Brigham and Women's Hospital
Founding Member, Mass General Brigham

Pneumonia in Hospitalized Patients

Intensive Review of Internal Medicine

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Disclosures

- Grant funding
  - Centers for Disease Control and Prevention
  - Agency for Healthcare Research and Quality
  - Massachusetts Department of Public Health

- Royalties
  - UpToDate for chapters on pneumonia

Objectives

- How accurate are clinical signs for pneumonia?
- Is pneumonia in hospitalized patients viral or bacterial?
- What kind of imaging should we get?
- Is there a role for procalcitonin?
- Do we need to get cultures?
- What should we treat with?
- Do we need to give antibiotics if viral tests are positive?
- Should we give steroids?
- How long should we treat for?

American Journal of Respiratory and Critical Care Medicine

Diagnosis and Management of Community-acquired Pneumonia. An Official American Thoracic Society Clinical Practice Guideline

Barbara E. Jones ; Julio A. Ramirez , Eyal Oren , Nilam J Soni ; Liam R Sullivan , Marcos I. Restrepo , Daniel M Musher , Brian L. Erstad , Chiagozie Pickens , Valerie M Vaughn , Scott A Helgeson , Kristina Crothers , Joshua P. Metlay , Brittany D. Bissell Turpin , Bin Cao , James D. Chalmers , Charles S. Dela Cruz , Inessa Gendlina , Leila S Hojat , Maryrose Laguio-Vila , Stephen Y Liang , Grant W Waterer , Marilynn Paine , Conall Hawkins , and Kevin Wilson ; ... Show less

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Abstract PDF

Abstract

Background: Understanding of the diagnosis and treatment of adults with community-acquired pneumonia (CAP) has evolved thanks to new evidence, experience, and emerging technologies. This document updates evidence-based clinical practice guidelines on four key questions for the diagnosis and management of adult patients with CAP. Methods: A multidisciplinary panel integrated systematic reviews of comparative evidence with other relevant research and clinical experience, then applied Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology to produce recommendations using the Evidence to Decision Framework. Results: The panel formulated clinical recommendations that address questions related to CAP, including lung ultrasound for diagnosis, empiric antibacterial therapy if a test for a respiratory virus is positive, antibiotic duration, and the use of systemic corticosteroids. Conclusions: The panel formulated and provided the rationale for recommendations on selected diagnostic and treatment strategies for adult patients with CAP.

Keywords: pneumonia; lower respiratory tract infection; practice guidelines; guideline update

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Covers just 4 questions:

1. **Is lung ultrasound an acceptable alternative to chest x-ray?**
2. **Do patients with CAP who test positive for a respiratory virus require antibacterials?**
3. **Can patients with CAP be treated with <5 days of antibiotics?**
4. **Should patients with CAP receive corticosteroids?**

AMERICAN THORACIC SOCIETY DOCUMENTS

Published 2019

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Joshua P. Metlay*, Grant W. Waterer*, Ann C. Long, Antonio Anzueto, Jan Brozek, Kristina Crothers, Laura A. Cooley, Nathan C. Dean, Michael J. Fine, Scott A. Flanders, Marie R. Griffin, Mark L. Metersky, Daniel M. Musher, Marcos I. Restrepo, and Cynthia G. Whitney; on behalf of the American Thoracic Society and Infectious Diseases Society of America

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY MAY 2019 AND THE INFECTIOUS DISEASES SOCIETY OF AMERICA AUGUST 2019

Background: This document provides evidence-based clinical practice guidelines on the management of adult patients with community-acquired pneumonia.

management decisions. Although some recommendations remain unchanged from the 2007 guideline, the availability of results from new therapeutic trials and epidemiological investigations led to

Case Study

- A 74 year old man with a history of atrial fibrillation and mild dementia is admitted to hospital from a nursing home with confusion. He is tachypneic, has a non-productive cough, and looks short of breath.
- On exam, he is lethargic but easily arousable. Temperature 100°F (37.8°C), HR 118 irregular, BP 108/64, RR 24, SaO2 90% RA. JVP difficult to see. Possible crackles in the bases. Mild lower extremity edema.
- Labs are notable for WBC count of 10.2, hct 32, plt 240, Na 130, creatinine 1.4, LFTs normal.
- Urinalysis with 4-6 WBC/hpf
- Portable chest x-ray with edema +/- LLL infiltrate

Does this patient have pneumonia?

A. Yes

B. No

Would you start antibiotics?

A. Yes

B. No

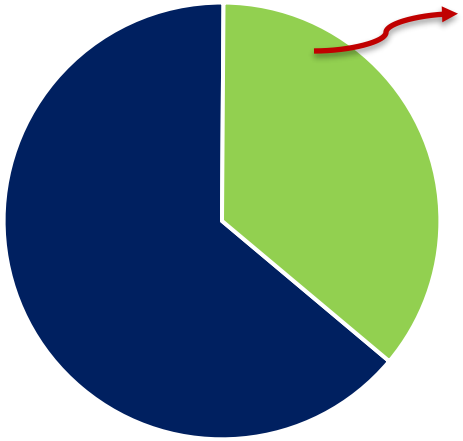
Why is Pneumonia So Difficult to Diagnose?

- Many medical conditions in hospitalized patients present with the same clinical signs as pneumonia
  - Radiographic opacities
  - Fever
  - Abnormal white blood cell count
  - Impaired oxygenation
  - Increased pulmonary secretions

Diagnostic Uncertainty in Pneumonia

Analysis of ED vs discharge diagnoses in 2,383,899 patients admitted to 118 VA hospitals, 2015-2022

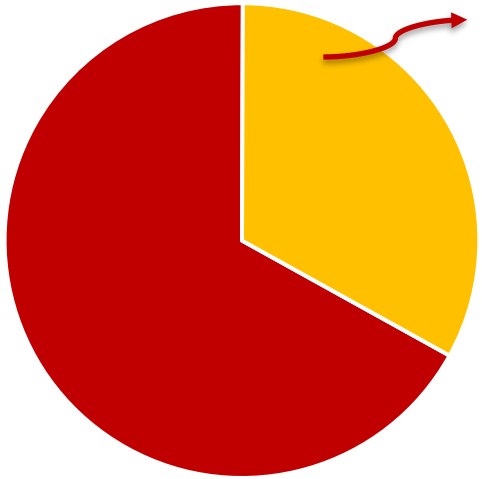
ED Diagnosis of Pneumonia



36% did not have a discharge diagnosis of pneumonia

- ED Pneumonia +, Discharge Pneumonia +
- ED Pneumonia +, Discharge Pneumonia -

Discharge Diagnosis of Pneumonia



33% did not have an ED diagnosis of pneumonia

- Discharge Pneumonia +, ED Pneumonia +
- Discharge Pneumonia+, ED Pneumonia -

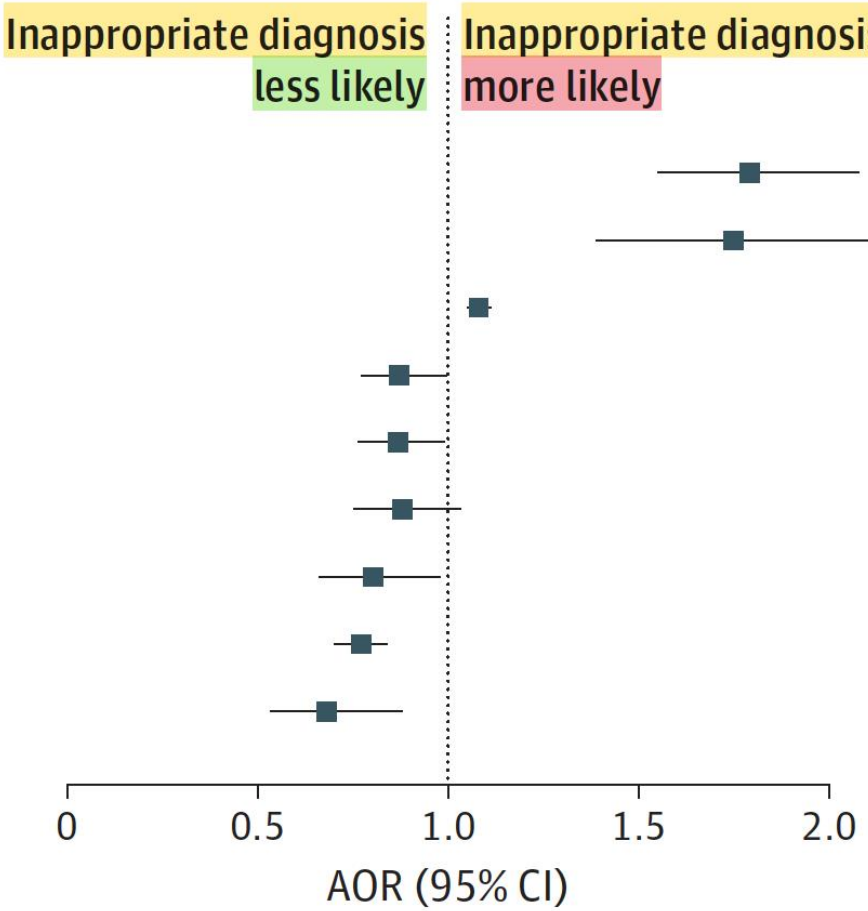
Uncertainty common! *51-58% of patients' clinical notes expressed uncertainty; 24% treated with diuretics, 38% treated with corticosteroids, 10% treated with all 3 of diuretics, steroids, and antibiotics*

Jones, *Ann Intern Med* 2024;177:1179-1189

Predictors of Inappropriate Diagnosis

Analysis of 17,290 patients admitted to 48 Michigan hospitals, 2017-2020.
Inappropriate diagnosis defined as <2 signs or symptoms of CAP or negative chest imaging.

Measure	AOR (95% CI)	*P* value
Dementia	1.79 (1.55-2.08)	<.001
Altered mental status, no dementia	1.75 (1.39-2.19)	<.001
Age, per 10 y	1.08 (1.05-1.11)	<.001
Home oxygen	0.87 (0.77-1.00)	.04
Chronic kidney disease	0.87 (0.76-0.99)	.03
Respiratory viral panel negative	0.88 (0.75-1.03)	.11
Respiratory viral panel positive	0.80 (0.66-0.98)	.03
≥2 SIRS criteria plus end organ dysfunction	0.77 (0.70-0.84)	<.001
History of pulmonary cancer	0.68 (0.53-0.88)	.003



Gupta, *JAMA IM* 2024;184:548-556

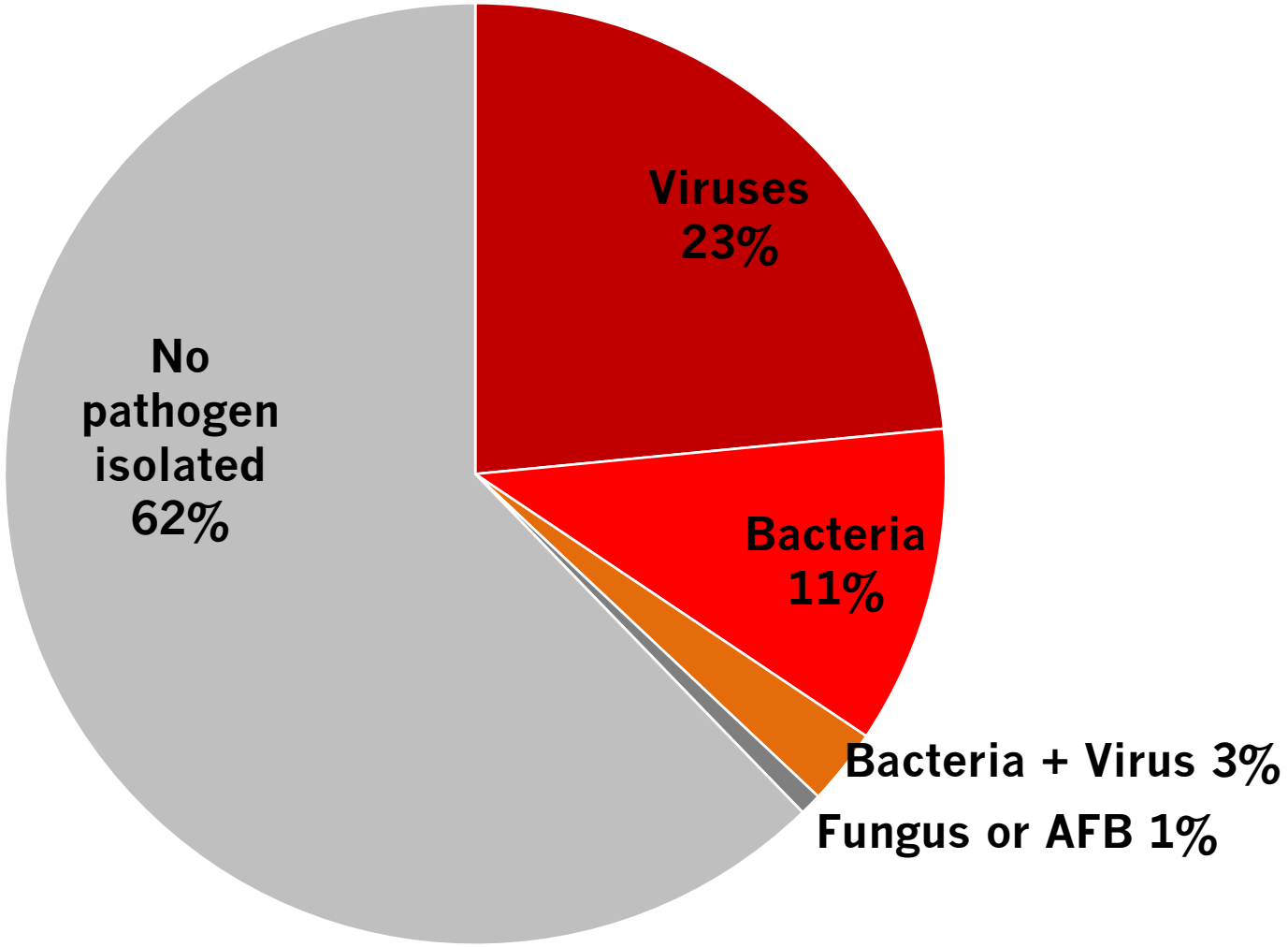
<u>If</u> the patient does have pneumonia, is it more likely bacterial or viral?

