



Update in Hospital Medicine

October 13, 2018

Audrey Corbett, MD

Department of Internal Medicine

University of Oklahoma School of Community Medicine

Tulsa, OK

No Financial Disclosures

Agenda

- ◆ Sepsis
 - ◆ Establish an overview of Sepsis Timeline
 - ◆ Discuss sepsis definitions, guidelines, and reimbursement
 - ◆ Review new evidence
- ◆ Myocardial Infarction
 - ◆ Discuss 2018 Guideline Updates
 - ◆ Review a Chest Pain Protocol
 - ◆ List New MI Definitions
- ◆ Clostridium Difficile
 - ◆ Review 2018 Updated Guidelines
 - ◆ Discuss Eosinopenia Prediction Score

Sepsis

Sepsis Facts

- ◆ **Leading Cause of Death**
- ◆ 1.5 Million Cases
 - ◆ 1 case **every 20 seconds**
- ◆ **20% Mortality**
- ◆ 92% Community Origin



**AT LEAST 250,000 AMERICANS
DIE FROM SEPSIS EACH YEAR.**

EVERYTHING
you need to know about
SEPSIS

**ANYONE CAN GET AN INFECTION,
AND ALMOST ANY INFECTION
CAN LEAD TO SEPSIS.**

**GET AHEAD
OF SEPSIS**



Sepsis - Organizations

- ◆ Surviving Sepsis Campaign

GUIDELINES

Surviving Sepsis
Campaign

- ◆ Sepsis-1, Sepsis-2, Sepsis-3

DEFINITIONS



- ◆ Medicare SEP-1

REIMBURSEMENT



Society of
Critical Care Medicine
The Intensive Care Professionals



A 32 year-old female presented with nausea, vomiting, + epigastric pain radiating to her back.

She drinks **1 pint of liquor daily**.

+Murphy's sign.

She is only oriented to person.

VS: T 38.0C HR 105 RR 32 BP 89/ 50 O2 sat 88% RA

Labs:

Lipase >3x ULN

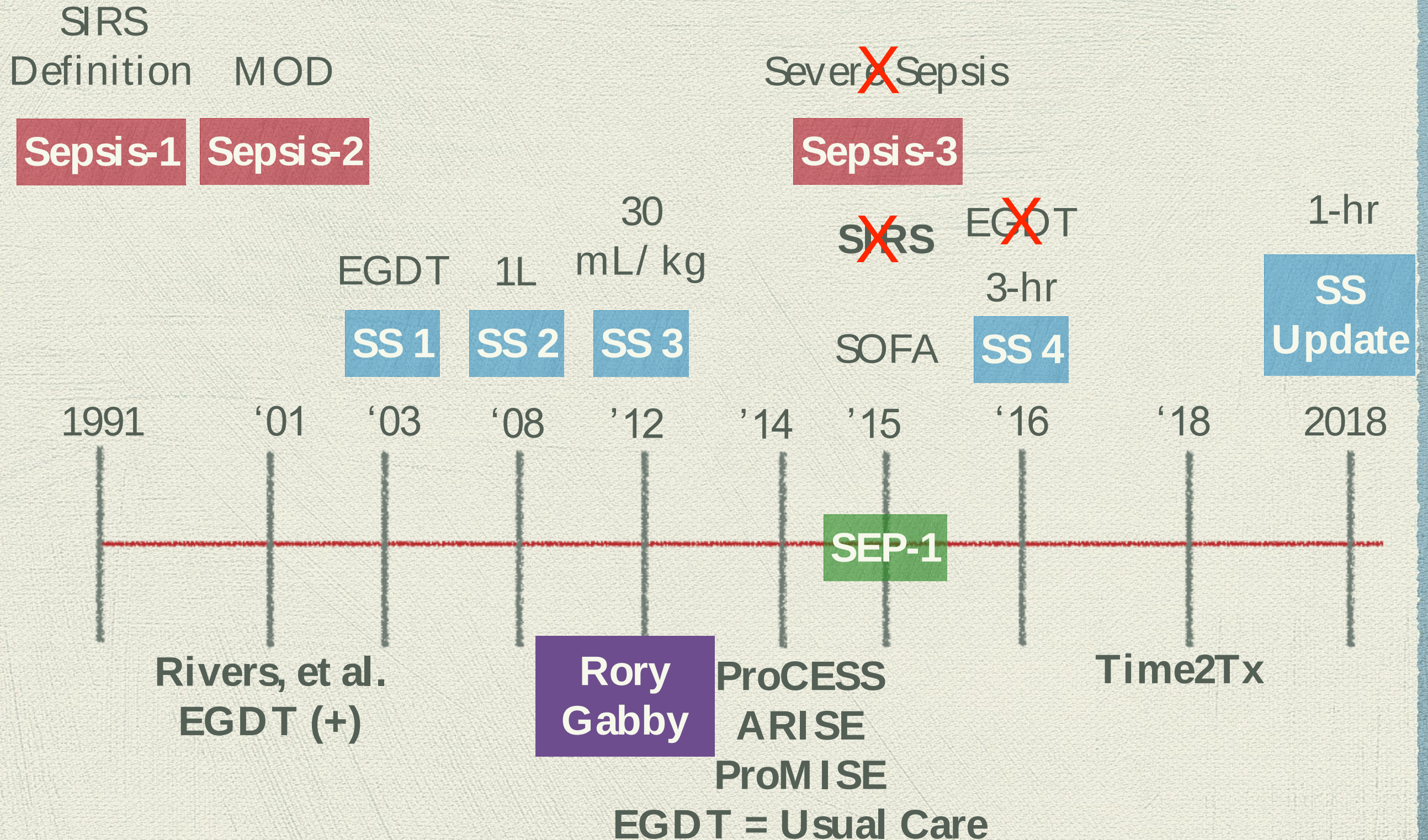
WBC 32,000 + 8% bands

Lactate 2.4 mmol/ L

Cr 1.6 mg/ dL

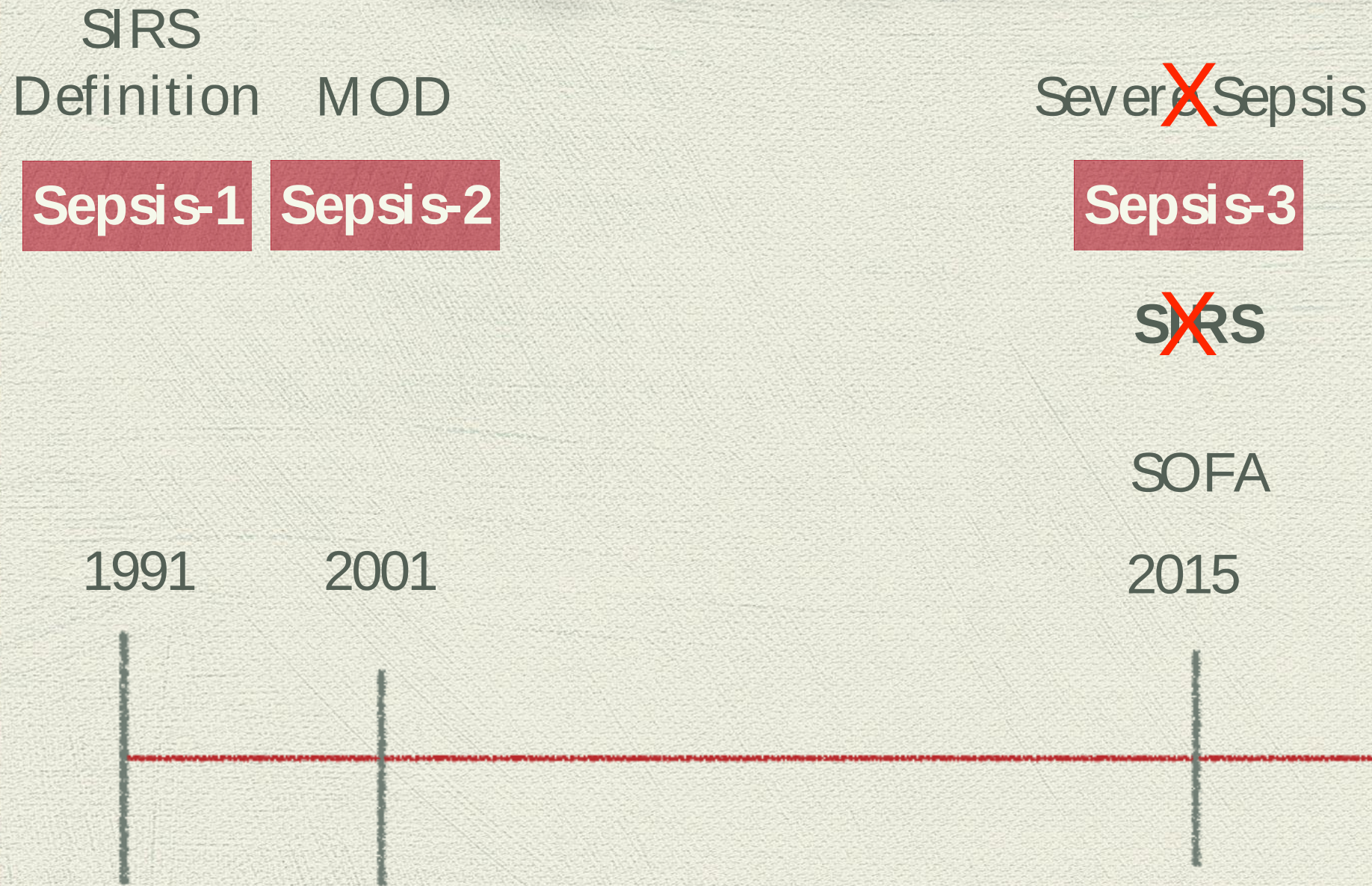
It is **2.5 hours** since triage, **Do you start antibiotics?**

