Il ruolo dei biomarcatori e delle terapie di supporto: strategie di companion test

Bruno Viaggi

Dipartimento di Anestesia
SOD Neuroanestesia e Rianimazione
A.O.U. Careggi, Firenze

Gian Maria Rossolini

Dip. Medicina Sperimentale e Clinica
Università di Firenze

SOD Microbiologia e Virologia
A.O.U. Careggi, Firenze

Meeting Antibiotic Stewardship

30 - 31 Maggio 2018, Ranica
Istituto di Ricerche Farmacologiche Mario Negri

Dichiarazione su potenziali conflitti di interesse
Consulenze, partecipazione advisory boards, speaker's bureau, contratti/contributi di ricerca e di eventi studio:
Abbott**, **Accelerate Diagnostics, Ada, Alifax, Angelini, Becton Dickinson, Bellco, Merck Sharp & Dohme, Pfizer, Thermofischer Scientific

Dichiarazione su potenziali conflitti di interesse
Consulenze, partecipazione advisory boards, speaker's bureau, contratti e contributi di ricerca, travel grants:
Accelerate, Achaogen, Alifax, Angelini ACRAF, Astra Zeneca, Basilea, Beckman Coulter, Becton-Dickinson, bioMérieux, Biotest, Cepheid, Checkpoints, Curetis, DID Diagnostics, Elitech, Merck, Menarini, Nordic Pharma, Novartis, Pfizer, Rempex-TMCo, Seegene, Shionogi, ThermoFisher, Zambon

Pros and cons of using biomarkers versus clinical decisions in start and stop decisions for antibiotics in the critical care setting

Albrich WC et al Intensive Care Med 2015

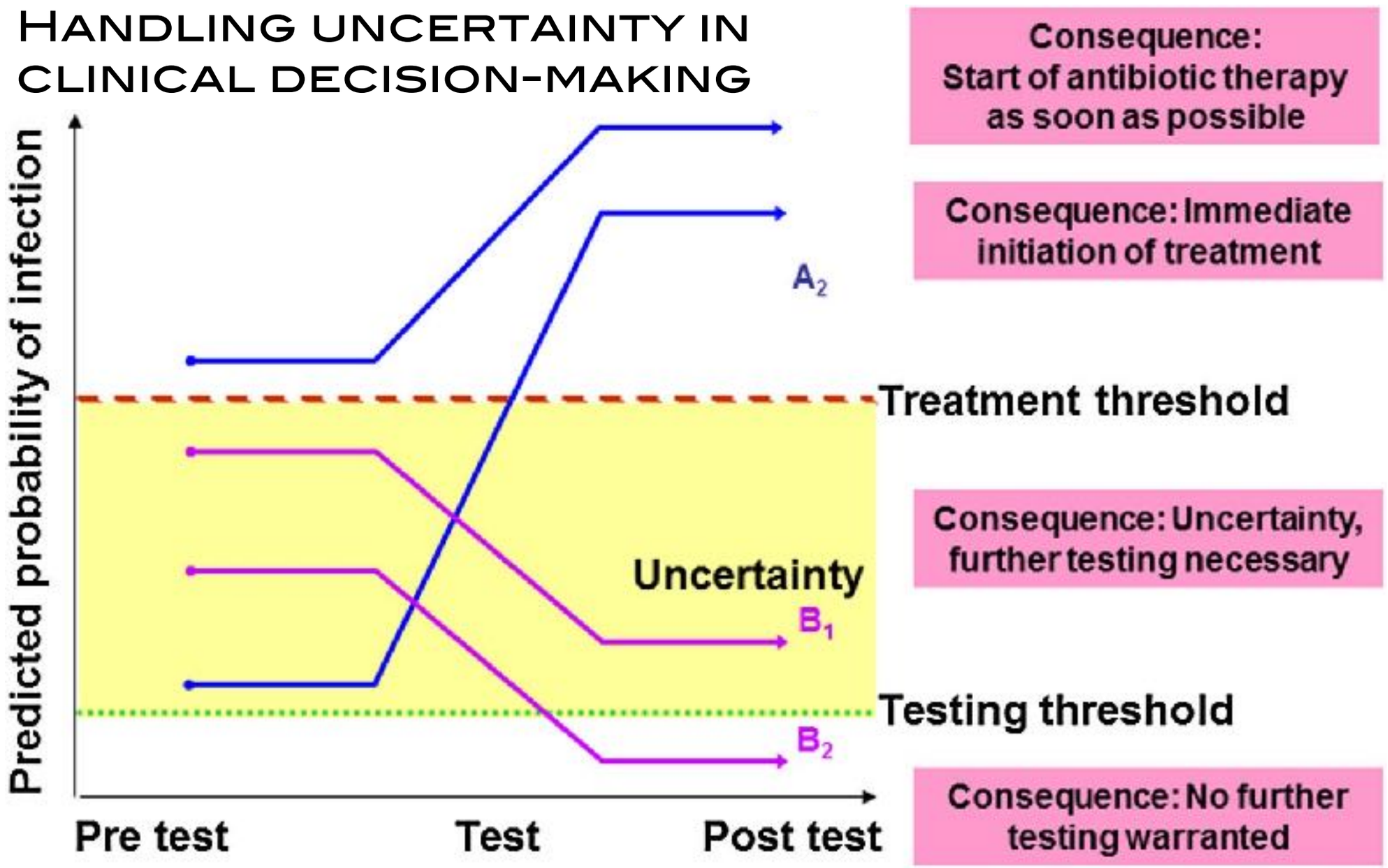
What to expect from a biomarker?

It has been suggested that biomarkers should be sensitive and specific, measurable with good precision and reproducibility, readily available, affordable, responsive to minor changes, and provide timely results

Pros and cons of using biomarkers versus clinical decisions in start and stop decisions for antibiotics in the critical care setting

Albrich WC et al Intensive Care Med 2015

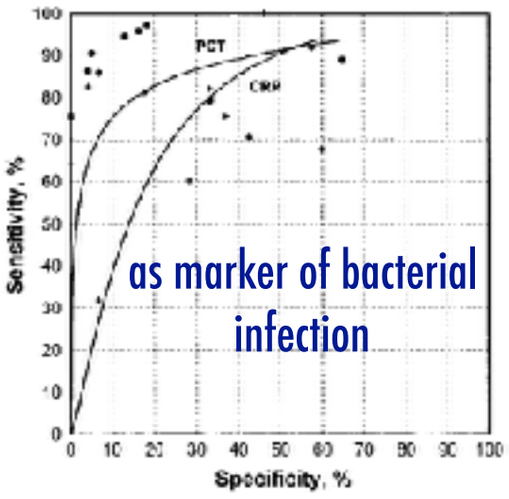
the real impact of a diagnostic test should be evaluated on the basis on how it will change the pretest probability and reclassify "uncertain" situations using Bayes computations or if multiple tests are used multivariable logistic regression analysis



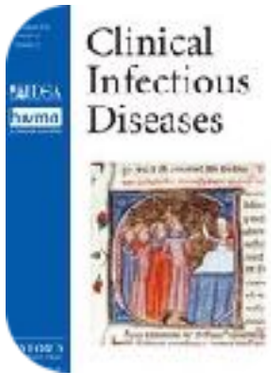
Serum Procalcitonin and C-Reactive Protein Levels as Markers of Bacterial Infection: A Systematic Review and Meta-analysis

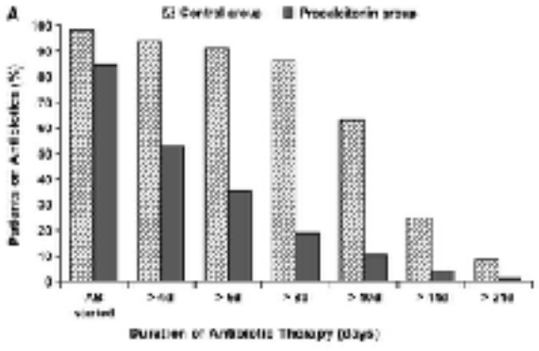
Simon Liliana

Clin Infect Dis 2004;39:206-217



as marker of bacterial infection





Reduction of antibiotic treatment duration from 12 to 5 days

ProCAP study

Procalcitonin Guidance of Antibiotic Therapy in Community-acquired Pneumonia

A Randomized Trial

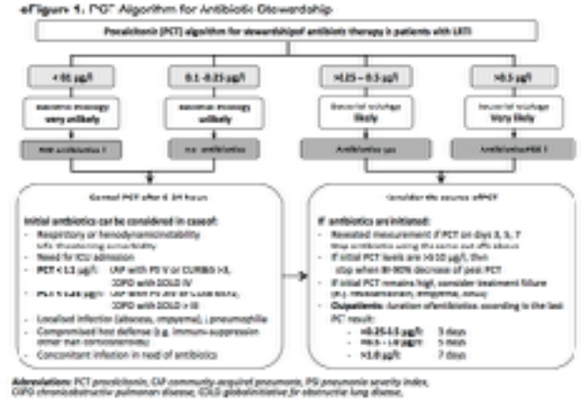
Christ-Crain M

Am J Respir Crit Care Med 2006;174:84-93

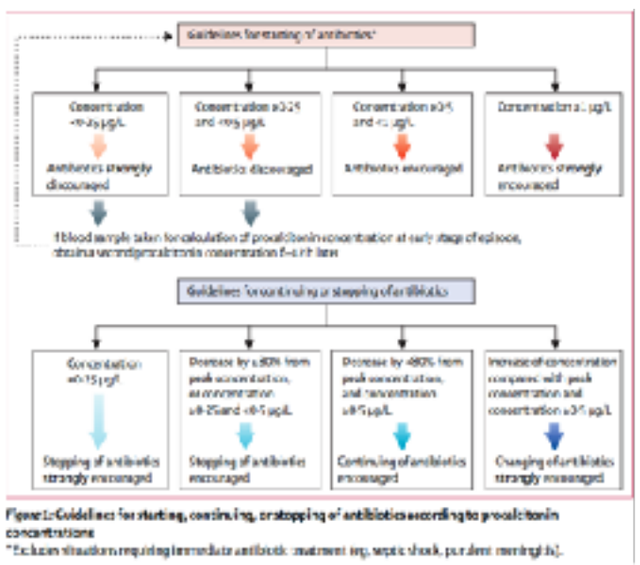
ProHOSP study

Effect of Procalcitonin-Based Guidelines vs Standard Guidelines on Antibiotic Use in Lower Respiratory Tract Infections

The ProHOSP Randomized Controlled Trial



JAMA 2009;302(10):1059-1066



PRORATA trial

Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial

Lancet 2010;375:463-74

Procalcitonin to Initiate or Discontinue Antibiotics in Acute Respiratory Tract Infections

The Cochrane Library 2012;Issue 9

THE COCHRANE COLLABORATION®

Analysis 1.1. Comparison 1 Procalcitonin algorithm versus no procalcitonin algorithm stratified by clinical setting, Outcome 1 Mortality at 30 days.

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

Comparison: 1 Procalcitonin algorithm versus no procalcitonin algorithm stratified by clinical setting

Outcome: 1 Mortality at 30 days

Study or subgroup	PCT Algorithm n/N	No PCT Algorithm n/N	Odds Ratio M-H,Random,95% CI	Odds Ratio M-H,Random,95% CI
1 Primary care trials				
Briel 2008	0/232	1/226		0.32 [0.01, 7.98]
Burkhardt 2010	0/275	0/275		0.0 [0.0, 0.0]
Subtotal (95% CI)	**507**	**501**		**0.32 [0.01, 7.98]**
Total events: 0 (PCT Algorithm), 1 (No PCT Algorithm)				
Heterogeneity: Tau² = 0.0; Chi² = 0.0, df = 0 (P = 1.00); I² =0.0%				
Test for overall effect: Z = 0.69 (P = 0.49)				
2 Emergency department trials				
Christ-Crain 2004	4/124	3/119		1.29 [0.28, 5.88]
Christ-Crain 2006	18/151	20/151		0.89 [0.45, 1.75]
Stolz 2007	3/102	2/106		1.58 [0.26, 9.63]
Schuetz 2009	349/671	330/688		1.06 [0.85, 1.33]
Kristoffersen 2009	2/103	1/107		2.10 [0.19, 23.51]
Long 2009	0/63	0/64		0.0 [0.0, 0.0]
Long 2011	0/77	0/79		0.0 [0.0, 0.0]
Subtotal (95% CI)	**1291**	**1314**		**1.05 [0.72, 1.52]**
Total events: 61 (PCT Algorithm), 59 (No PCT Algorithm)				
Heterogeneity: Tau² = 0.0; Chi² = 0.82, df = 4 (P = 0.94); I² =0.0%				
Test for overall effect: Z = 0.26 (P = 0.80)				
3 Intensive care unit trials				
Nobre 2008	5/25	8/27		0.59 [0.16, 2.14]
Hochreiter 2009	7/24	5/19		1.15 [0.30, 4.44]
Schroeder 2009	0/4	0/4		0.0 [0.0, 0.0]

0.01 0.1 1 10 100

Favours PCT Algorithm | Favours No PCT Algorithm

(Continued . . .)

14 RCTs of adult **(4221)** with ARIs who received an antibiotic treatment either based on a procalcitonin algorithm or usual care/guidelines.

PRIMARY ENDPOINT

- mortality at days 30
- treatment failure at 30 days

SECONDARY ENDPOINT

- antibiotic use
- length of hospital stay
- length of ICU stay

Analysis 1.2. Comparison 1 Procalcitonin algorithm versus no procalcitonin algorithm stratified by clinical setting, Outcome 2 Treatment failure at 30 days.

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

Comparison: 1 Procalcitonin algorithm versus no procalcitonin algorithm stratified by clinical setting

Outcome: 2 Treatment failure at 30 days

Study or subgroup	PCT Algorithm n/N	No PCT Algorithm n/N	Odds Ratio M-H,Random,95% CI	Odds Ratio M-H,Random,95% CI
1 Primary care trials				
Briel 2008	73/232	68/226		1.07 [0.72, 1.59]
Burkhardt 2010	86/275	96/275		0.85 [0.59, 1.21]
Subtotal (95% CI)	**507**	**501**		**0.94 [0.72, 1.22]**
Total events: 159 (PCT Algorithm), 164 (No PCT Algorithm)				
Heterogeneity: Tau² = 0.0; Chi² = 0.71, df = 1 (P = 0.40); I² =0.0%				
Christ-Crain 2006	36/151	56/151		0.53 [0.32, 0.87]
Stolz 2007	13/102	15/106		0.89 [0.40, 1.97]
Kristoffersen 2009	8/103	6/107		1.42 [0.47, 4.24]
Long 2009	4/63	6/64		0.66 [0.18, 2.44]
Schuetz 2009	103/671	130/688		0.78 [0.59, 1.03]
Long 2011	8/77	7/79		1.19 [0.41, 3.47]
Subtotal (95% CI)	**1291**	**1314**		**0.78 [0.62, 0.96]**
Total events: 182 (PCT Algorithm), 228 (No PCT Algorithm)				
Heterogeneity: Tau² = 0.0; Chi² = 5.01, df = 6 (P = 0.54); I² =0.0%				
Test for overall effect: Z = 2.30 (P = 0.021)				
3 Intensive care unit trials				
Nobre 2008	5/25	8/27		0.59 [0.16, 2.14]
Stolz 2009	8/51	12/50		0.59 [0.22, 1.59]
Schroeder 2009	0/4	0/4		0.0 [0.0, 0.0]
Hochreiter 2009	7/24	5/19		1.15 [0.30, 4.44]
Bouadma 2010	37/183	49/211		0.84 [0.52, 1.36]
Subtotal (95% CI)	**287**	**311**		**0.79 [0.53, 1.17]**
Total events: 57 (PCT Algorithm), 74 (No PCT Algorithm)				
Heterogeneity: Tau² = 0.0; Chi² = 0.88, df = 3 (P = 0.83); I² =0.0%				
Test for overall effect: Z = 1.18 (P = 0.24)				
Total (95% CI)	**2085**	**2126**		**0.83 [0.71, 0.97]**
Total events: 398 (PCT Algorithm), 466 (No PCT Algorithm)				
Heterogeneity: Tau² = 0.0; Chi² = 7.88, df = 12 (P = 0.79); I² =0.0%				
Test for overall effect: Z = 2.37 (P = 0.018)				
Test for subgroup differences: Chi² = 1.28, df = 2 (P = 0.53), I² =0.0%				

0.01 0.1 1 10 100

Favours experimental Favours control

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Conclusions

- Use of procalcitonin to guide initiation and duration of antibiotic treatment in patients with ARI was not associated with higher mortality rates or treatment failure.
- Antibiotic consumption was significantly reduced
- Lower risk of side effects and reduced antimicrobial resistance

Promising New Assays and Technologies for the Diagnosis and Management of Infectious Diseases

S. F. Mitsuma,[1,a] M. K. Mansour,[1,a] J. P. Dekker,[2] J. Kim,[2] M. Z. Rahman,[1] A. Tweed-Kent,[3] and P. Schuetz[4]

tial for clinical use in the near future. The scope of this review is broad and includes topics such as the serum marker procalcitonin, gene expression profiling, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), and nucleic acid aptamers. Principles that underlie each assay or technology, their clinical applications, and potential strengths and limitations are addressed.

Matteo Bassetti
Jan J. De Waele
Philippe Eggimann
Josè Garnacho-Montero
Gunnar Kahlmeter
Francesco Menichetti
David P. Nicolau
Jose Arturo Paiva
Mario Tumbarello
Tobias Welte
Mark Wilcox
Jean Ralph Zahar
Garyphallia Poulakou

Preventive and therapeutic strategies in critically ill patients with highly resistant bacteria

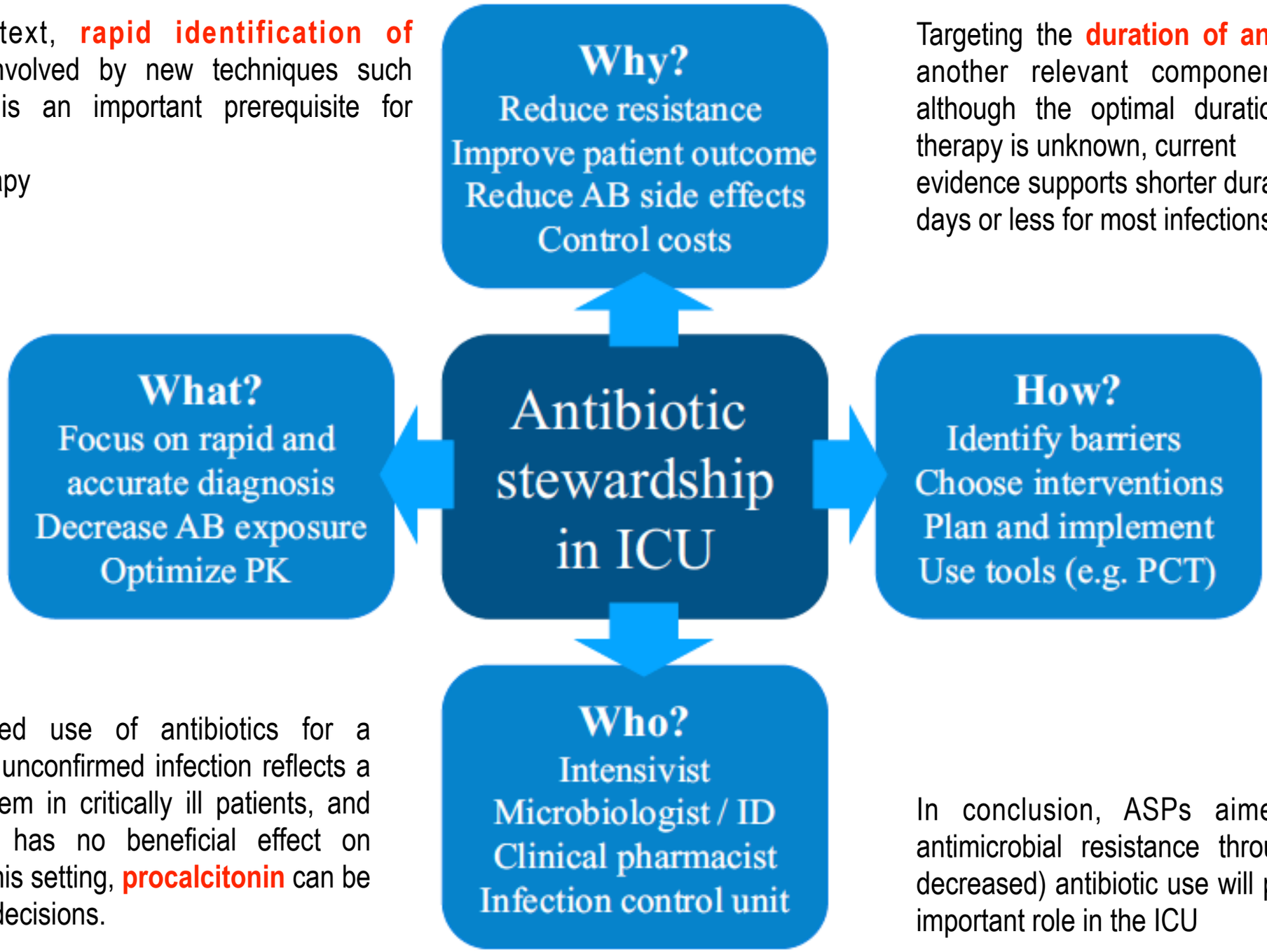
…Systematic reduction of the duration of antimicrobial treatment according to the clinical evolution and the kinetics of biomarkers such as PCT of…..

