Nuovi score e loro valore predittivo nelle infezioni gravi

Maddalena Giannella

Conflicts of interest

- Grants from MSD, Pfizer, Shionogi, Gilead, BioMerieux as a speaker

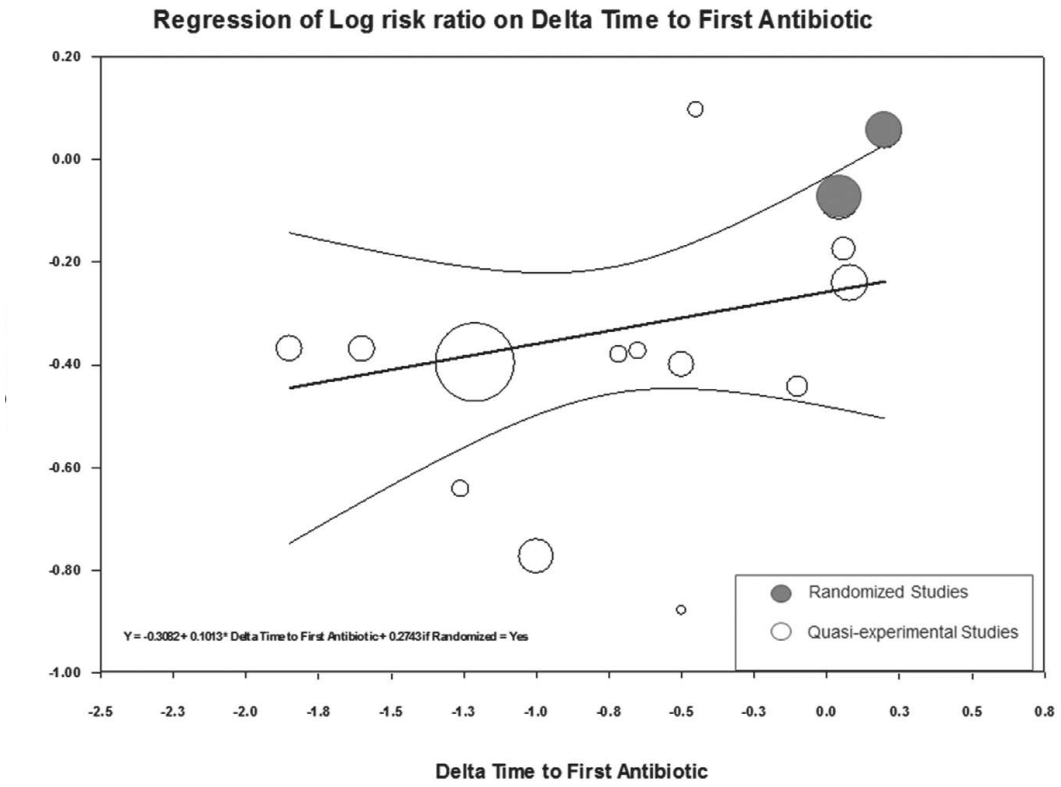
Surviving Sepsis Campaign Guidelines 2016 vs. 2021

Rhodes A et al. Intensive Care Med 2017; 43:304–377	Evans L et al. Intensive Care Med 2021; 47: 1181–1247
We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and **within 1 h for both sepsis and septic shock** (strong recommendation, moderate quality of evidence, grade applies to both conditions)	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 of evidence)
	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 of evidence)

Early goal-directed therapy for sepsis: A novel solution for discordant survival outcomes in clinical trials

Kalil AC et al Crit Care Med 2017; 45:607–614

- 31 Obs studies (n = 15,656), 6 RCTs (n=4,342)
  - ✓ Obs mortality reduction (RR = 0.73, 0.67–0.80)
  - ✓ RCTs non significant mortality reduction (RR = 0.92 0.78–1.07)