Sepsis Timeline



Sepsis Definition

Sepsis Definitions

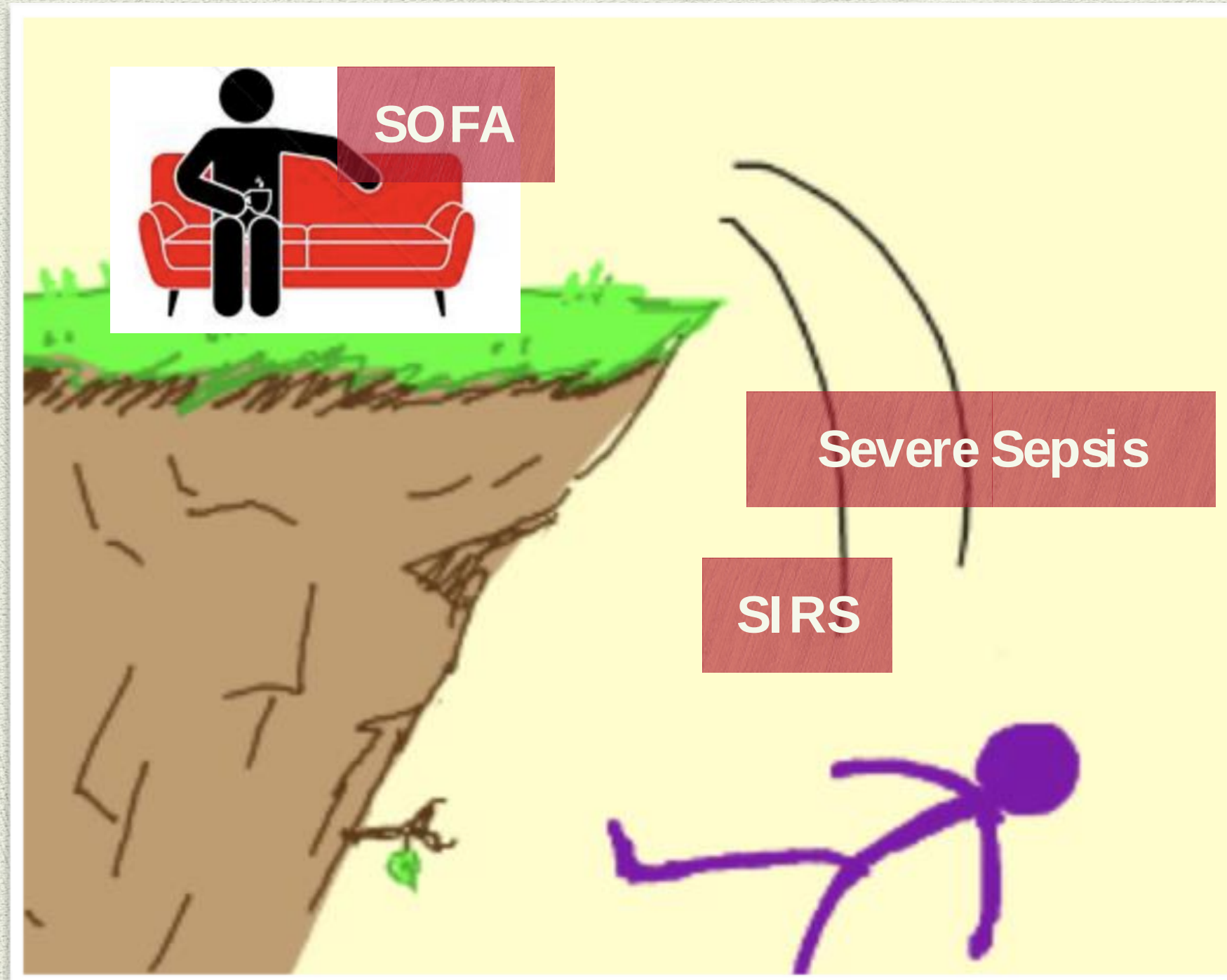


(Rivers, Nguyen et al. 2001)

(Bone, Balk et al. 1992)

2015: Definition

Sepsis-3



Sepsis-3

Sepsis = SEVERE sepsis:

A life threatening **dysfunction** caused by a dysregulated host response to infection.

Organ dysfunction:

SOFA **2 points** increase from baseline

Septic Shock:

Requiring Vasopressors with **Lactate >2 + MAP <65**
Absence of Hypovolemia

(Singer et al. 2016, JAMA)

A 32 year-old female presented with nausea, vomiting, + epigastric pain radiating to her back.

She drinks 1 **pint of liquor daily**.

+Murphy's sign.

She is only oriented to person.

VS: T 38.0C HR 105 RR 32 BP 89/ 50 O2 sat 88% RA

Labs:

Lipase >3x ULN

WBC 32,000 + 8% bands

Lactate 2.4 mmol/ L

Cr 1.6 mg/ dL

SOFA >2 = Sepsis

SIRS = 2/4

qSOFA = 3/3

It is **2.5 hours** since triage, **Do you start antibiotics?**

SIRS vs SOFA vs qSOFA

SIRS/qSOFA = NON-ICU
SOFA = ICU

	Use	Required	Mortality Risk
SIRS	Screen	WBC HR, T, RR	
SOFA	ICU** Mortality	ABG, Tbili, Cr, Plt, BP, GCS	2pts > 10%
qSOFA	Non-ICU** Mortality Screen	GCS, RR, BP	2:/3 Risk X3 3/3: Risk X14

(Singer et al. 2016)

February 2018

REVIEW

Annals of Internal Medicine

Prognostic Accuracy of the Quick Sequential Organ Failure Assessment for Mortality in Patients With Suspected Infection

A Systematic Review and Meta-analysis

Shannon M. Fernando, MD, MSc; Alexandre Tran, MD; Monica Taljaard, PhD; Wei Cheng, PhD; Bram Rochwerf, MD, MSc; Andrew J.E. Seely, MD, PhD; and Jeffrey J. Perry, MD, MSc

	Sensitivity	Specificity
SIRS	88%	26%
qSOFA	61%	72%

qSOFA ICU Specificity = 33%

(Fernando et al. 2018, Ann Intern Med)

Sepsis Guidelines

Sepsis Guidelines

Fluids!
Pressors!
Blood!

EGDT 1L 30
mL/ kg

SS 1 SS 2 SS 3

~~EGDT~~
3-hr
SS 4

1-hr
SS
Update

'01 '03 '08 '12 '14 '16 '17 2018

Rivers, et al.
EGDT (+)

Rory
Gabby

ProCESS
ARISE
ProMISE

Time2Tx

EGDT = Usual Care

THE RORY STAUNTON FOUNDATION

FOR SEPSIS PREVENTION



- ◆ 2013 N Y Law
- ◆ Rory's Regulations
- ◆ Sepsis Measures



<https://rorystauntonfoundationforsepsis.org/>

Gabby's Law



- ◆ 2016 Illinois
- ◆ Gabby's Law
- ◆ Sepsis Measures



<https://www.sepsis.org/faces/gabriella-galbo/>

The Rule of Rescue

“A single death is a **tragedy**, a million deaths is a statistic”

—*J. Stalin*

Who killed more than 17 million of his own Russian people

2017: EBM

Antibiotics vs Fluids

The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

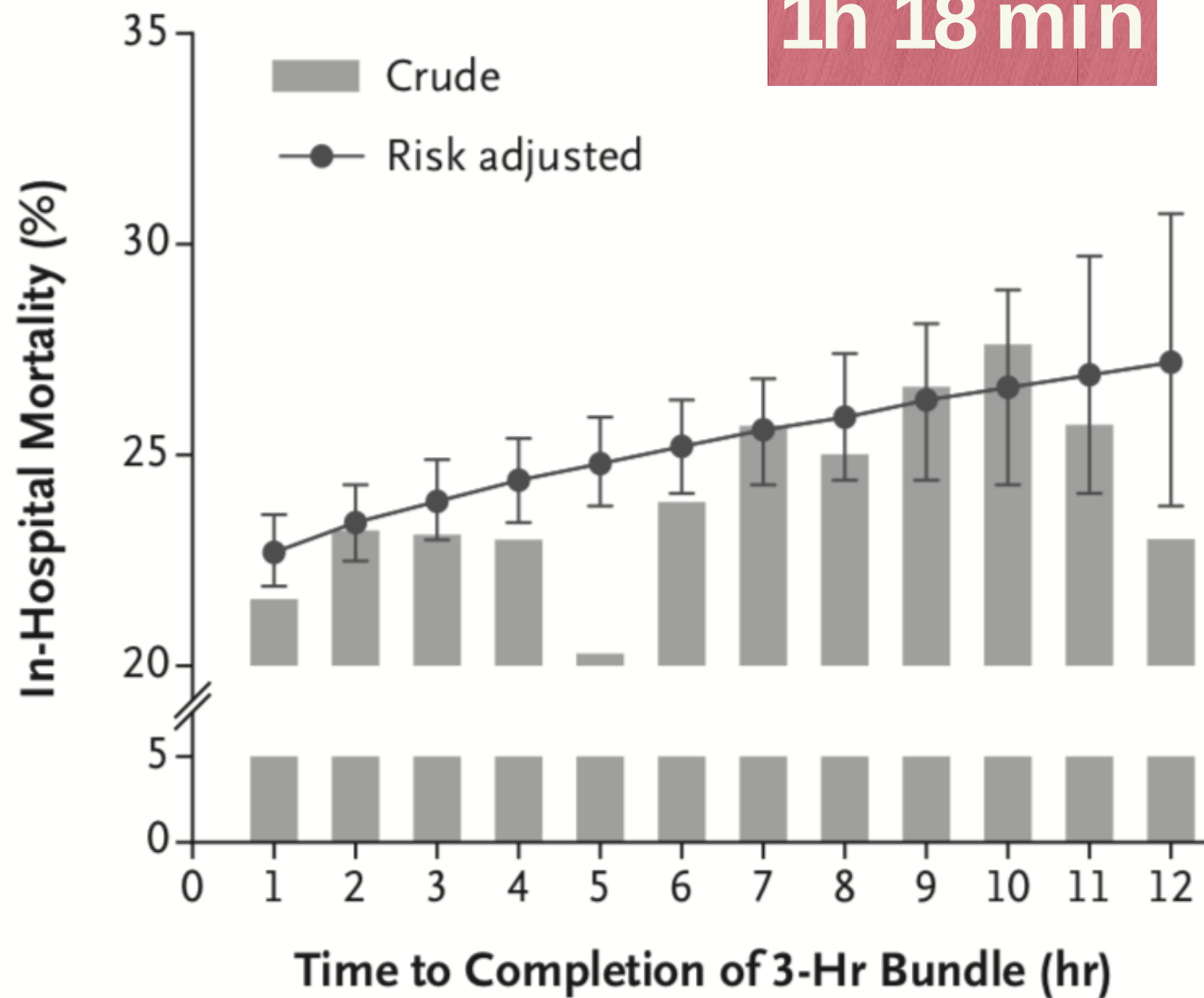
Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

Christopher W. Seymour, M.D., Foster Gesten, M.D., Hallie C. Prescott, M.D.,
Marcus E. Friedrich, M.D., Theodore J. Iwashyna, M.D., Ph.D.,
Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H.,
Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M.D.

