09,40-12,10	**Resistenze batteriche: nuove molecole e nuove modalità terapeutiche**
	Moderatori: P. Grossi (Varese), C. Mussini (Modena)
09,40-10,10	Il piano nazionale contro l'antibiotico resistenza – M. Tinelli (Lodi)
10,10-10,40	Ruolo in terapia di Ceftazidime-Avibactam nelle infezioni sostenute da Gram negativi resistenti – M. Bassetti (Udine)
10,40-11,10	Ruolo della early switch e early discharge in antibioticoterapia – C. Tascini (Napoli)
11,10-11,40	Terapia empirica dei batteri Multi Drug Resistant – P. Grossi (Varese)
11,40-12,10	Patogeni respiratori difficili: il ruolo di NAC - Gian Maria Rossolini (Firenze)

Dr Carlo Tascini
I Divisione Malattie Infettive
Ospedale Cotugno
Napoli
3480623360
c.tascini@gmail.com

Il sottoscritto Carlo Tascini
ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

che negli ultimi due anni ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- *Astra*
- *Merck*
- *Pfizer*
- *Astellas*
- *Angelini*
- *Gilead*
- *Novartis.*

Terapia empirica

- Universalmente accettata per ridurre il fallimento della terapia antibiotica nelle infezioni gravi e mortali:
- Tempestiva
- Ampio spettro per coprire tutti i potenziali patogeni
- Rischio di selezionare germi MDR
- Rischio di eventi avversi

Antibiotic de-escalation (ADE)

- ADE è un semplice approccio alla terapia antibiotica empirica che tenta di bilanciare la necessità di una terapia iniziale appropriata con la limitazione della esposizione non necessaria agli antibiotici, al fine di ridurre l'emergenza di resistenza e gli eventi avversi

2. Kollef MH. What can be expected from antimicrobial de-escalation in the critically ill? Intensive Care Med **2014**; 40:92–5.

Surviving sepsis campaign

- Iniziare antibiotici nello shock settico nella prima ora
- Terapia ampio spettro
- Rivalutazione giornaliera del paziente per ADE

Accuracy of point-of-care ultrasound to identify the source of infection in septic patients: a prospective study—comment

Carlo Tascini[1] · Emanuela Sozio[2] · Francesco Sbrana[3] · Giacomo Bertolino[4] · Andrea Ripoli[3]

lower risk-adjusted in-hospital mortality, and (3) for each hour of delay in time to blood cultures' collection, the risk of in-hospital deaths increases by 4%, especially in Gram-negative bacteraemia [2].

2. Seymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, Lemeshow S, Osborn T, Terry KM, Levy MM (2017) Time to treatment and mortality during mandated emergency care for sepsis. N Engl J Med 376:2235–2244. doi:10.1056/NEJMoa1703058

Intensive Care Med (2014) 40:284–285
DOI 10.1007/s00134-013-3166-7

EDITORIAL

Matteo Bassetti
José-Artur Paiva
Robert G. Masterton

The case for de-escalation in antimicrobial therapy: time to change our strategy in the management of septic shock?

Table 1 The potential benefits of antimicrobial de-escalation in clinical practice

Benefit
• Unaltered clinical outcomes compared to maintenance of initial therapy
• Improved antimicrobial resistance surveillance
• Decreased antibiotic-related adverse events
• Reduced overall antimicrobial costs

Intensive Care Med (2014) 40:284–285
DOI 10.1007/s00134-013-3166-7

EDITORIAL

Matteo Bassetti
José-Artur Paiva
Robert G. Masterton

The case for de-escalation in antimicrobial therapy: time to change our strategy in the management of septic shock?

concerned about its feasibility and worthiness. In its pivotal systematic review on antimicrobial stewardship, the Infectious Diseases Society of America concluded: (1) there is good evidence to support a recommendation for its use, but (2) this conclusion is based on moderate quality evidence from well-designed clinical studies and (3) prospective randomised controlled trials are missing

ADE: definizione

- Non esiste una definizione univoca
- Riduzione dello spettro (ranking degli antibiotici) e/o
- Passaggio alla terapia orale (non necessariamente si riduce lo spettro)
- Riduzione del numero delle molecole
- (in genere deve avvenire tra il 2° ed il 5° giorno di terapia, periodo della risposta degli esami microbiologici, ma potrebbe cambiare in futuro)
- In alcuni studi viene considerato anche la riduzione dei giorni di terapia, pertanto l'interruzione precoce

definizione

- Leone et al lo hanno definito come l'interruzione degli antibiotici partner quando non necessari

23. Leone M, Bechis C, Baumstarck K, et al. De-escalation versus continuation of empirical antimicrobial treatment in severe sepsis: a multicenter non-blinded randomized noninferiority trial [published erratum appears in Intensive Care Med 2014; 40:1794]. Intensive Care Med **2014**; 40:1399–408.

ADE e Italia

- Si intende passaggio da terapia parenterale a terapia orale o terapia intramuscolo domiciliare

ADE: su cosa si basa

- Riduzione del SOFA
- Riduzione del CPIS
- Riduzione dello score APACHE

16. Joung MK, Lee JA, Moon SY, et al. Impact of de-escalation therapy on clinical outcomes for intensive care unit-acquired pneumonia. Crit Care **2011**; 15:R79.

20. Knaak E, Cavalieri SJ, Elsasser GN, Preheim LC, Gonitzke A, Destache CJ. Does antibiotic de-escalation for nosocomial pneumonia impact intensive care unit length of stay? Infect Dis Clin Pract **2013**; 21:172–6.

22. Garnacho-Montero J, Gutierrez-Pizarraya A, Escoresca-Ortega A, et al. De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock. Intensive Care Med **2014**; 40:32–40.

Intensive Care Med
DOI 10.1007/s00134-013-3077-7

ORIGINAL ARTICLE

J. Garnacho-Montero
A. Gutiérrez-Pizarraya
A. Escoresca-Ortega
Y. Corcia-Palomo
Esperanza Fernández-Delgado
I. Herrera-Melero
C. Ortiz-Leyba
J. A. Márquez-Vácaro

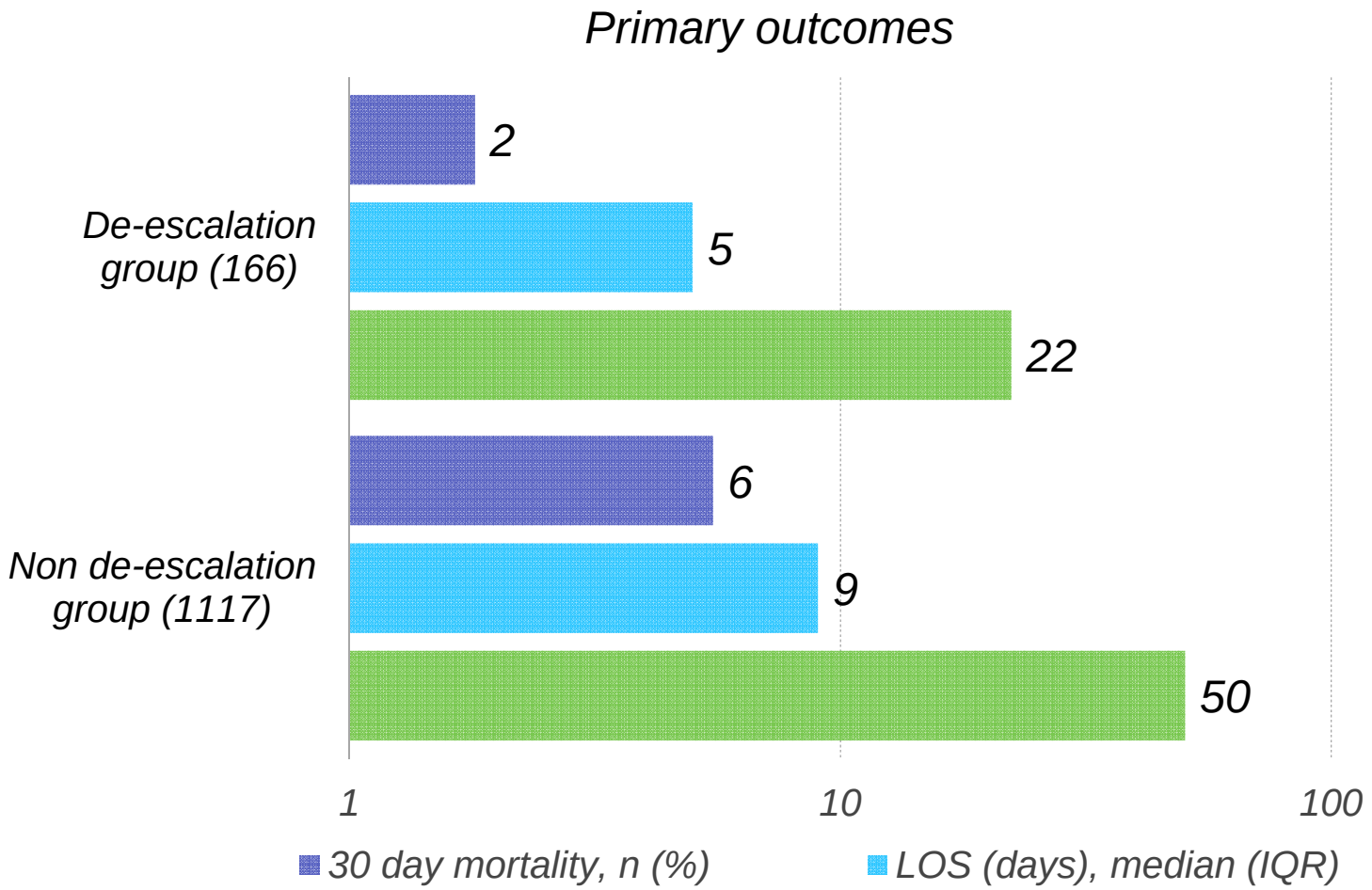
De-escalation of empirical therapy is associated with lower mortality in patients with severe sepsis and septic shock

De-escalation was defined as discontinuation of an antimicrobial agent or change of antibiotic to one with a narrower spectrum once culture results were available. To control for con-

90-day mortality. *Conclusions:* De-escalation therapy for severe sepsis and septic shock is a safe strategy associated with a lower mortality. Efforts to increase the frequency of this strategy are fully justified.

Role of Impact of ANTIBIOTIC DE-ESCALATION on clinical outcomes in community-acquired pneumococcal pneumonia

Viasus G et al. J Antimicrob Chemother Feb 2017



ADE nei programmi di anti-microbial stewardship

Eur J Clin Microbiol Infect Dis
https://doi.org/10.1007/s10096-017-3117-2

ORIGINAL ARTICLE

A 72-h intervention for improvement of the rate of optimal antibiotic therapy in patients with bloodstream infections

R. Murri[1] &F. Taccari[1] &T. Spanu[2] &T. D'Inzeo[2] &I. Mastrorosa[1] &F. Giovannenze[1] &
G. Scoppettuolo[1] &G. Ventura[1] &C. Palazzolo[1] &M. Camici[1] &S. Lardo[1] &B. Fiori[2] &
M. Sanguinetti[2] &R. Cauda[1] &M. Fantoni[1]

Rapid diagnostic tests and 72 h re-evaluation of empirical therapy for BSI significantly correlated with an improved rate of optimal antibiotic therapy and decreased duration of antibiotic therapy and length of stay.