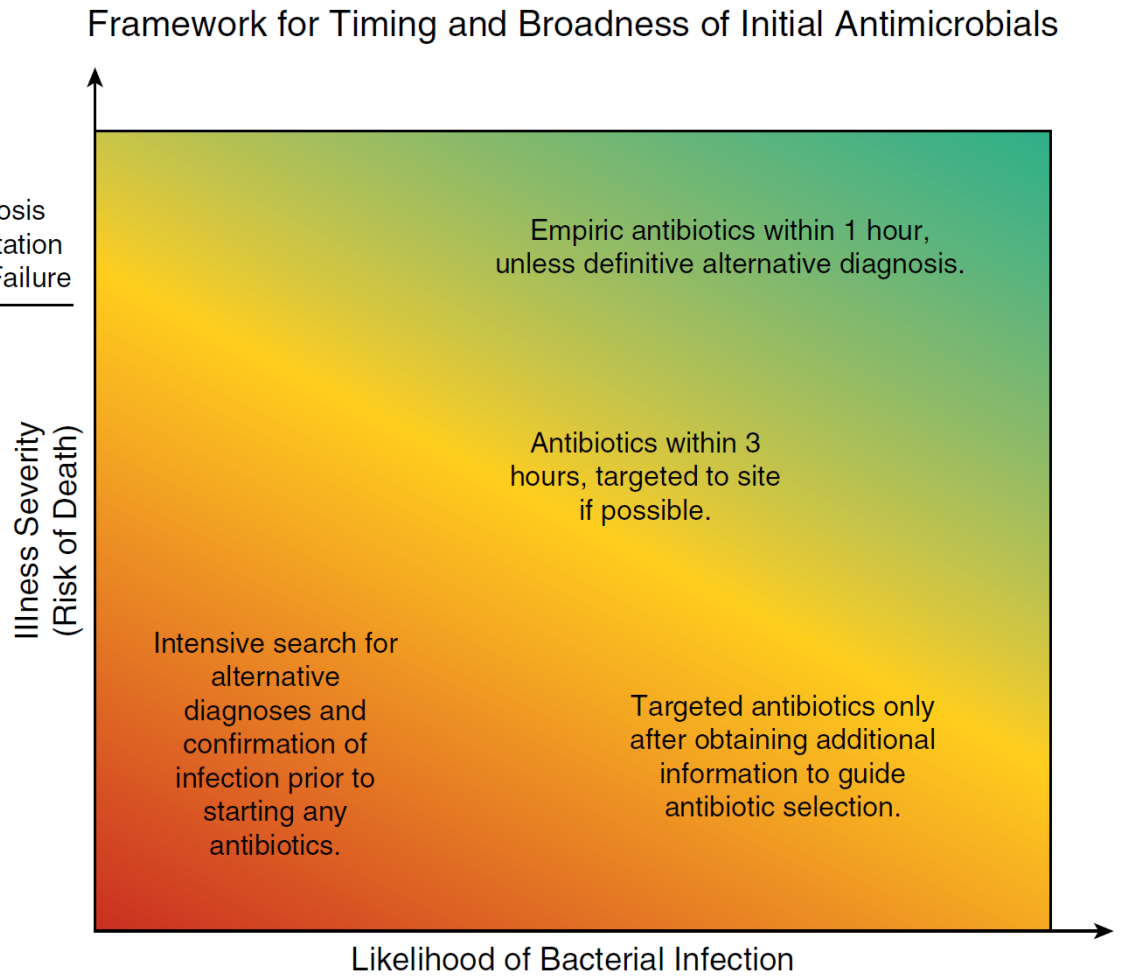


- Factors that explained the statistically significant mortality differences between RCT and obs studies **were time-to-first antibiotic [6 hours (R2 = 94%), 4 hours (R2 = 99%), 3 hours (R2 = 99%)], and appropriate antibiotic use (R2 = 96%)**

Improving Sepsis Treatment by Embracing Diagnostic Uncertainty

Prescott Annals ATS Volume 16 Number 4| April 2019

Illness Severity: assessment of the patient's risk of death based on pre-existing risk factors (e.g. age, chronic medical condition, immune-suppression) and acute physiological derangements



Likelihood of Bacterial infection: assessment of clinical signs and symptoms of infection, initial laboratories, imaging

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Conditions that can Mimic Sepsis & Septic Shock

GI Disease
- Intestinal perforation
- Bowel obstruction
- Volvulus
- Pancreatitis
- Inflammatory bowel disease

Pulmonary disease
- ARDS
- Pulmonary embolism
- Hypersensitivity pneumonitis
- Aspiration pneumonitis
- Pneumothorax
- COPD/asthma exacerbation

CNS disease
- Seizure
- Intracranial hemorrhage

Drugs & toxins
- Drug overdose
- Drug withdrawal
- Medication toxicity
- Alcohol intoxication

Malignancies
- Lymphoma
- Hemophagocytic syndrome
- Tumor lysis syndrome

Vascular disease
- Mesenteric ischemia
- Antiphospholipid syndrome
- Cholesterol emboli
- Air emboli
- Vasculitis

Cardiac disease
- Congestive heart failure
- Myocardial infarction
- Cardiac arrhythmias

Endocrine disease
- Adrenal insufficiency
- Hyperthyroid storm
- Diabetic ketoacidosis

Others
- Compartment syndrome
- Severe burns
- Urinary retention

Heffner, Clin Infect Dis 2010;50:814-820
Contou, Critical Care 2016;20:360
Klein Klouwenberg, Crit Care 2015;19:319

Recognition of Sepsis in the Immunocompromised Patient

- 109,663 ICU pts with infection and organ failure
- SIRS missed one patient in eight with severe sepsis
- SIRS neg
  - **Immunosuppression OR 1.28**
  - **End stage liver diseases OR 1.37**
  - **Leukemia OR 1.50**

Kirsi-Maija Kaukonen et al. N Engl J Med 2015;372:1629

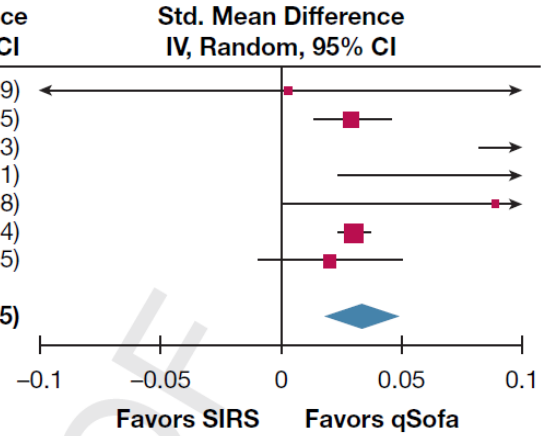
A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality: A Systematic Review and Meta-Analysis.

Serafim R et al Chest 2017 Dec 28.

Mortality

Study or Subgroup	qSOFA Mean	qSOFA SD	qSOFA Total	SIRS Mean	SIRS SD	SIRS Total	Weight	Std. Mean Difference IV, Random, 95% CI
April, 2017	0.66	2.61	214	0.65	2.61	214	0.7%	0.00 (–0.19 to 0.19)
Churpek, 2017	0.69	1.34	30,677	0.65	1.34	30,677	31.9%	0.03 (0.01 to 0.05)
Finkelsztein, 2017	0.74	0.47	152	0.59	0.5	152	0.5%	0.31 (0.08 to 0.53)
Freund, 2017	0.8	1.59	879	0.65	0.83	879	2.8%	0.12 (0.02 to 0.21)
Park, 2017	0.733	1.54	1,009	0.599	1.46	1,009	3.2%	0.09 (0.00 to 0.18)
Raith, 2017	0.607	0.88	184,875	0.58	0.88	184,875	42.6%	0.03 (0.02 to 0.04)
Williams, 2017	0.73	0.48	8,871	0.72	0.48	8,871	18.3%	0.02 (–0.01 to 0.05)
Total (95% CI)			**226,677**			**226,677**	**100.0%**	**0.03 (0.02 to 0.05)**

