July 27, 2021

The Clock is Ticking: Using the 'TIMED' Acronym for Successful De-escalation of Vancomycin at 48-72 Hours

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Disclosures

- The presenters have no real or perceived conflicts of interest related to this presentation

Note: This program may contain the mention of suppliers, brands, products, services or drugs presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any particular supplier, brand, product, service or drug.

Learning Objectives

At the end of this session, participants should be able to:

1. Identify collateral damage associated with vancomycin overuse for hospitalized patients and the benefits of vancomycin de-escalation in a hospital setting

2. Describe key components of reducing inappropriate vancomycin utilization as recommended by the CDC Core Elements of Hospital Antibiotic Stewardship Programs

3. Discuss the impact of a standardized, pharmacist-driven process on vancomycin de-escalation rates

Audience Poll Question

Does your facility currently have stewardship initiatives in place to reduce inappropriate vancomycin utilization?

a. Yes

b. No

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An Overview of Vancomycin Utilization Trends, Collateral Damage & Recommended Stewardship Practices

Dr. Kayihura Manigaba, PharmD, BCIDP

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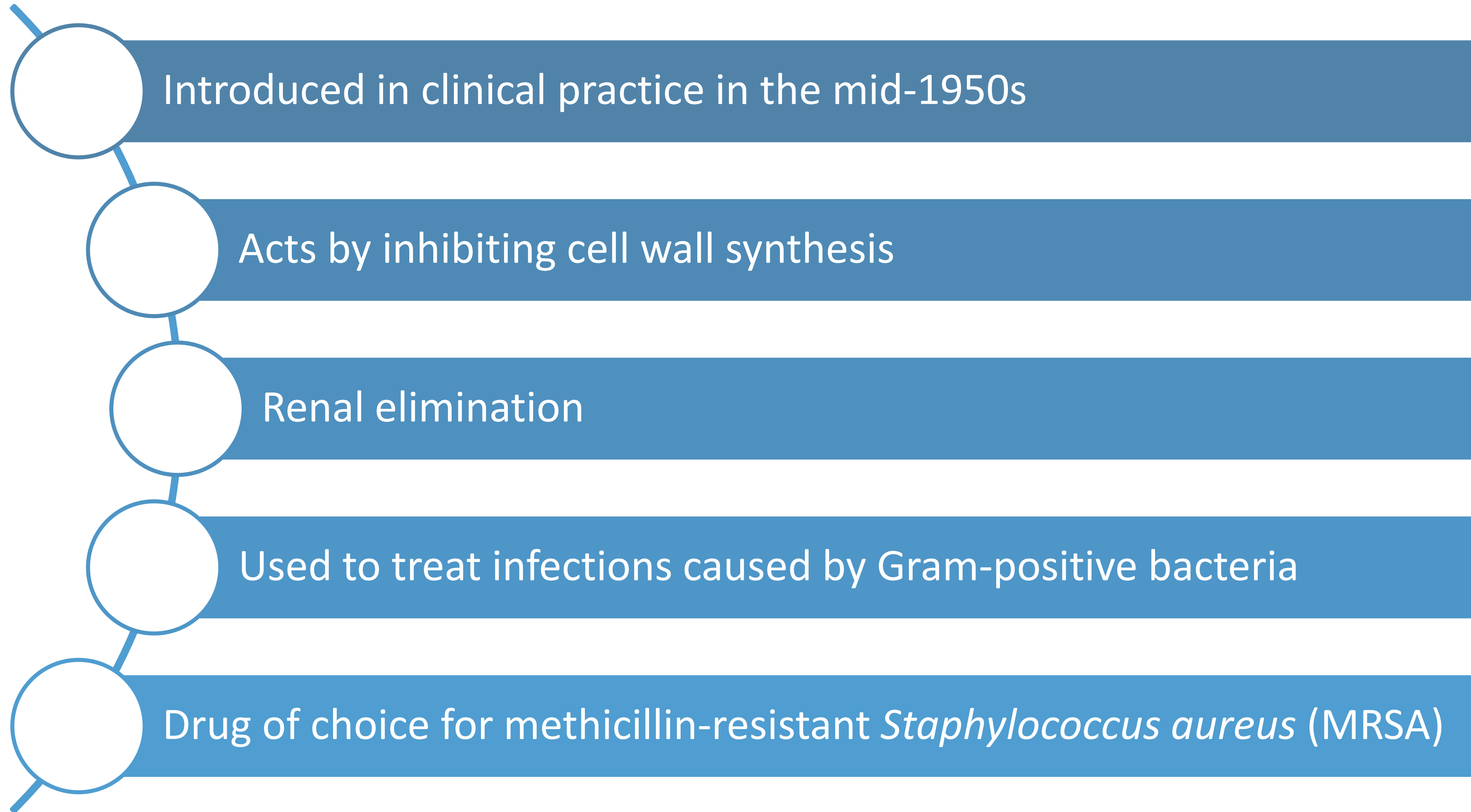
Vancomycin Overview



Zamoner W, et al. *Clin Exp Pharmacol Physiol*. 2019;46:292–301

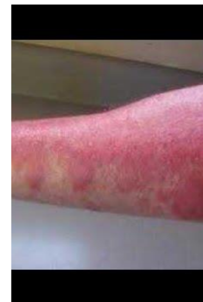
Collateral Damage Associated with Vancomycin Utilization

Development of super bugs

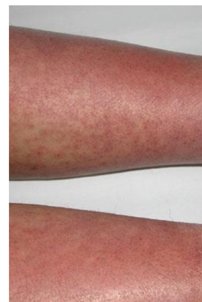
(i.e: vancomycin-resistant enterococci)

Nephrotoxicity

Ototoxicity



Redman syndrome



Hypersensitivity reactions, such as drug rash with eosinophilia and systemic symptoms (DRESS)

Centers for Disease Control and Prevention (CDC): https://www.cdc.gov/hai/organisms/vre/vre.html
Zamoner W, et al. *Clin Exp Pharmacol Physiol*. 2019;46:292–301

Serious Threat

CDC Biggest Threats and Data. https://www.cdc.gov/drugresistance/pdf/threats-report/vre-508.pdf

Every Day Matters

- National Veterans Affairs study of more than 79,000 surgical patients from October 2008 to September 2013
  - Analyzed effect of duration of postoperative antimicrobial prophylaxis on acute kidney injury (AKI) and *Clostridioides difficile* incidence
  - Antimicrobial prophylaxis regimens included vancomycin, aminoglycosides, and beta-lactams

- Vancomycin receipt was a **significant risk factor** for AKI

Number of Patients Needed to Harm

Duration (hours)	AKI	*C. difficile* Infection
24 to <48	9	2000
48 to <72	6	90
≥72	4	50

Branch-Elliman W, et al. *JAMA Surg*. 2019;154(7):590-598

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Increased Antimicrobial Utilization During COVID-19

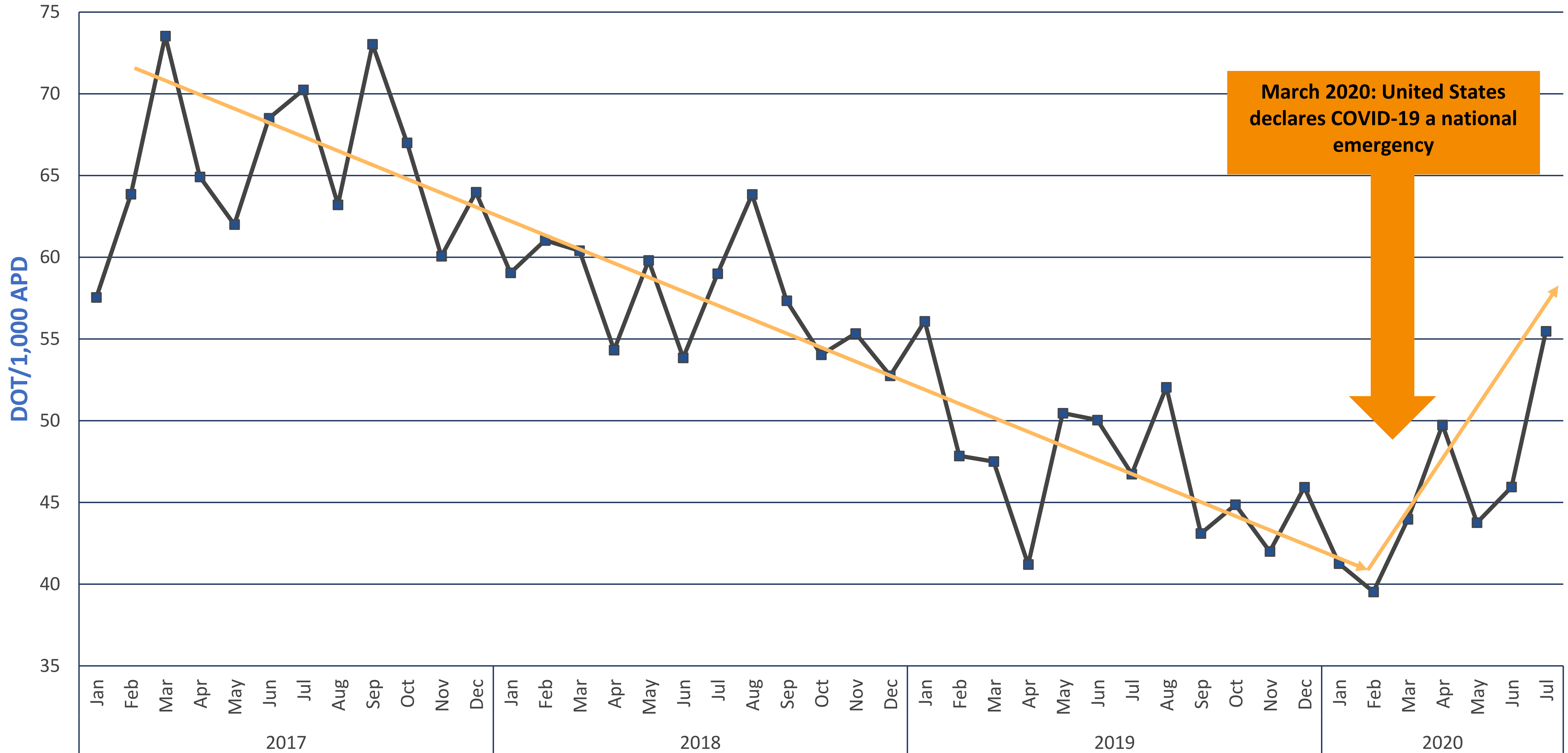
Antimicrobial stewardship was severely challenged during the early stages of the pandemic due to scarcity of data on bacterial co-infections

