KNAPPSCHAFT KLINIKEN
UNIVERSITÄTSKLINIKUM
KNAPPSCHAFTSKRANKENHAUS BOCHUM

UK RUB UNIVERSITÄTSKLINIKUM DER
RUHR-UNIVERSITÄT BOCHUM

Infektionsbiomarker im Klinikalltag

CRP, PCT & Co.

RUB

RUHR-UNIVERSITÄT BOCHUM

Interessenskonflikte

u.a. Vortragshonorare, Beratertätigkeit, Reise- und Kongressunterstützung

- Astellas Pharma GmbH
- Bayer Vital GmbH
- Biotest AG
- Bristol-Myers Squibb GmbH & Co. KGaA
- CSL Behring GmbH
- Mitsubishi Tanabe Pharma GmbH
- MSD Sharp & Dohme GmbH
- Pfizer Deutschland GmbH

Antibiotika – ja oder nein?

A 40-year-old man with no underlying lung disease has a 7-day history of mild shortness of breath with exertion, as well as cough that is now productive of purulent sputum. He reports no paroxysms of cough and no contact with ill persons in his community. He does not appear to be in distress. His temperature is 37° C, his pulse 84 beats per minute, and his respiratory rate 17 breaths per minute. On auscultation of the lungs, no rales are heard; scattered wheezes are heard in the lung bases. How should he be evaluated and treated?

Beispiel: „Akute Bronchitis“

➔ Typischerweise viraler Erreger – trotzdem in ca. 80% der Fälle Einsatz von Antibiotika...

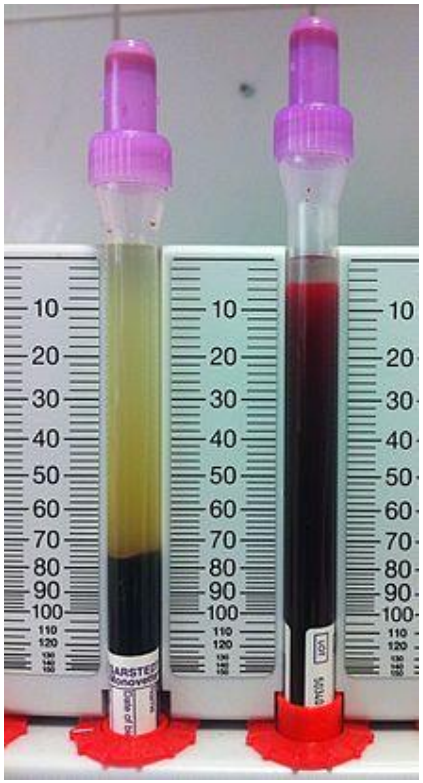
Wenzel RP et al. N Engl J Med 2006; 355:2125-2130.

Sepsis

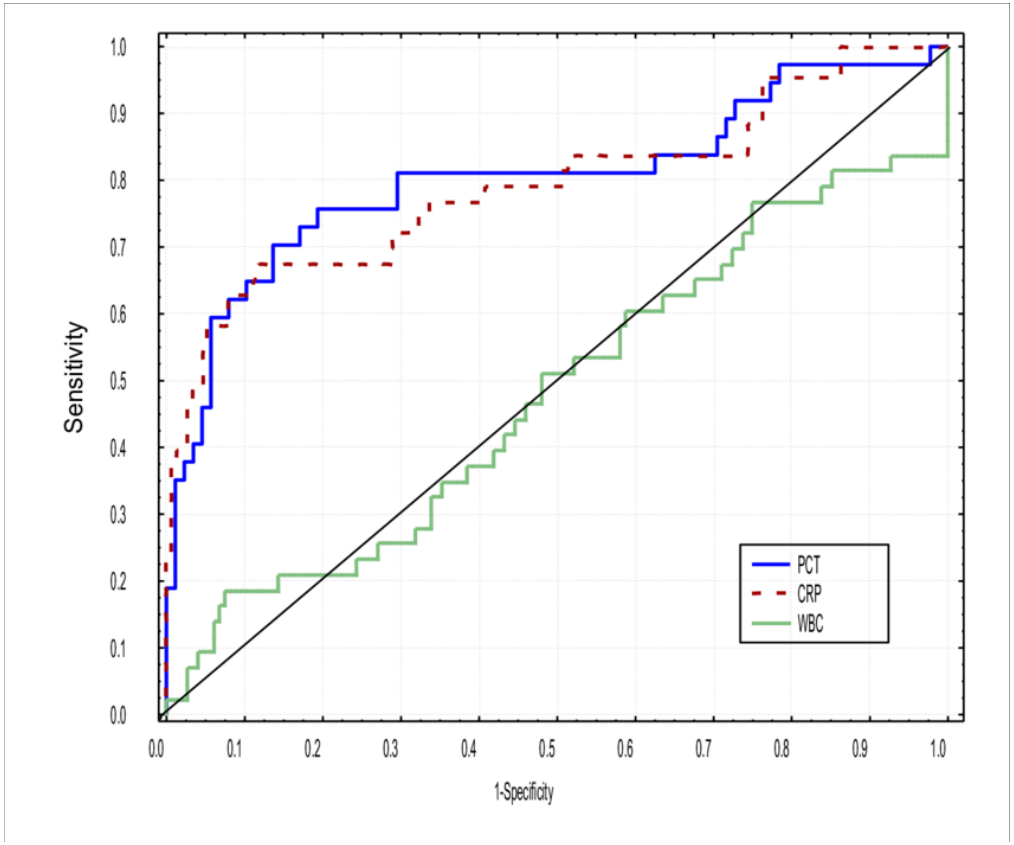
vs.

Nicht-septisches SIRS

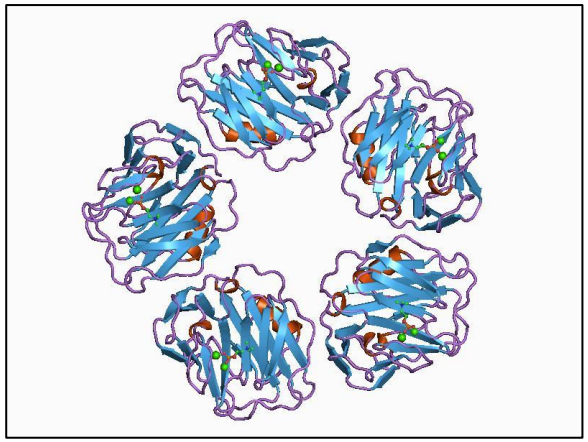
Blutsenkungsgeschwindigkeit



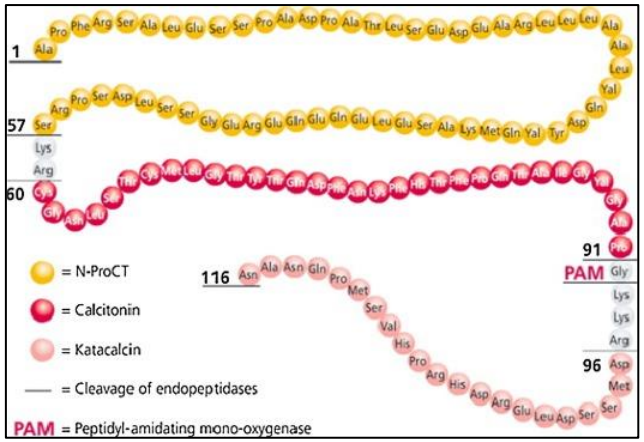
Leukozyten


Sensitivity
1-Specificity
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
PCT
CRP
WBC

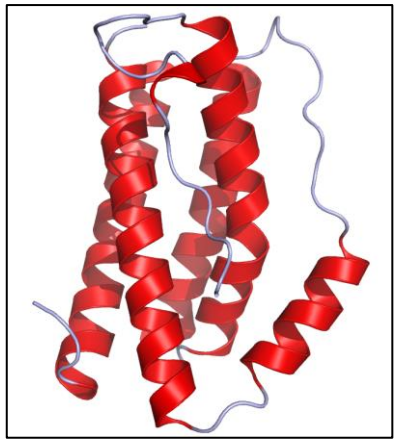
„Klassische“ Biomarker



CRP

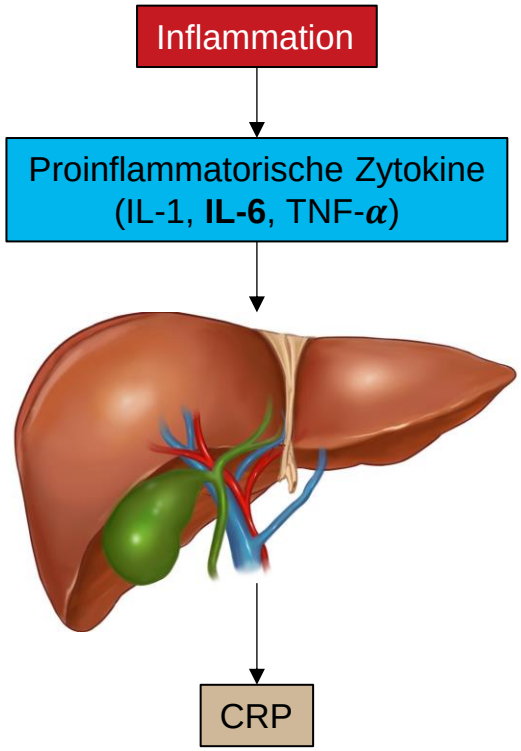


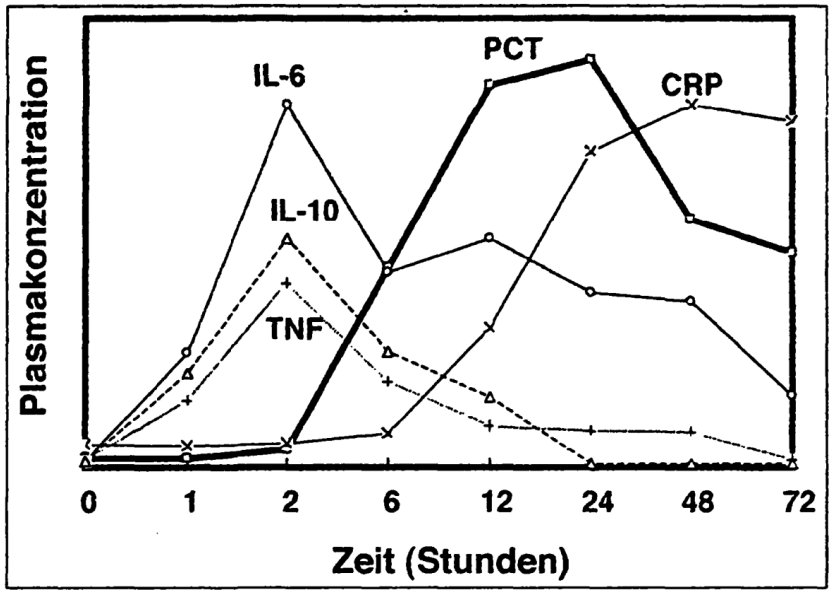
PCT



IL-6

C-reaktives Protein (CRP)



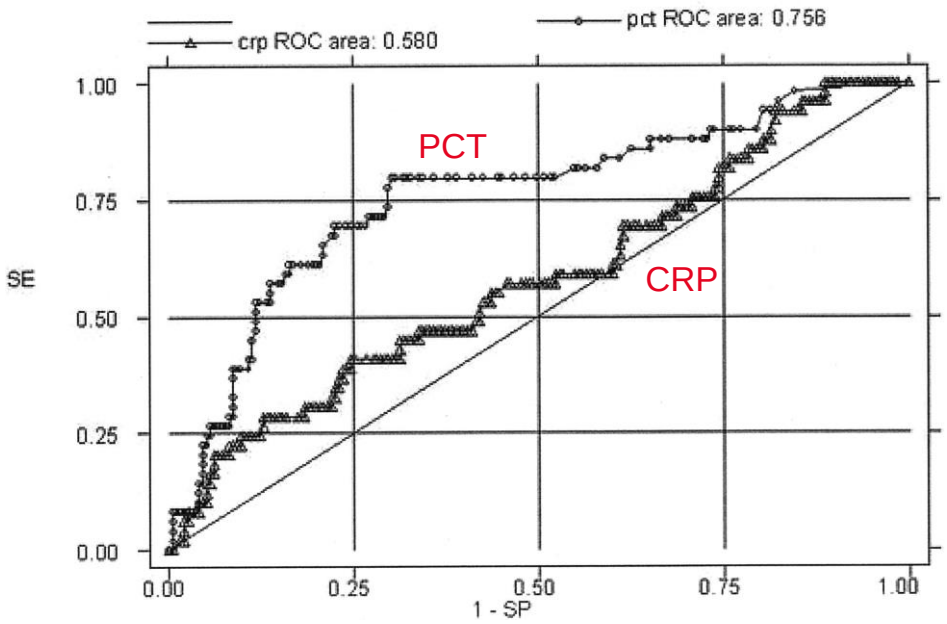


Halbwertszeit (HWZ) 19 Stunden

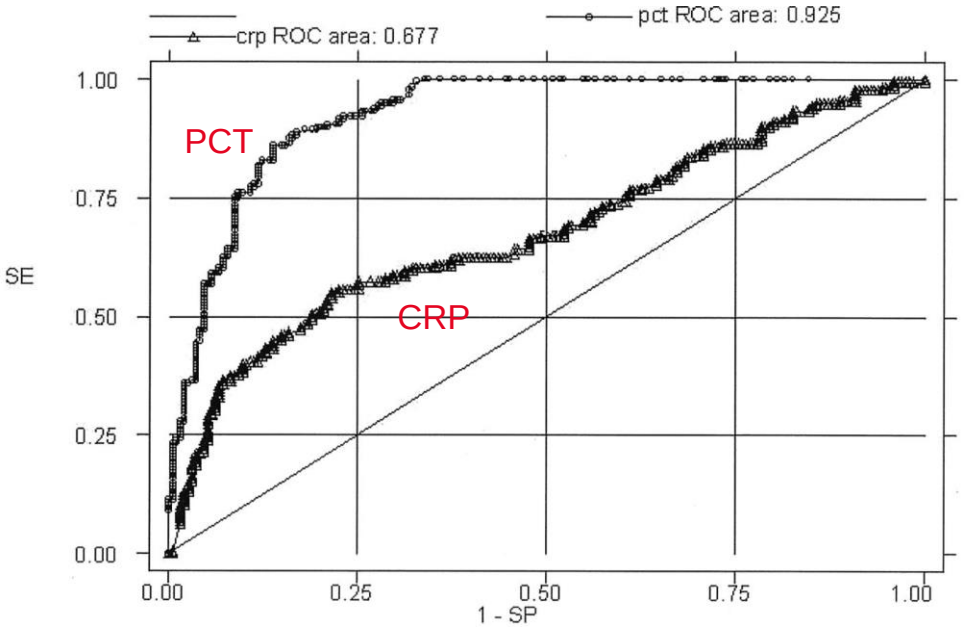
Spitzenkonzentration nach ca. 48-72 Stunden

Meisner M. J Lab Med 1999; 23:263-72.

