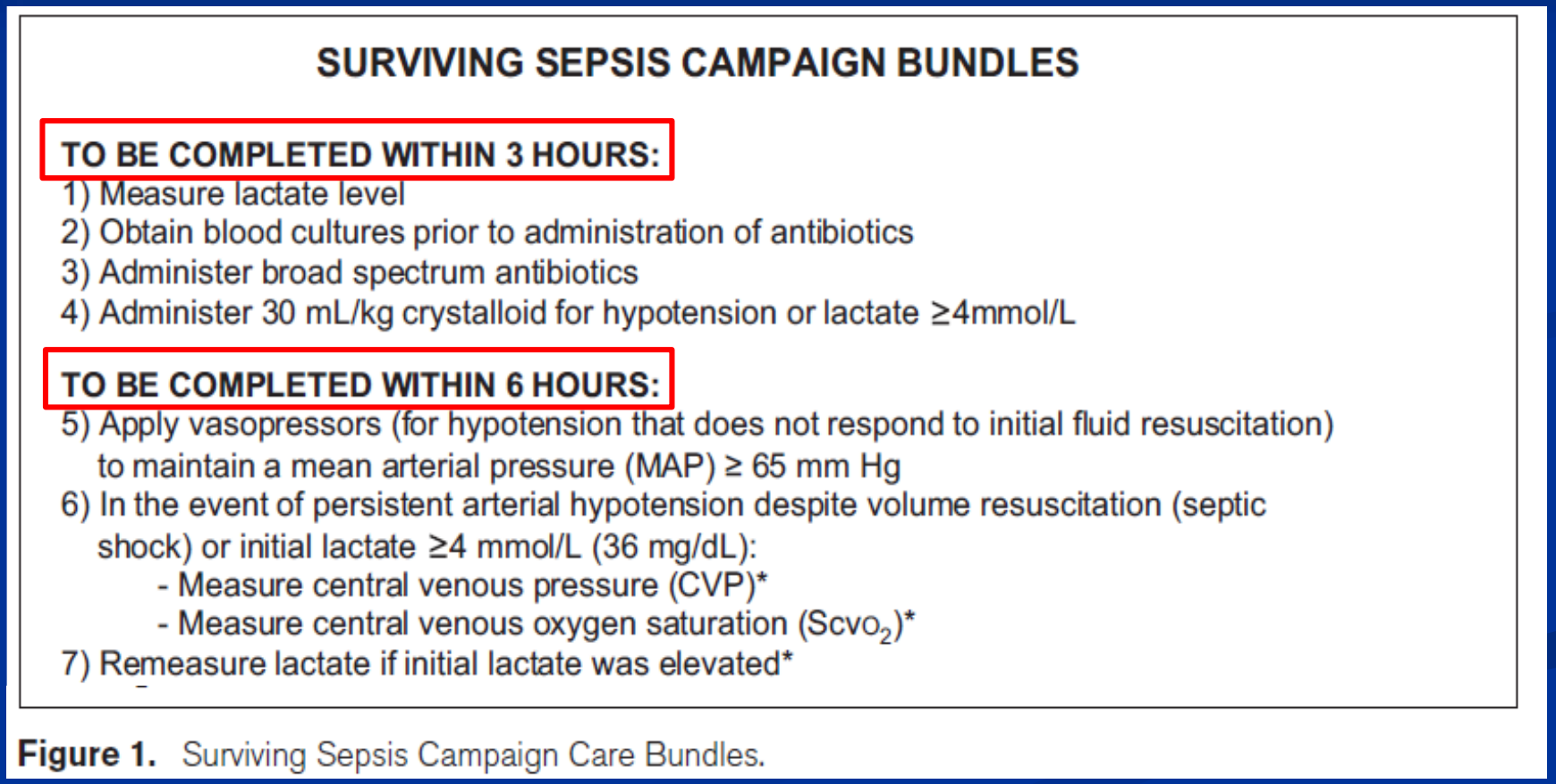
- What do we know that works for sepsis?
  - Early antibiotics
  - Goal-directed shock reversal
  - **“Bundled” care**

Protocolized ("Bundled") Care Improves Sepsis Survival



Thiel et al, *Crit Care Med*, 2009

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012



SURVIVING SEPSIS CAMPAIGN BUNDLES

TO BE COMPLETED WITHIN 3 HOURS:

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

TO BE COMPLETED WITHIN 6 HOURS:

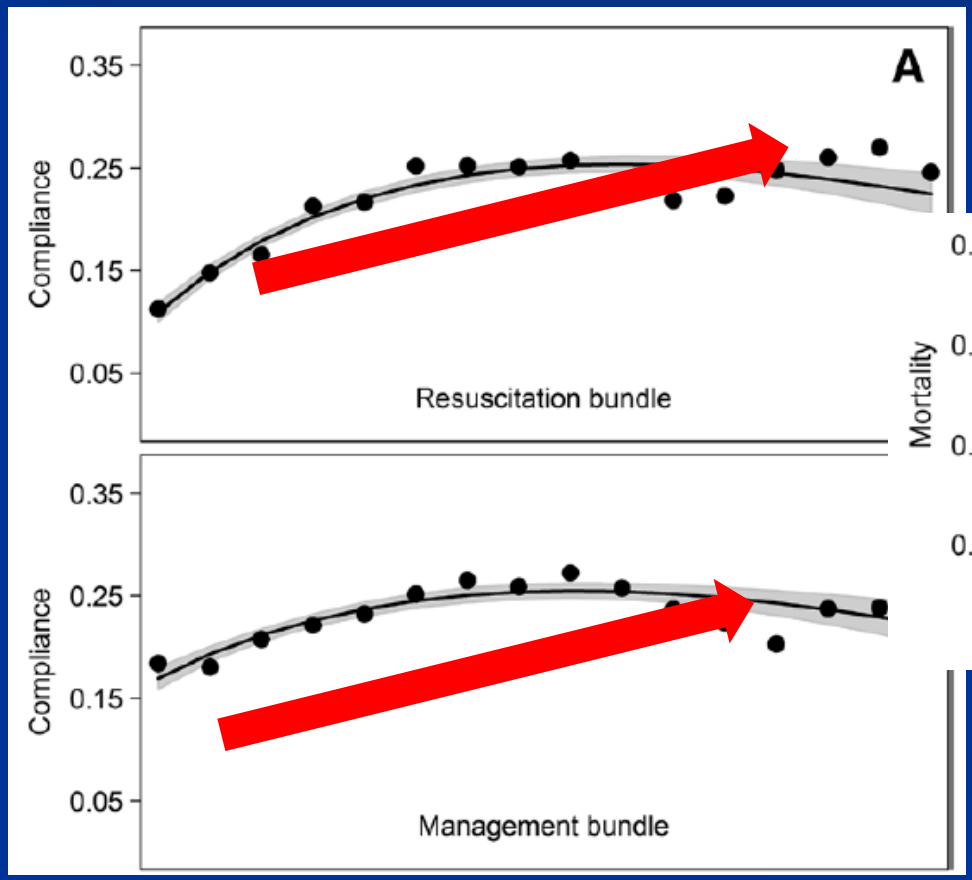
5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36 mg/dL):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation ($Scvo_2$)*
7) Remeasure lactate if initial lactate was elevated*

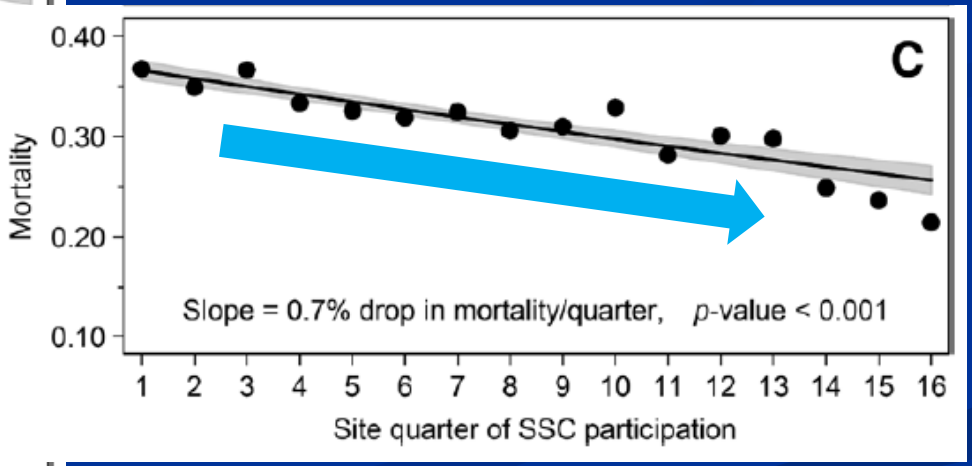
Figure 1. Surviving Sepsis Campaign Care Bundles.