A meta-analysis found that **71.9%** of patients hospitalized with COVID-19 before mid-April 2020 received antibiotics (only 6.9% of these admissions were associated with bacterial infections)

Various studies report increased antibiotic days of therapy (DOT) during COVID-19 compared to pre-COVID-19 DOT

CDC and Infectious Diseases Society of America (IDSA): https://www.idsociety.org/covid-19-real-time-learning-network/disease-manifestations--complications/co-infection-and-Antimicrobial-Stewardship/
Staub MB, et al. *Infect Control Hosp Epidemiol*. 2020;1-7.
Russell CD, et al. *Lancet Microbe*. 2021.
Langford BJ, et al. *Clin Microbiol Infect*. 2020;12:1622-29.

North Florida Regional Medical Center Vancomycin DOT: COVID-19 Impact



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Call for Action – Reduce Unsupported Use of Vancomycin by 95%

Cross-sectional study conducted by the CDC from 10 Emerging Infections Program sites.
Study period: May 1 to Sept. 30, 2015

Evaluated:
- Appropriateness of antimicrobial use for community-acquired pneumonia (CAP) or urinary tract infections (UTIs)
- Appropriateness of vancomycin and fluoroquinolones in hospitalized patients for all indications

Treatment was unsupported:
- Overall: 876 of 1566 patients (55.9%)
- **Vancomycin: 110 of 403 (27.3%)**
- Fluoroquinolones: 256 of 550 (46.5%)
- Diagnosis of UTI: 347 of 452 (76.8%)
- Diagnosis of CAP: 174 of 219 (79.5%)

Based on the Centers for Disease Control and Prevention (CDC) study published in the Journal of the American Medical Association (JAMA):

- Reduce unsupported prescribing when treating CAP and UTI by **90%**
- Reduce unsupported prescribing of fluoroquinolones and **vancomycin** by **95%**

JAMA Network Open. 2021;4(3):e212007
CDC: https://blogs.cdc.gov/safehealthcare/new-study-antibiotic-prescribing-hospitals/

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CDC Core Elements of Hospital Antibiotic Stewardship Programs, 2019

Interventions to Improve Antibiotic Use

- Prospective audit and feedback
- Preauthorization
- Facility-specific treatment guidelines
- Antibiotic "timeouts"
- Assessing penicillin allergies

 CDC: https://www.cdc.gov/antibiotic-use/core-elements/hospital.html

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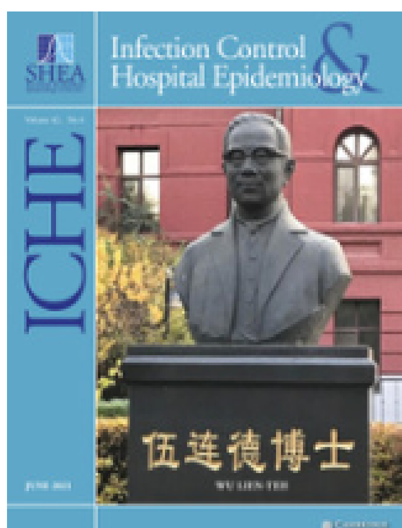
Assessment Question #1 of 3

What are some negative patient impacts that are caused by vancomycin overuse?

a. Greyman syndrome
b. Yellowing of the teeth
c. Nephrotoxicity
d. All of the above

Taking Vancomycin Consults to the Next Level:
Stop and ReConsider Advancing CoNsult (SCAN)



SCAN: A novel approach for vancomycin time-out

Published online by Cambridge University Press: **10 October 2018**

Kayihura Manigaba , Samuel J. Borgert , Kenneth P. Klinker , Kartikeya Cherabuddi and Veena Venugopalan

Show author details

Article Figures Metrics

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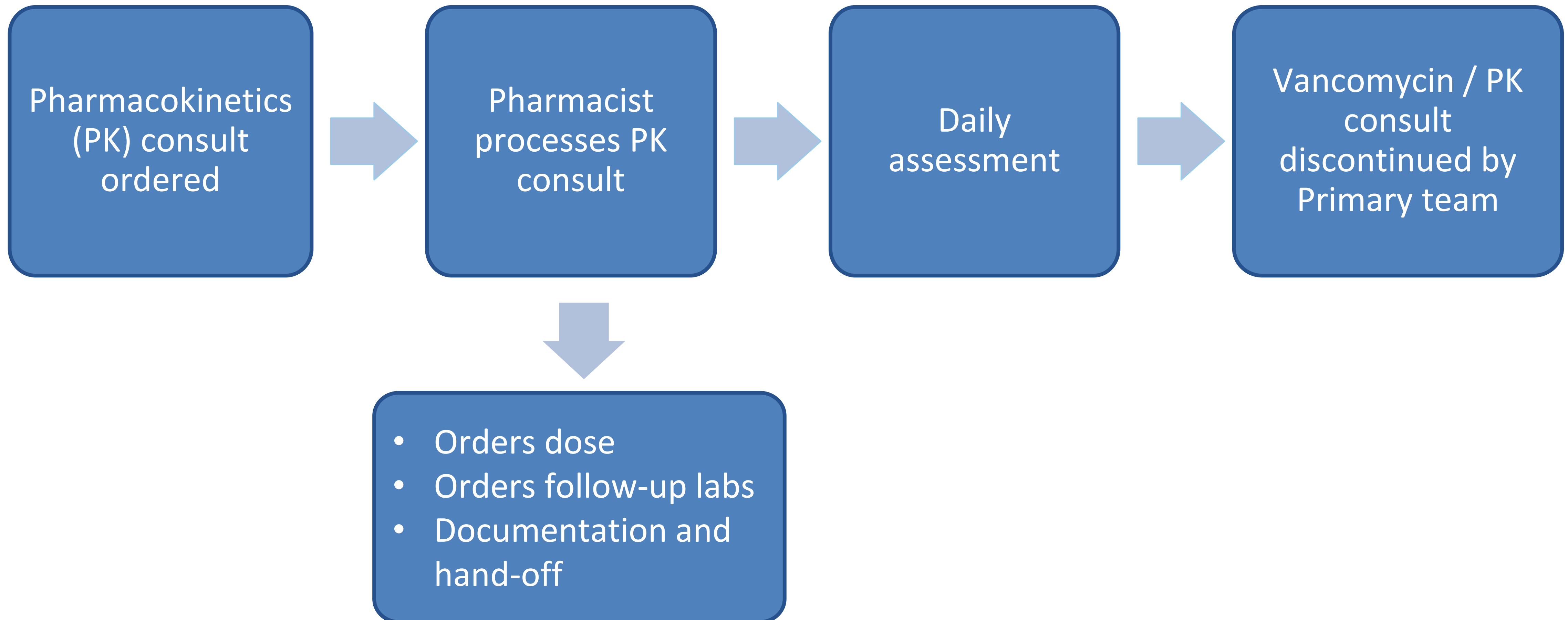
SCAN Study

Traditional Vancomycin Consultation Process



 Manigaba K, et al. *Infect Control Hosp Epidemiol*. 2018;39(12):1501-3.

