COMMUNITY ACQUIRED PNEUMONIA:
DIAGNOSIS AND TREATMENT DURING THE COVID-19 ERA

Tuesday, January 26, 2021
1:00 p.m. – 2:00 p.m. ET

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Norman Moore, PhD - Moderator/Speaker

Director of Infectious Disease and Scientific Affairs
Abbott Rapid Diagnostics

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ThermoFisher SCIENTIFIC

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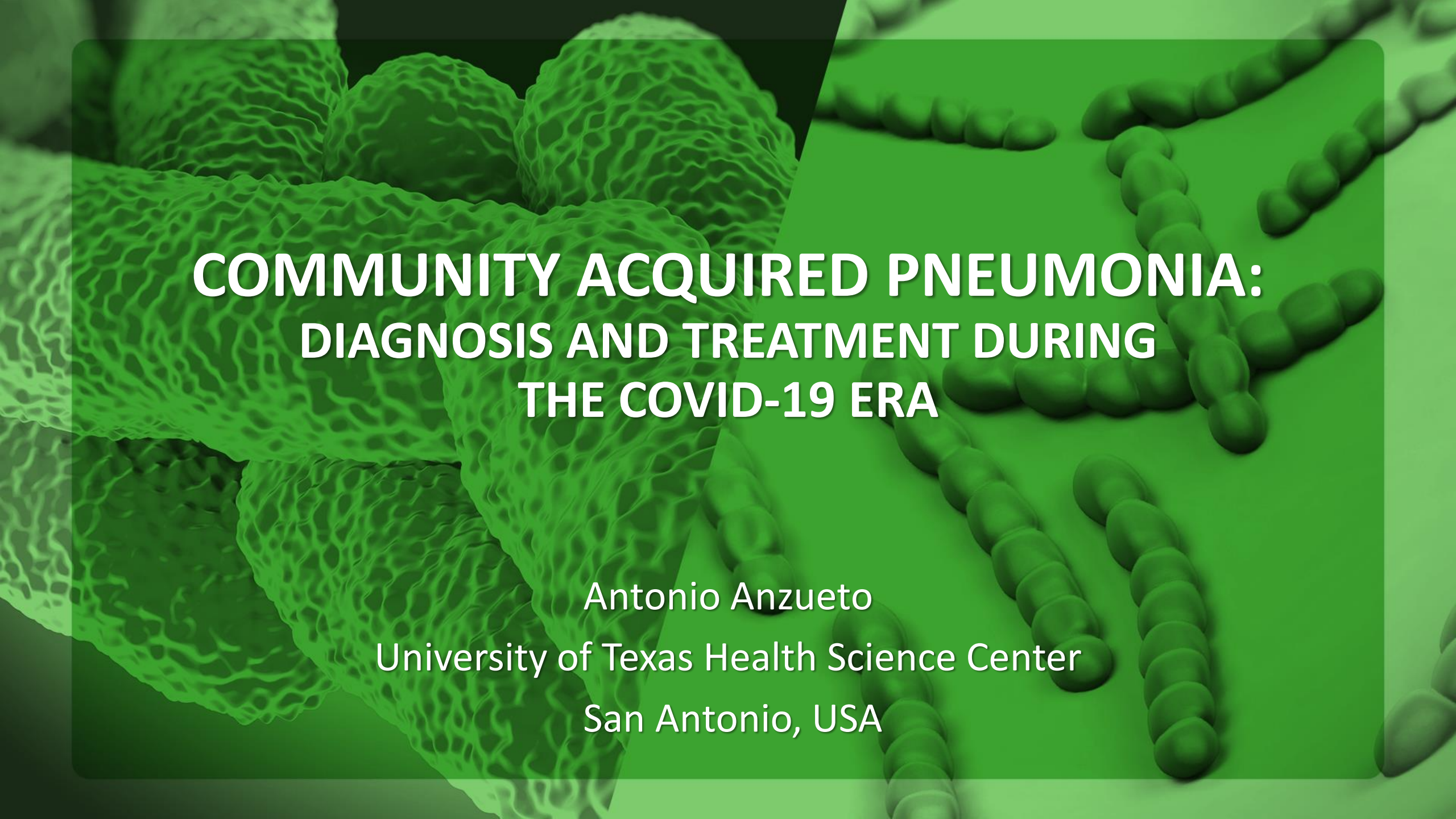
This program provides P.A.C.E. and AARC continuing education credits.
This provides does not provide continuing medical education (CME) credits.

Program Objectives

- Describe the relationship between COVID-19 and pneumonia and the associated public health risks
- Examine experiences and best practices for evaluating and managing COVID-19 patients with pneumonia
- Explain the guidance and practical clinical value of urinary antigen testing (UAT), including mortality reduction and antibiotic stewardship
- Discuss UAT performance characteristics and potential value related to laboratory workflow in times of strained respiratory testing resource



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Antonio Anzueto

University of Texas Health Science Center

San Antonio, USA

Faculty Disclosures

Dr. Anzueto

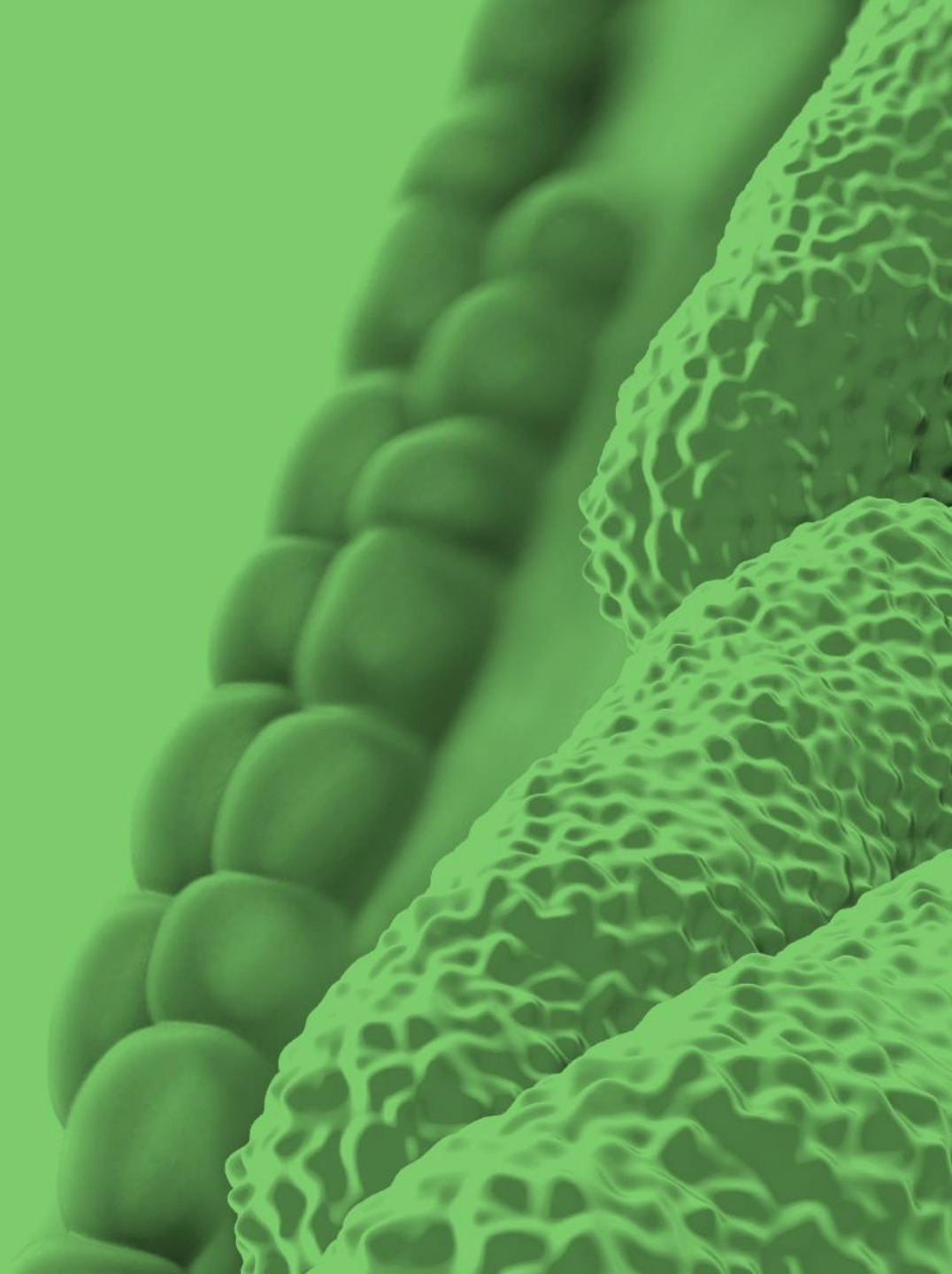
Personal financial interests in commercial entities that are relevant to my presentation:

- Being compensated by ABBOTT to give this presentation

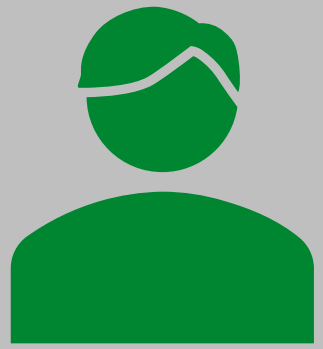
Non-commercial, non-governmental interests relevant to my presentation :

- Member of the ATS/ERS Task force on COPD and COPD Exacerbations,
- Member of the ATS/IDSA CAP Guidelines committee
- GOLD Past Member of the Executive and current member Scientific Committee

CASE STUDY



Case Study



55-year-old male presented to ED complaining 2-3 days of left chest pain, cough and chills.

Medications: Metoprolol and ASA 650 mg/day

Case Study

Physical Examination:

- Fever 101.7°F, HR 87/bpm, RR 32/min, BP 70/40
- Bilateral Crackles and dullness at bases

Other Information:

- WBC 14.6 x 10^3/mL
- Oxygen Saturation at rest 85%

Case Study

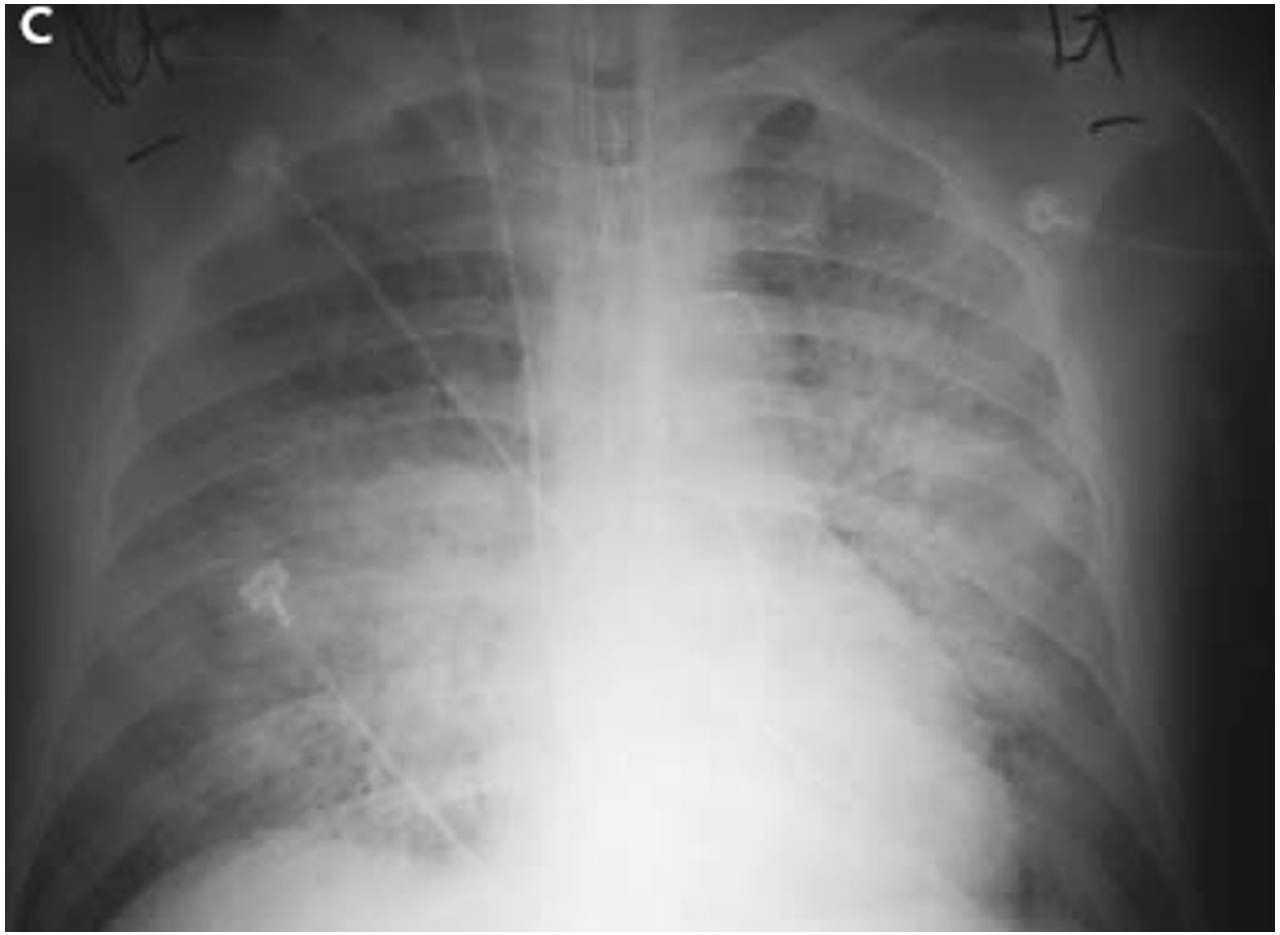
What questions do we need to ask?

Case Study

What questions do we need to ask?

- Any Travel history?
- Any use of electronic cigarette or Vaping?
- Sick contacts ?