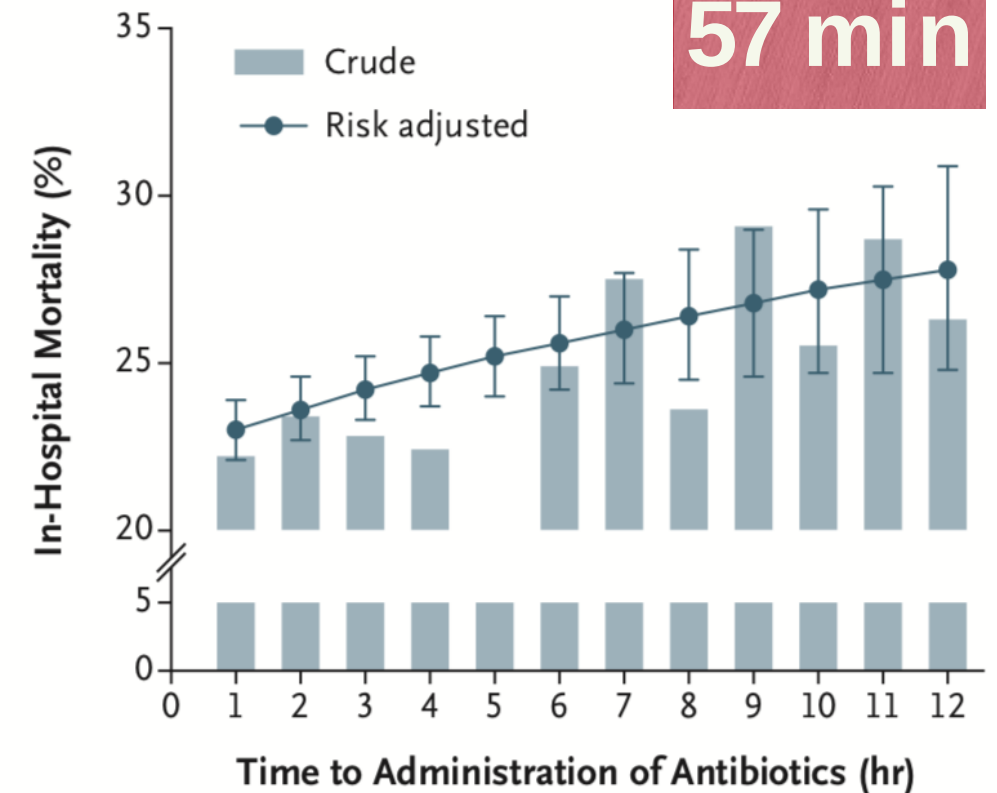
Antibiotics, Antibiotics, Antibiotics!

Mortality increases 14% Antibiotics >3hr

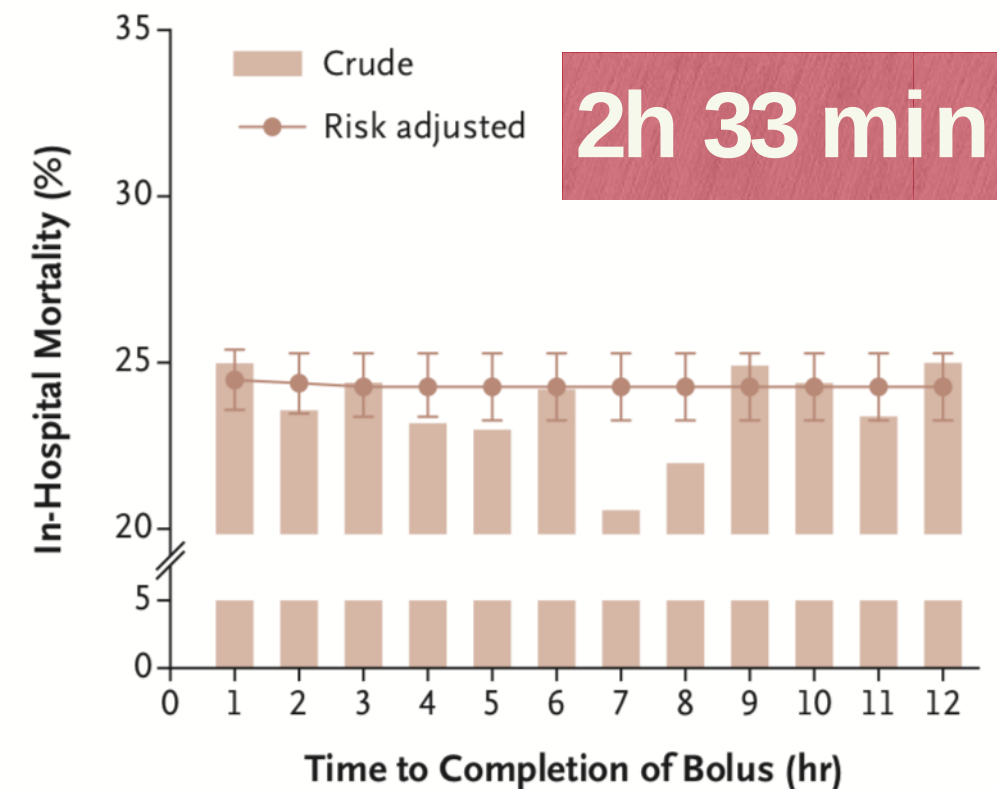
A 3-Hr Bundle



B Administration of Antibiotics



C Initial Bolus of Intravenous Fluids



2018: Guidelines

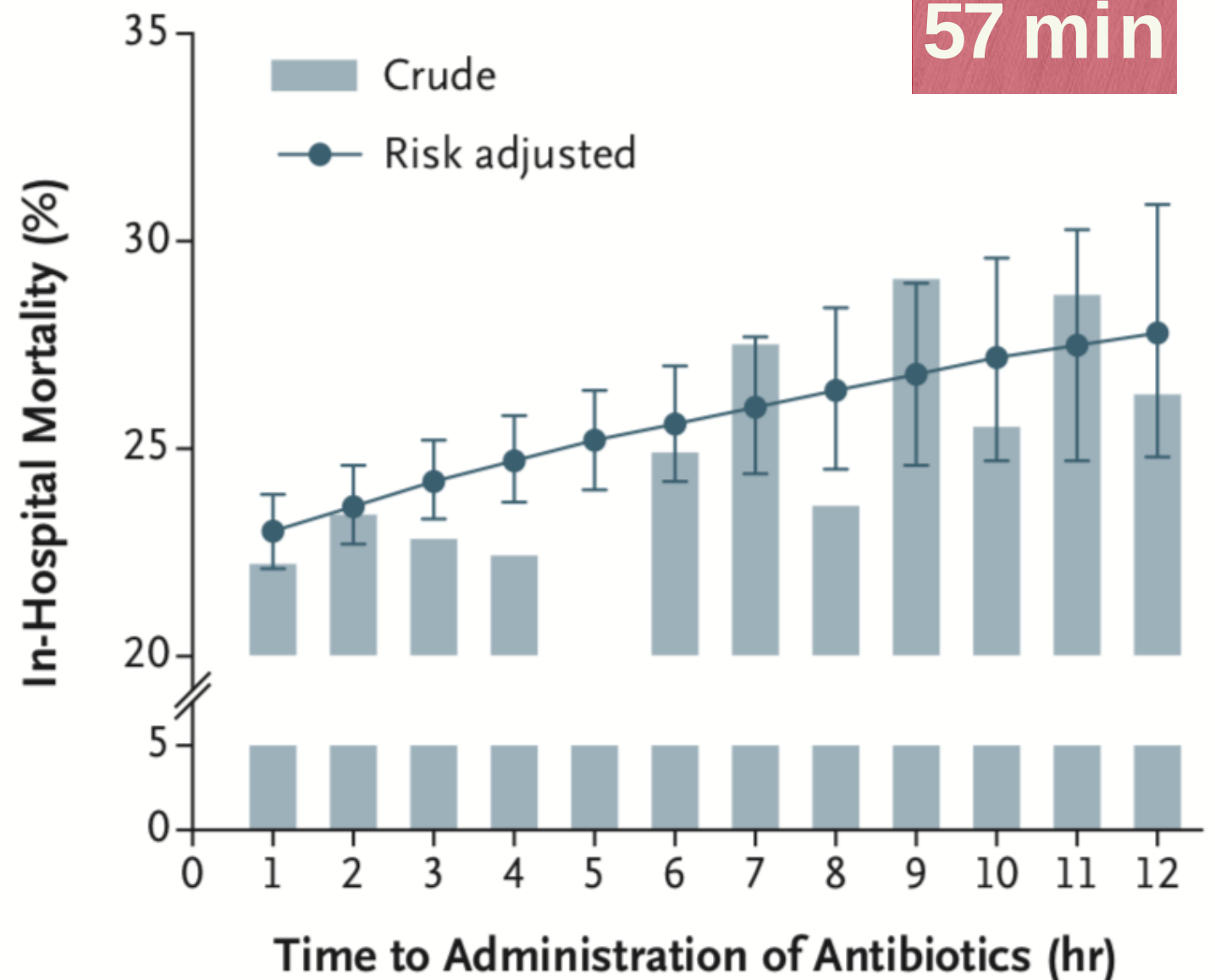
Surviving Sepsis Revision

1 hour bundle



B Administration of Antibiotics

57 min



A 32 year-old female presented with nausea, vomiting, + epigastric pain radiating to her back.