A. Bacterial

B. Viral

Etiology of Community-Acquired Pneumonia

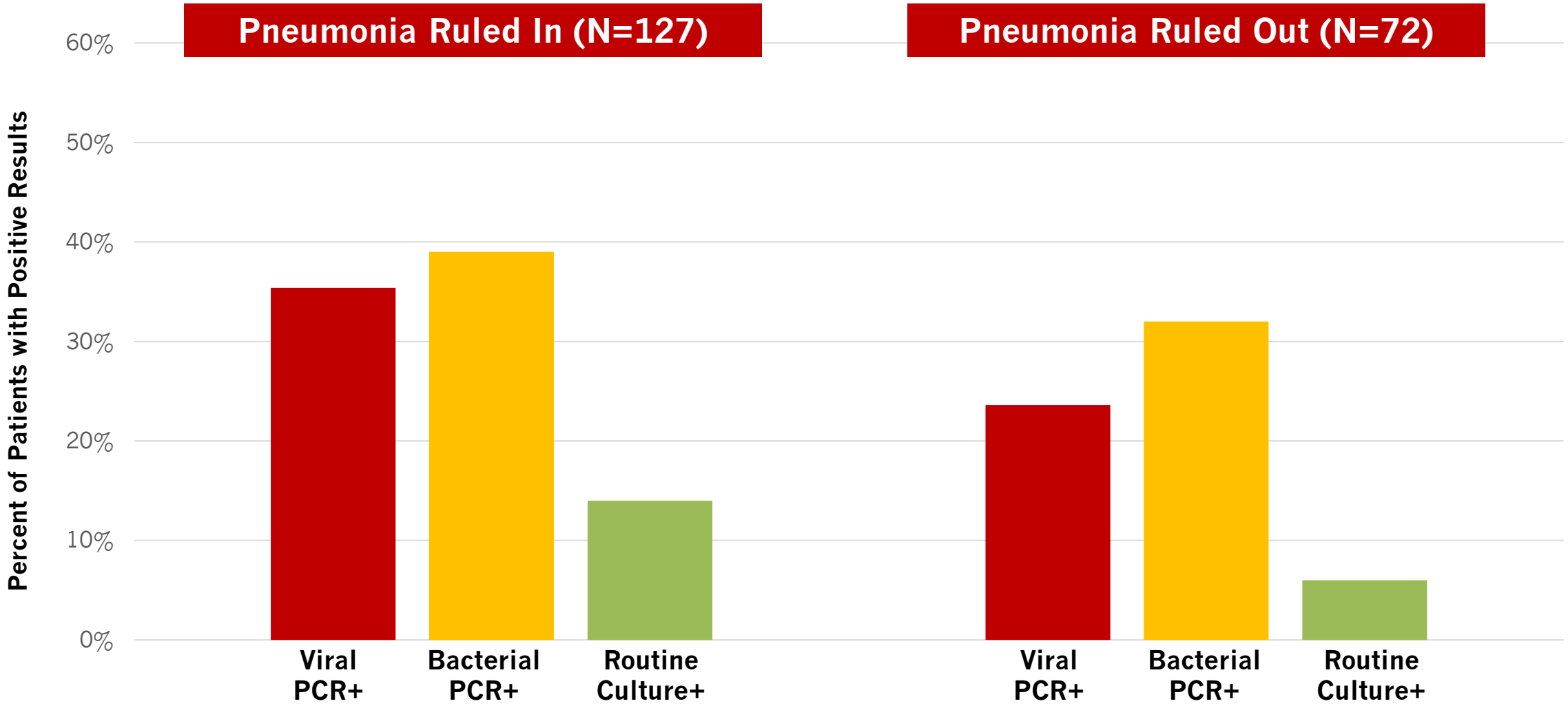
2,259 adults admitted to 5 hospitals in Chicago and Nashville, Jan 2010-Jun 2012



Jain, *N Engl J Med* 2015;373:415-427

Not every positive test indicates pneumonia…

199 elderly patients started on antibiotics for suspected pneumonia; pneumonia then ruled in or out by chest CT



Prendki, *Eur Respir J* 2018; 51:1702375

Could further imaging help?

A. Yes

B. No

Accuracy of Ultrasound and CXR vs Chest CT

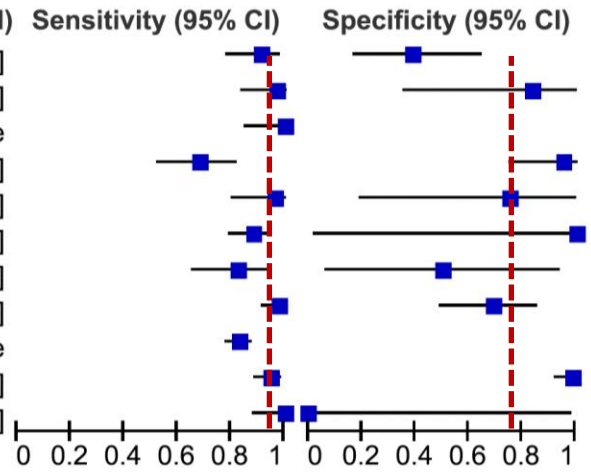
Meta-analysis of 11 studies, 939 patients. Chest CT used as reference standard

Accuracy of Ultrasound vs CT

Sensitivity: 95%

Specificity: 75%

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Amatya 2018	40	11	4	7	0.91 [0.78, 0.97]	0.39 [0.17, 0.64]
Bitar 2019	31	1	1	5	0.97 [0.84, 1.00]	0.83 [0.36, 1.00]
Bourcier 2014	23	0	0	0	1.00 [0.85, 1.00]	Not estimable
Corradi 2015	30	1	14	19	0.68 [0.52, 0.81]	0.95 [0.75, 1.00]
Cortallero 2012	25	1	1	3	0.96 [0.80, 1.00]	0.75 [0.19, 0.99]
Dhawan 2022	74	0	10	1	0.88 [0.79, 0.94]	1.00 [0.03, 1.00]
Fares 2015	28	2	6	2	0.82 [0.65, 0.93]	0.50 [0.07, 0.93]
Gibbons 2021	79	9	2	20	0.98 [0.91, 1.00]	0.69 [0.49, 0.85]
Karimi 2019	232	0	48	0	0.83 [0.78, 0.87]	Not estimable
Liu 2014	106	1	6	66	0.95 [0.89, 0.98]	0.99 [0.92, 1.00]
Taghizadieh 2015	29	1	0	0	1.00 [0.88, 1.00]	0.00 [0.00, 0.97]

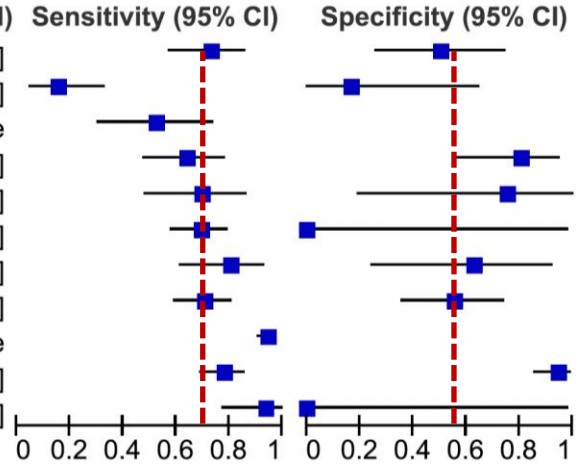


Accuracy of Chest X-Ray vs

Sensitivity: 70%

Specificity: 55%

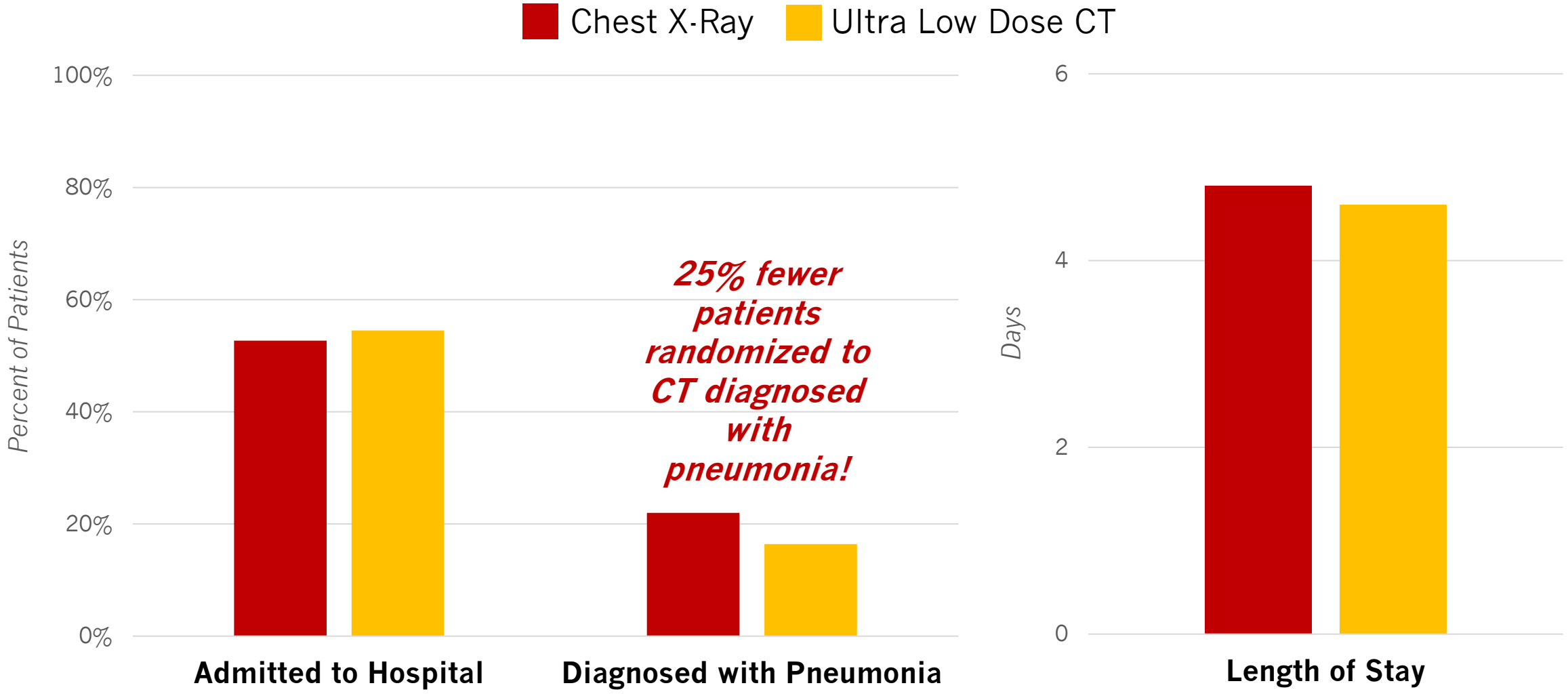
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Amatya 2018	32	9	12	9	0.73 [0.57, 0.85]	0.50 [0.26, 0.74]
Bitar 2019	5	5	27	1	0.16 [0.05, 0.33]	0.17 [0.00, 0.64]
Bourcier 2014	12	0	11	0	0.52 [0.31, 0.73]	Not estimable
Corradi 2015	28	4	16	16	0.64 [0.48, 0.78]	0.80 [0.56, 0.94]
Cortallero 2012	18	1	8	3	0.69 [0.48, 0.86]	0.75 [0.19, 0.99]
Dhawan 2022	58	1	26	0	0.69 [0.58, 0.79]	0.00 [0.00, 0.97]
Fares 2015	24	3	6	5	0.80 [0.61, 0.92]	0.63 [0.24, 0.91]
Gibbons 2021	57	13	24	16	0.70 [0.59, 0.80]	0.55 [0.36, 0.74]
Karimi 2019	263	0	17	0	0.94 [0.90, 0.96]	Not estimable
Liu 2014	87	4	25	63	0.78 [0.69, 0.85]	0.94 [0.85, 0.98]
Taghizadieh 2015	27	1	2	0	0.93 [0.77, 0.99]	0.00 [0.00, 0.97]



ATS 2025 CAP Guidelines (PMID 40679934)

CT vs CXR for Suspect Pulmonary Disease in the ED

2,418 ED patients with suspected pulmonary disease randomized to ultra-low dose CT vs CXR, Netherlands, 2017-8

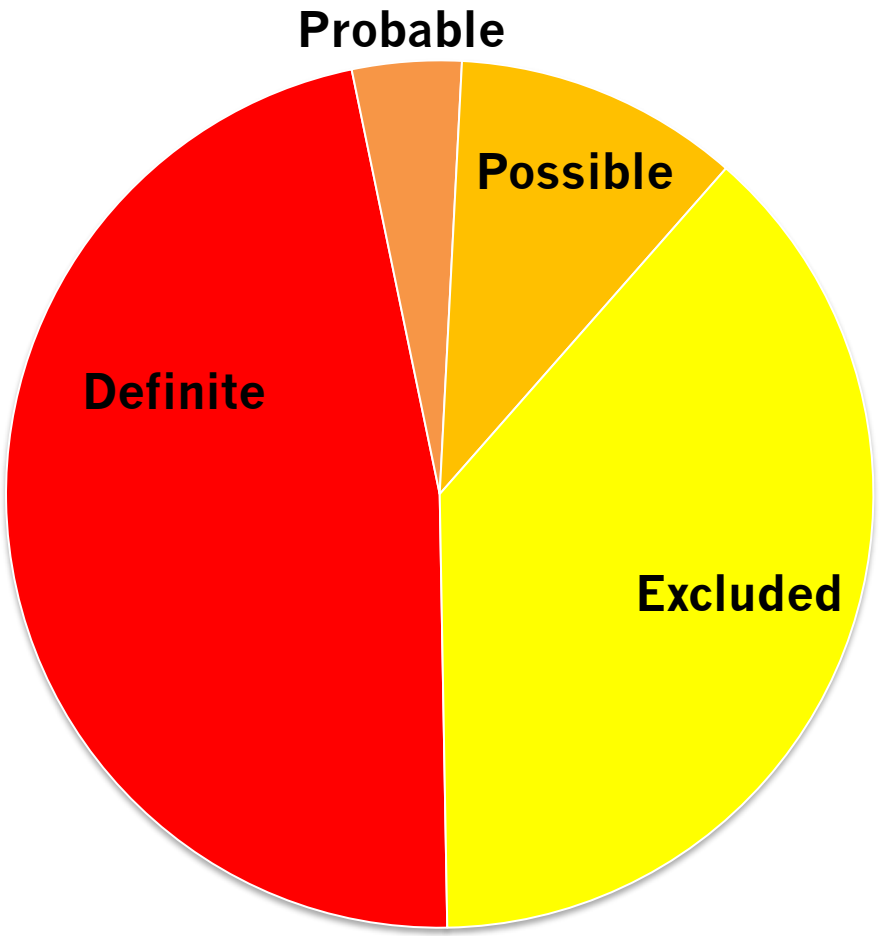


van den Berk, *Thorax* 2023;78:515-522

Chest X-Ray vs CT Scan

319 patients with clinically suspected community-acquired pneumonia referred for immediate CT chest to confirm or rule out pneumonia, 4 tertiary emergency departments, France

Final Pneumonia Classification:



Claessens, *AJRCCM* 2015;192:974-982

Intensive Care Med 2016;42:1159-63

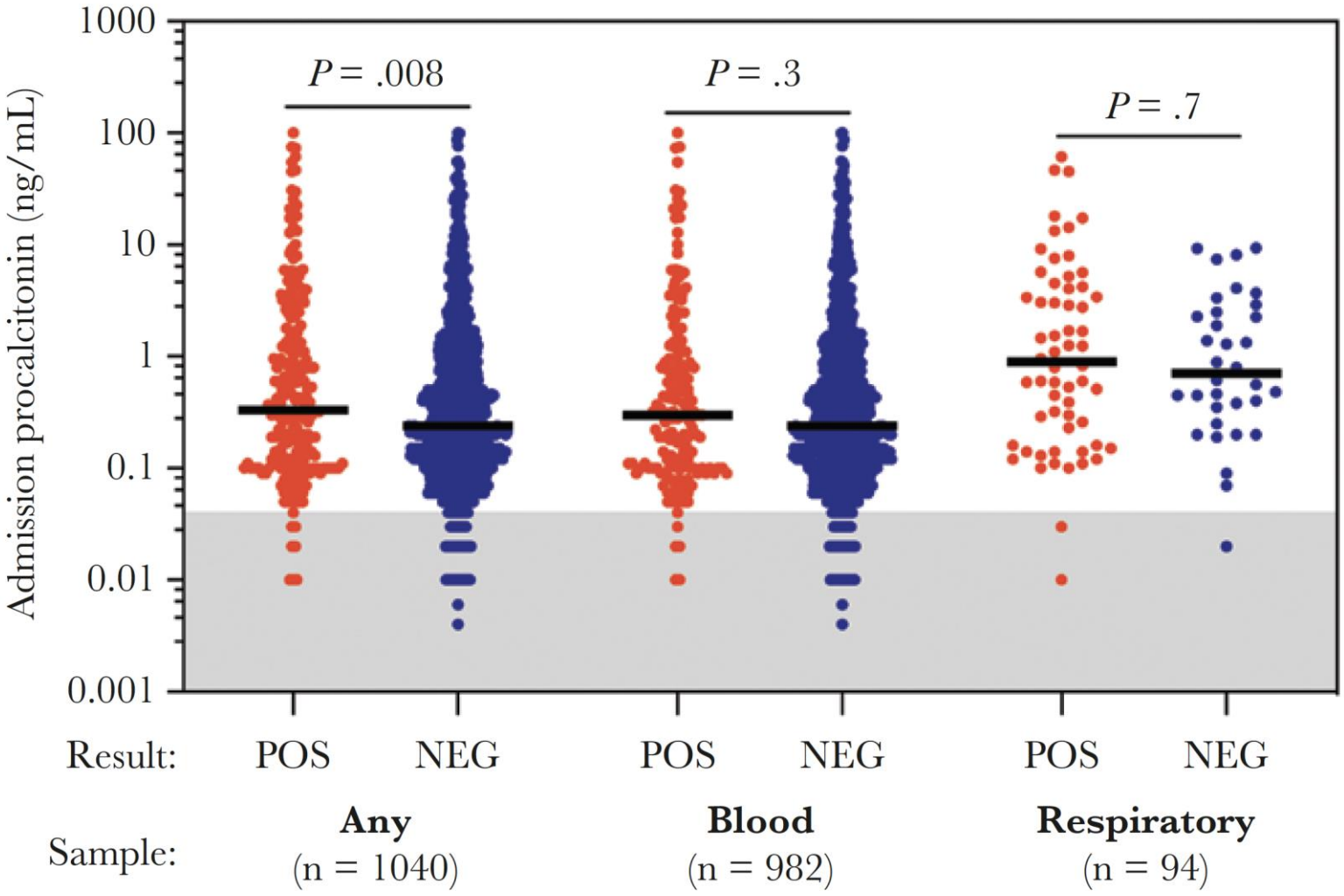
Could procalcitonin help?

A. Yes

B. No

Limited correlation between procalcitonin and bacterial cultures

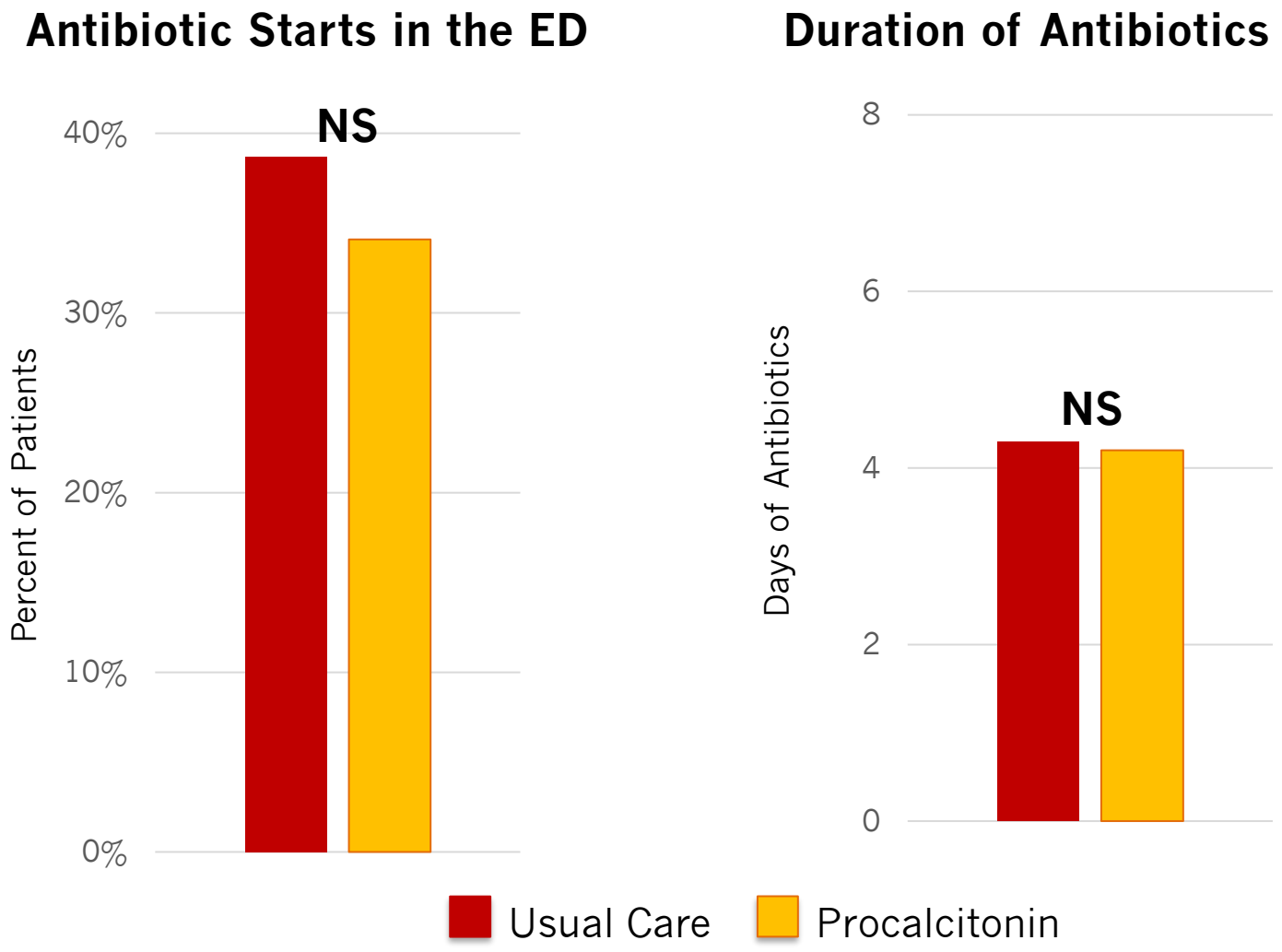
1,040 patients admitted to 260 UK hospitals with COVID-19; PCT & blood or respiratory cultures obtained within 48h of admission



Ralph, *Open Forum Infect Dis* 2022; doi.org//10.1093/ofid/ofac179

Procalcitonin for ?Pneumonia

1656 patients with possible pneumonia randomized to procalcitonin vs routine care



Huang, *N Engl J Med* 2018;379:236-249

Should we culture for bacteria and test for viruses?

A. Yes

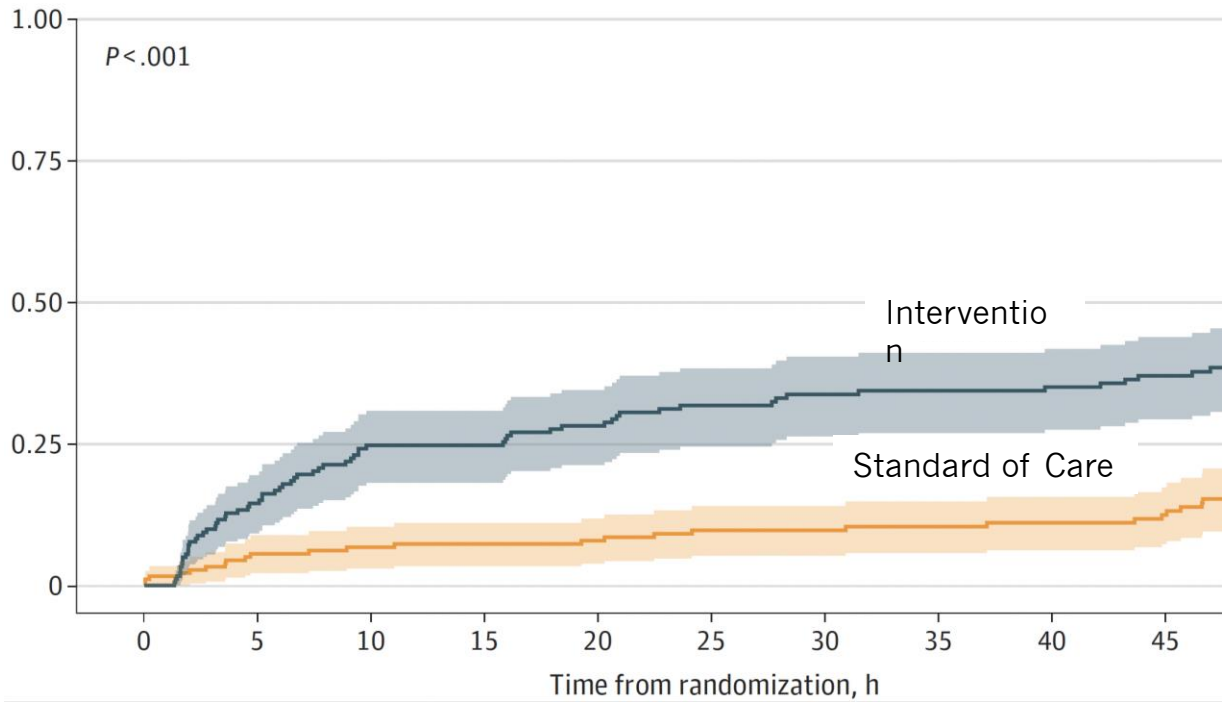
B. No

Impact of Multiplex Respiratory PCR on Outcomes

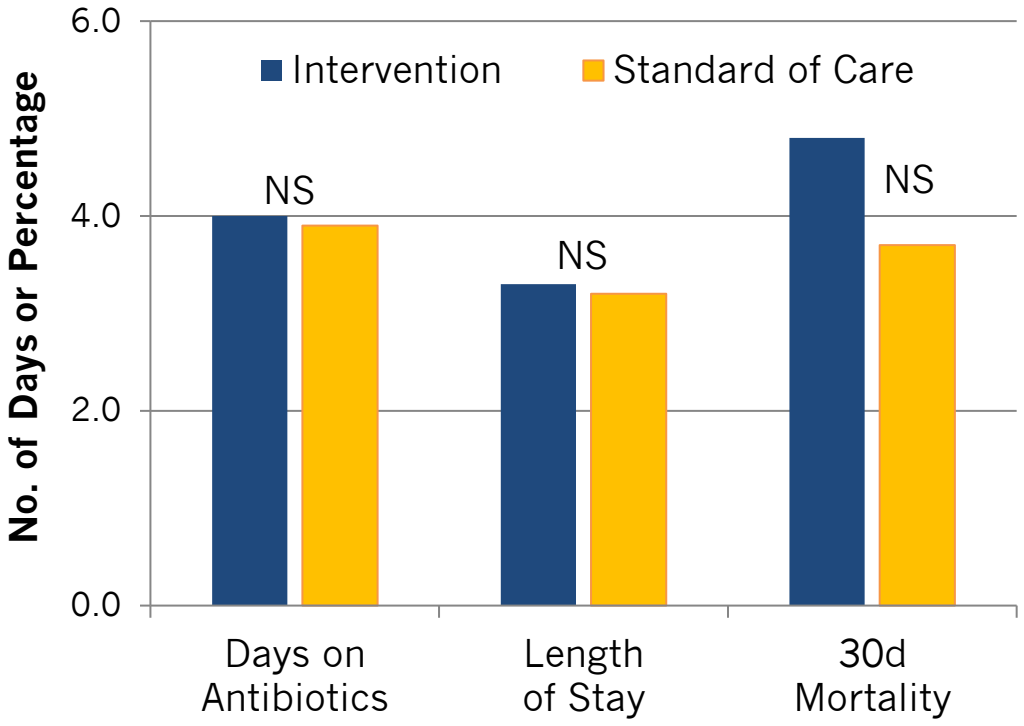
374 patients with suspected CAP in a large Norwegian hospital randomized to multiplex PCR vs routine care

More patients randomized to multiplex received pathogen-directed therapy (35% vs 13%) and in less time (35h vs 44h) but no difference in antibiotic days, length-of-stay, readmissions, or deaths

Proportion of Patients with Pathogen Directed Therapy



Outcomes



Markussen, *JAMA Network Open* 2024;7(3):e240830

Check for updates

AMERICAN THORACIC SOCIETY DOCUMENTS

Released 2021

Nucleic Acid–based Testing for Noninfluenza Viral Pathogens in Adults with Suspected Community-acquired Pneumonia

An Official American Thoracic Society Clinical Practice Guideline

Outpatients: we suggest not performing routine NAAT testing for respiratory viral pathogens other than influenza.

Inpatients: we suggest performing NAAT testing for respiratory viruses other than influenza in patients with severe CAP or immunocompromised state

ATS Guidelines

Obtain sputum gram stain & culture in inpatients if:

Any of the following:

- the patient has severe pneumonia
- you believe empiric coverage for MRSA or Pseudomonas is necessary
- the patient has a prior history of MRSA or Pseudomonas infection
- patient was been hospitalized and received IV antibiotics within the preceding 90 days

Test for influenza if influenza is circulating in the community. Test for other respiratory viruses if severe pneumonia or immunocompromised.

My Opinion

Obtain sputum gram stain & culture + viral studies in <u>all</u> inpatients

My reasons:

- Risk factors for resistant organisms are ill defined
- Positive cultures can help you tailor treatment
- Negative cultures can facilitate stopping antibiotics early
- Culture data is critical to generate hospital antibiograms to inform future empiric treatment choices
- Many viruses cause pneumonia & they circulate year-round (Covid!)
- Viral diagnosis has infection control implications

Which antibiotics should we use?

