Appropriateness of procalcitonin guided antimicrobial therapy utilization in hospitalized veteran patients

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The speaker has no actual or potential conflicts of interest in relation to this presentation.

OUTLINE

- Medical Center Overview
- Background/Literature Review
- Purpose
- Methods
- Results
- Self-Assessment Questions
- Q&A Session

CLEMENT J. ZABLOCKI VETERANS AFFAIRS MEDICAL CENTER (ZVAMC)

- Located in Milwaukee, WI
- Associated with Medical College of Wisconsin
- Unique users – 63,444
  - 185 acute care beds (Medical/Surgical/Psychiatry/Rehab/SCI)
    - ❖ Inpatients treated - 7,717
  - 113 long-term care beds
- Antimicrobial Stewardship Program
  - Prospective audit
  - Antibiotic protocols and restrictions
  - IV to PO conversions

BACKGROUND

Inappropriate antimicrobial use

- Bacterial or viral etiology is difficult to predict based on clinical signs and symptoms[1]
- 30-50% of antimicrobials used in the inpatient setting are inappropriate[2,3]

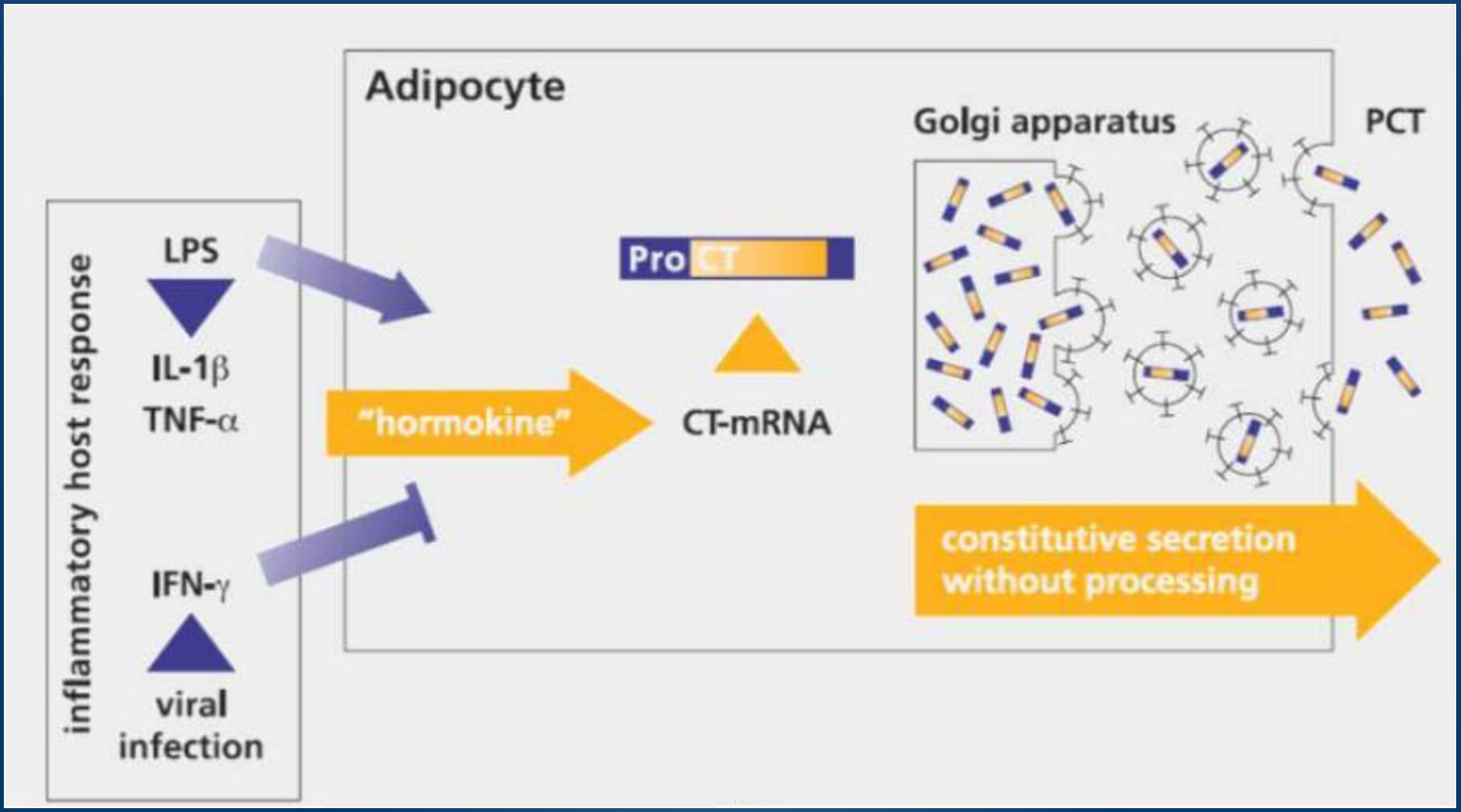
Unnecessary and inappropriate antimicrobial use leads to negative outcomes[1]

- Increased bacterial resistance
- Increased drug-related adverse events
- Increased health-care associated costs

Infection biomarkers are useful when determining the potential etiology of undifferentiated infections[4]

- Erythrocyte Sedimentation Rate (ESR)
- C-Reactive Protein (CRP)
- Cytokines
- Fever
- Leukocytes
- Procalcitonin (PCT)

PROCALCITONIN (PCT)[1,5,6]



PROCALCITONIN ASSAY

VIDAS® BRAHMS PCT[7]

- Enzyme-linked fluorescent immunoassay (ELFA) for the quantitative measurement of PCT with results in 20 minutes
- **FDA approval in 2008:** to aid in the risk assessment of critically ill patients on the first day of ICU admission for progression to severe sepsis or septic shock *in conjunction with other lab findings and clinical assessments*
- **FDA *expanded* approval in 2016:** to help assess the response of septic patients to treatment by comparing baseline PCT measurement with a PCT value taken on day four[8]

LITERATURE REVIEW

ProCAP[5]

- ***Design:*** Prospective, single-blinded, randomized study [n=200 with community acquired pneumonia (CAP)]
- ***Purpose:*** evaluate the impact of serial PCT testing and antibiotic discontinuation following PCT level results of less than 0.25 ng/mL to reduce antibiotic duration in CAP
- ***Results:*** no difference in mortality between PCT guided therapy and control despite a reduction in mean duration of antibiotic therapy in the PCT group (6.2 $\pm$ 6.2 days vs. 14.2 $\pm$ 7.3 days, $p<0.001$)

