Identifying Exposures and Outcomes: Inpatient Considerations

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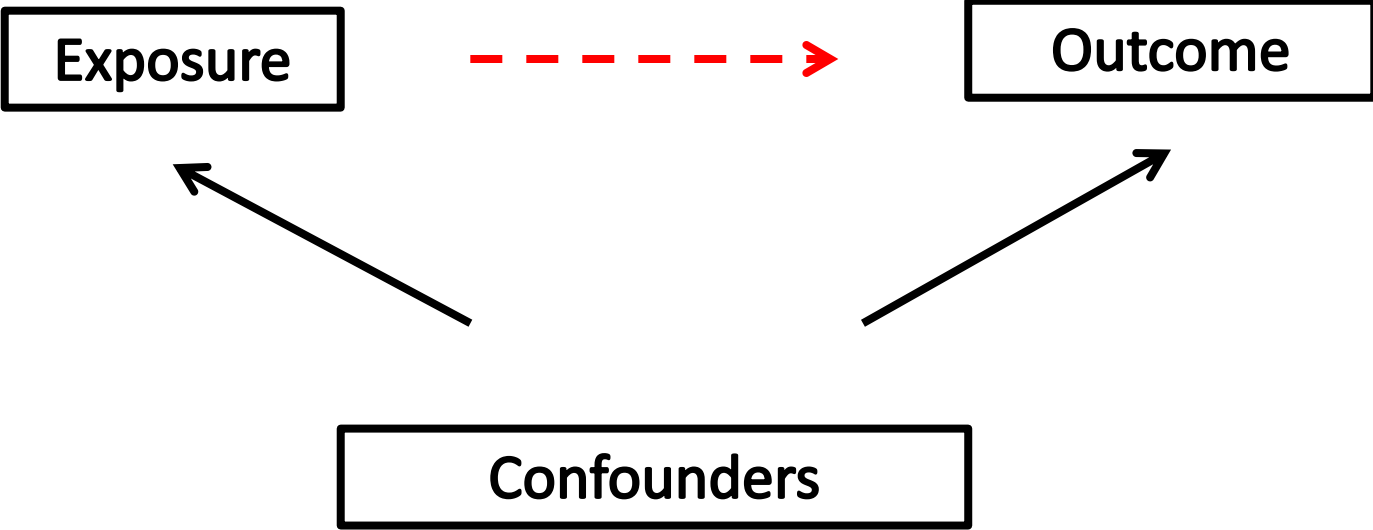Johns Hopkins University School of Medicine

Disclosures

- I have received non-federally funded support and speaker fees from the following extramural organizations in the past 12 months
  - Pfizer
  - Merck

- I have served on an advisory panel for Allergen

| Exposure | → | Outcome |

Syndrome-Specific Stewardship

- Easier to provide education and gather meaningful evidence for a specific infectious indication

- Focused message facilitates provider learning
  - Intervention seen as educational compared with broader stewardship methods
  - Learning = sustainable change

- Can broaden impact of interventions to appropriate diagnostics, imaging, etc.