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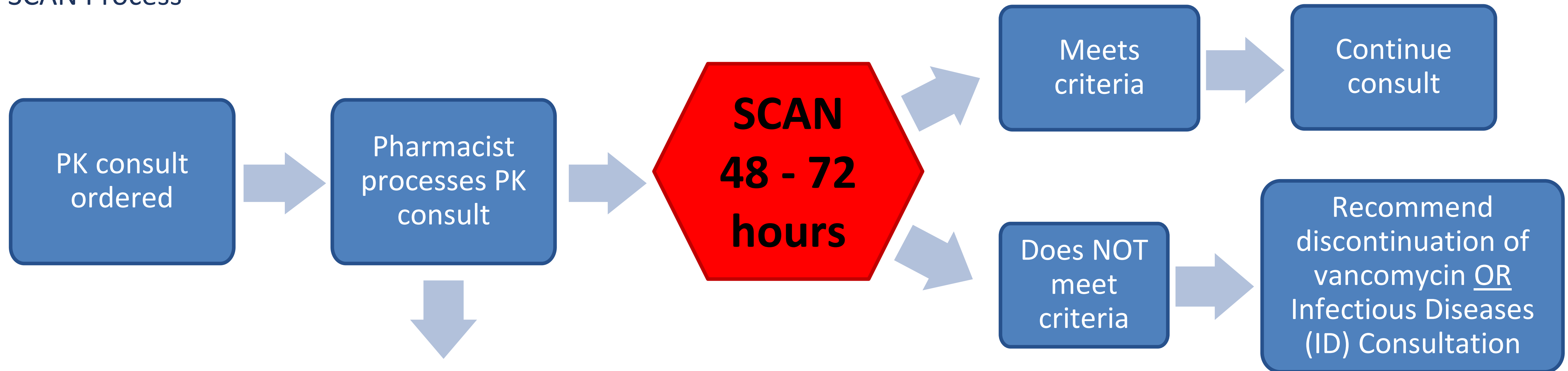
SCAN Study

SCAN Process



- Ensure appropriate cultures are obtained
- Orders dose
- Orders follow-up labs
- Documentation

Criteria:

1. Positive cultures for MRSA
2. History of MRSA
3. Culture results less than 24-48 hours
4. Severe beta-lactam allergy with no alternatives
5. Purulent cellulitis

Manigaba K, et al. *Infect Control Hosp Epidemiol*. 2018;39(12):1501-3.

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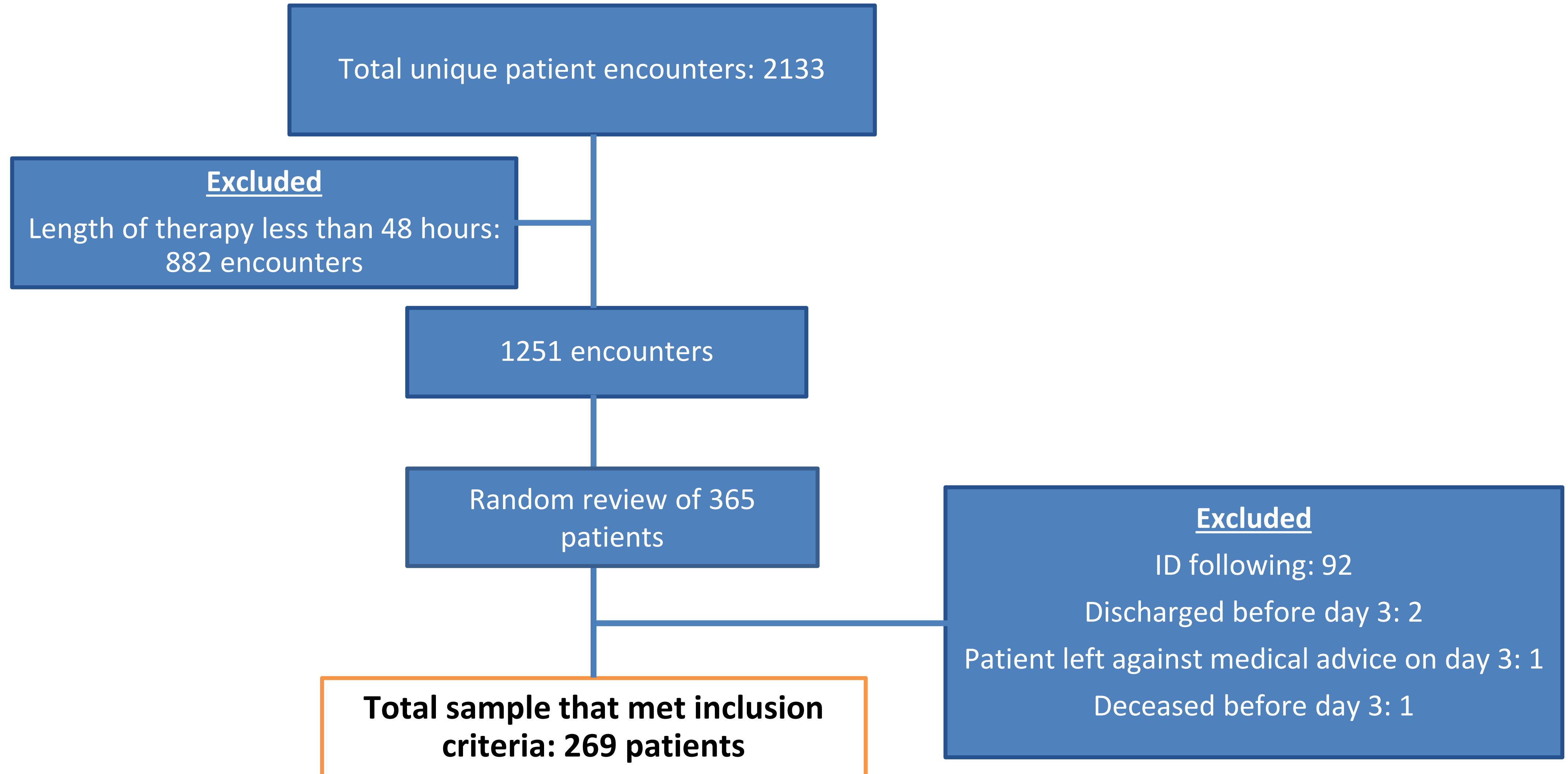
SCAN Study

Screening & Enrollment



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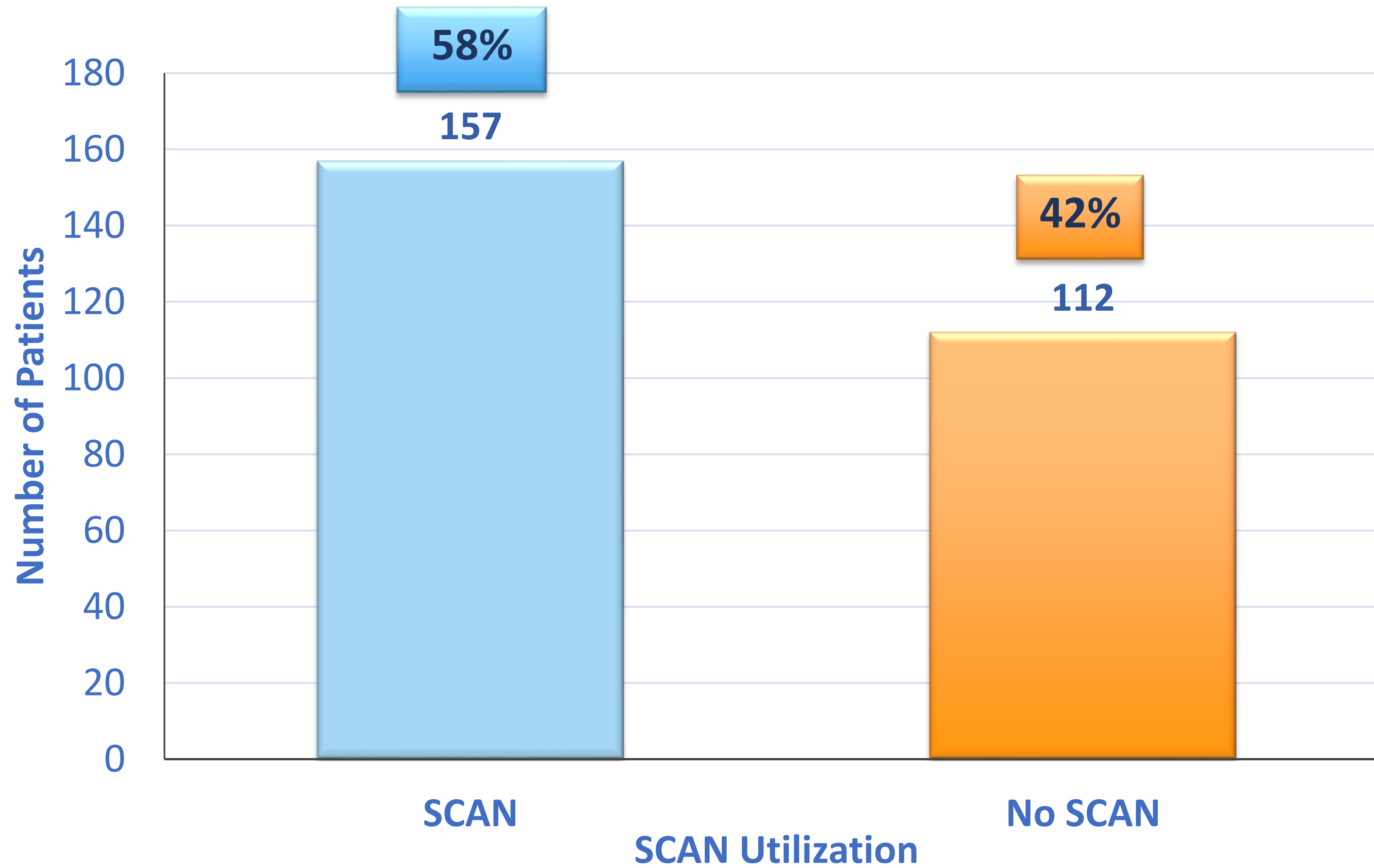
SCAN Study

