ATS/IDSA Guidelines for Community Acquired Pneumonia in Adults

Joshua P. Metlay, MD, PhD

April 2022

MASSACHUSETTS GENERAL HOSPITAL
DIVISION OF GENERAL INTERNAL MEDICINE

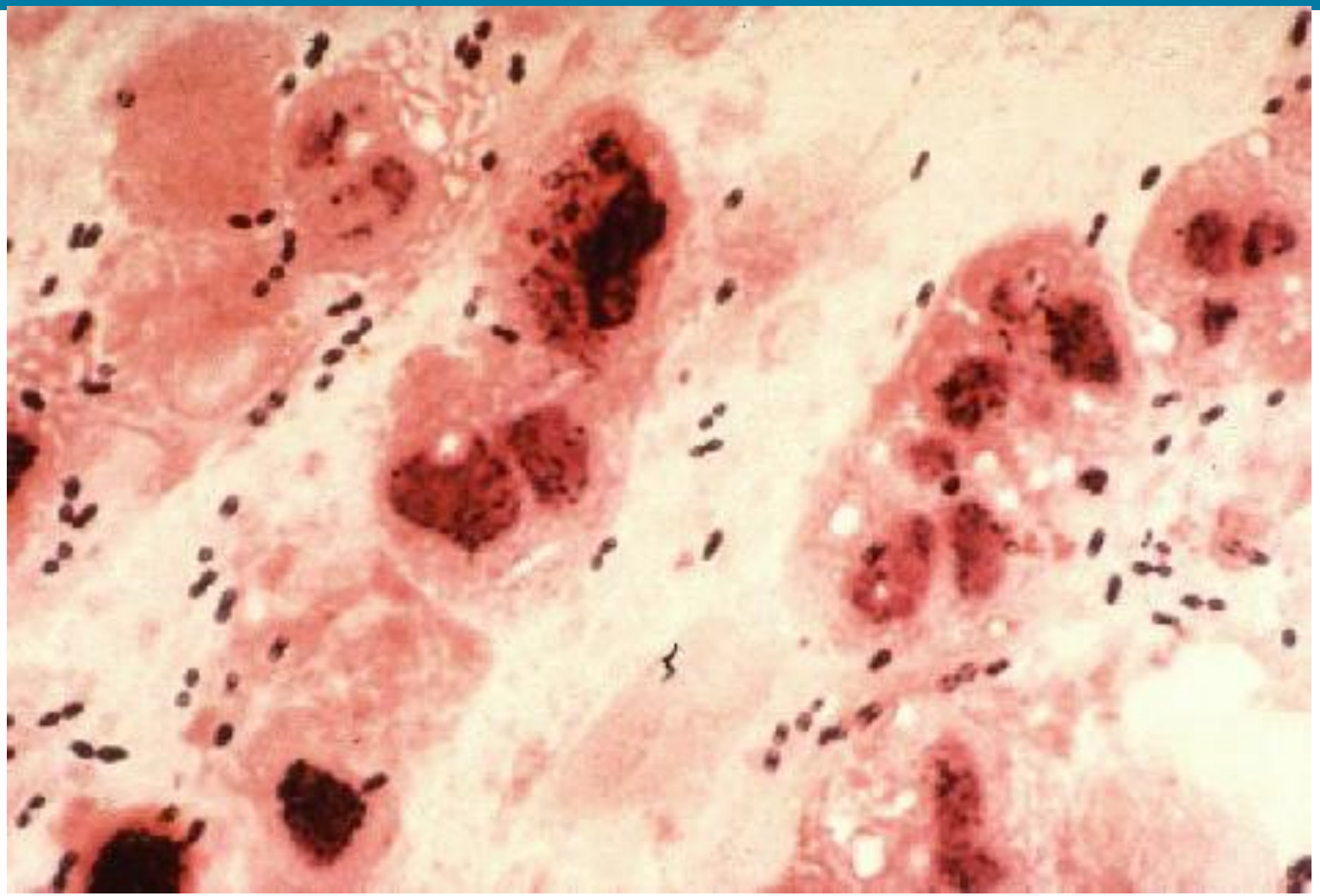
Disclosure

In accord with the disclosure policy of the Mass General Brigham HealthCare System as well as standards set forth by the Accreditation Council on Continuing Medical Education, speakers, I, my spouse or partner, do not have any relationship to companies producing pharmaceuticals, medical equipment or devices.

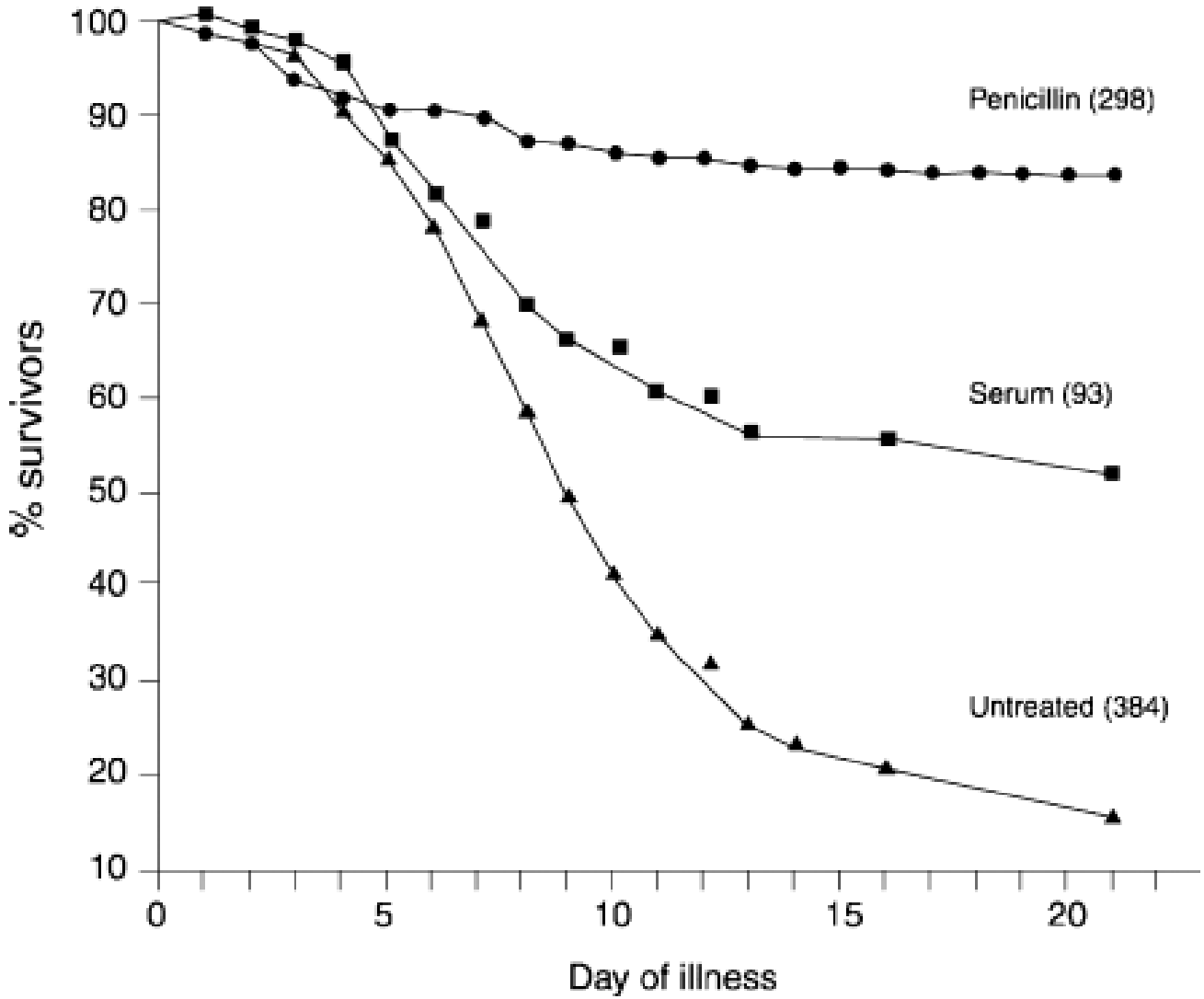
Learning Objectives

- Understand the process of creating a clinical practice guideline for pneumonia
- Review updates to the ATS/IDSA Community-Acquired Pneumonia in Adults practice guideline in diagnostics and therapeutics
- Identify management challenges created by the COVID-19 pandemic