Intensive Care Med 2015

Understanding antibiotic stewardship for the critically ill

De Waele et al Intensive Care Med 2015

In this context, **rapid identification of pathogens** involved by new techniques such MALDI–TOF is an important prerequisite for optimizing
antibiotic therapy



Targeting the **duration of antibiotic therapy** is another relevant component of ASPs and, although the optimal duration of antimicrobial therapy is unknown, current
evidence supports shorter durations of therapy—8 days or less for most infections

Also, prolonged use of antibiotics for a suspected but unconfirmed infection reflects a common problem in critically ill patients, and antibiotic use has no beneficial effect on outcomes. In this setting, **procalcitonin** can be used to guide decisions.

In conclusion, ASPs aimed at combatting antimicrobial resistance through improved (i.e. decreased) antibiotic use will play an increasingly important role in the ICU

From 32 eligible RCTs including 18 new trials for this 2017 update, we obtained individual participant data from 26 trials including 6708 participants, which we included in the main individual participant data meta-analysis. We did not obtain individual participant data for four trials, and two trials did not include people with confirmed ARIs. According to GRADE, the quality of the evidence was high for the outcomes mortality and antibiotic exposure, and quality was moderate for the outcomes treatment failure and antibiotic- related side effects.

Cochrane Library

Cochrane Database of Systematic Reviews

October 2017

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

Main results

Figure 4. Funnel plot of comparison: 1 Procalcitonin algorithm versus no procalcitonin algorithm stratified by clinical setting, outcome: 1.1 Mortality at 30 days.

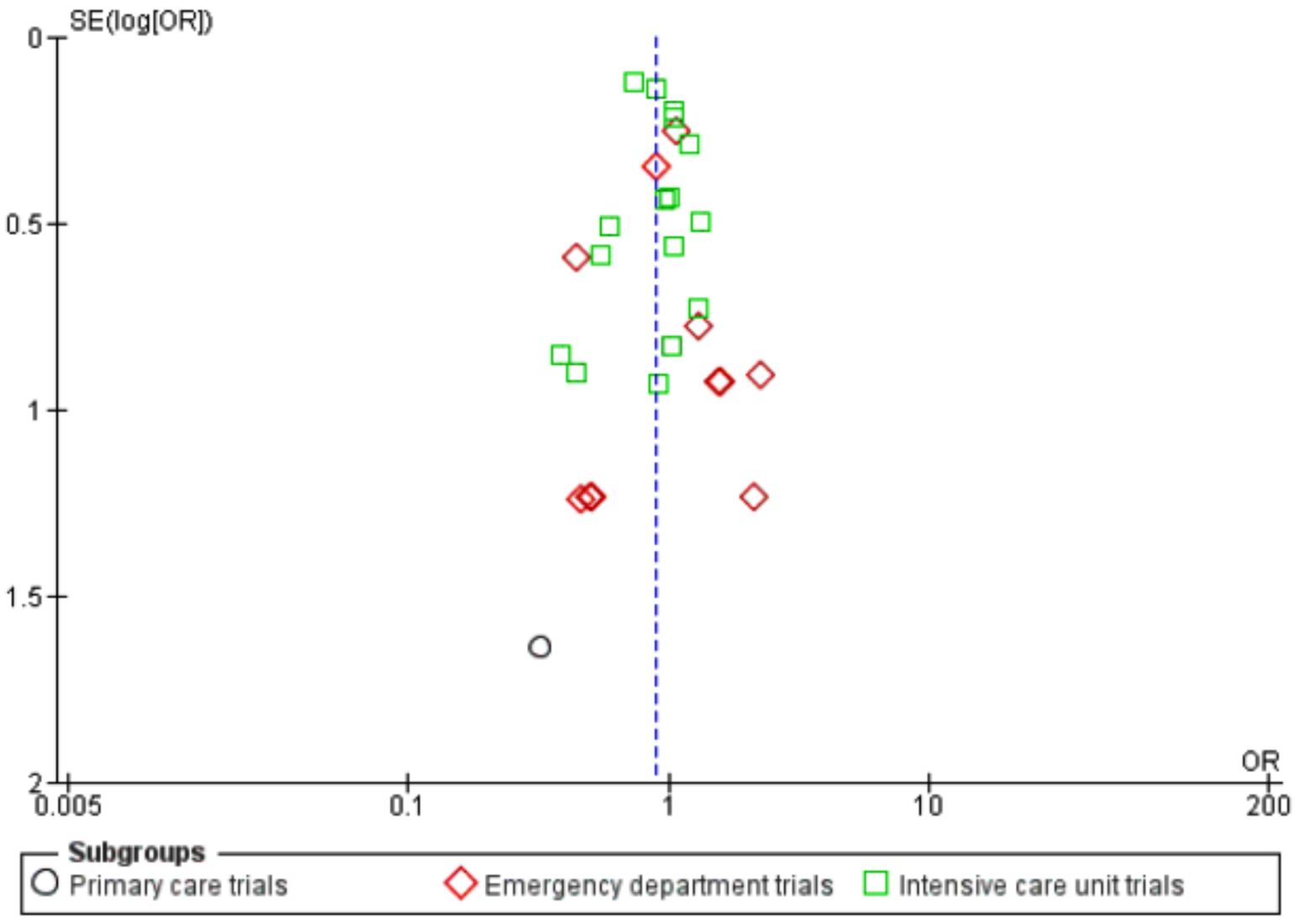
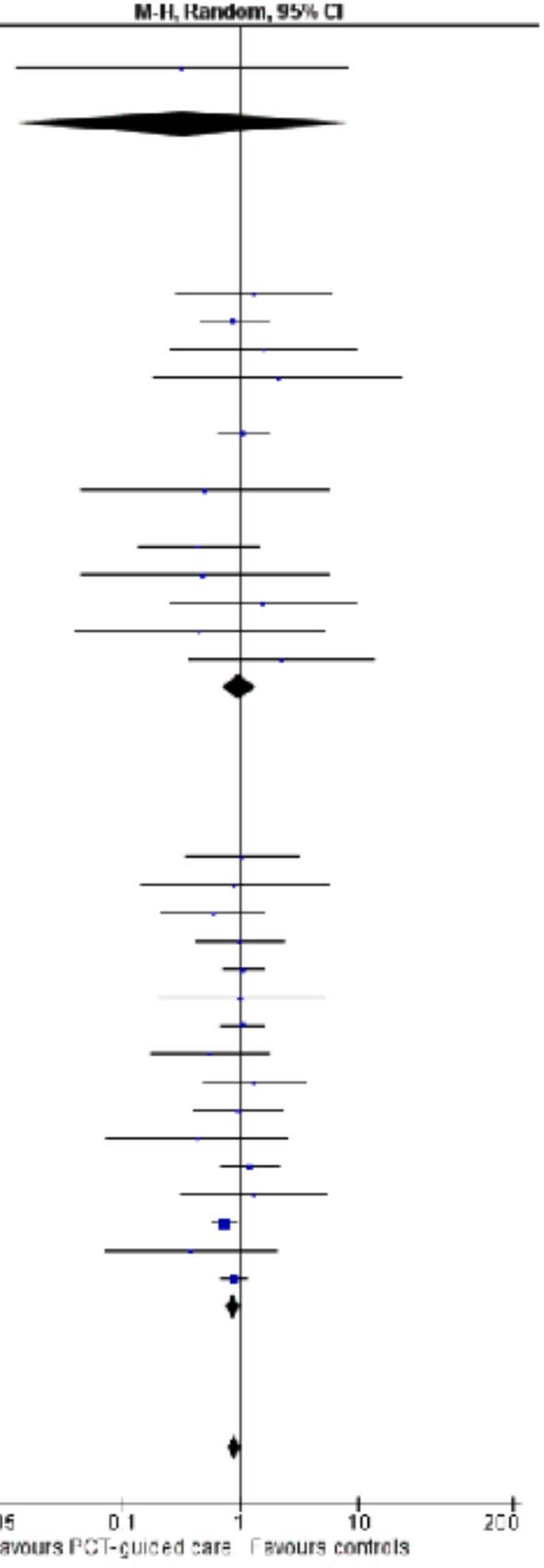


Figure 5. Forest plot of comparison: 1 Procalcitonin algorithm versus no procalcitonin algorithm stratified by clinical setting, outcome: 1.1 Mortality at 30 days.

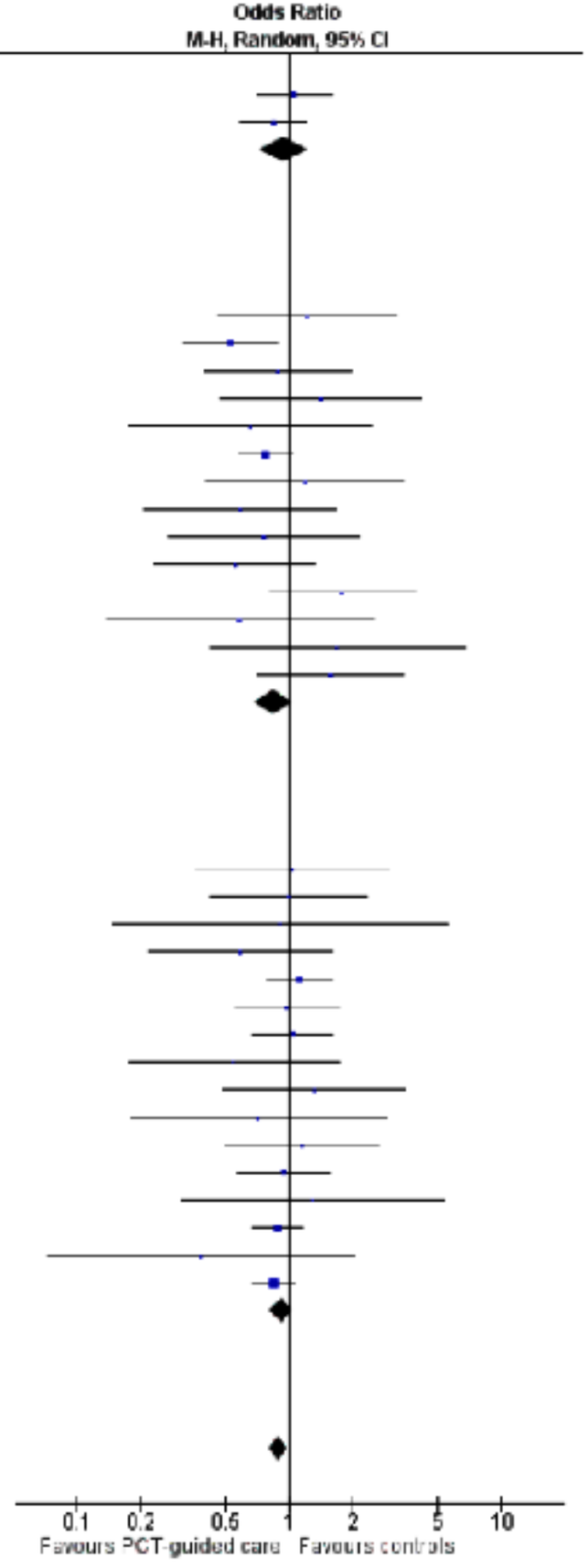
Study or Subgroup	PCT-guided care Events	Total	Controls Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.1.1 Primary care trials							
Briel 2009	0	232	1	226	0.2%	0.32 [0.01, 7.90]	2009
Burkhardt 2010	0	275	0	275		Not estimable	2010
Subtotal (95% CI)		**507**		**501**	0.2%	**0.32 [0.01, 7.98]**	
Total events	0		1				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.69 (P = 0.49)							
1.1.2 Emergency department trials							
Christ-Crain 2004	4	124	3	119	0.7%	1.29 [0.28, 5.88]	2004
Christ-Crain 2006	18	151	20	151	3.4%	0.89 [0.45, 1.75]	2006
Stolz 2007	3	102	2	106	0.5%	1.58 [0.26, 9.63]	2007
Kristoffersen 2009	2	103	1	107	0.3%	2.10 [0.19, 23.51]	2009
Long 2009	0	63	0	84		Not estimable	2009
Schuetz 2009	34	671	33	658	6.5%	1.06 [0.65, 1.73]	2009
Long 2011	0	77	0	79		Not estimable	2011
Tang 2013	1	132	2	133	0.3%	0.50 [0.04, 5.58]	2013
Long 2014	0	90	0	90		Not estimable	2014
Ogasawara 2014	5	48	10	48	1.2%	0.44 [0.14, 1.41]	2014
Branche 2015	1	151	2	149	0.3%	0.49 [0.04, 5.46]	2015
Verduri 2015	3	88	2	90	0.5%	1.55 [0.25, 9.53]	2015
Corli 2016	1	62	2	58	0.3%	0.46 [0.04, 5.20]	2016
Lima 2016	4	30	2	31	0.5%	2.29 [0.38, 13.20]	2016
Subtotal (95% CI)		**1892**		**1913**	14.3%	**0.97 [0.70, 1.36]**	
Total events	76		79				
Heterogeneity: Tau² = 0.00; Chi² = 4.83, df = 10 (P = 0.90); I² = 0%							
Test for overall effect: Z = 0.16 (P = 0.88)							
1.1.3 Intensive care unit trials							
Nobre 2008	0	39	0	40		1.00 [0.04, 3.09]	2008
Schroeder 2009	3	14	3	13	0.5%	0.91 [0.15, 5.50]	2009
Stolz 2009	8	51	12	50	1.6%	0.59 [0.22, 1.59]	2009
Hochreiter 2009	15	57	14	59	2.2%	0.99 [0.43, 2.32]	2009
Bouadma 2010	65	307	64	314	10.4%	1.05 [0.71, 1.55]	2010
Muravić-Stojković 2011	3	102	3	103	0.6%	1.01 [0.20, 5.13]	2011
Layios 2012	56	258	53	251	8.7%	1.04 [0.68, 1.58]	2012
Annane 2013	7	30	10	28	1.2%	0.55 [0.17, 1.72]	2013
Ding 2013	21	33	20	35	1.6%	1.31 [0.49, 3.48]	2013
Oliveira 2013	16	49	15	45	2.1%	0.97 [0.41, 2.29]	2013
Deliberato 2013	2	42	4	39	0.5%	0.44 [0.08, 2.54]	2013
Shehabi 2014	30	196	26	190	4.9%	1.20 [0.60, 2.41]	2014
Najafi 2015	5	30	4	30	0.8%	1.30 [0.31, 5.40]	2015
De Jong 2016	149	761	196	785	27.0%	0.73 [0.57, 0.93]	2016
Wang 2016	2	96	5	95	0.6%	0.38 [0.07, 2.02]	2016
Bloos 2016	140	552	149	537	21.6%	0.88 [0.68, 1.16]	2016
Subtotal (95% CI)		**2617**		**2616**	85.6%	**0.88 [0.77, 1.00]**	
Total events	530		588				
Heterogeneity: Tau² = 0.00; Chi² = 8.75, df = 15 (P = 0.89); I² = 0%							
Test for overall effect: Z = 1.92 (P = 0.06)							
Total (95% CI)		**5016**		**5030**	100.0%	**0.89 [0.78, 1.01]**	
Total events	606		666				
Heterogeneity: Tau² = 0.00; Chi² = 14.30, df = 27 (P = 0.98); I² = 0%							
Test for overall effect: Z = 1.86 (P = 0.06)							
Test for subgroup differences: Chi² = 0.72, df = 2 (P = 0.70), I² = 0%							



Main results

Figure 6. Forest plot of comparison: 1 Procalcitonin algorithm versus no procalcitonin algorithm stratified by clinical setting, outcome: 1.2 Treatment failure at 30 days.

