Thermo Scientific B·R·A·H·M·S PCT
Improving infection management

bacterial infections and sepsis

procalcitonin testing

Contributes to early diagnosis • indicates infection severity • reflects efficacy of initiated therapy • comforts decision to stop antibiotic therapy • allows reduction of antibiotic exposure and related side-effects • optimizes patient management and resource allocation

Thermo SCIENTIFIC

Diagnosis and monitoring of sepsis

Clinical need for earlier detection of sepsis

Early detection and specific clinical intervention has been shown to be crucial for the improved outcome of patients with sepsis. Sepsis can be difficult to distinguish from other, non-infectious conditions in critically ill patients with clinical signs of acute inflammation. Therefore, in the early phase of the disease process it may be difficult to decide on the appropriate therapeutic measures for the individual patient.

Additional **specific information** would be helpful **to increase the accuracy of sepsis diagnosis at an early stage**. A parameter which fulfills these demands to a high degree is Procalcitonin (PCT).

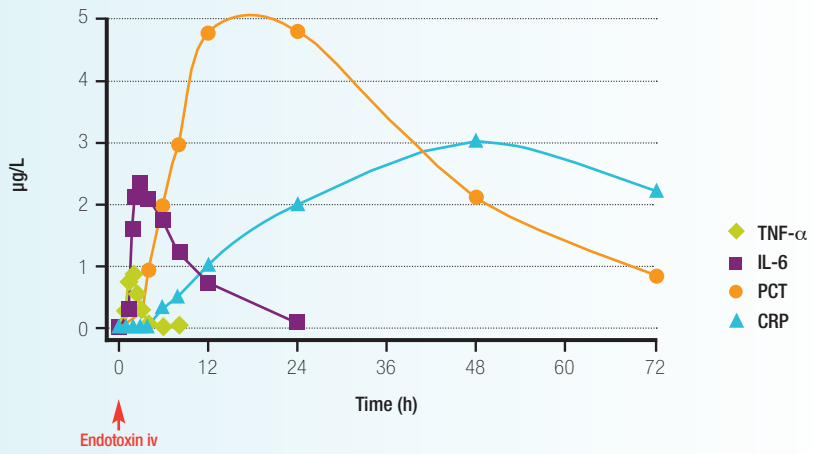
PCT – fast and highly specific increase in bacterial infection and sepsis

One **major advantage** of PCT compared to other parameters is its **early and highly specific increase in response to bacterial infections and sepsis**.[17,28,31] Thus, in septic conditions increased PCT levels can be observed 3-6 hours after infectious challenge.

Low PCT values (<0.25 µg/L) in patients with clinical signs of infection (CAP, UTI) indicate a low probability for blood culture proof of bacterial infection, whereas elevated PCT values (>0.25 µg/L) seem to correlate with the bacterial load and positive blood culture result.[32,47]

PCT levels in sepsis are generally greater than 1-2 µg/L and often reach values between 10 and 100 µg/L, or considerably higher in individual cases, thus enabling the diagnostic differentiation between various clinical conditions and a severe bacterial infection (sepsis).

Figure 1: **Kinetics of PCT compared to other inflammatory markers upon infection** [6,13,17,28]



PCT – best parameter for early sepsis diagnosis

PCT has been shown to be the best marker for differentiating patients with sepsis from those with systemic inflammatory reaction not related to infectious cause (Figure 2a, b).[17,31,46,48]

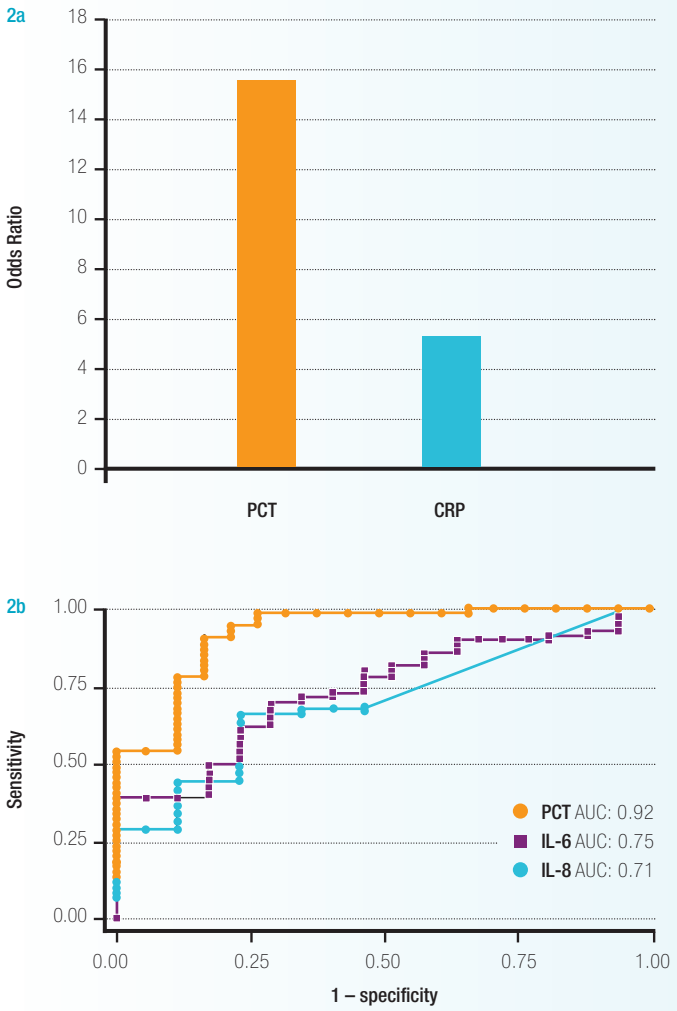
Figure 2a: PCT versus CRP [46]
PCT: Better differentiation of bacterial infection from non-infectious causes of inflammation

Global odds ratios for diagnosis of infection complicated by systemic inflammation were 15.7 for the 25 studies (2966 patients) using PCT (95% confidence interval, 9.1-27.1) (PCT; ●) and 5.4 for the 15 studies (1322 patients) using C-reactive protein (95% confidence interval, 3.2-9.2) (CRP; ●)

Figure 2b: PCT versus IL-6 and IL-8 [17]
PCT: More accurate diagnosis of sepsis than IL-6 and IL-8

Receiver operating characteristics (ROC) curves comparing serum procalcitonin (PCT), interleukin 6 (IL-6) and interleukin 8 (IL-8) for detection of sepsis on day of admission to ICU.