She drinks **1 pint of liquor daily**.

+Murphy's sign.

She is only oriented to person.

VS: T 38.0C HR 105 RR 32 BP 89/ 50 O2 sat 88% RA

Labs:

Lipase >3x ULN
WBC 32,000 + 8% bands
Lactate 2.4 mmol/ L
Cr 1.6 mg/ dL

**Guidelines:
SIRS
1 hour Bundle!**

It is **2.5 hours** since triage, **Do you start antibiotics?**

Sepsis Reimbursement

Sepsis Reimbursement



SEP-1

'15

SEP-1:
Version 5.4

'18

(Pepper et al. 2018, Ann Intern Med)

2015: Medicare SEP-1 Version 5.4 (2018)

3-Hour Bundle

- ◆ Blood Cultures
- ◆ Broad Spectrum Abx
- ◆ 30 mL/kg (hypotension)
 - ◆ Lactate

6-Hour Bundle

- ◆ Remeasure Lactate >2
SHOCK
- 2+ Hypotension - Pressor
- Specific Bedside PE or
 - 2/4 Advanced Interventions

Severe Sepsis

2+ SIRS

- SBP < 90 Or MAP < 70
 - Plt < 100K
- Cr > 2 OR UOP < 0.5
 - Tbili > 2
 - Lactate > 2
- INR > 1.5 or aPTT > 60s

Value Based Purchasing

2018 = 2% Medicare Reimbursement

Medicare Value Programs

CMS Hospital Value Programs

Hospital Value Based Purchasing

Rewards hospitals for improving the quality of care by redistributing payment among hospitals with higher quality performance than lower performing hospitals

Readmission Reduction Program

Hospitals with excess readmissions receive a negative payment adjustment

Hospital Acquired Conditions

Hospitals that rank in the worst performing quartile based on quality metrics receive a negative payment adjustment

Promoting Interoperability

Electronic quality measures
Pay for reporting

2% Medicare Reimbursement

Affordable Care Act (ACA)

Fiscal Year	Value Based Purchasing Program	Hospital Readmission Reduction Program*	Hospital Acquired Conditions Program*	Overall Potential Payment Reduction Risk
2013	1%	1%	N/A	2%
2014	1.25%	2%	N/A	3.25%
2015	1.50%	3%	1%	5.50%
2016	1.75%	3%	1%	5.75%
2017	2%	3%	1%	6%
2018	2%	3%	1%	6%

*Potential Reduction in Payment by Fiscal Year

A 32 year-old female presented with nausea, vomiting, + epigastric pain radiating to her back.

She drinks 1 **pint of liquor daily**.

+Murphy's sign.

She is only oriented to person.

VS: T 38.0C HR 105 RR 32 BP 89/ 50 O2 sat 88% RA

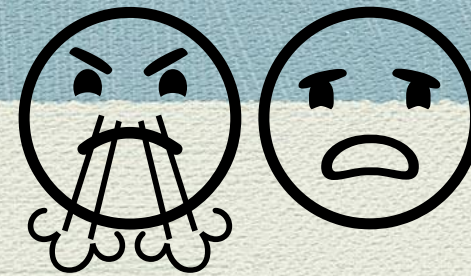
Labs:

Lipase >3x ULN
WBC 32,000 + 8% bands
Lactate 2.4 mmol/ L
Cr 1.6 mg/ dL

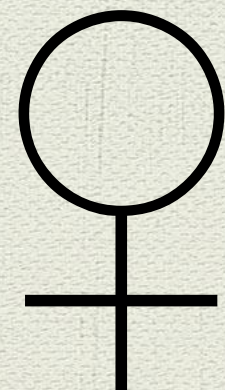
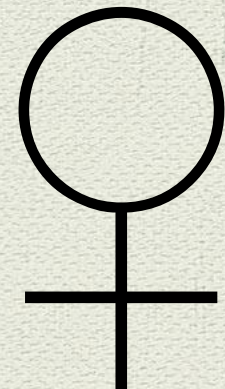
Yes!
3 hr bundle
Documentation:
SIRS
Severe Sepsis

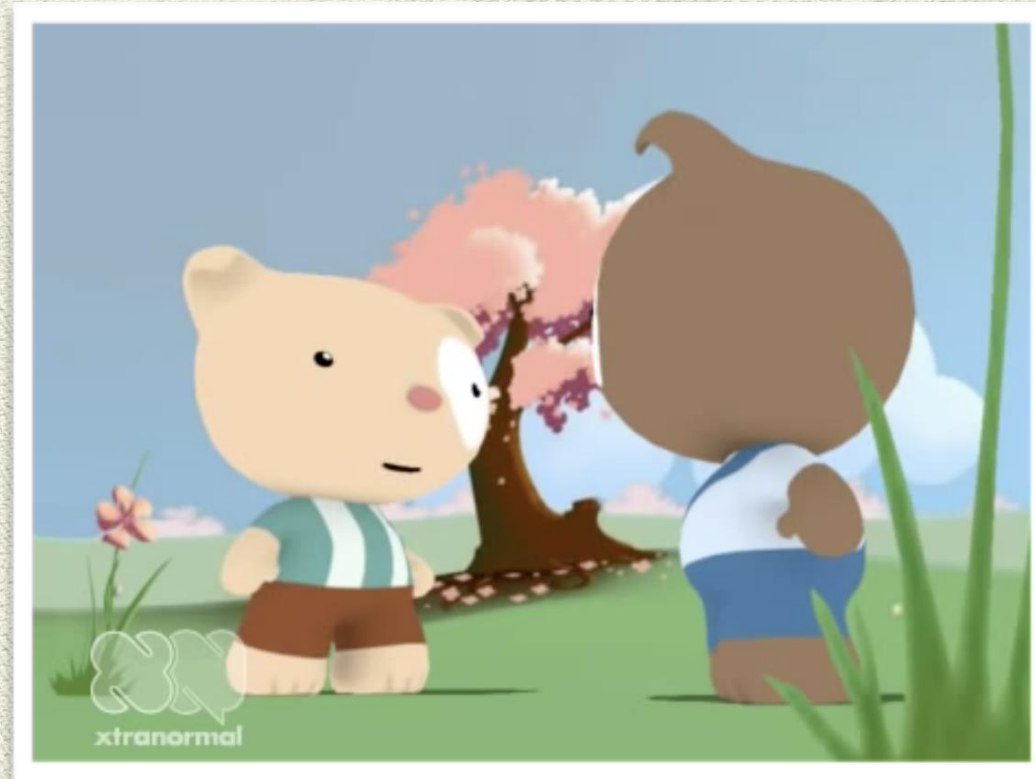
It is **2.5 hours** since triage, **Do you start antibiotics?**

What do we do?



- Evidence Based Medicine
- Hospital Reimbursement
- Patient Outcomes
- Mix?





Students, How do you know you are on a
surgery or medicine rotation?

– *Fluid Selection*

SALT-ED: March 2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Noncritically Ill Adults

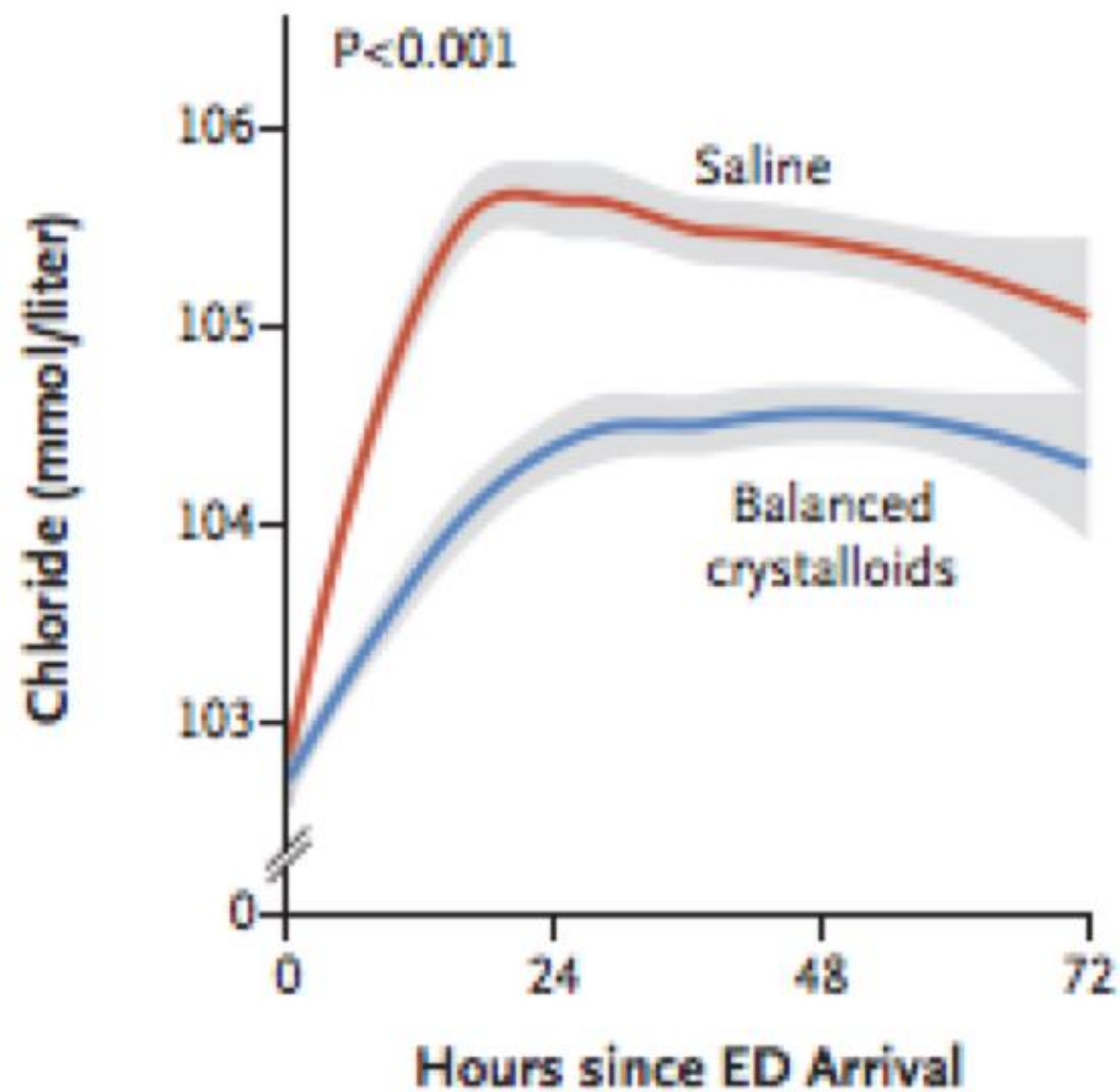
Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D.,
Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S.,
Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D.,
Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D.,
Andrew D. Shaw, M.B., Gordon R. Bernard, M.D.,
and Todd W. Rice, M.D., for the SALT-ED Investigators*

