울산대학교병원
ULSAN UNIVERSITY HOSPITAL

BASIC ICU care of SEPSIS

울산대학교병원 호흡기내과
박 철
cholssak21@gmail.com

ULSAN UNIVERSITY HOSPITAL

Timeline of Definition and Management guideline

Early recognition

Fluid resuscitation

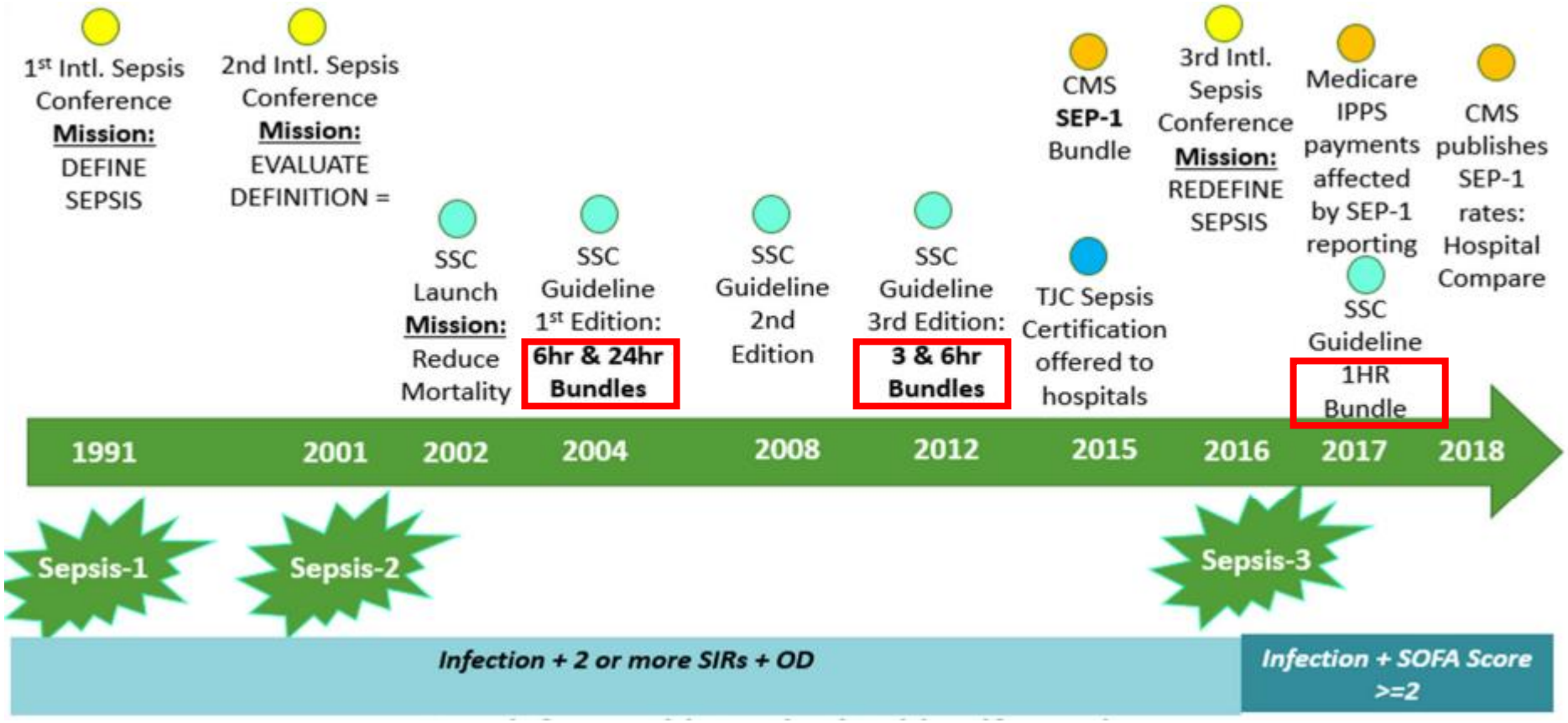
Vasoactive agents

Antibiotics

Source control

Timeline of Definition and Management guideline

Definition


1st Intl. Sepsis Conference
Mission: DEFINE SEPSIS
2nd Intl. Sepsis Conference
Mission: EVALUATE DEFINITION =
SSC Launch
Mission: Reduce Mortality
SSC Guideline 1st Edition: 6hr & 24hr Bundles
SSC Guideline 2nd Edition
SSC Guideline 3rd Edition: 3 & 6hr Bundles
CMS SEP-1 Bundle
TJC Sepsis Certification offered to hospitals
3rd Intl. Sepsis Conference
Mission: REDEFINE SEPSIS
Medicare IPPS payments affected by SEP-1 reporting
SSC Guideline 1HR Bundle
CMS publishes SEP-1 rates: Hospital Compare
1991
2001
2002
2004
2008
2012
2015
2016
2017
2018
Sepsis-1
Sepsis-2
Sepsis-3
Infection + 2 or more SIRs + OD
Infection + SOFA Score >=2

Brand new definition of sepsis

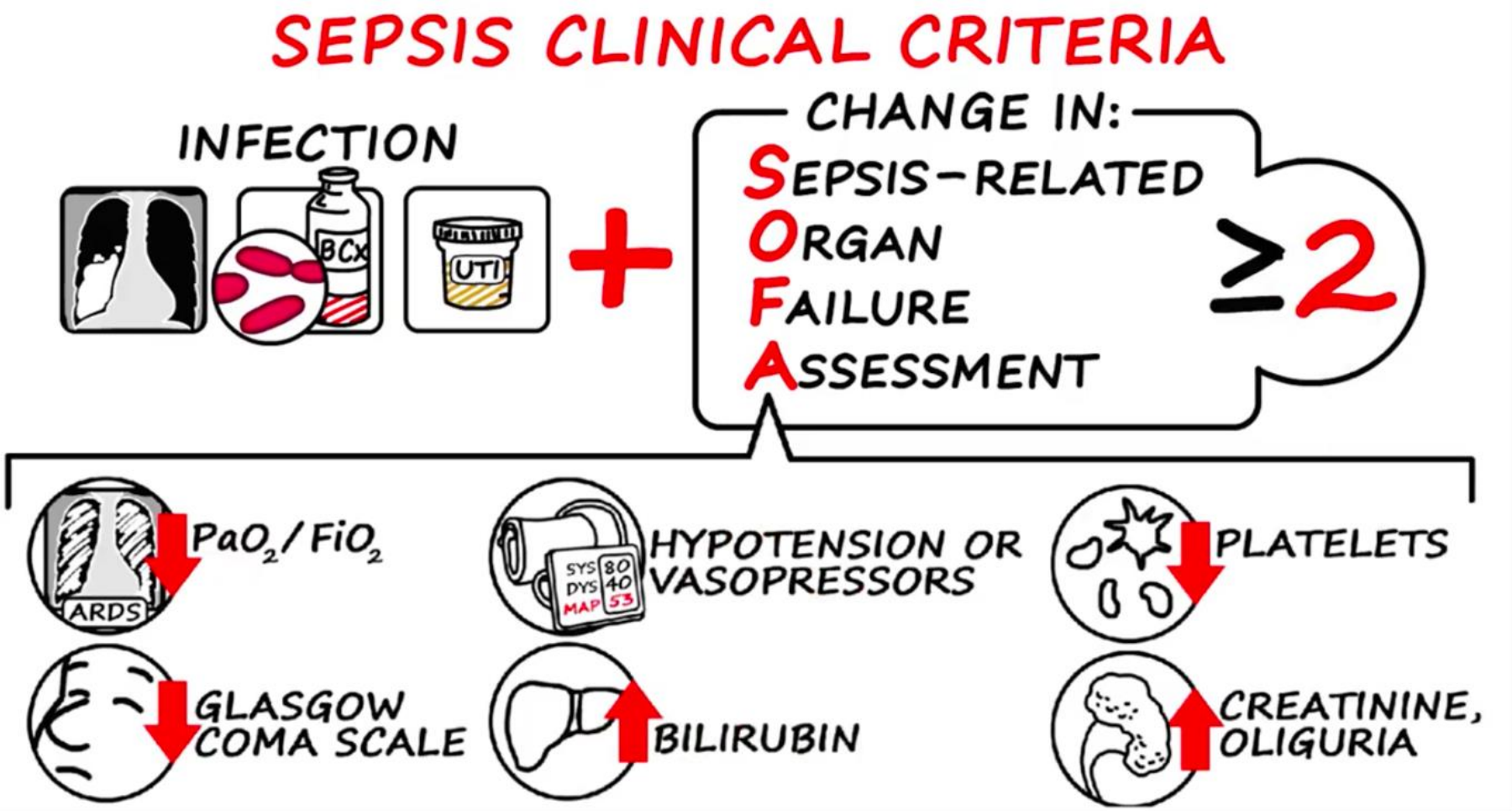
"Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs"

Jean-Louis Vincent et al. ***Lancet* 2013; 381: 774–75**

"life-threatening organ dysfunction caused by a dysregulated host response to infection"

SingerM et al. ***JAMA.2016;315[8]:801-810***

Brand new definition of sepsis (sepsis-3)