Study or Subgroup	PCT-guided care Events	Total	Controls Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.2.1 Primary care trials							
Briel 2009	73	232	69	226	6.0%	1.07 [0.72, 1.59]	2009
Burkhardt 2010	86	275	96	275	7.5%	0.85 [0.59, 1.21]	2010
Subtotal (95% CI)		**507**		**501**	**13.6%**	**0.94 [0.72, 1.22]**	
Total events	159		164				
Heterogeneity: Tau² = 0.00; Chi² = 0.71, df = 1 (P = 0.40); I² = 0%							
Test for overall effect: Z = 0.45 (P = 0.64)							
1.2.2 Emergency department trials							
Christ-Crain 2004	10	124	8	119	1.0%	1.22 [0.46, 3.20]	2004
Christ-Crain 2006	36	151	56	151	3.8%	0.53 [0.32, 0.87]	2006
Stolz 2007	13	102	15	106	1.5%	0.89 [0.40, 1.97]	2007
Kristoffersen 2009	6	103	6	107	0.8%	1.42 [0.47, 4.24]	2009
Long 2009	4	63	6	64	0.6%	0.66 [0.18, 2.44]	2009
Schuetz 2009	103	671	130	688	11.8%	0.78 [0.59, 1.03]	2009
Long 2011	6	77	7	79	0.8%	1.19 [0.41, 3.47]	2011
Tang 2013	6	132	10	133	0.9%	0.59 [0.21, 1.66]	2013
Long 2014	7	90	9	90	0.9%	0.76 [0.27, 2.13]	2014
Ogasawara 2014	12	48	18	48	1.2%	0.56 [0.23, 1.33]	2014
Verduri 2015	10	88	12	90	1.5%	1.79 [0.31, 3.95]	2015
Branche 2015	3	151	5	149	0.5%	0.58 [0.14, 2.49]	2015
Lima 2016	6	30	4	31	0.5%	1.69 [0.42, 6.70]	2016
Corti 2016	22	62	15	58	1.5%	1.58 [0.72, 3.46]	2016
Subtotal (95% CI)		**1892**		**1913**	**27.4%**	**0.85 [0.69, 1.05]**	
Total events	257		301				
Heterogeneity: Tau² = 0.01; Chi² = 14.08, df = 13 (P = 0.37); I² = 8%							
Test for overall effect: Z = 1.53 (P = 0.13)							
1.2.3 Intensive care unit trials							
Nobre 2008	9	39	9	40	0.8%	1.03 [0.36, 2.96]	2008
Hochreiter 2009	10	67	14	68	1.3%	0.69 [0.43, 2.32]	2009
Schroeder 2009	3	14	3	13	0.3%	0.91 [0.15, 5.58]	2009
Stolz 2009	8	51	12	50	1.0%	0.59 [0.22, 1.59]	2009
Bouadma 2010	85	307	80	314	7.5%	1.12 [0.78, 1.60]	2010
Maravić-Stojković 2011	40	102	41	103	3.0%	0.98 [0.56, 1.71]	2011
Layios 2012	66	268	53	261	5.3%	1.04 [0.68, 1.58]	2012
Annane 2013	7	30	10	28	0.7%	0.55 [0.17, 1.72]	2013
Ding 2013	21	33	20	35	1.0%	1.31 [0.49, 3.48]	2013
Deliberato 2013	4	42	5	39	0.5%	0.72 [0.18, 2.88]	2013
Oliveira 2013	19	49	16	46	1.4%	1.16 [0.50, 2.66]	2013
Shehabi 2014	36	196	38	198	3.7%	0.95 [0.57, 1.57]	2014
Najafi 2015	2	30	4	30	0.5%	1.30 [0.31, 5.40]	2015
Bloos 2016	140	552	149	537	13.2%	0.88 [0.68, 1.16]	2016
Wang 2016	2	96	5	95	0.3%	0.38 [0.07, 2.02]	2016
De Jong 2016	187	761	219	786	18.6%	0.84 [0.67, 1.06]	2016
Subtotal (95% CI)		**2617**		**2616**	**59.0%**	**0.92 [0.81, 1.05]**	
Total events	637		678				
Heterogeneity: Tau² = 0.00; Chi² = 6.02, df = 15 (P = 0.98); I² = 0%							
Test for overall effect: Z = 1.28 (P = 0.20)							
Total (95% CI)		**5016**		**5030**	**100.0%**	**0.90 [0.81, 0.99]**	
Total events	1053		1143				
Heterogeneity: Tau² = 0.00; Chi² = 21.69, df = 31 (P = 0.09); I² = 0%							
Test for overall effect: Z = 2.15 (P = 0.03)							
Test for subgroup differences: Chi² = 0.50, df = 2 (P = 0.78), I² = 0%							

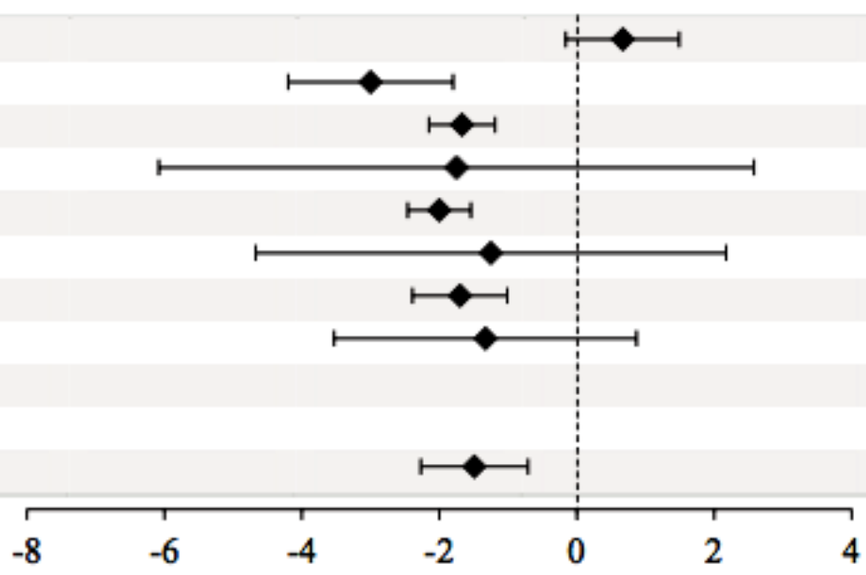


Main results

Efficacy and Safety PCT *Guidance in ptz with suspected or confirmed* SEPSIS: *A Systematic Review and Meta-Analysis*

Iankova I et al Crit Care Med 2018;46:691-698

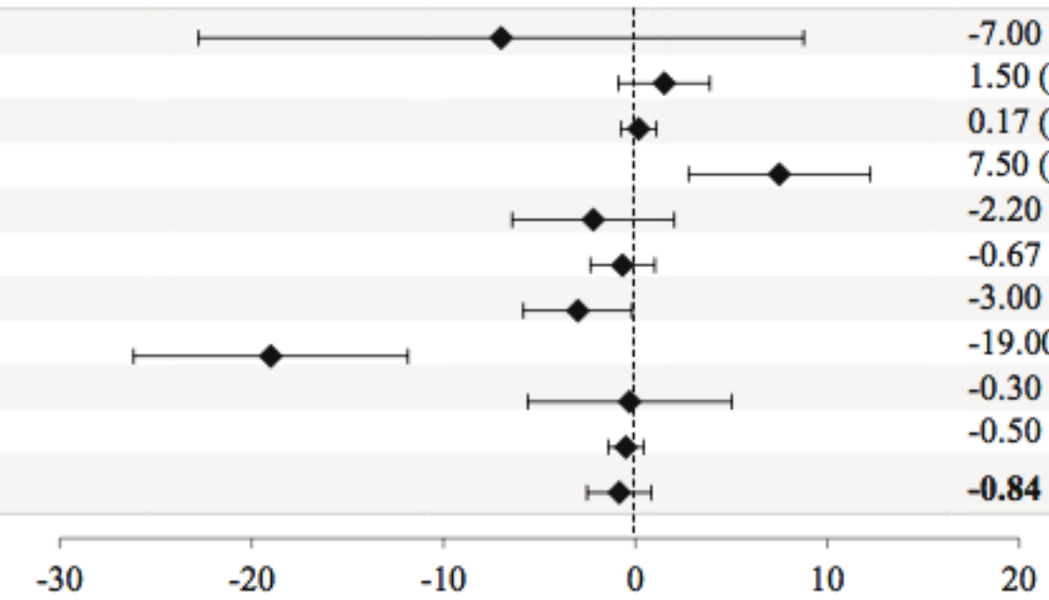
First author, year	AB duration (days), mean (SD) PCT	AB duration (days), mean (SD) Standard care	WMD (95% CI)	Weight %
Annane, 2013[24]	4.67 (0.7)	4.00 (2.2)	0.67 (-0.16, 1.49)	16.50
Bouadma, 2010[25]	10.30 (7.7)	13.30 (7.6)	-3.00 (-4.20, -1.80)	13.65
de Jong, 2016[26]	5.67 (4.4)	7.33 (5.2)	-1.67 (-2.15, -1.19)	18.79
Deliberato, 2013[27]	15.50 (9.0)	17.25 (10.8)	-1.75 (-6.08, 2.58)	2.79
Hochreiter, 2009[28]	5.90 (1.7)	7.90 (0.5)	-2.00 (-2.46, -1.54)	18.90
Nobre, 2008[31]	12.25 (7.8)	13.50 (7.8)	-1.25 (-4.67, 2.17)	4.14
Schroeder, 2009[32]	6.60 (1.1)	8.30 (0.7)	-1.70 (-2.39, -1.01)	17.47
Shehabi, 2014[33]	11.67 (10.4)	13.00 (11.9)	-1.33 (-3.53, 0.87)	7.76
Layios, 2012[29]			(Excluded)	
Najafi, 2015[30]			(Excluded)	
Overall (Heterogeneity: I^2=81.3%, p<0.001, T^2=0.782)			**-1.49 (-2.27, -0.71)**	**100.00**



Efficacy and Safety PCT *Guidance in ptz with suspected or confirmed* SEPSIS*: A Systematic Review and Meta-Analysis*

Iankova I et al Crit Care Med 2018;46:691-698

First author, year	ICU LOS (days), mean (SD) PCT	ICU LOS (days), mean (SD) Standard care	WMD (95% CI)	Weight %
Annane, 2013[24]	24.00 (25.2)	31.00 (37.0)	-7.00 (-22.77, 8.77)	1.07
Bouadma, 2010[25]	15.90 (16.1)	14.40 (14.1)	1.50 (-0.88, 3.88)	12.94
de Jong, 2016[26]	10.17 (8.9)	10.00 (9.6)	0.17 (-0.76, 1.09)	16.61
Deliberato, 2013[27]	16.25 (14.0)	8.75 (6.8)	7.50 (2.77, 12.23)	7.32
Hochreiter, 2009[28]	15.50 (12.5)	17.70 (10.1)	-2.20 (-6.43, 2.03)	8.29
Layios, 2012[29]	9.00 (8.9)	9.67 (10.4)	-0.67 (-2.35, 1.01)	14.89
Najafi, 2015[30]	7.50 (4.5)	10.50 (6.5)	-3.00 (-5.83, -0.17)	11.69
Nobre, 2008[31]	7.50 (5.0)	26.50 (22.5)	-19.00 (-26.15, -11.85)	4.20
Schroeder, 2009[32]	16.40 (8.3)	16.70 (5.6)	-0.30 (-5.61, 5.01)	6.37
Shehabi, 2014[33]	6.17 (4.8)	6.67 (4.4)	-0.50 (-1.42, 0.42)	16.63
Overall (Heterogeneity: I^2=80.1%, p<0.001, T^2=4.201)			**-0.84 (-2.52, 0.84)**	**100.00**



Given the growing threat of antimicrobial resistance, the reduction in duration of AB treatments due to better-targeted treatment under PCT guidance could also have important societal implications.

Systematic Review and Meta-Analysis of PCT vs Usual Care for Antimicrobial Management in Critically Ill Ptz

Lam SW et al Crit Care Med 2018;46:684-690

Focus on Subgroups based on Antibiotic Initiation, Cessation, or Mixed Strategies

A Forest plot for antibiotic duration. Df = degrees of freedom, PCT = procalcitonin.

	Procalcitonin			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.1.2 Cessation									
Bloos 2016	7.3	6.7	552	7.3	6.7	537	11.4%	0.00 [-0.80, 0.80]	
de Jong 2016	5.7	4.5	761	7.3	5.2	785	12.3%	-1.60 [-2.08, -1.12]	
Deliberato 2013	15.5	8.3	42	17.3	10	39	2.8%	-1.80 [-5.82, 2.22]	
Hochreiter 2009	5.9	1.7	57	7.9	0.5	53	12.4%	-2.00 [-2.46, -1.54]	
Nobre 2008	12.3	7.2	39	13.5	7.2	40	4.0%	-1.20 [-4.38, 1.98]	
Oliveira 2013	8.1	3.7	49	7.2	3.5	45	8.8%	0.90 [-0.56, 2.36]	
Schroeder 2009	6.6	1.1	14	8.3	0.7	13	11.7%	-1.70 [-2.39, -1.01]	
Shehabi 2014	11.7	10.5	196	13	8.2	198	7.3%	-1.30 [-3.16, 0.56]	
Stolz 2009	10.6	7.6	51	16	9.9	50	3.5%	-5.40 [-8.85, -1.95]	
Subtotal (95% CI)			**1761**			**1760**	**74.3%**	**-1.26 [-1.98, -0.54]**	
Heterogeneity: Tau² = 0.67; Chi² = 34.10, df = 8 (P < 0.0001); I² = 77%									
Test for overall effect: Z = 3.43 (P = 0.0006)									
2.1.3 Mixed									
Annane 2013	4	2.3	30	4.3	1.6				
Bouadma 2010	6.1	6	307	9.9	7.1				
Ding 2013	8.7	6.6	33	14.5	5.2				
Subtotal (95% CI)			**370**						
Heterogeneity: Tau² = 6.19; Chi² = 28.87, df = 2 (P < 0.0									
Test for overall effect: Z = 2.03 (P = 0.04)									
Total (95% CI)			**2131**						
Heterogeneity: Tau² = 1.16; Chi² = 66.82, df = 11 (P < 0.									
Test for overall effect: Z = 4.25 (P < 0.0001)									
Test for subgroup differences: Chi² = 1.38, df = 1 (P = 0.									

Conclusion: *When evaluating all studies of procalcitonin-guided antibiotics management in critically ill patients, no difference in short-term mortality was observed. However, when only examining procalcitonin-guided cessation of antibiotics, lower mortality was detected.*

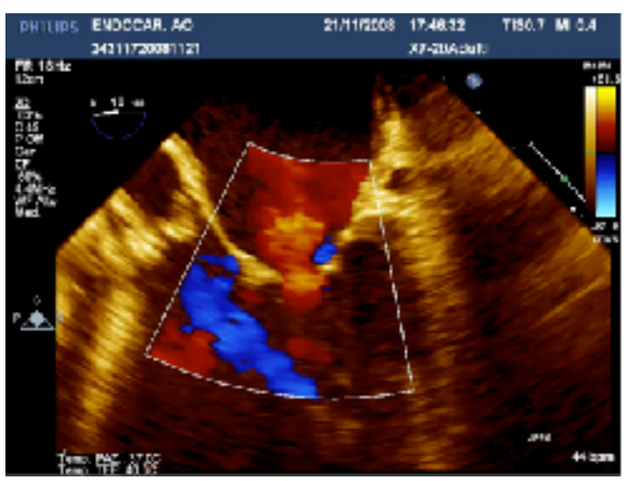
Procalcitonin in 759 Patients Clinically Suspected of Infective Endocarditis

Knudsen JB et al Am J Med 2010;123:1121-1127

Table 5 Procalcitonin Level in Various Microorganisms in Patients with Positive Blood Culture among 759 Patients Suspected of Infective Endocarditis

	Procalcitonin (ng/mL), Median (interquartile range)
Staphylococcus aureus (n = 62)	0.49 (0.19-2.29)
Coagulase-negative staphylococci (n = 41)	0.28 (0.11-0.71)
Streptococcus viridans (n = 57)	0.23 (0.09-0.52)
Enterococci (n = 35)	0.19 (0.12-0.64)
HACEK (n = 4)	1.00 (0.20-2.67)
Gram-negative species other than HACEK (n = 17)	0.42 (0.27-1.21)
Other microorganisms (n = 17)	0.13 (0.09-1.78)

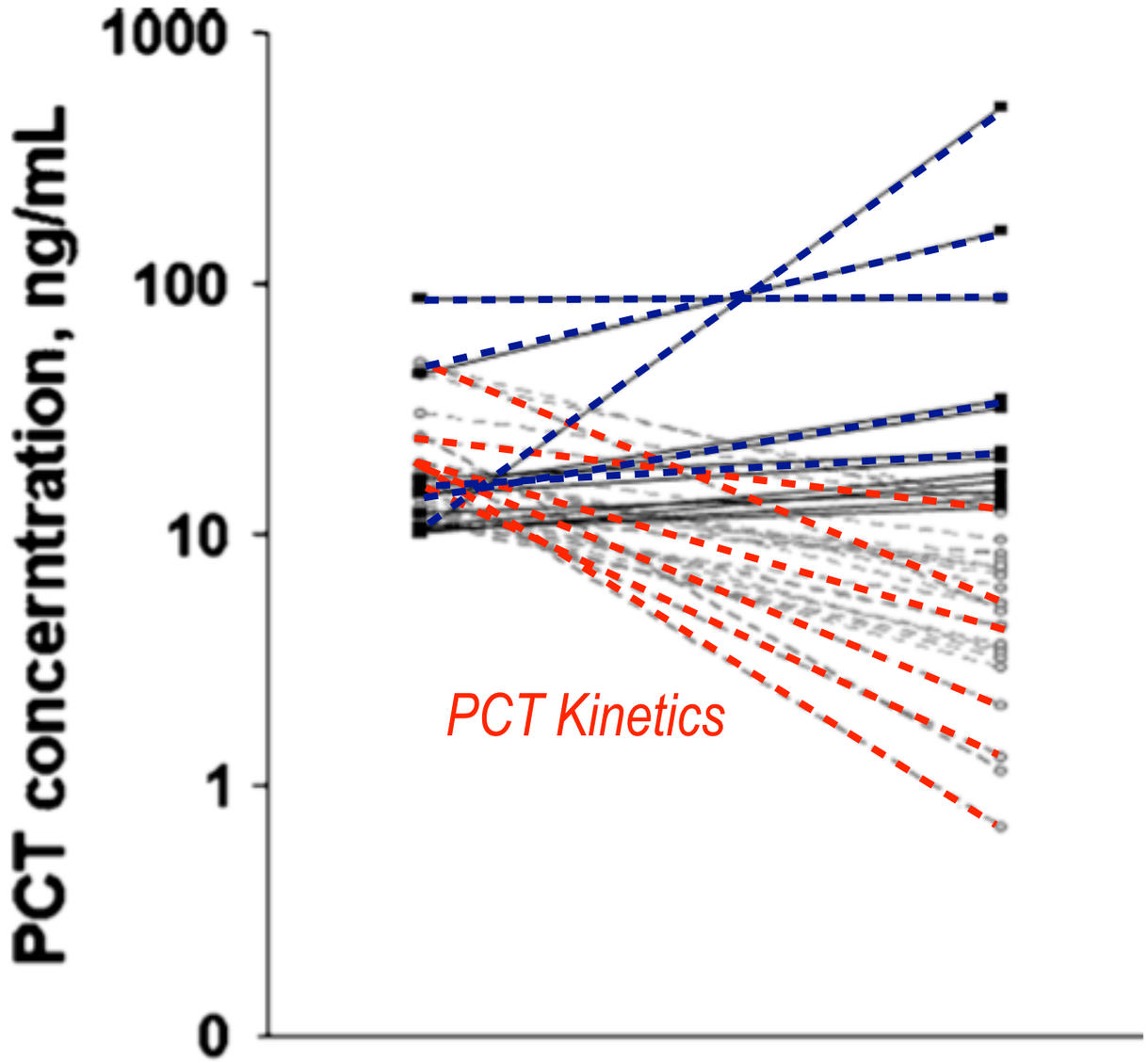
H*aemophilus*
A*ggregatibacter*
C*ardiobacterium*
E*ikenella*
K*ingella*



DYNAMIC CHANGE OF PROCALCITONIN, RATHER THAN CONCENTRATION ITSELF, IS PREDICTIVE OF SURVIVAL IN SEPTIC SHOCK PATIENTS WHEN BEYOND 10 NG/ML

Jun Guan,* Zhaofen Lin,* and Hong Lue†

**Shanghai Changzheng Hospital, Second Military Medical University, Shanghai; and †Taicang Chinese Medicine Hospital, Taicang, Jiangsu, China*



Is a Single Initial Procalcitonin Test Sufficient in Septic, Critically Ill Patients to Minimize Antibiotic Use?

To the Editor:

Research on PCT has shifted toward serial PCT measurements for the discontinuation of antimicrobial therapy.

We believe an initial PCT measurement followed by daily measurements will allow earlier and safe discontinuation of antibiotics in septic ICU patients.