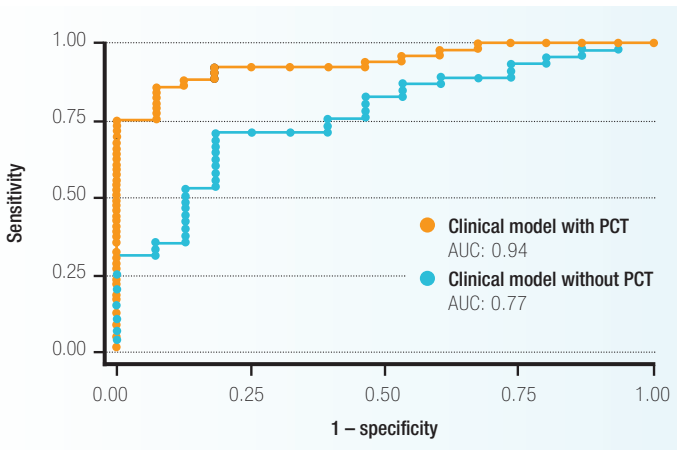
Figure 2: Comparison of diagnostic performances of various markers for diagnosis of bacterial infection/sepsis



Only PCT significantly improves accuracy of clinical sepsis diagnosis

PCT is the only laboratory parameter that made a significant contribution to the clinical diagnosis of sepsis (Figure 3).[17] In contrast to PCT, for IL-6, IL-8 and CRP such effect could not be demonstrated.

Figure 3: Accuracy of sepsis diagnosis based on a clinical model with and without PCT [17]



Increased PCT values – best indicator for the severity of infection and organ dysfunction

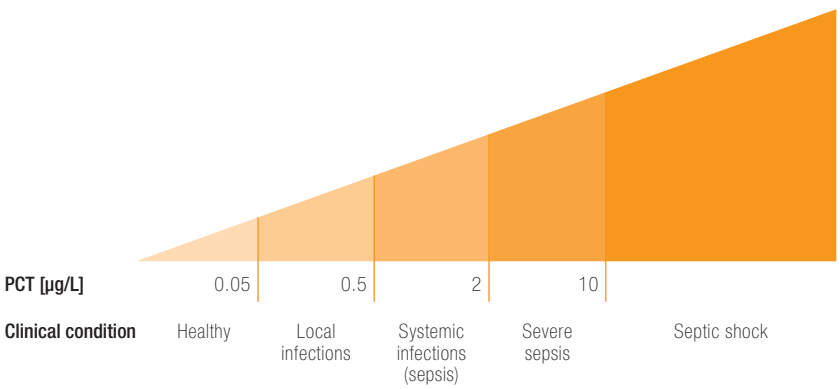


Figure 4: PCT increase reflects the continuous development from a healthy condition to the most severe states of disease (severe sepsis and septic shock)

Figure 5a, b: Differentiation between SIRS (Systemic Inflammatory Response Syndrome), sepsis, severe sepsis and septic shock by PCT and IL-6 [17]

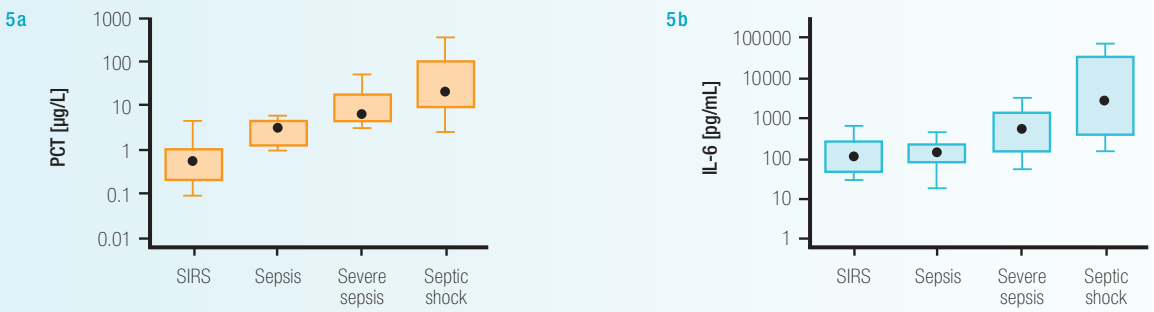
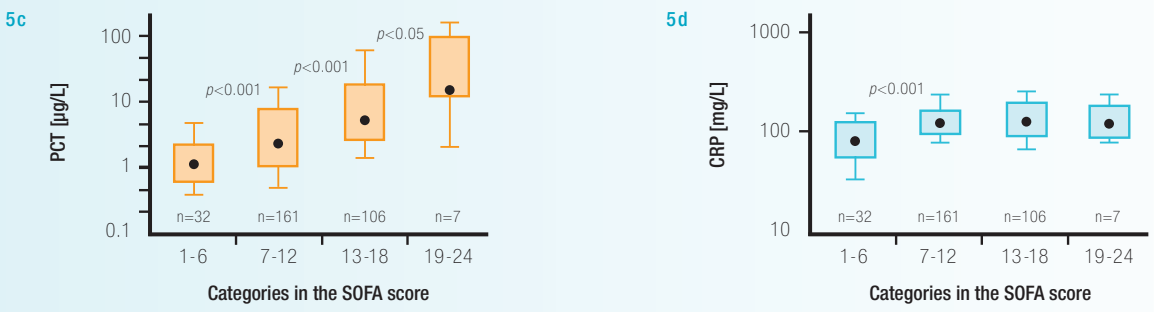


Figure 5c, d: Assessment of severity of disease (increasing organ dysfunction) by PCT and CRP [29]



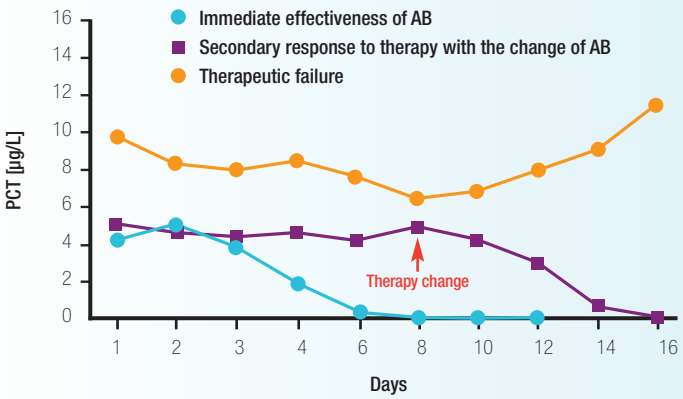
PCT development accurately reflects the progression of the disease during infection and is more reliable than other parameters.