Mervyn Singer, et al. JAMA 2016

Pathogenesis of Sepsis

Infectious Agents

- Endotoxin/LPS
- Lipopeptides
- Lipoteichoic acid
- DNA
- Flagellin

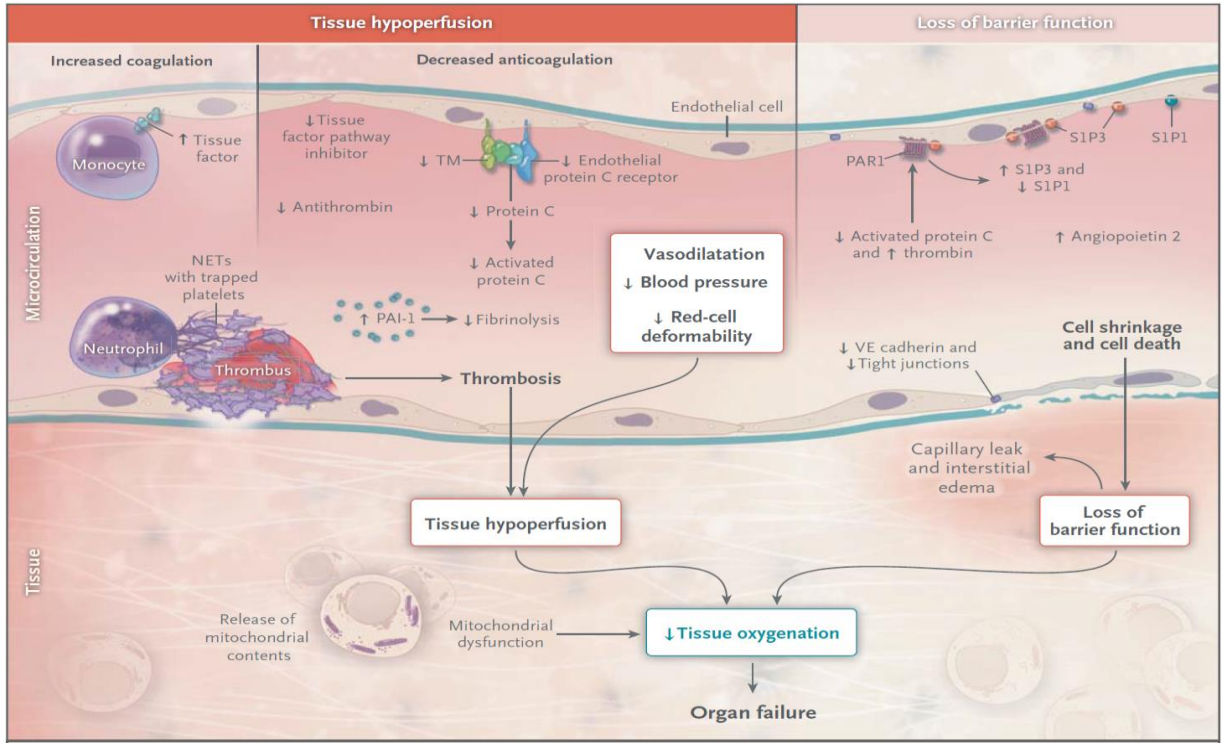
Susceptible Host

- Co-morbidities
- Age
- Genetic polymorphisms

SEPSIS

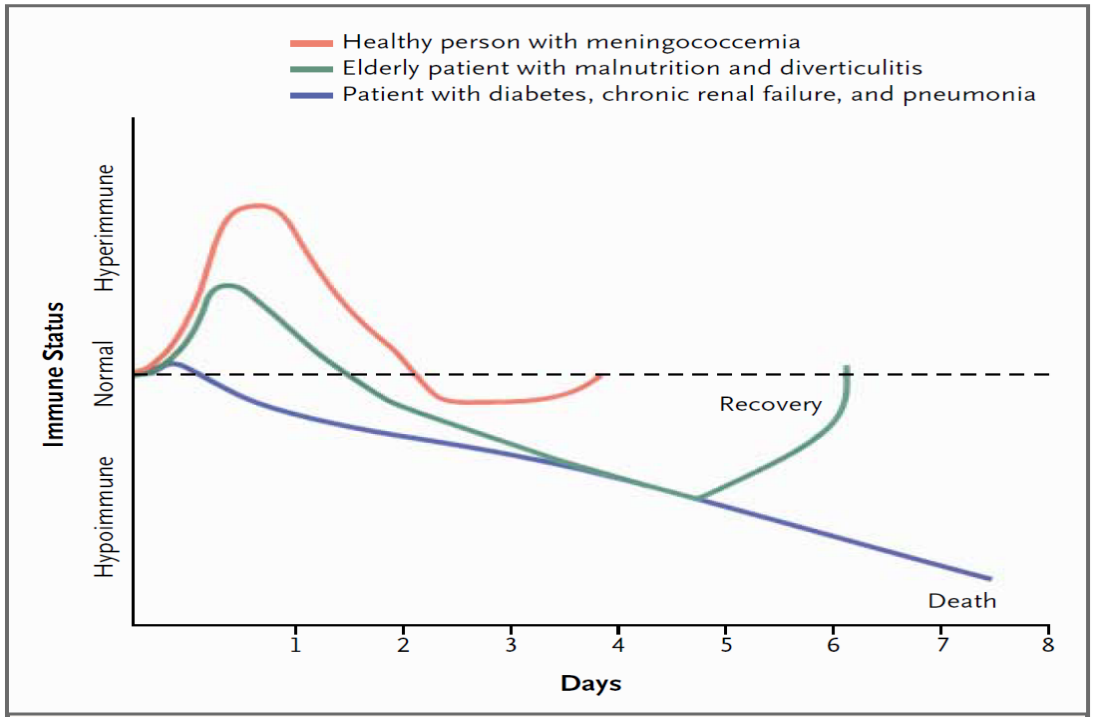
Response to Stimulus

- Inflammation
- Immunosuppression
- Coagulopathy
- Mitochondrial dysfunction



N Engl J Med 2013; 369:840-85

Host factor of Sepsis



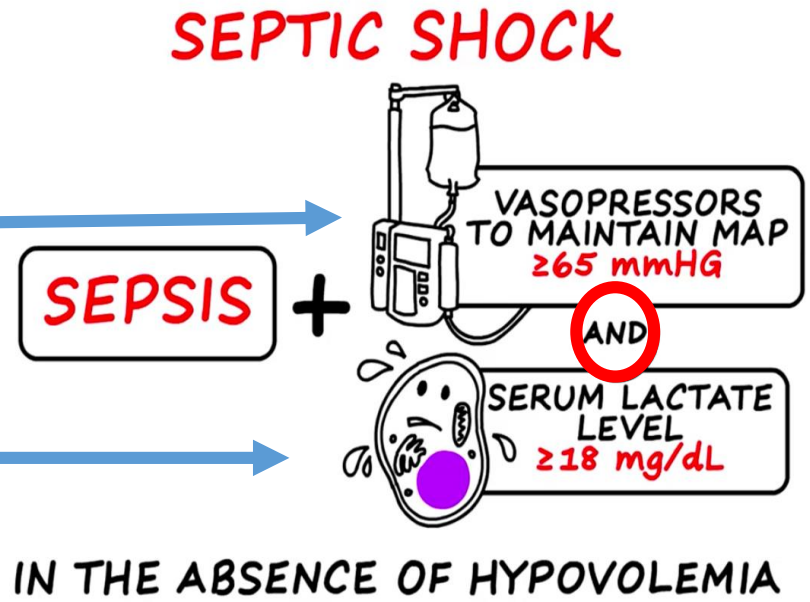
Co-morbidity	Immune dysfunction
DM	↓ Neutrophil chemotaxis after stimulation Blunted inflammatory response to endotoxemia
Uremia	Functional abnormalities of neutrophils, monocytes, dendritic cells, and lymphocytes
Liver Cirrhosis	↓Numbers and functions of Kuepfer cells, Impaired phagocytic function of neutrophils Downregulation of pro-inflammatory cytokine production
Heart Failure	NK cells have decreased sensitivity to activation by IL-2 and IFN-r

N Engl J Med 2003; 348:138-150

Definition of septic shock

"Septic Shock is defined as a **subset of sepsis** in which underlying circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone"

SingerM et al. ***JAMA.2016;315[8]:801-810***



Management of septic shock

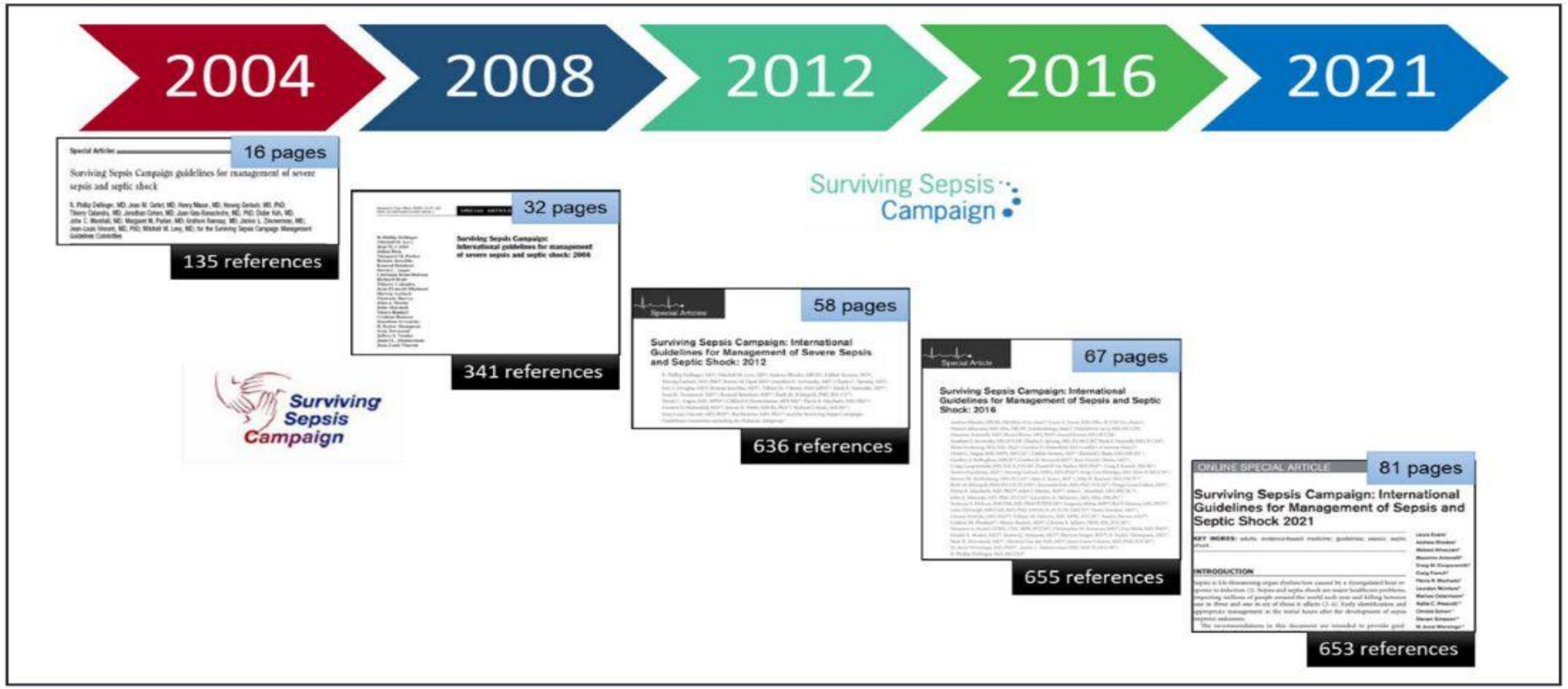


Figure 1. Surviving Sepsis Campaign (SSC) guidelines publication timeline and metrics. Guideline mastheads are displayed from original 2004 publication through the 2021 revision. The timeline displays and contrasts page numbers and numbers of references. To the left is the original SSC logo (2004 and 2008 editions) and the revised logo (2012 and forward).

Recommendations in SSc guideline

1. Screening and early treatment (n=10)
2. Infection (n=21)
3. Hemodynamic management (n=14)
4. Ventilation (n=12)
5. Additional therapies (n=16)
6. Long-term outcomes and goals of care (n=20)

Recommendations in surviving sepsis campaign 2021 Guideline (n=93)

Early recognition

quick SOFA, SIRS, NEWS or MEWS

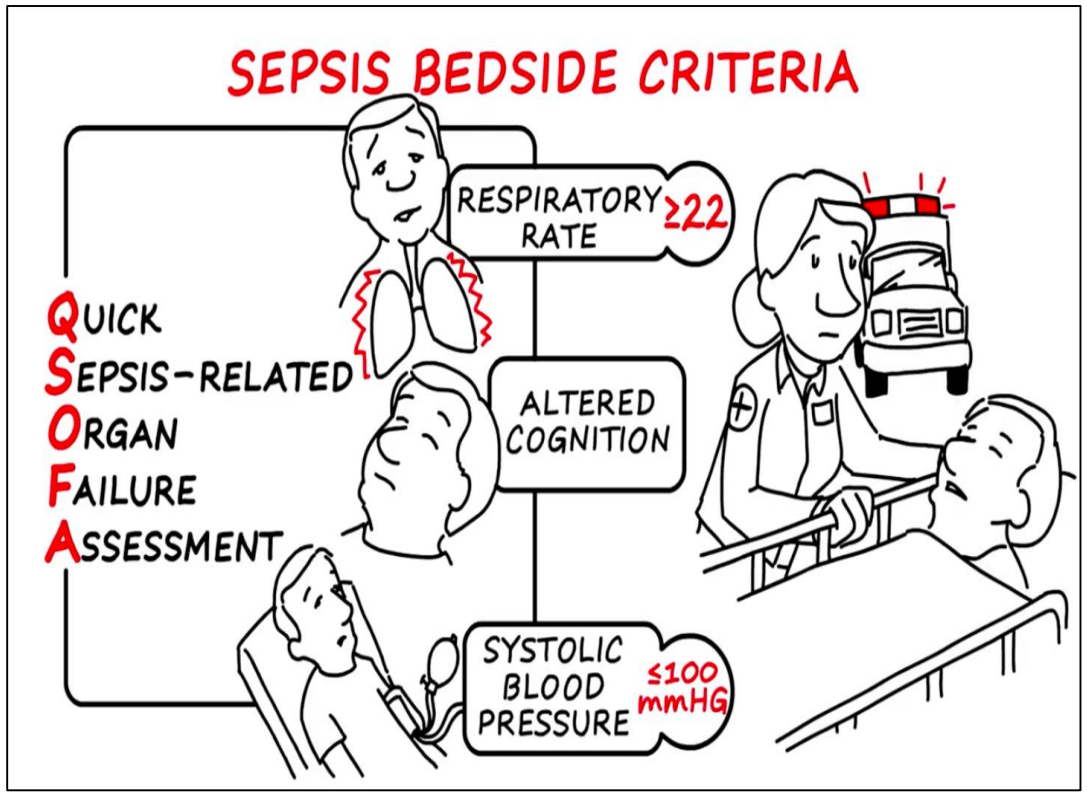


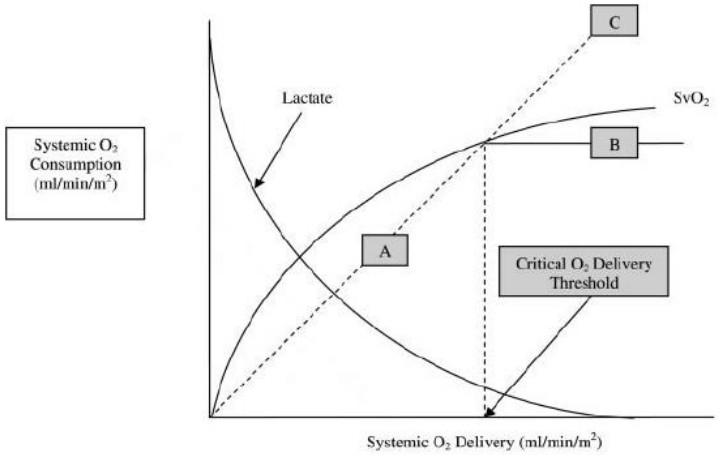
Table 2. Distribution of Signs Meeting SIRS Criteria in Patients with Severe Sepsis, According to SIRS-Positive and SIRS-Negative Status.*

