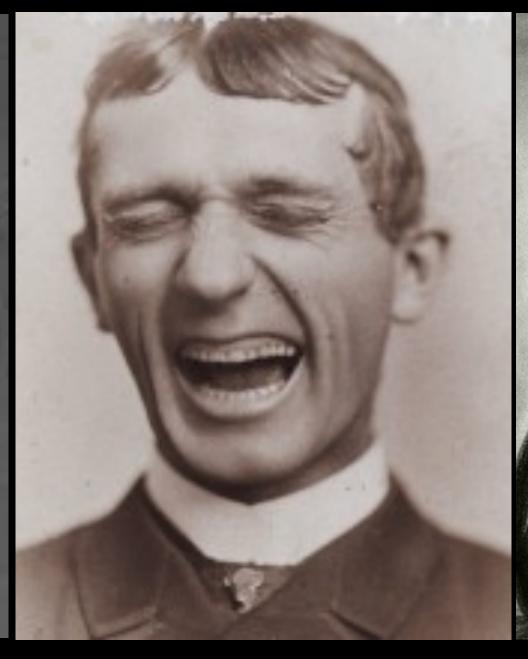
SEPSISHYSTERIA

CHALLENGING THE DOGMA





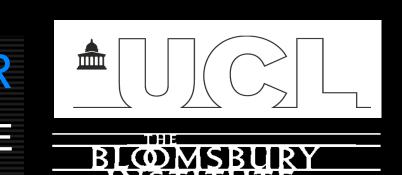






MERVYN SINGER

BLOOMSBURY INSTITUTE OF INTENSIVE CARE MEDICINE
UNIVERSITY COLLEGE LONDON, UK



AGENDA

- Sepsis hype
- Do patients die 'of' or 'with' sepsis?
- How many sepsis deaths are potentially 'saveable'?
- Are we fed fact or propaganda?
- Common sense is returning ...

DISCUSSION SOME MONTHS AGO ...

Singer to daughter of elderly patient:

"Your father has a chest infection"

Daughter:

"Thank God. I was so worried. The doctor I spoke to in the Emergency Department told me he had sepsis so I thought he was going to die"



Highlight a problem

Blow it up

Keep blowing it up

Sensationalise it

Weaponise it

Create Project Fear





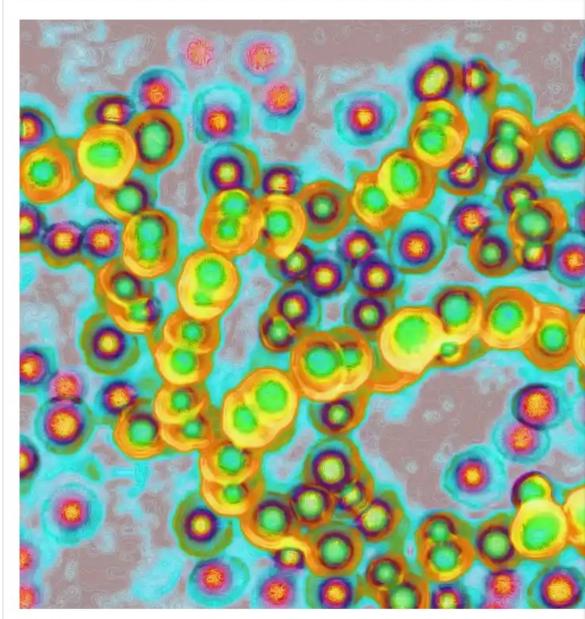






Strep A: fears NHS will s as seventh child reporte

Nadhim Zahawi says parents should look out infection, such as fever, headache or skin ras



Streptococcus A bacteria can cause many health issues invasive group A streptococcal disease (iGAS). Photograph