Crit Care Med 2013

Surviving Sepsis Campaign: Association Between Performance Metrics and Outcomes in a 7.5-Year Study

Mitchell M. Levy, MD, FCCM[1]; Andrew Rhodes, MB BS, MD (Res)[2]; Gary S. Phillips, MAS[3]; Sean R. Townsend, MD[4]; Christa A. Schorr, RN, MSN[5]; Richard Beale, MB BS[6]; Tiffany Osborn, MD, MPH[7]; Stanley Lemeshow, PhD[8]; Jean-Daniel Chiche, MD[9]; Antonio Artigas MD, PhD[10]; R. Phillip Dellinger, MD, FCCM[11]





Crit Care Med 2014

Treatment of Pediatric Septic Shock With the Surviving Sepsis Campaign Guidelines and PICU Patient Outcomes*

Jennifer K. Workman, MD[1]; Stefanie G. Ames, MD[1]; Ron W. Reeder, MS, PhD[1,2]; E. Kent Korgenski, MS, MT (ASCP)[3]; Susan M. Masotti, BA[4]; Susan L. Bratton, MD, MPH[1]; Gitte Y. Larsen, MD, MPH[1]

N=321 ED/PICU pediatric septic shock

Outcome Variable	Surviving Sepsis Campaign Compliant		Unadjusted *p* Values[a]
	No (*n* = 204)	Yes (*n* = 117)	
Organ dysfunction			
New or progressive multiple organ dysfunction syndrome	25 (12.3%)	9 (7.7%)	0.26
Mortality	13 (6.4%)	4 (3.4%)	0.31

Pediatr Crit Care 2016

The Surviving Sepsis Campaign Bundle: 2018 Update

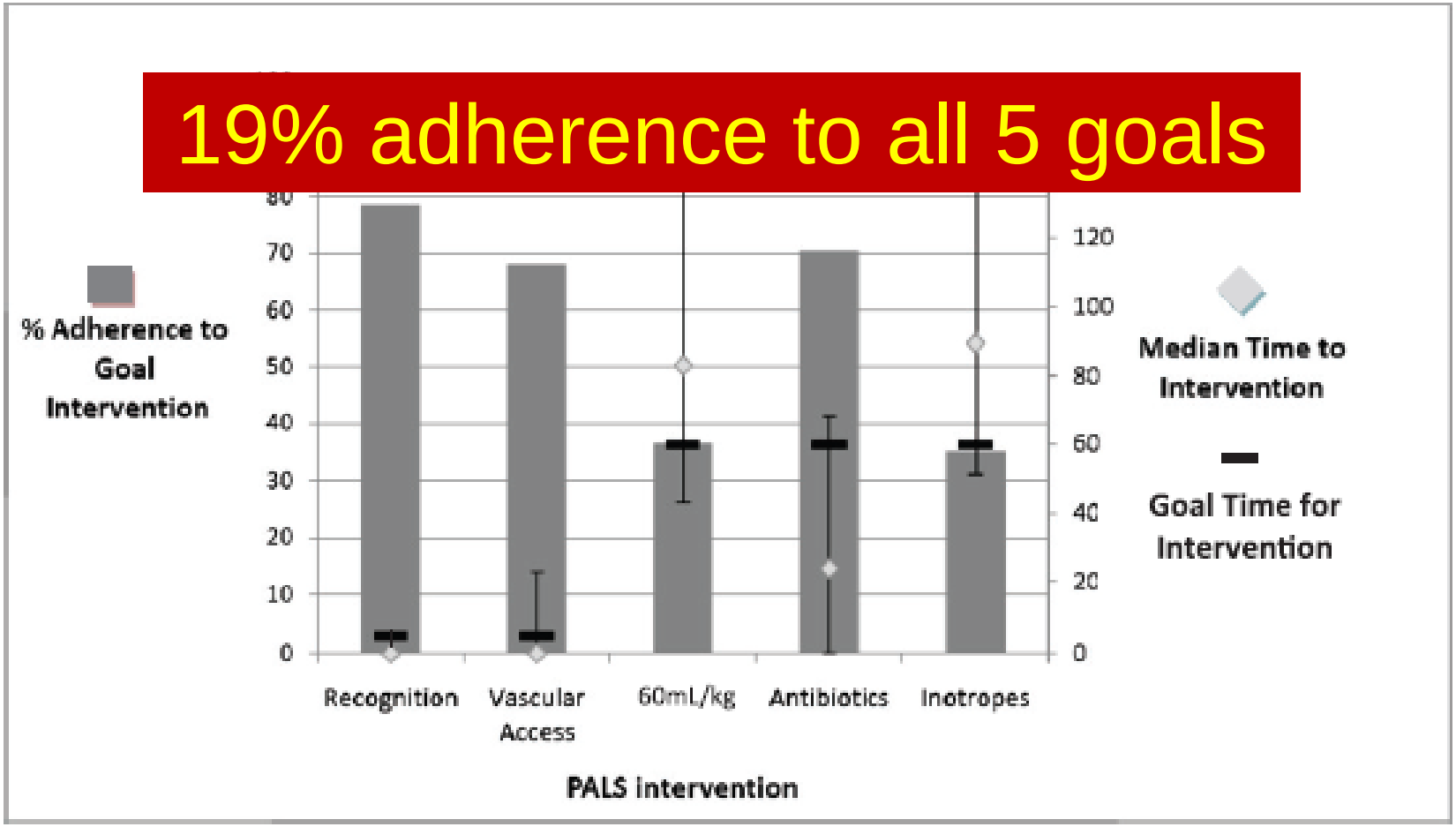
Mitchell M. Levy, MD, MCCM[1]; Laura E. Evans, MD, MSc, FCCM[2]; Andrew Rhodes, MBBS, FRCA, FRCP, FFICM, MD (res)[3]