Variable	All Patients (N=109,663)	Patients with SIRS-Positive Severe Sepsis (N=96,385)	Patients with SIRS-Negative Severe Sepsis (N=13,278)
SIRS criterion met — no. (%)†			
Abnormal temperature	64,365 (58.7)	62,430 (64.8)	1,935 (14.6)
High	33,059 (30.1)	32,605 (33.8)	454 (3.4)
Low	36,130 (32.9)	34,599 (35.9)	1,531 (11.5)
Increased heart rate	83,493 (76.1)	80,747 (83.8)	2,746 (20.7)
Increased respiratory rate or decreased $Paco_2$	76,558 (69.8)	74,043 (76.8)	2,515 (18.9)
Abnormal white-cell count	76,823 (70.1)	73,365 (76.1)	3,458 (26.0)
High	64,720 (59.0)	61,602 (63.9)	3,118 (23.5)
Low	12,967 (11.8)	12,616 (13.1)	351 (2.6)
No. of SIRS criteria met			
Median	3	3	1
Interquartile range	2–4	2–4	1–1
Distribution			
>1	96,385 (87.9)	96,385 (100)	0
0	2,624 (2.4)	0	2,624 (19.8)
1	10,654 (9.7)	0	10,654 (80.2)
2	26,820 (24.5)	26,820 (27.8)	0
3	41,315 (37.7)	41,315 (42.9)	0
4	28,250 (25.7)	28,250 (29.3)	0

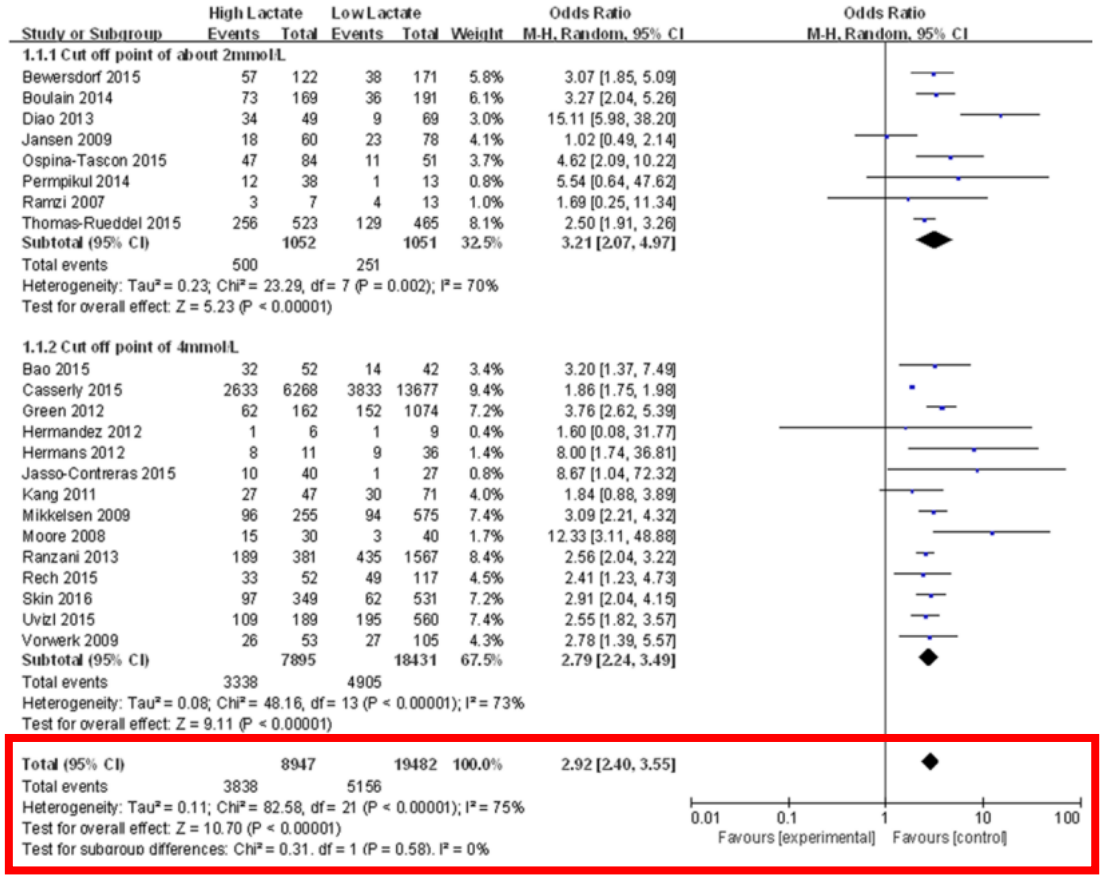
We recommend **against** using qSOFA compared to SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock (Strong recommendation, moderate-quality evidence)

N Engl J Med March 17, 2015

Lactate



	MAP	CVP	ScvO2	Lactate	Cardiac Index	Systemic Vascular Resistance	Treatment and Comments
Hypovolemia	Variable	↓	↓	↑	↓	↑	Volume
Compensated and vasodilatory	Normal or ↓	Normal	↑	Variable	↑	↓	Vasopressors, low dose corticosteroids
Myocardial Suppression	Variable	↑	↓	↑	Normal or ↓	Normal or ↑	Increased BNP levels, Inotropic Therapy
Impairment of tissue O_2 utilization	Variable	Normal	↑	↑	Variable	↓ , Normal or ↑	Vasodilators, r-APC

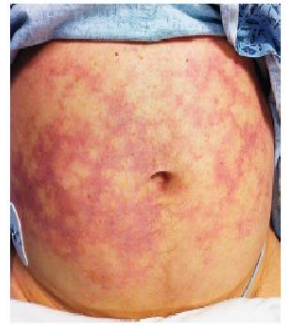


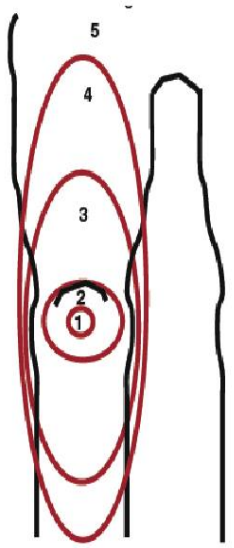
For adults suspected of having sepsis, we suggest measuring blood lactate (Weak recommendation, low-quality evidence)

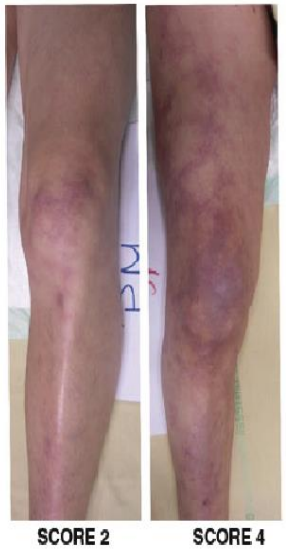
Otero RM, et al. Chest 2006
Genglong Liu, et al. Int J Exp Med 2017

Tissue perfusion

Category	Parameter	Endpoint	Suggested measurement interval
Peripheral perfusion	Capillary refill time	< 4.5 sec	15-60 min
	Skin mottling	Absent	
	Peripheral temperature	Warm	
	Peripheral perfusion index	≥ 1.4	Continuous
	Tissue oxygen saturation	≥ 70%	
Venous oxygen saturation	Central	≥ 65-70%	Continuous
	Mixed	≥ 60-65%	
Arterial lactate	Absolute value	< 2 mmol/L	2 hours
	Clearance	> 20%/2 hours	
Urine output		≥ 0.5 mL/kg per hour	15-60 min







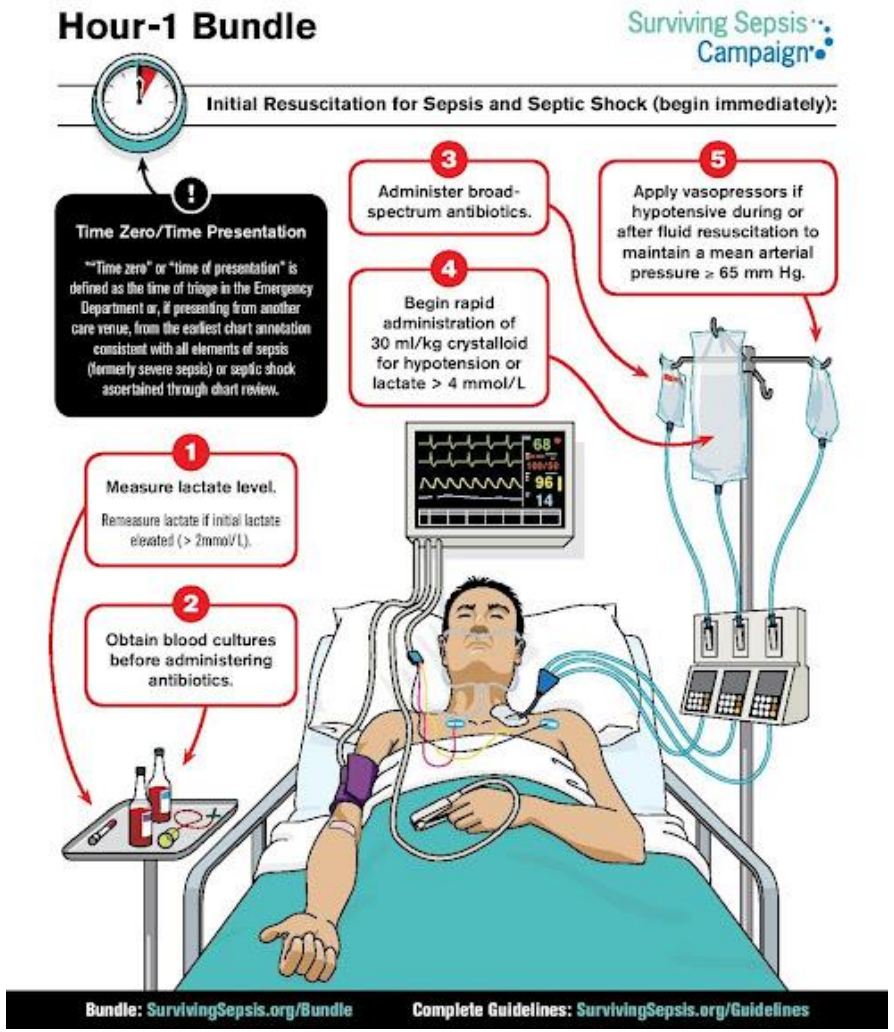
- Skin mottling (knee, abdomen)
- Capillary refill time (15 sec pressure)
  - Index finger (2.4 sec)
  - knee (4.9 sec)

For adults with septic shock, we suggest using **capillary refill time** to guide resuscitation as an adjunct to other measures of perfusion (Weak recommendation, low-quality evidence)

Dünser et al. Critical Care 2013

Fluid resuscitation

Initial resuscitation



The Five key elements of hour-1 bundle
1. Measure lactate level. Re-measure if initial lactate is >2mmol/L
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad-spectrum antibiotics.
4. Begin rapid administration of 30 ml/kg crystalloid for hypotension or lactate ≥ 4mmol/L.
5. Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥ 65mmHg

Critical Care Reviews 2021

Fluid management

Recommendation in SSc 2021

For adults with sepsis or septic shock, we recommend using **crystalloid** as firs-line fluid for resuscitation
(Strong recommendation, moderate-quality evidence)

For adults with sepsis or septic shock, we suggest using **balanced crystalloids** instead of normal saline for resuscitation
(Weak recommendation, low-quality evidence)

