L'esperienza di Antimicrobial Stewardship in ICU : l'esigenza al letto del paziente

G. Foti

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Regione Lombardia

ASST Monza

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Conflitto interessi

- Thermo Fisher
- Pfizer
- Drager
- Carefusion
- Dimar

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Personal bias

- **Troppi** Antibiotici
- Per **troppo** tempo
- Con un spettro **troppo** ampio

- Sepsi diagnosi troppo frequente
  - *Embolia polmonare in epoca pre Angio TC*
- Rule out sepsi difficile
- Medicina Difensiva
- Effetti collaterali ABT poco percepiti

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JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

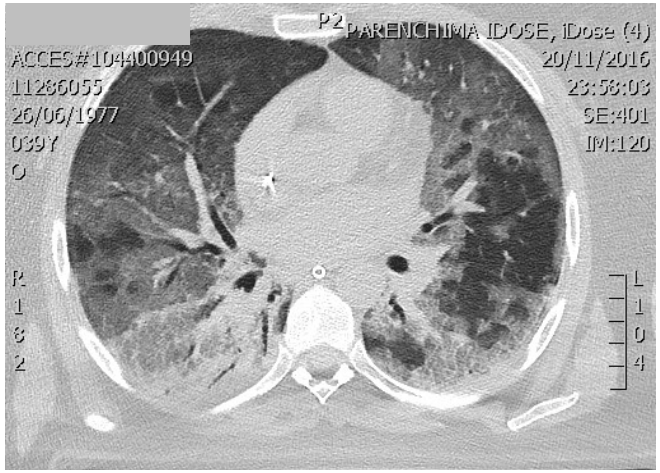
Giacomo Bellani, MD, PhD; John G. Laffey, MD, MA; Tài Pham, MD; Eddy Fan, MD, PhD; Laurent Brochard, MD, HDR; Andres Esteban, MD, PhD; Luciano Gattinoni, MD, FRCP; Frank van Haren, MD, PhD; Anders Larsson, MD, PhD; Daniel F. McAuley, MD, PhD; Marco Ranieri, MD; Gordon Rubenfeld, MD, MSc; B. Taylor Thompson, MD, PhD; Hermann Wrigge, MD, PhD; Arthur S. Slutsky, MD, MASc; Antonio Pesenti, MD; for the LUNG SAFE Investigators and the ESICM Trials Group

Risk factor for ARDS, No. (%)[a]	
Pneumonia	1794 (59.4)
Extrapulmonary sepsis	484 (16.0)
Aspiration	430 (14.2)
Noncardiogenic shock	226 (7.5)
Trauma	127 (4.2)
Blood transfusion	118 (3.9)
Pulmonary contusion	97 (3.2)
Inhalation	72 (2.3)
Drug overdose	56 (1.9)
Pulmonary vasculitis	41 (1.4)
Burn	9 (0.3)
Drowning	2 (0.1)
Other risk factor	82 (2.7)

Con ABT terapia spesso ci si becca

…prova…prova a pensare un po' diverso… ♫♯

B.M.S



Febbre
Tosse
Espettorato

S. Autoimmune Antifosfolipidi (ARDS Cortisono Sensibile)

21-nov-2016		21-nov 07:00	10:00	16:00	22-nov 06:00	16:00	
WBC	10 3/uL	19.07			18.42	16.28	
RBC	10 6/uL	3.6			3.27	2.96	
Hb	g/dL	9.7			8.9	7.9	
PLT	10 3/uL	445			418	368	
Ht	%	29			27	24.5	
Proteina C Reattiva	mg/dL	16.61			12.47		
Procalcitonina (45 Euro)	ng/mL				0.24		

ABT:
-di tutto e di +

Da dove salta fuori la medicina difensiva

- I° Giornata
  - Intervento NCH elettivo (venerdì)
  - Profilassi ABT
  - Anemia emolitica : 10Hgb, Hematocrit 15%
- III° giornata
  - Plasmaferesi
    - Nel we non si fa
- V°
  - MOF ingravescente
- IX°
  - Candidemia
- X°
  - Decesso

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Denuncia: focus del CTU

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Risk Factors for Adult Nosocomial Meningitis after Craniotomy Role of Antibiotic Prophylaxis

OBJECTIVES: To evaluate incidence and risk factors of postoperative meningitis, with special emphasis on antibiotic prophylaxis, in a series of 6243 consecutive craniotomies.

METHODS: Meningitis was individualized from a prospective surveillance database of surgical site infections after craniotomy. Ventriculitis related to external ventricular drainage or cerebrospinal fluid shunt were excluded. From May 1997 until March 1999, no antibiotic prophylaxis was prescribed for scheduled, clean, lasting less than 4 hours craniotomies, whereas emergency, clean-contaminated or long lasting craniotomies received cloxacillin or amoxicillin-clavulanate. From April 1999 till December 2003, prophylaxis was given to every craniotomy. Independent risk factors for meningitis were studied by a multivariate analysis. Efficacy of antibiotic prophylaxis in preventing meningitis was studied as well as consequences on bacterial flora.

RESULTS: The overall meningitis rate was 1.52%. Independent risk factors were cerebrospinal fluid leakage, concomitant incision infection, male gender, and surgical duration. Antibiotic prophylaxis reduced incision infections from 8.8% down to 4.6% ($P < 0.0001$) but did not prevent meningitis: 1.63% in patients without antibiotic prophylaxis, and 1.50% in those who received prophylaxis. Bacteria responsible for meningitis were mainly non-cutaneous in patients receiving antibiotics and cutaneous in patients without prophylaxis. In the former, micro organisms tended to be less susceptible to the prophylactic antibiotics administered. Mortality rate was higher in meningitis due to non cutaneous bacteria as compared to those due to cutaneous microorganisms.

CONCLUSION: Per-operative antibiotic prophylaxis, though clearly effective for the prevention of incision infections, does not prevent meningitis and tends to select prophylaxis resistant microorganisms.

KEY WORDS: Antibiotic prophylaxis, craniotomy, CSF leakage, nosocomial meningitis, risk factors for infection.

