PROCALCITONIN-GUIDED ANTIBIOTIC THERAPY
Selection of publications
2021 EDITION

PIONEERING DIAGNOSTICS
“50% of antibiotics prescribed for acute respiratory conditions are unnecessary” [1]

“... antibiotic therapy is of great importance in critically ill patients, but overly long antimicrobial treatment is undesirable because of increasing antibiotic resistance” [2]

“Use of sensitive procalcitonin measurements in clinical algorithms can reduce antimicrobial overuse, decreasing the risk of side effects and controlling emerging bacterial multiresistance” [3]

INTRODUCTION

Inappropriate and unnecessary use of antibiotics represents a significant healthcare burden, in terms of costs of treatment and the increased risk of resistant microorganisms. Rising rates of antimicrobial resistance and the serious issue of Clostridioides difficile infections call for more effective antibiotic stewardship efforts to reduce the unnecessary and prolonged use of antibiotics in self-limiting non-bacterial and resolving bacterial infections.

Procalcitonin (PCT) is a useful diagnostic biomarker, which is more specific for bacterial infections compared to other inflammatory markers (i.e. C-reactive protein) and helps to distinguish bacterial infections from other inflammatory reactions or viral infections.

PCT levels increase substantially within 4-6 hours upon stimulation and decrease daily by around 50% if the bacterial infection is controlled by the immune system supported by effective antibiotic therapy [4]. These kinetics set PCT apart from other markers, and have proven to be of diagnostic and prognostic value since they correlate with the extent and severity of infection as well as the resolution of illness [4, 5].

Based on PCT regulation and kinetics, many studies have documented the clinical utility of PCT in different settings (outpatients, Emergency Departments and Intensive Care Units) to help guide decisions to start, continue or stop antibiotic therapy using both initial PCT levels and serial measurements [6, 7].

In the case of lower respiratory tract infections (LRTI), measurement of the initial PCT level upon hospital admission has been found to significantly reduce the initiation of antibiotic treatment, whereas in septic patients, monitoring of PCT kinetics has led to shorter durations of antibiotic exposure through early cessation of therapy [5].

Today, a growing body of evidence-based literature supports the use of PCT to improve the clinical management of patients with suspicion of sepsis or LRTI and to contribute to antibiotic stewardship initiatives [8]. Importantly, PCT-guided antibiotic therapy strategies have been demonstrated to be safe and effective for patients, without increasing the risk for mortality, adverse effects, complications, length of stay, or treatment failure [6-10]. Currently, PCT is the only biomarker included in Second WHO Model List of Essential In Vitro Diagnostics to guide antibiotic therapy or discontinuation in sepsis and lower respiratory tract infection [11].

This document provides summaries of major publications demonstrating the medical value of PCT-guided antibiotic therapy in an easy-to-read format.

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Role of Procalcitonin Use in the Management of Sepsis.

Gregorac CS, Heilmann E, Mäliker A, Schuetz P. 


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Schröter R, Bretsch C, Bernasconi L, Mueller B. 


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HEALTH ECONOMICS AND OUTCOMES STUDIES OF PCT

Myers JC, Faia ME, Mansour MR, Broyles MR, Bryant Nguyen H, Steuten LM.

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AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 2020; doi.10.1164/rccm.202004-1201OC.

Impact of Procalcitonin Levels Combined with Active Intervention on Antimicrobial Stewardship in a Community Hospital.
Newton JA, Robinson S, Li Ling CL, Zimmer L, Kuper K, Trivedi KK.

Effect of Procalcitonin-Guided Antibiotic Treatment on Mortality in Acute Respiratory Infections: A Patient Level Meta-Analysis.

Efficacy and Safety of Procalcitonin in Patients with Suspected or Confirmed Sepsis: A Systematic Review and Meta-Analysis.

Impact of Procalcitonin Guidance with an Educational Program on Management of Adults Hospitalized with Pneumonia.

Impact of Procalcitonin (PCT)-Guided Antibiotic Management on Antibiotic Exposure and Outcomes: Real World Evidence.
Broyles MR.

Effect of Procalcitonin Testing on Health-care Utilization and Costs in Critically Ill Patients in the United States.
Balk RA, Kahi SS, Cao Z, Robinson SB, lipkin C, Bazzette S.

ADDITIONAL RECOMMENDED READING

Procalcitonin-guided Diagnosis and Antibiotic Stewardship Revisited.

CLINICAL CHEMISTRY AND LABORATORY MEDICINE 2018;56(5):177-77.

Procalcitonin as an Early Marker of the Need for Invasive Respiratory or Vasopressor Support in Adults with Community-Acquired Pneumonia.
Sefl WH, Griska CG, Williams DJ, et al.


Role of Procalcitonin in Managing Adult Patients with Respiratory Tract Infections.
Schuetz P, Amin D, Greenwald J.

Procalcitonin for Reduced Antibiotic Exposure in the Critical Care Setting: A Systematic Review and an Economic Evaluation.
Heyland DK, Johnson AP, Reynolds SB, et al.
CRITICAL CARE MEDICINE 2013;41(7):1792-93.

Procalcitonin Guidance of Antibiotic Therapy in Community-Acquired Pneumonia: A Randomized Trial.
Christ-Crain M, Stolz D, Bingisser R, et al.


Stojanovic I, Schneider J, Wei L, et al.

Economic Evaluation of Procalcitonin-Guided Antibiotic Therapy in Acute Respiratory Infections: A Chile Health System Perspective.
Schneider J, Stojanovic I, Vargas C, et al.

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Serial Procalcitonin Predicts Mortality in Severe Sepsis Patients: Results from the Multicenter Procalcitonin Monitoring Sepsis (MOSES) Study.


CONCLUSIONS
The objective of this study was to investigate the relationship between a PCT decrease of >80% from baseline to day 4 and 28-day mortality in patients with severe sepsis or septic shock. This was a blinded, prospective, multicenter, observational trial involving 13 US-based emergency departments and ICUs.

STUDY DESIGN
Eight hundred and fifty-eight (858) patients who met criteria for severe sepsis or septic shock, were admitted to the ICU, and had PCT measured over the first five days were enrolled in this study. Six hundred and forty-six (646) of those patients were alive and in the hospital on day 4 and were included in the intent-to-diagnose analysis. A 28-day follow-up was additionally conducted to verify vital status.

RESULTS
28-day mortality was nearly double in patients whose PCT levels did not decrease >80% from baseline at day 4 compared with those whose PCT decreased >80% (20% vs. 10.4%; p=0.001). Patients with a PCT increase from baseline to day 1 had an almost three-fold higher mortality than those with a short-term decrease (29% vs. 12%; p=0.001). This study demonstrates that PCT is a significant independent predictor of mortality even after adjusting for other clinical outcome predictors such as demographics, sepsis severity, and patient location (ICU or ward). PCT values for non-survivors were higher at baseline and stayed higher on all days compared to survivors.

CONCLUSIONS
In conclusion, monitoring of PCT changes over time aids in risk assessment, and kinetics of PCT over the first 4 days were predictive of survival of patients diagnosed with sepsis or septic shock. Initial PCT changes (baseline to day 1) also provide important information for mortality prediction and may prove useful during early critical care management. Furthermore, the first draw in the emergency room is crucial for later risk assessment.

“Results of this large, prospective multicenter U.S. study indicate the inability to decrease procalcitonin by more than 80% is a significant independent predictor of mortality and may aid in sepsis care.”

Efficacy and Safety of Procalcitonin Guidance in Reducing the Duration of Antibiotic Treatment in Critically Ill Patients: A Randomised, Controlled, Open-Label Trial.


OBJECTIVE
This trial evaluated the safety and efficacy of procalcitonin guidance in reducing duration of antibiotic use in critically ill ICU patients with a presumed bacterial infection.

STUDY DESIGN
This was a prospective, multicenter, randomized, controlled, open-label interventional trial in 15 hospitals in the Netherlands, where 3,575 patients were randomized (1:1 ratio) to a PCT-guided (n=1776) or standard-of-care antibiotic (n=1799) group. In the PCT-guided group, physicians were advised to discontinue antibiotics if the PCT level decreased by 80% or more from peak value or to 0.5 µg/L or lower. Patients in the standard-of-care group were treated according to local antibiotic protocols. The primary outcome for this study was consumption of antibiotics and duration of antibiotic treatment. The primary safety outcome was mortality at 28 days and 1 year. Secondary outcomes were the percentage of patients with recurrent infections, hospital and ICU length of stay (LOS), cost of antibiotics, and cost of PCT. The analyses for this study were intent-to-treat.

RESULTS
In the PCT-guided therapy group, 71% of the patients discontinued antibiotics in the ICU, with a median consumption of antibiotics of 7.6 daily doses vs. 9.3 daily doses for the standard-of-care group (p=0.0000). Mortality at 28 days was 18.6% for the PCT-guided group vs. 25% for the standard-of-care group (p=0.0122) and mortality at 1 year was 34.8% for the PCT group vs. 40.9% for standard of care (p=0.0158). The median reduction of antibiotic costs in the PCT-guided group was 34 Euros per patient (p=0.0006).

CONCLUSIONS
This large multi-center study in critically ill patients shows that PCT concentrations help physicians in deciding whether or not a presumed bacterial infection is truly of bacterial origin. Furthermore, use of a PCT-guided algorithm reduces duration of antibiotic therapy, which is one of the pillars of antibiotic stewardship. This reduction of antibiotic duration was associated with a significant decrease in mortality.

“Procalcitonin guidance stimulates reduction of duration of treatment and daily defined doses in critically ill patients with a presumed bacterial infection. This reduction was associated with a significant decrease in mortality.”