Fluid type

For patients with sepsis induced hypoperfusion or septic shock, we suggest that **at least 30 mL/kg of intravenous (IV) crystalloid fluid should be given within the first 3 hours** of resuscitation.
(Weak recommendation, low-quality evidence)

Volume

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021, Intensive Care Med 2021

Balanced crystalloid vs Normal saline

Crystalloid Fluids

Fluid	Na^+ mEq/L	Cl^- mEq/L	K^+ mEq/L	Ca^{2+} mEq/L	Glucose g/L	Buffer	Osmolarity mOsm/L	Tonicity	Typical Indication
Normal plasma	~ 140	~ 100	~ 4	~ 2.4	~ 0.85	HCO_3^- ~ 24 mEq/L	~ 290	N/A	N/A
0.9% saline (a.k.a. "normal saline" or NS)	154	154	0	0	0	0	308	"Isotonic"	Resuscitation
0.45% saline (a.k.a. ½ NS)	77	77	0	0	0	0	154	Hypotonic	Maintenance
3% saline	513	513	0	0	0	0	1026	Hypertonic	Severe Hyponatremia
D5 ½NS + 20 meq KCL	77	97	20	0	50	0	446	Hypertonic → Hypotonic	Maintenance
D5W	0	0	0	0	50	0	252	Hypotonic	Hypernatremia Hypoglycemia
Lactated Ringer's (LR) / Hartmann's solution*	130	109	4	3	0	Lactate 28 mEq/L	273	Isotonic	Resuscitation

Fluid	Advantages	Disadvantages
0.9% Saline	Isotonic	Hyper-chloremic acidosis, Worsens AKI (pH ⇩)
Lactated Ringer's solution	Balanced	Hypotonic, lactate, Ca++
Plasma solution	Isotonic, Balanced	Acetate, Gluconate

GrepMed

Controversies on balanced crystalloid vs normal saline

Trial (enrolled number)	Main outcome
SPLIT (n = 2,278)	(through Day 90) **No difference** RRT (Log-rank P=.85), mortality (Log-rank P=.32)
SMART (n = 15,802)	**Decreased** major adverse kidney event (adjusted OR 0.90 (0.82-0.99), p = 0.04) **No difference** in 30 d mortality (adjusted OR 0.90 (0.80-1.01), p = 0.06) **Decreased** mortality in sepsis (OR 0.80 (0.67-0.94), p = 0.01)
Network Meta-analysis of 23 studies (n = 14,659)	**Decreased** mortality (OR 0.84 (95% CI, 0.74-0.95)
BaSIC (n = 11,052)	**No difference** in 90d mortality (adjusted hazard ratio 0.97 (95% CI 0.90-1.05), P = .47) **No difference** in 90d mortality in sepsis (adjusted hazard ratio 0.93 (95% CI 0.82-1.06), P = .39)
PLUS (n = 5,037)	**No difference** in 90d mortality (adjusted hazard ratio 0.97 (95% CI 0.90-1.05), P = .47) **No difference** in 90d mortality in sepsis (adjusted hazard ratio 0.93 (95% CI 0.82-1.06), P = .39)

Paul Young, et al. JAMA 2015
Metthew W Semler, et al. NEJM 2018
Chien-Hua Tseng ,et al. Crit Care 2020
Fernando G Zempieri, et al. JAMA 2021
Simon Finfer, et al. NEJM 2022

Fluid volume and outcome

Variable	Mortality		Delayed Hypotension		ICU Admit		ICU LOS		Intubation	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	β (95% CI)	*p*	OR (95% CI)	*p*
30after3[a]	1.52 (1.03–2.24)	*0.035*	1.42 (1.02–1.99)	*0.040*	0.77 (0.6–1.0)	0.088	2.0 (0.5–3.6)	*0.010*	1.20 (0.78–1.84)	0.416
MEDS score[b]	1.18 (1.13–1.23)	*<0.001*	1.01 (0.98–1.05)	0.546	1.08 (1.0–1.1)	*<0.001*	0.2 (0.1–0.4)	*0.002*	1.03 (0.99–1.08)	0.172
Time to ABx[c]	1.02 (0.98–1.07)	0.362	1.02 (0.97–1.08)	0.392	1.01 (1.0–1.1)	0.695	0.02 (−0.2–0.3)	0.886	1.00 (0.95–1.06)	0.919
Obesity	0.74 (0.48–1.13)	0.158	1.03 (0.72–1.46)	0.882	1.11 (0.8–1.5)	0.527	−0.2 (−1.8–1.4)	0.816	1.46 (0.95–2.26)	0.088
Male Sex	0.63 (0.44–0.89)	*0.009*	0.75 (0.56–1.00)	0.053	0.93 (0.7–1.2)	0.580	−0.7 (−2.0–0.6)	0.305	1.06 (0.72–1.56)	0.762
ESRD	1.23 (0.70–2.17)	0.471	1.62 (0.94–2.80)	0.084	1.35 (0.8–2.2)	0.222	1.0 (−1.2–3.2)	0.371	0.83 (0.42–1.64)	0.583
HF	1.34 (0.90–2.00)	0.149	1.48 (1.02–2.16)	*0.038*	1.71 (1.2–2.4)	*0.002*	0.4 (−1.2–1.9)	0.653	0.88 (0.55–1.40)	0.590
Shock	1.05 (0.69–1.60)	0.822	7.80 (5.59–10.90)	*<0.001*	2.98 (2.2–4.0)	*<0.001*	−1.0 (−2.7–0.7)	0.234	1.98 (1.23–3.21)	*0.005*

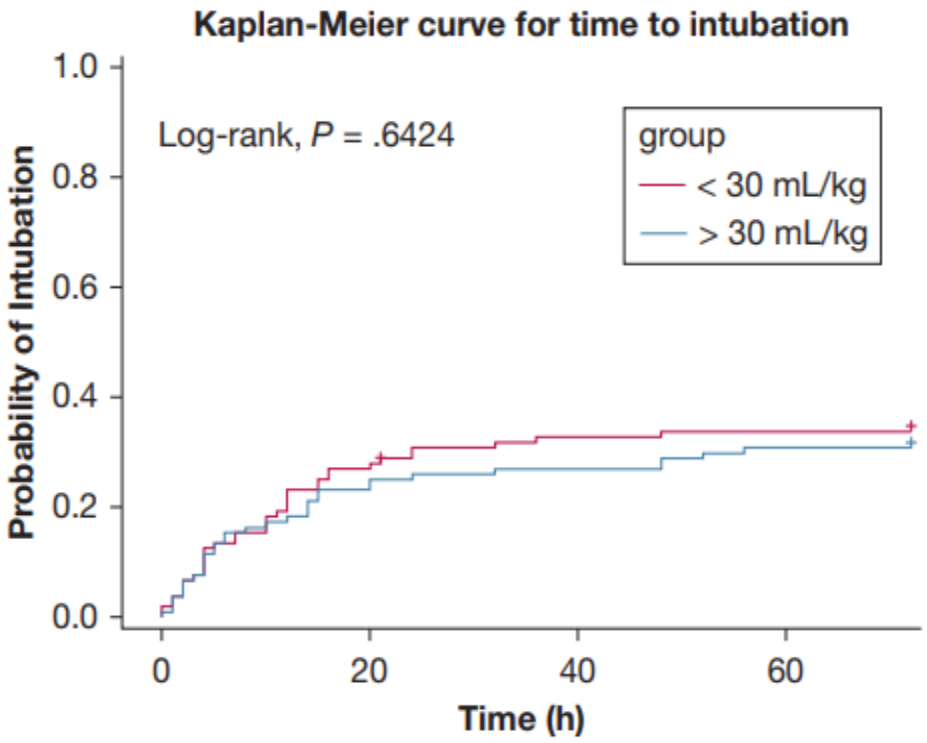
Protocol based “golden hours” in the initial management of septic shock (EGDT)

- Protocolized Care for Early Septic Shock (ProCESS) trial-US
- Australasian Resuscitation in Sepsis Evaluation (ARISE) trial-ANZIC
- Protocolised Management in Sepsis (ProMISe) trial-UK

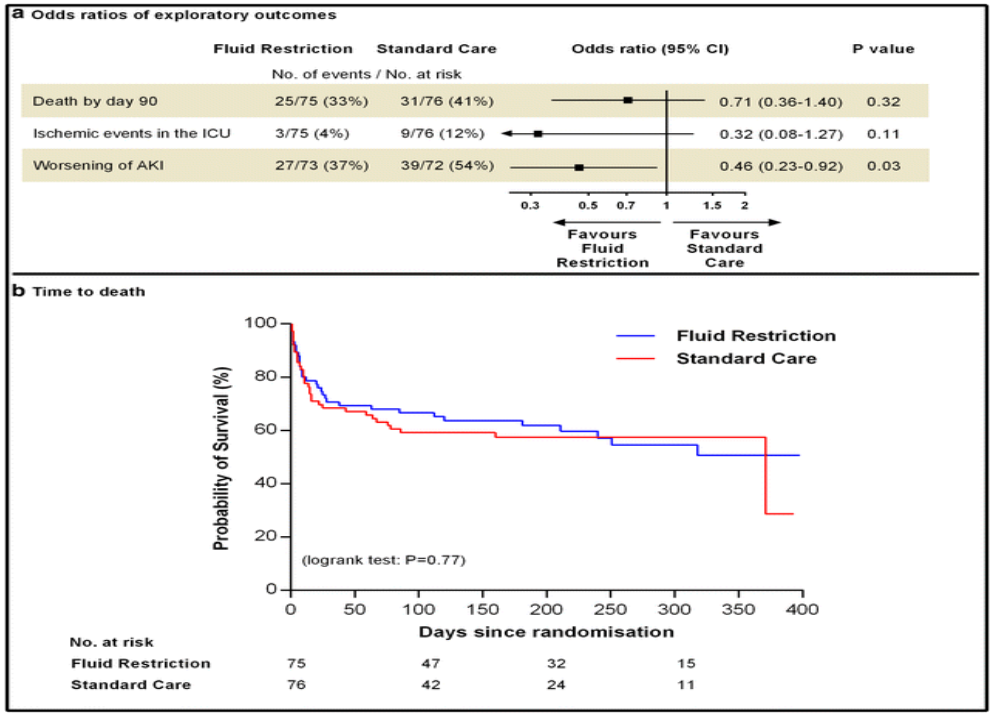
HI Kuttab, et al. Crit Care Med 2019
SSC guideline 2021, Intensive Care Med 2021

Fluid volume and outcome

Association Between Volume of Fluid Resuscitation and Intubation in High-Risk Patients With Sepsis, HF, ESRD, LC



Restricting volumes of resuscitation fluid in adults with septic shock after initial management: the CLASSIC trial