Intensive Care Med. 1998;24(8):888-9

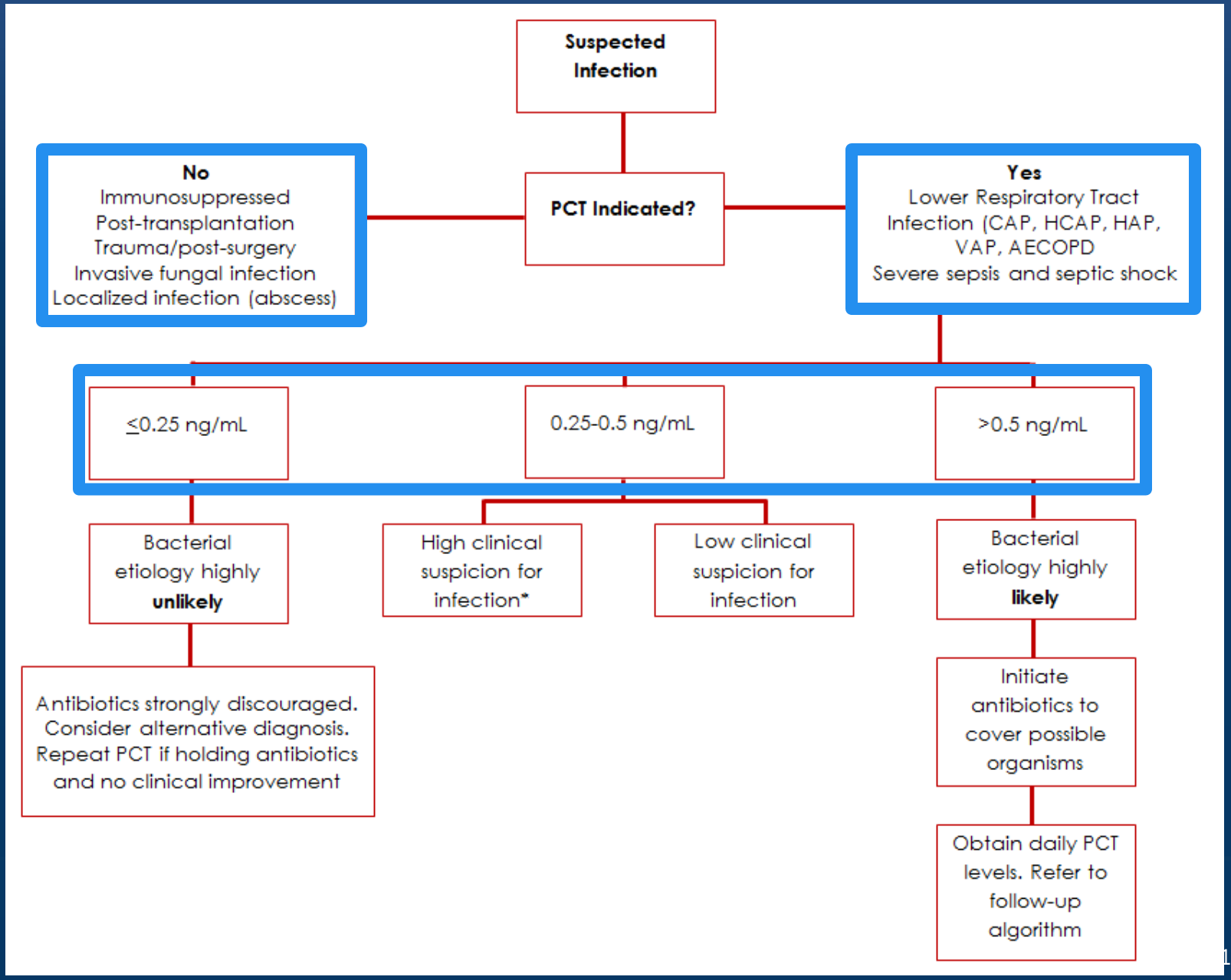
LITERATURE REVIEW

ProHOSP[1]

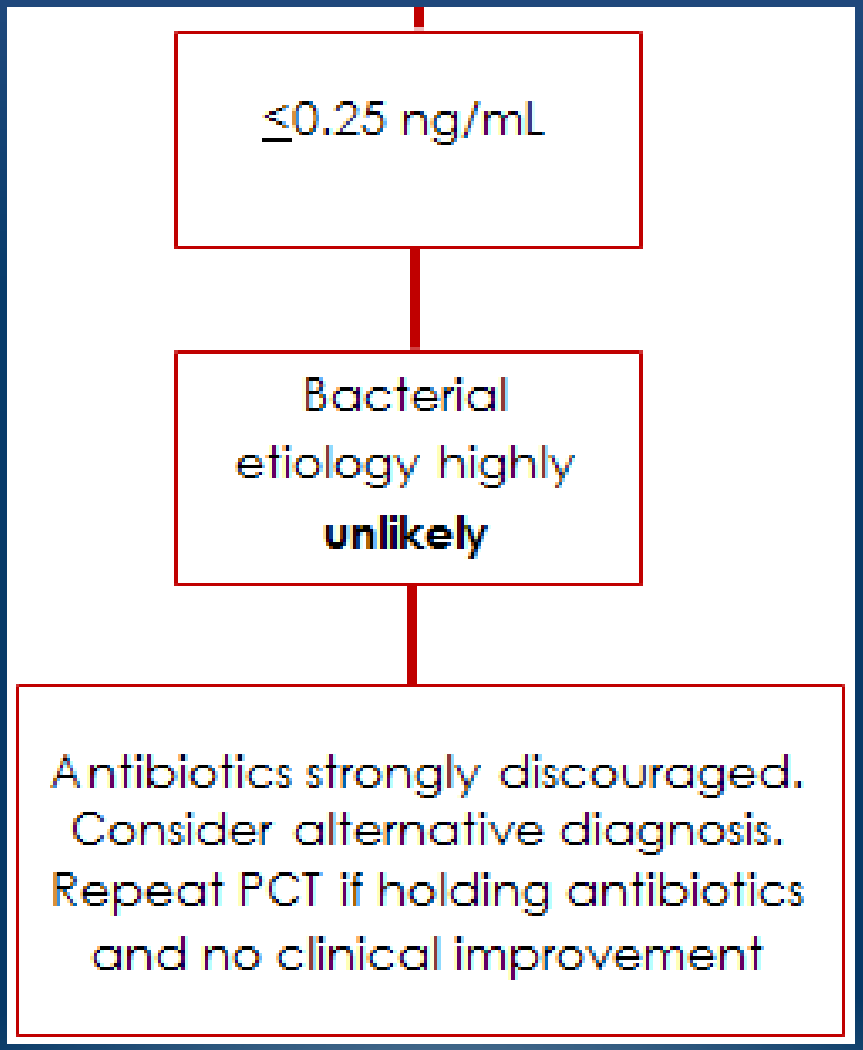
- ***Design:*** multicenter, non-inferiority, randomized controlled trial of ERs in 6 Swiss tertiary care hospitals [n=1359 presenting with lower respiratory infection (LRTI)]
- ***Purpose:*** assess the utility of a PCT algorithm in reducing antibiotic exposure without increasing adverse outcome risk in patients with LRTIs
- ***Results*** (PCT compared to control)*:*
  - Reduction in mean duration of antibiotic exposure (5.7 vs. 8.7 days; relative change -34.8%, 95% CI -40.3% to -28.7%)
  - Reduction of 8.2% in the incidence of antibiotic-related adverse effects without an increase in adverse outcomes (95% CI -12.7% to -3.7%)