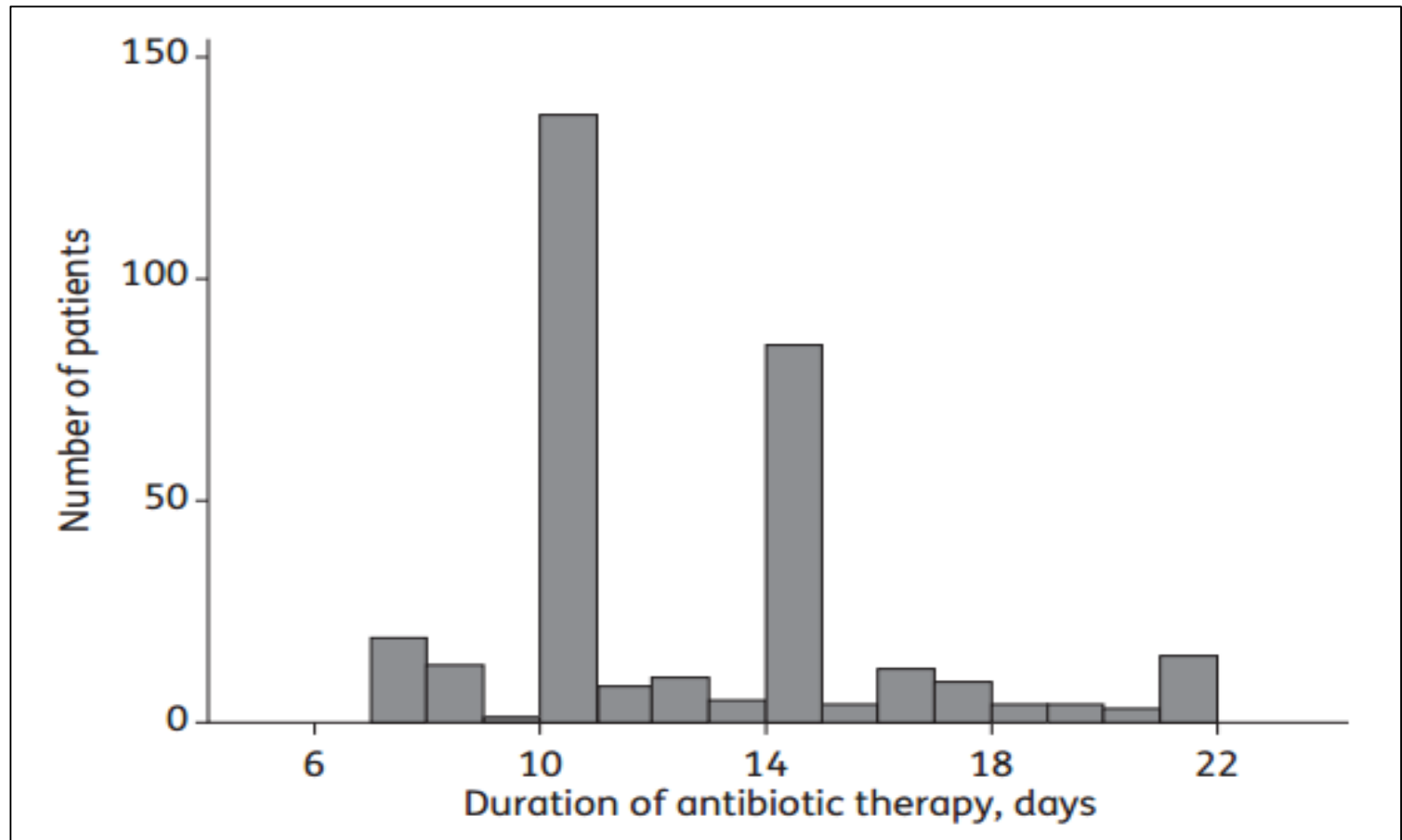- Less confounding when measuring outcomes

No Ceiling for Opportunities….

- Urinary tract infections
- Community-acquired pneumonia
- Healthcare-associated pneumonia
- Bacteremia
- Intra-abdominal infections
- Skin and soft tissue infections
- Central nervous system infections
- Surgical drain prophylaxis
- Hardware-associated infections
- *C. difficile* infections

Duration of Therapy for Gram-Negative Bacteremia

- The optimal duration of antibiotic therapy for gram-negative bacteremia remains unclear

- The IDSA guidelines suggests a duration between 7-14 days

- Some existing studies since IDSA guidelines indicating patients receiving 7 days of therapy may have equal outcomes as 14 days