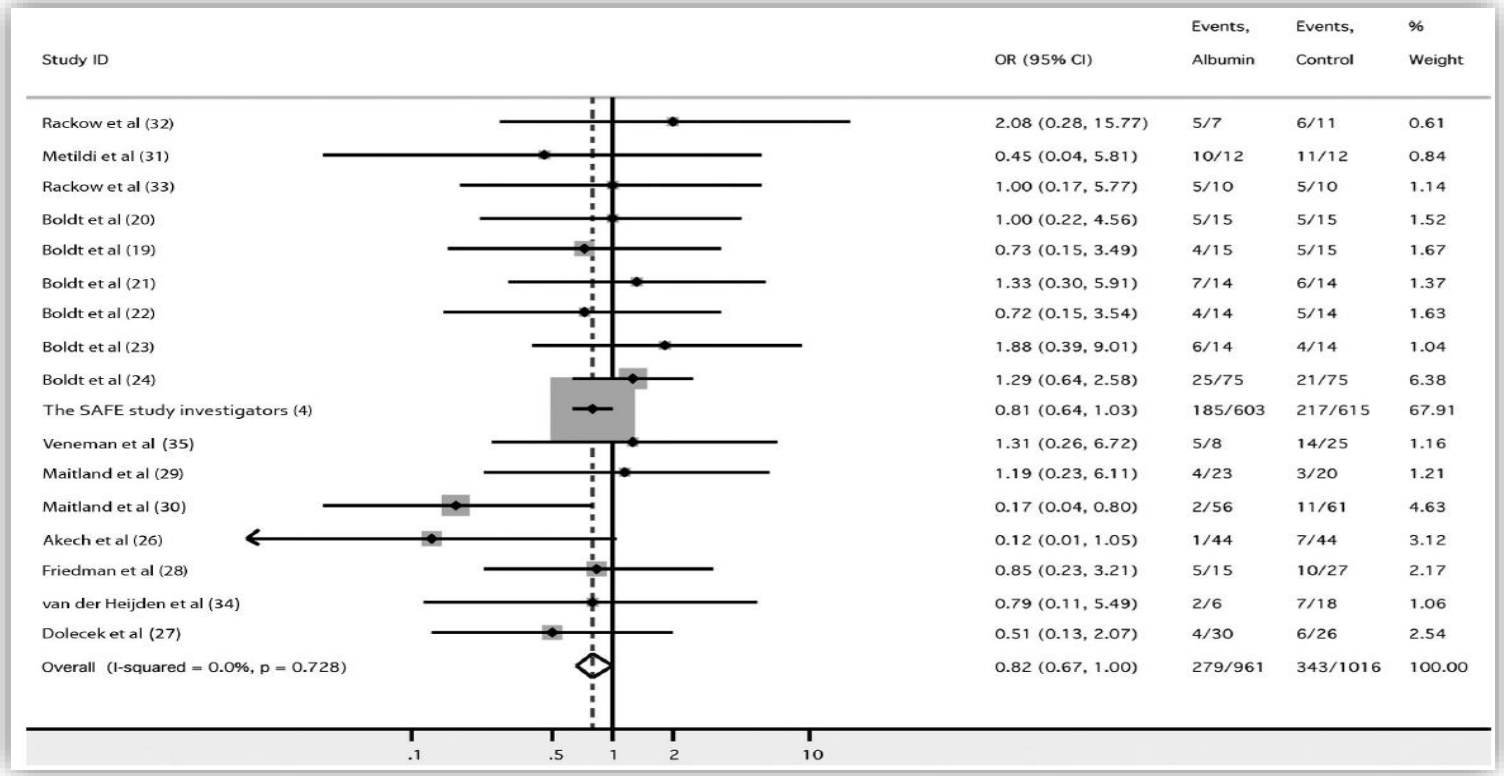


CHEST 2020; 157(2):286-292
Intensive Care Med 2016; 42, 1695–1705

Albumin in sepsis

The role of albumin as a resuscitation fluid for patients with sepsis: A systematic review and meta-analysis*

Anthony P. Delaney, MD, FCICM; Arina Dan, MD, FCICM; John McCaffrey, MD, FCICM; Simon Finfer, MD, FCICM



17 Trials, N=1977

OR 0.82 95% CI (0.67-1.00)

20% albumin (8 trials)
OR 1.08 95% CI (0.7-1.68)

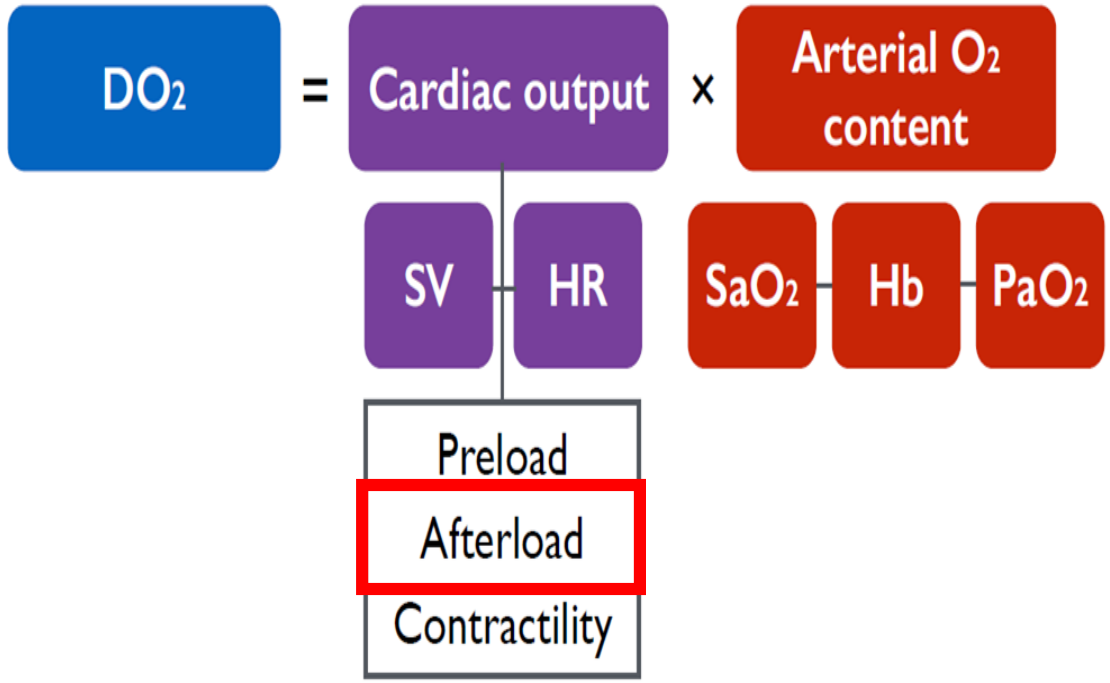
4-5% albumin (9 trials)
OR 0.76 95% CI (0.61-0.95)

vs. Saline (7 trials)
OR 0.78 95% CI (0.62-0.99)

Crit Care Med 2011; 39:386 –391
Pietro C, et al. N Eng J Med 2014

Vasoactive agents

Vascular properties of Vasoactive agents



	CI	PVR	SVR	PVR/SVR	Tachycardia	Renal[a]/metabolic
Vasopressors				Dose related		
NE	+	+	++	+/-	+	Lactic acidosis
PHE	-	++	+	+	-	-
Low-dose AVP	+/-	+/-	++	-	-	Diuresis ++
Inotropes						
Dobutamine	++	-	-	-	+	
< 5 µg/kg/min						
Dopamine	+	+/-	+	+	++	Natriuresis
Epinephrine	++	-	++	-	++	Lactic acidosis
Inodilators						
PDE IIIs	++	-	-	-	+/-	-
Levosimendan	++	-	-	-	-	-

Critical Care 2010;14:R169

Timing & First-line vasoactive agents

Recognize decreased mental status and perfusion.
Begin high flow O_2. Establish IV/IO access.

Initial resuscitation: Push boluses of 20 cc/kg isotonic saline or colloid up to & over 60 cc/kg until perfusion improves or unless rales or hepatomegaly develop.
Correct hypoglycemia & hypocalcemia. Begin antibiotics.

If 2nd PIV start inotrope.

shock not reversed?

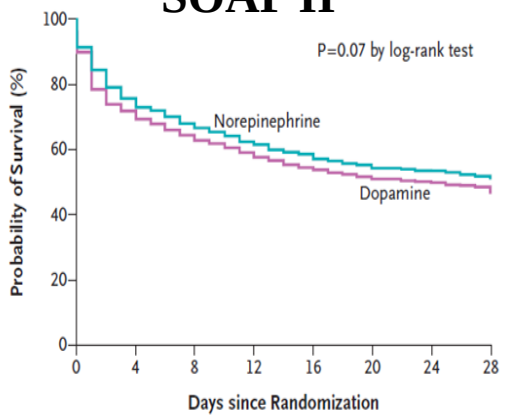
Fluid refractory shock: Begin inotrope IV/IO.
use atropine/ketamine IV/IO/IM
to obtain central access & airway if needed.
Reverse cold shock by titrating central dopamine
or, if resistant, titrate central epinephrine
Reverse warm shock by titrating central norepinephrine.

dose range: dopamine up to 10 mcg/kg/min, epinephrine 0.05 to 0.3 mcg/kg/min.

shock not reversed?

Catecholamine resistant shock: Begin hydrocortisone if at risk for absolute adrenal insufficiency

SOAP II

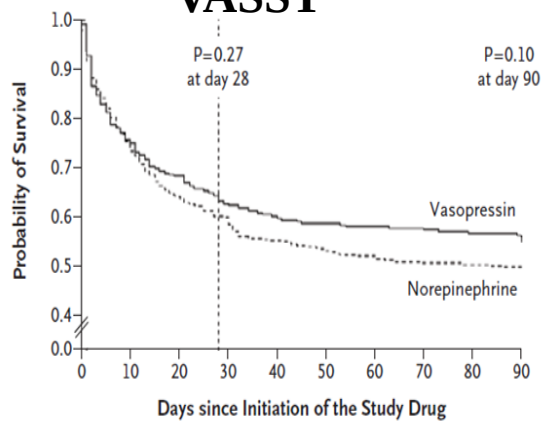


No. at Risk								
Norepinephrine	821	617	553	504	467	432	412	394
Dopamine	858	611	546	494	452	426	407	386

Figure 2. Kaplan–Meier Curves for 28-Day Survival in the Intention-to-Treat Population.

N. Engl. J. Med. 2010

VASST



No. at Risk										
Vasopressin	397	301	272	249	240	234	232	230	226	220
Norepinephrine	382	289	247	230	212	205	200	194	193	191

Figure 2. Kaplan–Meier Survival Curves for Patients Who Underwent Randomization and Infusion.

N. Engl. J. Med. 2008

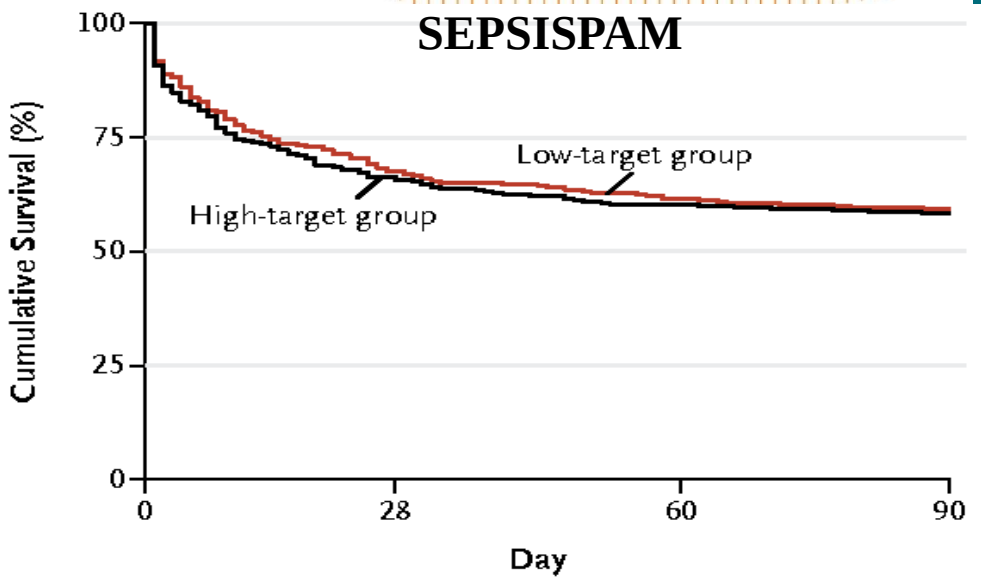
Decreased Mortality: RR 0.98 (95% CI 0.81-0.98)
Decreased Arrythmia: RR 0.48 (95% CI 0.40-0.58)

For adults with septic shock, we recommend using **norepinephrine as the first-line agent** over other vasopressors. (Strong recommendation, high-quality evidence)

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

Blood pressure target

Reference	Study design	No. of patients	Target MAP (mmHg)
LeDoux et al. (2000)	Prospective cohort	10	65,75,85
Bourgoin et al. (2005)	RCT	28	65, 85
Deruddre et al. (2007)	Prospective cohort	11	65,75,85
Jhanji et al. (2009)	Prospective cohort	16	60, 70, 80, 90
Thooft et al. (2011)	Prospective cohort	13	65,75,85, 95
Dubin et al. (2009)	Prospective cohort	20	65,75,85
Asfar et al. (2014)	RCT	776	65, 85



Valuable	Low	High	p value
Primary outcome			
Death at day 28	132 (34.0)	142 (36.6)	0.57
Serious adverse events			
Any	69 (17.8)	74 (19.1)	0.64
Atrial fibrillation	11 (2.8)	26 (6.7)	0.02

For adults with septic shock on vasopressor, we recommend an **initial target mean atrial pressure (MAP) of 65 mmHg** over higher MAP targets. (Strong recommendation, moderate-quality of evidence)

