Corso di Alta Formazione in Gestione delle Infezioni e delle Multi-Resistenze
GIN Project

ANTONINO MAZZONE
Direttore Dipartimento Area Medica
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Vice Presidente FISM
Cabina di Regia Patologie Croniche
Ministero della Salute
FADOI HONORARY FELLOW

15 maggio 2020

LIUC Università Cattaneo

CREMS Centro di Ricerca in Economia e Management in Sanità e nel Sociale

FONDAZIONE FADOI FORMAZIONE - RICERCA

Istituto Superiore di Sanità

Università degli Studi di Firenze

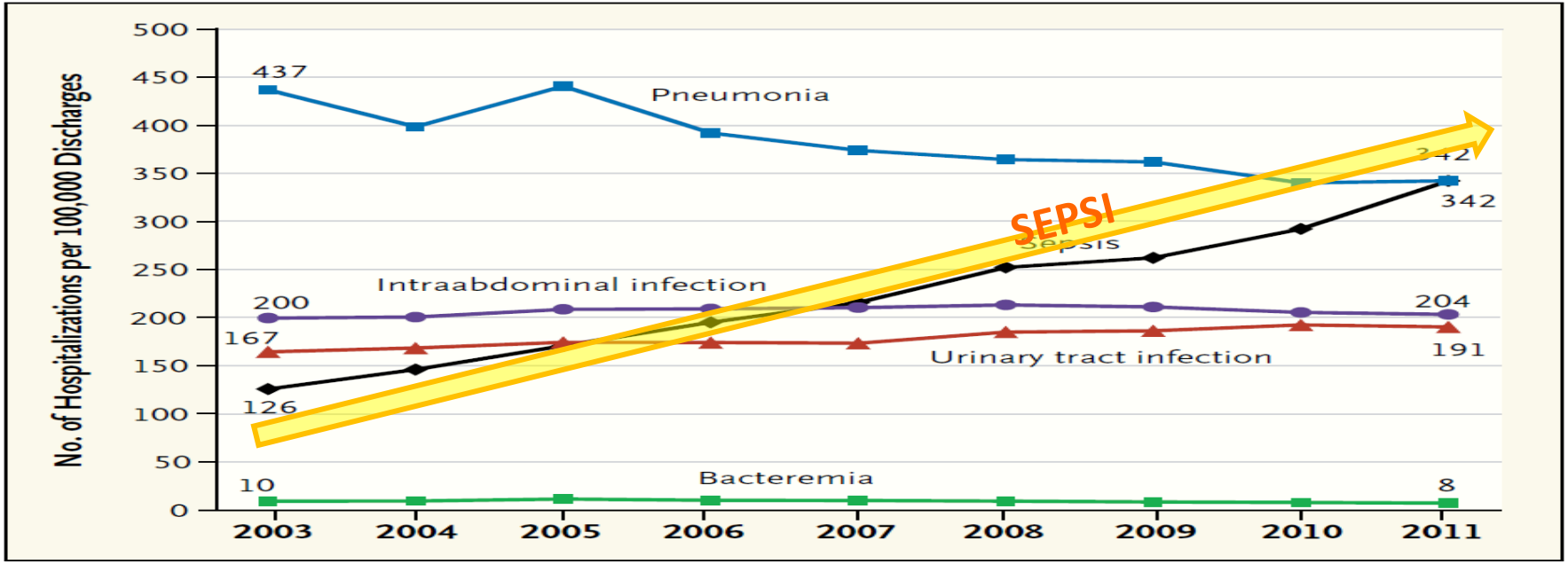
Agenda

- ✓ Epidemiologia della sepsi
- ✓ Studio Snoopii
  1. Obiettivi
  2. Risultati clinici
  3. Resistenze batteriche
  4. Mortalita'
  5. Costi

Regulatory Mandates for Sepsis Care — Reasons for Caution

Chanu Rhee, M.D., Shruti Gohil, M.D., M.P.H., and Michael Klompas, M.D., M.P.H.

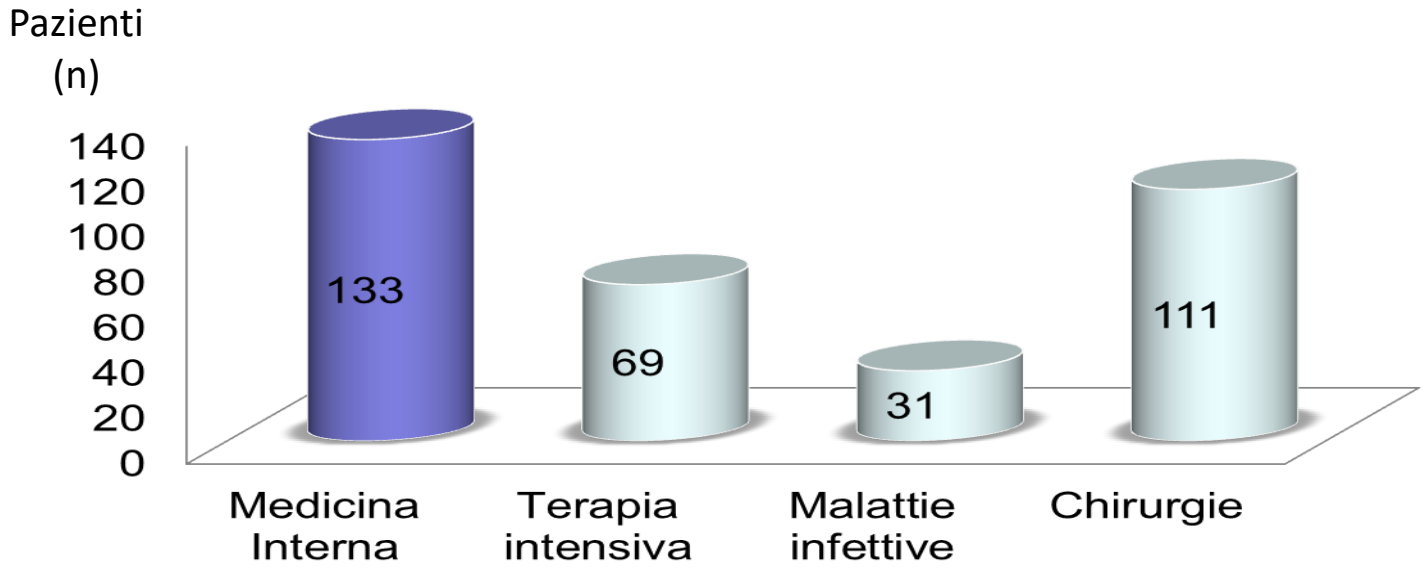
The NEW ENGLAND JOURNAL of MEDICINE



Hospitalizations for Which Certain Infection Codes Were Listed as a Primary Diagnosis, 2003–2011.

NEJM 2014; 370:1673-76

Epidemiologia delle batteriemie– Anno 2017



Clerici et al Microbiologia Legnano

SEPSI: CONFRONTO CON ALTRE PATOLOGIE MAGGIORI

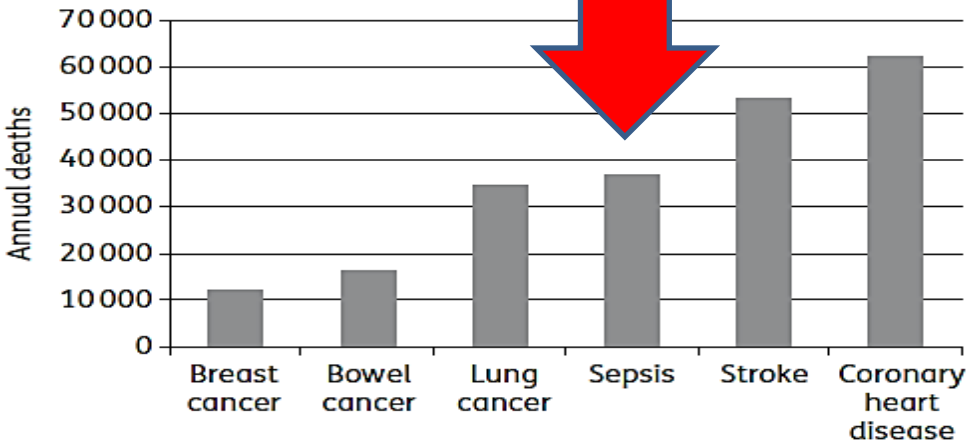


Figure 1. Chart showing relative mortality figures in 1 year for the UK for common conditions. Sources: sepsis, ICNARC data 2006. For all others: for England and Wales, Office for National Statistics 2008; for Scotland, General Register Office Registrar General Annual Report 2008; and for Northern Ireland, Statistics and Research Agency Registrar General Annual Report 2008.