PCT kinetics can be used to assess the effectiveness of treatment

Effective antibiotic (AB) treatment is reflected by declining PCT values,[7] consistent with its half-life time of about 20-24 hours.[28] 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 (Figure 6).[39,44]

This has been demonstrated for a variety of clinical conditions, *e.g.* for the case management of patients with ventilator-associated pneumonia (VAP),[24,43] with community-acquired pneumonia (CAP),[11,27] and for patients with sepsis or septic shock.[3,19,33] **Appropriate empiric antibiotic treatment was found to be reflected by a significant decline of PCT from D2 to D3.**[7]

Figure 6: Typical course of PCT serum level according to patient's response to antibiotic treatment (n=109)[44]



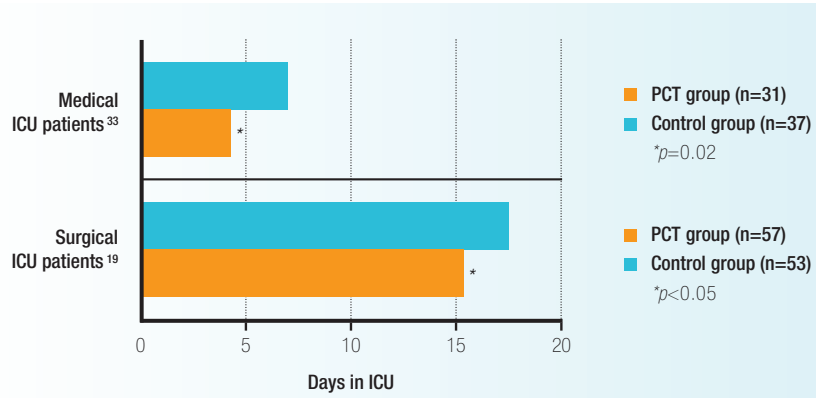
PCT impact on diagnostic and therapeutic decisions and resource allocation

Initial studies on the implication of utilizing PCT showed that **systematic use of PCT has an impact both on the decision on additional diagnostic measures**, such as microbiological tests, invasive procedures or imaging,[2,23,36] **as well as on duration of antibiotic therapy and length of stay in ICU** (Figure 7).[3,11,18,19,26,33,38]

This allows

- **a more individualized approach for each patient**
- **a more judicious, shorter use of antibiotics**
- **shorter stay in ICU**
- **cost savings**[49]

Figure 7: Length of ICU stay for patients treated according to PCT-based algorithm compared to control group treated according to routine practice[19,33]



PCT impact on antibiotic therapy

The duration of antibiotic therapy in critically ill patients with sepsis is still based on empirical rules, which may lead to antibiotic overuse and selection pressure.

It has been demonstrated now in more than 1000 ICU patients that the application of a **decision algorithm** based on the relative decrease of plasma PCT levels over time (Figure 8) allows a **significant reduction in the duration of antibiotic therapy and potentially also on ICU stay**, without apparent harm to patients with severe sepsis and septic shock (Figure 9-10).[21,39]

PCT-guided algorithm allows **significant reduction of antibiotic treatment duration** compared to routine practice (Figure 9).[21] Shorter antibiotic therapy is associated with reduced costs, particularly when broad-spectrum antibiotics are used.

An even more impressive impact on the treatment-related costs may be expected from the possible **reduction of ICU length of stay** as demonstrated in one study in medical and another in surgical ICU patients treated for sepsis. In both studies the patients in the PCT group were disposed from ICU to normal ward 2 days earlier than standard group patients (Figure 7).[19,33]

PCT-guidance strategy was shown to be non-inferior regarding 28 day mortality compared to routine practice (Figure 10).[21]

Figure 8: **PCT algorithm for stopping antibiotics in patients with sepsis in the ICU**[39]

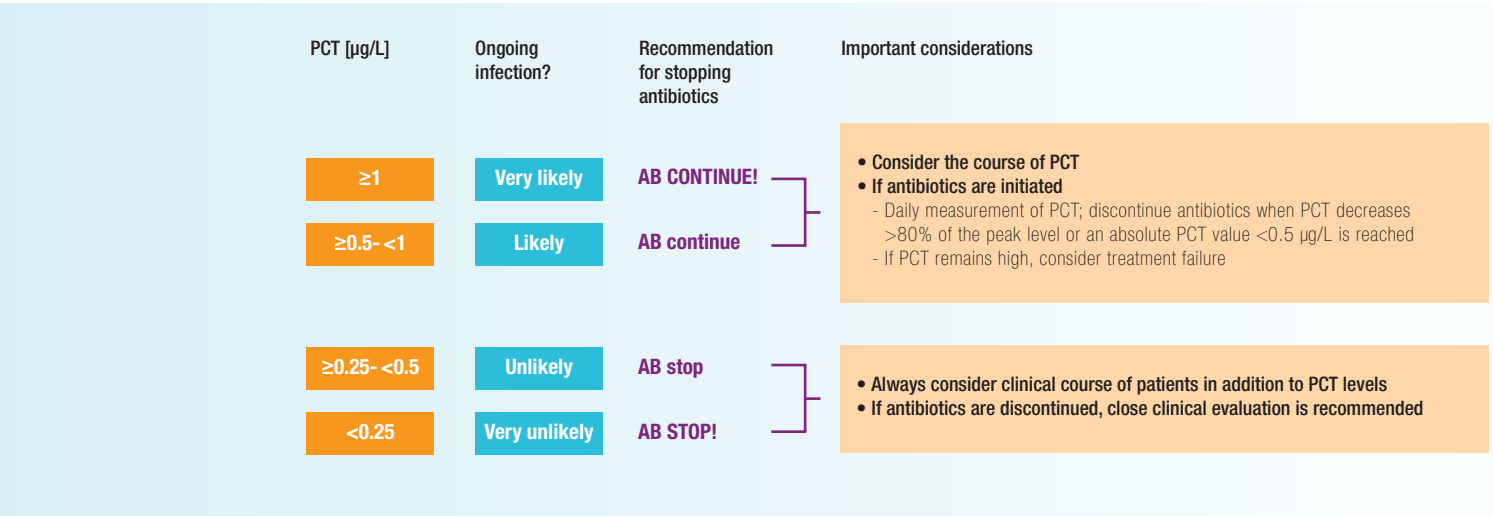


Figure 9: Duration of AB treatment guided by a PCT-based algorithm versus routine practice [21]

9a: Duration of AB treatment for first episode of infection

The implementation of procalcitonin-guided algorithms **decreased the duration of antibiotic therapy for the first episode of infection by approximately 2 days** (weighted mean difference 2.36 days; 95% confidence interval, 3.11 to 1.61).