Chest Radiograph



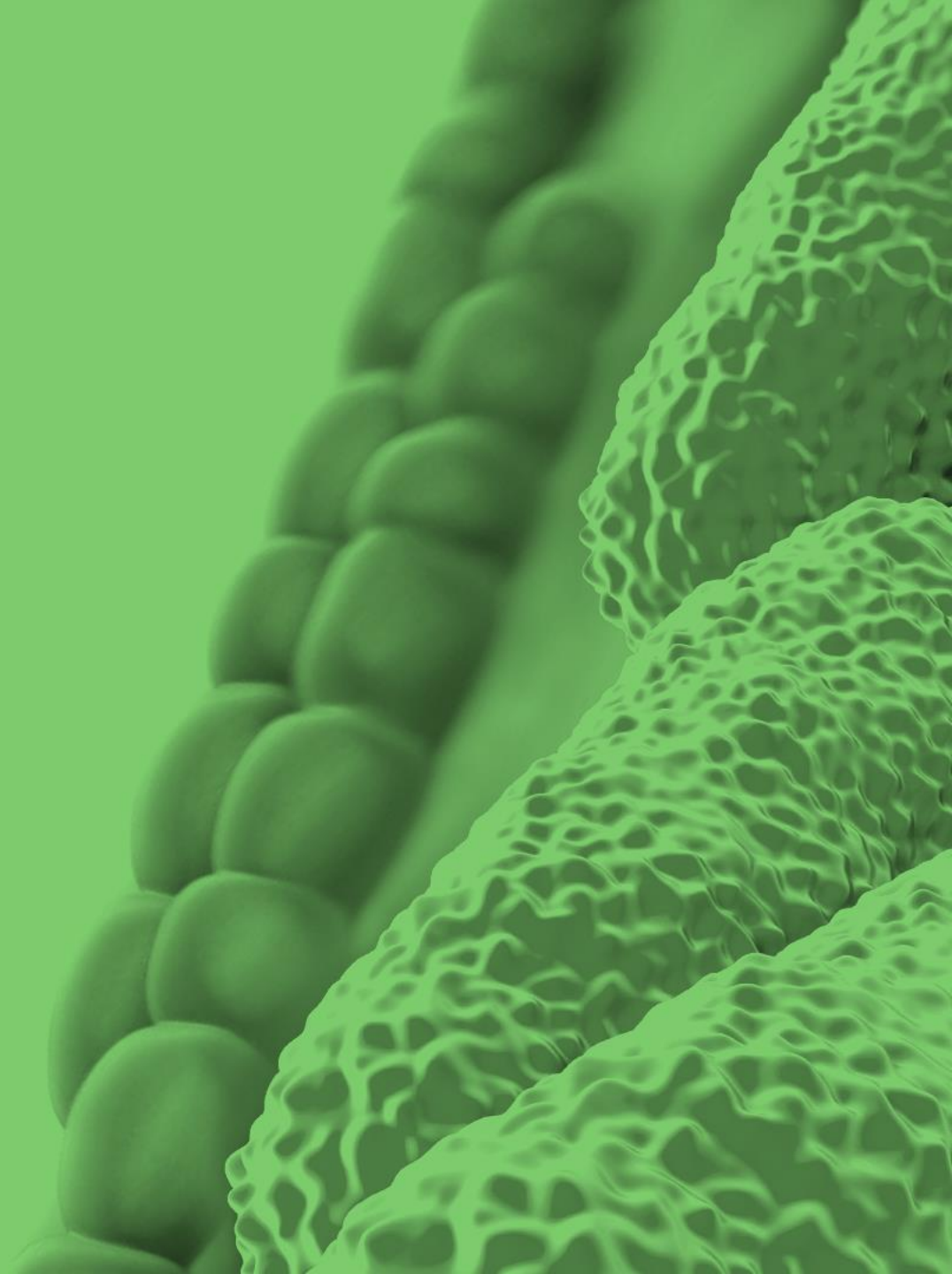
Respiratory Viral PCR

NEGATIVE

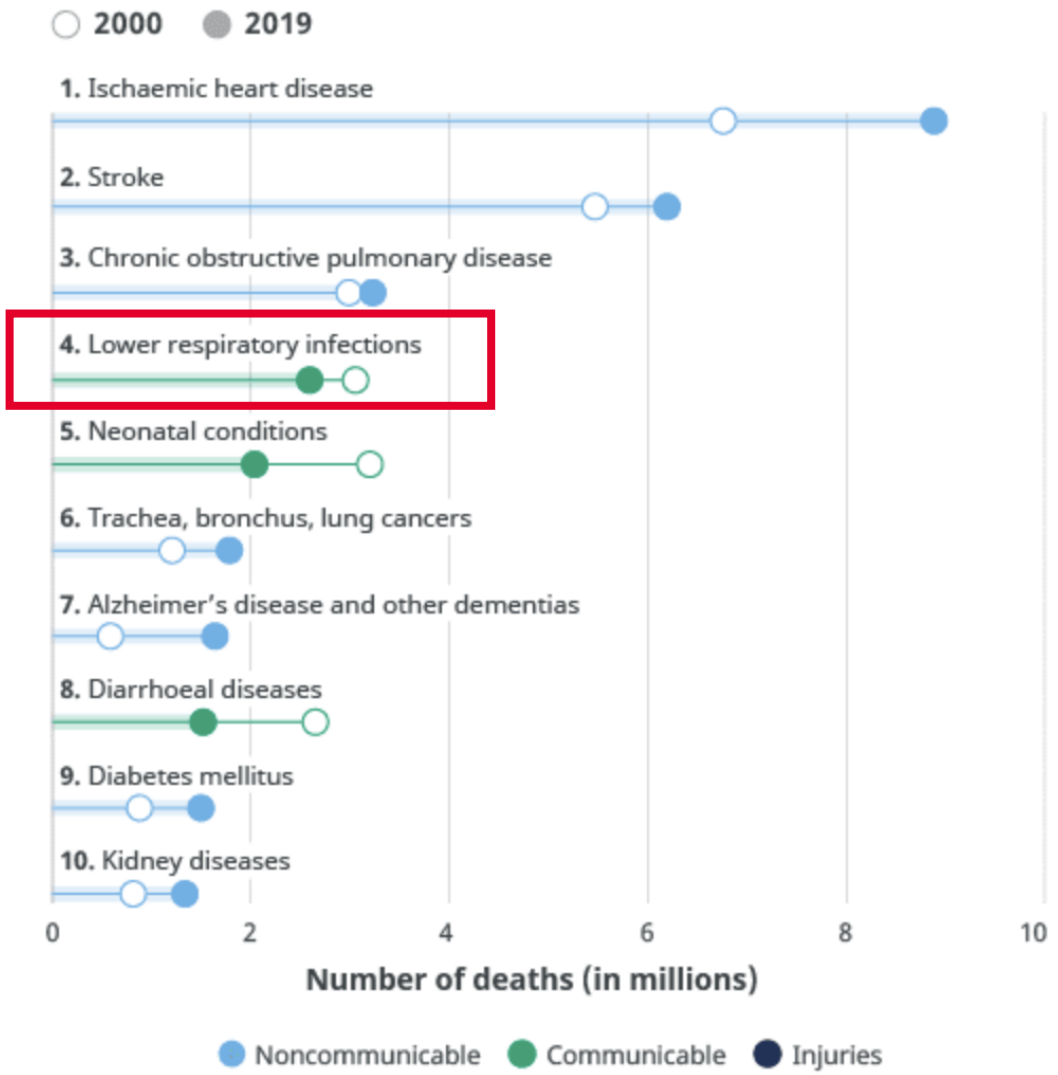
Need to order COVID Test

PUI

CAP and Risk Factors



Top 10 Global Causes of Death, 2019



World Health Organization Global Health Estimates. The top 10 causes of death. 2019 https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death. Accessed Jan 20, 2021.

Defining CAP, HCAP, HAP, and VAP

CAP (Community Acquired Pneumonia)

- Signs and symptoms of pneumonia with radiographic confirmation

HCAP (Healthcare-Associated Pneumonia)

- Prior hospitalization (within 90 days)
- Resided in nursing home or long-term care facility
- Received recent IV antibiotics (within 30 days)

Kalil AC, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society, *Clinical Infectious Diseases*, Volume 63, Issue 5, 1 September 2016, Pages e61–e111, https://doi.org/10.1093/cid/ciw353
Metlay JP, et al. 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. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

CAP

- Etiological agent is often not isolated or is identified late in course of treatment[1]
- Broad-spectrum antibiotics are prescribed early and empirically to reduce mortality[2]
- Inappropriate antibiotic use can cause antimicrobial resistance and C. difficile infections[3]
- Pathogen identification allows for targeted treatment[3]

1. Musher DM, et al. Can an etiologic agent be identified in adults who are hospitalized for community-acquired pneumonia: results of a one-year study. J Infect. 2013 Jul;67(1):11-8. doi: 10.1016/j.jinf.2013.03.003. Epub 2013 Mar 19.
2. *Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Arch Intern Med. 2004 Mar 22;164(6):637-44.*
3. Dellit TH, et al. IDSA/SHEA guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis. 2007 Jan 15;44(2):159-77. doi: 10.1086/510393. Epub 2006 Dec 13.

OPEN ACCESS

Risk factors for community-acquired pneumonia in adults in Europe: a literature review

Antoni Torres,[1] Willy E Peetermans,[2] Giovanni Viegi,[3,4] Francesco Blasi[5]

Table 4 Bundles for lifestyle interventions to reduce the risk of CAP in adults

Risk factor	Evidence	Recommendation
Smoking	Risk of CAP increased in current and former smokers (9 studies)[19–23 38 42 46 47]	Smoking cessation
Alcohol consumption	Risk of CAP increased with high consumption or history of alcohol abuse (4 studies)[21 23 38 47]	Reduce alcohol consumption
Nutritional status	Being underweight was generally associated with an increased risk of CAP (4 studies)[23 38 44 47]	Dietary advice to ensure good nutritional status
Contact with children	Regular contact with children increased the risk of CAP (3 studies)[23 38 44]	Avoid contacts with children with lower respiratory tract infections
Dental hygiene	Risk of CAP decreased in individuals with a recent (within past year) dental visit (2 studies)[23 38]	Ensure regular dental visits
Vaccination against influenza and *Streptococcus pneumoniae*	Current guidelines[88 89]	Ensure compliance with guidelines

CAP, community-acquired pneumonia.

Torres A, et al. Risk factors for community-acquired pneumonia in adults in Europe: a literature review. *Thorax*. 2013;68(11):1057-1065.

Differential Dx of COVID-19 and Pneumonia

	COVID-19 $n = 304$	SN-CAP $n = 138$	*P*-value
Age, mean (SD), y	61.5(13.3%)	61.6(16.1)	0.921
Female	166 (54.61%)	56(40.58%)	<0.01
Male	138 (45.39%)	82(59.42%)	
Signs and symptoms at admission, patient no			
Fever	172 (56.58%)	42 (30.43)	<0.01
Cough	134 (44.08%)	74 (53.62)	0.06
Dyspnea	29 (9.54%)	3 (2.17%)	<0.01
Fatigue	32 (10.53)	5 (3.62%)	0.02
Chest distress	24 (7.89%)	3 (2.17%)	0.02
Expectoration	10 (3.29%)	53 (38.41%)	<0.01
Sore throat	5 (1.64%)	5 (3.62%)	0.2
Diarrhea	5 (1.64%)	1 (0.72%)	0.4
Asymptomatic	39 (12.83%)	6 (4.35%)	<0.01
Chronic medical illness, patient no			
Hypertension	83 (27.3%)	34 (24.64%)	0.56
CAD	21 (6.91%)	8 (5.8%)	0.66
Diabetes	40 (13.16%)	25 (18.12%)	0.17
COPD	7 (2.3%)	27 (19.57%)	<0.01
Renal failure	27 (8.88%)	18 (13.04%)	0.18
Malignancy	3 (0.99%)	15 (10.87%)	<0.01

	COVID-19 $n = 304$	SN-CAP $n = 138$	*P*-value
Laboratory result abnormalities, patient no			
WBC count, <3.7 × 109/L	42 (13.82%)	4 (2.9%)	<0.01
Lymphocyte count, <0.8 × 109/L	97 (41.91%)	68 (49.28%)	<0.01
Lymphocyte ratio <20%	134 (44.08%)	93 (67.39%)	<0.01
Neutrophil count, x109/L	51 (16.78%)	37 (26.81%)	0.01
Platelet <85 × 109/L	15 (4.93%)	7 (5.07%)	0.95
CRP >10 mg/L	127 (41.78%)	98 (71.01%)	<0.01
Albumin <35 g/L	139 (45.72%)	95 (68.84%)	<0.01
ALT/AST abnormal	99 (32.57%)	42 (30.43%)	0.66
Creatinine >73 μmol/L	60 (19.74%)	28 (20.29%)	0.89
BUN, >8 mmol/L	87 (28.62%)	30 (21.74%)	0.13
LDH >250 U/L	42 (13.82%)	60 (43/48%)	<0.01
Creatine kinase >195 U/L	21 (6.91%)	6 (4.35%)	0.3
Troponin-I >0.4 ug/L	49 (16.12%)	25 (18.12%)	0.6
Patients tested for procalcitonin, no.	31	117	
Procalcitonin >0.05 ng/mL	13 (41.94%)	55 (47.01%)	0.61

P-value indicates differences between COVID-19 and SN-CAP, P < 0.05 was considered statistically significant.

SN-CAP, SARS-CoV-2 negative-community acquired pneumonia

Zhou Y, et al. COVID-19 Is Distinct From SARS-CoV-2-Negative Community-Acquired Pneumonia. *Front Cell Infect Microbiol.* 2020;10:322.