[Daniels R. *Surviving the first hours in sepsis: getting the basics right (an intensivist's perspective)* J Antimicrob Chemother 2011; 66 Suppl 2: ii11–ii23]

WHO, February 2019

OMS: LISTA PATOGENI DIFFICILI

A.baumannii

P.aeruginosa

Klebsiellla KPC

VRE

S.aureus

H.pylori

Campylobacter

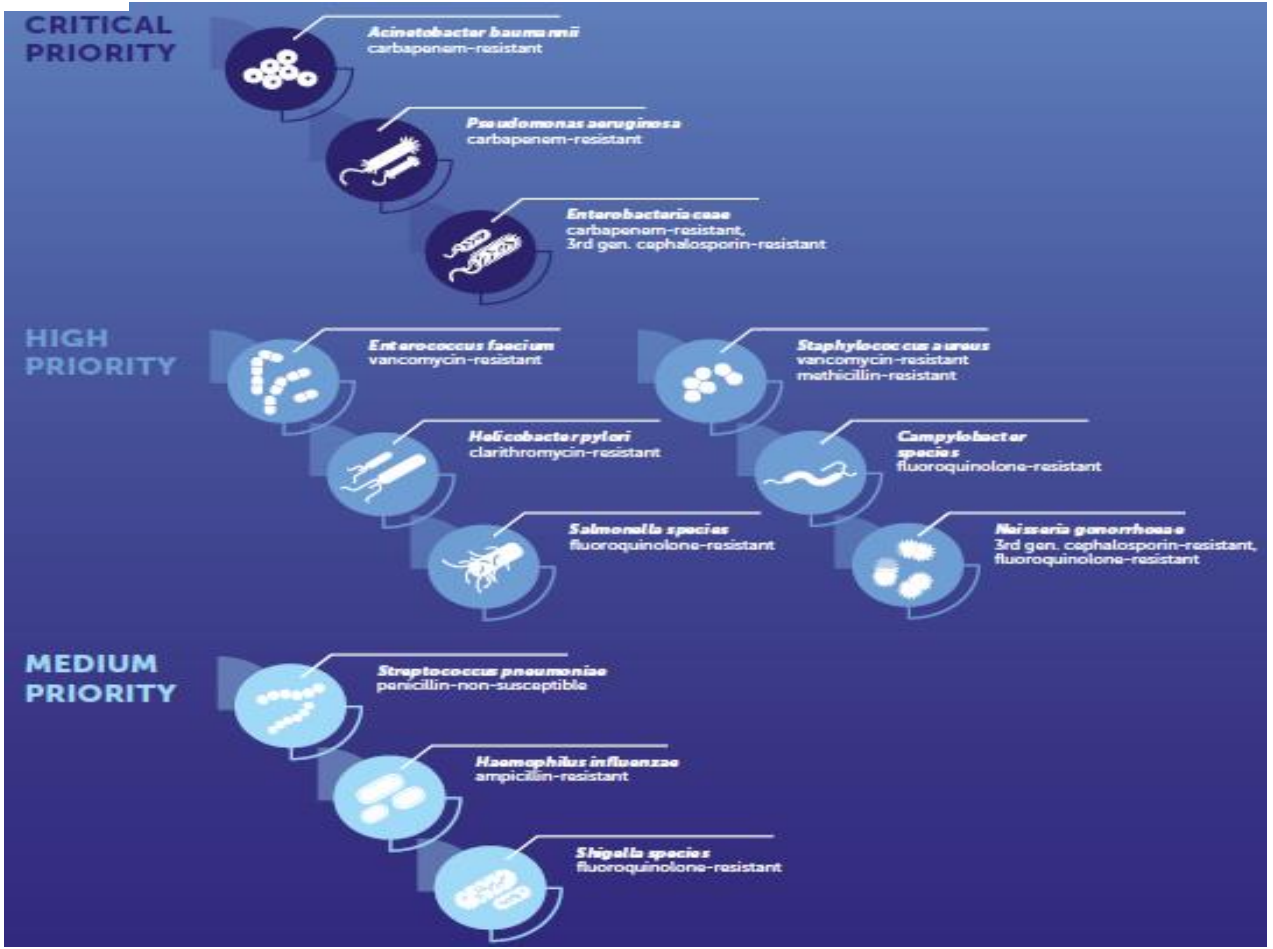
Salmonella

N.gonorrhoea

S.pneumoniae

H.influenzae

Shigella



IMPATTO DELLA RESISTENZA ANTIMICROBICA SULLA SOPRAVVIVENZA DEL PAZIENTE

Below is a table summarising available data on differences in death rates (mortality) between resistant and sensitive bacteria.

Bacteria	Death rate *resistant* strain	Death rate *sensitive* strain
E. coli[23]	32%	17%
A. baumannii[25]	16.4%	5.4%
A. baumannii[19]	53.8%	31.0%*
K. pneumoniae[26]	42.9% (CRKP)	18.9%
K. pneumoniae[27]	43.8% (CRKP)	12.5%
K. pneumoniae[10]	38%	12%
S. aureus[28]	36.4% (MRSA)	27.0%
S. aureus[14]	23.6% (MRSA)	11.5%

Table 2: Comparison of death rates (mortality) in patients with resistant or sensitive strains of bacteria. *=not fully sensitive.

Riorganizzazione della rete di assistenza sanitaria

ASSISTENZA OSPEDALIERA SOLO PER MALATI GRAVI

- ✓Aumento dei pazienti critici
- ✓Pz con comorbidità, età avanzata
- ✓Posti limitati
- ✓[illegible] adramento sciplanare

ECCESSI[illegible] LA [illegible]RIA

- [illegible]nto UOC/Strutture Complesse
- ✓Depotenziamento dei reparti ultraspecialistici
- ✓Conversione di attività verso DH
- ✓Scarsa redittività di alcuni reparti in base al DRG