CRP als Infektionsmarker



Lokale Infektion

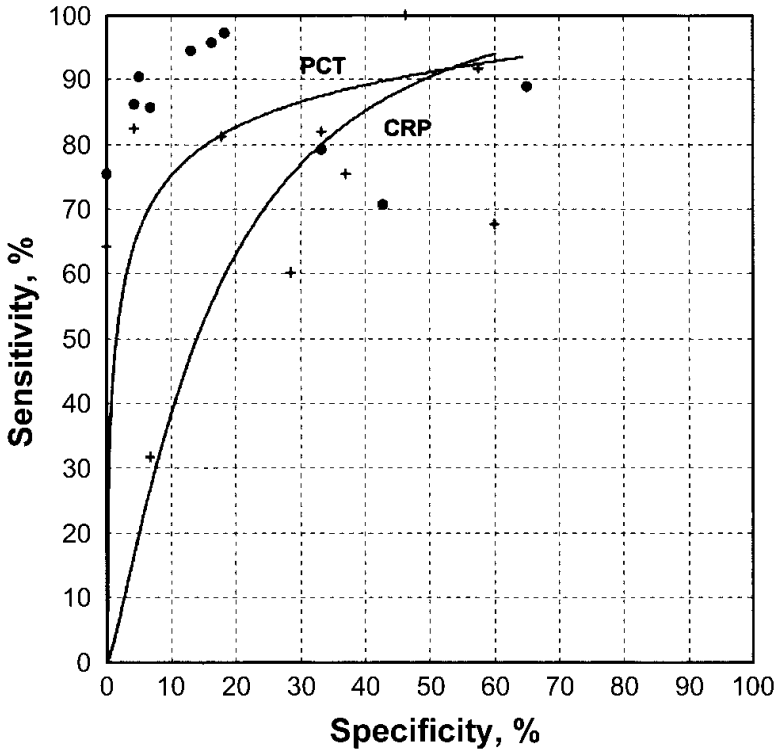


Sepsis

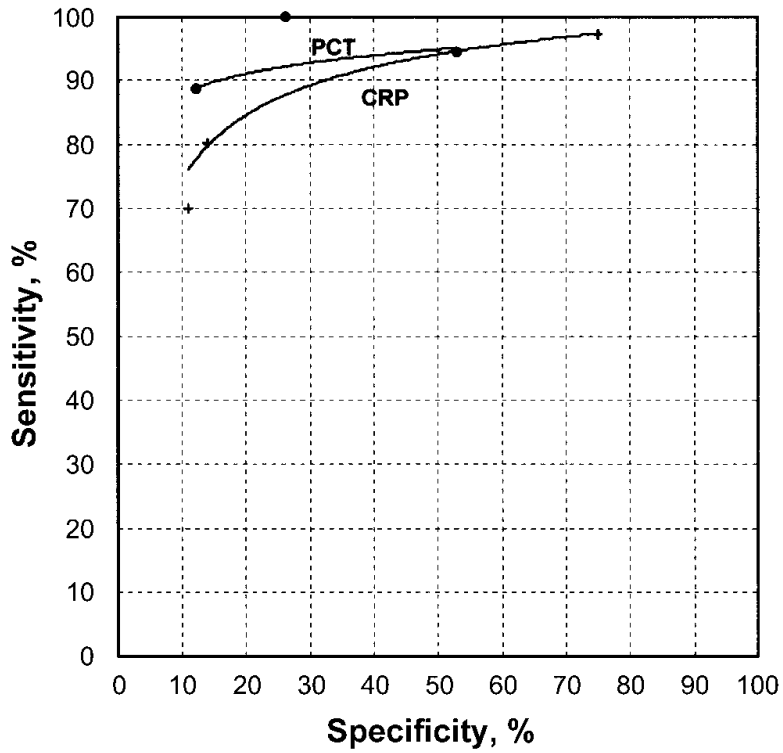
Luzzani A et al. Crit Care Med 2003; 31(6):1737-1741.

Clinical Infectious Diseases

Serum Procalcitonin and C-Reactive Protein Levels as Markers of Bacterial Infection: A Systematic Review and Meta-analysis



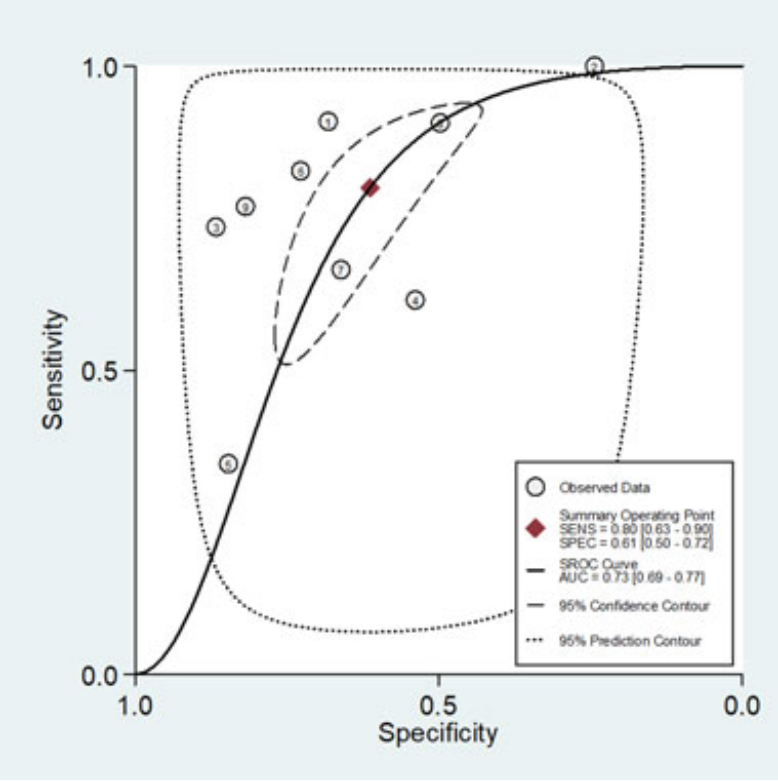
Bakterielle Infektion vs. Inflammation



Bakterielle vs. Virale Infektion

Simon L et al. Clinical Infectious Diseases 2004; 39:206-17.

C-reaktives Protein (CRP) zur Sepsis-Diagnose



AUC = 0.73 (95% CI, 0.69-0.77)

Sensitivität = 0.80 (95% CI, 0.63-0.90)

Spezifität = 0.61 (95% CI, 0.50-0.72)

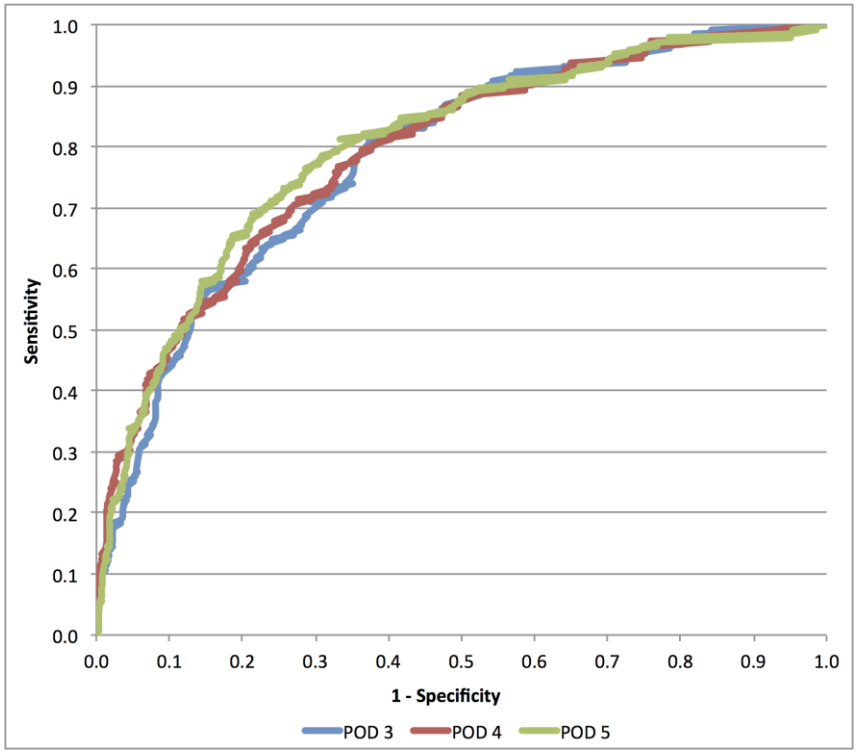
Tan M, et al. J Cell Biochem. 2018; 1-8.

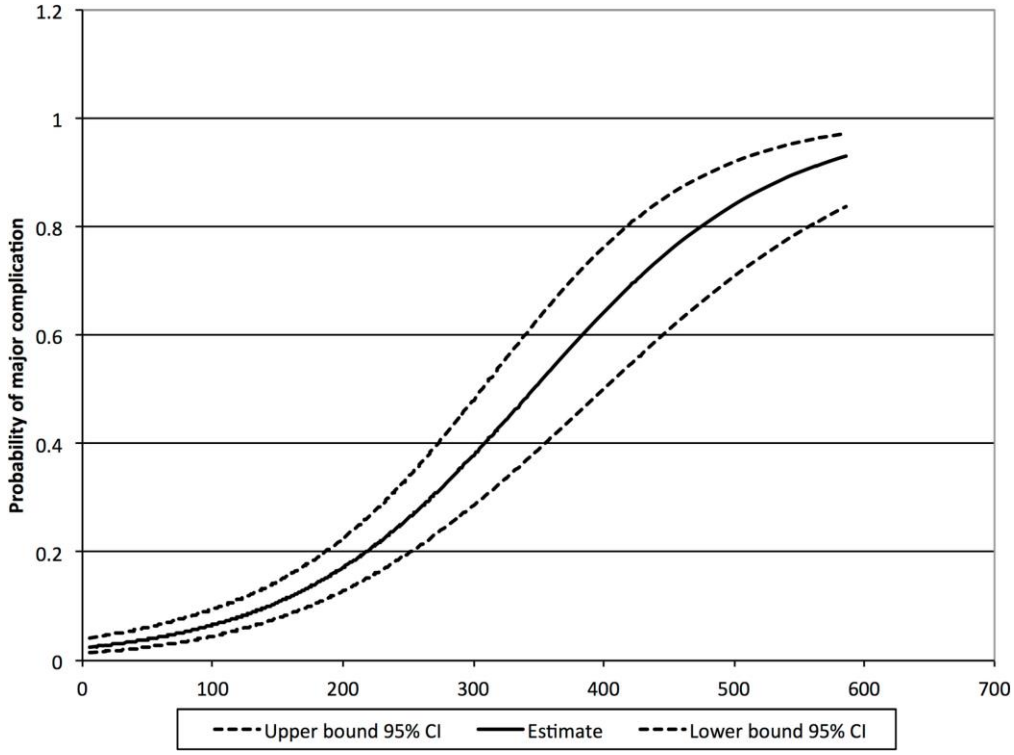
(unspezifische) Erhöhung des CRP

- Infektionen
- Nicht-infektiöse Entzündungen / Inflammation
  - Erkrankungen des rheumatischen Formenkreises
  - Autoimmunerkrankungen
  - Chronisch-entzündliche Darmerkrankungen
  - Malignome
  - Nekrosen / Gewebsuntergang
  - Trauma
  - Operative Eingriffe
  - ...

RESEARCH ARTICLE

Predictive Value of C-Reactive Protein for Major Complications after Major Abdominal Surgery: A Systematic Review and Pooled-Analysis

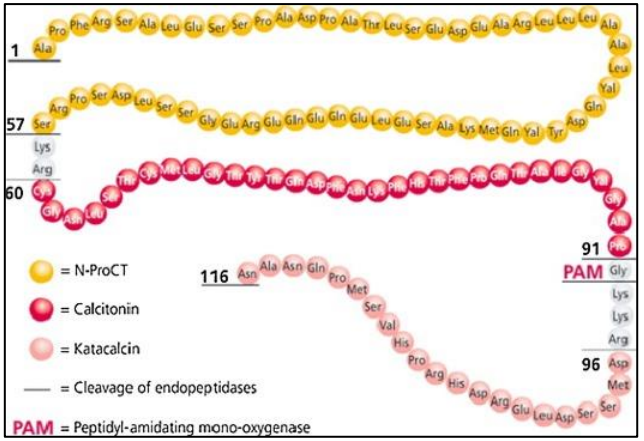


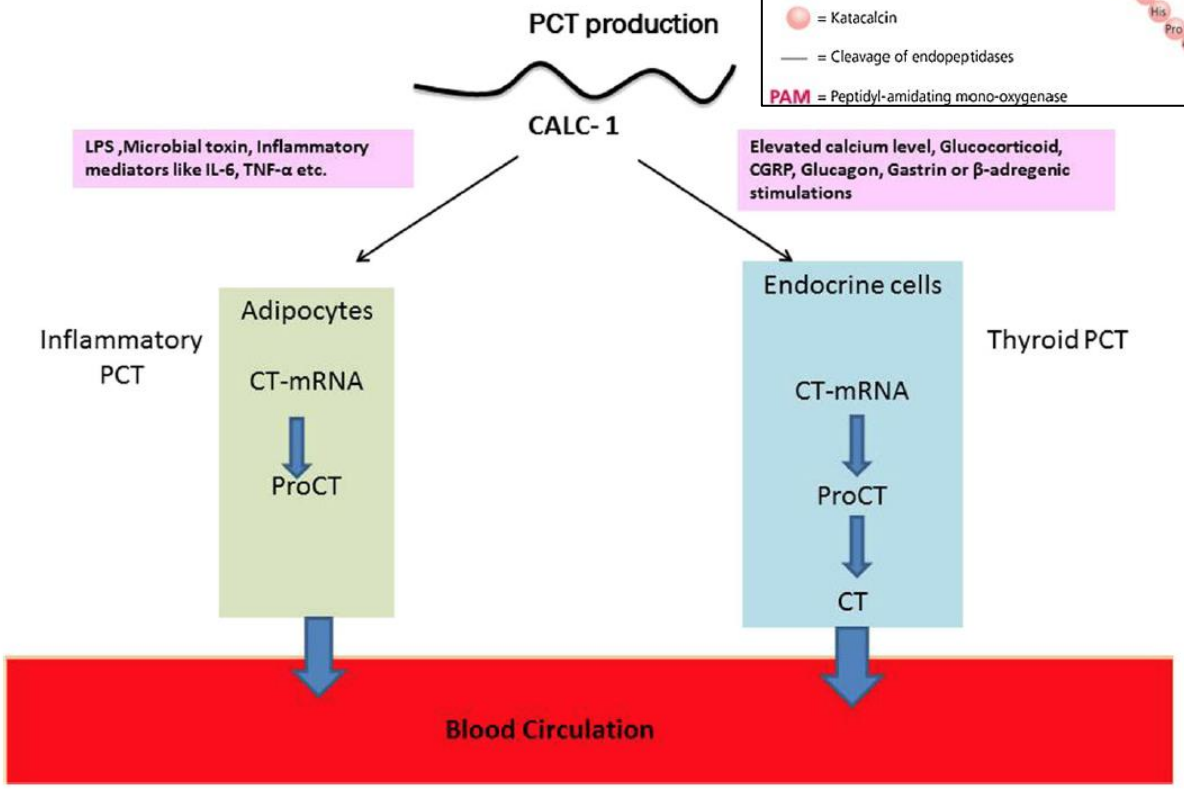


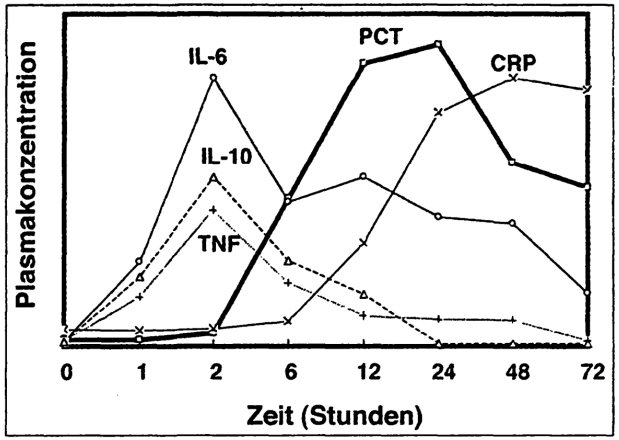
Tag 3: CRP < 75 mg/L → *sichere Verlegung*
Tag 3: CRP > 215 mg/L → *CT-Abdomen*

Straatman J et al. PLoS ONE 2015; 10(7):e0132995.

