

Procalcitonin

Best Practices and Clinical Guidelines

Comprehensive Guide for 2025

Background

Procalcitonin (PCT) consists of 116 amino acids and is the prohormone of calcitonin (Figure 1). Under normal metabolic conditions, PCT is produced by the thyroid gland's C cells, where it undergoes proteolysis to yield the hormone calcitonin. This hormone is involved in calcium homeostasis. Several cell types and tissues have been shown to produce PCT when facing pro-inflammatory stimuli, particularly stemming from bacterial insult.^{1,2}

In contrast, elevated PCT levels can also occur in the absence of bacterial infections due to various non-infectious conditions, such as major surgery, severe burns, neonates at birth, allergic disorders, autoimmune disorders or organ transplant. PCT levels may temporarily rise followed by a return to baseline levels in these cases.³

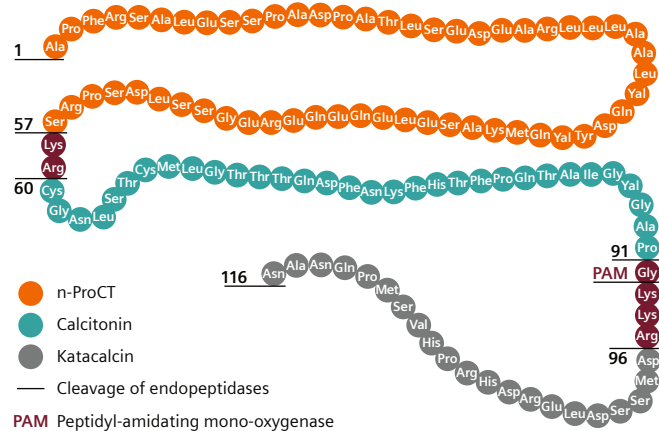


Figure 1. Structure of PCT (adapted from Le Moullec et al. 1984.⁴) PCT is enzymatically degraded into lower molecular weight peptides. The final product consists of 32 amino acids and is named calcitonin. All precursors, including PCT and the mature peptide hormone, can be detected in the serum of healthy humans. In septic patients, only the 3-116 fragment (lacking the N-terminal dipeptide Ala-Pro) is detected, not the complete molecule.⁵

PCT ✓
25+
YEARS

For more than 25 years, PCT has been recognized and utilized in European countries—where most early clinical trials were conducted—and in other countries (including the United States) as a crucial blood marker for distinguishing severe bacterial infections from other pro-inflammatory conditions such as viral infections.³

Meanwhile, antimicrobial resistance, in which microorganisms no longer respond to treatments like antibiotics, has become a growing global health threat.⁶ This issue is exacerbated by the misuse and overuse of these drugs, making infections harder to treat and leading to more prolonged illnesses, higher healthcare costs, and increased mortality. To combat this, healthcare institutions should implement antimicrobial stewardship programs to optimize the use of antimicrobials, reduce resistance, and improve patient outcomes with appropriate treatment.



The utility of PCT in antimicrobial stewardship programs aimed at optimizing antimicrobial use has been documented, providing evidence as to how PCT could help physicians optimize the use of antibiotics for common clinical conditions such as lower respiratory tract infections and sepsis.

Overall, numerous studies conducted worldwide have evaluated the clinical utility of PCT for differential diagnosis, severity assessment, prognosis of severe bacterial infections, and proper antibiotic management. The outcomes of these studies have been presented in more than 10,000 publications.[†] The objective of this clinical brief is to review and summarize the clinical practice guidelines (CPGs) from international medical societies for the use of PCT.



In 2020, Tujula et al. conducted a meta-analysis focusing specifically on clinical practice guidelines (CPGs) published between 2009 and 2018, and assessing the recommendations regarding PCT use.⁷ Seventy percent of those recommendations found PCT to be a useful biomarker, supported by low to moderate evidence for differential diagnosis and/or guidance of antibiotic therapy (AT) in multiple and various diseases and situations including sepsis, pneumonia, lower respiratory tract infections, and monitoring of treatment in the intensive care unit (ICU).

Since this review, new evidence has been generated and other recommendations have been published more recently. Between 2020 and 2025, a PubMed search (with the filters: “Guideline,” “Meta-analysis,” “Practice Guideline,” “Systematic review,” and “English”) yielded approximately 220 results, with about one third related to PCT use in the context of COVID-19 research. Of course, it wouldn’t be possible to review in detail here all this evidence, and this clinical brief issue focuses only on the three most recent documents highlighted in orange in figure 2.