Chest 2017

J Shock 2011;36(6):570-574

PCT and CR-BSI

Theodorou V P et al BMC Infectious Dis 2012;12:247

BMC Infectious Diseases

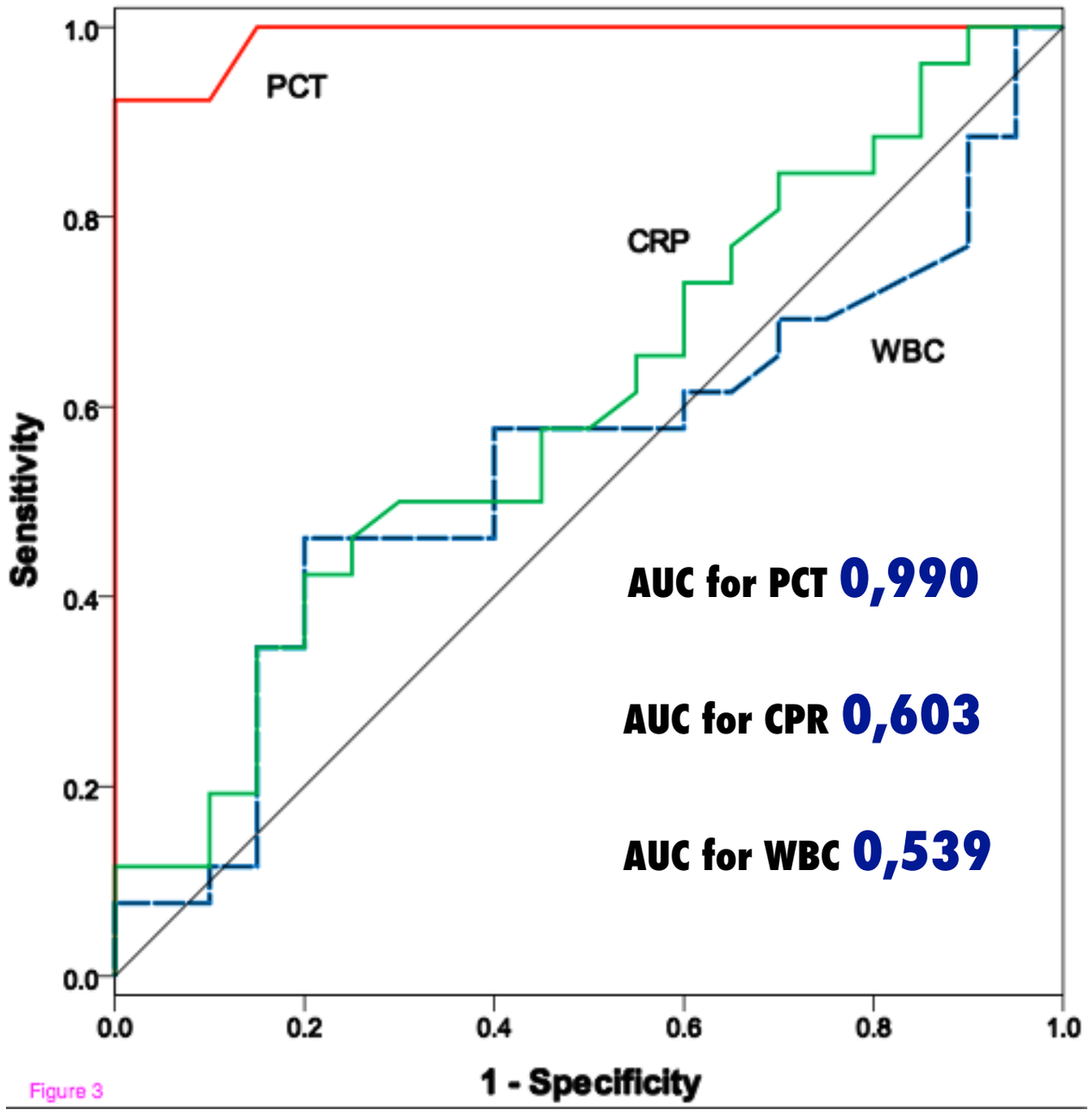
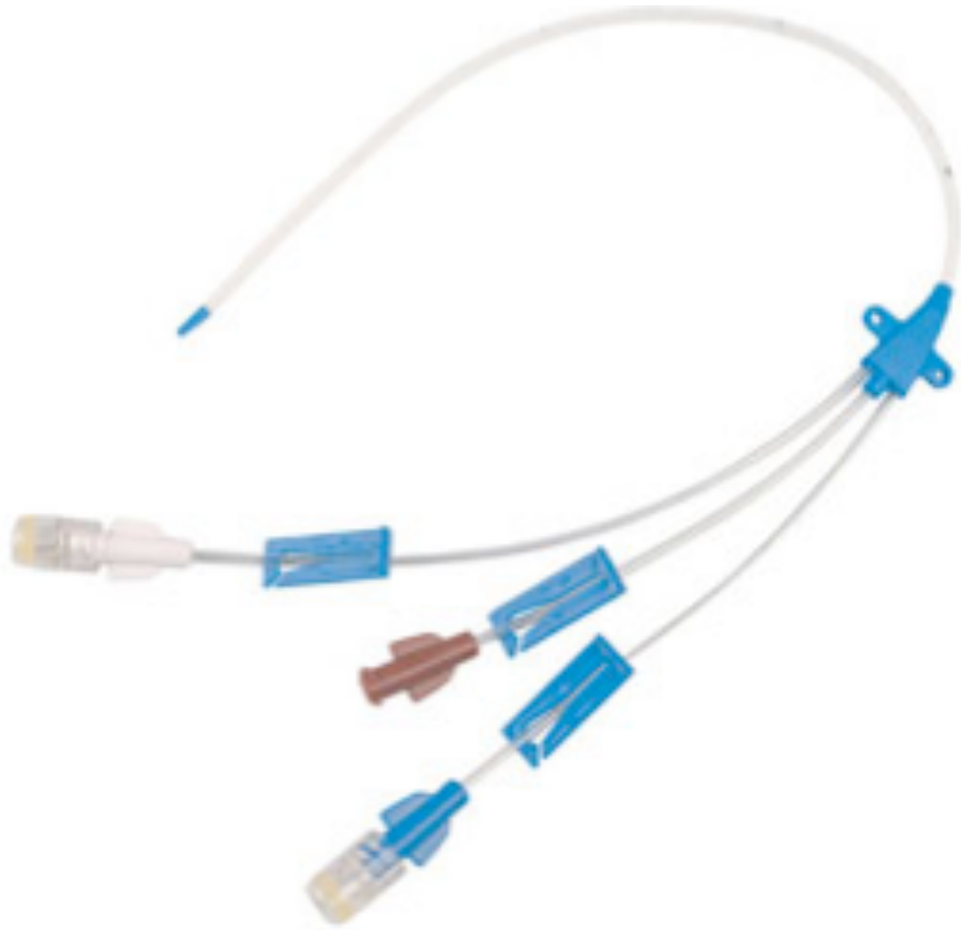


Figure 3

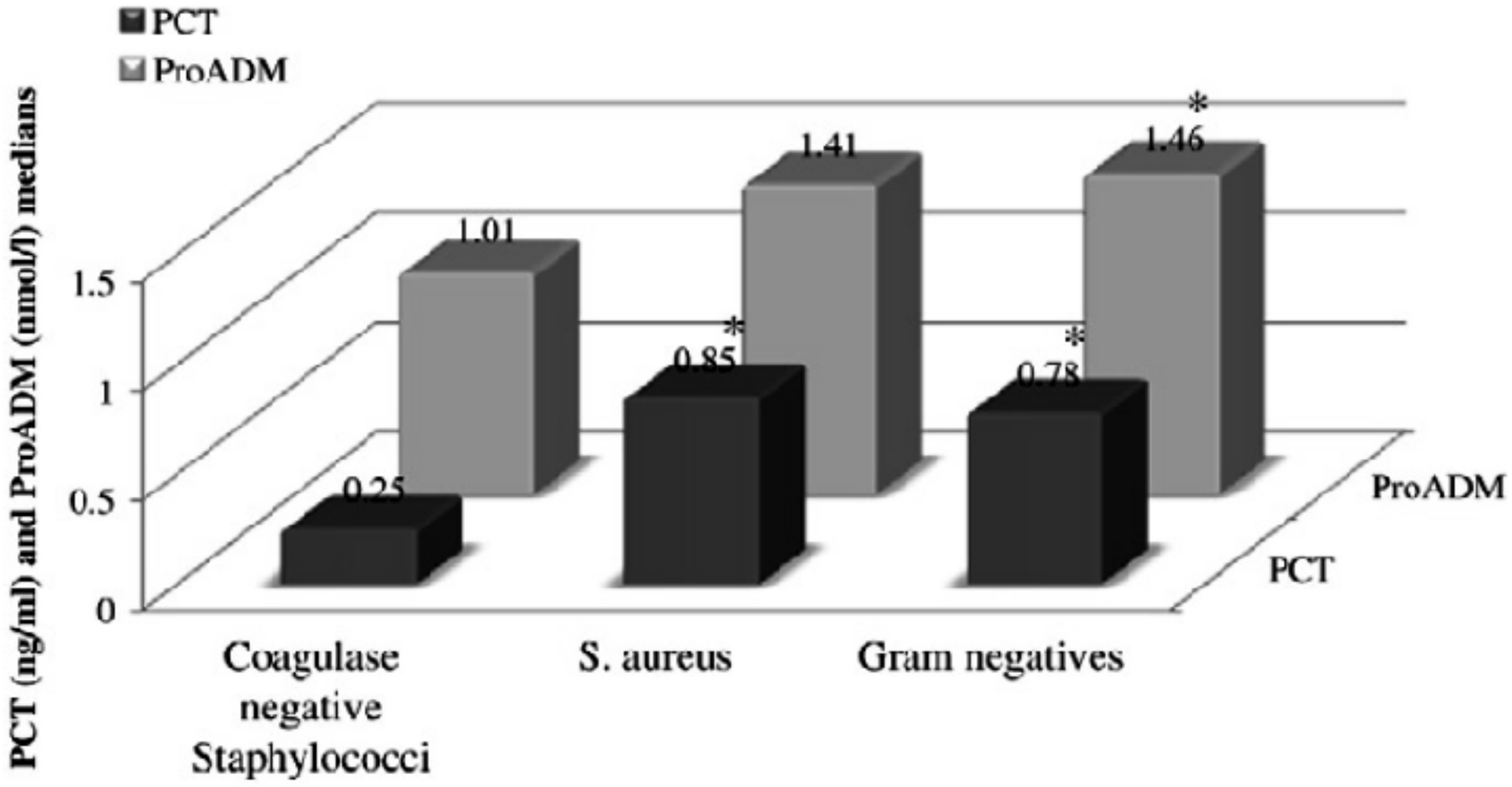


Can PCT differentiate Staphylococcus aureus from CoNS in clustered Gram-positive BSI?

Shomali et al Diagn Microbiol Infect Dis 2013;76:158-161

PCT and ProADM levels in different groups.

Group	N	Median PCT (range) (ng/mL)	Median ProADM (range)
CoNS	95	0.25 (0.075–43.8)	1.01 (0.075–15)
CoNS contamination	69	0.24 (0.075–43.8)	0.97 (0.075–15)
CoNS true bacteremia	26	0.26 (0.075–14.1)	1.14 (0.17–6.5)
S. aureus bacteremia	24 (21*)	0.85 (0.075–47.4)	1.41 (0.33–4.7)
Gram negative bacteremia	44 (42*)	0.78 (0.075–129.3)	1.46 (0.1–12.4)



*$P < 0.05$ when compared to Coagulase negative staphylococci

On the basis of our results, we conclude that **PCT** (and to a lesser extent ProADM) may be useful in differentiating the pathogenic *S. aureus* from the skin commensals CoNS in clustered gram-positive bacteremia

Could PCT differentiate Gram-negative sepsis from Gram-positive and fungal sepsis?

Brodska et al Clin Exp Med 2013;13:165-170

Table 3 Reliability of PCT in G– bacteremia

PCT > 0.5 pg/mL	PCT > 5 pg/mL	PCT > 15 pg/mL

Intensive Care Med
DOI 10.1007/s00134-009-1623-0

BRIEF REPORT

PCT and Fungal infections

Intensive Care Med 2009;35(12):2146-50

Pierre Emmanuel Charles
Carmen Castro
Sergio Ruiz-Santana
Cristóbal León
Pedro Saavedra
Estrella Martín

Serum procalcitonin levels in critically ill patients colonized with *Candida* spp: new clues for the early recognition of invasive candidiasis?

36 ICU's
136 PATIENTS> 7 DAYS
NO BACTERIAL INFECTION

Table 4 Diagnostic accuracy of serum procalcitonin and Candida Score for the discrimination between *Candida* spp multifocal colonization and infection in critically ill patients who have been hospitalized for at least 7 days

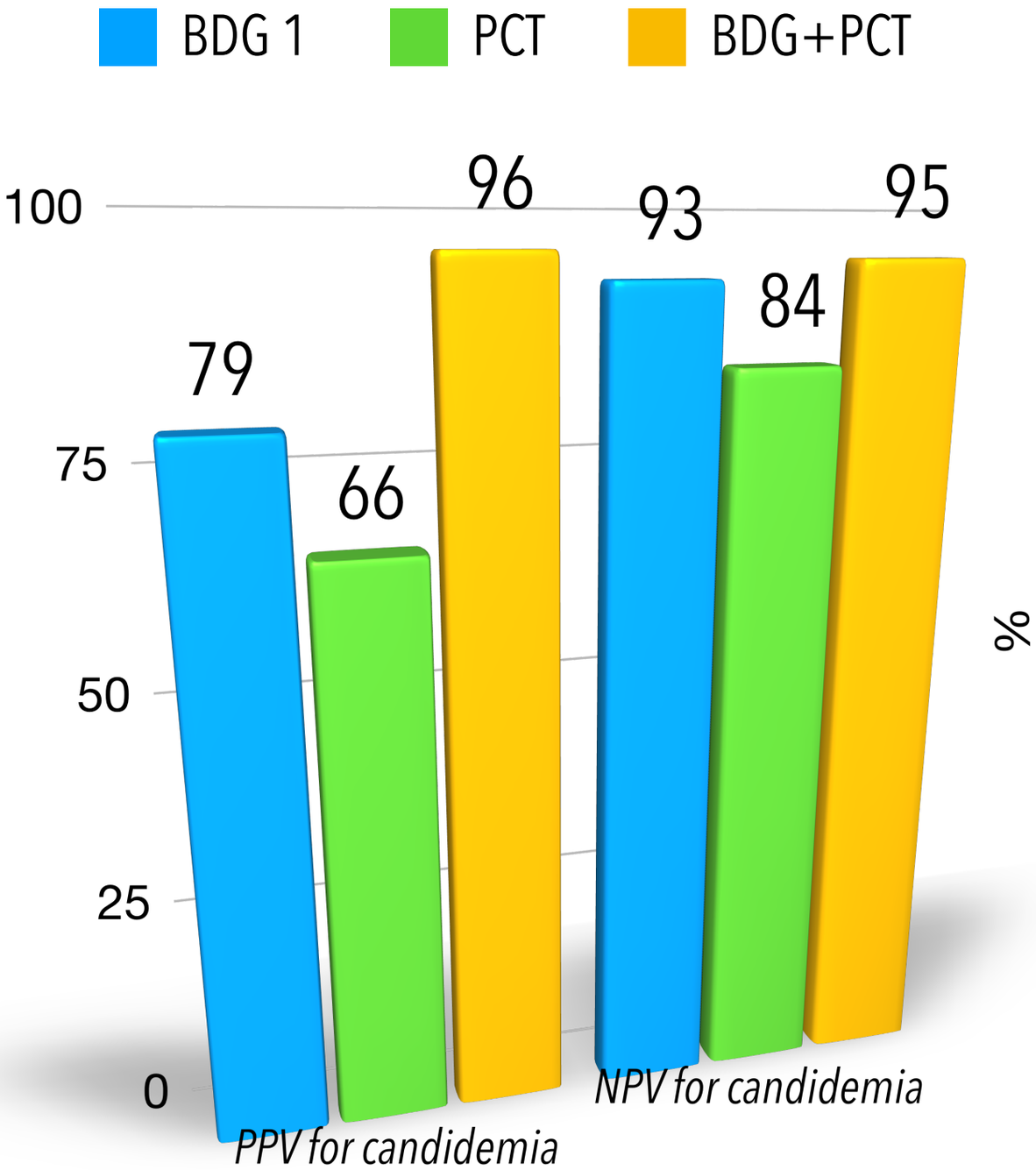
	Optimal cutoff	AUROCC 95% CI	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
PCT-D7	≥0.30 ng/ml	0.713 [0.587–0.839]	90.0%	53.5%	47.4%	92.0%	1.9	0.2
CS	≥3.0 points	0.728 [0.603–0.850]	85.0%	51.2%	44.7%	88.0%	1.7	0.3
PCT-D7 + CS	≥0.30 ng/ml ≥3.0 points	0.768 [0.645–0.891]	80.0%	74.4%	59.3%	88.9%	3.1	0.3

CS Candida Score maximal value measured during the ICU stay, *PCT-D7* procalcitonin measured on day 7 after ICU admission, *AUROCC* area under the receiver-operating characteristics curve, *CI* confidence interval

Early antifungal therapy might be considered in patients with a CS >3 points combined with a PCT >0.3 ng/ml.

Combined use of serum (1,3)-β-D-glucan and procalcitonin for the early differential diagnosis between candidaemia and bacteraemia in ICU

Giacobbe DR et al Crit Care 2017;21:176



Cut-offs for candidaemia used for the comparisons in the graph are ≥80 pg/ml for BDG and <2 ng/ml for PCT.

Diagnostic adds-on for candidemia, useful for antifungal stewardship

- Colonisation data (useful for some scores: CS, CI)
- Fungal biomarkers
- Molecular biology from positive blood cultures for rapid ID of *Candida* spp.
- Molecular biology from blood specimens for rapid detection of *Candida* spp.