Treatment Strategy for Inpatients with CAP

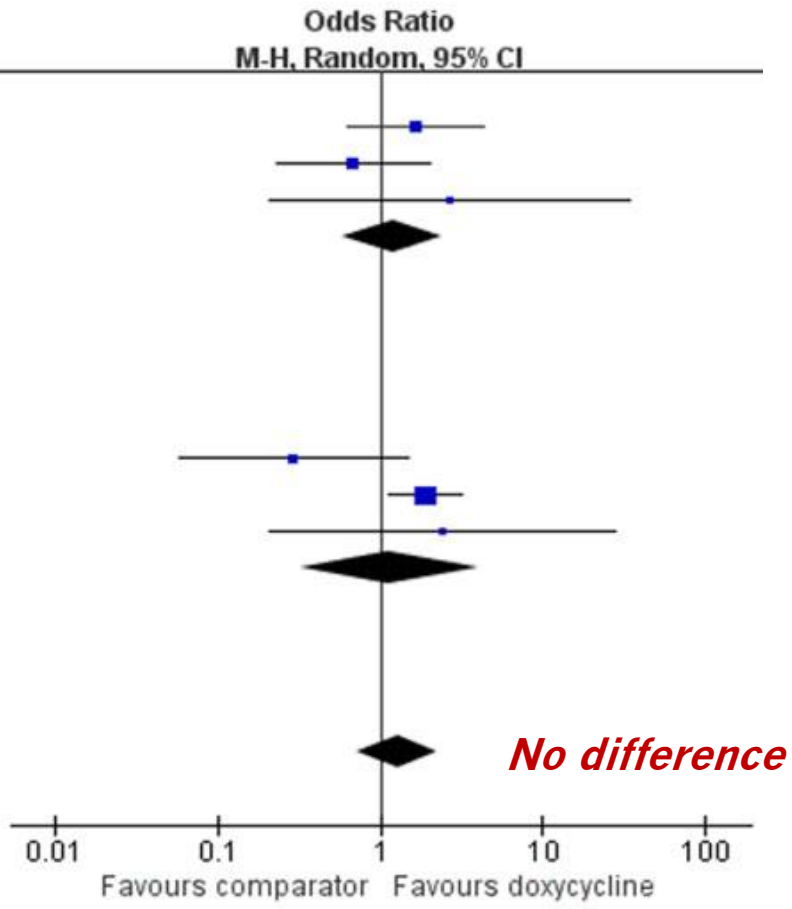
	Standard Regimen	MRSA coverage?	Pseudomonas coverage?
Mild disease	**B-lactam + macrolide or Fluoroquinolone**	If prior history of respiratory MRSA then cover for MRSA If risk factors alone, get cultures & nasal PCR. Only cover MRSA if cultures or nasal PCR positive	If prior history of respiratory Pseudomonas then cover for Pseudomonas If risk factors alone, get cultures. Only cover for Pseudomonas if cultures positive
Severe disease	**B-lactam + (macrolide or fluroquinolone)**	If prior history of respiratory MRSA or risk factors for MRSA then get cultures and cover MRSA upfront	If prior history of respiratory Pseudomonas or risk factors for Pseudomonas get cultures and cover for Pseudomonas upfront

AJRCCM 2019;7:e45-e67

What about doxycycline?

*Meta-analysis of 6 randomized trials of doxy vs comparator for **mild-to-moderate** CAP*

	Doxycycline Events	Doxycycline Total	Comparator Events	Comparator Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
vs Macrolides							
Biermann 1988	46	55	37	49	21.8%	1.66 [0.63, 4.36]	1988
Charpin 1988	65	75	57	63	19.1%	0.68 [0.23, 2.00]	1988
Wiesner 1993	12	13	9	11	4.6%	2.67 [0.21, 34.20]	1993
Subtotal (95% CI)		**143**		**123**	**45.5%**	**1.19 [0.60, 2.37]**	
Total events	123		103				
Heterogeneity: Tau² = 0.00; Chi² = 1.86, df = 2 (P = 0.39); I² = 0%							
Test for overall effect: Z = 0.49 (P = 0.62)							
vs Quinolones							
Harazim 1987	62	69	60	62	10.3%	0.30 [0.06, 1.48]	1987
Norrby 1997	162	190	137	182	39.2%	1.90 [1.13, 3.21]	1997
Mokabberi 2010	34	35	28	30	5.0%	2.43 [0.21, 28.20]	2010
Subtotal (95% CI)		**294**		**274**	**54.5%**	**1.14 [0.32, 4.06]**	
Total events	258		225				
Heterogeneity: Tau² = 0.73; Chi² = 4.78, df = 2 (P = 0.09); I² = 58%							
Test for overall effect: Z = 0.21 (P = 0.84)							
Overall		**437**		**397**	**100.0%**	**1.29 [0.73, 2.28]**	
Total events	381		328				
Heterogeneity: Tau² = 0.14; Chi² = 7.14, df = 5 (P = 0.21); I² = 30%							
Test for overall effect: Z = 0.87 (P = 0.39)							
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%							



No difference

Caveats: old trials, most comparators no longer used, 4/6 trials at increased risk of bias

Choi, *Clin Infect Dis* 2023;76:683-691

Should we add steroids?

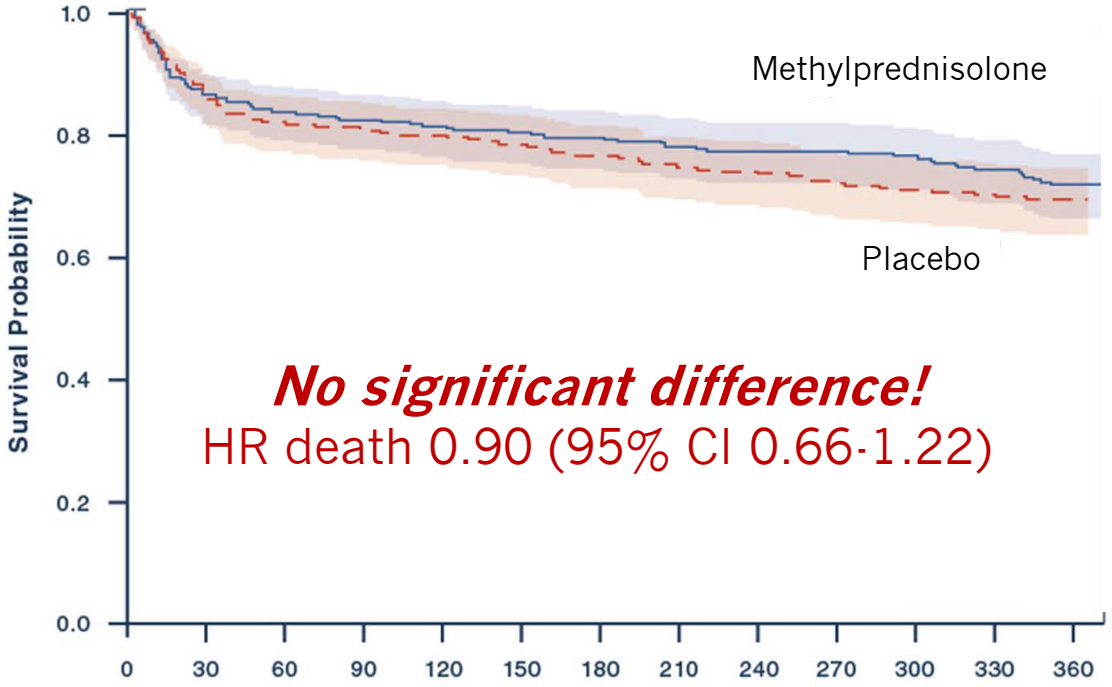
A. Yes

B. No

Two Recent RCTs

584 ICU & intermediate care patients with CAP randomized to methylprednisolone 40mg/day x7d then 13d taper

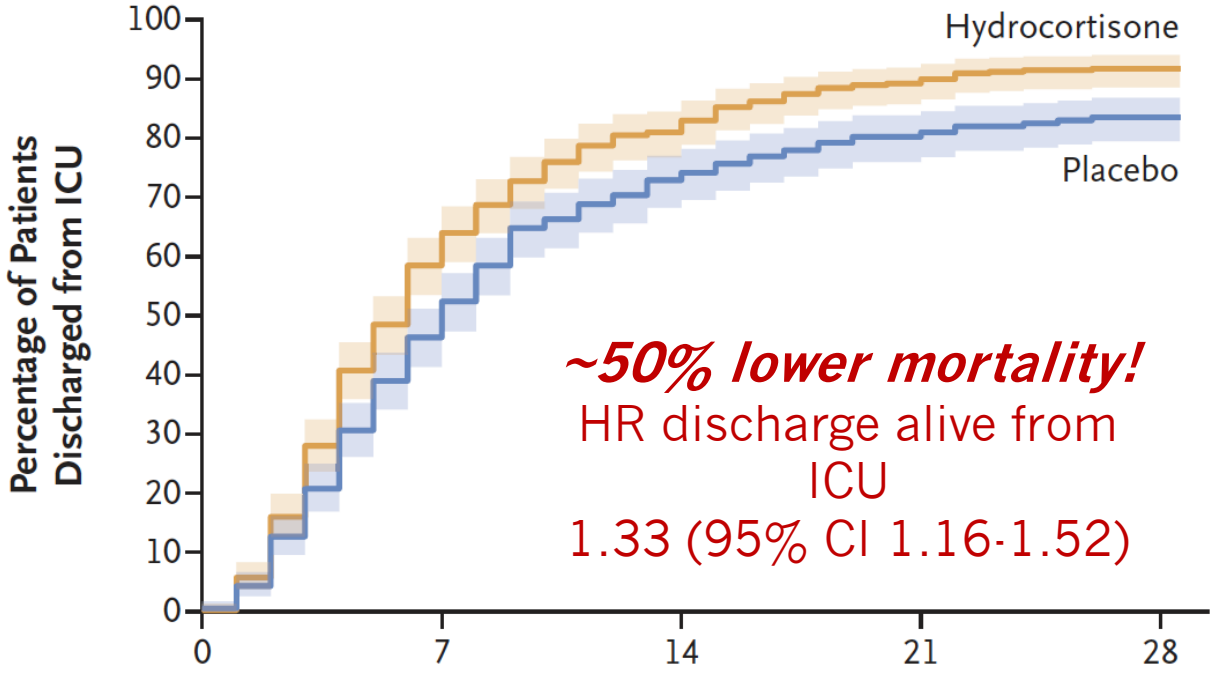
Treatment started up to 96h after admission
96% of participants were male
~10% of patients had influenza



Meduri, Intensive Care Med 2022;48:1009–1023

795 patients ICU patients with severe CAP randomized to hydrocortisone 200mg/day x 4-8d

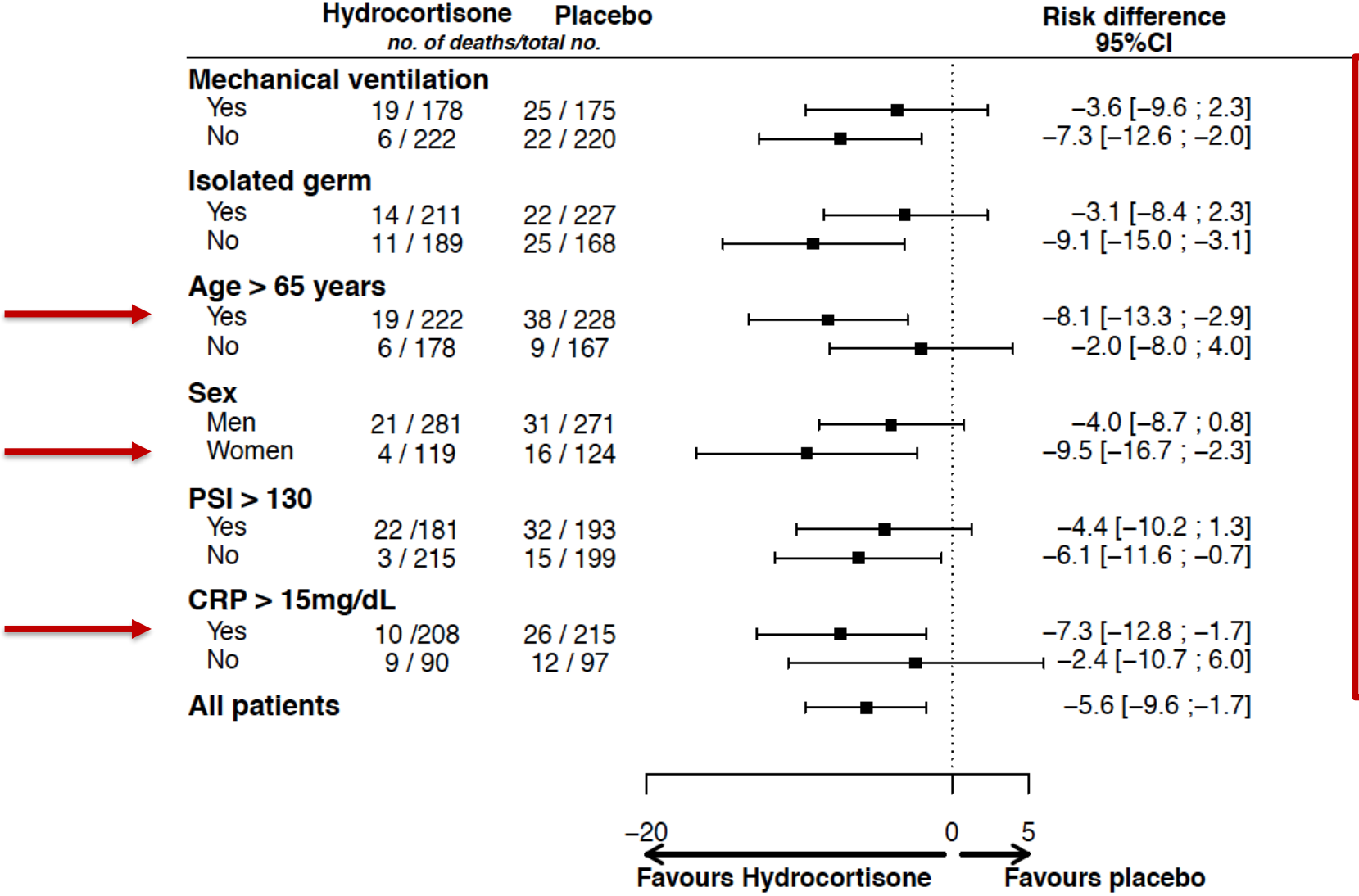
Treatment started within 24h after admission
31% of participants were female
Excluded patients with influenza



Dequin, NEJM 2023;288:1931-1941

Who Is Most Likely to Benefit?

