

**39th KSCCM Annual Congress and
Acute Critical Care Conference 2019
26th, April, 2019**

Procalcitonin-guided treatment in pneumonia

Jinsoo Min, M.D., M.P.H.

The Catholic University of Korea

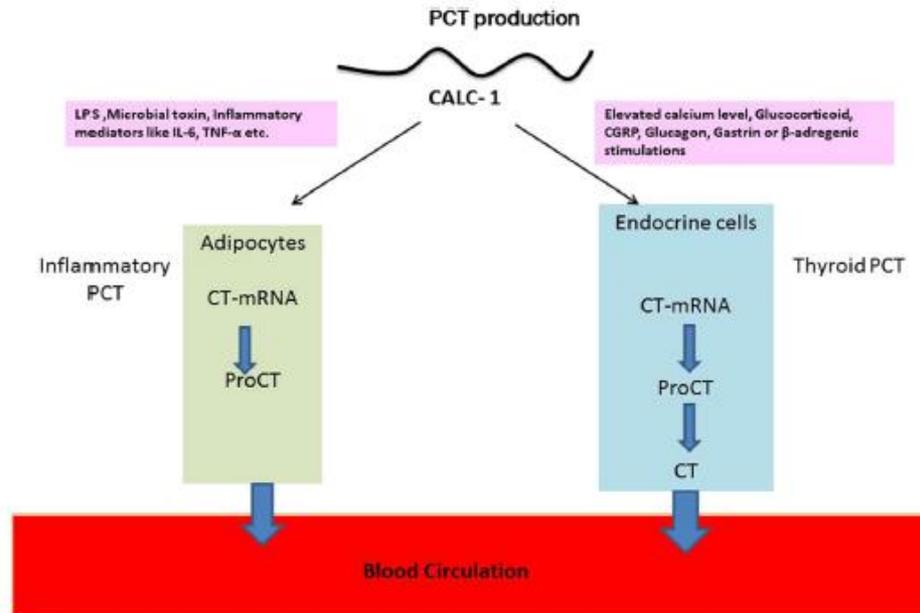
Contents

- Introduction and physiology of procalcitonin (PCT)
- Lower respiratory tract infections (LRTIs)
- Clinical implication of procalcitonin
- What do the guidelines say?
- Conclusions

Procalcitonin

- A serum biomarker that helps **distinguish bacterial infection from other causes of infection or inflammation**
- Serve as a helpful adjunct to clinical judgment for **guiding antibiotic therapy and resolving diagnostic uncertainty** in patients with **lower respiratory tract infections**
- A precursor hormone of calcitonin that **undetectable in healthy states**

Fate of Procalcitonin during inflammation and normal condition



Vijayan *et al.* J Int Care. 2017

- Serum PCT levels rise **rapidly in response to systemic inflammatory insults**, with peak levels that correlate with the intensity of the stimulus.
- PCT has a **short half-life** (25–30 hours), and its levels decline rapidly with resolution of inflammation.

Issues in LRTIs

- Lower respiratory tract infections (LRTIs) are among the most common reasons for antibiotic prescription.
- An estimated 30-85% of these prescriptions are **unnecessary or inappropriate**.
- Even when indicated, antibiotic treatment course often **exceed recommended duration**.
- The predilection for **antibiotic overuse for LTRIs** is in part due to the **difficulty in distinguishing between viral and bacterial infections**.

Grijalva CG *et al.* JAMA. 2009

Hecker MT *et al.* Arch Intern Med. 2003

Clinical Implication of Procalcitonin...

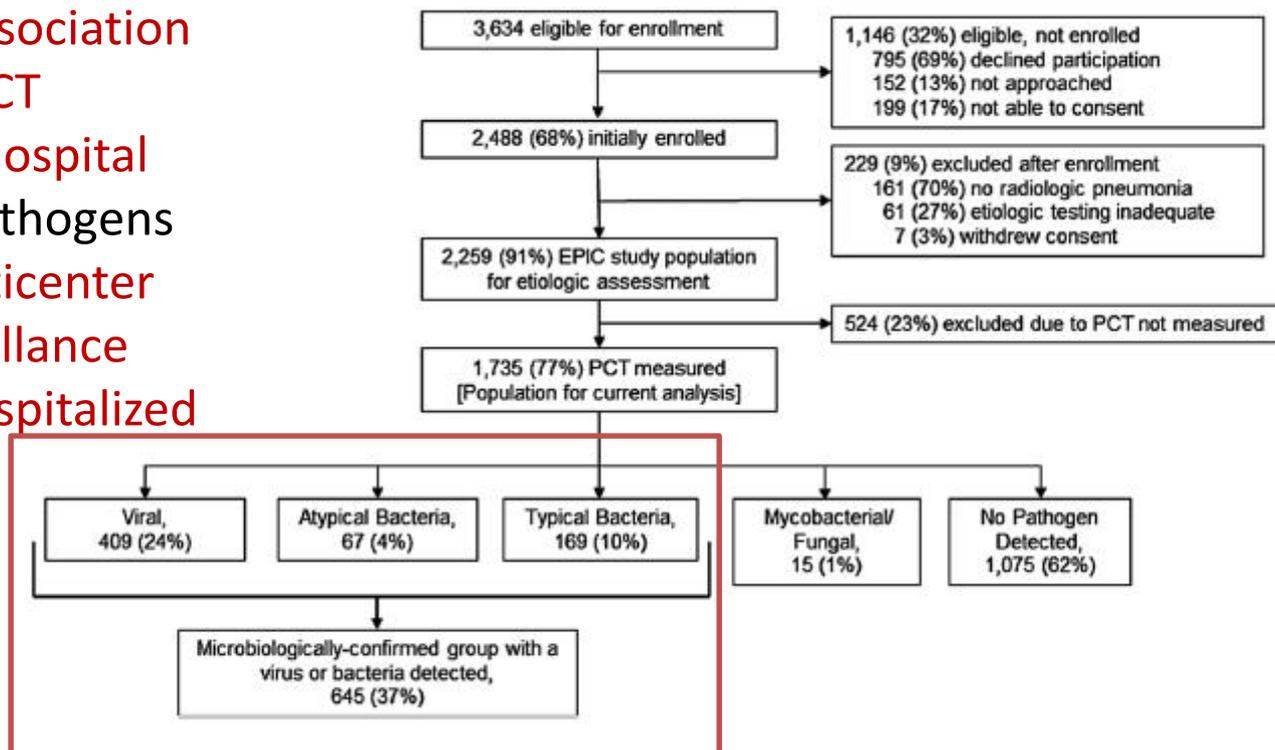
- 1. for Differential Diagnosis**
 - 2. for Guiding Antibiotic Therapy**
 - 3. for Prognosis?**
-

Use of Procalcitonin for Differential Diagnosis

Procalcitonin as a Marker of Etiology in Adults Hospitalized With Community-Acquired Pneumonia

Wesley H. Self,¹ Robert A. Balk,² Carlos G. Grijalva,¹ Derek J. Williams,¹ Yuwei Zhu,¹ Evan J. Anderson,³ Grant W. Waterer,^{4,5} D. Mark Courtney,⁵ Anna M. Bramley,⁶ Christopher Trabue,⁷ Sherene Fakhran,⁸ Anne J. Blaschke,⁹ Seema Jain,⁶ Kathryn M. Edwards,¹ and Richard G. Wunderink⁵

- To evaluate the **association between serum PCT concentration at hospital admission** with pathogens detected in a **multicenter prospective surveillance study of adults hospitalized with CAP**