ORIGINAL ARTICLE

Implementing criteria-based early switch/early discharge programmes: a European perspective

D. Nathwani[1], W. Lawson[2], M. Dryden[3], J. Stephens[4], S. Corman[4], C. Solem[4], J. Li[5], C. Charbonneau[6], N. Baillon-Plot[6], S. Haider[7] and C. Eckmann[8]

- Early switch: passagio prima possibile alla terapia orale
- Early switch: si può fare in Italia prevalentemente per i gram positivi

ORIGINAL ARTICLE

Implementing criteria-based early switch/early discharge programmes: a European perspective

D. Nathwani[1], W. Lawson[2], M. Dryden[3], J. Stephens[4], S. Corman[4], C. Solem[4], J. Li[5], C. Charbonneau[6], N. Baillon-Plot[6], S. Haider[7] and C. Eckmann[8]

hospitals showed that the majority of patients with hospital-acquired infections (70%) received IV antibiotic therapy, although the rate ranged from a low of 50% in Scotland and Wales (UK) and Sweden to a high of 90% in Greece and Romania [1]. The duration of IV antibiotic therapy and hospital stays also varied widely among European countries [2,3]. Results from a study evaluating the treatment of patients with methicillin-resistant *Staphylococcus aureus* (MRSA) complicated skin and soft-tissue infections (cSSTIs) showed that duration of IV antibiotic therapy ranged from a low of 10.1 days in the UK to a high of 18.6 days in Poland. Mean hospital length of stay

Implementing criteria-based early switch/early discharge programmes: a European perspective

D. Nathwani[1], W. Lawson[2], M. Dryden[3], J. Stephens[4], S. Corman[4], C. Solem[4], J. Li[5], C. Charbonneau[6], N. Baillon-Plot[6], S. Haider[7] and C. Eckmann[8]

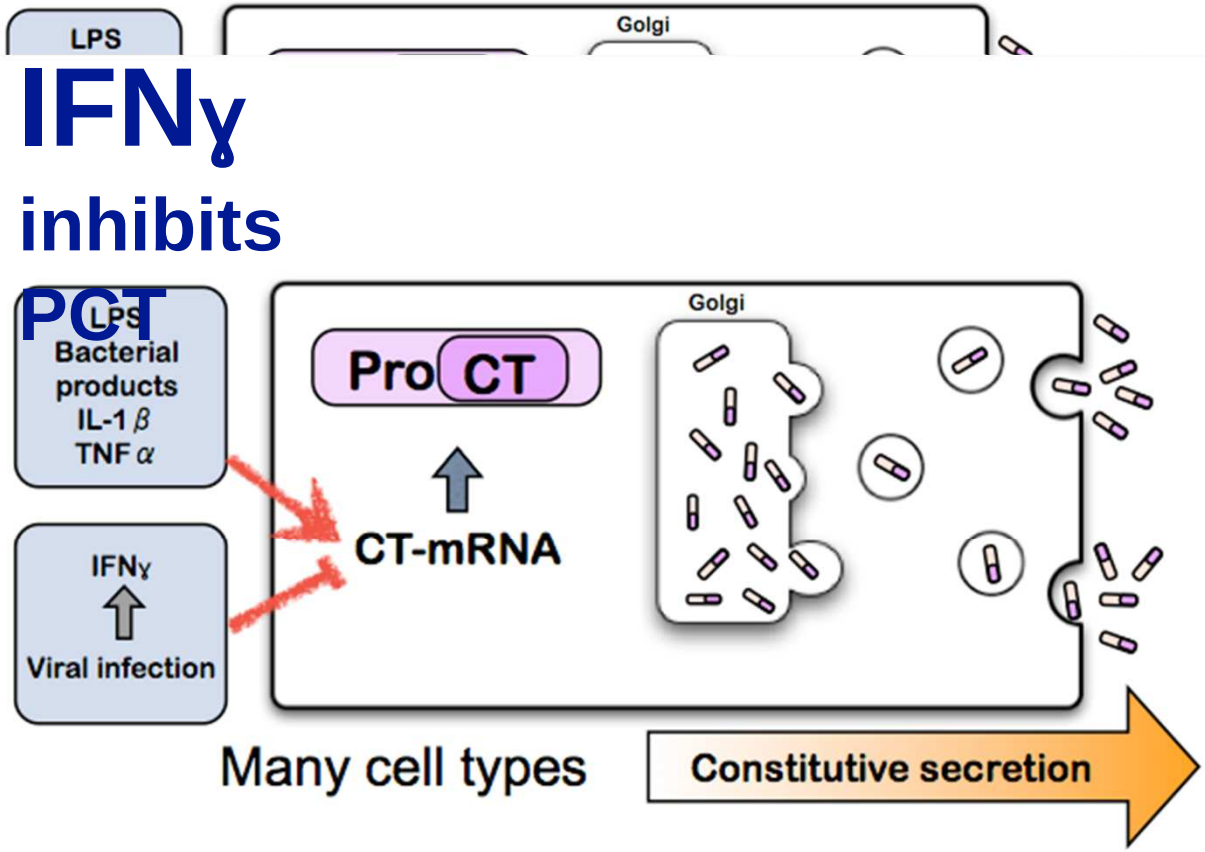
TABLE 1. Criteria used to determine patient eligibility for intravenous to oral antimicrobial switch therapy

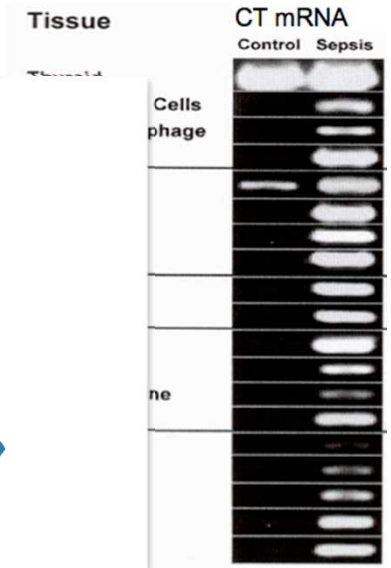
Criteria
Temperature <38°C or >36°C for 24–48 h; normalizing body temperature; afebrile for at least 8–24 h [5,9,12,14,16–18,20,21,23,25]
No unexplained tachycardia, haemodynamic instability [7,9,14,16,21,23,25]
Clinical improvement, no clinical indication for intravenous therapy [5,7,9,12,17–20,23,25]
Oral fluids/food tolerated, no reason to believe oral absorption of antimicrobials may be poor; may be by nasogastric/gastric feeding tube [5,7,9,12,14–20,22,23,25]
Improving white blood cell count [5,9,12,14,16,17,20,23,25]
Improving C-reactive protein [5,9]
Suitable oral antimicrobial therapy [9,12,23,24,33]
No surgery scheduled within next 24–36 h [16,25]

Early switch e PCT

Biochemistry of PCT
during bacterial infection

IFNγ inhibits PCT





ted from Muller 2001

uctural
uences
→ PCT

Inflamm Res 2012 DOI 10.1007/s00011-012-0439-5

Luzzani Aldo

Comparison of procalcitonin and C-reactive protein as markers of sepsis

as marker of severity of infection and organ dysfunction

Table 3. PCT and CRP plasma concentrations in the SOFA score groups

SOFA Score	PCT Median (Interquartile Range)	CRP Median (Interquartile Range)
1–6	3.1 (1.2–4.9)	135.9 (85.8–178.9)
7–12	3.9 (1.8–7.3)[a]	82.9 (59.4–149.2)[a]
13–18	31.0 (4.8–62.1)[a]	113.5 (107.9–222.9)[a]

PCT, procalcitonin; CRP, C-reactive protein; SOFA, sepsis-related organ failure assessment.
[a] $p < .001$.

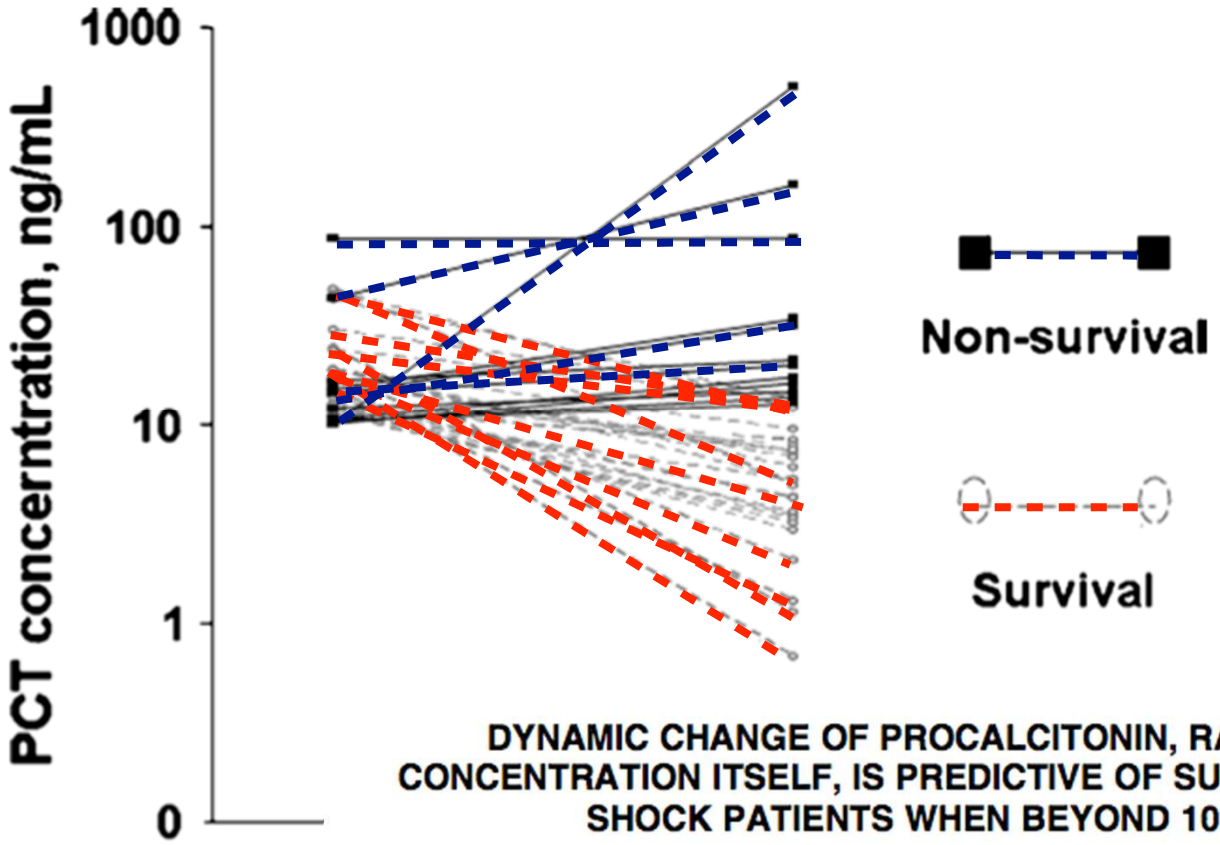
Conclusion: PCT is a better marker of sepsis than CRP. The course of PCT shows a closer correlation than that of CRP with the severity of infection and organ dysfunction.

Crit Care Med 2003;31:1737-1741

.. The dynamic change is more important than the PCT value

Guan J

PCT Kinetics



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*

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

	Procalcitonin group (n=307)	Control group (n=314)	Between-group absolute difference	p value
Primary endpoints				
28-day mortality*	65 (21·2%)	64 (20·4%)	0·8% (–4·6 to 6·2)	NA
60-day mortality*	92 (30·0%)	82 (26·1%)	3·8% (–2·1 to 9·7)	NA
Number of days without antibiotics	14·3 (9·1)	11·6 (8·2)	2·7 (1·4 to 4·1)	<0·0001
Secondary endpoints (days 1–28)				
Relapse	20 (6·5%)	16 (5·1%)	1·4% (–2·3 to 5·1)	0·45
Superinfection	106 (34·5%)	97 (30·9%)	3·6% (–3·8 to 11·0)	0·29
Number of days without mechanical ventilation	16·2 (11·1)	16·9 (10·9)	–0·7 (–2·4 to 1·1)	0·47
SOFA score				
Day 1	7·5 (4·4)	7·2 (4·4)	0·3 (–0·4 to 1·0)	0·39
Day 7	4·1 (4·2)	4·0 (4·2)	0·1 (–0·6 to 0·8)	0·73
Day 14	2·8 (3·5)	2·8 (3·6)	0 (–0·6 to 0·7)	0·87
Day 21	2·1 (3·3)	1·9 (3·1)	0·2 (–0·4 to 0·8)	0·52
Day 28	1·5 (3·0)	0·9 (2·4)	0·6 (0·0 to 1·1)	0·0370
Length of stay in ICU from inclusion (days)	15·9 (16·1)	14·4 (14·1)	1·5 (–0·9 to 3·9)	0·23
Length of stay in hospital from inclusion (days)	26·1 (19·3)	26·4 (18·3)	–0·3 (–3·2 to 2·7)	0·87
Multidrug-resistant bacteria†	55 (17·9%)	52 (16·6%)	1·3% (–4·6 to 7·2)	0·67
Days of antibiotic exposure per 1000 inpatient days	653	812	–159 (–185 to –131)	<0·0001
Duration of first episode of antibiotic treatment (number [%]; days [SD])				
Overall population	307 (100%); 6·1 (6·0)	314 (100%); 9·9 (7·1)	–3·8 (–4·8 to –2·7)	<0·0001
Community-acquired pneumonia	79 (26%); 5·5 (4·0)	101 (32%); 10·5 (6·4)	–5·0 (–6·6 to –3·4)	<0·0001
Ventilator-associated pneumonia	75 (24%); 7·3 (5·3)	66 (21%); 9·4 (5·7)	–2·1 (–4·0 to –0·3)	0·0210
Intra-abdominal infection	14 (5%); 8·1 (7·7)	20 (6%); 10·8 (6·7)	–2·7 (–7·7 to 2·4)	0·29
Urinary tract infection	24 (8%), 7·4 (6·3)	18 (6%), 14·5 (9·3)	–7·1 (–11·9 to –2·2)	0·0053
Infection with positive blood culture	55 (18%), 9·8 (7·7)	53 (17%), 12·8 (8·1)	–3·0 (–6·0 to 0·1)	0·06

Data are number (%), difference (95% CI), or mean (SD), unless otherwise indicated. NA–not applicable. SOFA–sequential organ-failure assessment. ICU–intensive care unit.
*Difference (90% CI).