- Prolonged antibiotic exposure has been associated with adverse drug events, emergence of antibiotic resistance, *Clostridium difficile* infections, Candidal superinfections, etc.
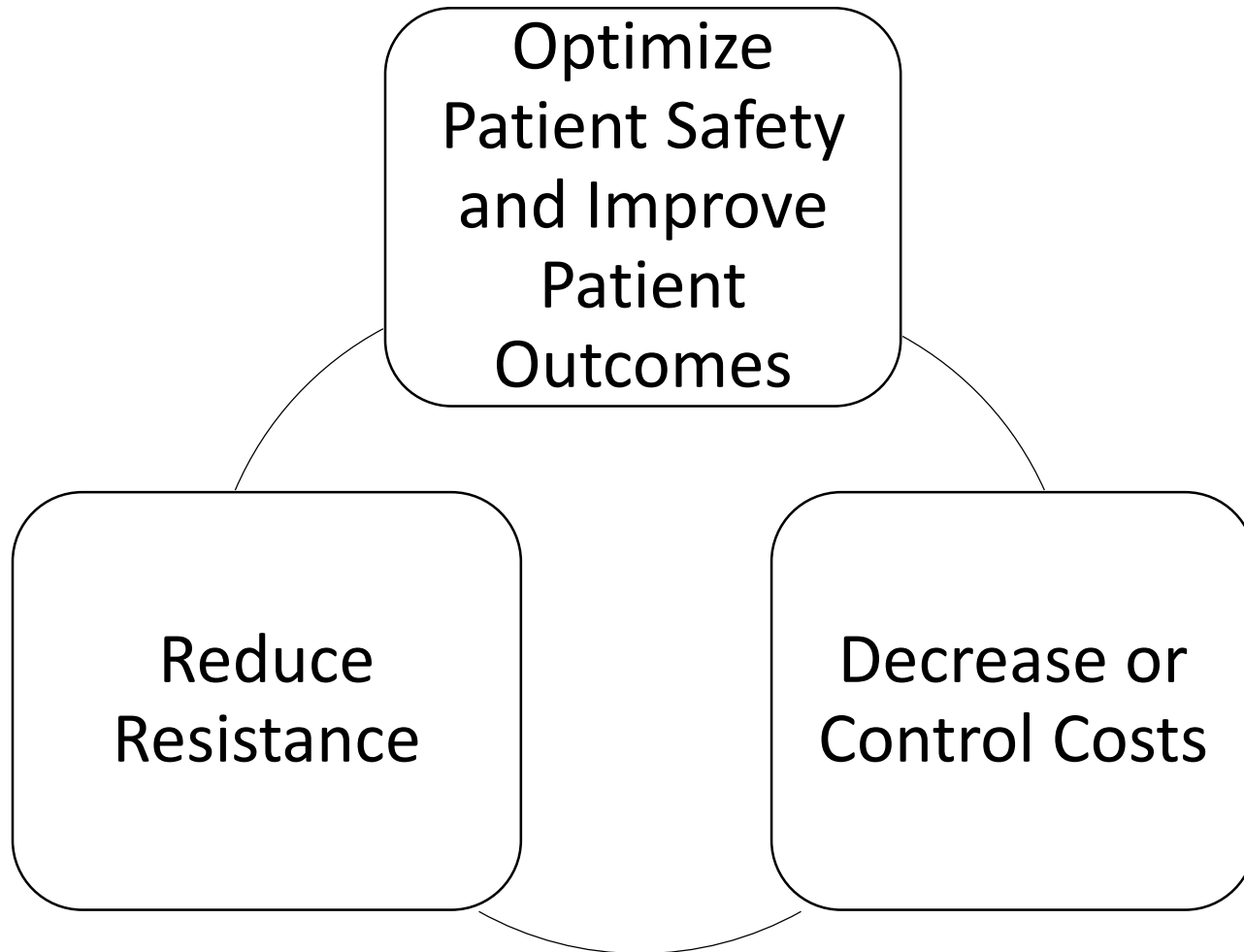
Mermel LA, et al. Clin Infect Dis 2009; 49:1-45. Park SH, et al. J Antimicrob Chemother 2014;69:779-85.

Continuous Versus Categorical Exposure?

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┌─────────────────────┐                        ┌─────────────────────┐
│    Short course     │ ─────────────────────▶ │      Outcome        │
│  antibiotic therapy │                        │                     │
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Goals of Antibiotic Stewardship Programs

Goals of Antibiotic Stewardship Programs

Optimize Patient Safety and Improve Patient Outcomes

Reduce Resistance

Decrease or Control Costs
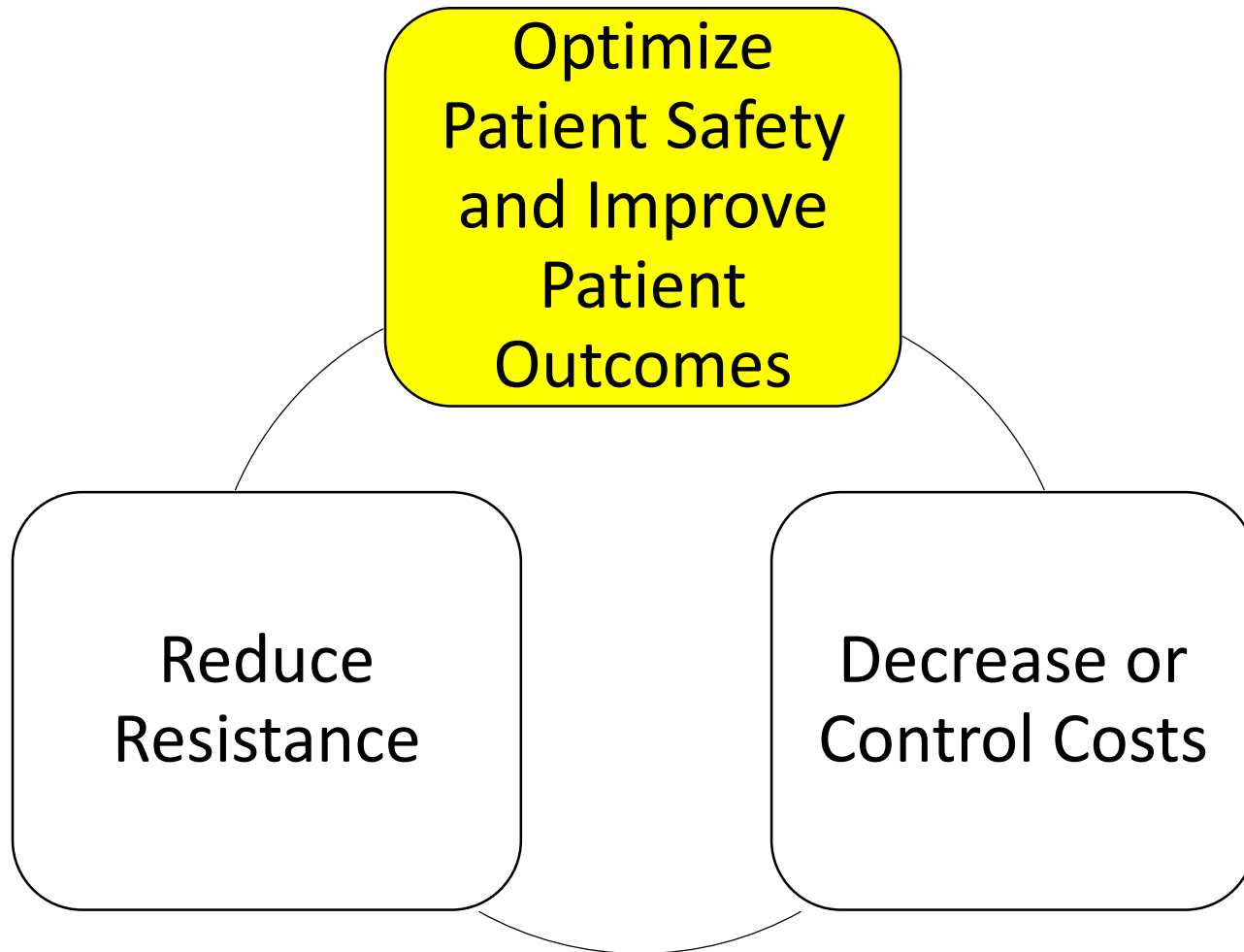
What Outcomes Appeal to Clinicians?

