

Manage infections safely and effectively

B·R·A·H·M·S PCT: Early infection
diagnosis and antibiotic guidance

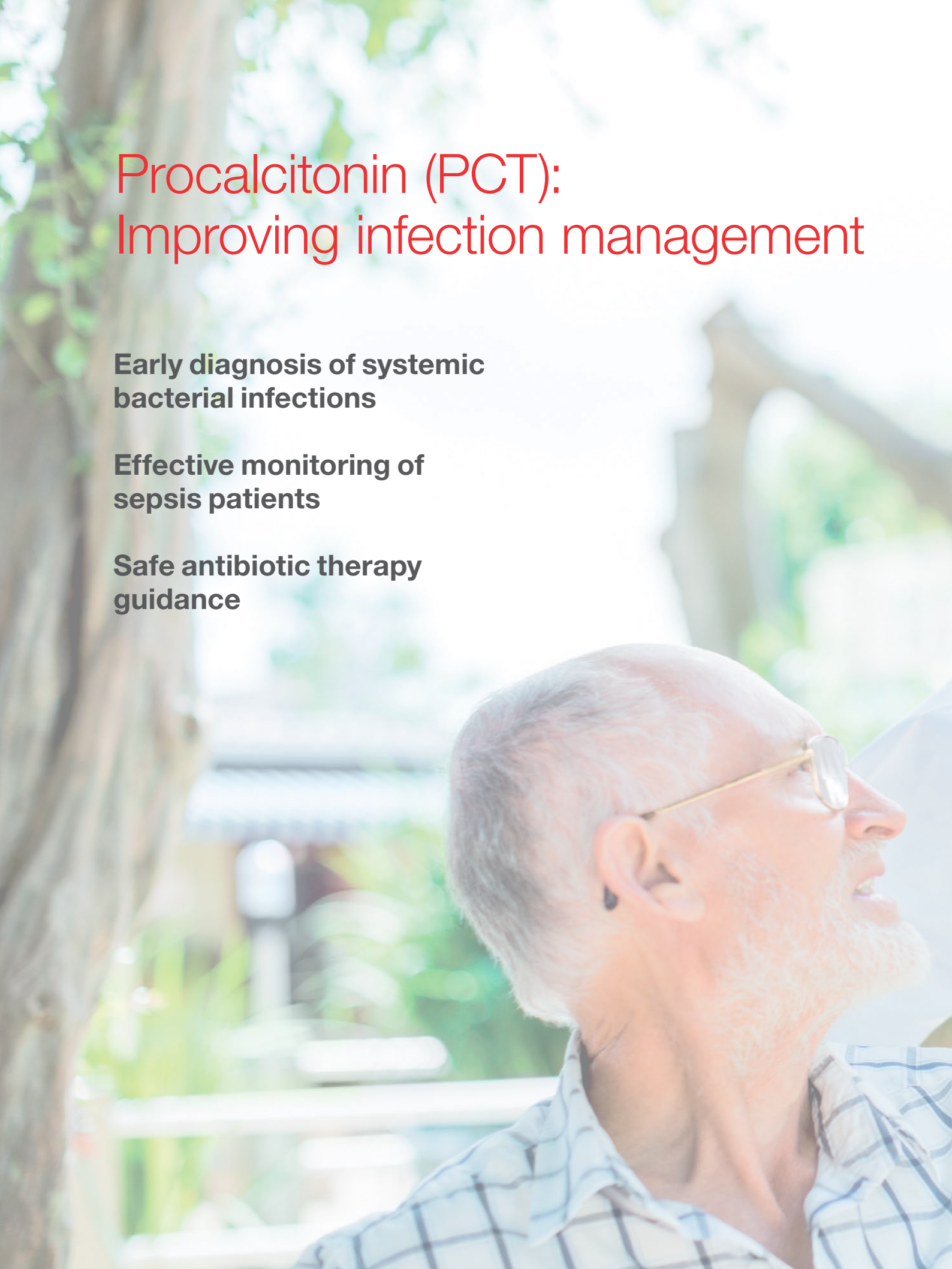


Procalcitonin (PCT): Improving infection management

**Early diagnosis of systemic
bacterial infections**

**Effective monitoring of
sepsis patients**

**Safe antibiotic therapy
guidance**





PCT – the infection marker

Early and highly specific increase in bacterial infections

Procalcitonin (PCT) is a precursor peptide of the hormone Calcitonin. In systemic microbial infections, circulating PCT increases up to several thousand-fold.¹ The PCT level correlates with the severity of the illness. Because of its highly specific induction due to bacterial infection PCT supports earlier and better diagnosis and clinical decision-making for systemic bacterial infections and therapy guidance.^{2,3,4}