Results



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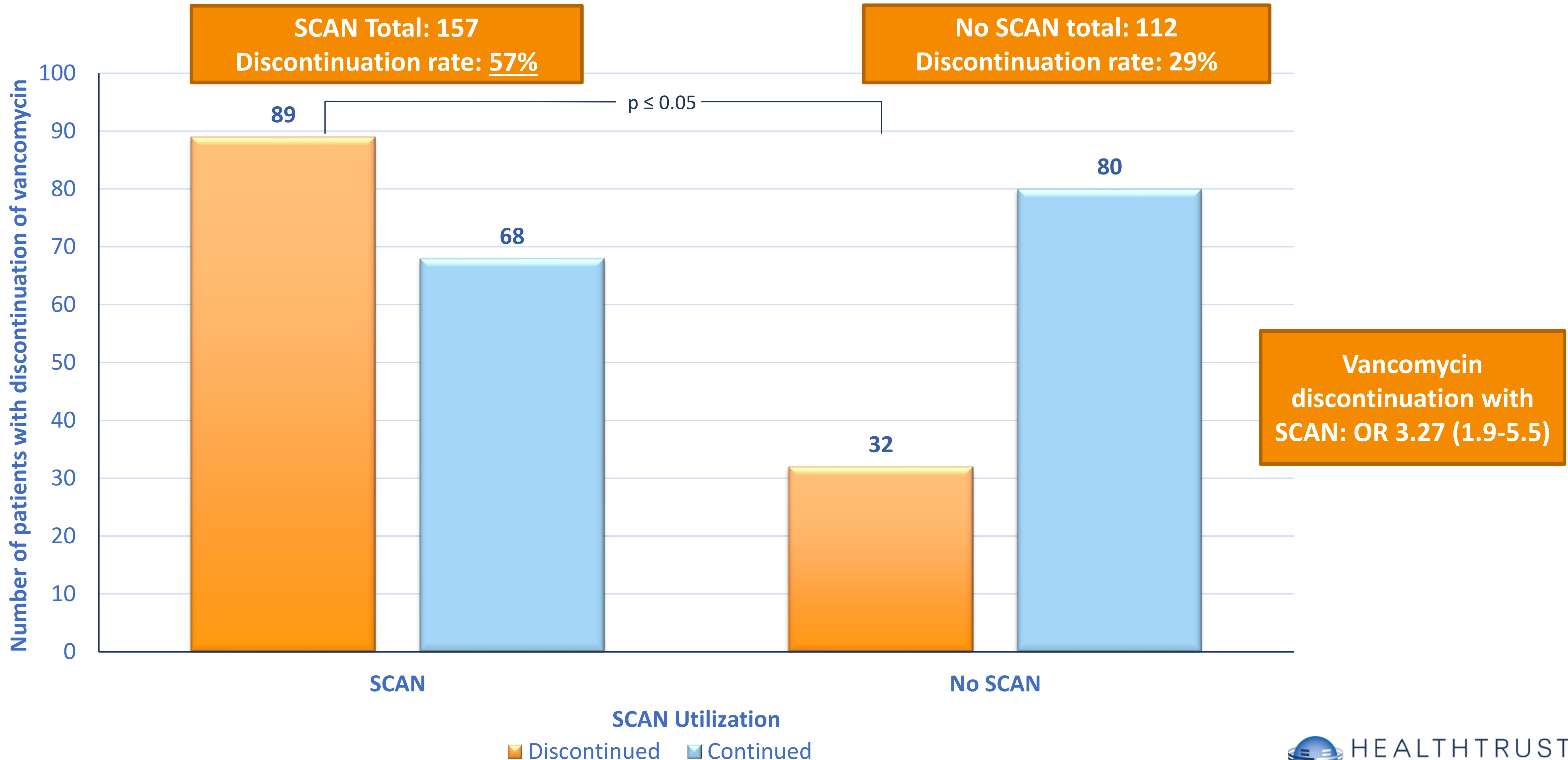
SCAN Study

Results



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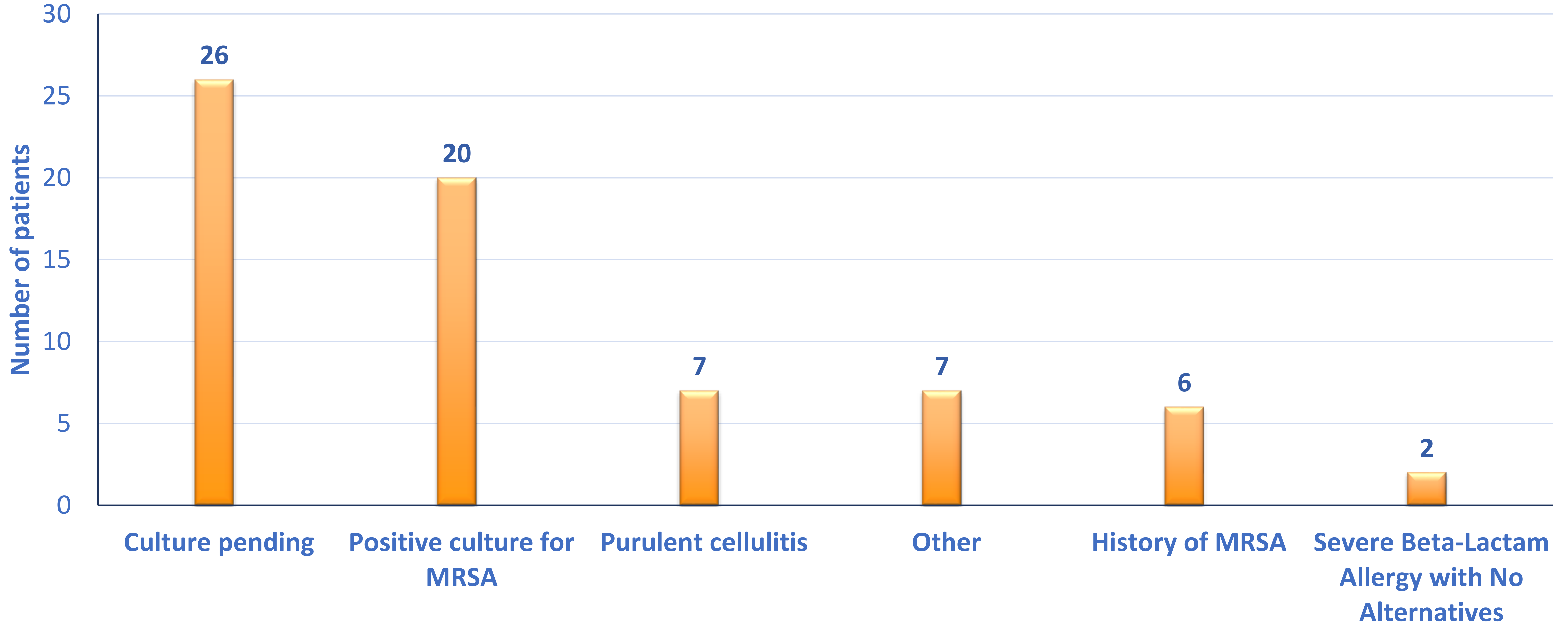
SCAN Study

Results



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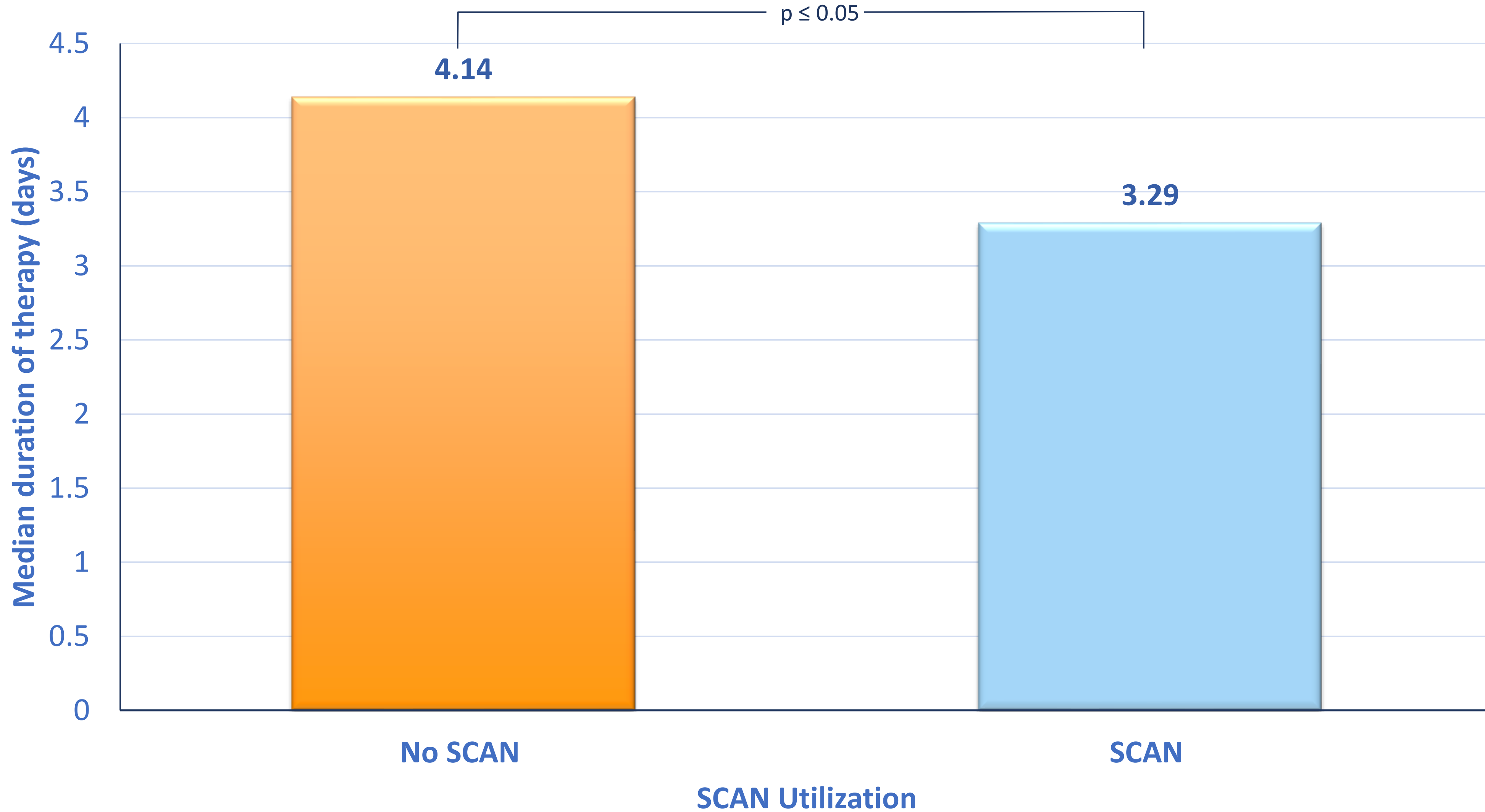
SCAN Study