AUMENTO DEI PAZIENTI A RISCHIO INFETTIVO IN MEDICINA INTERNA

Features of patients hospitalized in Internal Medicine wards

1.Transfer from **ICU or Sub-intensive** medical wards

2.Residence in **long-term care facilities or nursing homes**

3.Acutely ill pts coming from **Emergency Department**

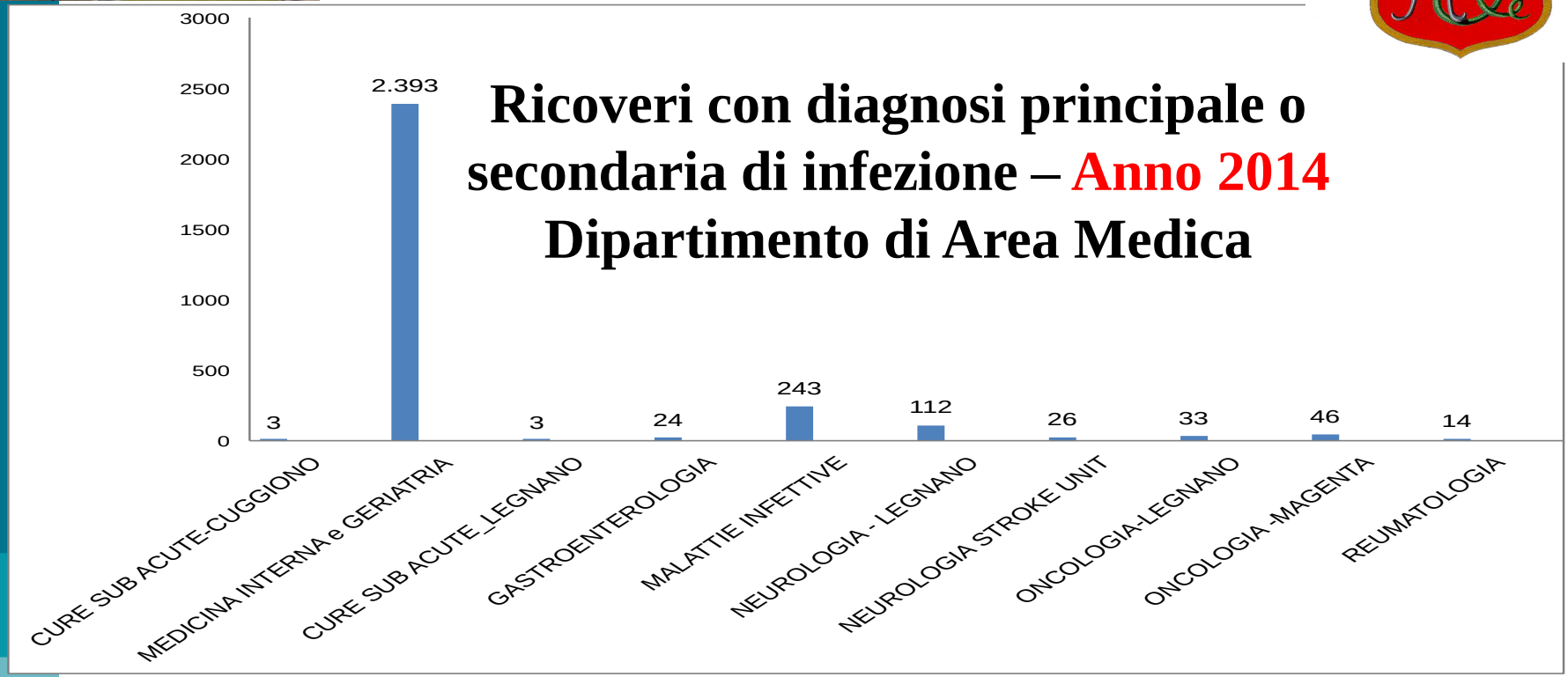
4.Pts with cancer in **chemotherapy**

5.Pts in chronic treatments with **immunosoppressive drugs**

6.Pts with multiple comorbidities with **devices and NPT**

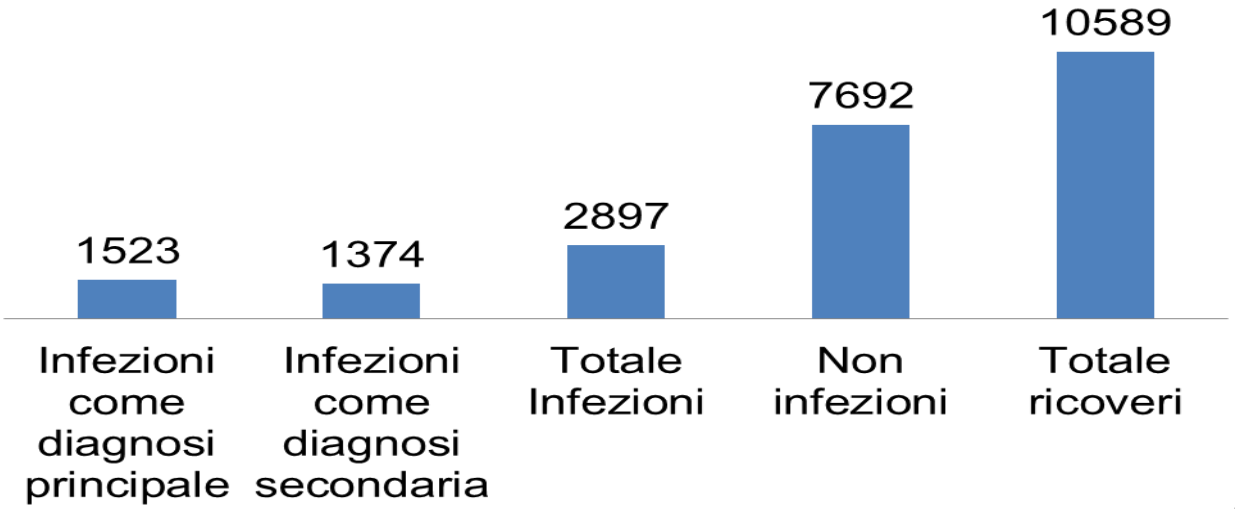
7.Pts with **post surgical** complications

Ricoveri con diagnosi principale o secondaria di infezione – Anno 2014 Dipartimento di Area Medica