Table 2: **Main outcome variables**

RESULTS

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

2016

De Jong E

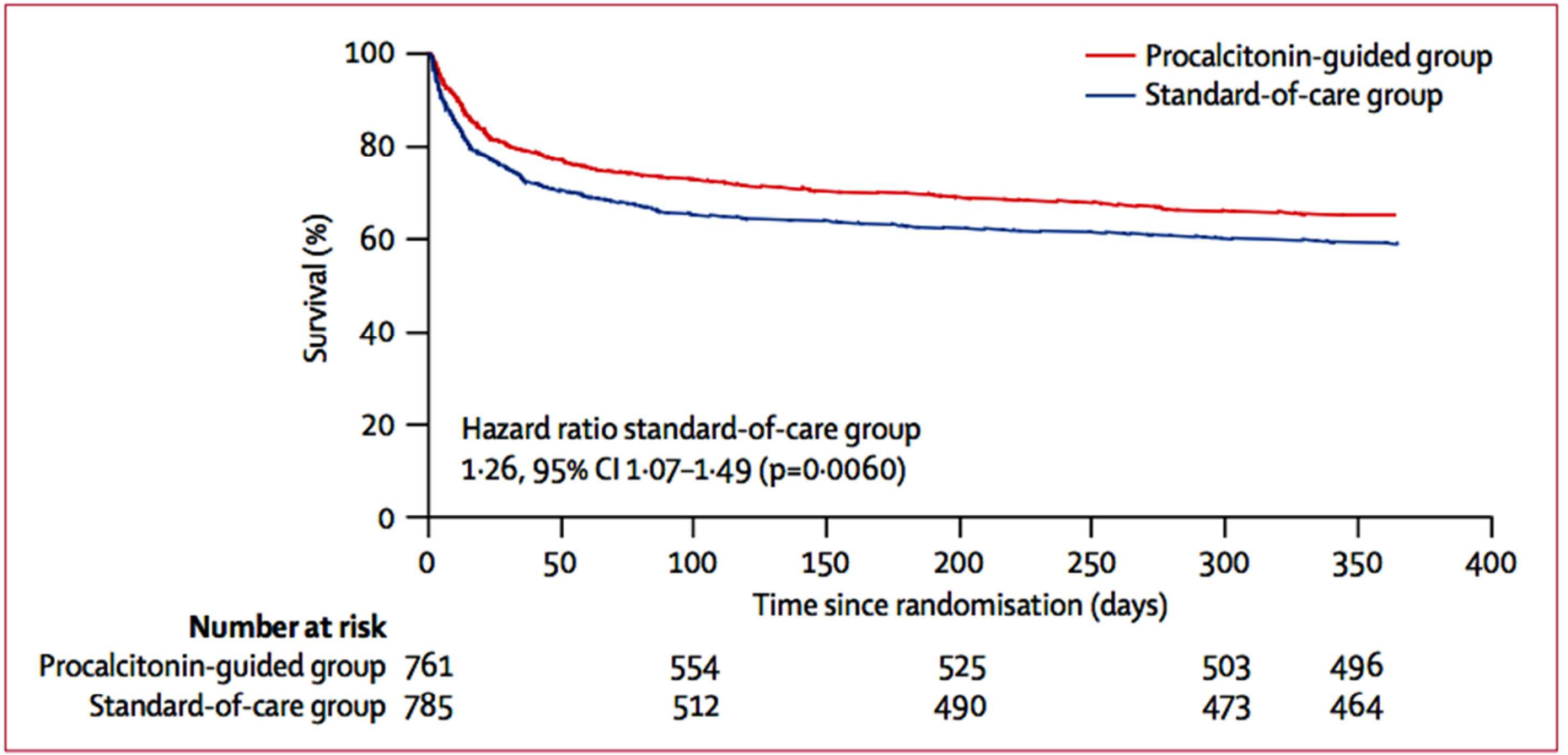
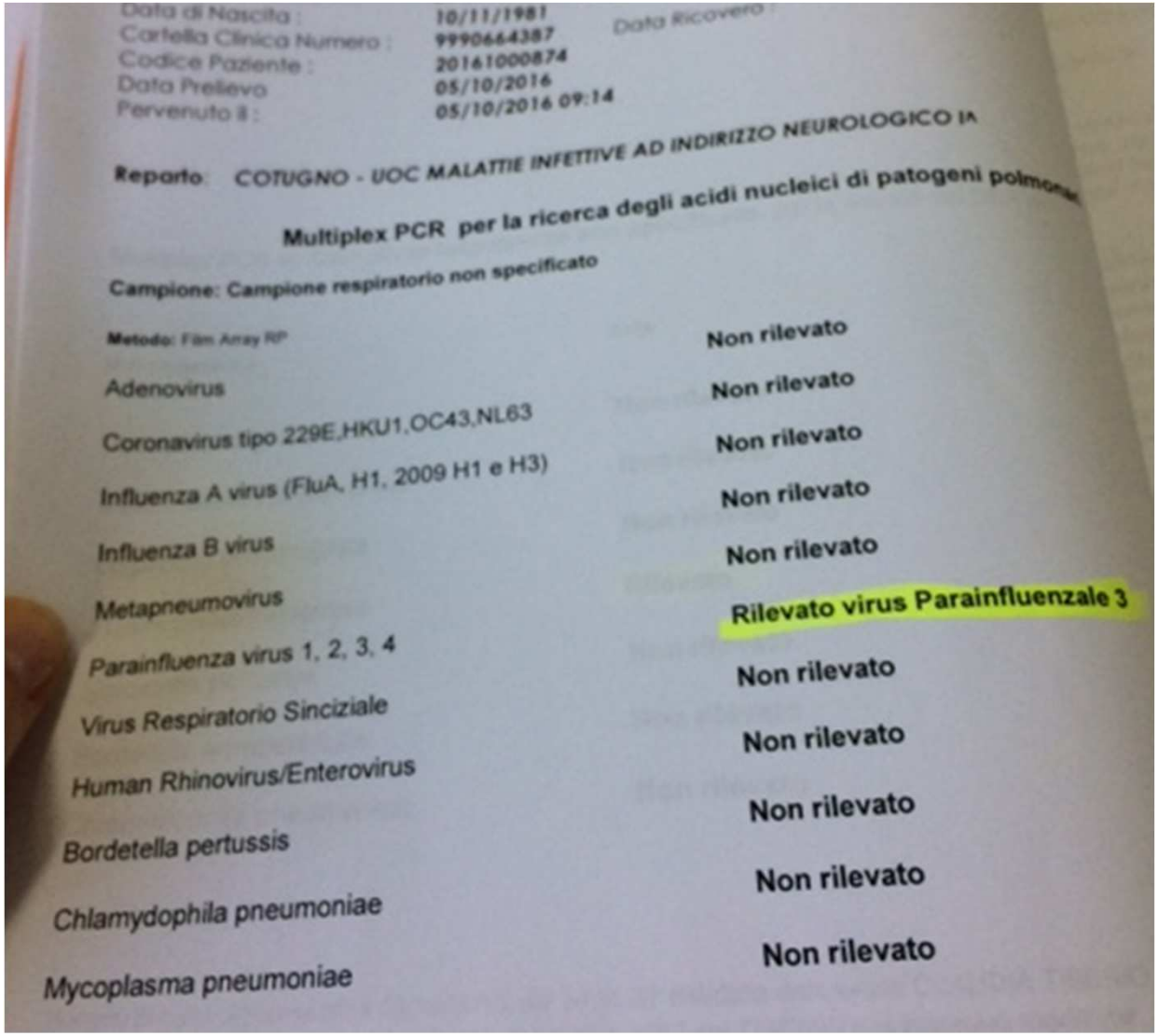


Figure 2: **Kaplan-Meier plot for probability of survival from random assignment to day 365, in the modified intention-to-treat population**

Lancet Infect Dis 2016

Otite e meningite da *H. influenzae*



Data di Nascita : 10/11/1981
Cartella Clinica Numero : 9990664387 Data Ricovero :
Codice Paziente : 20161000874
Data Prelievo 05/10/2016
Pervenuto il : 05/10/2016 09:14

Reparto COTUGNO - UOC MALATTIE INFETTIVE AD INDIRIZZO NEUROLOGICO IA

Multiplex PCR per la ricerca degli acidi nucleici di patogeni polmo

Campione: Campione respiratorio non specificato

Metodo: Film Array RP

Adenovirus	Non rilevato
Coronavirus tipo 229E,HKU1,OC43,NL63	Non rilevato
Influenza A virus (FluA, H1, 2009 H1 e H3)	Non rilevato
Influenza B virus	Non rilevato
Metapneumovirus	Non rilevato
Parainfluenza virus 1, 2, 3, 4	Rilevato virus Parainfluenzale 3
Virus Respiratorio Sinciziale	Non rilevato
Human Rhinovirus/Enterovirus	Non rilevato
Bordetella pertussis	Non rilevato
Chlamydophila pneumoniae	Non rilevato
Mycoplasma pneumoniae	Non rilevato

Paziente con meningite a liquor limpido e polmonite interstiziale

Campione: Campione respiratorio non specificato

Metodo: Real time PCR.

Influenza A virus (FluA-H1, FluA-H1pdm09,Flu A-H3)	**Non rilevato**
Influenza B virus	**Non Rilevato**
Virus Respiratorio Sinciziale	**Non rilevato**
Adenovirus	**Non rilevato**
Metapneumovirus	**Non rilevato**
Enterovirus	**Non rilevato**
Parainfluenza virus 1, 2, 3, 4	**Non rilevato**
Bocavirus	**Non rilevato**
Rhinovirus	**Non rilevato**
Coronavirus tipo 229E,OC43,NL63	**Non rilevato**

Multiplex PCR su **Campione respiratorio non specificato**, per la ricerca del DNA di:

Microorganismo	**Esito**
Mycoplasma pneumoniae	**Rilevato**
Streptococcus pneumoniae	**Non rilevato**

OSPEDALI DEI COLLI
MONALDI - COTUGNO - C.T.O.

"AZIENDA OSPEDALIERA SPECIALISTICA DEI COLLI"
Monaldi - Cotugno - C.T.O.

Azienda Ospedaliera dei Colli

UOC MICROBIOLOGIA E VIROLOGIA

Direttore: f.f. Dott. Luigi Atripaldi

Tel. – Fax 0817062438 Tel - Fax 0817067319

Batteriologia 0817067242-7239- Micobatteriologia - Tubercolare 0817067234-7343-7344

Parassitologia 0817067399 - Virologia: Biologia molecolare 0817067403-7372-7409-7308

Sierologia 0817067279-7523

Accettazione Monaldi 0817062713- Accettazione Cotugno 0817067340-7601

Cognome e Nome :
Data di Nascita :
Cartella Clinica Numero :
Codice Paziente :
Data Prelievo
Pervenuto il :

Reparto: -

Multiplex PCR su **Tampone Faringeo**, per la ricerca del DNA di:

Microorganismo	Esito
Mycoplasma pneumoniae	**Non rilevato**
Streptococcus pneumoniae	**Non rilevato**
Legionella pneumophila	**Non rilevato**
Haemophilus influenzae	**Rilevato**
Bordetella pertussis	**Non rilevato**
Bordetella parapertussis	**Non rilevato**
Chlamydophila pneumoniae	**Non rilevato**

e nel 2016 dai Laboratori aderenti al *Si.Re.Ar.* sulle antibiotico resistenze di *S. pneumoniae*.

