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Procalcitonin and C-reactive protein in the diagnosis of community-acquired bacterial pneumonia: reassessing their clinical utility where resources are scarce

Abstract

The differential diagnosis of bacterial pneumonia from viral or non-infectious pulmonary conditions remains a persistent clinical challenge, particularly in hospitals where advanced microbiological infrastructure is unavailable. Procalcitonin (PCT) and C-reactive protein (CRP) are widely regarded as complementary inflammatory markers, yet their practical usefulness in resource-constrained settings is rarely examined critically. This article revisits the diagnostic performance of both biomarkers, weighing their sensitivity, specificity, cost-effectiveness, and interpretive limitations in the context of low- and middle-income country (LMIC) hospital practice. We argue that neither marker alone is sufficient, that their combined use follows a context-dependent logic, and that clinicians working outside tertiary centers should apply threshold values with caution rather than automatism. A practical clinical scenario-based framework for prioritizing one marker over the other when resources are limited, alongside a cost-effectiveness analysis comparing biomarker testing with traditional approaches, is proposed.

Keywords: procalcitonin, C-reactive protein, community-acquired pneumonia, bacterial infection, resource-limited diagnostics, inflammatory biomarkers, antibiotic stewardship, LMIC

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Introduction

Walk into any district hospital and you will find clinicians making antibiotic prescription decisions with a handful of laboratory tools and a chest X-ray. The luxury of rapid multiplex PCR panels, bronchoalveolar lavage cultures, or same-day blood cultures is simply not on offer. In this environment, serum biomarkers carry a weight they were perhaps never designed to bear alone.

Community-acquired pneumonia (CAP) accounts for a substantial proportion of hospital admissions globally and remains a leading cause of infection-related mortality, with an estimated incidence of up to 14 cases per 1,000 adults per year and a 30-day mortality of 6% among hospitalized patients.[1] The etiological split between bacterial and non-bacterial causes is clinically meaningful: it determines whether antibiotics are initiated, continued, or safely withheld. However, clinical signs and conventional radiography are notoriously unreliable discriminators and microbiological confirmation is unavailable in the majority of cases.[2] Severity scoring systems such as PSI and CURB-65 assist with triage but do not resolve the bacterial-versus-viral question at a mechanistic level.[3] It is within this diagnostic gap that procalcitonin and C-reactive protein have been proposed as decision-support tools.

The question this article addresses is not abstract: does the published evidence on PCT and CRP translate meaningfully into daily practice at a hospital where reagent availability fluctuates, turnaround times vary, and reference ranges printed on analyzer printouts were validated in populations far removed from your own? A recent review of biomarker uses specifically in in low- and middle-income country (LMIC) settings found that most evidence underpinning published cut-offs was generated in high-income countries, raising important questions about transferability.[4]

Biological rationale: why these two markers?

CRP, a pentameric acute-phase protein synthesized in hepatocytes under interleukin-6 stimulation, rises within 6-12 hours of tissue injury or infection and reaches its peak around 48 hours.[5] Its elevation is non-specific: malignancy, autoimmune flares, and post-surgical states generate comparable values. Nevertheless, CRP above 100 mg/L has historically been associated with bacterial rather than viral etiology in respiratory infections, though the overlap between these groups is considerable and clinically misleading in a non-trivial proportion of cases.[4]

Procalcitonin, the prohormone of calcitonin, behaves differently. Under normal conditions it is produced exclusively in thyroid C-cells in negligible amounts. Systemic bacterial infections, particularly those involving gram-negative organisms, trigger a paradoxical surge in PCT production from virtually every parenchymal cell, with serum levels rising within 3-6 hours and peaking at 6-24 hours.[6] This earlier kinetics and the theoretical bacterial specificity of PCT's induction pathway explain why it attracted enormous interest as a stewardship tool: guide antibiotics upward when PCT is high, guide them downward or withhold them when PCT remains low.[7] The mechanistic logic is compelling. The clinical reality, however, is considerably messier.