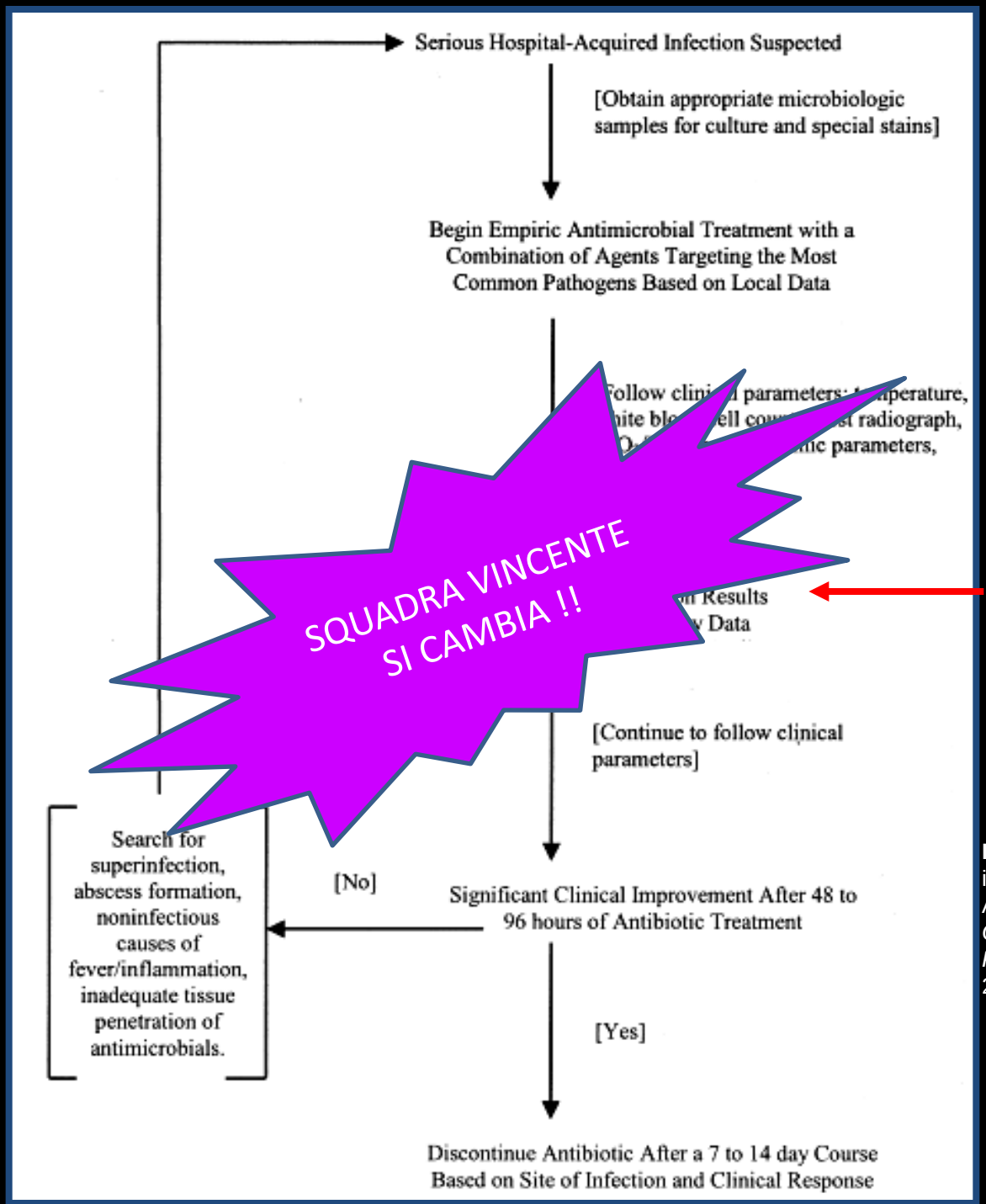
DE-ESCALATION THERAPY

Stage 1

- Administering the broadest-spectrum antibiotic therapy to improve outcomes (decrease mortality, prevent organ dysfunction, and decrease length of stay)

Stage 2

- Focusing on de-escalating as a means to minimize resistance and improve cost-effectiveness



SQUADRA VINCENTE
SI CAMBIA !!

When microbiologic data are known, narrow antibiotic coverage

Kollef M. Why appropriate antimicrobial selection is important: Focus on outcomes. *In:* Owens RC Jr, Ambrose PG, Nightingale CH., eds. *Antimicrobial Optimization: Concepts and Strategies in Clinical Practice*. New York:Marcel Dekker Publishers, 2005:41-64.

International Journal of Critical Illness and Injury Science
Medknow Publications

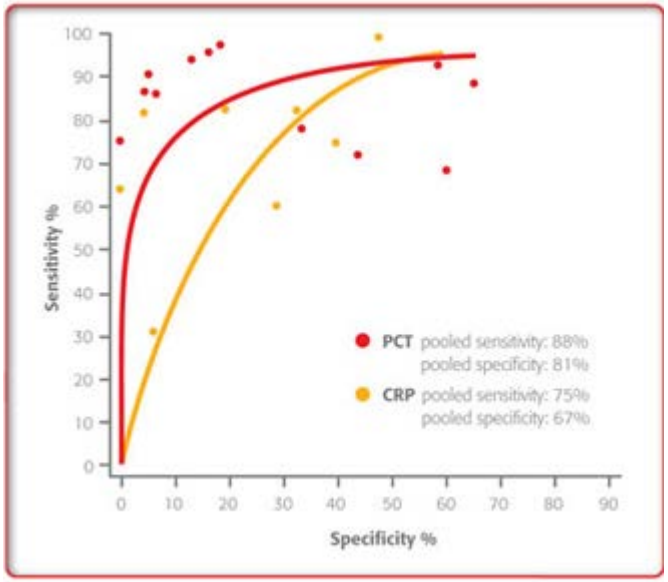
Procalcitonin versus C-reactive protein: Usefulness as biomarker of sepsis in ICU patient

