International Guidelines for Management of Sepsis and Septic Shock 2021

Surviving Sepsis Campaign

Les Vendredis de la Réanimation

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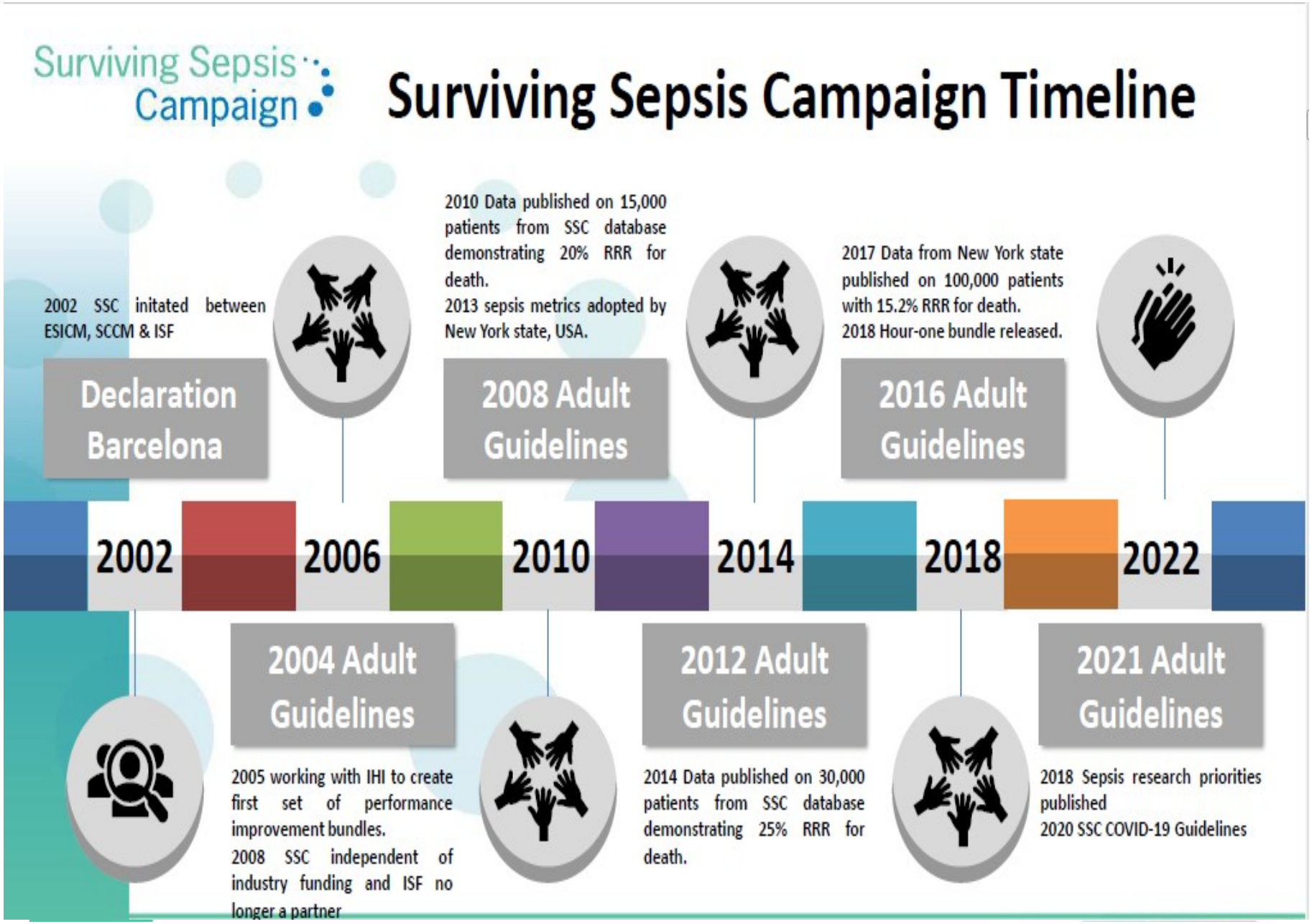
Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE
The Intensive Connection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Surviving Sepsis Campaign Timeline
2002 SSC initated between ESICM, SCCM & ISF
Declaration Barcelona
2004 Adult Guidelines
2005 working with IHI to create first set of performance improvement bundles.
2008 SSC independent of industry funding and ISF no longer a partner
2008 Adult Guidelines
2010 Data published on 15,000 patients from SSC database demonstrating 20% RRR for death.
2013 sepsis metrics adopted by New York state, USA.
2012 Adult Guidelines
2014 Data published on 30,000 patients from SSC database demonstrating 25% RRR for death.
2016 Adult Guidelines
2017 Data from New York state published on 100,000 patients with 15.2% RRR for death.
2018 Hour-one bundle released.
2021 Adult Guidelines
2018 Sepsis research priorities published
2020 SSC COVID-19 Guidelines
2002
2006
2010
2014
2018
2022

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What is new in the 2021 guidelines recommendations?
A few highlights

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PLAN :

1. SREENING AND EARLY TREATEMENT
2. INFECTION
3. HEMODYNAMIC MANAGEMENT
4. VENTILATION
5. ADDITION THERAPIES
6. LONG-TERM OUTCOMES AND GOALS OF CARE

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I. SCREENINIG AND EARLY TREATEMENT

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1. Screening for patients with Sepsis and Septic Shock:

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
1. For hospitals and health systems, we recommend using a performance improvement program for sepsis, including sepsis screening for acutely ill, high-risk patients and standard operating procedures for treatment.	**Strong**, moderate-quality evidence (for screening) **Strong**, very low-quality evidence (for standard operating procedures)	**Changed from Best practice statement** "We recommend that hospitals and hospital systems have a performance improvement program for sepsis including sepsis screening for acutely ill, high-risk patients."

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Contents lists available at ScienceDirect

Computer Methods and Programs in Biomedicine

journal homepage: www.elsevier.com/locate/cmpb

Prediction of sepsis patients using machine learning approach: A meta-analysis

Table 1
Baseline characteristic of included studies.

