UWTASP

tele-antimicrobial stewardship program

August 20th, 2019

Announcements

- Cases and questions

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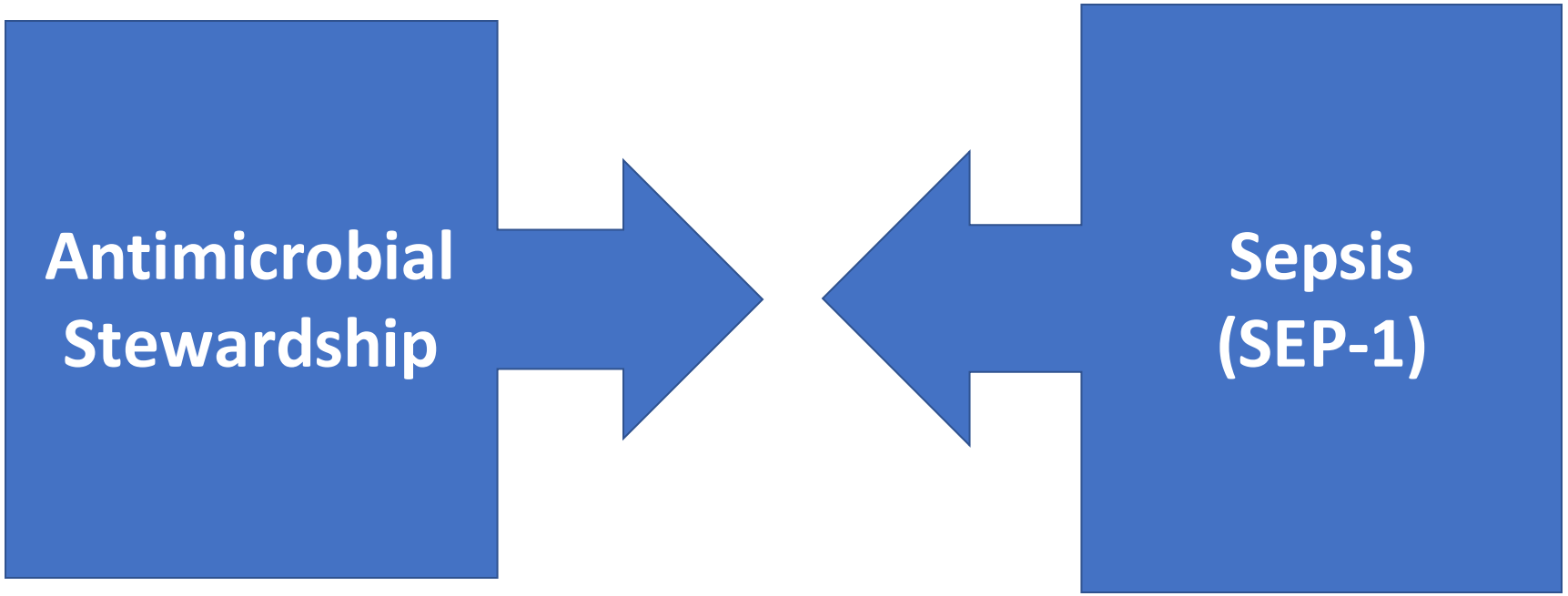
August 20th, 2019

Didactic

- Sepsis 2

Clash of Goals?