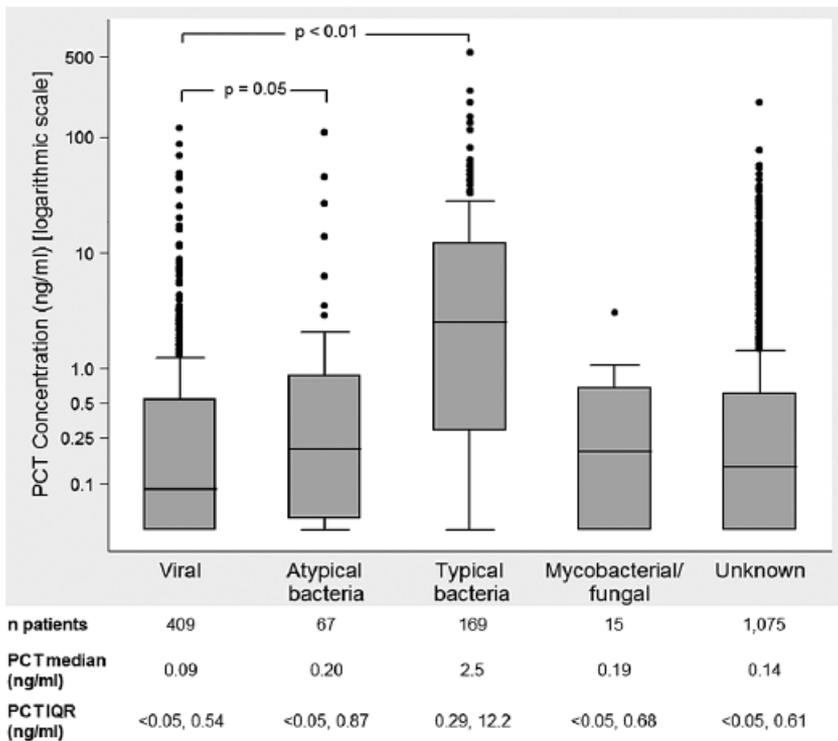
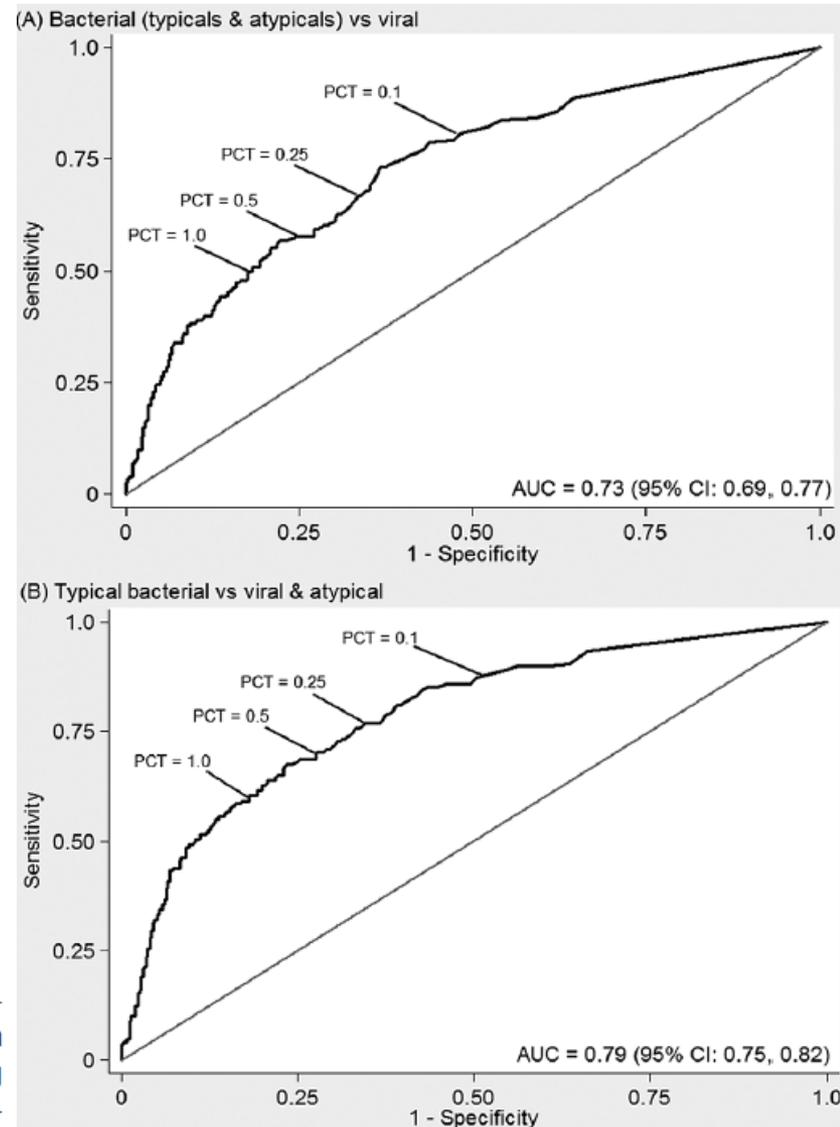
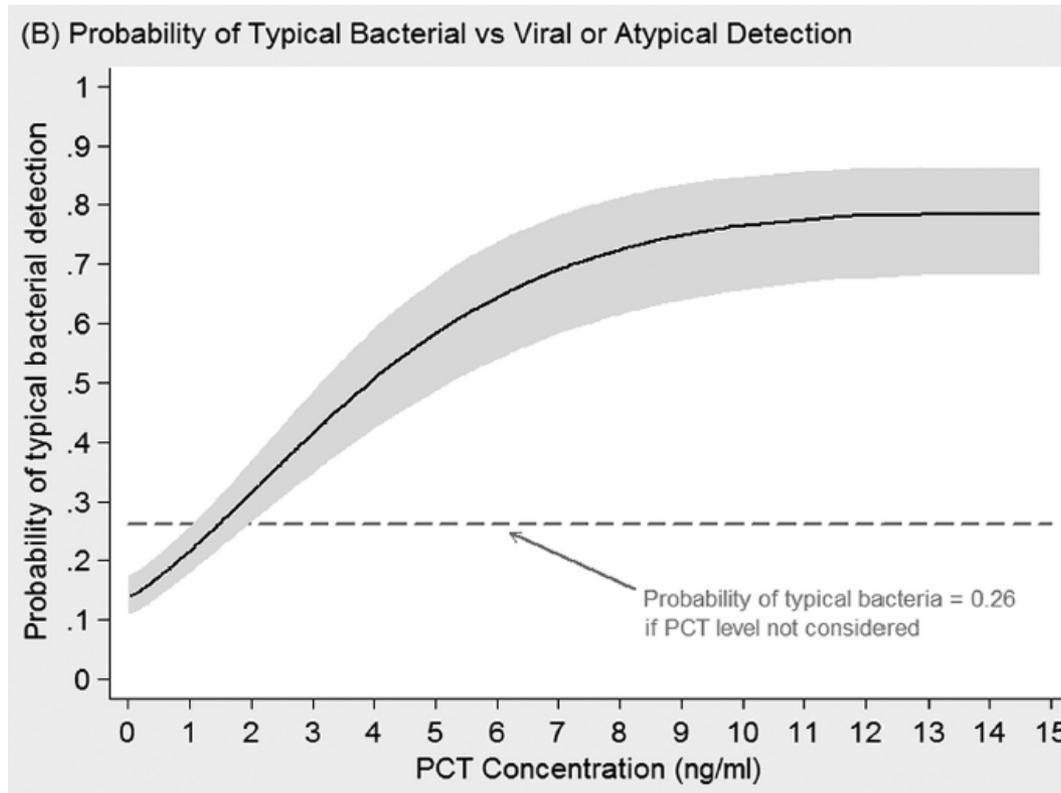


Figure 2. Box plot of serum procalcitonin (PCT) concentration by pathogen group. The center of each box plot represents the median, with the box denoting the interquartile range (IQR), the whiskers representing 1.5 times the IQR, and dots showing outliers beyond the whiskers. Displayed *P* values were calculated with the rank-sum test.

Figure 3. Receiver operating characteristic curves for procalcitonin (PCT) to discriminate bacterial (including typical and atypical bacteria) from viral pneumonia (A), typical bacterial from viral and atypical pneumonia (B), and bacterial (including typical and atypical bacteria) from nonbacterial pneumonia (C). Selected PCT cut-points (0.1 ng/mL, 0.25 ng/mL, 0.5 ng/mL, 1.0 ng/mL) are displayed. Abbreviations: AUC, area under the curve; CI, confidence interval.





Conclusion:

No PCT threshold perfectly discriminated between viral and bacterial pathogens, but **higher PCT strongly correlated with increased probability of bacterial pathogens, particularly typical bacteria.**

The role of serum procalcitonin in the differential diagnosis of pneumonia from pulmonary edema among the patients with pulmonary infiltrates on chest radiography

Young Kyung Yoon, MD, PhD^a, Min Ja Kim, MD, PhD^a, Kyung Sook Yang, PhD^b, Soo-Youn Ham, MD, PhD^{c,*}

Table 1

Comparison of demographic and baseline characteristics of 231 patients with pulmonary infiltration on chest x-ray.

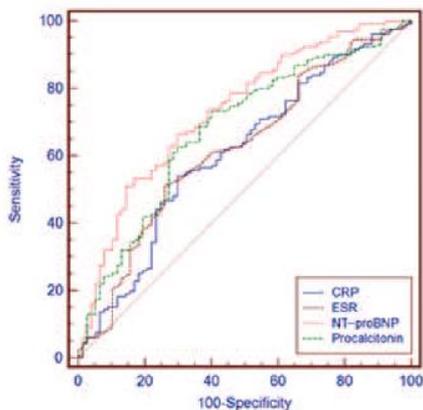
Variables ^a	All (n=231)	Pneumonia (n=143, 61.9%)	Pulmonary edema (n=88, 38.1%)	P ^b
Male sex, n (%)	132 (57.1)	80 (55.9)	52 (59.1)	.639
Age (y), median (IQR)	76 (69–82)	77 (69–83)	75 (69–82)	.424
Comorbidity, n (%)				
Cardiovascular	176 (76.2)	93 (65.0)	83 (94.3)	<.001
Cerebrovascular	64 (27.7)	51 (35.7)	13 (14.8)	.001
Diabetes mellitus	93 (40.3)	45 (31.5)	48 (54.4)	.001
Renal	48 (20.8)	17 (11.9)	31 (35.2)	<.001
Charlson comorbidity Index, median (IQR)	2 (1–4)	2 (1–3)	3 (2–6)	<.001
Symptoms, n (%)				
Fever	101 (43.7)	88 (61.5)	13 (14.8)	<.001
Cough	93 (40.3)	79 (55.2)	14 (15.9)	<.001
Sputum	98 (42.4)	83 (58.0)	15 (17.0)	<.001
Chest pain	35 (15.2)	20 (14.0)	15 (17.0)	.529
Dyspnea	160 (69.3)	93 (65.0)	67 (76.1)	.076
Clinical severity, n (%)				
Shock	51 (22.1)	35 (24.5)	16 (18.2)	.263
ICU care	75 (32.5)	48 (33.6)	27 (30.7)	.649
Mechanical ventilation	50 (21.6)	33 (23.1)	17 (19.3)	.501
Antibiotic therapy, n (%)	197 (85.3)	141 (98.6)	56 (63.6)	<.001
Outcome				
Morbidity, median (IQR)	9 (6–17)	9 (5–18)	9 (6–17)	.745
In-hospital mortality, n (%)	17 (7.4)	10 (7.0)	7 (8.0)	.800

ICU = intensive care unit, IQR = interquartile range.