Author	Publication year	Data collection period	Sepsis patients	Prediction models	Data source	Sepsis definition/ identification	Department	Prediction before sepsis	AUROC	External validation	Model discrimination
Desautels	2016	2001–08	2577	Insight	MIMIC-III	SIRS criteria	ICU	0 and 4 h before	ML = 0.88 SIRS = 0.61 SOFA = 0.73 QSOFA = 0.77 MEWS = 0.80	N	NR
Horng	2017	2008–13	32,103	SVM	MIMIC-III	ICD-9 code	ICU	4 h	ML = 0.86	N	NR
Mao	2017	2011–16	140	InSight	University of California, San Francisco and MIMIC-III	SIRS criteria, and ICD-9 code: 995.91	ICU	0 and 4 h before	ML = 0.92 MEWS = 0.76 SOFA = 0.63 SIRS = 0.75	Y	NR
Nemati	2017	2013–15	2,375	APeX	Emory University Hospitals And MIMIC-III	Third International Consensus Definitions	ICU	4 h before	ML = 0.85 SOFA = 0.87	Y	NR
Calvert	2016	2001–08	159	InSight	MIMIC-III	SIRS criteria, and ICD9 code: 995.9	ICU	3 h before	ML = 0.83	N	NR
Kam	2017	2001–12	360	Deep neural network	MIMIC-III	SIRS criteria, and ICD9 code: 995.9	ICU	3 h before	ML = 0.92	N	NR
Faisal	2018	2014–15	4,909	Logistic regression	York hospital, and Northern Lincolnshire and Google Hospital	ICD-10	ICU	4 h before	ML = 0.78	Y	0.186

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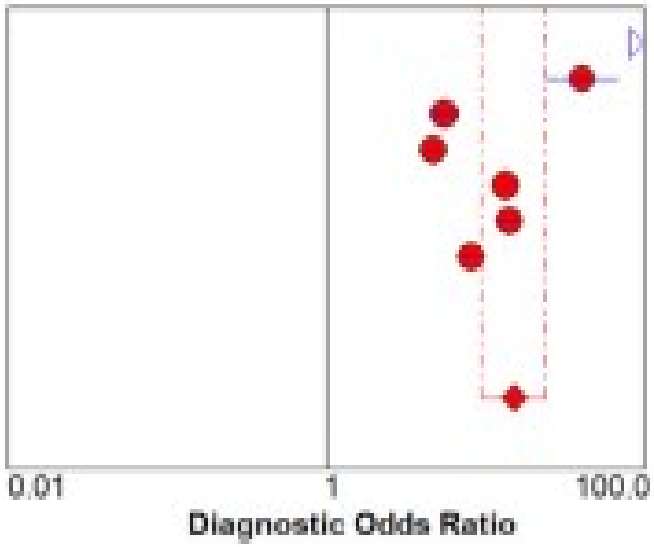
D.



	Diagnostic OR (95% CI)
Kam (2017)	160.45 (109.74 - 234.59)
Calvert (2016)	40.69 (23.85 - 69.42)
Faisal (2018)	5.49 (4.48 - 6.73)
Desautels (2016)	4.70 (4.25 - 5.20)
Horng (2017)	13.34 (12.96 - 13.72)
Mao (2017)	14.12 (12.26 - 16.26)
Nemati (2017)	8.11 (7.28 - 9.03)

Random Effects Model
Pooled Diagnostic Odds Ratio = 15.17 (9.51 to 24.20)
Cochran-Q = 702.99; df = 6 (p = 0.0000)
Inconsistency (I-square) = 99.1 %
Tau-squared = 0.3799

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Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
2. We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock.	**Strong**, moderate-quality evidence	**NEW** 

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JAMA Network Open

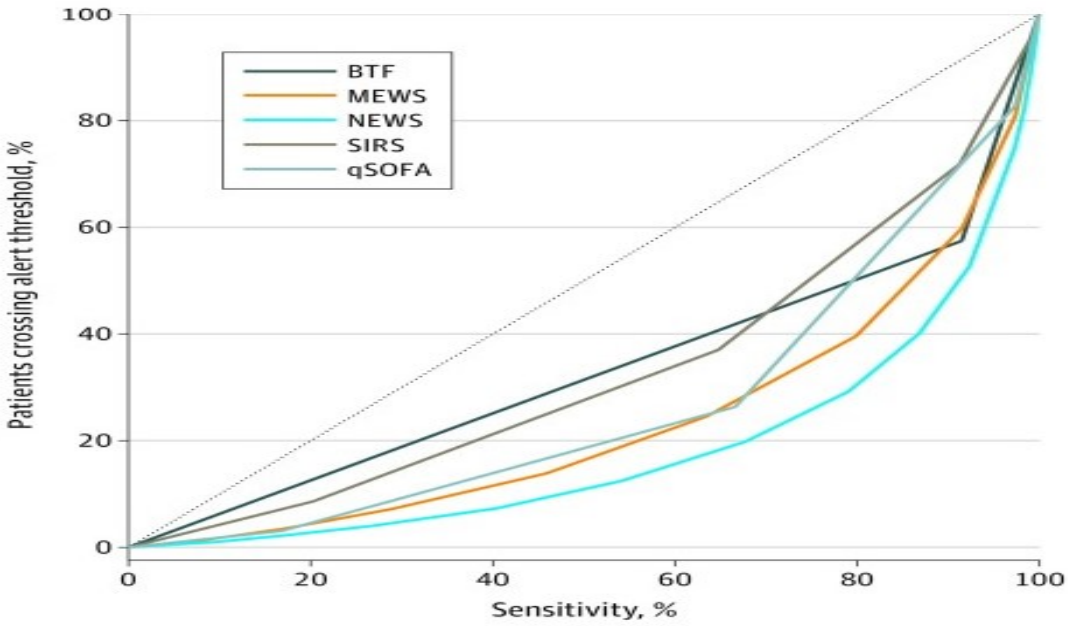
View Article

JAMA Netw Open. 2020 May; 3(5): e205191.
Published online 2020 May 19. doi: 10.1001/jamanetworkopen.2020.5191

PMCID: PMC7237982
PMID: 32427324

Comparison of Early Warning Scoring Systems for Hospitalized Patients With and Without Infection at Risk for In-Hospital Mortality and Transfer to the Intensive Care Unit

[Figure 3.



-Early Warning Score Efficiency Curves for Patients With Suspected Infection

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Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
3. For adults suspected of having sepsis, we suggest measuring blood lactate.	**Weak**, low quality of evidence	

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2. Initial resuscitation:

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
4. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately.	**Best practice statement**	
5. For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30mL/ kg of IV crystalloid fluid should be given within the first 3hr of resuscitation	**Weak**, low quality of evidence	**DOWNGRADE** from **Strong**, low quality of evidence

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- The 2016 SSC guideline issued a recommendation for using a minimum of 30 mL/kg (ideal body weight) of IV crystalloids in initial fluid resuscitation: based on observational evidence .

- There are no prospective intervention studies comparing different volumes for initial resuscitation in sepsis or septic shock.

- A retrospective analysis of adults presenting to an emergency department with sepsis or septic shock showed that failure to receive 30 mL/kg of crystalloid fluid therapy within 3 hours of sepsis onset was associated with increased odds of in-hospital mortality, delayed resolution of hypotension and increased length of stay in ICU, irrespective of comorbidities.

