Antimicrobial Stewardship in Pneumonia

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Financial Disclosure

- Presenter is co-principle investigator on research study on RSV epidemiology sponsored by Pfizer
- Presenter has no financial interests or other relationships related to the content of this presentation.
- No commercial support was provided for this educational activity.

Objectives

Describe opportunities to apply antimicrobial stewardship principles in the management of pneumonia

Define the rate of bacterial co-infection in patients hospitalized with COVID-19 pneumonia

Bacterial Pneumonia Classification

- CAP, HCAP/HAP/VAP
  - Epidemiology
    - MRSA
    - MDR gram-negative bacteria (*Pseudomonas aeruginosa*)
  - Empiric antibiotic selection
  - CAP core measure
- 2016 – IDSA Management of Adults with HAP and VAP Guideline
  - HCAP?
- 2019 – IDSA Diagnosis and Treatment of Adults with CAP Guideline

Metley JP, et al. Am J Respir Crit Care Med 2019;200:7. e45–e67
Kalil AC, et al. Clin Infect Dis 2016;63:5. e61-e111

Routine Epidemiology

CAP	• *Streptococcus pneumoniae* • Atypical (e.g. *Legionella* spp)
HAP/VAP	• MSSA • *Pseudomonas aeruginosa* (Not MDRO)
Aspiration	• Anaerobic coverage not needed unless lung abscess or empyema suspected

Metley JP, et al. Am J Respir Crit Care Med 2019;200:7. e45–e67
Kalil AC, et al. Clin Infect Dis 2016;63:5. e61-e111

Broad therapy needed?

IT DEPENDS

Risk Factors for MDRO CAP – Non-severe

MRSA

- Prior respiratory isolation of MRSA
- Nasal MRSA PCR positive

Anti-pseudomonal

- Prior respiratory isolation of *P. aeruginosa*

Metley JP, et al. Am J Respir Crit Care Med 2019;200:7. e45–e67

Risk Factors for MDRO CAP - Severe

MRSA

- Prior respiratory isolation of MRSA
- Recent hospitalization
- Prior intravenous antibiotic use within 90 days
- Locally validated risk factors

Anti-pseudomonal (monotherapy)

- Prior respiratory isolation of *P. aeruginosa*
- Recent hospitalization
- Prior intravenous antibiotic use within 90 days
- Locally validated risk factors

Metley JP, et al. Am J Respir Crit Care Med 2019;200:7. e45–e67

Risk Factors for MDRO HAP

MRSA

- Prior intravenous antibiotic use within 90 days
- >20% of unit *S. aureus* isolates are MRSA
- Prevalence of MRSA is unknown
- High risk for mortality
  - Requiring ventilatory support or
  - Septic shock

Dual anti-pseudomonal

- Prior intravenous antibiotic use within 90 days
- High risk for mortality
  - Requiring ventilatory support or
  - Septic shock

Kalil AC, et al. Clin Infect Dis 2016;63:5. e61-e111

Risk Factors for MDRO VAP

MRSA

- >10%-20% of unit *S. aureus* isolates are MRSA
- Prevalence of MRSA is unknown

Dual anti-pseudomonal

- Prior intravenous antibiotic use within 90 days
- Septic shock at time of VAP
- ARDS preceding VAP
- Five or more days of hospitalization prior to the occurrence of VAP
- Acute renal replacement therapy prior to VAP onset
- >10% Gram negative isolates are resistant to beta-lactam
- Local resistance rates are unknown

Kalil AC, et al. Clin Infect Dis 2016;63:5. e61-e111

Confused yet?

Antimicrobial stewardship programs

Review local epidemiology

Develop empiric treatment guidelines

Assist with de-escalation

Monitor duration of therapy

How long should we treat CAP?