9b: Total duration of AB treatment

The implementation of procalcitonin-guided algorithms **decreased the total duration of antibiotic treatment by 4 days** (fixed effect model: weighted mean difference: 4.19 days; 95% confidence interval, 4.98 to 3.39).

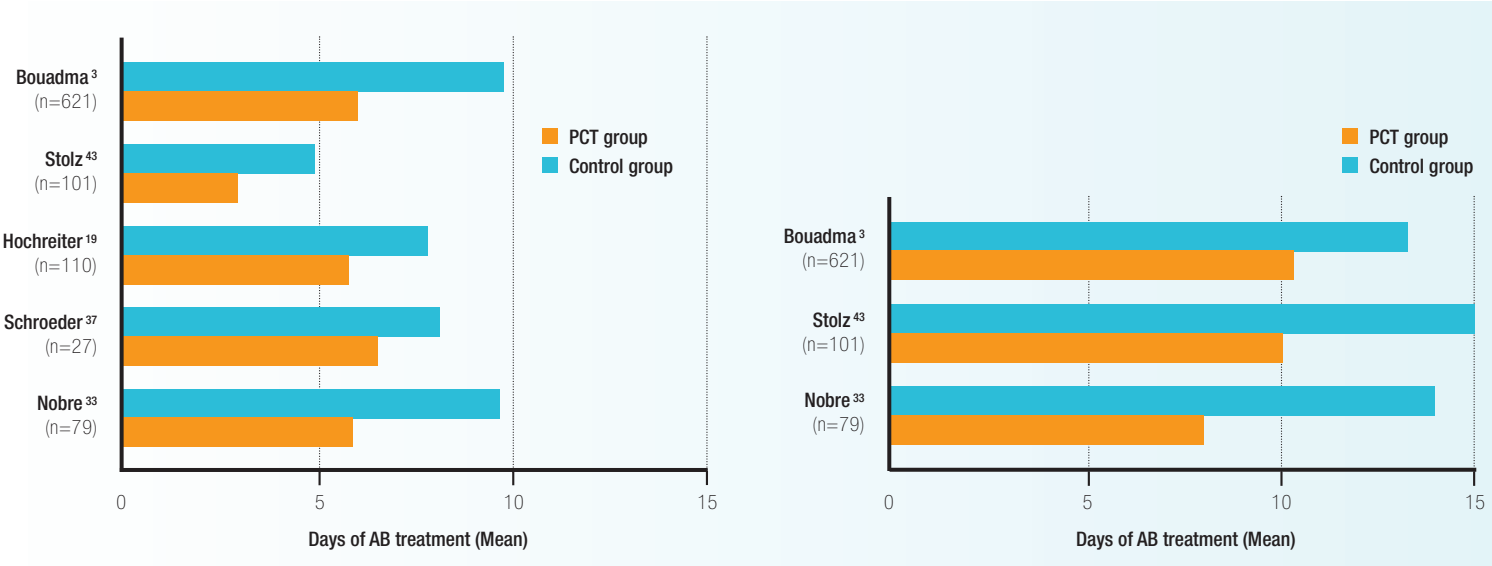
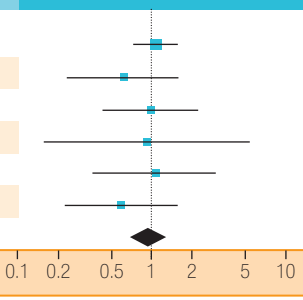


Figure 10: 28 day mortality in patients treated based on PCT-guided algorithm compared to those patients treated according to routine practice [21]

Study or sub-category	PCT-guided group		OR (fixed) 95% CI	Routine practice	
	n	Events (n)		Events (n)	n
Bouadma 3	307	65		64	314
Stolz 43	51	8		12	50
Hochreiter 19	57	15		14	53
Schroeder 37	14	3		3	13
Nobre 33	39	8		8	40
Svoboda 45	38	10		13	34
Total (95% CI)	**506**	**109**		**114**	**504**



Forest plot showing the comparison of PCT-guided algorithms vs. routine practice. The size of each square represents the proportion of information provided by each study. The vertical line depicts the point of "no difference" between the two groups, and the horizontal lines correspond to the 95% confidence intervals (CIs). Diamonds represent the pooled odds ratio (OR) for all studies.

With PCT guidance, the duration of antibiotic therapy of critically ill patients can be significantly reduced compared to the standard approach, with a similar outcome in both groups.[21]

Diagnosis and monitoring
of clinically relevant bacterial LRTI

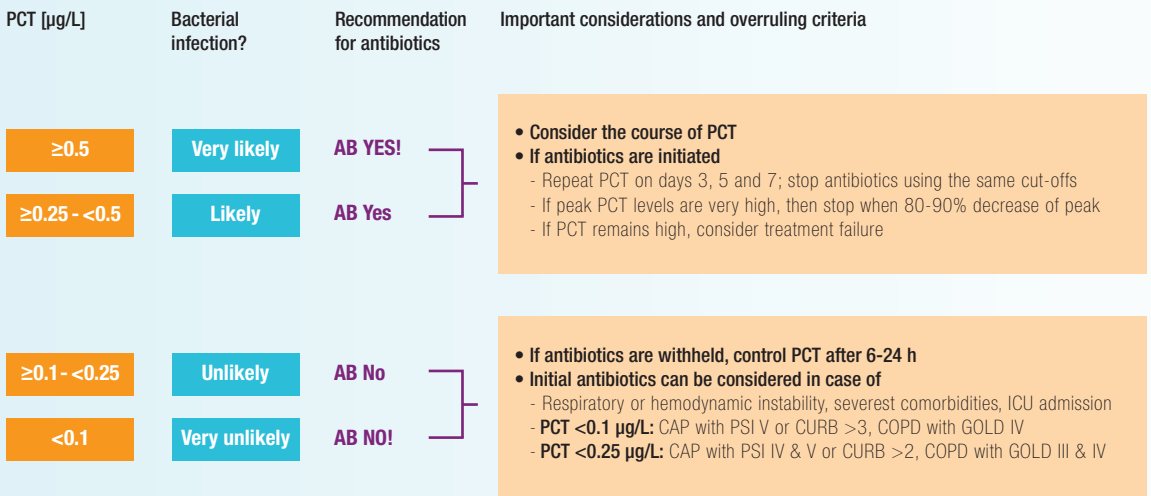
Lower respiratory tract infection (LRTI) – major cause of sepsis

It is common knowledge that the majority of septic cases in the ICU are caused by pneumonia.[10] LRTI should be considered as a potential pre-septic condition which requires early diagnosis and treatment. Such an approach may help to decrease the number of patients developing sepsis and, subsequently, increase their chance of survival.