^a Values represent the number of subjects (%) or median (interquartile range).

^b P values were obtained using Student *t* test, Mann–Whitney *U* test, or chi-square test as appropriate.

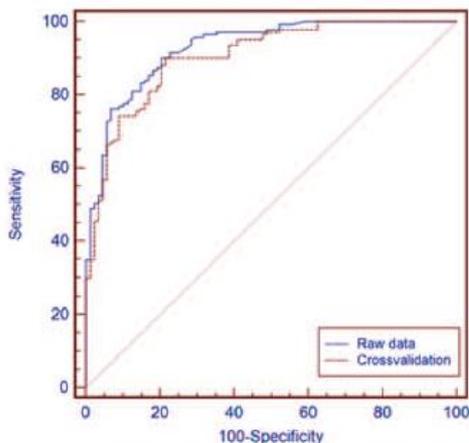
- To evaluate the usefulness of serum PCT as a diagnostic biomarker for **distinguishing pneumonia from pulmonary edema** in patients presenting with pulmonary infiltrates on CXR



Variables	Cut-off values	AUC (95% CI)
CRP level	18.0 mg/L	0.609 (0.540-0.676)
ESR level	35.0 /mm ³	0.622 (0.553-0.688)
NT-proBNP level	200.0 mg/L	0.735 (0.669-0.793)
PCT level	0.25 ng/dL	0.680 (0.612-0.743)

Multivariate logistic regression analysis for diagnosis of pneumonia among patients with pulmonary infiltration on chest x-ray.

Independent variable	OR (95% CI for OR)	P
Fever (BT ≥38°C)	5.89 (2.23–15.59)	<.001
Purulent sputum	3.80 (1.45–9.97)	.007
Cardiomegaly on chest x-ray	0.24 (0.08–0.73)	.012
Underlying cerebrovascular diseases	4.01 (1.44–11.16)	.008
Charlson comorbidity index (per 1-point increment)	0.65 (0.53–0.81)	<.001
PCT ≥0.25 ng/mL	3.96 (1.66–9.45)	.002
CRP ≥18.0 mg/dL	2.68 (1.07–6.67)	.035
ESR ≥35.0 mm/h	3.66 (1.46–9.17)	.006
NT-proBNP ≥200 pg/mL	0.17 (0.04–0.73)	.017



Variables	AUC (95% CI)	% (95% CI)			
		Sensitivity	Specificity	PPV	NPV
Raw data	0.929 (0.896–0.961)	90.2 (84.1–94.5)	79.6 (69.6–87.4)	87.8 (81.3–92.6)	83.3 (73.6–90.6)
LOOCV	0.904 (0.866–0.943)	90.2 (84.1–94.5)	78.4 (68.4–86.5)	87.2 (80.7–92.1)	83.1 (73.3–90.5)

AUC, area under the receiver operating characteristic curve; 95% CI, 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value; LOOCV, leave-one-out cross validation

Figure 2. Receiver-operating characteristic curve for pneumonia, obtained using the predictive probability of multivariate logistic regression model and validation results.

Conclusion:

Practical use of PCT in conjunction with clinical data can be valuable in the differential diagnosis of pulmonary infiltrates and guidance for clinicians to prevent antibiotic misuse.

Clinical Implication of Procalcitonin...

- 1. for Differential Diagnosis**
 - 2. for Guiding Antibiotic Therapy**
 - 3. for Prognosis?**
-

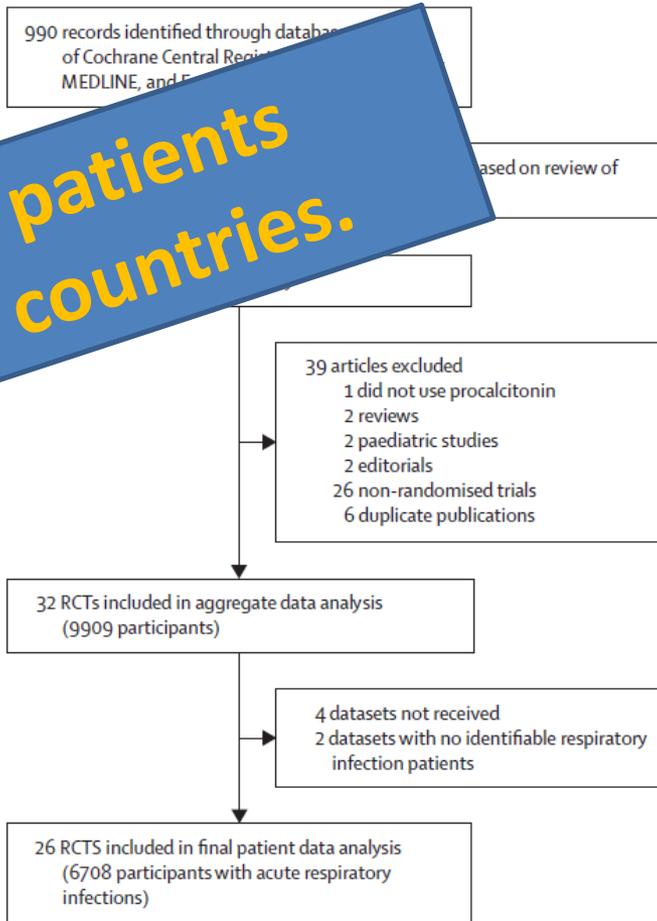
Use of Procalcitonin for Guiding Antibiotic Therapy

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

Philipp Schuetz*, Yannick Wirz*, Ramon Sager*, Mirjam Christ-Crain, Daiana Stolz, Michael Tamm, Lila Bouadma, Charles E Luyt, Michel Wolff, Jean Chastre, Florence Tubach, Kristina B Kristoffersen, Olaf Burkhardt, Tobias Welte, Stefan Schroeder, Vandack Nobre, Long Wei, Heiner C Bucher, Djillali Annane, Konrad Reinhart, Ann R Falsey, Angela Branche, Pierre Damas, Maarten Nijsten, Dylan W de Lange, Rodrigo O Deliberato, Carolina F Oliveira, Vera Maravić-Stojković, Alessia Verduri, Bianca Beghé, Bin Cao, Yahya Shehabi, Jens-Ulrik S Jensen, Caspar Corti, Jos A H van Oers, Albertus Beishuizen, Armand R J Girbes, Evelien de Jong, Matthias Briel*, Beat Mueller

	Control (n=3372)	Procalcitonin group (n=3336)
Age, years	61.2 (18.4)	60.7 (18.8)
Sex		
Men	1910 (57%)	1898 (57%)
Women	1462 (43%)	1438 (43%)
Clinical setting		
Primary care	149 (4%)	149 (4%)
Emergency department	67 (2%)	73 (2%)
ICU	46 (1%)	61 (2%)
Other	3092 (92%)	3044 (91%)
Lower acute respiratory infection		
Community-acquired pneumonia	1468 (44%)	1442 (43%)
Hospital-acquired pneumonia	262 (8%)	243 (7%)
Ventilator-associated pneumonia	186 (6%)	194 (6%)
Acute bronchitis	287 (9%)	257 (8%)
Exacerbation of COPD	631 (19%)	621 (19%)
Exacerbation of asthma	127 (4%)	143 (4%)
Other lower acute respiratory infection	131 (4%)	144 (4%)

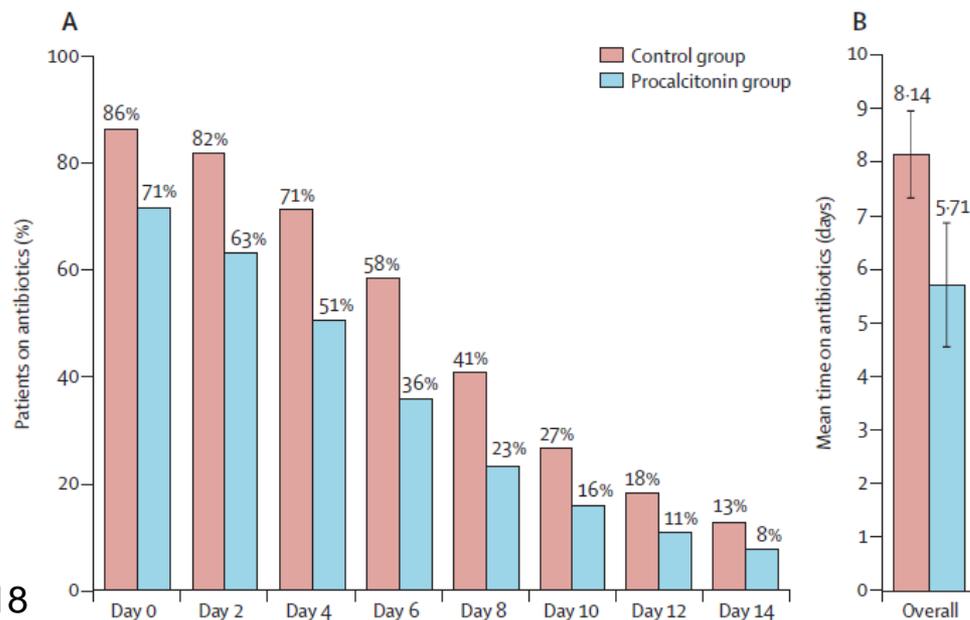
We collected data on 6708 patients from 26 eligible trials in 12 countries.



	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	..