Clin Infect Dis. 2015; rr(5): 651-662

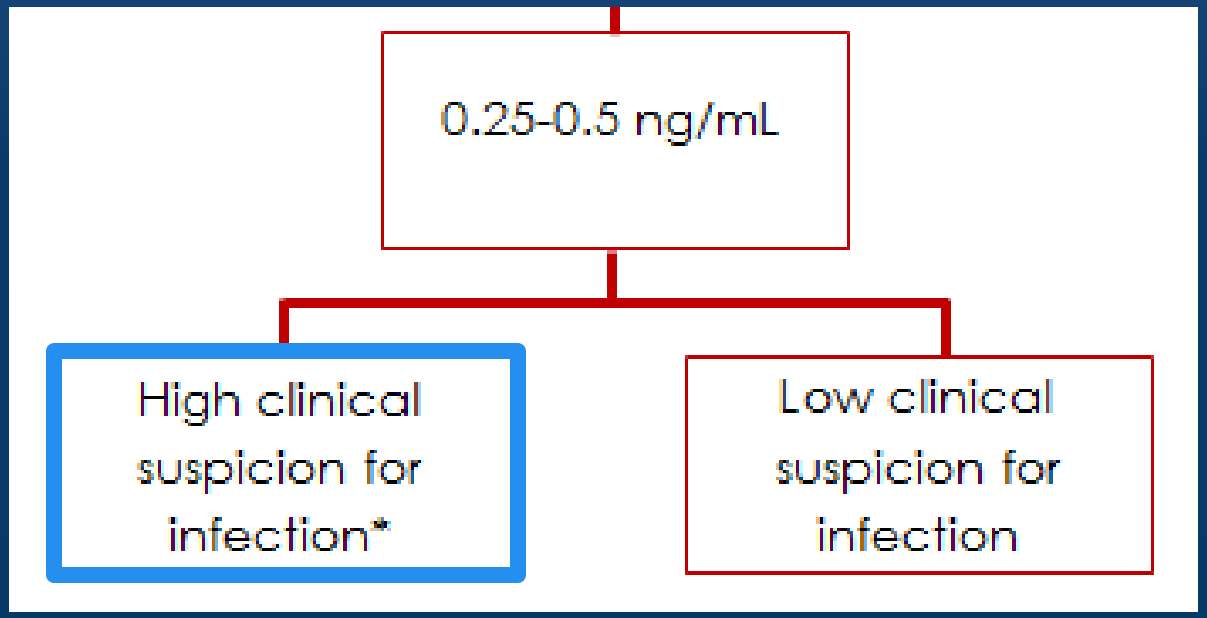
ZVAMC INITIAL PCT LEVEL ALGORITHM



ZVAMC INITIAL PCT LEVEL ALGORITHM

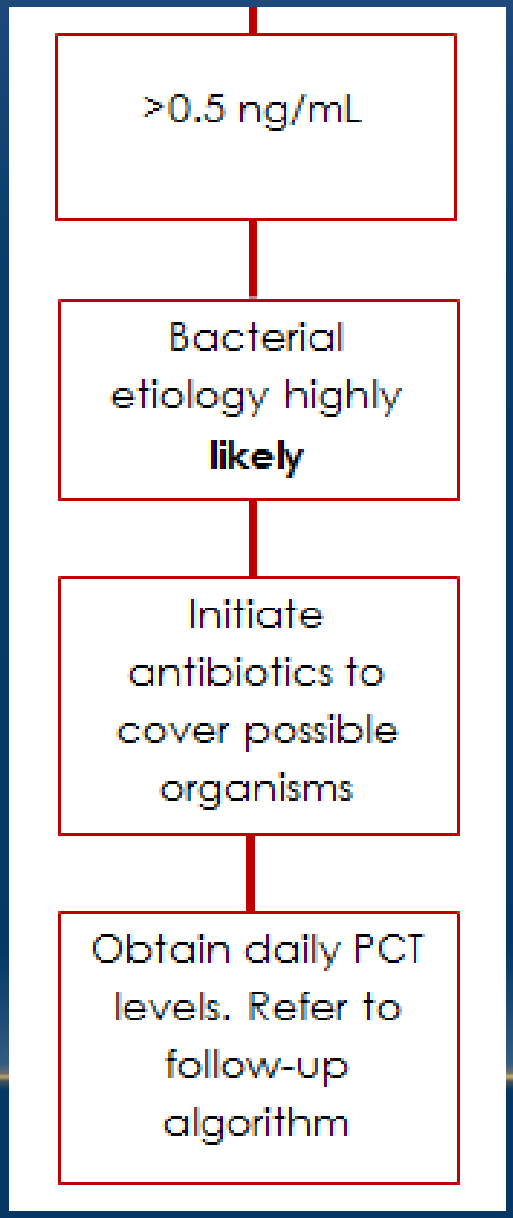


ZVAMC INITIAL PCT LEVEL ALGORITHM



***Continue empiric antimicrobials and redraw a level after 12 hours to assess for a subsequent rise in PCT.**

ZVAMC INITIAL PCT LEVEL ALGORITHM



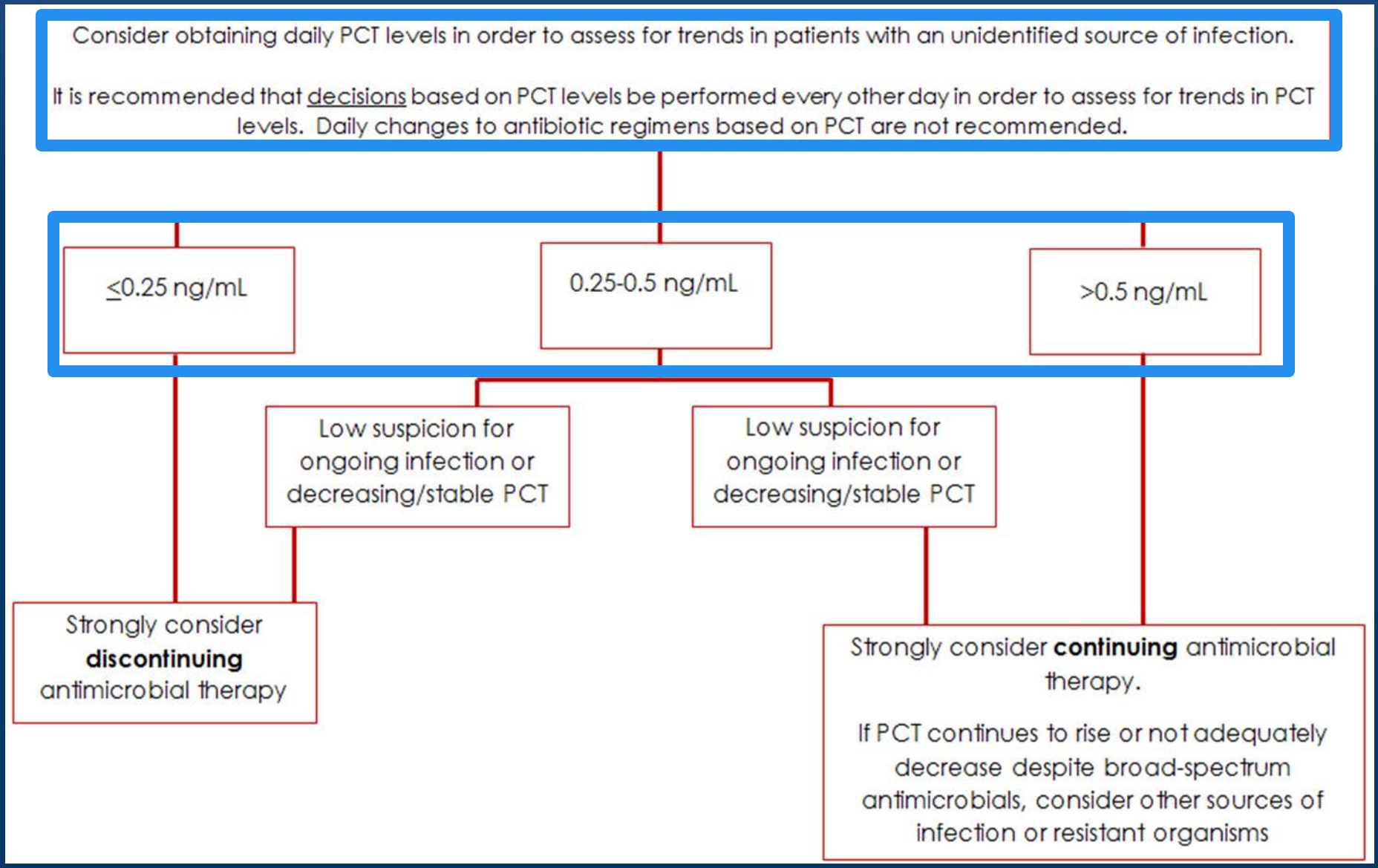
ZVAMC FOLLOW-UP PCT LEVEL ALGORITHM