TUTTI I MATERIALI Numero di isolati = 223						SANGUE e LIQUOR Numero di isolati = 35						RESPIRATORI Numero di isolati = 150					
Codice	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**	**Codice**	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**	**Codice**	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**
AMP**	184	**15,8**	4,9	79,3	10,5-21,0	AMP**	28	**7,1**	0	92,9	0,0-16,7	AMP**	127	**16,5**	6,3	77,2	10,1-23,0
PEN**	174	**11,5**	31,6	56,9	6,8-16,2	PEN**	26	**3,8**	11,5	84,6	0,0-11,2	PEN**	114	**12,3**	38,6	49,1	6,3-18,3
ERY	218	**62,4**	0,5	37,2	56,0-68,8	ERY**	34	**52,9**	0	47,1	36,2-69,7	ERY	147	**61,9**	0,7	37,4	54,1-69,8
CLI	210	**46,2**	0	53,8	39,4-52,9	CLI**	33	**45,5**	0	54,5	28,5-62,4	CLI**	144	**43,8**	0	56,2	35,6-51,9
CTX**	221	**7,2**	5,4	87,3	3,8-10,7	CTX**	34	**2,9**	2,9	94,1	0,0-8,6	CTX**	150	**7,3**	6	86,7	3,2-11,5
CRO**	159	**8,8**	11,9	79,2	4,4-13,2	CRO**	27	**3,7**	3,7	92,6	0,0-10,8	CRO**	112	**8,9**	12,5	78,6	3,6-14,2
LNZ	197	**0**	0	100	0,0-0,0	LNZ	34	**0**	0	100	0,0-0,0	LNZ	135	**0**	0	100	0,0-0,0
LVX**	222	**4,1**	0	95,9	1,5-6,6	LVX**	35	**2,9**	0	97,1	0,0-8,4	LVX**	150	**4,7**	0	95,3	1,3-8,0
TCY	221	**45,2**	0,9	53,8	38,7-51,8	TCY**	35	**42,9**	0	57,1	26,5-59,3	TCY**	150	**41,3**	1,3	57,3	33,5-49,2
SXT**	221	**18,6**	5	76,5	13,4-23,7	SXT**	35	**14,3**	0	85,7	2,7-25,9	SXT**	150	**18,7**	6	75,3	12,4-24,9
VAN	222	**0,9**	0	99,1	0,0-2,1	VAN	35	**0**	0	100	0,0-0,0	VAN**	150	**1,3**	0	98,7	0,0-3,2

enere una variabilità della stima di %R inferiore al 10%

ze di *E. coli*.

URINA Numero di isolati = 6.908					
Codice	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**
AMP	5.256	**69,7**	0	30,3	68,5-71,0
AMC	6.381	**35**	0	65	33,8-36,2
TZP	6.539	**9,9**	2,9	87,2	9,2-10,6
CTX	6.899	**26,7**	0,8	72,5	25,7-27,8
CAZ	6.899	**18,9**	7,2	73,9	18,0-19,8
FEP	5.805	**18**	8,7	73,3	17,0-19,0
CIP	6.899	**43,5**	1,1	55,4	42,3-44,6
LVX	901	**34,9**	0,2	64,9	31,7-38,0
AMK	4.158	**3,3**	10,2	86,5	2,8-3,9
GEN	6.899	**18,7**	1	80,3	17,7-19,6
IPM	5.213	**0,8**	1,8	97,5	0,5-1,0
MEM	6.878	**1,2**	0,8	98	0,9-1,4
ETP	6.541	**3,4**	0,5	96,1	3,0-3,8
SXT	6.892	**38**	0,1	61,8	36,9-39,2
FOS	6.560	**5**	0	95	4,5-5,6
NIT	6.524	**3,4**	0	96,6	3,0-3,8

volte nel 2016 dai Laboratori aderenti al *Si.Re.Ar.* sulle antibiotico resistenze di *K. pneumoniae.*

TUTTI I MATERIALI Numero di isolati = 4.402						SANGUE E LIQUOR Numero di isolati = 518						RESPIRATORI Numero di isolati = 964					
Codice	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**	**Codice**	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**	**Codice**	**Num.**	**%R**	**%I**	**%S**	**%R 95%C.I.**
AMP	2246	**99,8**	0	0,2	99,6-100	AMP	256	**99,6**	0	0,4	98,8-100	AMP	294	**100**	0	0	100 -100
AMC	4309	**60,8**	0	39,2	59,3-62,3	AMC	517	**75,2**	0	24,8	71,5-79,0	AMC	954	**67,6**	0	32,4	64,6-70,6
TZP	4300	**56,2**	5,7	38,1	54,7-57,7	TZP	509	**71,5**	4,7	23,8	67,6-75,4	TZP	960	**63,8**	4,9	31,4	60,7-66,8
CTX	4402	**57,2**	0,4	42,4	55,7-58,6	CTX	518	**73**	0	27	69,1-76,8	CTX	964	**64,6**	2,1	33,3	61,6-67,6
CAZ	4399	**55,7**	3	41,3	54,2-57,2	CAZ	517	**72**	3,1	25	68,1-75,8	CAZ	964	**65,1**	0,4	34,4	62,1-68,2
FEP	3811	**47,6**	6,6	45,8	46,0-49,2	FEP	448	**60**	5,1	34,8	55,5-64,6	FEP	851	**57**	6	37	53,7-60,3
CIP	4398	**55,8**	2,5	41,7	54,3-57,2	CIP	517	**74,3**	2,3	23,4	70,5-78,0	CIP	961	**63,4**	2,4	34,2	60,3-66,4
LVX	1268	**57,7**	0,2	42,1	55,0-60,4	LVX	241	**77,2**	0,4	22,4	71,9-82,5	LVX	274	**60,2**	0,4	39,4	54,4-66,0
AMK	3888	**21,5**	5,2	73,3	20,2-22,8	AMK	518	**24,1**	5	70,8	20,4-27,8	AMK	963	**24,7**	5,9	69,4	22,0-27,4
GEN	4398	**34,7**	10,1	55,2	33,3-36,1	GEN	516	**42,2**	12,2	45,5	38,0-46,5	GEN	963	**38,9**	13,2	47,9	35,9-42,0
IPM	3940	**32,8**	11,4	55,8	31,3-34,3	IPM	492	**42,1**	17,9	40	37,7-46,4	IPM	908	**43,9**	12,8	43,3	40,7-47,2
MEM	4391	**38,8**	4	57,2	37,3-40,2	MEM	514	**54,3**	5,1	40,7	50,0-58,6	MEM	964	**52,4**	3,7	43,9	49,2-55,5
ETP	4254	**44,1**	1	54,9	42,6-45,6	ETP	498	**60**	1,2	38,8	55,7-64,3	ETP	937	**56**	0,5	43,4	52,9-59,2
FOS	4294	**25,7**	0	74,3	24,4-27,0	FOS	508	**22**	0	78	18,4-25,7	FOS	958	**26,7**	0	73,3	23,9-29,5
TGC	3733	**29,4**	23,4	47,2	27,9-30,8	TGC	502	**36,9**	24,1	39	32,6-41,1	TGC	930	**34,6**	23,9	41,5	31,6-37,7
SXT	4397	**52,7**	0,3	46,9	51,3-54,2	SXT	516	**65,9**	0,4	33,7	61,8-70,0	SXT	963	**58,3**	0,4	41,3	55,1-61,4

Implementing criteria-based early switch/early discharge programmes: a European perspective

D. Nathwani[1], W. Lawson[2], M. Dryden[3], J. Stephens[4], S. Corman[4], C. Solem[4], J. Li[5], C. Charbonneau[6], N. Baillon-Plot[6], S. Haider[7] and C. Eckmann[8]

efits of ES programmes that facilitate switching from IV to oral antimicrobial therapy include the following: improved patient comfort and mobility [5,17], reduced incidence of IV-line related adverse effects such as catheter-related bacteraemia and phlebitis [5,16,29], reduced nursing or pharmacy time spent preparing IV antimicrobials [5,17,30], decreased hospital length of stay [2,5,17,18,20,24,29,31] and reduced antimicrobial purchasing and administration costs [17,24]. Additionally, when clinical outcomes are equivalent, patients prefer oral therapy to IV therapy [32]. Benefits of ES followed by ED programmes include a lower risk of line-related infections [29], less patient deconditioning [5,23], and a shorter recovery time [23].

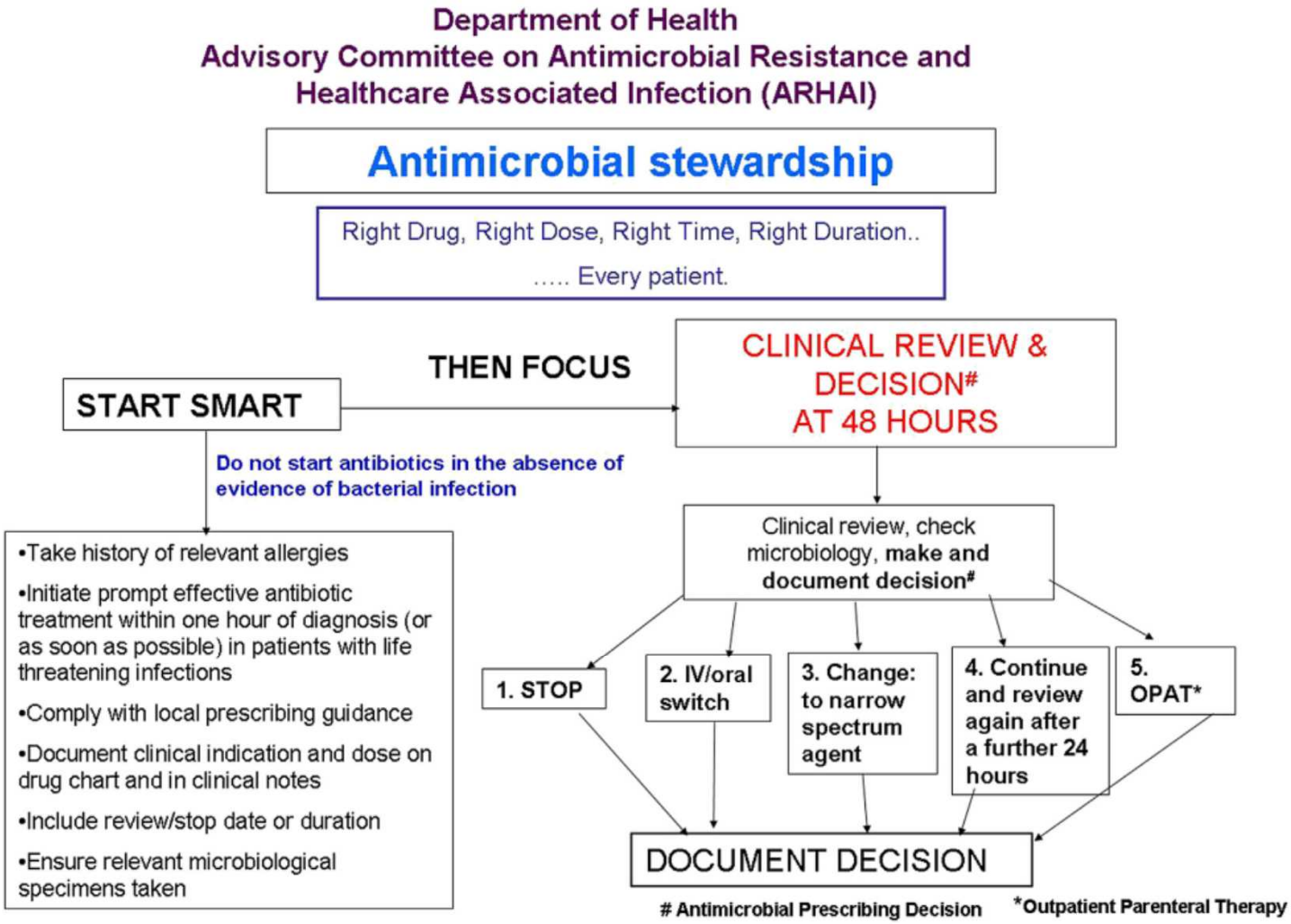


FIG. 1. Antimicrobial Stewardship in Secondary Care, Antimicrobial Stewardship Algorithm [26].

INTRAVENOUS ANTIBIOTICS

HAS **YOUR** PATIENT BEEN ON IV ANTIMICROBIALS FOR MORE THAN 48 HOURS?

CONSIDER THE 5 ANTIMICROBIAL DECISION OPTIONS

STOP
IF NO EVIDENCE OF INFECTION

SWITCH
IV-TO-ORAL

CHANGE
TO NARROW SPECTRUM ANTIMICROBIAL AGENT

CONTINUE
AND REVIEW AGAIN AT 72 HOURS

OPAT
OUTPATIENT PARENTERAL ANTIMICROBIAL THERAPY

INTRAVENOUS ANTIBIOTICS

HAS **YOUR** PATIENT BEEN ON IV ANTIMICROBIALS FOR MORE THAN 48 HOURS?