Within ONE hour:

1. Measure lactate
2. Blood culture (before antibiotics)
3. Administer antibiotics
4. Fluid 30 ml/kg if shock present
5. Vasopressors if shock persists

Crit Care Med 2018

Children's Hospital Boston



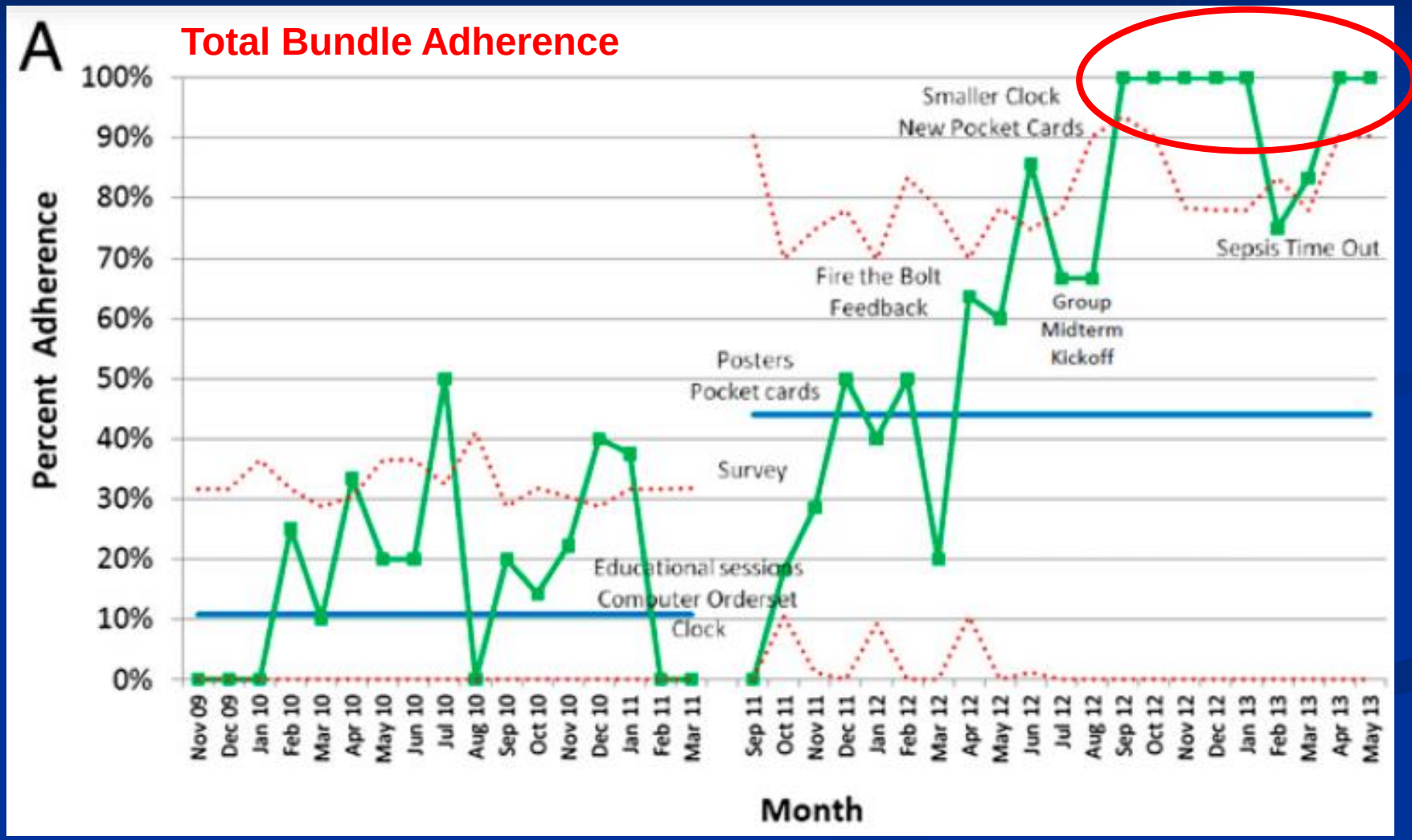
Paul et al *Pediatrics* 2012

Improving Adherence to PALS Septic Shock Guidelines

AUTHORS: Raina Paul, MD,[a] Elliot Melendez, MD,[b,c] Anne Stack, MD,[b] Andrew Capraro,[b] Michael Monuteaux, ScD,[b] and Mark I. Neuman, MD, MPH[b]