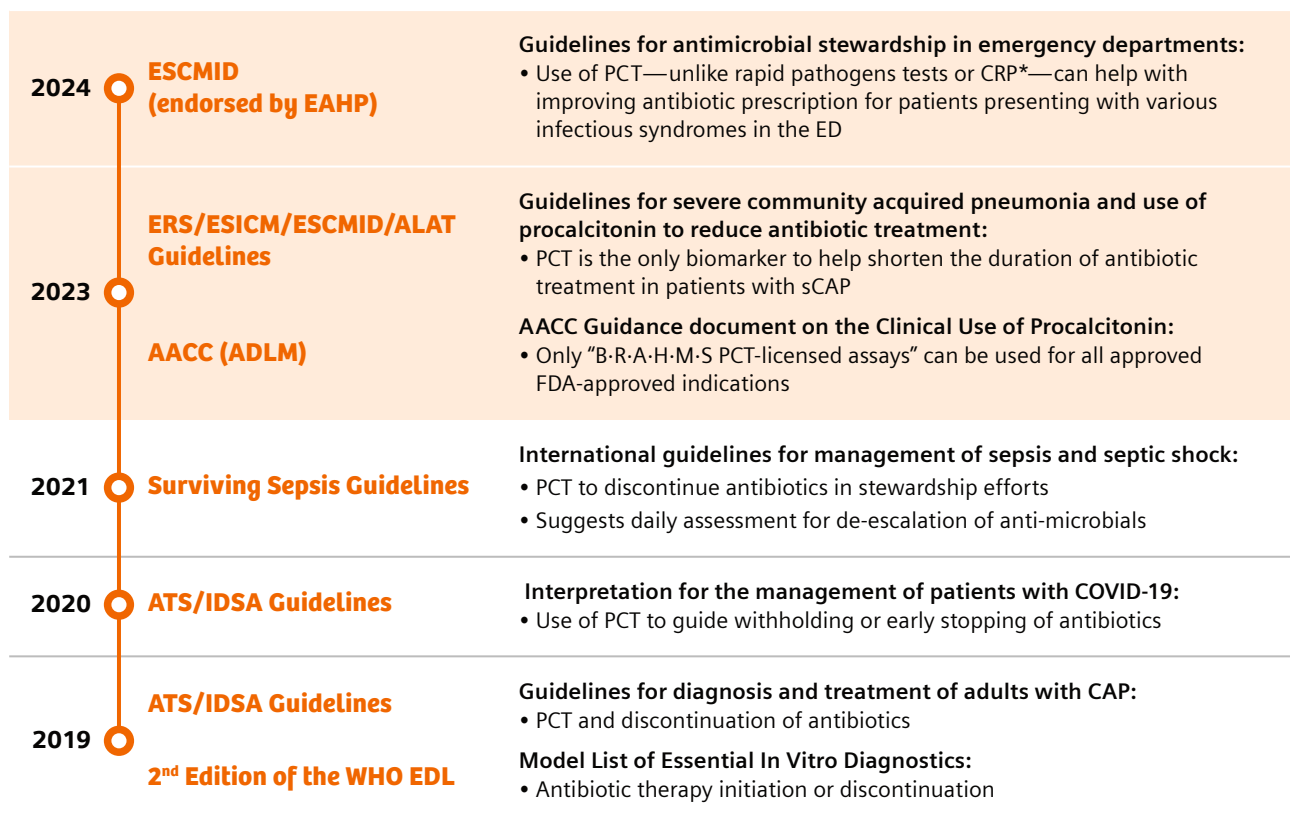


Figure 2. Selection of guidelines with their key recommendations

[†]Based on a PubMed search for “Procalcitonin” (1984 to 2025)

2023 ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia

Cases of CAP

1–25
per 1000

inhabitants
annually

40%

require
hospitalization

5%

require ICU
admission

In Europe and Latin America, four international scientific societies—the ERS, ESICM, ESCMID, and ALAT[†] combined their resources and efforts for the management of severe community-acquired pneumonia (sCAP), the form of the disease requiring supportive therapy in an ICU environment and presenting a higher mortality rate. As indicated by the authors, guidelines had been available, but as part of general management guidelines for CAP, yet not for sCAP.⁸