Procalcitonin (PCT)





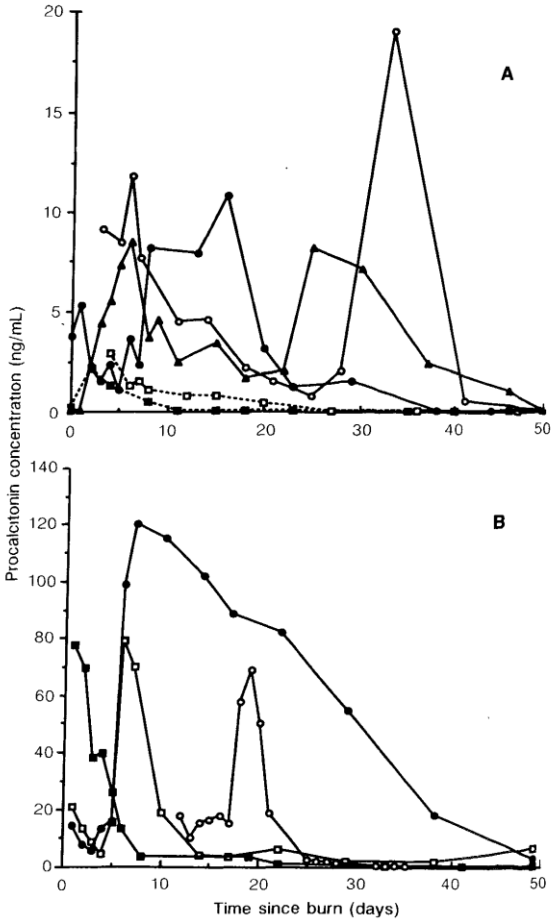


Halbwertszeit (HWZ) 24 Stunden

Spitzenkonzentration nach ca. 12 Stunden

Vijayan AL et al. Journal of Intensive Care 2017; 5:51.
Meisner M. J Lab Med 1999; 23:263-72.

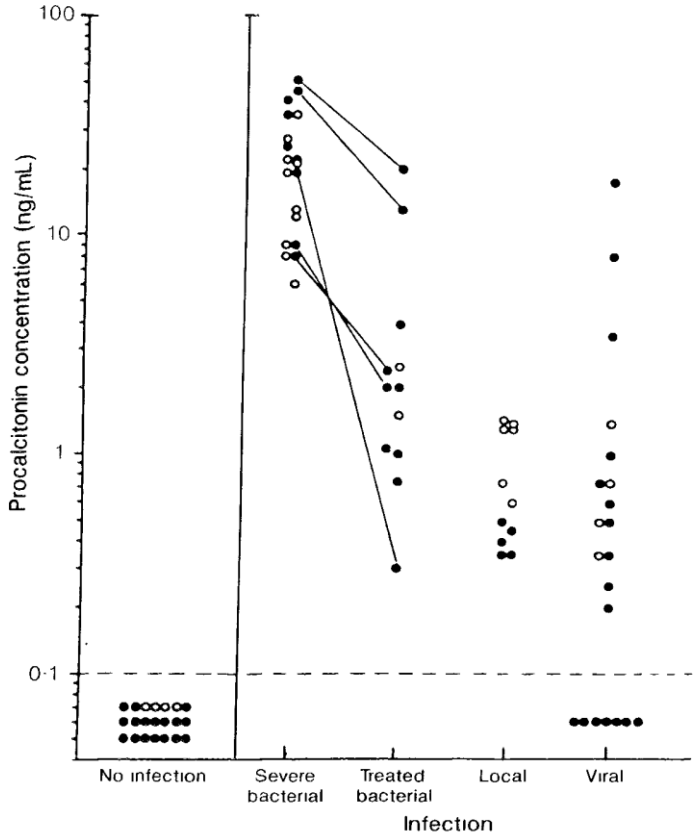
High serum procalcitonin concentrations in patients with sepsis and infection



__ = Sepsis
.... = keine Sepsis

__ = Sepsis

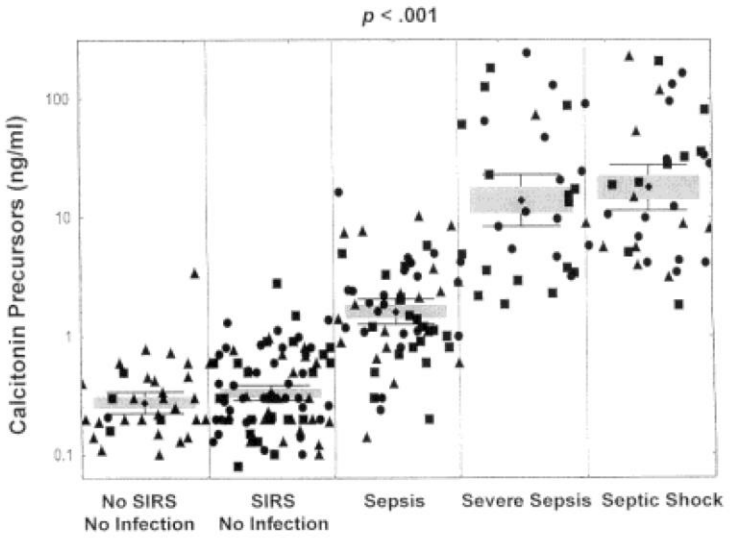
Verbrennungspatienten

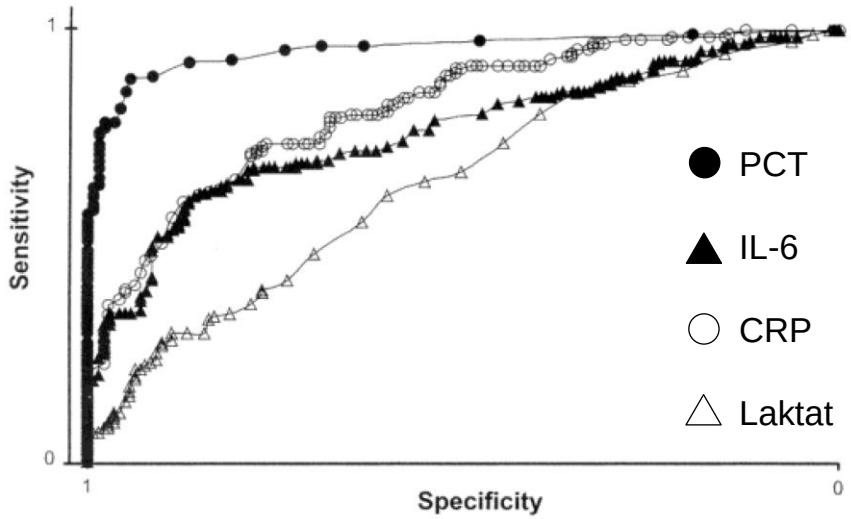


Kinder und Neugeborene

Assicot M et al. Lancet 1993; 341:515-518

Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit





Muller B et al. Critical Care Medicine 2000; 28(4):977–983.

Clinical Infectious Diseases

Serum Procalcitonin and C-Reactive Protein Levels as Markers of Bacterial Infection: A Systematic Review and Meta-analysis

Table 4. Results derived from the 2 × 2 tables of individual studies involving procalcitonin and C-reactive protein levels as markers for bacterial infections versus noninfective causes of inflammation.

	Procalcitonin markers				C-reactive protein markers			
	No. of results		Sensitivity,	Specificity,	No. of results		Sensitivity,	Specificity,
Study	TP/FN	FP/TN	% (95% CI)	% (95% CI)	TP/ FN	FP/TN	% (95% CI)	% (95% CI)
Aouifi et al. [117]	46/2	8/41	96 (85–99)	84 (70–92)	50/33	4/10	60 (49–71)	71 (42–90)
Enguix et al. [118][a]	19/3	1/23	86 (64–96)	96 (77–100)	19/4	1/22	83 (61–94)	96 (76–100)
Hatherill et al. [119][a]	103/3	9/40	97 (91–99)	82 (68–91)	73/0	37/43	100 (95–100)	54 (42–65)
Muller [121][a]	52/3	6/40	95 (84–99)	87 (73–95)	41/9	17/34	82 (68–91)	67 (52–79)
Penel et al. [122][a]	43/14	0/5	75 (62–85)	100 (48–100)	43/24	0/1	64 (52–75)	100 (3–100)
Rothenburger et al. [123][a]	12/2	3/42	86 (56–97)	93 (81–98)	14/30	1/14	32 (19–48)	93 (66–100)
Selberg et al. [125]	19/5	3/6	79 (57–92)	67 (31–91)	19/9	3/2	68 (48–83)	40 (7–83)
Suprin et al. [126][a]	49/6	26/14	89 (77–95)	35 (21–52)	55/5	19/14	92 (81–97)	42 (26–61)
Ugarte et al. [127][a]	75/31	36/48	71 (61–79)	57 (46–68)	80/26	3/53	75 (66–83)	63 (52–73)
Viallon et al. [128][a]	19/2	2/38	90 (68–98)	95 (82–99)	13/3	8/37	81 (54–95)	82 (67–91)
Total[b]	…	…	88 (80–93)	81 (67–90)	…	…	75 (62–84)	67 (56–77)

NOTE. FN, false negative; FP, false positive; TN, true negative, TP, true positive.

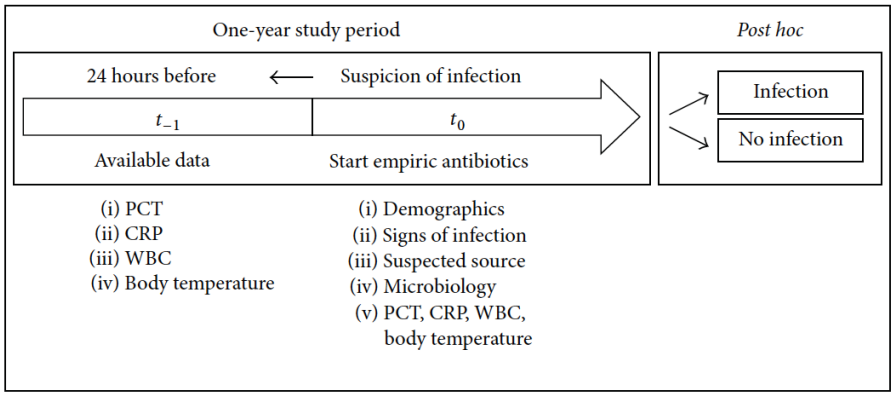
[a] Data confirmed by original author.

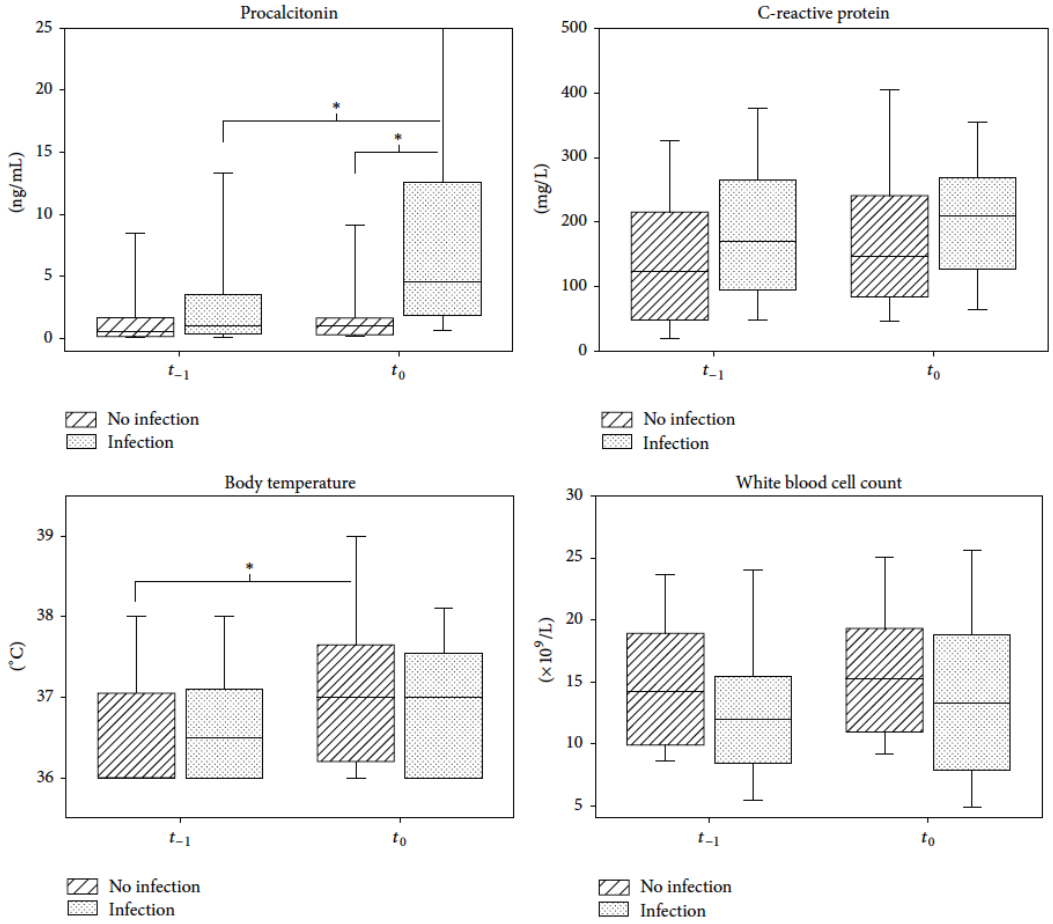
[b] Pooled data from a random effects model.

Simon L et al. Clinical Infectious Diseases 2004; 39:206-17.

Research Article

Delta Procalcitonin Is a Better Indicator of Infection Than Absolute Procalcitonin Values in Critically Ill Patients: A Prospective Observational Study

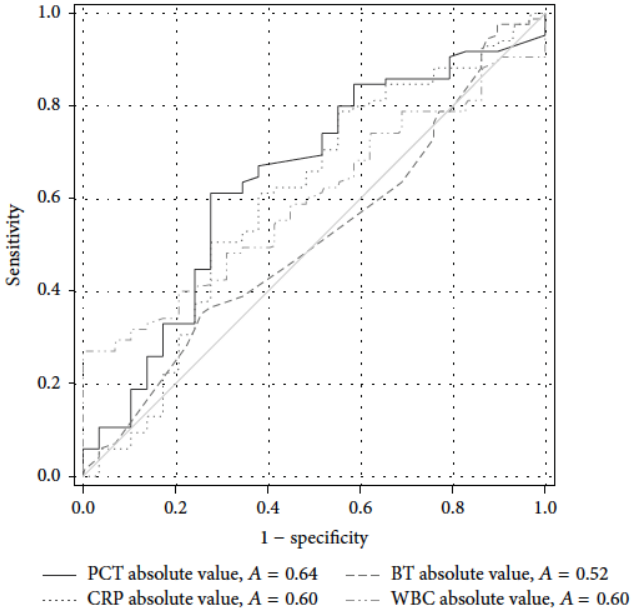




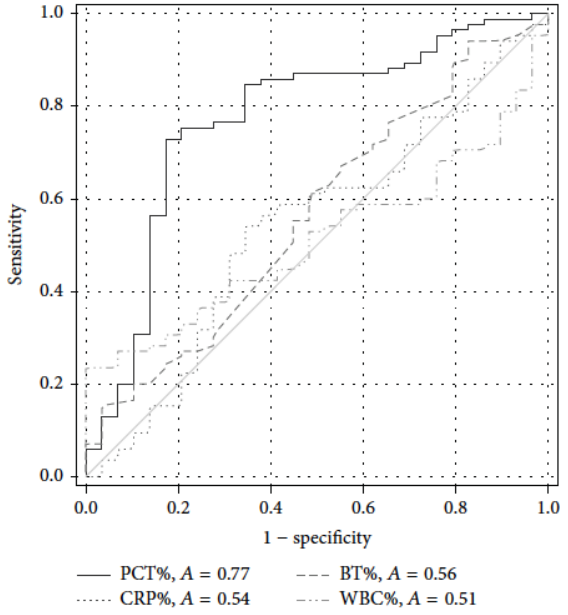
Trásy D et al. Journal of Immunology Research 2016; 3530752.