	Control (n=3372)	Procalcitonin group (n=3336)	Adjusted OR or difference (95% CI), p value*	p _{interaction}
Overall				
Initiation of antibiotics	2894 (86%)	2351 (70%)	0.27 (0.24 to 0.32), p<0.0001	..
Duration of antibiotics, days†	9.4 (6.2)	8.0 (6.5)	-1.83 (-2.15 to -1.5), p<0.0001	..
Total exposure of antibiotics, days‡	8.1 (6.6)	5.7 (6.6)	-2.43 (-2.71 to -2.15), p<0.0001	..

Conclusion:
 Use of PCT to guide antibiotic treatment in patients with ARI reduces antibiotic exposure and side-effects, and improves survival.



Impact of Procalcitonin Guidance with an Educational Program on Management of Adults Hospitalized with Pneumonia



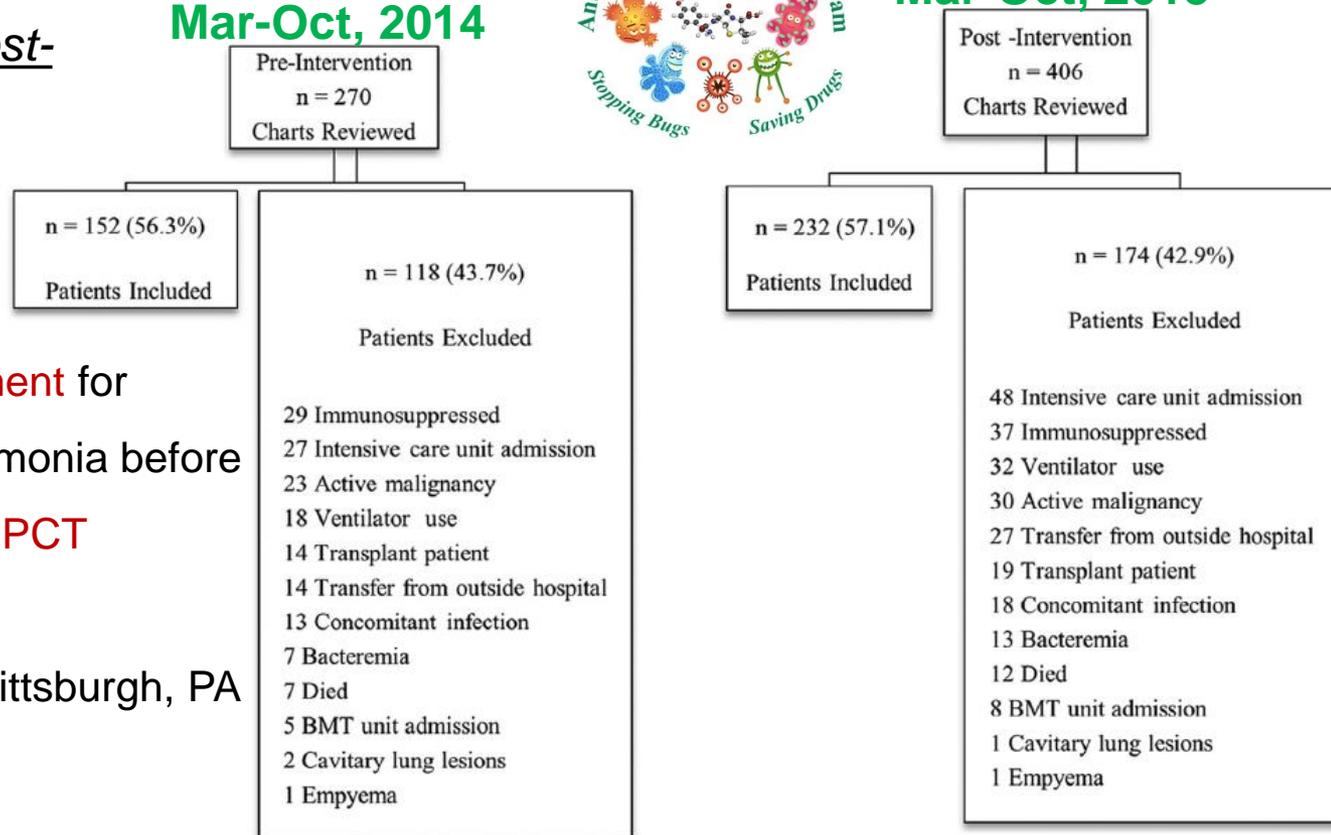
Thomas L. Walsh, MD,^{a,b} Briana E. DiSilvio, MD,^c Crystal Hammer, MD,^c Moezullah Beg, MD,^c Swati Vishwanathan, MD,^c Daniel Speredelozzi, MD,^c Matthew A. Moffa, DO,^{a,b} Kurt Hu, MD,^c Rasha Abdulmassih, MD,^{a,b} Jina T. Makadia, MD,^{a,b} Rikinder Sandhu, MD,^{a,b} Mouhib Naddour, MD,^c Noreen H. Chan-Tompkins, PharmD BCPS-AQ ID,^d Tamara L. Trienski, PharmD,^d Courtney Watson, MPH,^e Terrence J. Obringer, DO,^f Jim Kuzyck, MT,^g Derek N. Bremmer, PharmD, BCPS^h

Retrospective, pre-/post-intervention study

Mar-Oct, 2014



Mar-Oct, 2015



Aim : To **compare management** for patients admitted with pneumonia before and after **implementation of PCT guidance**

At 2 teaching hospitals in Pittsburgh, PA

Table 2 Antibiotic Treatment Duration

Variable	Preintervention (n = 152)	Postintervention (n = 232)	P Value
Total antibiotic duration (d)*	9.9 (3.3)	6.0 (3.8)	<.001
Intravenous antibiotic duration (d)*	5.0 (3.1)	3.3 (2.4)	<.001
Total antibiotic duration, n (%)			<.001
0-1 d	0 (0)	40 (17.2)	
2-5 d	11 (7.2)	51 (22.0)	
6-7 d	30 (19.7)	63 (27.2)	
8-10 d	55 (36.2)	52 (22.4)	
11-14 d	39 (25.7)	21 (9.1)	
>14 d	17 (11.2)	5 (2.2)	

Table 3 Postintervention Analysis Comparing Management in Patients with Low Peak Procalcitonin Levels Versus Patients with Elevated Peak Procalcitonin Levels

Variable	Peak Procalcitonin Level <0.25 µg/L (n = 136)	Peak Procalcitonin Level >0.25 µg/L (n = 96)	P Value
Total antibiotic duration (d)*	4.6 (3.6)	8.0 (3.3)	<.001
Intravenous antibiotic duration (d)*	2.7 (2.2)	4.3 (2.3)	<.001
Total antibiotic duration, n (%)			<.001
0-1 d	37 (27.2)	3 (3.2)	
2-5 d	37 (27.2)	14 (14.7)	
6-7 d	34 (25.0)	29 (30.5)	
8-10 d	21 (15.4)	31 (32.6)	
11-14 d	6 (4.4)	15 (15.8)	
>14 d	1 (0.7)	3 (3.2)	
Hospital length of stay (d)*	3.2 (2.5)	4.0 (2.3)	.02
30-Day readmission, n (%)			
All-cause	19 (14.0)	16 (16.7)	.58
Pneumonia-related	3 (2.2)	7 (7.3)	.10

*Mean ± standard deviation.

Conclusion:

In this **real-world study**, PCT guidance **led to shorter durations of total antibiotic therapy** and abridged inpatient length of stay **without affecting hospital readmissions**.

ORIGINAL ARTICLE

Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection

D.T. Huang, D.M. Yealy, M.R. Filbin, A.M. Brown, C.-C.H. Chang, Y. Doi, M.W. Donnino, J. Fine, M.J. Fine, M.A. Fischer, J.M. Holst, P.C. Hou, J.A. Kellum, F. Khan, M.C. Kurz, S. Lotfipour, F. LoVecchio, O.M. Peck-Palmer, F. Pike, H. Prunty, R.L. Sherwin, L. Southerland, T. Terndrup, L.A. Weissfeld, J. Yabes, and D.C. Angus, for the ProACT Investigators*

Procalcitonin Antibiotic Consensus Trial - ProACT

- Patient-level, 1:1 randomized trial
- 14 U.S. hospitals with high adherence to quality measures for the treatment of pneumonia
- Primary efficacy and safety outcome (co-primary)
 - Mean No. of antibiotic-days : PCT-guided antibiotic prescription would be superior.
 - Safety outcome : PCT-guided antibiotic prescription would be non-inferior.