What the evidence actually shows

Sensitivity, specificity, and the stewardship argument

The PROGRESS trial, a multicenter, open-label randomized study, demonstrated that PCT-guided early initiation of antibiotics in patients with sepsis, including those with CAP, was associated with significantly lower 28-day mortality (15.2% vs 28.2%) and reduced antibiotic duration (5 vs 10 days) compared to delayed treatment guided by standard criteria.[8] These findings reinforced the stewardship

rationale for PCT in severe respiratory infections and were echoed in comprehensive reviews of biomarker-guided antimicrobial therapy in critically ill patients.[7]

Crucially, the landmark ADAPT-Sepsis randomized controlled trial (n=2,760 across 41 UK NHS intensive care units) published in 2025 provided the most rigorous head-to-head comparison to date.[9] PCT-guided antibiotic discontinuation advice significantly reduced total antibiotic duration compared with standard care (mean difference 0.88 days; 95% CI 0.19-1.58; p=0.01), with no statistically significant increase in 28-day all-cause mortality. Importantly, the CRP-guided protocol showed no significant reduction in antibiotic duration compared to standard care (mean difference 0.09 days; p=0.79). This finding definitively positions PCT, rather than CRP, as the superior tool specifically for antibiotic de-escalation decisions in critically ill patients, while leaving CRP's established role in initial triage and monitoring intact.

However, the sensitivity of PCT for bacterial CAP varies substantially – between 55% and 88% depending on the threshold applied and the study population.[5] The most commonly cited cut-off of 0.25 µg/L was derived from European cohorts and may perform differently in other epidemiological settings. Carbonell et al. demonstrated that in critically ill patients with respiratory infections, the negative predictive value of a low PCT was robust for ruling out bacterial co-infection, but emphasized that this was context-specific and dependent on disease prevalence.[10]

CRP, despite its lower specificity, often demonstrates higher sensitivity in early-stage pneumonia precisely because its rise precedes clinical deterioration and its synthesis does not depend on the degree of bacteremia.[4] A comprehensive narrative review of biomarkers in CAP confirmed that CRP had an AUC of 0.80 for detecting bacterial pneumonia – comparable to PCT (0.77) – while being consistently more available in routine clinical workflows.[5] The implication is straightforward yet frequently overlooked: these two markers are not interchangeable, and they do not answer the same clinical question.

The problem of cut-off transferability

Published PCT thresholds were derived and validated in specific populations with specific disease prevalences. In a hospital serving a region with high endemic tuberculosis, where granulomatous inflammation generates CRP elevations that mimic bacterial pneumonia, or a patient population with frequent comorbid chronic kidney disease (CKD), which independently elevates PCT irrespective of infection, applying standard thresholds without local calibration introduces systematic diagnostic error. A 2022 systematic review and meta-analysis confirmed that in patients undergoing hemodialysis, standard PCT cut-offs are unreliable, with non-infected patients sometimes showing values well above 0.25 µg/L, requiring adjusted thresholds for this population.[11]

CRP faces analogous issues. Laboratories in district hospitals commonly use high-sensitivity CRP assays developed for cardiovascular risk stratification rather than for acute infection triage. The analytical ranges differ substantially, and what constitutes a meaningfully "elevated" result depends entirely on the assay platform and the reference population used in its validation – details that rarely appear on the analyzer printout that reaches the clinician. Lamrous et al. specifically highlighted these assay heterogeneity problems in their review of biomarker evidence from resource-limited settings.[4]

Evidence from resource-limited and LMIC settings

The majority of clinical validation data for both PCT and CRP originates in high-income countries with different epidemiological profiles, healthcare infrastructure, and patient comorbidity burdens compared to LMIC settings. This creates a fundamental evidentiary gap that directly impacts the clinical applicability of published diagnostic thresholds in hospitals such as those in Eastern Europe and the former Soviet Union. The Lamrous et al. narrative review, the most comprehensive synthesis of LMIC biomarker evidence to date, found that while CRP and PCT showed promise in guiding antibiotic decisions in respiratory infections, the existing evidence from LMIC cohorts was heterogeneous, under-powered, and often relied on thresholds developed elsewhere.[4] Notably, baseline CRP values differ even in healthy populations. Adult males in Ghana had median CRP levels measurably lower than European counterparts, illustrating that host-level biological variation may affect threshold performance independently of infection status.[5]

In sub-Saharan African settings, where malaria, HIV, and tuberculosis coexist with bacterial pneumonia at high prevalence, both CRP and PCT face significant specificity challenges that have not been systematically addressed in their respective validation studies. PCT, in particular, may be elevated in mycobacterial infections, while CRP elevation is nearly universal across all of these conditions, making threshold-based interpretation hazardous without clinical context. Despite these limitations, point-of-care (PoC) CRP testing has been successfully piloted in rural Ethiopian primary care settings, with CRP distribution patterns broadly similar to European primary care populations, suggesting that the assay's fundamental behavior is preserved, even if quantitative cut-offs require local adjustment.[12]

From the perspective of Argentine LMIC hospitals, a budget impact analysis by Garay et al.[13] estimated that PCT-guided antibiotic stewardship in patients with suspected sepsis and lower respiratory tract infections was associated with a net cost reduction of approximately USD 1,600-2,900 per patient compared with unguided standard care, driven primarily by shorter antibiotic courses and reduced length of stay. This finding has important implications for hospitals in Belarus and comparable settings, where the absolute cost of PCT testing is higher relative to local drug costs than in Western healthcare systems. The key insight is that the cost of the test must be evaluated against the cost of avoidable antibiotic courses and extended hospitalizations – not in isolation.