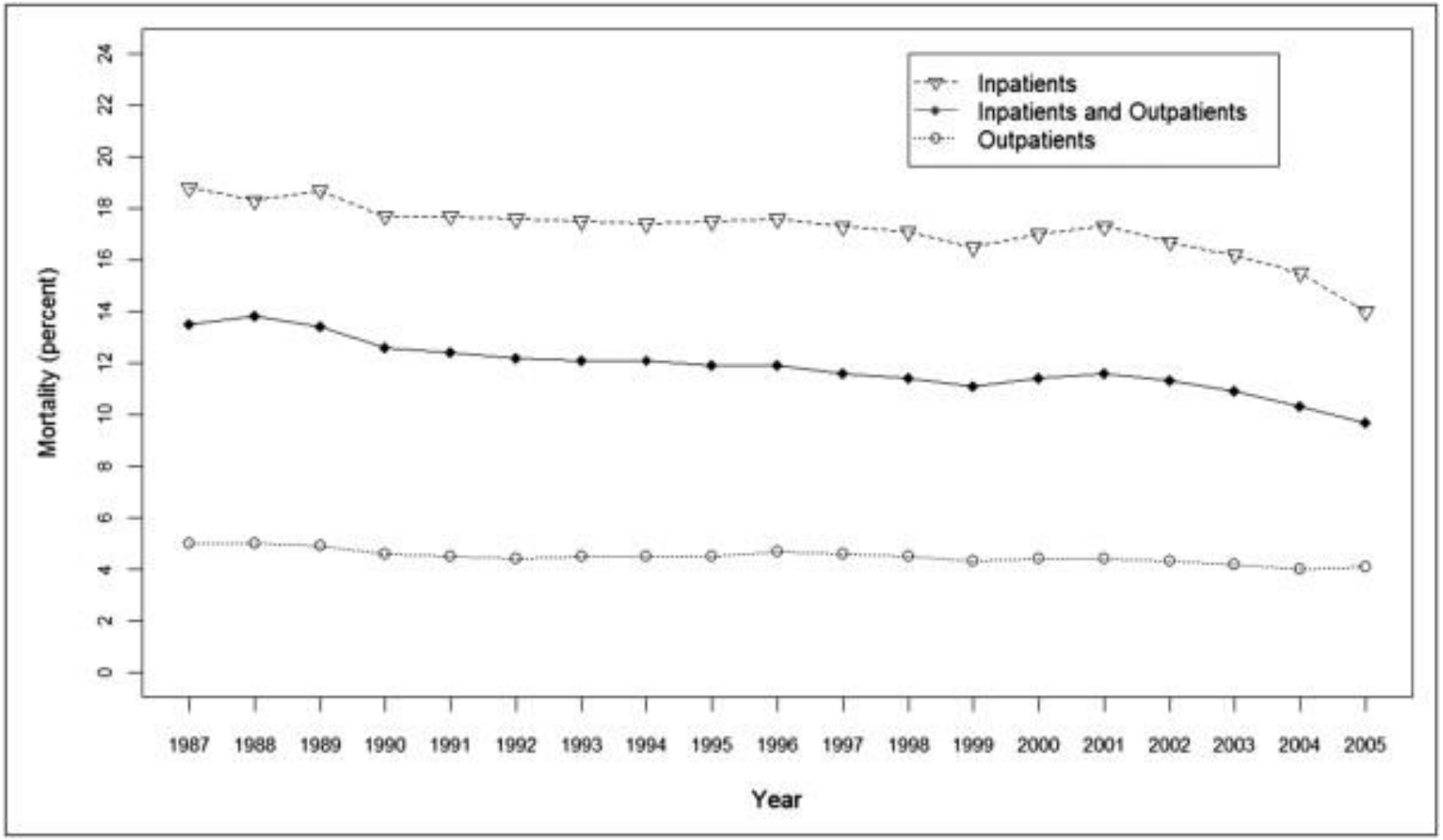
The Good Old Days



Survival from pneumococcal bacteremia 1952-1962



CAP Remains a Serious Illness



Ruhnke. AJM 2011

CAP GUIDELINE CIRCA 2007

Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults

Lionel A. Mandell,[1,a] Richard G. Wunderink,[2,a] Antonio Anzueto,[3,4] John G. Bartlett,[7] G. Douglas Campbell,[8] Nathan C. Dean,[9,10] Scott F. Dowell,[11] Thomas M. File, Jr.[12,13] Daniel M. Musher,[5,6] Michael S. Niederman,[14,15] Antonio Torres,[16] and Cynthia G. Whitney[11]

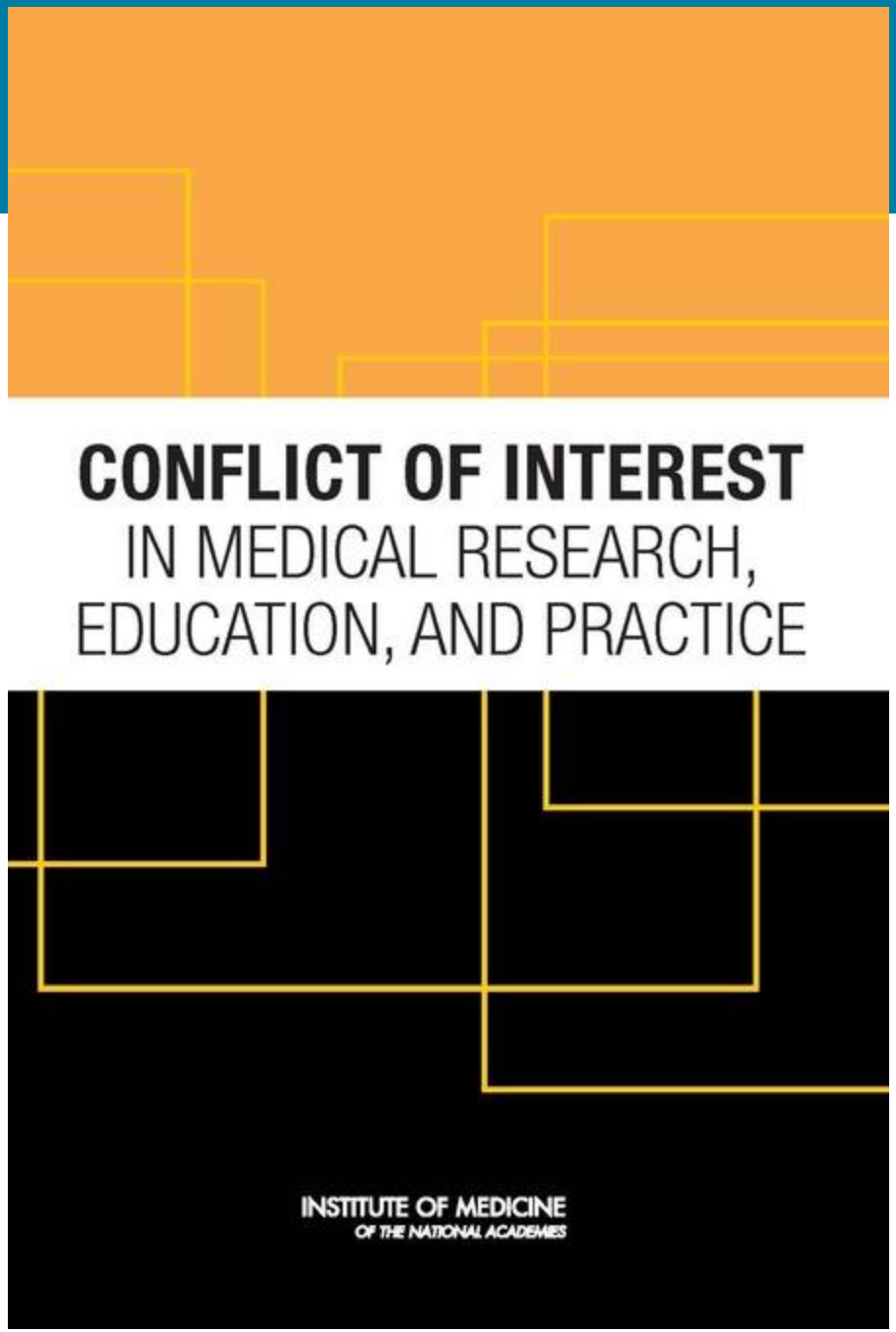
UPDATING THE GUIDELINE TAKES 12 YEARS

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


CONFLICT OF INTEREST
IN MEDICAL RESEARCH,
EDUCATION, AND PRACTICE
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

RECOMMENDATION 7.1 Groups that develop clinical practice guidelines should generally exclude as panel members individuals with conflicts of interest and should not accept direct funding for clinical practice guideline development from medical product companies or company foundations. Groups should publicly disclose with each guideline their conflict of interest policies and procedures and the sources and amounts of indirect or direct funding received for development of the guideline.

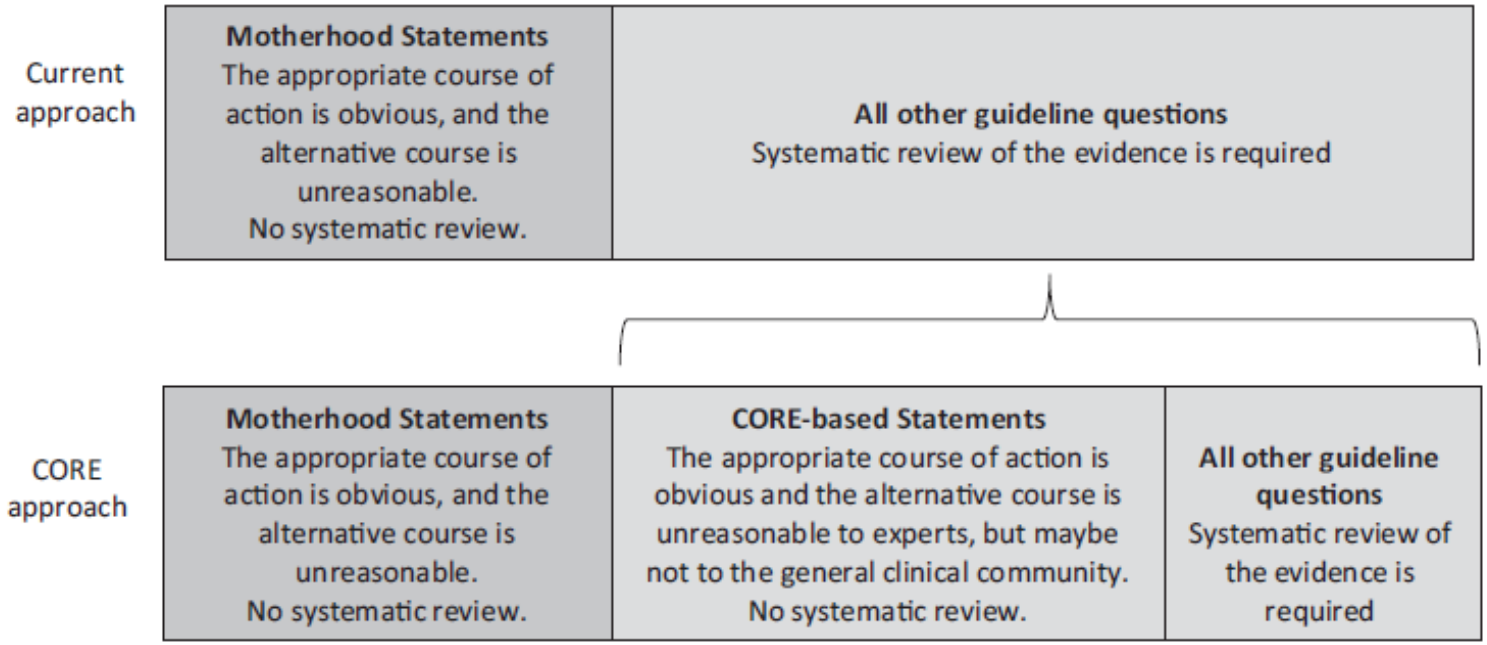
GRADE

- Systematic retrieval
- Meta-analytic summary when possible
- Grading of Recommendations: Assessment, Development, and Evaluation
  - Risk of bias
  - Precision
  - Consistency
  - Directness of Evidence
  - Magnitude of Effect