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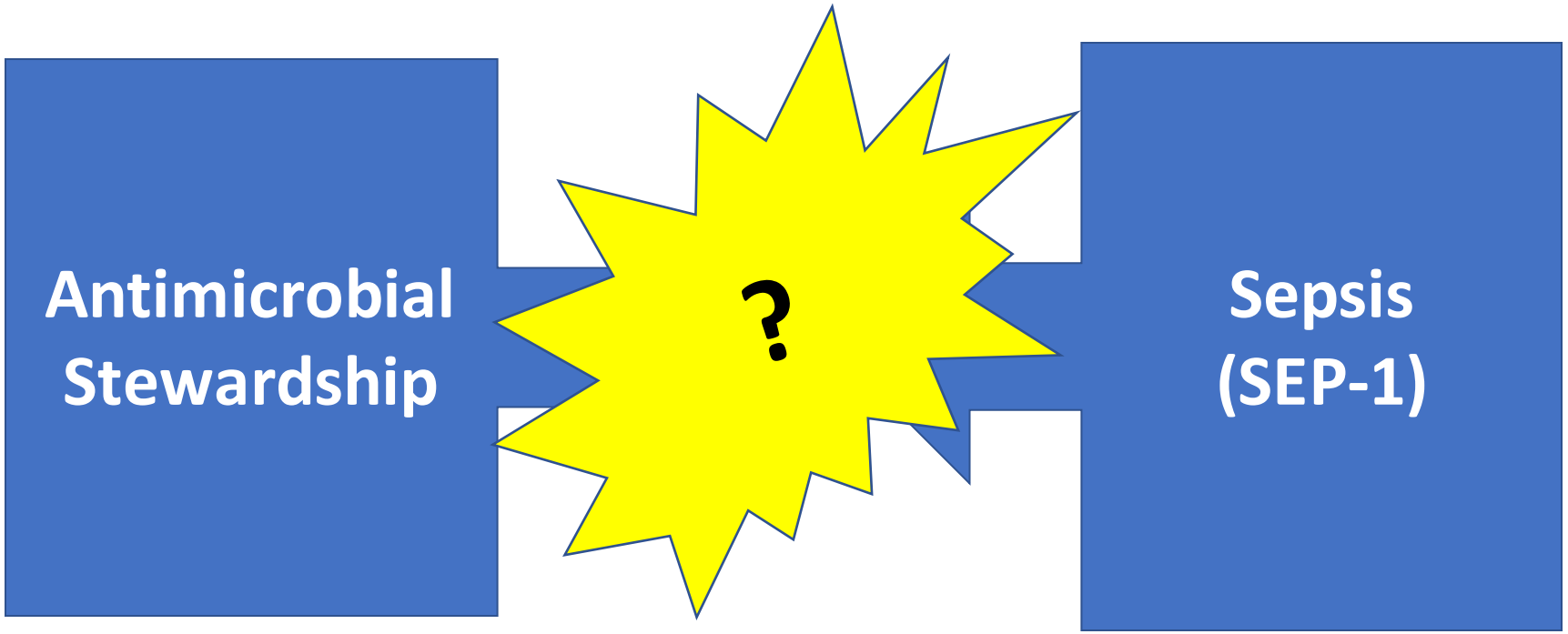

Image: Ministry of Health Singapore

Clash of Definitions?