- PCT levels are not indicated if antimicrobial therapy has been discontinued, if the source of the infection has been identified, or if the infection is well controlled

- PCT levels are not recommended for more than 5 days

- Patients should be treated for a duration based on established guidelines for the diagnosed infection

ZVAMC FOLLOW-UP PCT LEVEL ALGORITHM



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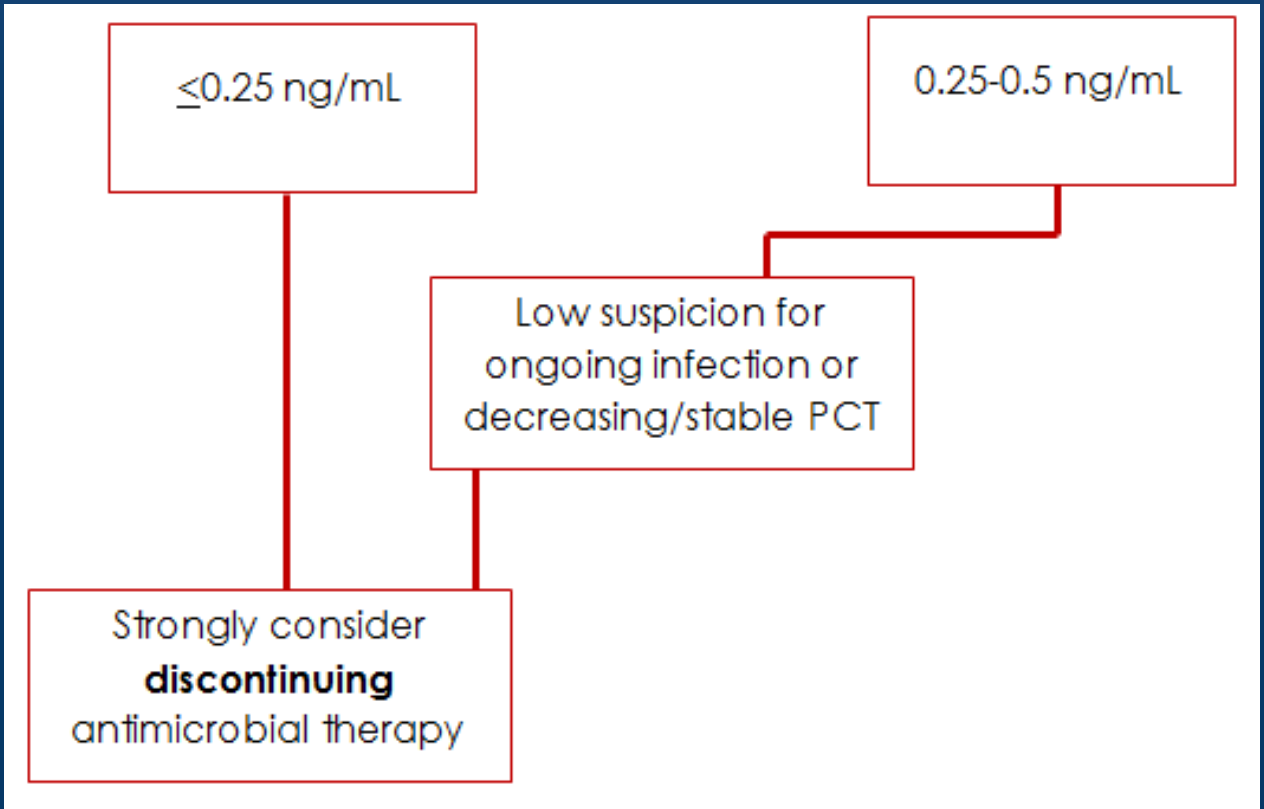