CAP is a common respiratory infectious disease and a life-threatening condition with high rates of mortality and morbidity and an incidence ranging from one to 25 cases per 1,000 inhabitants annually.⁹

Approximately 40 percent of CAP patients necessitate hospitalization, and 5 percent of these require admission to the ICU for supportive therapy, such as vasopressors and/or mechanical ventilation.¹⁰⁻¹²

Current treatment options encompass antibiotics, systemic corticosteroids, and hemodynamic and respiratory support.^{13,14}

The objective was to get guidance from a panel of 18 European and four non-European experts on the most effective ways to treat and manage patients with sCAP and provide recommendations for healthcare workers in respiratory and intensive care medicine: general internists, infectious disease specialists, pharmacists, and microbiologists who manage adults with sCAP, as well as policymakers.

The expert panel faced eight clinical questions about sCAP diagnosis and treatment. One of them is of particular interest for this clinical brief as it pertains to the use of biomarkers to assist physicians in guiding sCAP antibiotic therapy. Since the experts had decided to focus on a single biomarker—PCT (the initial question on biomarkers was intended to review both PCT and C-reactive protein (CRP);* but the expert panel chose to focus solely on PCT due to the stronger clinical evidence supporting PCT)—they reviewed whether serial measurements of this biomarker in patients with sCAP could help reduce the duration of antibiotic therapy and improve other outcomes compared to the standard of care. It should be noted that studies investigating biomarkers for reducing or discontinuing antibiotics are predominantly conducted in CAP with only limited data available for sCAP. Out of 1,696 references screened, three randomized clinical trials (RCTs) were deemed relevant for sCAP and duration of antibiotic treatment (AT).¹⁵⁻¹⁷ All three were focused on patients with sepsis.

Based on the available evidence, the guidelines recommend using PCT to help shorten the duration of AT in patients with sCAP. However, this is a conditional recommendation as supported by low-quality evidence, due to the lack of studies specifically including sCAP populations and the imprecision of estimates regarding AT duration. The use of PCT should be considered alongside clinical assessment, and PCT may not be useful for discontinuation once clinical stability is reached and the antibiotic therapy duration is between 5 and 7 days. Also, the experts noted that they didn't systematically investigate the cost-effectiveness of a PCT-guided strategy.¹⁵

2024 European Society of Clinical Microbiology and Infectious Diseases guidelines for antimicrobial stewardship in emergency departments

The following year, in 2024, ESCMID published its guidelines (endorsed by EAHP⁶) for implementing antimicrobial stewardship programs, which was aimed at optimizing antibiotic use in patients presenting in emergency departments (ED).¹⁸ This very recent document is of significant interest because, despite the high volume of antibiotics prescribed at the ED for patients with suspected infections, there was a lack of specific guidance on antimicrobial stewardship for this clinical setting. These recommendations are for healthcare professionals treating adult patients presenting to the ED with suspected infection (i.e., ED physicians, infectious diseases physicians, or other internists, pulmonologists, clinical microbiologists, pharmacists or advanced practice providers).

The document reviews four antimicrobial stewardship topics that can affect antibiotic prescription. One of them questions the utility of biomarkers (PCT and CRP*) in improving antibiotic prescription for patients presenting to the ED with various infectious syndromes. The experts' conclusions and guidelines are outlined below, along with references to the supporting evidence.



PCT ✓
LRTI
Asthma
COPD

The guidelines recommend using PCT to help guide the initiation of antibiotics in adult patients who present to the ED and are likely to be admitted to the hospital for a suspicion of LRTI (recommendation for use: weak, certainty of evidence: moderate),¹⁹⁻²⁵ an acute exacerbation of asthma^{26,27} (recommendation for use: weak, certainty of evidence: low) and an acute exacerbation of chronic obstructive pulmonary disease (COPD)^{28,29} (recommendation for use: weak, certainty of evidence: moderate).

However, the experts do not suggest using PCT to guide the initiation of antibiotics for patients with dyspnea and suspected or known heart disease^{30,31} who are likely to be admitted to the hospital (recommendation against use: weak, certainty of evidence: low) and patients based on the criterion of fever alone^{32,33} (recommendation against use: weak, certainty of evidence: very low).^{34,35} Finally, regarding the choice of a specific biomarker, the expert panel recommends against using CRP* to guide the initiation of antibiotics for patients with respiratory tract infections (recommendation against use: weak, certainty of evidence: very low).