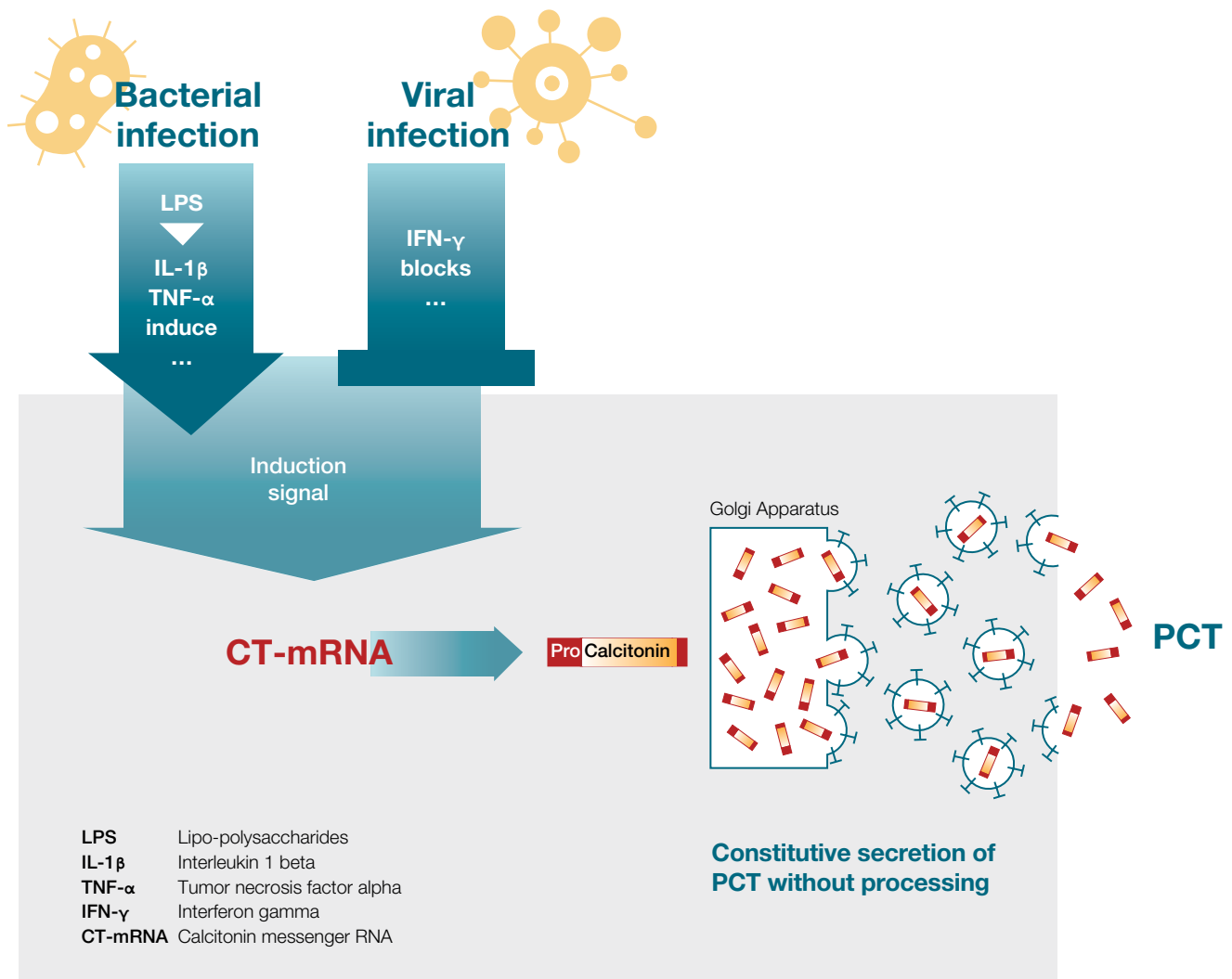


Figure 1 Schematic diagram of Calcitonin I Gene expression in adipocytes¹: Lipo-polysaccharides (LPS) from the bacterial cell wall lead to the production of IL-1 β and TNF- α . These proinflammatory mediators induce CT-mRNA and ProCT (Procalcitonin, PCT) production. In contrast to thyroidal cells, adipocytes and other parenchymal cells lack secretory granules, and hence, unprocessed ProCT is released in a nonregulated, constitutive manner. On the other hand IFN- γ released from tissues in viral infection blocks the endocrine signal. Thus, PCT levels do not rise in viral infections.