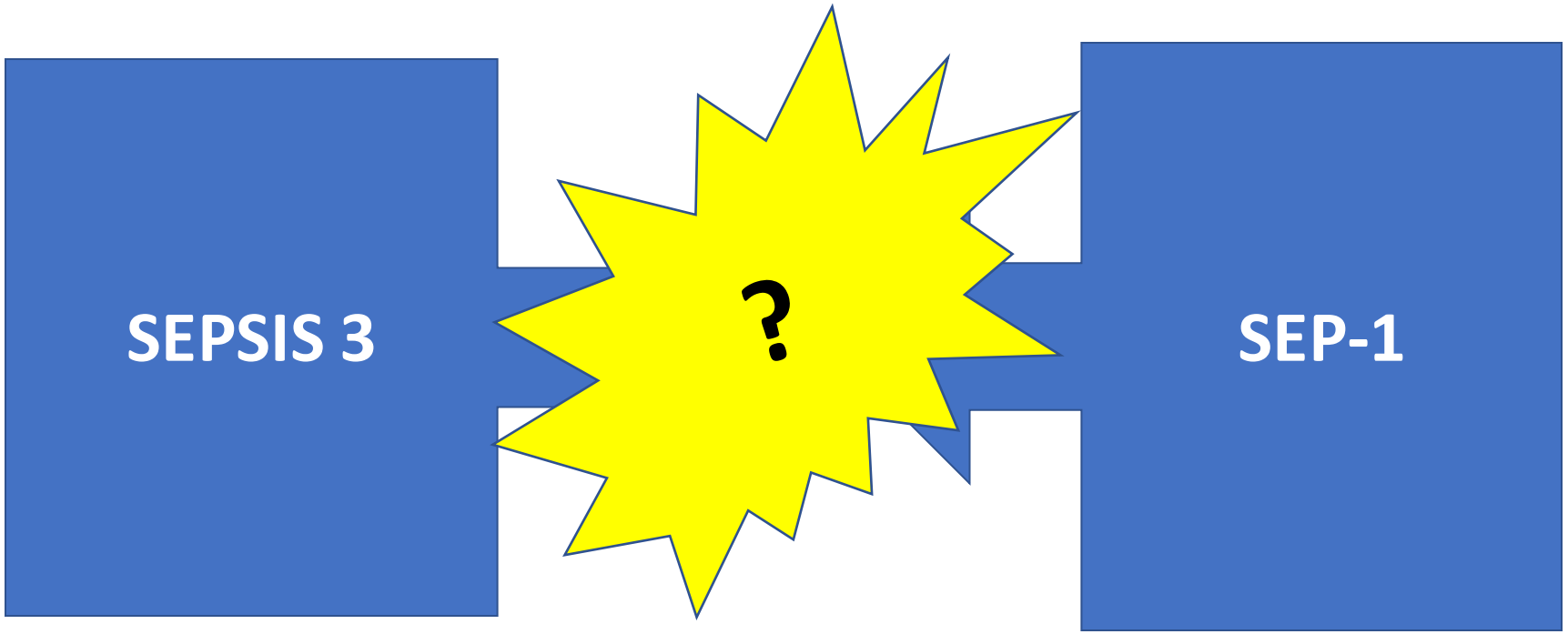

Image: Ministry of Health Singapore

What are the Antimicrobial Rights?

- **Right patient**
- **Right drug**
- **Right time**
- **Right dose**
- **Right duration**
- **And….right allergy assessment**

Image: Ministry of Health Singapore

Evolution of Definitions – SEPSIS III

SIRS + Sepsis

- <36 degrees C or >38 degrees
- HR > 90/minute
- RR >20/minute
- PaCO2 32 mmHg and
- WBC <4,000 or 12,000 and/or >10% bands

➢2 or more + concern for infection =

Sepsis

Sepsis to Severe Sepsis and Shock

- **Sepsis** +
  - End-organ dysfunction
  - <90 mmHg
  - And/or lactate >4 mmol/L

- Persistent hypotension, end-organ damage

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Sepsis to Severe Sepsis and Shock

- **Sepsis** +
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= Severe Sepsis

- Persistent hypotension, end-organ damage **= Septic Shock**

Sepsis-3

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

Singer, JAMA, 2016

Sepsis-3

- Sepsis: Life-threatening organ dysfunction cause by dysregulated host response to infection
- Suspected or documented infection and an acute increase of ≥2 SOFA points (ICU) or ≥2 qSOFA