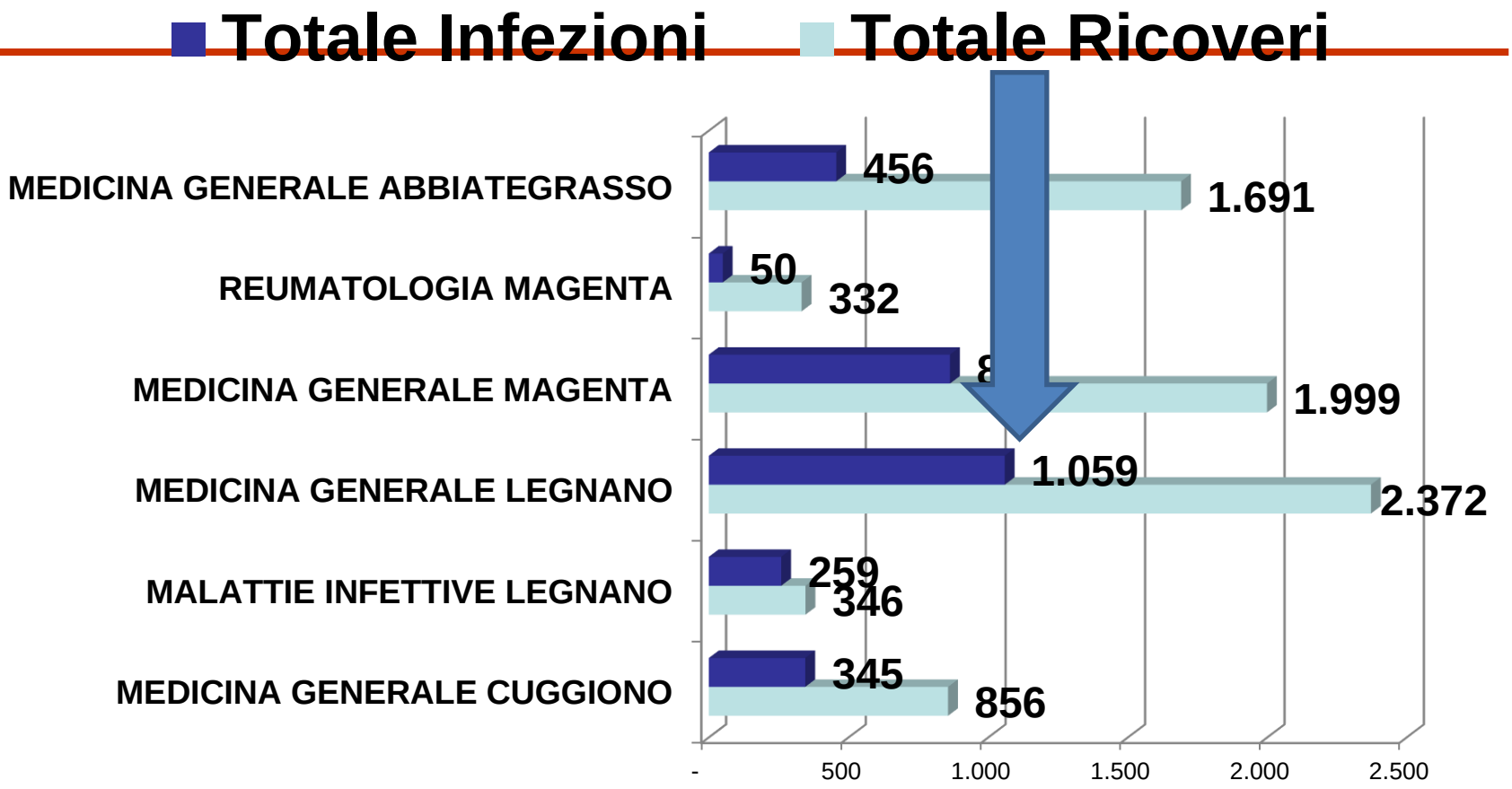
DIPARTIMENTO DI AREA MEDICA

Ricoveri con diagnosi principale o secondaria di infezione



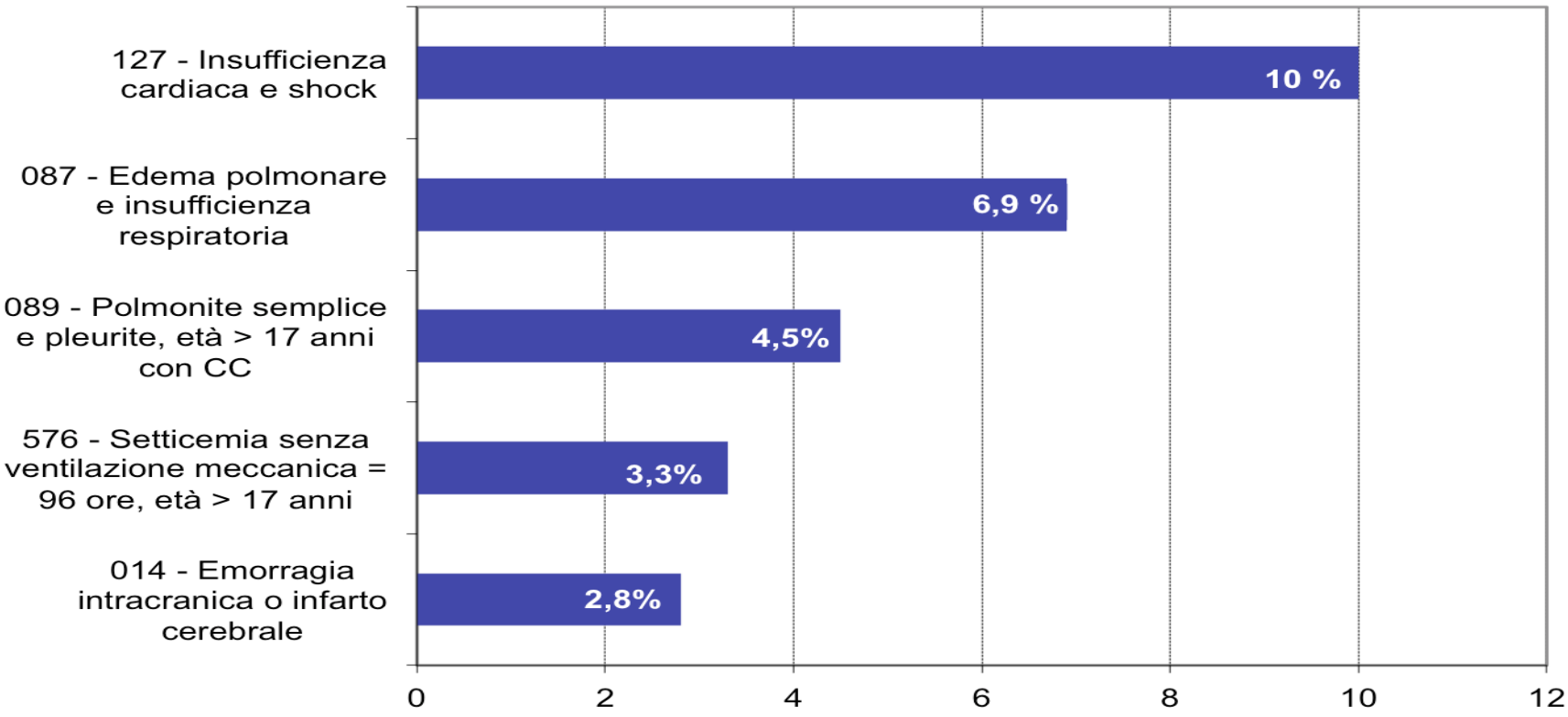
27,8% SUL TOTALE DELLE SDO

Azienda Ospedaliera "Ospedale Civile di Legnano
Anno 2014

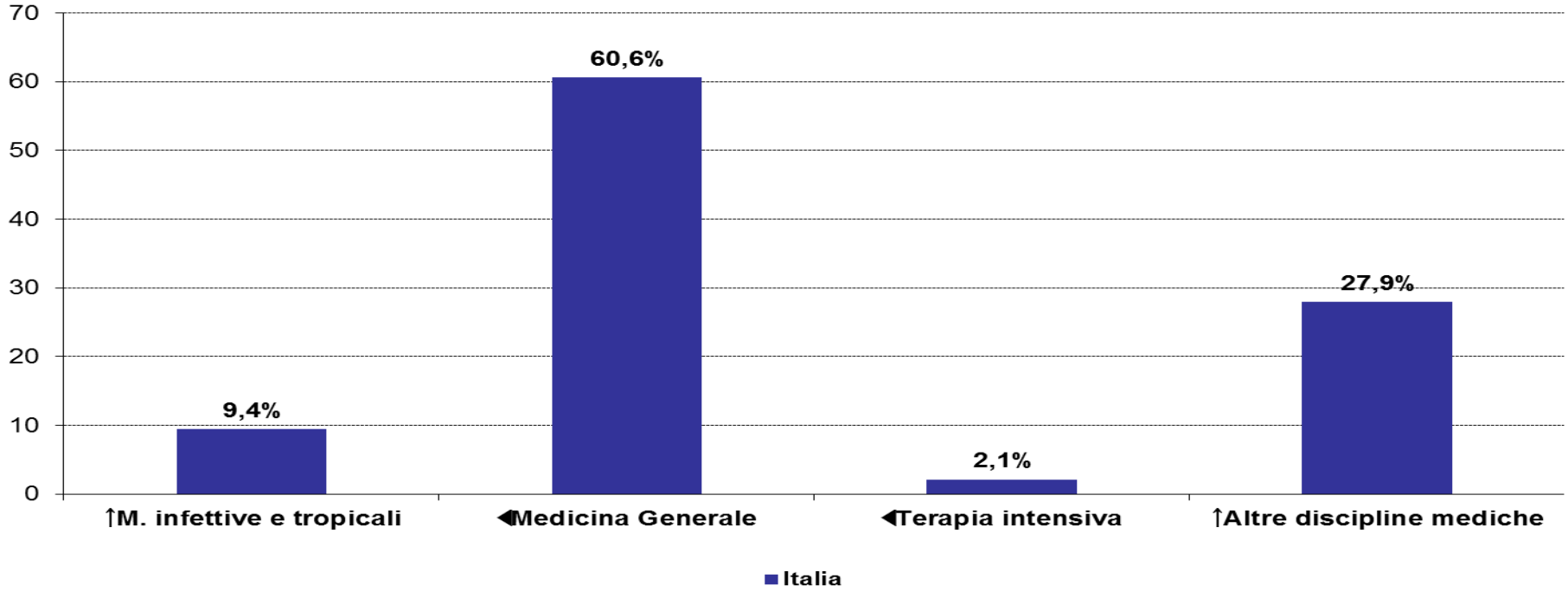


SDO 2018 DIAGNOSI DI INFEZIONE PRIMA O SECONDA DIAGNOSI

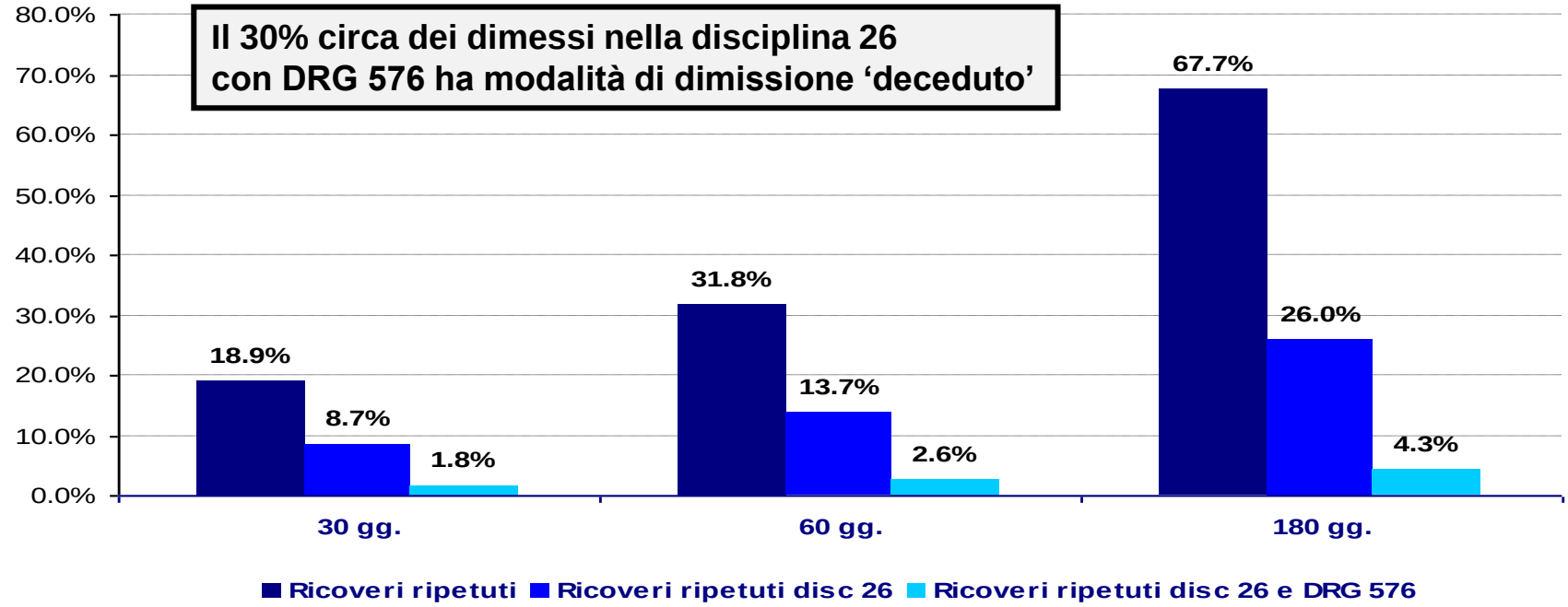
Ricoveri ordinari, primi 5 DRG Medici in ordine di frequenza
Disciplina 26. Valori %. Italia, 2014



Ricoveri con DRG 576 nella Disciplina 26 e in alcune altre Discipline mediche
Valori %. Italia, 2014



Ricoveri ripetuti a 30, 60 e 180 giorni in tutte le Discipline, nella Disciplina 26, nella Disciplina 26 e con DRG 576 - SEPSI