Waheeda Nargis, Md Ibrahim, and Borhan Uddin Ahamed

Table 3

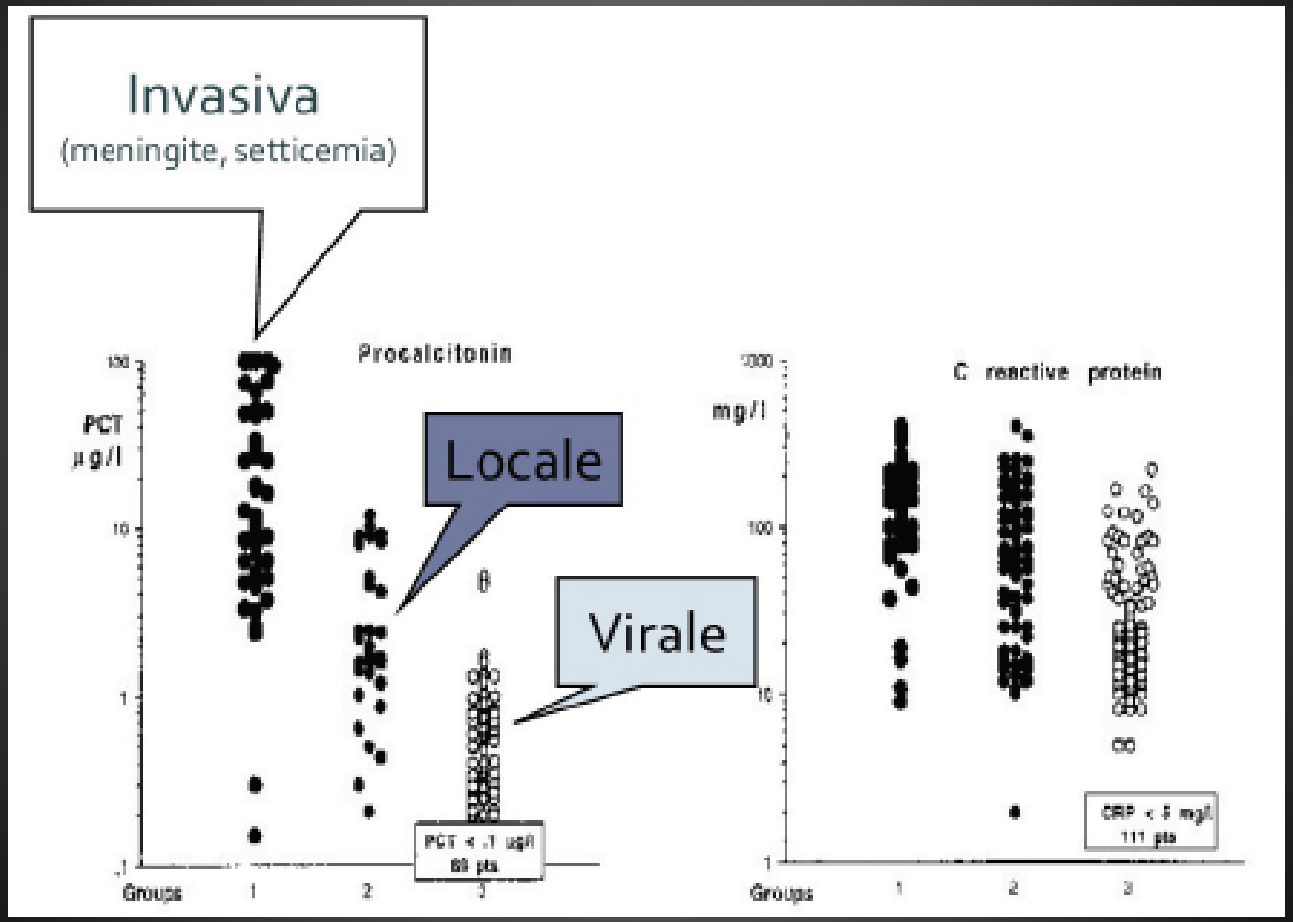
Validity tests	High to any possibilities of sepsis (%)	
	PCT	CRP
Sensitivity	76.36 (62.98-86.7)	85.45 (73.3-93.5)
Specificity	72.2 (46.52-90.31)	33.3 (13.34-59)
(+) ve LR	2.75 (1.29-5.87)	1.28 (0.91-1.81)
(−) ve LR	0.33 (0.19-0.57)	0.44 (0.17-1.09)
PPV	89.36 (76.9-96.45)	79.66 (67.1-89)
NPV	50 (29.93-70.07)	42.86 (17.6-71.1)
Accuracy	75.34	72.6

(+) ve LR: Positive likelihood ratio; (-) ve LR: Negative likelihood ratio; PPV: Positive predictive value; NPV: Negative predictive value, PCT: Procalcitonin, CRP: C-reactive protein



Comparison of the validity tests of PCT, CRP in the diagnosis of high to any possibilities of sepsis (overall)

PCT e PCR a confronto



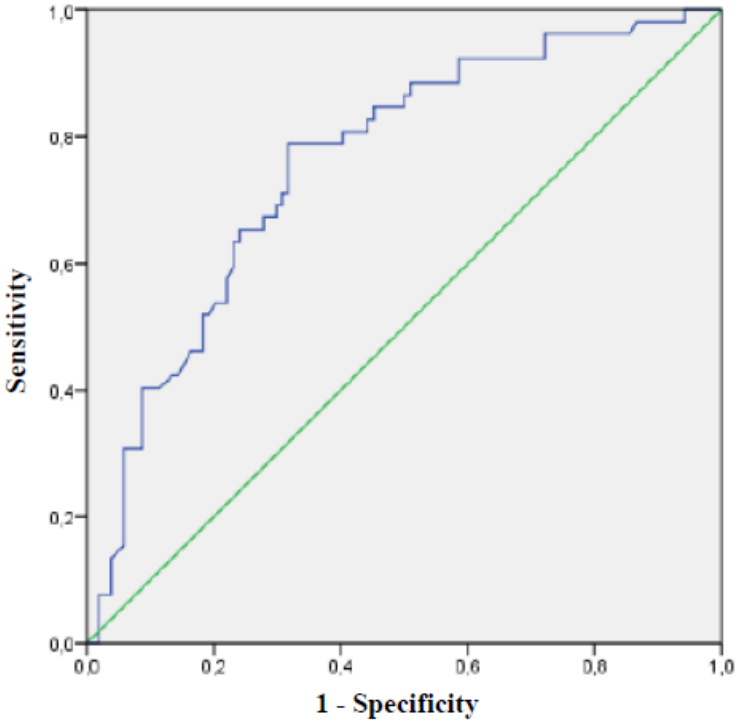
PCT

PCR

Receiver-operating-characteristic (ROC) curve of procalcitonin for the identification of *Candida* spp. by blood cultures.

