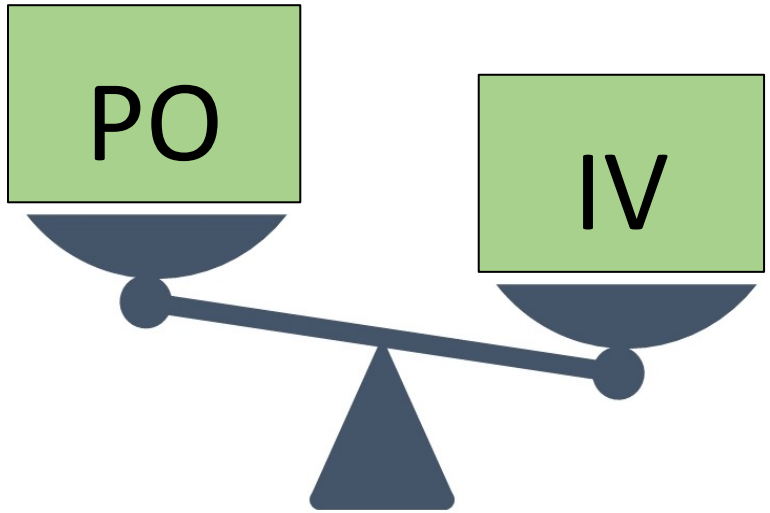
Using Veins in Vain: the Benefit of PO

Whitney Hartlage, PharmD

Intravenous (IV) versus oral (PO)

- **Outcomes in adult patients with CAP**
  - Clinical success at the end of treatment: **no difference**
  - Clinical success at follow-up: **no difference**
- **Benefits of PO**
  - Reduces cost
  - Shortens length of hospital stay
  - Improves workflow and nursing capacity
  - Smaller carbon footprint
  - Impact on bloodstream infection rates



Teng G, et al. JGAR. 2023.

Oral treatment for pneumonia shortens length of hospital stay

- Two RCTs in adult patients with severe CAP

IV → PO on day 3 vs all IV	IV → PO on day 2 vs all IV
• Length of hospital stay 2 days shorter in early switch to PO arm	• Length of inpatient days 5 days shorter in early switch to PO arm

- Cost for each day of reduction in LOS* for CAP: **$2,273-2,373/day (2009)**

*LOS = length of stay

Oosterheert, et al. BMJ. 2006.
Castro-Guardiola, et al. Am J Med. 2001.
Weycker D, et al. Pharmacoecon Open. 2021.
McDermott K, et al. AHRQ. 2021.
Kozma C, et al. Journal of Medicine Economics. 2010.

Underrated finding: PO antibiotics decrease nursing medication preparation and administration times

- Timed:
  - 140 oral administrations
  - 87 intravenous administrations

What about pharmacy prep and delivery time???

- Median time for nursing to prepare and administer:

Oral formulations: 80 seconds

Intravenous injection/infusions: 22 minutes 5 seconds

Slide credit: Abi Jenkins, ECMID 2023.

Carbon footprint of IV antibiotics is higher than PO equivalents

- Medications are responsible for 22% of the UK NHS's carbon footprint
  - Carbon footprint of an antimicrobial drug = the greenhouse gas emissions associated with its lifecycle from development through to use and disposal ('cradle to grave')

- Carbon footprint of one week treatment with IV versus PO:
  - **Amoxicillin**: **11 times higher with IV**
  - **Ciprofloxacin**: **71 times higher with IV**

Walpole S, et al. Antibiotics. 2023.
Walpole S, et al. Federation of Infection Societies Conference. 2021.

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- Carbon footprint of one week treatment with IV versus PO:
  - **Amoxicillin**: **11 times higher with IV**
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- IV ciprofloxacin x 7 days =

  - CO_2 emissions from: 11.3 gallons of gasoline consumed

  - Greenhouse gas emission from: 256 miles driven from vehicle

Walpole S, et al. Antibiotics. 2023.
Walpole S, et al. Federation of Infection Societies Conference. 2021.

Risk of bloodstream infections with peripheral IV catheters

- Short-term peripheral venous catheters (PVCs) are common → **200 million successfully inserted in adult patients** in the United States per year

- PVC-related bloodstream infection (BSI) rate = **0.18%** (n=85,083 PVCs)

Incidence rate may be low, but high volume of use equates to 360,000 PVC BSI per year in US

Mermel L, et al. Clin Infect Dis. 2017.