Early clinical assessment of LRTI by sensitive PCT measurement

Sensitive PCT measurement techniques will capture minor elevations of PCT in the blood circulation [12,30,41] – therefore the **detection of clinically relevant bacterial infection is possible at a much earlier stage of the disease.**

Figure 11: **PCT algorithm for patients with LRTI** [39]



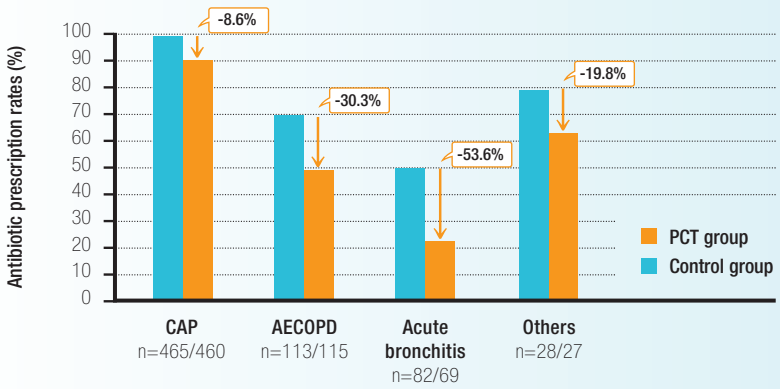
Identification of LRTI patients who require antibiotic therapy

Due to the high specificity of PCT for bacterial infection, **PCT measurement at relatively low concentrations can help to differentiate patients with clinically relevant LRTI who require antibiotic therapy (AB)** from those with viral infection or minor bacterial infection who do not require antibiotic treatment.[10]

For patients who are clinically assessed as requiring treatment with antibiotics, but who have low PCT values (<0.25 µg/L), it is recommended that antibiotics should not be administered. For patients with very low PCT values (<0.1 µg/L), AB treatment is strongly discouraged (see decision algorithm, Figure 11).

Data are available now from randomized controlled trials in about 3000 patients with LRTI, demonstrating that with this approach **AB exposure can be significantly reduced without impairment of the outcome compared to standard treatment** (Figure 12).[38,39]

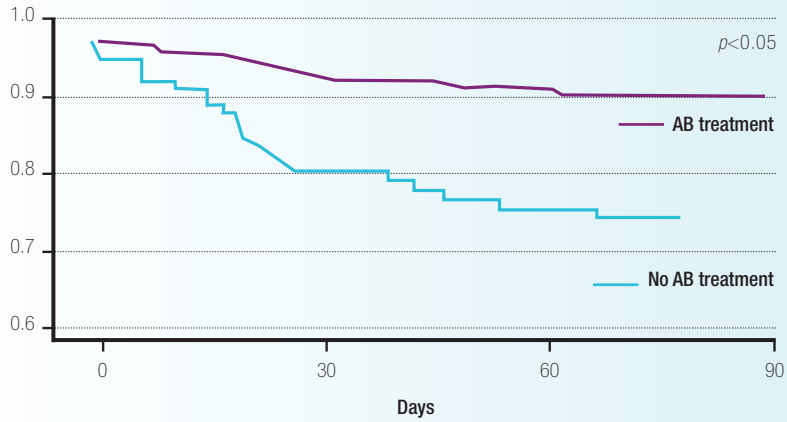
Figure 12: AB treatment based on standard clinical assessment of LRTI and guided by PCT level [38]
Patient groups with LRTI and relative reduction of AB prescription by PCT guidance: CAP (community-acquired pneumonia); AECOPD (acute exacerbation of chronic obstructive pulmonary disease); acute bronchitis; others



Consider infection also in patients with other primary diagnosis

PCT may also be helpful in patients presenting to the emergency department with other primary disease, *e.g.* with cardiac insufficiency, but who have concomitant infection, *e.g.* pneumonia. It was observed that acute heart failure patients with elevated PCT levels who received antibiotic treatment had a better outcome than the control group not treated with antibiotics (Figure 13).[25]

Figure 13: Survival probability by days in acute heart failure patients with accompanying pneumonia and PCT values >0.2 µg/L treated or not treated with AB [25]



Tailoring the duration of antibiotic therapy to the individual need of patients with LRTI

LRTI patients will usually be treated with AB for 7-10 days, patients with community-acquired pneumonia (CAP) for 10-14 days.

Several mono- and multicenter randomized controlled trials demonstrate that the duration of therapy can be guided for each patient individually by **monitoring the development of PCT concentration** over the course of antibiotic treatment.

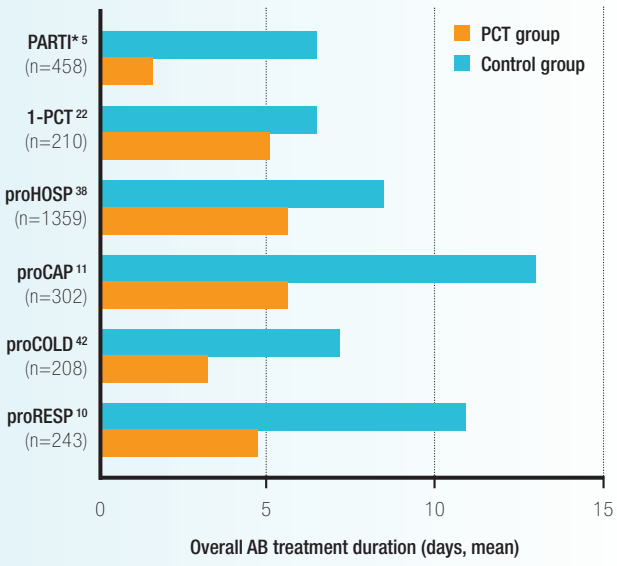
It is recommended that AB therapy conclude when PCT levels fall below 80-90% of peak value and it is strongly recommended that AB therapy conclude when PCT levels fall below 0.1 µg/L (Figure 11).[39]

The integration of PCT into diagnostic and treatment algorithms allows a better identification of patients with clinically relevant bacterial infection and a **more judicious AB prescription. In addition it becomes possible to tailor the duration of therapy** to the individual clinical situation **of each patient**.