KEY FINDINGS
- Hospitalized patients whose PCT levels did not decrease >80% from baseline at day 4 had two times greater likelihood of dying from any cause at day 28.
- Changes in PCT levels from baseline to day 4:
  - are strongly correlated with risk of death,
  - provide important information for prognosis,
  - can aid in the decision to discharge patients from the ICU.
**OBJECTIVE**
The purpose of this study was to evaluate whether using PCT-guided therapy in patients with sepsis is non-inferior to standard of care for mortality; this was an intent-to-treat analysis.

**STUDY DESIGN**
This study was a randomized (1:1 ratio), multicenter, prospective, parallel-group, open-label trial, of 630 patients in the PCT (n=311 patients) or control (n=319) groups. Since this was an open-label design, the investigators were not blinded to the randomization assignment.

The primary endpoints were all-cause mortality at 28 and 60 days (non-inferiority) and the number of days without antibiotics at 28 days after inclusion (superiority). The secondary endpoints were relapse of superinfection, number of days without mechanical ventilation, length of stay in the hospital and ICU, days of exposure to antibiotics per 1,000 inpatient days, duration of antibiotic treatment, and percentage of emerging multi-drug resistant bacteria isolated.

**RESULTS**
The outcomes of this trial demonstrated that the use of a PCT-based approach was non-inferior to standard of care in mortality at day 28 and 60. The number of days without antibiotics at 28 days was statistically significant for the PCT-guided therapy group, with an average reduction of 2.7 days of treatment ($p<0.0001$) and a 10% non-inferiority margin for mortality. The secondary endpoints were relapse of superinfection, number of days without mechanical ventilation, length of stay in the hospital and ICU, days of exposure to antibiotics per 1,000 inpatient days, duration of antibiotic treatment, and percentage of emerging multi-drug resistant bacteria isolated.

**CONCLUSIONS**
This study showed that PCT-guided care in non-surgical patients in the ICU could substantially reduce antibiotic exposure and selective pressure with no apparent adverse outcomes. Reduction of selection pressure could be potentially beneficial in the current era of multi-drug resistance.

**KEY FINDINGS**
- PCT-guided therapy to treat sepsis leads to fewer days of antibiotic use (23% relative reduction in antibiotic exposure).
- Mortality in the PCT-guided therapy group is non-inferior when compared to standard of care.

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**OBJECTIVE**
In this secondary analysis of a prospective, multicenter, observational study of 148 ICUs in Spain, the authors’ main objective was to determine which specific biomarkers and variables are associated with co-infection in patients admitted to the ICU, using the CHAID (Chi-square Analysis Interaction Detection) analysis.

**STUDY DESIGN**
During three pre-determined time periods, 972 patients were admitted to the ICU for influenza symptoms (also PCT-tested), who were found positive for Influenza A (H1N1), and subsequently confirmed with or without CARC (community acquired respiratory co-infection). A CHAID decision tree model was utilized in order to analyze independent variables in each subgroup of cases.

**RESULTS**
Findings showed that PCT levels were higher in co-infected patients, making it the most important variable for identifying co-infection (84% sensitivity, 94% negative predictive value (NPV), area under the curve (AUC) 0.716 (95% CI 0.67-0.75)), especially in the absence of shock (Figure 1).

**CONCLUSIONS**
In ICU patients with confirmed influenza A (H1N1) infection without shock, PCT was found to have a high negative predictive value (94%) and seemed to be useful for excluding co-infection (for ruling out the presence of CARC). Also, in this study, PCT was more accurate than CRP.

**KEY FINDINGS**
- PCT has a high negative predictive value (94%) and low PCT levels could be a good tool for ruling out the presence of CARC in ICU patients with confirmed influenza A (H1N1) infection and without shock.
- In this study, PCT was shown to be a more accurate biomarker than CRP to define CARC.
PCT-GUIDED ANTIBIOTIC THERAPY IN LOWER RESPIRATORY TRACT INFECTIONS (LRTI)
PCT-GUIDED ANTIBIOTIC THERAPY IN LRTI


OBJECTIVE
This study investigated the effects of PCT guidance on inpatients and outpatients in hospitals and general physician offices in 3 countries with diverse antibiotic-prescribing patterns.

Most evidence regarding PCT-guided antibiotic stewardship comes from randomized controlled trials (RCTs), with minimal data from real-world practice. The objective of this international multicenter surveillance trial was to study the “real-life” effects of PCT-guided antibiotic stewardship in daily practice in patients with lower respiratory tract infections (LRTI).

STUDY DESIGN
The study was conducted in 14 centers in Switzerland (10), France (3), and the United States (1). One thousand eight hundred and fifty (1,850) adults with LRTI presenting to emergency departments or outpatient offices were enrolled.

The primary endpoint was duration of antibiotic therapy within 30 days and secondary endpoints were duration of antibiotic therapy at the index presentation, adherence to the PCT algorithm, and adverse medical outcomes in the index hospitalization.

The PCT algorithm used pre-defined cut-off ranges for initiating or stopping antibiotics. There were pre-specified criteria for overruling, but in some cases, the algorithm advice was overruled based only on clinical judgment (Figure 1).

RESULTS
Of 1,520 patients with LRTIs, the mean duration of antibiotic therapy was 6.9 days. This study demonstrated that antibiotic duration was significantly shorter (1.51 days) if the PCT algorithm was followed compared with when it was overruled (6.9 vs. 7.4 days; p<0.001).

CONCLUSIONS
When the PCT algorithm was followed for non-initiation of antibiotics on hospital admission and early cessation of antibiotics, no increase in the risk of adverse outcomes within 30 days of follow-up was observed.

“We demonstrate that good compliance with the PCT algorithm is possible in real-life conditions but has to be reinforced to achieve optimal benefit.”

KEY FINDINGS
- This study shows that in “real-life” conditions, a PCT-guided algorithm can significantly reduce antibiotic use without increasing risk of complications.
- Good compliance with a PCT algorithm depends on antibiotic-prescribing cultures, and has to be reinforced to achieve optimal benefits.
- Both VIDAS® and KRYPTOR (Thermo Fisher) demonstrated similar PCT results. VIDAS® showed ease-of-use in different settings (ED, primary care).

Figure 1: PCT Algorithm for Antibiotic Stewardship in patients with LRTI - ProREAL

Adapted from Albrich WC et al. Arch Intern Med. 2012;172(9):755-22

| PCT algorithm for stewardship of antibiotic therapy in patients with LRTI |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| If antibiotic therapy is initiated: | If antibiotic therapy is initiated: |
| Repeated PCT measurement within 6–24 hours (also in outpatients if symptoms persist/worsen) | Check PCT on control days 1–3, 4–6, 8, and every 2 days after day 8 for guidance of antibiotic therapy |
| Differential diagnosis? eg, pulmonary embolism, congestive heart failure, tumor, BOOP, sepsis, fungal | To stop ongoing antibiotic therapy, use the same cutoff values as above |
| Antibiotic therapy can be considered for: | For outpatients, duration of antibiotic therapy depends on last PCT value (≥0.25 ng/mL x 3 days, ≥0.5 ng/mL x 5 days, ≥2 ng/mL x 7 days) |
| 1. Admission to the ICU or IMC: (a) respiratory instability (respiratory rate ≥30/min or O2 saturation <90% with 6 L O2/min); (b) hemodynamic instability (systolic blood pressure for at least 1 h <90 mm Hg, despite adequate volume replacement or need for vasopressors) | For initially very high PCT (eg, >5 ng/mL) follow the relative decline of PCT if patients show clinical improvement |
| 2. Life-threatening comorbidity: (a) imminent death; (b) severe immunosuppression (neutrophils <500/μL; for HIV: CD4 <350/μL); (c) chronic infection or other nonrespiratory infection requiring antibiotics (eg, endocarditis, TB) | – Decline ≥80% of peak: stop recommended |
| 3. Complications and difficult-to-treat-organisms: Legionella (antibiotics ≥30 days), sepsis, empyema | – Decline ≥80% of peak: Stop strongly recommended |
| 4. (a) PCT <0.1 ng/mL: CAP PSI V (>130) or CURB 65 >3 points, COPD GOLD IV; (b) PCT 0.1–0.25 ng/mL: CAP PSI V or V ≤90, CURB 65 >2, COPD/GOLD stages III and IV, SatsO2 ≤90% despite 30 minutes of intensive oxygen therapy | Persistently elevated PCT: suspect complicated course (resistant organism, MOF, abscess,…) |
| (c) chronic infection or other nonrespiratory infection requiring antibiotics (eg, endocarditis, TB) | Falsely elevated PCT: eg, severe SIRS and shock, ARDS, trauma, postoperative, tumor (eg, mediastinal thyroid cancer, SCLC), fungal, malaria |

Abbreviations:
- ARDS: acute respiratory distress syndrome; BOOP: bronchiolitis obliterans with organizing pneumonia; CAP: community-acquired pneumonia; COPD-GOLD: chronic obstructive pulmonary disease Global Initiative for Chronic Obstructive Lung Disease; CURB-65: confusion, serum urea nitrogen, respiratory rate, blood pressure, and age 65 years or older; HIV: human immunodeficiency virus; ICU: intensive care unit; IMC: intermediate care unit; MOF: multiple organ failure; PSI: Pneumonia Severity Index; SCLC: small-cell lung cancer; SIRS: sepsis inflammatory response syndrome; and TB: tuberculosis.
**OBJECTIVE**

This multi-center, non-inferiority, randomized controlled trial investigated the effects of PCT guidance on patients admitted to the emergency departments (ED) of 6 Swiss tertiary care hospitals with symptoms of severe lower respiratory tract infection (LRTI).

The objective of the study was to examine whether a PCT algorithm can reduce antibiotic exposure without increasing the risk for serious adverse outcomes in the ED setting.