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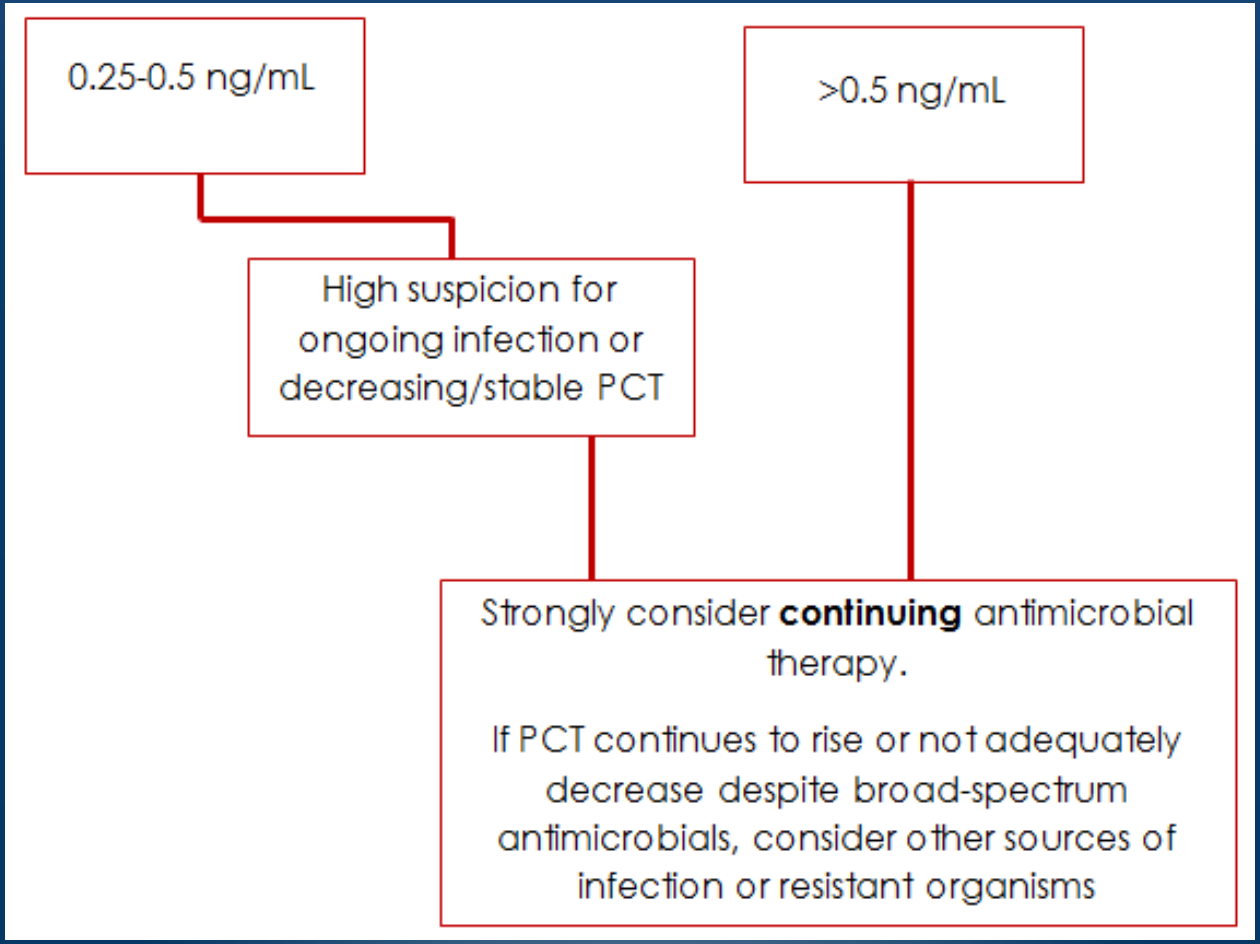


PURPOSE

- To assess the long-term appropriateness of initial and serial PCT testing and the impact of PCT testing on antibiotic management in the Intensive Care Unit (ICU) and Emergency Department (ED) per the ZVAMC PCT protocol

OUTCOMES

Primary outcome:

- Appropriate utilization assessment of PCT testing in the ED and ICU per the current PCT protocol in patients with LRTIs and/or sepsis

Secondary outcomes:

- Antibiotic duration
- Antibiotic de-escalation (antibiotic days saved)
- Total and ICU length of stay (LOS)
- Readmission at 30 days
- Economic analysis (antibiotic cost)

METHODS: STATISTICS

Primary outcome:

- *Chi-square*

Baseline characteristics:

- *Chi-square, Fisher's exact test, 2-sample t-test*

Secondary outcomes:

- Antibiotic duration: *Negative binomial regression*
- Antibiotic de-escalation (antibiotic days saved): *Poisson regression*
- Total and ICU LOS: *Negative binomial regression*
- Readmission at 30 days: *Chi-square*
- Economic analysis (antibiotic cost)

STUDY DESIGN

Quality assurance, single-center study

Intervention:

- Implementation of pharmacy-assisted PCT serial ordering and guidance of antimicrobial therapy per protocol for patients with PCT tests drawn in the ED or ICU

Retrospective review

October 1 – December 31, 2014

Prospective review with intervention

October 1 – December 31, 2015

STUDY DESIGN

Data collected:

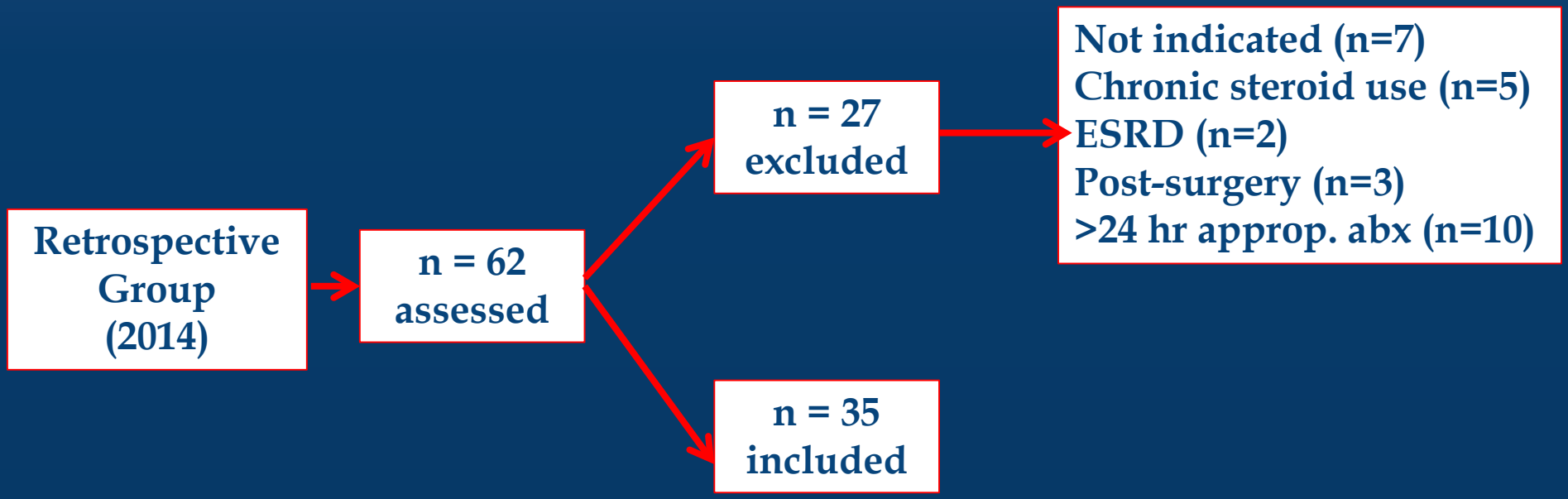
- Patient demographics
- PCT level
- Diagnosis at time of test
- Signs/symptoms related to sepsis and/or LRTI
- Systemic Inflammatory Response Syndrome criteria
- Pertinent microbiology
- Antimicrobial therapy
- Total and ICU LOS
- 30-day readmission rates