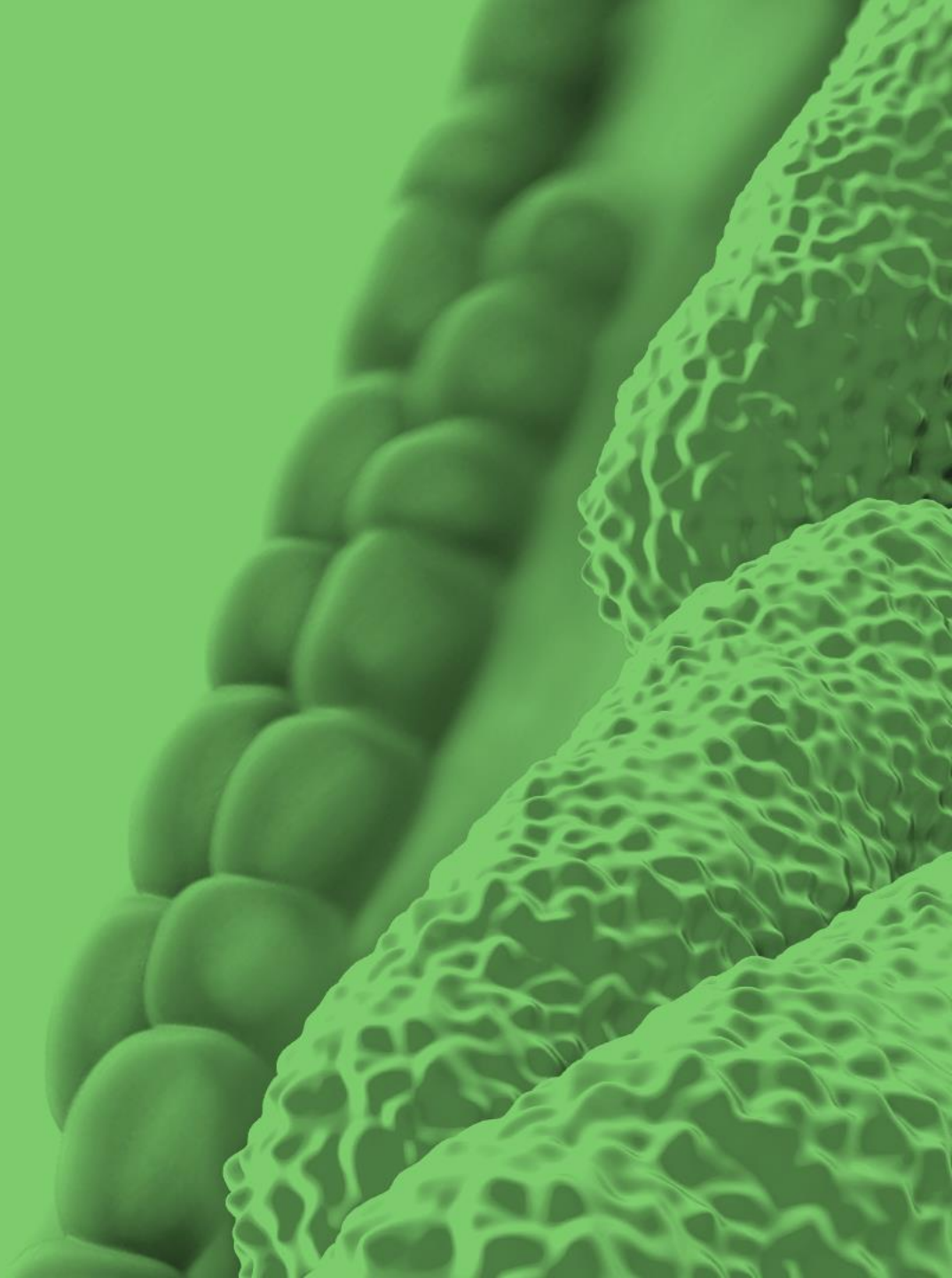
Poll Question #1

The following tests are performed to detect pathogens for community acquired pneumonia (CAP) in my facility (select all that apply):

a. Blood culture
b. Sputum culture
c. Sputum gram stain
d. Urinary antigen testing (UAT)
e. Molecular pneumonia panel
f. ELISA
g. Other
h. We send out all pneumonia testing
i. Don’t know or n/a

Pathogens:

S. pneumoniae and *Legionella*



S. pneumoniae

- Leading cause of CAP[1]
- Leading cause of pneumonia mortality[1]
- May cause secondary bacteremia[2,3]
- Difficult to diagnose using traditional culture methods[4-6]
  - Long turnaround time
  - Difficult to obtain high-quality sputum sample
  - Blood cultures have low sensitivity
  - Empiric antibiotics impact yield

1. Ramirez JA, File TM, and Bond S. Overview of community-acquired pneumonia in adults. UpToDate. December 28, 2020. https://www.uptodate.com/contents/overview-of-community-acquired-pneumonia-in-adults/print.
2. File TM Jr, et al. What can we learn from the time course of untreated and partially treated community-onset Streptococcus pneumoniae pneumonia? A clinical perspective on superiority and noninferiority trial designs for mild community-acquired pneumonia. *Clin Infect Dis*. 2008;47 Suppl 3:S157-S165.
3. Pneumococcal Disease. Centers for Disease Control and Prevention. https://www.cdc.gov/pneumococcal/clinicians/clinical-features.html. Published September 6, 2017. Accessed December 14, 2020.
4. Vernet G, et al. Laboratory-based diagnosis of pneumococcal pneumonia: state of the art and unmet needs. *Clin Microbiol Infect*. 2011;17 Suppl 3:1-13.
5. Blaschke AJ. Interpreting assays for the detection of Streptococcus pneumoniae. *Clin Infect Dis*. 2011;52 Suppl 4(Suppl 4):S331-S337.
6. Sordé R, et al. Current and potential usefulness of pneumococcal urinary antigen detection in hospitalized patients with community-acquired pneumonia to guide antimicrobial therapy. *Arch Intern Med*. 2011;171(2):166-172.

Etiology of CAP

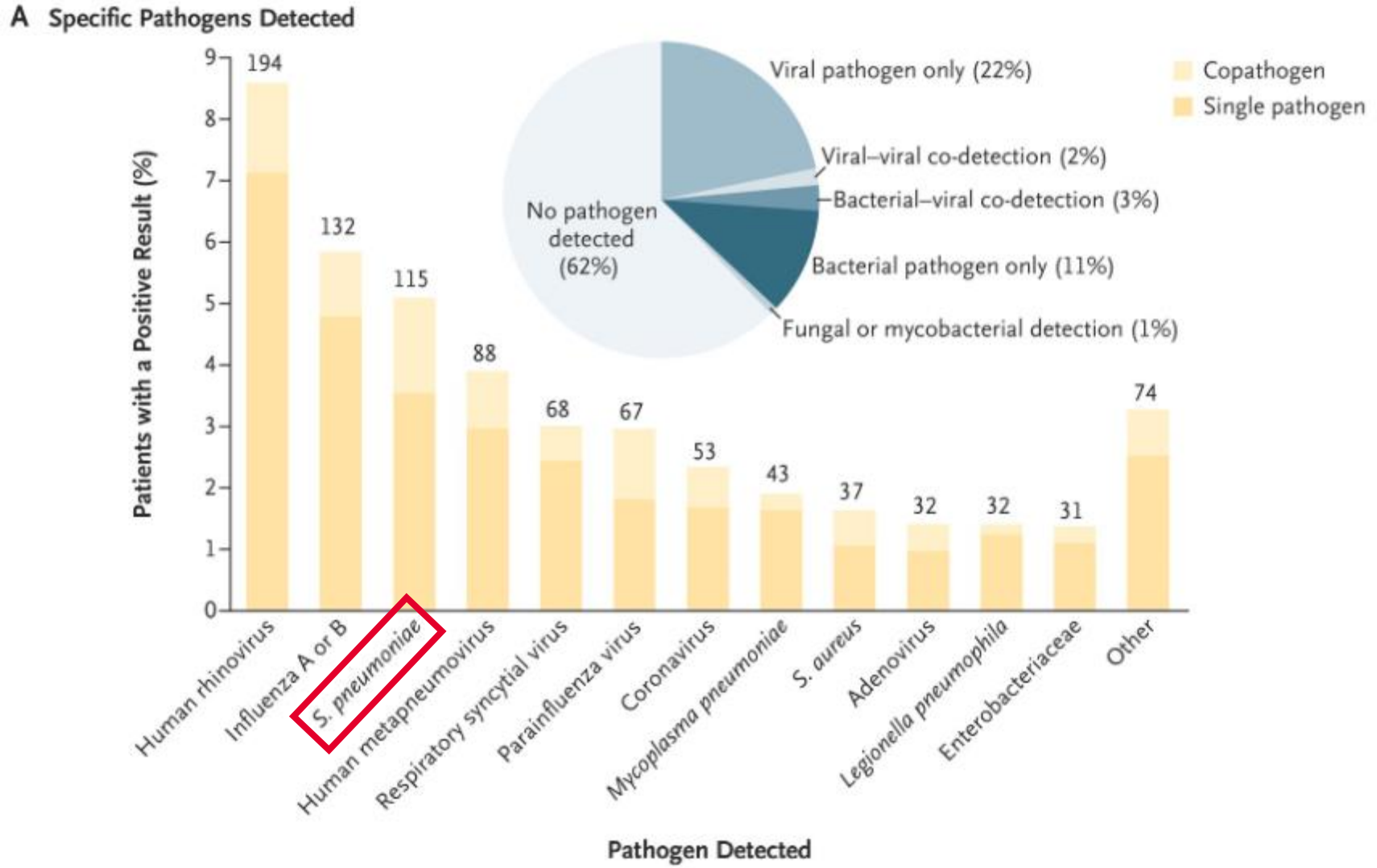
AMBULATORY PATIENTS	HOSPITALIZED (NON-ICU)	SEVERE (ICU)
S. pneumoniae	*S. pneumoniae*	*S. pneumoniae*
M. pneumoniae *H. influenzae* *C. pneumoniae* Respiratory viruses*	*M. pneumoniae* *C. pneumoniae* *H. influenzae* *Legionella* spp. Aspiration Respiratory viruses*	*H. influenzae* *Legionella* spp. Gram-negative bacilli *S. aureus* **Viral: H1N1**

ICU = Intensive care unit

*Influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza

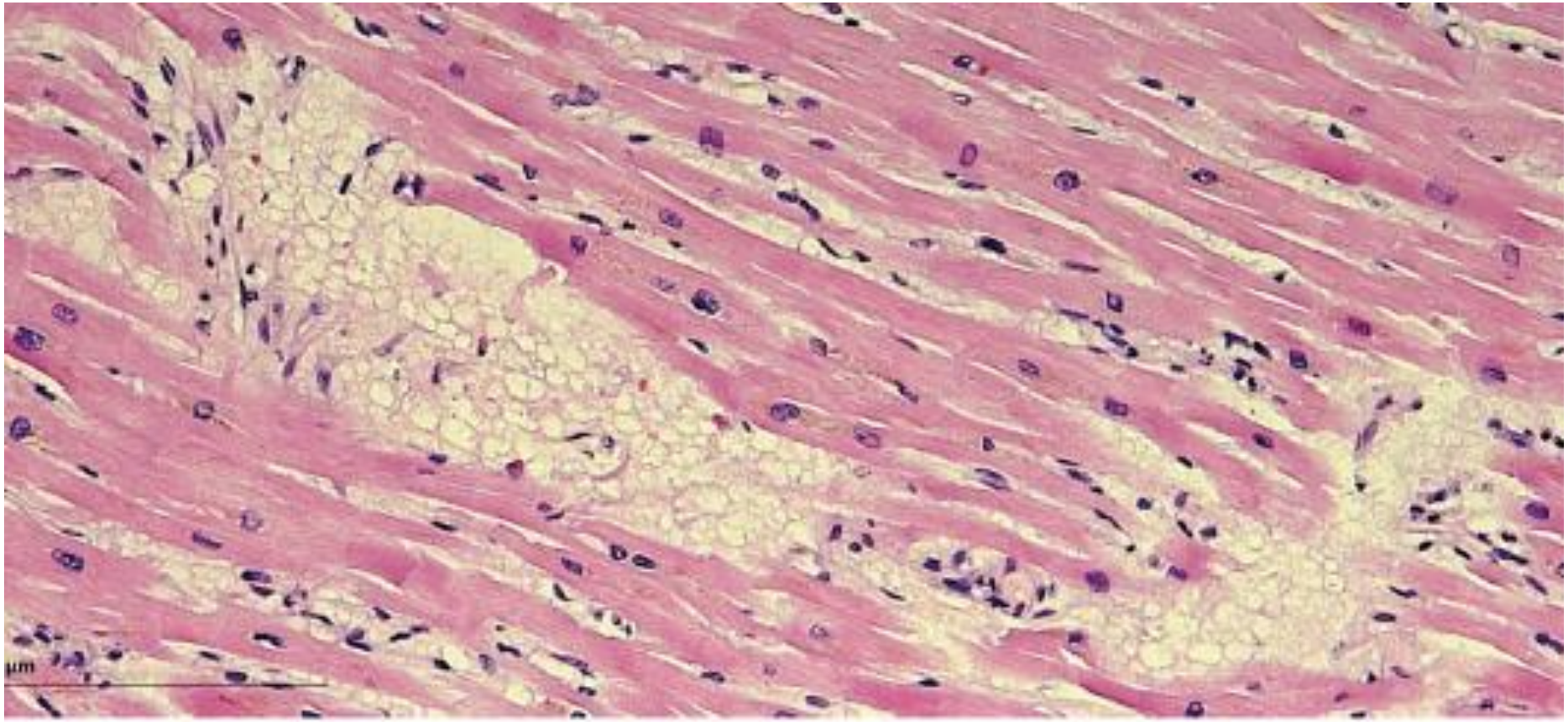
Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-S72.

Etiology of Community-Acquired Pneumonia



Jain S, et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. *N Engl J Med*. 2015;373(5):415-427.

Invasive Pneumococcal Disease
Cardiac lesion



Brown AO, et al PLoS Pathog 2014; 10: e1004383.

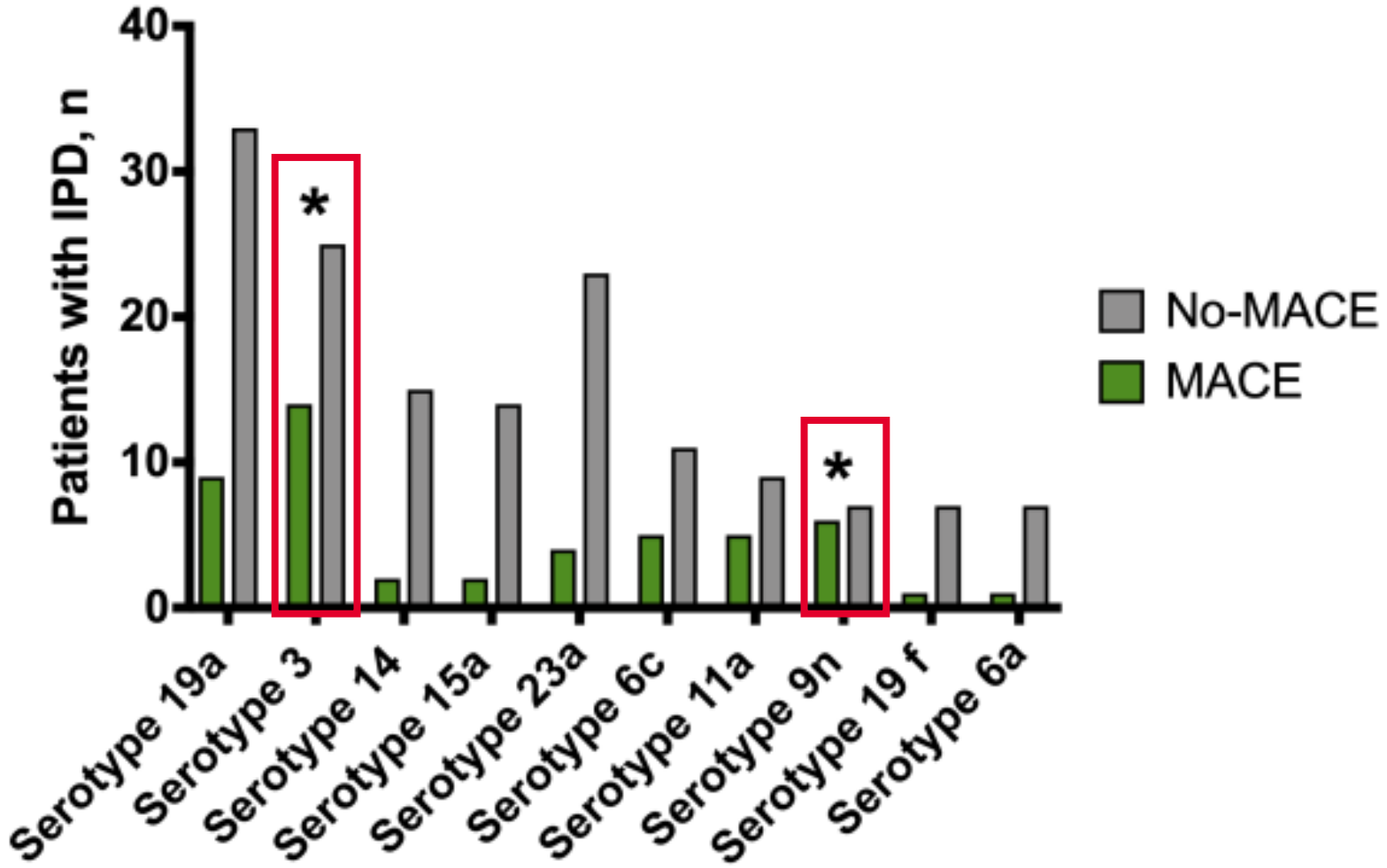
Mortality of Hospital Admitted Patients with Invasive Pneumococcal Disease

1952–62	1966–95	1995–97
↑	↑	↑
13% Mortality[1]	**12% Mortality[2]**	**12% Mortality[3]**
n = 1130	n = 4432	n = 5837

Although the management of critically ill patients has improved by far and there are no resistance problems with regard to *S. pneumoniae*, mortality of IPD remains tremendous.