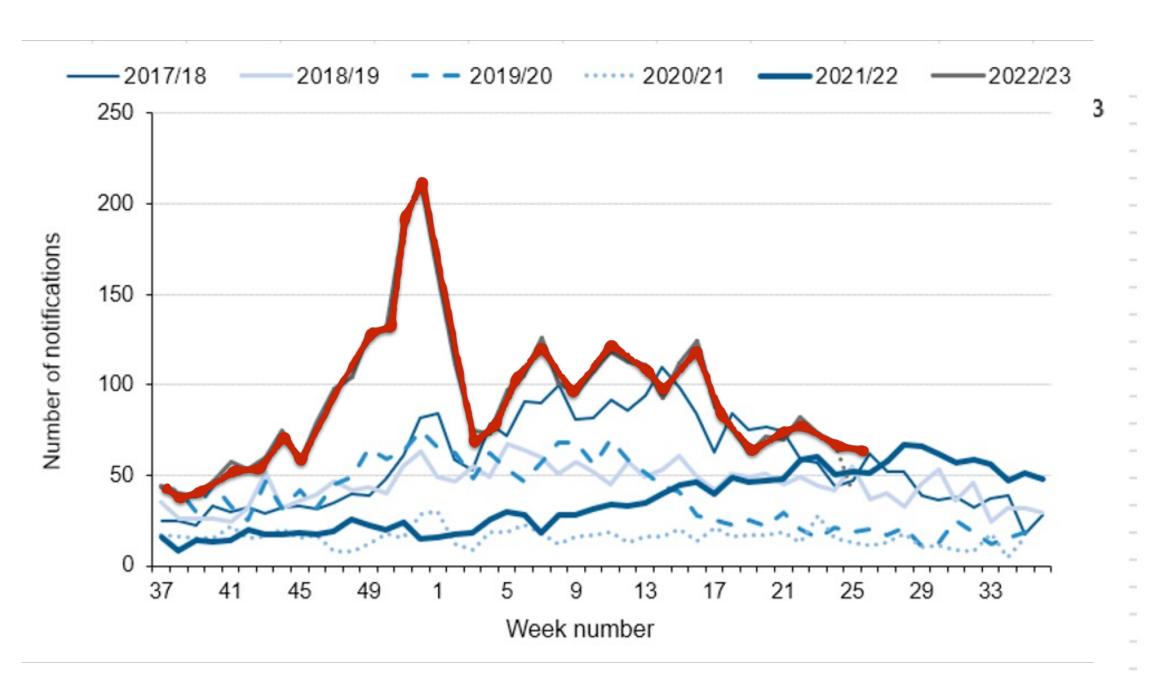


Research and analysis

Group A streptococcal infections: 15th update on seasonal activity in England

Updated 29 June 2023

Figure 2. Weekly laboratory notifications of iGAS, England, by season, 2017 to 2018 onwards



our vid

he last month







Sepsis kills over 52,000 every year - each death a preventable tragedy. So we're introducing new guidance to use #data to identify & treat sepsis faster - and save more lives



NHS hospitals could face fines for breaches of new sepsis rules

NHS England staff told to look out for signs of sepsis in patients attending A&E theguardian.com

SEPSIS IS THE TIP OF THE INFECTION ICEBERG



INFECTION SEPSIS ... DEATH

Sepsis hysteria: excess hype and unrealistic expectations

www.thelancet.com Vol 394 October 26, 2019 1513-14

*Mervyn Singer, Matt Inada-Kim, Manu Shankar-Hari

DO SC

1

Estimated population in England (2018)

55.6 million

EAV

General
practitioner
antibiotic prescriptions
(2017–18)²

33.6 million

wi h disch rge of caterial i fection or epsis (2017–18) 73 m ic

- Critical care admissions with sepsis (2015)⁴ 44115
- In-hospital deaths, including admission to critical care
 (2015)⁴ 13 455

Sepsis hysteria: excess hype and unrealistic expectations

*Mervyn Singer, Matt Inada-Kim, Manu Shankar-Hari

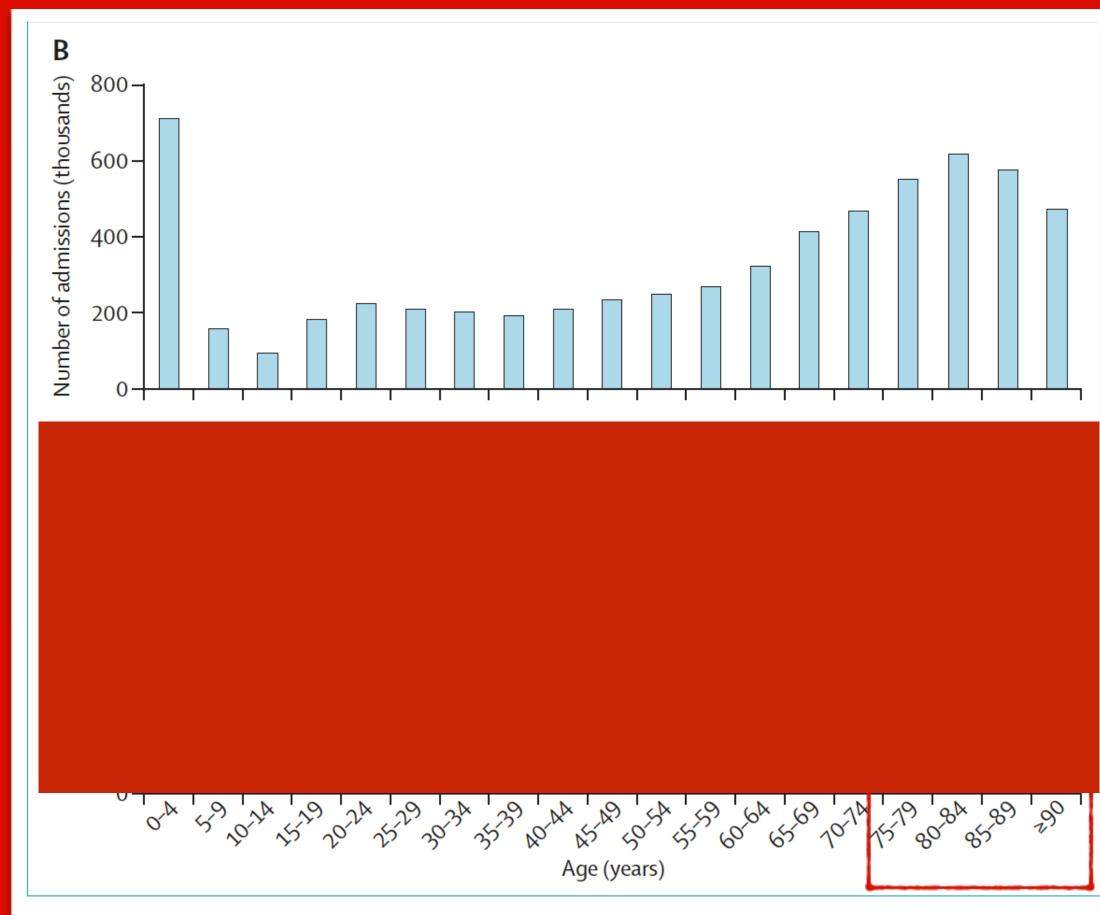


Figure: Data for infection, sepsis, and emergency hospital admissions for sepsis or bacterial infection in England