Recommendations

- Quality of Evidence
  - High, Moderate, Low, Very low
- Strength of Recommendation
  - Strong
  - Conditional
- Consensus voting

GUIDELINE PROCESSES IN THE FUTURE



Wilson et al. Clinical Infectious Diseases.2020

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

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DIAGNOSIS

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QUESTION 1

- A 53-year-old, otherwise healthy patient presents with 5 days of cough develops worsening sputum production and fever to 101. He has had 2 negative PCR tests for SARS CoV-2. A chest radiograph demonstrates a right middle lobe infiltrate. Vital signs are stable. A procalcitonin value is < .2 ng/ml. In the absence of other laboratory results, should you:

A. Order sputum gram stain and culture and then decide on antibiotics

B. Empirically prescribe guideline concordant antibiotics

C. Withhold antibiotics with a plan for close 24-48 hour follow-up.

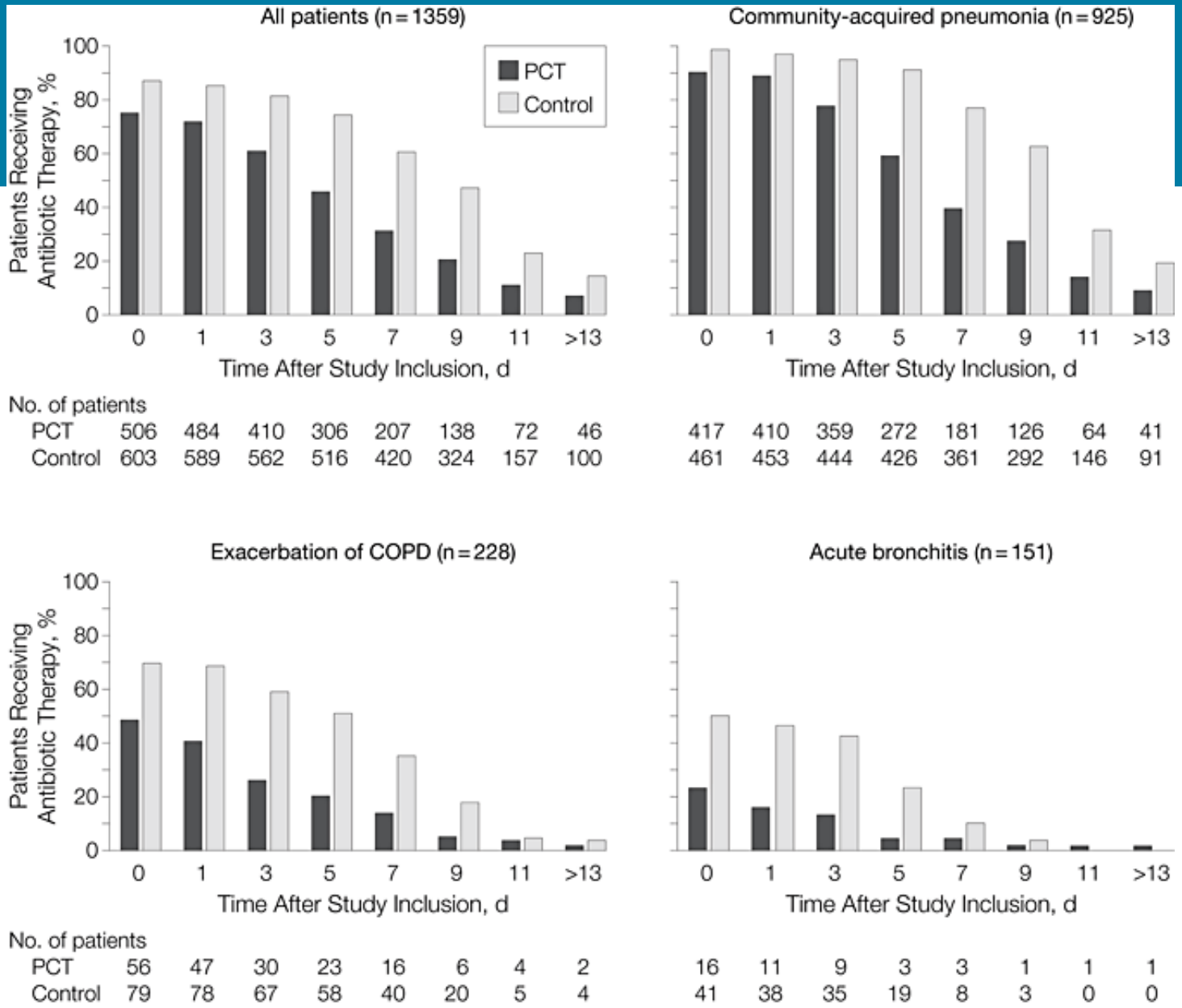
Should you measure procalcitonin?

2007

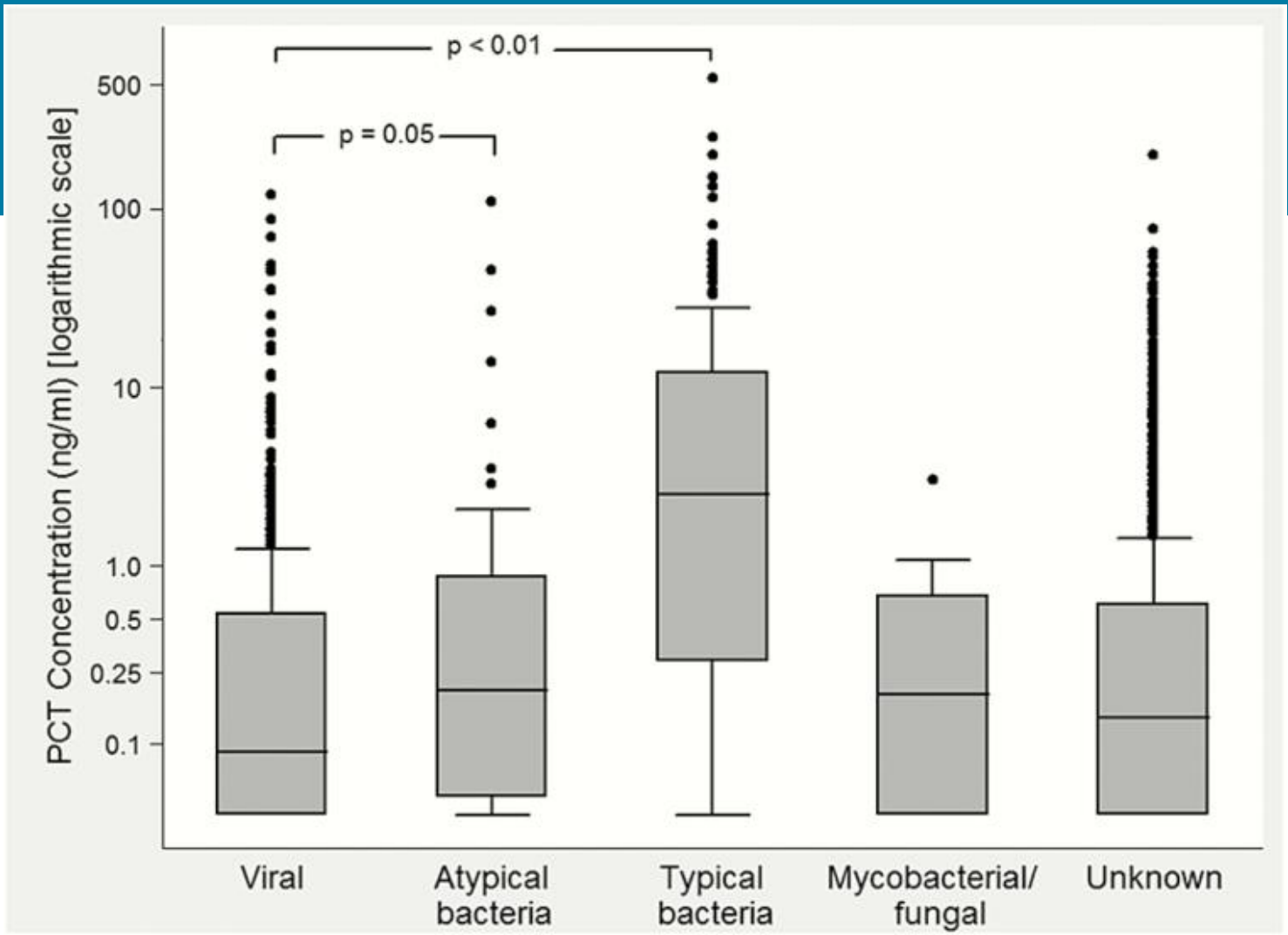
- No mention of procalcitonin

2019

- Don’t use for initial treatment decision
- Only measure serially if planned duration of treatment is > 5-7 days



Schuetz.JAMA.2009



	Viral	Atypical bacteria	Typical bacteria	Mycobacterial/ fungal	Unknown
n patients	409	67	169	15	1,075
PCT median (ng/ml)	0.09	0.20	2.5	0.19	0.14
PCT IQR (ng/ml)	<0.05, 0.54	<0.05, 0.87	0.29, 12.2	<0.05, 0.68	<0.05, 0.61

Self.CID.2017

HOW CAN AN ID GUIDELINE BE SO NIHILISTIC ABOUT PATHOGEN TESTING?