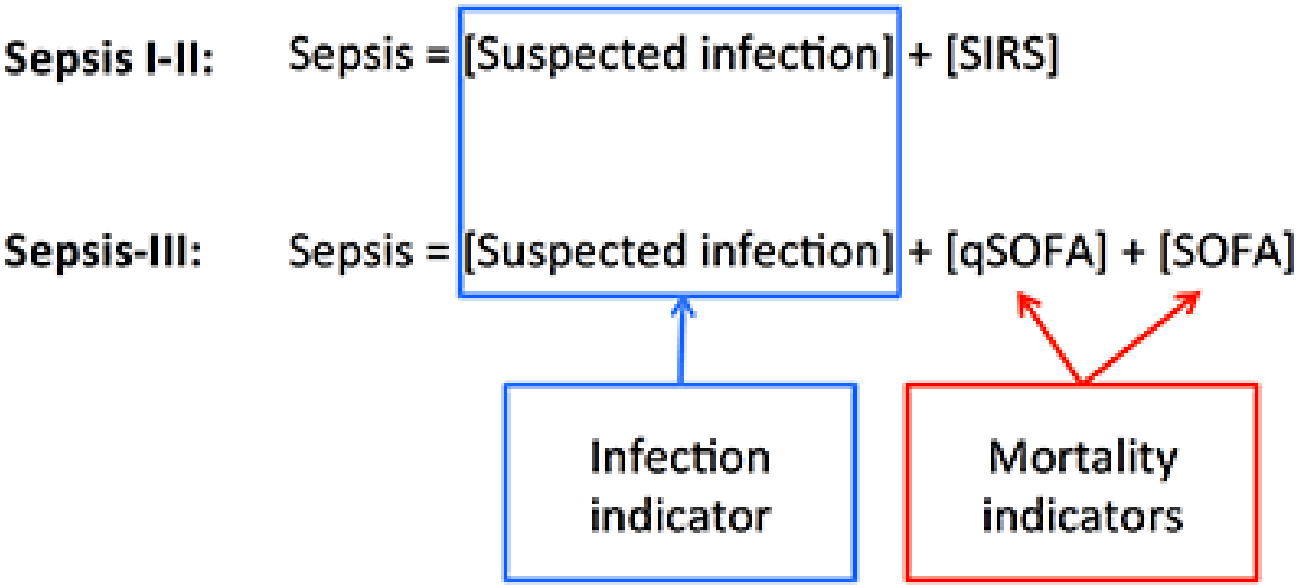
Singer, JAMA, 2016

New Definitions – Septic Shock

- Septic shock: Sepsis with circulatory and cellular/metabolic abnormalities profound enough to substantially increase mortality
- Sepsis and vasopressor therapy needed to elevate MAP ≥ 65 mmHg and lactate >2 mmol/L after adequate fluid resuscitation

New Definitions

- No more SIRS
- Many inpatients met criteria, sometime for benign conditions, so not specific



Sequential Organ Failure Assessment Score

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

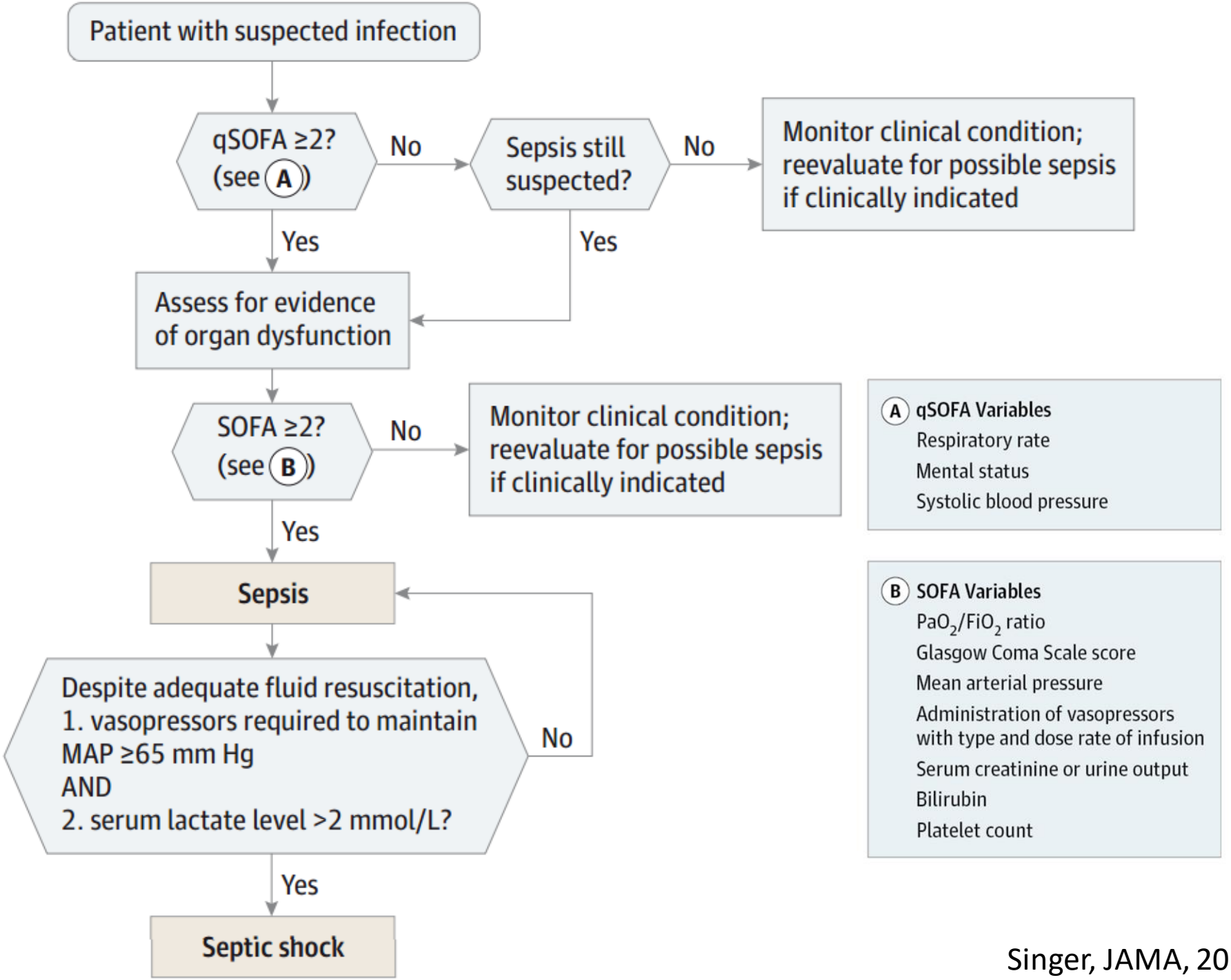
aka SOFA score acute = >2 indicates organ dysfunction