Best parameter for early diagnosis and monitoring of severe bacterial infections and sepsis

- **Fast increase after bacterial infection** within 3–6 hours after infectious challenge (faster than CRP) facilitates early diagnosis^{2,3,4}
- **High sensitivity and specificity for bacterial infection** enables therapeutic decision making^{2,3,4}
- **Suitable for monitoring**^{2,3,4}
 - Half-life of ~24 h
 - PCT-levels correlate to the patient's clinical condition
- **Convenient to measure**^{2,3,4}
 - Very stable molecule
 - High in-vitro stability

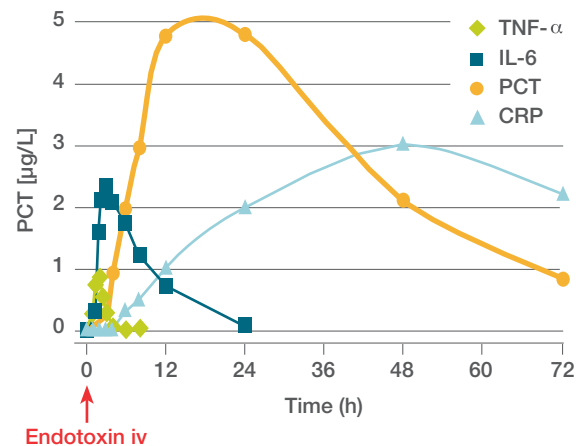


Figure 2 Kinetics of PCT compared to other inflammatory markers upon infection^{2,3,5,6}