- The guideline is driven by patient outcomes not microbiological results or epidemiological knowledge
- Very few RCTs of diagnostic tests with patient outcomes
- Empiric antibiotic therapy is very effective
- Except for influenza, what we mostly miss are BENIGN viral pathogens (or so we thought)

TREATMENT

What to use for outpatient therapy

2007

- Macrolides monotherapy is first line for outpatients
- Beta-lactam monotherapy not recommended

2019

- Macrolides no longer first line if local resistance is > 25%
- Beta-lactam monotherapy (amoxicillin) is recommended for uncomplicated CAP

RISING PNEUMOCOCCAL RESISTANCE

Topic

Antibiotic resistance

Year ☐ Single year

From

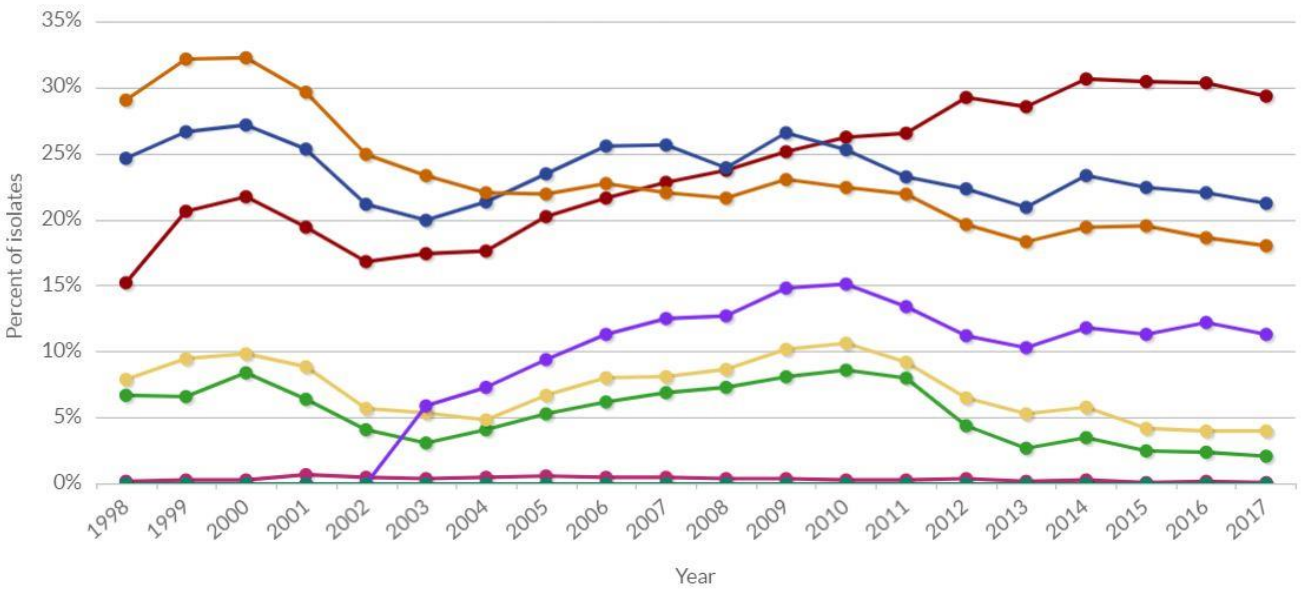
1998

To

2017

- ☑ Cefotaxime[4]
- ☑ Erythromycin
- ☑ Levofloxacin
- ☑ Penicillin[1]
- ☑ Penicillin[2]
- ☑ Tetracycline[3]
- ☑ TMPsulfa

Percent of invasive *Streptococcus pneumoniae* isolates that were resistant* to select antibiotics in ABCs areas



*Resistant includes those isolates intermediate or fully resistant to antibiotics tested.

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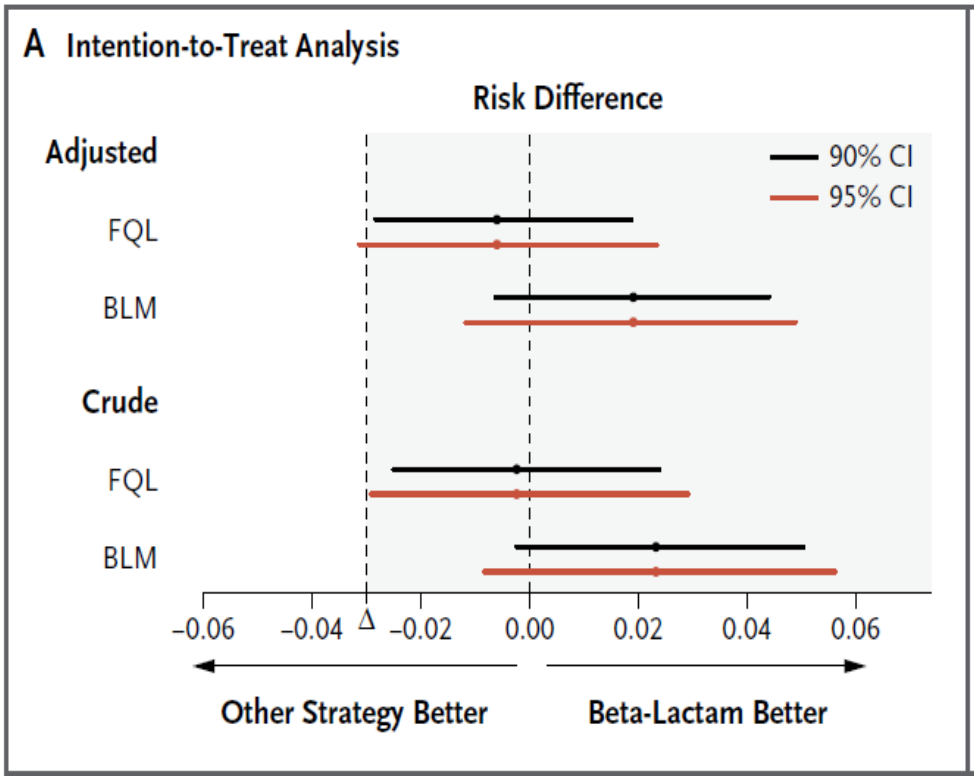
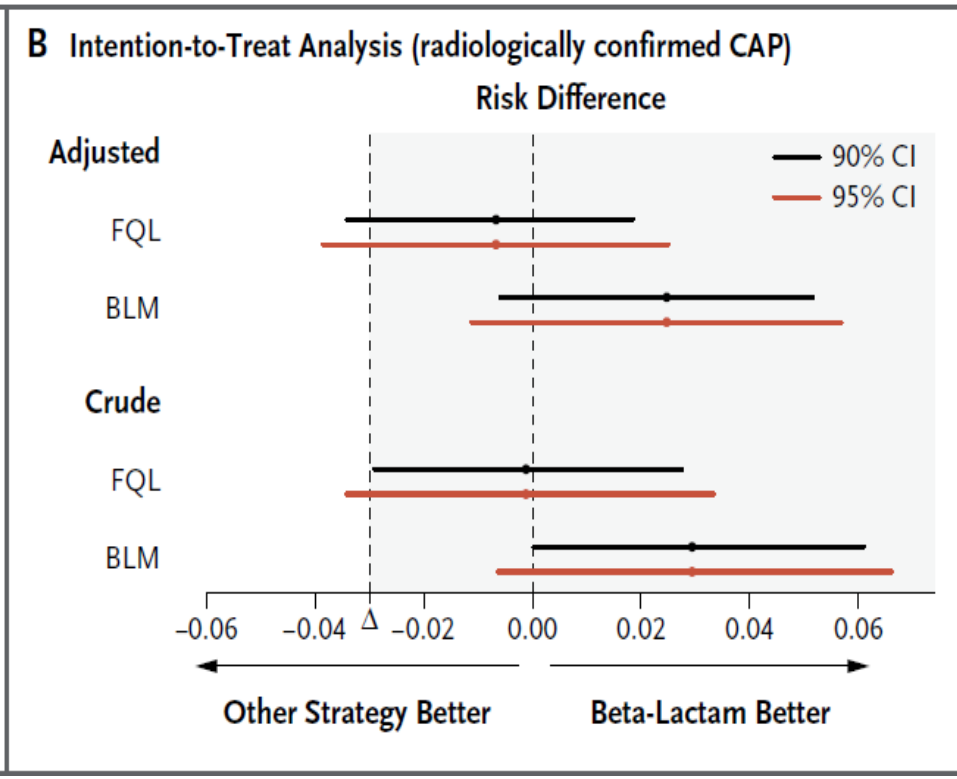
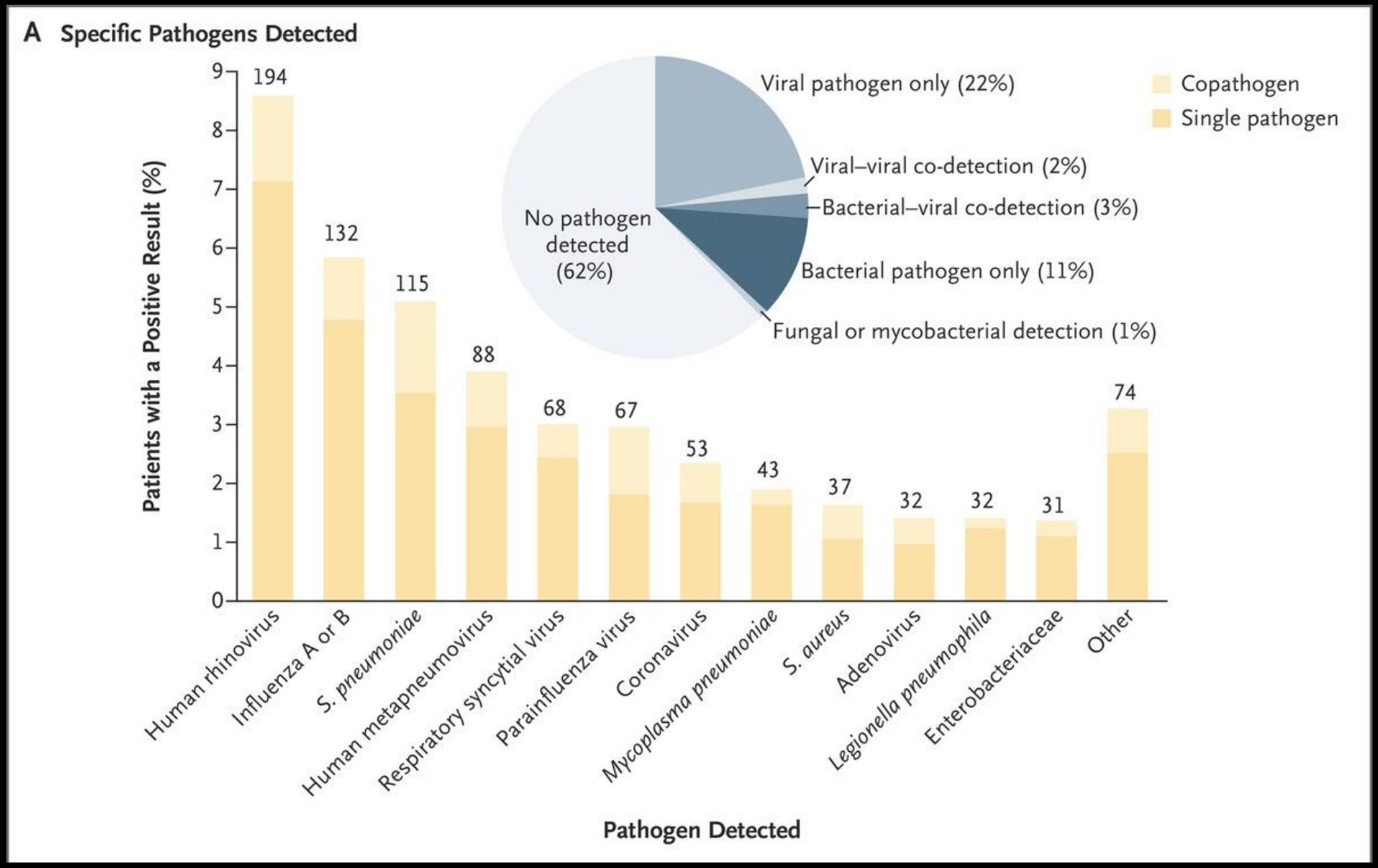