2011–17

THE PRINCIPLES AND PRACTICE OF MEDICINE

DESIGNED FOR THE USE OF PRACTITIONERS
AND STUDENTS OF MEDICINE

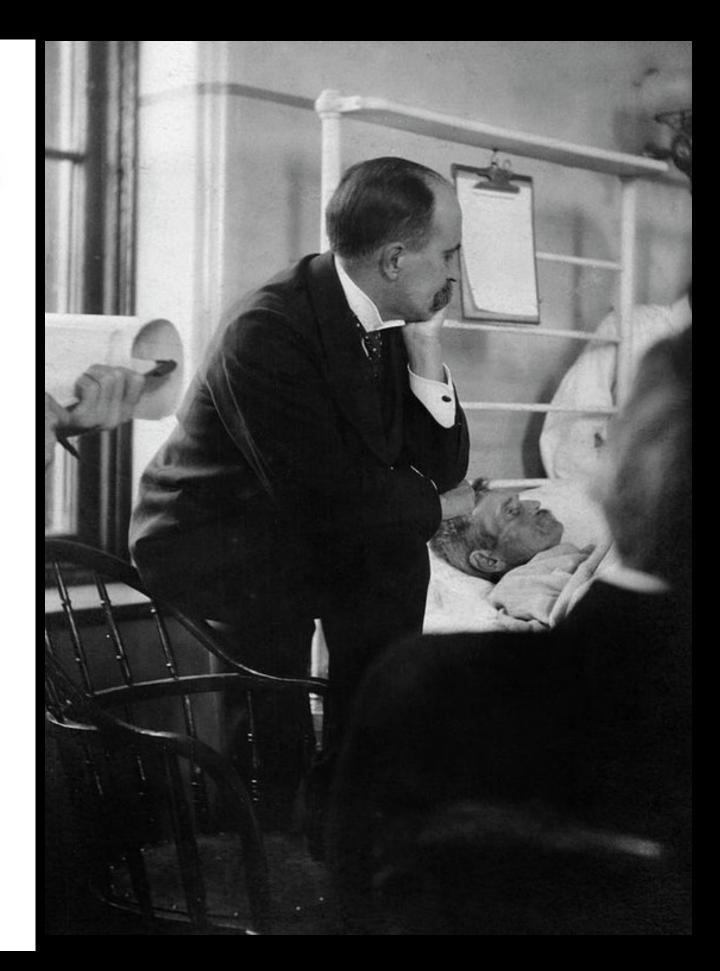
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WILLIAM OSLER, M. D.

Fellow of the Royal Society; Fellow of the Royal College of Physicians,
London; Professor of Medicine in the Johns Hopkins University and
Physician-in-chief to the Johns Hopkins Hospital, Baltimore;
formerly Professor of the Institutes of Medicine, McGill
University, Montreal; and Professor of Clinical Medicine
in the University of Pennsylvania, Philadelphia