IDSA/ATS Guidelines: at least 5 days

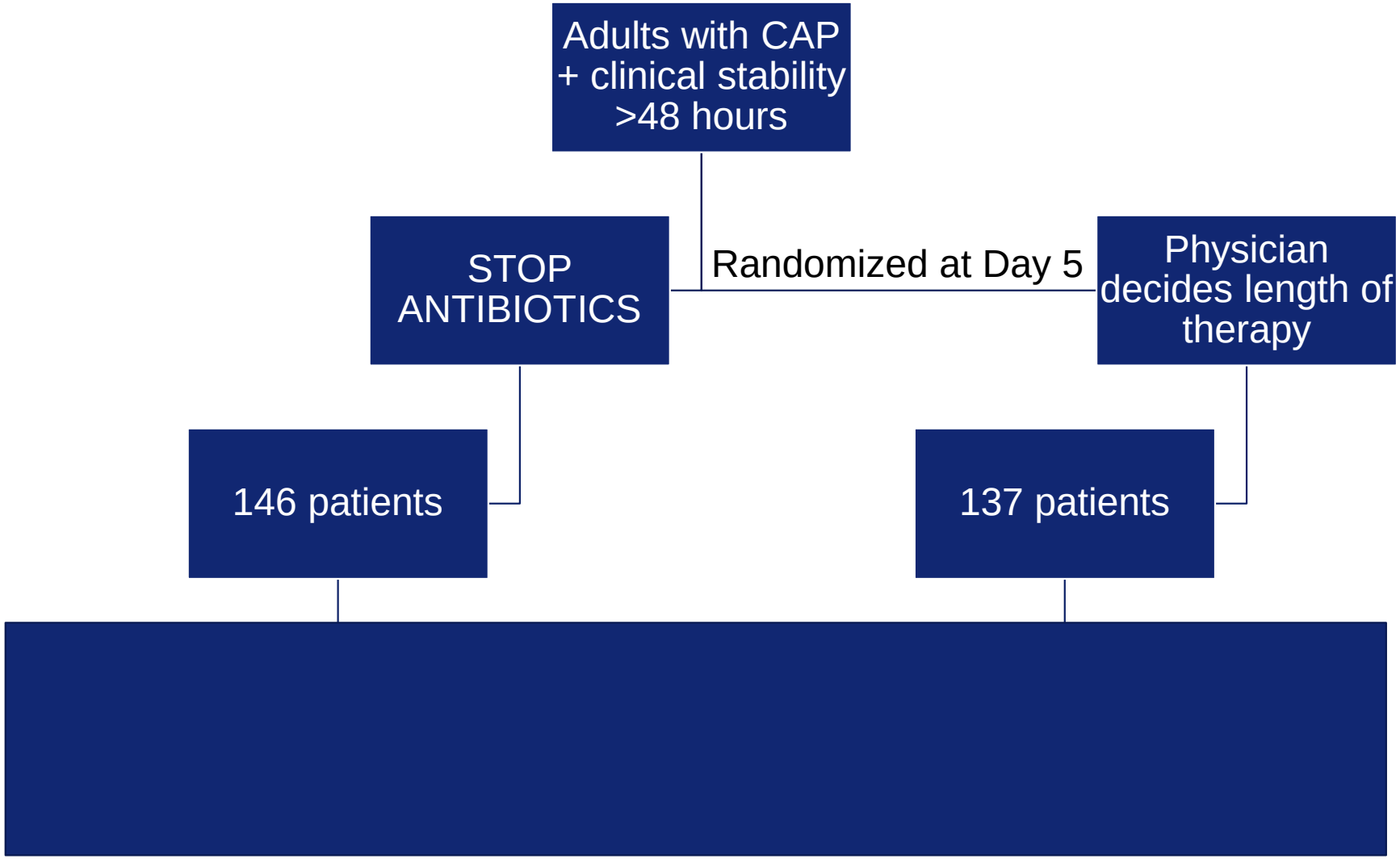
Applies to patients who achieve clinical stability

- Normal vital signs
- Eating
- Normal mental status

Continue until patient reaches clinical stability

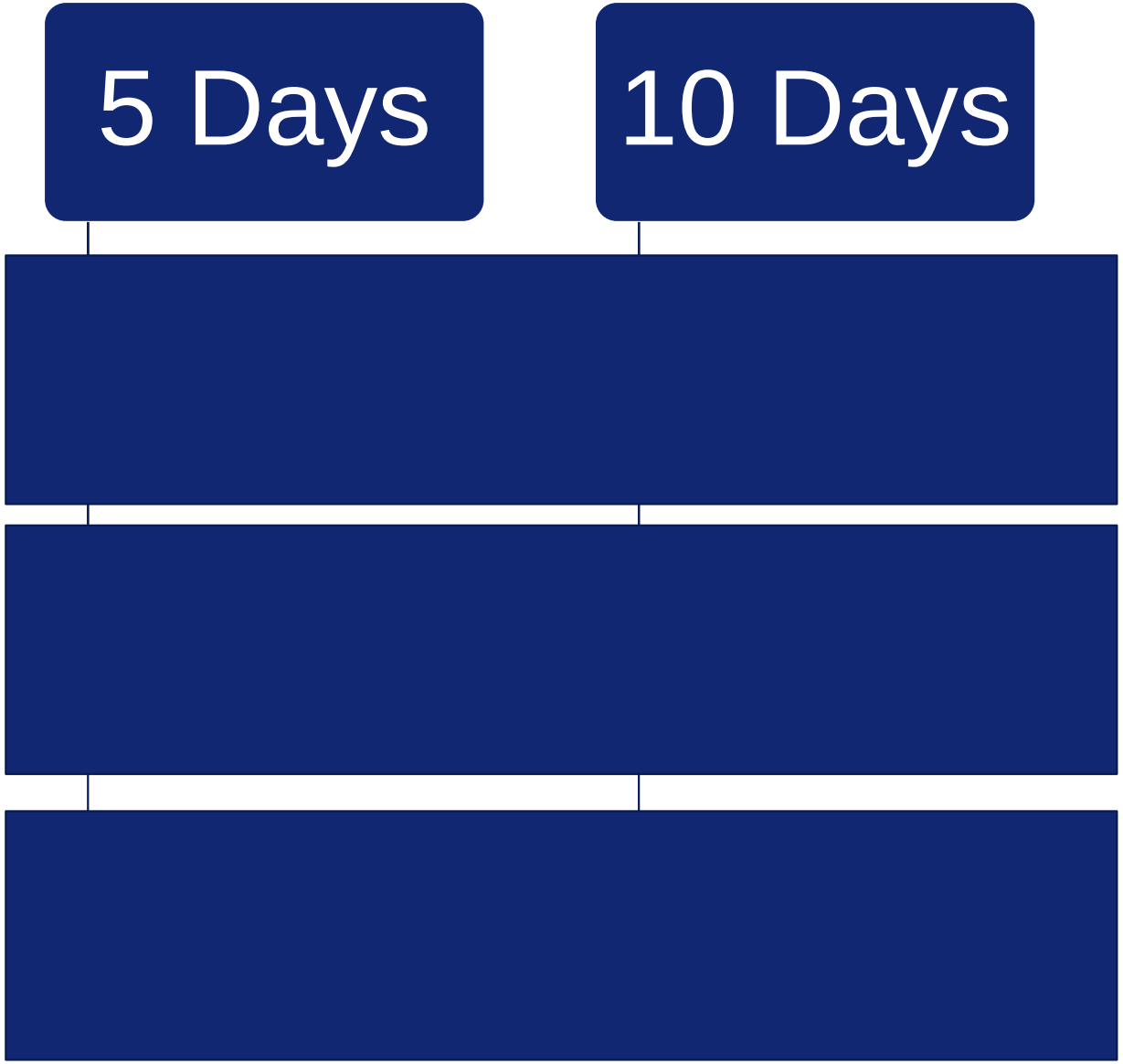
Metlay JP, *Am J Respir Crit Care Med.* 2019. 200(7): e45-67