PCT levels rise with increasing severity of infection²

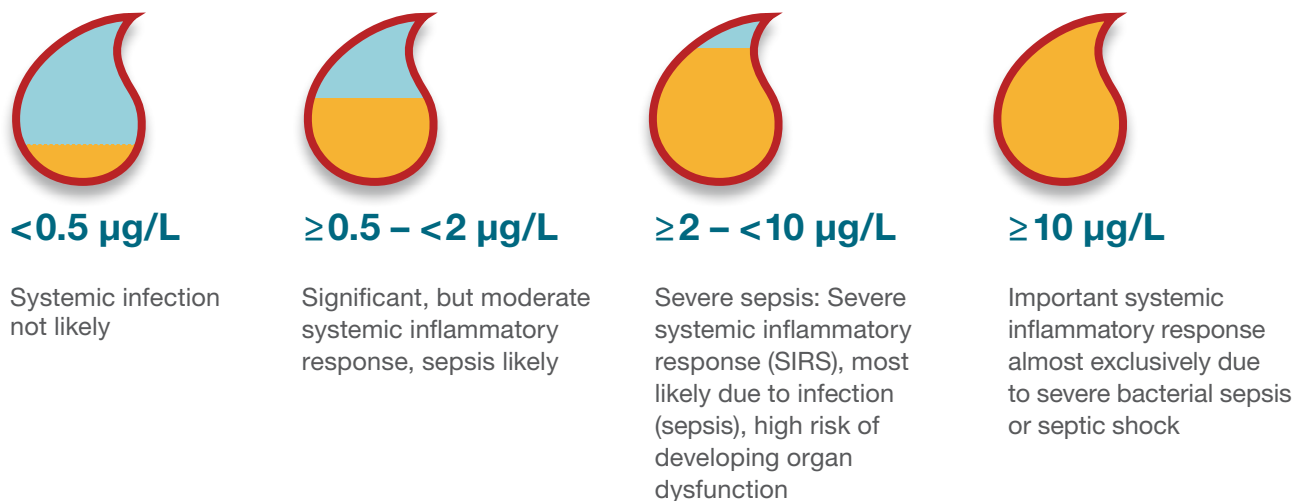


Figure 3 PCT reference ranges and their correlation with the patient's clinical condition.² As an expression of individually different immune responses and different clinical situations, the same focus of infection may be associated with varying individual elevations in PCT concentrations. Therefore, PCT results should be interpreted in context of the patient's clinical condition and other laboratory findings.

B·R·A·H·M·S PCT facilitates early sepsis diagnosis

PCT levels increase within 3-6 hours after bacterial challenge and make a significant contribution to the clinical diagnosis of sepsis. In patients with $>0.5 \mu\text{g/L}$ PCT a bacterial infection is likely and the administration of antibiotics is recommended.^{2,3,4}

Early detection and specific clinical intervention is crucial for the improved outcome of patients with sepsis

Every hour delay in receiving antibiotics is associated with 7.6% decrease in survival in adults with septic shock.

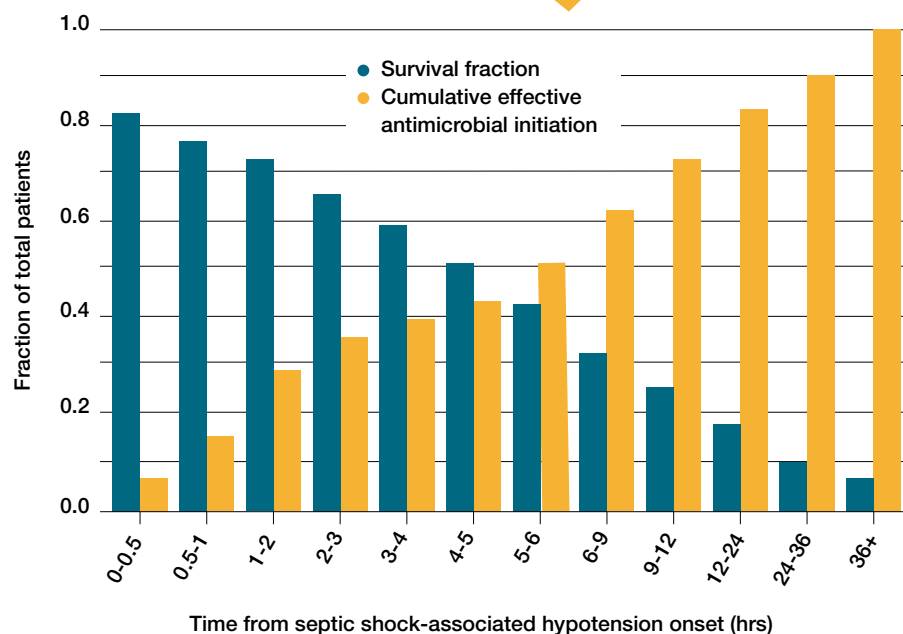
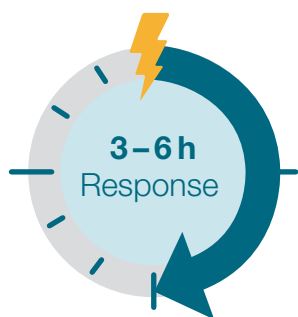