Singer, JAMA, 2016

qSOFA Score

- RR >21, alt mentation, SBP <100
- Study used SOFA, SIRS and LODS to evaluate 148,907 patients with suspected sepsis
- Among ICU pts, SOFA superior to SIRS as predictor
- Outside the ICU, qSOFA better predictor of in-hospital mortality
- Based on retrospective data, more research is needed

Seymour, JAMA, 2016



Singer, JAMA, 2016

Issues with New Definitions

- Based on retrospective data
- “Consensus” of 2 organizations
- Diagnosis delay?
- No more SIRS, so mortality increases as the denominator population decreases in size, even if the hospital is diagnosing and treating sepsis better

Immediate Actions – Sepsis

- Time Zero = meets SEPSIS criteria*
  - ED, acute care, ICU
  - Early recognition is critical, hence the push
- Resuscitation bundles
  - 3 and 6 hours bundles
  - Key elements are antibiotics and resuscitation (EGDT)

SEP-1*– 3 hour bundle

- Measure lactate level
- Blood cultures prior to antibiotics
- Administer broad spectrum antibiotics
- Administer 30 mL/kg crystalloid or lactate $\geq$4 mmol/L

***Lactate >2 or organ dysfunction (2 SIRS + suspected infection)**

SEP-1*– 6 hour bundle

- Repeat lactate if initial >2
- Vasopressor administration (if hypotension persists after fluid)
- Repeat volume status assessment

***Lactate >2 or organ dysfunction (2 SIRS + suspected infection)**

Right Drug - SEP-1

MONOTHERAPY	OR	Column A +	Column B
Doripenem		Amikacin	Cefazolin
Ertapenem		Gentamicin	Cefoxitin
Imipenem/Cilastatin		Tobramycin	Cefuroxime
Meropenem		Aztreonam	Clindamycin IV
Cefotaxime		Ciprofloxacin	Daptomycin
Ceftazidime			Telavancin
Ceftriaxone			Vancomycin
Ceftazidime			Linezolid
Cefepime			Azithromycin
Ceftaroline fosamil			Erythromycin
Moxifloxacin			Ampicillin
Levofloxacin			Nafcillin
Amoxicillin/clavulanate			Oxacillin
Ampicillin/sulbactam			Penicillin G
Piperacillin/tazobactam			

Right Drug?

MONOTHERAPY	OR	Column A +	Column B
Doripenem		[redacted]	Cefazolin
Ertapenem		Gentamicin	[redacted]
Imipenem/Cilastatin		[redacted]	[redacted]
Meropenem		[redacted]	[redacted]IV
[redacted]		Ciprofloxacin	Daptomycin
[redacted]			Telavancin
Ceftriaxone			Vancomycin
[redacted]			Linezolid
Cefepime			Azithromycin
Ceftaroline fosamil			[redacted]
Moxifloxacin			Ampicillin
Levofloxacin			Nafcillin
[redacted]			Oxacillin
Ampicillin/sulbactam			[redacted]
Piperacillin/tazobactam			

Antibiotic Therapy for Severe Sepsis/Septic Shock

ABX choice should be based on site of infection and risk factors for drug resistant organisms (prior abx, SNF, LTACH, h/o MDROs)

Single drug therapy options:

- Ceftriaxone
- Cefepime
- Piperacillin/Tazobactam
- Ertapenem
- Meropenem
- Levofloxacin

(ADD VANCOMYCIN if risk factors for MRSA present)