Asfar et al. N Eng J Med 2014

Vascular approach in vasoactive agents

Delayed initiation of vasopressor until central venous catheterization

VS

Immediately initiation of vasopressor on peripheral vein

Vasopressor induced digit necrosis and gangrene

Foot & Ankle Surgery: Techniques, Reports & Cases 2. 2022
J Korean Foot Ankle Soc. 2019

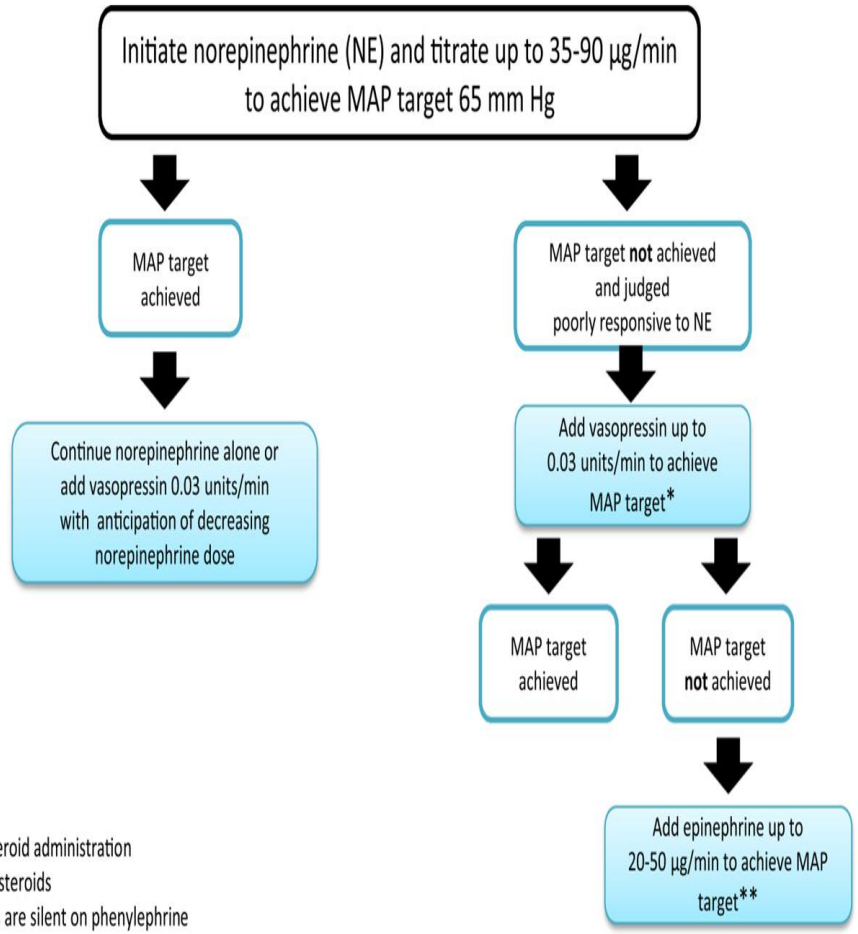
Vascular approach in vasoactive agents

Peripheral vs Central	iPVC (N=389)	iCVC (N=548)	P-value
Median time (h) from ED to vasopressor commencement (IQR)	2.4 (1.3-4.1)	4.9 (3.5-6.6)	< 0.001
Median [IQR] time (hours) from ED to commencement of norepinephrine	3.0 (1.7-4.7)	5.0 (3.6-6.6)	<0.001
Extravasation Incidence	Local tissue injury (N=204)	Extravasation (N=114)	
38 events (3.4%, 95% CI 2.5-4.7)			
Distal (saphenous vein, hand, forearm, leg, wrist, foot, arm)	174 (85.3%)	39 (34.2)	
Proximal (Antecubital fossa, neck, thigh, scalp/head, trunk)	120 (9.8)	13 (11.4)	

For adults with septic shock, we suggest starting vasopressors **peripherally** to restore MAP rather than delaying initiation until a central venous access is secured. When the using vasopressor peripherally, they should be administered only for a short period of time and vein **in or proximal to the antecubital fossa**. (Weak recommendation, very low quality of evidence)

Anthony Delaney, et al., Emerg Med Australas. 2020
David H tian, et al., Emerg Med Australas. 2020
Osama M Loubani, et al., J Crit Care. 2015

Refractory shock state on NE CIV



Recommendation in SSc 2021

For adults with septic shock on norepinephrine with inadequate MAP levels, we suggest adding **vasopressin** instead of escalating the dose of norepinephrine
(Weak recommendation, moderate-quality evidence)

In our practice, vasopressin is usually started when the dose of norepinephrine is the range of **0.25-0.5 mcg/kg/min**
(Weak recommendation, low-quality evidence)

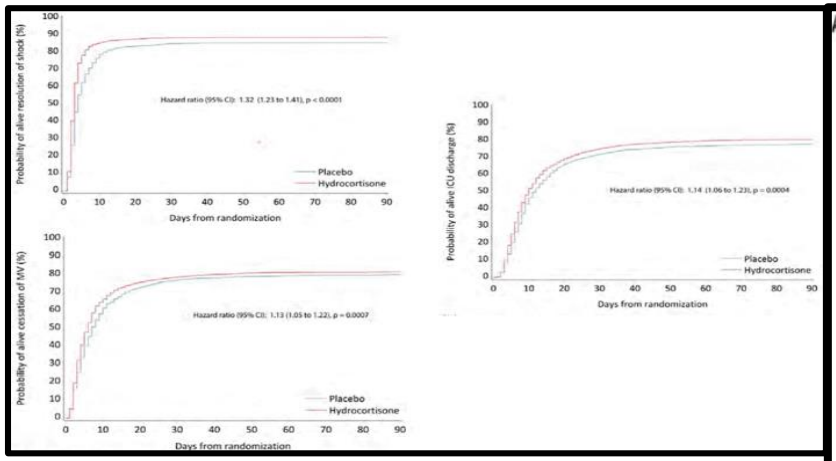
For adults with septic shock and inadequate MAP levels despite norepinephrine and vasopressin, we suggest adding **epinephrine**
(Weak recommendation, low-quality evidence)

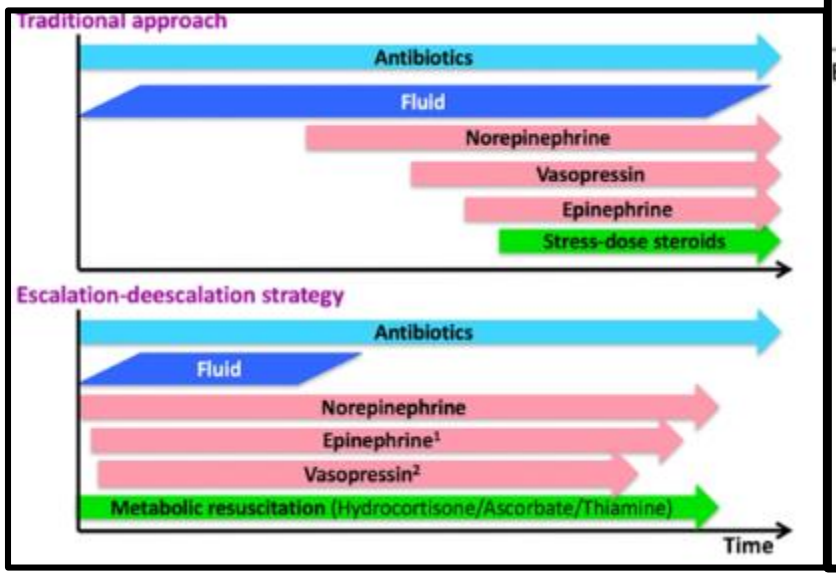
For adults with septic shock and **cardiac dysfunction** with persistent hypoperfusion despite adequate volume status and arterial blood pressure, we suggest either **adding dobutamine to norepinephrine** or **using epinephrine alone** (Weak recommendation, low-quality evidence)

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021, Intensive Care Med 2021

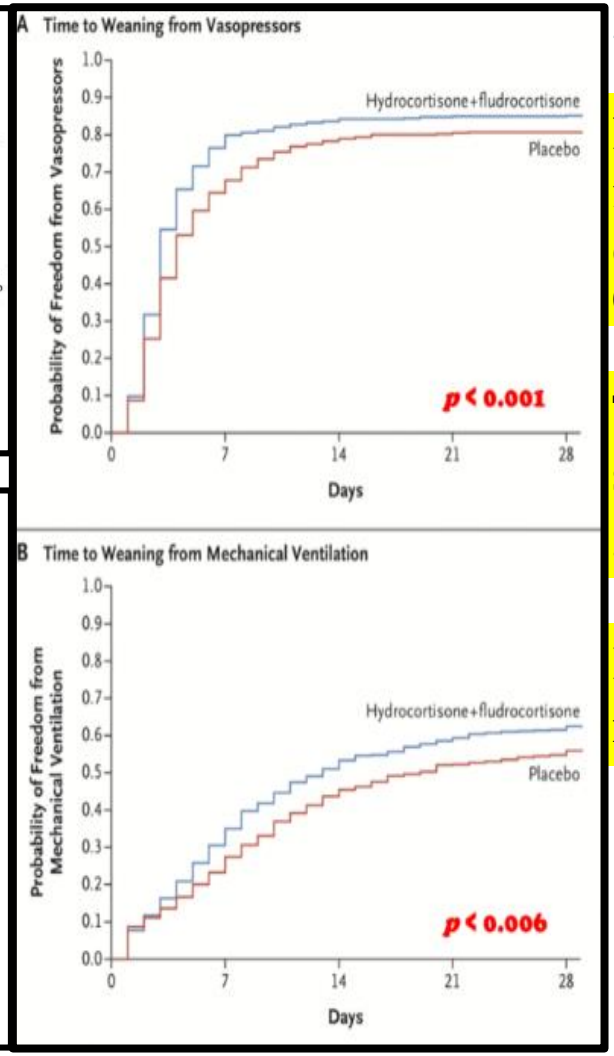
Consider IV steroid administration

ADRENAL





APROCCHSS



Recommendation in SSc 2021

For adults with septic shock and an ongoing requirement for vasopressor therapy, we suggest using IV corticosteroids
(Weak recommendation, moderate-quality evidence)

The typical corticosteroid used in adults with septic shock is **IV hydrocortisone** at a dose of **200mg/day** given as 50mg IV every 6 h or as a continuous infusion

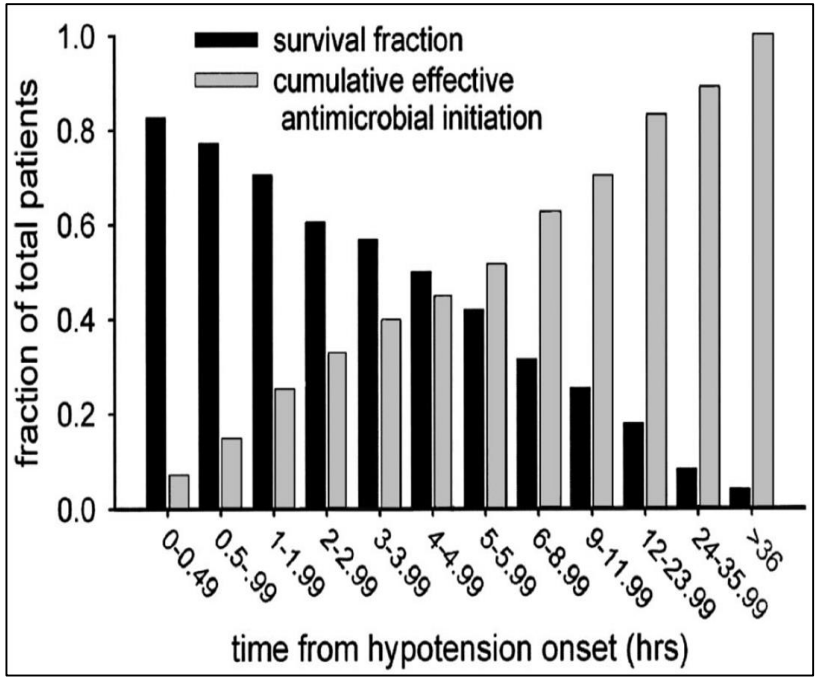
It is suggested that this is commenced at a dose of norepinephrine or epinephrine **≥ 0.25-0.5 mcg/kg/min**