Study period:
Nov 2015 – May 2017

Enrolled **adult Pt** in the **ED** for whom the treating clinician had given an **initial Dx of acute LRTI**

8360 Patients with acute (<28 days in duration) lower respiratory tract infection were assessed for eligibility

Screening: 8360

- Had clinician not willing to consider procalcitonin in antibiotic decision making
- 3540 Met exclusion criteria
 - 1369 Received antibiotics previously
 - 787 Had severe immunosuppression
 - 587 Had metastatic cancer
 - 300 Were receiving long-term prophylactic antibiotic treatment
 - 251 Were undergoing long-term dialysis
 - 239 Had accompanying nonrespiratory infection
 - 106 Were <18 yr of age
 - 91 Were homeless
 - 85 Had undergone surgery in past 7 days
 - 48 Had endotracheal intubation
 - 22 Had lung abscess or empyema
 - 11 Were incarcerated
 - 10 Had been enrolled in ProACT in past 30 days
 - 8 Were receiving intravenous vasopressors
- 2122 Were excluded for other reasons
 - 1251 Had logistic issues
 - 737 Declined to participate
 - 195 Had language barrier and no LAR
 - 124 Lacked mental capacity to consent and had no LAR
 - 69 Did not have staff available

<Procalcitonin Group>

- Real-time initial PCT assay results
- Antibiotic use guideline based on four tiers of PCT levels

1664 Underwent randomization

Randomization: 1664

830 Were assigned to procalcitonin
826 Were eligible for inclusion in analysis
4 Requested removal of all data

PCT: 830

826 Were included in primary outcome analysis
675 Completed 30-day follow-up
40 Completed 15-day follow-up only

834 Were assigned to usual care
830 Were eligible for inclusion in analysis
4 Requested removal of all data

UC: 834

830 Were included in primary outcome analysis
670 Completed 30-day follow-up
45 Completed 15-day follow-up only

<Usual-care Group>

- Real-time initial PCT assay : the results were clinically unuavailable

NATIONAL ANTIBIOTIC GUIDELINES

COMMUNITY-ACQUIRED PNEUMONIA

Antibiotic duration - 5d min, afebrile 48-72h, and ≤ 1 sign of clinical instability (Moderate recommendation, level II evidence, IDSA/ATS 2007)

COPD

Antibiotics if all 3 cardinal symptoms* (Evidence B) or 2 symptoms if one is sputum purulence (Evidence C), for 5-10 days (Evidence D) (GOLD 2015). (*increased dyspnea, sputum volume, sputum purulence)

ASTHMA

Antibiotics not generally recommended for the treatment of acute asthma exacerbations (Evidence B) (NIH Expert Panel Report 3, 2007); Do not initiate antibiotics (GINA 2015)

ACUTE BRONCHITIS

Antibiotics not recommended for uncomplicated bronchitis (CDC/ACP 2016)

PROCALCITONIN ANTIBIOTIC GUIDELINE

PROCALCITONIN LEVEL ($\mu\text{g/L}$)	BACTERIAL ETIOLOGY	RECOMMENDATION
< 0.1	Very Unlikely	Antibiotics Strongly Discouraged
0.1 - 0.25	Unlikely	Antibiotics Discouraged
> 0.25 - 0.5	Likely	Antibiotics Recommended
> 0.5	Very Likely	Antibiotics Strongly Recommended

1. Initial antibiotics can be considered for Legionella, empyema, critical illness. Procalcitonin should be evaluated in context with all data; clinical judgment always necessary.
2. For outpatients, antibiotic duration based on level (> 0.25-0.5 $\mu\text{g/L}$: 3 days; > 0.5-1.0 $\mu\text{g/L}$: 5 days; >1.0 $\mu\text{g/L}$: 7 days).

ProACT (Procalcitonin Consensus Trial) is a NIH-funded trial of procalcitonin implementation in ED patients with lower respiratory tract infection

Fig. 1 ProACT guidelines. The ProACT Coordinating Center provided posters of this Figure to all centers. Other study education, in-service training, and promotion materials contain the same content

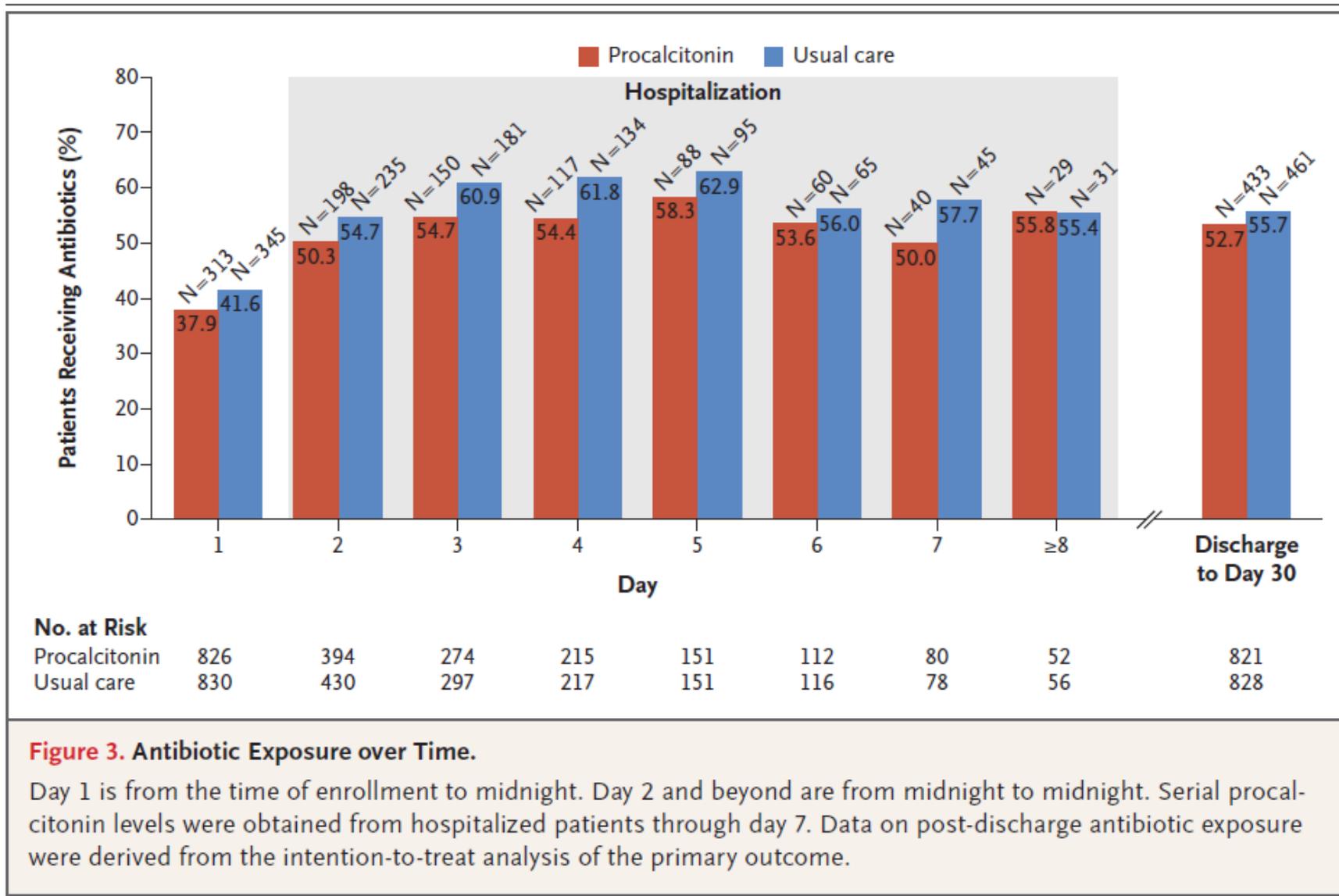


Figure 3. Antibiotic Exposure over Time.

Day 1 is from the time of enrollment to midnight. Day 2 and beyond are from midnight to midnight. Serial procalcitonin levels were obtained from hospitalized patients through day 7. Data on post-discharge antibiotic exposure were derived from the intention-to-treat analysis of the primary outcome.

Table 2. Antibiotic Exposure.*

Outcome	Procalcitonin (N = 826)	Usual Care (N = 830)	Difference (95% or 99.86% CI)†
Intention-to-treat population‡			
Antibiotic-days by day 30§	4.2±5.8	4.3±5.6	-0.05 (-0.6 to 0.5)
Received any antibiotics by day 30 — estimated no. (%)¶	471 (57.0)	513 (61.8)	-4.8 (-12.7 to 3.0)
Antibiotic prescription in ED — estimated no. (%)¶	282 (34.1)	321 (38.7)	-4.6 (-12.2 to 3.0)
Antibiotic-days during hospital stay	2.6±3.3	2.7±3.0	-0.1 (-0.8 to 0.6)
Hospital length of stay — days	5.0±4.4	4.7±3.5	0.3 (-0.2 to 0.9)

Table S5. - Adverse outcomes by day 30*

	Procalcitonin (n = 826)	Usual Care (n = 830)	% Risk Difference (95% CI)
All patients (intention-to-treat)	n = 826	n = 830	
Overall adverse outcome	96 (11.7%)	109 (13.1%)	-1.5% (-4.6% to 1.7%)
Death	16 (1.9%)	10 (1.2%)	0.7% (-0.5% to 2.0%)
Endotracheal intubation	13 (1.6%)	20 (2.4%)	-0.8% (-2.2% to 0.6%)
Vasopressors	11 (1.3%)	21 (2.6%)	-1.3% (-2.7% to 0.1%)
Renal failure	3 (0.4%)	4 (0.5%)	-0.1% (-0.8% to 0.6%)
Lung abscess / empyema	4 (0.5%)	5 (0.6%)	-0.1% (-0.9% to 0.7%)
Pneumonia development in non-CAP patient	8 (1.0%)	9 (1.0%)	-0.1% (-1.1% to 1.0%)
Hospital readmission	62 (7.6%)	70 (8.5%)	-0.9% (-3.6% to 1.8%)

Conclusion:

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

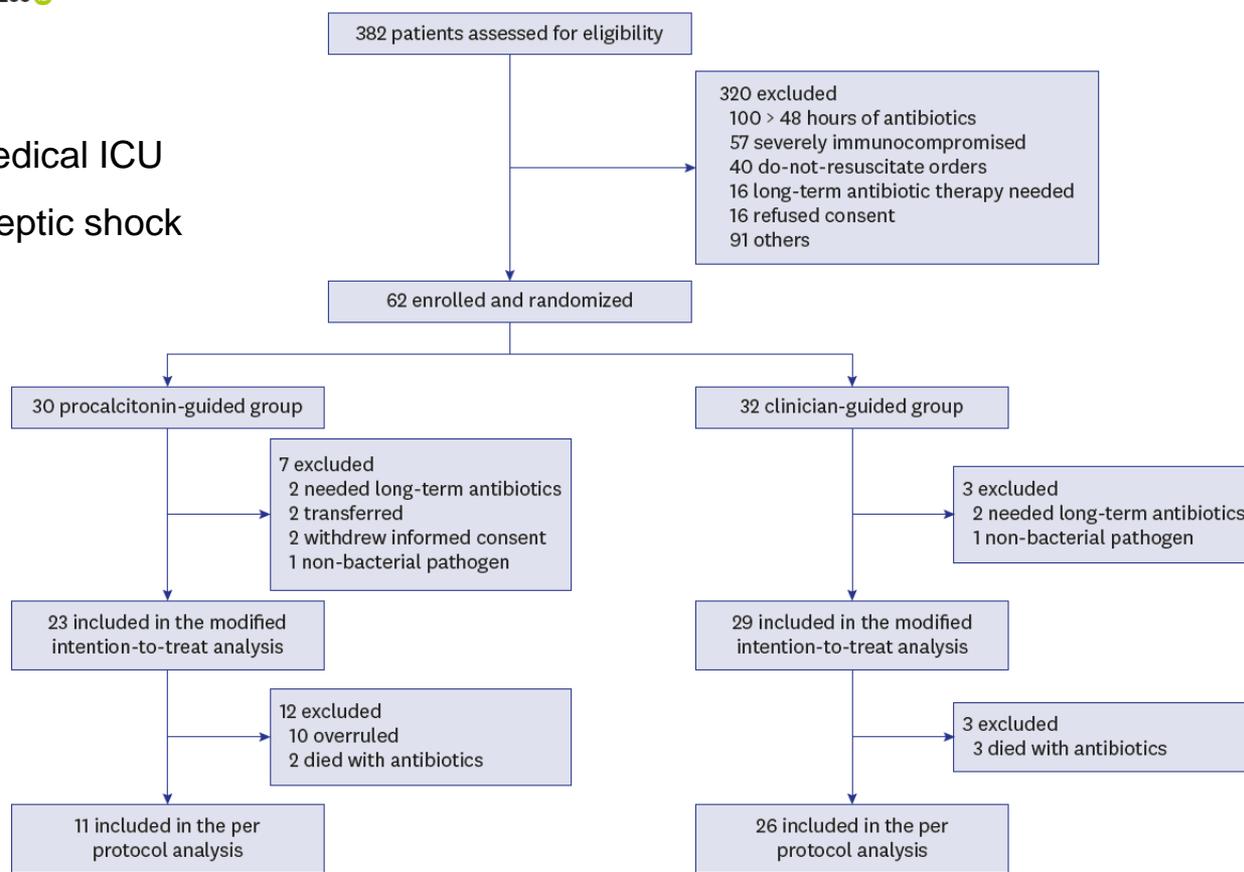
Procalcitonin-Guided Treatment on Duration of Antibiotic Therapy and Cost in Septic Patients (PRODA): a Multi-Center Randomized Controlled Trial

Kyeongman Jeon ,^{1,2*} Jae Kyung Suh ,^{3*} Eun Jin Jang ,^{3,4} Songhee Cho ,³ Ho Geol Ryu ,⁵ Sungwon Na ,⁶ Sang-Bum Hong ,⁷ Hyun Joo Lee ,⁸ Jae Yeol Kim ,⁹ and Sang-Min Lee ¹⁰

OPEN ACCESS

Check for updates

Adult patients
within 24 hours of admission to medical ICU
with suspected severe sepsis or septic shock
July 2014 ~ June 2015



Characteristics	Modified intention-to-treat analysis			Per-protocol analysis		
	Procalcitonin group (n = 23)	Control group (n = 29)	P value	Procalcitonin group (n = 11)	Control group (n = 26)	P value
Age, yr	69 (61-75)	70 (63-77)	0.537	69 (63-74)	71 (61-77)	0.781
Gender, men	8 (33)	14 (48)	0.272	4 (36)	12 (46)	0.723
Comorbidities						
Diabetes	13 (54)	11 (38)	0.237	6 (55)	9 (35)	0.295
Cardiovascular disease	7 (29)	8 (28)	0.899	3 (27)	6 (23)	> 0.999
Chronic lung disease	6 (25)	7 (24)	0.942	3 (27)	5 (19)	0.672
Chronic renal disease	8 (33)	7 (24)	0.459	4 (36)	5 (19)	0.404
Chronic liver disease	6 (25)	4 (14)	0.482	2 (18)	4 (15)	> 0.999
Malignancy	5 (21)	7 (24)	0.775	2 (18)	6 (23)	> 0.999
Charlson comorbidity index	4 (2-5)	3 (2-4)	0.301	2 (2-4)	3 (2-4)	0.919
Acquisition of infection						
Community-acquired	9 (37)	14 (48)	0.387	4 (36)	14 (54)	0.293
Healthcare-associated	9 (37)	10 (35)		4 (36)	8 (31)	
Hospital-acquired	6 (25)	5 (17)		3 (27)	4 (15)	
Sites of infection						
			0.927			0.908
Pulmonary	5 (21)	10 (35)	0.927	2 (18)	8 (31)	0.908
Intraabdominal	8 (33)	11 (38)		5 (46)	11 (42)	
Urinary	9 (38)	4 (14)		3 (27)	4 (15)	
Skin and soft tissue	1 (4)	0		0	0	
Catheter-related	0	0		0	0	
Others	1 (4)	3 (10)		1 (9)	2 (8)	
Unknown	0	1 (3)		0	1 (4)	

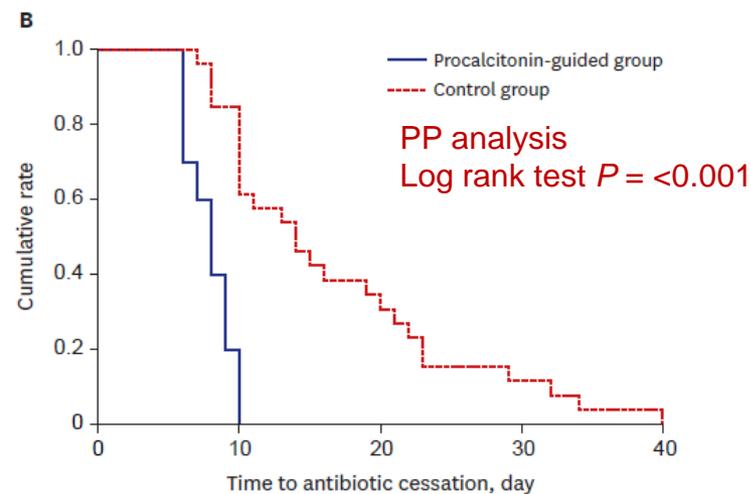
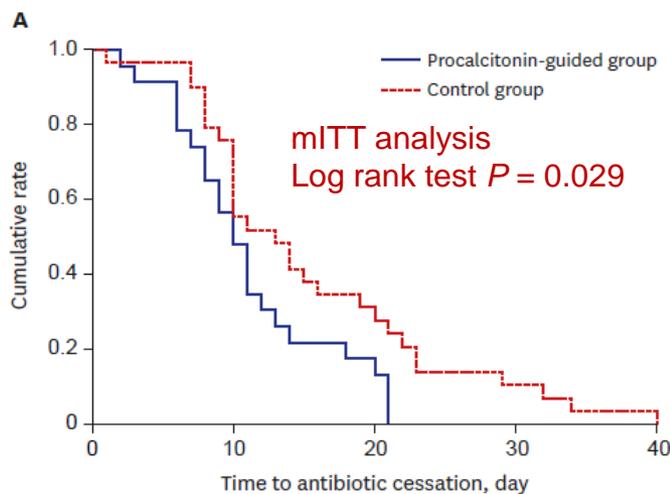


Table 3. Primary and secondary outcome measures according to per-protocol analysis

Variables	Procalcitonin group (n = 11)	Control group (n = 26)	P value
Primary outcome			
Duration of antibiotic therapy, day	8 (6-9)	14 (10-22)	< 0.001
Secondary outcomes			
Clinical cure	10 (91)	23 (85)	0.829
Recurrence of the first episode of infection	0	0	-
28-day mortality	1 (9)	3 (12)	> 0.999
In-hospital mortality	1 (9)	4 (15)	> 0.999
Length of ICU stay, day	4 (4-7)	5 (3-8)	0.523
Length of hospital stay, day	17 (10-29)	21 (12-33)	0.454

Table 5. Total cumulative costs per patient with sepsis

Variables	Modified intention-to-treat analysis		Per-protocol analysis	
	Procalcitonin group (n = 23)	Control group (n = 29)	Procalcitonin group (n = 11)	Control group (n = 26)
Hospital costs				
General ward	6,968.1	4,758.1	6,572.9	6,117.5
ICU stay	4,510.1	4,121.3	3,818.4	3,500.7
Treatment				
Antibiotics	240.5	270.1	206.2	258.8
Laboratory test				
PCT	242.8	-	207.3	-
Total cost	11,721.0	8,879.4	10,598.6	9,618.2

Conclusion:

PCT-guided antibiotic discontinuation in critically ill patients with sepsis **could reduce the duration of antibiotic use and its costs** with no apparent adverse outcomes.

Clinical Implication of Procalcitonin...