Institutional Approach & Considerations

When to switch patients with pneumonia from IV to PO? Rapid transition for most.

1) Based on clinical response

- Per IDSA Guidelines: when hemodynamically stable, improving clinically, and tolerating PO – **usually occurs within 3 days**
  - Subjective response: 1-3 days
  - Objective (based on ATS/IDSA 2007 criteria): within 3 days

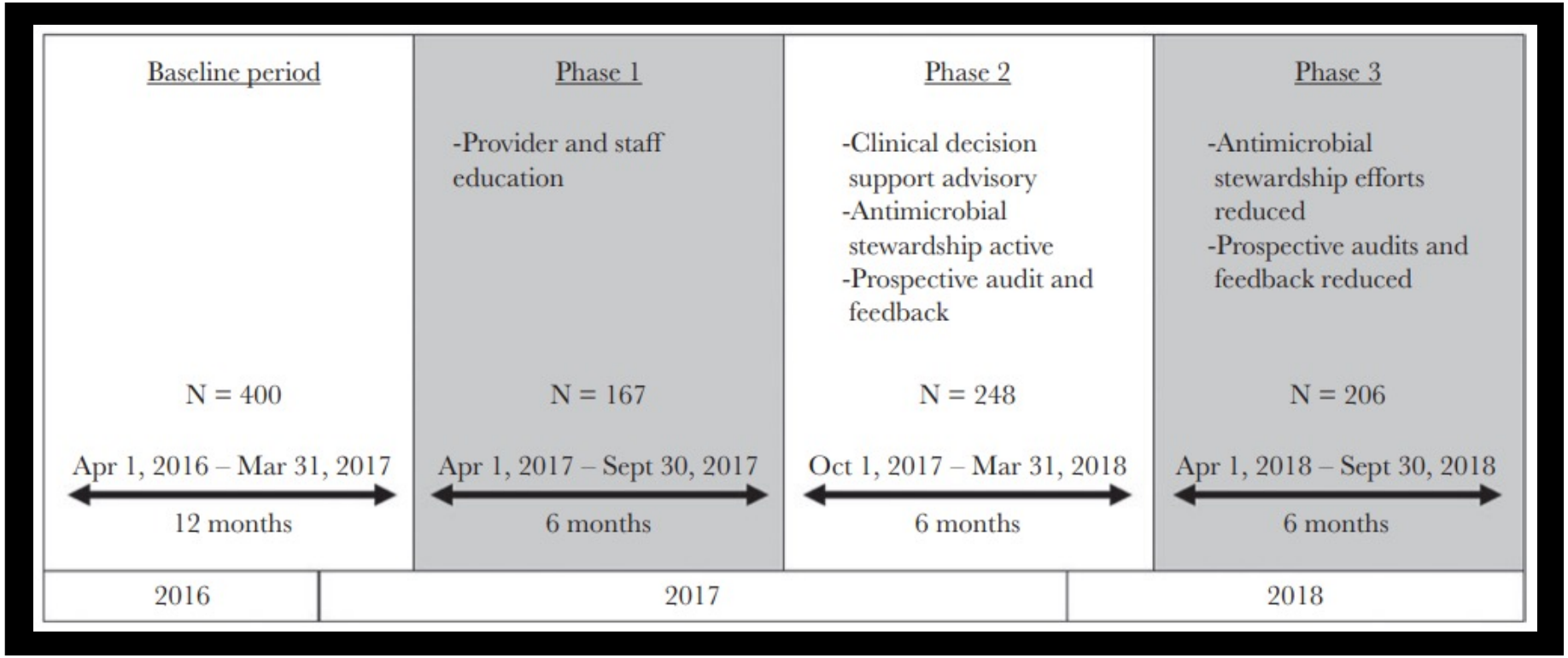
2) Automatic switch to PO regardless of clinical response

- Alternative approach quoted in IDSA Guidelines
- Similar outcomes in studies that observed this approach in inpatients with CAP

Bartlett, et al. Clin Infect Dis. 2000.
Aliberti, et al. Eur Respir J. 2013.
Castro-Guardiola, et al. Am J Med. 2001.