Research Article

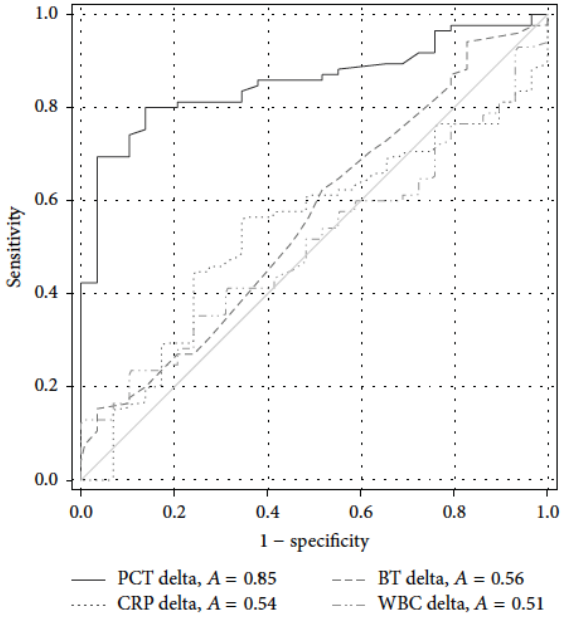
Delta Procalcitonin Is a Better Indicator of Infection Than Absolute Procalcitonin Values in Critically Ill Patients: A Prospective Observational Study



absolut



%



Delta

Our results suggest that delta-PCT values are superior to absolute values in indicating infection in intensive care patients.

Trásy D et al. Journal of Immunology Research 2016; 3530752.

RESEARCH Open Access

Influence of pathogen and focus of infection on procalcitonin values in sepsis patients with bacteremia or candidemia

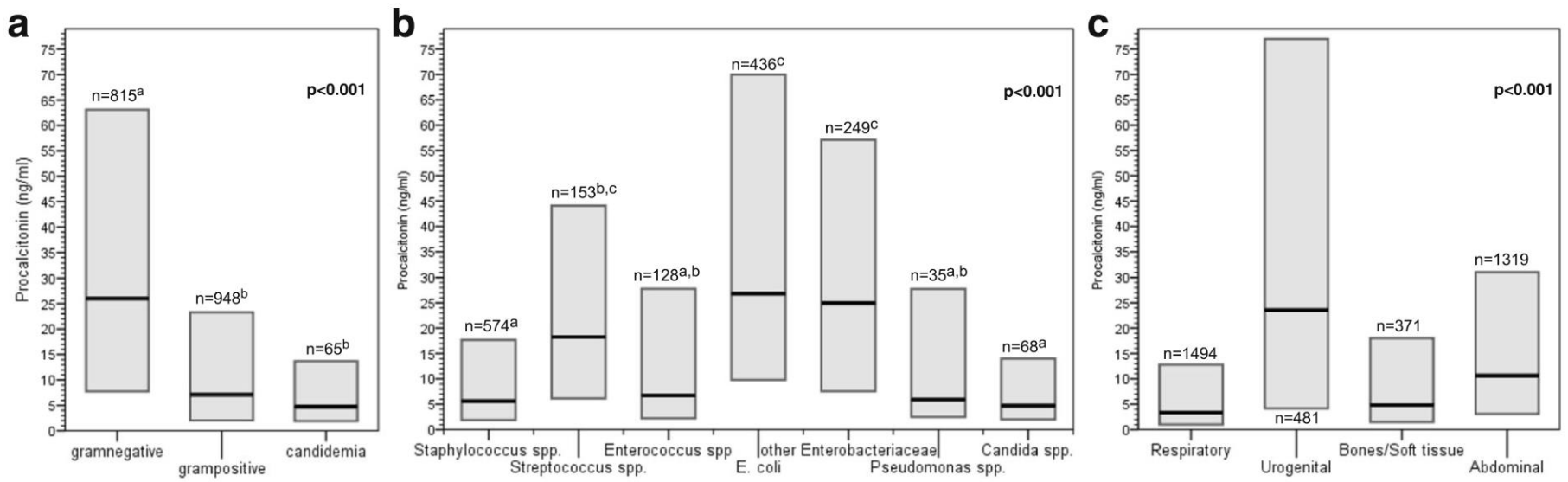
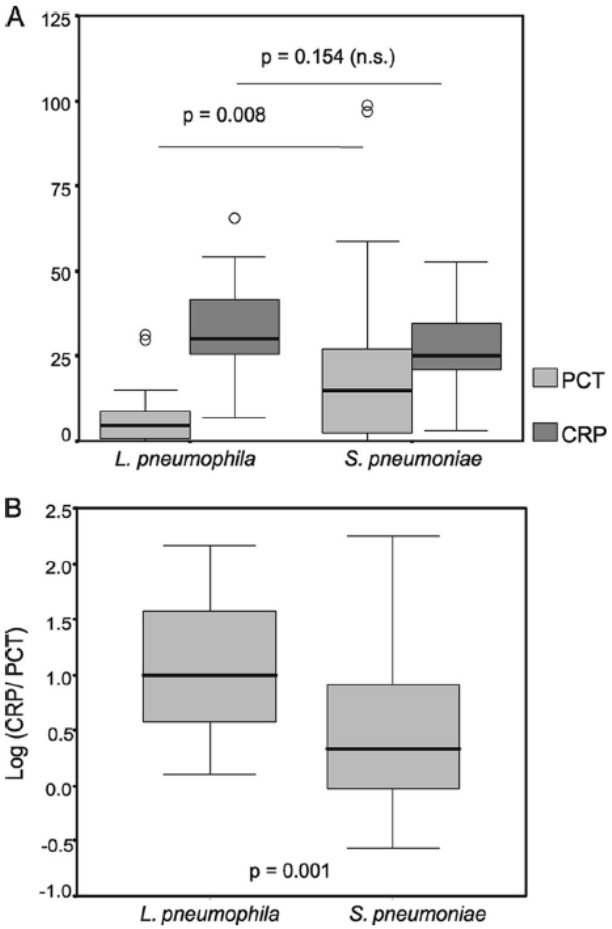
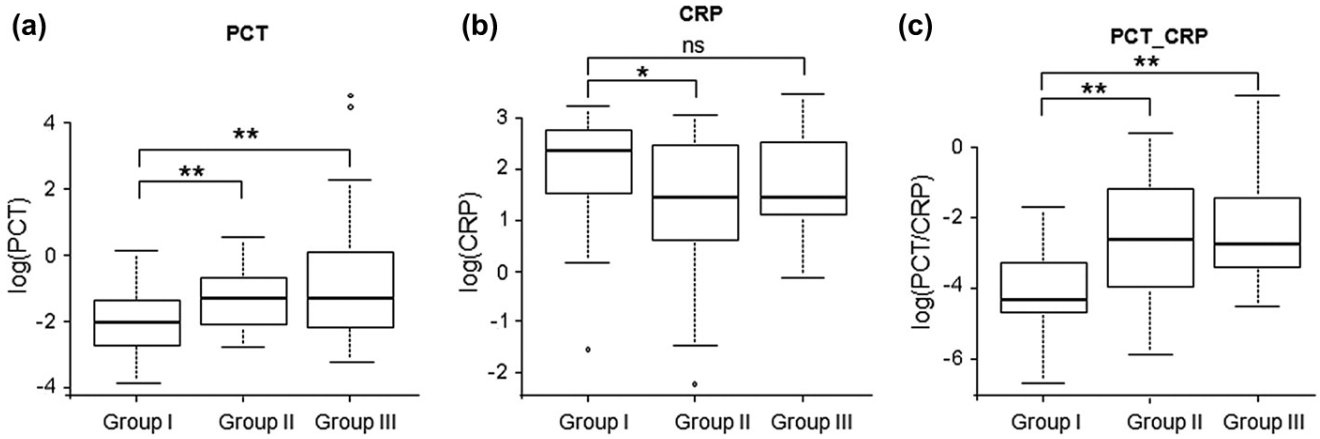


Fig. 1 Initial PCT concentrations (ng/ml, median and IQR) associated with Gram stain (**a**) or type of pathogen (**b**) detected in blood culture drawn at sepsis onset, or associated with focus of infection (**c**). Significantly different ($p < 0.001$) in all three comparisons. n denotes number of cases represented by each bar and superscript letters denote homogeneous subsets

Thomas-Rüddel DO et al. Critical Care 2018; 22.128.

CRP/PCT-Ratio



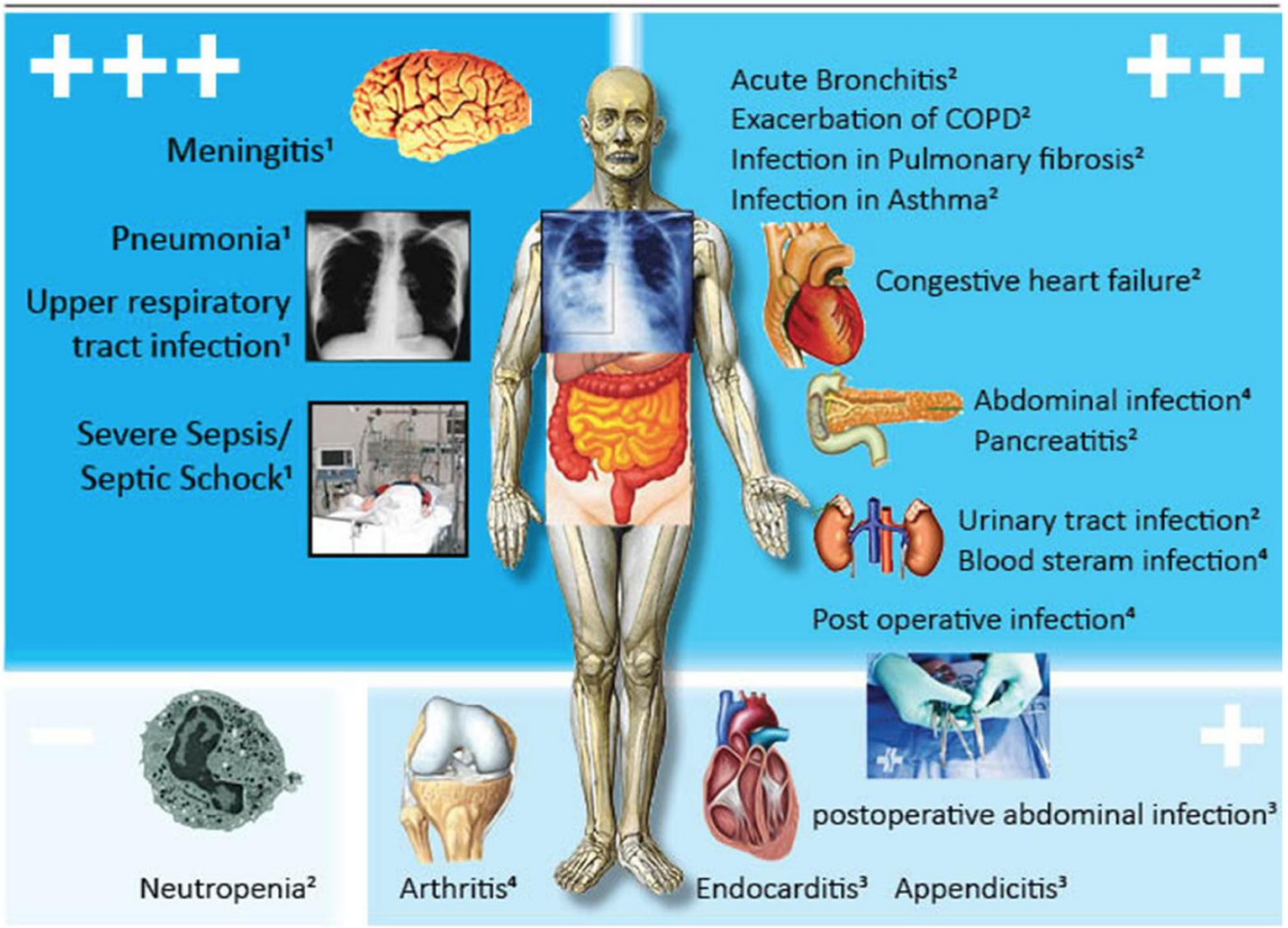


Gruppe 1
Tumorfieber
- Neg. Blutkulturen
- Negativer Rö-Tx oder andere Bildgebung
- Neg. Urin-Kulturen
- Kein Hinweis auf Infektion

Gruppe 2
Infektion
- Pos. Blutkulturen
- Positiver Rö-Tx oder andere Bildgebung
- Pos. Urin-Kulturen

Gruppe 3
Schwere Infektion
- Unter Chemotherapie
- Pos. Blutkultur

Bellmann-Weiler R et al. Journal of Clinical Microbiology 2010; 48(5):1915-1917.
Hangai S et al. Leukemia & Lymphoma 2015; 56(4):910-914.



Sager R et al. BMC Medicine 2017; 15:15.


Antibiotic
Stewardship

Use of Procalcitonin to Shorten Antibiotic Treatment Duration in Septic Patients

A Randomized Trial

BLUE JOURNAL

RCT
Single Centre

Patienten mit schwerer Sepsis oder septischem Schock (per protocol)

PCT
n = 31

Kontrolle
n = 37

- **PCT > 1 µg/L → Reevaluation Tag 5**
  Absetzen bei:
  - PCT < 90% des Baseline-Peaks
  - PCT < 0.25 µg/L
- **PCT < 1 µg/L → Reevaluation Tag 3**
  Absetzen bei:
  - PCT < 0.1 µg/L

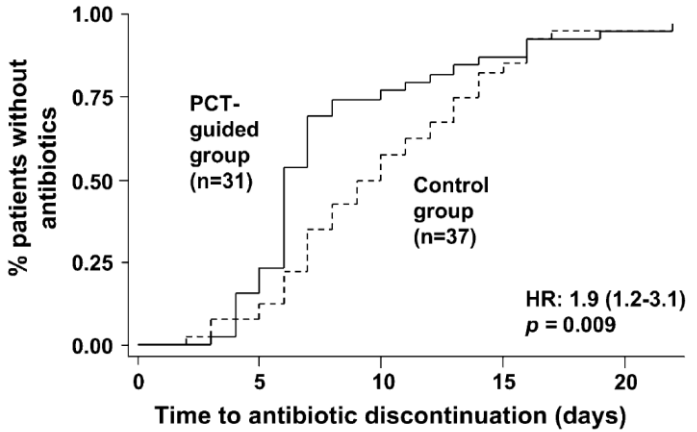


TABLE 3. OUTCOMES USING PER-PROTOCOL ANALYSIS

Per-Protocol Analysis	Control Group (*n* = 37)	PCT Group (*n* = 31)	RR (95% CI)	*P* Value
Primary outcomes				
Duration of antibiotic therapy, first episode of infection, median d (range)	10 (3–33)	6 (4–16)	Mean difference: 3.2 (1.1 to 5.4)	0.003
Total antibiotic exposure days/1,000 d	655	504	1.3 (1.1 to 1.5)*	0.0002
Days alive without antibiotics, mean ± SD	13.6 ± 7.6	17.4 ± 7.6	Mean difference: 3.8 (0.1 to 7.5)	0.04
Secondary outcomes				
Clinical cure, n (%)	31 (83.8)	28 (90.3)	0.8 (0.5 to 1.3)	0.48
28-d mortality, n (%)	6 (16.2)	5 (16.1)	1.0 (0.5 to 1.8)	0.74
In-hospital mortality, n (%)	7 (18.9)	6 (19.4)	0.9 (0.6 to 1.7)	0.79
Sepsis-related death, n (%)	1/6 (16.6)	3/5 (60)	0.3 (0.1 to 2.0)	0.44
Primary infection relapse rate, n (%)	1 (2.7)	1 (3.2)	0.9 (0.9 to 3.7)	0.70
ICU length of stay, median d (range)	5 (1–30)	3 (1–18)	Mean difference: 4.3 (0.4 to 8.3)	0.03
Hospital length of stay, median d (range)	21 (5–89)	14 (5–64)	Mean difference: 2.2 (−1.9 to 6.3)	0.16