Fungal biomarkers for IC: (1→3)-β-D-glucan in serum

McCarthy et al - Int J Mol Sci 2017

Positive in:

Candida spp. invasive

Pneumocystis jirovecii pneumonia

Aspergillus spp. invasive

Fusariosis

Negative in:

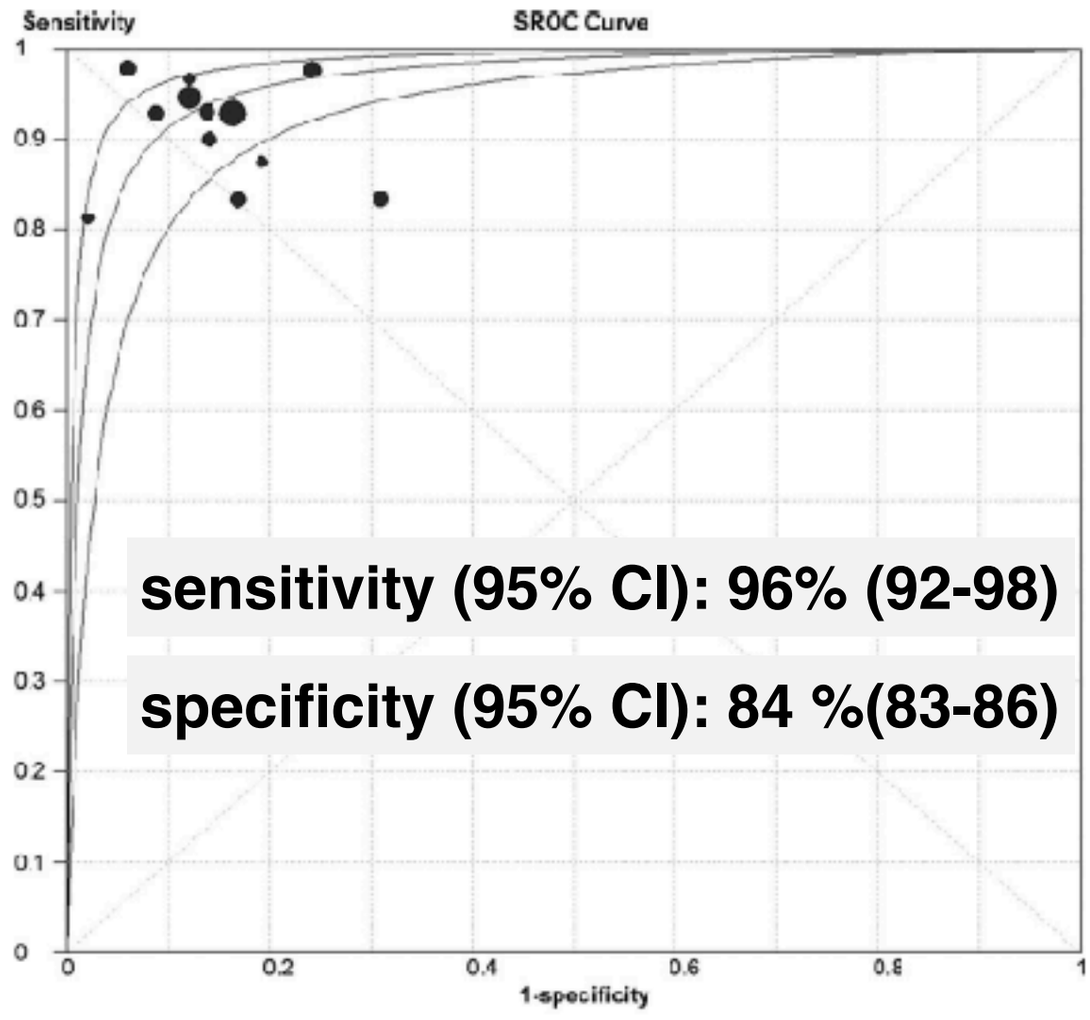
Cryptococcosis

Zygomycoses (Mucor, Absidia, Rhyzopus)

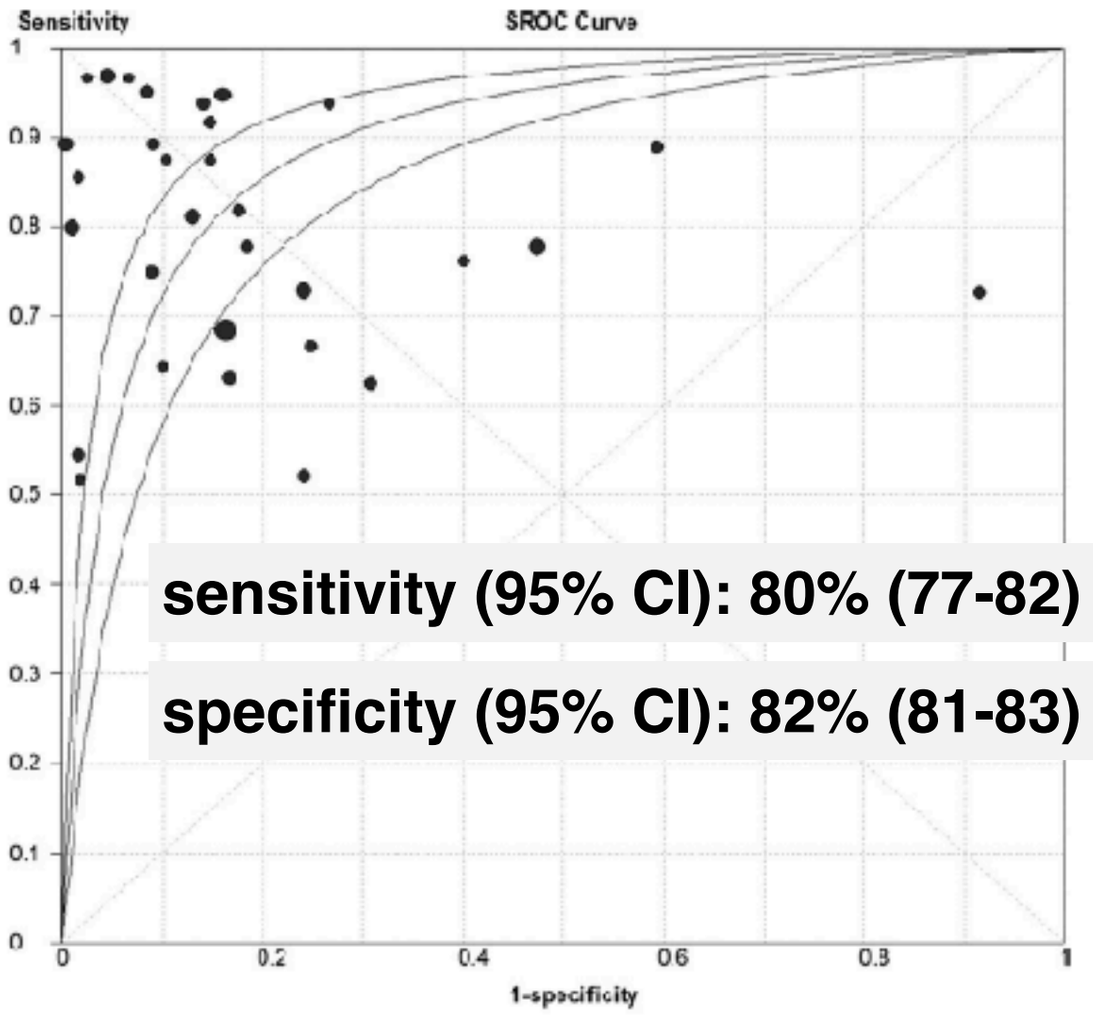
JCM 2012
Journals.ASM.org

Diagnostic Accuracy of Serum 1,3-β-D-Glucan for *Pneumocystis jiroveci* Pneumonia, Invasive Candidiasis, and Invasive Aspergillosis: Systematic Review and Meta-Analysis

Akira Onishi,[a] Daisuke Sugiyama,[a] Yoshinori Kogata,[a] Jun Saegusa,[a] Takeshi Sugimoto,[b] Seiji Kawano,[b] Akio Morinobu,[b] Kunihiro Nishimura,[a,c] and Shunichi Kumagai[a,d]



Pneumocystis jiroveci pneumonia

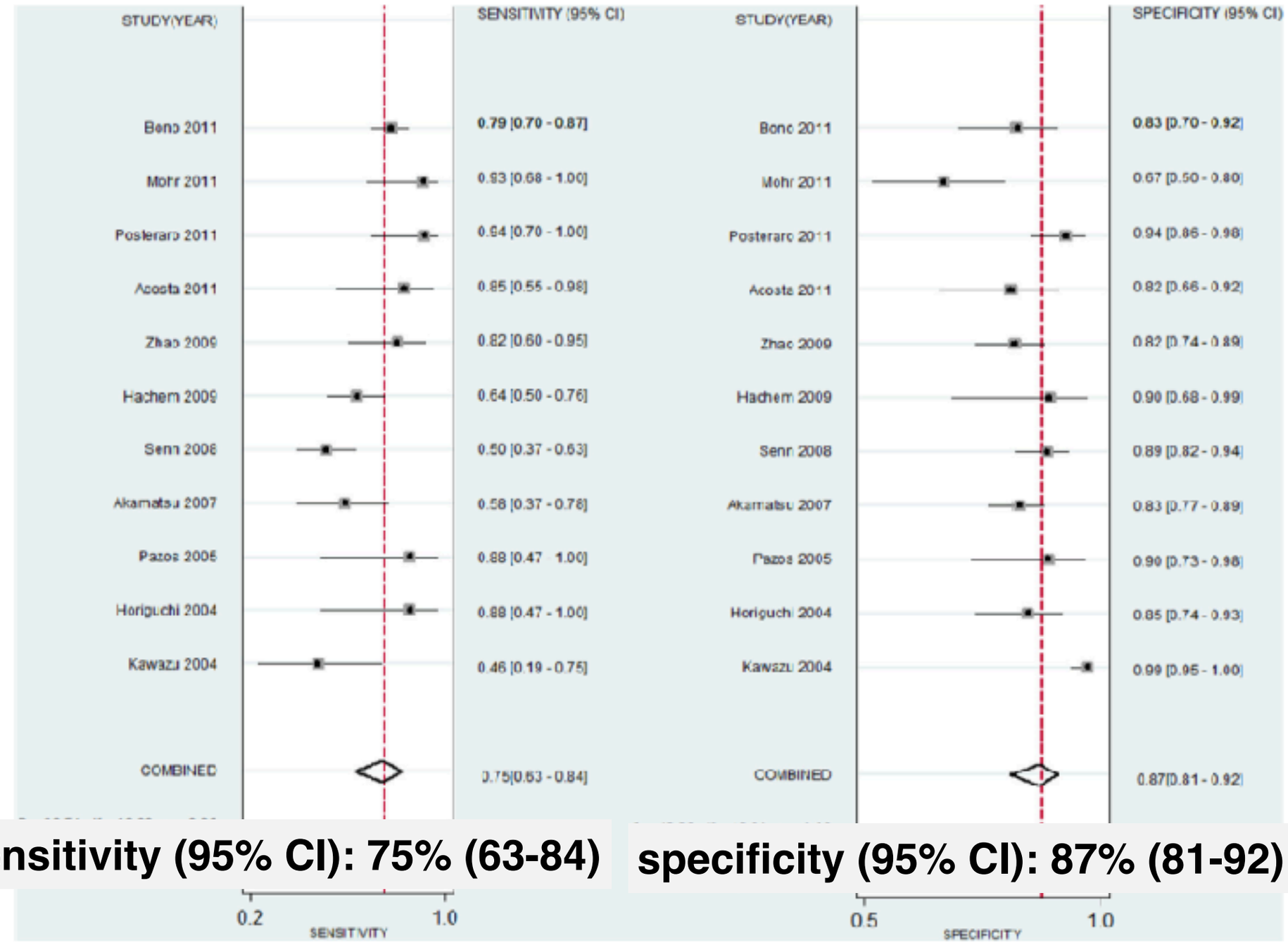


Invasive fungal infection

RESEARCH ARTICLE

The Screening Performance of Serum 1,3-Beta-D-Glucan in Patients with Invasive Fungal Diseases: A Meta-Analysis of Prospective Cohort Studies

Tie-Ying Hou[1], Shou-Hong Wang[2], Sui-Xin Liang[3], Wen-Xin Jiang[4], Dan-Dong Luo[5], De-Hong Huang[6]*



sensitivity (95% CI): 75% (63-84)

specificity (95% CI): 87% (81-92)

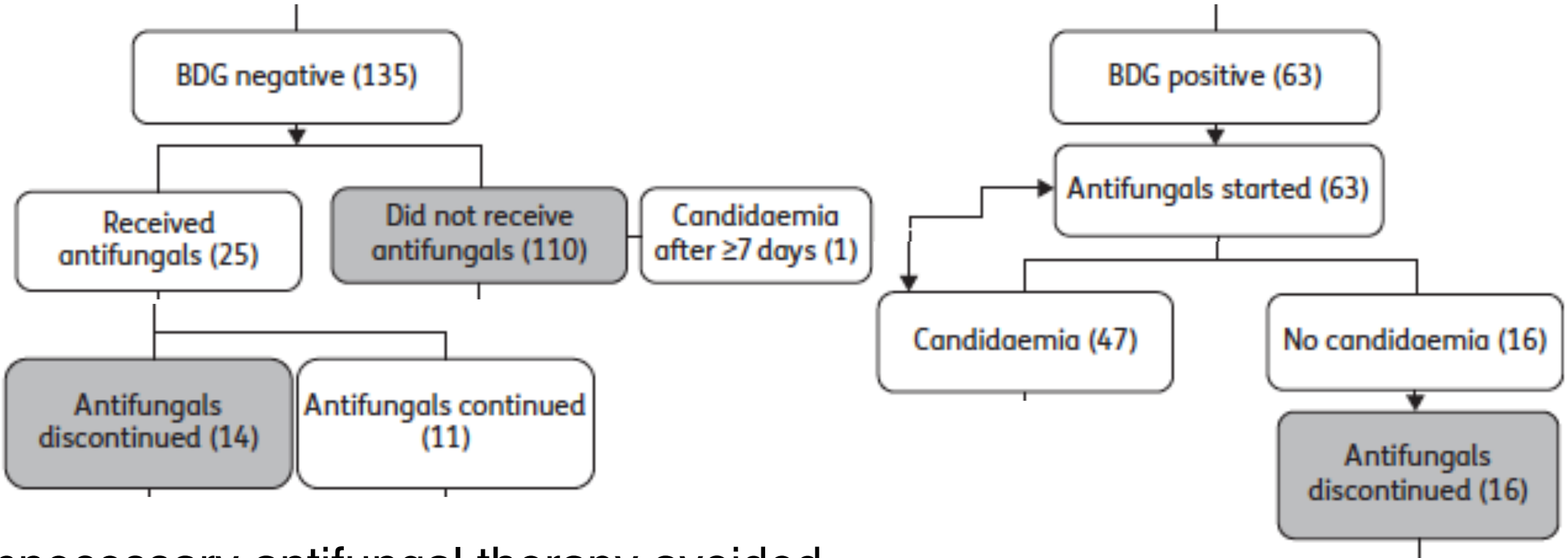
J Antimicrob Chemother 2016; **71**: 2262–2269
doi:10.1093/jac/dkw112 Advance Access publication 28 April 2016

Journal of Antimicrobial Chemotherapy

(1,3)-β-D-Glucan-based antifungal treatment in critically ill adults at high risk of candidaemia: an observational study

Brunella Posteraro[1]†, Mario Tumbarello[2]†, Gennaro De Pascale[3], Elvira Liberto[4], Maria S. Vallecoccia[3], Elena De Carolis[4], Valentina Di Gravio[3], Enrico M. Trecarichi[2], Maurizio Sanguinetti[4]* and Massimo Antonelli[3]

Septic patients with CS ≥3 tested for BDG



Unnecessary antifungal therapy avoided in ca. 70% of potentially treatable patients

J Antimicrob Chemother 2016; **71**: 2628–2633
doi:10.1093/jac/dkw188 Advance Access publication 10 June 2016

Journal of Antimicrobial Chemotherapy

Discontinuation of empirical antifungal therapy in ICU patients using 1,3-β-D-glucan

Marcio Nucci[1]*, Simone A. Nouér[1], Patricia Esteves[2], Thais Guimarães[3], Giovanni Breda[4], Bianca Grassi de Miranda[3], Flavio Queiroz-Telles[4] and Arnaldo L. Colombo[2]

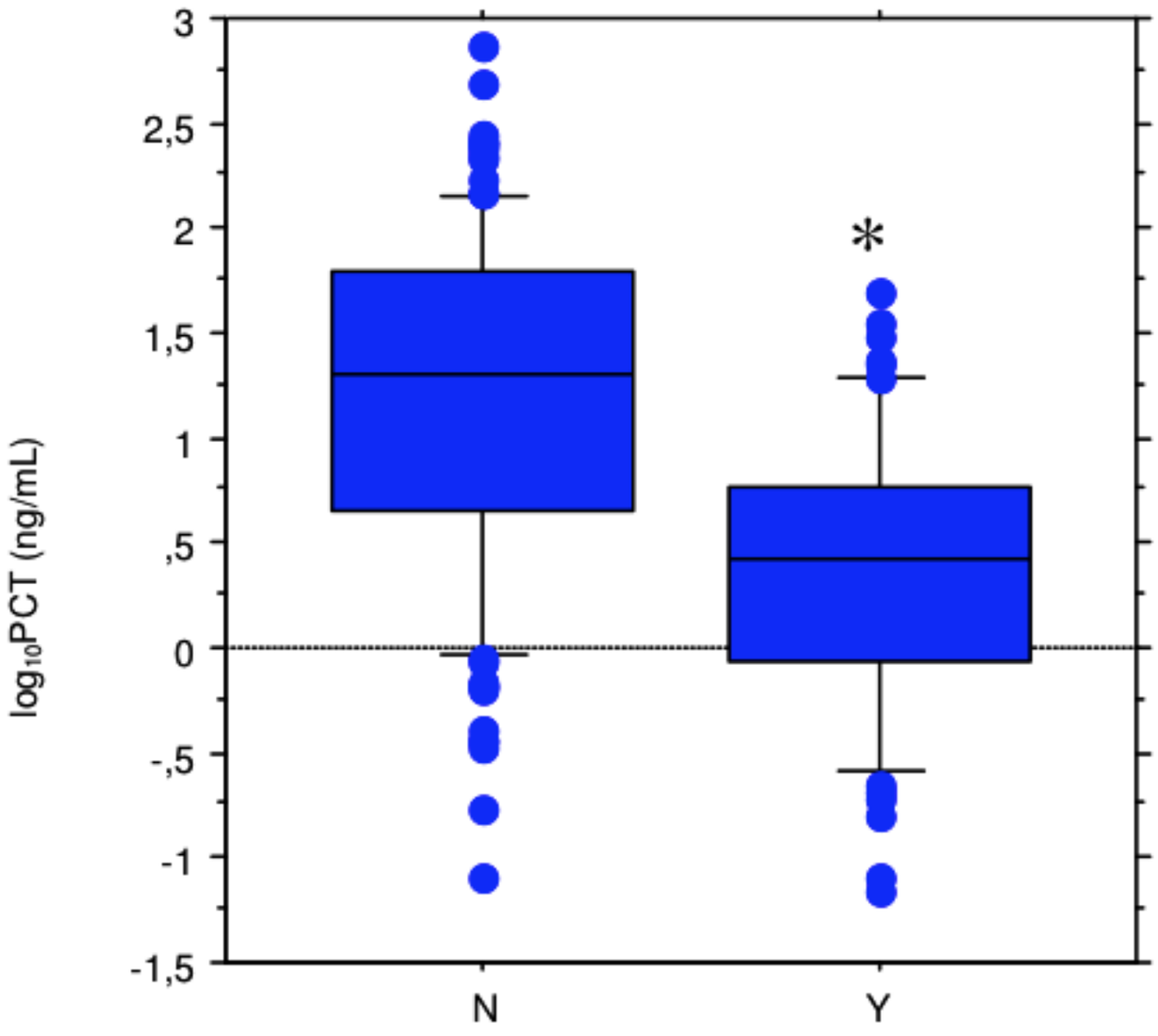
Table 5. Comparison of outcome variables between the three cohorts

	Candidaemia, *N*=7	Positive biomarker cohort, *N*=57	Negative biomarker cohort, *N*=21	*P*
Duration (days) of antifungal therapy, median (range)	14 (1–37)	10 (1–20)	3 (2–12)	<0.001
Breakthrough candidaemia	0	0	0	1.0
Discharged from the ICU on day 14 of study, *n* (%)	3 (42.8)	12 (21.0)	6 (28.6)	0.40
14 day mortality, *n* (%)	1 (14.3)	25 (45.6)	5 (23.8)	0.09
Discharged from the ICU on day 30, *n* (%)	4 (57.1)	18 (31.6)	7 (33.3)	0.40
30 day mortality, *n* (%)	2 (28.6)	32 (56.1)	9 (42.8)	0.28