- Most clinicians want to see improvements in patient-centered outcomes
  - Reduction in antibiotic use is usually not enough

- The status quo is harming patients, necessitating a change in practice

- A new treatment approach will not worsen clinical outcomes

- Ideally, a stewardship intervention will result in both of these

Short-course Empiric Antibiotic Therapy for Patients with Pulmonary Infiltrates in the Intensive Care Unit
A Proposed Solution for Indiscriminate Antibiotic Prescription

NINA SINGH, PAUL ROGERS, CHARLES W. ATWOOD, MARILYN M. WAGENER, and VICTOR L. YU
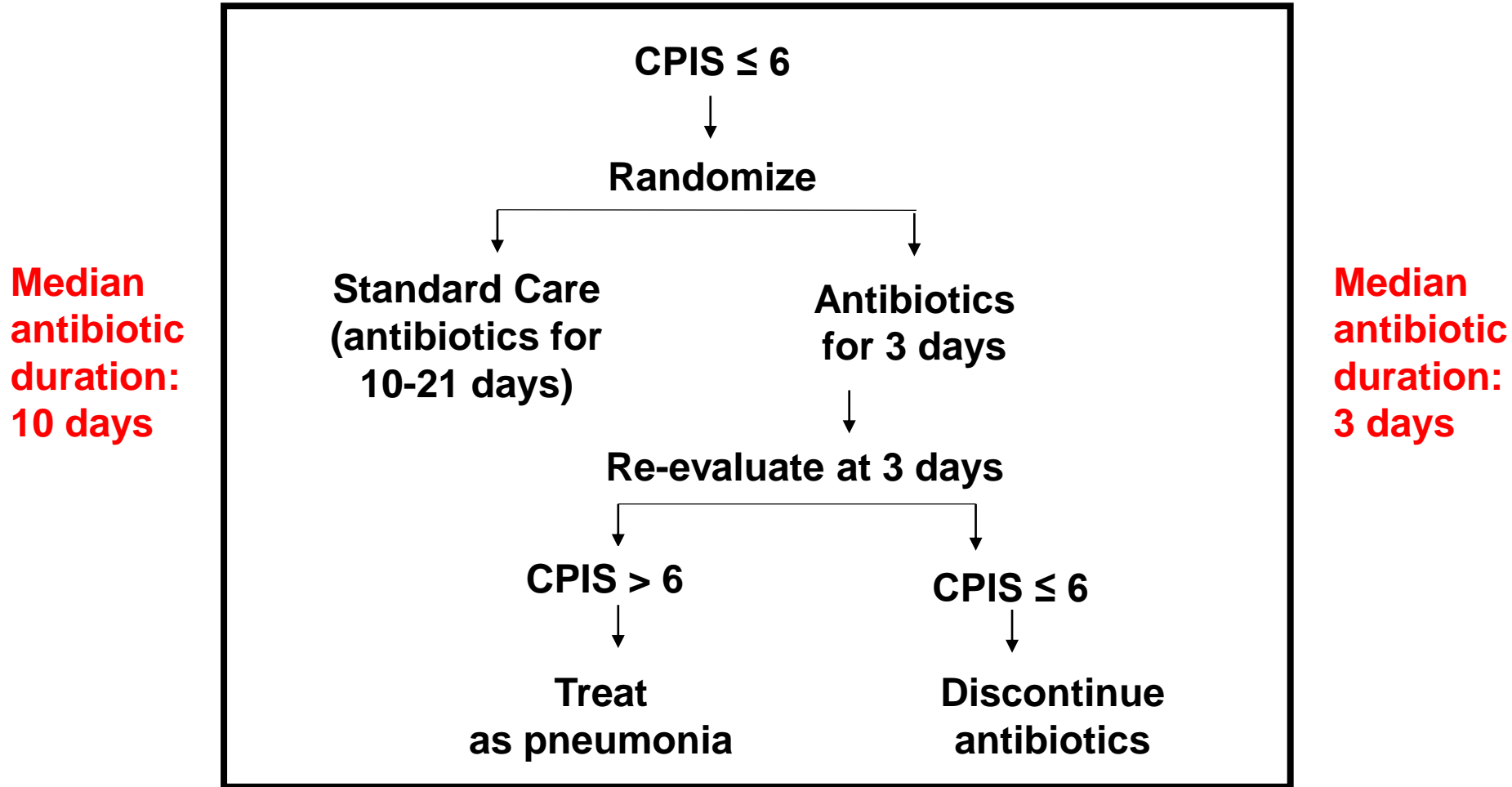
- Components of CPIS
  - Temperature
  - Peripheral white blood cell count
  - Tracheal sections
  - Oxygenation
  - Progression of pulmonary infiltrate
  - Culture of tracheal aspirate