This PCT-based approach enables a more targeted use of clinical and financial resources by

- More targeted initiation of diagnostic measures like blood culture and imaging
- Reducing expenditures on antibiotics both in hospital and primary care
- Reducing number of treatment days and overall AB exposure
- Reducing risk of AB resistance development

Figure 14: **Impact of PCT-guided treatment algorithm on antibiotic treatment duration of patients with LRTI: Results of randomized controlled studies** [39]



* PARTI study: primary care treatment; all other studies: hospital treatment

With PCT guidance the duration of antibiotic therapy of LRTI patients can be significantly reduced compared to the standard approach, with a similar outcome in both groups. [10,11,21,38,39,42]

Clinical evidence and medical impact of PCT

Due to the high level of evidence for the impact of a PCT-assisted clinical strategy (more than 2000 clinical and scientific publications with 14 randomized controlled interventional studies), PCT has been included into a number of national and international clinical recommendations.

The American guidelines for evaluation of new fever in critically ill adult patients recommend serum PCT levels as an adjunctive diagnostic tool for discriminating infection as the cause for fever or sepsis presentations.[34]

PCT is recommended for early sepsis diagnosis and discontinuation of antibiotic therapy *e.g.* by German Sepsis Guidelines [15] and Surviving Sepsis Guidelines.[14]

The German guidelines for the management of adult lower respiratory tract infections (LRTI) recommend PCT for antibiotic stewardship in patients with AECOPD and community-acquired pneumonia.[35]

Recently, PCT was also included into the European guidelines for management of adult LRTI.[50]

References

1 American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference, Crit Care Med 1992, 20 (6): 864-874
2 Blanchais T et al. Arch Pediatr 2011, 18 (9): 955-61
3 Bouadma L et al. Lancet 2010, 375 (9713): 463-474
4 B·R·A·H·M·S internal data
5 Briel M et al. Arch Intern Med 168 (18): 2000-7
6 Brunkhorst FM et al. Intensive Care Medicine 1998, 24: 888-892
7 Charles PE et al. Crit Care 2009, 13 (2): R38
8 Chiesa C et al. Clin Infect Dis 1998, 26: 664-672
9 Chiesa C et al. Clin Chem 2003, 49 (1): 60-68
10 Christ-Crain M et al. Lancet 2004, 363 (9409): 600-607
11 Christ-Crain M et al. Am J Respir Crit Care Med. 2006, 174, 84-93
12 Christ-Crain M & Müller B, Swiss Med Wkly 2005, 135: 451-460
13 Dandona P, J. Clin. Endocrinol. Metab. 1994, 79: 1605-1608
14 Dellinger P, 41st Critical Care Congress (SCCM), Houston (Texas) 2012
15 Reinhardt K et al. Ger Med Sci. 2010; 8: Doc14
16 Falcoz PE et al. Eur J Cardiovasc Surg 2005, 27 (6): 74-78
17 Harbarth S et al. Am J Respir Crit Care Med 2001, 164: 396-402
18 Heyland DK et al. Crit Care Med 2011, 39 (7): 1792-1799
19 Hochreiter M et al. Crit Care 2009, 13 (3): R83
20 Joram N et al. Eur J Clin Microbiol Inf Dis 2011, 30 (8): 1005-1013
21 Kopterides P et al. Crit Care Med 2010, 38 (11): 2229-41
22 Kristoffersen KB et al.Clin Microbiol Infect 2009, 15 (5): 481-7
23 Leroy S et al. J Pediatr 2007, 150 (1): 89-95
24 Luyt CE et al. AJRCCM 2005, 171: 48-53
25 Maisel A et al. Eur J Heart Fail doi:10.1093/eurjhf/hfr177
26 Marc E et al. Arch Pédiatr 2002, 9: 1-7
27 Masia M et al. Chest 2005, 128 (4): 2223-2229
28 Meisner M, Procalcitonin – Biochemistry and Clinical Diagnosis, ISBN 978-3-8374-1241-3, UNI-MED, Bremen 2010
29 Meisner M et al. Critical Care 1999, 3: 45-50
30 Morgenthaler N et al. Clin Lab 2002, 48 (5-6): 263-270
31 Müller B et al. Crit Care Med 2000, 28 (4): 977-983
32 Müller F et al. Chest 2010, 138 (1): 121-9
33 Nobre S et al. Am J Respir Crit Care Med 2008, 177 (5): 498-505
34 O'Grady NP et al. Crit Care Med 2008, 36 (4): 1330-49.
35 Höffken G et al. Pneumologie 2009, 63: e1-e68
36 Rau B et al. Ann Surg 2007, 245: 745-754
37 Schroeder S et al. Langenbecks Arch Surg 2009, 394: 221–226
38 Schuetz P et al. JAMA 2009, 302 (10): 1059-66
39 Schuetz P et al. Expert Rev Anti Infect Ther 2010, 8 (5): 575-87
40 Schuetz P et al. Clin Biochem 2010, 43 (3): 341-4
41 Steinbach G et al. Clin Chem Lab Med 2004, 42 (4): 440-449
42 Stolz D et al. Chest 2007, 131 (1): 9-19
43 Stolz D et al. Eur Respir J 2009, 34 (6): 1364-75
44 Stüber F, 21st Int. Congress of Intensive Care and Emergency Medicine (ISICEM), Brussels 2001
45 Svoboda P et al. Hepato-Gastroenterology 2007, 54: 359-363
46 Uzzan B et al. Crit Care Med 2006, 34: 1996-2003
47 van Niewkoop et al. Critical Care 2010, 14: R206
48 van Rossum AM et al. Lancet Infect Dis 2004, 4 (10): 620-630
49 Wilke MH et al. Eur J Med Res 2011, 16 (12): 543-8
50 Woodhead M et al. Clin Microbiol Infect 2011, 17 (Suppl. 6): E1-E59

Interpretation of results

Healthy individuals: Determination of normal values with a highly sensitive assay revealed normal values to be below 0.05 µg/L.[30]

PCT serum concentrations are elevated in clinically relevant bacterial infections and continue to rise with the increasing severity of the disease. However, 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, clinicians should use the PCT results in conjunction with the patient's clinical signs and other laboratory findings, and interpret the values in the context of the patient's clinical situation.* The reference ranges below are provided for guidance purposes only.