Figure 2

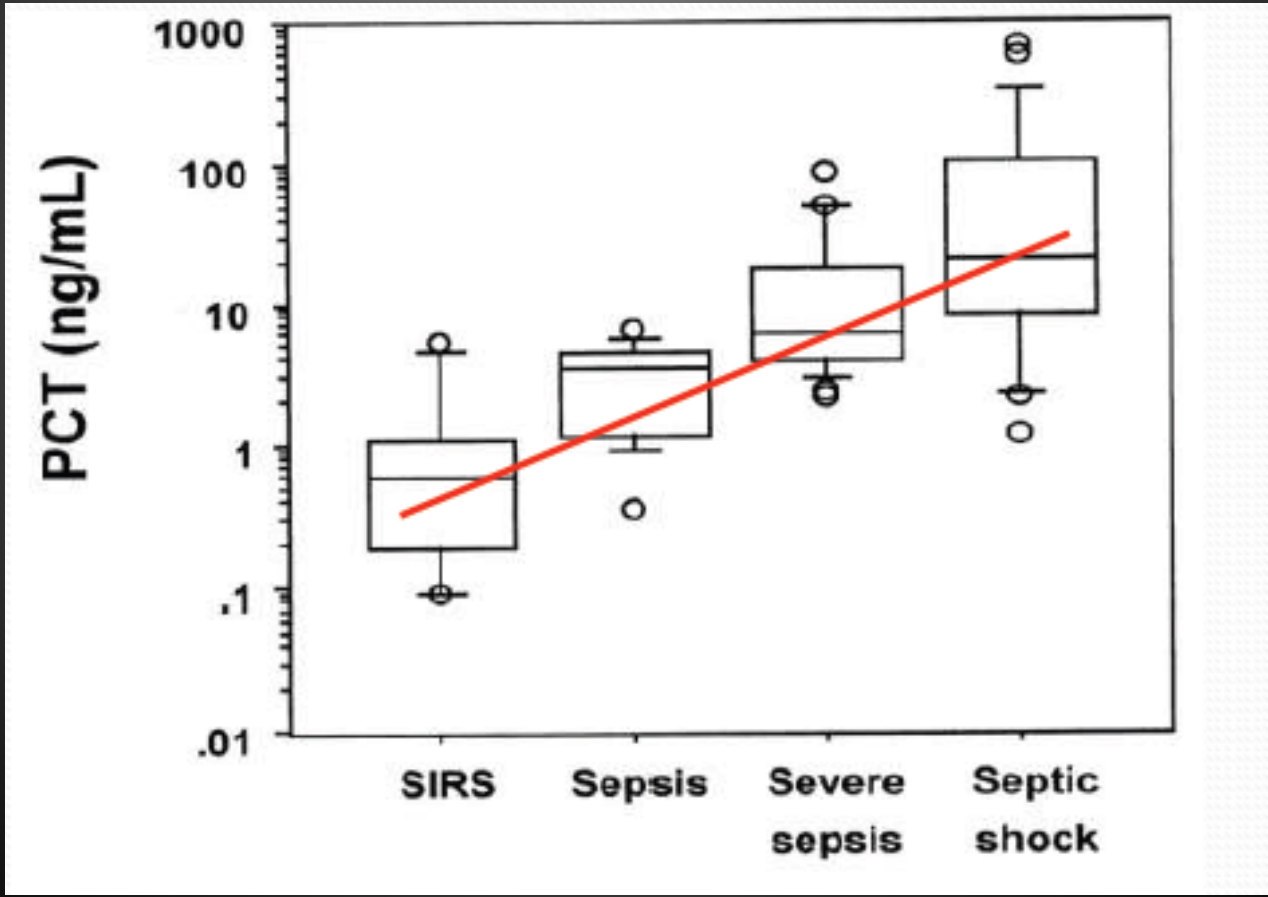
At ROC curve analysis, values of PCT more than 2.5 ng/ml had a negative predictive value (NPV) of 98,3% with an AUC of 0.76 (0.68-0.84 95% CI) for the identification of *Candida* spp. from blood cultures. **At multivariate analysis a PCT value < 2.5 ng/mL showed an Odds Ratio of 5.43 (95% CI 1.52-19.43; p= 0.009) for candidemia.**