Figure 4 Cumulative effective antimicrobial initiation following onset of septic shock-associated hypotension and associated survival⁷

B·R·A·H·M·S PCT meets the needs of sepsis diagnosis



Early response

Levels increase within 3-6 hours after bacterial challenge⁵



Fast results

Incubation time 16-30 minutes (except B·R·A·H·M·S PCT™ LIA)



Highly sensitive and specific

A mean sensitivity of 0.77 and a mean specificity of 0.79 to discriminate sepsis from SIRS of non-infectious origin – based on meta-analysis of 3244 patients⁸



“In sepsis it’s all about time.
Fast PCT results support me in early
and safe clinical decision making.”



PCT – a useful marker for monitoring sepsis patients

PCT kinetics indicates prognosis

Serial PCT measurement gives information about patient's prognosis. In a prospective, multi-centre observational clinical trial, the 28-day all-cause mortality was two-fold higher when PCT did not show a decrease of more than 80% from baseline to day 4 (20% vs 10%).⁹

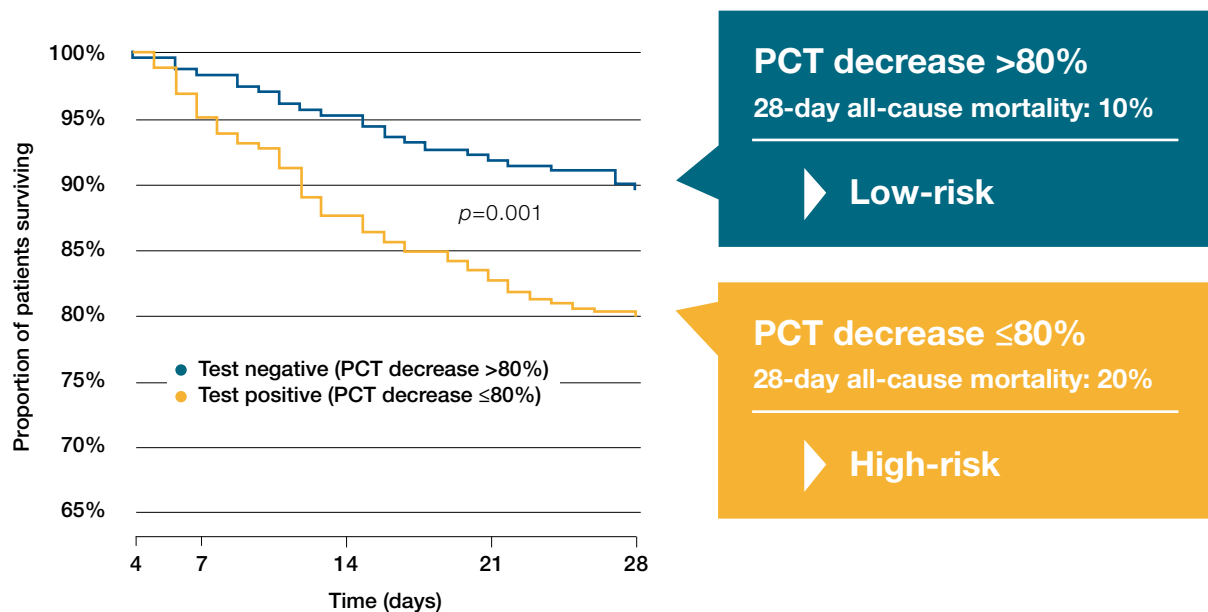


Figure 6 Kaplan-Meier survival curves comparing the survival of patients with PCT decrease of at least 80% (●) and patients with PCT decrease >80% (●) (n=646)⁹

Monitoring with PCT provides therapeutic guidance

Effective antibiotic (AB) treatment is reflected by declining PCT values,¹⁰ consistent with its half-life time of about 24 hours.³ Consequently, serial determinations of PCT can be used to monitor the course and prognosis of life-threatening systemic bacterial infections and to tailor the therapeutic interventions more efficiently.^{11,12}