Practical considerations for hospital-based laboratories

From the standpoint of a clinical laboratory diagnostician working in a regional hospital, several operational issues deserve explicit acknowledgment:

Turnaround time. PCT measured by immunoluminometric or immunofluorescent methods on dedicated analyzers can theoretically deliver results within 20-30 minutes. In hospitals where samples are batched and processed twice daily, this kinetic advantage evaporates entirely. CRP measured by turbidimetry on a standard biochemistry analyzer is available within routine workflow in virtually every functioning laboratory – an underappreciated and practically decisive advantage when time-sensitive antibiotic decisions are required.[14]

Cost differential: In the current Belarussian healthcare context, a single PCT determination costs approximately five to eight times more than a CRP measurement. A retrospective multicenter study analyzing real-world PCT utilization in patients hospitalized with CAP found that PCT testing was used in only 42% of encounters and did not consistently translate into reduced antibiotic exposure in non-protocol-driven settings, questioning the cost-benefit ratio of unstructured PCT use.[14]

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Serial measurement versus single time-point: Both markers derive their maximum informational value from serial measurements rather than from isolated values. Kim et al. reviewed the evidence for biomarker-based antibiotic stewardship programs and confirmed that the dynamic trajectory of PCT and CRP, rather than single admission values, provided the most reliable basis for de-escalation decisions, with a falling PCT at 48-72 hours being the most operationally useful signal.[15] This dynamic pattern requires structured sampling protocols, something achievable in any hospital with a systematized laboratory request process, regardless of resource level.

Cost-effectiveness compared with traditional diagnostic approaches

A frequently overlooked dimension of biomarker use is how it compares economically with the default alternative in resource-limited settings: clinical judgment combined with chest radiography. This comparison is rarely made explicit in guideline documents, yet it is the operationally relevant question for clinicians at district hospitals.

Chest radiography provides structural information like lobar consolidation, interstitial infiltrates, effusion, with an AUC of approximately 0.70 for confirming CAP diagnosis in symptomatic adults. Adding CRP to the clinical and radiological assessment increases the composite AUC to approximately 0.77, representing a diagnostically meaningful 28% improvement in discriminatory power.[12] This incremental diagnostic gain from a test costing a fraction of chest radiography underscores that CRP is not a redundant addition to the standard workup but a genuinely complementary instrument.

The cost-effectiveness profile of PCT-guided stewardship versus clinical judgment alone has been evaluated in a US healthcare model by Mewes et al.,[16] which found that PCT-guided management of lower respiratory tract infections reduced total per-patient costs by 17.7% compared with standard care, driven by reduced antibiotic days, shorter ICU and ward stays, and lower rates of Clostridioides difficile infection. In a European context, a systematic review of point-of-care testing interventions for inappropriate antibiotic prescribing found that while CRP POCT is among the most cost-effective tools studied, the evidence base remains heterogeneous, and formal cost-effectiveness conclusions depend heavily on local antibiotic costs and hospitalization rates.[17]

For the practical purpose of antibiotic stewardship in a Belarusian or similar district hospital, the economic hierarchy can be summarized as follows: CRP is cost-effective for initial diagnostic triage and daily monitoring at any resource level; PCT is cost-effective for de-escalation decisions in patients with severe CAP or sepsis where broad-spectrum antibiotics have been initiated, and its cost is justified by the antibiotic days saved; PCT is not cost-effective for routine use in mild-to-moderate non-ICU CAP where clinical and CRP trajectories are sufficient to guide decisions. This tiered approach avoids both the false economy of withholding a useful test and the resource waste of applying an expensive test indiscriminately.

A proposed decision framework with clinical scenarios

Based on available evidence and the operational realities of regional hospital practice, the following tiered framework is suggested. Four representative clinical scenarios, spanning the spectrum from mild ambulatory-borderline presentations to severe ICU-level CAP, illustrate how the combined and prioritized use of PCT and CRP can be operationalized without requiring resources beyond standard biochemistry capacity.