Diagnosis of systemic bacterial infection/sepsis [1,17]

SIRS, sepsis, severe sepsis, and septic shock are categorized according to the criteria of the consensus conference of the American College of Chest Physicians/Society of Critical Care Medicine.[1]

PCT <0.5 µg/L	
Systemic infection (sepsis) is not likely.	Low risk for progression to severe systemic infection (severe sepsis).
Local bacterial infection is possible.	**Caution:** PCT levels below 0.5 µg/L do not exclude an infection, because localized infections (without systemic signs) may be associated with such low levels. Also if the PCT measurement is performed immediately after bacterial challenge (usually <6 hours), these values may still be low. In this case, PCT should be re-assessed 6-24 hours later.[10]
PCT ≥0.5 - <2 µg/L	
Systemic infection (sepsis) is possible, but various conditions are known to induce PCT as well.*	Moderate risk for progression to severe systemic infection (severe sepsis). The patient should be closely monitored both clinically and by re-assessing PCT within 6-24 hours.
PCT ≥2 - <10 µg/L	
Systemic infection (sepsis) is likely, unless other causes are known.*	High risk for progression to severe systemic infection (severe sepsis).
PCT ≥10 µg/L	
Important systemic inflammatory response, almost exclusively due to severe bacterial sepsis or septic shock.	High likelihood of severe sepsis or septic shock.

Differential diagnosis of Lower Respiratory Tract Infections [10,39]

PCT <0.1 µg/L	
Indicates absence of bacterial infection.	Use of antibiotics strongly discouraged, also in the presence of impaired pulmonary reserve in AECOPD.
PCT ≥0.1 - <0.25 µg/L	
Bacterial infection unlikely.	The use of antibiotics is discouraged.
PCT ≥0.25 - <0.5 µg/L	
Bacterial infection is possible.	Advice to initiate antimicrobial therapy.
PCT ≥0.5 µg/L	
Suggests the presence of bacterial infection.	Antibiotic treatment strongly recommended.

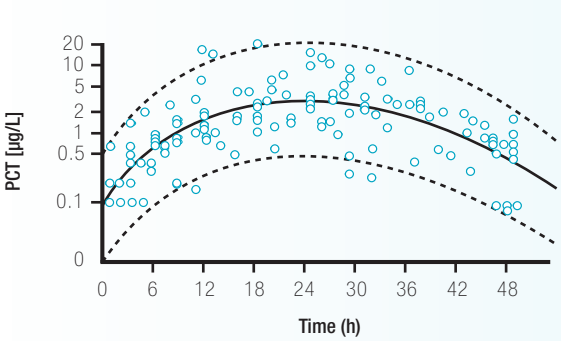
PCT reference ranges in neonates

Early and reliable differentiation of infected and non-infected newborns is possible with **PCT determination directly after birth from cord blood** when neonatal infection is suspected. **A value <0.5 µg/L practically excludes the presence of infection** (calculated best cut-off 0.6 µg/L with a negative predictive value of 99% and a post-test probability of 0.001%).[20]

After birth the PCT values of the newborn increase over the first 24 hours and stay elevated during the first 2 days of life.

Therefore separate, well-defined reference ranges apply to newborn infants at different hours of age during the first 48 hours of life (Figure 15a). However, **also during these first 2 days of life, the PCT values of newborns suffering from early sepsis are significantly higher than those of non-infected newborns (Figure 15b), so that PCT can be used for sepsis diagnosis**.

The adult reference range applies from day 3 after birth.[8,9]



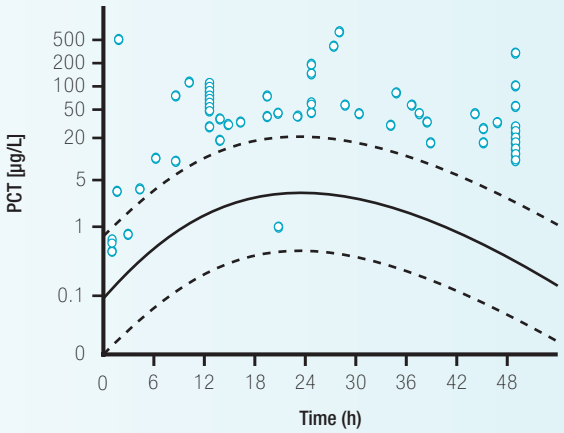


Figure 15a: Healthy newborns
95% reference range of PCT in healthy newborns (n=83) in the first 48 hours after birth. Individual measurements are illustrated. The unbroken line characterizes the geometric mean and the dotted lines the 95% reference range.[8]

Figure 15b: Septic newborns
PCT values in neonates presenting symptoms of sepsis within the first 48 hours of birth. Individual measurements are displayed. The unbroken line refers to the geometric mean while the dotted lines refer to the 95% reference range in the non-infected normal population.[8]

* NOTE:
Increased PCT levels may not always be related to systemic bacterial infection.[28]
There are a few situations described where PCT can be elevated by non-bacterial causes. These include, but are not limited to
- neonates <48 hours of life (physiological elevation) (see reference values Figure 15)
- the first days after a major trauma, major surgical intervention, severe burns, treatment with OKT3 antibodies and other drugs stimulating the release of pro-inflammatory cytokines
- patients with invasive fungal infections or acute attacks of plasmodium falciparum malaria
- patients with prolonged or severe cardiogenic shock or prolonged severe organ perfusion anomalies
- patients with severe liver cirrhosis and acute or chronic viral hepatitis
- patients with small cell lung cancer or medullary C-cell carcinoma of the thyroid.

Low PCT levels do not automatically exclude the presence of bacterial infection.[28]
Such low levels may be obtained, *e.g.*, during the early course of infections, in localized infections and in subacute endocarditis. Therefore, follow-up and re-evaluation of PCT in clinical suspicion of infection is pivotal. The PCT measuring technique should be chosen depending on the intended clinical use (see Figure 16).