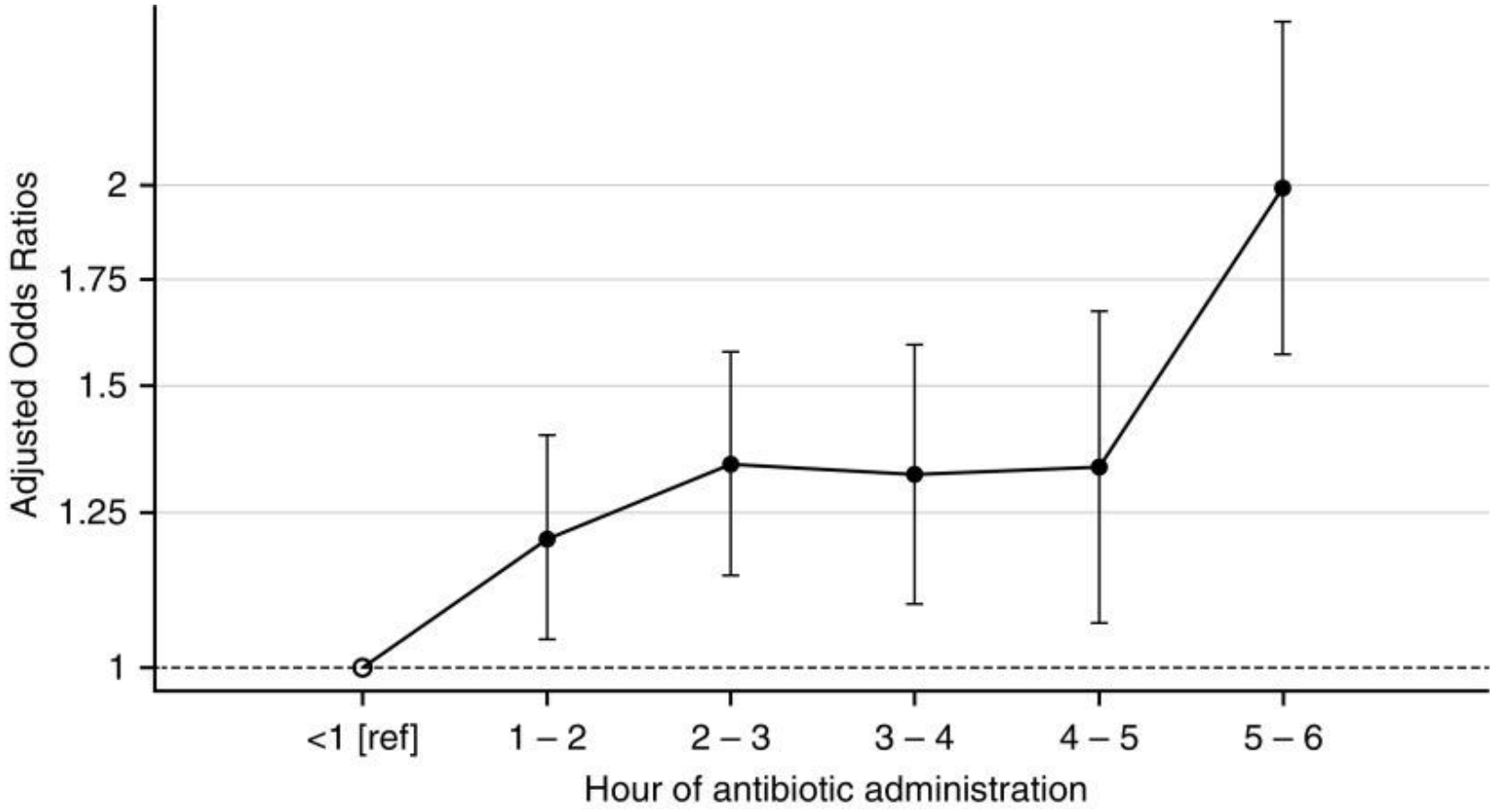
For patients with severe beta-lactam allergy:

Aztreonam OR Ciprofloxacin OR Aminoglycoside

PLUS Vancomycin regardless of risk factors for MRSA

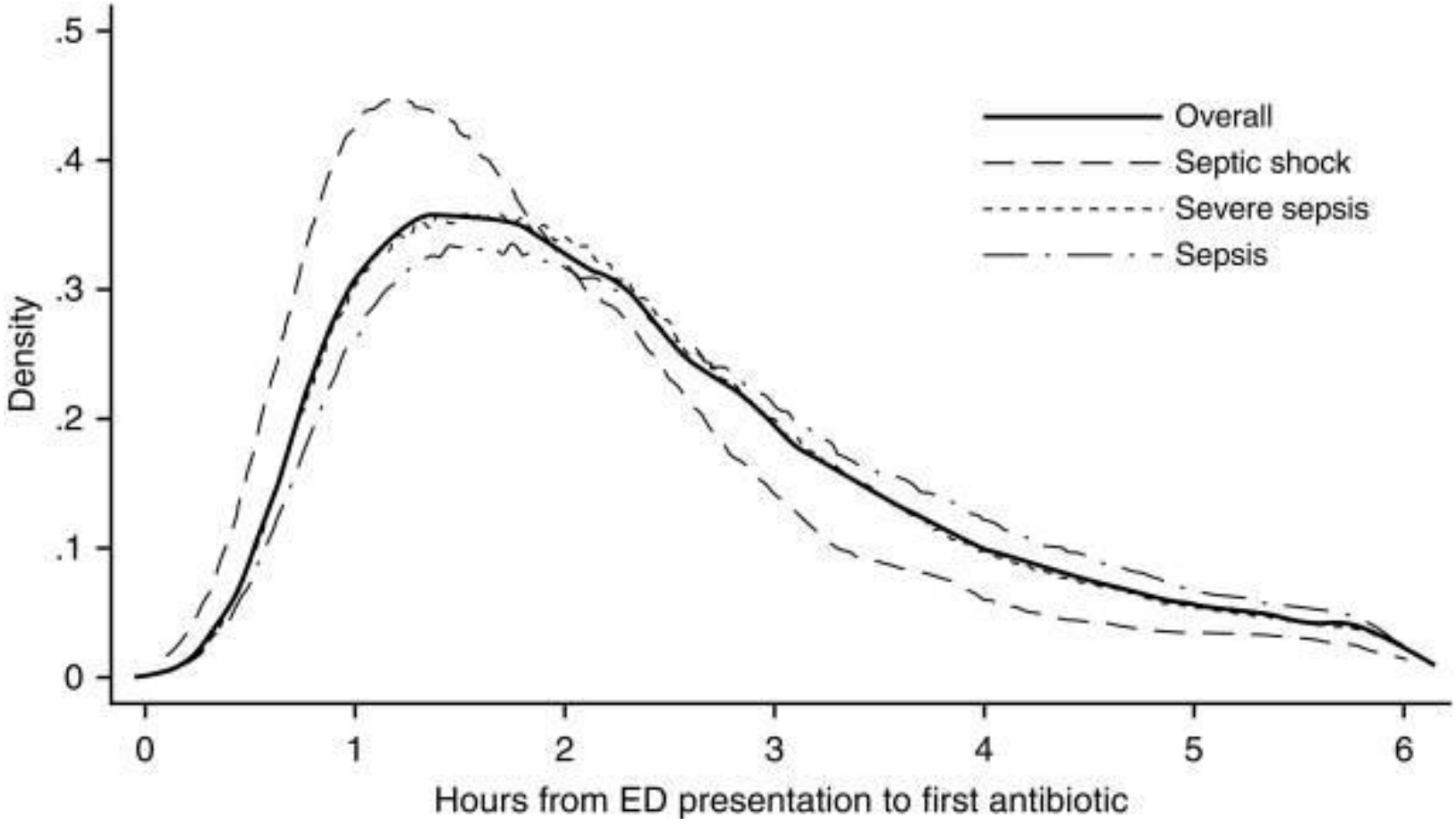
Contact Infectious Disease Consult or Antimicrobial Stewardship with questions