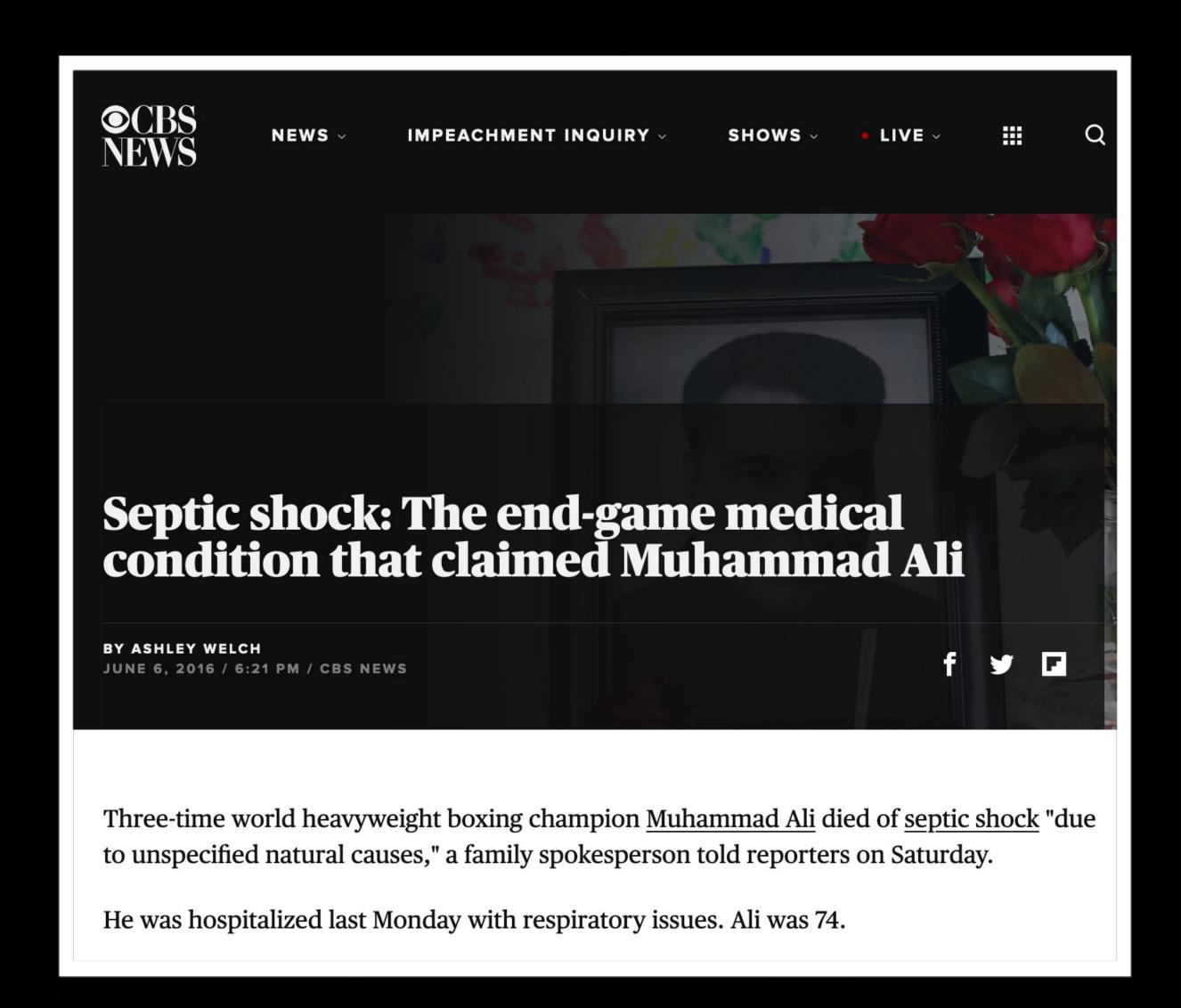
FOURTH EDITION

NEW YORK
D. APPLETON AND COMPANY



Pneumonia may well be called the friend of the aged. Taken off by it in an acute, short, not often painful illness, the old man escapes those "cold gradations of decay" so distressing to himself and to his friends.

DO PEOPLE DIE OF OR WITH SEPSIS?

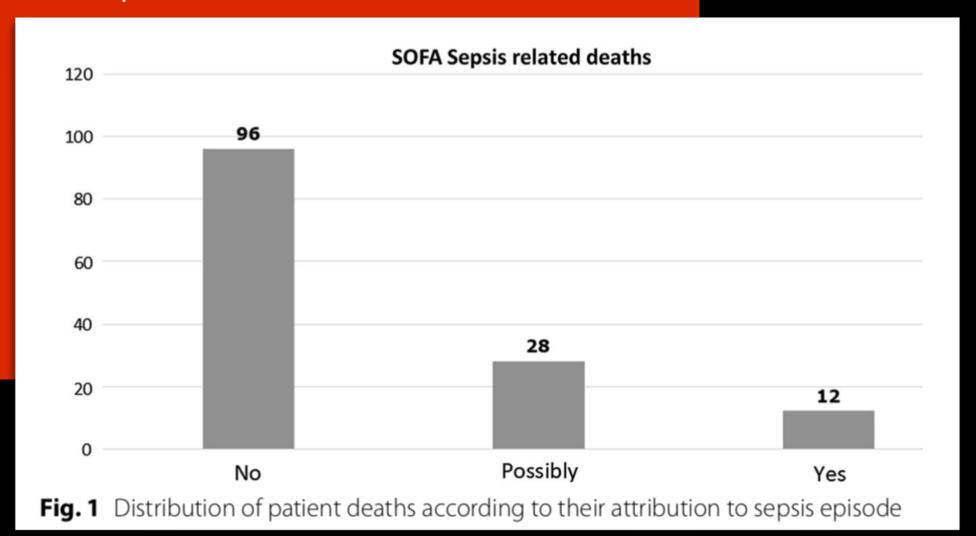


Sepsis-related deaths in the at-risk population on the wards: attributable fraction of mortality in a large point-prevalence study

Maja Kopczynska¹, Ben Sharif¹, Sian Cleaver¹, Naomi Spencer¹, Amit Kurani¹, Camilla Lee¹, Jessica Davis¹, Carys Durie¹, Jude Joseph-Gubral¹, Angelica Sharma¹, Lucy Allen¹, Billie Atkins¹, Alex Gordon¹, Llewelyn Jones¹, Amy Noble¹, Matthew Bradley¹, Henry Atkinson¹, Joy Inns¹, Harriet Penney¹, Carys Gilbert¹, Rebecca Walford¹, Louise Pike¹, Ross Edwards¹, Robyn Howcroft¹, Hazel Preston¹, Jennifer Gee¹, Nicholas Doyle¹, Charlotte Maden¹, Claire Smith¹, Nik Syakirah Nik Azis¹, Navrhinaa Vadivale¹ and Tamas Szakmany^{1,2*} on behalf of Welsh Digital Data Collection Platform Collaborators

- 12,477 patients screened over two 24-hr periods in 14 Welsh hospitals
- 839 patients identified, of whom 521 fulfilled Sepsis-3 criteria (SOFA ≥2)
- 136 died in hospital, 96 for non-sepsis reasons
- Of 40 sepsis-attributable deaths (12 definite, 28 possible):
 - 77.5% had high frailty score (≥6)
 - 70% had existing DNA-CPR order
 - 42.5% had limitation-of-care order

Kopczynska et al. BMC Res Notes (2018) 11:720



Prevalence, Underlying Causes, and Preventability of Sepsis-Associated Mortality in US Acute Care Hospitals

Chanu Rhee, MD, MPH; Travis M. Jones, PharmD; Yasir Hamad, MD; Anupam Pande, MD, MPH; Jack Varon, MD; Cara O'Brien, MD; Deverick J. Anderson, MD, MPH; David K. Warren, MD, MPH; Raymund B. Dantes, MD, MPH; Lauren Epstein, MD, MS; Michael Klompas, MD, MPH; for the Centers for Disease Control and Prevention (CDC) Prevention Epicenters Program

Findings In this cohort study reviewing the medical records of 568 patients who were admitted to 6 hospitals and died in the hospital or were discharged to hospice and not readmitted, sepsis was present in 300 hospitalizations (52.8%) and directly caused death in 198 cases (34.9%). However, most underlying causes of death were related to severe chronic comorbidities and only 3.7% of sepsis-associated deaths were judged definitely or moderately preventable.