Fluid Components

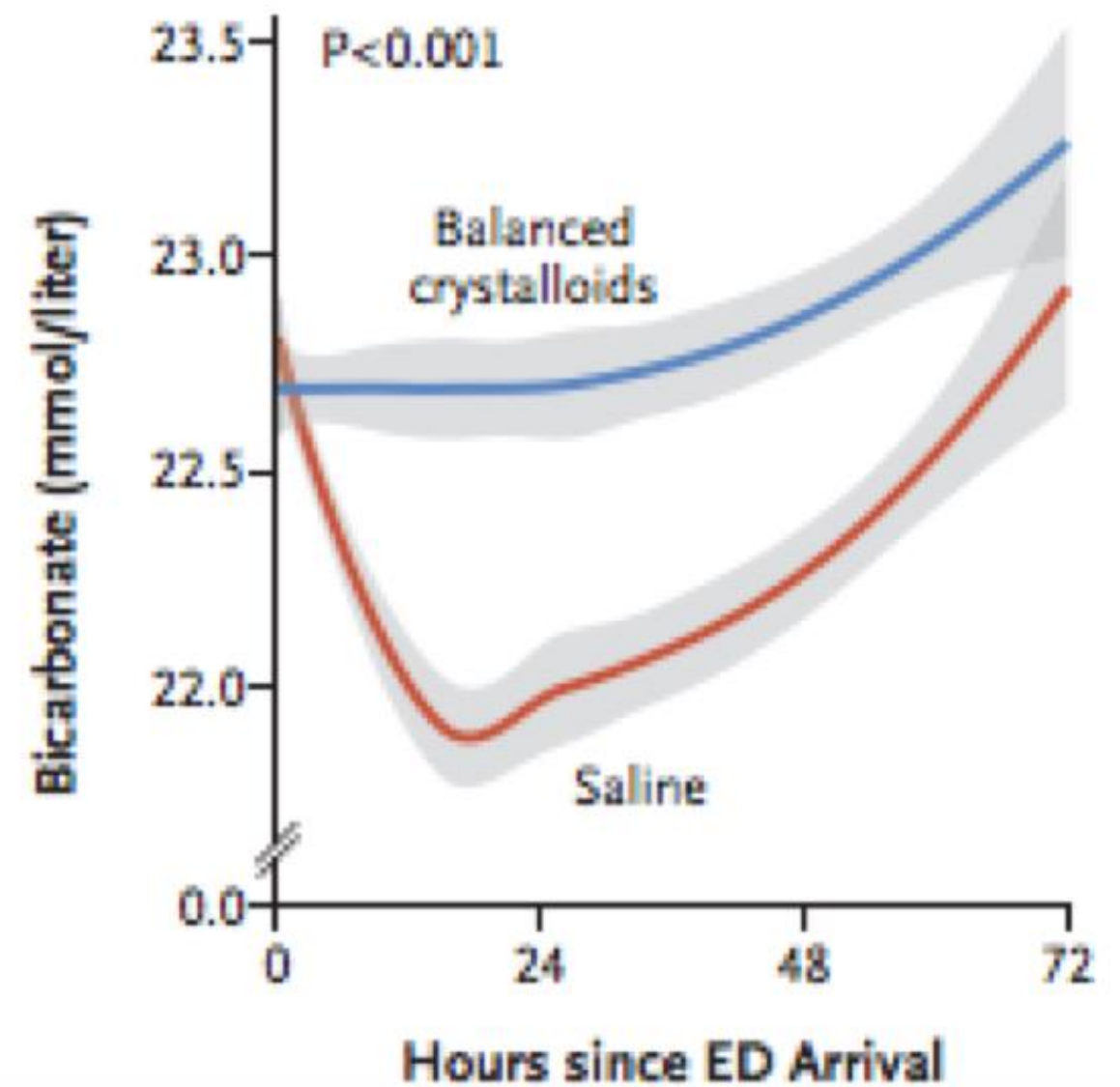
	Normal Saline	LR	Plasma-Lyte
Na ⁺	154	130	140
K ⁺	0	4	5
Ca ²⁺	0	3	0
Mg ²⁺	0	0	3
Cl ⁻	154	109	98
Lactate	0	28	0
Osmolarity	308	275	294
pH	5.5	6.75	7.4

SALT-ED

B Chloride



E Bicarbonate



SALT-ED

	NS	Balanced	P value
Hospital Free Days	25	25	0.41
MAKE-30	5.6%	4.7%	0.01
AKI (>Stage II)	8.6%	8.0%	0.14
In Hospital Death	1.6%	1.4%	0.36

MAKE-30: Major Adverse Kidney Event in 30 days

Death, Renal Replacement, 2x Cr @Discharge

NNT = 111

CONFOUNDING, Single Center

2017: Vitamin C and Sepsis

CITRIS-ALI: Phase 2

- Single Center, unblinded
- MICU + Severe sepsis/ Septic shock + Procalcitonin >2
- IV vitamin C 6g, thiamine, Hydrocortisone 50 q6

41% vs 9% (intervention)

(Marik et al. 2017, CHEST)

Sepsis Review

- ◆ Timely Antibiotics!
- ◆ Consider LR
- ◆ Still Document Severe Sepsis \$\$\$
- ◆ Do not use qSOFA in the ICU

Chest Pain

Updates

- ◆ Last Updates
 - ◆ STEMI 2015
 - ◆ NSTEMI 2014
 - ◆ DAPT 2016
- ◆ Discuss new chest pain scores
- ◆ Review Imaging vs Standard Care
- ◆ List new MI definition

Chest Pain Facts

- 6% of all ED visits
 - \$14 Billion
- 75% Noncardiac
 - <20% ACS
- Missed ACS largest ED malpractice
 - 2-8% misdiagnosed/ discharged



A 55 year-old female with no PMH presented to the ED with substernal chest pain at rest.

Worse with exertion, better with nitroglycerin.
Non reproducible, No radiation, No diaphoresis
Worse with Inspiration

High sensitivity troponin negative at 0h + 6h

EKG No changes

BMI 40

What prediction scores?

CENTRAL ILLUSTRATION: Performance of the EDACS Versus Modified HEART Score Among Emergency Department Patients With Chest Pain



EDACS & mHEART perform similarly in terms of NPV

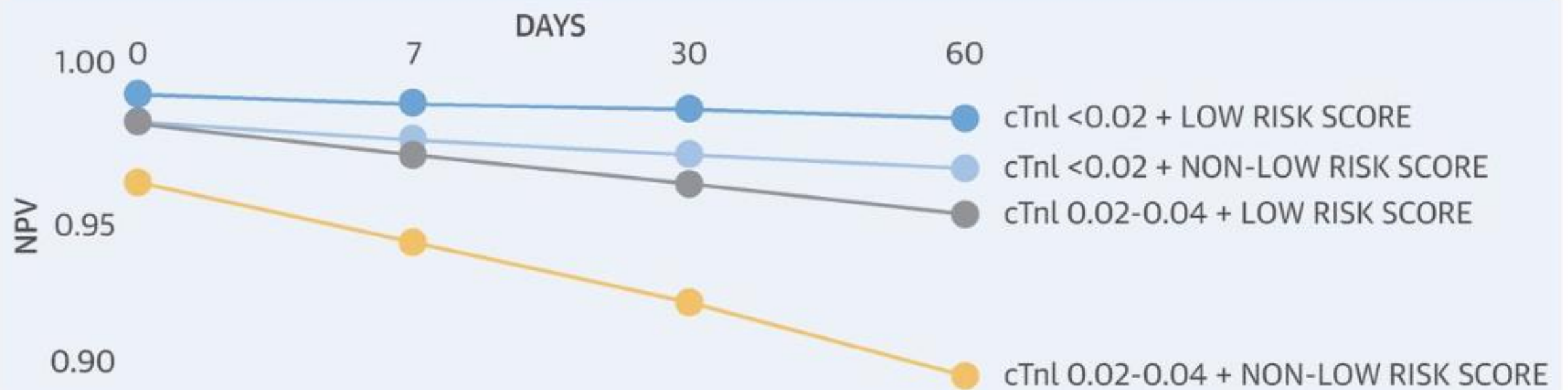


EDACS



mHEART

EDACS categorizes more patients as low risk



Lower troponin cut-off to define low risk is superior

(Mark et al. 2018, JACC)

A 55 year-old female with no PMH presented to the ED with substernal chest pain at rest.

Worse with exertion, better with nitroglycerin.
Non reproducible, No radiation, No diaphoresis
Worse with Inspiration

High sensitivity troponin negative at 0h + 6h

EKG No changes

BMI 40

What prediction scores?