Italia, 1 gen. 2012-30 giu. 2014



Editoriale

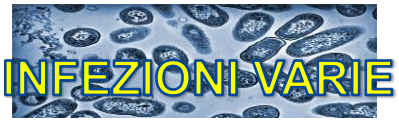
Editorial

Roberto Nardi, Magda Mazzetti

di rischio nelle infezioni dell'anzian

INFEZIONE URINARIA

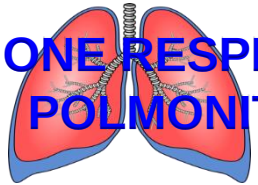
INFEZIONE DEL TRATTO DIGESTIVO



INFEZIONI VARIE

INFEZIONE DELLA CUTE E DEI TESSUTI MOLLI

GERMI MULTIRESISTENTI, STATO DI COLONIZZAZIONE CRONICA



INFEZIONE RESPIRATORIA, POLMONITE

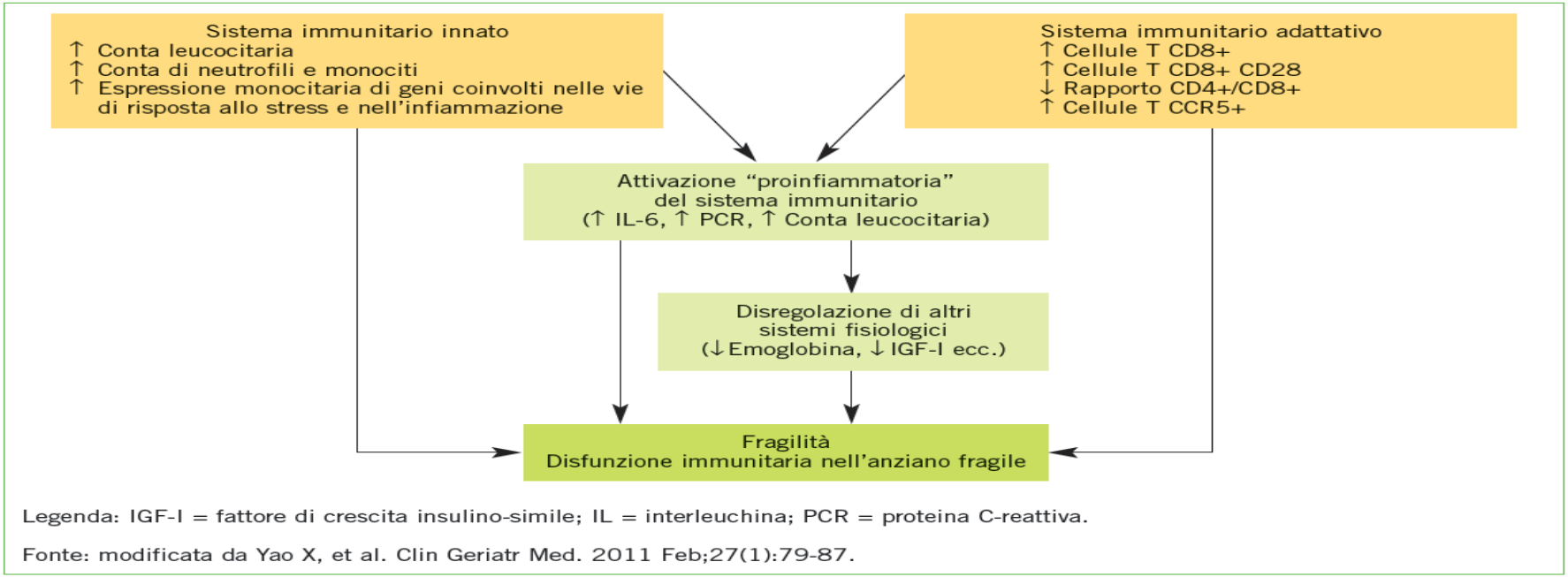
TUBERCOLOSI, HERPES ZOSTER

Editoriale

Editorial

Roberto Nardi, Magda Mazzetti

Azienda USL di Bologna, Ospedale Maggiore, Medicina Interna



Legenda: IGF-I = fattore di crescita insulino-simile; IL = interleuchina; PCR = proteina C-reattiva.