What's the Evidence?



Uranga, Ane, et al. *JAMA Internal Med* (2016)

What's the Evidence?



Uranga, Ane, et al. *JAMA Internal Med* (2016)

Who Wasn't Studied?

- Immunocompromised
- *Pseudomonas* infection risk
- Need for chest tube
- Pregnancy + Breastfeeding
- Previously failed other antibiotics
- Other site of infection

Dunbar LM *Clin Infect Dis* 2003;37(6):752-60. ;
Uranga, Ane, et al. *JAMA Internal Med* (2016)

Key Takeaway

5 days of antibiotics is as effective as longer courses

Shorter is Better

Shorter Is Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	14
Atypical CAP	1	3	Equal	1
Possible PNA in ICU	3	14-21	Equal	1*
VAP	8	15	Equal	2
cUTI/Pyelonephritis	5 or 7	10 or 14	Equal	9**
Intra-abd Infection	4	10	Equal	2
Complex Appendicitis	2	5	Equal	1
GNB Bacteremia	7	14	Equal	3†
Cellulitis/Wound/Abscess	5-6	10	Equal	4‡
Osteomyelitis	42	84	Equal	2
Osteo Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2φ
Septic Arthritis	14	28	Equal	1
AECB & Sinusitis	≤5	≥7	Equal	>25
Variceal Bleeding	3	7	Equal	1
Neutropenic Fever	AFx72h/3 d	+ANC>500/9 d	Equal	2
Post Op Prophylaxis	0-1	1-5	Equal	55Ψ
Erythema Migrans (Lyme)	7	14	Equal	1
P. vivax Malaria	7	14	Equal	1
Total: 19 Conditions				>125 RCTs