Thanks to Dr. A, Mazzone

Sistema Socio Sanitario
Regione Lombardia
ASST Ovest Milanese

PROCALCITONINA e gravità infezione



Treatment Duration

CHEST®
Official publication of the American College of Chest Physicians

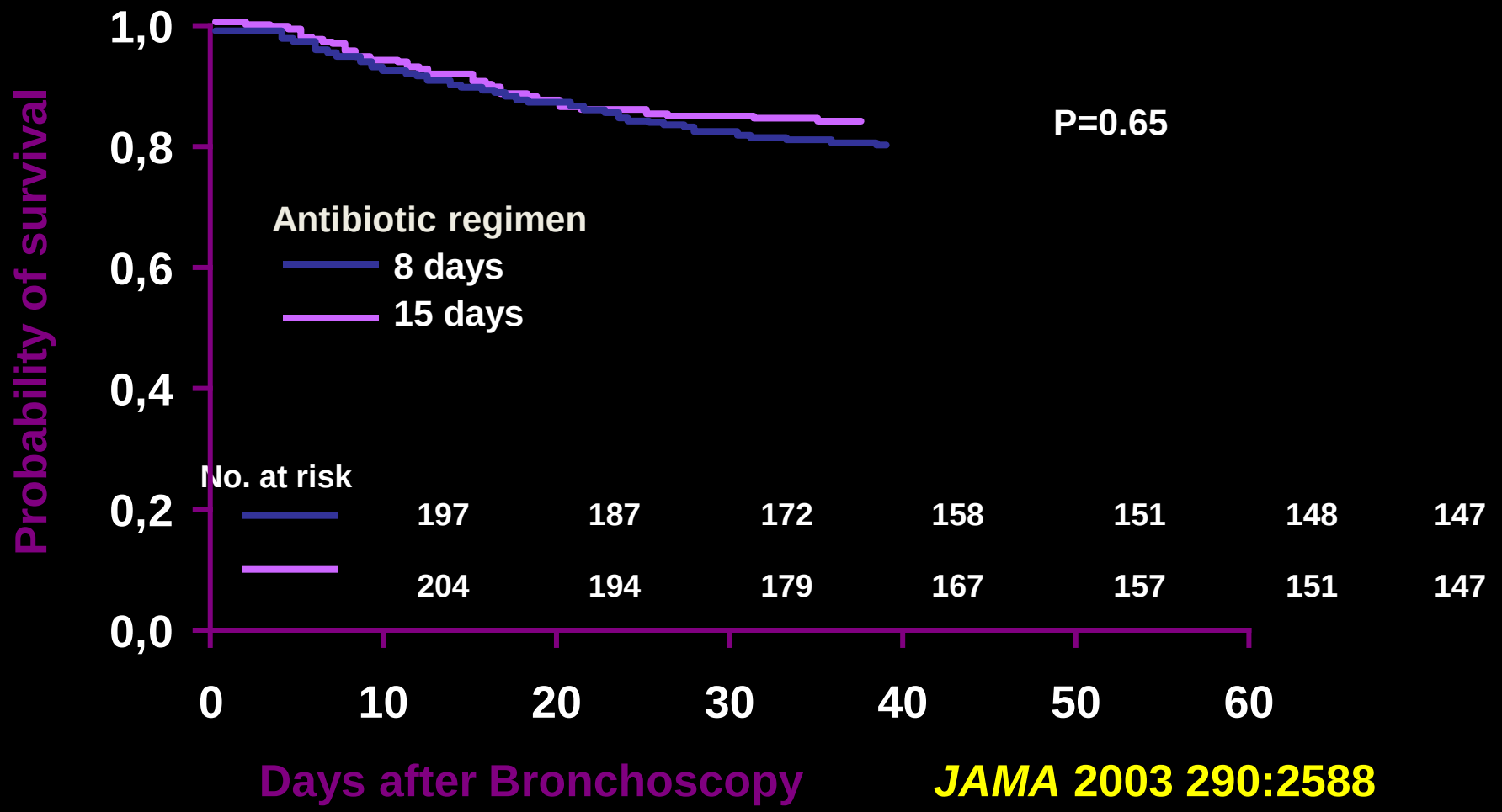
ONLINE FIRST

Short- versus long-duration antibiotic regimens for ventilator-associated pneumonia: a systematic review and meta-analysis

George Dimopoulos MD, PhD, [1], Garyphallia Poulakou, MD, PhD [2], Ioannis A. Pneumatikos, MD, PhD [3], Apostolos Armaganidis, MD, PhD [1], Marin H. Kollef, MD [4], Dimitrios K. Matthaiou MD [1]

8 vs 15 Day Treatment of VAP

No difference in outcome except if P. aeruginosa involved



JAMA 2003 290:2588

Using procalcitonin-guided algorithms to improve antimicrobial therapy in ICU patients with respiratory infections and sepsis

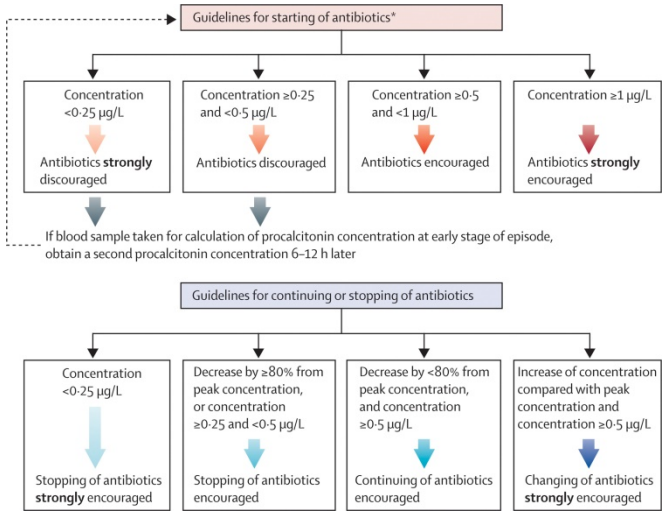
Philipp Schuetz[a], *Issam Raad*[b], *and Devendra N. Amin*[c]

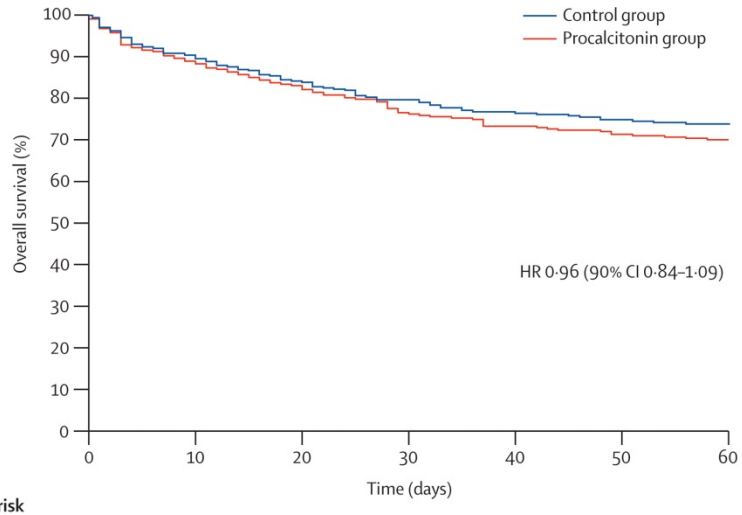
Table 2. Outcomes associated with PCT monitoring in ICU studies (adapted from [42])