Fonte: modificata da Yao X, et al. Clin Geriatr Med. 2011 Feb;27(1):79-87.

Figura 1 Alterazioni del sistema infiammatorio e del sistema immunitario associate alla fragilità

Fattori di rischio per le infezioni in medicina interna

- Insufficienza renale cronica
- Sindrome nefrosica
- Epatopatia
- Epatiti autoimmuni
- Diabete mellito
- Tumori solidi in fase avanzata
- Tossicodipendenza/alcolismo

Deficit immunitario	Apparati coinvolti
Immunità cellulo-mediata – Alterata chemiotassi dei neutrofili e monociti – Deficit fagocitico Immunità umorale perdita di IgG sia per dispersione con le urine che per aumentato catabolismo Immunità legata al complemento perdita di fattori del complemento	Tratto genito-urinario e gastroenterico
Immunità cellulo mediata – Alterata chemiotassi dei neutrofili e monociti – Deficit fagocitico Immunità umorale Attivazione dei linfociti T→ attivazione dei linfociti B e produzione di autoanticorpi	Cute, tratto gastro-enterico
Immunità cellulo-mediata - Deficit fagocitico Alterata chemiotassi dei granulociti neutrofili e dei monociti	Cute, tratto genito-urinario e gastroenterico Raro coinvolgimento della colecisti, del naso e dei seni paranasali da Mucorales (Mucor, Absidia, Rhizopus)
Immunità cellulo-mediata ed umorale Fattori predisponenti: utilizzo di chemioterapici e steroidi, stato di malnutrizione, ampio uso di antibiotici a largo spettro e nutrizione parenterale totale	Ampia variabilità delle sedi coinvolte anche in base alla localizzazione del tumore e allo stadio
Diminuzione della fagocitosi e chemiotassi Diminuzione dell'attività dei linf T e B Diminuzione delle citokine infiammatorie Deficit dell'attività del complemento	Incremento infezioni opportunistiche, TBC, listeria

Fattori di rischio per le infezioni in medicina interna

- Obesità
- Senescenza
- Patologie autoimmuni
- Patologie ematologiche
- Cattivo stato nutrizionale
- Uso di devices

Deficit immunitario	Apparati coinvolti
multifattoriale	Cute, app respiratorio, app gastroenterico vie urinarie, ecc
multifattoriale	Cute, app respiratorio, vie urinarie, app gastroenterico, SNC, SNP
multifattoriale	Cute, app respiratorio, vie urinarie, app gastroenterico, SNC
Neutropenia, linfocitopenia, agranulocitosi	Cute, app respiratorio, vie urinarie, app gastroenterico, SNC, mucose
multifattoriale	
	Cute, app respiratorio, vie urinarie, app gastroenterico, SNC, mucose

World Health Organization

WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella spp., fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

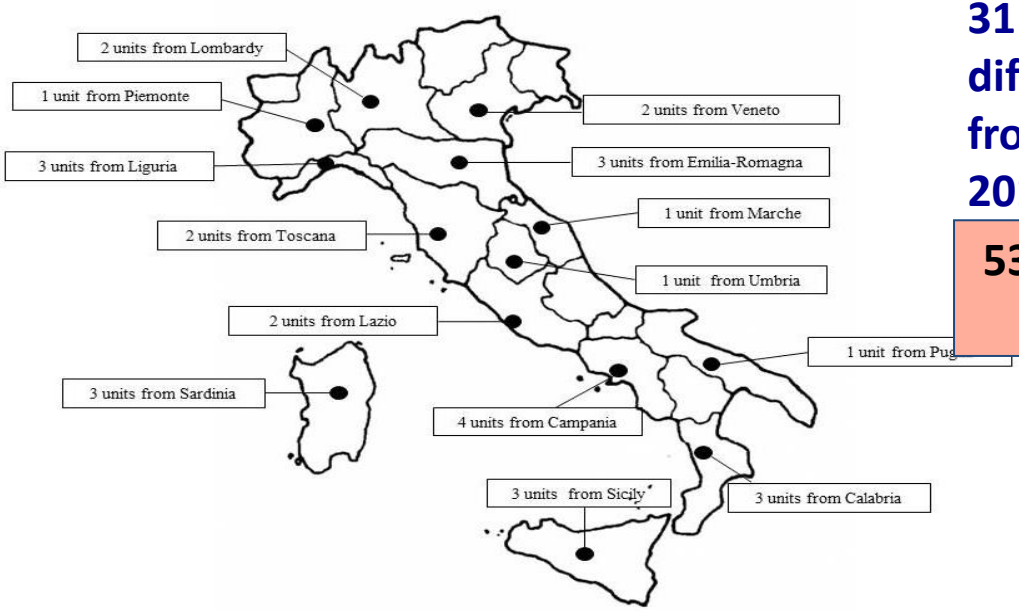
Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella spp., fluoroquinolone-resistant

The SNOOPII study on bloodstream infections: data from FADOI



31 internal medicine units from 14 different Italian regions was conducted from March 1, 2012, to December 31, 2012 (SNOOPII Study)

533 bloodstream infections from different region of Italy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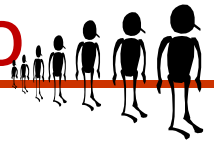
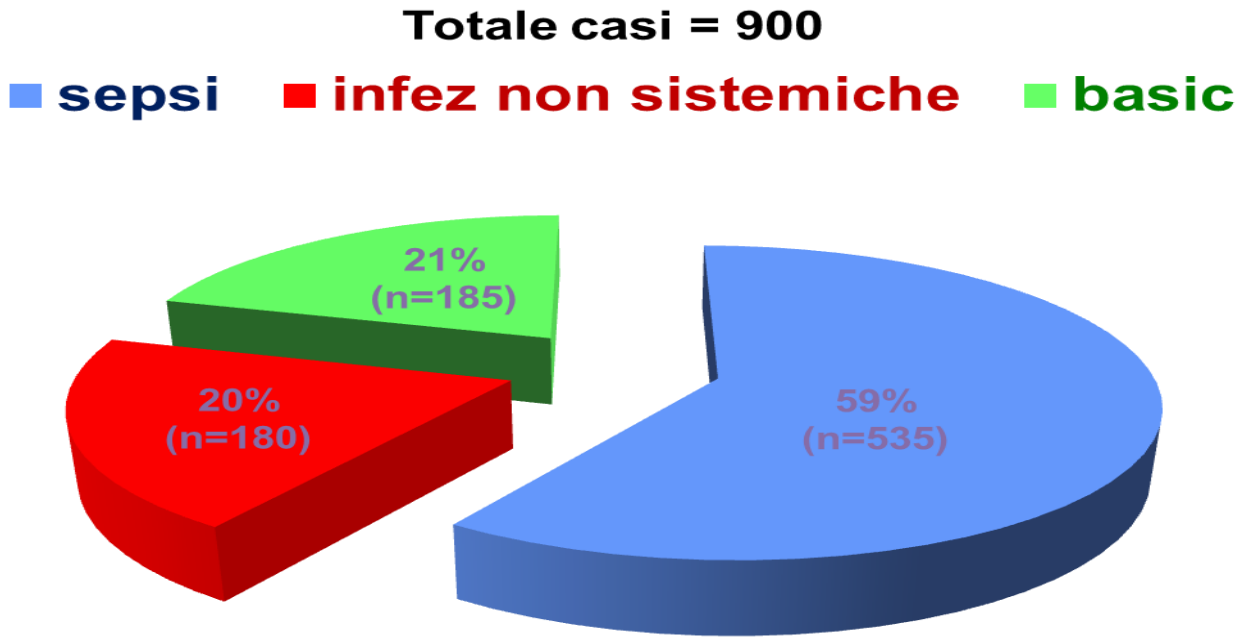
Clinical Features, Short-Term Mortality, and Prognostic Risk Factors of Septic Patients Admitted to Internal Medicine Units
Results of an Italian Multicenter Prospective Study
Antonino Mazzone, MD, Francesco Dentali, MD, Micaela La Regina, MD, Emanuela Foglia, MEcon, Maurizia Gambacorta, MD, Elisabetta Garagiola, MEng, Giorgio Bonardi, MD, Pierangelo Clerici, MD, Ercole Concia, MD, Fabrizio Colombo, MD, and Mauro Campanini, MD