Right Timing



Liu, Am J Respir Crit Care Med, 2017

Right Timing



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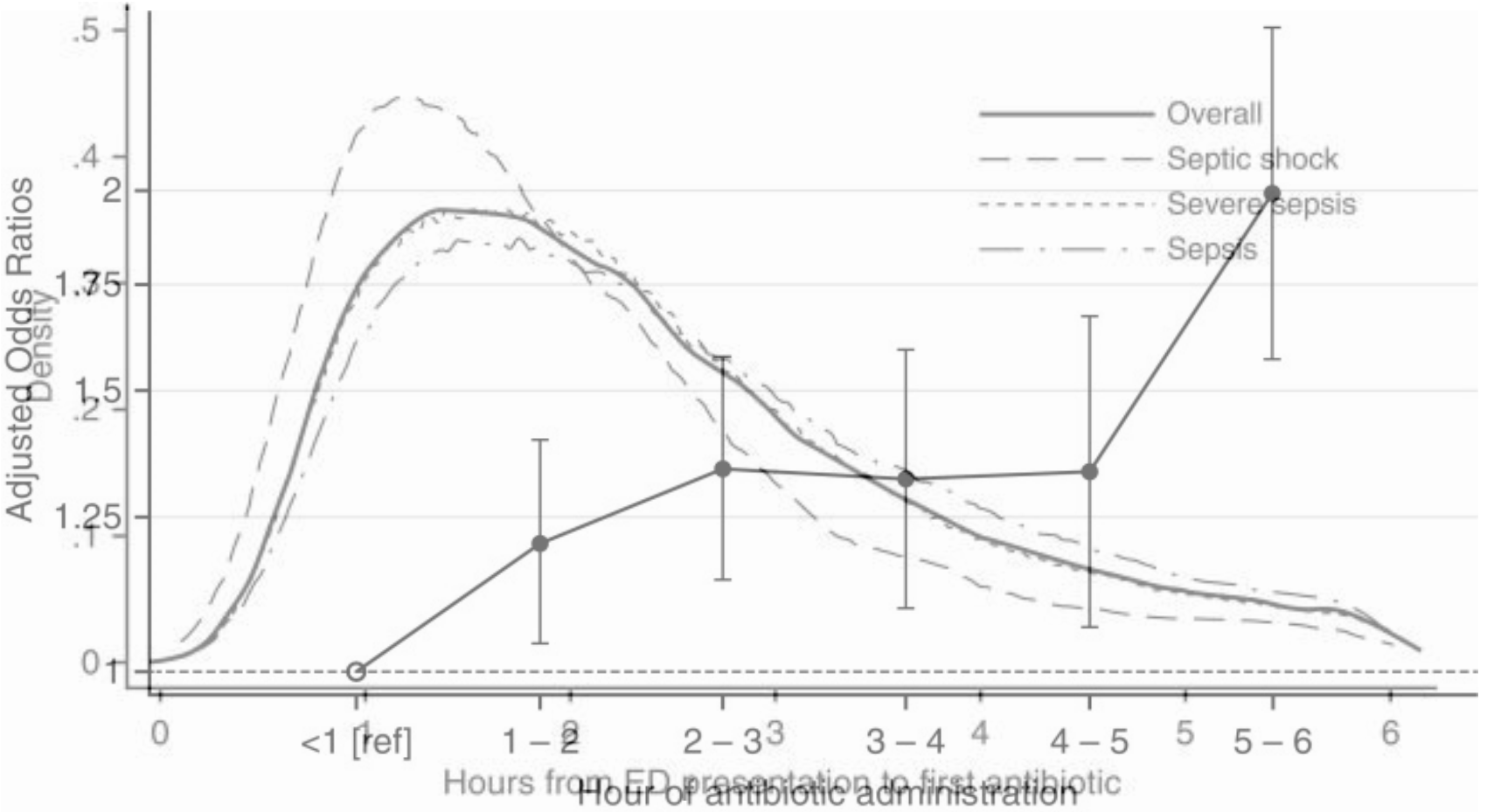

Liu, Am J Respir Crit Care Med, 2017

Right Duration

Stewardship: Shorter = Better

Diagnosis	Short (d)	Long (d)	Result
CAP	3 or 5	7, 8, or 10	Equal
HAP	7	10-15	Equal
VAP	8	15	Equal
Pyelo	7 or 5	14 or 10	Equal
Intra-abd	4	10	Equal
Gram Neg Bacteremia	7	14	Equal
AECB	≤5	≥7	Equal
Cellulitis	5-6	10	Equal
Osteo	42	84	Equal
Septic Arthritis	14	28	Equal
Neutropenic Fever	AF x 72 h	+ANC > 500	Equal

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Brad Spellberg, UCLA-USC, Twitter

Right Allergies

A reported penicillin allergy is associated with:

- Increase time to antibiotic administration
- Increased breadth of antimicrobials administered
- Increased use of 2nd and 3rd line agents
- Increase morbidity
- Increased mortality
- Increased length of stay
- And…..is usually wrong!

Discussion, questions, comments?