Results



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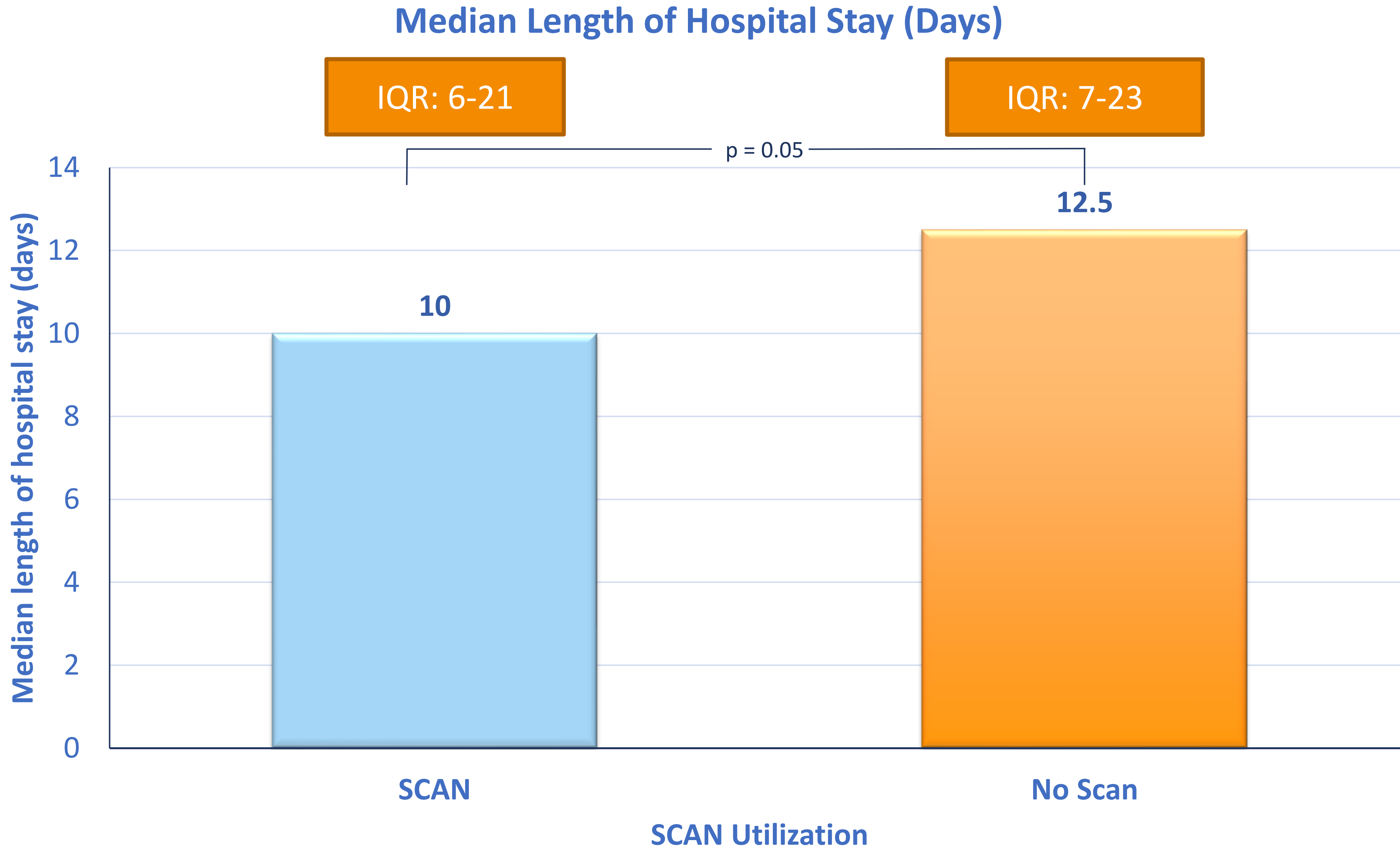
SCAN Study

Results



Manigaba K, et al. *Infect Control Hosp Epidemiol*. 2018;39(12):1501-3.

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SCAN Study

Conclusions

- Of patients evaluated ~60% were SCANned (i.e., evaluated at day 3)
- Patients who were SCANned had a greater antibiotic discontinuation rate **(57% vs. 29%, p≤ 0.05)**
- Median length of vancomycin therapy was lower in SCAN arm **(3.3 vs 4.1 days, p≤ 0.05)**
- Median hospital length of stay was numerically lower in SCAN arm (10 vs 12, not significant)
- Pharmacists can contribute greatly in the reduction of inappropriate continuation of vancomycin

Manigaba K, et al. *Infect Control Hosp Epidemiol*. 2018;39(12):1501-3.

Assessment Question: #2 of 3

Which of the following are key components of reducing inappropriate vancomycin utilization as recommended by the CDC?

a. Preauthorization

b. Antibiotic “timeouts”

c. Assessing penicillin allergies

d. All of the above

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Vancomycin De-Escalation:

A Multi-Faceted Approach at North Florida Regional Medical Center

Dr. Nora Bairagdar, PharmD, BCPS, AAHIVP

1. 'TIMED' Acronym

Introduced December 2020

- Included in a vancomycin de-escalation guide disseminated to pharmacists

A. To guide the process for daily assessment of vancomycin de-escalation, remember "TIMED": **Every day matters in order to prevent acute kidney injury or *C. difficile* infections!**

Time on vancomycin therapy

- Assess patients daily for an appropriate indication for continuation of vancomycin. Recommend discontinuation of vancomycin **by day 3** of therapy if no indication for continuation exists.

Indication

- Indications to continue vancomycin include: positive culture(s)/nasal swab for MRSA (PBP2 positive), gram-positive infection for which vancomycin is a drug of choice based on susceptibility, culture results less than 48 hours, severe allergy to beta-lactams with no alternative antibiotics, purulent cellulitis, documented infection but no site cultures available (recommend Infectious Diseases [ID] consult)[5]

Microbiology

- Assess cultures for growth and if organisms are a colonizer, contaminant, or true pathogen. True pathogens are unlikely to grow after cultures have demonstrated no growth in 48 hours.[5,6]
- Ensure that all pneumonia patients on vancomycin have a MRSA nasal swab ordered within 48 hours of vancomycin initiation per the NFRMC screening protocol.

Evaluate symptoms, vitals, labs, and imaging

- Evaluate patient for clinical, lab, or imaging indicators of infection
  - *Vitals*: Temperature, blood pressure, heart rate, respiratory rate, O_2 saturation
  - *Labs*: WBC, neutrophils, C-reactive protein, erythrocyte sedimentation rate

De-escalate if appropriate

- Recommend discontinuation of vancomycin to the provider when there is no valid indication for continuation of therapy.
- If provider does not accept the recommendation, consider recommending an ID consult. Document the provider rejection in VigiLanz.