1. Austrian R, Gold J. *Ann Intern Med* 1964;60:759-76.
2. Fine MJ, et al. *JAMA* 1996;275(2):134-41.
3. Feikin DR, et al. *Am J Public Health* 2000;90(2):223-9.

S. pneumoniae Serotypes and Risk of Cardiac Events



MACE, major adverse cardiac events

Africano HF, Serrano-Mayorga CC, Ramirez-Valbuena PC, Bustos IG, Bastidas A, Vargas HA, Gómez S, Rodriguez A, Orihuela CJ, Reyes LF. Major Adverse Cardiovascular Events During Invasive Pneumococcal Disease are Serotype Dependent. Clin Infect Dis. 2020 Sep 22:ciaa1427.

AMBULATORY PATIENTS	HOSPITALIZED (NON-ICU)	SEVERE (ICU)
S. pneumoniae	*S. pneumoniae*	*S. pneumoniae*
M. pneumoniae *H. influenzae* *C. pneumoniae* Respiratory viruses*	*M. pneumoniae* *C. pneumoniae* *H. influenzae* *Legionella* spp. Aspiration Respiratory viruses*	*H. influenzae* *Legionella* spp. Gram-negative bacilli *S. aureus* **Viral:** **Influenza** **COVID-19**

ICU = Intensive care unit

*Influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza

ICU, intensive care unit

Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-S72.

Antimicrobial Resistance - Status

Urgent Threats

These germs are public health threats that require urgent and aggressive action

Carbapenem-resistant *Acinetobacter*
Candida auris
Clostridioides difficile
Carbapenem-resistant Enterobacteriaceae
Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

These germs are public health threats that require prompt and sustained action:

Drug-resistant *Campylobacter*
Drug-resistant *Candida*
ESBL-producing Enterobacteriaceae
Vancomycin-resistant *Enterococci*
Multidrug-resistant *Pseudomonas aeruginosa*
Drug-resistant nontyphoidal *Salmonella*
Drug-resistant *Salmonella* serotype Typhi
Drug-resistant *Shigella*
Methicillin-resistant *Staphylococcus aureus*
Drug-resistant *Streptococcus pneumoniae*
Drug-resistant Tuberculosis

Concerning Threats

These germs are public health threats that require careful monitoring and prevention action

Erythromycin-resistant group A *Streptococcus*
Clindamycin-resistant group B *Streptococcus*

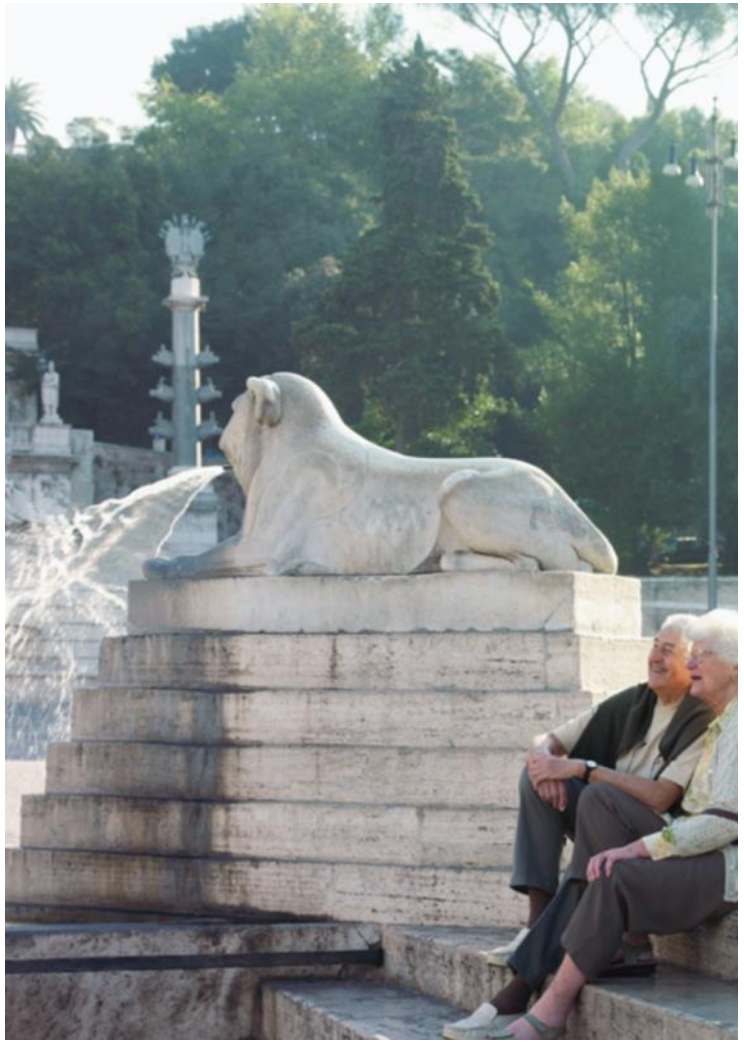
Watch List

Azole-resistant *Aspergillus fumigatus*
Drug-resistant *Mycoplasma genitalium*
Drug-resistant *Bordetella pertussis*

CDC. Antibiotic Resistance Threats In The United States 2019. Revised December 2019. https://www.Cdc.Gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.Pdf. Accessed January 18, 2021

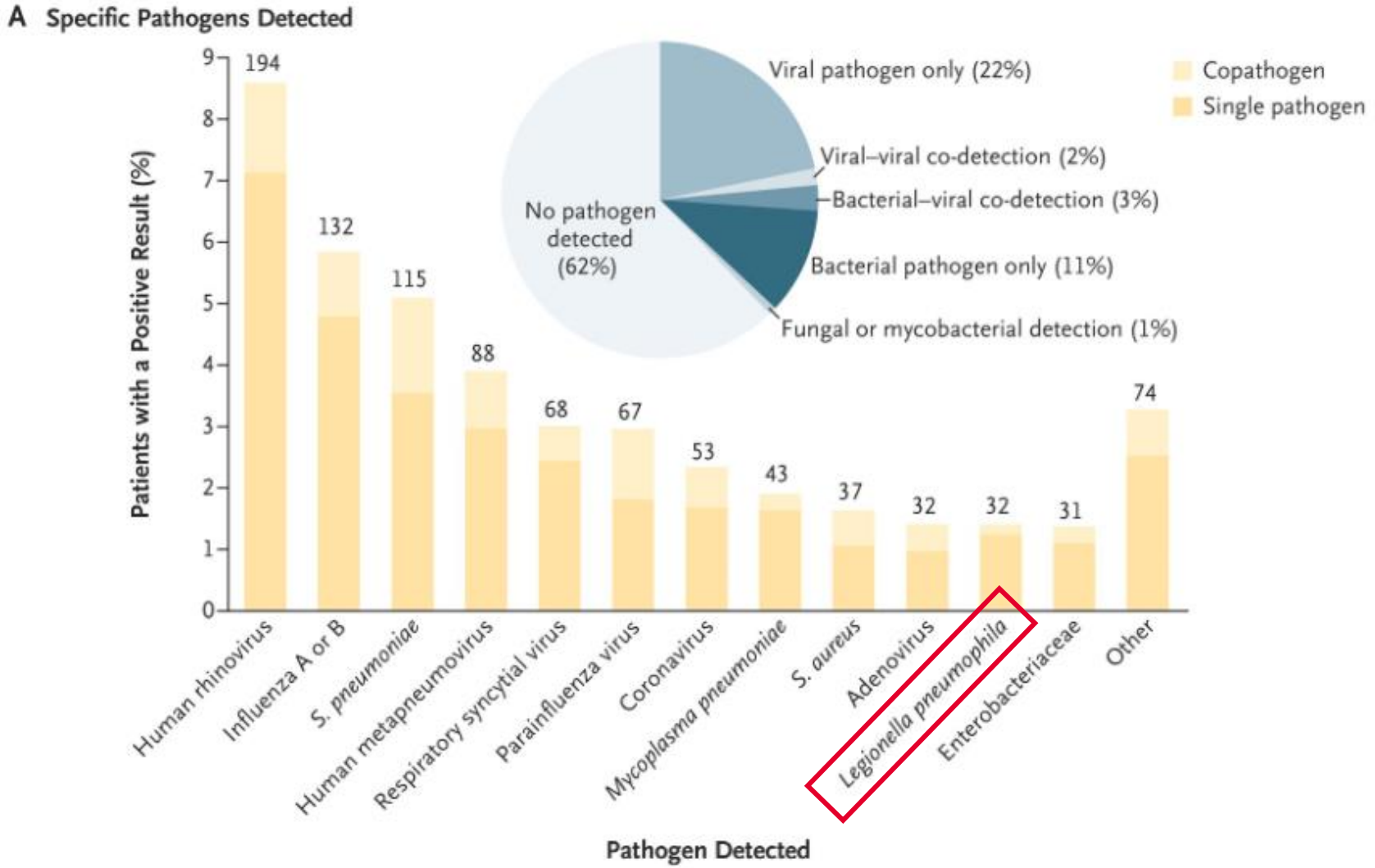
Legionella

- Leading cause of waterborne disease outbreaks[1]
- The deadliest pneumonia – up to 25% fatality rate[2]
- Disease incidence continues to rise, and likely underdiagnosed[3] – impact of shut-downs/reopenings?
- Outbreaks can lead to costly legal action with lasting negative impact on facility reputations[4]
- Initial symptom presentation similar to COVID[5]
- Risk factors[6]:
  - Age ≥ 50 years
  - Smoking
  - Underlying illness
  - Recent travel
  - Exposure to water sources



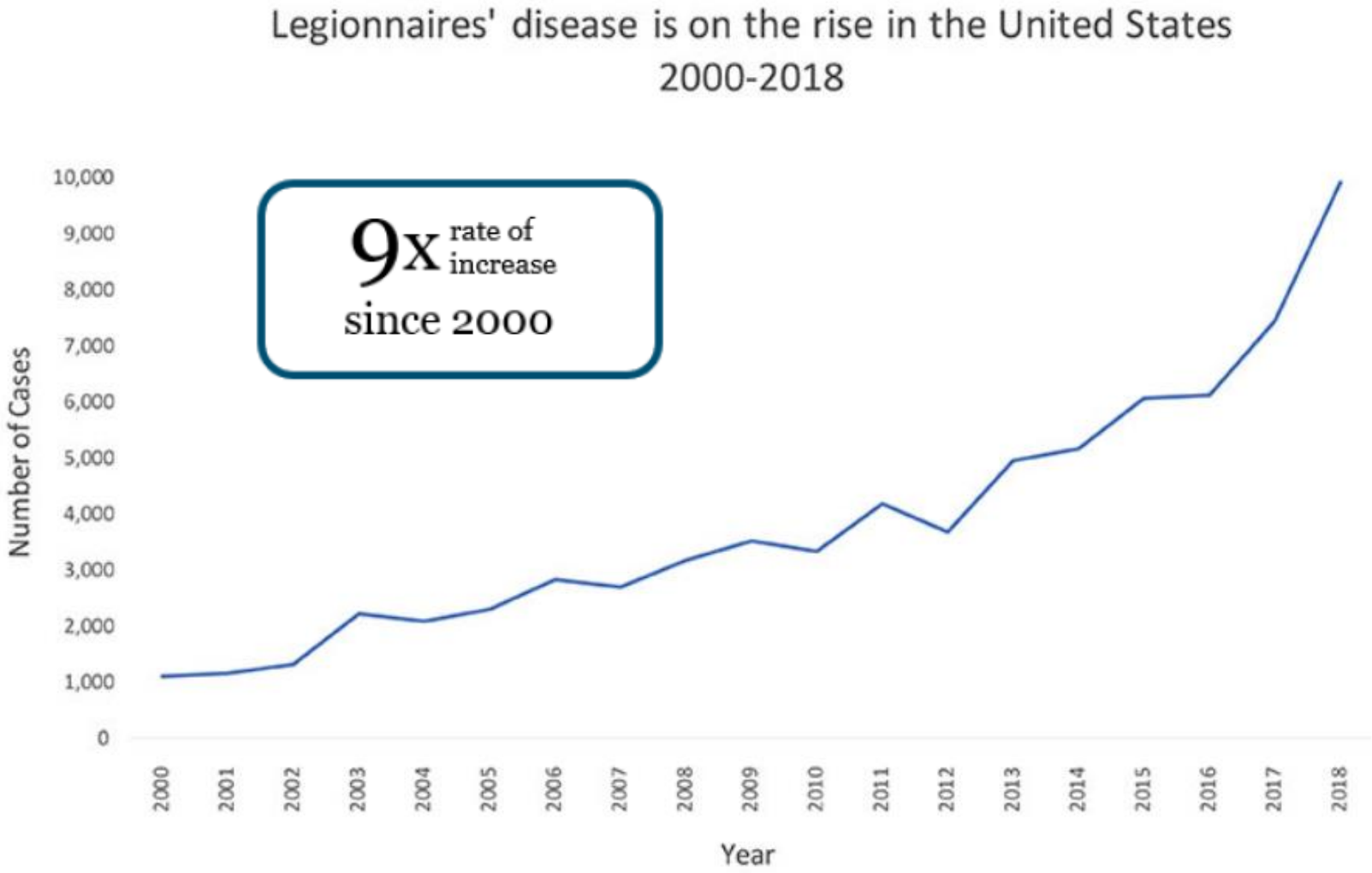
1. Craun GF, et al. Causes of outbreaks associated with drinking water in the United States from 1971 to 2006. *Clinical Microbiology Reviews*. 2010;23(3): 507–528.
2. Soda EA, et al. Vital Signs: Health Care-Associated Legionnaires' Disease Surveillance Data From 20 States and a Large Metropolitan Area-United States, 2015. *Am J Transplant*. 2017;17(8):2215-2220.
3. CDC, Nationally Notifiable Diseases Surveillance System, https://www.cdc.gov/legionella/images/national-incidence.jpg
4. Puri S, et al. Clinical Presentation of Community-Acquired Legionella Pneumonia Identified by Universal Testing in an Endemic Area. *Int J Environ Res Public Health*. 2020;17(2):533.
5. Dey R, Ashbolt NJ. Legionella Infection during and after the COVID-19 Pandemic. ACS ES&T Water. 2020;acsestwater.0c00151. Published 2020 Sep 23.
6. Legionnaires Disease Specifics. Centers for Disease Control and Prevention. https://www.cdc.gov/legionella/clinicians/disease-specifics.html. Published April 30, 2018. Accessed January 14, 2021.