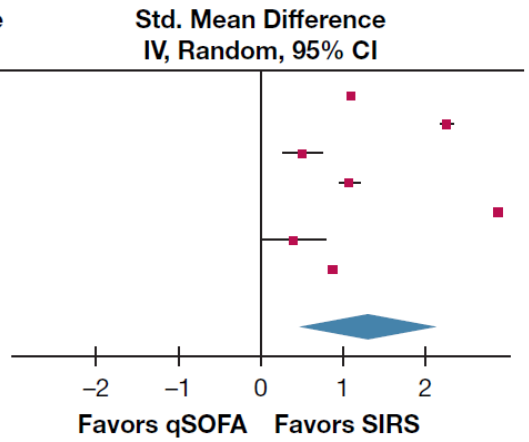
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 11.39$, df = 6 ($P = .08$); $I^2 = 47\%$
Test for overall effect: $Z = 4.12$ ($P < .0001$)



Diagnosis of sepsis

Study or Subgroup	SIRS Mean	SIRS SD	SIRS Total	qSOFA Mean	qSOFA SD	qSOFA Total	Weight	Std. Mean Difference IV, Random, 95% CI
Churpek, 2017	0.88	0.45	30,677	0.38	0.45	30,677	14.4%	1.11 (1.09 to 1.13)
Donnelly, 2017	0.54	0.02	2,593	0.12	0.26	2,593	14.3%	2.28 (2.21 to 2.35)
Dorsett, 2017	0.39	0.5	152	0.16	0.38	152	14.2%	0.52 (0.29 to 0.75)
Freund, 2017	0.74	0.45	879	0.25	0.45	879	14.3%	1.09 (0.99 to 1.19)
Raith, 2017	0.86	0.11	184,875	0.54	0.11	184,875	14.4%	2.91 (2.90 to 2.92)
Siddiqui, 2017	0.62	0.47	58	0.42	0.51	58	14.0%	0.41 (0.04 to 0.77)
Williams, 2017	0.47	0.48	8,871	0.1	0.34	8,871	14.4%	0.89 (0.86 to 0.92)
Total (95% CI)			**228,105**			**228,105**	**100.0%**	**1.32 (0.40 to 2.24)**

Heterogeneity: $Tau^2 = 1.53$; $Chi^2 = 43948.08$, df = 6 ($P < .00001$); $I^2 = 100\%$
Test for overall effect: $Z = 2.81$ ($P = .005$)



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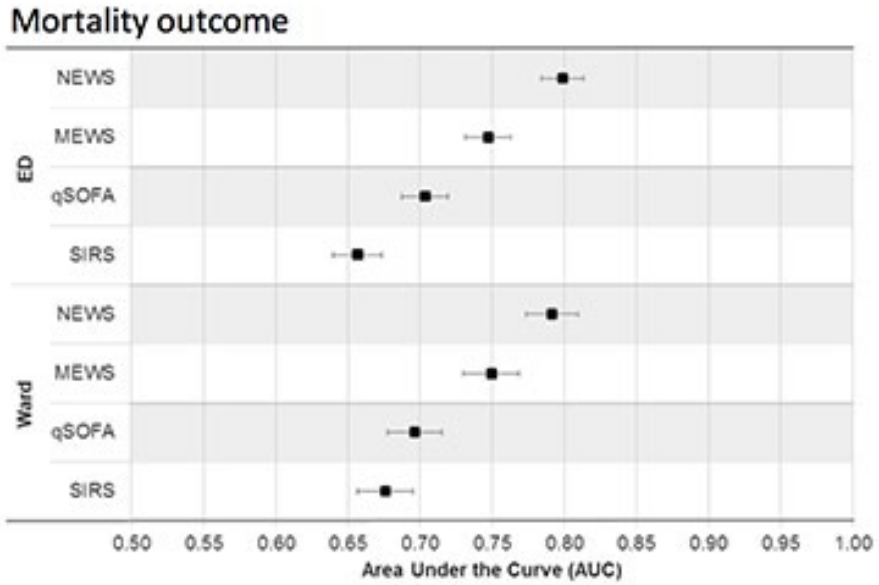
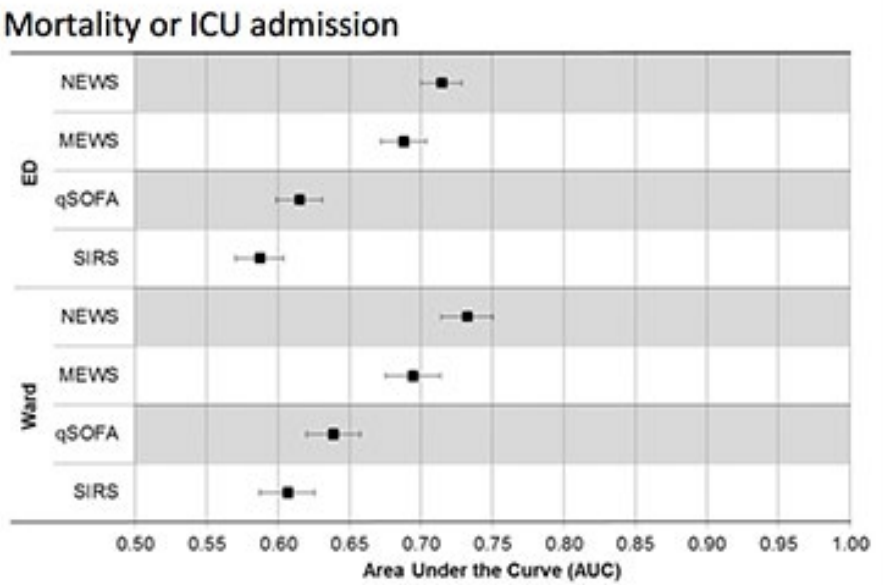
30,677 patients in the emergency department and ward at the University of Chicago