Nobre V et al. Am J Respir Crit Care Med 2008; 177(5):498-505.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection

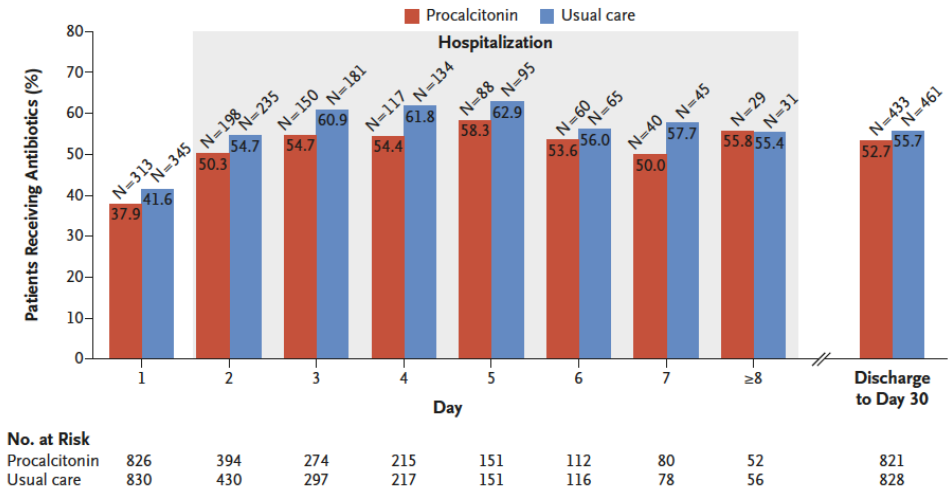
14 U.S.-Krankenhäuser → Schulungsmaßnahmen zur Interpretation von PCT-Assays → Patienten in Notaufnahme mit unterer Atemwegsinfektion → Unsichere Indikation für Antibiotikum

< 0.1 µg/L	dringend abgeraten
0.1 – 0.25 µg/L	abgeraten
0.25 – 0.5 µg/L	empfohlen
> 0.5 µg/L	dringend empfohlen

→ PCT-Gruppe n = 826

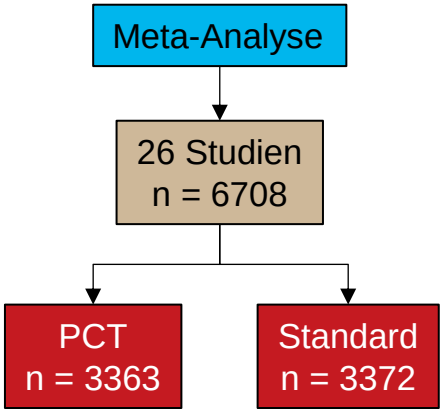
Kontroll-Gruppe n = 830

The provision of procalcitonin assay results, along with instructions on their interpretation, to emergency department and hospital-based clinicians did not result in less use of antibiotics than did usual care among patients with suspected lower respiratory tract infection.



Huang DT et al. N Eng J Med 2018; 379:236-49.

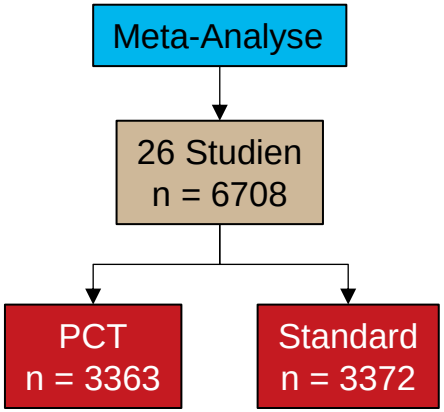
Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis



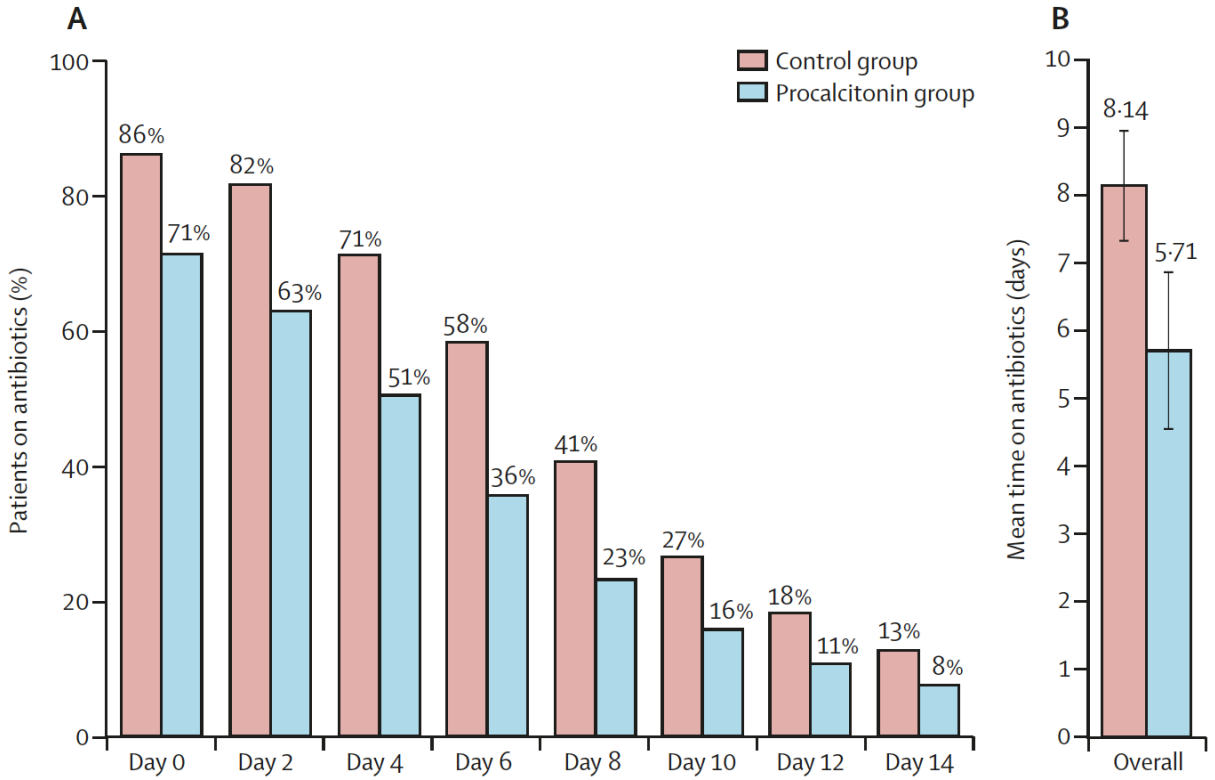
	Control (n=3372)	Procalcitonin group (n=3336)	Adjusted OR (95% CI)*, p value	$p_{interaction}$
Overall				
30-day mortality	336 (10%)	286 (9%)	0·83 (0·7 to 0·99), p=0·037	..
Treatment failure	841 (25%)	768 (23%)	0·90 (0·80 to 1·01), p=0·068	..
Length of ICU stay, days	13·3 (16·0)	13·7 (17·2)	0·39 (–0·81 to 1·58), p=0·524	..
Length of hospital stay, days	13·7 (20·6)	13·4 (18·4)	–0·19 (–0·96 to 0·58), p=0·626	..
Antibiotic-related side-effects	336/1521 (22%)	247/1513 (16%)	0·68 (0·57 to 0·82), p<0·0001	..

Schuetz P et al. Lancet Inf Dis 2018; 18:95-107.

Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis



Use of procalcitonin to guide antibiotic treatment in patients with acute respiratory infections reduces antibiotic exposure and side-effects, and improves survival. Widespread implementation of procalcitonin protocols in patients with acute respiratory infections thus has the potential to improve antibiotic management with positive effects on clinical outcomes and on the current threat of increasing antibiotic multiresistance.



Schuetz P et al. Lancet Inf Dis 2018; 18:95-107.

Meta-Analyse

11 RCTs

(ICU-Patienten mit Sepsis)

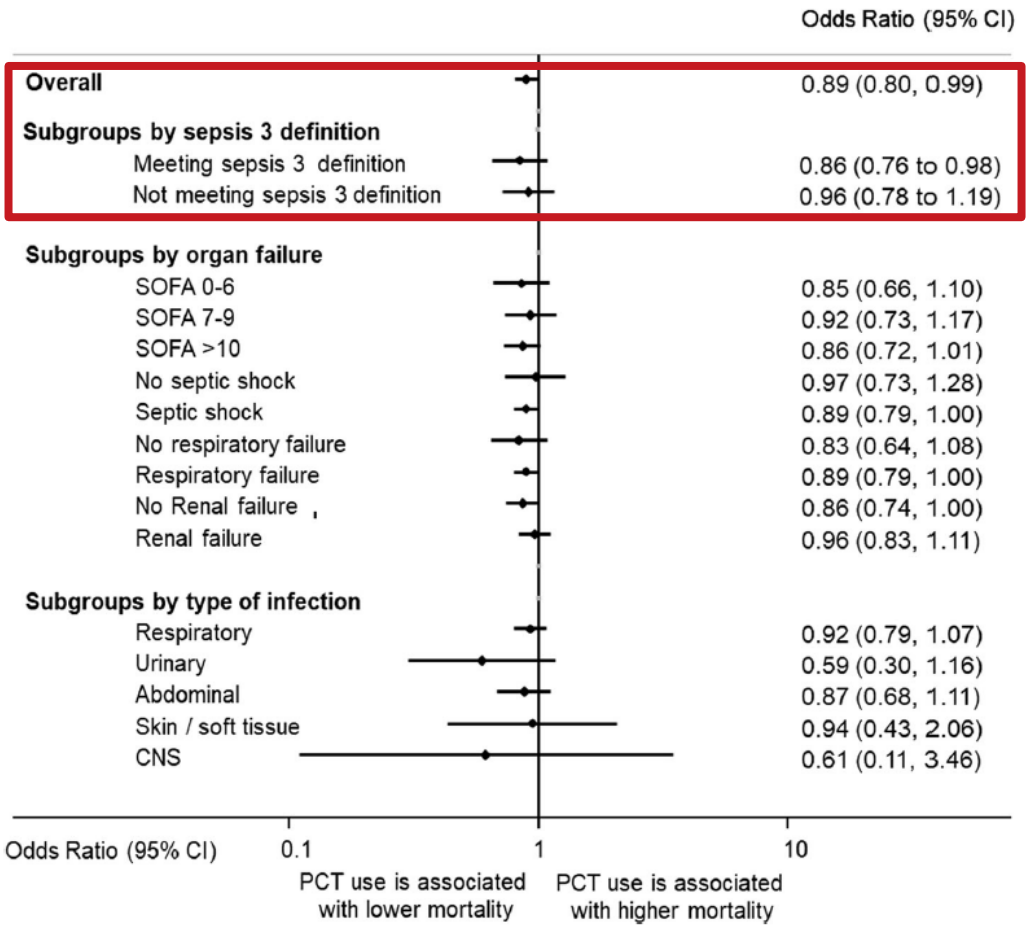
n = 4482

PCT-Gruppe n = 2252 ⟷ **Kontroll-Gruppe** n = 2230

Primärer Endpunkt:

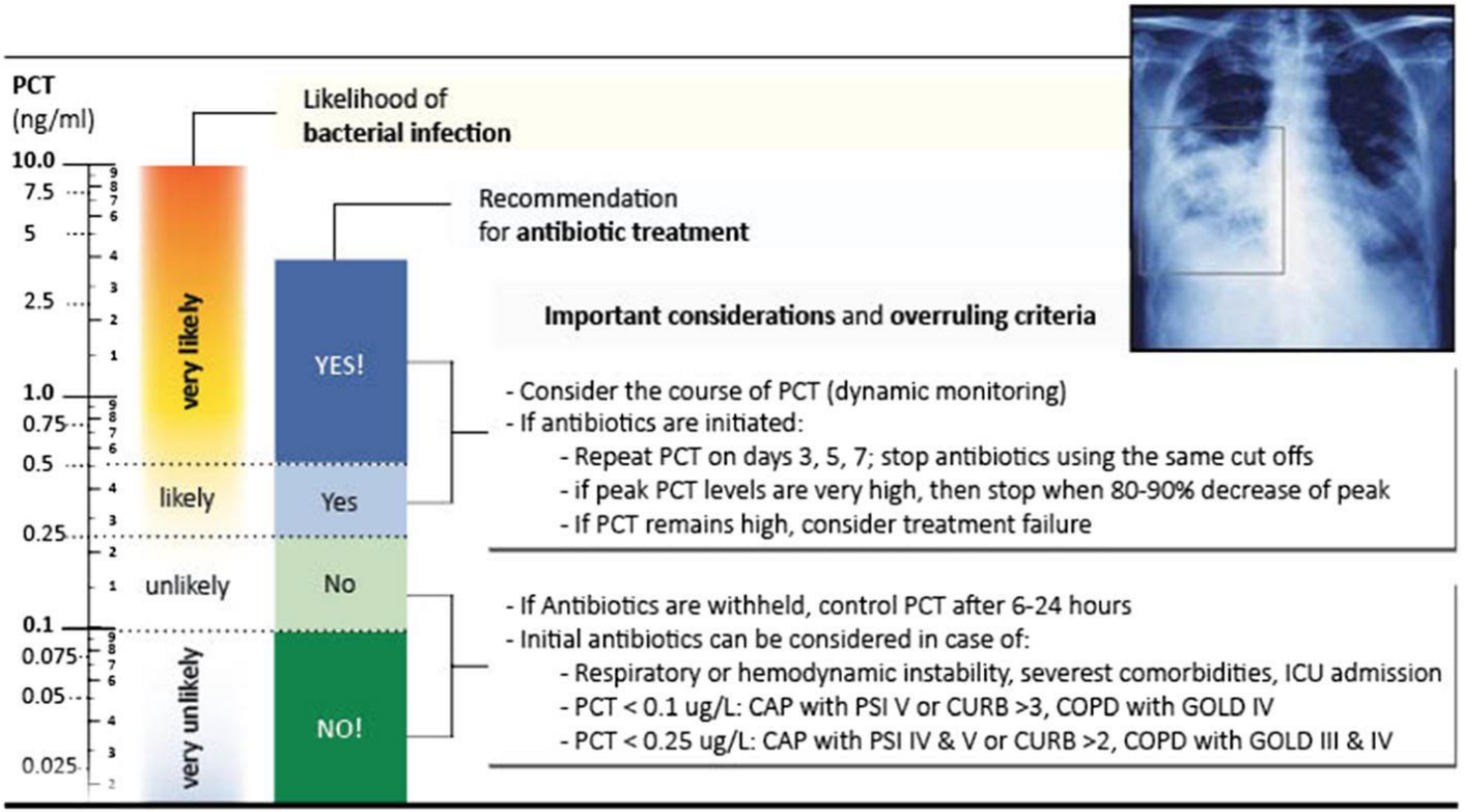
→ Mortalität

Procalcitonin guidance also facilitated earlier discontinuation of antibiotics, with a reduction in treatment duration (9.3 vs 10.4 days; adjusted coefficient −1.19 days, 95% CI −1.73 to−0.66; p < 0.001).