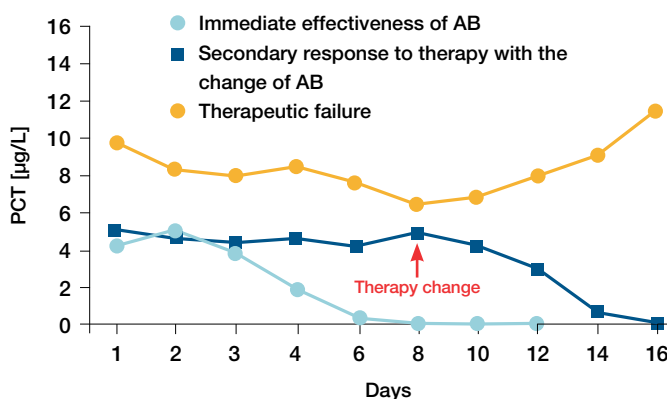


Figure 5 Typical course of PCT serum level according to patient's response to antibiotic treatment (n=109)¹²

“Monitoring with PCT levels
gives me confidence that the
treatment is working fine.”

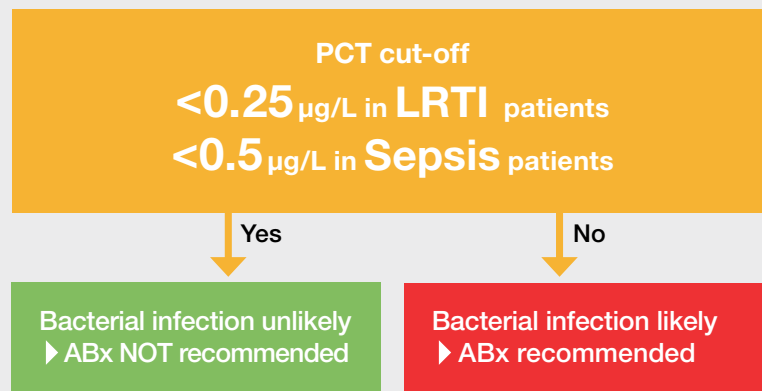


PCT helps tailor antibiotic therapy to individual patient needs

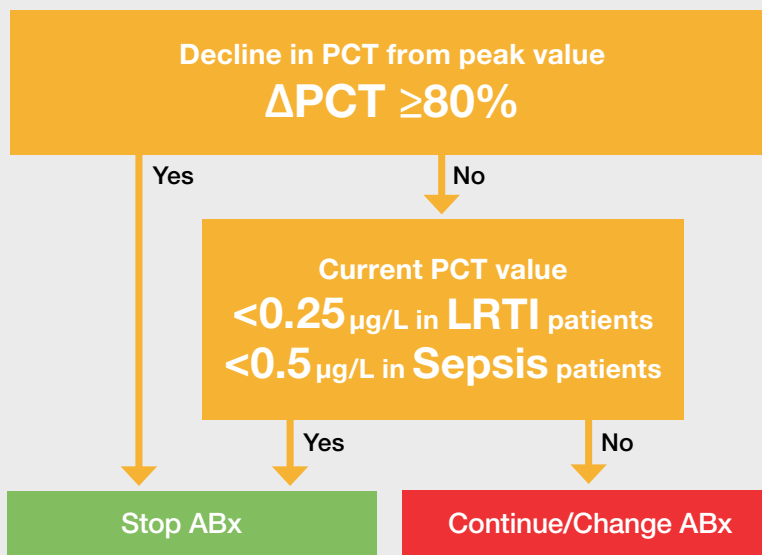
B·R·A·H·M·S PCT guided algorithms for antibiotic therapy



When to START antibiotics?