14 RCTs in CAP

https://www.bradspellberg.com/shorter-is-better

Duration of Therapy at Discharge

Retrospective

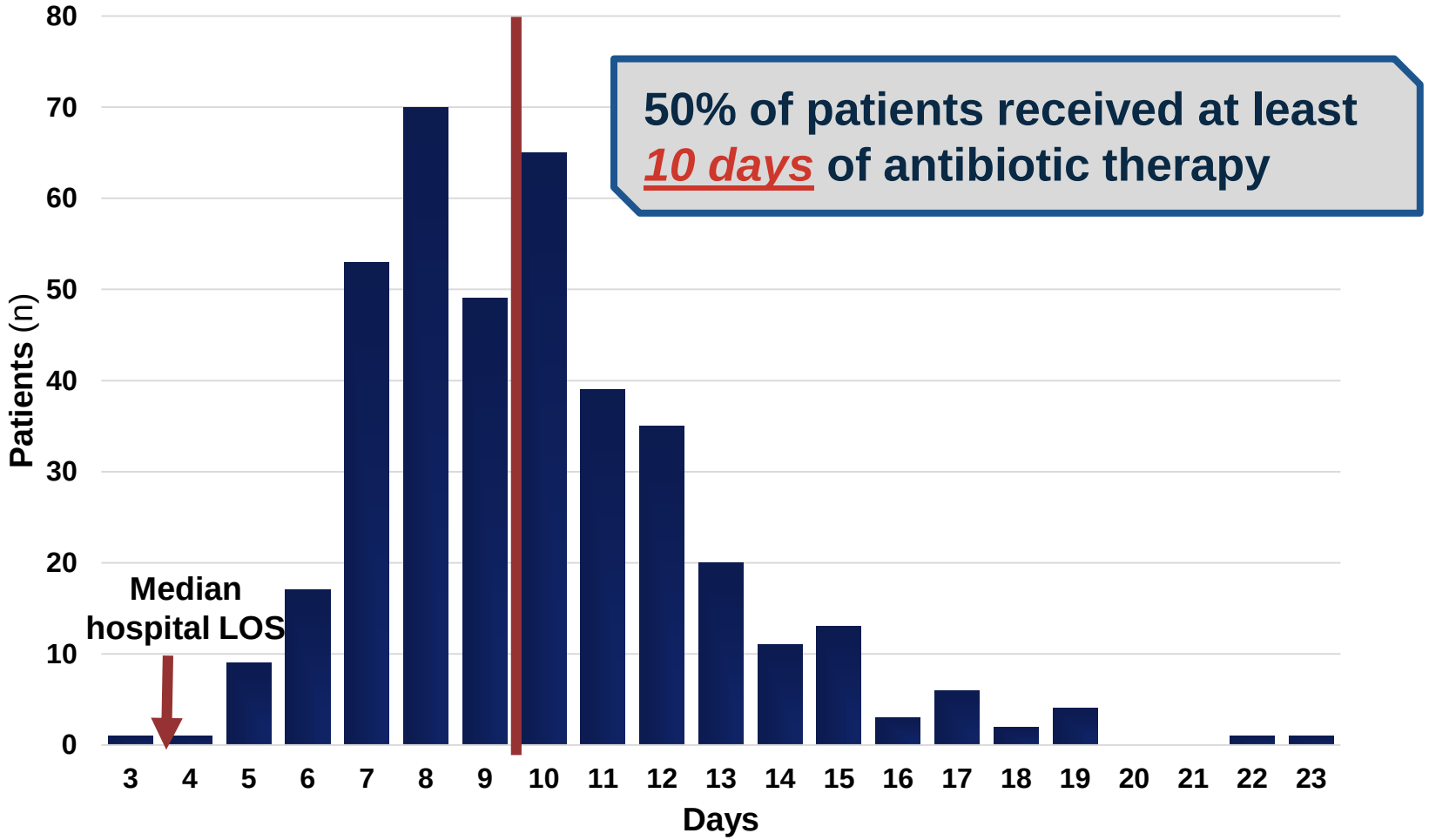
- Patients ≥ 18 years old hospitalized with CAP at Norton Healthcare
- Reviewed based on ICD-10 codes

Design

Key Results

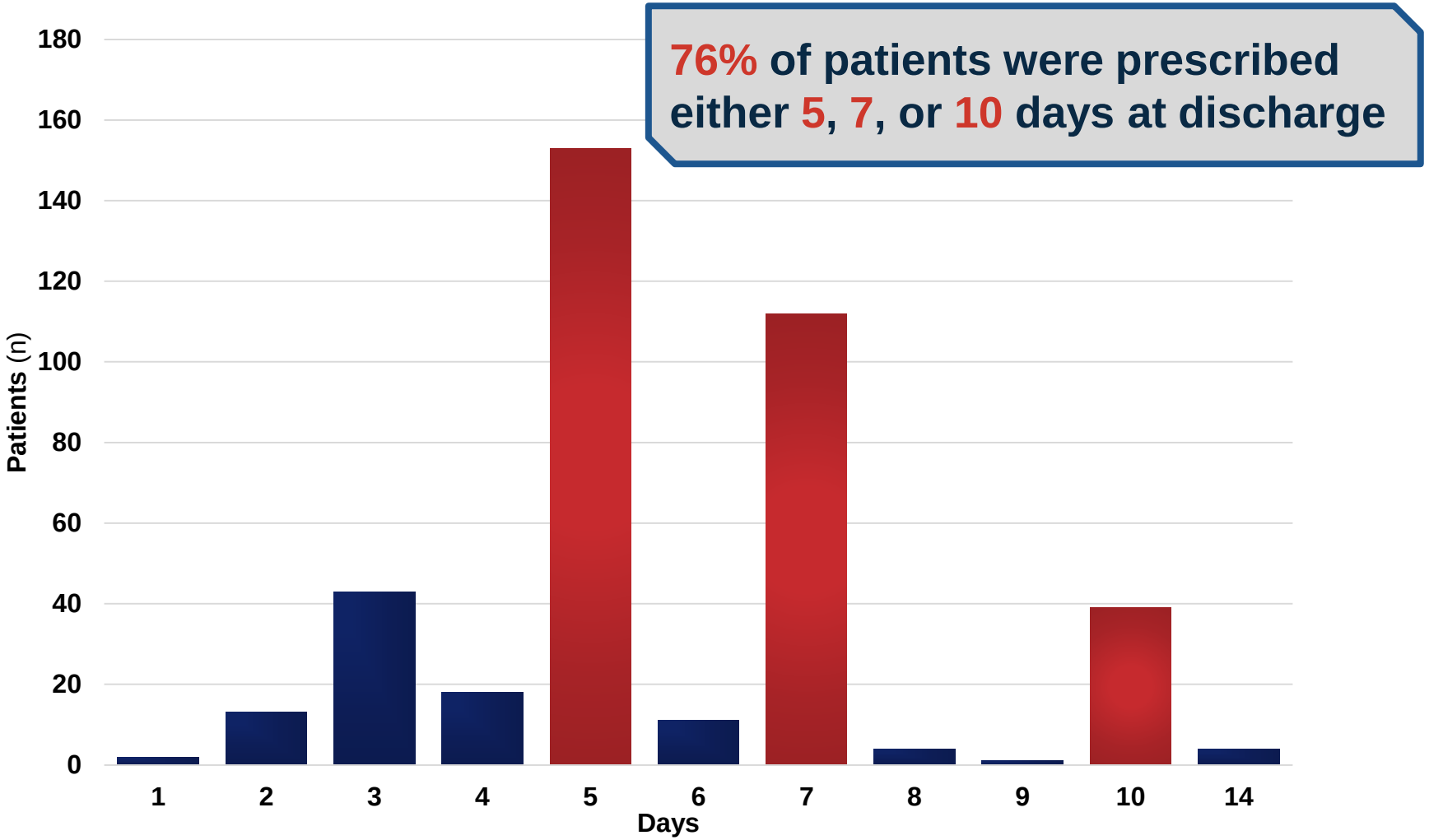
Whitman CW *Univ Louisville J Resp Infect*; 2022;6(1):Article 16.