795 patients ICU patients with severe CAP randomized to hydrocortisone 200mg/day x 4-8d vs placebo



Bottom Line

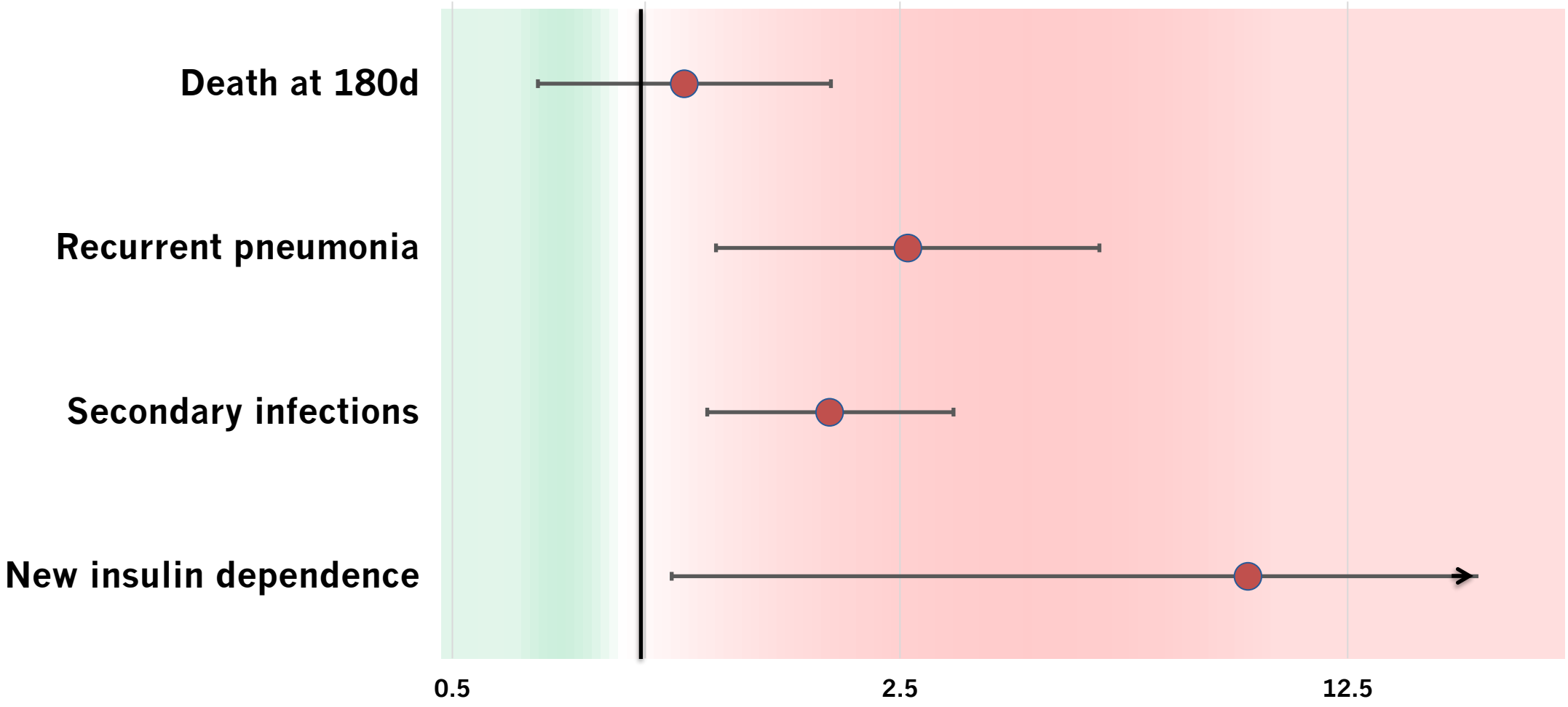
Consider steroids for:

- **severe CAP (ICU)**
  and
- **<24h since admission**
  and
- **CRP >150mg/L**

Dequin, NEJM 2023;288:1931-1941

Long-term impact of steroids for CAP

785 patients hospitalized with CAP randomized to prednisone 50mg PO x 7d vs placebo, 180-day outcomes



Blum, *BMC Pulm Med* 2023;23:500

American Journal of Respiratory and Critical Care Medicine

Diagnosis and Management of Community-acquired Pneumonia. An Official American Thoracic Society Clinical Practice Guideline

Barbara E. Jones ; Julio A. Ramirez , Eyal Oren , Nilam J Soni ; Liam R Sullivan , Marcos I. Restrepo , Daniel M Musher , Brian L. Erstad , Chiagozie Pickens , Valerie M Vaughn , Scott A Helgeson , Kristina Crothers , Joshua P. Metlay , Brittany D. Bissell Turpin , Bin Cao , James D. Chalmers , Charles S. Dela Cruz , Inessa Gendlina , Leila S Hojat , Maryrose Laguio-Vila , Stephen Y Liang , Grant W Waterer , Marilynn Paine , Conall Hawkins , and Kevin Wilson ; ... Show less
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Abstract PDF

Abstract

Background: Understanding of the diagnosis and treatment of adults with community-acquired pneumonia (CAP) has evolved thanks to new evidence, experience, and emerging technologies. This document updates evidence-based clinical practice guidelines on four key questions for the diagnosis and management of adult patients with CAP. Methods: A multidisciplinary panel integrated systematic reviews of comparative evidence with other relevant research and clinical experience, then applied Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology to produce recommendations using the Evidence to Decision Framework. Results: The panel formulated clinical recommendations that address questions related to CAP, including lung ultrasound for diagnosis, empiric antibacterial therapy if a test for a respiratory virus is positive, antibiotic duration, and the use of systemic corticosteroids. Conclusions: The panel formulated and provided the rationale for recommendations on selected diagnostic and treatment strategies for adult patients with CAP.

Keywords: pneumonia; lower respiratory tract infection; practice guidelines; guideline update

Corticosteroids:

Non-severe CAP:
steroids not recommended
(strong recommendation)

Severe CAP:
steroids suggested
(conditional recommendation)

Do we need to cover for atypicals?

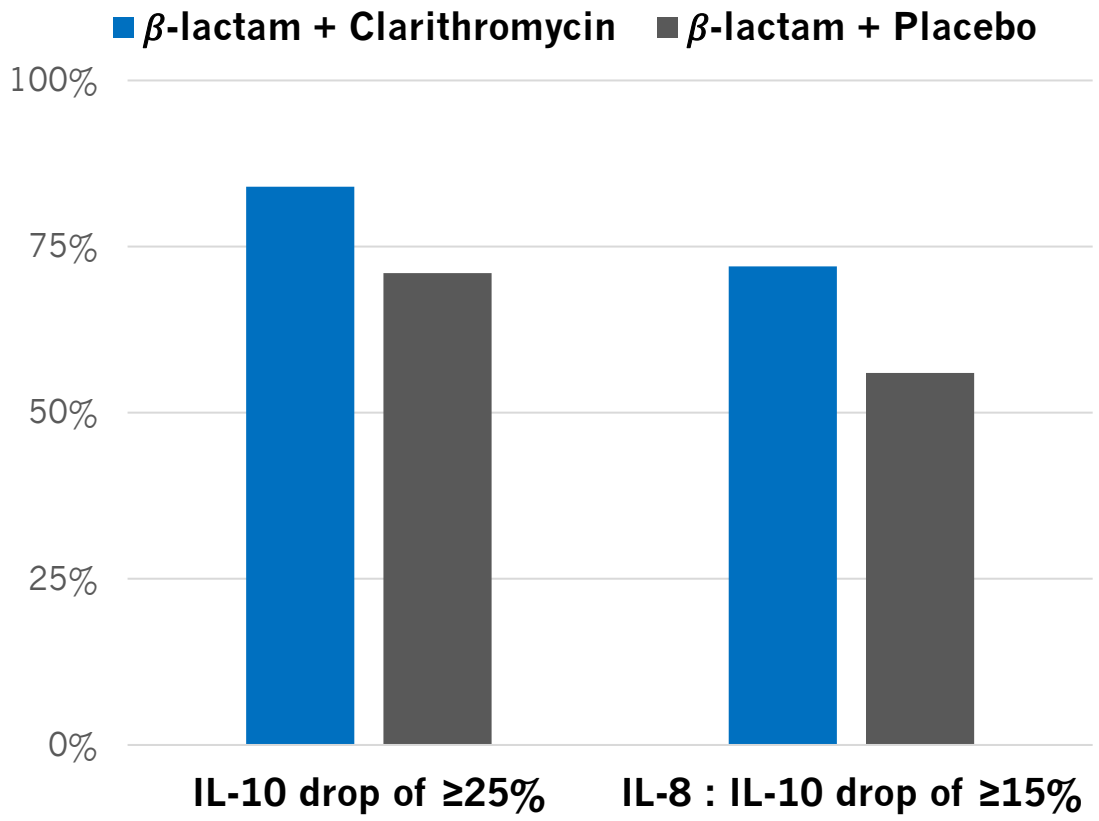
A. Yes

B. No

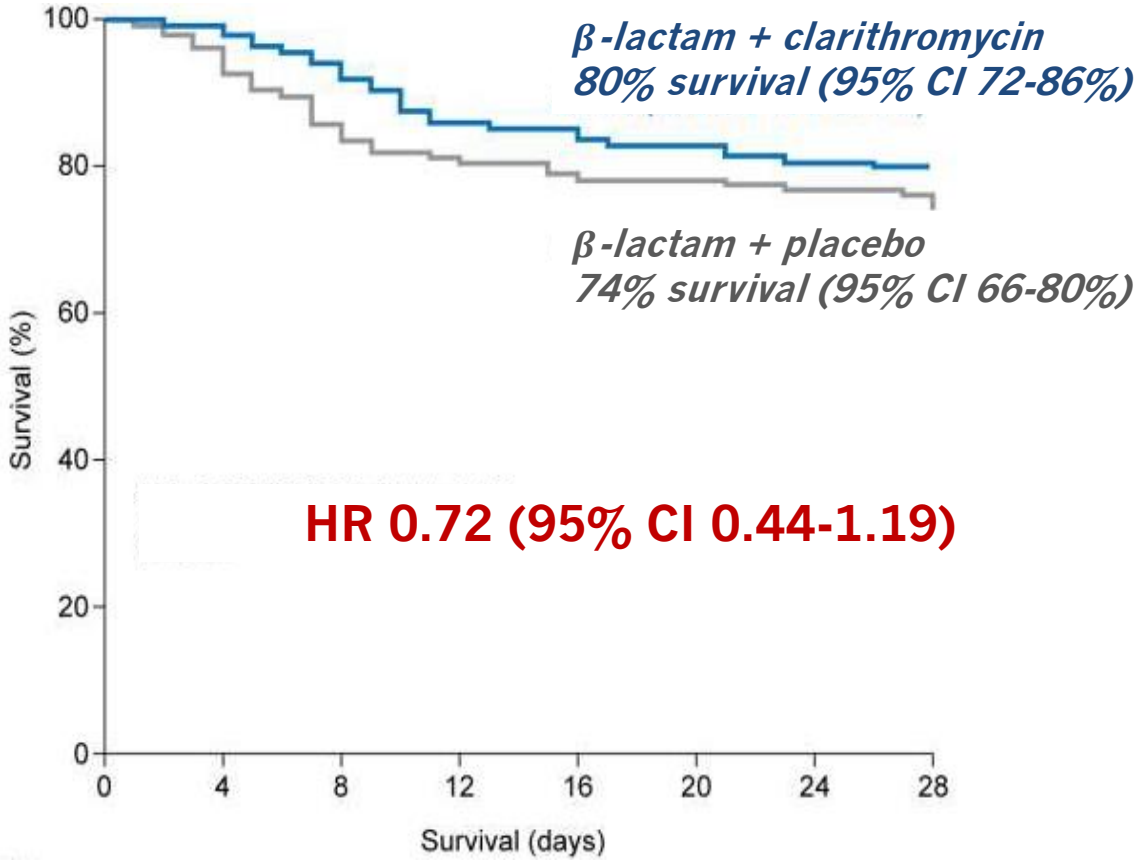
β-lactam alone vs β-lactam+macrolide

*278 patients hospitalized with CAP in Greece randomized to **β-lactam+placebo** vs **β-lactam+clarithromycin**.*
Greater drop in inflammatory markers, less sepsis, less hospital death, no difference in 28d or 90d mortality