Etiology of Community-Acquired Pneumonia



Jain S, et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. *N Engl J Med*. 2015;373(5):415-427.

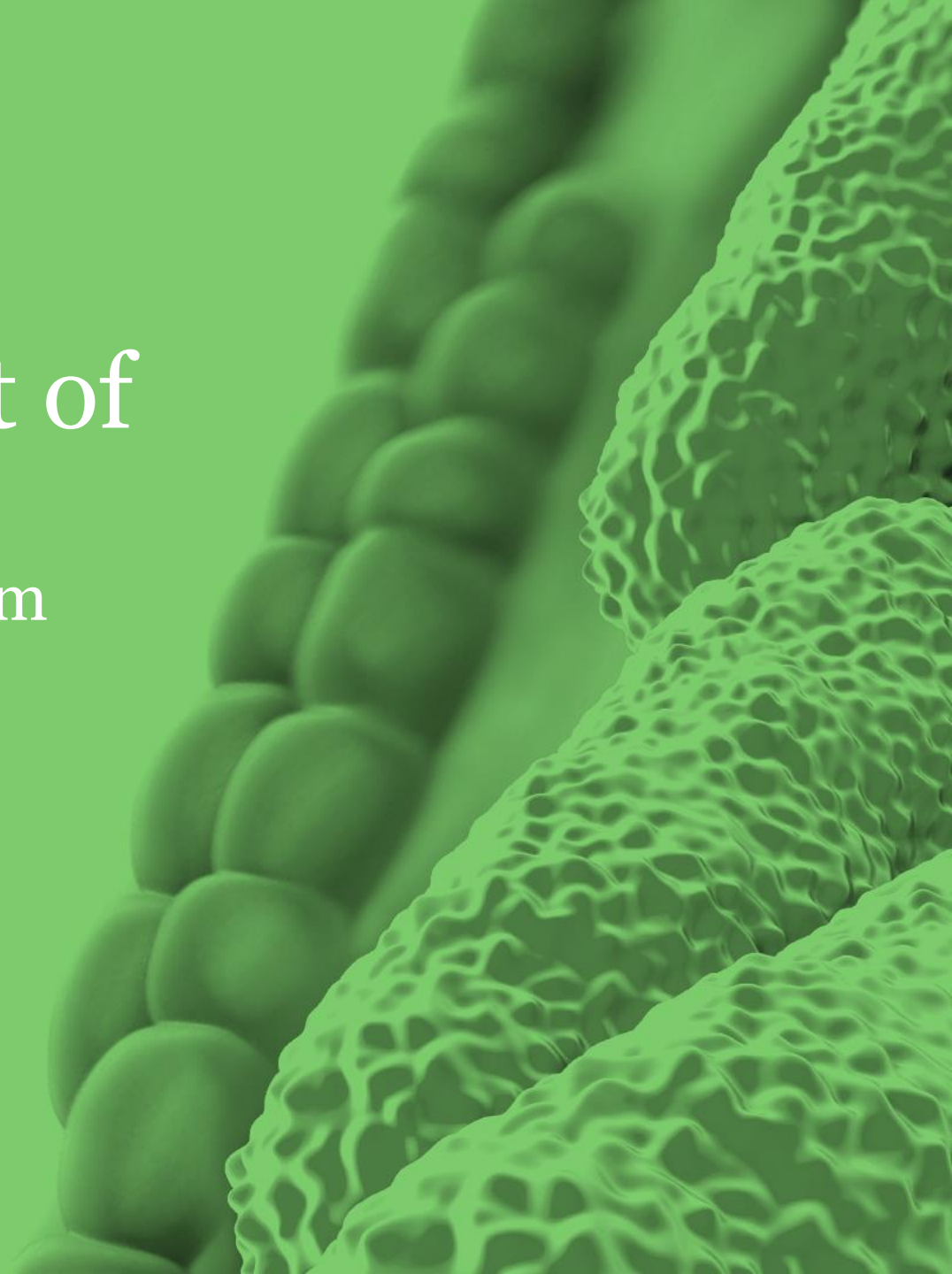
Legionnaire's Disease: Likely Underdiagnosed



CDC, Nationally Notifiable Diseases Surveillance System, https://www.cdc.gov/legionella/images/national-incidence.jpg

Diagnosis and Treatment of Adults with CAP

Official Clinical Practice Guidelines from ATS/IDSA



AMERICAN THORACIC SOCIETY DOCUMENTS

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.

Methods: A multidisciplinary panel conducted pragmatic systematic reviews of the relevant research and applied Grading of Recommendations, Assessment, Development, and Evaluation methodology for clinical recommendations.

Results: The panel addressed 16 specific areas for recommendations spanning questions of diagnostic testing, determination of site of care, selection of initial empiric antibiotic therapy, and subsequent management decisions. Although some recommendations remain unchanged from the 2007 guideline, the availability of results from new therapeutic trials and epidemiological investigations led to revised recommendations for empiric treatment strategies and additional management decisions.

Conclusions: The panel formulated and provided the rationale for recommendations on selected diagnostic and treatment strategies for adult patients with community-acquired pneumonia.

Keywords: community-acquired pneumonia; pneumonia; patient management

Contents

*Co-first authors.

Endorsed by the Society of Infectious Disease Pharmacists July 2019.

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Supported by the American Thoracic Society and Infectious Diseases Society of America.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. CDC.

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This article has an online supplement, which is accessible from this issue's table of contents at www.atsjournals.org.

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DOI: 10.1164/rccm.201908-1581ST
Internet address: www.atsjournals.org

16 Questions

Diagnosis

Treatment

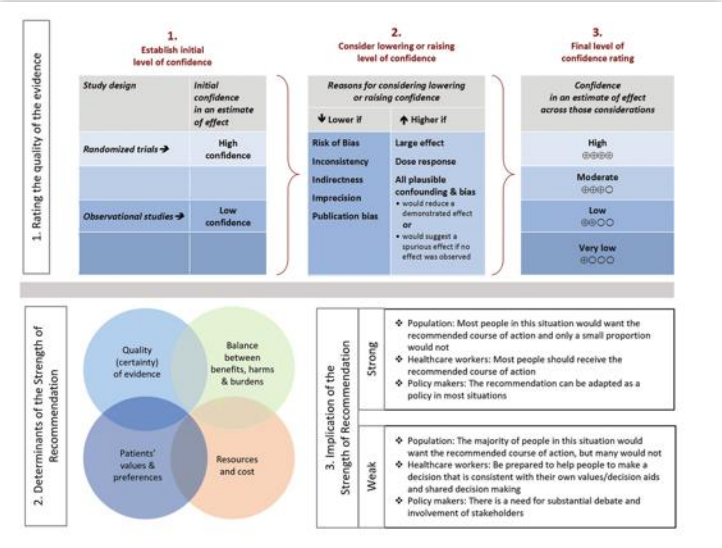
Other therapies

Duration Therapy

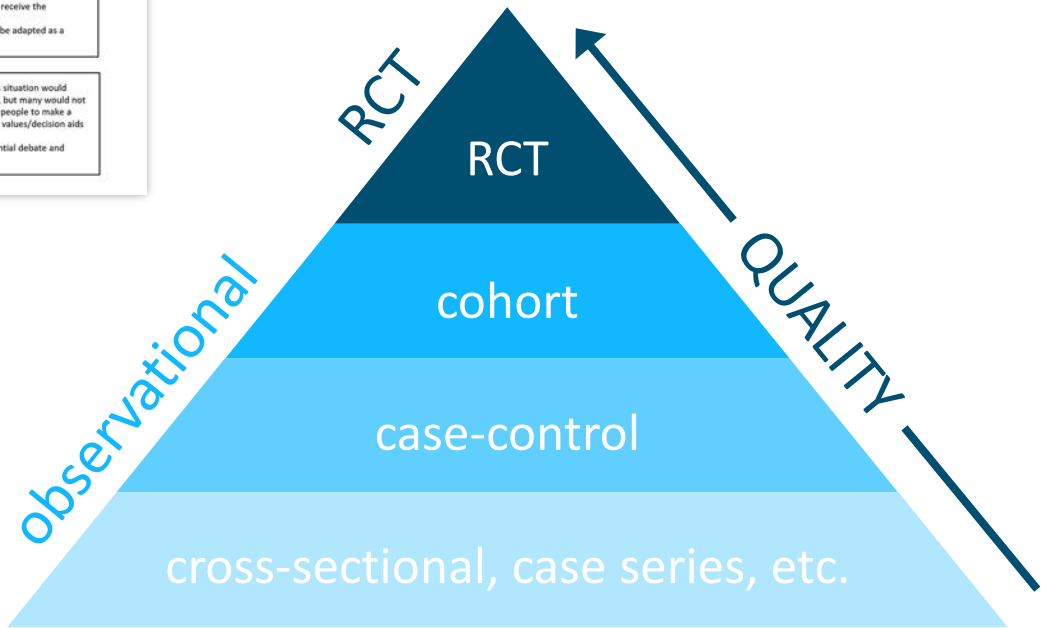
Follow up

Metlay JP, et al. 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. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Evaluating Recommendations



Quality



Interpretation

Strong

Weak

C

Conditional

Shane AL, Mody RK, Crump JA, et al. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. *Clin Infect Dis*. 2017;65(12):1963-1973.
Metlay JP, et al. 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. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Recommendations for Specific Management Questions:
Initial Diagnostic Evaluation

Question 1

In adults with CAP, should **Gram stain and culture of lower respiratory secretions be obtained** at the time of diagnosis?

Recommendation

In the setting of **severe CAP**, especially if they are intubated

Or, are being **empirically treated for MRSA or *P. aeruginosa***

Interpretation
Strong

Quality
Very low quality of evidence

Or, were previously infected with MRSA or P. aeruginosa, especially those with prior respiratory tract infection

Or, were hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days

Interpretation
Conditional

Quality
Very low quality of evidence

Metlay JP, et al. 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. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Recommendations for Specific Management Questions:
Initial Diagnostic Evaluation

Question 2

In adults with CAP, should **blood cultures be obtained** at the time of diagnosis?

Recommendations

Obtain pretreatment **blood cultures in the setting of severe CAP**

Or, if being empirically **treated for MRSA or *P. aeruginosa***

Interpretation
Strong

Quality
Very low quality of evidence

Or, were previously infected with MRSA or P. aeruginosa, especially those with prior respiratory tract infection

Or, were hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days

Interpretation
Conditional

Quality
Very low quality of evidence

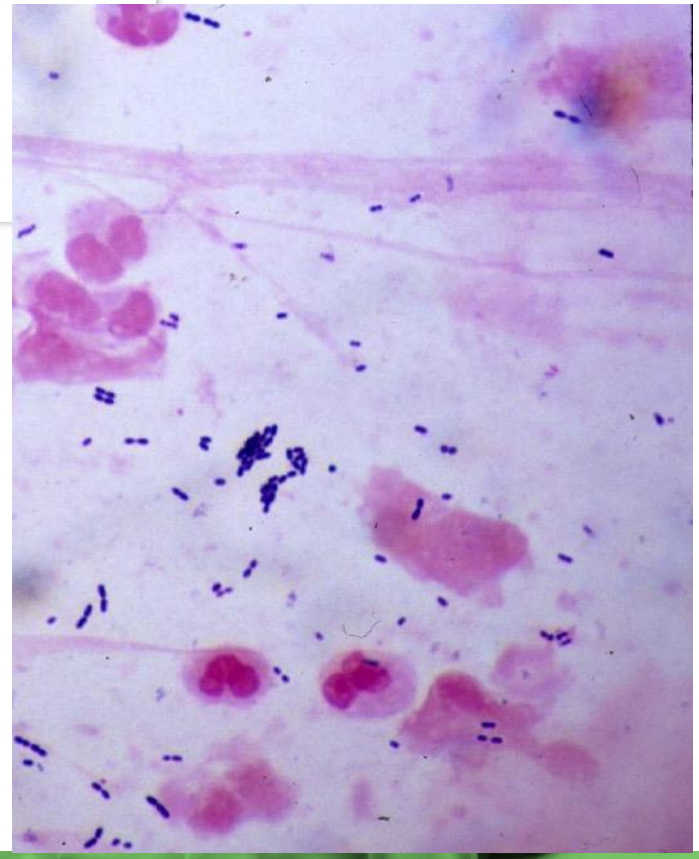
Metlay JP, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Clinical Infectious Diseases

MAJOR ARTICLE

Sputum Gram Stain for Bacterial Pathogen Diagnosis in Community-acquired Pneumonia: A Systematic Review and Bayesian Meta-analysis of Diagnostic Accuracy and Yield

Hiroaki Ogawa,[1] Georgios D. Kitsios,[2] Mitsunaga Iwata,[1] and Teruhiko Terasawa,[1]



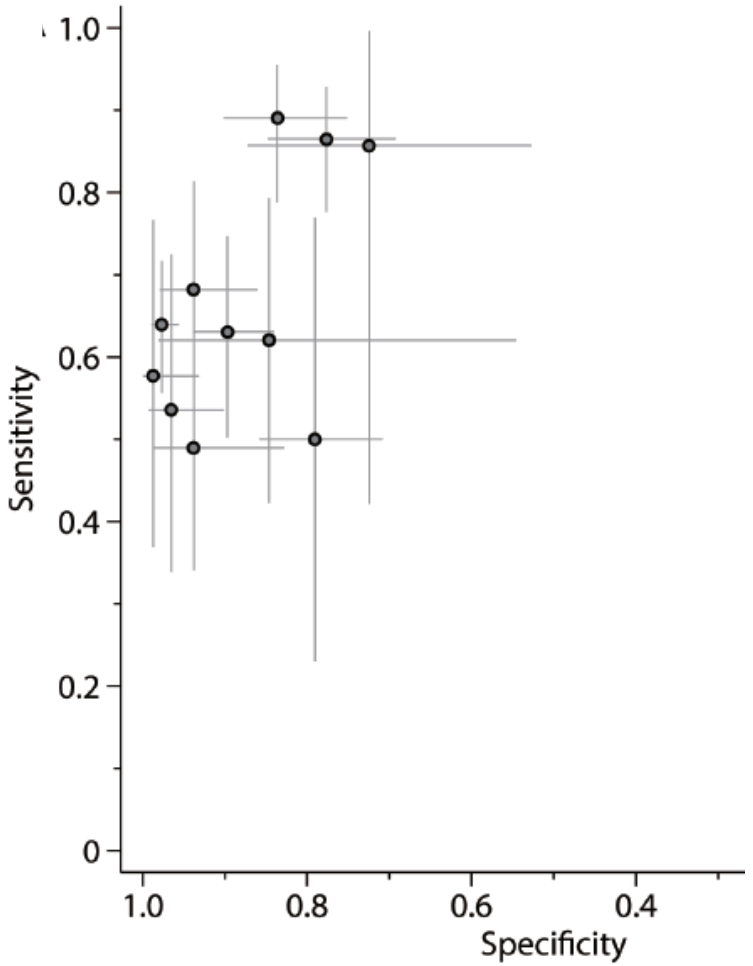
Ogawa H, et al. Sputum Gram Stain for Bacterial Pathogen Diagnosis in Community-acquired Pneumonia: A Systematic Review and Bayesian Meta-analysis of Diagnostic Accuracy and Yield. Clin Infect Dis. 2020 Jul 27;71(3):499-513.