Parameter	PCT group	Control group	Adjusted[a] OR or absolute difference (95% CI)[a]	*P*
Initiation of antibiotics, *n* (%)	286 (100%)	311 (100%)	–	–
Duration[b] of antibiotics (days), median (IQR)	8 (5–15)	12 (8–18)	–3.17 (–4.28, –2.06)	<0.0001
Total exposure[c] of antibiotics (days), median (IQR)	8 (5–15)	12 (8–18)	–3.21 (–4.32, –2.10)	<0.0001
Mortality, *n* (%)	57 (19.9%)	74 (23.8%)	0.84 (0.54, 1.31)	0.443
ICU length-of-stay, median (IQR)	12 (6–23)	12 (6–22)	1.01 (–1.26, 3.28)	0.385
Hospital length-of-stay, median (IQR)	21 (11–38)	24 (14–38)	–1.36 (–4.5, 1.77)	0.393

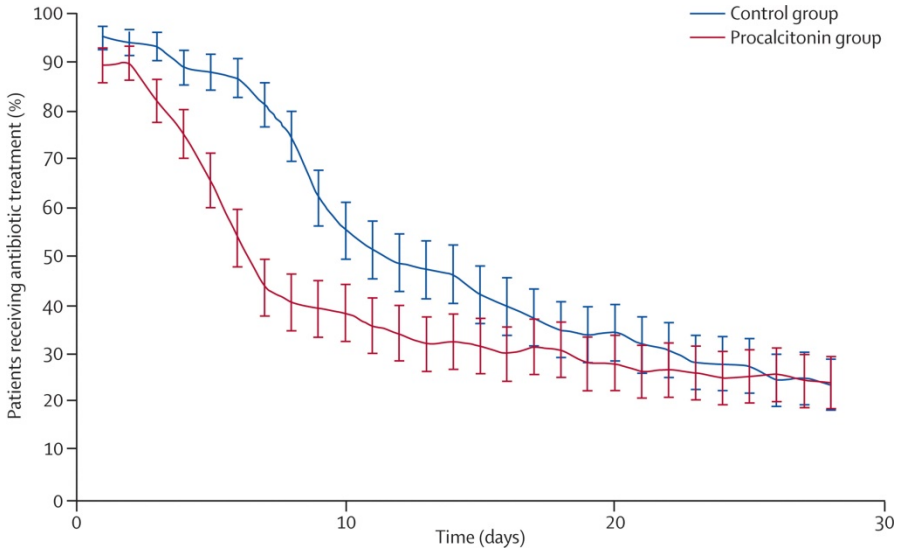
Curr Opin Crit Care 2013, 19:453–460

Prorata Trial





Number at risk							
Procalcitonin group	307	273	255	235	225	219	215
Control group	314	284	264	249	240	234	231



Quenot *et al. Annals of Intensive Care* 2013, **3**:21
http://www.annalsofintensivecare.com/content/3/1/21

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Role of biomarkers in the management of antibiotic therapy: an expert panel review II: clinical use of biomarkers for initiation or discontinuation of antibiotic therapy

PCT-based algorithms cannot be used in:

- Endocarditis
- Bone and joint infection
- Acute mediastinitis
- Intracerebral , intrabdominal abscess

Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial

Evelien de Jong, Jos A van Oers, Albertus Beishuizen, Piet Vos, Wytze J Vermeijden, Lenneke E Haas, Bert G Loef, Tom Dormans, Gertrude C van Melsen, Yvette C Kluiters, Hans Kemperman, Maarten J van den Elsen, Jeroen A Schouten, Jörn O Streefkerk, Hans G Krabbe, Hans Kieft, Georg H Kluge, Veerle C van Dam, Joost van Pelt, Laura Bormans, Martine Bokelman Otten, Auke C Reidinga, Henrik Endeman, Jos W Twisk, Ewoudt M W van de Garde, Anne Marie G A de Smet, Jozef Kesecioglu, Armand R Girbes, Maarten W Nijsten, Dylan W de Lange