- A score >6 is suggestive of pneumonia

Singh N et al. Am J Respir Crit Care Med 2000;162:505-11.

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Median antibiotic duration: 10 days

Median antibiotic duration: 3 days

CPIS ≤ 6

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Randomize

Standard Care (antibiotics for 10-21 days) — Antibiotics for 3 days

Re-evaluate at 3 days

CPIS > 6 → Treat as pneumonia

CPIS ≤ 6 → Discontinue antibiotics

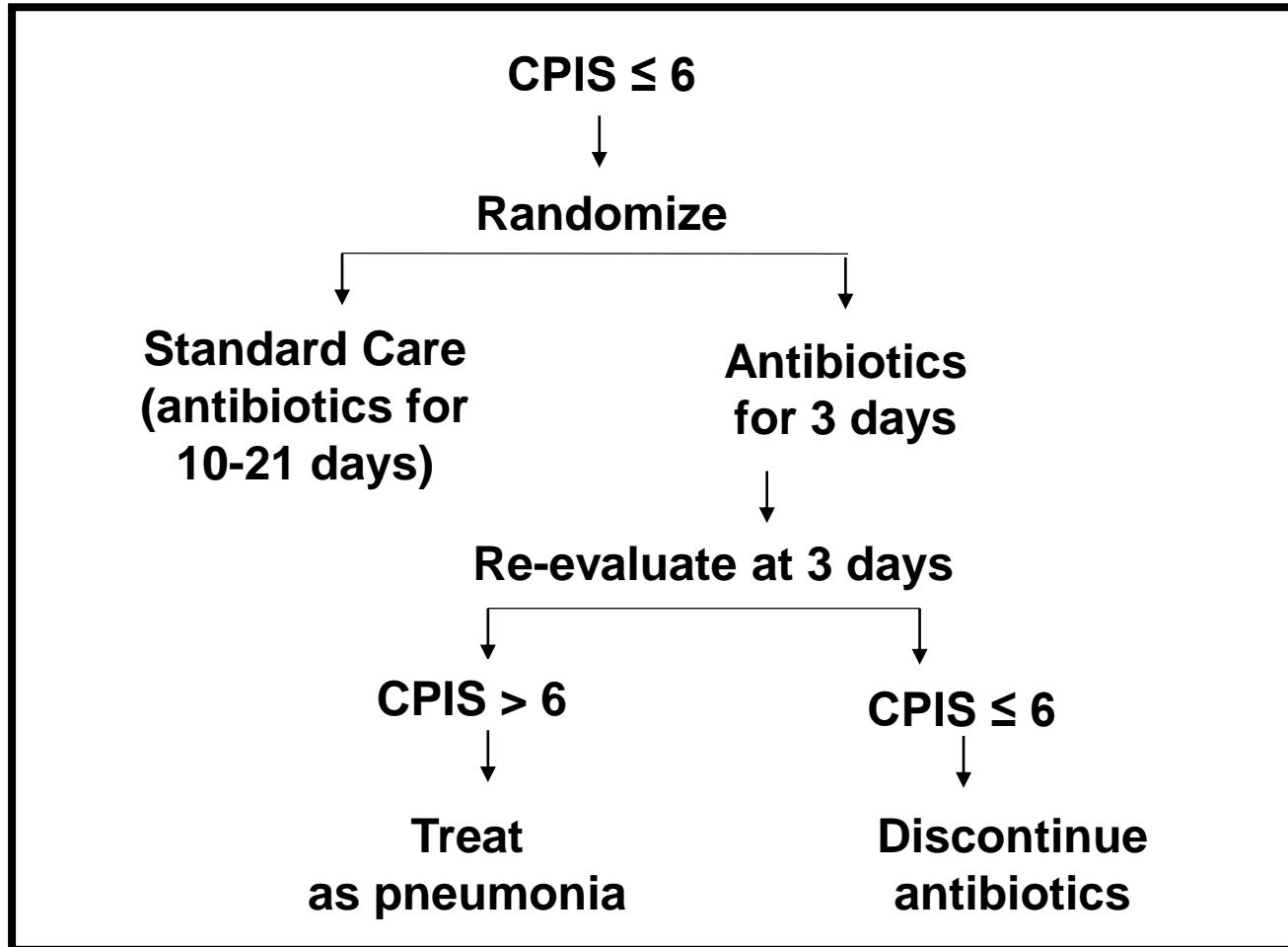Singh N, et al. Am J Respir Crit Care Med 2000;162:505-11.