Successful approach: Order set + prospective audit and feedback

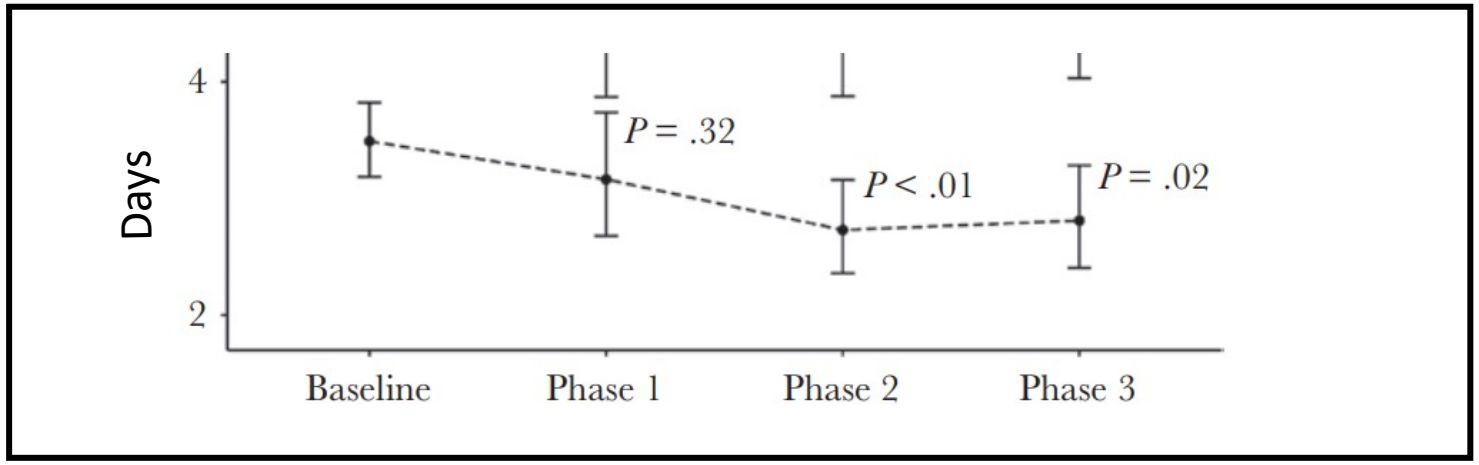
- Pathway for community-acquired pneumonia with rapid conversion to oral therapy



Ciarkowski C, et al. OFID. 2020.

Successful approach: Order set + prospective audit and feedback

- **Outcome results**: length of intravenous antibiotic therapy



- **Inpatient mortality, 30-day readmission, length of stay**: no difference
- Compared to baseline, CAP pathway + active AS in Phase 2 associated with **20% reduction in total cost per visit**
  - Most notable in pharmacy costs

Ciarkowski C, et al. OFID. 2020.

Barriers for IV-to-oral switch

- Belief that IV > than oral
- Concern to switch unless there is a direct oral equivalent
- Lack of awareness and access to IV to oral switch guidelines
- Practical considerations
- Patient specific factors (ie. comorbidities)

Solution?

Engel M, et al. European Respiratory Journal. 2013.
Broom J, et al. Journal of Antimicrobial Chemotherapy. 2016.

Pharmacokinetics of PO agents

- Oral beta-lactams have notable PK differences

Drug Class	Antibiotic	Bioavailability (%)	Half-life (hours)
Oral penicillins	Amoxicillin	74-92	1.0
	Amoxicillin-clavulanate	60	1.0
Oral cephalosporins	Cephalexin	90-100	0.6-1.3
	Cefuroxime	30-52	1.0-2.0
	Cefdinir	21-25	1.7
	Cefpodoxime	29-53	2.2-2.8

- Optimizing dosing helps maximize free time above MIC

Mogle B, et al. Pharmacotherapy. 2019.

What about orals for pneumonia with pneumococcal bacteremia?

- **2007 IDSA Guidelines on Management of CAP in Adults**

"Even in the presence of pneumococcal bacteremia, a **switch to oral therapy can be safely done once clinical stability** is achieved and prolonged intravenous therapy is not needed."

Mandell L, et al. Clin Infect Dis. 2007.

So why do we use so much IV in everyone?

Quote from 1998 IDSA CAP Guidelines:

"As cost considerations increase and hospital bed closures become commonplace, there is rising interest in the use of oral therapy whenever possible. For many pathogens, **there is no clear advantage of intravenous therapy over oral therapy**. **However, for most patients admitted to the hospital, the common practice is at least to begin therapy with intravenous drugs.** There are no studies that verify superior outcomes when drugs are administered intravenously rather than orally (when the drugs are well absorbed). The panel endorses use of oral antimicrobial agents for patients who tolerate these drugs if oral bioavailability and activity are adequate."

Bartlett, et al. Clin Infect Dis. 1998.