25 sepsis-associated deaths (8.3%) were considered possibly preventable.

Meaning Sepsis is a leading cause of death in US hospitals, but most of these deaths are unlikely to be preventable through better hospital-based care.

Most common underlying causes of death in patients with sepsis:

- cancer 31.0%,
- chronic heart disease 15.3%,
- dementia 9.7%

JAMA Network Open. 2019;2(2):e187571.

FACT OR PROPAGANDA?





• ... but don't want unnecessary or prolonged delay in giving appropriate antibiotics

Sepsisital diagnos morvear.

Sepsisital diagnos morvear.

J.S. 27 billion each year.

J.S. 27 billion each year.

s is the cause

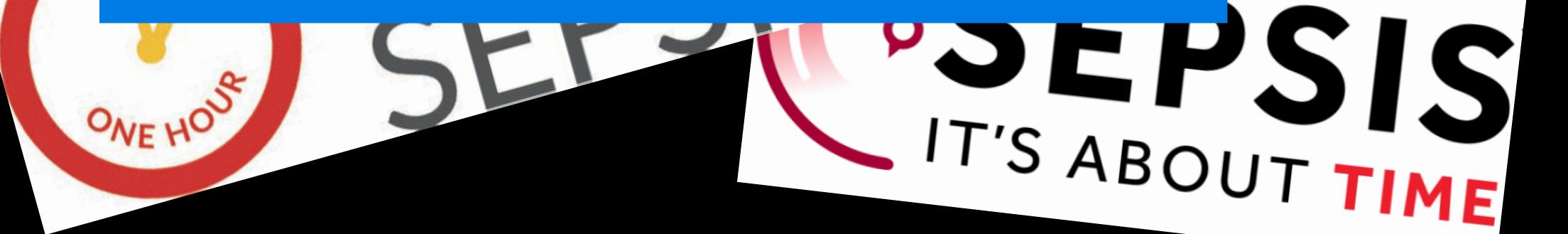
Antibiotics for Sepsis: Does Each Hour Really Count, or Is It Incestuous Amplification?

Mervyn Singer, M.D., F.R.C.P.

Bloomsbury Institute of Intensive Care Medicine
University College London
London, United Kingdom

Incestuous amplification—the (extreme) reinforcement of ideas and/or beliefs that occurs when like-minded people communicate with each other (1).

American Journal of Respiratory and Critical Care Medicine Volume 196 Number 7 | October 1 2017



Narrative Review

Impact of time to antibiotic therapy on clinical outcome in patients with bacterial infections in the emergency department: implications for antimicrobial stewardship

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P. Nauclér <sup>1</sup>, A. Huttner <sup>2</sup>, C.H. van Werkhoven <sup>3</sup>, M. Singer <sup>4</sup>, P. Tattevin <sup>5</sup>, S. Einav <sup>6</sup>, T. Tängdén <sup>7, *</sup>
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Sources: A literature search was performed in the PubMed/MEDLINE database using combined search terms for various infectious syndromes (sepsis/septic shock, bacterial meningitis, lower respiratory tract infections, urinary tract infections, intra-abdominal infections and skin and soft tissue infections), time to antibiotic treatment, and clinical outcome.

Content: The literature search generated 8828 hits. After screening titles and abstracts and assessing potentially relevant full-text papers, 60 original articles (four randomized controlled trials, 43 observational studies) were included. Most articles addressed sepsis/septic shock, while few studies evaluated early initiation of therapy in mild to moderate disease. The lack of randomized trials and the risk of confounding factors and biases in observational studies warrant caution in the interpretation of results.

Implications: For patients presenting with suspected bacterial infections, withholding antibiotic therapy until diagnostic results are available and a diagnosis has been established (e.g. by 4–8 h) seems acceptable in most cases unless septic shock or bacterial meningitis are suspected. This approach promotes the use of ecologically favourable antibiotics in the ED, reducing the risks of side effects and selection of resistance.

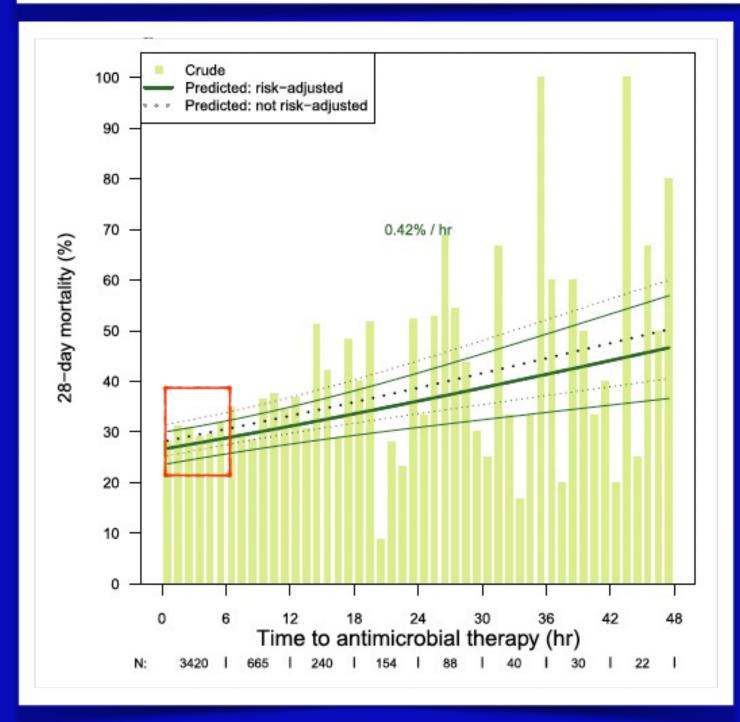
Adverse effects of delayed antimicrobial treatment and surgical source control in adults with sepsis: results of a planned secondary analysis of a cluster-randomized controlled trial