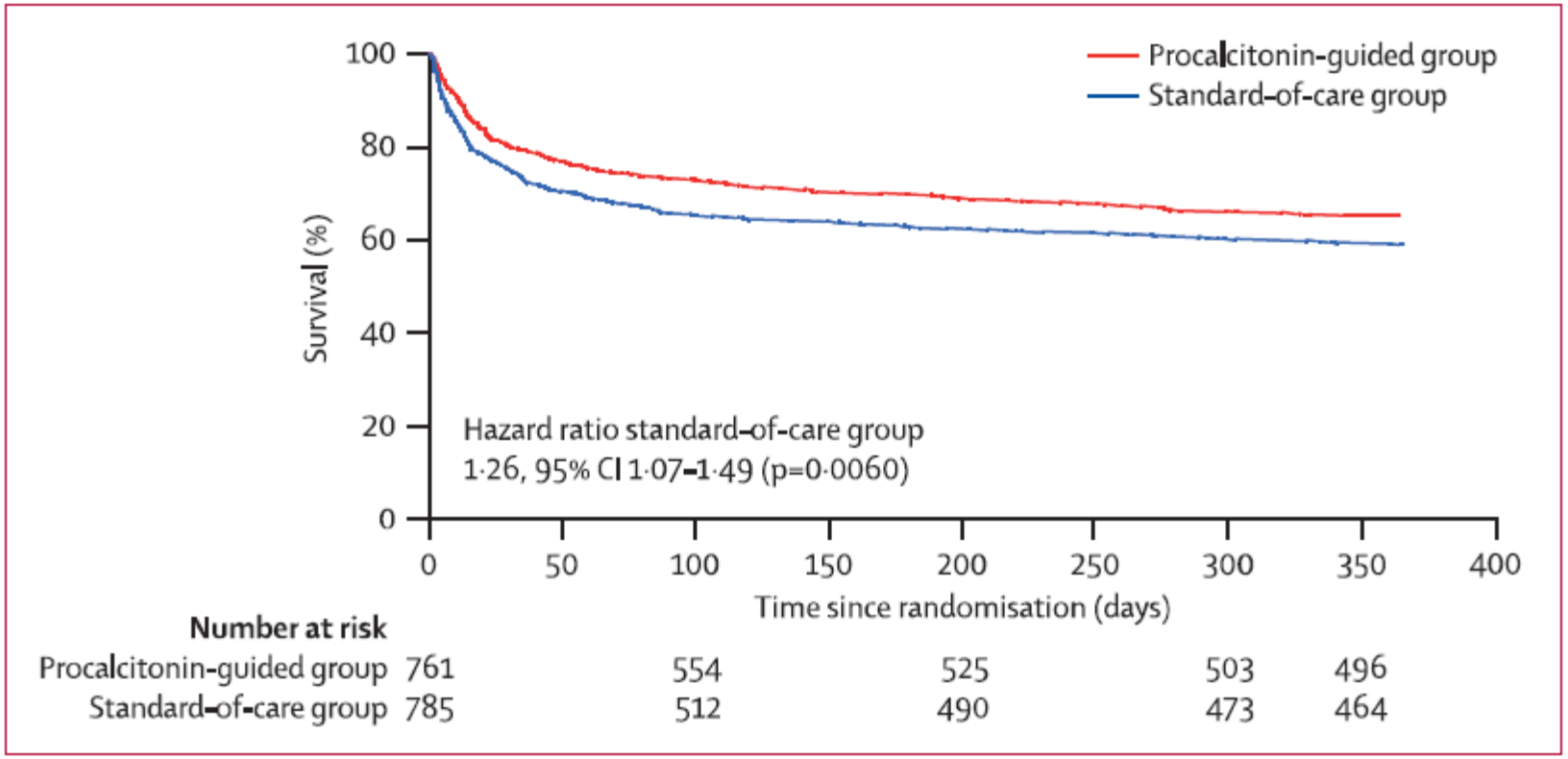


Figure 2: **Kaplan-Meier plot for probability of survival from random assignment to day 365, in the modified intention-to-treat population**

Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial

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	Procalcitonin-guided group (n=761)	Standard-of-care group (n=785)	Between-group absolute difference in means (95% CI)	p value
Costs				
Total cumulative costs of antibiotics	€150 082	€181 263	NA	NA
Median cumulative costs antibiotics per patient	€107 (51 to 229)	€129 (66 to 273)	€33·6 (2·5 to 64·8)	0·0006

Economicamente vantaggiosa se PCT < 4 €

Impact of Regular Collaboration Between Infectious Diseases and Critical Care Practitioners on Antimicrobial Utilization and Patient Outcome*

Ramzy H. Rimawi, MD[1]; Mark A. Mazer, MD[2]; Dawd S. Siraj, MD, MPH, TM[1]; Mike Gooch, MS, RPH[3]; Paul P. Cook, MD[1]

TABLE 3. Types of Recommendations Made by the Infectious Diseases Fellow

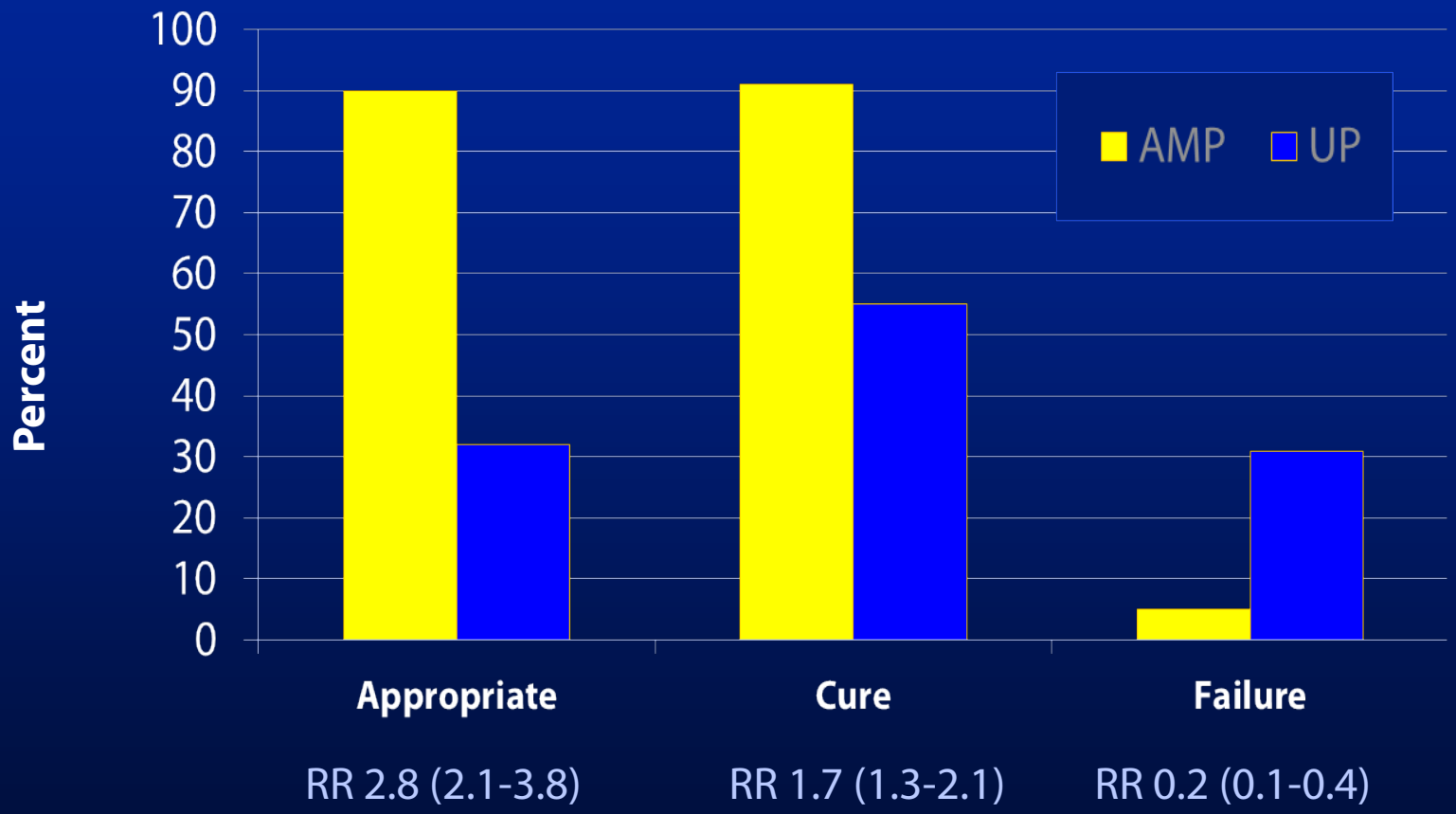
Type of Recommendation	Number of Recommendations ($n = 180$) (%)	Recommendation Followed (%)
Shorten duration	77 (43)	63 (82)
Stop antibiotic	53 (29)	44 (83)
Narrow based on culture and susceptibility results	34 (19)	31 (91)
Convert to oral administration	8 (4)	5 (63)
Broaden based on culture and susceptibility results	4 (2)	4 (100)
Change due to adverse effect	4 (2)	4 (100)