PCT *impact of previous sepsis on the accuracy for diagnosis of BSI in critically ill patients*

Charles PE et al BMC Infect Dis 2008

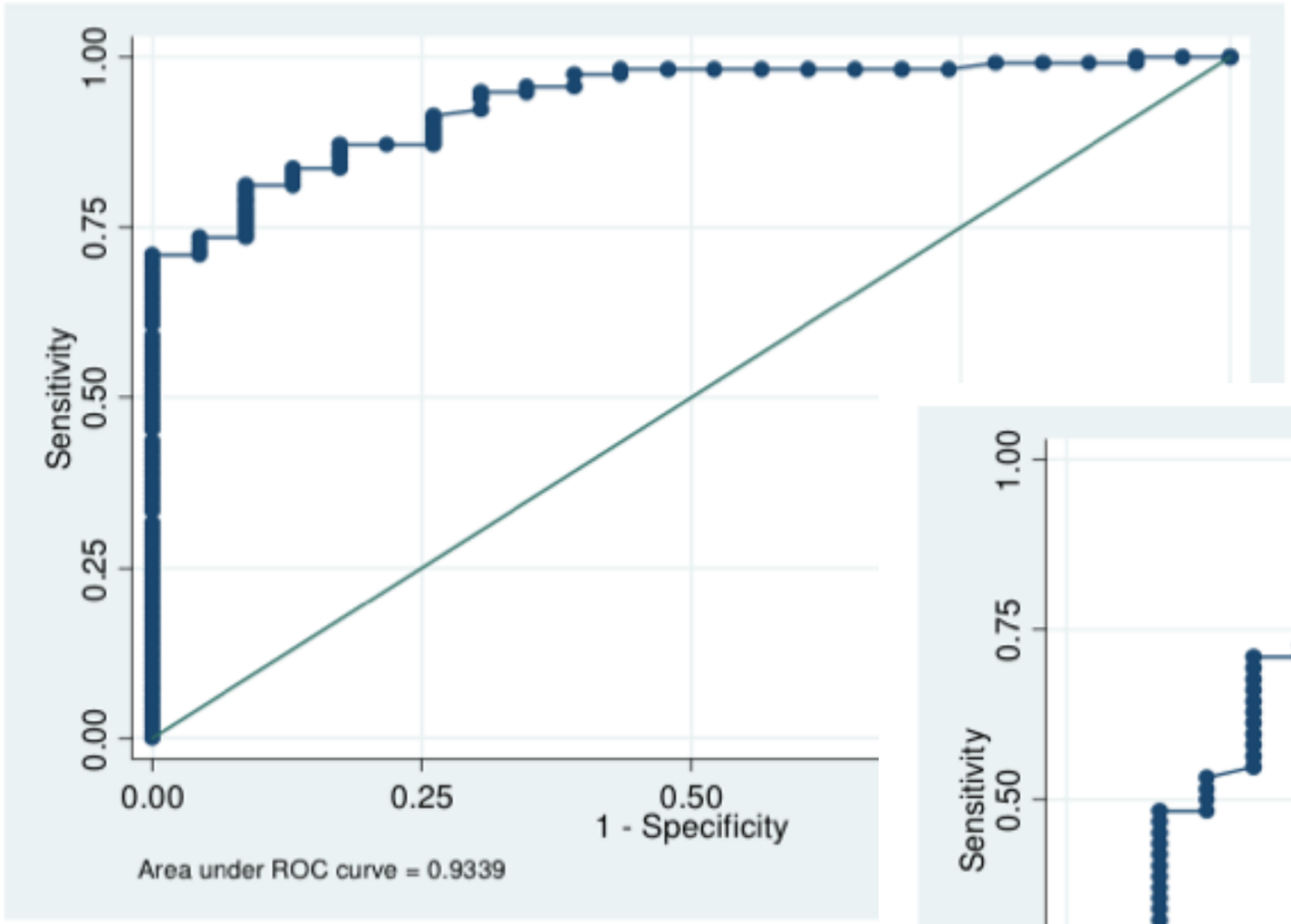
179 EPISODES OF EITHER PRIMARY (N = 117) OR SECONDARY (N = 62) SEPSIS WERE INCLUDED

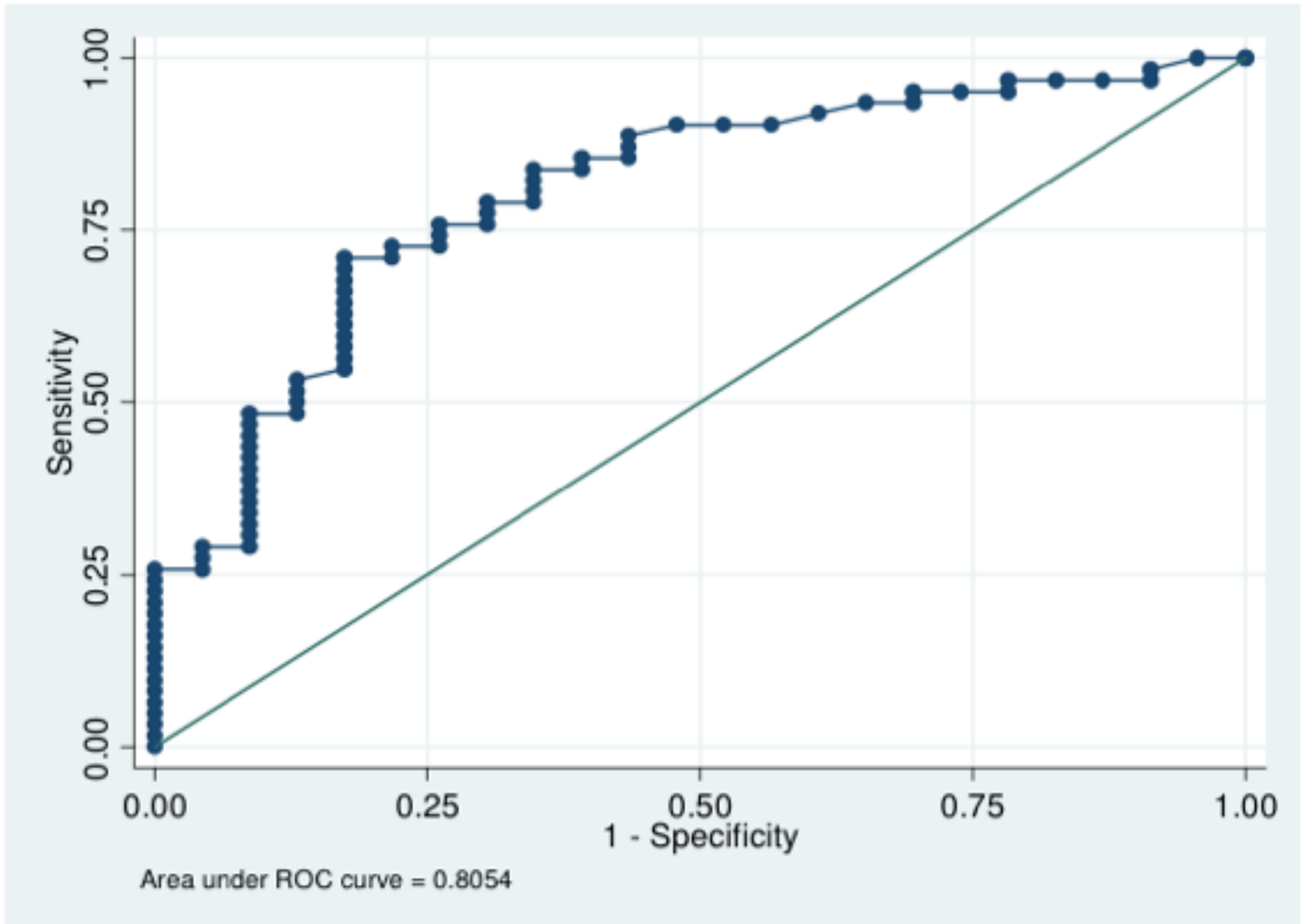


Serum procalcitonin (PCT) level at the onset of blood stream infection according to its primary (left boxes, n = 127) or secondary status (right boxes, n = 62) in critically ill patients with clinical sepsis

PCT *impact of previous sepsis on the accuracy for diagnosis of BSI in critically ill patients*

Charles PE et al BMC Infect Dis 2008





ROC curve of serum PCT for the diagnosis of BSI in critically ill patients with either primary or secondary sepsis. Plain circles indicate PCT values. Area under the ROC curve = 0.934, vs. 0.805 respectively; P < 0.050.

PCT *impact of previous sepsis on the accuracy for diagnosis of BSI in critically ill patients*

Charles PE et al BMC Infect Dis 2008

Since PCT elevation reflects the inflammatory cytokine response to one bacterial insult, such a difference could be explained by the so-called **IMMUNE PARALYSIS PARADIGM**

in the former group were more likely to have received **STEROIDS** and **EFFECTIVE ANTIBIOTIC THERAPY** prior to the BSI episode

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Dec. 1999, p. 2984–2989 Vol. 43, No. 12
0066-4804/99/$04.00+0

Antibiotic-Induced Cell Wall Fragments of *Staphylococcus aureus* Increase Endothelial Chemokine Secretion and Adhesiveness for Granulocytes

P. VAN LANGEVELDE, E. RAVENSBERGEN, P. GRASHOFF, H. BEEKHUIZEN, P. H. P. GROENEVELD, AND J. T. VAN DISSEL*
Department of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands

Received 21 May 1998/Returned for modification 6 August 1998/Accepted 2 October 1999

PCT *impact of previous sepsis on the accuracy for diagnosis of BSI in critically ill patients*

Charles PE et al BMC Infect Dis 2008

IT MAY BE ADVISABLE TO USE LOWER CUT-OFF VALUES IN THE SETTING OF SECONDARY SEPSIS

Since PCT elevation reflects the inflammatory cytokine response to one bacterial insult, such a difference could be explained by the so-called **IMMUNE PARALYSIS PARADIGM**

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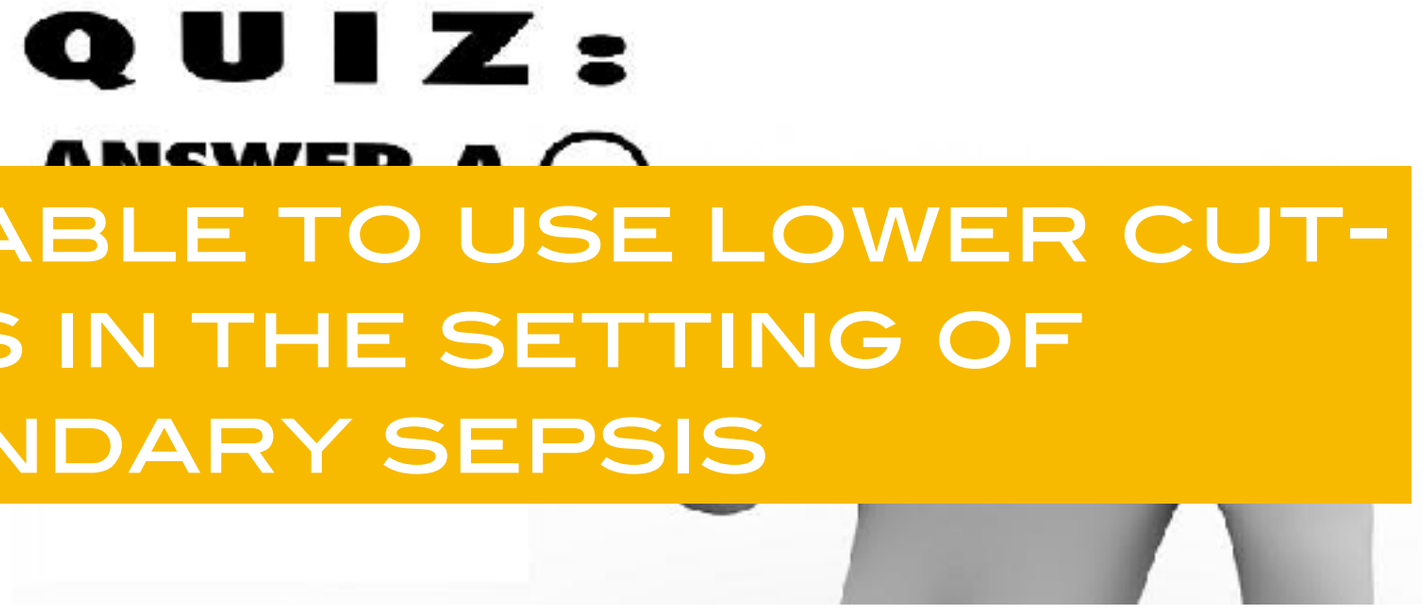

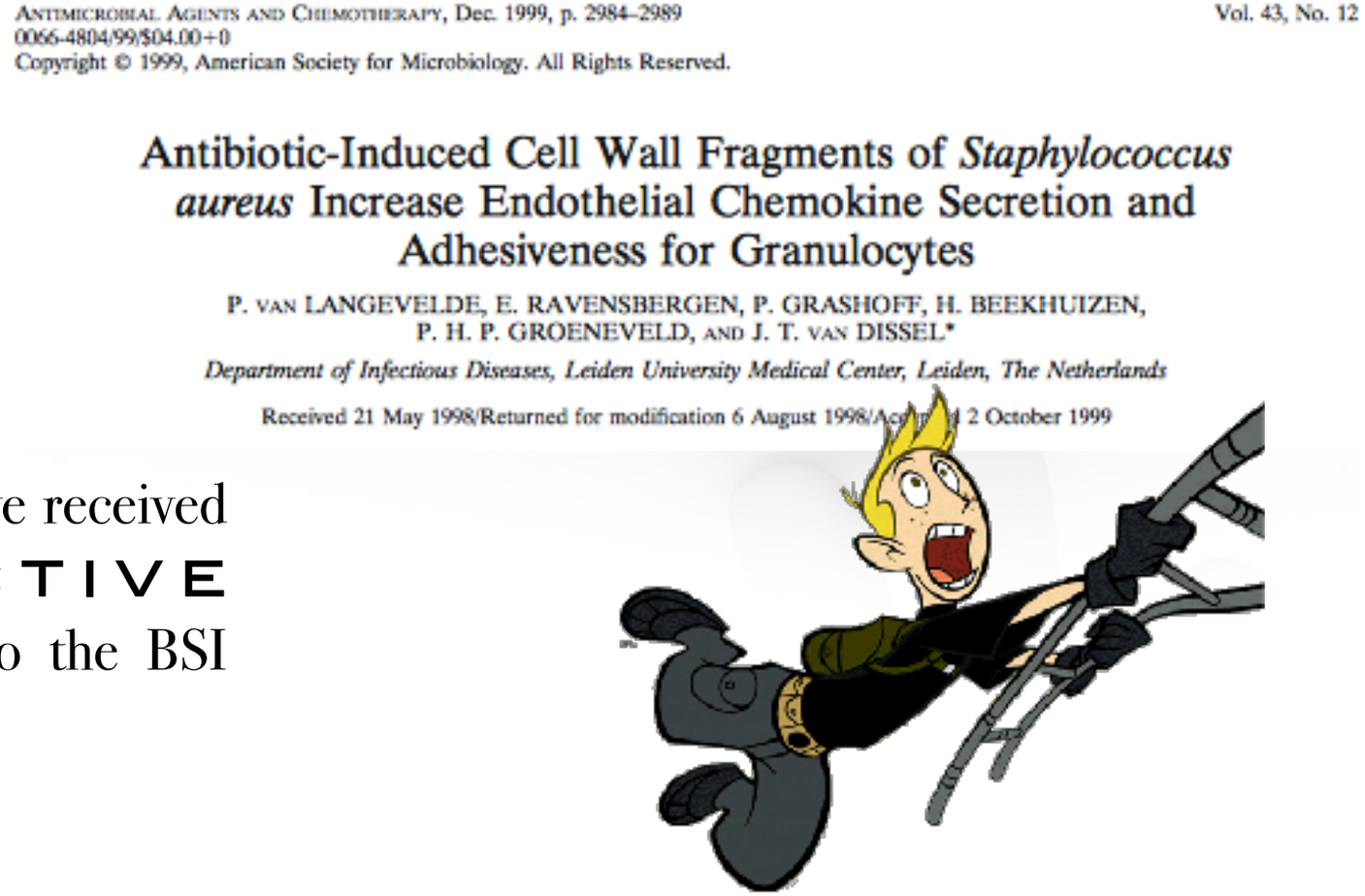

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Dec. 1999, p. 2984–2989 Vol. 43, No. 12
0066-4804/99/$04.00+0
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Department of Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands

Received 21 May 1998/Returned for modification 6 August 1998/Accepted 2 October 1999

Combination Biomarkers to Diagnose Sepsis in the Critically Ill Patient

Sébastien Gibot[1,2], Marie C. Béné[3], Robin Noel[4], Frédéric Massin[5], Julien Guy[6], Aurélie Cravoisy[1], Damien Barraud[1], Marcelo De Carvalho Bittencourt[3], Jean-Pierre Quenot[4], Pierre-Edouard Bollaert[1],

FOCUS ON SEPSIS

Nature Medicine 2012;18(7):999

New biomarkers sought for improving sepsis management and care

For something so deadly, sepsis is surprisingly difficult to characterize. The body's response to a severe blood infection can be virtually identical to its response to other noninfectious triggers such as trauma. And even though approximately one-quarter of all people with severe sepsis eventually die from the disease, it's not easy for physicians to tell who the sickest ones are.

"You'd really like to be able to identify [severe sepsis] before it's obvious," says Mitchell Levy, medical director of the intensive care unit (ICU) at the Rhode Island Hospital in Providence. Right now, he points out, "you have to wait until organs fail until you can really tell how sick someone is."

To overcome this problem, researchers are hunting for new biomarkers that could be used to diagnose the condition earlier and single out individuals who are most likely to benefit from aggressive treatment. To date, however, even the best validated biomarkers can't differentiate sepsis caused by infections from other inflammatory causes and conditions.

Take procalcitronin (PCT), a precursor to a hormone involved in calcium metabolism that Frank Gu, a bioengineer who studies sepsis biomarkers at the University of Waterloo in Ontario, describes as "the champion so far" when it comes to identifying bacterial infections. PCT levels in the blood typically jump 1,000-fold within hours of severe sepsis or septic shock setting in. However, concentrations of the peptide also spike after major trauma, elective surgery, severe burns and even some forms of cancer, which means it might not be specific enough to serve as a diagnostic marker of infection-caused sepsis.

That doesn't mean PCT can't be useful in the critical-care setting, however. In a study published online in May, Czech researchers reported that PCT levels were significantly higher in patients with sepsis infected with Gram-negative bacteria than in patients with either Gram-positive bacterial or fungal infections (*Clin. Exp. Med.* doi:10.1007/s10238-012-0191-8, 2012). This finding suggests that the biomarker could help doctors narrow down appropriate treatment options. Still, most experts in the field agree that a more specific indicator of at-risk patients is needed.