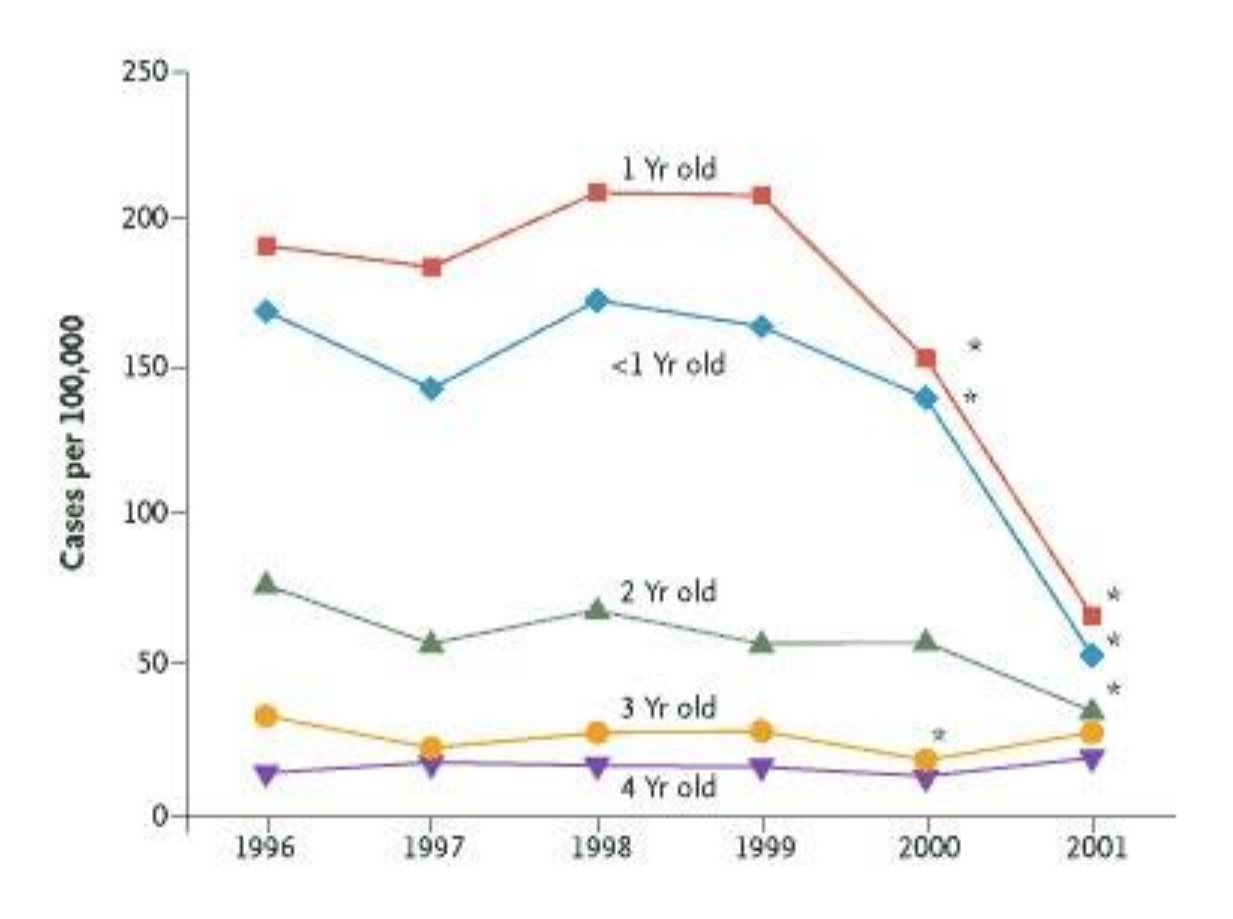


Postma. NEJM.2015



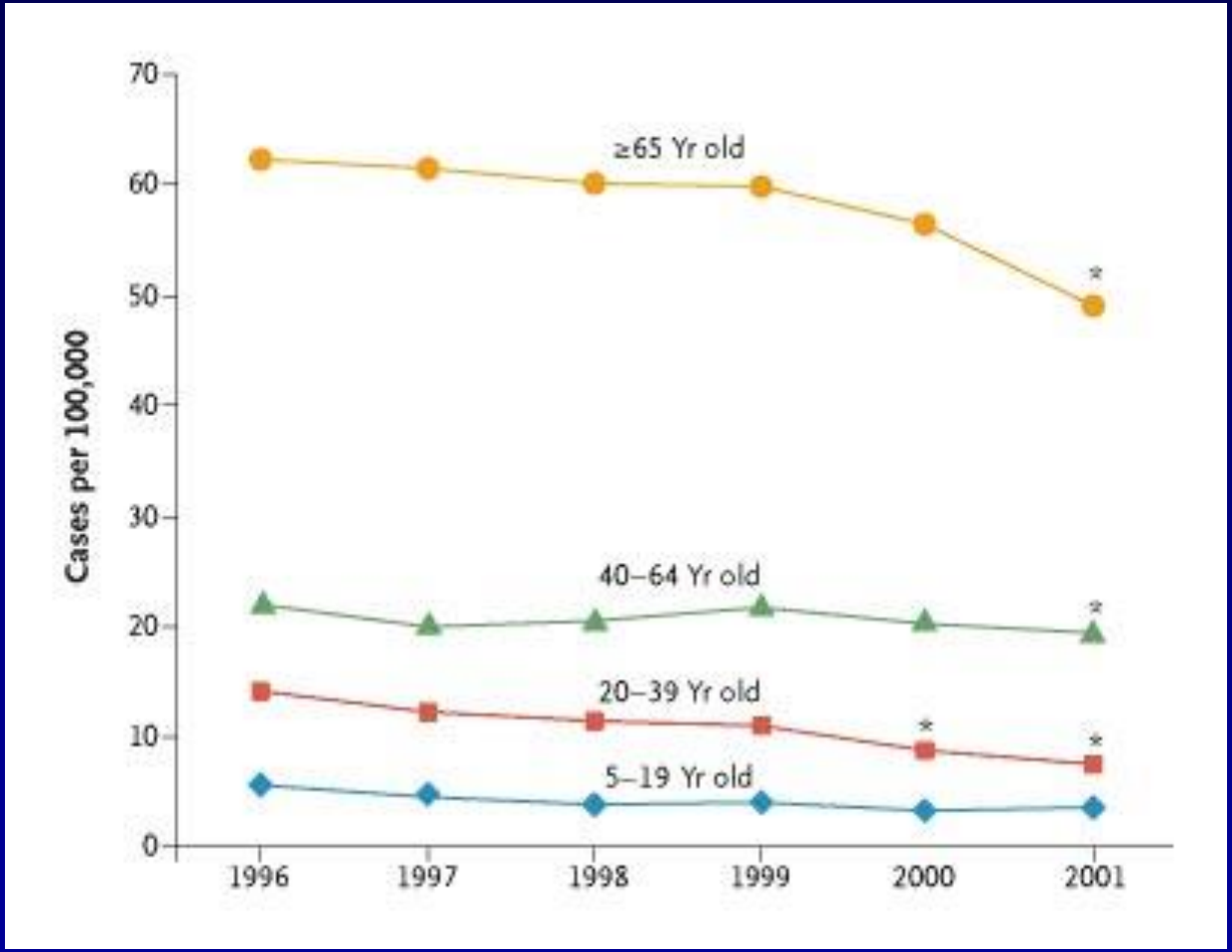
Jain S et al. N Engl J Med 2015;373:415-427.