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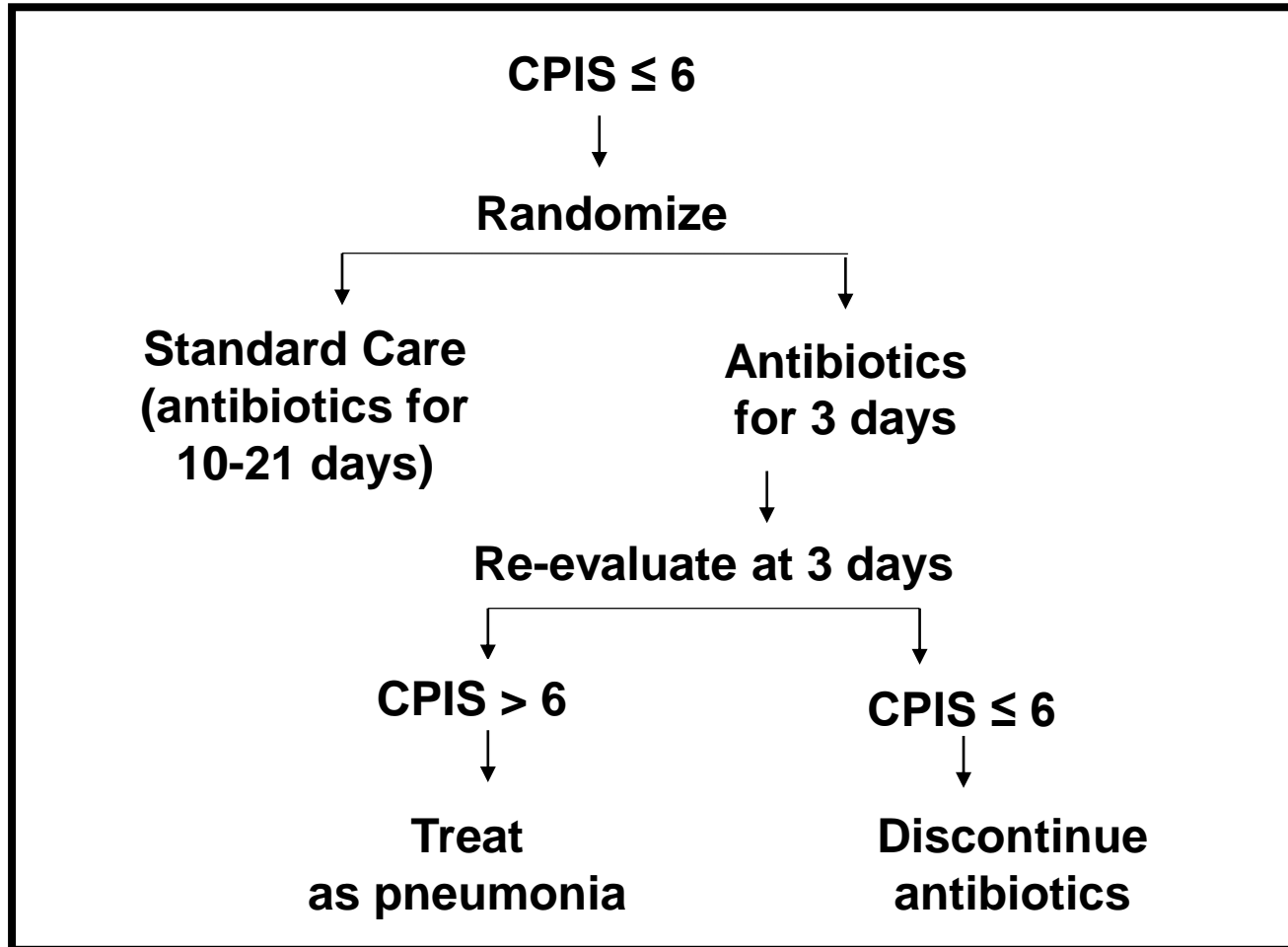NINA SINGH, PAUL ROGERS, CHARLES W. ATWOOD, MARILYN M. WAGENER, and VICTOR L. YU