**STUDY DESIGN**

One thousand three hundred and fifty-nine (1,359) patients admitted to the ED with symptoms of severe LRTI were randomized into 2 groups:

- PCT guided group: pre-defined cut-off ranges were used to initiate or stop antibiotics (Figure 1)
- Control group: patients received antibiotic therapy according to standard guidelines.

The primary endpoint was adverse outcomes, within 30 days of ED admission, including death, ICU admission, disease-specific complications or recurrent LRTI requiring antibiotic treatment. The secondary endpoints were antibiotic prescription rates, duration of antibiotic therapy and adverse effects.

**RESULTS**

Results showed that the overall adverse outcome rate was similar in the PCT and control groups (15.4% vs. 18.9%), however, the mean duration of antibiotic exposure was lower in the PCT group in all patients (5.7 vs. 8.7 days = -34.8%), and in patient sub-groups.

**CONCLUSIONS**

Compared to the standard care group, PCT guidance resulted in significant reductions in antibiotic exposure: lower antibiotic prescription rates, shorter mean duration of antibiotic treatment and reduced side-effects from antibiotics.

“PCT guidance will have substantial clinical and public health implications to reduce antibiotic exposure and associated risks of adverse effects and antibiotic resistance.”

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**KEY FINDINGS**

- Multicenter study performed in a mix of non-academic and academic tertiary care hospitals.
- This study demonstrates that within all LRTI subgroups, a PCT-guided treatment algorithm reduced antibiotic usage with no increased adverse patient outcomes.
- First study to include a primary end-point composed of many adverse outcome parameters within 30 days of ED admission.

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**Abbreviations:**

PCT: procalcitonin; CAP: community-acquired pneumonia; PSI: pneumonia severity index; COPD: chronic obstructive pulmonary disease; GOLD: global initiative for obstructive lung disease; CURB-65: confusion, serum urea nitrogen, respiratory rate, blood pressure, and age 65 years or older; ARDS: acute respiratory distress syndrome.
**PCT-GUIDED ANTIBIOTIC THERAPY IN LRTI**

**CLINICAL CHEMISTRY LABORATORY MEDICINE**
2018; 56(8):1200-09

**Procalcitonin Guidance in Patients with Lower Respiratory Tract Infections: A Systematic Review and Meta-Analysis.**


**OBJECTIVE**
As part of a regulatory submission to the US FDA, a systematic review and meta-analysis of randomized controlled trials of PCT-guided therapy versus standard of care was performed. This study was conducted to summarize existing evidence on the safety and efficacy of PCT guidance in adult patients with lower respiratory tract infections (LRTI), comprising acute bronchitis, exacerbations of chronic obstructive pulmonary disease (COPD), and pneumonia.

**STUDY DESIGN**
Eleven English-language papers evaluating PCT use in this population and published between 2004 and 2016 were included. In the PCT-guided treatment arm of these studies, physicians used both clinical judgment and PCT values when deciding whether to initiate and when to discontinue antibiotic use. To evaluate the effectiveness of PCT in guiding antibiotic therapy among adults with LRTI compared to standard care, the study examined the proportion of patients initiating antibiotics and length of antibiotic treatment. Safety was measured by length of hospital stay (LOS) and all-cause mortality.

**RESULTS**
When compared to patients treated according to standard care, patients whose treatment was guided by PCT had lower odds of initiating antibiotic treatment (odds ratio: 0.26, 95% confidence interval [CI]: 0.13; 0.52); and fewer days of antibiotic use (weighted mean difference [WMD]: -2.15 days, 95% CI: -3.30; -0.99). Patients in the PCT arm did not have a statistically different length of hospital stay (WMD: -0.15, 95% CI: -0.60; 0.30); or a statistically different risk of mortality (relative risk [RR]: 0.94, 95% CI: 0.69; 1.28). Patients in the PCT arm did not have a statistically different length of hospital stay (LOS) and all-cause mortality.

**CONCLUSIONS**
The use of PCT as a biomarker for adults with LRTI reduced antibiotic use with no adverse effects on LOS or mortality.

“PCT is an effective biomarker in guiding [antibiotic] AB therapy in LRTI by reducing AB initiation and use compared to the standard of care, with no observed adverse effects on hospital LOS and all-cause mortality.”

**KEY FINDINGS**
- PCT is a biomarker that can help guide decision-making for both the initiation and cessation of antibiotics in patients with LRTIs.
- PCT-guidance had no adverse impact on mortality or LOS in this population.
- The reduction in antibiotic use can have important implications for antimicrobial resistance and side-effects from prescribing unneeded antibiotics.

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**PCT-GUIDED ANTIBIOTIC THERAPY IN LRTI**

**CLINICAL INFECTIOUS DISEASES**
2017; 65(2):183-90

**Procalcitonin as a Marker of Etiology in Adults Hospitalized with Community-Acquired Pneumonia.**


**OBJECTIVE**
This research article describes a large cohort study with comprehensive pathogen testing to evaluate the accuracy of PCT for discriminating between viral and bacterial pneumonia. The analysis was performed on 1,735 patient samples collected upon hospital admission for the CDC Etiology of Pneumonia in the Community (EPIC) study, a prospective, multicenter, active surveillance study conducted in the United States.

**STUDY DESIGN**
All enrolled patients had clinical signs of community-acquired pneumonia (CAP) and radiographic evidence of pneumonia. Each enrolled patient underwent extensive systemic pathogen testing for bacterial and viral pathogens, and patients were grouped as follows: (1) typical bacteria (detection of any bacteria other than atypicals); (2) atypical bacteria (M. pneumoniae, C. pneumoniae, or Legionella); (3) viral (detection of a virus without co-detection of bacteria); (4) mycobacterial/fungal; and (5) unknown (no pathogen detected). PCT concentrations were measured for each patient.

**RESULTS**
Median PCT was higher in the typical bacterial group (2.5 ng/mL) than the viral (0.09 ng/mL) or atypical bacterial (2.5 ng/mL) groups. Typical bacteria were detected in 21% of patients with PCT ≥0.5 ng/mL, and only in 3% of patients with PCT <0.1 ng/mL and 4% of patients with PCT <0.25 ng/mL. The presence of typical bacterial pathogens in patients with PCT levels <0.25 ng/mL indicates that no PCT threshold perfectly predicts the presence or absence of typical bacteria. However, higher PCT concentrations strongly correlated with increased probability of detecting bacterial pathogens, particularly typical bacteria. The authors constructed receiver operating characteristic (ROC) curves to evaluate the accuracy of PCT for identifying bacterial CAP. The area under the curve (AUC) was 0.73 for distinguishing between any bacterial pathogens and viral pathogens, and 0.79 for distinguishing between typical bacterial CAP versus viral and atypical CAP. A PCT cut-point of ≥0.1 ng/mL discriminated between any bacterial pathogens and viral pathogens with a sensitivity of 80.9% and a specificity of 51.6%, and discriminated between typical bacterial pathogens and atypical bacterial or viral pathogens with a sensitivity of 87.6% and a specificity of 49.3%. A PCT cut-point of ≥0.1 ng/mL discriminated between bacterial CAP and all nonbacterial CAP with a sensitivity of 80.0% and a specificity of 46.2%.

**CONCLUSIONS**
Taken together, these data demonstrate that PCT has clinical utility as an indicator of pneumonia etiology, as higher PCT values strongly correlated with increased probability of typical bacteria.

“Serum PCT concentration, which can be available to clinicians within 60 minutes after a simple blood draw, could be a useful adjunct in the etiologic assessment of patients hospitalized with CAP.”

**KEY FINDINGS**
- Higher levels of serum PCT at hospital admission strongly correlated with increased probability of a bacterial pathogen.
- PCT is a useful tool for judging the relative likelihood of whether an infection is caused by a virus or bacteria.
PCT-GUIDED ANTIBIOTIC THERAPY IN PEDIATRICS
PCT-GUIDED ANTIBIOTIC THERAPY IN PEDIATRICS

LANCET
2017;390(10097):871-81

Procalcitonin-guided Decision Making for Duration of Antibiotic Therapy in Neonates with Suspected Early-Onset Sepsis: A Multicentre, Randomised Controlled Trial (NeoPIns).


OBJECTIVE

The Neonatal Procalcitonin Intervention Study (NeoPIns) investigated whether PCT-guided decision making could safely shorten the duration of antibiotic therapy in newborns with suspected early onset sepsis.

STUDY DESIGN

This multi-center randomized controlled interventional trial was carried out in a large cohort of neonates from high-income countries with a low incidence of proven early-onset sepsis: 18 hospitals in Holland (n=11), Switzerland (n=4), Canada (n=2), and the Czech Republic (n=1).

The study population included 1,710 neonates aged ≥ 34 weeks or older presenting with signs of early-onset sepsis in the first 72 hours of life and who required antibiotic therapy. The babies were randomized in a 1:1 ratio to either PCT-guided therapy (n=866) or standard therapy (n=844). Analyses were intention to treat and per-protocol. 1,408 neonates were included in the per-protocol analysis (745 in the PCT group and 663 in the standard group).

Primary outcomes were superiority of duration of antibiotic therapy and non-inferiority for re-infection or death in the first month of life (margin 2.0%). Secondary outcome was length of hospital stay (LOS).

RESULTS

PCT-guided decision making was shown to be superior to standard care in significantly reducing the median duration of antibiotic therapy (intention to treat: 55.1 vs. 65.0 hours, p=0.0001; per protocol: 51.8 vs. 64.0 hours, p=0.0001).