abstract

BACKGROUND AND OBJECTIVES: Few studies have demonstrated im-



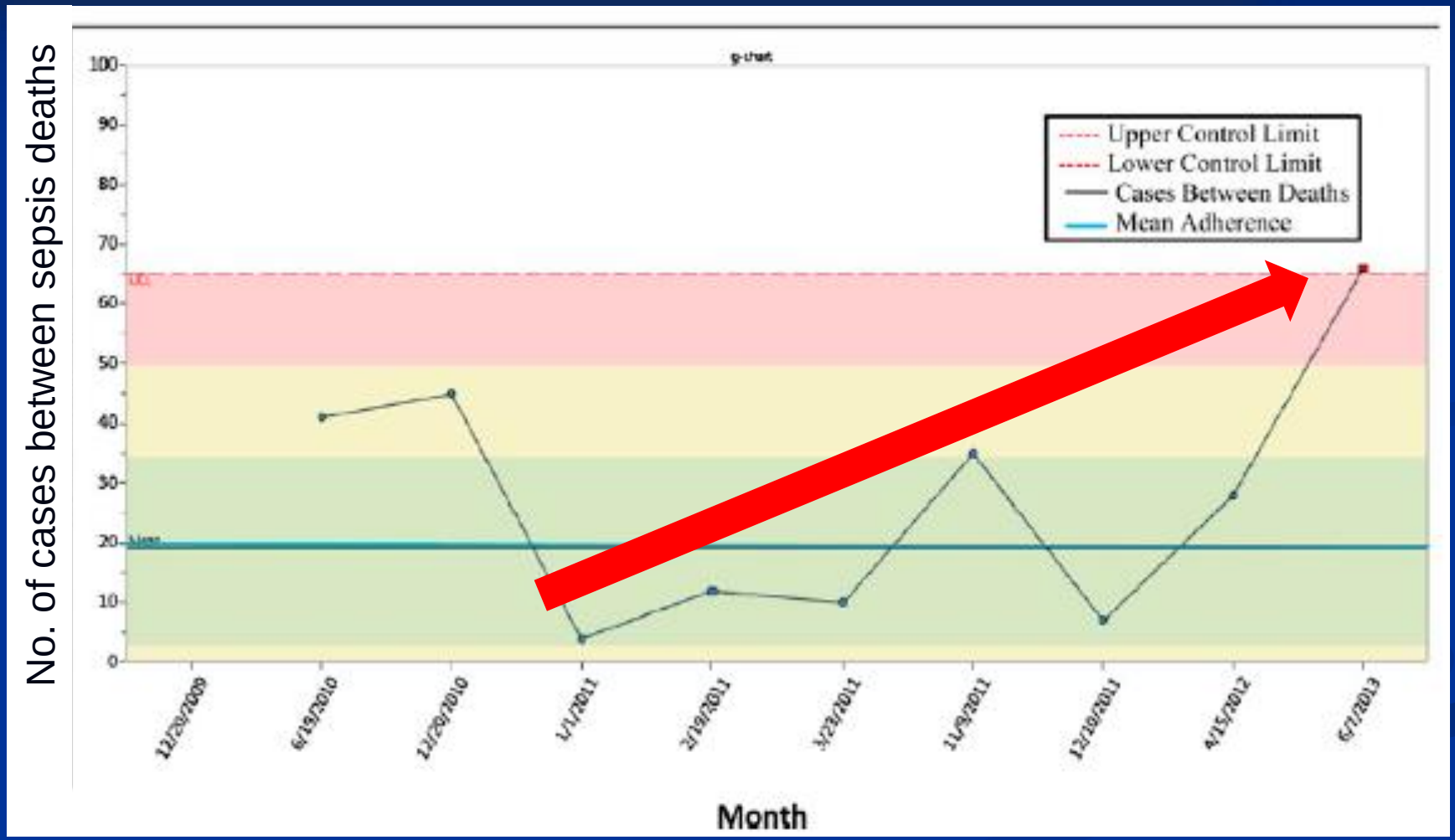
Pediatrics 2014

Improving Adherence to PALS Septic Shock Guidelines

AUTHORS: Raina Paul, MD,[a] Elliot Melendez, MD,[b,c] Anne Stack, MD,[b] Andrew Capraro,[b] Michael Monuteaux, ScD,[b] and Mark I. Neuman, MD, MPH[b]

abstract

BACKGROUND AND OBJECTIVES: Few studies have demonstrated im-



Paul et al *Pediatrics* 2014

Protocolized Treatment Is Associated With Decreased Organ Dysfunction in Pediatric Severe Sepsis*