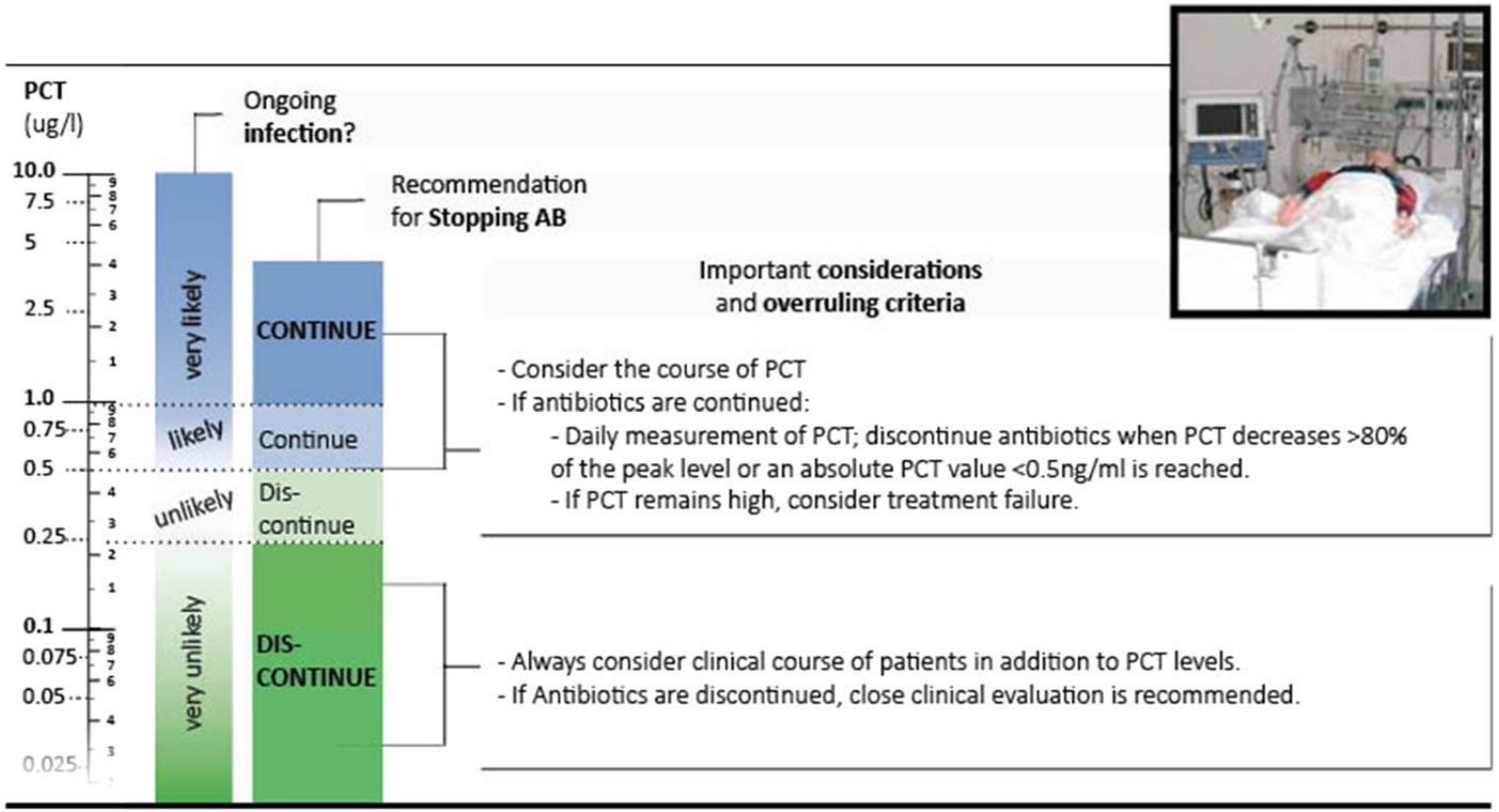
Wirz Y et al. Critical Care 2018; 22:191.

PCT-basierte AB-Therapie (Atemwegsinfektionen)



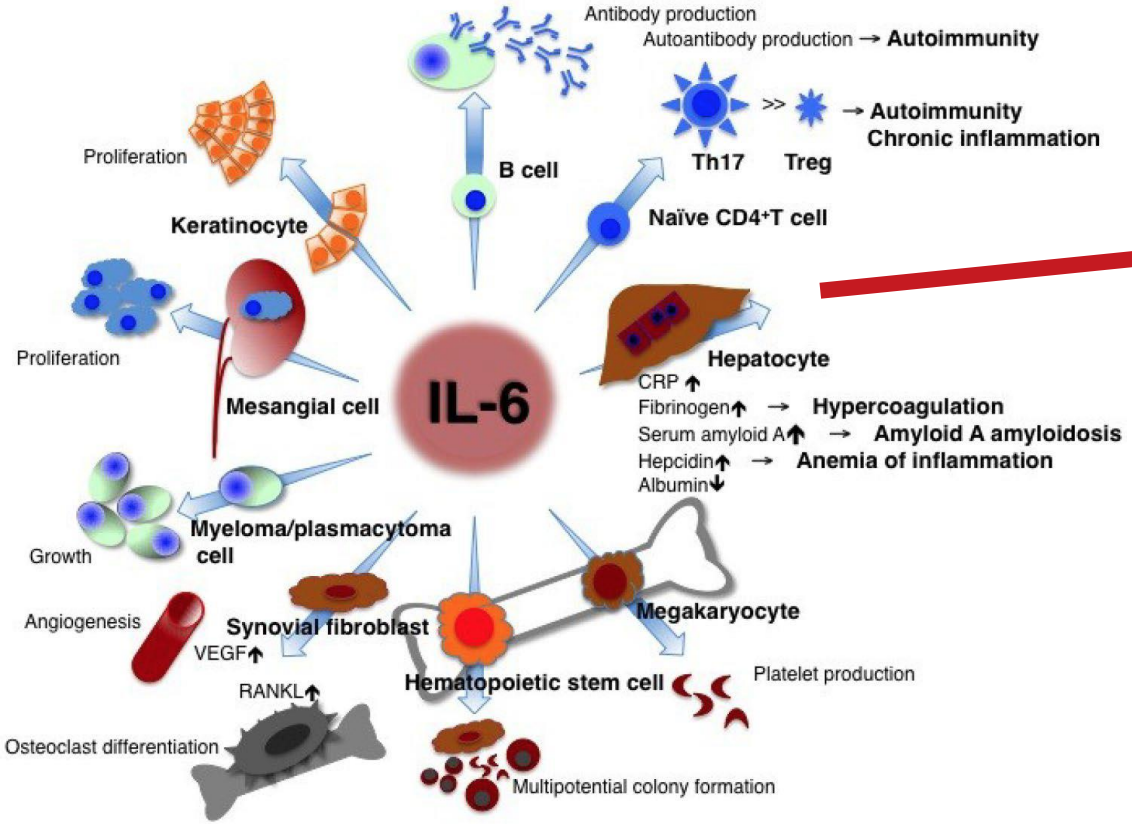
Sager R et al. BMC Medicine 2017; 15:15.

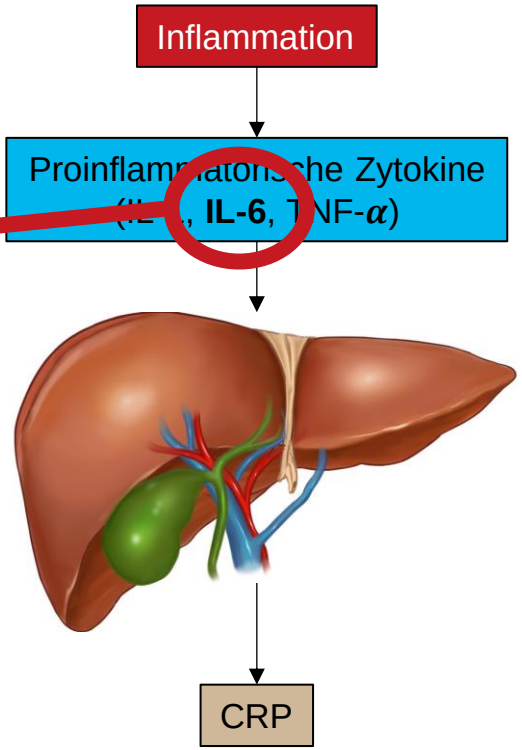
PCT-basierte AB-Therapie (Sepsis)



Sager R et al. BMC Medicine 2017; 15:15.

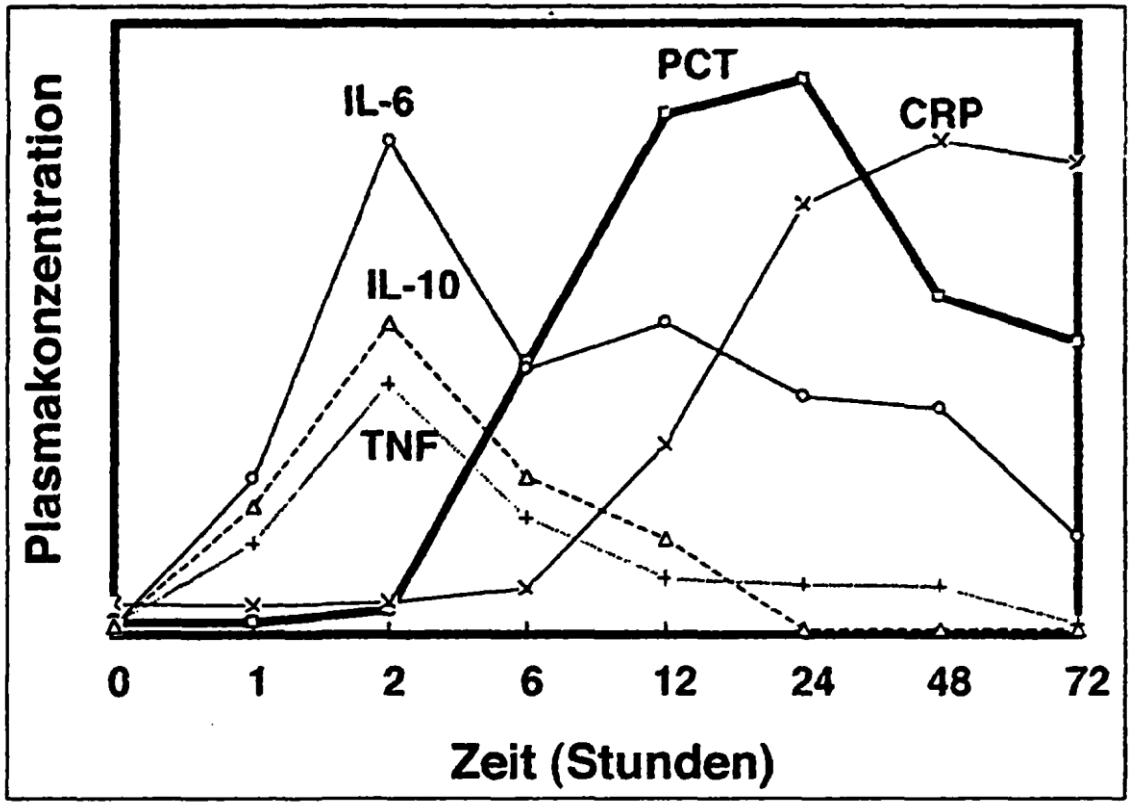
Interleukin-6 (IL-6)





Tanaka T et Kishimoto T. Int J Biol Sci 2012; 8(9):1227-1236.

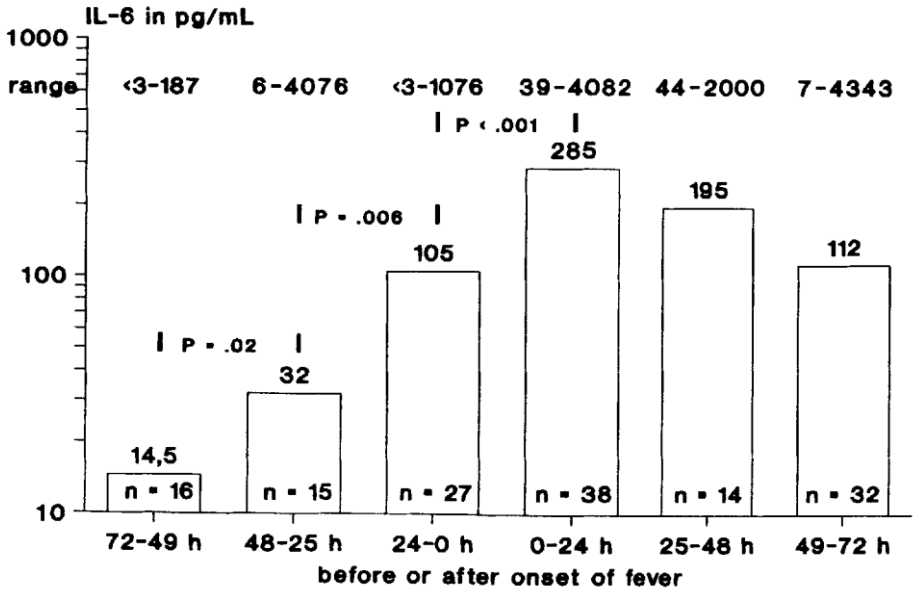
Interleukin-6 (IL-6)

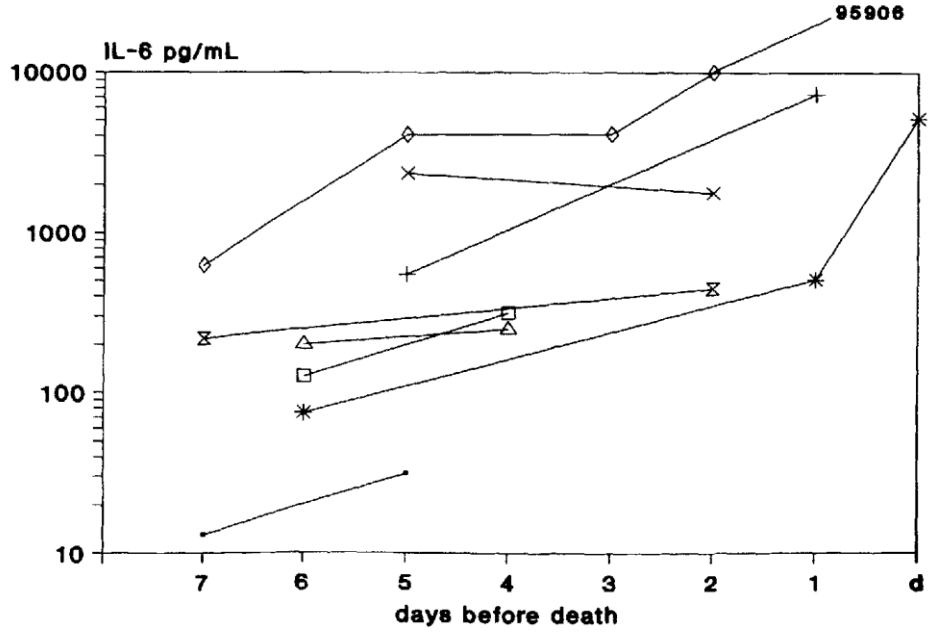


Meisner M. J Lab Med 1999; 23:263-72.