Poll Question #2

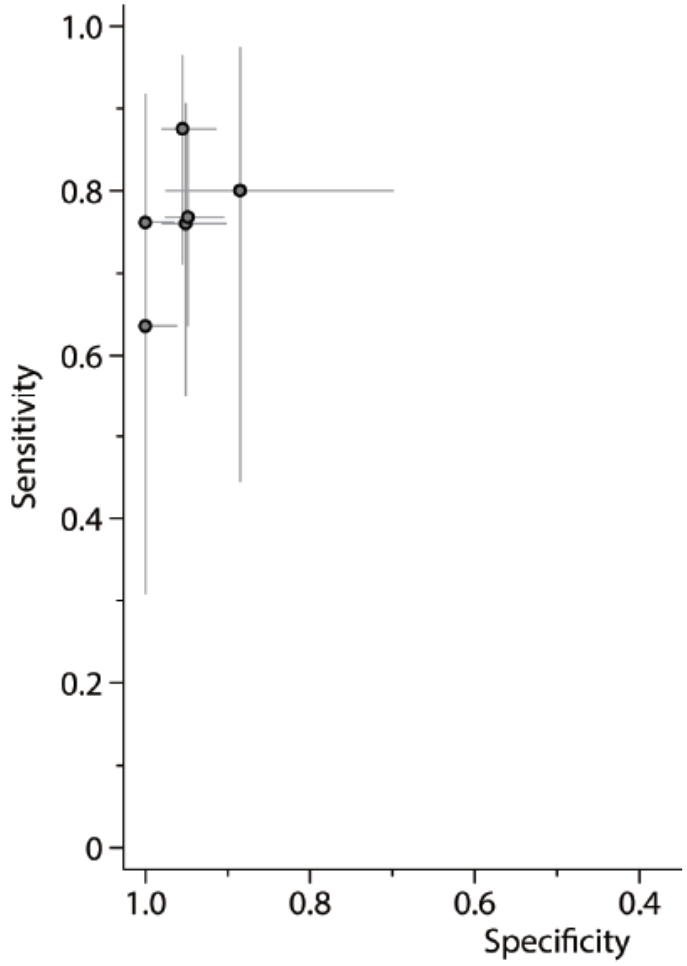
The following UAT are performed in-house:

a. *S. pneumoniae*
b. *L. pneumophila*
c. Both
d. Neither
e. n/a

Streptococcus pneumoniae



Haemophilus influenzae



Ogawa H, et al. Sputum Gram Stain for Bacterial Pathogen Diagnosis in Community-acquired Pneumonia: A Systematic Review and Bayesian Meta-analysis of Diagnostic Accuracy and Yield. Clin Infect Dis. 2020 Jul 27;71(3):499-513.

Recommendations for Specific Management Questions:
Initial Diagnostic Evaluation

Question 3

In adults with CAP, should ***Legionella*** **and pneumococcal urinary antigen testing be performed** at the time of diagnosis?

Recommendation

Legionella and *S. pneumoniae* antigen testing

- In **adults with severe CAP**
  - ***(Legionella)*** also collect lower respiratory tract secretions for culture or NAAT
- Where indicated by **epidemiological factors** (***Legionella***)
  - i.e., known outbreaks or recent travel

Interpretation
Conditional

Quality
Low quality of evidence

Metlay JP, et al. 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. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

UAT Guideline Recommendation Based On Observed Mortality Reduction in Large Observational Studies

Costantini, et al. 2016

Table 5 Multivariable regression analyses for in-hospital and 30-day mortality, length of hospital stay and duration of antibiotic therapy

	In-hospital mortality		30-day mortality		Length of hospital stay		Duration of antibiotic therapy	
	N = 561		*N* = 495		*N* = 561		*N* = 505	
	OR	95 % CI	OR	95 % CI	MD	95 % CI	MD	95 % CI
Socio-demographic characteristics and other potential confounders								
Age in years (continuous)	**1.081**	**1.049, 1.114**	**1.105**	**1.068, 1.143**	**0.052**	**0.016, 0.089**	−0.003	−0.038, 0.033
Male gender (vs. female gender)	0.803	0.454, 1.419	0.628	0.348, 1.133	0.850	−0.424, 2.124	0.411	−0.792, 1.615
Admission from nursing home (vs. from own home)	1.118	0.544,2.300	1.409	0.648, 3.063	**−3.222**	**−5.232, −1.213**	−1.770	−3.619, 0.079
Five or more comorbidities (vs. less than five)	1.601	0.827, 3.102	1.243	0.627, 2.464	1.150	−0.621, 2.921	1.421	−0.233, 3.075
ATS criteria for CAP severity (continuous)	**1.743**	**1.383, 2.196**	**1.868**	**1.462, 2.385**	-0.287	−0.903, 0.329	**−1.111**	**−1.694, −0.527**
Admission in 2012 (vs. admission in 2015)	1.081	0.491, 2.377	0.863	0.387, 1.923	1.297	−0.723, 3.318	0.659	−1.224, 2.541
Stay in a respiratory ward (vs. stay in a non-respiratory ward)	0.847	0.351, 2.042	0.750	0.304, 1.851	**4.225**	**2.152, 6.299**	**4.363**	**2.377, 6.349**
Mechanical ventilation	0.968	0.289, 3.243	1.102	0.340, 3.575	**4.638**	**1.688, 7.587**	**5.017**	**2.115, 7.919**
Adherence to diagnostic procedures								
Blood culture	0.677	0.377, 1.213	0.600	0.328, 1.097	**2.631**	**1.259, 4.003**	**2.728**	**1.417, 4.039**
Urinary Antigen tests	**0.427**	**0.215, 0.850**	**0.341**	**0.170, 0.685**	0.033	−1.407, 1.473	−0.164	−1.535, 1.207

57% lower odds of in-hospital mortality and 66% lower odds of 30-day mortality compared to patients not tested

(Adjusted for baseline demographic/ clinical differences)

Costantini E, Allara E, Patrucco F, Faggiano F, Hamid F, Balbo PE. Adherence to guidelines for hospitalized community-acquired pneumonia over time and its impact on health outcomes and mortality. Intern Emerg Med. 2016;11(7):929-940.

UAT Guideline Recommendation Based On Observed Mortality Reduction in Large Observational Studies

Uematsu, et al. 2014

Table 3 Crude mortality and the association of microbiological tests with 30-day mortality, stratified by disease severity

	Severity class							
	Very severe		Severe		Moderate		Mild	
Death[a]/total (%)	2075/7935 (26.1)		977/8224 (11.9)		1214/36 186 (3.4)		41/12 213 (0.3)	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Sputum tests	0.93 (0.82–1.05)	0.24	1.22 (1.05–1.41)	0.009	1.11 (0.98–1.26)	0.11	1.00 (0.50–2.00)	0.99
Blood cultures	0.81 (0.70–0.93)	0.004	0.71 (0.60–0.85)	<0.001	0.79 (0.68–0.93)	0.003	1.67 (0.79–3.53)	0.18
Urine antigen tests	0.75 (0.64–0.87)	<0.001	0.75 (0.63–0.89)	0.001	0.80 (0.69–0.94)	0.005	0.39 (0.16–0.99)	0.047
Cumulative no. performed								
0	Reference		Reference		Reference		Reference	
1	0.97 (0.85–1.12)	0.69	1.03 (0.87–1.21)	0.74	0.81 (0.70–0.93)	0.003	1.03 (0.50–2.11)	0.93
2	0.74 (0.63–0.86)	<0.001	0.78 (0.64–0.94)	0.010	0.78 (0.66–0.92)	0.004	0.50 (0.17–1.47)	0.21
3	0.51 (0.40–0.64)	<0.001	0.70 (0.54–0.91)	0.008	0.83 (0.66–1.04)	0.11	1.08 (0.36–3.26)	0.89

[a]In-hospital deaths within 30 days of admission.

25% reduced odds of 30-day mortality

Uematsu H, Hashimoto H, Iwamoto T, Horiguchi H, Yasunaga H. Impact of guideline-concordant microbiological testing on outcomes of pneumonia. Int J Qual Health Care. 2014;26(1):100-107.

Testing Warranted in Endemic Populations

- Identifies cases that would otherwise remain undetected
- Facilitates targeted antibiotic therapy
- Provides surveillance for potential outbreaks

"Routine *Legionella* testing affords confidence that cases were not missed…and infection prevention protocols remained effective."

International Journal of *Environmental Research and Public Health*

MDPI

Article

Clinical Presentation of Community-Acquired Legionella Pneumonia Identified by Universal Testing in an Endemic Area

Shruti Puri [1], Monique Boudreaux-Kelly [2], Jon D. Walker [2], Cornelius J. Clancy [2,3] and Brooke K. Decker [2,3,*]

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2 Statcore, VA Pittsburgh Healthcare System, Pittsburgh, PA 15240, USA; Monique.Kelly@va.gov (M.B.-K.); Jon.Walker4@va.gov (J.D.W.); cjc76@pitt.edu (C.J.C.)
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check for updates

Abstract: The rapid identification of *Legionella* pneumonia is essential to optimize patient treatment and outcomes, and to identify potential public health risks. Previous studies have identified clinical factors which are more common in *Legionella* than non-*Legionella* pneumonia, and scores have been developed to assist in diagnosing cases. Since a *Legionella* pneumonia outbreak at VA Pittsburgh in 2012, nearly all patients with pneumonia have been tested for *Legionella*. The purpose of this study was to evaluate distinguishing characteristics between *Legionella* and non-*Legionella* pneumonia with the application of universal testing for *Legionella* in all cases of community-acquired pneumonia. We performed a retrospective case-control study matching *Legionella* and non-*Legionella* pneumonia cases occurring in the same month. Between January 2013 and February 2016, 17 *Legionella* and 54 non-*Legionella* cases were identified and reviewed. No tested characteristics were significantly associated with *Legionella* cases after Bonferroni correction. Outcomes of *Legionella* and non-*Legionella* pneumonia were comparable. Therefore, in veterans who underwent routine *Legionella* testing in an endemic area, factors typically associated with *Legionella* pneumonia were non-discriminatory.

Puri S, Boudreaux-Kelly M, Walker JD, Clancy CJ, Decker BK. Clinical Presentation of Community-Acquired Legionella Pneumonia Identified by Universal Testing in an Endemic Area. *Int J Environ Res Public Health*. 2020;17(2):533. Published 2020 Jan 15. doi:10.3390/ijerph17020533

Clinical Infectious Diseases

MAJOR ARTICLE

Pneumococcal and *Legionella* Urinary Antigen Tests in Community-acquired Pneumonia: Prospective Evaluation of Indications for Testing

Shawna Bellew,[1] Carlos G. Grijalva,[1] Derek J. Williams,[1] Evan J. Anderson,[2] Richard G. Wunderink,[3] Yuwei Zhu,[1] Grant W. Waterer,[4] Anna M. Bramley,[5] Seema Jain,[5] Kathryn M. Edwards,[1] and Wesley H. Self[1]

A **SP**

IDSA/ATS indications for SP UAT

	Positive	Negative	
SP UAT positive	49 (4.1%)	32 (4.2%)	81
SP UAT negative	1135 (95.9%)	725 (95.8%)	1860
	1184	757	1941

B **LP**

IDSA/ATS indications for LP UAT

	Positive	Negative	
LP UAT positive	20 (1.6%)	12 (1.8%)	32
LP UAT negative	1238 (98.4%)	671 (98.2%)	1909
	1258	683	1941

Bellew S, Grijalva CG, Williams DJ, Anderson EJ, Wunderink RG, Zhu Y, Waterer GW, Bramley AM, Jain S, Edwards KM, Self WH. Pneumococcal and Legionella Urinary Antigen Tests in Community-acquired Pneumonia: Prospective Evaluation of Indications for Testing. Clin Infect Dis. 2019 May 30;68(12):2026-2033.