Duration of CAP Therapy



Whitman CW *Univ Louisville J Resp Infect*; 2022;6(1):Article 16.

Discharge Prescription



Whitman CW *Univ Louisville J Resp Infect*; 2022;6(1):Article 16.

How long should we treat VAP?

Comparison of 8 vs 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults

A Randomized Trial

Jean Chastre, MD; Michel Wolff, MD; Jean-Yves Fagon, MD; et al

Chastre J, Wolff M, Fagon J, et al. *JAMA.* 2003;290(19):2588–2598.

Short vs Long Course – HAP/VAP

Short course associated with:

- Increased 28-day antibiotic free days
- Reduced recurrent VAP due to MDROs

No difference in:

- Mortality
- Recurrent pneumonia
- Treatment failure
- Hospital length of stay
- Duration of mechanical ventilation

Non-lactose fermenting gram-negative bacteria?

Chastre J, Wolff M, Fagon J, et al. *JAMA.* 2003;290(19):2588–2598.

Every Day Matters

Duration of Exposure to Antipseudomonal β-Lactam Antibiotics in the Critically Ill and Development of New Resistance

Besu F. Teshome, Scott Martin Vouri, Nicholas Hampton, Marin H. Kollef, Scott T. Micek

- Retrospective cohort study >7000 adults
- Cefepime, piperacillin/tazobactam, meropenem
- New resistance within 60 days
- Each additional day of antibiotic exposure resulted in a small, but statistically significant increase in risk of new resistance development

Teshome BF, et al. Pharmacotherapy 2018;39: 261-270

Antimicrobial Stewardship in COVID-19

…and the impact on antimicrobial resistance

Antimicrobial Stewardship in COVID-19

- Antimicrobial Stewardship Programs: focus on preventing resistance
- Core antimicrobial stewardship activities
  - Prospective audit and feedback
  - Formulary restriction/preauthorization
  - Antibiotic “timeouts”
  - Engagement with microbiology and infection prevention
  - Guideline development
  - Education

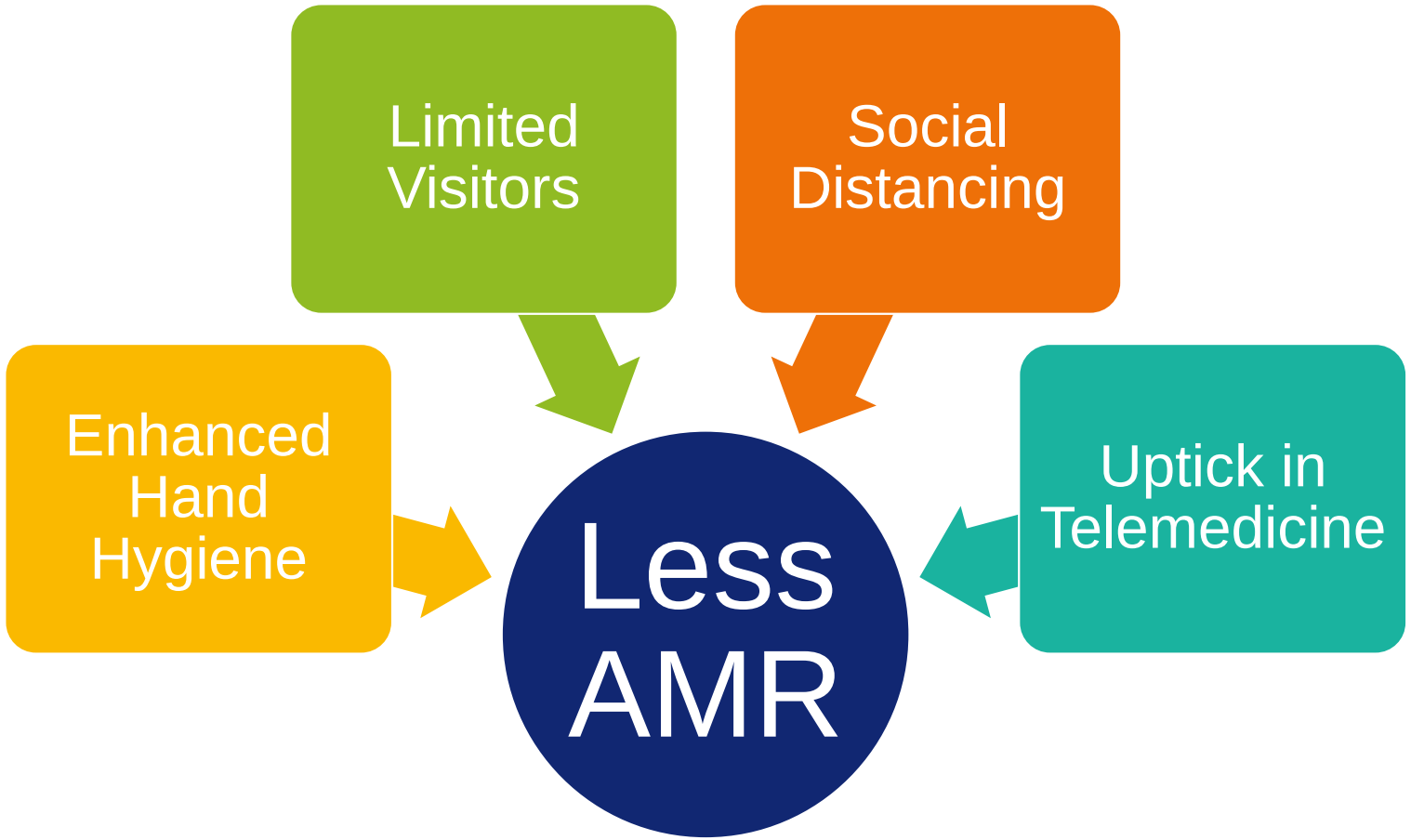
Mazdeyasna H, et al. *Curr Infect Dis Rep* 22, 23 (2020)