Non-inferiority for re-infection or death could not be shown due to the low occurrence of infections in the first 9 (<1%) of 1,710 neonates, and the absence of study-related death. LOS was significantly shorter in the PCT group. In the intention-to-treat analysis, there was a median reduction of 3.5 hours in hospital LOS between the PCT group and the standard group (223.0 hours vs. 226.5 hours, respectively, p=0.0039). In the per-protocol analysis, neonates in the PCT arm had a shorter median hospital stay of 5.2 hours (115.8 hours vs. 121.0 hours, respectively, p=0.0039).

CONCLUSIONS

In conclusion, standardized risk assessment for suspected early-onset sepsis and PCT-guided decision making reduced the duration of antibiotic therapy and hospital stay, with a low rate of re-infection and without study-related mortality.

“Combining serial procalcitonin measurements with initial assessment […] supports antimicrobial stewardship and helps physicians to decide to discontinuate antibiotic treatment sooner in neonates classified as having low or moderate risk of infection.”

KEY FINDINGS

- First neonatal intervention study on suspected early-onset sepsis to show superiority (reduced duration of antibiotic treatment) of PCT-guided antibiotic therapy – thereby improving antimicrobial stewardship.
- PCT-guided decision making was shown to significantly reduce the median duration of antibiotic therapy by 9.9 hours and hospital stay by 3.3 hours compared to standard care.

PCT-GUIDED ANTIBIOTIC THERAPY IN PEDIATRICS

PLOS ONE
2013; 8: e68419

Procalcitonin Guidance to Reduce Antibiotic Treatment of Lower Respiratory Tract Infection in Children and Adolescents (ProPAED): A Randomized Controlled Trial.


OBJECTIVE

The ProPAED trial investigated whether PCT-guided treatment could reduce antibiotic prescribing rates and therapy duration in children and adolescents with lower respiratory tract infections (LRTI) presenting to an emergency department (ED) using cut-off ranges established in trials of adults with LRTI.

STUDY DESIGN

The study included all children and adolescents, from 1 month to 18 years of age, presenting with LRTI to the EDs of two pediatric hospitals in Switzerland between 01/2009 and 02/2010. Eligible patients were randomized in a 1:1 ratio to either PCT-guided antibiotic treatment established for adult LRTI patients (PCT group) or to clinically guided standard care (control group).

The primary endpoint was antibiotic prescribing rate within 14 days of randomization. Secondary endpoints included duration of antibiotic treatment, antibiotic side effects, hospitalization and impairment of daily activities due to LRTI during the same period.

The analysis for this study was intention-to-treat.

RESULTS

In total, 337 children, mean age 3.8 years (range 0.1–18), were included. In the PCT-guided group, 104 of 168 (62%) patients and in the control group, 93 of 165 (56%) patients received antibiotics. Antibiotic prescribing rates were not found to be significantly different in the PCT-guided group compared to the control group (Odds Ratio 1.26: 95% CI 0.81, 1.95). Mean duration of antibiotic exposure was reduced from 6.3 to 4.5 days in the PCT-guided group (-1.8 days: 95% CI -3.1, -0.5; p=0.039) for all LRTI and from 9.1 to 5.7 days for pneumonia (-3.4 days: 95% CI -4.9, -1.7; p<0.001). No apparent difference in impairment of daily activities between PCT-guided and control patients was observed. Rates of antibiotic side effects and hospitalizations were similar in both groups.

CONCLUSIONS

This trial demonstrates that PCT-guided antibiotic therapy in children and adolescents can contribute to reduced antibiotic exposure by shortening the duration of antibiotic treatment. In this study, the antibiotic prescribing rate was not affected. However, Switzerland has a low baseline prescribing rate for pediatric LRTI and the use of adult LRTI cut-off values may be too low for use in pediatric patients. Further research is recommended to define optimal PCT cut-off values for children with LRTI.

“Reducing antibiotic treatment in pediatric patients through PCT guidance could have an impact on overall antibiotic prescribing, as the burden of viral respiratory tract infections in this population is high, and there is a paucity of reliable tests to guide prudent antibiotic use.”

KEY FINDINGS

- First major trial to investigate the impact of PCT-guided therapy in pediatric patients (children and adolescents).
- In this trial, PCT-guided therapy led to reduced antibiotic exposure in children with LRTI by reducing the duration of antibiotic treatment.
- Antibiotic prescribing rates were not significantly different in the PCT-guided group compared to the control group.
**PCT-GUIDED ANTIBIOTIC THERAPY IN PEDIATRICS**

**Procalcitonin Accurately Identifies Hospitalized Children with Low Risk of Bacterial Community-Acquired Pneumonia.**


**OBJECTIVE**

This retrospective study assessed whether serum PCT concentrations are associated with disease severity and the presence of viral, “typical” bacterial, or “atypical” bacterial pathogens. The study further evaluated whether PCT thresholds can identify children at low risk for CAP caused by typical bacterial pathogens so they may be spared unnecessary antibiotic therapy.

**STUDY DESIGN**

The study involved 532 children hospitalized with radiologically confirmed CAP and enrolled in the CDC’s Etiology of Pneumonia in the Community (EPIC) study. Each patient sample was comprehensively tested for pathogens and classified as (1) typical bacterial pathogen(s), with or without viral and/or atypical bacteria; (2) atypical bacterial pathogen(s), with or without viral detection; (3) viral pathogen(s) only; or (4) no pathogen detected. Typical pathogens included *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Haemophilus influenzae*, *Staphylococcus aureus*, certain streptococci, and Gram-negative bacteria. Atypical bacteria were *Chlamydia pneumoniae* or *Mycoplasma pneumoniae*.

**RESULTS**

Median PCT concentrations were significantly higher in children with typical bacterial pathogens (6.10 ng/mL) than in those with atypical bacteria (0.10 ng/mL), viral pathogens only (0.33 ng/mL) or no pathogens (0.44 ng/mL). No typical bacterial pathogens were detected in children with PCT concentrations <0.1 ng/mL. Thus, the PCT <0.1 ng/mL threshold had a 100% negative predictive value, which is the probability that subjects with values below this threshold do not have typical bacterial CAP. In this study, children with PCT <0.1 ng/mL accounted for 23% of the population; therefore, adoption of this cutoff may substantially reduce antibiotic exposure in children with CAP.

Elevated PCT levels were also associated with higher severity of clinical disease. The median PCT concentration was significantly higher for children admitted to the ICU (0.61 ng/mL) compared with children not in the ICU (0.24 ng/mL). PCT concentrations <0.25 ng/mL were strongly associated with a lower likelihood of detection of typical bacteria and decreased disease severity, reduced odds of ICU admission, and a 2.3 day decrease in the average hospital length of stay. The area under the curve (AUC) and diagnostic accuracy of this study are illustrated in Figure 1.

**CONCLUSIONS**

In this large cohort, PCT cut-offs of <0.1 and <0.25 ng/mL accurately identified children at lower risk of typical bacterial CAP, helping to improve patient management and decreasing the use of unnecessary antibiotics. The study findings suggest that PCT may be safely incorporated into treatment algorithms for children with CAP to reduce both antibiotic use and duration.

“...PCT may safely be incorporated into treatment algorithms for children with CAP to reduce antibiotic administration and duration.”

**KEY FINDINGS**

- **PCT concentrations <0.25 ng/mL were strongly associated with a decreased likelihood of detecting typical bacteria and decreased disease severity.**
- **PCT concentrations <0.1 ng/mL have a very high negative predictive value. A PCT threshold of 0.1 ng/mL accurately identifies children at extremely low risk of typical bacterial infection.**
- **Lower PCT concentrations were associated with less severe disease. Higher PCT concentrations were associated with an increased likelihood of ICU admission, empyema, and increased hospital length of stay.**

---

**Figure 1. Discriminatory performance of several procalcitonin cutoffs in identifying children hospitalized without typical bacterial community-acquired pneumonia (CAP)**

PCT-GUIDED ANTIBIOTIC THERAPY CONSENSUS & PROTOCOLS
**PCT-GUIDED ANTIBIOTIC THERAPY CONSENSUS & PROTOCOLS**

**CLINICAL CHEMISTRY AND LABORATORY MEDICINE**

2019;57(9):1308-18

**Procalcitonin (PCT)-guided Antibiotic Stewardship: An International Experts Consensus on Optimized Clinical Use.**


**OBJECTIVE**

The purpose of this international meeting was to reach agreement on algorithms for use in patients with suspicion of bacterial infection and that are easy to implement in clinical settings.

**CONSENSUS PROCESS**

The consensus process took place during a 1-day workshop in Berlin in late September 2018. The consensus was developed by a multidisciplinary team of 19 experts on PCT use in clinical practice, from 12 countries mirroring the different medical specialties participating in hospital ABS (antibiotic stewardship) programs.

**CONSENSUS OUTCOMES AND UPDATES**

The group agreed that there is strong evidence that PCT guided ABS supports individual decisions on initiation and duration of antibiotic treatment in patients with acute respiratory infections and sepsis from any source, thereby reducing overall antibiotic exposure and associated side effects, and improving clinical outcomes.

To simplify practical application, the expert group refined the established PCT algorithms by incorporating severity of illness and that are easy to implement in clinical settings.

Further, guidance on interpretation of PCT results to initiate, withhold or discontinue antibiotic treatment was included.

**"...integration of PCT into [antibiotic stewardship] algorithms has the potential to improve the diagnostic and therapeutic management of patients presenting with respiratory illnesses and sepsis"**

**KEY FINDINGS**

- International consensus achieved by a multidisciplinary team of 19 experts on PCT usage in clinical practice.
- PCT has shown promising results to help tailor antibiotic treatment to the individual patient, thereby reducing antibiotic exposure and improving clinical outcomes for patients with acute respiratory infections and sepsis.
- PCT supports the move from standardized care to more personalized treatment decisions, and contributes to the fight against bacterial resistance.