Hendrik Rüddel^{1,2}, Daniel O. Thomas-Rüddel^{1,2}, Konrad Reinhart^{3,4}, Friedhelm Bach⁵, Herwig Gerlach⁶, Matthias Lindner⁷, John C. Marshall⁸, Philipp Simon⁹, Manfred Weiss¹⁰, Frank Bloos^{1,2}, Daniel Schwarzkopf^{1,2,11*} and the MEDUSA study group

Critical Care (2022) 26:51

Using a

categorized timing variable, there were no significant differences comparing treatment within 1 h versus 1-3 h, or 1 h versus 3-6 h. Delays of more than 6 h significantly increased mortality (OR = 1.41 [1.17, 1.69]).



Predictor	No. of patients	Observed mortality	Risk-adjusted mortality	OR (95% CI)	Decreasing Increasing mortality mortality	P-valu
Timing of antimicrobial therapy	4659/4792					0,008
0-1 hr		364/1270 (28.7)	25.3 (22, 28.9)	1		
1-3 hrs		418/1352 (30.9)	27.8 (24.4, 31.6)	1.14 (0.95, 1.36)	i . • →	0.14
3-6 hrs		255/836 (30.5)	26 (22.3, 30.2)	1.04 (0.85, 1.27)	⊢• ⊢1	0.7
>6 hrs		437/1201 (36.4)	31.5 (27.5, 35.7)	1.36 (1.12, 1.63)	⊢∙⊣	0.0
Timing of surgical source control	1563/1595					0.2
0-1 hr		92/327 (28.1)	25.1 (19.1, 32.3)	1		
1-3 hrs		85/287 (29.6)	26.4 (20.8, 32.9)	1.07 (0.71, 1.61)	⊢ •−−−1	0.7
3-6 hrs		93/293 (31.7)	27.1 (21.3, 33.8)	1.11 (0.71, 1.72)	- • − − 1	0.6
>6 hrs		240/656 (36.6)	31.9 (26.7, 37.5)	1.4 (0.94, 2.08)	l :	0.1
Success of source control	1563/1595					
Not successful		179/262 (68.3)	68.7 (60.7, 75.7)	1		
Successful		331/1301 (25.4)	20.2 (16.5, 24.5)	0.12 (0.08, 0.16)	M	<=0,0
					0 0.2 0.4 0.6 0.8 1 1.2 1.4 1.6 1.8 2 2.2 2.4 Adjusted odds ratio for 28-day mortality	

Infectious Diseases Society of America Position Paper: Recommended Revisions to the National Severe Sepsis and Septic Shock Early Management Bundle (SEP-1) Sepsis Quality Measure

Chanu Rhee,^{1,2} Kathleen Chiotos,^{3,a} Sara E. Cosgrove,^{4,b} Emily L. Heil,^{5,c} Sameer S. Kadri,^{6,©} Andre C. Kalil,⁷ David N. Gilbert,⁸ Henry Masur,⁶ Edward J. Septimus,^{1,9} Daniel A. Sweeney,¹⁰ Jeffrey R. Strich,⁶ Dean L. Winslow,¹¹ Michael Klompas,^{1,2}; for the Infectious Diseases Society of America Sepsis Task Force^d

^dThis position paper is endorsed by the American College of Emergency Physicians, Pediatric Infectious Diseases Society, Society for Healthcare Epidemiology of America, Society of Hospital Medicine, and Society of Infectious Disease Pharmacists.

Concerns:

- Antibiotic overuse
 - high rate of over-diagnosis of sepsis
 - mandate encourages aggressive a/b use for all patients,
 regardless of certainty of diagnosis or severity of illness
- Overlooks treatment for non-infectious conditions
- Evidence base does not support immediate a/b for all sepsis
- Complex 'time-zero' definition non-evidence-based

Clinical Infectious Diseases 2021;72(4):541–52

Infectious Diseases Society of America Position Paper: Recommended Revisions to the National Severe Sepsis and Septic Shock Early Management Bundle (SEP-1) Sepsis Quality Measure

Chanu Rhee,^{1,2} Kathleen Chiotos,^{3,a} Sara E. Cosgrove,^{4,b} Emily L. Heil,^{5,c} Sameer S. Kadri,^{6,©} Andre C. Kalil,⁷ David N. Gilbert,⁸ Henry Masur,⁶ Edward J. Septimus,^{1,9} Daniel A. Sweeney,¹⁰ Jeffrey R. Strich,⁶ Dean L. Winslow,¹¹ Michael Klompas,^{1,2}; for the Infectious Diseases Society of America Sepsis Task Force^d

IDSA's core recommendation is to limit SEP-1 to septic shock, for which the evidence supporting the benefit of immediate antibiotics is greatest. Prompt empiric antibiotics are often appropriate for suspected sepsis without shock, but IDSA believes there is too much heterogeneity and difficulty defining this population, uncertainty about the presence of infection, and insufficient data on the necessity of immediate antibiotics to support a mandatory treatment standard for all patients in this category.