High Rates of Antibiotic Prescribing in COVID-19

- Michigan hospitals
  - 56.6% received early antibiotics
  - 3.5% had confirmed community-onset bacterial infections
- NYC
  - 70% started on empiric antibiotics
  - 3%-8% had confirmed community-onset bacterial infections
- London ICU
  - 100% started on empiric antibiotics
  - 6% had confirmed community-onset bacterial infections

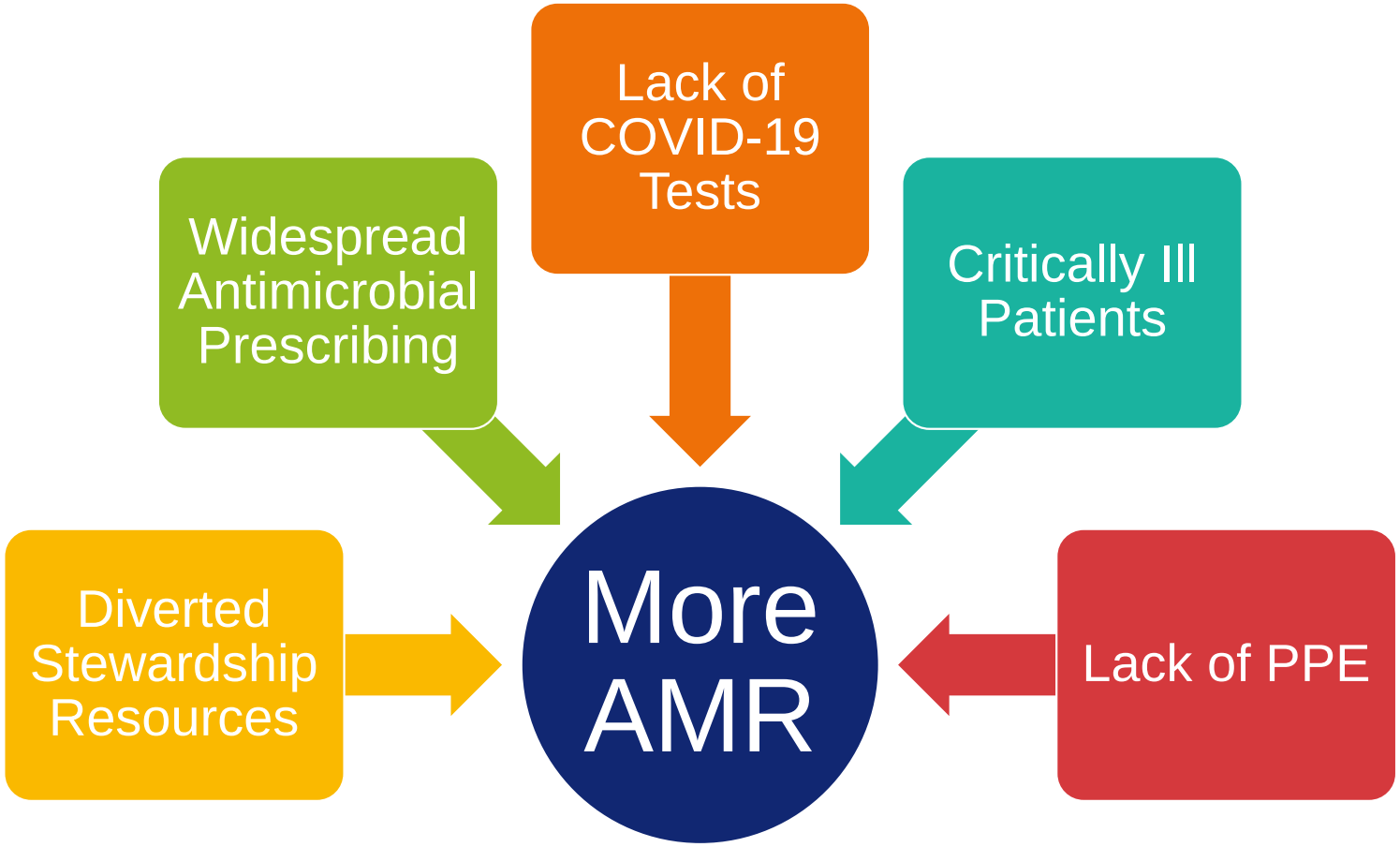
Vaughn VM, et al. *Clin Infect Dis* 2021;72:10
Kubin CJ, et al. *Am J Health-Sys Pharm* 2021;78:8
Stevenson DR, et al. *Clin Infect Dis* 2021;72:11