Mazzone A et al. Medicine (Baltimore). 2016;95:e2124.

Il campione studiato





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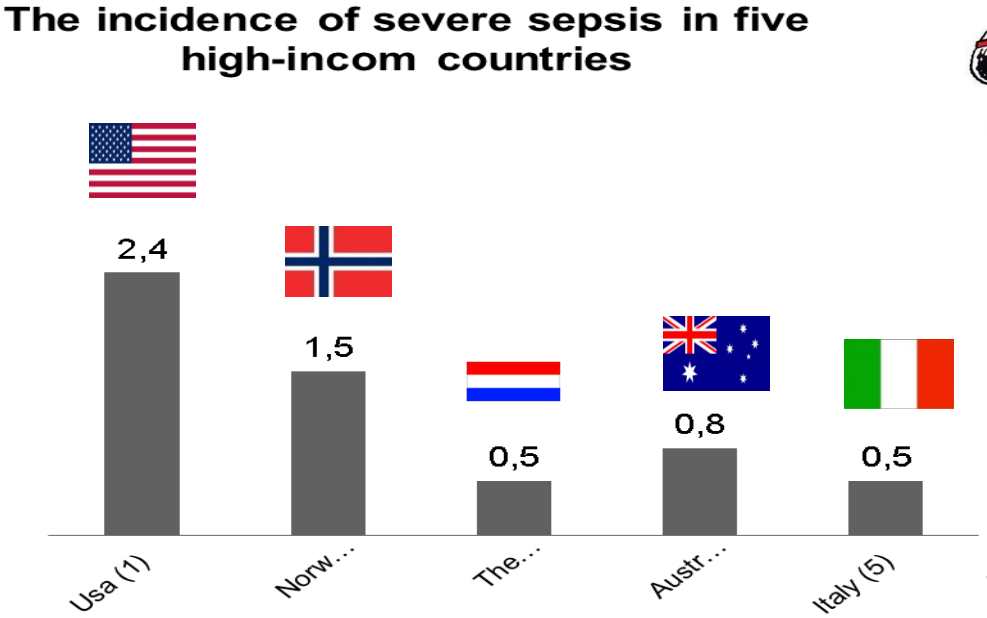
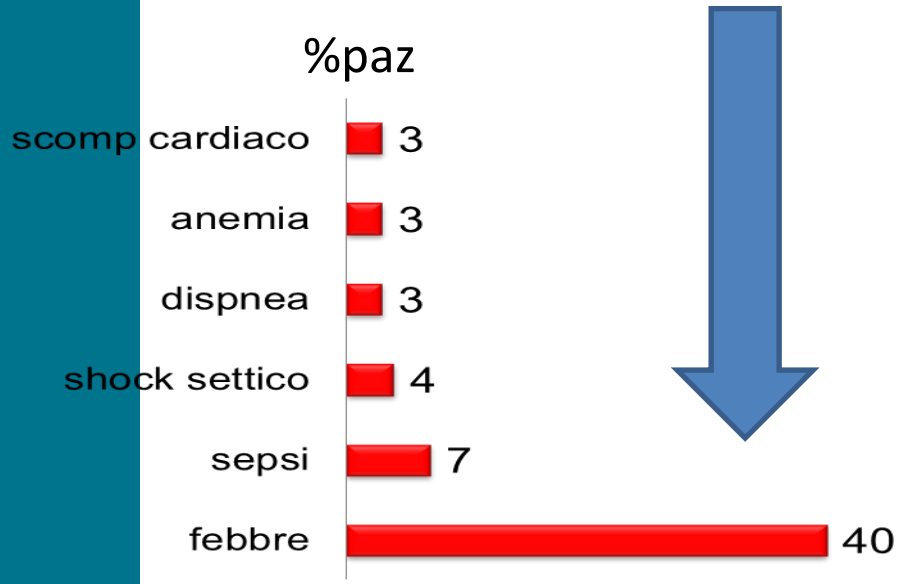
Incidenza sepsi sul totale dei ricoverati



Il **2.36%** (min 0.44%-max 5.46%)
di tutti i pazienti ospedalizzati nelle UO nel periodo di raccolte dati presentavano sepsi

Motivo dell'attuale ricovero – Sepsi



In altri termini…

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I SEI SUPERBATTERI RESISTENTI INDICATI DALL'OMS

World Health Organization

- ESCHERICHIA COLI — Fluorochinoloni, Cefalosporine
- KLEBSIELLA PNEUMONIAE — Carbapenemi, Cefalosporine
- STAPHILOCOCCO AUREO — Meticillina
- PSEUDOMONAS
- ACINETOBACTER BAUMANII
- ENTEROCOCCO


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The SNOOPII study on bloodstream infections: data from FADOI

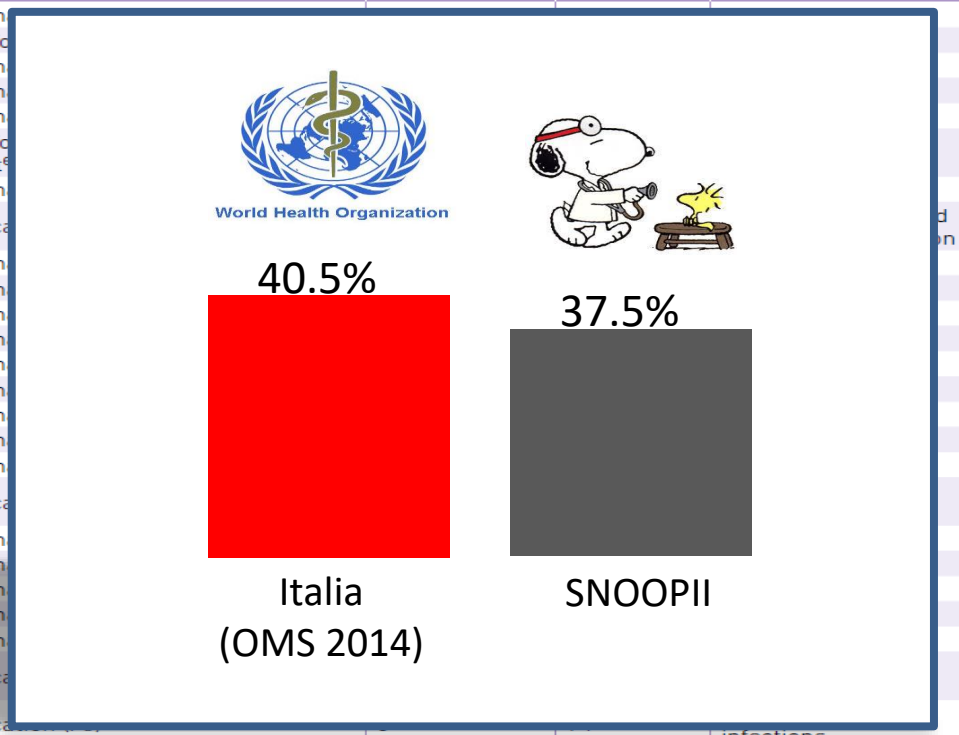
TABLE 2. Main Isolates at Blood Cultures