HEART = 4
Intermediate

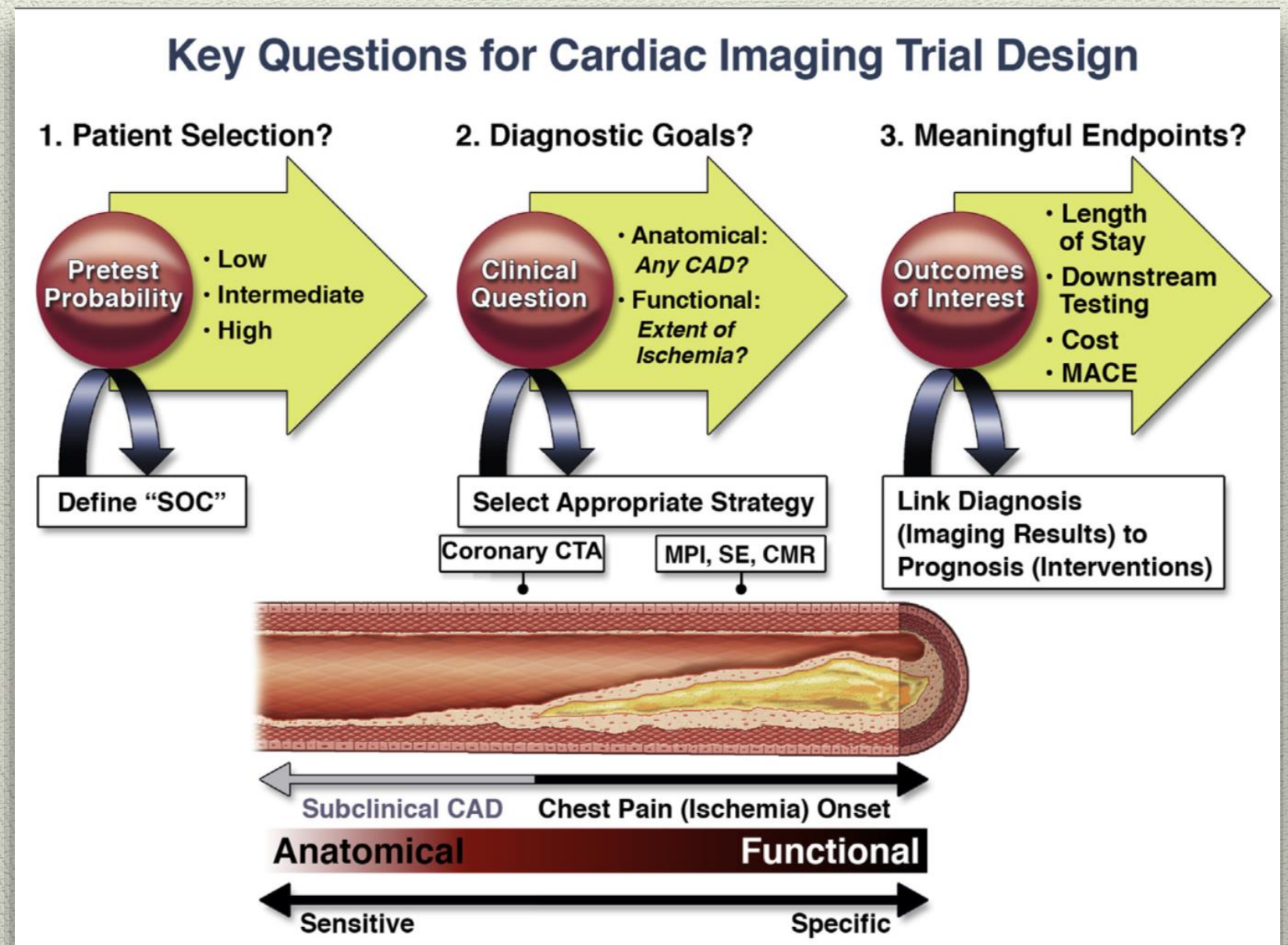
ED ACS = 2
Low

Out with the Old: Coronary CTA

No Difference

\$300 Less

54% Reduction in
time to diagnosis

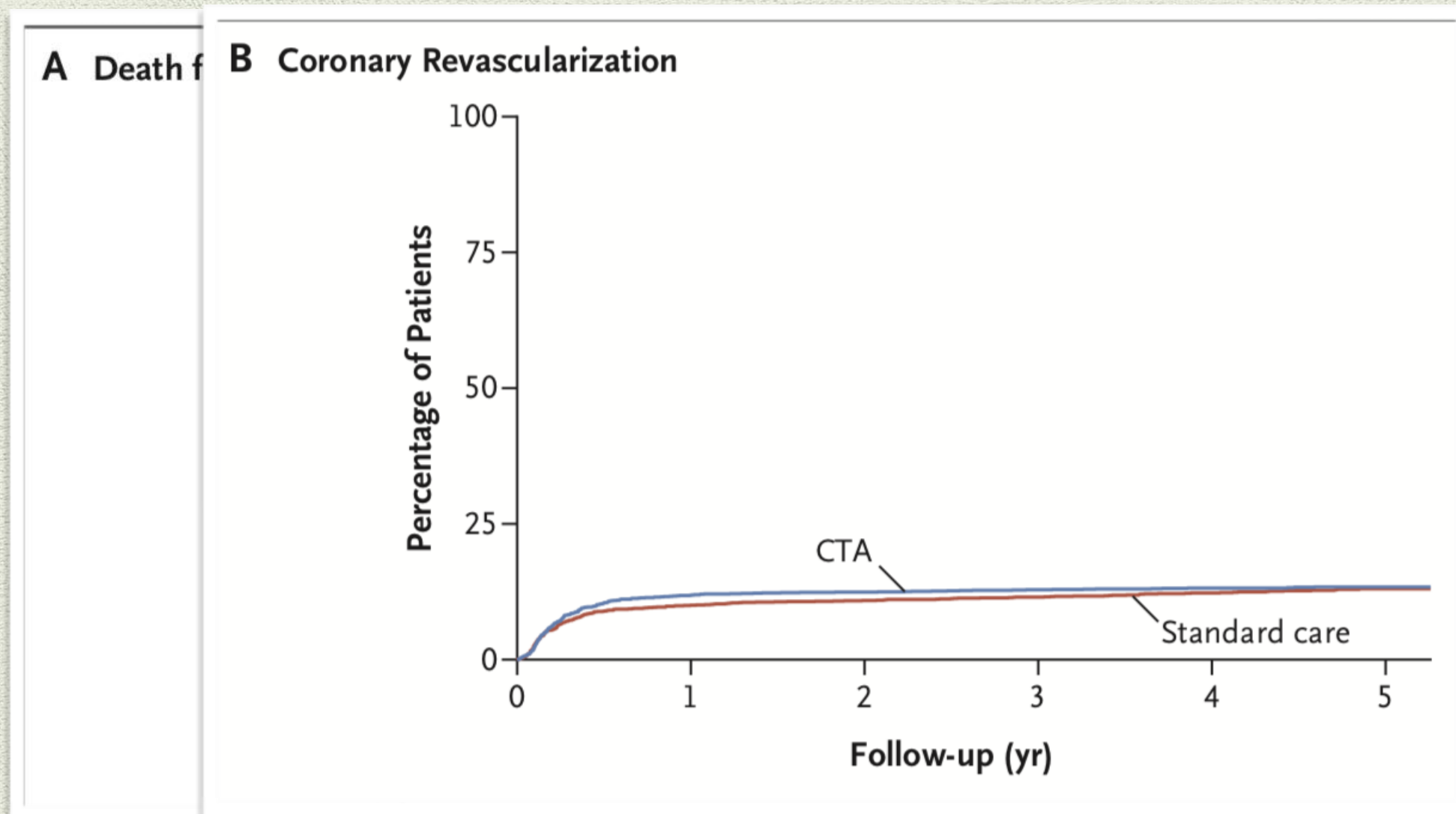


(Bhatt et al. 2017, JACC)

August 2018: Cardiac Imaging

A SCOT-HART Trial - 5 years

- CTA vs Standard Care for **Stable Chest Pain**



(Newby et al. 2018, NEJM)

September 2018: CTA vs Stress Echo

No history of CAD
Negative Troponin
Resolution of chest pain

	CTA	Stress Echo	P value
Hospitalization	19%	11%	0.026
LOS	58h	34h	0.002

No difference in outcomes

(Levsky et al. 2018, JACC)

December 2017: Shared Decision Making

Shared Decision Making or Usual Care CTA or Stress

- No significant difference:
 - # ED visits
 - Imaging studies
 - Procedures
- SDM = 125.6 fewer tests/ 100 patients

(Shaffer et al. 2017)

A 55 year-old female with no PMH presented to the ED with
substernal chest pain at rest.

Worse with exertion, better with nitroglycerin.
Non reproducible, No radiation, No diaphoresis
Worse with Inspiration