**PCT-GUIDED ANTIBIOTIC THERAPY CONSENSUS & PROTOCOLS**

**Figure 1. Use of PCT in patients with moderate illness outside the ICU**


**Patient with moderate illness outside ICU**

(Defined by setting specific scores, e.g. qSOFA, SOFA, APACHE)

<table>
<thead>
<tr>
<th>Initial clinical assessment (including microbiology)</th>
<th>Bacterial infection uncertain</th>
<th>Bacterial infection highly suspected</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT result (μg/L)</td>
<td>≤0.25</td>
<td>≥0.25</td>
</tr>
<tr>
<td>Probability of bacterial infection based on PCT level</td>
<td>Low probability</td>
<td>High probability</td>
</tr>
<tr>
<td>Overall interpretation</td>
<td>Bacterial infection unlikely</td>
<td>Bacterial infection likely</td>
</tr>
</tbody>
</table>

**Antibiotic management**

Use empiric Abx based on clinical judgement, consider other diagnostic tests

Use Abx based on clinical judgement

Use empiric Abx based on clinical judgement, consider other diagnostic tests

Use Abx based on clinical judgement

**Recommendations for follow-up of patients**

Use repeated PCT test within 6–24 h to early stop Abx if PCT <0.25 μg/L.

Consider 2nd PCT test within 24 h to stop Abx if PCT <0.5 μg/L.

*Caution in patients with immuno-suppression (including HIV), COPD, severe trauma, high-volume transfusion, malaria. PCT-guided stewardship should not be applied to patients with chronic infections (e.g. abscess, osteomyelitis, endocarditis).*

**Figure 2. Use of PCT in patients with severe illness in the ICU**


**Patient with severe illness in ICU**

(Defined by setting specific scores, e.g. qSOFA, SOFA, APACHE)

<table>
<thead>
<tr>
<th>Initial clinical assessment (including microbiology)</th>
<th>Bacterial infection uncertain</th>
<th>Bacterial infection highly suspected</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT result (μg/L)</td>
<td>≤0.5</td>
<td>≥0.5</td>
</tr>
<tr>
<td>Probability of bacterial infection based on PCT level</td>
<td>Low probability</td>
<td>High probability</td>
</tr>
<tr>
<td>Overall interpretation</td>
<td>Bacterial infection unlikely</td>
<td>Bacterial infection likely</td>
</tr>
</tbody>
</table>

**Antibiotic management**

Use empiric Abx based on clinical judgement, consider other diagnostic tests

Use Abx based on clinical judgement

Use empiric Abx based on clinical judgement, consider other diagnostic tests

Use Abx based on clinical judgement

**Recommendations for follow-up of patients**

Use PCT every 24–48 h for monitoring and discontinuation of Abx if PCT ≤0.5 μg/L or drop by 80%.

Consider 2nd PCT test within 24 h to stop Abx if PCT ≤0.25 μg/L or drop by 80%.

*Caution in patients with immuno-suppression (including HIV), COPD, severe trauma, high-volume transfusion, malaria. PCT-guided stewardship should not be applied to patients with chronic infections (e.g. abscess, osteomyelitis, endocarditis).*
**PCT-GUIDED ANTIBIOTIC THERAPY CONSENSUS & PROTOCOLS**

**Figure 1. Algorithm for use of PCT in critically ill patient populations**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial infection uncertain</td>
<td>Use empiric Abx based on clinical judgment, consider to do a baseline PCT level and other diagnostic tests</td>
</tr>
<tr>
<td>Bacterial infection highly suspected</td>
<td>Consider treatment failure; Monitor PCT for discontinuation of Abx if PCT &lt;0.25 μg/L or drop by 80%</td>
</tr>
<tr>
<td>Suspected tropical disease*</td>
<td>PCT kinetics may help to assess prognosis</td>
</tr>
</tbody>
</table>

**Figure 2. Algorithm for use of PCT in non-critically ill patient populations**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial infection uncertain</td>
<td>Use Abx based on clinical judgment</td>
</tr>
<tr>
<td>Bacterial infection likely</td>
<td>Use empiric Abx based on clinical judgment, look for other diagnoses</td>
</tr>
<tr>
<td>Bacterial infection possible</td>
<td>Use repeated PCT monitoring and discontinuation of Abx if PCT &lt;0.25 μg/L or drop by 80%</td>
</tr>
<tr>
<td>Bacterial infection highly likely</td>
<td>Use repeated PCT monitoring and discontinuation of Abx if PCT &lt;0.25 μg/L or drop by 80%</td>
</tr>
</tbody>
</table>

*Caution in patients with immunosuppression (including HIV), CF, pancreatitis, trauma, pregnancy, high volume transfusion. PCT-guided stewardship should not be applied to patients with chronic infections (e.g., abscess, osteomyelitis, endocarditis). Tropical diseases include, but not limited to, malaria, dengue fever, hemorrhagic fever, typhus and others.

**KEY FINDINGS**

- The expert group agreed that the existing evidence for PCT-guided antibiotic stewardship in patients with acute respiratory infections and sepsis is also largely valid for Asia-Pacific countries.
- The experts decided that two adapted algorithms, one for the critically ill and one for the non-critically ill patient population would be most relevant to optimize use of PCT in critical care in Asia-Pacific countries.
- Following patient stratification based on clinical criteria and probability of bacterial infection, PCT should be added to patient assessment based on the following cut-offs:
  - <0.25 μg/L in critically ill patients indicating low likelihood of bacterial infection.
  - <0.5 μg/L in non-critically ill patients.

**CONSENSUS PROCESS**

During a 1-day workshop in Bangkok on September 23, 2019, a multidisciplinary team of 36 experts from 12 Asia-Pacific countries discussed practical experience with PCT-guided AMS, and the applicability of the Berlin consensus algorithms for the Asia-Pacific region.

**CONSENSUS OUTCOMES**

The expert group observed that, overall, the existing evidence for PCT-guided AMS in patients with acute respiratory infections and sepsis is also generally valid for Asia-Pacific countries. The group reached consensus on an approach based on two adapted PCT algorithms, one for critically ill (Figure 1) and one for non-critically ill (Figure 2) patients. This approach aims to simplify optimal use of PCT in clinical routine in Asia-Pacific countries. Initially, patients should be stratified according to clinical criteria and probability of bacterial infection (uncertainty vs. high suspicion of bacterial infection), followed by a PCT test based on the following cut-offs:

- <0.25 μg/L in critically ill patients indicating low likelihood of bacterial infection.
- <0.5 μg/L in non-critically ill patients.

However, due to an insufficient database on patients with tropical diseases in the Asia-Pacific patient population, the experts do not currently recommend use of these algorithms in such patients. Furthermore, the algorithms should be used in acute infections, but not in patients with chronic infections (e.g., abscess, osteomyelitis, endocarditis). These points are reflected in the adapted algorithms.

**CONCLUSIONS**

Use of PCT to guide antibiotic stewardship can significantly improve the utilization of antibiotic treatment in Asia-Pacific countries. However, adaptations of existing PCT algorithms are required due to differences in types of infections and routine clinical care. In particular, the lack of scientific data for tropical diseases underlines the need for further research to understand the optimal use of PCT and interpretation of results in such cases.

*“Use of PCT to guide antibiotic stewardship in conjunction with continuous education and regular feedback to all stakeholders has high potential to improve the utilization of antibiotic treatment also in Asia-Pacific countries.”*
This review covered the following aspects of procalcitonin (PCT) use in the treatment of critically ill patients with sepsis based on existing study results.

**OBJECTIVE**

The purpose of this review was to provide an overview about the current knowledge of procalcitonin (PCT) use in the treatment of critically ill patients with sepsis.

**REVIEW FINDINGS**

This review covered the following aspects of procalcitonin:

- **Procalcitonin as a diagnostic biomarker for bacterial infection and sepsis**
  
  PCT is one of the most investigated host-directed biomarkers. Its synthesis pathway can vary depending on different inflammatory states. Due to cytokines released during viral infections that inhibit the production of TNF alpha, PCT synthesis is not induced in most viral infections. Furthermore, PCT has a wide biological range, is rapidly induced following bacterial stimulation and has a long half-life. It therefore has good discriminatory properties for the differentiation between bacterial and viral infections with rapidly available results. PCT per se cannot isolate or detect specific pathogens, but the level of PCT may be useful to estimate the probability of a severe bacterial infection.

- **Procalcitonin as a prognostic biomarker for risk assessment in patients with severe infection and sepsis**
  
  PCT values correlate with severity of illness and serial measurements have prognostic implications. PCT kinetics over time can improve the monitoring of critically ill patients with sepsis, since decreasing PCT values correlate with good outcomes and increasing values are associated with adverse outcomes, such as mortality.

- **Procalcitonin as a therapeutic biomarker for antibiotic stewardship in patients with severe infection and sepsis**
  
  In 2017, the US Food and Drug Administration (FDA) approved the use of PCT for antibiotic stewardship. This decision was based on systematic reviews and meta-analyses of randomized controlled trials (RCTs) which analyzed infections of varying severity in different clinical settings ranging from primary care to ICU. These RCTs investigated and demonstrated the efficacy and safety of PCT-guided antibiotic therapy.

- **Practical considerations for use of procalcitonin testing**

  The proACT1 trial showed low compliance rates with the PCT protocol, indicating a lack of experience by physicians in the use of PCT-guided antibiotic therapy. In 2017, the US Food and Drug Administration (FDA) approved the use of PCT for antibiotic stewardship. This decision was based on systematic reviews and meta-analyses of randomized controlled trials (RCTs) which analyzed infections of varying severity in different clinical settings ranging from primary care to ICU. These RCTs investigated and demonstrated the efficacy and safety of PCT-guided antibiotic therapy.