The Journal of Infectious Diseases

Increase in Interleukin-6 Serum Level Preceding Fever in Granulocytopenia and Correlation with Death from Sepsis

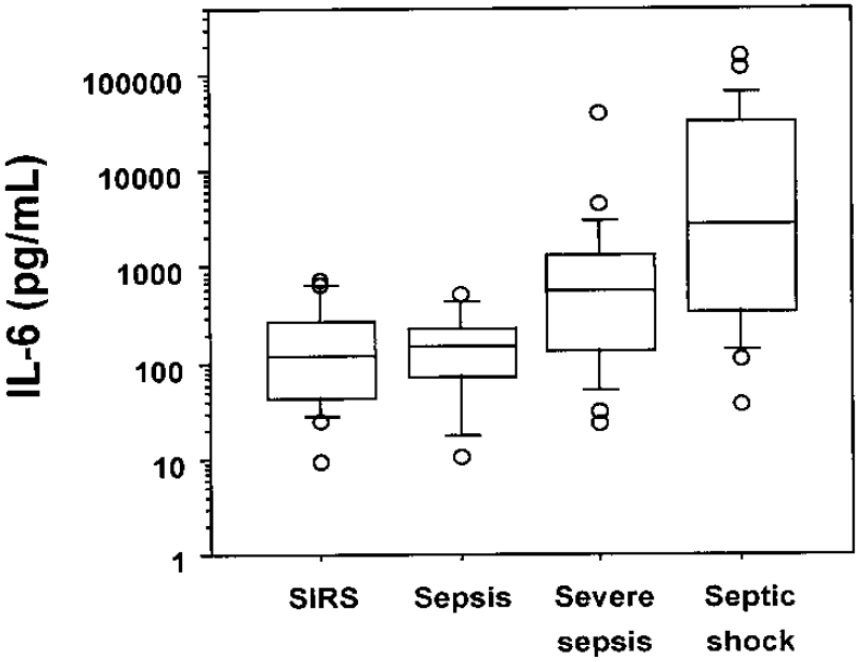


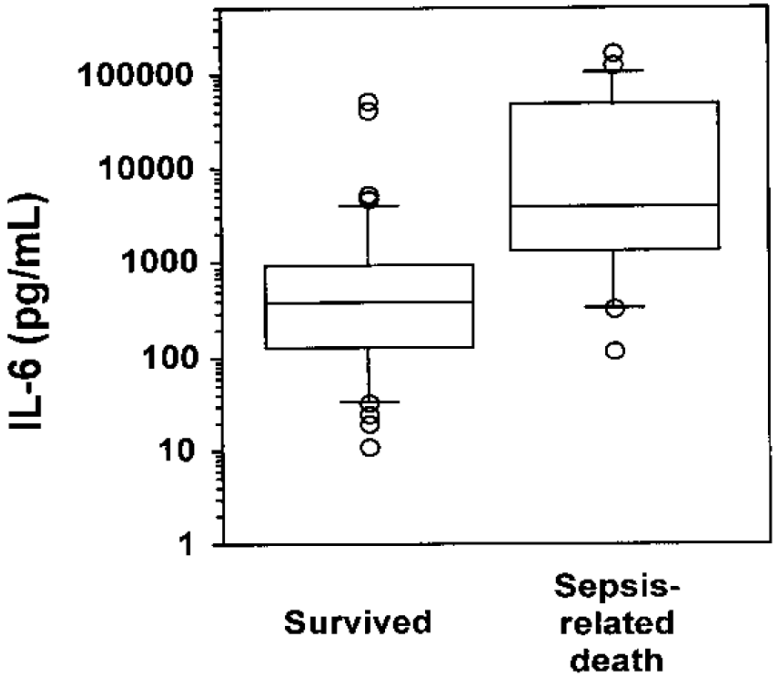


We conclude that determination of IL-6 during granulocytopenia may be helpful in early detection of risk for fever. It may be useful for assessment of fever and as a factor for predicting the severity of disease.

Steinmetz HT et al. J Infect Dis 1995; 171(1):225-228.

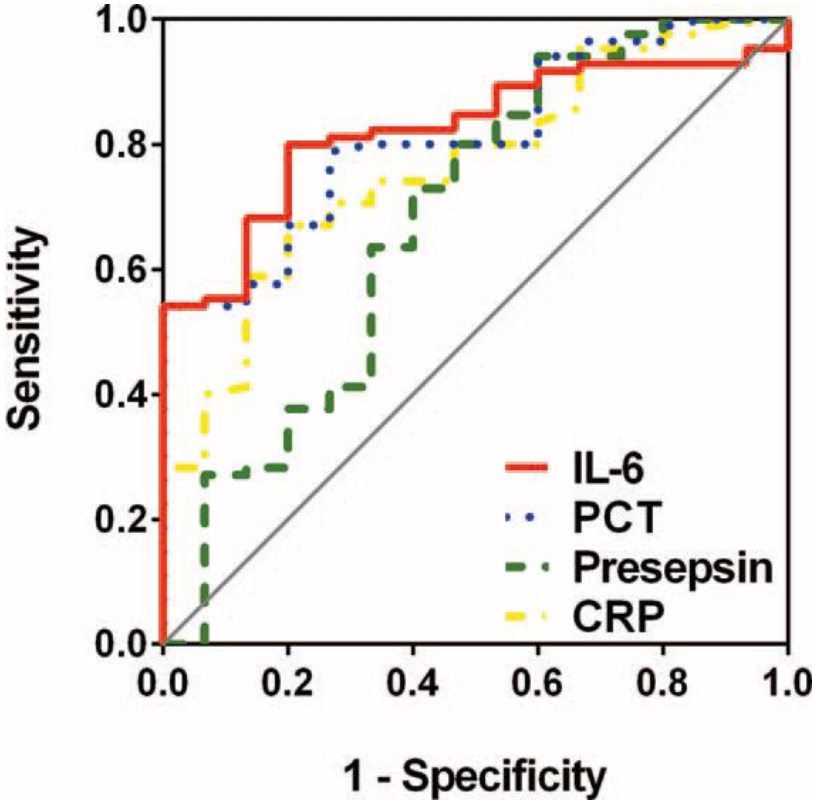
BLUE JOURNAL Diagnostic Value of Procalcitonin, Interleukin-6, and Interleukin-8 in Critically Ill Patients Admitted with Suspected Sepsis



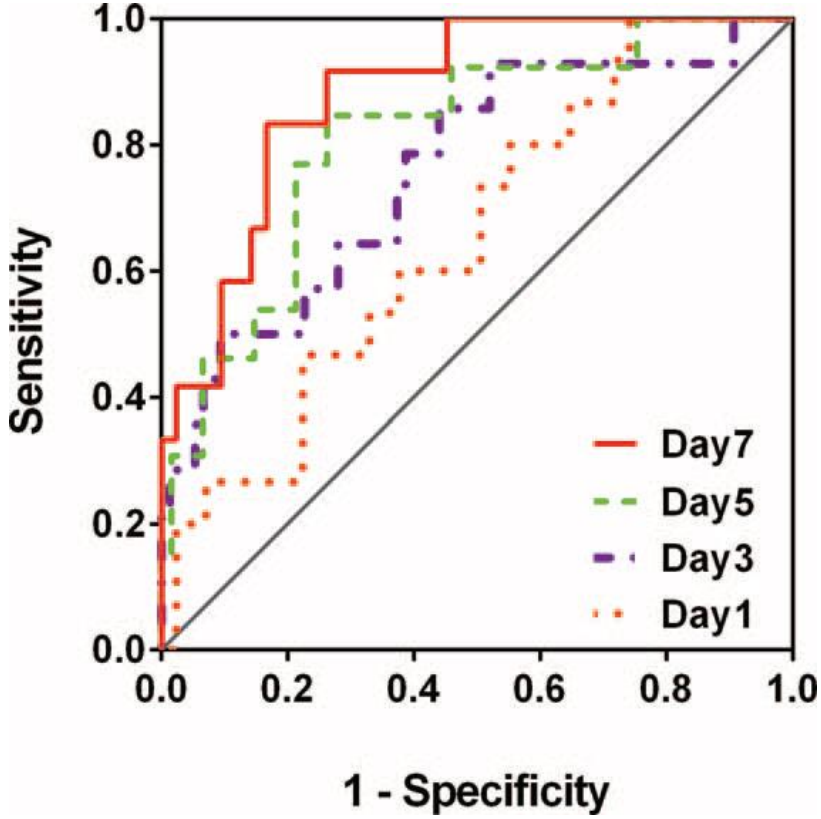


Harbarth S et al. Am J Respir Crit Care Med 2001; 164:396-402.

INTERLEUKIN-6 LEVELS ACT AS A DIAGNOSTIC MARKER FOR INFECTION AND A PROGNOSTIC MARKER IN PATIENTS WITH ORGAN DYSFUNCTION IN INTENSIVE CARE UNITS



Diagnose einer Infektion



Prädiktion 28-Tages-Mortalität

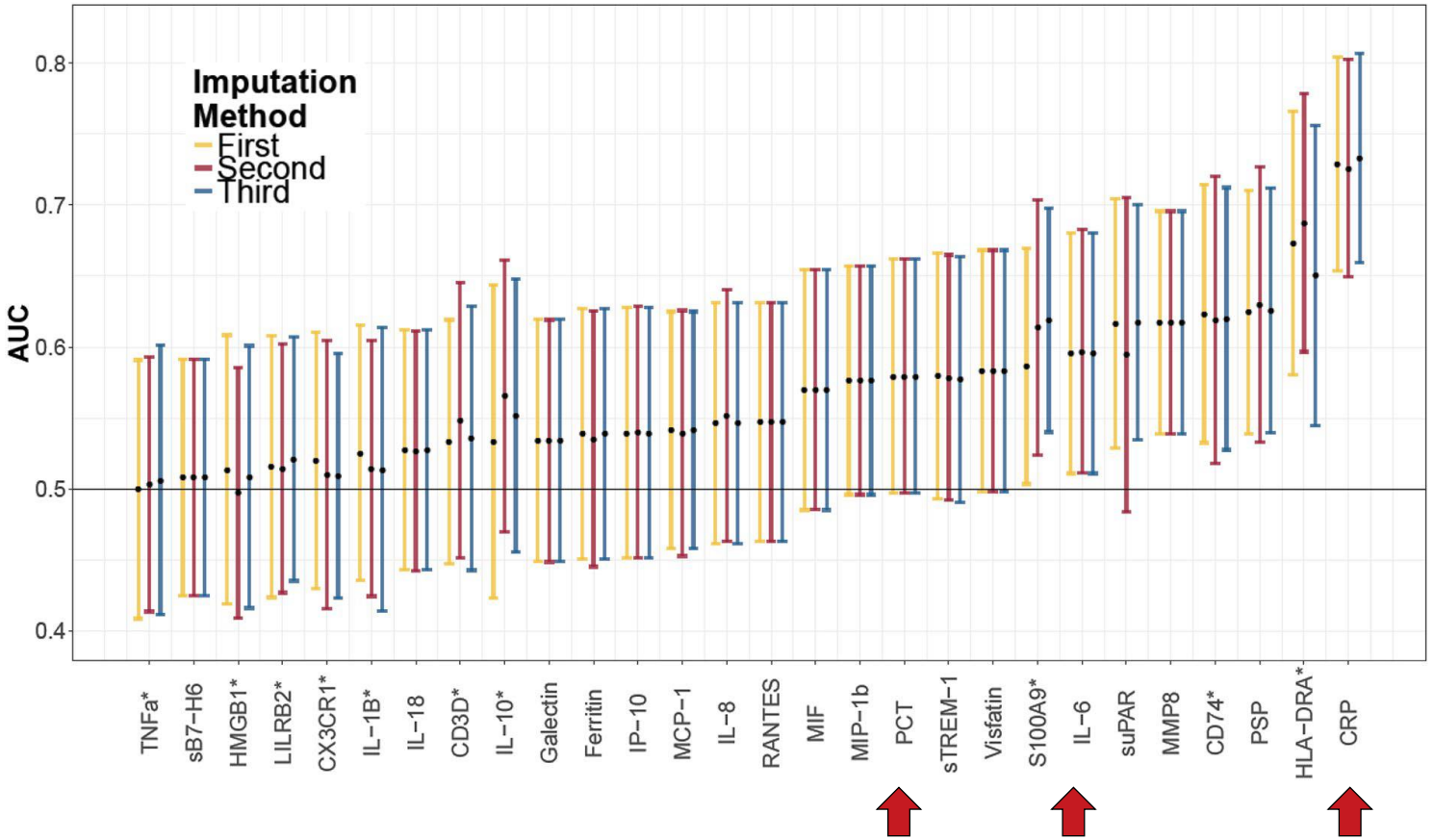
Takahashi W et al. Shock 2016; 46(3):254-260.

Zusammenfassung – Stellenwert der Biomarker

	CRP	PCT	IL-6
Frühmarker	-	+(+)	+++
DD bakteriell / viral	+	+++	+
Prognose	(+)	+	+++
Therapieerfolg	+	+++	++

ORIGINAL

Circulating biomarkers may be unable to detect infection at the early phase of sepsis in ICU patients: the CAPTAIN prospective multicenter cohort study



Parlato M et al. Intensive Care Med 2018; 44:1061-1070.

Sepsis

Sepsis-Verdacht
Infektion/Infektionsverdacht + qSOFA-Score ≥ 2

Sepsis
Infektion/Infektionsverdacht + Anstieg SOFA-Score ≥ 2

Septischer Schock
Sepsis + MAP < 65 mmHg + Serum-Laktat ≥ 2 mmol/l

Singer M et al., JAMA 2016, 315(1):801-810

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Ruhr-Universität


Schauspielhaus

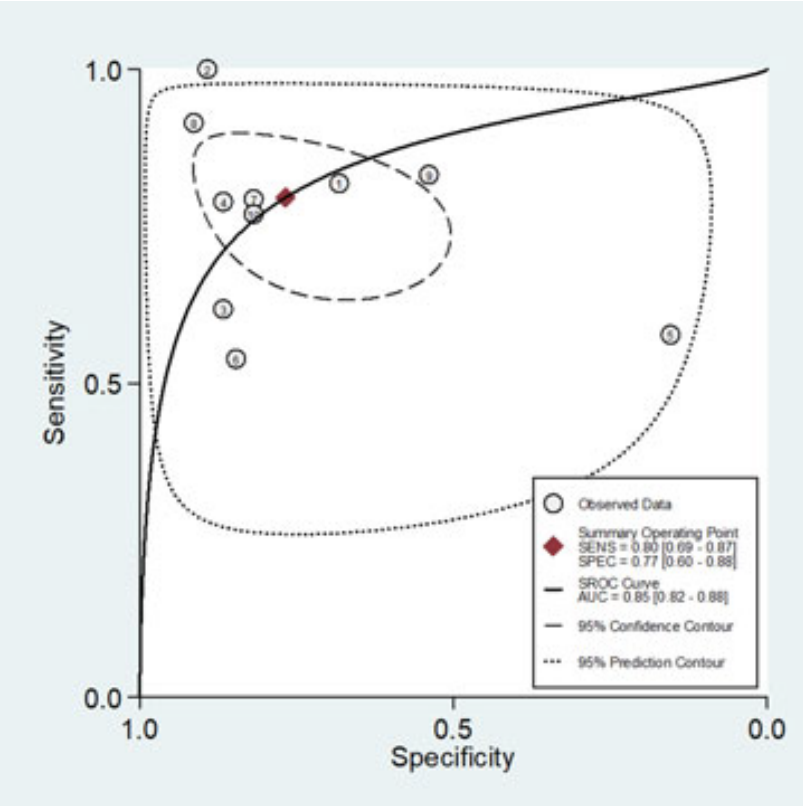
Vielen Dank für Ihre Aufmerksamkeit!