Overall test performance





Select cutoffs to predict mortality or ICU transfer

	Sensitivity	Specificity
SIRS ≥ 2	91%	13%
qSOFA ≥ 2	54%	67%
NEWS ≥ 7	77%	53%
NEWS ≥ 8	67%	66%
NEWS ≥ 9	54%	78%

qSOFA is an insensitive and late indicator of deterioration

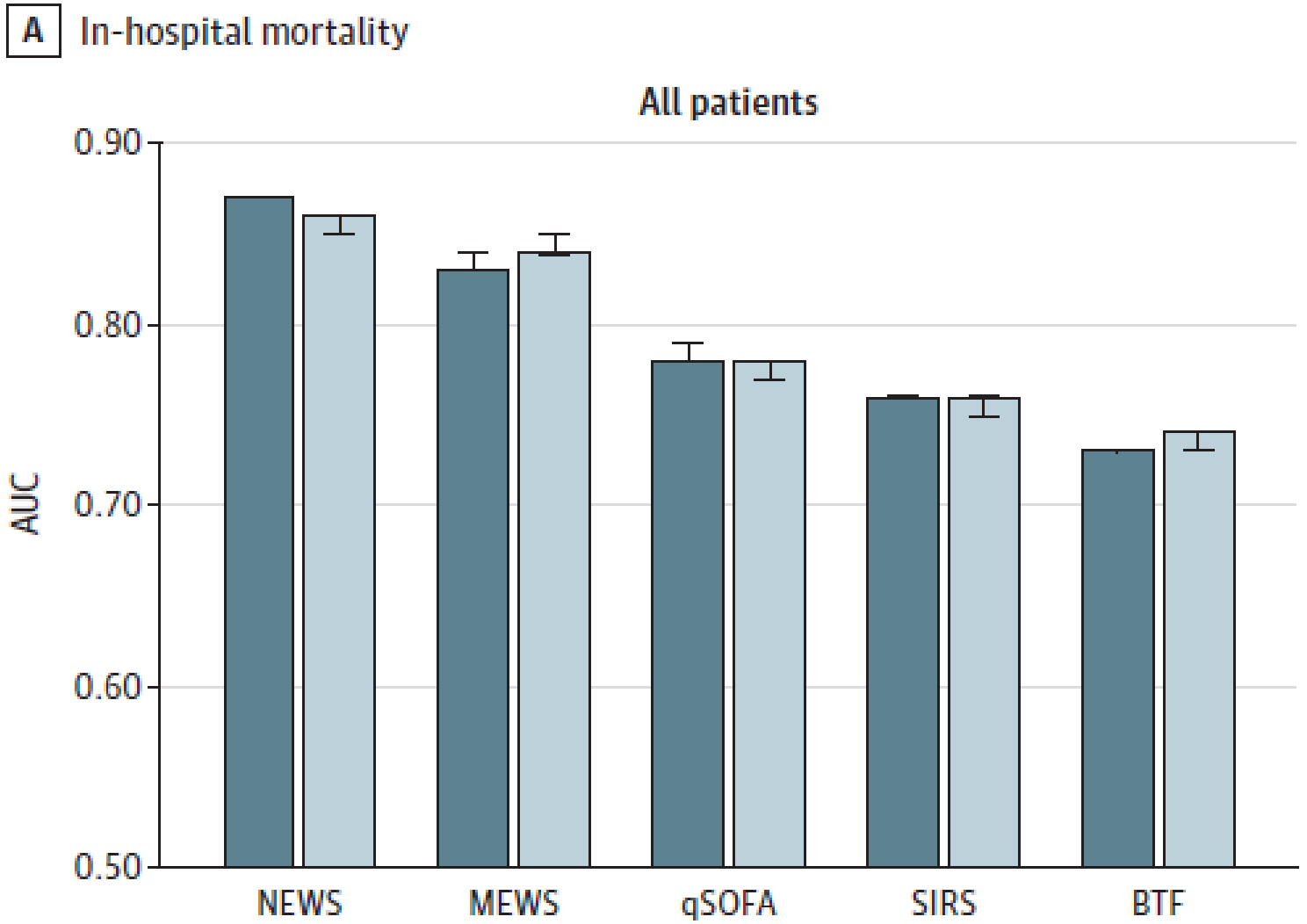
Churpek et al. American Journal of Respiratory and Critical Care Medicine 2016; 195 7

Components of SIRS, qSOFA, MEWS, and NEWS

	SIRS	qSOFA	MEWS	NEWS
Temperature	✓		✓	✓
Heart rate	✓		✓	✓
Blood pressure		✓	✓	✓
Respiratory rate	✓	✓	✓	✓
Oxygen saturation				✓
Use of supplemental oxygen				✓
Mental status		✓	✓	✓
Leukocyte count	✓			
Urine Output			✓	

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

Liu V JAMA Netw Open 2020 May 1;3(5):e205191.



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nature medicine

ARTICLES

https://doi.org/10.1038/s41591-022-01894-0

Check for updates

Prospective, multi-site study of patient outcomes after implementation of the TREWS machine learning-based early warning system for sepsis

Roy Adams[1,2], Katharine E. Henry[2,3], Anirudh Sridharan[4], Hossein Soleimani[5], Andong Zhan
Nishi Rawat[6], Lauren Johnson[7], David N. Hager[8], Sara E. Cosgrove[8], Andrew Markowski[9],
Eili Y. Klein[10], Edward S. Chen[8], Mustapha O. Saheed[10], Maureen Henley[7], Sheila Miranda[11],
Katrina Houston[7], Robert C. Linton[4], Anushree R. Ahluwalia[7], Albert W. Wu[6,8,12,13,14] ✉ and
Suchi Saria[1,3,8,12,15] ✉

npj | digital medicine

www.nature.com/npjdigitalmed

ARTICLE OPEN

Check for updates

Effectiveness of automated alerting system compared to usual care for the management of sepsis