Declining risk of invasive pneumococcal disease: children

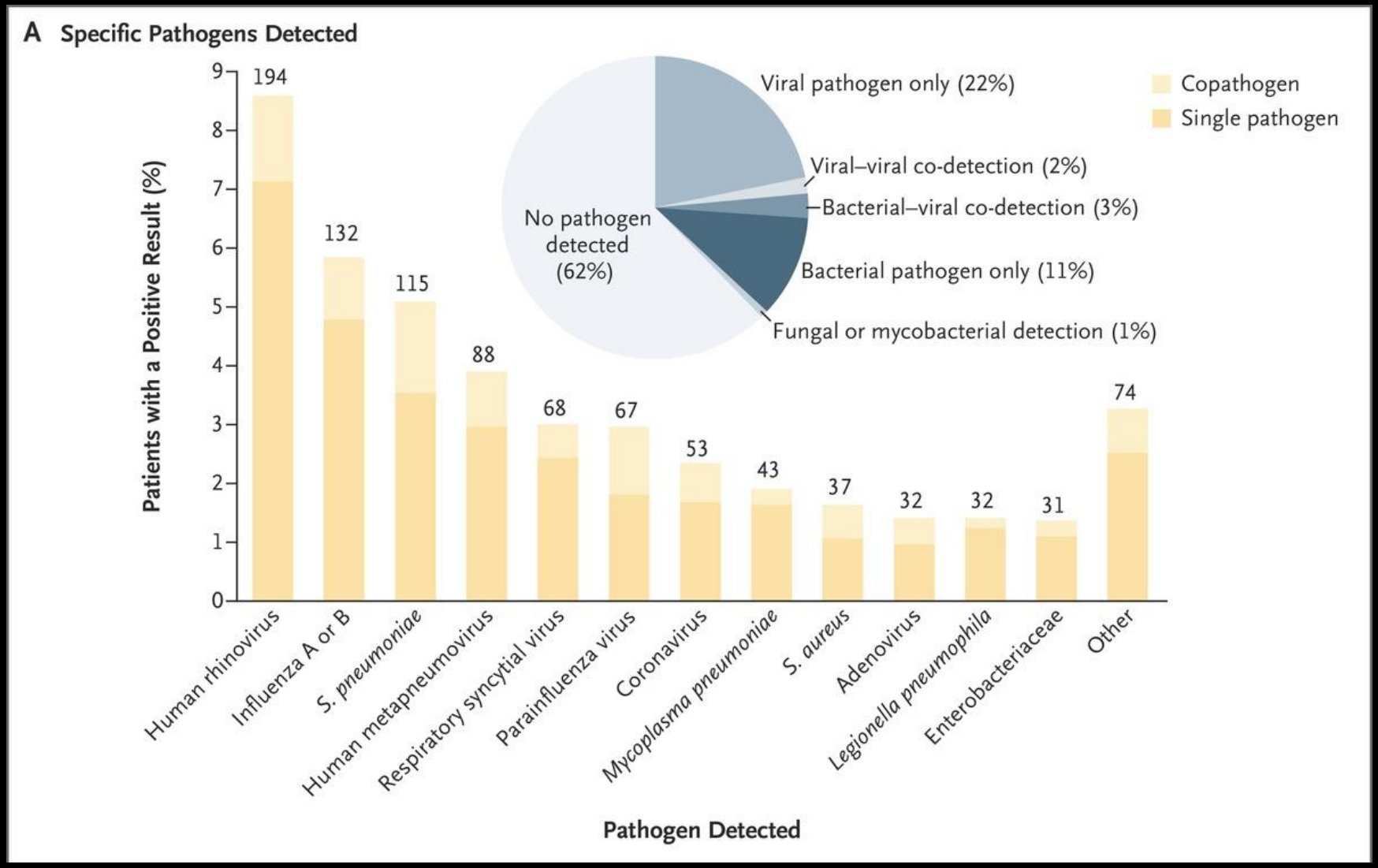


Whitney. NEJM. 2003

Declining risk of invasive pneumococcal disease: adults



Whitney. NEJM. 2003



Jain S et al. N Engl J Med 2015;373:415-427.

What to do about influenza

2007

- Oseltamivir for uncomplicated influenza if symptoms < 48 hours
- Treat with oseltamivir regardless of duration of symptoms if pneumonia present.

2019

- Same
- Initially treat with antibacterial drugs too
- Role for PCT?

QUESTION 2

- A 67-year-old with a history of hypertension and hyperlipidemia presents with rapid onset of dyspnea, fever and productive cough. He was admitted to the hospital for knee replacement 3 months ago. He is mildly tachypneic with O2 sat of 88% on room air, corrected with 2 L NC. Chest radiograph demonstrates left lower lobe consolidated pneumonia. He is admitted to the hospital. Treatment choices:

A. Ceftriaxone alone

B. Ceftriaxone plus azithromycin

C. Levofloxacin

D. Vancomycin plus ceftriaxone plus azithromycin

What happened to HCAP?

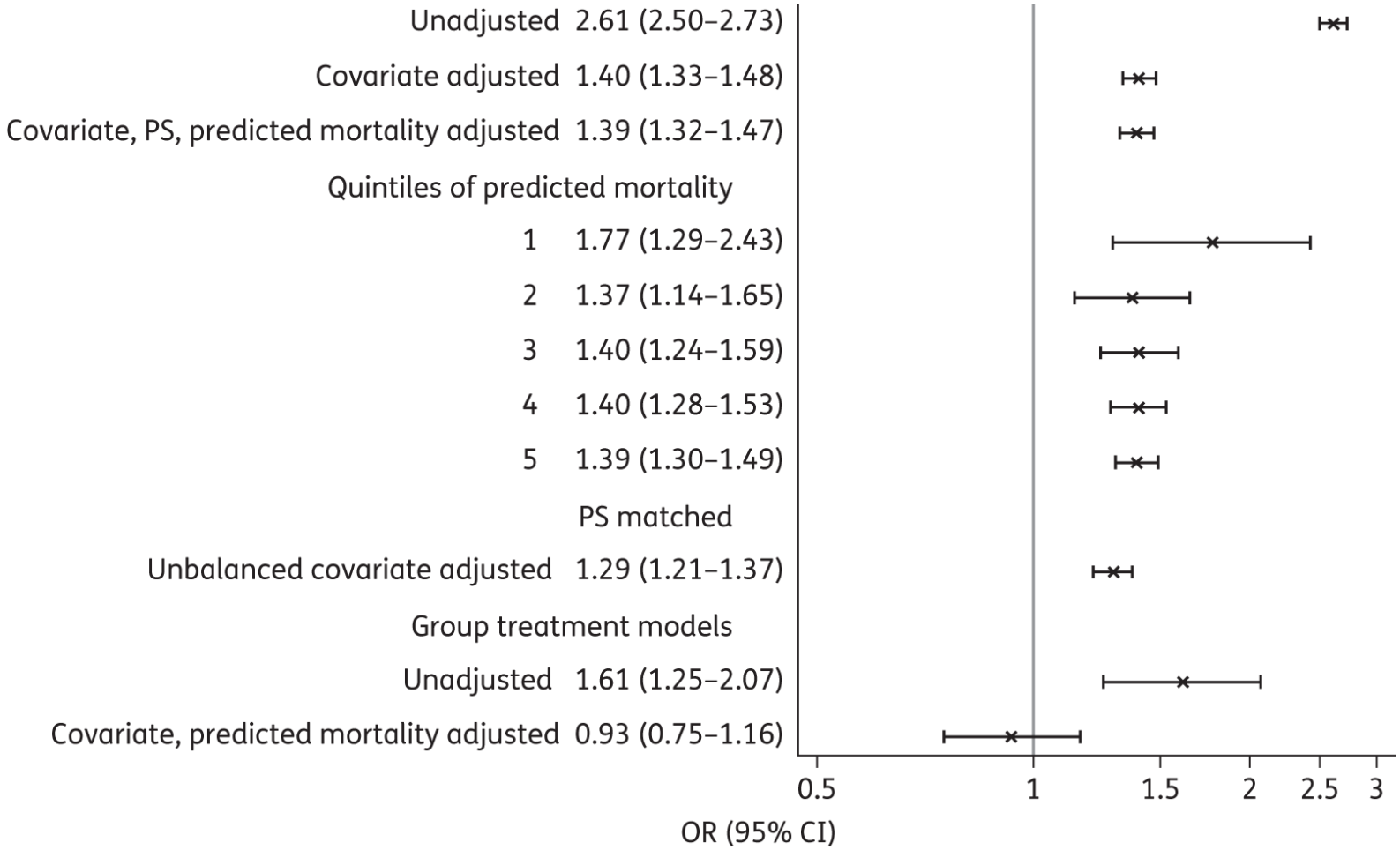
2007

- Endorsed HCAP as a category
  - Nursing home residence
  - HD
  - Home iv antibiotics
  - Hospitalization in last 90 days
  - Home wound care
  - Household member with MDR infection

2019

- Eliminate HCAP as a category
  - Empiric treatment for MRSA and P. aeruginosa based on prior culture data
  - Always get cultures if treatment initiated
  - De-escalate if cultures are negative (including MRSA nasal swab)

HCAP Treatment Associated with Worse Outcomes



Rothberg, JAC 2015

Should I worry about drug resistance?

Outpatients

- Antibiotic resistant *S. pneumoniae*
  - Macrolides
- Beta-lactamase producing H flu
- MRSA

Inpatients

- Antibiotic resistant *S. pneumoniae*
- MRSA
- *P. aeruginosa* and other enteric pathogens

Table 4. Initial Treatment Strategies for Inpatients with Community-acquired Pneumonia by Level of Severity and Risk for Drug Resistance

	Standard Regimen	Prior Respiratory Isolation of MRSA	Prior Respiratory Isolation of *Pseudomonas aeruginosa*	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for *P. aeruginosa*
Nonsevere inpatient pneumonia*	β-Lactam + macrolide† or respiratory fluroquinolone‡	Add MRSA coverage§ and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for *P. aeruginosa*‖ and obtain cultures to allow deescalation or confirmation of need for continued therapy	Obtain cultures but withhold MRSA coverage unless culture results are positive. If rapid nasal PCR is available, withhold additional empiric therapy against MRSA if rapid testing is negative or add coverage if PCR is positive and obtain cultures	Obtain cultures but initiate coverage for *P. aeruginosa* only if culture results are positive
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Definition of abbreviations: ATS = American Thoracic Society; CAP = community-acquired pneumonia; HAP = hospital-acquired pneumonia; IDSA = Infectious Diseases Society of America; MRSA = methicillin-resistant *Staphylococcus aureus*; VAP = ventilator-associated pneumonia.

*As defined by 2007 ATS/IDSA CAP severity criteria guidelines (*see* Table 1).

†Ampicillin + sulbactam 1.5–3 g every 6 hours, cefotaxime 1–2 g every 8 hours, ceftriaxone 1–2 g daily, or ceftaroline 600 mg every 12 hours AND azithromycin 500 mg daily or clarithromycin 500 mg twice daily.

‡Levofloxacin 750 mg daily or moxifloxacin 400 mg daily.

§Per the 2016 ATS/IDSA HAP/VAP guidelines: vancomycin (15 mg/kg every 12 h, adjust based on levels) or linezolid (600 mg every 12 h).

‖Per the 2016 ATS/IDSA HAP/VAP guidelines: piperacillin-tazobactam (4.5 g every 6 h), cefepime (2 g every 8 h), ceftazidime (2 g every 8 h), imipenem (500 mg every 6 h), meropenem (1 g every 8 h), or aztreonam (2 g every 8 h). Does not include coverage for extended-spectrum β-lactamase–producing Enterobacteriaceae, which should be considered only on the basis of patient or local microbiological data.