High sensitivity troponin negative at 0h + 6h

EKG No changes

BMI 40

Positive at 12 hours

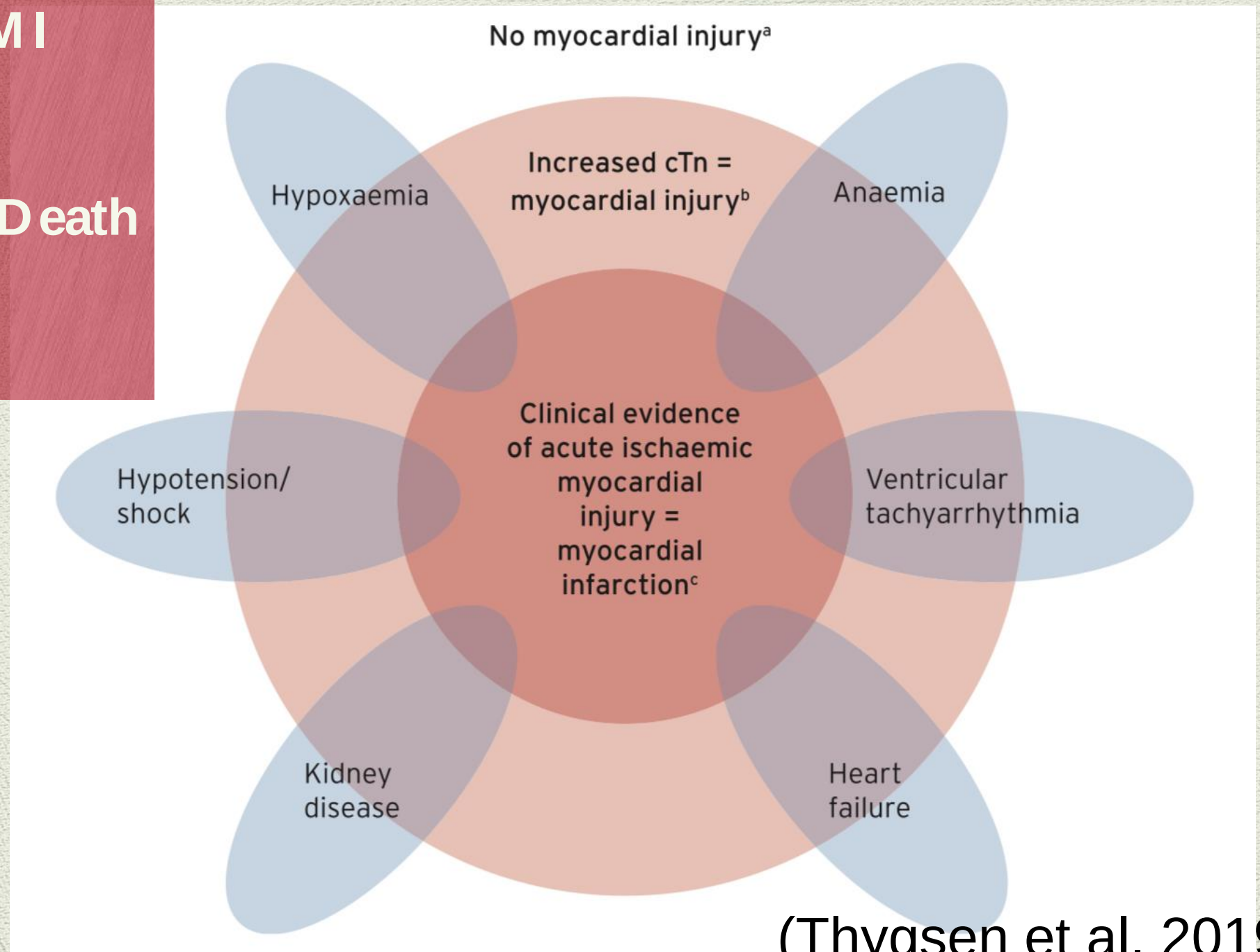
BP 212/115

Is this an Type II NSTEMI?

August 2018: 4th Universal MI Definition Revision

5 TYPES NSTEMI

1. Ischemic
2. Demand
3. Sudden Cardiac Death
4. PCI
5. CABG



(Thygsen et al. 2019)

Criteria for type 2 MI

Detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL, and evidence of an imbalance between myocardial oxygen supply and demand unrelated to coronary thrombosis, requiring at least one of the following:

- Symptoms of acute myocardial ischaemia;
- New ischaemic ECG changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology.

A 55 year-old female with no PMH presented to the ED with substernal chest pain at rest.

Worse with exertion, better with nitroglycerin.
Non reproducible, No radiation, No diaphoresis
Worse with Inspiration

High sensitivity troponin negative at 0h + 6h

EKG No changes

BMI 40

Positive at 12 hours

BP 212/115

Is this an Type II NSTEMI?

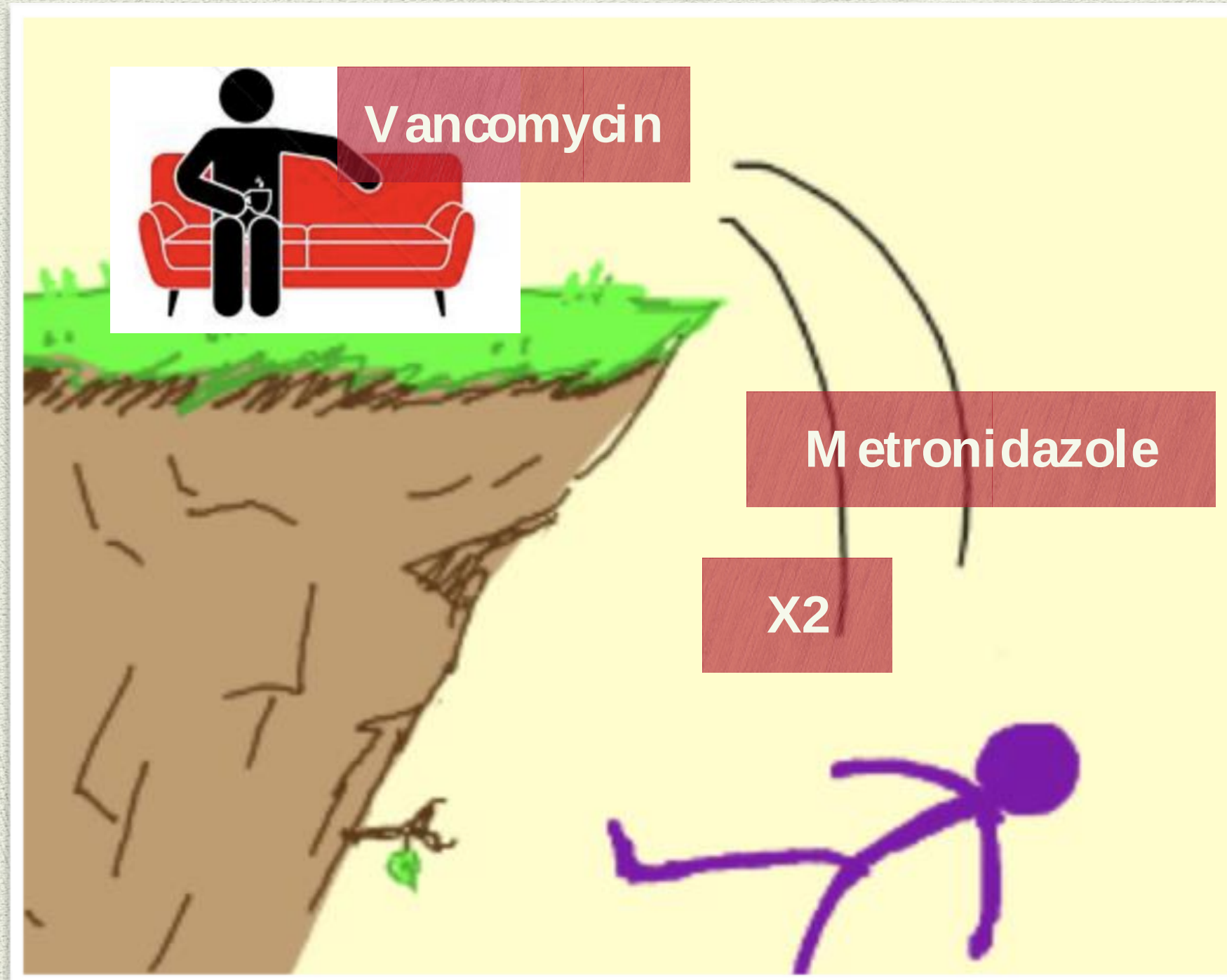
YES: SYMPTOMS

Chest Pain Review

- Could consider **EDACS** if HEART intermediate
- Still on the fence about Coronary CTA rule out
- Type II NSTEMI now has **new criteria!**

Clostridium Difficile

2018 C. Diff Guidelines



IDSA 2017 Update

	Treatment
Non Severe Initial	Vanc 125 po QID x 10 FDX 200 po BID x10
Severe Initial	Same
Fulminant Initial	Vanc 500 po QID (Consider Rectal) + Flagyl IV
1st Recurrence	Vanc taper 2-8 weeks FDX (if van 1st)
2nd Recurrence	Vanc Taper FDX Fecal Transplant

Severe:
WBC >15,000 OR Serum Cr
>1.5

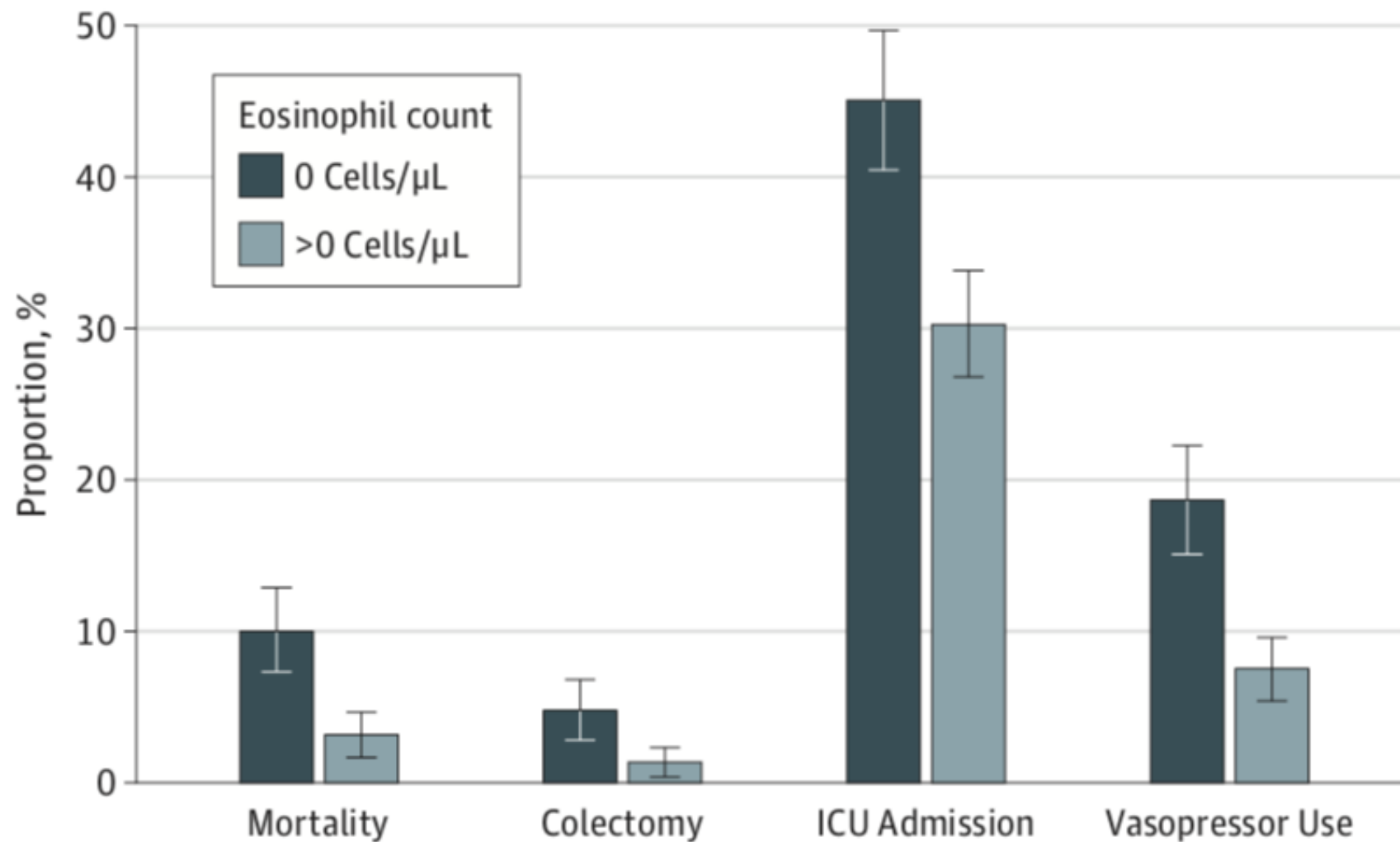
Fulminant:
Hypotension, Shock, Ileus,
or Megacolon