Impact of Regular Collaboration Between Infectious Diseases and Critical Care Practitioners on Antimicrobial Utilization and Patient Outcome*

Ramzy H. Rimawi, MD[1]; Mark A. Mazer, MD[2]; Dawd S. Siraj, MD, MPH, TM[1]; Mike Gooch, MS, RPH[3]; Paul P. Cook, MD[1]

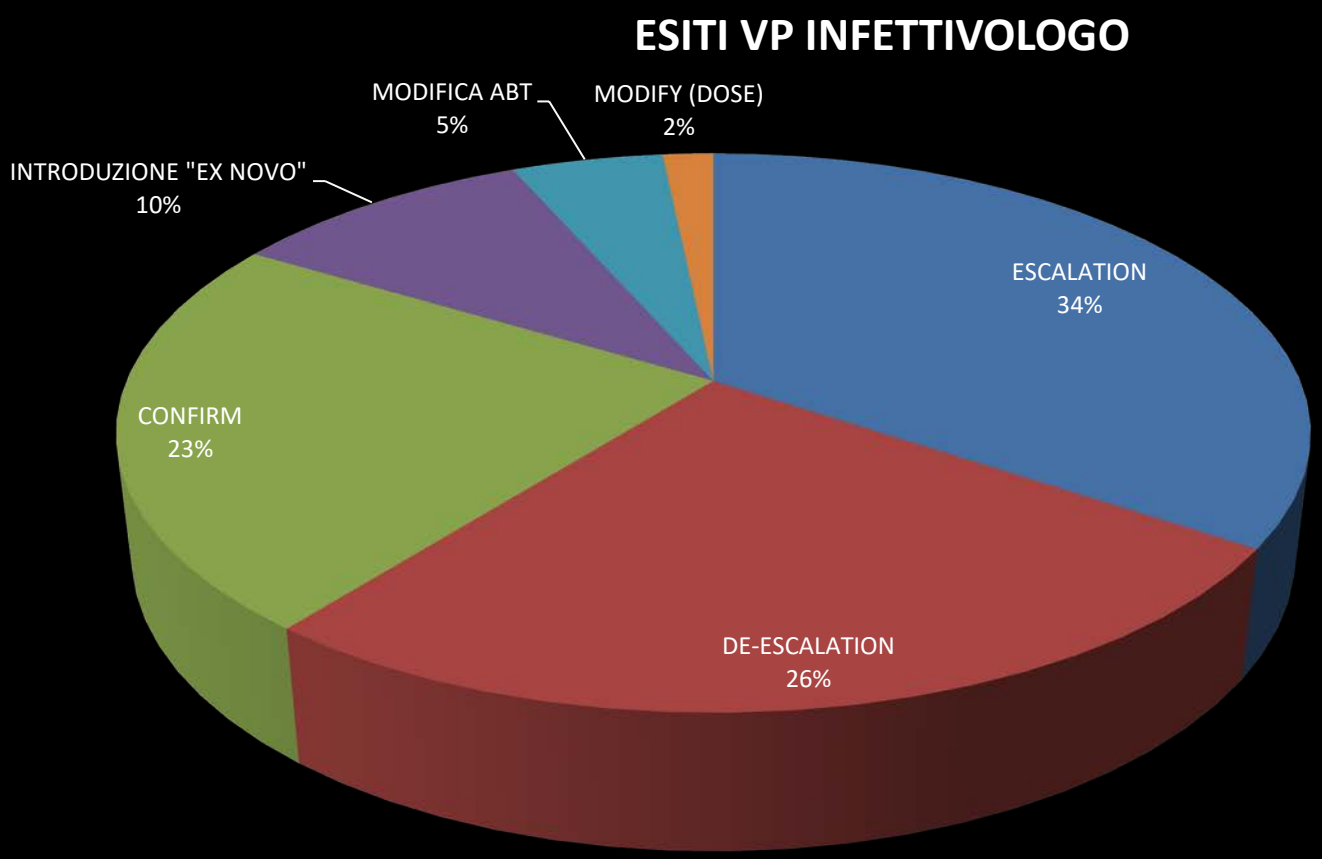
Groups	Variables	Period No. of Patients ($n = 123$) (%)	Period No. of Patients ($n = 123$) (%)	p
All-cause mortality	During medical ICU	34 (28)	29 (24)	0.4970
	Throughout hospitalization	45 (37)	29 (24)	0.0367
Appropriateness of antibiotic management	Appropriate	78 (63)	108 (88)	< 0.0001
	Inappropriate	45 (37)	15 (12)	

Antibiotic Stewardship Improves Clinical Outcomes



AMP = Antibiotic Management Program
UP = Usual Practice

Fishman N. *Am J Med* 2006;119:S53.


ESITI VP INFETTIVOLOGO
MODIFICA ABT
5%
MODIFY (DOSE)
2%
INTRODUZIONE "EX NOVO"
10%
ESCALATION
34%
CONFIRM
23%
DE-ESCALATION
26%

2014

Di cosa abbiamo bisogno

- Nuovi Antibiotici….bah
- Sistemi di diagnosi/monitoraggio sepsi
  - Sensibili
  - Specifici
  - Veloci

  - Test microbiologici in poche ore
  - PCT e oltre
  - β glucano etc.
- Linee Guida che proteggano le scelte "coraggiose"
  - Legge Gelli
- Pensare un pò diverso
  - La sepsi non spiega sempre tutto
  - I malati in UTI muoiono cmq di infezione con o senza ABT
    - Morire di s. settico senza ABT non è una eresia (desistenza terapeutica)