CONSIDER THE 5 ANTIMICROBIAL DECISION OPTIONS

STOP
IF NO EVIDENCE OF INFECTION

SWITCH
IV-TO-ORAL

CHANGE
TO NARROW SPECTRUM ANTIMICROBIAL AGENT

TABLE 4. Recommendations for implementing early switch/ early discharge programmes for antibiotics

- Identify the size of the problem locally and opportunities for early switch/early discharge through audit and harness local support from clinicians and administrators
- Outline an evidence-based plan of implementation with measurable criteria for success for implementation
- Engage a multidisciplinary team in the design of the programme, including key stakeholders from the clinical service and infection specialists (e.g Infectious Diseases, Microbiology, and Pharmacy and Nursing departments). Identify clinician champions where possible
- Use multiple intervention tools to promote good antibiotic prescribing practices, including educational activities and materials, audit and feedback, and reminders. Ensure these tools are tested/piloted before spread to all parts of the hospital; prevent duplication of process—embed or integrate into similar existing work such as review of need for peripheral venous cannulae
- Provide prescribers with timely and regular feedback that is clear and directive, and deliver specific recommendations for improved prescribing (e.g. antibiotic
  dose, route and frequency)
- Evaluate the programme performance regularly to demonstrate its value and benefits to key stakeholders

When to switch to an oral treatment and/or to discharge a patient with skin and soft tissue infections

- Hospitalization is often required to treat complicated

skin and soft tissue infections (cSSTIs) with intravenous
antibiotics, especially for infections caused by drug resistant
bacteria such as methicillin-resistant Staphylococcus aureus (MRSA).

- Early (<72 h from diagnosis) assessment of clinical

response to treatment can help clinician decisions to switch to oral treatment and discharge the patient.

- Early switch to oral treatment and early patient

discharge should always be considered in the management of cSSTIs in order to reduce hospital associated
costs and risks.

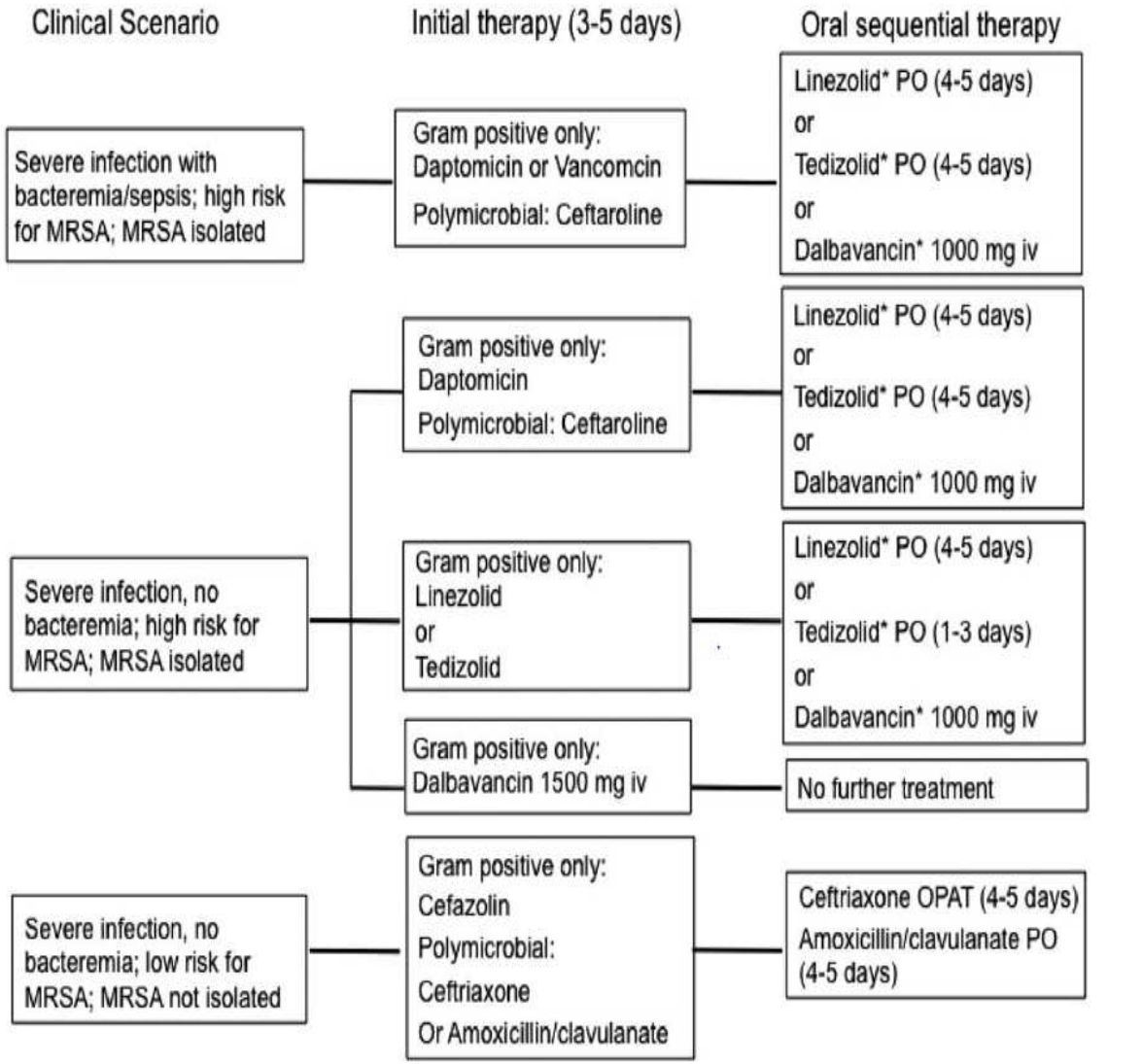
- New therapeutic options currently offer MRSA coverage

as well as the possibility for intravenous to oral switch
or weekly administration, allowing for patients' early discharge and reducing costs.

Early switch eligibility criteria for intravenous discontinuation
Intravenous antibiotics for more than 24 h
Stable clinical infection or clinical improvement
Afebrile/temperature of less than 38 °C for more than 24 h
WBC count not less than 4×10^9/l or more than 12×10^9/l
Absence of unexplained tachycardia
SBP of at least 100 mmHg
Patient tolerates p.o. fluids/diet and is able to take p.o. medications with no gastrointestinal absorption problems
Bacteria susceptible to p.o. treatment (if microbiological cultures available)
Early discharge (early discharge) eligibility criteria
All key early switch eligibility criteria listed above
No other reason to stay in hospital except for infection management
Stable mental status
Stable comorbid illness
Stable social situation

Data from [14,15]; p.o., oral; WBC, white blood cells.

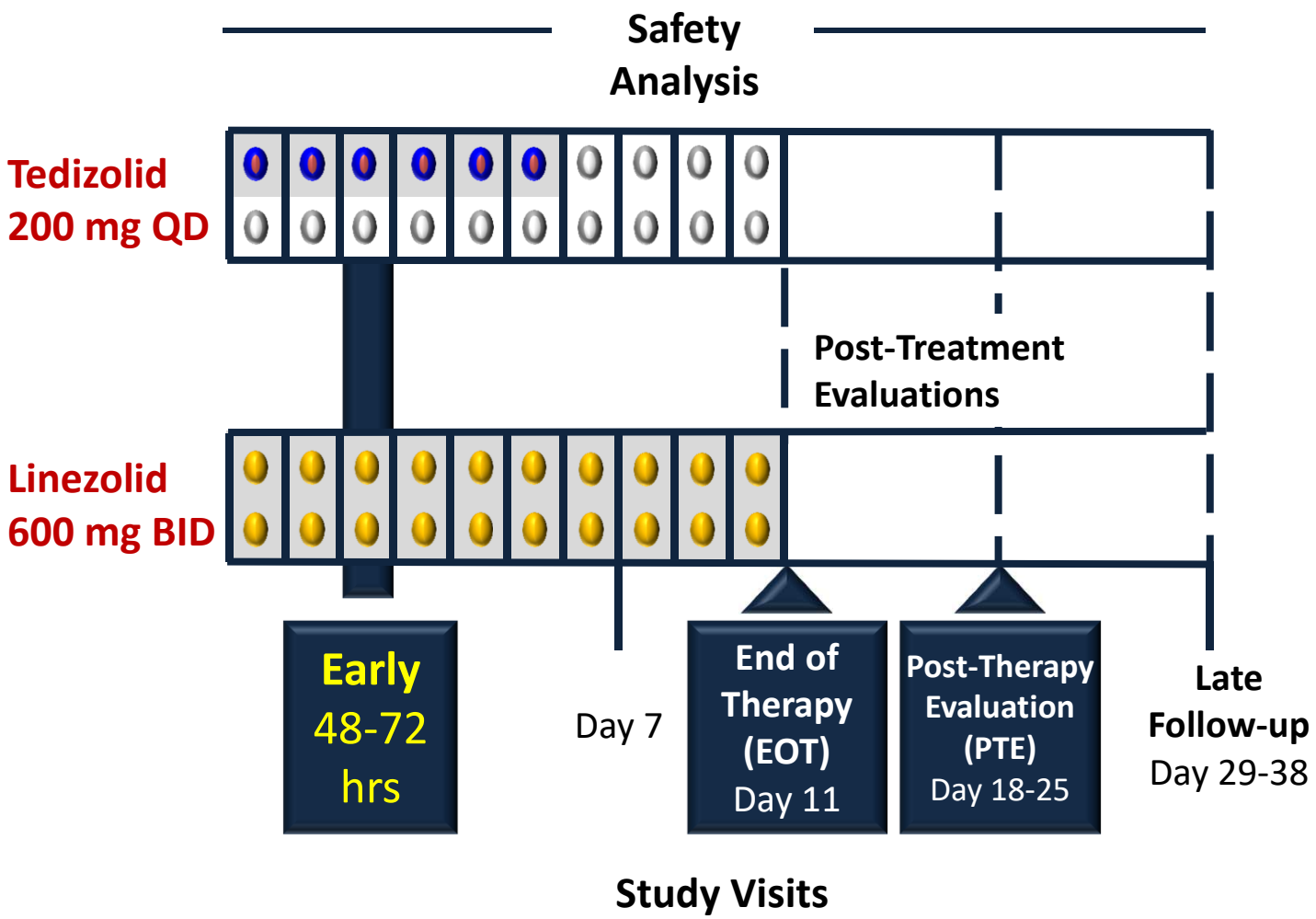
Bassetti M et al Curr Opin Infect Dis 2018, 31:163–169



MRSA, methcillin-resistant *S. aureus*; OPAT, outpatients parenteral antimicrobial therapy; p.o., oral.

Bassetti M et al Curr Opin Infect Dis 2018, 31:163–169

DISEGNO DEGLI STUDI DI FASE III

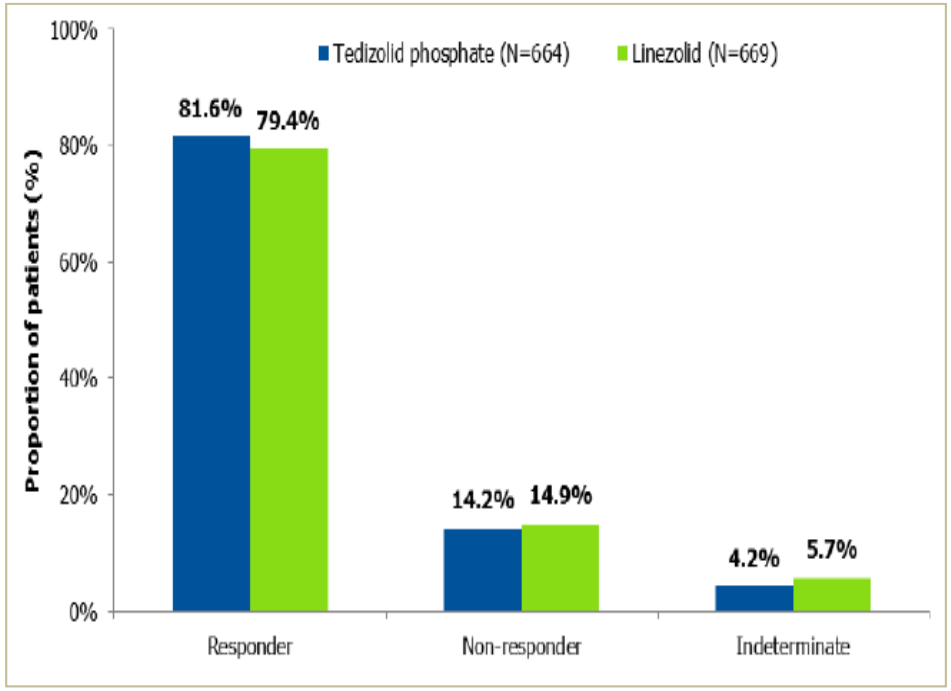


Shorr AF et al Antimicrob Agents Chemother. 2015 Feb;59(2):864-71

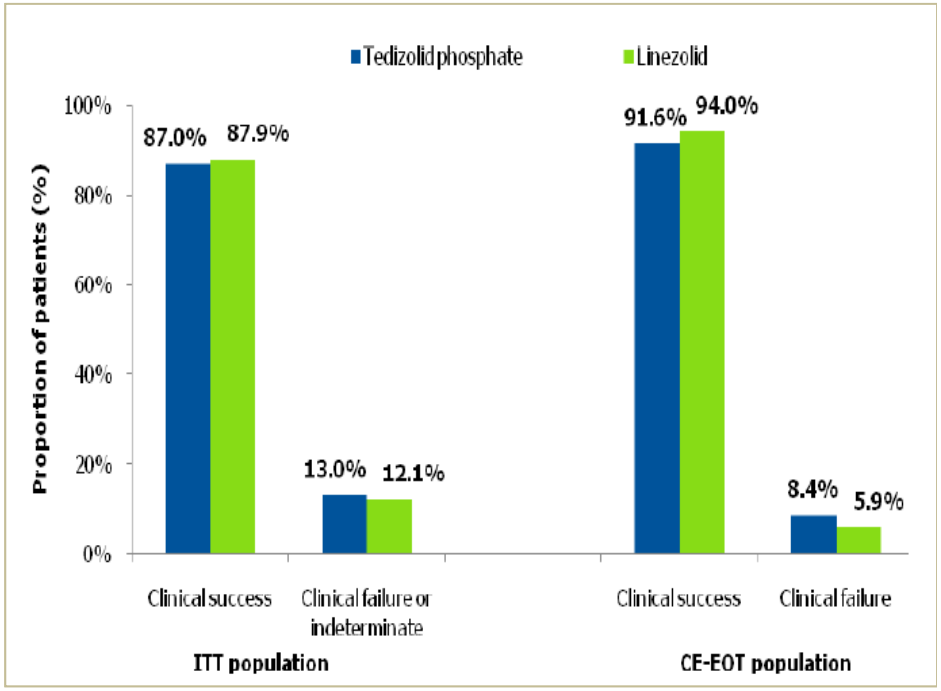
ANALISI AGGREGATA DEGLI STUDI REGISTRATIVI ESTABLISH 1&2:

Successo clinico precoce e a fine terapia **sovrapponibile a Linezolid**, ma con soli **6 giorni** di terapia anziché 10

% di pazienti con risposta clinica precoce, definita come riduzione ≥20% dell'area della lesione rispetto al baseline alla visita a 48-72h nella analisi dei dati aggregati (popolazione ITT)



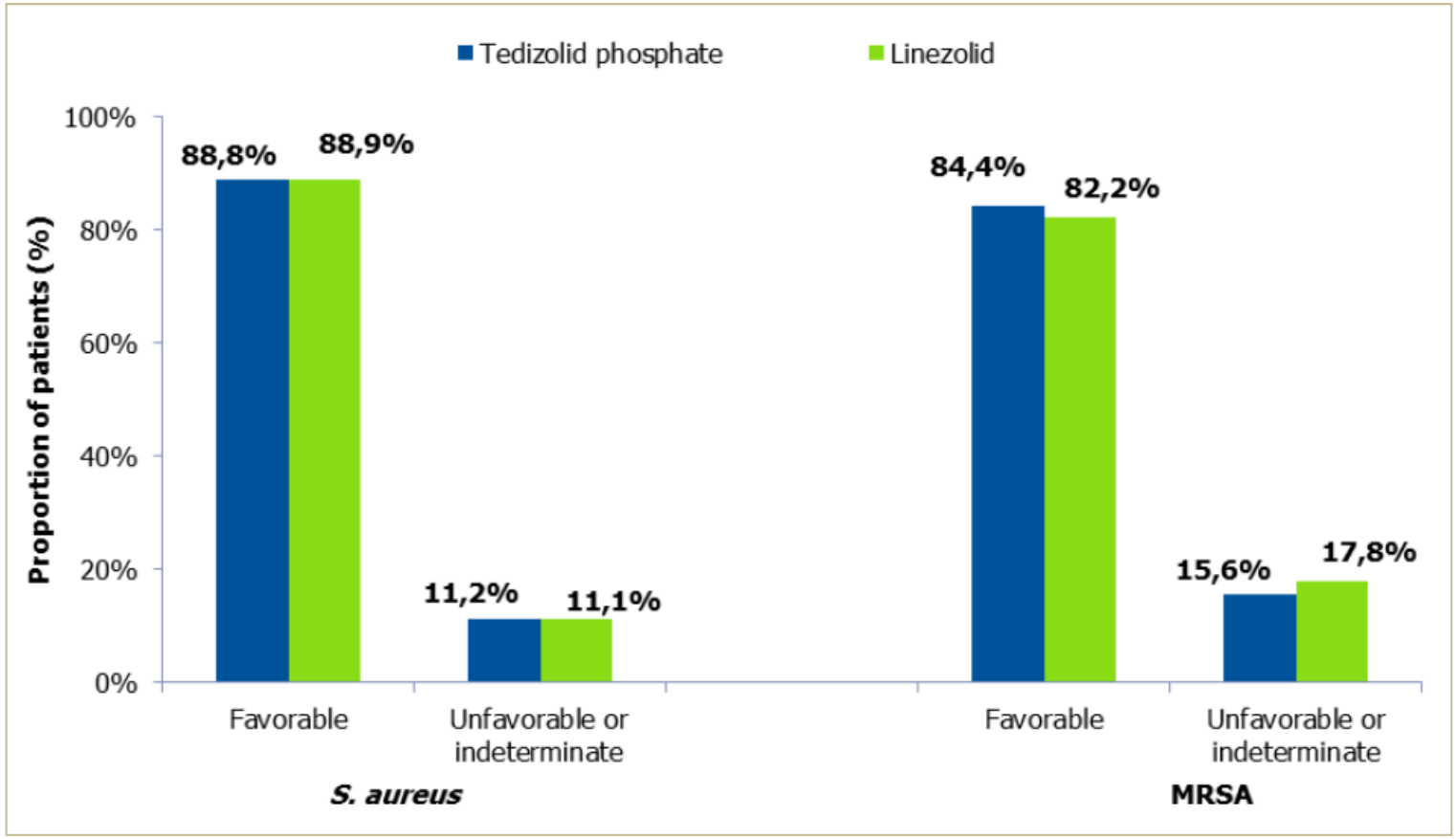
% di pazienti con successo clinico riscontrato alla visita EOT nell'analisi dei dati aggregati dei trials clinici di fase III (popolazioni ITT e CE-EOT)



Shorr AF et al Antimicrob Agents Chemother. 2015 Feb;59(2):864-71

ANALISI AGGREGATA: RISPOSTA MICROBIOLOGICA

% di pazienti con risposta microbiologica favorevole verso S. aureus ed MRSA alla visita PTE nell'analisi dei dati aggregati dei due studi di fase III (popolazione MITT)

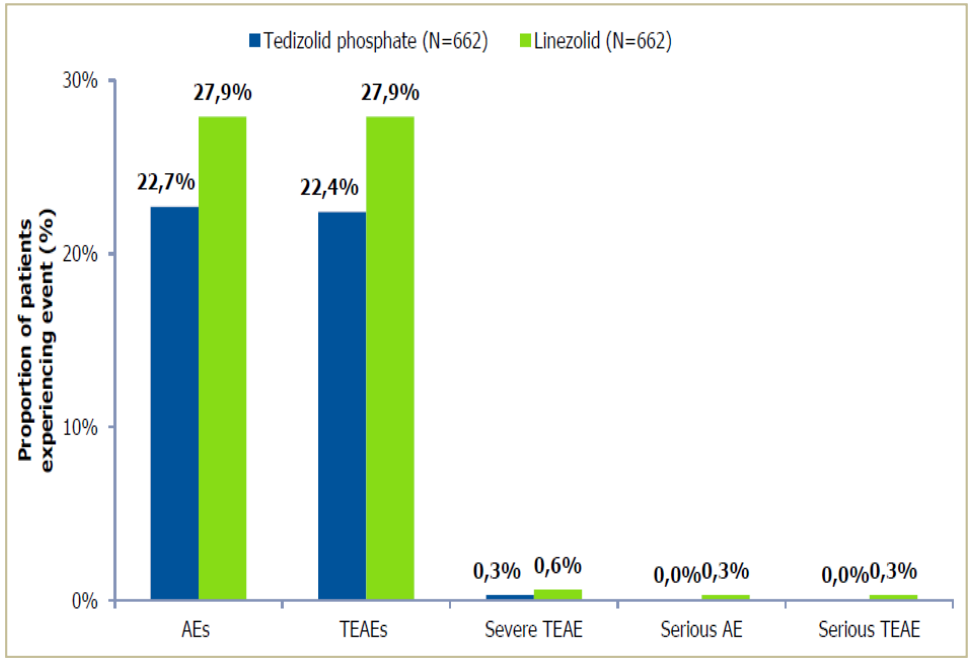


Shorr AF et al Antimicrob Agents Chemother. 2015 Feb;59(2):864-71

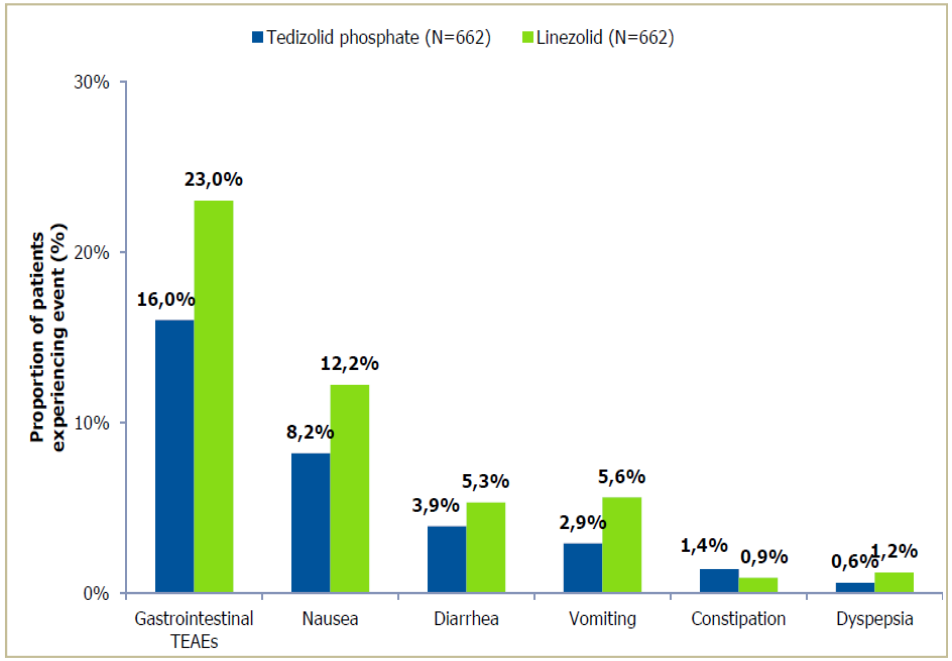
ANALISI AGGREGATA DEGLI STUDI REGISTRATIVI ESTABLISH 1&2:

miglior profilo di safety rispetto a Linezolid

Overview degli AE considerati correlate al farmaco in studio nell'analisi dai dati aggregati relativi alla sicurezza degli studi di fase III