- In the PROCESS , ARISE and PROMISE trials, the average volume of fluid received pre-randomization was also in the range of 30 mL/kg, suggesting that this fluid volume has been adopted in routine clinical practice

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Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
6. For adults with sepsis or septic shock, we suggest using dynamic measures to guide fluid resuscitation, over physical examination, or static parameters alone.	**Weak**, very low quality of evidence.	
7. For adults with sepsis or septic shock, we suggest guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate.	**Weak**, low quality of evidence	
8. For adults with septic shock, we suggest using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.	**Weak**, low quality of evidence	**NEW** 

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Review > Crit Care Med. 2017 Sep;45(9):1538-1545. doi: 10.1097/CCM.0000000000002554.

Incorporating Dynamic Assessment of Fluid Responsiveness Into Goal–Directed Therapy: A Systematic Review and Meta–Analysis

Study or Subgroup	Dynamic therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Kapoor 2008	0	15	0	15		Not estimable
Goepfert 2013	0	50	0	50		Not estimable
Kumar 2016	0	30	0	30		Not estimable
Colantonio 2015	0	42	4	44	1.4%	0.12 [0.01, 2.10]
Scheeren 2013	0	32	2	32	1.3%	0.20 [0.01, 4.01]
Buettner 2009	0	40	1	40	1.1%	0.33 [0.01, 7.95]
Parke 2015	0	70	1	74	1.1%	0.35 [0.01, 8.50]
Lopes 2007	2	17	5	16	5.1%	0.38 [0.08, 1.67]
Richard 2015	7	30	14	30	20%	0.50 [0.24, 1.06]
Pearse 2015	28	368	42	366	54.7%	0.66 [0.42, 1.05]
Jhanji 2010	9	90	6	45	12.1%	0.75 [0.28, 1.98]
Mayer 2010	2	30	2	30	3.2%	1.00 [0.15, 6.64]
Total (95% CI)		**814**		**772**	**100.0%**	**0.59 [0.42, 0.83]**
Total events	48		77			

Heterogeneity: Tau² = 0.00; Chi² = 3.28, df = 8 (P = 0.92); I² = 0%

Test for overall effect: Z = 3.04 (P = 0.002)

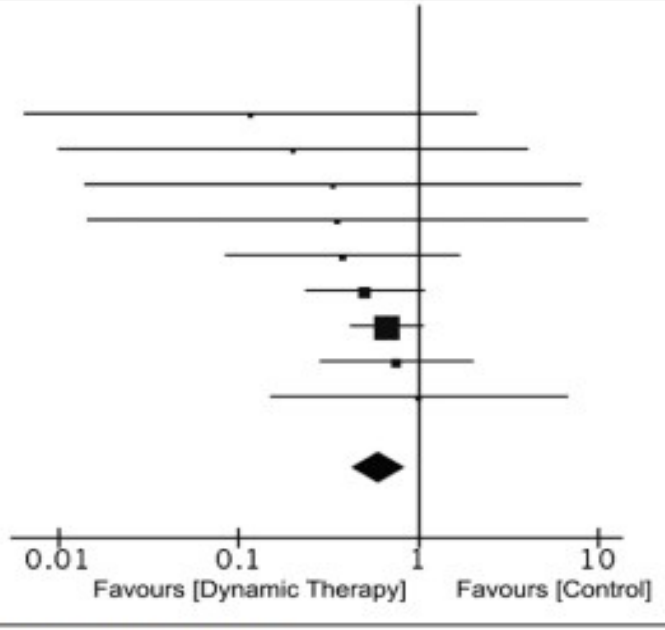

Figure 2. Effect of goal-directed fluid therapy guided by dynamic assessment of fluid responsiveness on mortality.

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Meta-Analysis > Intensive Care Med. 2015 Oct;41(10):1862-3. doi: 10.1007/s00134-015-3955-2. Epub 2015 Jul 8.

Early lactate clearance–guided therapy in patients with sepsis: a meta–analysis with trial sequential analysis of randomized controlled trials

Study or Subgroup	Lactate clearance Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Jansen 2010	20	68	30	67	35.2%	0.66 [0.42, 1.03]
Jones 2010	25	150	34	150	33.7%	0.74 [0.46, 1.17]
Tian 2012	14	43	12	19	24.0%	0.52 [0.30, 0.89]
Yu 2013	5	25	7	25	7.2%	0.71 [0.26, 1.95]
Total (95% CI)		**286**		**261**	**100.0%**	**0.65 [0.49, 0.85]**
Total events	64		83			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.02$, df = 3 (P = 0.80); $I^2 = 0\%$

Test for overall effect: Z = 3.16 (P = 0.002)

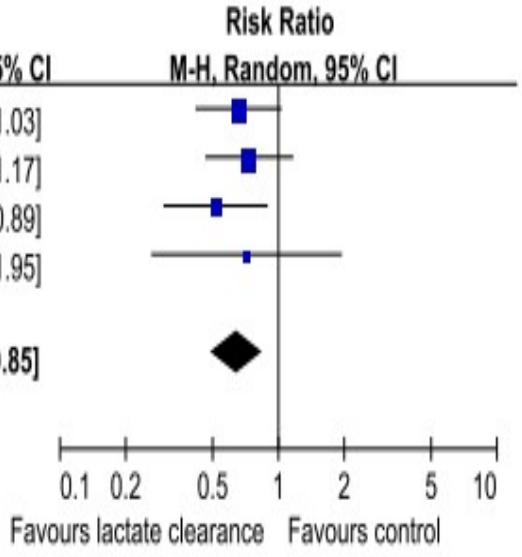

Fig. 1 Forest plot depicting mortality

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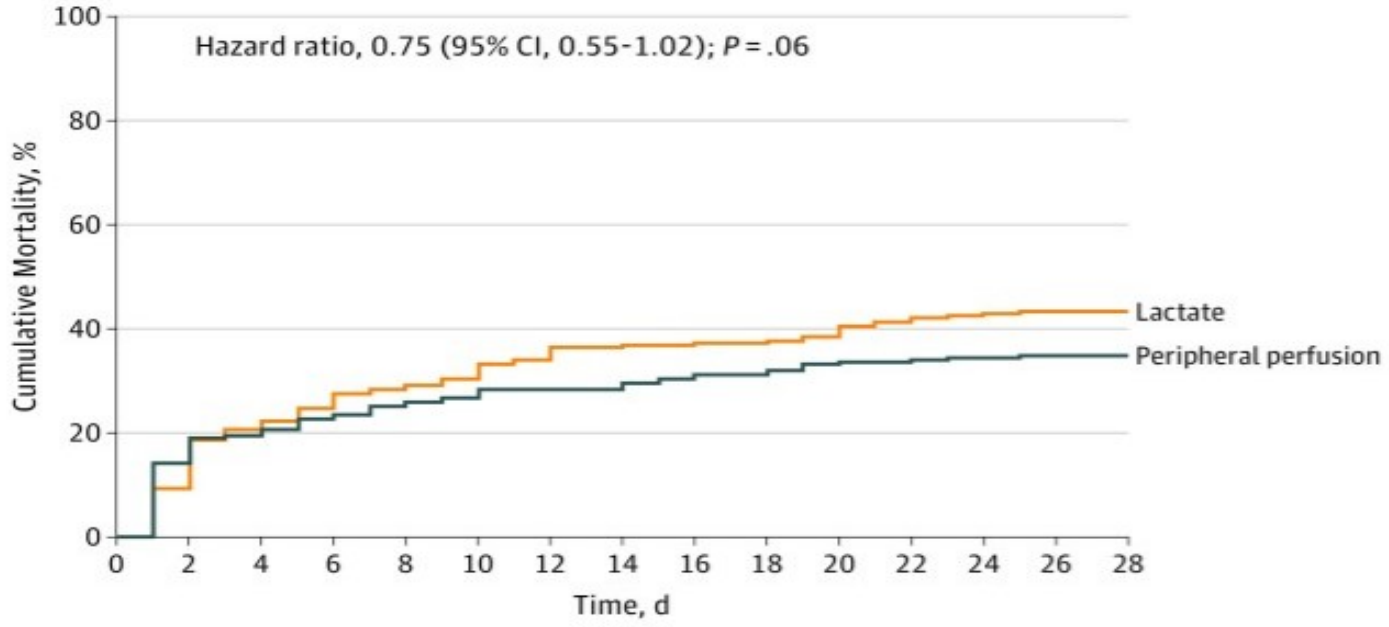
Randomized Controlled Trial > JAMA. 2019 Feb 19;321(7):654-664. doi: 10.1001/jama.2019.0071.