When to STOP antibiotics? ^{13,14}



$$\Delta PCT = \frac{\text{Peak PCT} - \text{Current PCT}}{\text{Peak PCT}} \times 100\%$$

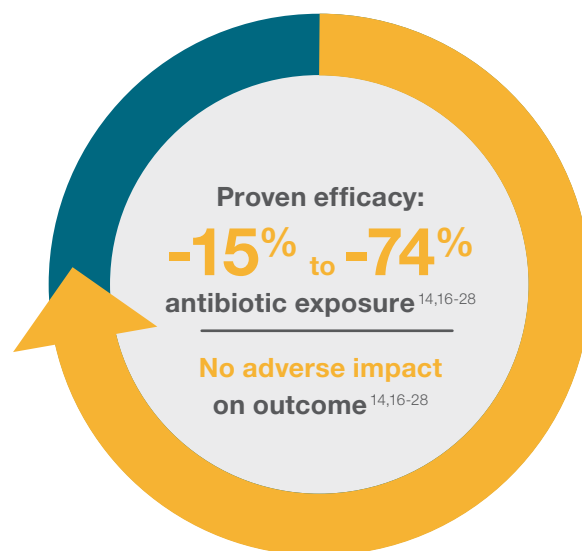
PCT values should always be interpreted in context of the patient's clinical condition. Antibiotic treatment should be started/continued on suspicion of infection, particularly in high-risk patients.

PCT guidance – to safely reduce antibiotic exposure

Numerous randomized intervention studies have proven the role of PCT in reducing antibiotic exposure across a range of clinical settings.¹⁴⁻²⁸ PCT measurement offers several potential benefits:

Reduction of

- initial AB prescription rates
- AB treatment duration
- average length of stay (LOS)
- AB resistance



“PCT helps me to prescribe antibiotics rationally and thus to save their power for future generations.”



B·R·A·H·M·S PCT – proven across diverse clinical settings



Intensive Care Medicine

Early detection and specific clinical intervention have been shown to be crucial for the improved outcome of patients with sepsis.

PCT can facilitate

- **early diagnosis of sepsis,**
- **patient monitoring and**
- **reduction in antibiotic exposure**

without any adverse impact on patient outcome.



Emergency Medicine

Many ED patients present with non-specific overlapping symptoms that may be caused by infection as well as other reasons.

PCT measurement can **confirm the initial suspicion of infection** thus helping to accelerate treatment decisions and to prioritize resources in an emergency department.



Surgery

Surgical site infections are a major source of nosocomial infections.

PCT can **promptly detect infectious complications** post surgery or after multiple trauma thus **reducing antibiotic exposure and length of hospital stay** in these patients.



Cardiology

Patients with Acute Heart Failure (AHF) or Lower Respiratory Tract Infection (LRTI) usually present to the ED with the common complaint of dyspnea. Differentiating AHF from LRTI is challenging due to overlapping clinical picture and radiological findings.

Including PCT in clinical diagnosis **increases diagnostic certainty of pneumonia in AHF patients.**



Pediatrics

In children with fever, it is at times difficult to assess the source, type and severity of the infection correctly. This often results in an overprescription of antibiotics.

PCT can rapidly **verify the initial clinical suspicion of bacterial infection** thus enabling a more judicious use of antibiotics.



Neonatology

Neonatal infection is a challenge for the treating physician.

The high sensitivity and specificity of PCT **support diagnosis of neonatal sepsis** from the first day of life on. Serial measurements can also **support significant reduction in antibiotic treatment duration**.

Safely reduce antibiotic exposure

Antibiotics are a limited resource. At the current pace of injudicious use, all antibiotics will soon become ineffective.

B·R·A·H·M·S PCT supports responsible use of antibiotics to prolong their effectiveness.

PCT guidance of antibiotic therapy has a proven utility across diverse clinical settings: ICU, ED, Surgery, Cardiology, Pediatrics, and Neonatology.



B·R·A·H·M·S PCT assays

Meeting the highest international quality standard

PCT cut-offs and clinical algorithms were established by use of the global reference standard Thermo Scientific™ B·R·A·H·M·S PCT™ sensitive KRYPTOR™ assay. All B·R·A·H·M·S PCT assays use **original raw material** from B·R·A·H·M·S GmbH, are **calibrated on the same standard** and offer excellent correlation and concordance at the **established clinical cut-offs**.