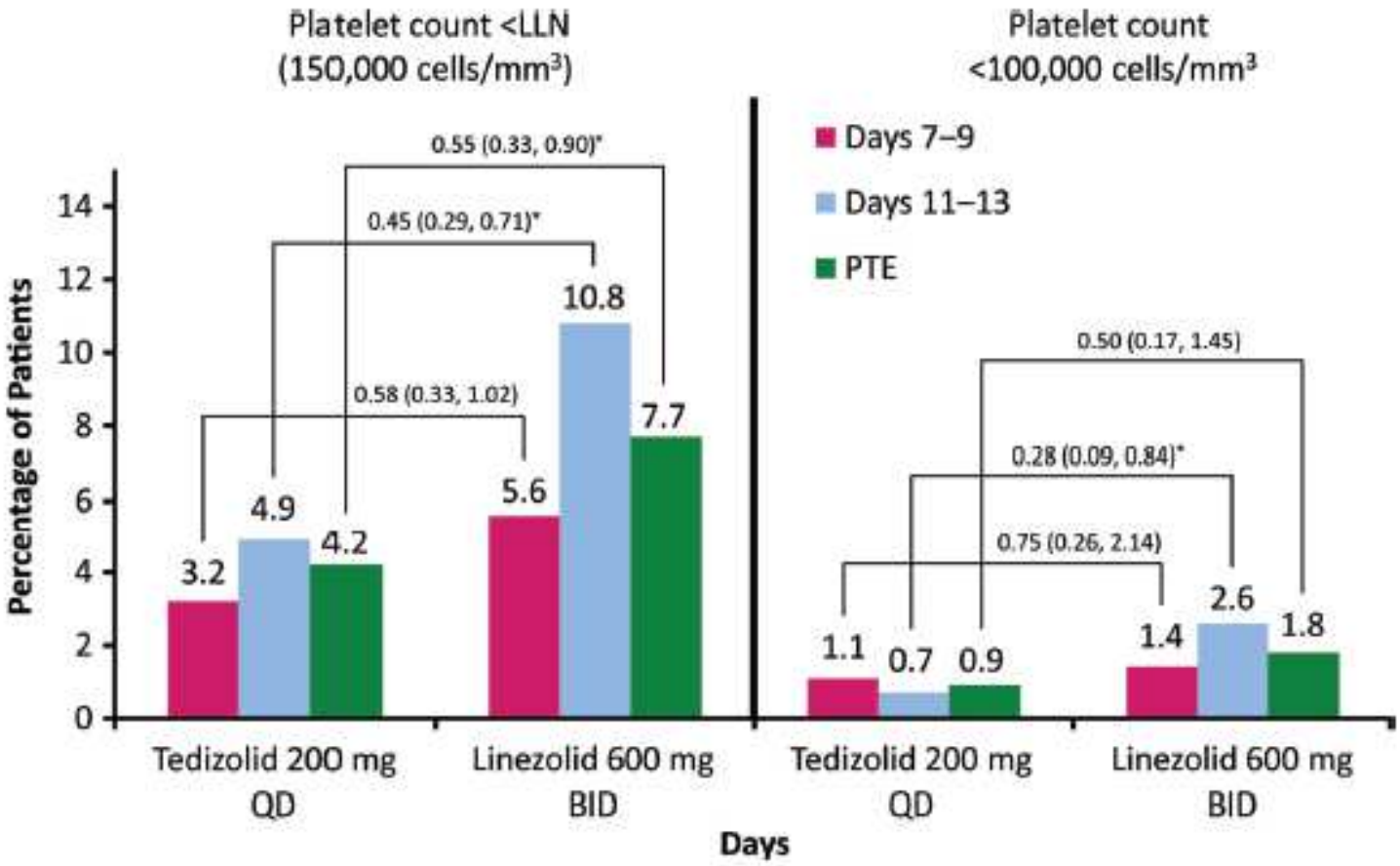
TEAE (eventi avversi emersi durante il trattamento) di natura gastrointestinale nell'analisi dei dati aggregati relativi alla sicurezza degli studi di fase III



Shorr AF et al Antimicrob Agents Chemother. 2015 Feb;59(2):864-71

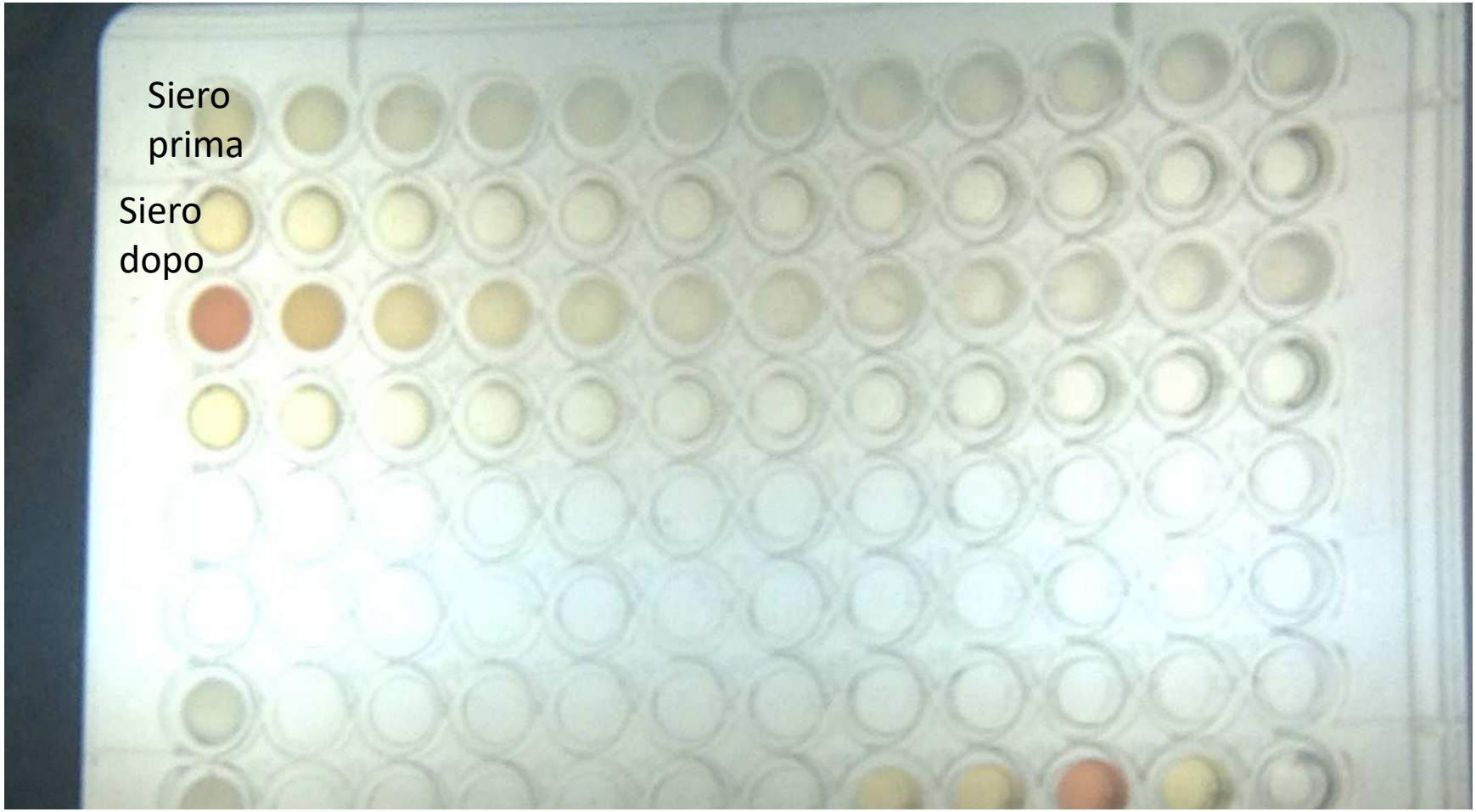
.

TEDIZOLID: MINORE PIASTRINOPENIA VS LINEZOLID (ESTABLISH 1 ED ESTABLISH 2)

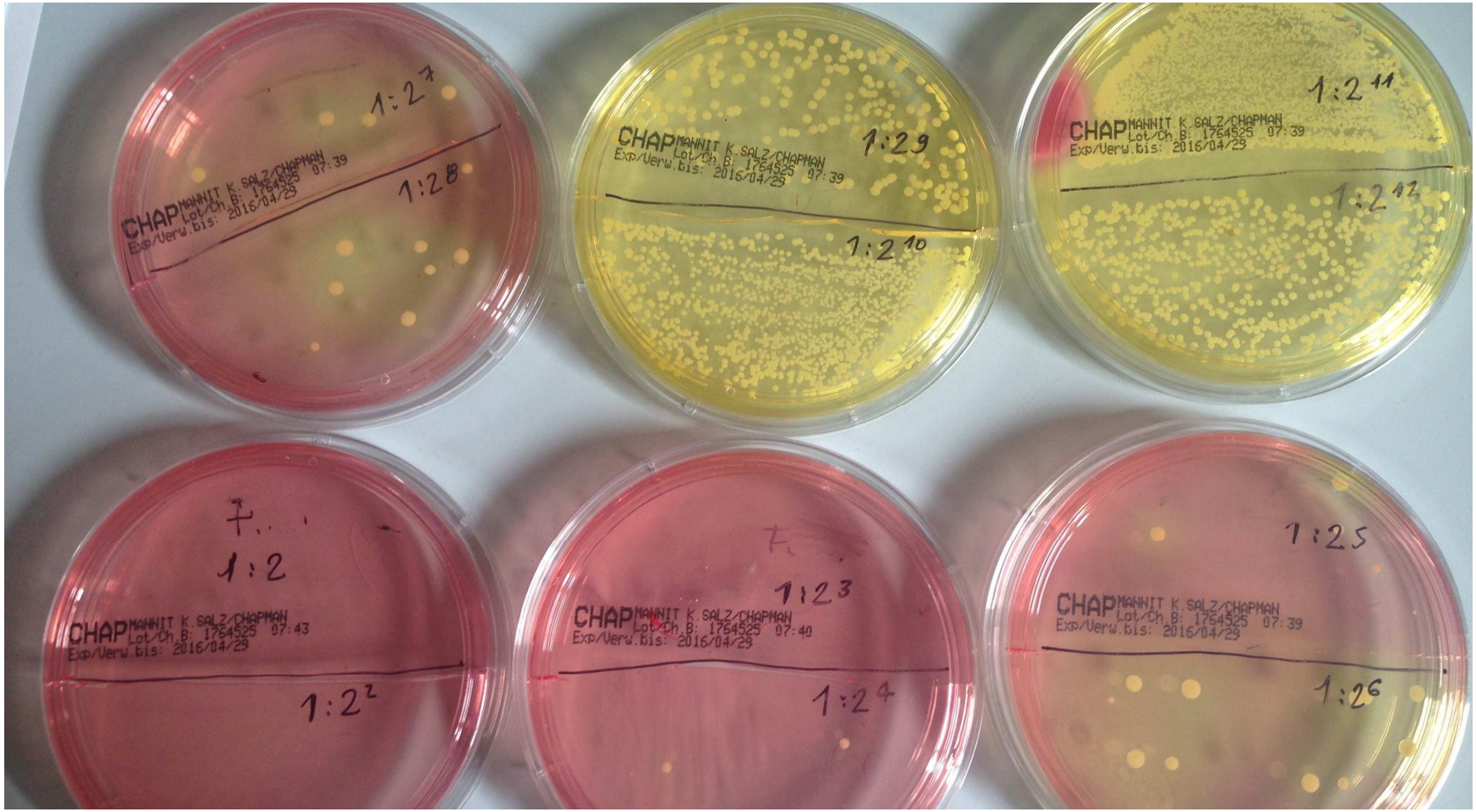


Lodise TP et al Antimicrob Agents Chemother. 2014 Dec;58(12):7198-204

Attività dalbavancina vs MRSA



Potere battericida di dalbavancina contro MRSA



Early discharge

- Riduce i costi del ricovero
- Riduce gli eventi avversi dell'ospedale: infezioni nosocomiali, cadute etc
- Ha un senso se è finito il ricovero e si può fare una terapia domiciliare sicura
- E' un obiettivo in molti sistemi di valutazione del servizio sanitario

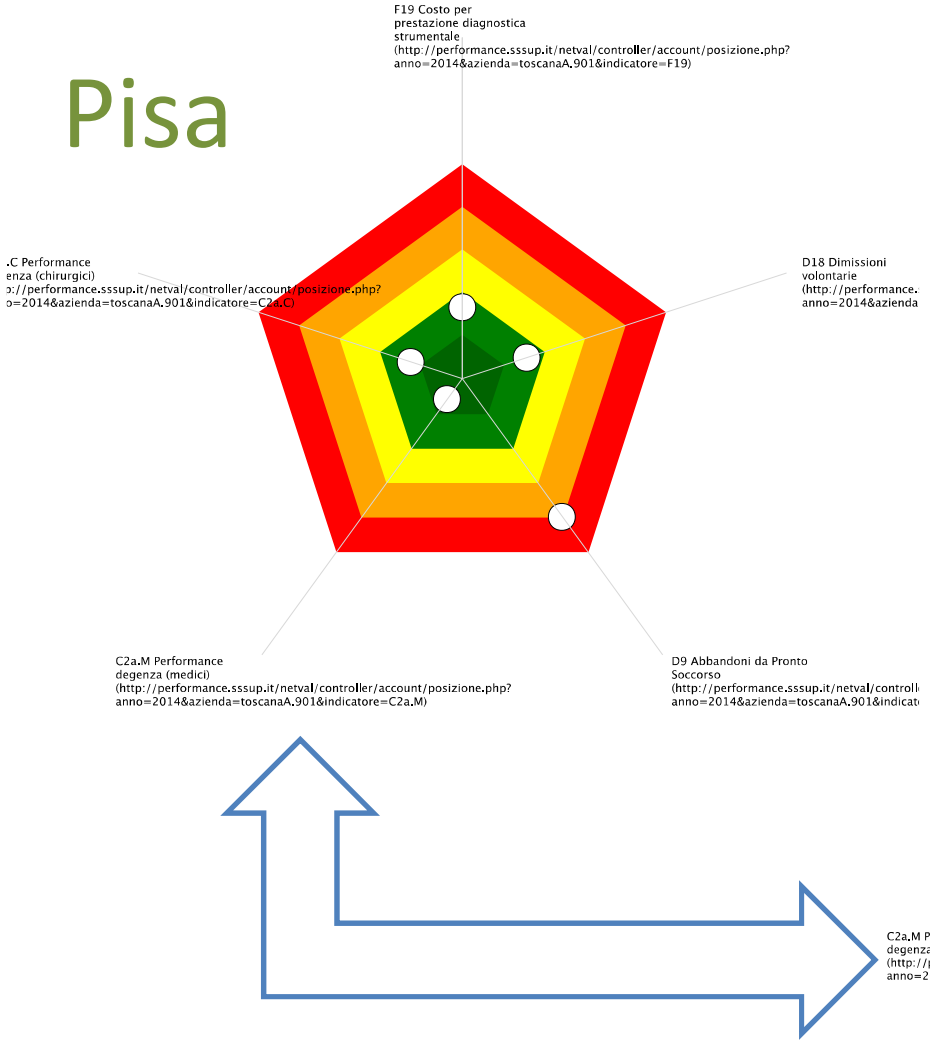
Candidemie Pisa/Udine/Firenze

Reparto	Durata degenza media (giorni) PISA	Rate/ 10000 days admission PISA	Durata degenza media (giorni) UDINE	Rate/ 10000 days admission UDINE	Durata degenza media (giorni) FIRENZE	Rate/ 10000 days admission FIRENZE
Popolazione globale	5,95	3,59	9,76	1,44	6,86	3,70
Medicine (interne + specialistiche)	6,29	4,37	12,72	0,95	4,67	11,70
UTI	5,7	9,95	18,3	2,16	6,08	1,13
Chirurgie	4,05	2,48	9,76	4,7	5,71	5,71
Solo medicina interna	5	10,38	8,7	1,04	6,15	2,60