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Why Was This Study So Successful?

- It focused on one syndrome with a clear and specific goal

- If focused on a syndrome with good evidence to support the treatment recommendations

- It involved multiple opportunities for interventions along the way that could be scalable to the comfort level of the provider

- It engaged all relevant stakeholders with the primary team ultimately making the decisions

- It showed that the stewardship outcome was safe
  - No increased mortality or increased ICU length of stay in the intervention group

- The "harm" caused by the status quo actually impacted the patients in the study
  - There is a perception by clinicians that antibiotic resistance is a theoretical problem
  - Evaluated resistance in the patients involved in the intervention

Outcome Measures

- **Process outcomes**
  - Antibiotic usage

- **Clinical outcomes**
  - Antibiotic resistance
  - *Clostridium difficile* infections
  - Central-line complications
  - End-organ toxicity
  - Mortality
  - Length of hospital stay
  - Infection recurrence

- **Balancing Measures**
  - Hospital readmissions

Selecting Practical Clinical Outcomes Interventions

Harm with the Status Quo

- **Antibiotic resistance**
  - Antibiograms?
- ***Clostridium difficile***
  - Also impacted by infection control
  - Relatively rare outcome
  - May occur months after intervention
  - Higher associations with certain agents
  - Confounding due to overtesting
- **PICC complications**
  - Infectious, thrombotic, mechanical
- **End-organ toxicity**
  - Except for acute kidney injury, relatively rare outcome

No Harm with the Intervention

- **Mortality**
  - Relatively rare outcome – especially attributable mortality
- **Length of stay**
  - Most useful for studies where promoting IV to oral switch or decreased antibiotic duration
- **Infection recurrence**
- **Hospital readmission**

Impact of an Antimicrobial Stewardship Intervention on Shortening the Duration of Therapy for Community-Acquired Pneumonia

- **Goal**
  - Reduce duration of therapy from baseline median of 10 days to 5 days of antibiotics for CAP

- **Approach**
  - Assess knowledge and behavior with a provider survey
  - Revision of treatment guidelines with involvement of medicine housestaff and simplification of recommendations
  - Educational lectures reviewing evidence for CAP recommendations
  - Direct, real-time discussion of management to providers caring for CAP patients
  - Feedback of results to housestaff

Avdic E, et al Clin Infect Dis 2012;54:1581.

Results

	Baseline n=56	Intervention n=63	P-value
Median duration of therapy	10 days	7 days	<0.001
30-day readmissions	14.5%	7.7%	0.22
C. difficile infections	4.8%	1.5%	0.28

Patients characteristics were similar between the two periods

Sustained Impact of an Antibiotic Stewardship Intervention for Community-Acquired Pneumonia

	Baseline n=56	Intervention n=63	3 years later n=72
Median duration of therapy	10 days	7 days	7 days
30-day readmissions	14.5%	7.7%	8%
C. difficile infections	4.8%	1.5%	1%

Patients characteristics were similar between the three periods

Decreased Antibiotic Utilization After Implementation of a Guideline for Inpatient Cellulitis and Cutaneous Abscess

JAMA

- **Goals**
  - Decrease duration of therapy for SSTI from median of 13 days

- **Approach**
  - Developed evidence-based guidelines regarding empiric antibiotic therapy and duration of therapy
  - Dissemination of guidelines via emails, website, postings in nursing stations and work areas
  - Development of a SSTI admission order set
  - Educational campaign by designated key physician peer champions from the emergency department, medicine, and surgery
  - Quarterly data regarding antibiotic use and harm to patients fed back to providers

Jenkins TC, et al. Arch Intern Med 2011; 171:1072.