Zhongheng Zhang[1,12] ✉, Lin Chen[2,12], Ping Xu[3,4,5,12], Qing Wang[6], Jianjun Zhang[3], Kun Chen[2], Casey M. Clements[7],
Leo Anthony Celi[8,9,10], Vitaly Herasevich[11] and Yucai Hong[1]

JAMA Network | Open

Original Investigation | Health Informatics

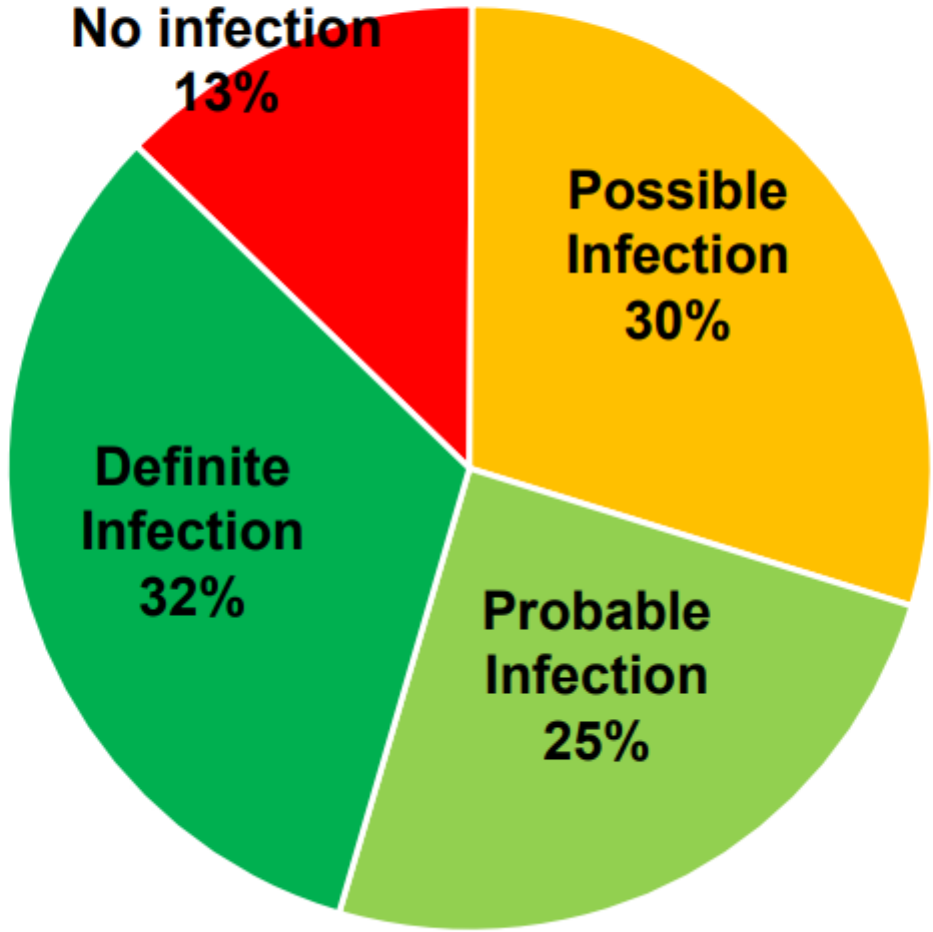
Sepsis Prediction Model for Determining Sepsis vs SIRS, qSOFA, and SOFA

Adam R. Schertz, MD, MS; Kristin M. Lenoir, MPH; Alain G. Bertoni, MD, MPH; Beverly J. Levine, PhD; Morgana Mongraw-Chaffin, PhD; Karl W. Thomas, MD

Sepsis was defined as receipt of 4 or more days of antimicrobials, blood cultures collected within 48 hours of initial antimicrobial, and at least 1 organ dysfunction (eSOFA)

Up to 40% of ICU Patients with “Sepsis” Are Not Infected…

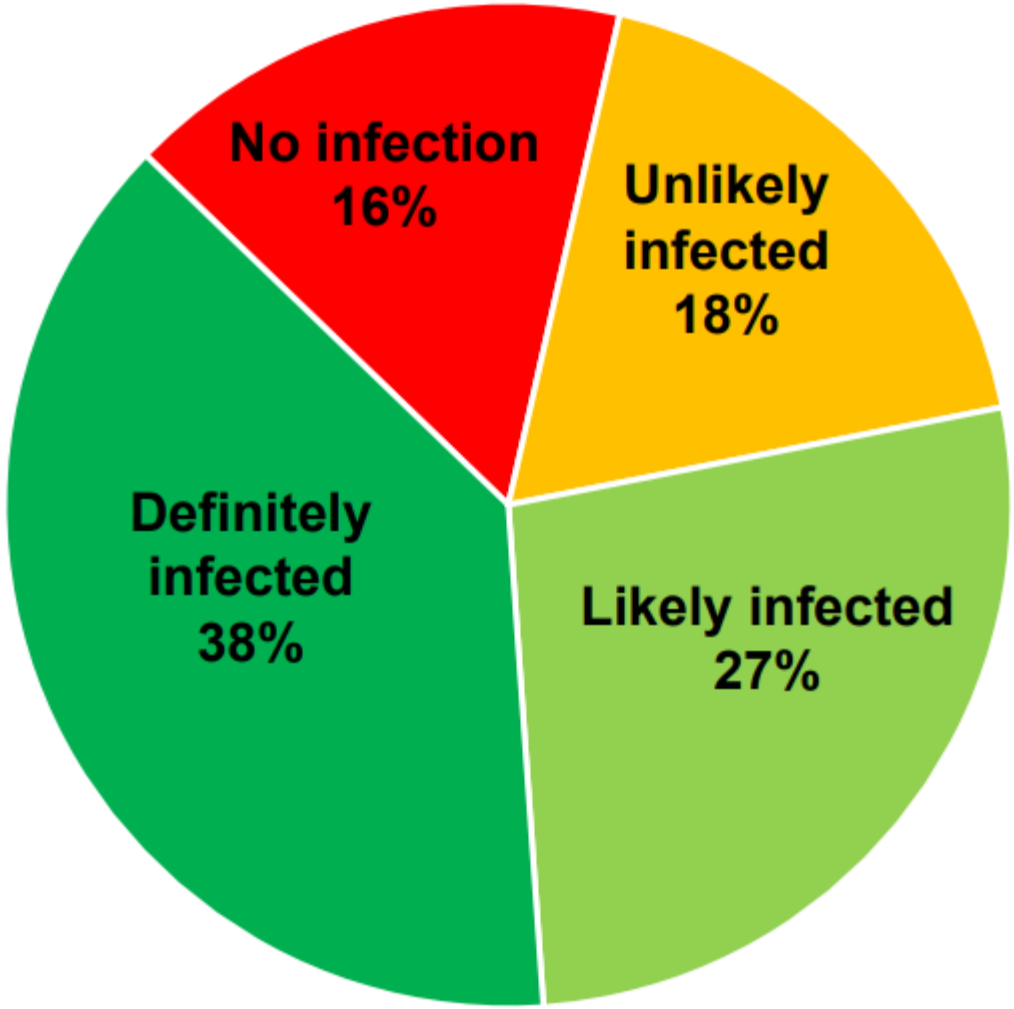
Retrospective analysis of 2,579 patients admitted to 2 Dutch ICUs and treated for sepsis