The ESCMID expert panel underscores the challenges in implementing and adhering to these recommendations. Although evidence is limited,³⁶⁻³⁹ reports reveal that low requests for biomarkers and suboptimal compliance with their results are significant issues. Consequently, the authors recommend focusing on improving these two areas.

PCT use in the United States

Following this review of two recent European CPGs, let's conclude this clinical brief by examining the recommendations for PCT use in the United States. In 2017, the U.S. Food and Drug Administration (FDA) made a significant advancement by expanding the indications for use of a PCT assay.⁴⁰ Initially, PCT was recommended to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock and to assess the cumulative 28-day risk of all-cause mortality for patients with severe sepsis or septic shock using changes in PCT levels over time. The revised indications now enable PCT to be used to assist clinicians in guiding AT for patients with lower respiratory tract infections and sepsis, including decision-making on antibiotic therapy for community-acquired pneumonia, acute bronchitis, acute exacerbations of chronic obstructive pulmonary disease, and antibiotic discontinuation for suspected or confirmed sepsis. Since 2017, additional assays have received FDA approval, though not all PCT assays available on the market have been approved. The 2023 AACC** Guidance Document on the Clinical Use of PCT⁴¹ clearly reminds us that only the "B·R·A·H·M·S PCT-licensed assays" like the Atellica IM B·R·A·H·M·S PCT assay can be used according to the above-mentioned FDA-approved indications.

Conclusion

In summary, PCT testing is recommended by multiple CPGs, and the FDA-approved indications have expanded. In the absence of a higher-order standard, and since the Thermo Fisher Scientific B·R·A·H·M·S PCT sensitive KRYPTOR was used in the clinical trials that established the FDA-approved clinical decision points, this method has become the gold standard. Unlike B·R·A·H·M·S PCT assays, non-B·R·A·H·M·S assays generally show lower agreement (especially at clinical decision points)—on average—than with the B·R·A·H·M·S PCT sensitive KRYPTOR assay, as supported by various publications.⁴²⁻⁴⁴ Therefore, use of these standardized assays with the validated clinical decision points can aid clinicians in optimizing their patient management.

Implementing new clinical practice guidelines in routine practice is always challenging due to several factors. Healthcare professionals often face barriers such as resistance to change, limited resources, and time constraints. Additionally, there may be a lack of training or familiarity with the new guidelines, leading to uncertainty and inconsistent application. Organizational culture and existing workflows can also hinder the adoption of new practices. Overcoming these challenges requires effective communication, ongoing education, and support from leadership to enable successful integration into daily routines.



Implementing PCT and new CPGs into clinical practice will require the education of healthcare professionals and consideration for modifications of their clinical practices. Regular evaluations of the new process to measure the impact of PCT testing will be critical to ensure its successful implementation.

Advance the fight against sepsis

The PCT assay provides valuable information that can help clinical decision-making in multiple settings, including risk assessment in the ICU for progression to severe sepsis or septic shock, aiding in decisions on starting antibiotics in specific cases, and guiding decisions on antibiotic discontinuance. This helps interventions to be timely and precisely tailored to achieve clinical excellence. The Atellica IM PCT Assay delivers B·R·A·H·M·S gold-standard performance with established algorithms and cut-offs. Through alignment to a validated gold standard, B·R·A·H·M·S PCT assays demonstrate excellent performance in multiple applications, giving physicians confidence when performing patient assessments.



Explore how the Atellica IM B·R·A·H·M·S PCT Assay helps enable confident sepsis risk assessment and antibiotic management.

*Siemens Healthineers has neither tested nor recommends the CRP method described herein. There can be no guarantee that this method proves itself in clinical practice and that clinical benefits will outweigh possible side-effects. Necessary conformity assessments have not yet been entered into submission for necessary market clearances or approvals have not yet been made. Siemens Healthineers assumes no liability whatsoever, if the CRP method described herein is applied despite missing evidence of safety and effectiveness and missing clearances respectively approvals.

Abbreviations

‡ERS (European Respiratory Society), ESICM (European Society of Intensive Care Medicine), ESCMID (European Society of Clinical Microbiology and Infectious Diseases),

ALAT (Latin American Thoracic Association)

§EAHP (European Association of Hospital Pharmacists)

**AACC (American Association for Clinical Chemistry, now Association for Diagnostics and Laboratory Medicine)

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