B·R·A·H·M·S PCT – Secured clinical decision making independent of platform



	B·R·A·H·M·S PCT™ sensitive KRYPTOR™	
	B·R·A·H·M·S PCT™ LIA	
	B·R·A·H·M·S PCT™-Q	
	B·R·A·H·M·S PCT™ direct	
	ALINITY i B·R·A·H·M·S PCT	
	ARCHITECT B·R·A·H·M·S PCT	
	VIDAS® B·R·A·H·M·S PCT	
	LIAISON® B·R·A·H·M·S PCT II GEN	
	Lumipulse® G B·R·A·H·M·S PCT	
	Elecsys® B·R·A·H·M·S PCT	
	Samsung IB B·R·A·H·M·S PCT	
	ADVIA Centaur® B·R·A·H·M·S PCT	
	Atellica® IM B·R·A·H·M·S PCT	



Automated sensitive assay



Manual assay



Point of care test

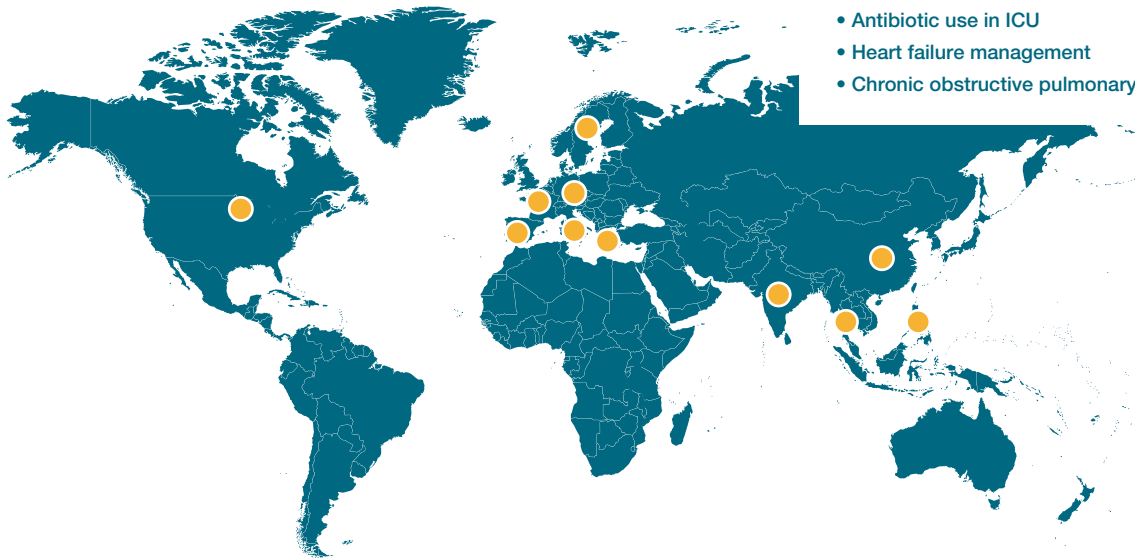
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PCT in guidelines

PCT is included in several clinical guidelines across the world

PCT is incorporated in guidelines for various clinical indications

- Sepsis
- Community acquired pneumonia
- Nosocomial pneumonia
- Neonatal infections
- Bacterial meningitis
- Pediatric sepsis
- Elderly with LRTI
- Antibiotic use in ICU
- Heart failure management
- Chronic obstructive pulmonary disease



Surviving Sepsis Campaign: “We suggest that measurement of procalcitonin levels can be used to support **shortening the duration of antimicrobial therapy** in sepsis patients.”

Source: International Guidelines for Management of Sepsis and Septic Shock, 2016²⁹

-9%
overall treatment costs³³

Cost savings

The economic impact of PCT-guided treatment has been studied through health economic modeling.³⁰⁻³²

Treatment cost reductions ranging from 9% to 12% have been demonstrated across various countries.³³



Save antibiotics for the future

B-R-A-H-M-S PCT supports responsible use of antibiotics to prolong their effectiveness

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Clinical Diagnostics

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