Practical aspects of PCT testing

	Frequently asked questions	Answers
PCT induction and kinetics	What is PCT and where is it produced?	PCT is the **prohormone of calcitonin**. Whereas calcitonin is secreted by the C-cells of the thyroid after hormonal stimulation, **PCT can be produced by numerous cell types and organs after proinflammatory stimulation**, especially when caused by bacterial challenge.[12]
	Rapid increase after bacterial infection	PCT increases ~3 hours after bacterial infection, reaching maximum values after 6-12 hours.[12]
	Half-life time in vivo	About 24 hours
Patient monitoring with PCT	Frequency of PCT measurement for patient monitoring	Minimum once per day
	Interpretation of PCT concentrations during **therapeutic monitoring***, *e.g.* after surgical removal of septic focus and/or after start of antibiotic therapy	~50% reduction of PCT concentration per day over several days → Indication for **success of therapeutic intervention** (surgery, antibiotic treatment) Persistent high or further increasing PCT levels → Indication for **non-controlled infectious process** justifying a re-assessment of therapeutic strategy [11,12,17,24,44]
	Interpretation of PCT concentrations during **infectious disease monitoring* of high-risk patients**, *e.g.* after extended surgery or polytrauma	Low PCT levels or a significant reduction of primarily increased PCT levels by ~50% per day over the subsequent 2-3 days to reach low values. → **No infectious complication** Persistent increased PCT levels or newly increasing PCT levels indicate infectious complication → **Infectious complication** [12,16]
Sample material and stability	**Sample material** for PCT measurement	Depending on the used assay format **human serum or plasma** may be used.* PCT values measured in patient samples of arterial blood are ~4% higher than in samples from venous blood.[28] Current assay formats are suitable for use with human serum or plasma only. Other human body fluids or samples from other species cannot be used.
	Stability	
	In vitro stability	**Very stable** in vitro,[28] no special requirements for pre-analytical sample handling and storage
	At room temperature	PCT is stable up to 24 hours in serum, plasma[25] and even in whole blood.[4] Individual deviations might occur due to individual proteolytic activities.
	At -20 °C	Stable for months[40]
	Freeze/thaw, 3 cycles	<2% loss of PCT in the sample
PCT and blood culture	What is the additive value of PCT measurement?	PCT allows the **fast identification of patients** who need antibiotic treatment and where a blood culture is useful.[32,47]
	Can PCT measurement replace blood cultures?	Blood cultures are needed for the identification of the causative microorganism in patients with suspected blood stream infection.

* For patient monitoring the same sample matrix should always be used.

Which assay to use? Today a rapid, semi-quantitative assay is available together with several different immunoassays for quantitative determination of PCT concentrations. All PCT determinations can be measured in either serum or plasma. Results are available within 18 minutes to 2.5 hours – depending on the choice of method used. **Choice of assay depends on intended clinical use (Figure 16).** (For detailed description of assays please see enclosed assay information.)

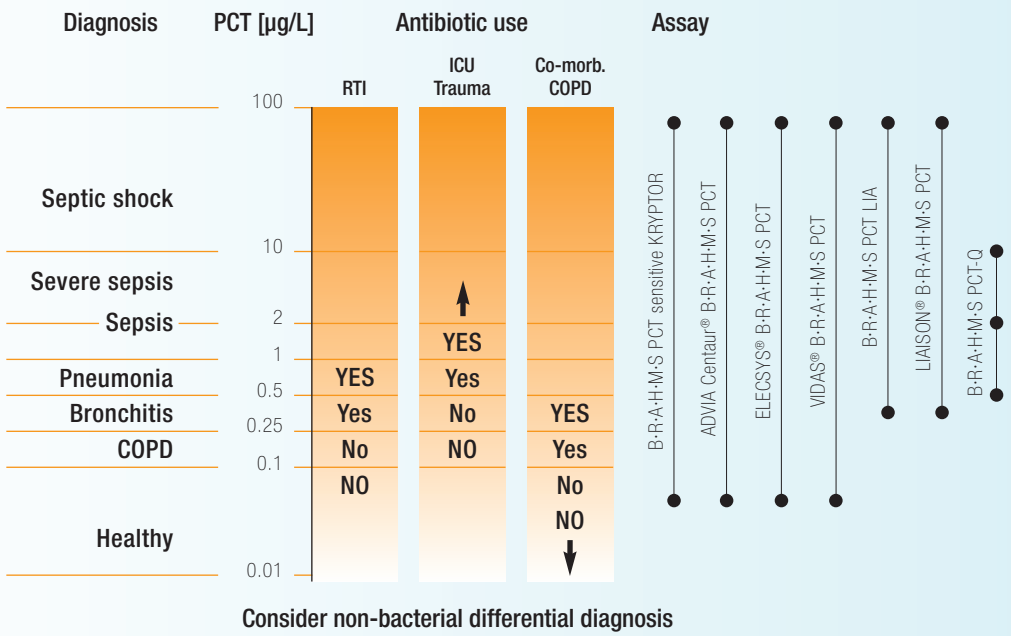


Figure 16: Application of available PCT assays for various clinical settings (adapted from Christ-Crain & Müller[12])

Cut-offs for clinical decision making (*e.g.* decision on prescription and duration of AB therapy) **depend on the clinical setting.** *E.g.*, for patients with COPD and suspicion of infection, antibiotics would be prescribed at a lower PCT value compared to a trauma patient without concomitant disease.

Decision to prescribe or withhold antibiotics should be re-assessed within the (second) 6-24 hours based on the patients clinical picture and PCT level. These values should also be considered in the clinical decision making process regarding the **duration of antibiotic therapy** as well as consideration of the clinical course of the disease.

Thermo Scientific PCT assays**

B·R·A·H·M·S **PCT sensitive** KRYPTOR*
B·R·A·H·M·S **PCT-Q**
B·R·A·H·M·S **PCT** LIA*

PCT assays** of other IVD providers

ADVIA Centaur® B·R·A·H·M·S **PCT**
ELECSYS® B·R·A·H·M·S **PCT**
LIAISON® B·R·A·H·M·S **PCT**
VIDAS® B·R·A·H·M·S **PCT***

* FDA-cleared. Please refer to US-specific instructions for use.

Other Thermo Scientific B·R·A·H·M·S Biomarkers for intensive care and emergency medicine

B·R·A·H·M·S **Neopterin-Screening** EIA
B·R·A·H·M·S **Neopterin** EIA
B·R·A·H·M·S **Neopterin** RIA

B·R·A·H·M·S **CRP ultrasensitive** KRYPTOR

B·R·A·H·M·S **MR-proADM** KRYPTOR
B·R·A·H·M·S **MR-proANP** KRYPTOR
B·R·A·H·M·S **Copeptin** KRYPTOR
B·R·A·H·M·S **Copeptin us** KRYPTOR

More about PCT and sepsis

thermoscientific.com/procalcitonin
facebook.com/AboutSepsis
twitter.com/AboutSepsis

** The manufacture and/or use of these products are covered by one or more of the following patents: AU686114, CA2142599, CN93118343, DE69317289, EP656121, JP3257796, RU2137130, US5639617, ZA9306042, DE19600875, EP880702, JP3095784, EP2028493, DE19903336, EP1026506, US7723492, EP2174143, US5569587, US5627027

Clinical Diagnostics

Thermo Fisher Scientific
B·R·A·H·M·S GmbH
Neuendorfstr. 25
16761 Hennigsdorf
Germany

+49-3302-883-0
+49-3302-883-100 fax
info.pct@thermofisher.com

www.thermoscientific.com/brahms
www.thermoscientific.com/copeptin
www.thermoscientific.com/procalcitonin
www.thermoscientific.com/kryptor

Thermo SCIENTIFIC
Part of Thermo Fisher Scientific

104656.16