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1. 'TIMED' Acronym

T = Time on vancomycin therapy

- Assess patients daily for an appropriate indication for continuation of therapy
  - Recommend discontinuation of vancomycin at 48-72 hours if no valid indication

I = Indication

- Valid indications for continuation of therapy:
  - Positive culture(s)/nasal swab for MRSA
  - Gram-positive infection for which vancomycin is a drug of choice based on susceptibility
  - Culture results less than 48 hours
  - Severe beta-lactam allergy with no alternative antibiotics
  - Purulent cellulitis
  - Documented infection but no site cultures available (recommend an Infectious Diseases consult)

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M = Microbiology

- Assess cultures for growth
- Ensure all pneumonia patients receiving vancomycin have an MRSA nasal swab ordered within 48 hours per hospital screening protocol

E = Evaluate symptoms, vitals, labs, and imaging

- Assess patients for indicators of active infection

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D = De-escalation if appropriate

- Recommend discontinuation of vancomycin to provider when there is no valid indication for duration of therapy
  - If provider does not accept recommendation, recommend an ID consult

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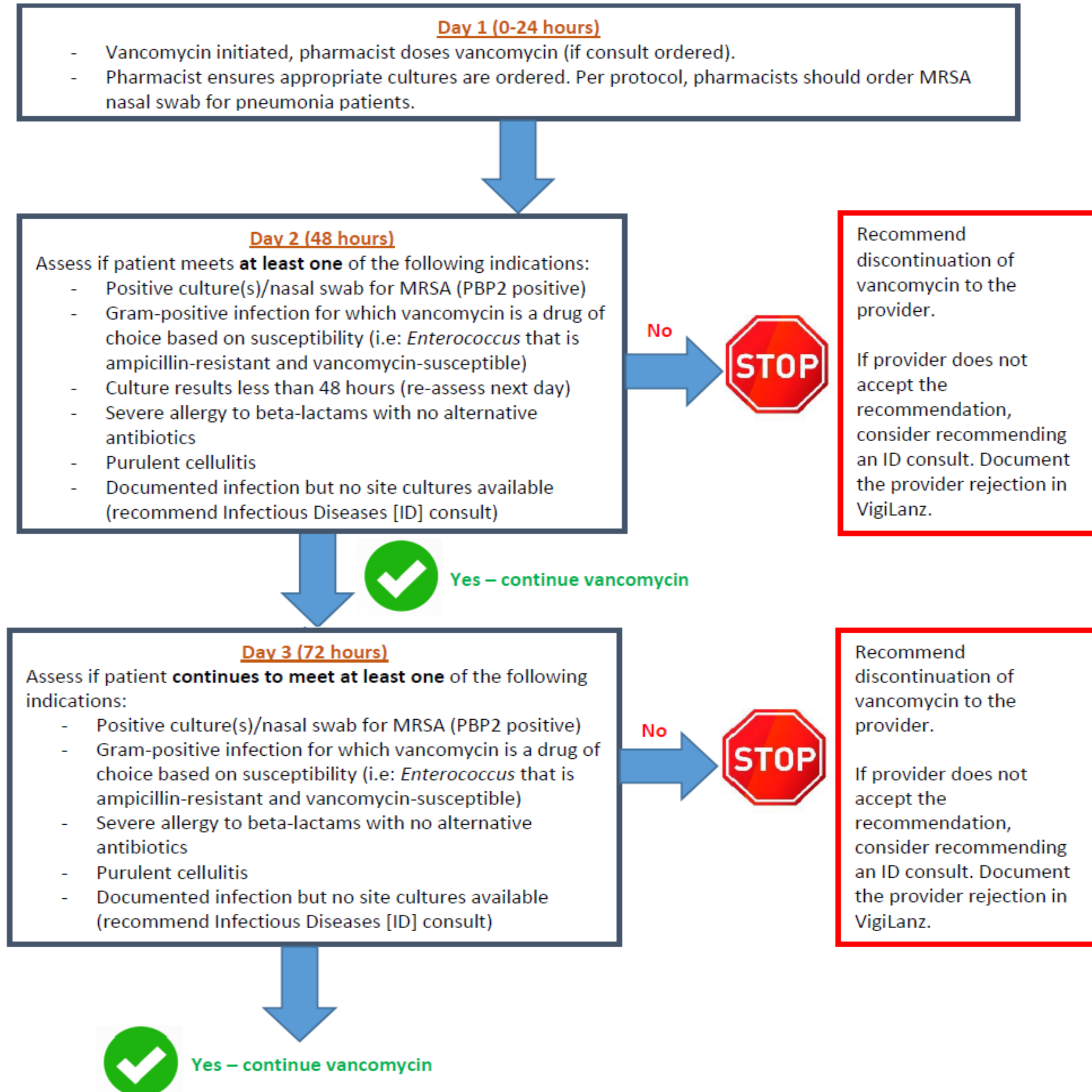
2. Vancomycin De-Escalation Algorithm

Introduced December 2020

- Included in a vancomycin de-escalation guide disseminated to pharmacists



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3. Vancomycin De-Escalation Competency

Introduced December 2020

- Following distribution of a comprehensive vancomycin de-escalation guide, pharmacists were required to complete a corresponding competency in 30 days
- If any questions were missed, the ID Pharmacist performed one-on-one education with the pharmacists
- Vancomycin de-escalation competency was added to training regimen for new pharmacists, residents and students

Please read the NFRMC Vancomycin De-escalation Guidance and answer the following questions.

1. What can inappropriate usage of vancomycin result in?
   - A. Severe adverse effects
   - B. Promotion of antibiotic resistance
   - C. Development of *Clostridioides difficile* infections
   - D. Increased hospital lengths of stay
   - E. All of the above

2. What does the '**TIMED**' acronym for daily assessment of vancomycin de-escalation stand for?

   T:

   I:

   M:

   E:

   D:

3. Vancomycin patients should be assessed daily for de-escalation opportunities. By what day of therapy does vancomycin need to be discontinued if there is no valid indication for continuation?
   - A. Day 1 (24 hours)
   - B. Day 2-3 (48-72 hours)
   - C. Day 4 (96 hours)
   - D. Day 5 (120 hours)

4. Which of the following is **NOT** an appropriate indication for continuing vancomycin therapy?
   - A. Positive culture or nasal swab for MRSA
   - B. Ampicillin-susceptible *Enterococcus* infection
   - C. Severe purulent cellulitis, cultures showing no growth to date at 48 hours
   - D. Patient with a severe allergy to beta-lactams requiring gram-positive coverage
   - E. Patient with a documented infection but no site cultures available

5. Where should you document the indication for continuation of vancomycin therapy?
   - A. Daily documentation in VigiLanz
   - B. Documentation in PDoc notes
   - C. Both A & B
   - D. Neither A or B – documentation of indication is not required

3. Vancomycin De-Escalation Competency

Introduced December 2020

- Competency was a mixture of 10 fact-based questions and clinical scenarios
- Informal verbal/written feedback solicited from pharmacists

Examples of clinical competency questions:

6. MM is a 75 YO male brought to the hospital from his assisted living facility after being diagnosed with pneumonia. He is currently on ampicillin/sulbactam 3 g IV q6h, doxycycline 100 mg PO BID, and vancomycin 1 g IV q12h. On day 2 of vancomycin therapy, his nasal swab returned negative for MRSA. His sputum culture shows no growth to date, and the patient is noted to be clinically improving.

What is the most appropriate course of action?

---

9. JR is a 59 YO male currently being treated with vancomycin 1.5 g IV q12h for uncomplicated left-sided native-valve endocarditis. At 24 hours, his blood cultures grow *Staphylococcus aureus*. While a susceptibility report is not yet available, the PBP2 test is negative. JR has no known drug allergies.

What is the most appropriate course of action?

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Pharmacy Huddles

- Twice daily pharmacist huddles (AM and PM), ~15 minutes
- General announcements, policy/procedure updates, education, great catches, patient care handoffs
- Virtual meetings

Pharmacist Staff Meetings

1-hour meeting every other month

Process changes, policy/procedure updates, P&T updates, Medication Safety and Antimicrobial Stewardship Committee reports, education

Virtual meetings, mandatory attendance

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Email Reminders

Initial guidance document and competency emailed in December 2020 to pharmacists

Bimonthly emails sent out to all pharmacists evaluating progress with pharmacy metrics and methods for improvement

Sent reminder of TIMED acronym to individual pharmacists when coaching required

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One-on-One Education

All competencies were graded by ID Pharmacist

If any competency answers were answered incorrectly, ID pharmacist spent one-on-one time doing education with the pharmacist