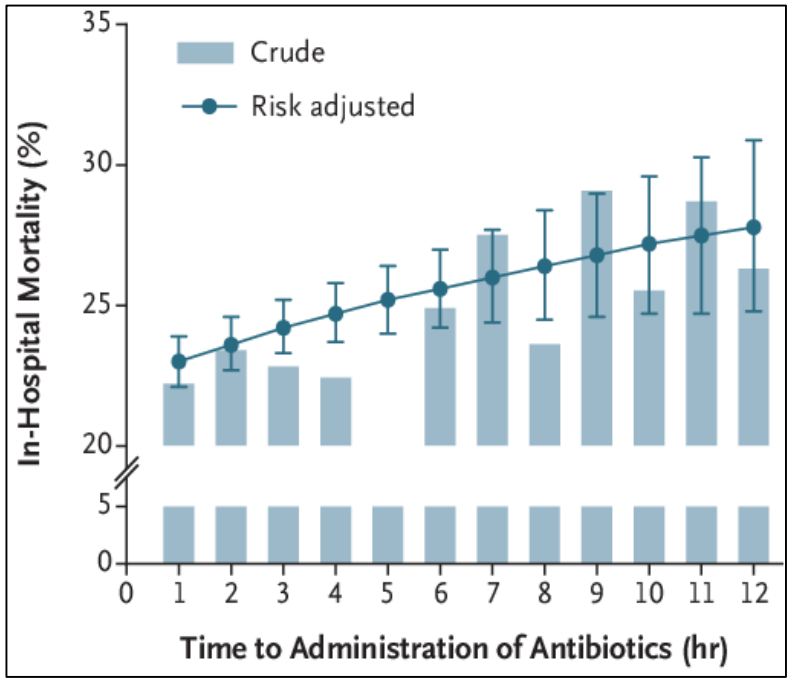
Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021, Intensive Care Med 2021

Antibiotics

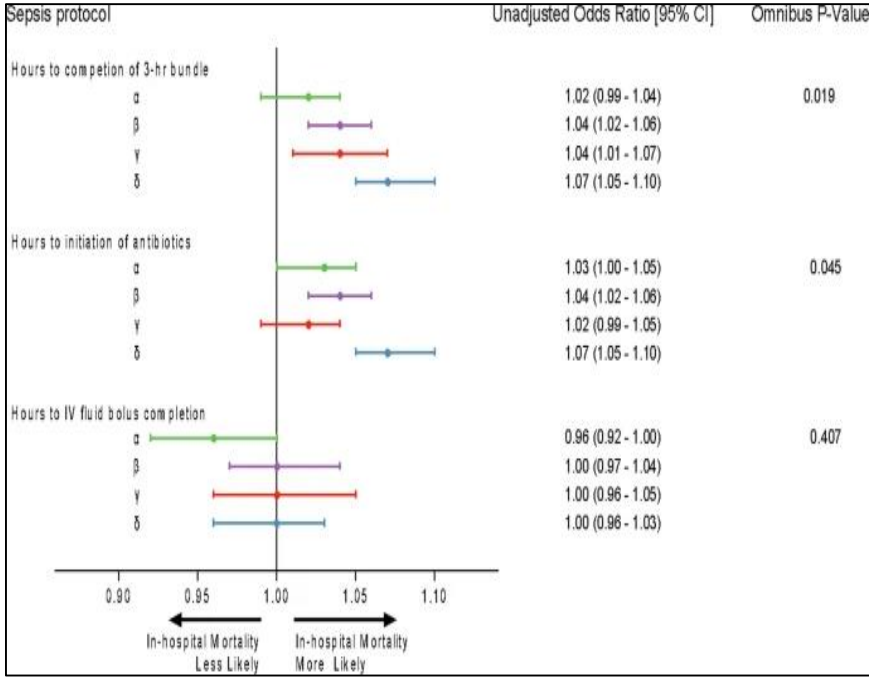
Time to antibiotics

Time to treatment and mortality





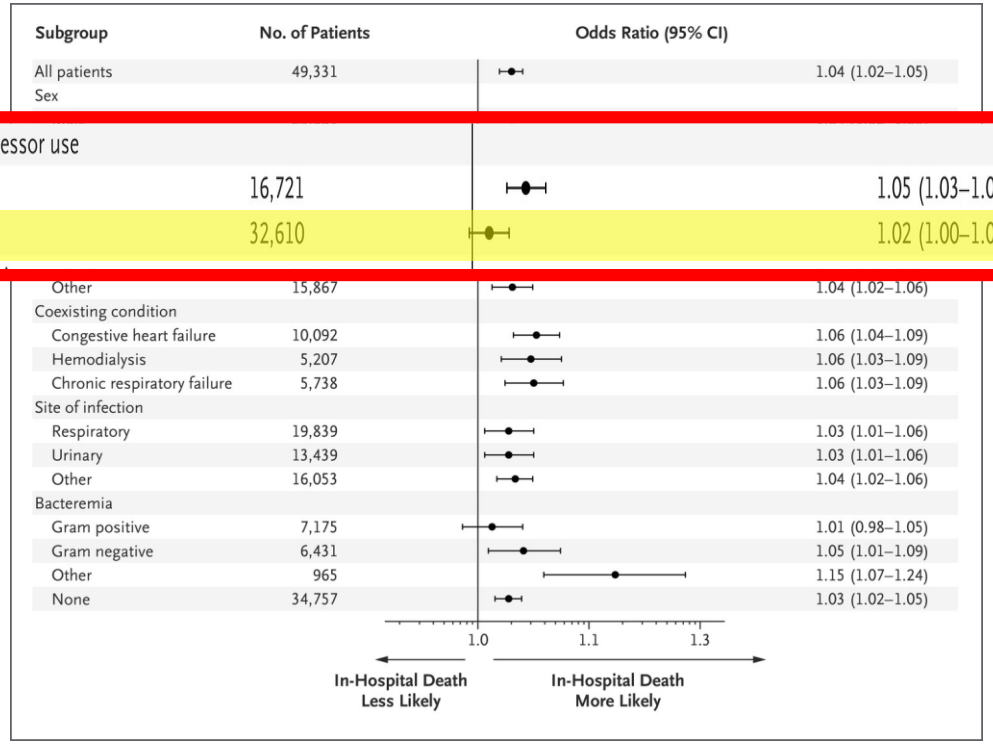
Adjusted odds ratios of in-hospital mortality, stratified by clinical sepsis subtype.



For adults with **possible septic shock** or **a high likelihood for sepsis**, we recommend administering antimicrobials **immediately, ideally within 1 h** of recognition (Strong recommendation, low-quality evidence)

Ferrer R, et al. Am J Respir Crit Care Med 2009
Seymour CW, et al. N Eng J Med 2017
Yang A, et al. Crit Care 2023

Time to antibiotics



Risk-adjusted odd ratios for in-hospital mortality associated with antibiotics in 1h

In-hospital mortality	Administration of broad spectrum antibiotics in 1h		p-value
	No	Yes OR (95% CI)	
All participants (n = 3035)			
Overall	Ref	**0.78 (0.61-0.99)**	**0.046**
Without septic shock	Ref	0.85 (0.64-1.15)	0.300
With septic shock	Ref	**0.66 (0.44-0.99)**	**0.049**

For adults with **possible sepsis without shock**, we suggest a time-limited course of rapid investigation and if concern for infection persists, the administration of antimicrobials **within 3 h** from the time when sepsis was first recognized

(Weak recommendation, very low-quality evidence)

Seymour CW, et al. N Eng J Med 2017

Yunjoo im et al. Crit Care 2022

Antimicrobial choice

Risk Factors for Multidrug Resistant (MDR) Pathogens

- Antimicrobial therapy in preceding 90 days
- Current hospitalization of 5 days or more
- High frequency of antibiotic resistance in the community or specific hospital unit
- Immunosuppressive disease and/or therapy
- Risk factors for healthcare associated pneumonia
  - Hospitalization for 2 days or more in the preceding 90 days
  - Residence in nursing home or extended care facility
  - Home infusion therapy
  - Chronic dialysis within 30 days
  - Home wound care
  - Family member with MDR pathogen

Preceding antibiotics therapy
Colonization MDR pathogen

For adults with sepsis or septic shock and **high risk** for multidrug resistant (MDR) organisms, we suggest using **two** antimicrobials with gram-negative coverage for empiric treatment over one gram-negative agent (Weak recommendation, very low quality of evidence)

For adults with sepsis or septic shock and low risk for MDR organisms, we suggest **against using two** Gram-negative agents for empiric treatment, as compared to one Gram-negative agent (Weak recommendation, very low quality of evidence)

Arulkumaran N, et al. Intensive Care Med 2020
Rottier WC, et al. Clin Microbiol Infect 2018

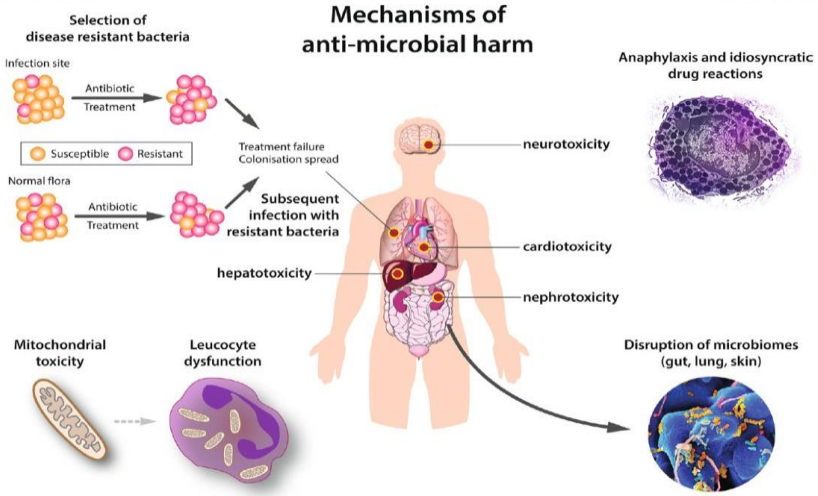
Antimicrobial-associated undesirable effects

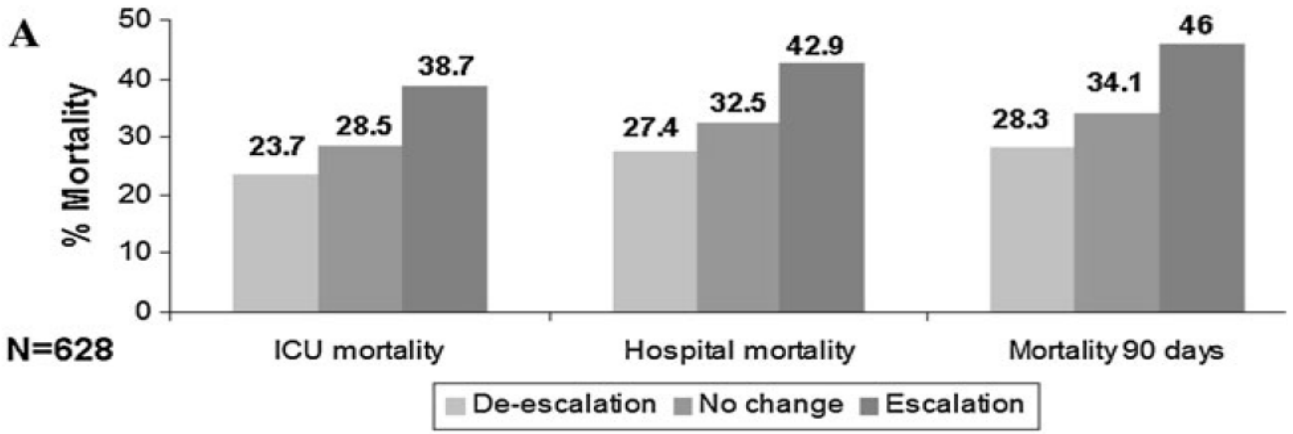
Intensive Care Med (2020) 46:225–235
https://doi.org/10.1007/s00134-020-05929-3