The Good



Jesús Rodríguez-Baño J, *Trans R Soc Trop Med Hyg* 2021;115:10

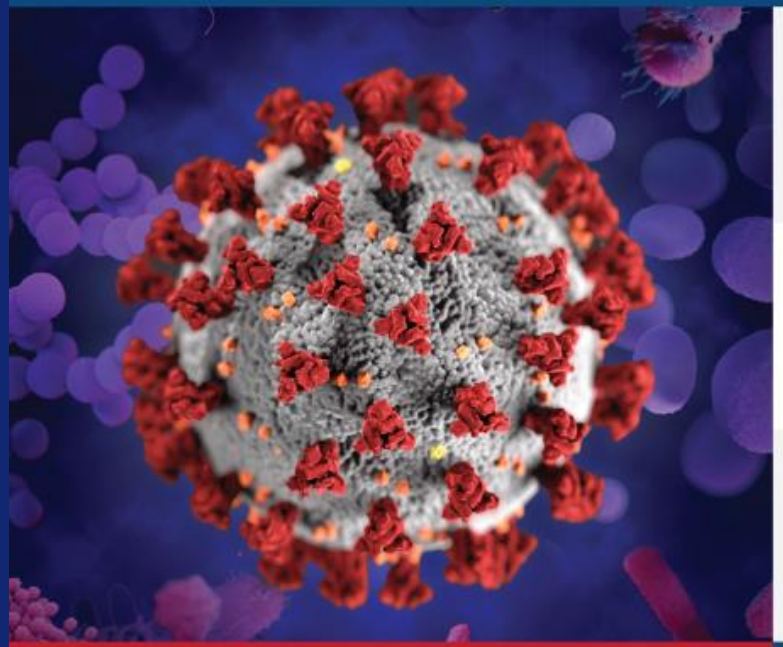
The Bad



Jesús Rodríguez-Baño J, *Trans R Soc Trop Med Hyg* 2021;115:10

The Ugly

2022 CDC Special Report



COVID-19 CREATED A PERFECT STORM

The U.S. lost progress combating antimicrobial resistance in 2020

↑15% Antimicrobal-resistant infections and deaths increased in hospitals in 2020.

~80% Patients hospitalized with COVID-19 who received an antibiotic March-October 2020.

Delayed or unavailable data, leading to resistant infections spreading undetected and untreated.

INVEST IN PREVENTION.

Setbacks to fighting antimicrobial resistance can and must be temporary.

CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2022

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

2022 CDC Special Report

CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2022

- Faster COVID-19 tests
- COVID-19 vaccines and therapeutics
- Renewed interest in infectious diseases
- Strengthening HAI/AR Program (SHARP)

Kentucky Antimicrobial Stewardship Innovation Consortium

KYMDRO.org/KASIC

Co-infection

- COVID-19 and other infection concurrently
- Community-acquired bacterial pneumonia

Secondary infection

- Develops after COVID-19
- Hospital-acquired pneumonia/ventilator-associated pneumonia