Clinical Infectious Diseases 2021;72(4):541–52

Early Care of Adults With Suspected Sepsis in the Emergency Department and Out-of-Hospital Environment: A Consensus-Based Task Force Report

This report has been organized by the American College of Emergency Physicians and has been endorsed by the

American Academy of Emergency Medicine, the American College of Osteopathic E American Osteopathic Board of Emergency Medicine, the Association of Academic Char the Council of Emergency Medicine Residency Directors, the Emergency Medicine R Emergency Nurses Association, the Infectious Diseases Society of America, the National Associety for Academic Emergency Medicine, the Society of Critical Care Medicine, and the

Donald M. Yealy, MD; Nicholas M. Mohr, MD, MS; Nathan I. Shapiro, MD; Arjun Venkatesh Wesley H. Self, MD, MPH once the diagnosis of sepsis is established, rapid and comprehensive therapy—not just antibiotic administration—is optimal. But the current data do not recommend a singular time target that clearly improves outcomes for all. In those

We recommend prompt administration of antibiotics in the ED, but we reserve very short time thresholds for those with infection and shock and note there are insufficient data to recommend a specific time threshold for administration of antibiotics.

of sepsis—septic shock—the nce support a shorter time ationship between time and

UKNATIONAL EARLY WARNING SCORE (NEWS-2)

Chart 1: The NEWS scoring system								
Physiological parameter	3	2	1	Score 0	1	2	3	
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25	
SpO ₂ Scale 1 (%)	≤91	92–93	94–95	≥96				
SpO ₂ Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen	

Chart 2: NEWS thresholds and triggers

NEW score	Clinical risk	Response	
Aggregate score 0–4	Low	Ward-based response	
Red score Score of 3 in any individual parameter	Low-medium	Urgent ward-based response*	
Aggregate score 5–6	Medium	Key threshold for urgent response*	
Aggregate score 7 or more	High	Urgent or emergency response**	

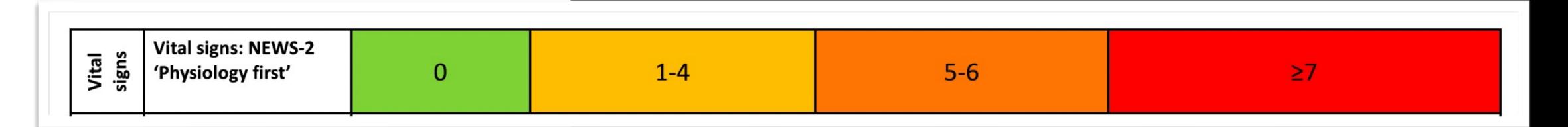
^{*} Response by a clinician or team with competence in the assessment and treatment of acutely ill patients and in recognising when the escalation of care to a critical care team is appropriate.

	≥93 on air	oxygen	oxygen	oxygen	
	Air				
101–110	111–219			≥220	
41–50	51–90	91–110	111–130	≥131	
	Alert			CVPU	
35.1–36.0	36.1–38.0	38.1–39.0	≥39.1		
© Royal College of Physicians 2017					

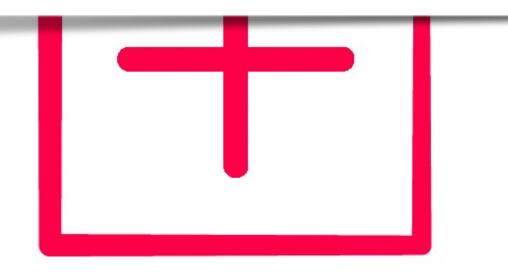
• ... used in all hospitals (ED, ward) ... ambulance crews, nursing homes ... and GPs

^{**}The response team must also include staff with critical care skills, including airway management.

The working group unanimously agreed with the principle that treatment urgency for adults and children in secondary care should initially be determined by severity of illness using NEWS2 or PEWS, respectively as part of clinical assessment.



The severity score should then be interpreted in the light of clinical assessment, to include rapidity of deterioration and trajectory, likely diagnosis (such as infection and sepsis), immune status, and evidence of organ dysfunction.



Academy of Medical Royal Colleges

Statement on the initial antimicrobial treatment of sepsis

If additional concerns are identified at this stage, the clinician can 'upgrade' the actions required at least to the next highest severity band.

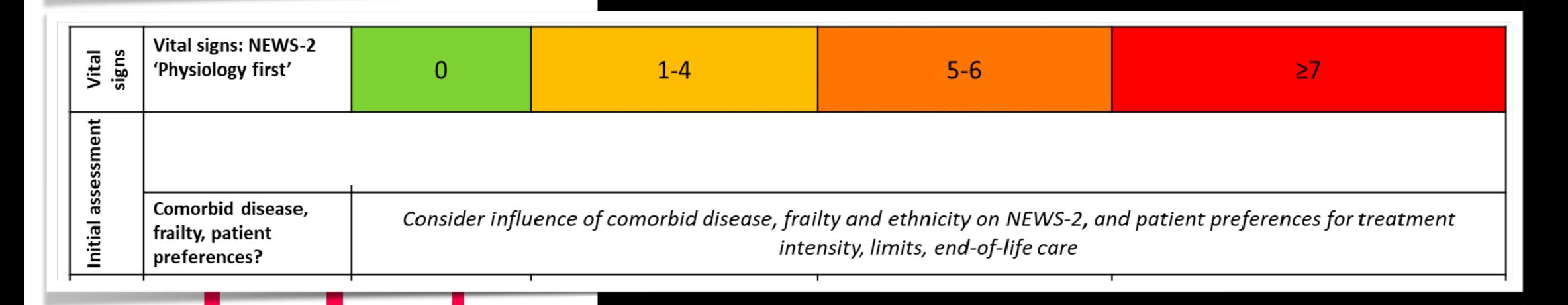
Vital signs	Yital signs: NEWS-2 'Physiology first' 0 1-4 5-6 ≥7						
Initial assessment	History, examination, lab results	-			epsis, neutropaenia, or blood gas / lab ctions at least to next NEWS-2 level ->		
iu							