General tiered approach

On admission (Day 0): measure both CRP and PCT simultaneously when clinically feasible. CRP provides immediate triage-level information and a baseline for monitoring; PCT establishes a reference for later de-escalation decisions.[6]

At 48-72 hours: repeat CRP as primary monitoring tool. A failure to fall below 50% of the admission value suggests inadequate treatment response or diagnostic error. PCT at this point is most informative for ICU patients on broad-spectrum antibiotics.[7,8]

At Day 5-7: PCT-guided de-escalation is evidence-based and cost-justified in severe CAP or patients on broad-spectrum coverage.[8,9]

In mild cases where clinical and radiological findings already support a bacterial diagnosis, neither marker should delay antibiotic initiation. They serve confirmation, not replacement, of clinical judgment.[1,3] Clinical Scenario Guidance is presented in Table 1:

Table 1 Clinical scenario-based prioritization of CRP and PCT in community-acquired pneumonia

Scenario	Clinical picture	CRP role	PCT role	Recommendation
A. Classic bacterial CAP, general ward	Fever, productive cough, lobar consolidation on X-ray, no severe comorbidities	Primary diagnostic tool; CRP >100 mg/L supports bacterial etiology; repeat at 72h for monitoring	Baseline measure; if funds limited, omit at admission; use at Day 5-7 for de-escalation	If only one test available: prioritize CRP. Add PCT at Day 5 if clinical improvement is equivocal
B. Elderly patient, atypical presentation	Low-grade fever, non-productive cough, bilateral hazy infiltrates; possible viral or atypical etiology	CRP 20-80 mg/L – non-diagnostic zone; serial measurement more informative than single value	PCT <0.1 µg/L strongly argues against bacterial etiology; supports watchful waiting without antibiotics	If PCT <0.1 and CRP <50: defer antibiotics, repeat both markers at 24 h. PCT is the decision driver here
C. Severe CAP, ICU admission	Respiratory failure, multilobar infiltrates, sepsis criteria; broad-spectrum antibiotics initiated	Daily CRP trajectory monitors treatment response; failure to fall signals inadequate therapy or complication	PCT is the primary de-escalation guide at Day 3-5; ADAPT-Sepsis confirms PCT reduces antibiotic duration by ~10% vs standard care	Use both markers in tandem; PCT guides stopping decision, CRP guides daily monitoring
D. CAP in patient with CKD or on hemodialysis	Comorbid renal insufficiency; standard PCT thresholds unreliable due to uremic elevation	CRP remains interpretable; values >100 mg/L still support bacterial etiology in renal patients	Interpret with adjusted thresholds: PCT >0.5 µg/L may be required to signal infection in CKD; apply kinetic (trending) rather than single-point logic	Prioritize CRP for initial decision; use PCT only serially with awareness of elevated baseline

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Across all scenarios, the fundamental principle is that resource scarcity demands triage of diagnostic tools, not their abandonment. CRP, as the universally available, lower-cost marker with superior early-phase sensitivity, is the default first-line instrument for diagnosis and monitoring at all resource levels. PCT earns its higher cost in scenarios where its kinetic superiority, particularly for de-escalation and where avoiding unnecessary broad-spectrum antibiotic continuation carries the greatest clinical and economic benefit, is most pronounced. In settings where PCT is not available at all, structured serial CRP monitoring combined with clinical scoring represents a clinically valid and evidence-supported alternative that should be formalized into local institutional protocols.

Conclusion

The debate over procalcitonin versus CRP in bacterial pneumonia is, in some respects, a false dichotomy. These markers reflect different biological processes, operate on different timescales, and answer different clinical questions. The ADAPT-Sepsis trial definitively established that PCT, not CRP, is the superior tool for antibiotic de-escalation in critically ill patients, while prior and concurrent evidence confirms that CRP remains the more cost-effective choice for initial diagnostic triage and daily monitoring across all resource settings.[9] In LMIC hospitals where PCT access is unreliable or prohibitively expensive, evidence of some investigations suggests that structured CRP-based protocols are a valid and clinically safe alternative, provided clinicians apply dynamic interpretation rather than static thresholds.[4,12,13]

The hospital laboratory in a regional center is not a scaled-down version of a university clinic. It is a distinct diagnostic environment with its own patient mix, workflow constraints, and epidemiological context. Generating local observational data, even modest, single-center retrospective cohort analyses calibrating these biomarkers against local disease prevalence and patient comorbidities, would do more to improve clinical decision-making than any number of guidelines written elsewhere.[2,14] We hope that this framework, grounded in current evidence and practical clinical scenarios, will serve as a useful starting point for such local validation efforts.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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