Individual coaching for missed de-escalation opportunities

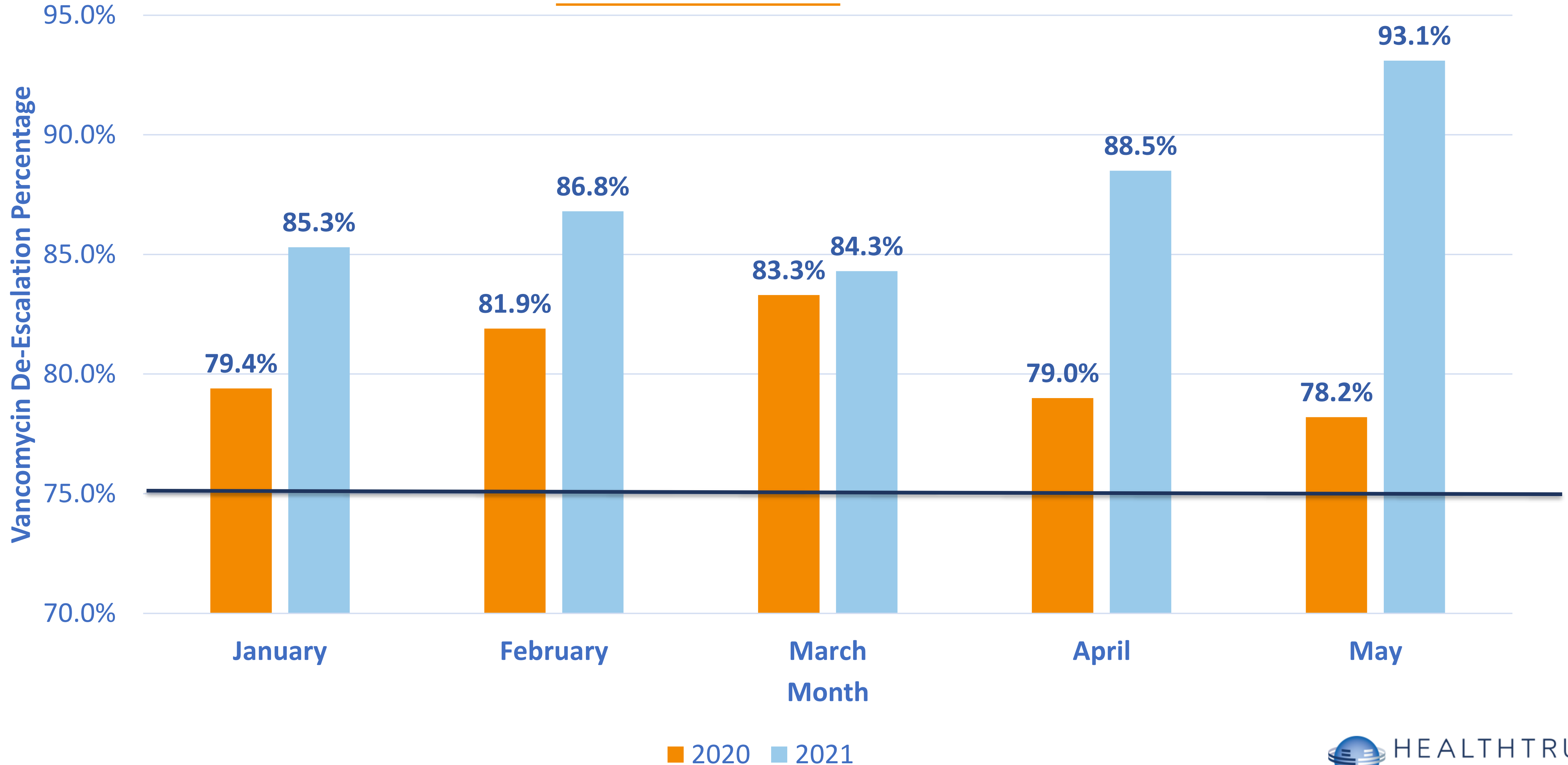
Results of Vancomycin De-Escalation Initiatives

HCA Healthcare Clinical Pharmacy Metric: Vancomycin De-Escalation

- **Metric:**
  - Percentage of patients on vancomycin who are de-escalated at **≤ 3 days**

- **Calculation:**
  - Number of vancomycin patients de-escalated at ≤ 3 days of therapy divided by the number of vancomycin de-escalation opportunities

HCA Healthcare Clinical Pharmacy Metric: Vancomycin De-Escalation



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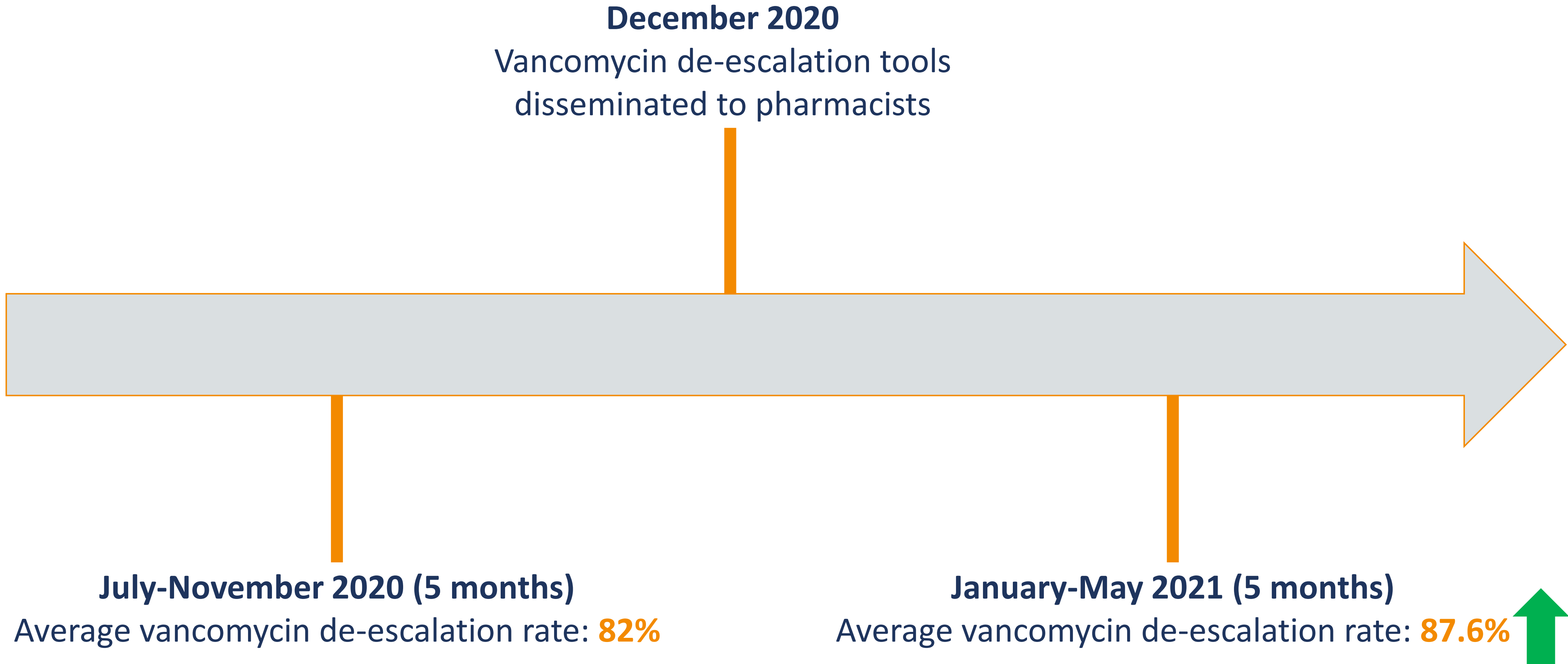
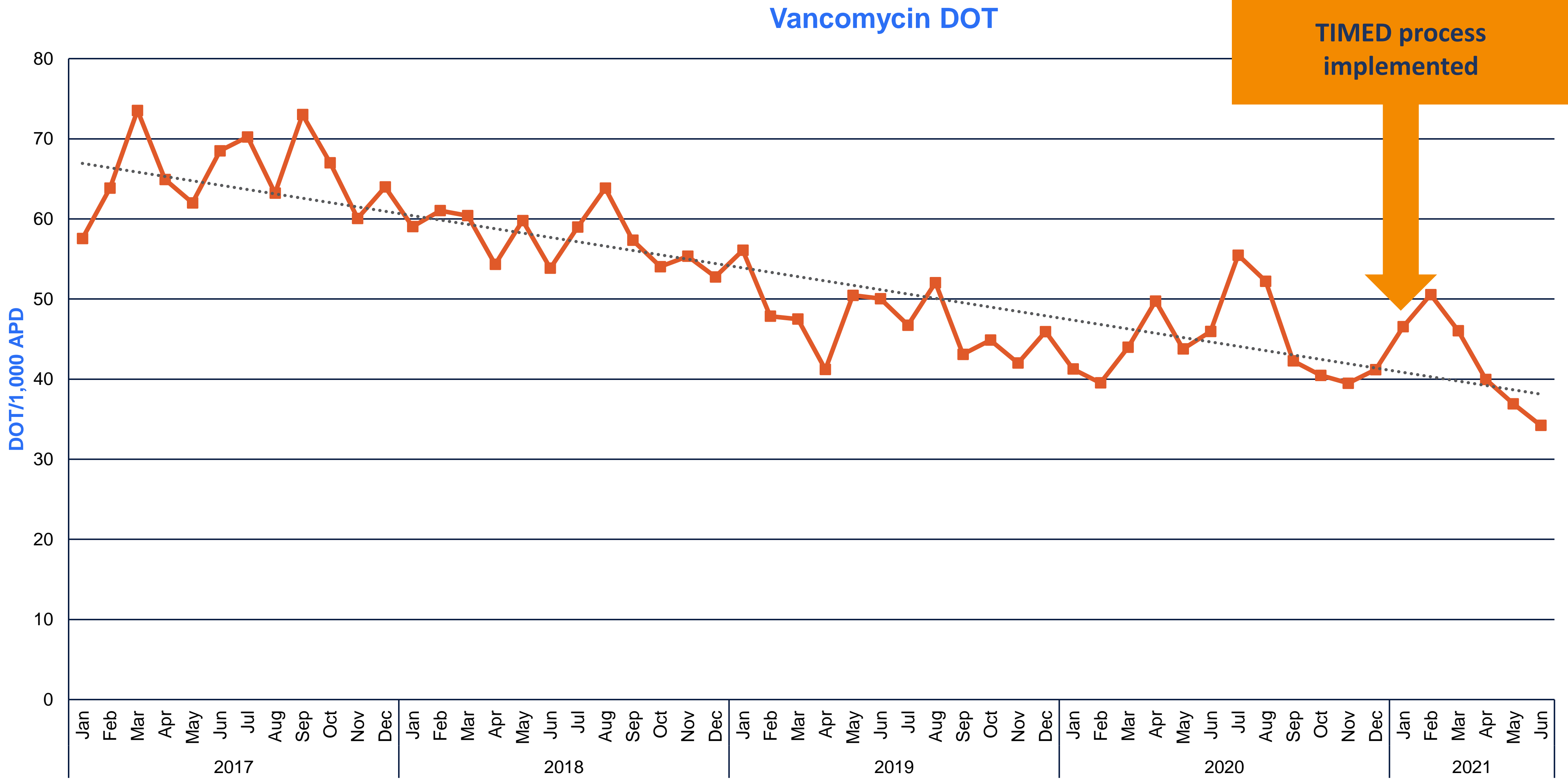
HCA Healthcare Clinical Pharmacy Metric: Vancomycin De-Escalation