What do we mean by "severe CAP"

Validated definition includes either one major criterion or three or more minor criteria

Minor criteria

- Respiratory rate ⩾ 30 breaths/min
- Pa_{O2}/F_{IO2} ratio ⩽ 250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (blood urea nitrogen level ⩾ 20 mg/dl)
- Leukopenia* (white blood cell count < 4,000 cells/μl)
- Thrombocytopenia (platelet count < 100,000/μl)
- Hypothermia (core temperature < 36°C)
- Hypotension requiring aggressive fluid resuscitation

Major criteria

- Septic shock with need for vasopressors
- Respiratory failure requiring mechanical ventilation

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Question 3

- The patient from the prior section was started on ceftriaxone plus azithromycin. On Day #2 his O2 requirement goes up to 4 L NC but he is otherwise stable. A repeat SARS-CoV-2 test is negative as are initial blood and sputum cultures. Options include:
  A. Continue current treatment
  B. Start prednisone 40 mg/day
  C. Add vancomycin to cover for MRSA (which you should have done in the first place!)
  D. Order Chest CT

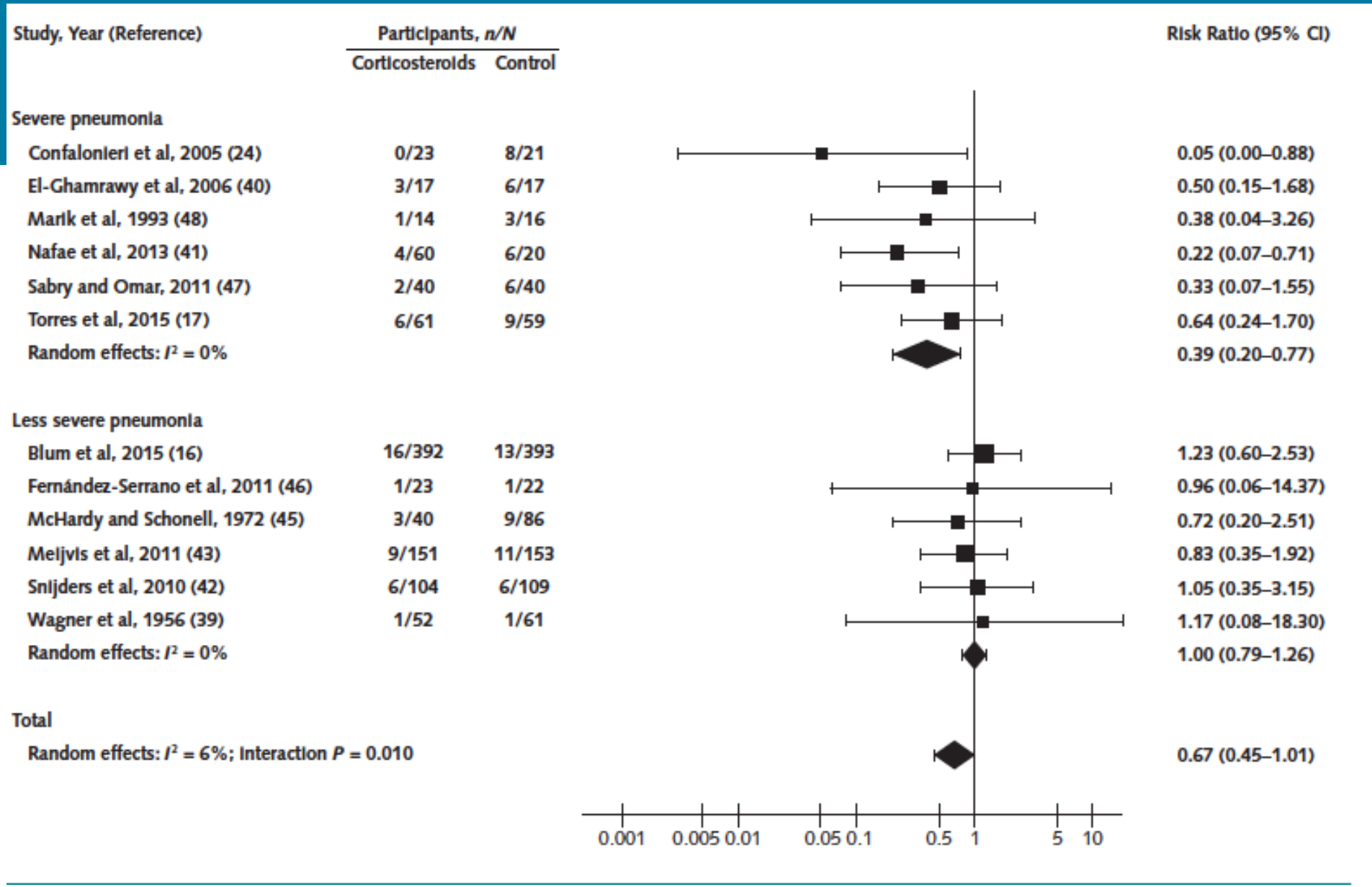
Should I use corticosteroids?