Inflammatory Markers



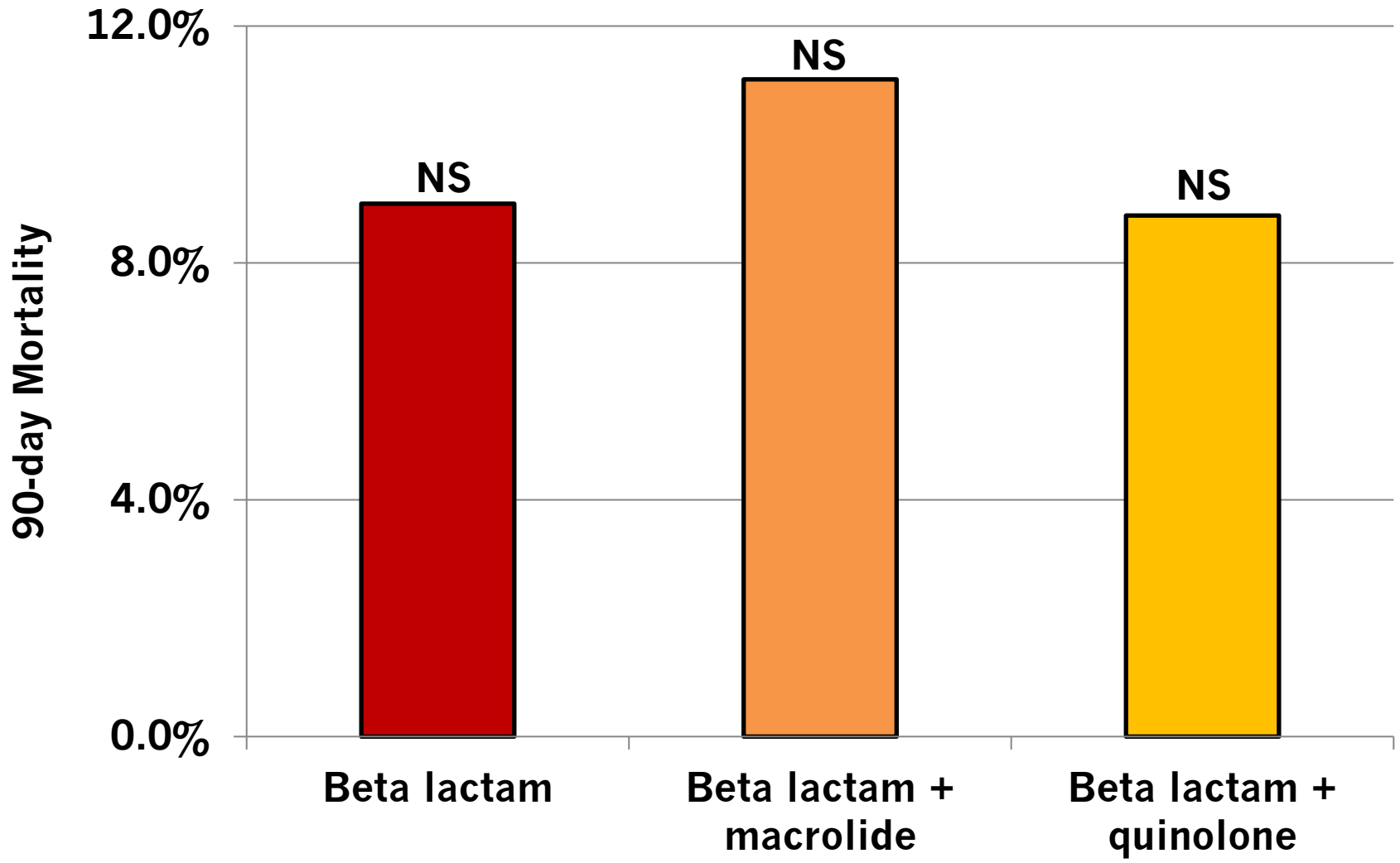
28d Survival



Giamarellos-Bourboulis, Lancet Respir Med 2024;12:294–304

βlactam vs βlactam+macrolide vs βlactam+quinolone

Cluster randomized trial of 2,283 non-ICU patients with CAP in the Netherlands



N Engl J Med 2015;372:1312-23

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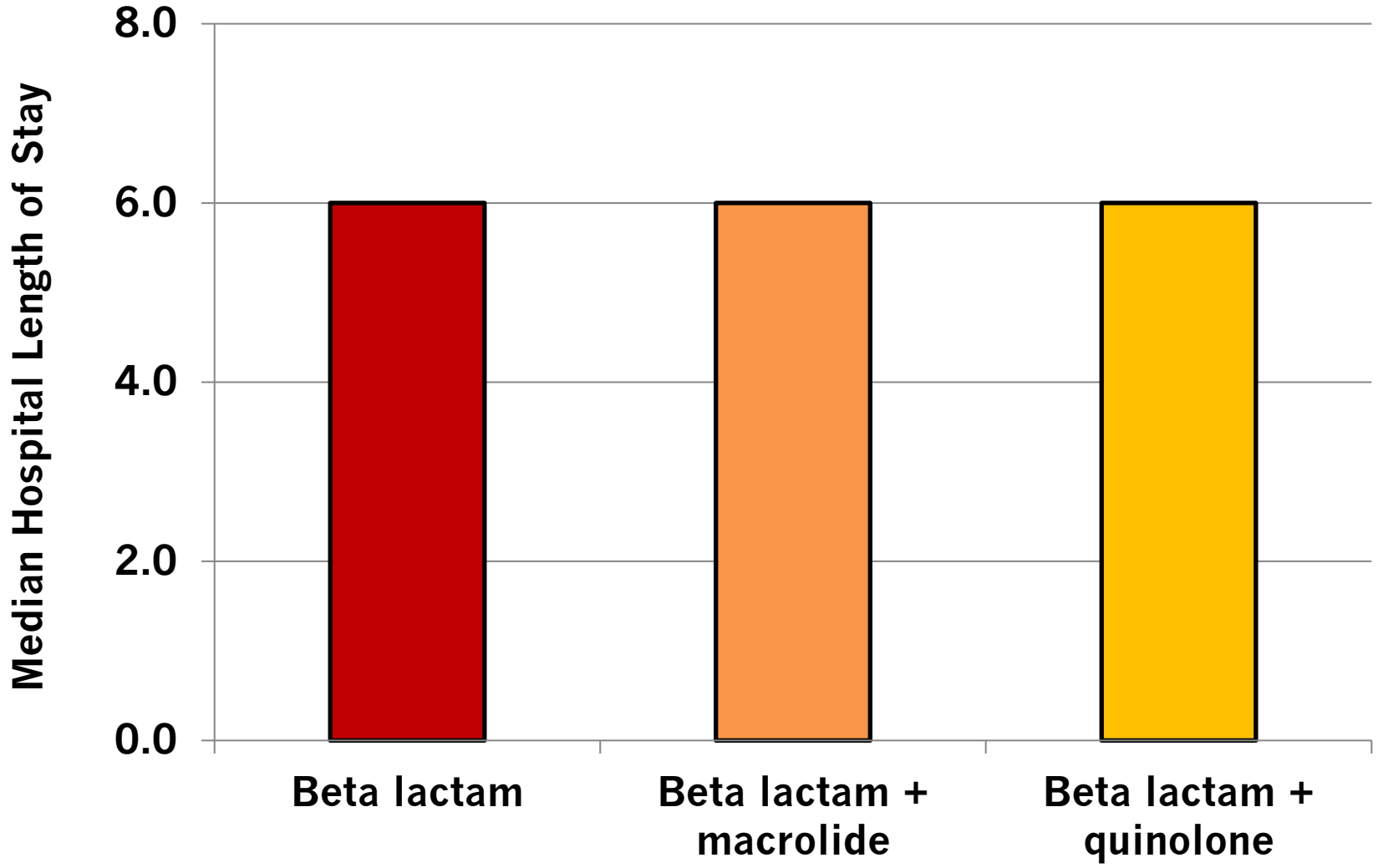


N Engl J Med 2015;372:1312-23

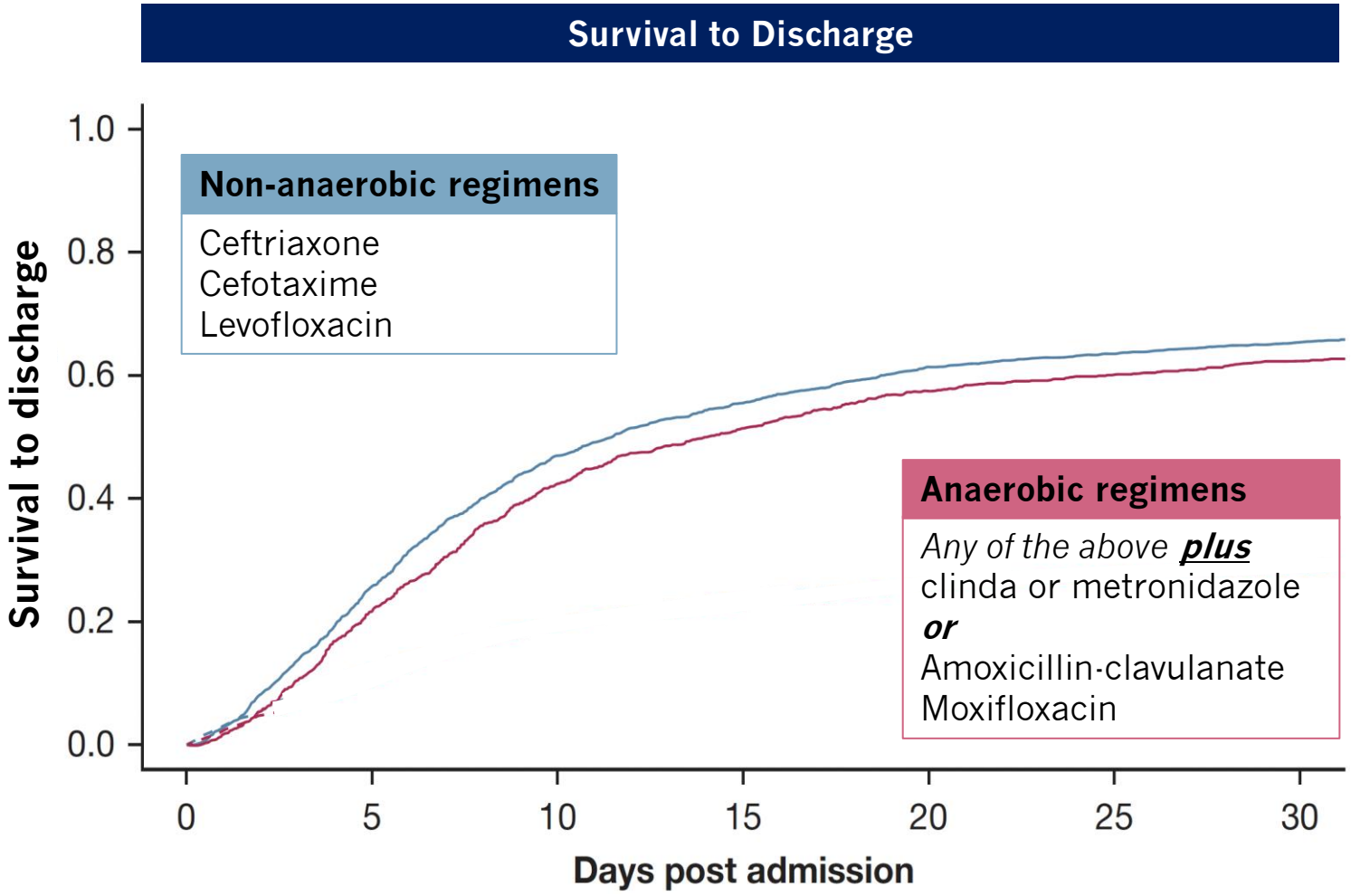
Do patients who aspirate need antibiotics?

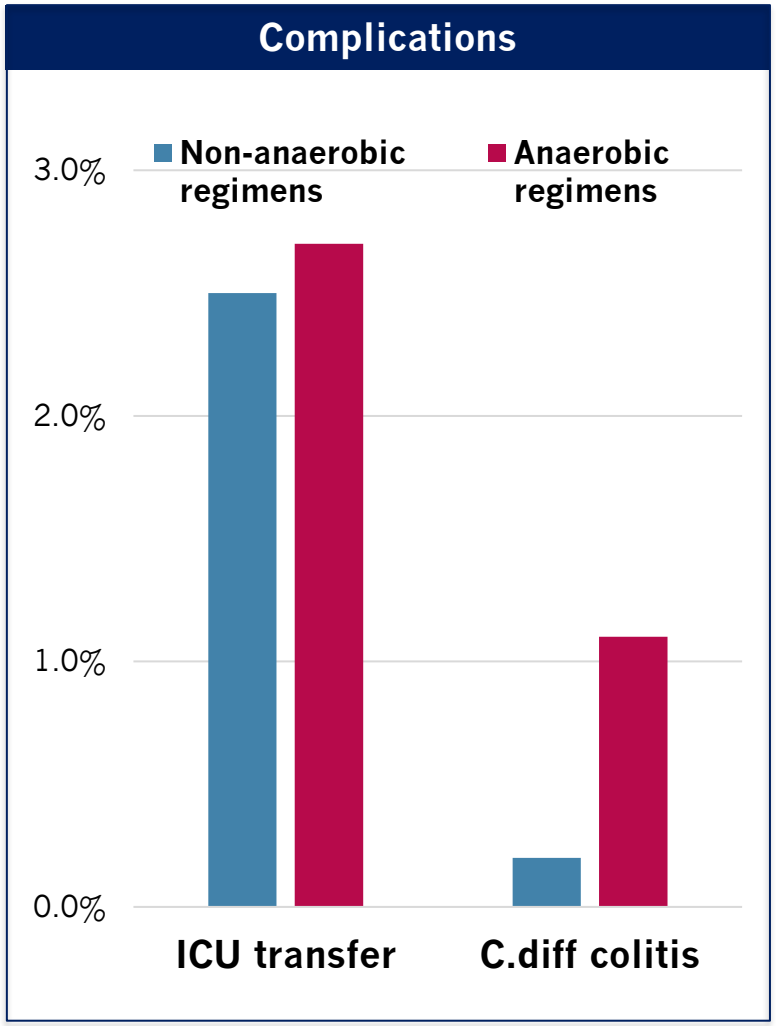
A. Yes

B. No

Adding anaerobic coverage: Same Outcomes, More *C.diff*

Propensity-matched comparison of anaerobic vs non-aerobic regimens for aspiration pneumonia, 18 hospitals, Ontario





Bai, *Chest* 2024;166:39-48

Do we still need antibiotics if the patient tests positive for a virus?

A. Yes

B. No

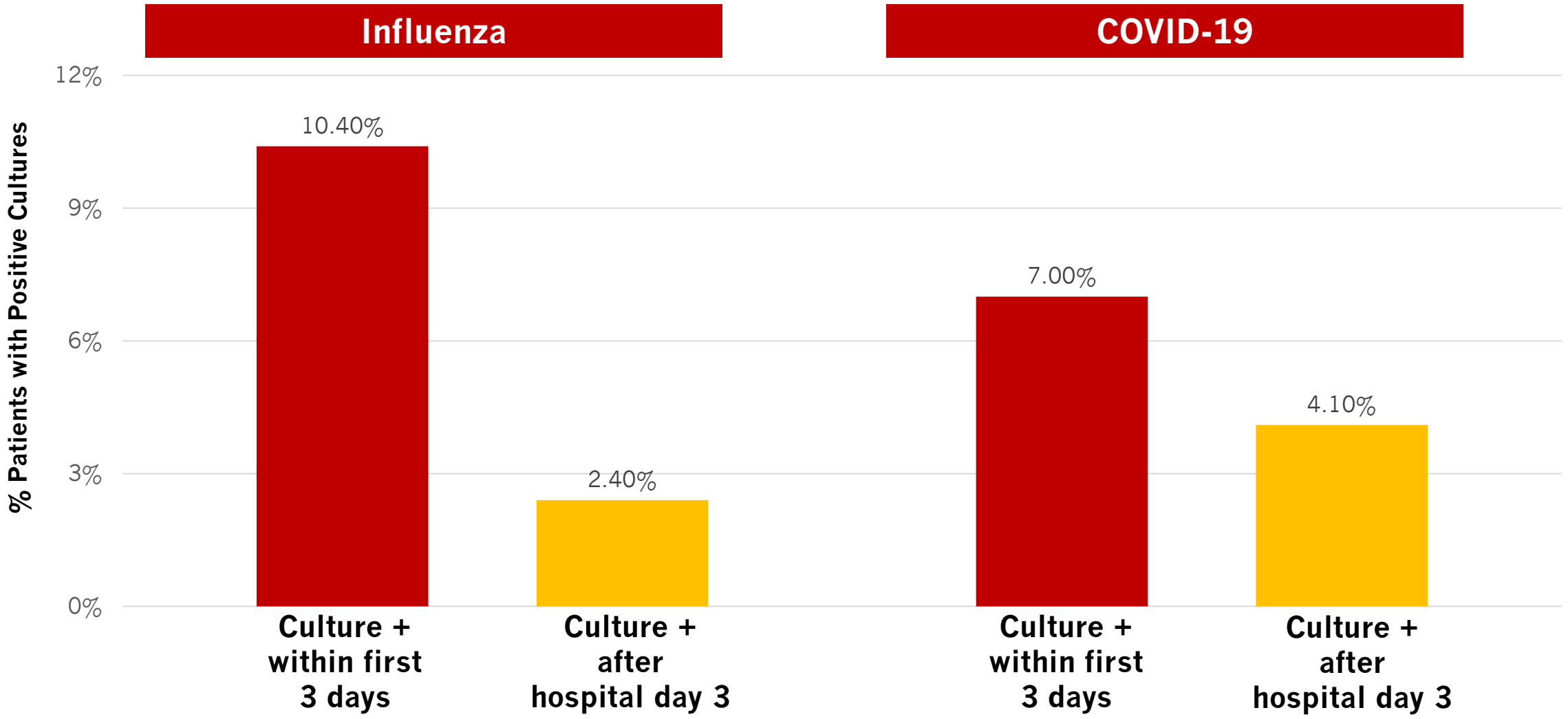
ATS Journals | American Journal of Respiratory and Critical Care Medicine

Infectious Diseases Society of America (IDSA) Position Statement: Why IDSA Did Not Endorse the Community-Acquired Pneumonia Guidelines 2025 Update

Frequency of Bacterial Coinfection* in Viral Pneumonia

*any body site (respiratory accounts for about 50% of positives)