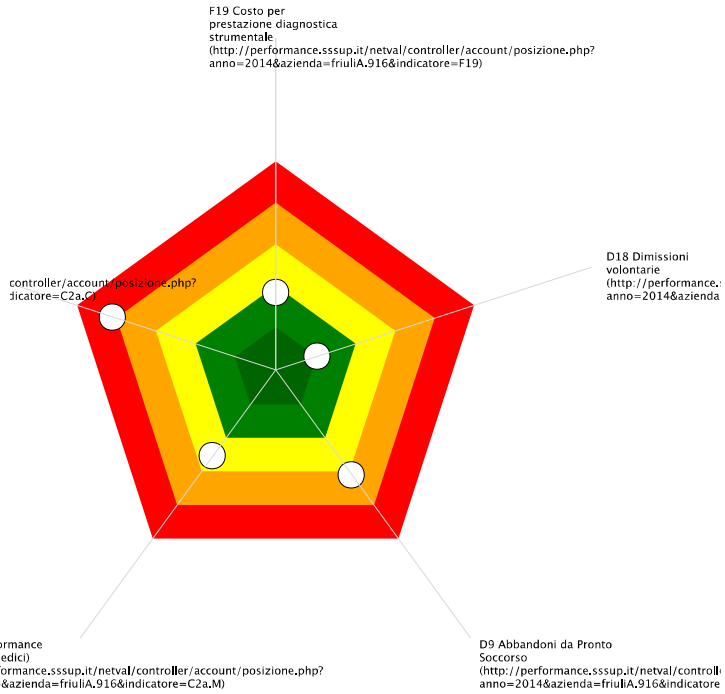
Tascini C et al., *Variable incidence of candidemia in patients admitted to ICUs or medical wards of large tertiary-care Italian hospitals,* Clinical Microbiology and Infection (2015), http://dx.doi.org/10.1016/j.cmi.2015.05.019

Bersagli MeS 2014 – Performance Degenza medicine

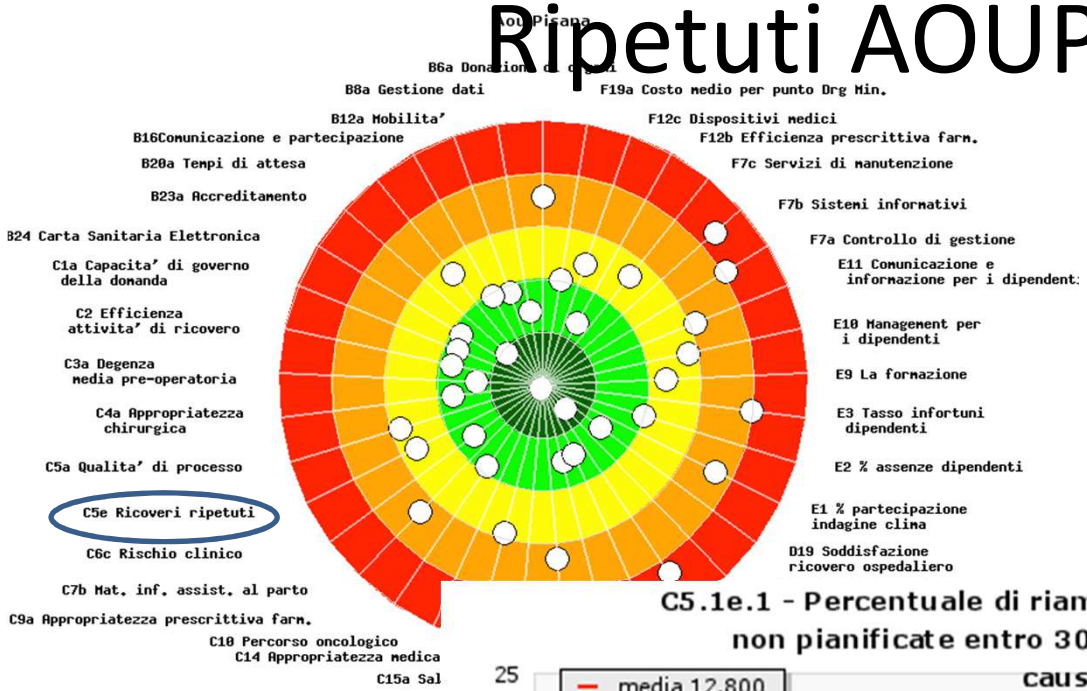
Pisa

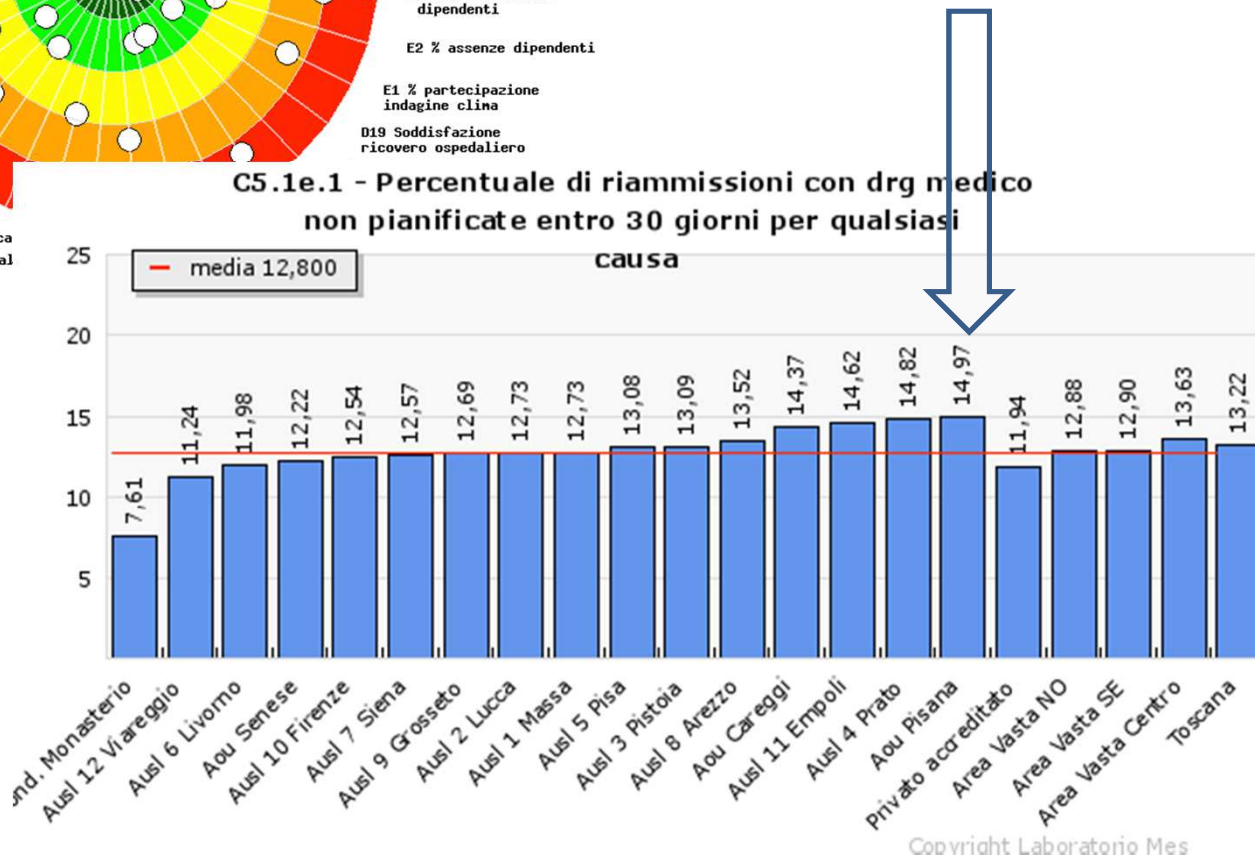


Udine



Bersagli Mes 2014 – Ricoveri Ripetuti AOUP





PICC e Candide

Intensive Care Med
DOI 10.1007/s00134-015-3892-0

Carlo Tascini
Emanuela Sozio
Giancarlo Tintori
Andrea Ripoli
Francesco Sbrana
Elena Rosselli Del Turco
Giacomo Bertolino
Simona Fortunato
Franco Carmassi
Gianluigi Cardinali
Francesco Menichetti

Peripherally inserted central catheter as a predominant risk factor for candidemia in critically ill patients in Internal Medicine wards in Italy

Accepted: 19 May 2015

Electronic supplementary material
The online version of this article (doi: 10.1007/s00134-015-3892-0) contains supplementary material, which is available to authorized users.

Table 1 Comparison of clinical characteristics and outcomes of patients in the general internal medicine wards versus those in the intensive care units

Clinical characteristics and outcomes of patients	All patients (n = 72)	Patients in General Internal Medicine wards (n = 50)	Patients in Intensive Care Units (n = 22)	p value
Clinical characteristics				
Age (years)	73 ± 14	78 ± 13	66 ± 12	<0.05
Charison score	6.82 ± 2.70	6.69 ± 2.52	7.16 ± 3.14	ns
Admission from home	36/72 (50 %)	34/50 (68 %)	2/22 (9 %)	≤0.001
Transfer from surgical ward	14/72 (19 %)	1/50 (2 %)	13/22 (59 %)	≤0.001
Hospital stay (days)	15 [8–35]	11 [6–20]	40 [30–72]	≤0.001
Time to onset of candidemia (days)	7 [2–17]	4 [1–11]	21 [9–36]	≤0.001
Very early onset candidemia (<48 h from admission)	24/72 (34 %)	23/50 (46 %)	1/22 (5 %)	≤0.001
Early onset candidemia (2–10 days from admission)	19/72 (26 %)	13/50 (26 %)	6/22 (27 %)	ns
Late onset candidemia (>10 days from admission)	29/72 (40 %)	14/50 (28 %)	15/22 (68 %)	<0.05
Patient therapy and outcomes				
Therapy with azole	39/72 (54 %)	33/50 (66 %)	6/22 (27 %)	<0.05
Therapy with echinocandins	17/72 (22 %)	2/50 (4 %)	14/22 (64 %)	≤0.001
No treatment	17/72 (24 %)	15/50 (30 %)	2/22 (9 %)	ns
Continuous infusions	48/72 (67 %)	29/50 (58 %)	19/22 (86 %)	<0.05
Nasogastric tube	33/72 (46 %)	16/50 (32 %)	17/22 (77 %)	≤0.001
Central venous catheter	26/72 (36 %)	9/50 (18 %)	17/22 (77 %)	≤0.001
Peripherally inserted central catheter	37/72 (52 %)	36/50 (72 %)	1/22 (5 %)	≤0.001
Overall mortality	31/72 (43 %)	17/50 (34 %)	14/22 (64 %)	≤0.001

Data are presented as the mean ± standard deviation, number with the percentage in parenthesis, or the median with the interquartile range in square brackets, as appropiate
ns Not significant

Conclusioni

- Ricordarsi rivalutazione a 48-72 ore
- Utilizzare biomarcatori
- Utilizzare le nuove tecniche microbiologiche
- Early discharge non deve diventare un ossessione