- **Limitations of procalcitonin**

  Very limited data about the use of PCT in immunosuppressed patients including patients with HIV, cystic fibrosis, pancreatitis, trauma, pregnancy and high-volume transfusion is available. Furthermore, certain non-infectious disorders, such as C-cell carcinoma or trauma, can lead to a systemic inflammation resulting in elevated PCT levels. The use of PCT-guided antibiotic stewardship is not recommended in patients suffering from a chronic infection such as osteomyelitis or endocarditis, since observational studies were unable to identify any benefit and interventional investigations in this context are still lacking.

**CONCLUSIONS**

Serial PCT measurement and continuous education for antibiotic stewardship could be advantageous for physicians.

**KEY FINDINGS**

- **PCT is the best studied biomarker regarding antibiotic stewardship and has good discriminatory properties to differentiate between bacterial and viral infections.**

- **PCT values are not intended to replace good clinical practice, but should be used as a complementary tool combined with available clinical and diagnostic parameters.**

**PCT-GUIDED ANTIBIOTIC THERAPY CONSSENSUS & PROTOCOLS**

**Overview of Procalcitonin Assays and Procalcitonin-Guided Protocols for the Management of Patients with Infections and Sepsis.**

**OBJECTIVE**

This review provides an overview of the strengths and limitations of currently available PCT assays and PCT-guided protocols when used in different clinical settings and patient populations.

**REVIEW FINDINGS**

Three algorithms based on setting have been suggested:

- **Low acuity, primary care settings, where admission PCT levels may provide guidance on whether antibiotics should be initiated:**
  
  - Moderate acuity settings, such as the emergency department and medical wards, where admission and follow-up PCT levels may guide initial use of antibiotics and duration of treatment.
  
  - Highest acuity settings, such as ICUs, where PCT changes over time provide guidance on discontinuation of antibiotic therapy.

  In patients with respiratory infections, sepsis and other infections, PCT-guided antibiotic stewardship protocols have shown utility in reducing unneeded antibiotic use (initiation and duration) and are associated with positive clinical outcomes.

  A number of fully automated PCT assays are currently available and have been validated for routine clinical use. Of these, the B·R·A·H·M·S PCT assays (based on B·R·A·H·M·S antibodies) have been studied most extensively, including on the KRYPTOR and VIDAS® platforms. In numerous published clinical studies, the assays have shown good correlation with the reference standard (KRYPTOR) and demonstrated similar performance and reproducibility. The VIDAS® B-R-A-H-M-S PCT assay has been recently cleared by the FDA for expanded use for antibiotic stewardship in patients with sepsis and lower tract respiratory infections.

  Before implementing any new PCT assay in clinical practice, rigorous assessment is essential to evaluate functional assay sensitivity and clinically relevant cut-off ranges by setting and patient population. Tests which are not based on B-R-A-H-M-S antibodies may have limited sensitivity at lower levels and require additional validation. Newly developed semi-quantitative point of care assays may be of limited use in clinical practice. The total internal reflection-based highly sensitive fluorescence immunoassay monoclonal antibody can detect very low levels of PCT but has yet to demonstrate clinical utility in diagnosis and antibiotic decision-making.

**CONCLUSIONS**

The review concludes that, along with physician judgment, PCT levels may be used to support clinical decisions on antibiotic therapy initiation and duration. Consideration should be given to assay sensitivity, cutoffs for a specific setting and patient population and type of infection.

“Use of sensitive procalcitonin measurements in clinical algorithms can reduce antimicrobial overuse, decreasing the risk of side effects and controlling emerging bacterial multiresistance.”

**KEY FINDINGS**

- **Interpretation of PCT levels should consider the clinical setting, type of infection and assay characteristics.**

- **Newly developed PCT assays should be evaluated carefully for functional sensitivities and concordance with reference tests before routine use in clinical practice.**
**PCT-GUIDED ANTIBIOTIC THERAPY CONSENSUS & PROTOCOLS**

**ARCHIVES OF INTERNAL MEDICINE**
2011;171(15):1322-31

**Procalcitonin Algorithms for Antibiotic Therapy Decisions: A Systematic Review of Randomized Controlled Trials and Recommendations for Clinical Algorithms.**

Schuetz P, DiPirro V, Briel M, Greppin I, L.

**OBJECTIVE**

The objective of this systematic review was to summarize the design, efficacy and safety of previous European randomized controlled trials (RCTs) suggesting that PCT-guided antibiotic therapy results in reduced antibiotic use without adverse effect on clinical outcome, and to propose algorithms for use in US healthcare settings.

**REVIEW FINDINGS**

A systematic search was made up to 2011 in MEDLINE and EMBASE databases and in the Cochrane Central Register of Controlled Trials for RCTs using PCT to make antibiotic therapy decisions in adults with respiratory tract infections (RTI) and sepsis from primary care, emergency department (ED) and intensive care unit (ICU) settings. Fourteen RCTs (n=4,467 patients) were included: 2 performed in the primary care setting (1,008 patients with LRTI*), 6 in the ED (2,449 patients with CAP** and AECOPD***), and 6 in the ICU (1,010 patients with severe sepsis/septic shock).

**REVIEW FINDINGS**

Overall, no significant difference in mortality was observed between the PCT-guided and control groups (odds ratio, 0.91; 95% CI, 0.79 to 1.04) or in primary care (OR, 0.13; 0.6-4.0), ED (OR, 0.95; 0.61-1.46), and ICU (OR, 0.89; 0.66-1.20) settings individually. None of the trials reported an increase in adverse outcomes, including mortality rate.

A marked reduction in antibiotic exposure was observed in the PCT-guided groups in all settings, levels of disease acuity and patient populations, mainly due to lower prescription rates in low-acuity infections (such as bronchitis, AECOPD) in the primary care and ED settings, and shorter duration of antibiotic courses in moderate- to high-acuity infections (pneumonia, sepsis) in the hospital and ICU settings.

**CONCLUSIONS**

The authors concluded that the use of PCT-guided algorithms for antibiotic therapy decisions in adult patients with RTI and sepsis can safely reduce antibiotic exposure without adversely impacting patient safety or the mortality rate. They also proposed specific PCT-guided algorithms for low-, moderate- and high-acuity patients for use in future trials in the United States aimed at reducing antibiotic overconsumption (Figure 1).

---

### **KEY FINDINGS**

- Major systematic review of 14 randomized controlled trials (4,467 patients).
- PCT-guided protocols for antibiotic therapy decisions can safely reduce use of antibiotics without adversely impacting patient safety.
- Proposal of PCT-guided protocols based on infection acuity levels for use in US-based trials aiming to reduce overuse of antibiotics.

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**PCT-GUIDED ANTIBIOTIC THERAPY CONSENSUS & PROTOCOLS**

Table: Proposed algorithms for use of PCT values to determine antibiotic treatment of infections

**Figure 1:** Proposed algorithms for use of PCT values to determine antibiotic treatment of infections


---

**A**

**LOW-ACUITY NON-PNEUMONIC INFECTIONS (i.e., LOW RISK) IN PRIMARY CARE AND ED SETTINGS**

**EVALUATION AT TIME OF ADMISSION**

<table>
<thead>
<tr>
<th>PCT result</th>
<th>0.10 μg/L</th>
<th>0.25 μg/L</th>
<th>≥0.25 μg/L</th>
<th>&gt;0.50 μg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>regarding use of Abx</td>
<td>Strongly discouraged</td>
<td>Discouraged</td>
<td>Encouraged</td>
<td>Strongly encouraged</td>
</tr>
<tr>
<td>Over ruling</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>the algorithm</td>
<td>Consider use of antibiotics if patients are clinically unstable, have strong evidence of pneumonia, or are at high risk (ie, COPD GOLD III-IV), or need hospitalization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up/other comments</td>
<td>Follow-up only needed if no symptom resolution after 1 to 2 days; if clinical situation is not improving; consider Abx if PCT level increases to ≥0.25 μg/L</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**FOLLOW-UP EVALUATION EVERY 2 TO 3 DAYS**

<table>
<thead>
<tr>
<th>PCT result</th>
<th>0.10 μg/L</th>
<th>0.25 μg/L</th>
<th>≥0.25 μg/L</th>
<th>&gt;0.50 μg/L</th>
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<tr>
<td>Recommendation</td>
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<tr>
<td>regarding use of Abx</td>
<td>Cessation of therapy</td>
<td>Cessation of therapy</td>
<td>Cessation of therapy</td>
<td>Cessation of therapy</td>
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<tr>
<td>Over ruling</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>the algorithm</td>
<td>Consider continuation of Abx if patients are clinically not stable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up/other comments</td>
<td>Clinical reevaluation as appropriate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**C**

**HIGH-ACUITY INFECTIONS (i.e., HIGH RISK) IN ICU SETTINGS**

**EVALUATION AT TIME OF ADMISSION**

<table>
<thead>
<tr>
<th>PCT result</th>
<th>0.25 μg/L</th>
<th>≥0.50 μg/L</th>
<th>&gt;1.0 μg/L</th>
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<tbody>
<tr>
<td>Recommendation</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>regarding use of Abx</td>
<td>Strongly discouraged</td>
<td>Discouraged</td>
<td>Encouraged</td>
</tr>
<tr>
<td>Over ruling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>the algorithm</td>
<td>Empirical therapy recommended in all patients with clinical suspicion of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up/other comments</td>
<td>Consider alternative diagnosis; reassess patients' condition and recheck PCT level every 2–3 days</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FOLLOW-UP EVALUATION EVERY 1 TO 2 DAYS**

<table>
<thead>
<tr>
<th>PCT result</th>
<th>0.25 μg/L</th>
<th>≥0.50 μg/L</th>
<th>&gt;1.0 μg/L</th>
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</thead>
<tbody>
<tr>
<td>Recommendation</td>
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<tr>
<td>regarding use of Abx</td>
<td>Cessation of Abx</td>
<td>Cessation of Abx</td>
<td>Cessation of Abx</td>
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<tr>
<td>Over ruling</td>
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<td></td>
</tr>
<tr>
<td>the algorithm</td>
<td>Consider continuation of Abx if patients are clinically unstable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up/other comments</td>
<td>Clinical reevaluation as appropriate</td>
<td></td>
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Abx: antibiotics; COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; PCT: pneumonia severity index.
OBJECTIVE
This review summarized published evidence regarding the utility of PCT in the critical care setting; discussed the potential benefits and limitations of the use of PCT for clinical decision-making; and illustrated how PCT can be applied to support risk-stratification of patients with presumed sepsis to safely individualize treatment and patient management decisions.