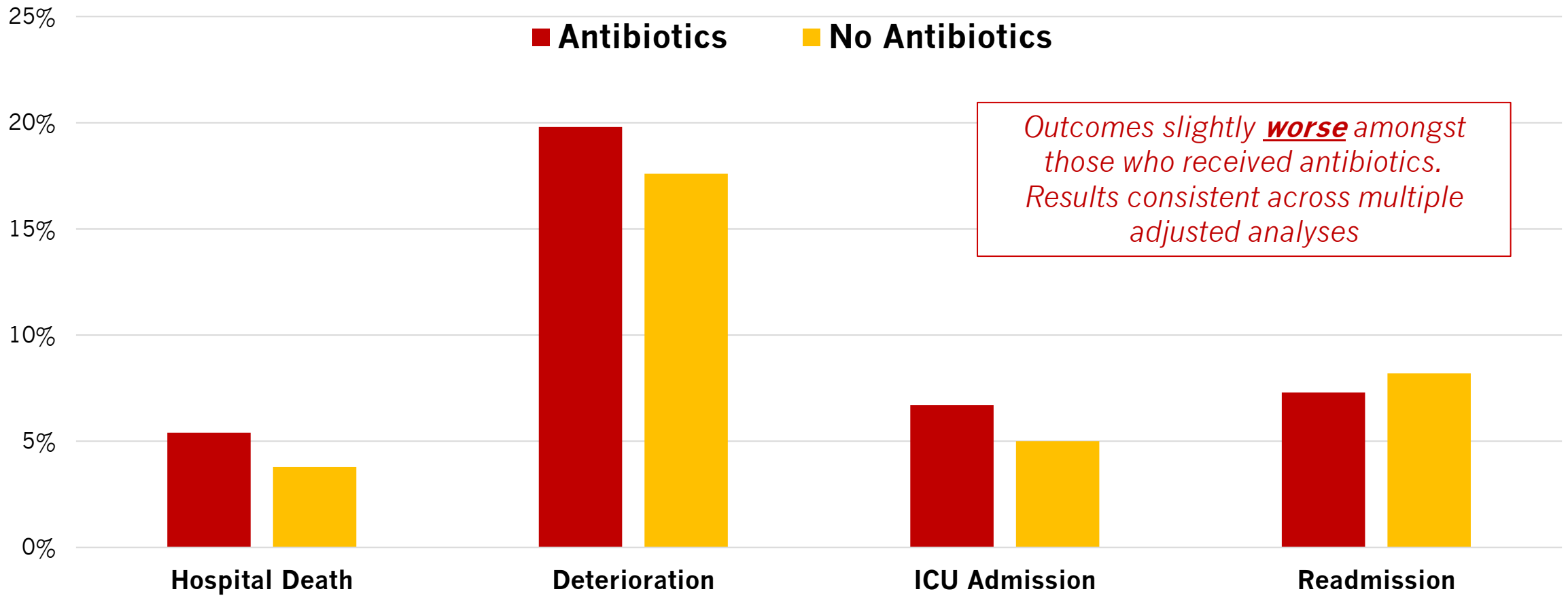
142,426 inpatients with influenza-like illness and 206,435 inpatients with COVID-19, 2019-2021 in 280 US hospitals



Baggs, *Clinical Infect Dis* 2022;75:S294-S297

Impact of Antibiotics in Patients Hospitalized with Covid

Retrospective comparison of 160,482 Covid patients treated with antibiotics versus 359,923 treated without antibiotics, 1,053 US hospitals, April 2020 – December 2023



*Outcomes slightly **worse** amongst those who received antibiotics. Results consistent across multiple adjusted analyses*

Pulia, *JAMA Network Open* 2025;8(5):e2511499

American Thoracic Society

Treat all patients with possible CAP who test positive for a respiratory virus with antibacterials

ATS's rationale:

- Bacterial coinfection is common and potentially deadly
- Delays in antibiotics may lead to worse outcomes

Infectious Disease Society of America

Use your judgement.

Reserve antibiotics for patients with severe illness or clinical signs suggestive of co-infection

- High WBC, positive sputum gram stain, + molecular assays, high procalcitonin…

IDSA's rationale:

- Most patients with +viral assays do not have bacterial coinfection. The vast majority will not benefit.
- Retrospective analyses show similar outcomes in patients who do and don't get antibiotics

How long should we treat for?

A. 3 days

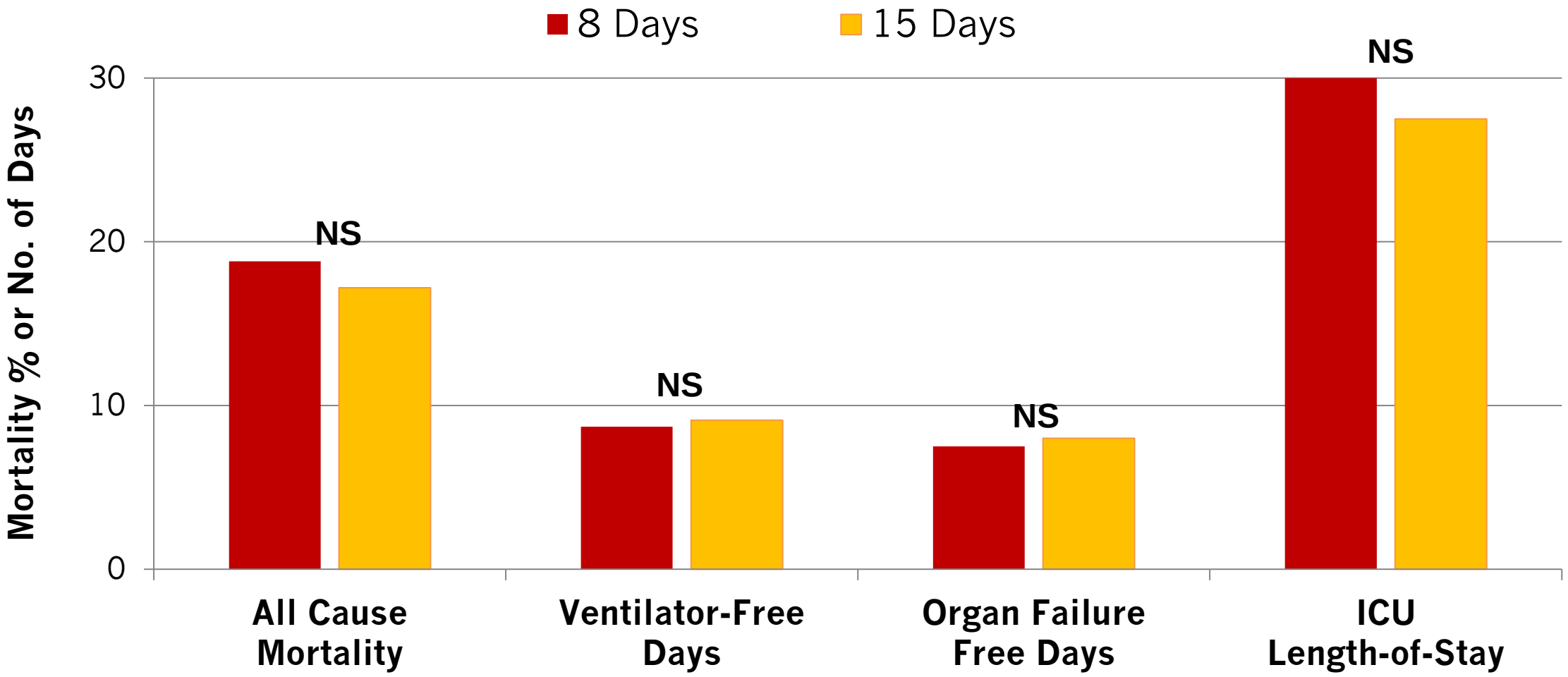
B. 5 days

C. 7 days

D. 10 days

Ventilator Associated Pneumonia

401 patients with ventilator-associated pneumonia randomized to 8 vs 15 days of antibiotics

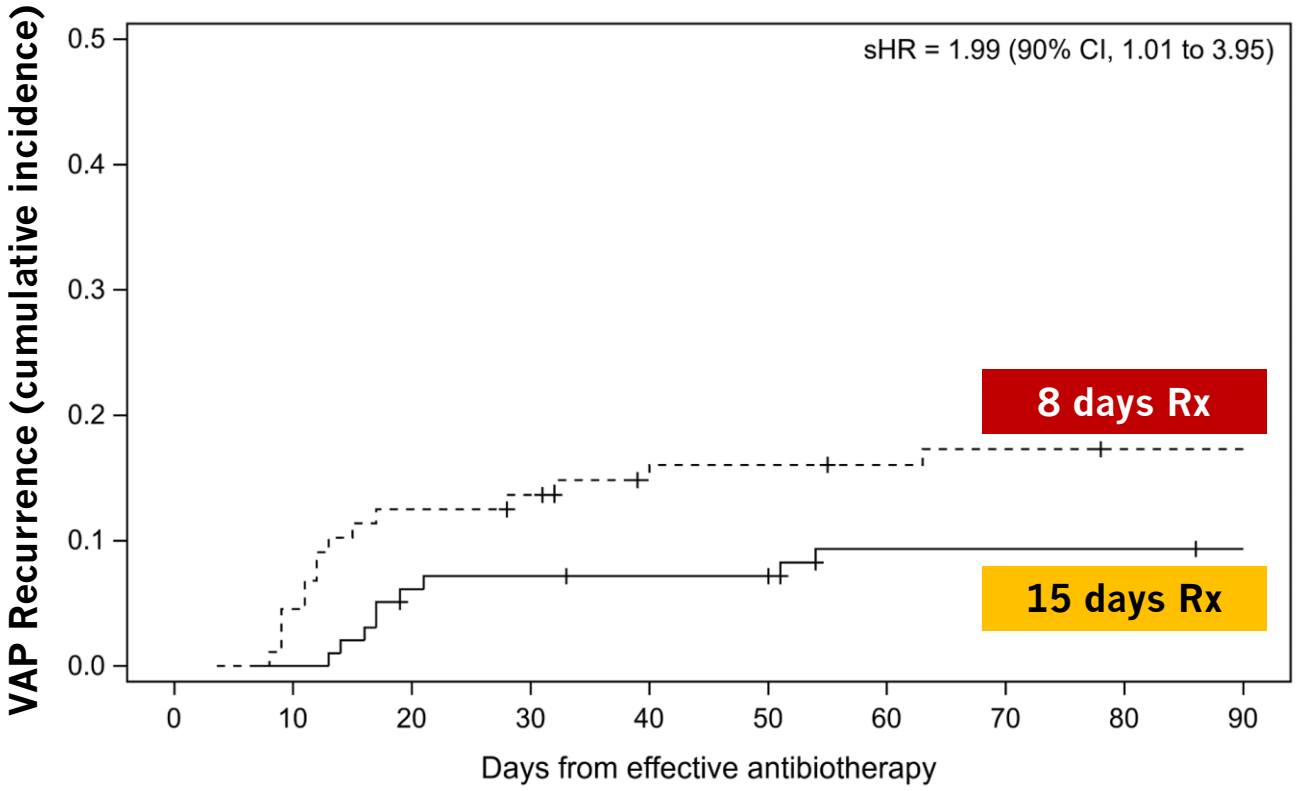


Chastre, *JAMA* 2003;290:2588-2598

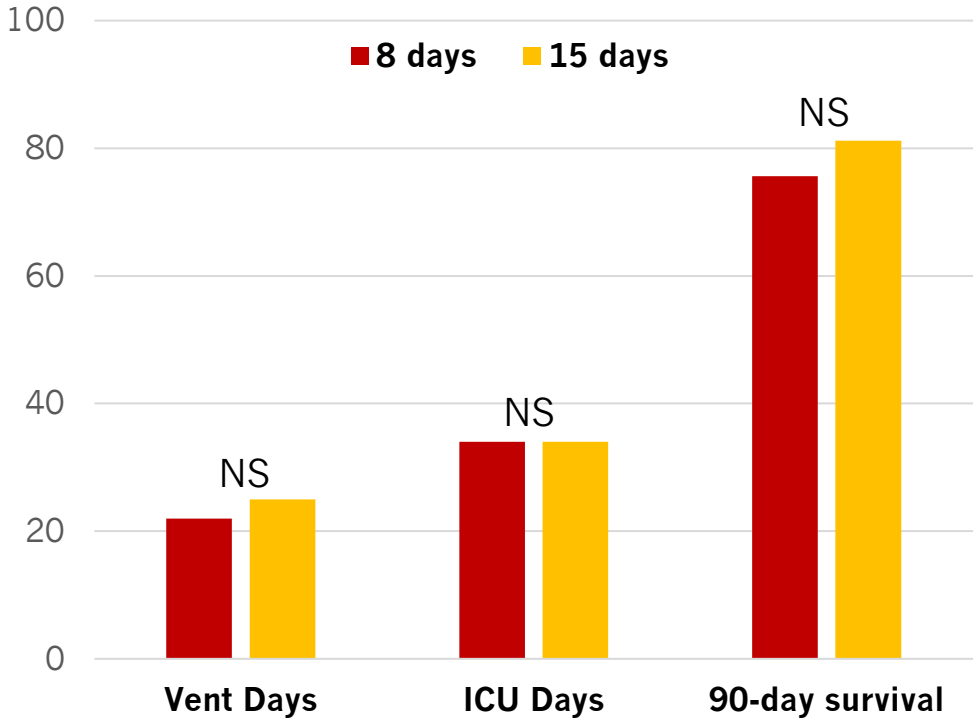
What about Pseudomonas???