Deutsches Bergbaumuseum

SYMBARA Systemmedizinbasierte personalisierte Sepsisanalyse

Backup-Folien

Procalcitonin (PCT) zur Sepsis-Diagnose



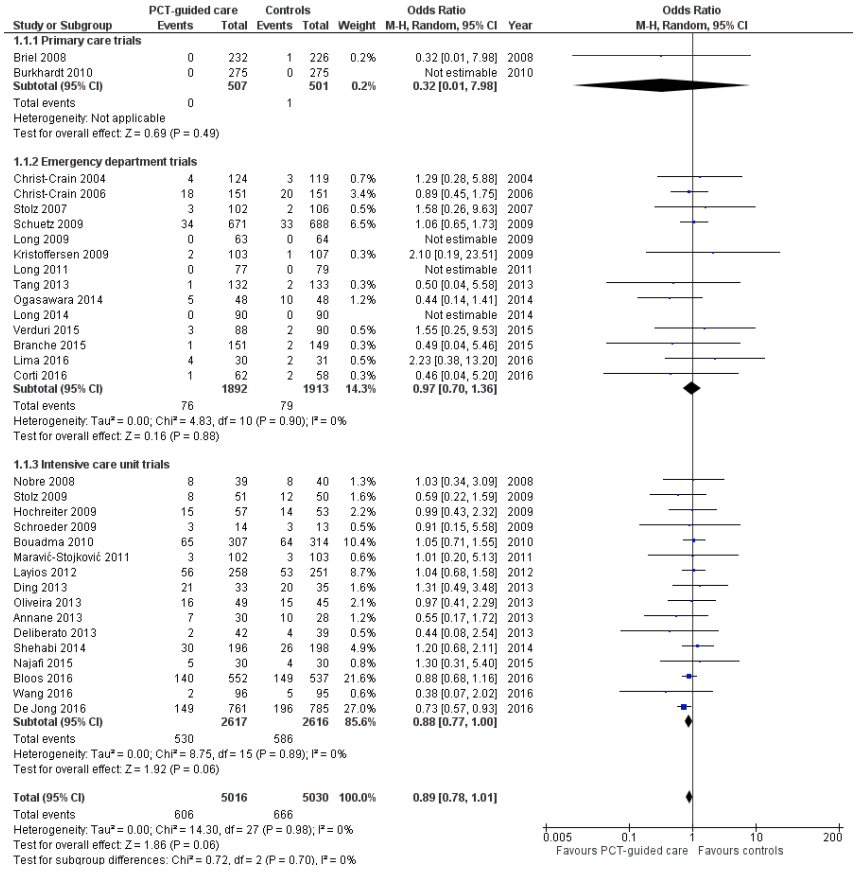
AUC = 0.85 (95% CI, 0.82-0.88)

Sensitivität = 0.80 (95% CI, 0.69-0.87)

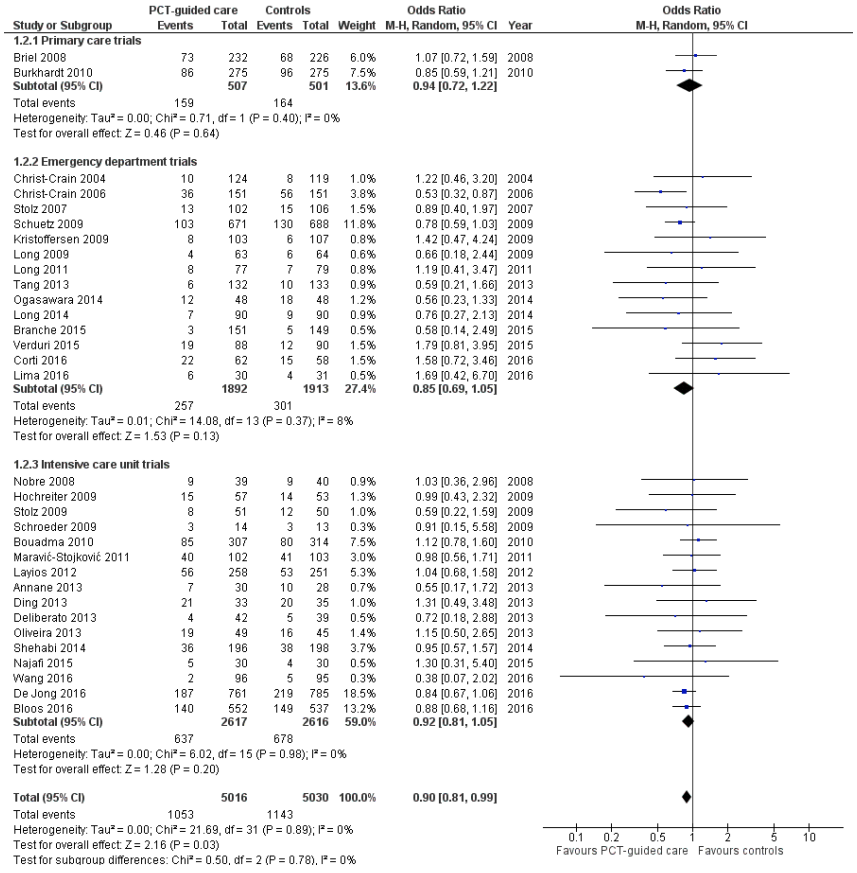
Spezifität = 0.77 (95% CI, 0.60-0.88)

Tan M, et al. J Cell Biochem. 2018; 1-8.

Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections (Review)



Mortalität



Therapieversagen an Tag 30

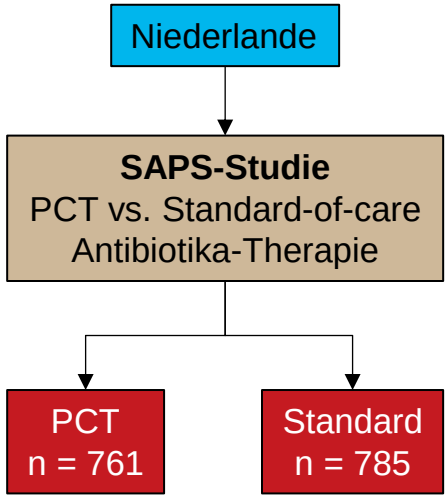
Schuetz P et al. Cochrane Database Syst Rev 2017; 10:CD007498.

Kosten-Effektivität

Table 1 Overview of model outcomes

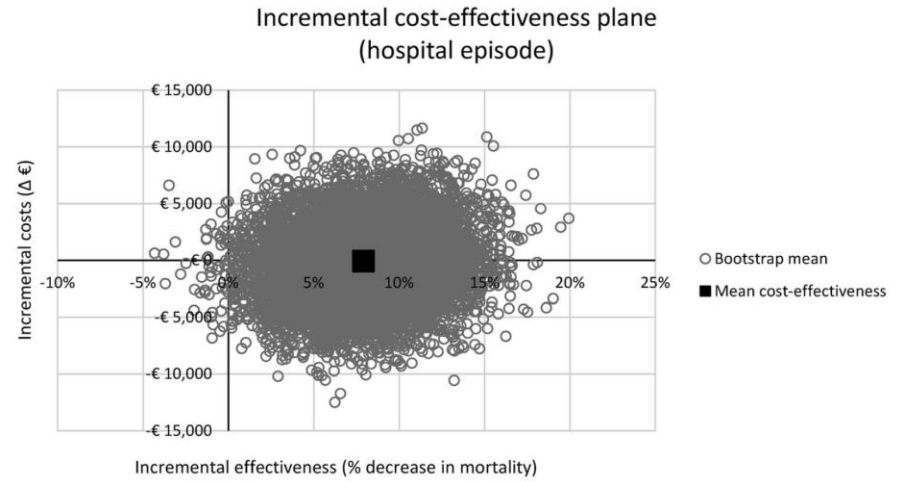
Type of parameter	Parameter	PCT, mean (95% CI)	Standard of care, mean (95% CI)	Effect, mean (95% CI)
Effectiveness outcomes				
Hospital stay	ICU stay, days (*n*)	14.6 (12.4 to 16.9)	14.3 (12.5 to 16.1)	0.3 (− 2.2 to 2.8)
	General ward stay, days (*n*)	16.9 (13.9 to 19.6)	17.6 (14.5 to 20.8)	− 0.4 (− 4.3 to 3.5)
Organ support	Mechanical ventilation, days (*n*)	4.7 (4.0 to 5.6)	5.4 (4.5 to 6.3)	− 0.6 (− 1.3 to 0.0)
	Renal replacement therapy, days (*n*)	0.8 (0.5 to 1.1)	0.9 (0.5 to 1.3)	− 0.1 (− 0.5 to 0.2)
Medication	Antibiotics, days (*n*)	6.9 (5.6 to 8.5)	8.2 (7.0 to 9.5)	− 1.2 (− 1.9 to − 0.4)
	SDD and SOD (*n*)	4.0 (0.7 to 8.2)	4.9 (0.9 to 9.9)	− 0.9 (− 2.1 to − 0.1)
Laboratory tests	Cultures (*n*)	4.2 (2.8 to 5.9)	4.8 (3.2 to 6.5)	− 0.5 (− 1.4 to 0.2)
	PCT (*n*)	6.4 (5.7 to 7.3)	0.0 (0.0 to 0.0)	6.4 (5.7 to 7.3)
	Other tests (including order tariff) (*n*)	14.3 (11.3 to 17.3)	14.7 (11.8 to 17.7)	− 0.4 (− 2.8 to 2.1)
In-hospital mortality		21.8% (17.1% to 26.4%)	29.8% (23.5% to 36.4%)	− 7.9% (− 13.9% to − 1.8%)
QALYs		0.52 (0.49 to 0.54)	0.47 (0.43 to 0.51)	0.05 (0.00 to 0.10)
Cost outcomes				
Hospital stay	ICU stay	€32,908 (€28,109 to €38,131)	€32,390 (€28,080 to €36,673)	€519 (− €5227 to €6118)
	General ward stay	€9594 (€6218 to €12,669)	€9972 (€6331 to €13,525)	− €378 (− €2206 to €1300)
Organ support	Mechanical ventilation	€1991 (€1667 to €2369)	€2259 (€1867 to €2671)	− €268 (− €555 to €9)
	Renal replacement therapy	€362 (€244 to €500)	€408 (€247 to €592)	− €46 (− €217 to €116)
Medication	Antibiotics	€203 (€131 to €283)	€237 (€168 to €317)	− €35 (− €73 to €6)
	SDD and SOD	€127 (€32 to €226)	€157 (€42 to €267)	− €30 (− €64 to − €1)
Laboratory tests	Cultures	€109 (€72 to €151)	€122 (€81 to €165)	− €13 (− €34 to €6)
	PCT	€204 (€181 to €232)	€0 (€0 to €0)	€204 (€181 to €232)
	Other tests (including order tariff)	€584 (€484 to €677)	€602 (€502 to €707)	− €19 (− €96 to €56)
Total hospital costs		€46,081 (€38,242 to €54,120)	€46,146 (€39,383 to €53,042)	− €65 (− €6314 to €6107)
Healthcare costs (follow up)		€27,585 (€26,031 to €29,261)	€24,815 (€22,311 to €27,056)	€2770 (€136 to €5550)
Total healthcare costs (up to 1 year follow up)		€73,665 (€66,065 to €81,344)	€70,961 (€64,776 to €77,082)	€2704 (− €4495 to €10,005)
Lost productivity		€6982 (€6582 to €7370)	€6923 (€6570 to €7276)	€59 (− €364 to €485)
Total societal costs (up to 1 year follow up)		€80,647 (€72,918 to €88,401)	€77,884 (€71,604 to €84,116)	€2763 (− €4491 to €10,172)

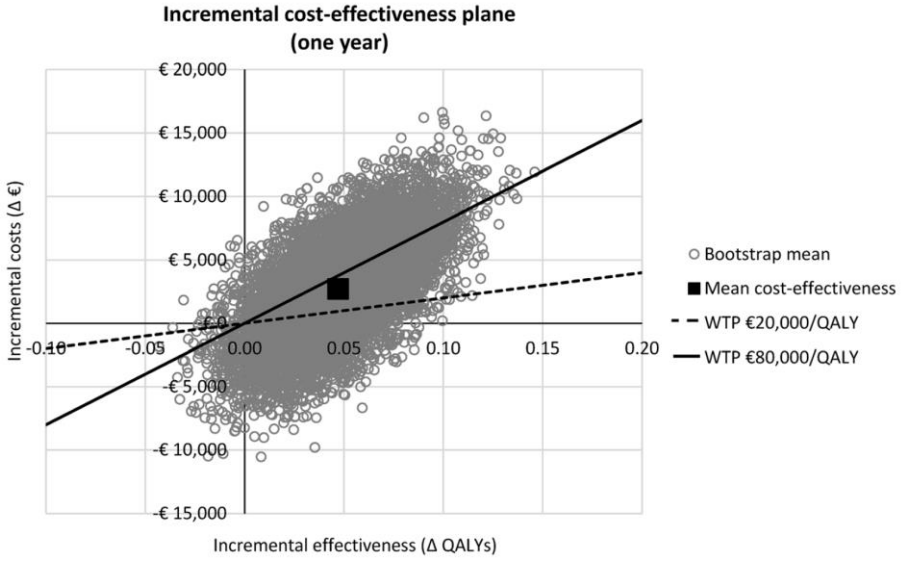
This table shows an overview of the model outcomes in terms of mean effectiveness and costs on an individual patient level. The mean model outcomes (and accompanying 95% CIs) are shown for the procalcitonin (PCT) group and the standard of care group. In addition, the differences between these groups (and accompanying 95% CIs) are provided
SDD selective digestive decontamination, *SOD* selective oral decontamination, *QALY* quality-adjusted life year

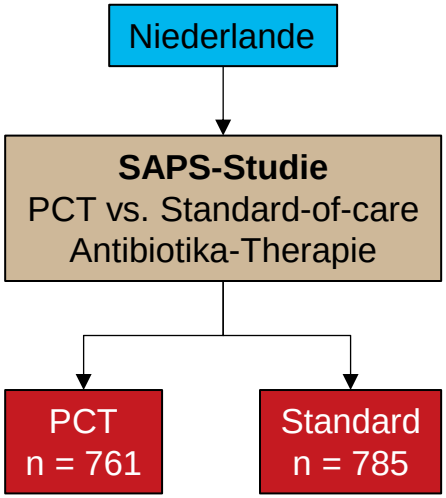


Kip MMA et al. Critical Care 2018; 22:293.

Kosten-Effektivität







Kip MMA et al. Critical Care 2018; 22:293.

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

TABLE 3] Matched, Regression Adjusted Outcomes (N = 132,112)

Variable	PCT		No PCT		Difference		*P* Value
	Mean of Adjusted Value	95% CI	Mean of Adjusted Value	95% CI	Mean of Adjusted Value	95% CI	
Total LOS	11.6	11.4 to 11.7	12.7	12.6 to 12.8	−1.2	−1.3 to −1.0	< .001
ICU LOS	5.1	5.1 to 5.2	5.3	5.3 to 5.4	−0.2	−0.3 to −0.1	.031
Total cost, $	30,454	29,968 to 31,033	33,213	32,964 to 33,556	−2,759	−3,321 to −2,156	< .001
ICU cost, $	20,155	20,625 to 19,798	21,465	21,270 to 21,710	−1,310	−1,702 to −847	< .001
Pharmacy cost, $	4,238	4,119 to 4,453	4,568	4,480 to 4,678	−331	−488 to −99	.002
Antibiotic cost, $	882	854 to 948	952	931 to 980	−70	−105 to 4	.074
Laboratory cost, $	1,807	1,778 to 1,839	1,726	1,710 to 1,744	81	51 to 114	.002
Total antibiotic exposure[a]	16.2	16.1 to 16.5	16.9	16.8 to 17.1	−0.7	−0.9 to −0.4	.006
Discharged to home	44.1%	43.7 to 44.6	41.3	41.0 to 41.6	2.8	2.3 to 3.3	.012
Discharged to hospice	6.3%	6.0 to 6.5	6.4	6.3 to 6.6	−0.2	−0.4 to 0.0	< .001
Discharged to other	1.8%	1.6 to 1.9	1.6	1.5 to 1.7	0.1	0.0 to 0.3	.779
Transfer to SNF/ICF/LTC	22.6%	22.2 to 23.0	25.2	24.9 to 25.5	−2.6	−3.1 to −2.2	< .001
Transfer to acute care	6.3%	6.0 to 6.5	7.2	7.0 to 7.3	−0.9	−1.2 to −0.6	< .001
Inpatient mortality[b]	19.0%	18.6 to 19.4	18.3	18.0 to 18.5	0.7	0.3 to 1.2	.001
Inpatient mortality[c]	19.1%	18.7 to 19.4	19.1	18.9 to 19.3	−0.0	−0.5 to 0.4	.93

95% CIs were calculated using bootstrap method with 500 replications. See Table 1 and 2 legends for expansion of abbreviations.
[a]Total antibiotic exposure comprises both total number of systemic antibiotics administered and duration of administration.
[b]All subjects.
[c]Analysis incorporating the CareScience Mortality Risk Model score; N = 127,809.

Balk RA et al. Chest 2017; 151(1):23-33.