Multivariable Models for Predicting Positive *Streptococcus pneumoniae* and *Legionella pneumophila* Urinary Antigen Tests

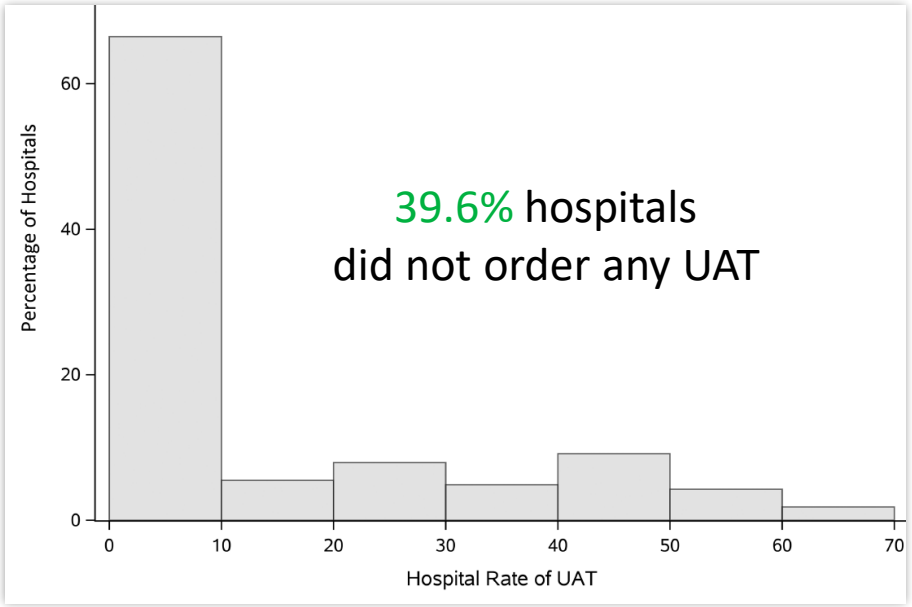
	Multivariable OR (95% CI)
Streptococcus pneumoniae (n = 81)	
Male sex	0.69 (0.43–1.09)
Age ≥65	1.04 (0.61–1.77)
Failure of outpatient antibiotics	0.67 (0.36–1.26)
Fever (>38°C)	1.50 (0.93–2.42)
Hyponatremia	1.81 (0.96–3.41)
ICU admission	1.29 (0.75–2.24)
Pneumonia Severity Index risk class ≥IV	1.46 (0.84–2.55)
Empiric broad spectrum antibiotics	1.16 (0.70–1.94)
Legionella pneumophila (n = 32)	
Recent travel	2.18 (0.99–4.76)
Fever (>38°C)	3.21 (1.56–6.60)
Hyponatremia	7.44 (3.5–15.67)
Diarrhea	2.88 (1.39–5.95)

Bellew S, Grijalva CG, Williams DJ, Anderson EJ, Wunderink RG, Zhu Y, Waterer GW, Bramley AM, Jain S, Edwards KM, Self WH. Pneumococcal and Legionella Urinary Antigen Tests in Community-acquired Pneumonia: Prospective Evaluation of Indications for Testing. Clin Infect Dis. 2019 May 30;68(12):2026-2033.

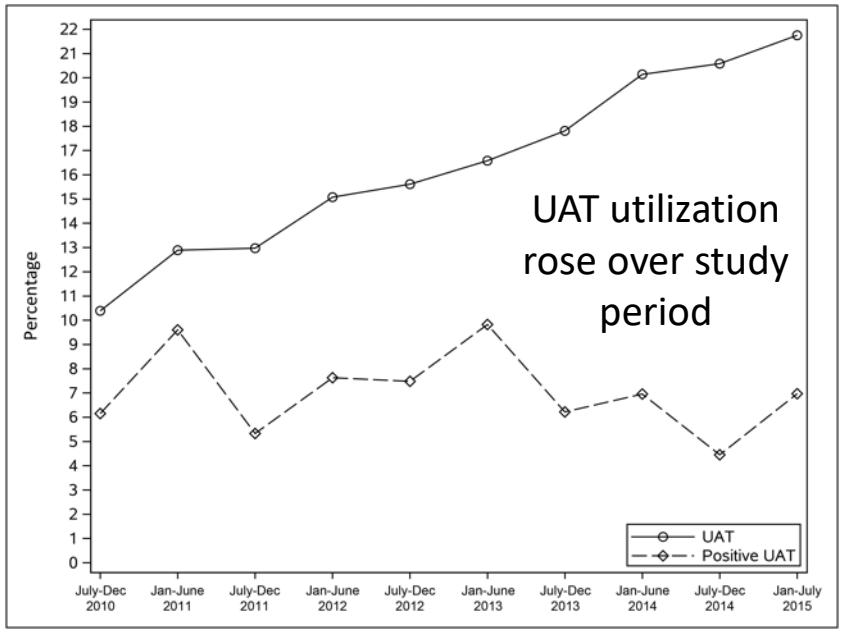
Clinical Infectious Diseases

MAJOR ARTICLE

Pneumococcal Urinary Antigen Testing in United States Hospitals: A Missed Opportunity for Antimicrobial Stewardship



39.6% hospitals did not order any UAT

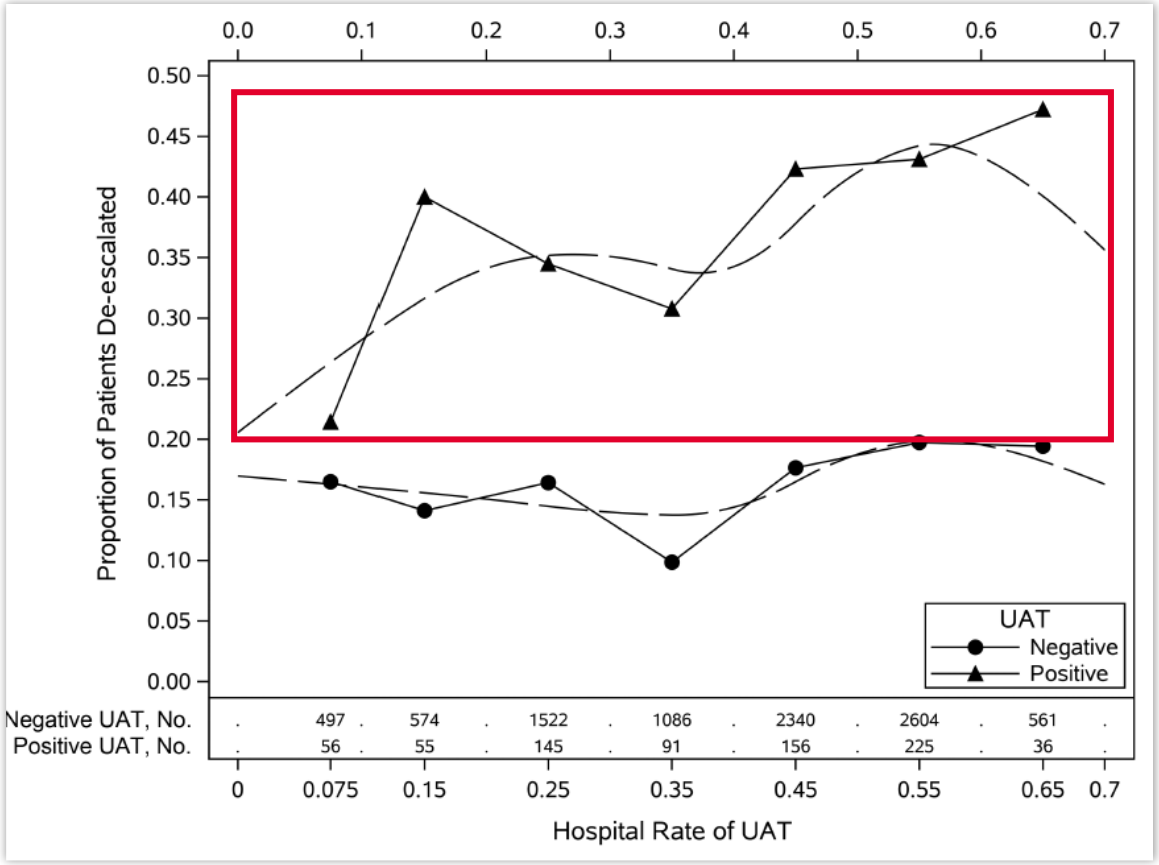


UAT utilization rose over study period

16.2% UAT in pneumonia population (n=159,894)

Schimmel JJ, Haessler S, Imrey P, Lindenauer PK, Richter SS, Yu PC, Rothberg MB. Pneumococcal Urinary Antigen Testing in United States Hospitals: A Missed Opportunity for Antimicrobial Stewardship. Clin Infect Dis. 2020 Sep 12;71(6):1427-1434.

Rate of De-escalation Following UAT Positivity Tended To Increase With Increasing Hospital Use



Hospital UAT use was strongly correlated with de-escalation following a positive test

Schimmel JJ, Haessler S, Imrey P, Lindenauer PK, Richter SS, Yu PC, Rothberg MB. Pneumococcal Urinary Antigen Testing in United States Hospitals: A Missed Opportunity for Antimicrobial Stewardship. Clin Infect Dis. 2020 Sep 12;71(6):1427-1434.

What are the clinical scenarios where UAT can be useful?

Hospitalized patients with CAP

COVID + patients – required hospitalization due to acute respiratory failure

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Hospitalized patient that you suspect a nosocomial pneumonia

Recommendations for Specific Management Questions:
Initial Diagnostic Evaluation

Question 5

In adults with CAP, should **serum procalcitonin plus clinical judgement versus clinical judgment alone** be used to withhold initiation of antibiotic treatment?

Recommendation

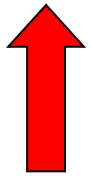
Serum procalcitonin should **not be used** **to withhold initiation of empiric antibiotic therapy** in adults with CAP.

Interpretation
Strong

Quality
Moderate quality of evidence

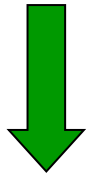
Metlay JP, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.

Procalcitonin Differentiates between Bacterial and Viral Infections



bacterial infections

(proinflammatory cytokines - IL-1, IL-6 and TNF-a - and endotoxin)



in viral infections

(interferon gama)

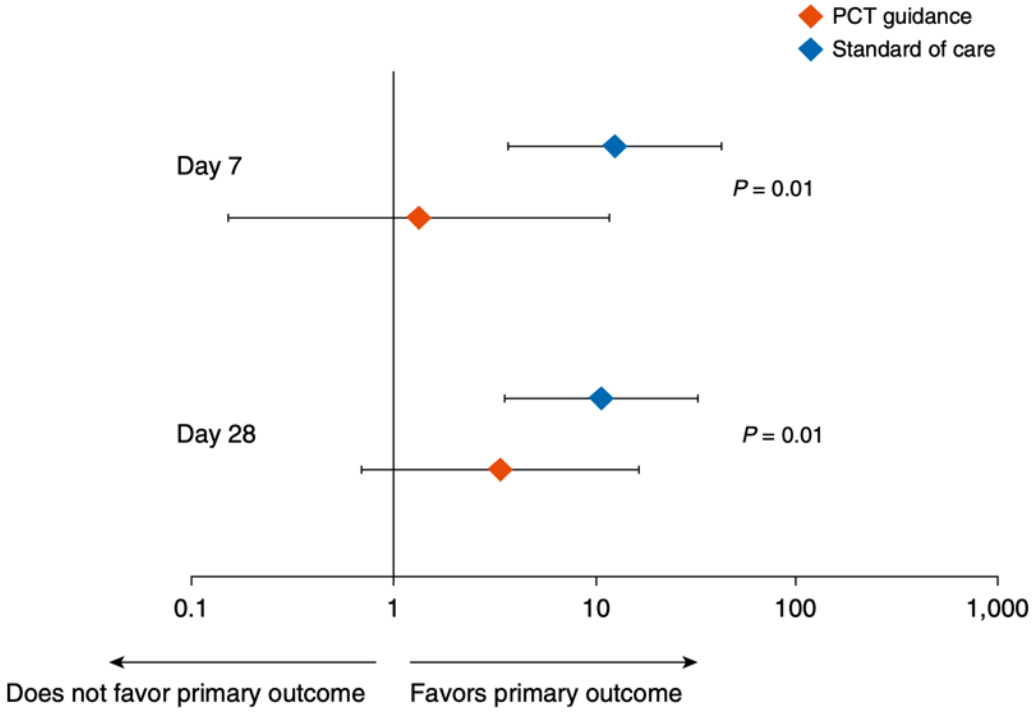
inflammation-mediated expression of the CALC I gene

Authors	Study name	Research question	Setting	*n=*	Mortality Control vs PCT group	AB exposure Control vs PCT	Relative AB reduction
Christ-Crain et al,	**ProRESP**	Reduction of antibiotic prescription for LRTI in the ED?	ED, single center	*243*	4/119 (3.4%) vs 4/124 (3.2%)	10.7 vs 4.8*	55.1%
Christ-Crain et al,	**ProCAP**	Reduction of antibiotic exposure in CAP in ED and hospital?	ED and hospital, single center	*302*	20/151 (13.2%) vs 18/151 (11.9%)	12.9 vs 5.7*	55.8%
Stolz et al,	**ProCOLD**	Reduction of antibiotic exposure in COPD exacerbation over 6 month?	ED, single center	*208*	9/106 (8.5%) vs 5/102 (4.9%)	7.0 vs 3.7*	47.1%
Briel et al,	**PARTI**	Safety & reduction of antibiotic exposure in upper and lower RTI?	Primary Care, multicenter	*458*	1/232 (0.4%) vs 0/226 (0%)	6.8 vs 1.5*	77.9%
Nobre et al,	**"ProSEP"**	Reduction of antibiotic exposure in septis in the ICU ?	ICU , single center	*79*	8/39 (20.5%) vs 8/40 (20%)	9.5 vs 6**	36.8%
Schuetz et al,	**ProHOSP**	Safety & feasability in LRTI in a multicenter setting?	ED and hospital, multicenter	*1359*	33/671 (4.9%) vs 34/688 (4.9%)	8.7 vs 5.7*	34.5%
Stolz et al,	**ProVAP**	Reduction of antibiotic exposure in VAP in different ICUs ?	ICU, multicenter	*101*	12/50 (24%) vs 8/51 (15.7%)	9.5 vs 13***	26.9%
Kristoffersen et al,	**1-PCT**	Reduction of antibiotic exposure for LRTI in Denmark?	ED and hospital, single center	*210*	1/107 (0.9%) vs 2/103 (1.9%)	6.8 vs 5.1*	25.0%
Hochreiter et al,	**ProSICU**	Guiding antibiotic therapy with PCT in a surgical ICU?	Surgical ICU, single center	*110*	14/53 (26.4%) vs 15/57 (26.3%)	7.9 vs 5.9*	25.3%
Bouadma et al,	**ProRATA**	Reduction of antibiotic exposure for sepsis in different french ICUs ?	ICU , multicenter	*621*	64/314 (20.4%) vs 65/307 (21.2%)	11.6 vs 14.3***	18.9%
Burckhardt et all	**"PARTI Germany"**	Safety & reduction of only initial PCT measurement in primary care?	Primary Care, multicenter	*550*	0/275 (0%) vs 0/275 (0%)	36.7% vs 21.5%****	42.0%
	Total			***4241***	**166/2117 (7.8%) vs 159/2124 (7.5%)**		