186 patients with VAP due to non-fermenting gram negatives randomized to 8 vs 15 days of antibiotics

Recurrent Pneumonia



Length of Stay and Mortality

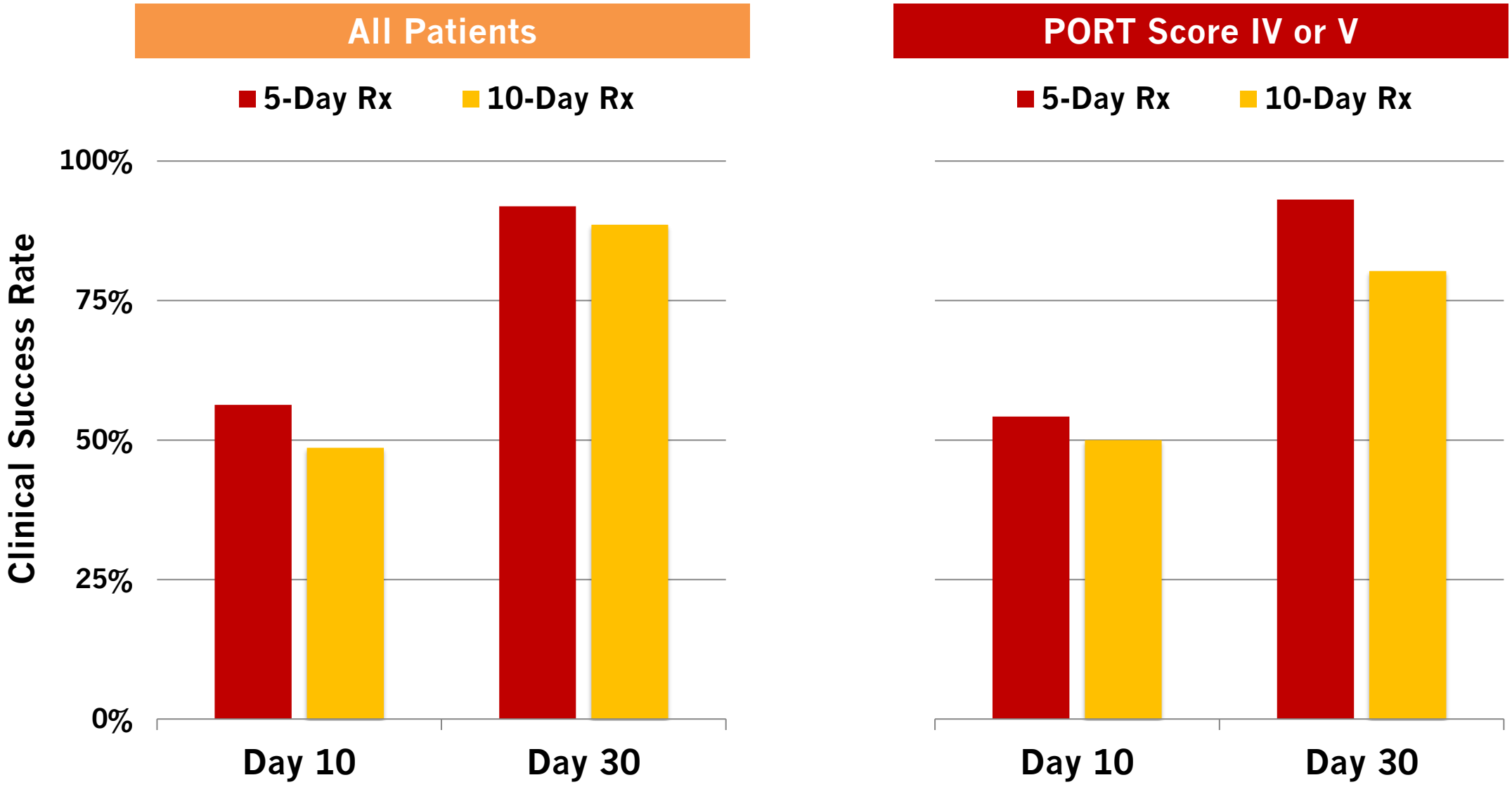


Bougle, *Intensive Care Med* 2022;48:841-848

Is less than 8 days feasible?

5 vs 10 Days for Community Acquired Pneumonia

Randomized controlled trial, 312 patients, 4 hospitals in Spain



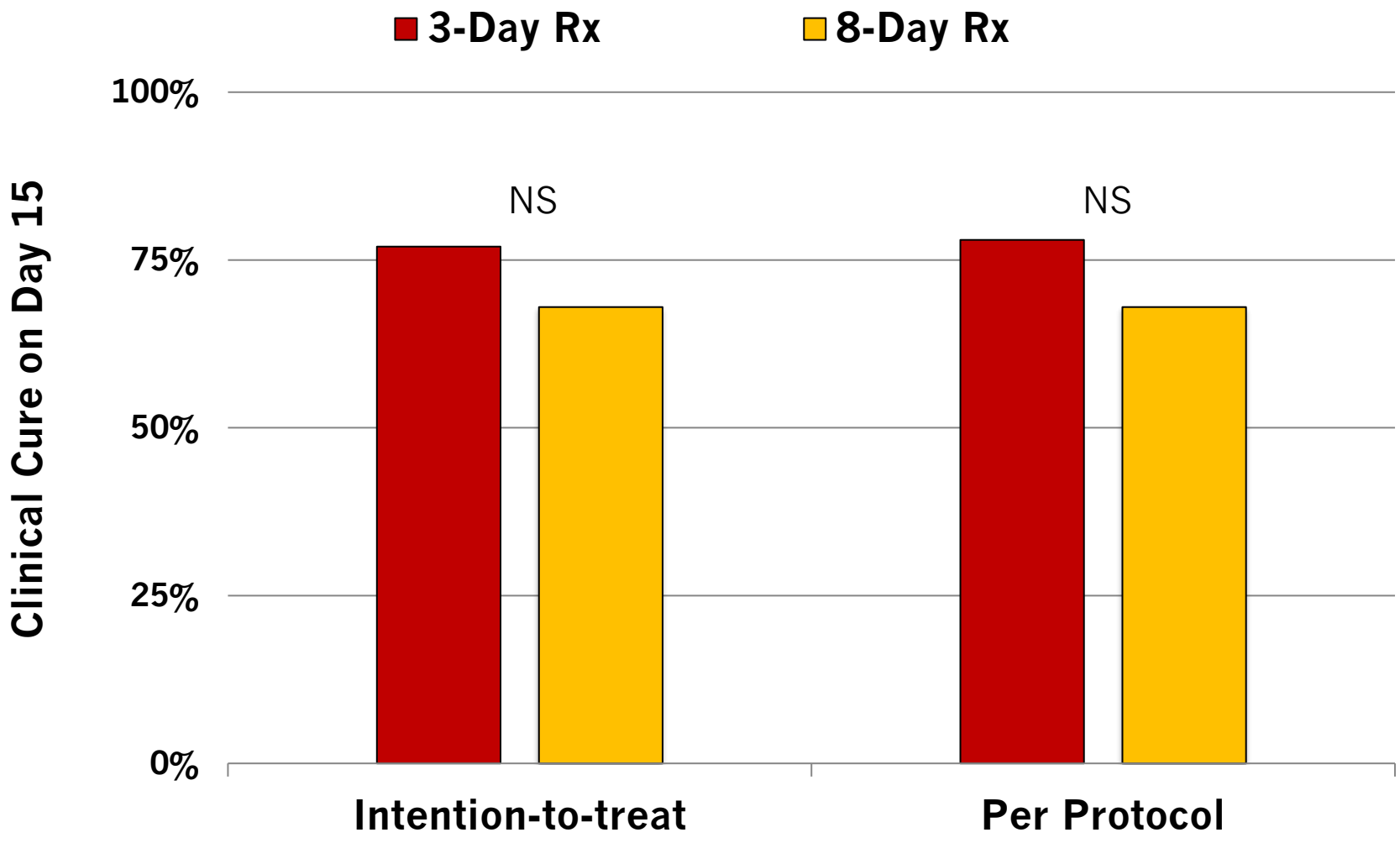
Uranga, JAMA Internal Medicine 2016;176:1257-1265

Is less than 5 days feasible?

Image: www.she.stir.ac.uk/env-carbon-management/challenge.php

3 vs 8 Days for Community Acquired Pneumonia

Randomized double-blind multicenter trial, 310 patients, 20 hospitals in France



Dinh et al. *Lancet* 2021;397:1195-1203

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Keywords: pneumonia; lower respiratory tract infection; practice guidelines; guideline update

Duration of Treatment:

(in patients who have stabilized)

Non-severe CAP:

<5 days of antibiotics

- minimum 3 days
- conditional recommendation

Severe CAP:

≥5 days of antibiotics

- strong recommendation

Contraindications to shorter courses:
bronchiectasis, necrotizing pneumonia, empyema, resistant or necrotizing organisms such as Staphylococcus aureus or Pseudomonas aeruginosa

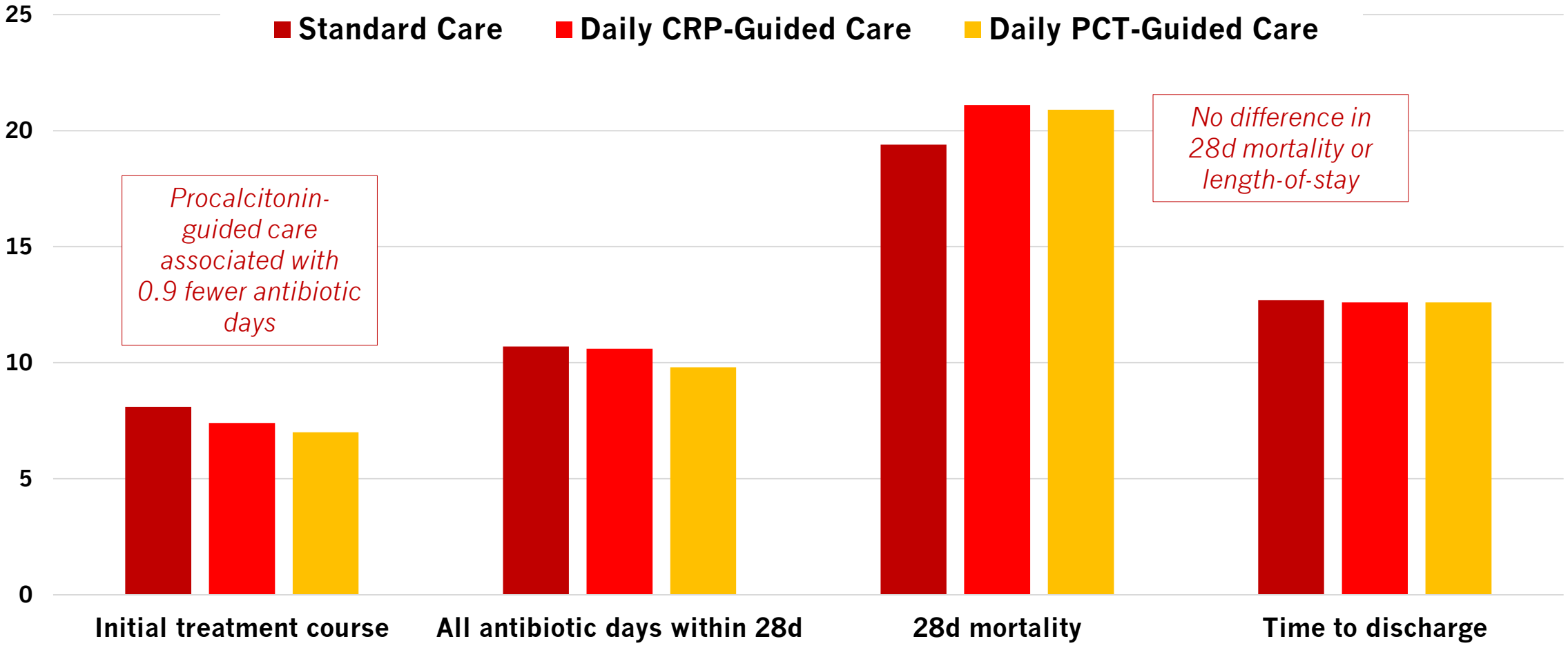
Could procalcitonin help?

A. Yes

B. No

Biomarker Guided Antibiotic Duration

2760 critically ill patients with suspected sepsis randomized to daily procalcitonin, CRP, or usual care to guide antibiotic duration, double-blinded, 41 ICUs in the United Kingdom, 2018-2024



Dark, *JAMA* 2025;333:682-693

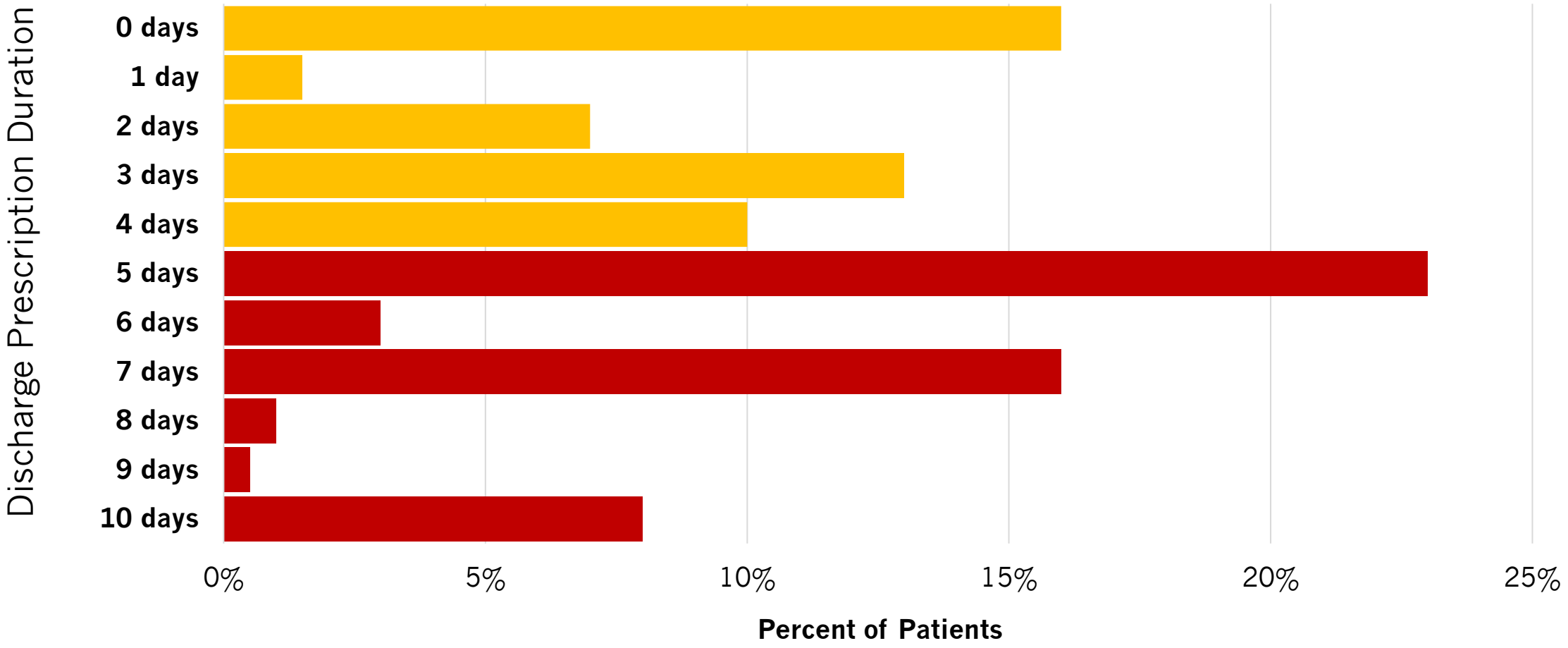
How many days of antibiotics does the patient need after discharge?

Typical Discharge Prescription Durations

6,481 patients treated for pneumonia in 43 Michigan hospitals

68% Overtreated. Discharge antibiotics accounted for 93% of unnecessary antibiotic days

Each additional day of treatment associated with 5% increase in risk of adverse events



Vaughn, *Ann Intern Med* 2019;171:153-163

Summary

- Diagnosing pneumonia is challenging. **We're often wrong.** CT may help.
- Many (?most) pneumonias are caused by **viruses.** Test for them.
  Most patients with viruses are **NOT** coinfected
- **Atypical coverage** most important for patients with severe disease or compromised immune systems.
- Consider **steroids** in patients with **severe CAP (ICU) with elevated CRP within 24h of arrival**
- **Short course regimens (3-5 days) usually adequate**. Serial procalcitonin measures may enable shorter courses. **Don't reset the clock at discharge!**

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Thank You!

For all the
lives we touch

Clean hands protect our patients.

Always perform hand hygiene
and help others do the same.

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THE LIVES WE TOUCH

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