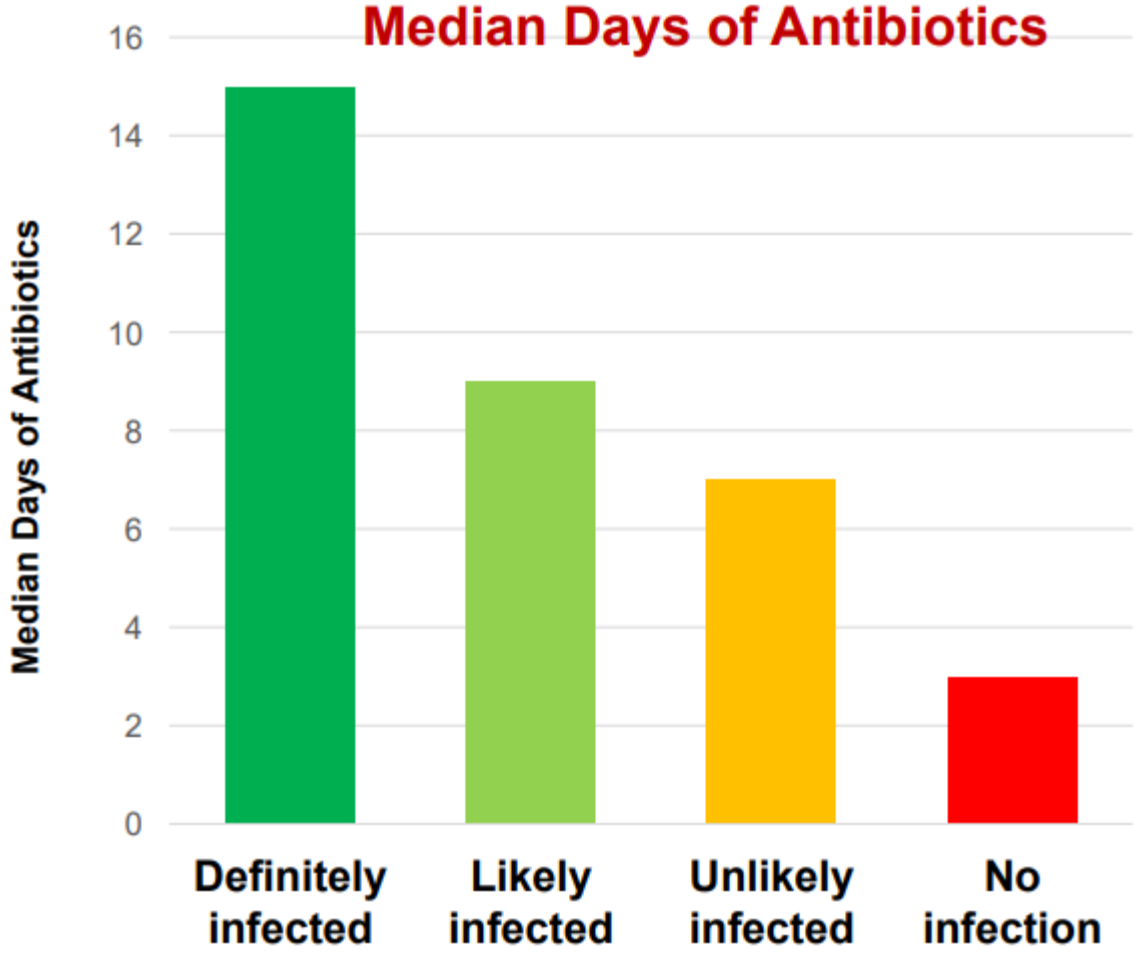


Critical Care 2015;19:319

Up to 35% of ED patients who get IV antibiotics uninfected

Retrospective analysis of 300 ED patients in whom blood cultures were drawn and IV antibiotics given, 4 Harvard Hospitals





Schappell, *Crit Care Med* 2021; doi:10.1097/CCM.0000000000005090

Clinical Infectious Diseases

MAJOR ARTICLE

Infectious Diseases Team for the Early Management of Severe Sepsis and Septic Shock in the Emergency Department

Pierluigi Viale,[1] Sara Tedeschi,[1] Luigia Scudeller,[2] Luciano Attard,[1] Lorenzo Badia,[1] Michele Bartoletti,[1] Alessandra Cascavilla,[1] Francesco Cristini,[1] Nicola Dentale,[1] Giovanni Fasulo,[1] Giorgio Legnani,[1] Filippo Trapani,[1] Fabio Tumietto,[1] Gabriella Verucchi,[1] Giulio Virgili,[1] Andrea Berlingeri,[3] Simone Ambretti,[3] Chiara De Molo,[3] Mara Brizi,[4] Mario Cavazza,[4] and Maddalena Giannella[1]