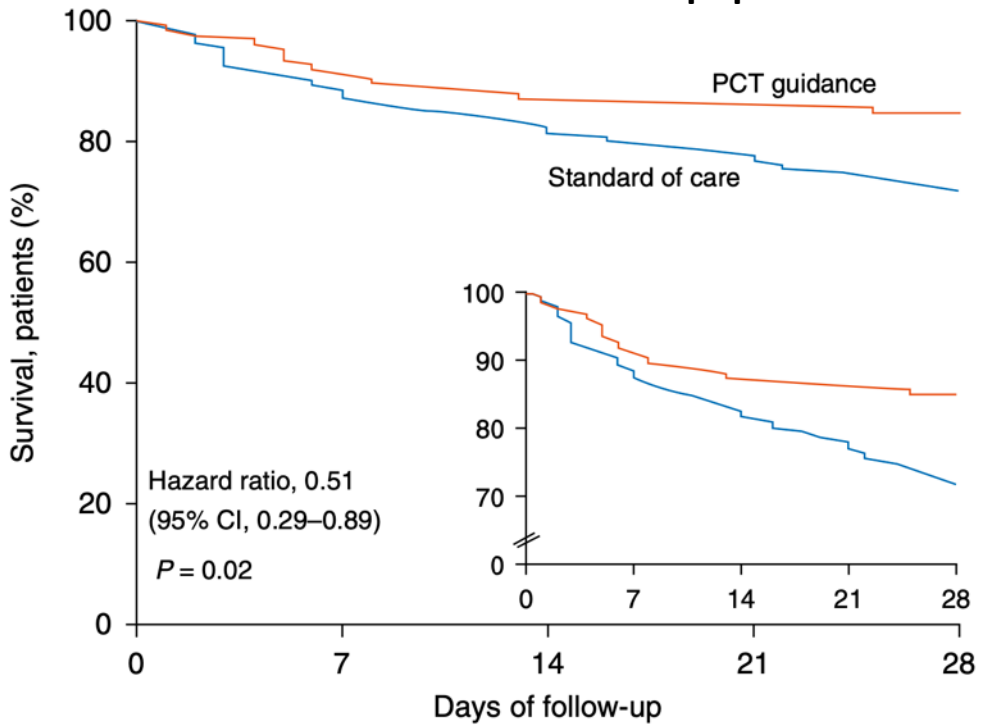
Schuetz P, Wirz Y, Sager R, et al. Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis. Lancet Infect Dis. 2018 Jan;18(1):95-107. doi: 10.1016/S1473-3099(17)30592-3. Epub 2017 Oct 13.

PCT-guidance treatment compared to standard-of-care after 180 days

Infection-associated adverse events (PCT vs. SOC)



28-day survival in the intention-to-treat population



Kyriazopoulou E, et al. Procalcitonin to Reduce Long-Term Infection-associated Adverse Events in Sepsis. A Randomized Trial. Am J Respir Crit Care Med. 2021 Jan 15;203(2):202-210.

What are the clinical scenarios where PCT levels can be useful?

Recognizing response to and shortening duration of antibiotic therapy

Determining the need for antibiotics in patients with LRTI (i.e., AECOPD)

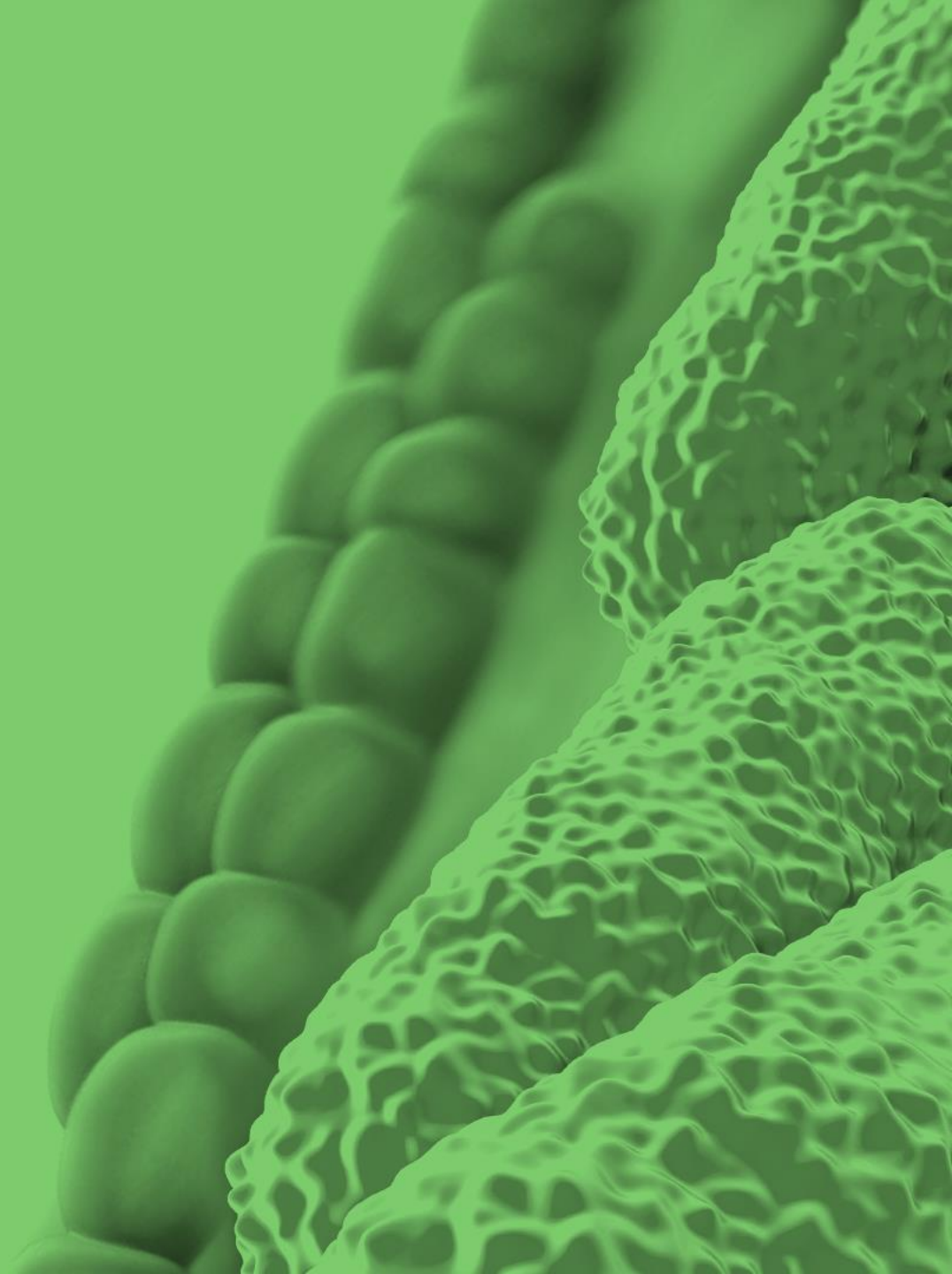
Determining severity of infection (e.g. localized versus systemic)

Differentiating between septic and other forms of shock

Distinguishing viral from bacterial infection in febrile patients

CAP Test Methods:

S. pneumoniae
Legionella



LEGIONELLA

METHODOLOGY	COMPONENT DETECTED	SAMPLE TYPE	SENSITIVITY	SPECIFICITY	TURNAROUND TIME
Culture	organism	sputum	Gold Standard*	Gold Standard*	4 - 10 days
UAT[1]	antigen	urine	95%	95%	15 minutes
DFA[2]	organism	sputum	33% - 70%	>95%	40 - 60 minutes
Serology/IFA[2]	antibody	serum	40% - 60%	>95%	60 - 90 minutes

STREPTOCOCCUS PNEUMONIAE

METHODOLOGY	COMPONENT DETECTED	SAMPLE TYPE	SENSITIVITY	SPECIFICITY	TURNAROUND TIME
UAT[3]	antigen	urine	86%**	94%**	15 minutes
Blood Culture	organism	blood	10% - 30%[4]	N/A	24 - 48 hours
Sputum Culture	organism	sputum	29% - 94%[5]	66%[6] - 94%[7]	24 - 48 hours
Sputum Gram Stain[8]	organism	sputum	15% - 100%	11% - 100%	15 minutes

* Sensitivity and specificity data for methodologies listed were obtained through comparison to clinical diagnosis including culture.
** Sensitivity and specificity data are retrospective for urine only.

1. BinaxNOW™ *Legionella* Urinary Antigen Card Package Insert.
2. Stout JE and Yu VL. Legionellosis, NEJM, 1997; 337:682-687.
3. Schrag SJ, et al. Resistant Pneumococcal Infections, WHO/CDS/CSR/DRS/2001.6.
4. BinaxNOW™ *S. pneumoniae* Urinary Antigen Card Package Insert.
5. Musher D, et al. Diagnostic Value of Microscopic Examination of Gram-Stained Sputum and Sputum Cultures Inpatients with Bacteremic Pneumococcal Pneumonia; CID: 2004:39..
6. Stralin K, et al. Etiologic Diagnosis of Adult Bacterial Pneumonia by Culture and PCR Applied to Respiratory Tract Samples, J Clin Micro, Feb. 2006, 643-645.
7. Garcia-Vazquez E, et al. Assessment of the Usefulness of Sputum Culture for Diagnosis of Community-Acquired Pneumonia Using the PORT Predictive Scoring System, Arch Inter Med/Vol. 164, Sept. 13, 2004, 1807-1811.
8. Reed, W, et al. Sputum Gram's Stain in Community Acquired Pneumococcal Pneumonia – A Meta-analysis; West J. Med 1996; 165:197-204.

UAT for *S. pneumoniae* and *Legionella*

Guideline-concordant testing[1]

Non-invasive, ease of urine sample collection[3]

No instrument required

Easy to use[2,3]

Rapid results[2,3]

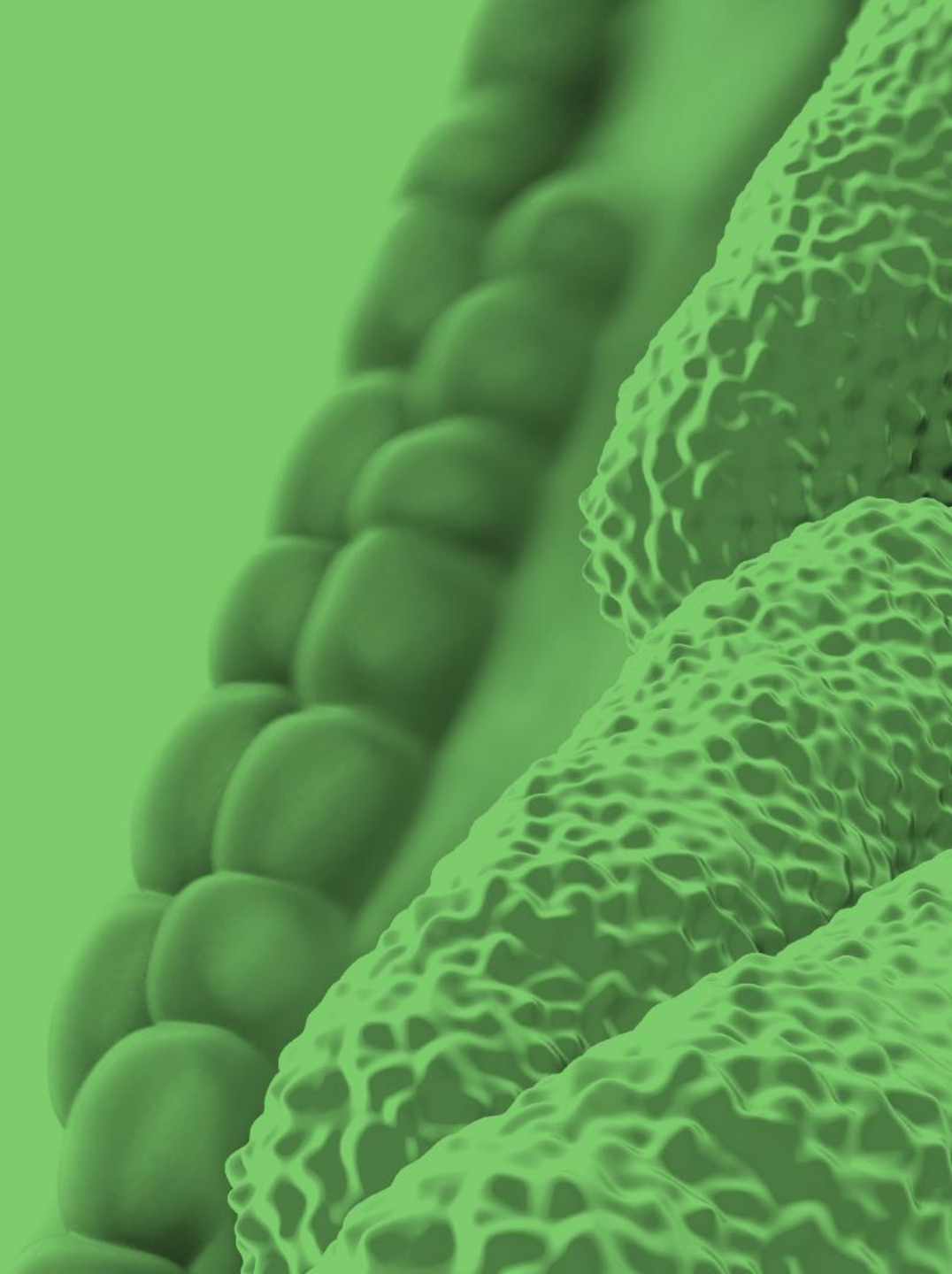
Low cost per test/Inexpensive[2,3]

Guide for antibiotic de-escalation[2,3]

UAT may provide cost-effective off-instrument testing option to avoid disrupting molecular workflows and higher technical demands

1. Metlay JP, et al. Am J Respir Crit Care Med. 2019;200(7):e45-e67.
2. Schimmel JJ, et al. Clin Infect Dis. 2020 Sep 12;71(6):1427-1434.
3. West, et al. Pneumococcal urinary antigen test use in diagnosis and treatment of pneumonia in seven Utah hospitals. Pneumococcal urinary antigen test use in diagnosis and treatment of pneumonia in seven Utah hospitals. ERJ Open Res 2016; 2: 00011-2016.

Summary



CAP Dx - Take Home Messages

- ✓ CAP is changing - clinical diagnosis is pivotal for patient's management
- ✓ UAT helps identify two important CAP pathogens associated with high mortality
  - ✓ *Legionella*, of increasing prevalence and poses new risks with building re-openings
  - ✓ *S. pneumoniae, the leading cause of CAP*
- ✓ Procalcitonin is important diagnosis tool for the diagnosis and management of CAP
- ✓ During COVID 19, CAP diagnosis and management should be managed according to the ATS/IDSA CAP Guidelines

"Problems are not stop signs,
***they are** guidelines"*

- Robert H. Schuller

THANK YOU