INCLUSION/EXCLUSION CRITERIA

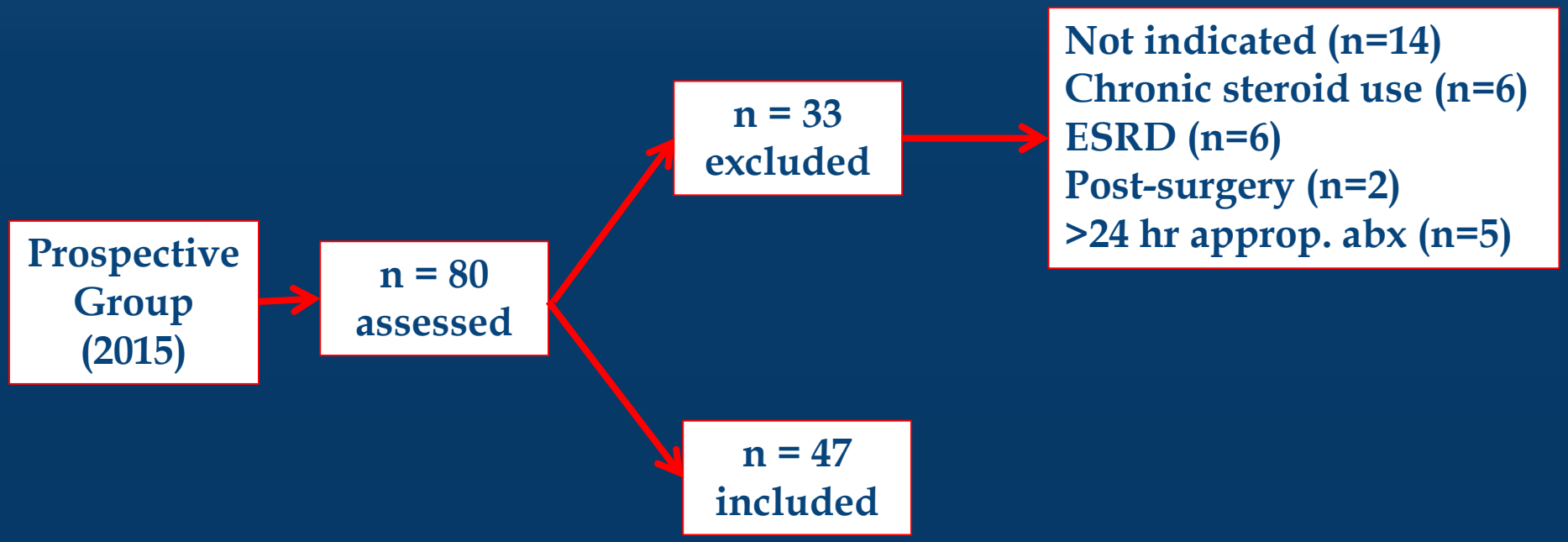
- Female or male veteran
- Age ≥ 18 years
- PCT in ED or ICU during retrospective or prospective time frames
- Diagnosis of LRTI and/or suspected sepsis

- Patients with >24 hours of appropriate antimicrobial therapy prior to initial PCT level
- Febrile neutropenia
- Acute and chronic graft-versus-host disease (GVHD)
- Immunosuppression
- Chronic steroid use (defined as >3 months of prednisone 7.5 mg/day or of a prednisone equivalent)
- End stage renal disease (CrCl <15 ml/min)
- Pregnancy, post-partum
- Immediately post-surgery, trauma, and/or burns

RESULTS


Retrospective Group (2014)
n = 62 assessed
n = 27 excluded
Not indicated (n=7)
Chronic steroid use (n=5)
ESRD (n=2)
Post-surgery (n=3)
>24 hr approp. abx (n=10)
n = 35 included

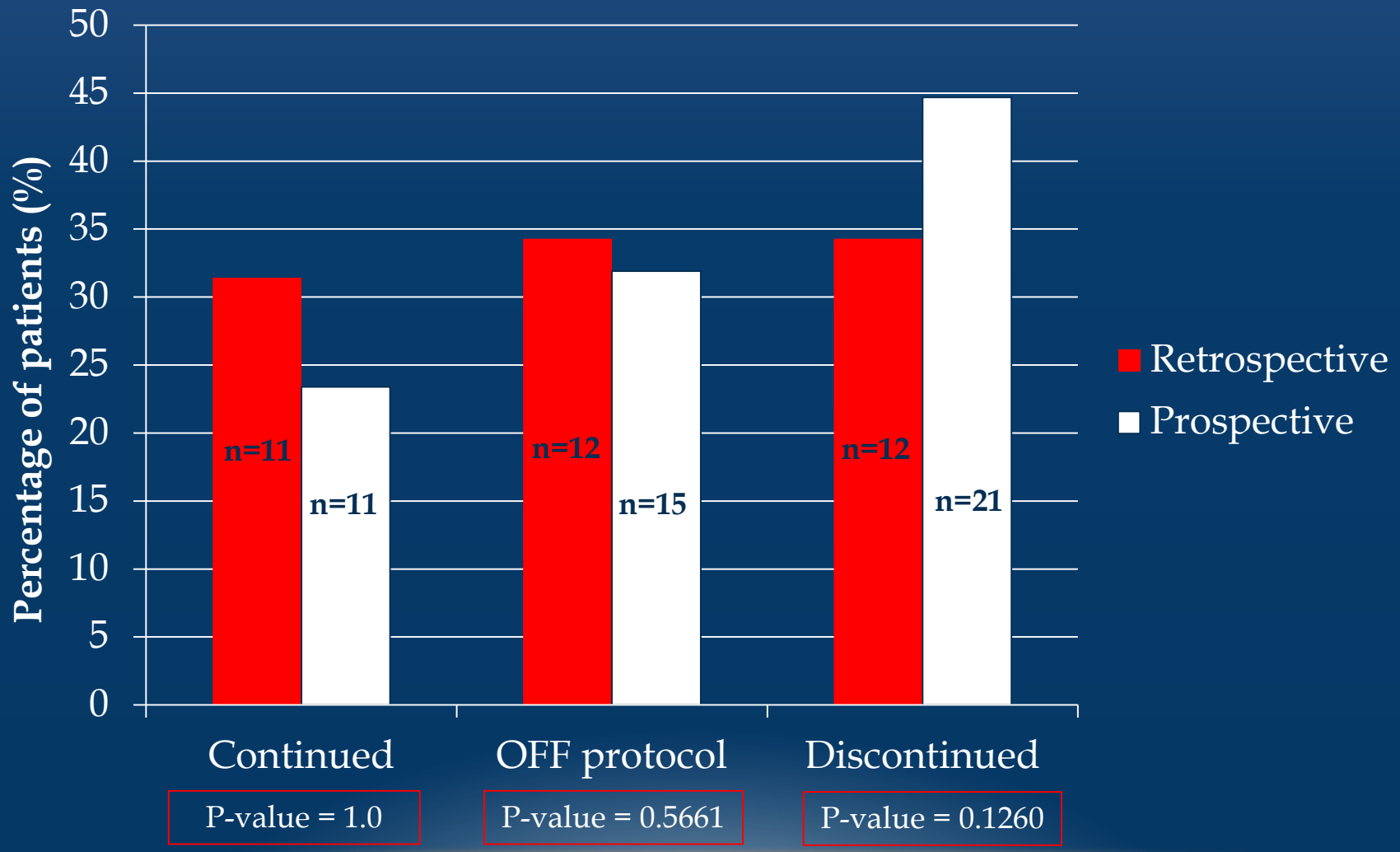
RESULTS


Prospective Group (2015)
n = 80 assessed
n = 33 excluded
Not indicated (n=14)
Chronic steroid use (n=6)
ESRD (n=6)
Post-surgery (n=2)
>24 hr approp. abx (n=5)
n = 47 included