Statement on the initial antimicrobial treatment

https://www.aomrc.org.uk/reports-guidance/

Assessment of

comorbid disease, frailty and patient preferences must also be considered to inform judgements about treatment intensity.

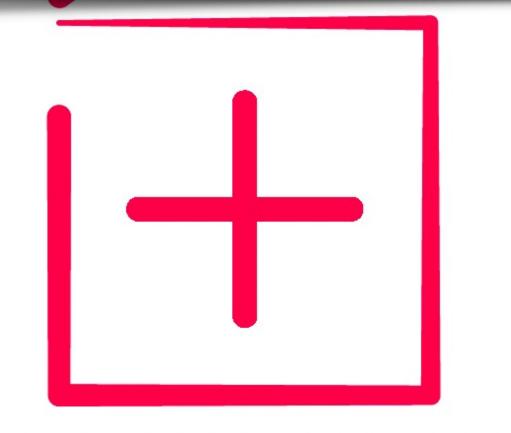


Statement on the initial antimicrobial treatment of sepsis

https://www.aomrc.org.uk/reports-guidance/

For

patients with possible, probable or definite infection, infection-specific diagnostic tests and administration of antimicrobials should be completed within 6, 3, or 1 hour of recording a NEWS2 of 1-4, 5-6, or ≥7, respectively, These are maximum periods, not targets.



October 2022 v2.0

(Replac

Academy of Medical Royal Colleges

Sta ant

ofs

	Vi t al signs	Vital signs: NEWS-2 'Physiology first'	0	1-4	5-6	≥7			
	essment	History, examination, lab results	If clinical or carer concern, continuing deterioration, surgically remediable sepsis, neutropaenia, or blood gas / lab evidence of organ dysfunction, including elevated serum lactate, upgrade actions at least to next NEWS-2 level ->						
	Initial ass	Comorbid disease, frailty, patient preferences?	Consider influence of comorbid disease, frailty and ethnicity on NEWS-2, and patient preferences for treatment intensity, limits, end-of-life care						
	Initial (generic) actions	Monitoring and escalation plan	Standard observations	 Registered nurse review <1 h Obs 4-6 hrly if stable. Escalate if no improvement 	 Obs hourly. Review <1 hr by clinician competent in acute illness assessment Escalate if no improvement 	 Obs every 30 mins. Review <30 min by clinician competent in acute illness assessment. Senior doctor review <1 hr if no improvement: refer to Outreach or ICU 			
		Initial treatment of precipitating condition	Standard care	<6 hr	<3 hr	<1 hr			
	Likelihood of infection & specific actions	Unlikely	Standard care	andard care Review daily and reconsider infection if diagnosis remains uncertain					
		Possible	Review at least daily	< 6 h • Source identification & control plan documented.	 < 3 h: • Microbiology tests • Antimicrobials: administer or revise 	 < 1 h: • Microbiology tests • Antimicrobials: administer or revise (broadspectrum if causative organism uncertain). 			
		Probable or definite	< 6 h Diagnostic tests & R plan 	 < 6 h Microbiology tests Antimicrobials: administer or revise Source identification & control plan. D/w ID/micro if uncertain, & review 	 Source identification & control plan documented. 6h Source control initiated 48 – 72 h Review antimicrobials with ID/micro/senior clinician 	 3 h Source identification 3-6 h Source control initiated according to clinical urgency 48 – 72 h: Review antimicrobials with ID/micro/senior clinician 			

Statement on the initial antimicrobial treatment of sepsis

https://www.aomrc.org.uk/reports-guidance/

The aim is not to delay treatment, but to allow sufficient time to make an informed clinical judgement. Antimicrobial treatment must be accompanied by source identification and control and antimicrobial stewardship through iterative review.

The frameworks aim to provide a balance between patient safety and antimicrobial stewardship, while allowing clinicians to exercise accountable judgement in the care of individual patients. As with all service delivery interventions, the framework should be subject to local audit and prospective research evaluation leading to future modifications and improvements.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Suspected sepsis in people aged 16 or over who are not and have not recently been pregnant

Draft for consultation, March 2023



Timing of antibiotics

Given the lack of direct evidence, the committee decided, by consensus, to recommend adopting the initial antimicrobial treatment of sepsis outlined in the 2022 AoMRC statement. That is, for people with low to moderate, moderate to high and high risk of severe illness or death from sepsis, antibiotics should be given, respectively within 6, 3, and 1 hour and, for people at low risk, on a need for basis, in line with local practice.

The committee highlighted that:

- the purpose of deferring antibiotic delivery is not to delay treatment, but to have extra time to gather information for a more specific diagnosis, allowing for more targeted treatment
- the 1-, 3- and 6-hour time limits are a maximum (rather than an aim) for each risk level
- clinical judgement is key when considering someone's specific care needs.