METHODS

RESULTS
This literature has largely demonstrated that the use of PCT-guided protocols to support earlier antibiotic de-escalation can significantly lower antibiotic exposure without increasing rates of mortality, relapsing infections or other adverse patient outcomes. In addition, serial PCT measurements have shown value for risk stratification of patients with sepsis in several studies. However, the use of PCT-guided protocols for escalation of antibiotics when PCT increases cannot yet be recommended in the sepsis setting.

CONCLUSIONS
The review concludes that integrating PCT data in clinical algorithms improves individualized antibiotic therapy decision-making in critically ill patients with sepsis or respiratory infections. Furthermore, adding the information derived from serial PCT measurements to a thorough clinical evaluation appears to be an effective evidence-based approach for antibiotic stewardship, resulting in a more rational use of these drugs. The authors recommend that future studies should focus on further validating the use of repeat PCT measurements to risk-stratify patients, and evaluate the impact of PCT guidance in the ICU on patient outcomes.

“Inclusion of PCT data in clinical algorithms improves individualized decision-making regarding antibiotic treatment in patients in critical care for respiratory infections or sepsis.”
OBJECTIVE
This study aimed to compare the effectiveness and costs of procalcitonin (PCT)-guided care versus standard care to optimize antibiotic prescription in hospitalized patients diagnosed with suspected sepsis or lower respiratory tract infection (LRTI) in the US.

STUDY DESIGN
A previously published health economic decision model was used to compare the costs and the effects of PCT-guided care (Figures 1 and 2). The analysis took into account the societal and hospital impact and costs over the length of hospital stay. The main outcomes analyzed were:
- total difference in costs per patient (including treatment costs and productivity losses),
- number of patients with antibiotic resistance or C. difficile infections,
- costs per antibiotic day avoided.

RESULTS
Table 1. Results of implementation of a PCT-guided algorithm on main outcomes analyzed

<table>
<thead>
<tr>
<th>Sepsis Patients</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in antibiotic therapy days</td>
<td>5.83</td>
</tr>
<tr>
<td>Reduction in LOS (ICU)</td>
<td>3.6</td>
</tr>
<tr>
<td>Reduction of mechanical ventilation days (ICU)</td>
<td>2</td>
</tr>
<tr>
<td>Savings per patient cost in PCT Arm VS Standard of Care (SOC)</td>
<td>$11,311</td>
</tr>
<tr>
<td>% sepsis patients with Antibiotic Resistance (ABR) was smaller in PCT arm</td>
<td>6.40%</td>
</tr>
<tr>
<td>Reduction in C. difficile infections</td>
<td>54.80%</td>
</tr>
</tbody>
</table>

CONCLUSIONS
PCT-guided care for hospitalized patients with suspected sepsis and LRTI was associated with:
- a reduction in antibiotic treatment days,
- shorter length of stay on the regular ward and the intensive care unit,
- shorter duration of mechanical ventilation,
- reduced risk of antibiotic-resistant or C. difficile infections.
Significant cost-savings were observed in the PCT-guided group vs. standard care for both sepsis and LRTI patient populations.

“Using a Procalcitonin-algorithm to guide antibiotic use in sepsis and hospitalised lower respiratory tract infection patients is expected to generate cost-savings to the hospital and lower rates of antibiotic resistance and C. difficile infections.”

KEY FINDINGS
- In the PCT group, total costs were reduced by 26.0% in sepsis and 17.7% in LRTI (total incremental costs of −$11,311 per patient and −$2,867 per patient respectively) vs. standard care.
- Using a PCT-guided algorithm can lead to hospital cost-savings and lower rates of antibiotic resistance and C. difficile infections.
**HEALTH ECONOMICS AND OUTCOMES STUDIES OF PCT**

**AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE**
2020; DOI:10.1164/RCCM.202004-1201OC

**Procalcitonin to Reduce Long-Term Infection-associated Adverse Events in Sepsis: A Randomized Trial.**


**OBJECTIVE**
The objective of this study was to assess the impact of PCT-guided discontinuation of antimicrobials on the incidence of infection-associated adverse events in septic patients.

**STUDY DESIGN**
This multicenter randomized trial was designed as a real-world pragmatic study. Performed in 7 internal medicine departments in Athens, Greece, the study enrolled 266 patients with lower respiratory tract infections (LRTIs), acute pyelonephritis, primary bloodstream infection, and meeting the Sepsis-3 definitions.

After 24 hours of antimicrobial treatment, patients were randomized into two arms: PCT-guided discontinuation or standard of care (SOC). In the PCT-guided arm, antibiotics were discontinued if ≥80% decrease in PCT level or PCT level ≤0.5 μg/L at day 5 or later. In the SOC arm, duration of antimicrobial treatment followed international guidelines.

**RESULTS**
- The rate of infection-associated adverse events was 7.2% in the PCT-guidance arm vs 15.3% in SOC arm (p=0.045).
- The 28-day mortality rate was 15.2% in PCT arm vs 28.2% in SOC arm (p=0.02).
- A trend for decreased mortality at day 180 was observed in the PCT arm (30.4%) compared to SOC arm (38.2%), but was not statistically significant.
- The median LOS was 5 days in PCT arm vs 10 in SOC arm (p<0.01).
- Costs were €956.99 in PCT arm vs €1,183.49 in SOC arm (p<0.01).

**CONCLUSIONS**
The PCT guidance approach was shown to be effective in reducing the rate of infection-associated adverse events, as well as 28-day mortality, LOS and related cost of hospitalization. In countries with high antimicrobial consumption and high antimicrobial resistance rates, this strategy could be beneficial from a public health standpoint.

"In the PROGRESS trial, we demonstrate for the first time that PCT-guided early discontinuation of antimicrobials in patients with sepsis prevents infection caused by MDRO and/or C. difficile."

**HEALTH ECONOMIES AND OUTCOMES STUDIES OF PCT**

**OPEN FORUM INFECTIOUS DISEASES**
2019;6(11):e02355

**Impact of Procalcitonin Levels Combined with Active Intervention on Antimicrobial Stewardship in a Community Hospital.**

Newton JA, Robinson S, Ling LL, Zimmer L, Kuper K, Traina KH.

**OBJECTIVE**
The objective of this study was to measure the impact of PCT with an antimicrobial stewardship program (ASP) on patient length of stay (LOS) and antimicrobial therapy (ABX) duration in a community hospital.

**STUDY DESIGN**
Patients with at least 1 PCT value and an ASP recommendation to alter medications were included in the study. Between May 2013 and April 2014, 857 patients were eligible. ASP recommendations were made based upon evidence-based guidelines, clinical experience and PCT results.

**RESULTS**
Patients were stratified into two groups based upon treating physician acceptance or rejection of ASP guidance (compliers versus non-compliers). Patients were also stratified by initial PCT level (normal versus elevated). Providers complied with 77.1% of ASP recommendations. LOS, length of ABX after ASP recommendations and total length of ABX were evaluated (Figure 1).

"Procalcitonin has the potential to improve provider decision making and support antimicrobial stewardship through reduction of both unnecessary antibiotic initiation and treatment duration."

**CONCLUSIONS**
PCT guided recommendations, when accepted by providers, resulted in shorter duration of ABX irrespective of whether PCT values were normal or elevated.

"Procalcitonin is an excellent tool for clinicians to use in making decisions regarding antimicrobial therapy. It has been shown to reduce the duration of therapy when used appropriately."

**KEY FINDINGS**
- In a 'real world' setting, compliance with PCT-guided recommendations provided by an ASP can decrease antimicrobial therapy duration.
- Duration of antibiotic therapy after ASP recommendations was significantly shorter (2.5 vs 3.9 days, p<0.0001) in the ASP complier group.
- ASPs play a key role in reducing inappropriate use of antimicrobials.
HEALTH ECONOMICS AND OUTCOMES STUDIES OF PCT

**Effect of Procalcitonin-Guided Antibiotic Treatment on Mortality in Acute Respiratory Infections: A Patient Level Meta-Analysis.**


**OBJECTIVE**

This meta-analysis comprehensively assessed the safety of procalcitonin-guided treatment in patients with acute respiratory infections (ARIs) in primary care, intensive care, surgical intensive care, or emergency department settings.

**STUDY DESIGN**

The analysis combined data from 6,708 patients enrolled in 26 separate randomized controlled trials in which patients with respiratory infections were randomly assigned to either a PCT-guided antibiotic treatment group or a control group. The meta-analysis relied on individual patient data rather than aggregated patient data, which allowed for harmonization of outcomes definitions. The primary endpoints were 30-day mortality and setting-specific treatment failure, secondary endpoints were antibiotic exposure, side-effects and length of stay.