BASELINE CHARACTERISTICS

Characteristic	Retrospective (n=35)	Prospective (n=47)	P-value
Age (years)	70.46 ±12.85	71.13 ± 11.39	0.8035
Male	33 (94.29%)	45 (95.74%)	0.7632
Indication			
LRTI	22 (62.9%)	33 (70.2%)	0.4833
Sepsis	6 (17.1%)	6 (12.8%)	0.5791
Both	7 (20.0%)	8 (17.0%)	0.7300
COPD diagnosis	12 (34.29%)	26 (55.32%)	0.0526
Undetectable PCT level (<0.05 ng/mL)	8 (22.86%)	23 (48.9%)	0.0215*
Detectable PCT level (ng/mL)	0.221±4.85	0.164±6.30	0.4439

ANTIBIOTIC ACTION PER PROTOCOL



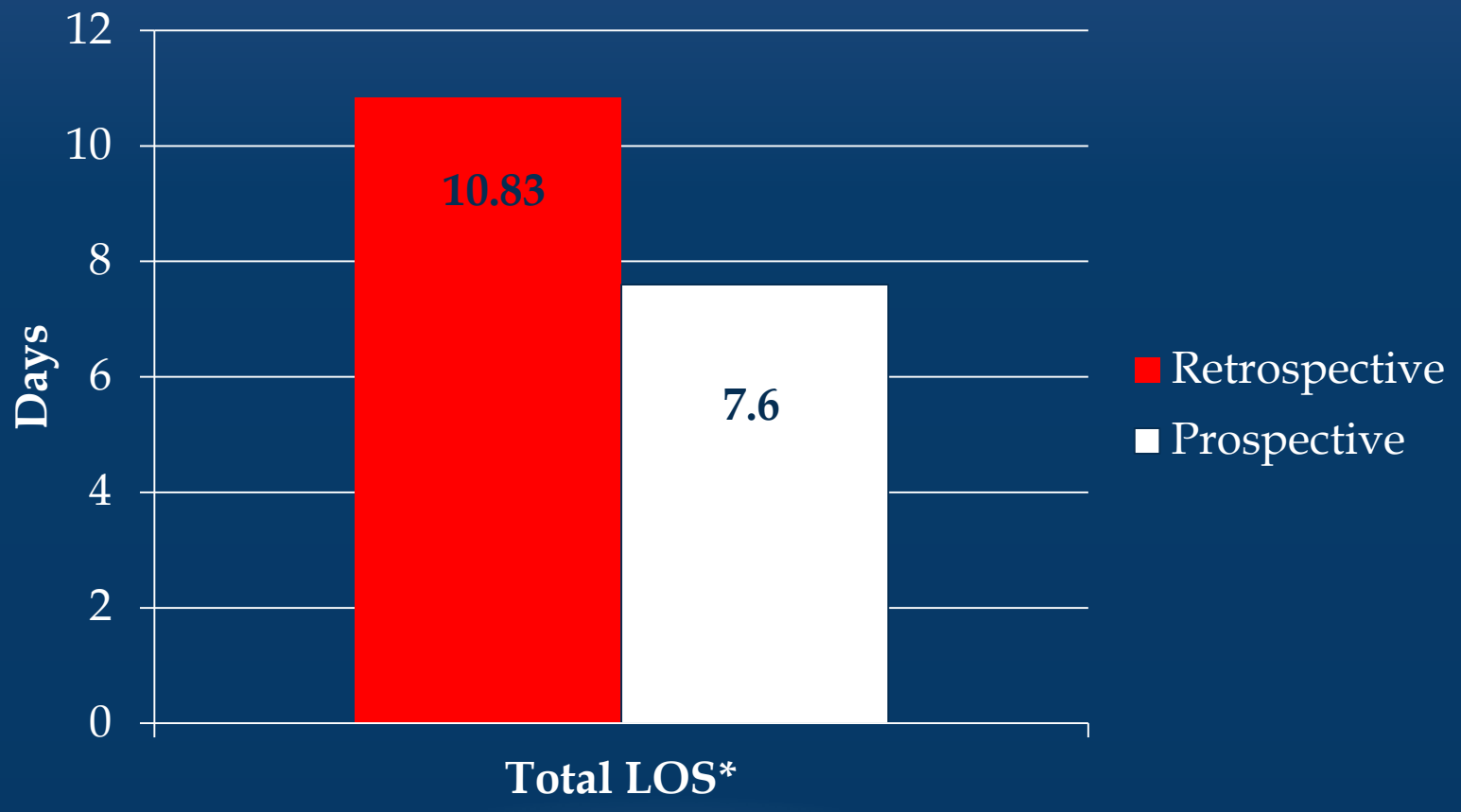
ANTIBIOTIC DAYS

Characteristic	Retrospective (n=36)	Prospective (n=47)	P-value	Percent change
Antibiotic duration (days)	6.94±8.75	4.26±4.41	0.0706	- 40%
Antibiotic days saved*	6.42±0.79 *(n=12)*	6.33±0.86 *(n=21)*	0.9273	- 7.06%

Total saved antibiotic cost due to de-escalation of antibiotics: $1126.40

*low initial PCT level or serial levels showing decline

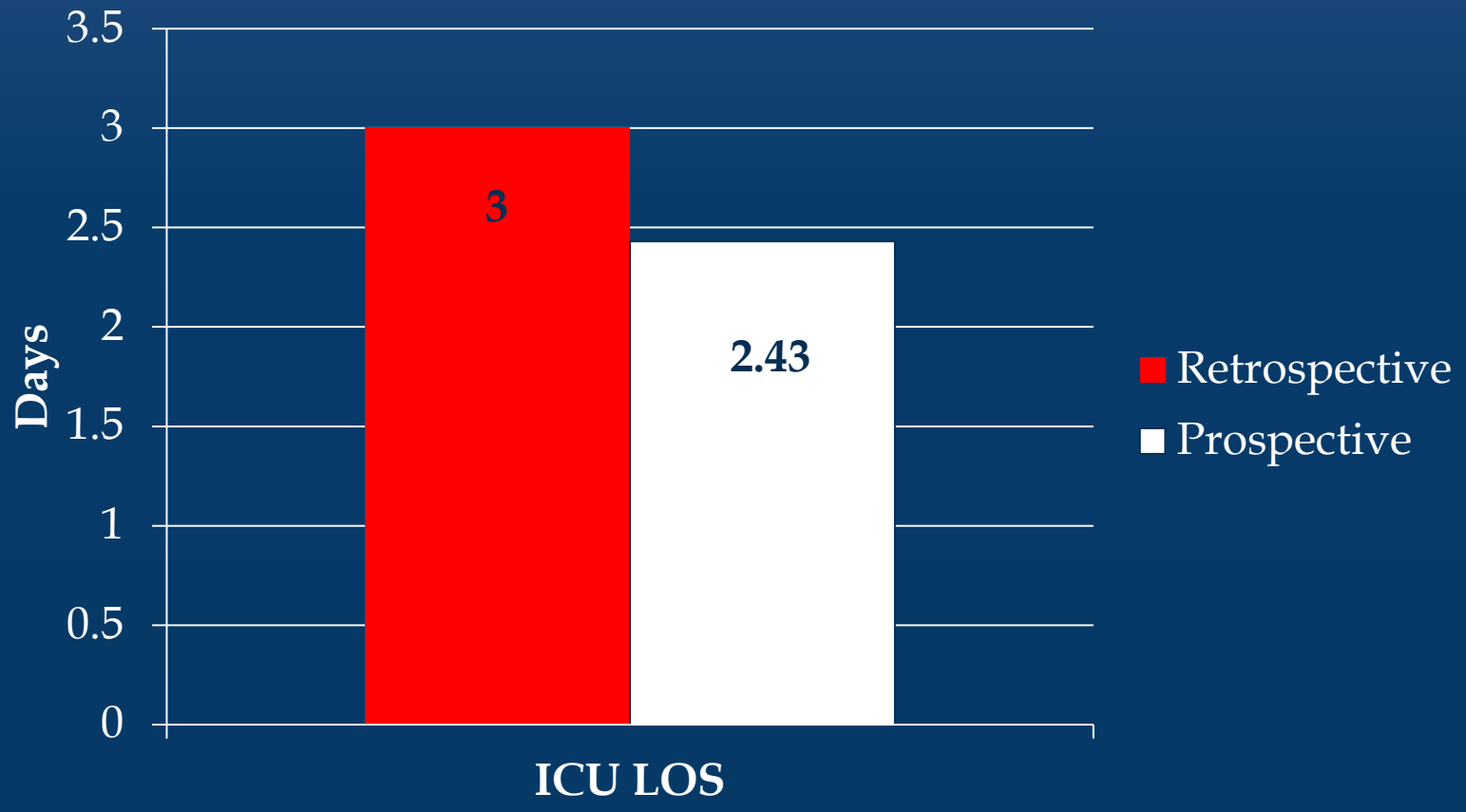
MEAN TOTAL LENGTH OF STAY (LOS)