Fran Balamuth, MD, PhD, MSCE[1,2]; Scott L. Weiss, MD, MSCE[3,4]; Julie C. Fitzgerald, MD, PhD[3,4]; Katie Hayes, BS[2]; Sierra Centkowski, BA[1]; Marianne Chilutti, MS[5]; Robert W. Grundmeier, MD[1,5]; Jane Lavelle, MD[1,2]; Elizabeth R. Alpern, MD, MSCE[6,7]

Organ Failure Free Day 2	OR (Adjusted)	*p*	95% CI
Emergency department sepsis protocol	4.23	0.002	1.7–10.4
Sex	1.23	0.59	0.6–2.6
Central line	0.95	0.98	0.3–2.8
Pediatric Index of Mortality-2 score	0.61	< 0.005	0.5–0.8
Any comorbidity	0.92	0.79	0.4–1.9
Antibiotics < 120 min	0.93	0.9	0.4–2.2
Bolus < 120 min	3.1	0.04	1.1–8.8

OR = odds ratio.
Variables were included in the model if $p < 0.2$ on univariate analysis.

Pediatric Crit Care 2016

American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock

Recognition Bundle

- Screen for septic shock using a trigger tool
- Clinician assessment within 15 minutes
- Begin resuscitation within 30 minutes

Resuscitation Bundle

- IV/IO access within 5 minutes
- Fluid within 30 minutes
- Antibiotics within 60 minutes
- Vasoactive within 60 minutes

PCCM 2017
CCM 2017

Sepsis QI Bundles → Law

CMS SEP-1

Within 3 hours:

- Measure serum lactate
- Obtain blood cultures
- Administer antibiotics
- Fluid 30 mL/kg

Within 6 hours:

- Volume, perfusion status
- Vasopressor administration

NY State Regulations

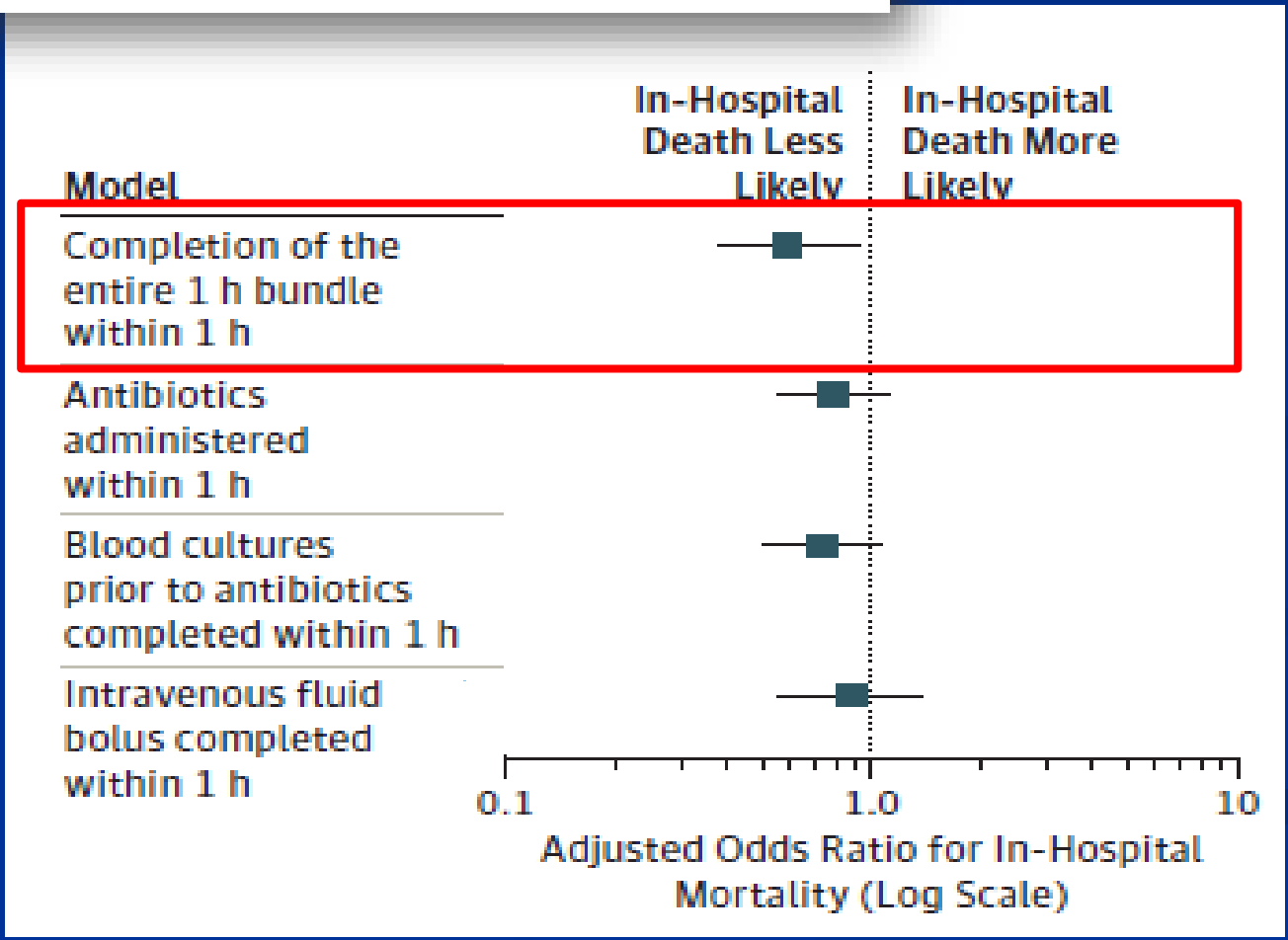
Within 1 hour:

- Obtain blood cultures
- Administer antibiotics
- Fluid 20 mL/kg

JAMA | Original Investigation

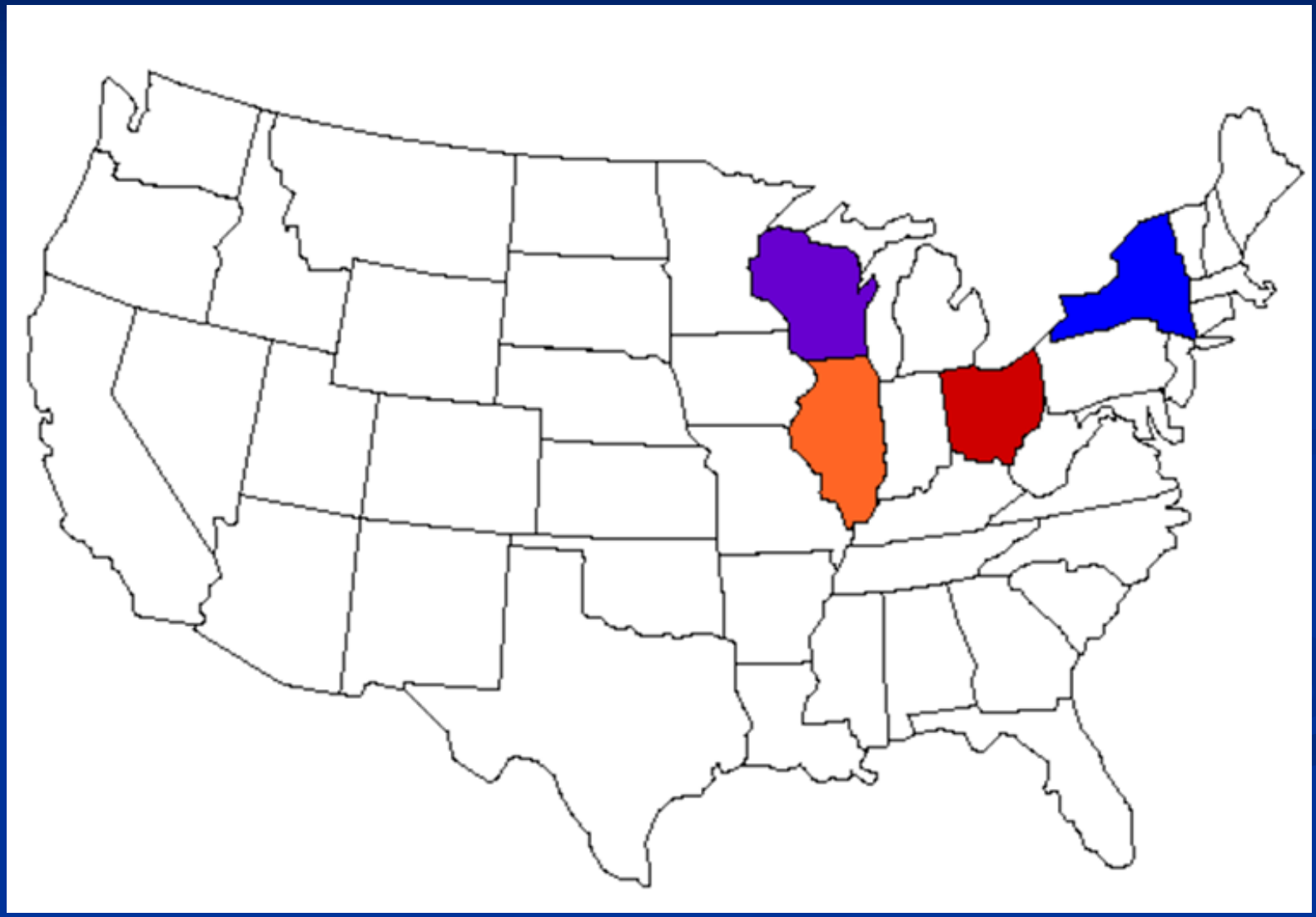
Association Between the New York Sepsis Care Mandate and In-Hospital Mortality for Pediatric Sepsis