2007

- No mention of corticosteroids

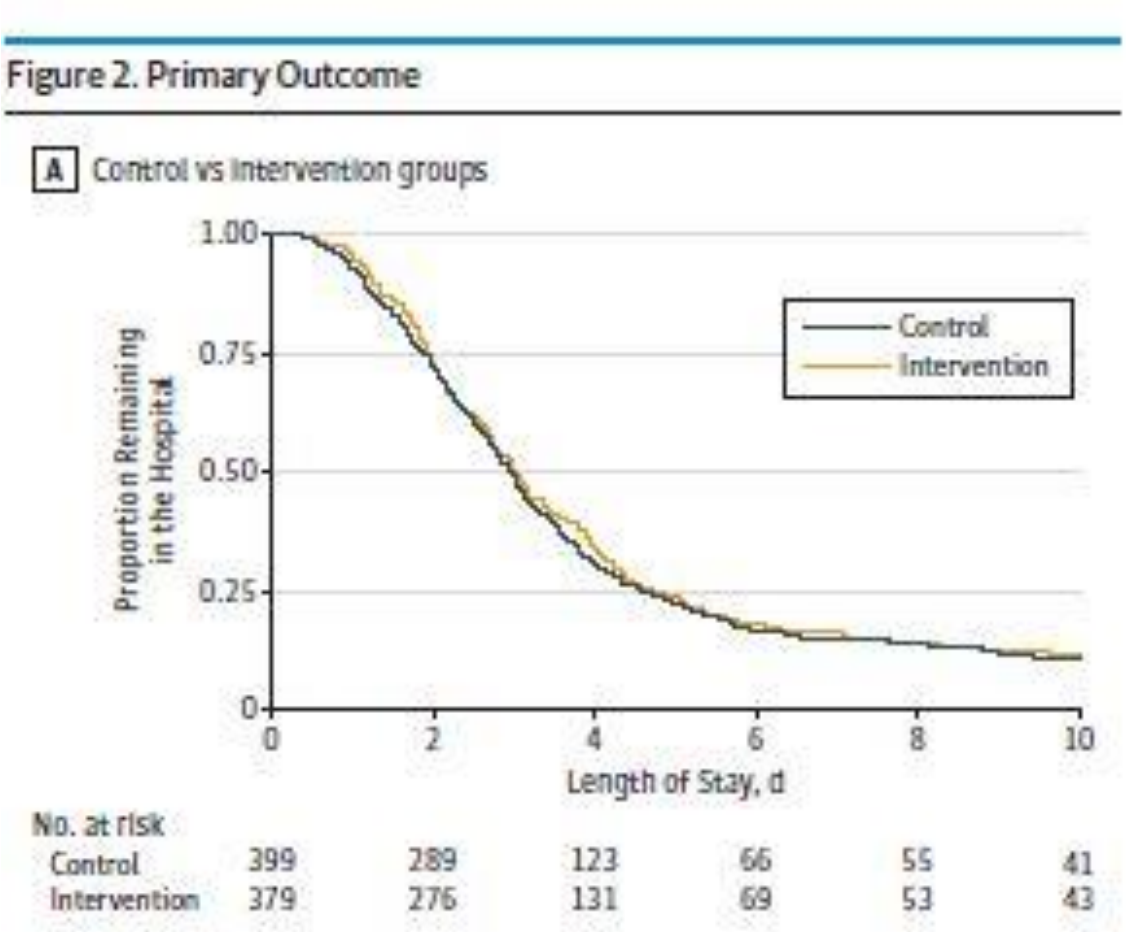
2019

- Don’t routinely use for CAP including severe CAP



Siemieniuk, Annals, 2015

Steroids and CAP

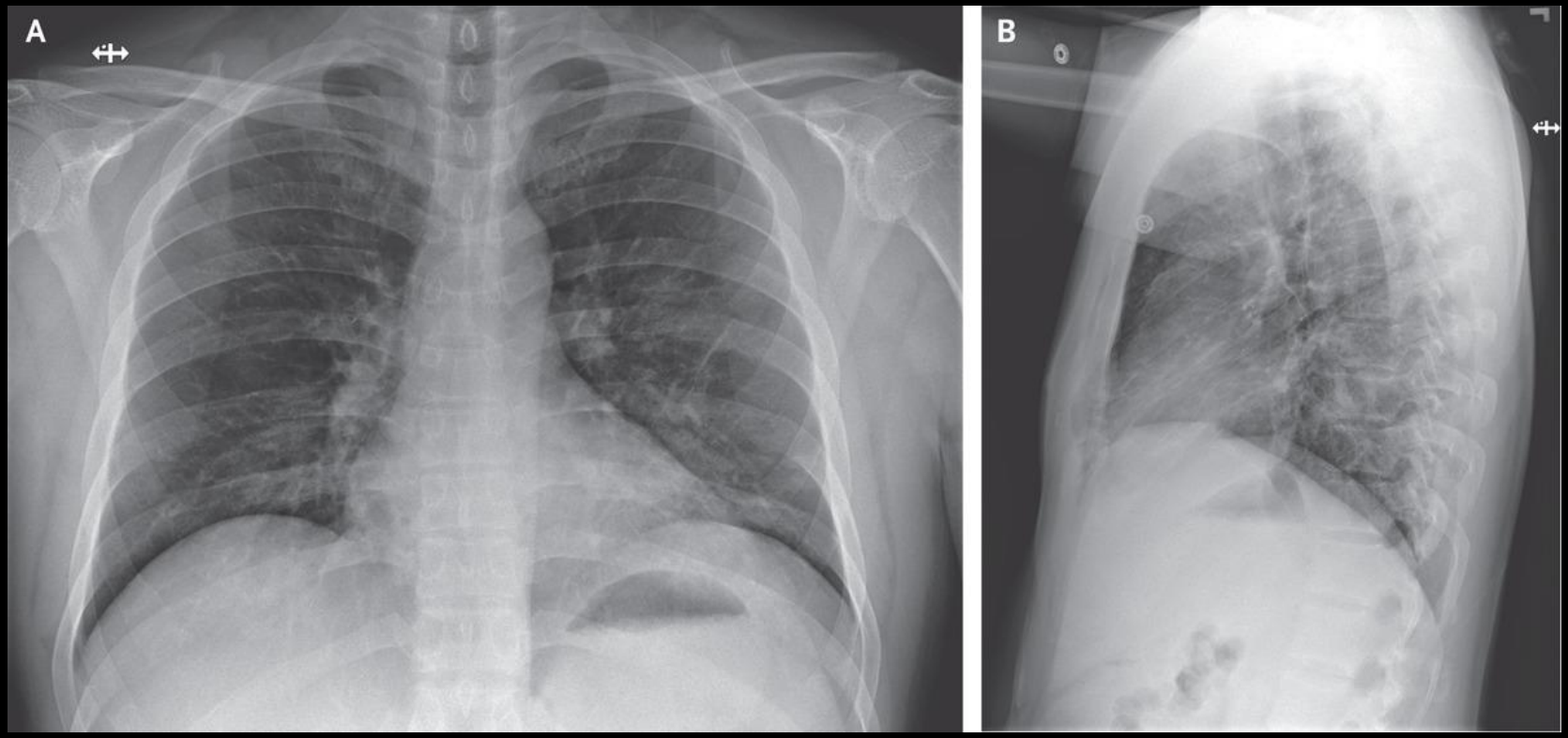


Lloyd, JAMA IM, 2019

AND THEN CAME 2020

MGH 1811 MASSACHUSETTS GENERAL HOSPITAL
DIVISION OF GENERAL INTERNAL MEDICINE

Anteroposterior and Lateral Chest Radiographs, January 26, 2020 (Illness Day 10, Hospital Day 6).



ML Holshue et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2001191

The NEW ENGLAND JOURNAL of MEDICINE

Clinical Infectious Diseases

MAJOR ARTICLE

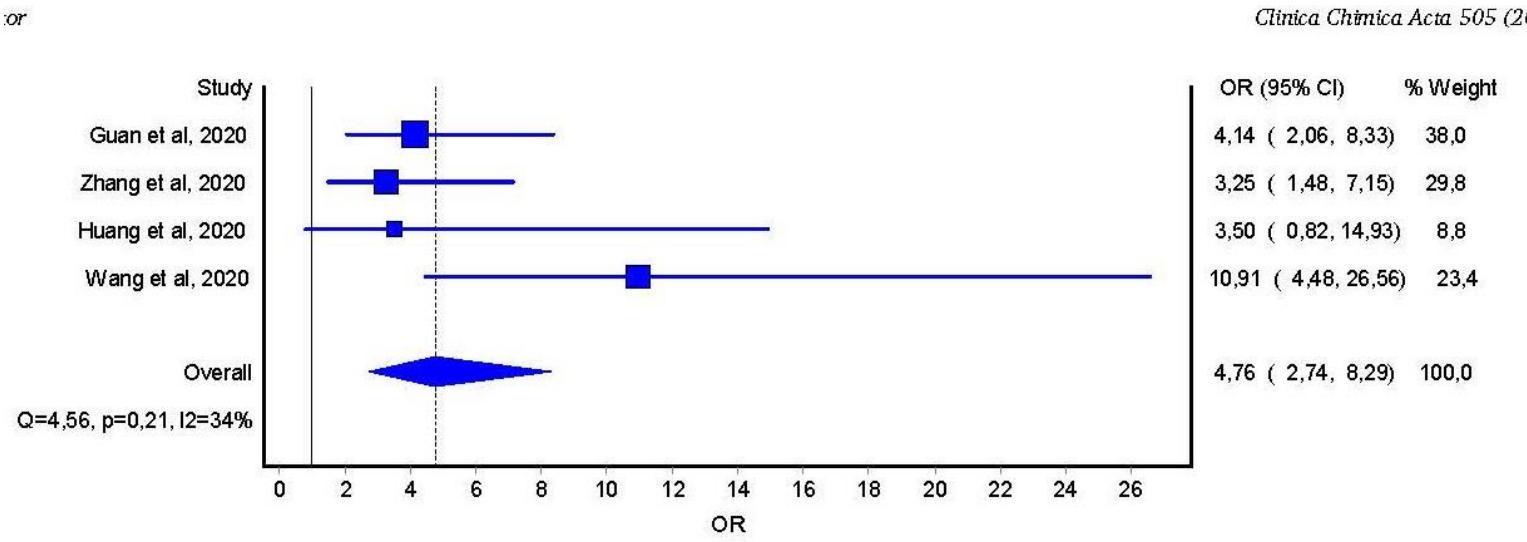
Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing

Timothy M. Rawson,[1,2,3] Luke S. P. Moore,[1,4,5] Nina Zhu,[1] Nishanthy Ranganathan,[3,4] Keira Skolimowska,[3,4] Mark Gilchrist,[3,4] Giovanni Satta,[3,4] Graham Cooke,[3,4] and Alison Holmes[1,2,3,4]

For COVID-19 (N=9 studies), 62/806 (8%) patients were reported as experiencing bacterial/fungal coinfection during hospital admission.

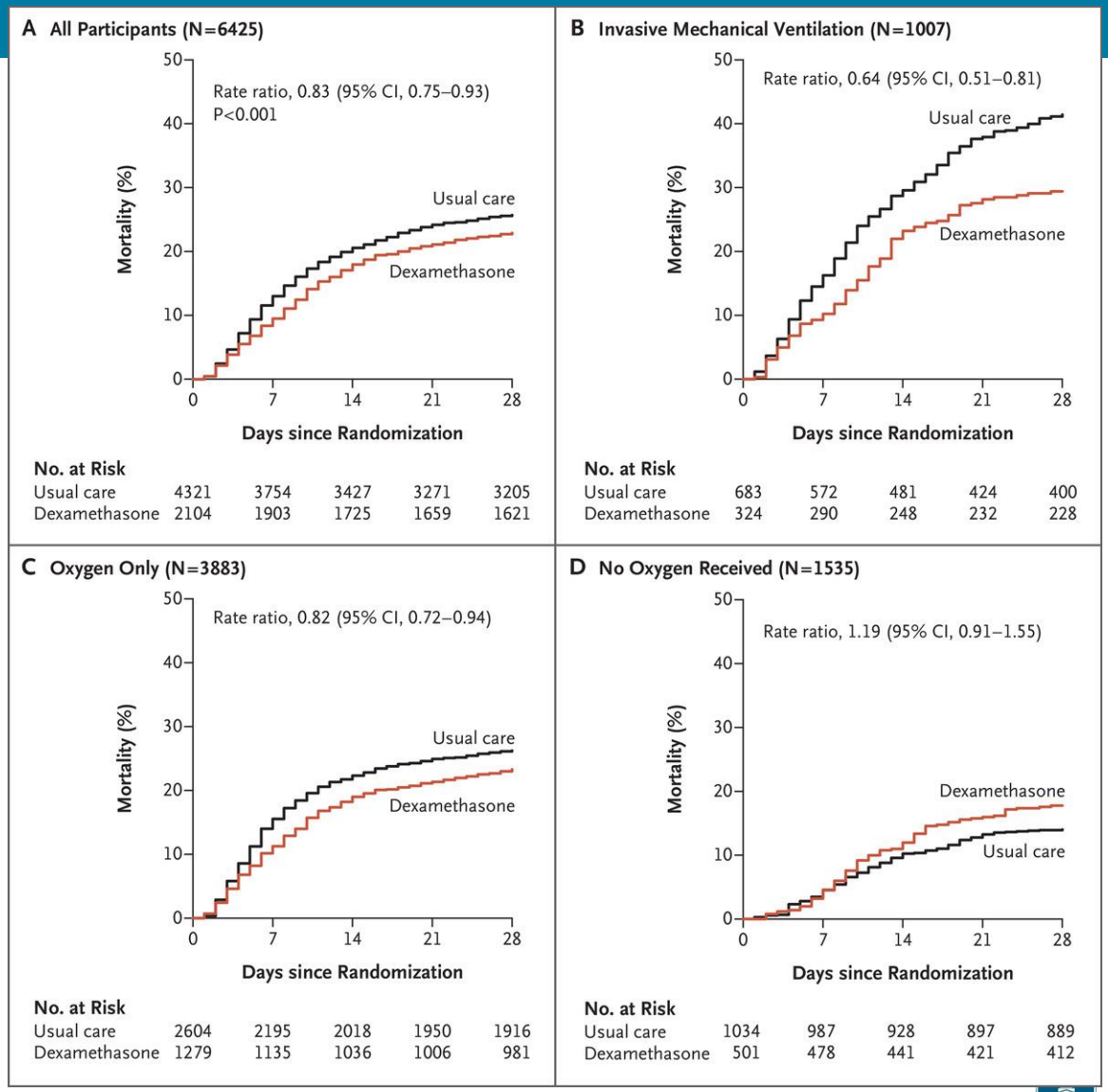
BUT 72% received antibacterial therapy.

THE RETURN OF PROCALCITONIN



PCT above normal range predicting odds of admission to ICU in COVID-19

MORTALITY AT 28 DAYS IN ALL PATIENTS AND ACCORDING TO RESPIRATORY SUPPORT AT RANDOMIZATION.



The RECOVERY Collaborative Group. N Engl J Med 2020.

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ADULT CAP GUIDELINE COMMITTEE

- Joshua Metlay Co-Chair
- Grant Waterer Co-Chair
- Ann Long
- Antonio Anzueto
- Jan Brozek
- Kristina Crothers
- Laura Cooley
- Nathan Dean
- Michael Fine
- Scott Flanders
- Marie Griffin
- Mark Metersky
- Daniel Musher
- Marcos Restrepo
- Cynthia Whitney

Take Home Points

- Pneumonia remains primarily a clinical diagnosis though emerging molecular platforms are changing some of the testing paradigms

- Antibiotic treatment is primarily empiric. Concern for drug resistant pathogens remains but should be guided by past infections and micro testing.

- Corticosteroids do not clearly improve outcomes for patients with bacterial pneumonia.