Parsing patients

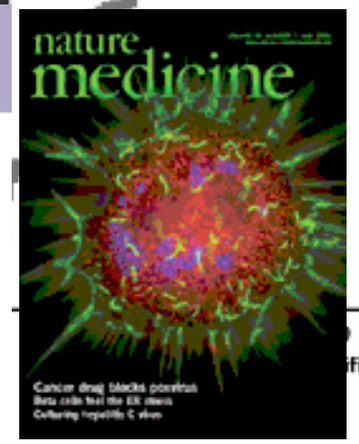
The 'soluble triggering receptor expressed on myeloid cells', sTREM-1, is one such candidate. In a study published last month, a Korean team measured plasma levels of sTREM-1 in 63 men with severe sepsis and found them to be significantly higher in individuals who ended up dying than in those who survived (*Shock* 37, 574–578, 2012).

A similar contender is suPAR (short for soluble urokinase-type plasminogen activator receptor). This protein is expressed on the surface of immune cells including neutrophils and macrophages and can differentiate dying patients from those who have both sepsis and pneumonia but will survive (*J. Infect.* 63, 344–350, 2011). In a 750-person observational trial, Austrian physicians are now evaluating whether measuring levels of suPAR and another biomarker shown to predict mortality in severe sepsis called ST2, a receptor involved in helper T cell responses, can help forecast not only clinical outcome but also infection type and treatment response.

Ultimately, this kind of biomarker combination approach will probably be more effective than any single biomarker would be. A team from the French University Hospital Centers in Nancy and Dijon has developed a 'Bioscore' that pools levels of three biomarkers: PCT, sTREM-1 and a type of glycoprotein expressed on the surface of neutrophils. Reporting in April, the French team showed that the composite metric performed better than each of the individual biomarkers—a finding that they validated in two separate cohorts (*Am. J. Respir. Crit. Care M* doi:10.1164/rccm.201201-0037OC, 2012

The hope now, says Francois Philippart, an immunologist at the Pasteur Institute in Paris who is developing his own combination index, is to move these kinds of analysis out of clinical trials and into routine practice. "If we find an interesting panel of biomarkers, it will be useful for [diagnosing sepsis in] any kind of ICU patient," he says.

Melinda Wenner Moyer



clu ve and validation cohorts of
, d nst the high performance of a
ind oget vith PCT and sTREM-1 serum
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Am J Respir Crit Care Med 2012;186(1):65-71

What is Adrenomedullin?

Presente

The measurement of ADM
is challenging due to a number of issues such as:

- a short half life of 22 minutes
- rapid degradation by proteases
- binding to complement factor H

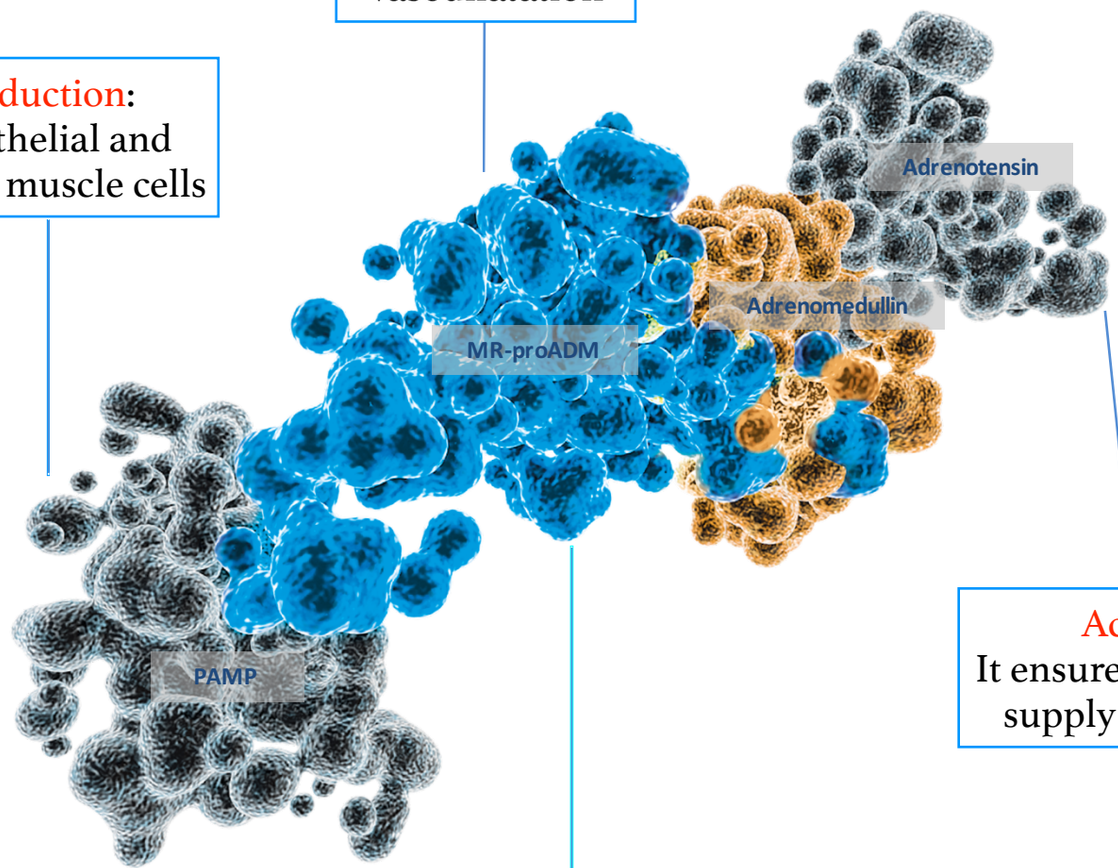
Futuro

MR-proADM provides the solution
as:

- it is a stable molecule
- it is a surrogate biomarker for the unstable ADM (1:1)
- standardized measurements

Production:
Endothelial and smooth muscle cells

Function:
Key mediator of vasodilatation



Action:
It ensures the blood supply to organs

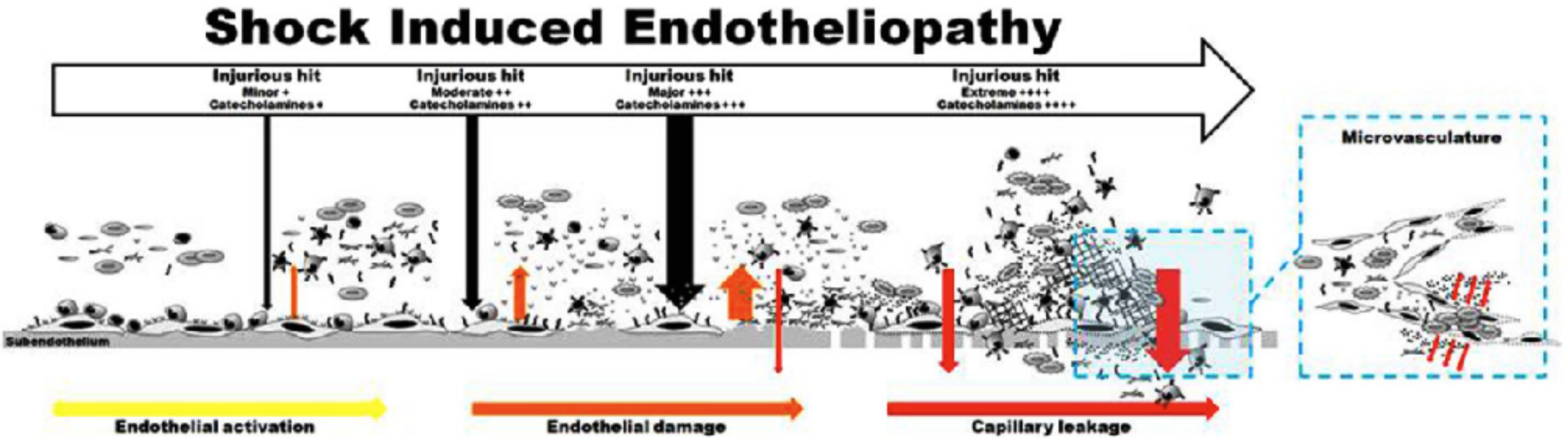
Mechanism of action:
Cyclic AMP
Nitric oxide

REVIEW Open Access

Shock induced endotheliopathy (SHINE) in acute critical illness - a unifying pathophysiologic mechanism

3000 ptz

We have investigated the degree of coagulopathy, sympatho-adrenal activation (plasma catecholamines) and endothelial injury (circulating biomarkers of endothelial cell (soluble thrombomodulin (**sTM**)) and glycocalyx (**syndecan-1**) damage) in three independent cohorts of severely injured patients

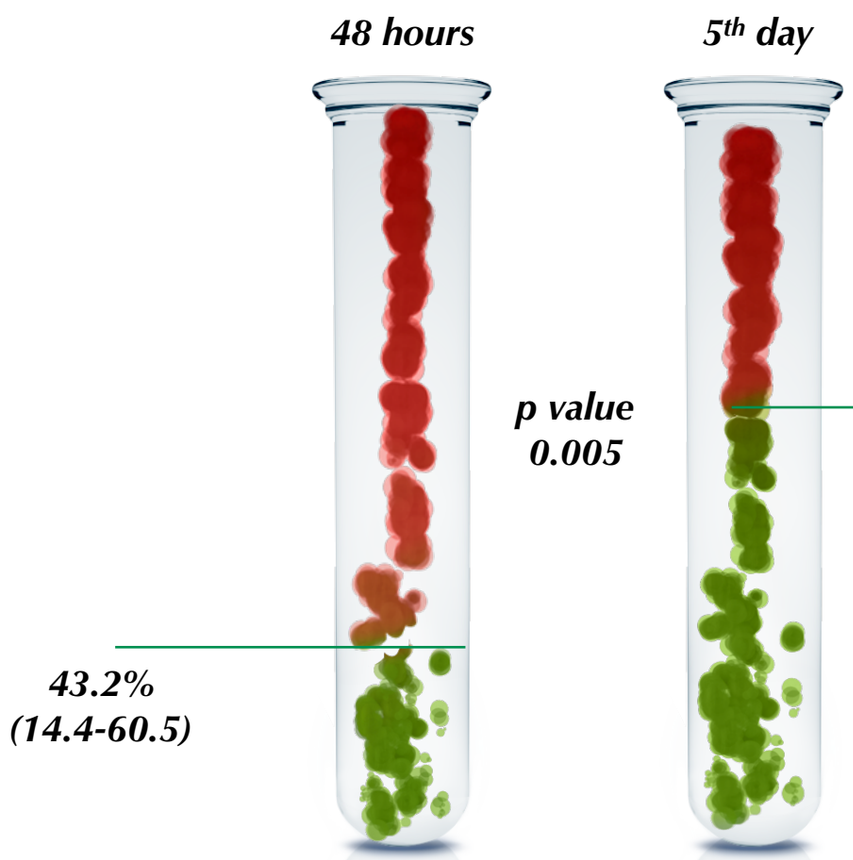


The catecholamine-induced damage to the endothelium is responsible for endothelial breakdown resulting in glycocalyx shedding, breakdown of tight junctions with capillary leakage and a pro- coagulant microvasculature that further reduces oxygen delivery due to increased tissue pressure and micro- vascular thrombosis creating a vicious circle that ultimately results in organ failure

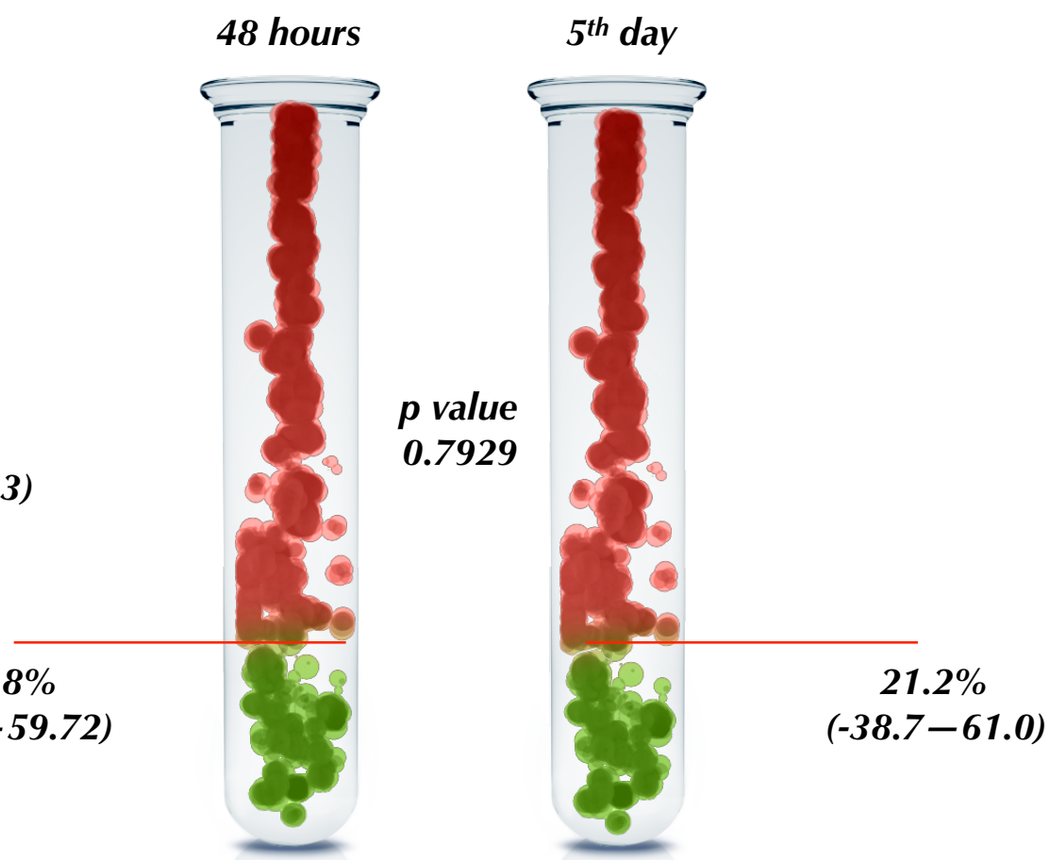
MR-proADM: increased clearance in survivors

Valenzuela-Sanchez et al. Diagnostic and prognostic usefulness of mid-regional pro-adrenomedullin levels with severe sepsis. in press

Septic survivors

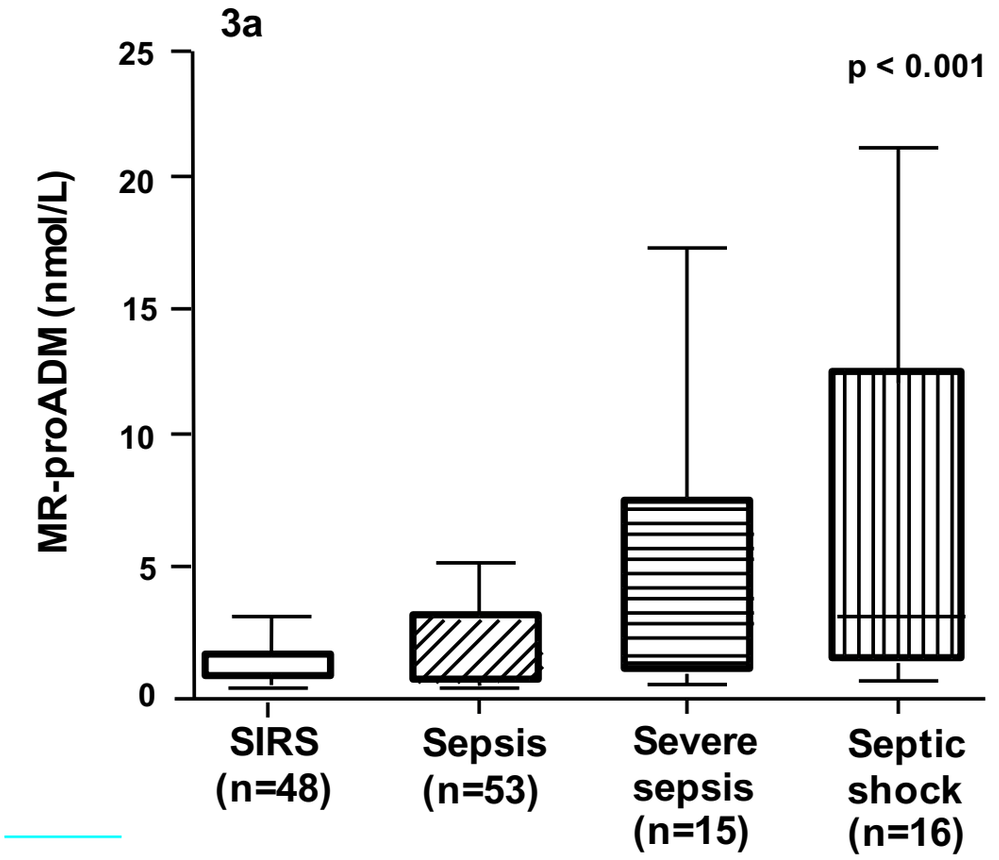


Septic non-survivors



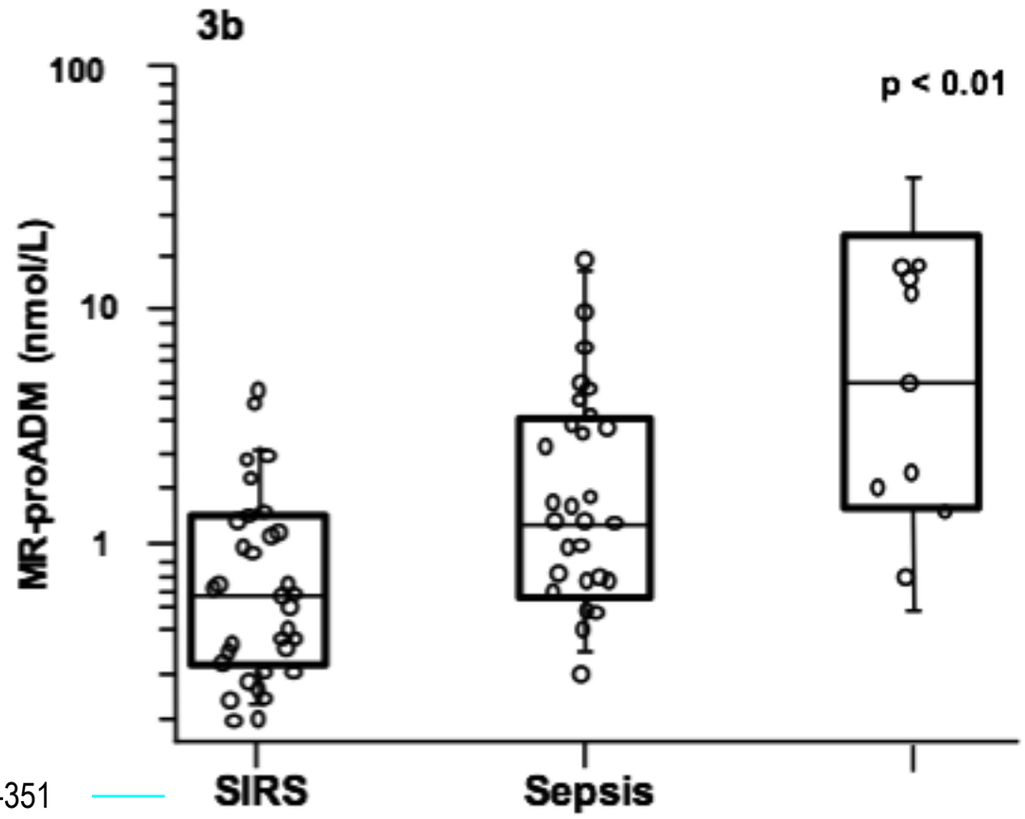
Survivors have increased Adrenomedullin clearance