Negative binomial regression percent change = 0.701; p-value =0.054

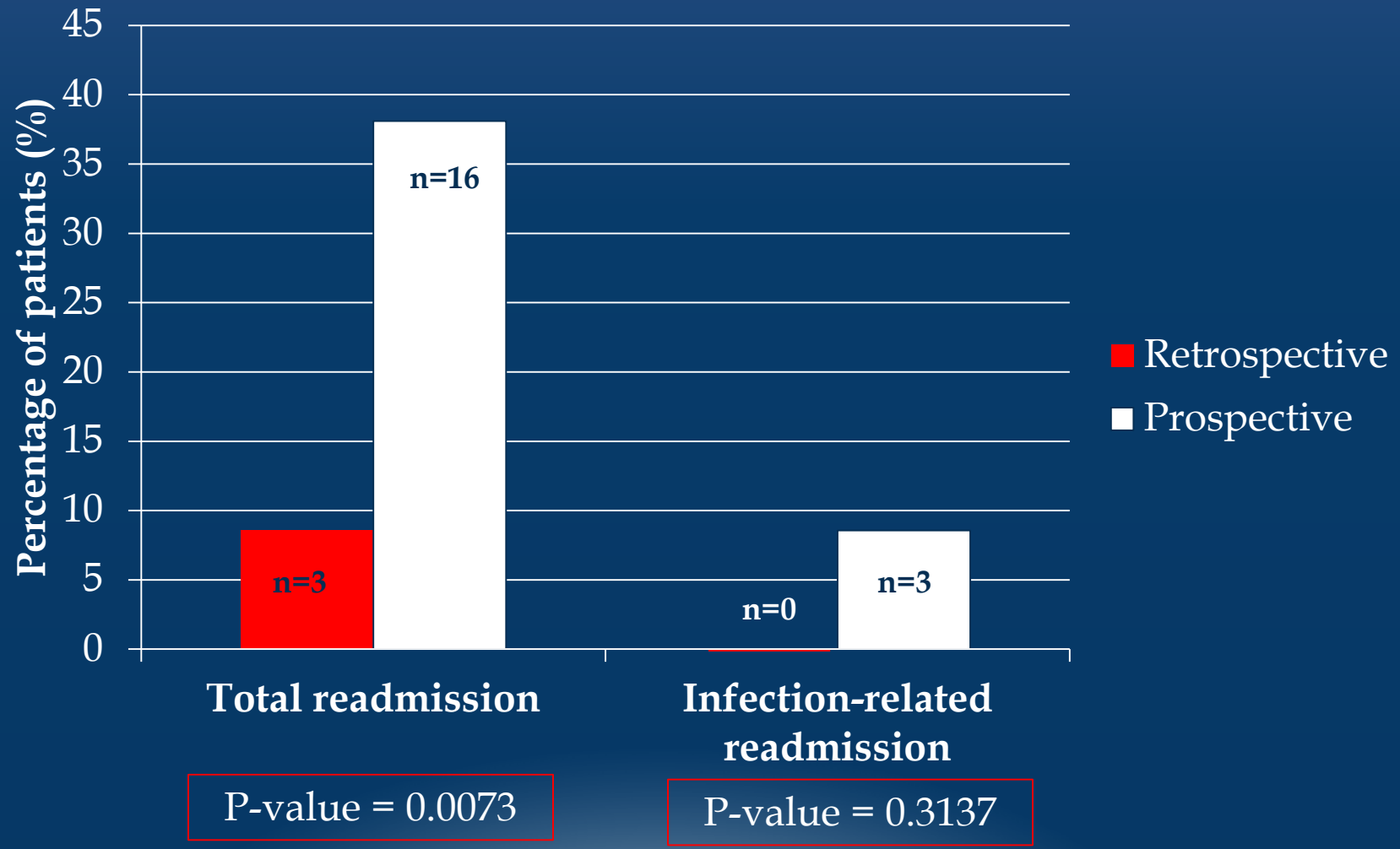
*Total LOS is truncated at 30 days

MEAN ICU LENGTH OF STAY (LOS)



Negative binomial regression percent change = 0.808; p-value =0.6244

READMISSIONS AT 30 DAYS



CONCLUSIONS

- PCT can reduce the duration of antibiotic days overall and increase the number of antibiotic days saved when compared to guideline antibiotic durations
- The number of patients impacted by antibiotic days saved is increased when a pharmacist is involved in the monitoring and follow-up of PCT
- A pharmacist monitoring PCT levels has the potential to decrease total LOS if protocol is followed

LIMITATIONS

- Small sample size
- Only conducted in patients who were in the ED and ICU at the time of the initial lab draw

FUTURE DIRECTIONS

- Implement pharmacy-assisted PCT follow-up into ZVAMC antimicrobial stewardship protocol and/or clinical pharmacist work-flow
- Education to providers regarding PCT protocol and how to interpret/act upon results
- Expansion of study timeframe to achieve power

ASSESSMENT QUESTION #1

Which of the following disease state combinations is procalcitonin clinically indicated for?

A. Suspected sepsis and/or lower respiratory tract infections
B. Cellulitis and/or onycholysis
C. Otitis externa and/or otitis media
D. Sinusitis and/or nasopharyngitis

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ASSESSMENT QUESTION #2

Based on current literature, procalcitonin is associated with which of the following?

A. Reduced mortality

B. Increased length of stay

C. Reduction in the duration of antibiotic therapy

D. Increased number of antibiotic-related adverse effects

ASSESSMENT QUESTION #2

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