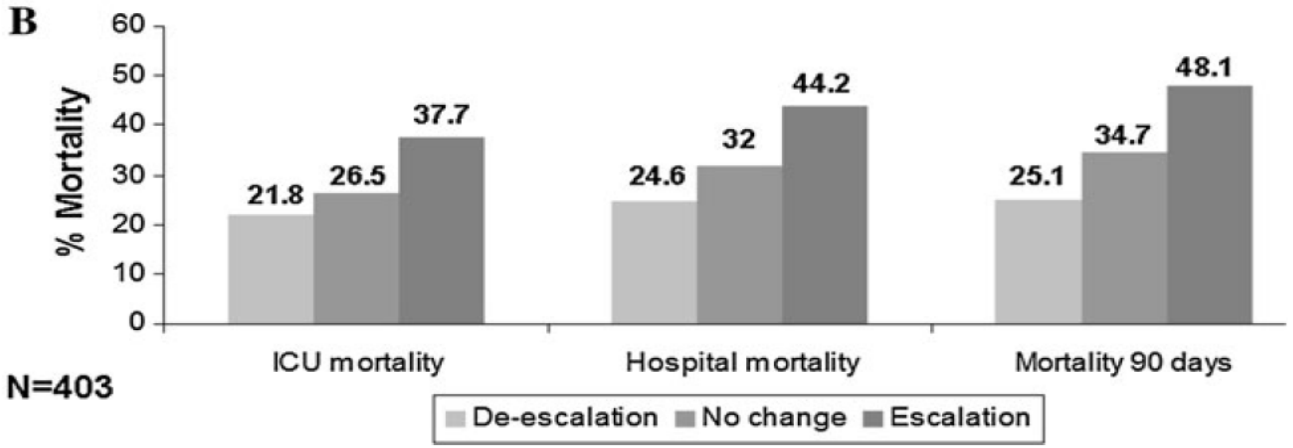
NARRATIVE REVIEW

Antimicrobial-associated harm in critical care: a narrative review

Nishkantha Arulkumaran[1], Matthew Routledge[2,3], Sanmarié Schlebusch[4,5], Jeffrey Lipman[4,6,7] and Andrew Conway Morris[8,9*]

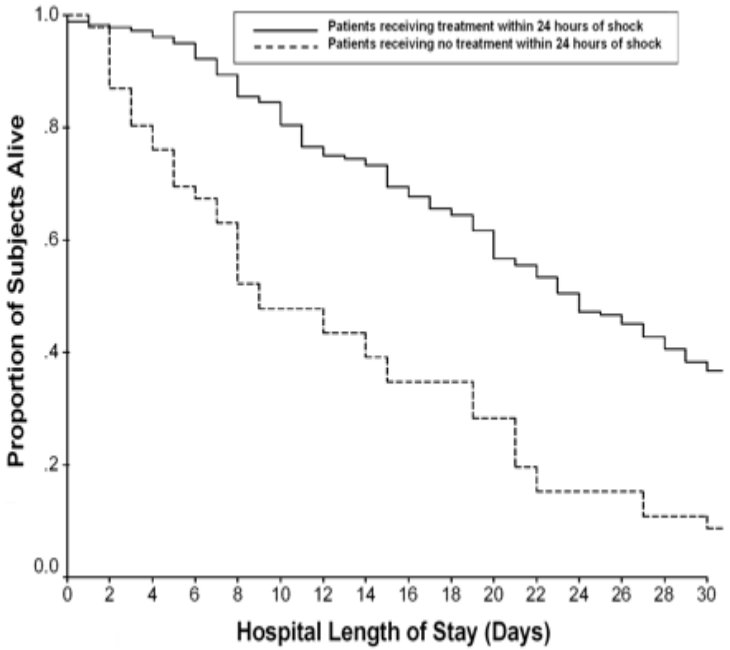


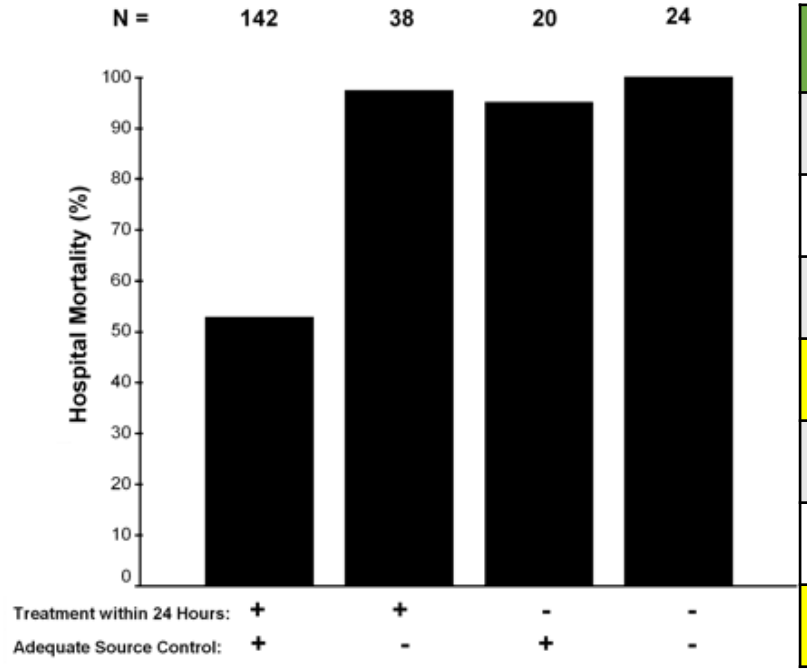




Nishkantha A, et al. Intensive Care Med 2020
Intensive Care Med 40:32–40 2014

Antifungal therapy





	AOR	95%CI	P value
Solid cell tumor with metastasis	6.01	2.97-12.10	.010
Class IV congestive heart failure	4.98	2.53-9.68	.017
APACHE II score (1-point increments)	1.37	1.26-1.48	< .001
Inadequate source control	77.40	21.52-278.38	.001
Red blood cell transfusion	6.49	4.06-10.38	< .001
Serum albumin (1g/dL increments)	0.42	0.30-0.59	.012
Delayed antifungal treatment	33.75	9.65-118.04	.005

For adults with sepsis or septic shock at **high risk** of fungal infection, we **suggest** using empiric antifungal therapy (Weak recommendation, low-quality evidence)

For adults with sepsis or septic shock at **low risk** of fungal infection, we **suggest against** using empiric antifungal therapy (Weak recommendation, low-quality evidence)

Kollef M, et al. Clin Infect Dis 2012

Risk factors for fungal infection

Candida sepsis	
Candida colonization at multiple sites	Persons who inject drugs
Surrogate markers (e.g. Beta-D-Glucan assay)	GI tract perforation
Neutropenia	GI tract anastomotic leaks
Immunosuppression	Emergency GI or hepatobiliary surgery
Severity of illness (High APACHE score)	Severe thermal injection
Longer ICU LOS	Prior surgery
CVC and other intravascular devices	Broad spectrum antibiotics
Total parenteral nutrition	Acute renal failure and hemodialysis

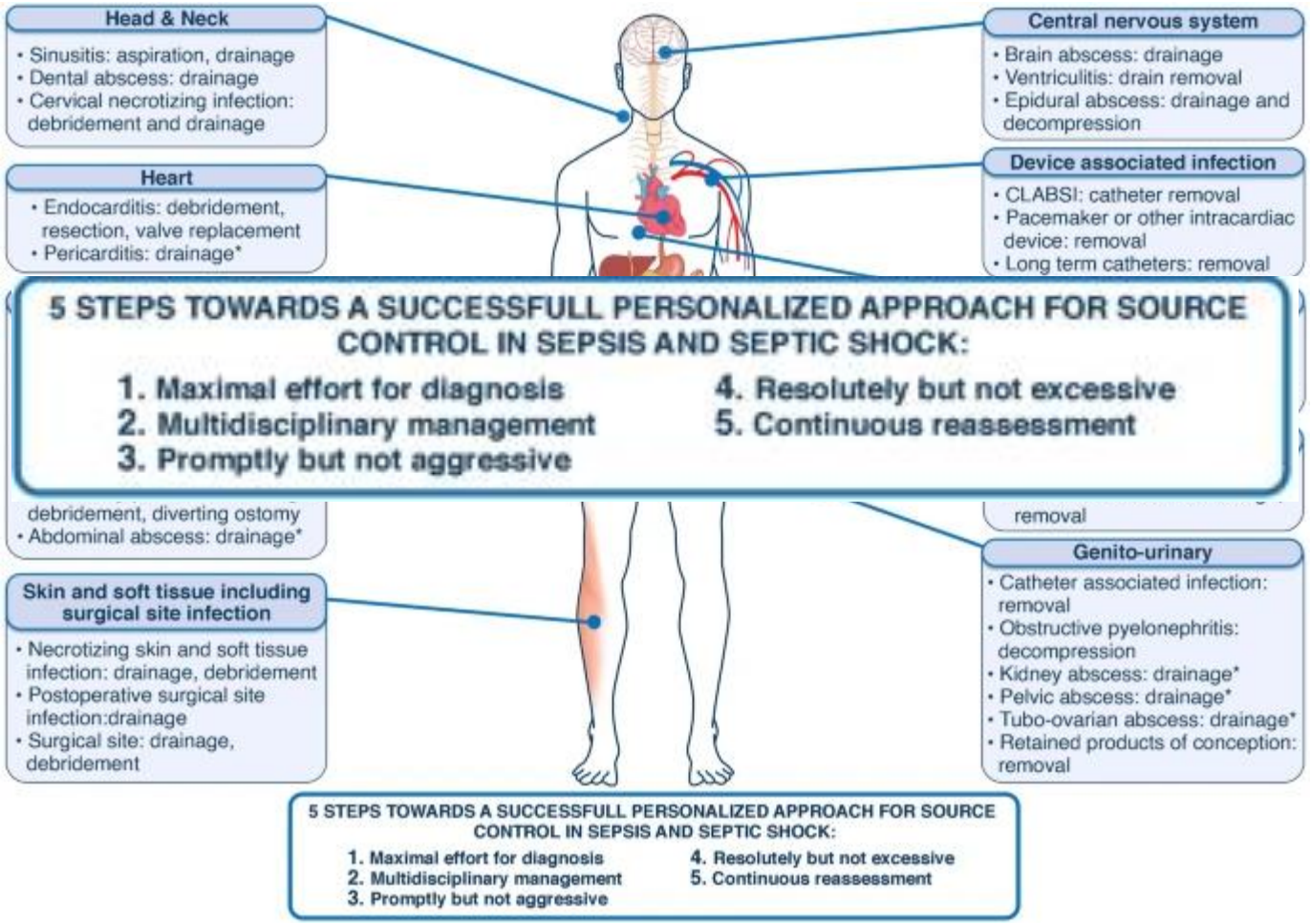
Endemic yeast (Cryptococcus, histoplasma, blastomyces, coccidiodomycosis)
Antigen marker (cryptococcal, histoplasma, blastomyces assays)
HIV infection
Sold organ transplantation
High dose corticosteroid therapy
Hematopoietic stem cell transplantation
Biologic response modifiers
Diabetes mellitus

Invasive mold infection
Neutropenia
Surrogate markers (Galactomannan assay)
Hematopoietic stem cell transplantation
High dose corticosteroid therapy
Biologic response modifiers

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Source control

Different types of infections where source control



For adults with sepsis or septic shock, we recommend rapidly identifying or excluding a specific anatomical diagnosis of infection that requires emergent source control and implementing any required source control intervention as soon as medically and logistically practical (Best Practice Statement)

For adults with sepsis or septic shock, we recommend prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established (Best Practice Statement)

De Waele, J.J., et al. Intensive Care Med 2022
Bloos F, et al. Crit Care 2014

Take home Message

❑Definition: sepsis-3

- Sepsis: infection + organ dysfunction (SOFA score)
- Septic shock: sepsis + vasopressor + hyperlacticemia

❑Early recognition

- qSOFA << SIRS, NEWS, MEWS
- Serum lactate, Capillary refill time

❑Fluid resuscitation

- Colloid << Crystalloid << Balanced crystalloid
- at least 30 mL/kg within the first 3 h

❑Vasoactive agents

- Fluid refractory shock state: Norepinephrine >> Vasopressin (NE ≥ 0.25 mcg/kg/min) >> epinephrine
- MAP target ≥ 65 mmHg
- Add corticosteroid (NE or Epi ≥ 0.25 mcg/kg/min)

❑Antibiotics and Source control

- Shock or probable sepsis: within 1h
- Possible sepsis without shock: within 3h
- High risk MDR, Fungal infection

울산대학교병원
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Thank you!

Q & A

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