**RESULTS**

The analysis demonstrated significant improvements in patient outcomes for the PCT-guided treatment group. Mortality at 30 days was significantly lower (9% vs. 10%, p=0.037), and antibiotic related side effects were significantly reduced (16% vs. 22%, p=0.0001) in PCT guided patients compared to control patients. Treatment failure, as specifically defined for each clinical setting, was less frequent in the PCT-guided patients, but not significantly (23.0% vs. 24.9%, p=0.068). Mean total antibiotic exposure was significantly lower in the PCT-guided group (5.7 days vs. 8.1 days, p=0.0001) and side-effects were also lower (10% vs. 22%, p=0.003). No significant differences in length of hospital stay or ICU stay were observed between the two groups.

**CONCLUSIONS**

This meta-analysis found that implementation of PCT-guided protocols in patients with ARIs led to positive effects on clinical outcomes and reduced antibiotic exposure. Given these positive findings, and the increasing threat of multi-drug resistance, this report strengthens the rationale to use procalcitonin to support antibiotic stewardship decisions in patients with ARIs.

“... [This patient-level meta-analysis] is the first report to describe significant and relevant improvements in clinical outcomes and specifically a decreased risk for mortality for patients with acute respiratory infections, when procalcitonin was used to guide antibiotic treatment decisions.”

**KEY FINDINGS**

- This patient-level meta-analysis demonstrates for the first time that PCT-guided treatment significantly improved clinical outcomes in patients with ARIs from different clinical settings.
- PCT-guided treatment is associated with a decreased risk of mortality, reduced antibiotic exposure (5.7 days vs. 8.1 days), and fewer antibiotic-related side effects compared to treatment without PCT guidance.
- The meta-analysis described in this paper is the basis for a 2017 Cochrane Systematic Review which concluded that the quality of the evidence for the mortality and antibiotic exposure outcomes was high.

HEALTH ECONOMICS AND OUTCOMES STUDIES OF PCT

**Efficacy and Safety of Procalcitonin Guidance in Patients with Suspected or Confirmed Sepsis: A Systematic Review and Meta-Analysis.**


**OBJECTIVE**

As part of a regulatory submission to the US FDA, a systematic review and meta-analysis of randomized controlled trials of PCT-guided therapy versus standard of care was performed. This study was conducted to summarize existing evidence on the safety and efficacy of PCT guidance in adult patients with sepsis.

**STUDY DESIGN**

Ten randomized controlled trials evaluating PCT use in this population and published between 2004 and 2016 were included in the meta-analysis. In the PCT-guided treatment arm of these studies, physicians used both clinical judgment and PCT values when deciding to discontinue antibiotic use. Clinicians whose patients were in the PCT cohort generally adhered to the PCT algorithm (47%-93%). Outcomes evaluated included antibiotic duration defined as number of days on treatment; length of intensive care unit (ICU) stay and mortality. Effectiveness of PCT was measured by the length of antibiotic treatment, and safety was measured by ICU length of stay and all-cause mortality.

**RESULTS**

A total of 3,489 patients were included in these studies. PCT-guided patients had shorter antibiotic duration compared to controls: (7.35 vs. 8.85 days; p=0.001). However, ICU length of stay was not statistically different between the two groups: 11.09 days in the PCT arm and 11.91 days in the control arm (p=0.329). The length of follow-up for mortality varied between studies: some studies considered in-hospital mortality and others 28-day mortality. PCT use had no adverse impact on mortality (p=0.114).

**CONCLUSIONS**

In this systematic review and meta-analysis, PCT-guided therapy was found to reduce antibiotic duration with no adverse effects on patient outcomes in adult patients with suspected or confirmed sepsis.

“In light of the positive effect of PCT on reducing antibiotic duration with no observed adverse impact on key safety outcomes, the use of PCT as a biomarker to guide antibiotic treatment decision-making has the potential to improve the quality of care for adults with confirmed or suspected sepsis.”

**KEY FINDINGS**

- PCT-guided care is associated with reduced antibiotic duration in patients with suspected and confirmed sepsis.
- PCT-guidance had no adverse impact on mortality or length of ICU stay in this population.
**OBJECTIVE**

This paper describes a real-world study of the impact of the introduction of a procalcitonin guidance algorithm on the duration of antibiotic use for adult patients with pneumonia in two teaching hospitals in Pittsburgh, Pennsylvania.

**STUDY DESIGN**

This retrospective cohort study compared patient data from before and after implementation of VIDAS® B·R·A·H·M·S PCT™ testing, accompanied by education and stewardship practices to encourage adherence to the algorithm. Standard PCT cutoffs were used to discourage or recommend therapy.

The primary outcome was antibiotic treatment duration, the secondary outcomes included duration of IV antibiotics; hospital length of stay (LOS); and percentage of patients with appropriate antibiotic therapy duration.

**RESULTS**

In the post-PCT guidance group, the primary outcome of antibiotic therapy duration was significantly reduced. Secondary outcomes were also positively impacted in the PCT group (Table 1). Among the PCT-guided group, total duration of antibiotic therapy for patients with low PCT levels (<0.25 µg/L) was compared to patients with elevated levels (≥0.25 µg/L), as shown in Table 2. Among this population, therapy duration was significantly shorter in the low PCT cohort.

**CONCLUSIONS**

In this real-world study, the implementation of a PCT guidance algorithm led to shorter durations of total antibiotic therapy and shorter hospital length of stay without affecting hospital readmissions.

“Our study demonstrates that implementation of PCT guidance, as part of a clinical decision-making algorithm, in a real-world setting in the United States represents a practical method to meaningfully and safely diminish antibiotic exposure in the management of adult patients admitted with uncomplicated pneumonia.”

**KEY FINDINGS**

- A real world study of PCT guidance in patients with pneumonia, which showed similar findings to randomized controlled trials, including significant reductions in duration of antibiotic therapy and hospital LOS compared to standard of care.
- Among patients with peak PCT values <0.25 µg/L, mean antibiotic duration was significantly shorter than in the PCT-guided groups with values of 0.25 µg/L or higher.
Impact of Procalcitonin (PCT)-Guided Antibiotic Management on Antibiotic Exposure and Outcomes: Real World Evidence

Broyles MR.

**OBJECTIVE**
This study evaluated the clinical impact of introduction of PCT testing and a PCT algorithm to guide antibiotic management in a rural community healthcare facility with an established stewardship program. PCT introduction was accompanied by education on use of a PCT algorithm and stewardship practices to encourage adherence to the algorithm.

**STUDY DESIGN**
Patient data from four years before and four years after implementation of VIDAS® B·R·A·H·M·S PCT™ testing were collected. A total of 985 patients managed without PCT-guidance (the Pre-PCT cohort) and 1,167 PCT-managed patients (the Post-PCT cohort) were included in the analysis.

**RESULTS**
Median days of antibiotic therapy decreased from 17 to 9 in the post-PCT implementation group (p<0.0001). Significant reductions in antibiotic exposure, hospital mortality rates, 30-day readmission rates, C. difficile (CDI) rates during hospitalization, and antimicrobial adverse drug event (ADE) rates during hospitalization were also observed (Figure 1).

![Figure 1: Comparison of outcomes measured in Pre vs. Post PCT cohorts.](image)

**CONCLUSIONS**
Implementing a PCT-guided antibiotic therapy algorithm in a community healthcare facility with an established stewardship program led to a significant reduction in antibiotic exposure and adverse outcomes. Use of the algorithm, together with thorough clinician education, made improved antibiotic management and outcomes achievable.

“Pairing clinical assessment with trends in PCT... led to significant reductions in antibiotic exposure, hospital mortality, 30-day readmission, CDI during hospitalization, and antimicrobial ADEs during hospitalization.”

**KEY FINDINGS**
- PCT-guided care resulted in better patient outcomes than care guided by a mature stewardship program without PCT.
- Days of antibiotic therapy, hospital mortality rates, 30-day readmission rates, antimicrobial adverse drug events and hospital C. difficile infection (CDI) rates were all significantly reduced in the PCT-managed group compared to the control group.
- The observed improvements in patient outcomes were achieved by integrating PCT guidance into routine care at a small community hospital and not in the context of a highly protocolized clinical trial.

**Effect of Procalcitonin Testing on Health-care Utilization and Costs in Critically Ill Patients in the United States.**

Balk RA, Kadri SS, Cao Z, Robinson SB, Lipkin C, Bouzette SA.

**OBJECTIVE**
This study evaluated the impact of PCT testing performed on the first day of ICU admission in critically ill adult patients with suspected or documented sepsis, with the aim of providing real-world data on healthcare utilization and cost.

**STUDY DESIGN**
This retrospective database analysis used the Premier Healthcare Database to evaluate the impact of PCT guidance on day 1 of ICU admission on healthcare use and costs among patients with suspected or documented sepsis. The comparison group included patients with similar clinical and demographic characteristics without PCT guidance on their first day in the ICU.

**RESULTS**
A total of 33,569 PCT managed patients were compared to 98,543 propensity-matched non-PCT patients. The differences observed between the PCT-guided group and the comparison group for the main outcomes are shown in Figure 1.

![Figure 1. Average Differences Between the Two Groups](image)

**CONCLUSIONS**
Use of PCT testing on ICU admission was associated with reduced antibiotic exposure, shorter hospital and ICU length of stay, and significant cost-savings for the hospital, ICU, and pharmacy.

“Use of PCT testing on ICU admission was associated with a significant decrease in hospital and ICU LOS, less systemic antibiotic exposure... and decreased hospital, ICU and pharmacy costs.”

**KEY FINDINGS**
- PCT-guided care is associated with reduced length of stay and lower costs.
- This study demonstrates the value and impact of PCT use in clinical practice.
NOTES

REFERENCES