- 1. for Differential Diagnosis**
 - 2. for Guiding Antibiotic Therapy**
 - 3. for Prognosis?**
-

Use of Procalcitonin
for Prognosis?

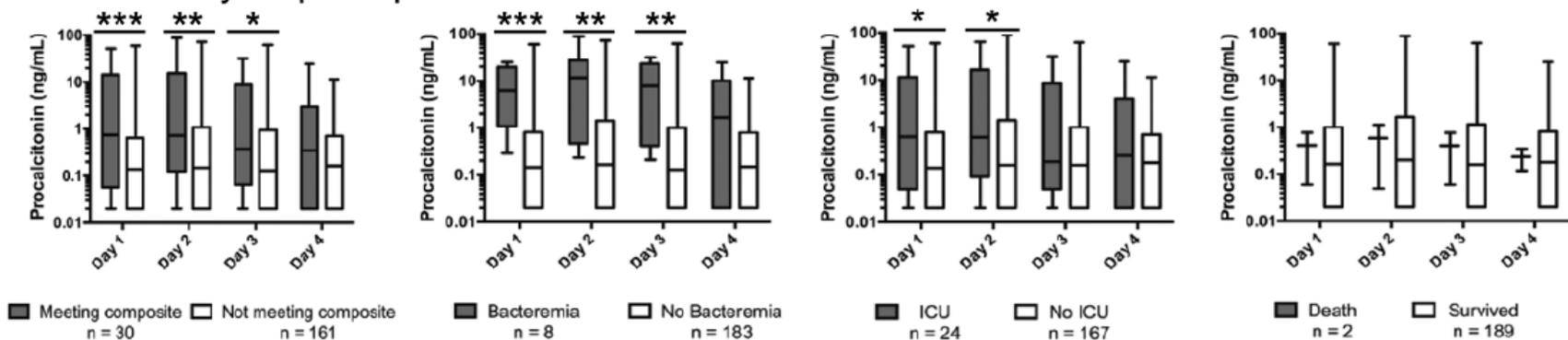
Serial Procalcitonin as a Predictor of Bacteremia and Need for Intensive Care Unit Care in Adults With Pneumonia, Including Those With Highest Severity: A Prospective Cohort Study

Suzanne M. McCluskey,¹ Philipp Schuetz,² Michael S. Abers,³ Benjamin Bearnot,³ Maria E. Morales,⁴ Debora Hoffman,⁴ Shreya Patel,³ Lauren Rosario,¹ Victor Chiappa,³ Blair A. Parry,⁴ Ryan T. Callahan,⁴ Sheila A. Bond,⁶ Kent Lewandrowski,⁵ William Binder,⁷ Michael R. Filbin,⁴ Jatin M. Vyas,¹ and Michael K. Mansour¹

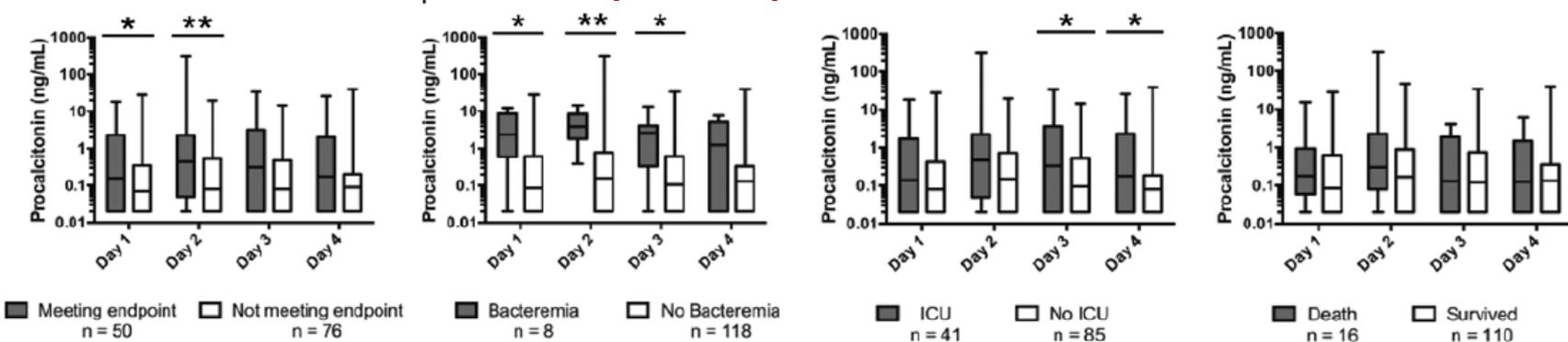
Primary outcome

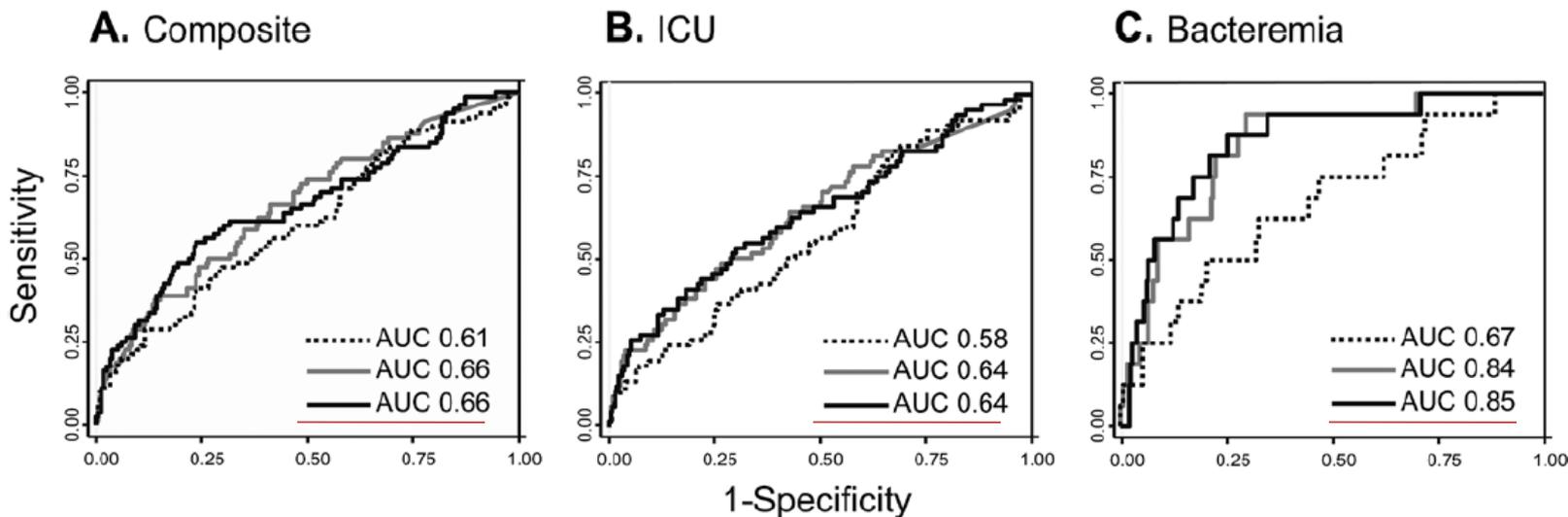
- **A composite outcome**, defined as
- (1) all cause mortality
 - (2) need for ICU-level care
 - (3) bacteremia