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



No. at risk															
Lactate	212	192	168	160	152	148	140	135	134	133	130	124	122	120	120
Peripheral perfusion	212	182	171	164	159	155	152	152	148	146	142	141	139	138	138

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3. Mean arterial pressure:

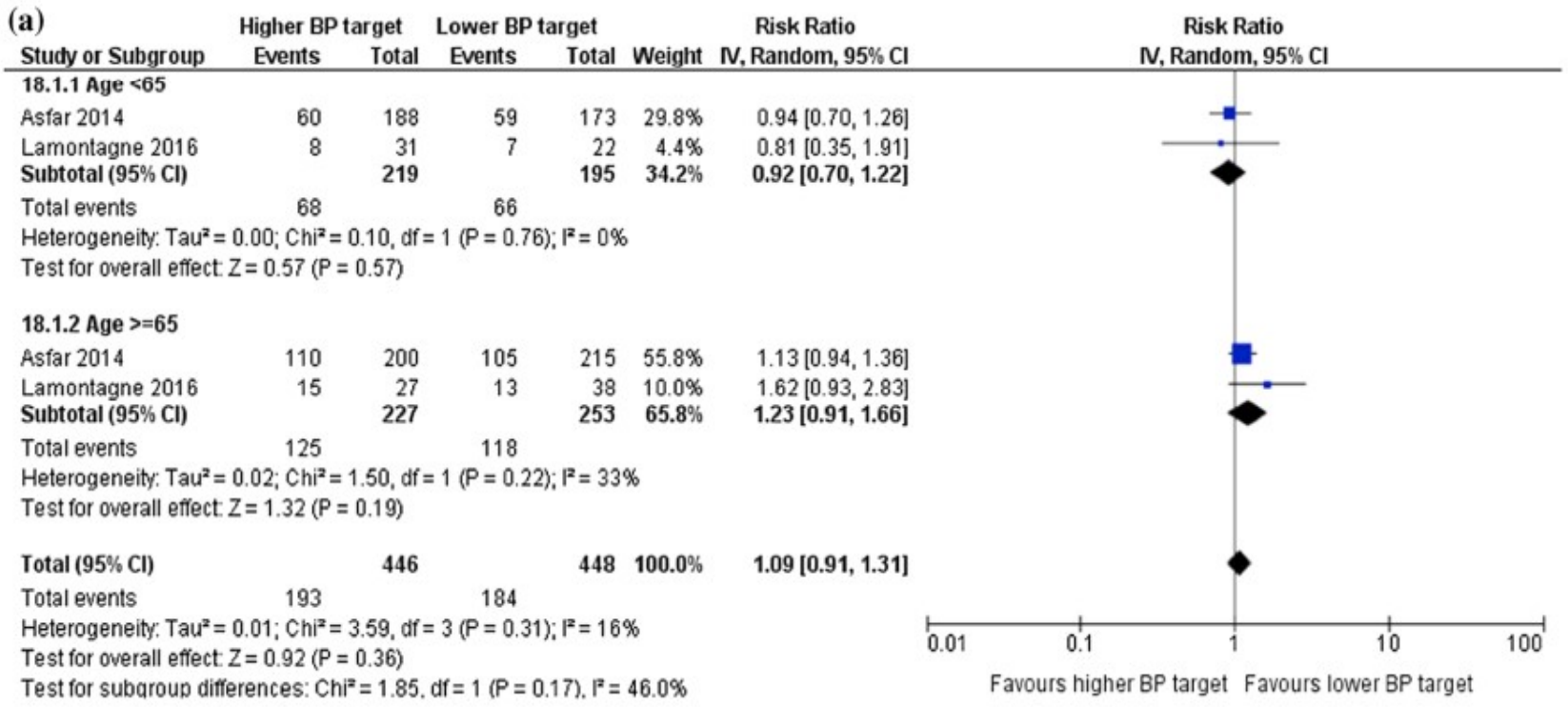
Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
9. For adults with septic shock on vasopressors, we recommend an initial target mean arterial pressure (MAP) of 65mm Hg over higher MAP targets	**Strong**, moderate-quality evidence	

Can J Anesth/J Can Anesth
DOI 10.1007/s12630-017-0877-1

REPORTS OF ORIGINAL INVESTIGATIONS

A systematic review of vasopressor blood pressure targets in critically ill adults with hypotension

Une revue systématique des cibles de tension artérielle sous vasopresseurs chez des adultes gravement malades atteints d'hypotension



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4. Admission to intensive care :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
10. For adults with sepsis or septic shock who require ICU admission, we suggest admitting the patients to the ICU within 6hr.	**Weak,** low quality of evidence	

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> Crit Care Med. 2007 Jun;35(6):1477-83. doi: 10.1097/01.CCM.0000266585.74905.5A.

Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit

Measurements and main results: Main outcomes were intensive care unit and hospital survival and intensive care unit and hospital length of stay. During the study period, 50,322 patients were admitted. Both groups (delayed, n = 1,036; nondelayed, n = 49,286) were similar in age, gender, and do-not-resuscitate status, along with Acute Physiology and Chronic Health Evaluation II score in the subgroup for which it was recorded. Among hospital survivors, the median hospital length of stay was 7.0 (delayed) vs. 6.0 days (nondelayed) ($p < .001$). Intensive care unit mortality was 10.7% (delayed) vs. 8.4% (nondelayed) ($p < .01$). In-hospital mortality was 17.4% (delayed) vs. 12.9% (nondelayed) ($p < .001$). In the stepwise logistic model, delayed admission, advancing age, higher Acute Physiology and Chronic Health Evaluation II score, male gender, and diagnostic categories of trauma, intracerebral hemorrhage, and neurologic disease were associated with lower hospital survival (odds ratio for delayed admission, 0.709; 95% confidence interval, 0.561-0.895).