[1]Infectious Diseases Unit, Department of Medical and Surgical Sciences, Hospital S. Orsola-Malpighi, University of Bologna, [2]Clinical Epidemiology and Biostatistics Unit, Scientific Direction, IRCCS Policlinic San Matteo Foundation, Pavia, and [3]Microbiology, Department of Diagnosis and Prevention, and [4]Emergency Department, Hospital S. Orsola-Malpighi, University of Bologna, Italy

	Pre Phase (N = 195)	Post Phase (N = 187)	P Value
Blood culture before antibiotics (%)	21	85	<.001
Etiological diagnosis (%)	9	42	<.001
Appropriate empiric antibiotic therapy (%)	30	79	<.001
De-escalation with microbiological data (%)	13	46	<.001
De-escalation without microbiological data (%)	17	16	.993
All-cause 14-day mortality (%)	40	29	.002

Clinical Infectious Diseases

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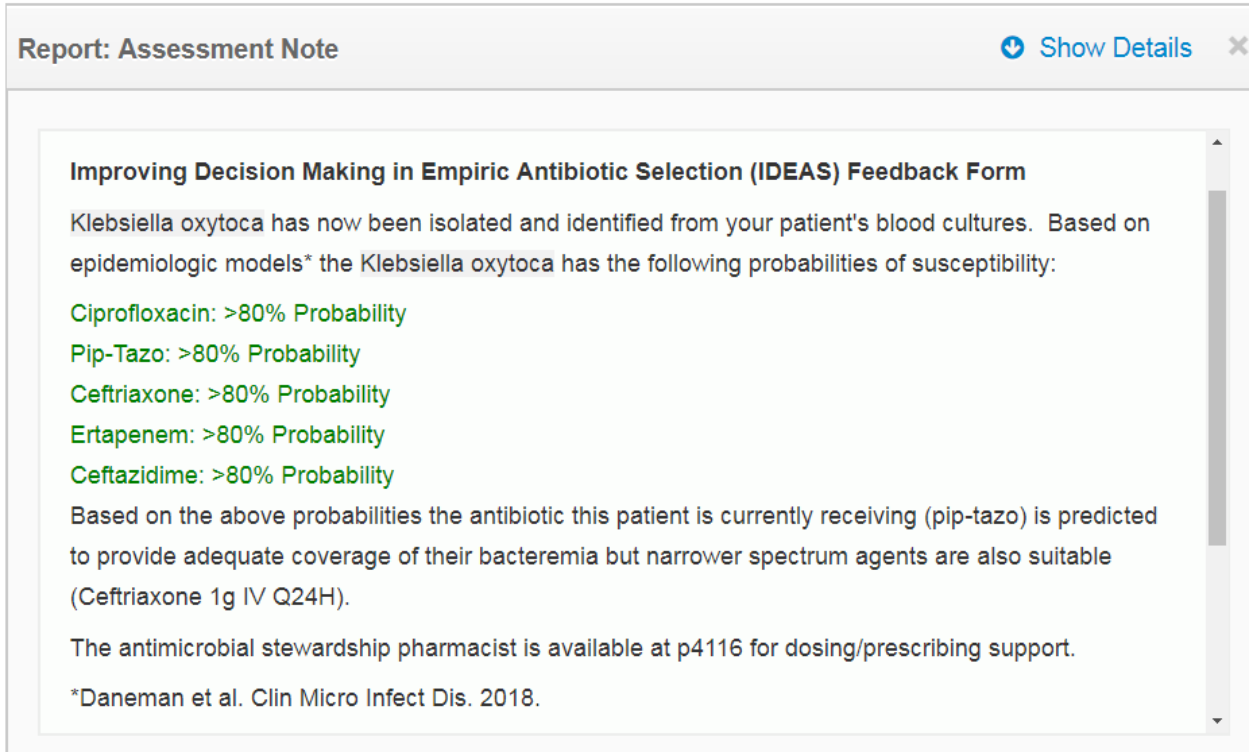
Variable	HR	95% CI	P Value
qSOFA score ≥ 2	1.68	1.15-2.45	.007
serum lactate ≥2 mmol/L	2.13	1,39-3.25	<.001
unknown infection source	2.07	1.42-3.02	<.001
being attended by «sepsis team» during post phase	0.64	0.43-0.94	.026

Improving Decision Making in Empiric Antibiotic Selection (IDEAS) for Gram-negative Bacteremia: A Prospective Clinical Implementation Study

Elligsen et al Clin Infect Dis 2020

- qSOFA <3, threshold of 80% coverage
- qSOFA ≥3, threshold of 90% coverage



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Improving Decision Making in Empiric Antibiotic Selection (IDEAS) for Gram-negative Bacteremia: A Prospective Clinical Implementation Study

Elligsen et al Clin Infect Dis 2020

	Control N=201 (%)	Intervention N=182 (%)	p
Narrowest adequate therapy at culture finalization	88 (44)	100 (55)	.04
E. coli and Klebsiella spp., n	160	121	
Narrowest adequate therapy at culture finalization	**75 (47)**	**77 (64)**	**.01**
Difficult-to-treat GN organisms, n	33	49	
Narrowest adequate therapy at culture finalization	**8 (24)**	**17 (35)**	**.45**