A. Community-acquired pneumonia (n = 191)



B. Healthcare-associated pneumonia (n = 126)

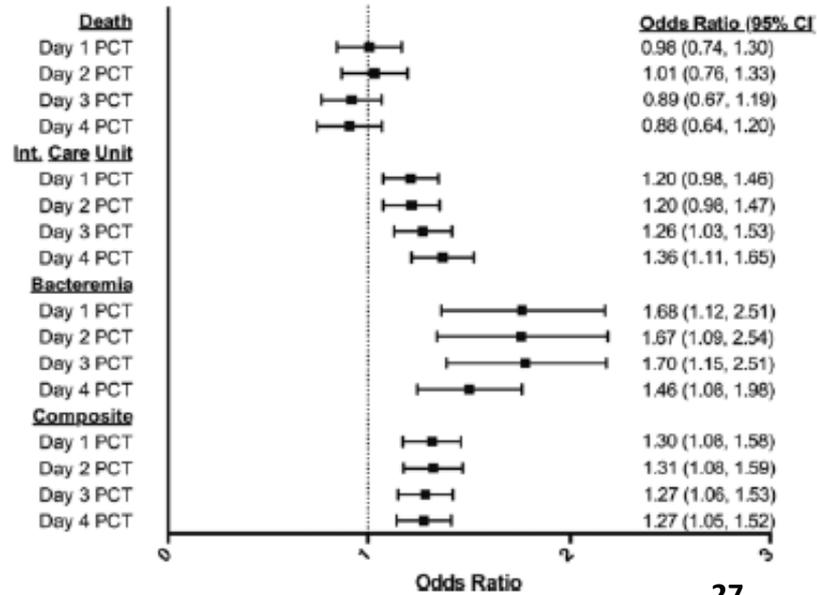




PSI PCT days 1 to 4 — PSI and PCT days 1 to 4 —

B. PSI >130

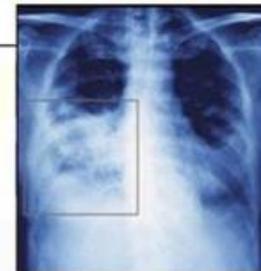
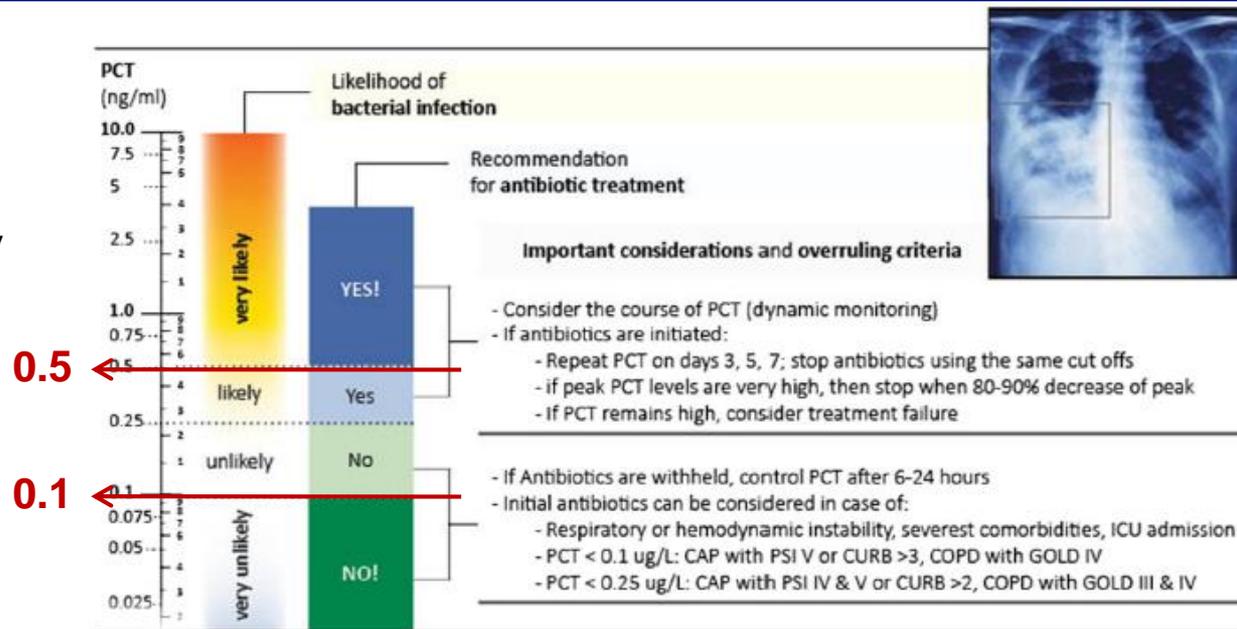
Conclusion:
 Serial PCT measurement in patients with pneumonia shows promise for predicting adverse clinical outcomes, including in those at highest mortality risk.



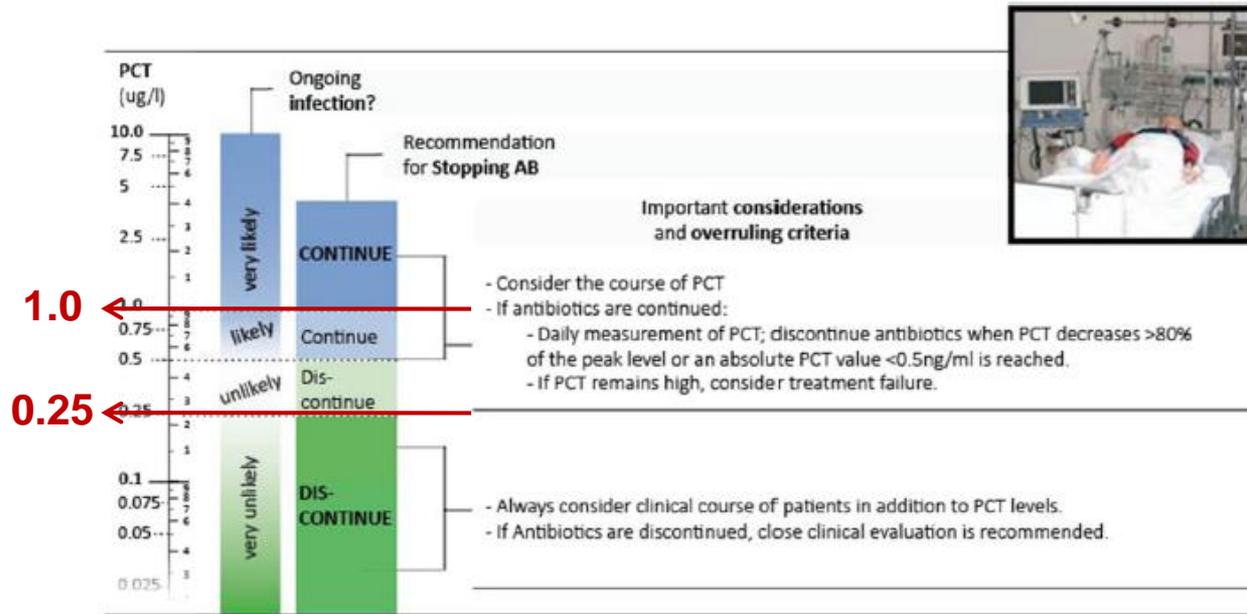
What do the guidelines say?

Procalcitonin algorithm

(a) Patients with respiratory tract infections in the ED



(b) Patients with sepsis with the ICU





Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

- We **suggest** that measurement of **procalcitonin** levels can be used to support **shortening the duration of antimicrobial therapy** in sepsis patients (weak recommendation, low quality of evidence).
- We **suggest** that **procalcitonin** levels can be used to support the **discontinuation of empiric antibiotics** in patients who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection (weak recommendation, low quality of evidence).

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

Tamar F. Barlam,^{1,a} Sara E. Cosgrove,^{2,a} Lilian M. Abbo,³ Conan MacDougall,⁴ Audrey N. Schuetz,⁵ Edward J. Septimus,⁶ Arjun Srinivasan,⁷ Timothy H. Dellit,⁸ Yngve T. Falck-Ytter,⁹ Neil O. Fishman,¹⁰ Cindy W. Hamilton,¹¹ Timothy C. Jenkins,¹² Pamela A. Lipsett,¹³ Preeti N. Malani,¹⁴ Larissa S. May,¹⁵ Gregory J. Moran,¹⁶ Melinda M. Neuhauser,¹⁷ Jason G. Newland,¹⁸ Christopher A. Ohl,¹⁹ Matthew H. Samore,²⁰ Susan K. Seo,²¹ and Kavita K. Trivedi²²

In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an antibiotic stewardship program (ASP) intervention to decrease antibiotic use (weak recommendation, moderate quality evidence).

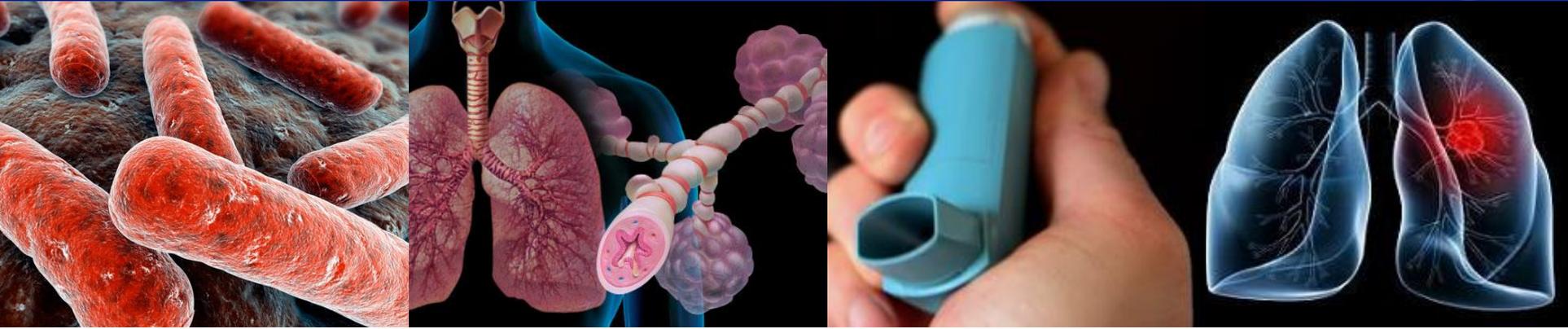
Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

Andre C. Kalil,^{1,a} Mark L. Metersky,^{2,a} Michael Klompas,^{3,4} John Muscedere,⁵ Daniel A. Sweeney,⁶ Lucy B. Palmer,⁷ Lena M. Napolitano,⁸ Naomi P. O'Grady,⁹ John G. Bartlett,¹⁰ Jordi Carratalà,¹¹ Ali A. El Solh,¹² Santiago Ewig,¹³ Paul D. Fey,¹⁴ Thomas M. File Jr,¹⁵ Marcos I. Restrepo,¹⁶ Jason A. Roberts,^{17,18} Grant W. Waterer,¹⁹ Peggy Cruse,²⁰ Shandra L. Knight,²⁰ and Jan L. Brozek²¹

For patients with **suspected HAP/VAP**, we recommend using **clinical criteria alone**, rather than using serum PCT plus clinical criteria, **to decide whether or not to initiate antibiotic therapy** (strong recommendation, moderate-quality evidence).

Conclusions

- PCT-guided treatment **improves the management of patients with LRTIs.**
- **Antibiotic stewardship** by monitoring PCT levels
 - Resulted in **shorter antibiotic treatment duration** by early cessation of antimicrobial therapy
 - Appear to be **safe** without increasing the risk for mortality, recurrent infections, or treatment failure
- The utility of PCT for guiding antibiotic therapy in patients with VAP is less certain than for CAP.



**Thank you
for
your attention!**