(McDonald et al. 2018, IDSA Guideline)

2018: Eosinophil Prediction

WBC >15K had no significance

Figure. Comparisons of Primary and Secondary Outcomes Between the Eosinophil Count Groups



(Kulaylet et al. 2018, JAMA Surgery)

PatientlyWaiting.....

Community Acquired Pneumonia

Questions?

Credits

- Bhatt, D. L., & Taqueti, V. R. (2017). Out With the Old Rule-Out: Raising the Bar for Acute Chest Pain Evaluation With Randomized Trials of Cardiac Imaging. *JACC Cardiovasc Imaging*, 10(3), 350-353. doi:10.1016/j.jcmg.2016.12.008
- Bone, R. C., Balk, R. A., Cerra, F. B., Dellinger, R. P., Fein, A. M., Knaus, W. A., . . . Sibbald, W. J. (1992). Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest*, 101(6), 1644-1655.
- Dellinger, R. P., Carlet, J. M., Masur, H., Gerlach, H., Calandra, T., Cohen, J., . . . Levy, M. M. (2004). Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Intensive Care Med*, 30(4), 536-555. doi:10.1007/s00134-004-2210-z
- Dellinger, R. P., Levy, M. M., Carlet, J. M., Bion, J., Parker, M. M., Jaeschke, R., . . . Critical Care, M. (2008). Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med*, 36(1), 296-327. doi:10.1097/01.CCM.0000298158.12101.41
- Dellinger, R. P., Levy, M. M., Rhodes, A., Annane, D., Gerlach, H., Opal, S. M., . . . Surviving Sepsis Campaign Guidelines Committee including The Pediatric, S. (2013). Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*, 39(2), 165-228. doi:10.1007/s00134-012-2769-8
- Fernando, S. M., Tran, A., Taljaard, M., Cheng, W., & Perry, J. J. (2018). Prognostic Accuracy of the Quick Sequential Organ Failure Assessment for Mortality in Patients With Suspected Infection. *Ann Intern Med*, 169(4), 264-265. doi:10.7326/L18-0291

Credits

- Ferrer, R., Martin-Loeches, I., Phillips, G., Osborn, T. M., Townsend, S., Dellinger, R. P., . . . Levy, M. M. (2014). Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. *Crit Care Med*, 42(8), 1749-1755. doi:10.1097/CCM.0000000000000330
- Investigators, A., Group, A. C. T., Peake, S. L., Delaney, A., Bailey, M., Bellomo, R., . . . Williams, P. (2014). Goal-directed resuscitation for patients with early septic shock. *N Engl J Med*, 371(16), 1496-1506. doi:10.1056/NEJMoa1404380
- Investigators, S.-H., Newby, D. E., Adamson, P. D., Berry, C., Boon, N. A., Dweck, M. R., . . . Williams, M. C. (2018). Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. *N Engl J Med*, 379(10), 924-933. doi:10.1056/NEJMoa1805971
- Kulaylat, A. S., Buonomo, E. L., Scully, K. W., Hollenbeak, C. S., Cook, H., Petri, W. A., Jr., & Stewart, D. B., Sr. (2018). Development and Validation of a Prediction Model for Mortality and Adverse Outcomes Among Patients With Peripheral Eosinopenia on Admission for Clostridium difficile Infection. *JAMA Surg*. doi:10.1001/jamasurg.2018.3174
- Kumar, A., Roberts, D., Wood, K. E., Light, B., Parrillo, J. E., Sharma, S., . . . Cheang, M. (2006). Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*, 34(6), 1589-1596. doi:10.1097/01.CCM.0000217961.75225.E9
- Levsky, J. M., Haramati, L. B., Spevack, D. M., Menegus, M. A., Chen, T., Mizrachi, S., . . . Garcia, M. J. (2018). Coronary Computed Tomography Angiography Versus Stress Echocardiography in Acute Chest Pain: A Randomized Controlled Trial. *JACC Cardiovasc Imaging*, 11(9), 1288-1297. doi:10.1016/j.jcmg.2018.03.024

Credits

- Levy, M. M., Fink, M. P., Marshall, J. C., Abraham, E., Angus, D., Cook, D., . . .
Sccm/Esicm/Accp/Ats/Sis. (2003). 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis
Definitions Conference. *Crit Care Med*, 31(4), 1250-1256.
doi:10.1097/01.CCM.0000050454.01978.3B
- Marik, P. E., Khangoora, V., Rivera, R., Hooper, M. H., & Catravas, J. (2017). Hydrocortisone,
Vitamin C, and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A
Retrospective Before-After Study. *Chest*, 151(6), 1229-1238. doi:10.1016/j.chest.2016.11.036
- Mark, D. G., Huang, J., Chettipally, U., Kene, M. V., Anderson, M. L., Hess, E. P., . . . Kaiser
Permanente, C. N. I. (2018). Performance of Coronary Risk Scores Among Patients With
Chest Pain in the Emergency Department. *J Am Coll Cardiol*, 71(6), 606-616.
doi:10.1016/j.jacc.2017.11.064
- Marshall, J. C., Cook, D. J., Christou, N. V., Bernard, G. R., Sprung, C. L., & Sibbald, W. J.
(1995). Multiple Organ Dysfunction Score: A reliable descriptor of a complex clinical outcome.
Critical Care Medicine, 23(10), 1638-1652. doi:10.1097/00003246-199510000-00007
- Mouncey, P. R., Osborn, T. M., Power, G. S., Harrison, D. A., Sadique, M. Z., Grieve, R. D., . . .
Pro, M. T. I. (2015). Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med*,
372(14), 1301-1311. doi:10.1056/NEJMoa1500896
- Pepper, D. J., Jaswal, D., Sun, J., Welsh, J., Natanson, C., & Eichacker, P. Q. (2018). Evidence
Underpinning the Centers for Medicare & Medicaid Services' Severe Sepsis and Septic Shock
Management Bundle (SEP-1): A Systematic Review. *Ann Intern Med*, 168(8), 558-568.
doi:10.7326/M17-2947

Credits

- Pro, C. I., Yealy, D. M., Kellum, J. A., Huang, D. T., Barnato, A. E., Weissfeld, L. A., . . . Angus, D. C. (2014). A randomized trial of protocol-based care for early septic shock. *N Engl J Med*, 370(18), 1683-1693. doi:10.1056/NEJMoa1401602
- Rhodes, A., Evans, L. E., Alhazzani, W., Levy, M. M., Antonelli, M., Ferrer, R., . . . Dellinger, R. P. (2017). Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Med*, 43(3), 304-377. doi:10.1007/s00134-017-4683-6
- Rivers, E., Nguyen, B., Havstad, S., Ressler, J., Muzzin, A., Knoblich, B., . . . Early Goal-Directed Therapy Collaborative, G. (2001). Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*, 345(19), 1368-1377. doi:10.1056/NEJMoa010307
- Salim Rezaie, M. (2018). Petition to Retire the Surviving Sepsis Campaign Guidelines. *R.E.B.E.L. EM*.
- Schaffer, J. T., Hess, E. P., Hollander, J. E., Kline, J. A., Torres, C. A., Diercks, D. B., . . . Shah, N. D. (2018). Impact of a Shared Decision Making Intervention on Health Care Utilization: A Secondary Analysis of the Chest Pain Choice Multicenter Randomized Trial. *Acad Emerg Med*, 25(3), 293-300. doi:10.1111/acem.13355
- Self, W. H., Semler, M. W., Wanderer, J. P., Wang, L., Byrne, D. W., Collins, S. P., . . . Investigators, S.-E. (2018). Balanced Crystalloids versus Saline in Noncritically Ill Adults. *N Engl J Med*, 378(9), 819-828. doi:10.1056/NEJMoa1711586
- Seymour, C. W., Gesten, F., Prescott, H. C., Friedrich, M. E., Iwashyna, T. J., Phillips, G. S., . . . Levy, M. M. (2017). Time to Treatment and Mortality during Mandated Emergency Care for Sepsis. *N Engl J Med*, 376(23), 2235-2244. doi:10.1056/NEJMoa1703058
- Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., . . . Angus, D. C. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, 315(8), 801-810. doi:10.1001/jama.2016.0287
- Surviving Sepsis Campaign. Retrieved from <http://www.survivingsepsis.org/Guidelines/Pages/default.aspx>
- Thygesen, K., Alpert, J. S., Jaffe, A. S., Chaitman, B. R., Bax, J. J., Morrow, D. A., . . . Group, E. S. C. S. D. (2018). Fourth universal definition of myocardial infarction (2018). *Eur Heart J*. doi:10.1093/eurheartj/ehy462