Opportunities for Antimicrobial Stewardship in COVID-19

Bacterial Co-infection

Bacterial co-infection rate is < 10%

National Institute of Health

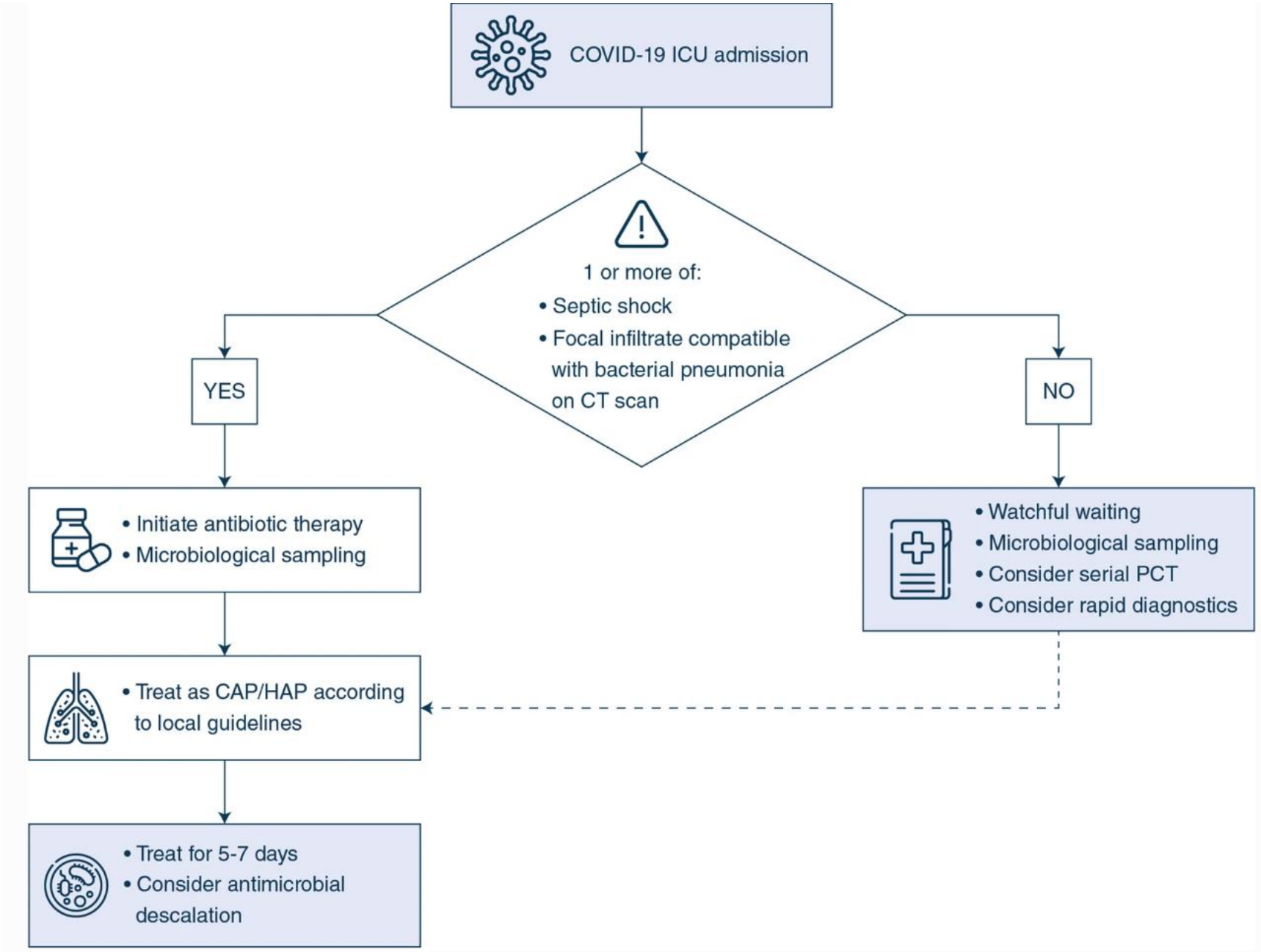
- Recommend against empiric broad-spectrum antibiotics in patients with severe or critical COVID-19
- Consider in specific situations
  - Lobar infiltrate on chest x-ray
  - Leukocytosis
  - Elevated serum lactate level
  - Shock
  - Microbiological data

COVID-19 Treatment Guidelines Panel. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed [Aug 25, 2022]
Evans L, Rhodes A, Alhazzani W, et al. *Intensive Care Med*. 2021;47(11):1181-1247.
Metlay JP, Waterer GW, Long AC, et al. *Am J Respir Crit Care Med.* 2019;200(7):e45-e67.
Moore SE, Wilde AM, Bohn BC, et al. *Infect Control Hosp Epidemiol*. 2021;1-3.

Procalcitonin in COVID-19

- Can be misleading in patients with COVID-19
  - May be elevated in absence of bacterial co-infection
- High negative predictive value
  - 99.3% in a study of 2,443 patients
  - Low procalcitonin should guide antibiotic de-prescribing
- Procalcitonin not recommended to aid in decision to initiate antibiotics

May M, et al. *Antimicrob Agents Chemother* 2021;65:e02167-20
Barlam TF, et al. *Infect Control Hosp Epidemiol* 2022



De Waele JJ, et al. *Intensive Care Med* 2021;**47**, 104–106

Secondary Infection Opportunities

Obtaining appropriate cultures

De-escalation

- Positive cultures
- Negative cultures
  - No MRSA and No Pseudomonas = Stop vancomycin and anti-pseudomonal
  - Difficult in critically ill – suggest step-wise approach

Defining durations of therapy early

- Adding stop dates

“Monitoring off antibiotics”

Conclusion

- Etiology of acute pneumonia varies greatly
- Apply antimicrobial stewardship principles to mitigate development of MDROs:
  - Select most narrow spectrum empiric option
    - Order sets aid in selection
  - De-escalate based on culture results
  - Use shortest duration of antibiotics (5 days CAP, 7 days HAP/VAP)
  - Discontinue antibiotics in viral pneumonia

Questions?

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