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II. Infection :

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1. Diagnosis of infection :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
11. For adults with suspected sepsis or septic shock but unconfirmed infection, we recommend continuously re-evaluating and searching for alternative diagnoses and discontinuing empiric antimicrobials if an alternative cause of illness is demonstrated or strongly suspected.	**Best practice statement**	

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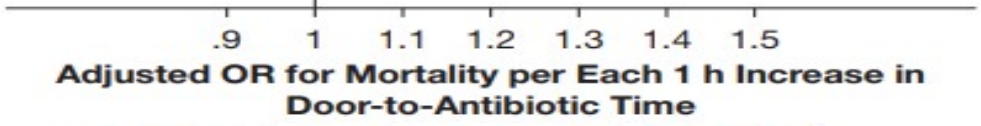
2. Time to antibiotics:

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
12. For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 hr of recognition.	**Strong**, low quality of evidence (Septic shock) **Strong**, very low quality of evidence (Sepsis without shock)	CHANGED from previous: **Strong recommendation** moderate quality of evidence:
13. For adults with possible sepsis without shock, we recommend rapid assessment of the likelihood of infectious versus noninfectious causes of acute illness	**Best practice statement**	

ED Door-to-Antibiotic Time and Long-term Mortality in Sepsis

Characteristic	N	Adjusted OR (95% CI)	*P* Value
Overall	10,811	1.10 (1.05-1.14)	< .001
High acuity score	5,735	1.11 (1.06-1.17)	.37
Low acuity score	5,076	1.08 (1.02-1.14)	
Hypotension	874	1.13 (1.00-1.28)	.57
No hypotension	9,937	1.09 (1.05-1.13)	
MEDS score 3-5	2,068	1.10 (1.02-1.19)	.77
MEDS score 2	3,120	1.11 (1.04-1.18)	
MEDS score 1	5,623	1.08 (1.02-1.14)	
Altered mental status	561	1.14 (0.98-1.32)	.58
Intact mental status	10,250	1.09 (1.05-1.14)	
Initial lactate > 2 mmol/L	3,860	1.10 (1.04-1.17)	.76
Initial lactate ≤ 2 mmol/L	6,951	1.09 (1.04-1.14)	
Female	5,972	1.12 (1.06-1.18)	.19
Male	4,839	1.07 (1.02-1.13)	



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Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
14. 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 3hr from the time when sepsis was first recognized.	**Weak**, very low quality of evidence	NEW from previous: **Strong recommendation**, moderate quality of evidence
15. For adults with a low likelihood of infection and without shock, we suggest deferring antimicrobials while continuing to closely monitor the patient	**Weak,** very low quality of evidence	NEW from previous: **strong recommendation**, moderate quality of evidence

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3. Biomarkers to start antibiotics :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
16. For adults with suspected sepsis or septic shock, we suggest against using procalcitonin plus clinical evaluation to decide when to start antimicrobials, as compared to clinical evaluation alone.	**Weak**, very low quality of evidence	

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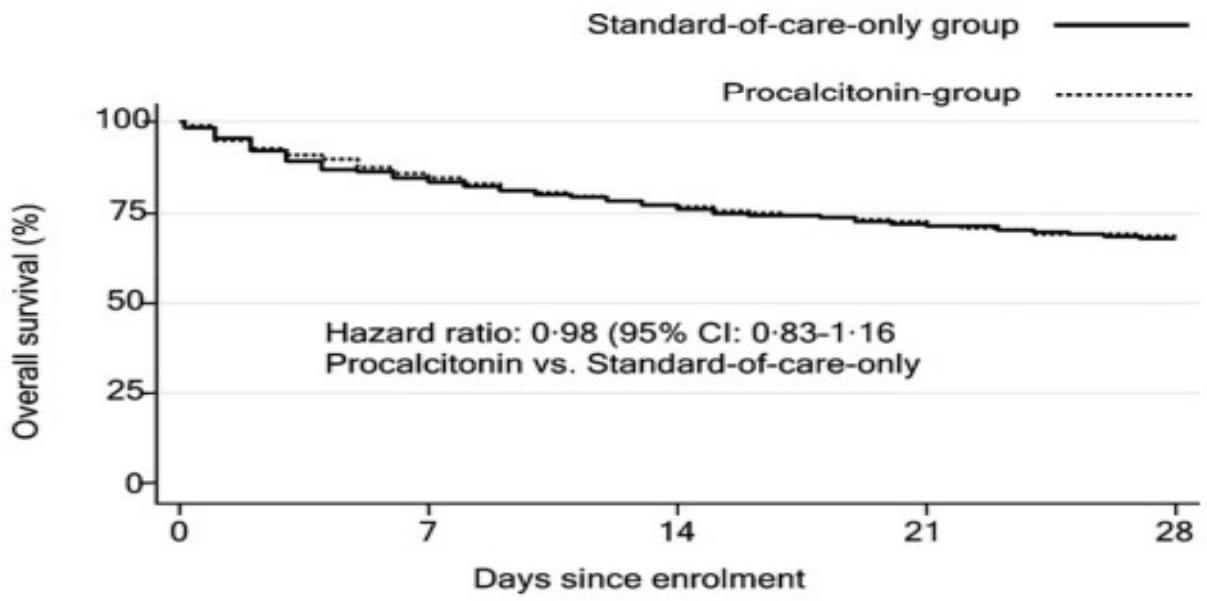
Randomized Controlled Trial > Crit Care Med. 2011 Sep;39(9):2048-58.
doi: 10.1097/CCM.0b013e31821e8791.

Procalcitonin–guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: a randomized trial



Number at risk:

Procalcitonin	604	518	466	436	414
Standard-of-care	596	505	458	429	405

Figure 3. Kaplan-Meier estimates of 28-day survival. The analysis is based on the intention-to-treat

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4. Antimicrobial choice:

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
17. For adults with sepsis or septic shock at high risk of MRSA, we recommend using empiric antimicrobials with MRSA coverage over using antimicrobials without MRSA coverage.	**Best practice statement**	**NEW from previous**: "We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage. **" Strong recommendation,** moderate quality of evidence
18. For adults with sepsis or septic shock at low risk of MRSA, we suggest against using empiric antimicrobials with MRSA coverage, as compared with using antimicrobials without MRSA coverage.	**Weak**, low quality of evidence	**NEW from previous: "Strong recommendation**, moderate quality of evidence

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> Clin Infect Dis. 2003 Jun 1;36(11):1418-23. doi: 10.1086/375057. Epub 2003 May 20.