Idris V. R. Evans, MD, MSc; Gary S. Phillips, MAS; Elizabeth R. Alpern, MD, MSCE; Derek C. Angus, MD, MPH; Marcus E. Friedrich, MD; Niranjan Kissoon, MD; Stanley Lemeshow, PhD; Mitchell M. Levy, MD; Margaret M. Parker, MD; Kathleen M. Terry, PhD; R. Scott Watson, MD, MPH; Scott L. Weiss, MD, MSCE; Jerry Zimmerman, MD, PhD; Christopher W. Seymour, MD, MSc



JAMA 2018

States with Sepsis Legislation



Public Campaigns

www.sepsis.org

FOR PATIENTS AND FAMILIES

GET AHEAD OF SEPSIS

KNOW THE RISKS. SPOT THE SIGNS. ACT FAST.

PROTECT YOURSELF AND YOUR FAMILY FROM SEPSIS.

Sepsis happens when an infection you already have—in your skin, lungs, urinary tract or somewhere else—triggers a chain reaction throughout your body.

It is life-threatening, and without timely treatment, sepsis can rapidly lead to tissue damage, organ failure, and death.

How can I get ahead of sepsis?

1. Talk with your doctor or nurse about steps you can take to prevent infections. Some steps include taking good care of chronic conditions and getting recommended vaccines.
2. Practice good hygiene, such as handwashing, and keeping cuts clean and covered until healed.
3. Know the symptoms of sepsis.
4. **ACT FAST. Get medical care IMMEDIATELY if you suspect sepsis or have an infection that's not getting better or is getting worse.**

To learn more about sepsis and how to prevent infections, visit, **www.cdc.gov/sepsis**.

CDC

PubNo. 300412

Improving Pediatric Sepsis Outcomes (IPSO) aims:

- To reduce sepsis mortality by 75 percent
- To reduce hospital-onset sepsis by 75 percent

47 participating hospitals

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes, MB BS, MD(Res) (Co-chair)[1]; Laura E. Evans, MD, MSc, FCCM (Co-chair)[2]; Waleed Alhazzani, MD, MSc, FRCPC (methodology chair)[3]; Mitchell M. Levy, MD, MCCM[4]; Massimo Antonelli, MD[5]; Ricard Ferrer, MD, PhD[6]; Anand Kumar, MD, FCCM[7]; Jonathan E. Sevransky, MD, FCCM[8]; Charles L. Sprung, MD, JD, MCCM[9]; Mark E. Nunnally, MD, FCCM[2]; Bram Rochwerg, MD, MSc (Epi)[3]; Gordon D. Rubenfeld, MD (conflict of interest chair)[10]; Derek C. Angus, MD, MPH, MCCM[11]; Djillali Annane, MD[12]; Richard J. Beale, MD, MB BS[13];

- **No "Pediatric Considerations"**
- ***Pediatric SSC – Expected 2019***

Crit Care Med 2017
Intensive Care Med 2017

Summary

- Pediatric sepsis remains a public health problem
- Systematic screening enhances sepsis recognition
- Guideline-based “bundles”, while not yet perfect, improve outcomes
- Numerous multidisciplinary and national programs (including laws) support the quest to “cure” sepsis

Acknowledgements

Julie Fitzgerald, MD PhD
(PICU)

Fran Balamuth, MD PhD MSCE
(ED)

Sharon Kaminski
Valerie Rigby
Sarah Hadley
Charlie Woods-Hill, MD
Jane Whitney, MD
Kate Chiotos, MD
Kristi McKenna, RN
Lauren Biedron, RN
Kelly Morris, RN
Octavia Cade
Susan Warrington, PharmD
Susan Ditaranto, RN
Allison Ballantine, MD MEd
Kathryn Roberts, RN
Geoff Bird, MD
Lakshmi Srinivasan, MD
Pamela Mazzeo, MD
Adelaide Barnes, MD
Kimberly DeGerolamo
Janine Cockerham
Christian Minich
Renee Bruhn
Ashley Woodford
Katie Hayes
Marlena Kittick
Mary Kate Abbadessa
Ron Keren, MD
Bob Berg, MD
Joseph St. Geme, MD

Est: Sept 2017

Children's Hospital of Philadelphia

Pediatric Sepsis Program

Recognize. Survive. Thrive.

www.chop.edu/sepsis

sepsis@email.chop.edu

Thank you!