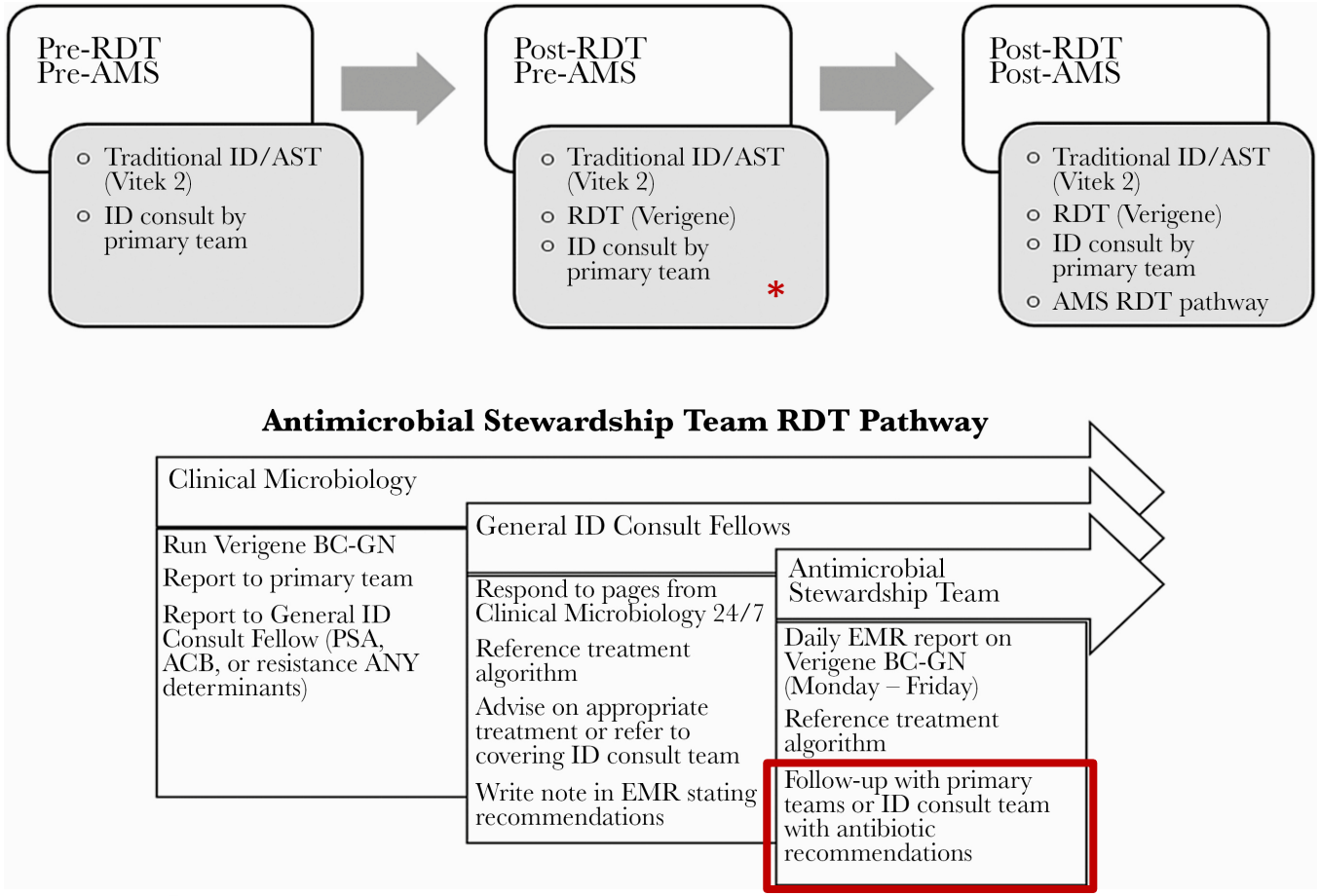
Management of Gram-Negative Bloodstream Infections in the Era of Rapid Diagnostic Testing: Impact With and Without Antibiotic Stewardship

Claeys KC et al. Open Forum Infect Dis 2020;7(10):ofaa427

	Pre-RDT Pre-AMS (n = 237)	Post-RDT Pre-AMS (n = 308)	Post-RDT Post-AMS (n = 287)	p
ID consult within 24 h	50.3%	67.8%	83.6%	<0.001
Optimal therapy (**narrowest spectrum**)	66.5%	78.9%	83.2%	<0.001
All-cause mortality	15.9%	14.9%	3.8%	<0.001

Management of Gram-Negative Bloodstream Infections in the Era of Rapid Diagnostic Testing: Impact With and Without Antibiotic Stewardship

Claeys KC et al. Open Forum Infect Dis 2020;7(10):ofaa427



***24h/7d**

Starting empirical antimicrobial treatment

1. Certainity of diagnosis

2. Risk of delaying treatment

3. Enviromental damage caused by the use of antimicrobial drugs

Starting appropriate empirical antimicrobial treatment

Clinical severity (septic shock, SOFA≥2)

- Site of infection acquisition
  - CA, HCA, HA
- Infection source
  - High (primary, lung) vs. low risk (urinary) sources
- **Individual patient risk factors for MDR and/or opportunistic pathogens**
  - Immunosuppression
  - Prior exposure to antibiotics
  - Prior colonization or infection with MDR pathogens
- **Local epidemiology**

Score building
AI support tool

Diagnostic workup
Fast microbiology

Impact of MDRO colonization

- Screening strategy (universal vs. high risk patients/units) – local epidemiology
- Detection methods (**culture-based vs/plus** molecular assays)
- Timing of colonization (before admission, **during admission**)
- Lower respiratory tract carriage (high PPV in VAP)
- Rectal carriage (**low PPV**, high NPV)

- Clinical factors
  - ✓ Hospital wide
  - ✓ Specific settings (**ICU, SOT, HM**)
- Microbiological factors
  - ✓ Multi-site colonization (e.g. throat)
  - ✓ Semiquantitative cultures
  - ✓ Relative abundance (16S rRNA)

Giannella M et al. Clin Microbiol Infect 2014;20:1357-62
Viale P et al. Clin Microbiol Infect 2015;21:242-7
Shimasaki T et al. Clin Infect Dis 2019;68:2053-2059
Andremont O et al. Intensive Care Med 2020; 46:1232-1242
Giannella M et al. Clin Infect Dis 2021;73:e955-e966
Cano A et al. Microbiol Spectr 2022;10:e0197021
Bredin S et al. Journal of Critical Care 2022; 71: 154068