Outcomes analysis of delayed antibiotic treatment for hospital-acquired Staphylococcus aureus bacteremia

Abstract

The objective of this study was to determine the effect of delayed therapy on morbidity and mortality associated with nosocomial Staphylococcus aureus bacteremia. The study included all episodes of S. aureus bacteremia that developed >2 days after hospital admission during 1999 to 2001. Classification and regression tree analysis (CART) was used to select the mortality breakpoint between early and delayed treatment. During the 25-month study period, 167 patients met the inclusion criteria. The breakpoint between delayed and early treatment derived using CART was 44.75 hours. On multivariate analysis, delayed treatment was found to be an independent predictor of infection-related mortality (odds ratio, 3.8; 95% confidence interval, 1.3-11.0; P=.01) and was associated with a longer hospital stay than was early treatment (20.2 days versus 14.3 days; P=.05). These findings support the notion that delay of therapy has deleterious effects on clinical outcomes, and efforts should be made to ensure that appropriate therapy is initiated promptly.

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Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
19. 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**, very low quality of evidence	
20. For adults with sepsis or septic shock and low risk for multidrug resistant (MDR) organisms, we suggest against using two gram-negative agents for empiric treatment, as compared to one gram-negative agent	**Weak,** very low quality of evidence	
21. For adults with sepsis or septic shock, we suggest against using double gram-negative coverage once the causative pathogen and the susceptibilities are known.	**Weak**, very low quality of evidence	

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Review > J Infect. 2017 Apr;74(4):331-344. doi: 10.1016/j.jinf.2016.11.013. Epub 2016 Dec 3.

Empirical mono- versus combination antibiotic therapy in adult intensive care patients with severe sepsis – A systematic review with meta-analysis and trial sequential analysis

Fredrik Sjövall [1], Anders Perner [2], Morten Hylander Møller [2]

Results: Thirteen RCTs (n = 2633) were included; all were judged as having high risk of bias. Carbapenems were the most frequently used mono-antibiotic (8 of 13 trials). There was no difference in mortality (RR 1.11, 95% CI 0.95-1.29; p = 0.19) or in any other patient-important outcomes between mono- vs. combination therapy. In TSA of mortality, the Z-curve reached the futility area, indicating that a 20% relative risk difference in mortality may be excluded between the two groups. For the other outcomes, TSA indicated lack of data and high risk of random errors.

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5. Antifugal therapy :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
22. For adults with sepsis or septic shock at high risk of fungal infection, we suggest using empiric antifungal therapy over no antifungal therapy.	**Weak,** low quality of evidence	**NEW from previous**: "We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage. " **Strong recommendation**, moderate quality of evidence.
23. For adults with sepsis or septic shock at low risk of fungal infection, we suggest against empiric use of antifungal therapy	**Weak**, low quality of evidence	**NEW from previous**: " **Strong recommendation**, moderate quality of evidence.

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TABLE 2.
Examples of Risk Factors for Fungal Infection

Risk Factors for Candida Sepsis
Candida Colonization at Multiple Sites (177–179)
Surrogate Markers Such as Serum Beta-D-Glucan Assay (177)
Neutropenia (180, 181)
Immunosuppression (173, 180, 181)
Severity of Illness (High APACHE score) (182, 183)
Longer ICU Length of Stay (183)
Central Venous Catheters and Other Intravascular Devices (168, 180, 181, 184)
Persons Who Inject Drugs (185)
Total Parenteral Nutrition (186)
Broad Spectrum Antibiotics (178, 187)
Gastrointestinal Tract Perforations and Anastomotic Leaks (186, 188–190)
Emergency Gastrointestinal or Hepatobiliary Surgery (190)
Acute Renal Failure and Hemodialysis (186, 188)
Severe Thermal Injury (191–193)
Prior Surgery (186)

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6. Antiviral Therapy :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
24. We make no recommendation on the use of antiviral agents.	No recommendation	

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7. Delivery of antibiotics :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
25. For adults with sepsis or septic shock, we suggest using prolonged infusion of beta-lactams for maintenance (after an initial bolus) over conventional bolus infusion.	**Weak**, moderate-quality evidence	

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Meta-Analysis > Lancet Infect Dis. 2018 Jan;18(1):108-120. doi: 10.1016/S1473-3099(17)30615-1. Epub 2017 Nov 5.

Prolonged versus short-term intravenous infusion of antipseudomonal β-lactams for patients with sepsis: a systematic review and meta-analysis of randomised trials