Increasing MR-proADM levels correlate to disease severity



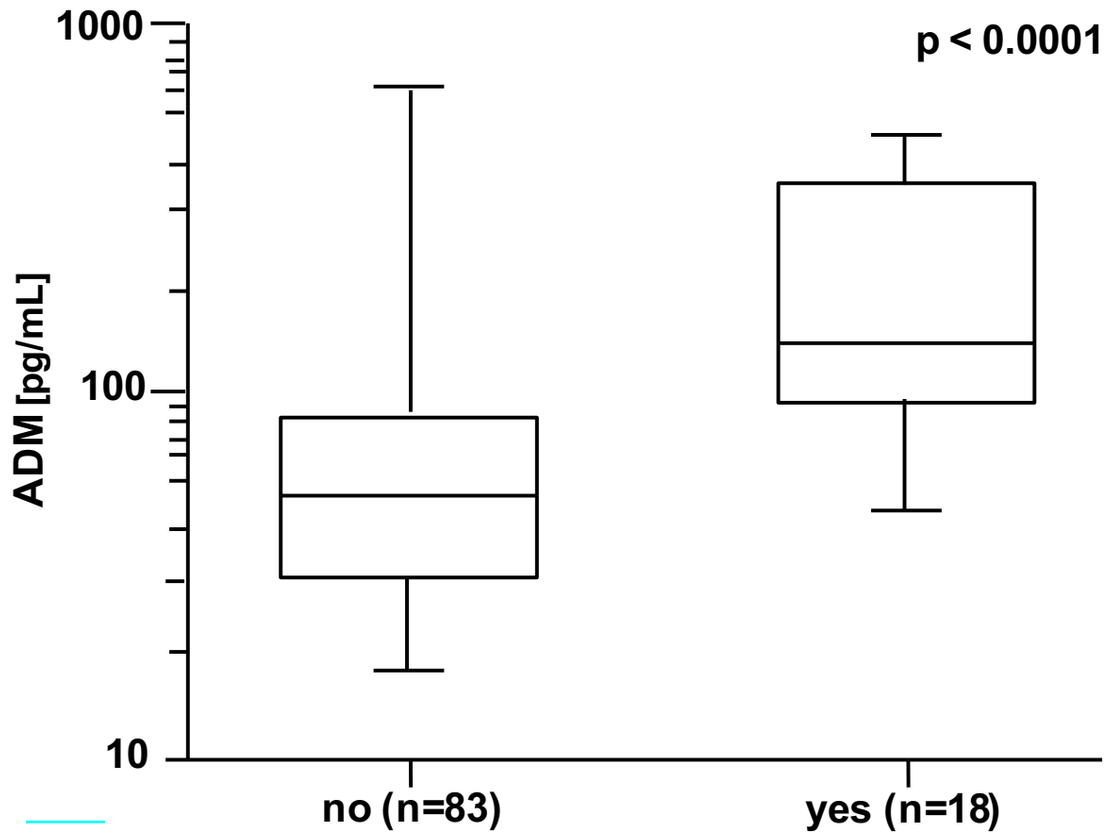
Christ-Crain et al. Crit Care 2005;9:R816-R824

Non- infectious SIRS and sepsis are clearly distinguishable



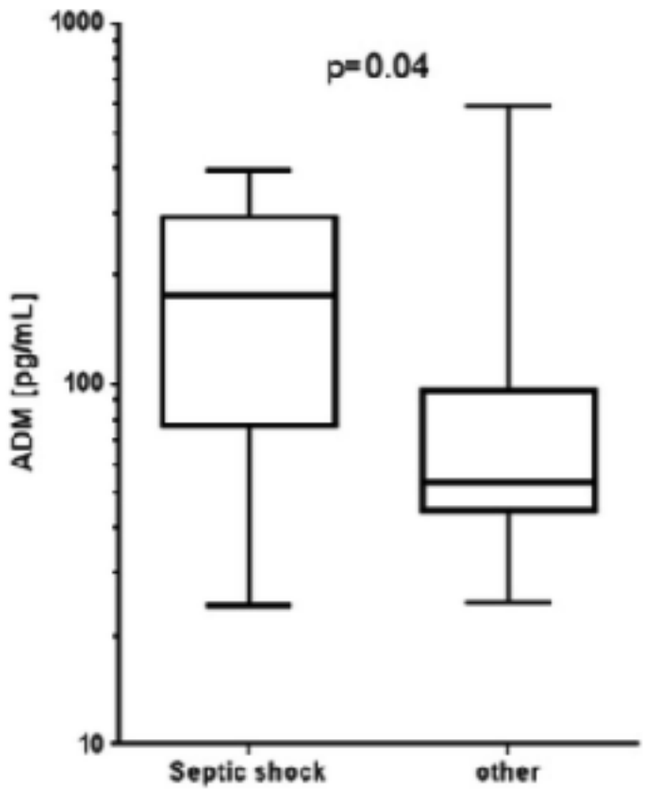
Shultz P et al. Endothelium 2007;14:345-351

Plasma adrenomedullin is associated vasopressor requirement in patients admitted with sepsis



Marino R et al. Crit Care 2014;18:R34

Plasma adrenomedullin is associated with short-mortality in patients admitted with sepsis



Activity Superior accuracy of MR-proADM for mortality prediction in sepsis with varying levels of illness severity

Andaluz-Ojeda D et al Ann Intensive Care 2017;7:15

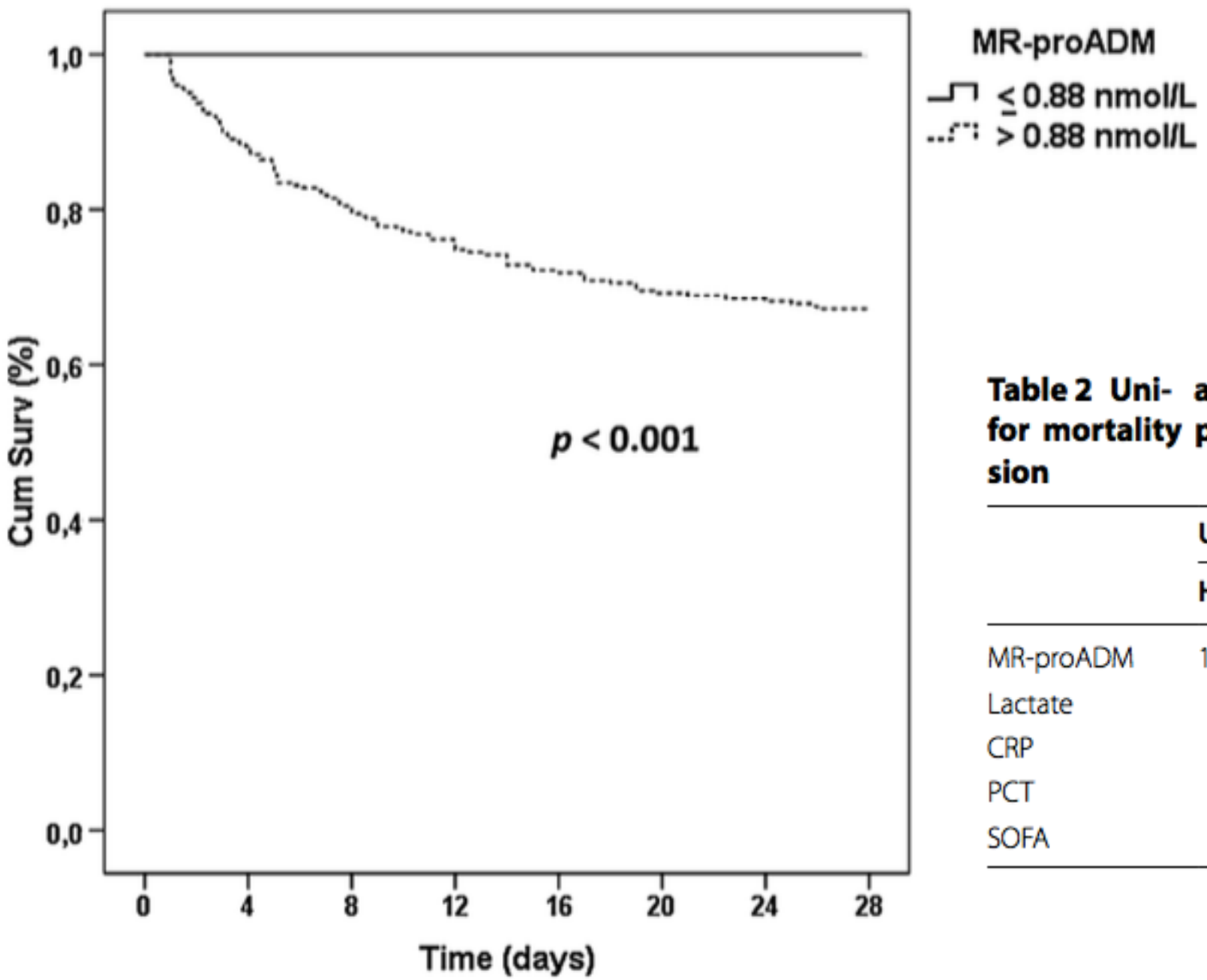


Fig. 1 Kaplan–Meier analysis for mortality prediction at 28 days

Methods: *a two-centre prospective observational cohort,* enrolling severe sepsis or septic shock patients admitted to the ICU

Plasma biomarkers were measured during the first 12 h of admission. The association between biomarkers and 28-day mortality was assessed by Cox regression analysis and Kaplan–Meier curves

Table 2 Uni- and multivariate Cox regression analysis for mortality prediction at 28 days following ICU admission

	Univariate		Multivariate	
	HR (95% CI)	*p*	HR (95% CI)	*p*
MR-proADM	11.2 (6.3–19.8)	<0.001	8.5 (4.2–17.4)	<0.001
Lactate	3.8 (2.6–5.5)	<0.001	3.4 (2.0–5.8)	<0.001
CRP	1.3 (0.8–1.9)	0.266	–	–
PCT	1.4 (1.2–1.8)	0.001	1.1 (0.9–1.4)	0.326
SOFA	1.2 (1.2–1.3)	<0.001	1.2 (1.1–1.3)	<0.001

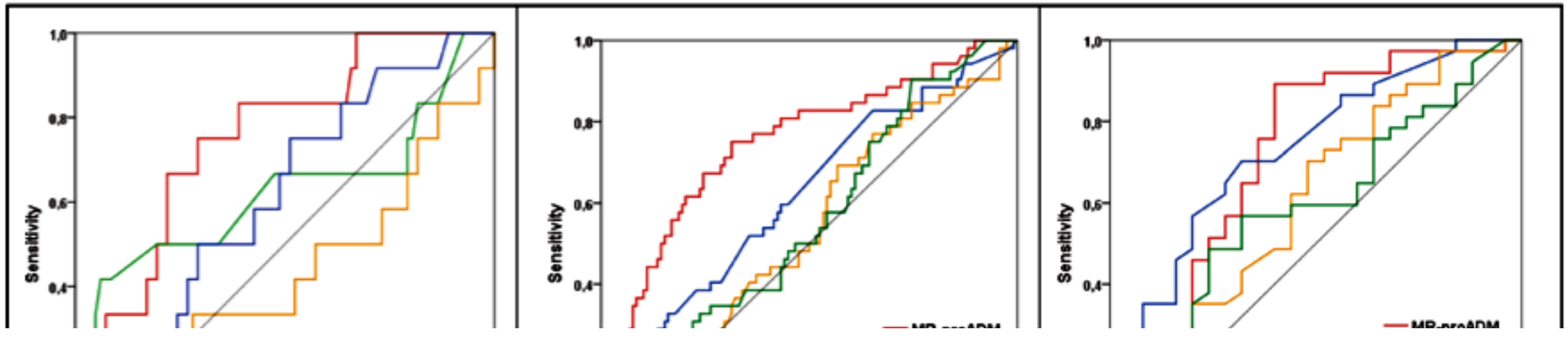
severe sepsis (21.7%) or septic shock (79.3%) were enrolled with a 28-day mortality rate of 31.0%

Activity Superior accuracy of MR-proADM for mortality prediction in sepsis with varying levels of illness severity

SOFA ≤ 6
N= 94 patients

SOFA 7-12
N= 170 patients

SOFA ≥ 13
N= 62 patients



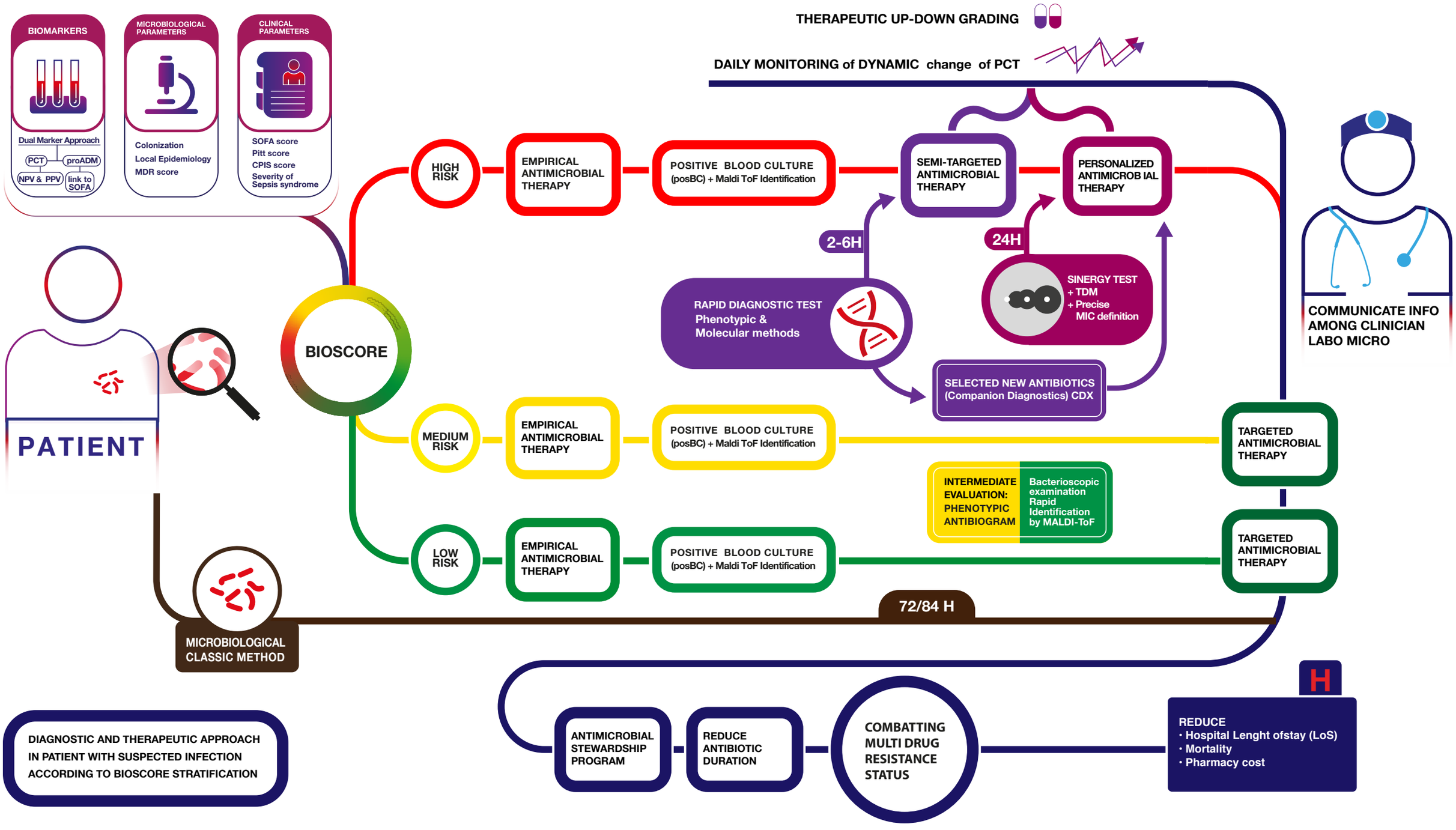
	[95%CI]	p
MR-proADM	0.75 [0.61 - 0.88]	0.006
Lactate	0.62 [0.41 - 0.83]	0.165
CRP	0.43 [0.23 - 0.62]	0.428
PCT	0.58 [0.44 - 0.73]	0.341

	[95%CI]	p
MR-proADM	0.74 [0.66 - 0.83]	0.000
Lactate	0.61 [0.52 - 0.71]	0.018
CRP	0.53 [0.44 - 0.62]	0.549
PCT	0.56 [0.46 - 0.65]	0.250

	[95%CI]	p
MR-proADM	0.73 [0.59 - 0.86]	0.003
Lactate	0.72 [0.59 - 0.86]	0.003
CRP	0.6 0 [0.46 - 0.75]	0.168
PCT	0.58 [0.44 - 0.73]	0.279

Conclusions: The performance of prognostic biomarkers in sepsis is highly influenced by disease severity. MR-proADM accuracy to predict mortality is not affected by the degree of organ failure. Thus, it is a good candidate in the early identification of sepsis patients with moderate disease severity but at risk of mortality.

Andaluz-Ojeda D et al Ann Intensive C


BIOMARKERS
Dual Marker Approach
PCT
proADM
NPV & PPV
link to SOFA
MICROBIOLOGICAL PARAMETERS
Colonization
Local Epidemiology
MDR score
CLINICAL PARAMETERS
SOFA score
Pitt score
CPIS score
Severity of Sepsis syndrome
THERAPEUTIC UP-DOWN GRADING
DAILY MONITORING of DYNAMIC change of PCT
PATIENT
BIOSCORE
HIGH RISK
EMPIRICAL ANTIMICROBIAL THERAPY
POSITIVE BLOOD CULTURE (posBC) + Maldi ToF Identification
SEMI-TARGETED ANTIMICROBIAL THERAPY
PERSONALIZED ANTIMICROB IAL THERAPY
2-6H
24H
RAPID DIAGNOSTIC TEST
Phenotypic & Molecular methods
SINERGY TEST
+ TDM
+ Precise MIC definition
SELECTED NEW ANTIBIOTICS (Companion Diagnostics) CDX
COMMUNICATE INFO AMONG CLINICIAN LABO MICRO
MEDIUM RISK
EMPIRICAL ANTIMICROBIAL THERAPY
POSITIVE BLOOD CULTURE (posBC) + Maldi ToF Identification
TARGETED ANTIMICROBIAL THERAPY
INTERMEDIATE EVALUATION: PHENOTYPIC ANTIBIOGRAM
Bacterioscopic examination
Rapid Identification by MALDI-ToF
LOW RISK
EMPIRICAL ANTIMICROBIAL THERAPY
POSITIVE BLOOD CULTURE (posBC) + Maldi ToF Identification
TARGETED ANTIMICROBIAL THERAPY
72/84 H
MICROBIOLOGICAL CLASSIC METHOD
DIAGNOSTIC AND THERAPEUTIC APPROACH IN PATIENT WITH SUSPECTED INFECTION ACCORDING TO BIOSCORE STRATIFICATION
ANTIMICROBIAL STEWARDSHIP PROGRAM
REDUCE ANTIBIOTIC DURATION
COMBATTING MULTI DRUG RESISTANCE STATUS
H
REDUCE
• Hospital Lenght ofstay (LoS)
• Mortality
• Pharmacy cost

Azienda Ospedaliero Universitaria Careggi

bruno.viaggi@gmail.com
gianmaria.rossolini@unifi.it