North Florida Regional Medical Center Vancomycin DOT: Impact of TIMED



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Future Directions

- Additional emphasis on overall antimicrobial de-escalation

- Multidisciplinary collaboration to reduce unsupported use of vancomycin and other antimicrobials

- Initiatives to target appropriateness of vancomycin initiation
  - Antibiogram
  - Pocket card
  - Utilize electronic health record prompts to guide appropriate initiation
    - INSPIRE Trial 1 & 2
    - Antibiotic indication screen

What impact can vancomycin stewardship practices have on patient care outcomes?

a. Reduce risk of nephrotoxicity

b. Increase de-escalation rates and reduce duration of vancomycin therapy

c. Reduce risk of antimicrobial resistance and development of ‘super bugs’

d. All of the above

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Role of Pharmacists in Reducing Vancomycin Overuse

"Highly effective hospital antibiotic stewardship programs have strong engagement of pharmacists."

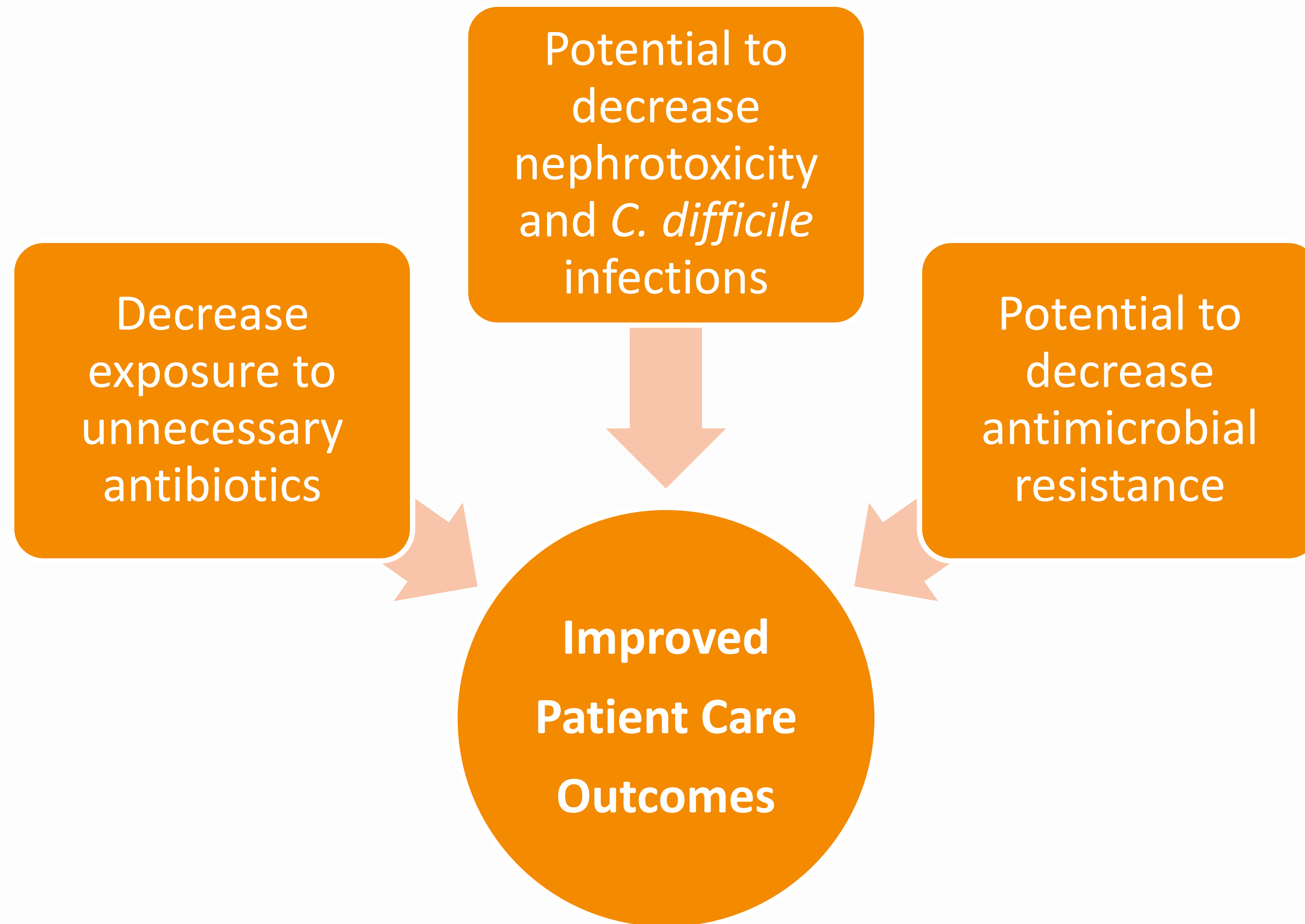
CDC Core Elements of Hospital Antibiotic Stewardship Programs, 2019

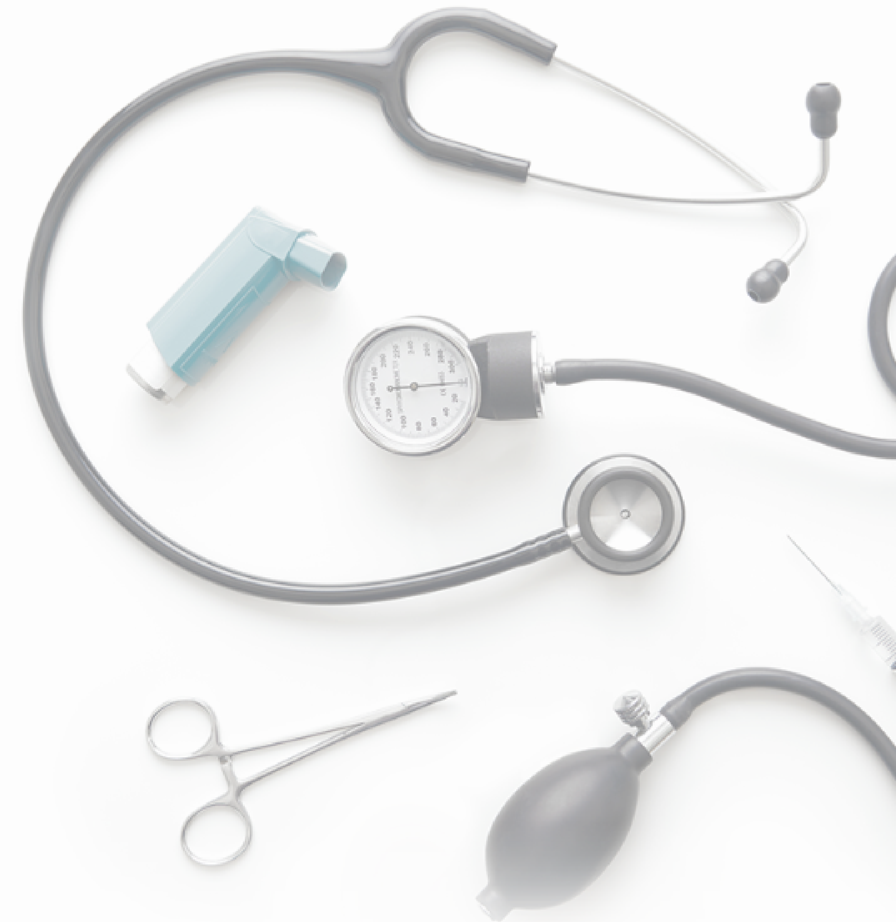
Pharmacists are responsible for dosing vancomycin in most hospitals

Pharmacists can contribute greatly in the reduction of inappropriate use of vancomycin

 CDC: https://www.cdc.gov/antibiotic-use/core-elements/hospital.html

Impact on Patient Care





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Impact on the Institution

Promotion of interdisciplinary collaboration

Robust antimicrobial stewardship program

Decreased hospital lengths of stay / costs

Compliance with The Joint Commission / Centers for Medicare & Medicaid Services requirements

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Summary

- Unnecessary use of vancomycin can lead to avoidable adverse events such as acute kidney injury, severe skin reactions, and increased incidence of multidrug resistance
- Reducing unnecessary use of vancomycin should be a high priority
- Pharmacists are in the unique position to significantly reduce the unnecessary use of vancomycin
- Antibiotic time-out works
- Don’t forget a catchy acronym! (e.g. SCAN & TIMED)

References

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12. Manigaba K, et al. *Infect Control Hosp Epidemiol*. 2018;39(12):1501-3.

Thank you…

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