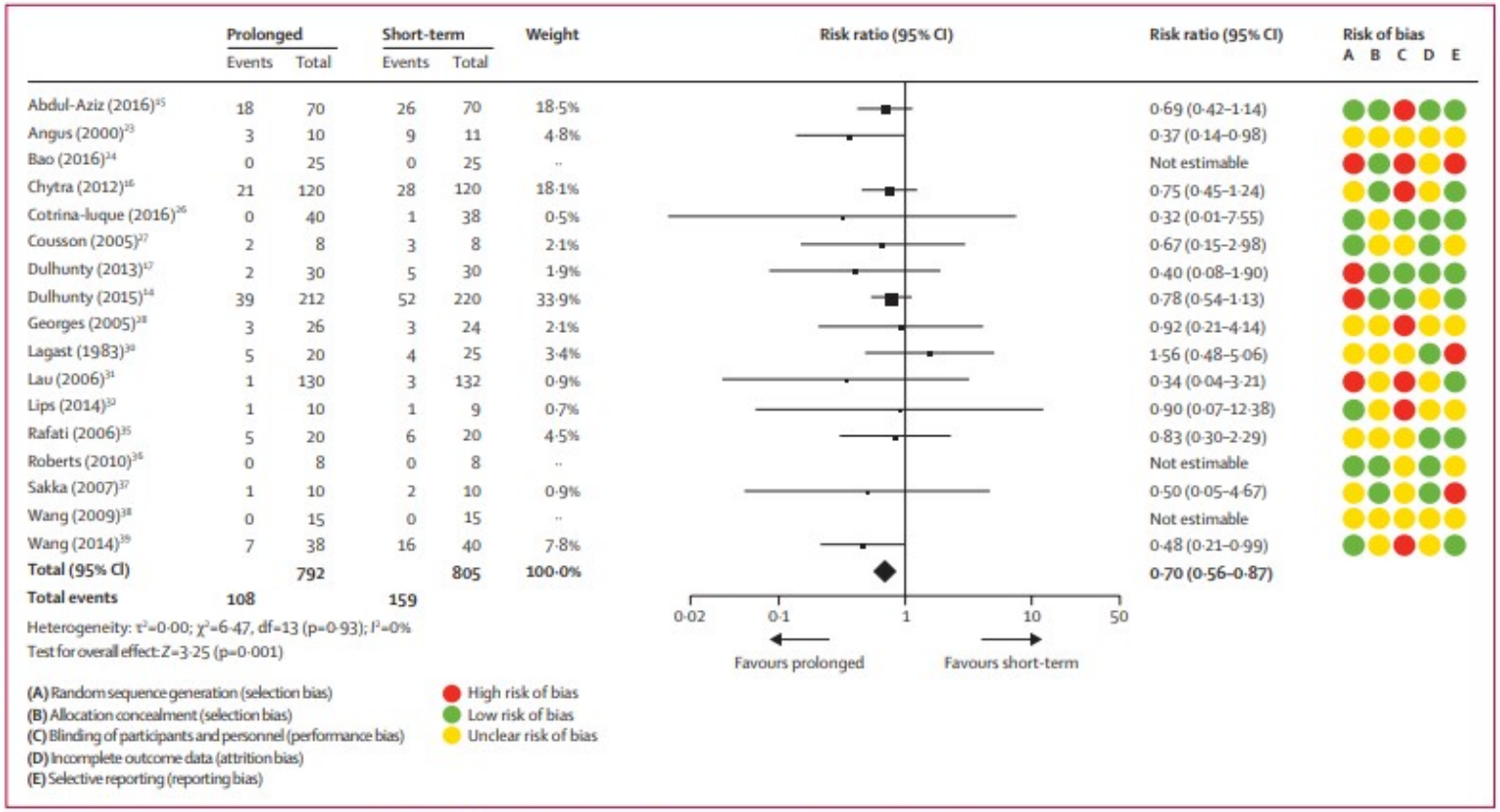

Figure 2: **Forest plot of mortality among patients treated with prolonged versus short-term infusion of antipseudomonal antibiotics**
The areas of squares are proportional to the weight given to each study. Risk ratios are the centres of each square. df=degrees of freedom.

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8. Pharmacokinetics and pharmacodynamics :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
26. For adults with sepsis or septic shock, we recommend optimising dosing strategies of antimicrobials based on accepted pharmacokinetic/ pharmacodynamic (PK/PD) principles and specific drug properties.	**Best practice statement**	

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TABLE 3.
Guidance for PK/PD-Based Dosing for Specific Drug Classes

Drug or Drug Class	PK/PD Index Associated With Bacterial Killing or Efficacy	Drug Concentration Target	Considerations for Optimized Dosing*	Reference Number
Antibacterials				
Aminoglycosides	$AUC_{0\text{-}24}$/MIC; C_{max}/MIC	AUC 70–100 C_{max}/MIC 8–10	Use extended interval dosing with patient weight and kidney function	237
Beta-lactams	$fT_{>MIC}$	C_{min} > MIC	Use prolonged infusions, consider patient weight and kidney function	253
Colistin	$AUC_{0\text{-}24}$/MIC	Unspecified	Use patient weight and kidney function	259
Daptomycin	$AUC_{0\text{-}24}$/MIC; C_{max}/MIC	$AUC_{0\text{-}24}$/MIC > 200	Use patient weight and kidney function	237
Fluoroquinolones	$AUC_{0\text{-}24}$/MIC; C_{max}/MIC	$AUC_{0\text{-}24}$/MIC 80–125	Use kidney function	237
Vancomycin	$AUC_{0\text{-}24}$/MIC	$AUC_{0\text{-}24}$/MIC 400	Use patient weight and kidney function	260
Antifungals				
Fluconazole	$AUC_{0\text{-}24}$/MIC	$AUC_{0\text{-}24}$/MIC 100	Use patient weight and kidney function	261
Posaconazole	$AUC_{0\text{-}24}$/MIC	C_{min} 1–4 mg/L	Use formulation-specific dose	261
Voriconazole	$AUC_{0\text{-}24}$/MIC	C_{min} 2–6 mg/L	Use patient weight	261

*Other considerations than those listed may have been listed in studies in critically ill patient subpopulations.
$AUC_{0\text{-}24}$–ratio of area under the concentration-time curve from 0–24 hours; MIC–minimum inhibitory concentration; $fT_{>MIC}$–time over-dosing interval that free (unbound) drug is maintained above the MIC; C_{max}–maximum concentration in a dosing interval; C_{min}–minimum concentration in a dosing interval.

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9. Source control :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
27. 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**	

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Observational Study > Crit Care Med. 2017 Jan;45(1):11-19.
doi: 10.1097/CCM.0000000000002011.

Impact of Source Control in Patients With Severe Sepsis and Septic Shock

María Luisa Martínez [1], Ricard Ferrer, Eva Torrents, Raquel Guillamat-Prats, Gemma Gomà, David Suárez, Luis Álvarez-Rocha, Juan Carlos Pozo Laderas, Ignacio Martín-Loeches, Mitchell M Levy, Antonio Artigas, Edusepsis Study Group

TABLE 3. Outcome Measurements in Source Control Group Versus Nonsource Control Group

Outcome Measurements	All Patients, *n* = 3,663	Patients Not Requiring Source Control, *n* = 2,490	Patients Requiring Source Control, *n* = 1,173	*p*
Duration of mechanical ventilation, d, mean (SD)	6.88 (13.2)	6.78 (13.0)	7.11 (13.6)	0.480
Duration of vasopressors, d, mean (SD)	4.26 (7.2)	4.01 (6.6)	4.8 (8.4)	0.002
ICU stay, d, mean (SD)	11.8 (15.4)	11.6 (15.03)	12.3 (16.02)	0.202
Hospital stay, d, mean (SD)	29.04 (28.6)	27.4 (27.8)	32.5 (30.1)	< 0.001
Mortality, *n* (%)				
ICU	875 (23.9)	626 (25.1)	249 (21.2)	0.010
Hospital	1,088 (29.7)	756 (30.4)	332 (28.3)	0.203

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Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
28. 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**	

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10. De-escalation of antibiotics :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
29. For adults with sepsis or septic shock, we suggest daily assessment for de-escalation of antimicrobials over using fixed durations of therapy without daily reassessment for de-escalation.	**Weak**, very low quality of evidence	

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Intensive Care Med
https://doi.org/10.1007/s00134-019-05866-w

CONFERENCE REPORTS AND EXPERT PANEL

Antimicrobial de-escalation in critically ill patients: a position statement from a task force of the European Society of Intensive Care Medicine (ESICM) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Critically Ill Patients Study Group

Effects of ADE

Q3: In critically ill patients receiving antimicrobials for an infection, what are the effects of antimicrobial de-escalation compared to no de-escalation on mortality and length of stay?

The ADE strategy is likely safe with regard to patients' outcomes. (Statement of fact; moderate quality of evidence.)

Q4: In critically ill patients receiving antimicrobials for an infection, what are the effects of antimicrobial de-escalation compared to no de-escalation on the total duration of antimicrobial therapy?

ADE is associated with a risk of increase in total duration of antimicrobial therapy. We recommend that ADE and duration of antimicrobial therapy are assessed separately but as part of the global stewardship strategy. (Statement of fact; low quality of evidence.)