Results

	Baseline n=56	**Intervention n=63**	**P-value**
Median duration of therapy	13 days	10 days	<0.001
Clinical failure	7.7%	7.4%	0.93
Hospital mortality	0	0	--
Length of hospital stay	4 days	4 days	0.43

Patients characteristics were similar between the two periods

Back to Our Study of Bacteremia: Outcomes

- **All-cause 30-day mortality (Secondary outcome)**
  - 6 (4%) and 5 (3%) deaths in short and prolonged groups, respectively

- **30-day bacteremic relapse (Primary outcome)**
  - 27 (16%) and 17 (10%) in short and prolonged groups, respectively

- ***Clostridium difficile* infections (Secondary outcome)**
  - 4 (2%) vs. 3 (2%) in short and prolonged groups, respectively

- **Incident MDRGN infection (Secondary outcome)**
  - 6 (4%) vs. 10 (6%) in short and prolonged groups, respectively

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│    Short course     │ ───────────────────────────▶ │  Bacteremic relapse  │
│  antibiotic therapy │                              └──────────────────────┘
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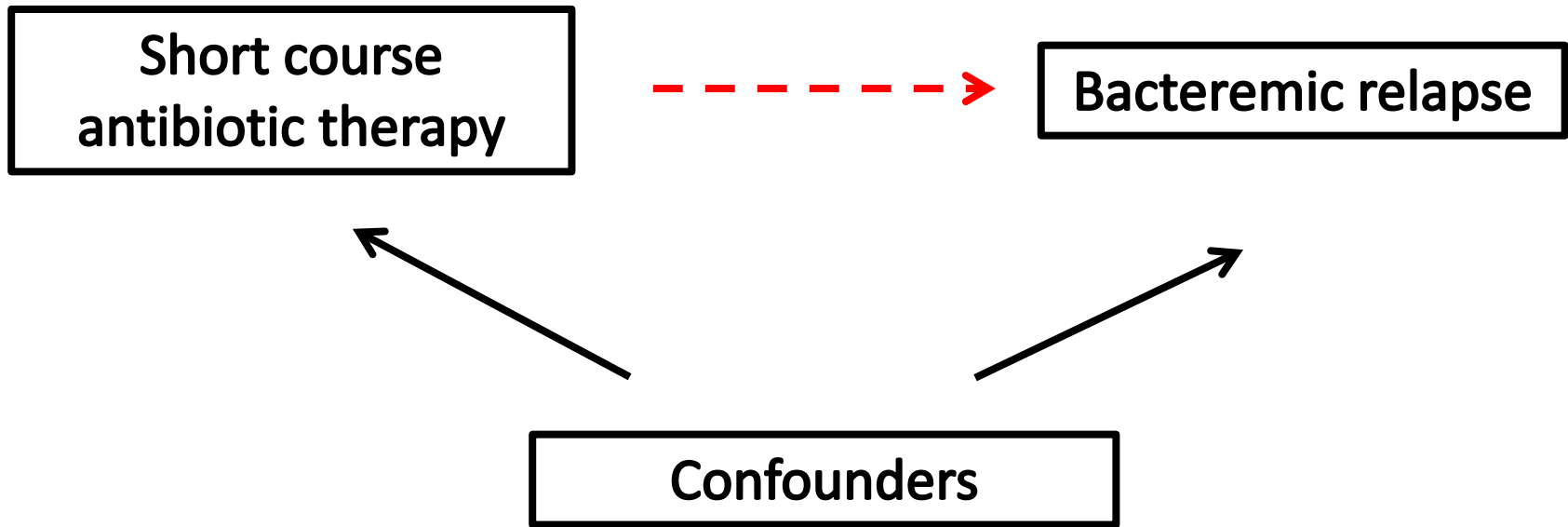
Confounders

- An unobserved exposure associated with the exposure of interest and a potential cause of the outcome of interest
  - Should not be an intermediate step in the causal pathway

- Can lead to bias that distorts the magnitude of the relationship between the exposure and outcome

Two Patients with *E. coli* Bacteremia….

7 days of antibiotics

14 days of antibiotics

Age = 75 years
Renal transplant
Intra-abdominal source
Intensive care unit
Pitt bacteremia score = 1

Age = 37 years
Otherwise healthy
Urinary Source
General ward
Pitt bacteremia score = 1

Syndrome-Specific Intervention Barriers

- **Prescribers think their patients are sicker**
  - Frequent conversations (face-to-face preferred)
  - Show they data frequently that their patients are not being harmed (ask clinicians what data they want)
  - Make compromises
  - Show that your recommendations are similar to those from similar institutions (peer-pressure)

- **Recommendations are too complex**
  - Make a single recommendation or provide no more than two options
  - Make sure all members of your stewardship team (and infections diseases consult team) are on board
  - Be confident!

- **They don't care about antibiotic stewardship**
  - Involve teams in selecting the issues and making guidelines
  - Provide positive reinforcement (encourage administration to do this)
  - Make them think interventions are their idea
  - Appeal to emotions

Thank You!