Q5: In critically ill patients receiving antimicrobials for an infection, what are the effects of antimicrobial de-escalation compared to no de-escalation on the development of resistance to antimicrobials?

No recommendation can be made

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11. Duration of antibiotics :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
30. For adults with an initial diagnosis of sepsis or septic shock and adequate source control, we suggest using shorter over longer duration of antimicrobial therapy	**Weak,** very low quality of evidence	

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TABLE 4.

Planned Duration of Empirical Antimicrobial Therapy in RCTs of Shorter vs Longer Duration of Therapy According to Clinical Syndrome

Population/Syndrome	RCT/Systemic Review (Data Extracted From)	Shorter Duration	Longer Duration	Outcomes
Pneumonia	Capellier 2012 (301)	8 days	15 days	No difference
	Chastre 2003 (301, 302)	8 days	15 days	No difference
	El Moussaoui 2006 (302)	3 days	8 days	No difference
	Fekih Hassen 2009 (301–303)	7 days	10 days	No difference
	File 2007 (302, 303)	5 days	7 days	No difference
	Kollef 2012 (302, 303)	7 days	10 days	No difference
	Leophonte 2002 (302, 303)	5 days	10 days	No difference
	Medina 2007 (301)	8 days	12 days	No difference
	Siegel 1999 (302, 303)	7 days	10 days	No difference
	Tellier 2004 (302, 303)	5 days	7 days	No difference
Bacteremia	Chaudhry 2000 (302)	5 days	10 days	No difference
	Runyon 1991 (302)	5 days	10 days	No difference
	Yahav 2018 (304)	7 days	14 days	No difference
Intra-abdominal infection	Montravers 2018 (305)	8 days	15 days	No difference
	Sawyer 2015 (293)	Max. 5 days	Max. 10 days	No difference
Urinary tract infection	Peterson 2008 (290)	5 days	10 days	No difference

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12. Biomarkers to discontinue antibiotics :

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
31. For adults with an initial diagnosis of sepsis or septic shock and adequate source control where optimal duration of therapy is unclear, we suggest using procalcitonin AND clinical evaluation to decide when to discontinue antimicrobials over clinical evaluation alone.	**Weak,** low quality of evidence	

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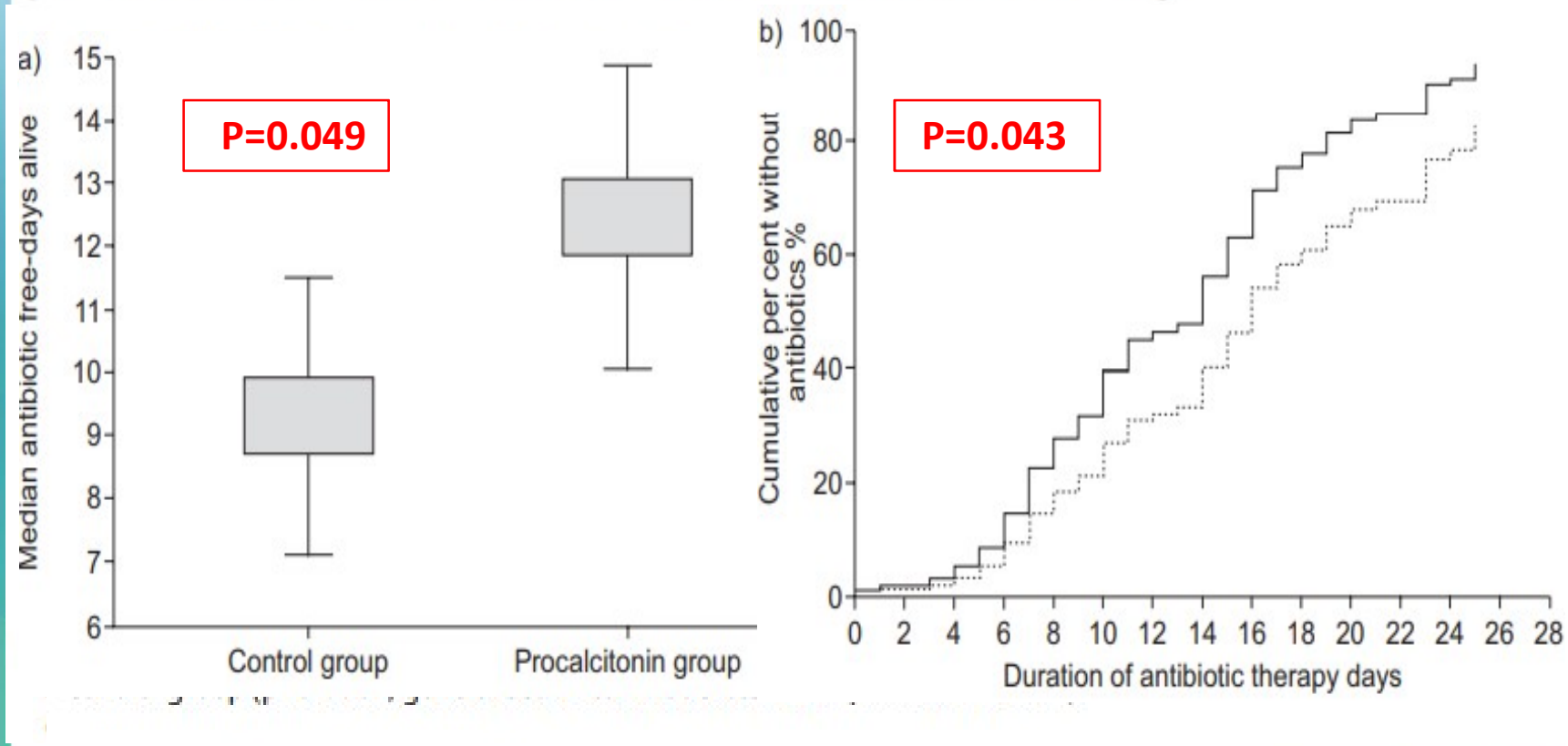
Eur Respir J 2009; 34: 1364–1375
DOI: 10.1183/09031936.00053209

Procalcitonin for reduced antibiotic exposure in ventilator-associated pneumonia: a randomised study



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TAKE HOME MESSAGES

- **Screening:**
  - **Systèmes informatisés/IA**
  - **≠ qSOFA**
  - **30 ml/kg de cristalloïdes**
  - **Indices dynamiques +++**
  - **clearance de lactate**
  - **TRC**
- **PEC:**
  - **Délai d'admission < 6h**
  - **ATB la 1ére heure : Golden hour +++**
  - **ß lactamines en perfusion continue**
  - **Mono vs Bithérapie anti MDR ? Risque**
  - **ATB visant MRSA? Risque**
  - **Raccourcir la durée++**
  - **PCT pour l'arret de l'ATB**

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Merci pour votre attention !