Isolate or Micro-organism	N (%)
Escherichia coli	184 (29.4)
Staphylococcus aureus	75 (12.0)
Staphylococcus epidermidis	75 (12.0)
Enterococcus faecalis	46 (7,3)
Klebsiella pneumoniae	36 (5,8)
Staphylococcus hominis	29 (4.6)
Enterobacter cloacae	13 (2.1)
Proteus mirabilis	10 (1.6)
Streptococcus pneumoniae	10 (1.6)
Pseudomonas aeruginosa	9 (1.4)

Mazzone A et al. Medicine (Baltimore). 2016;95:e2124.

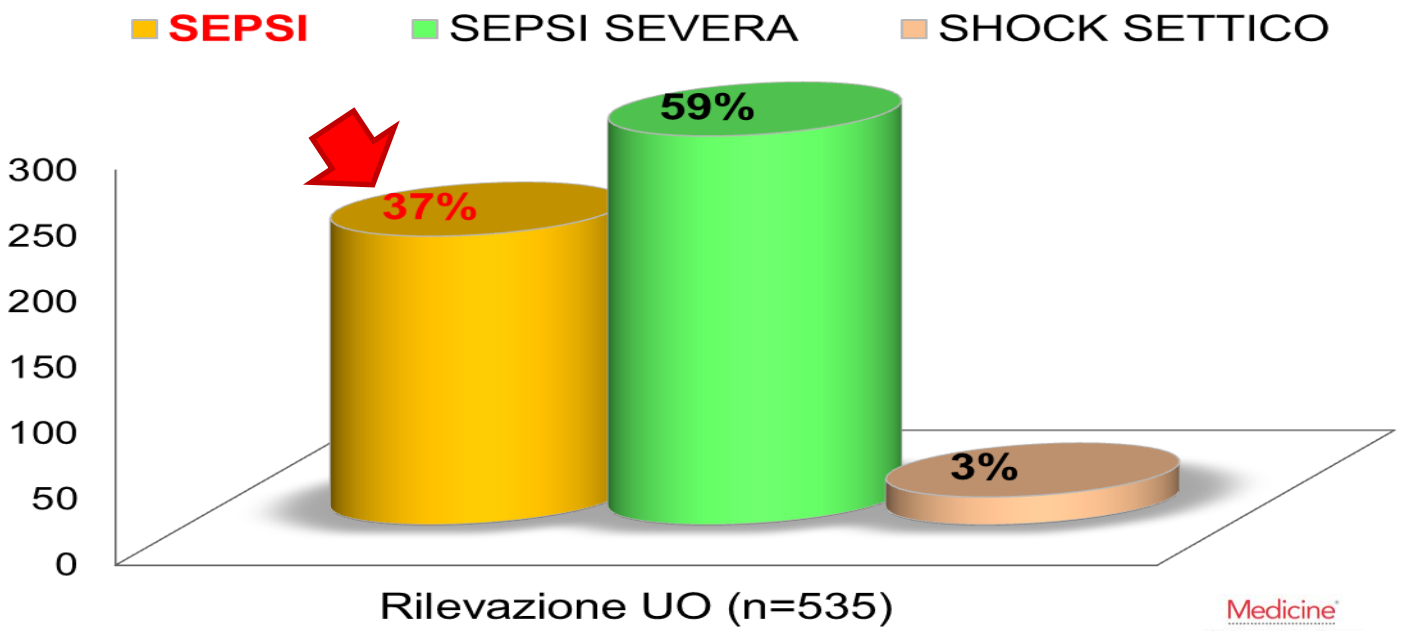
Escherichia coli: resistenze ai fluorochinoloni

Countries, territories and other areas or groupings	Data source[b, c, d]	Resistance (%)	No. tested isolates	Type of surveillance, population or samples[c]	Period for data collection	Year of publication or report
Albania	Nation					2013
Andorra	No info					
Armenia	Nation					2013
Austria	Nation				2011	2013
Azerbaijan	Nation					2013
Belarus	No info report[e]					
Belgium	Nation				2011	2013
Bosnia and Herzegovina	Publica				2004	2010
Bulgaria	Nation				2011	2013
Croatia	Nation				2012	2013
Cyprus	Nation				2011	2013
Czech Republic	Nation				2011	2013
Denmark	Nation				2011	2013
Estonia	Nation				2011	2013
Finland	Nation				2011	2013
France	Nation				2011	2013
Georgia	Nation					2013
Georgia	Publica				2003–2004	2009
Germany	Nation				2011	2013
Greece	Nation				2011	2013
Hungary	Nation				2011	2013
Iceland	Nation				2011	2013
Ireland	Nation				2011	2013
Israel	Publica				(1997)–2004[f]	2008
Israel	Publica			infections	1995–2004	2009
Italy	National data	40.5	1899	Invasive isolates	2011	2013



ANTIMICROBIAL RESISTANCE
Global Report on surveillance 2017

Categorizzazione pazienti – Sepsi



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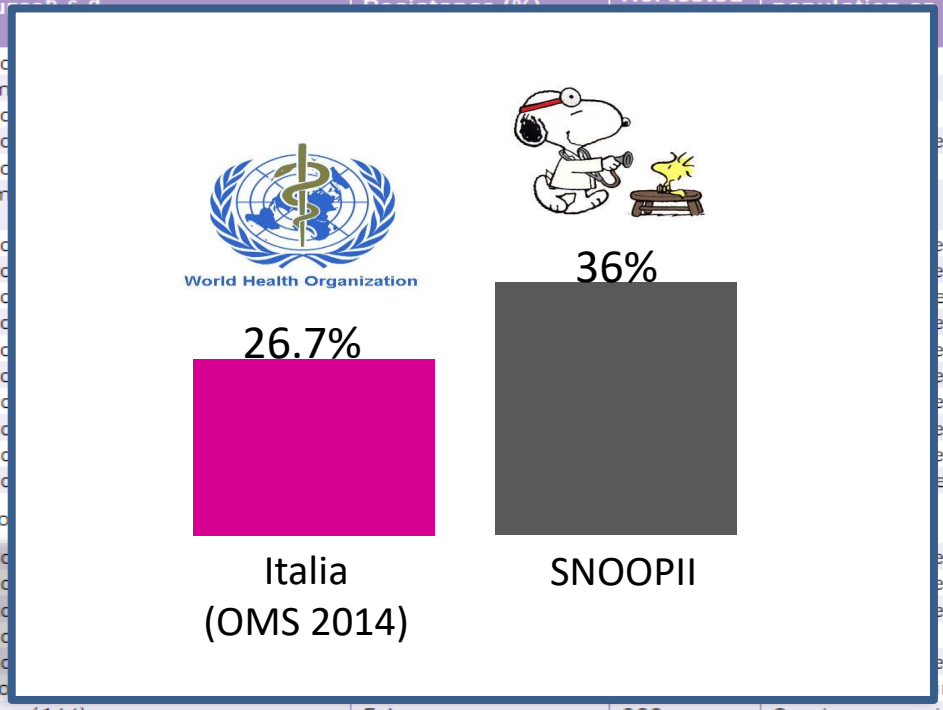
Klebsiella pneumoniae: resistenze ai carbapenemi

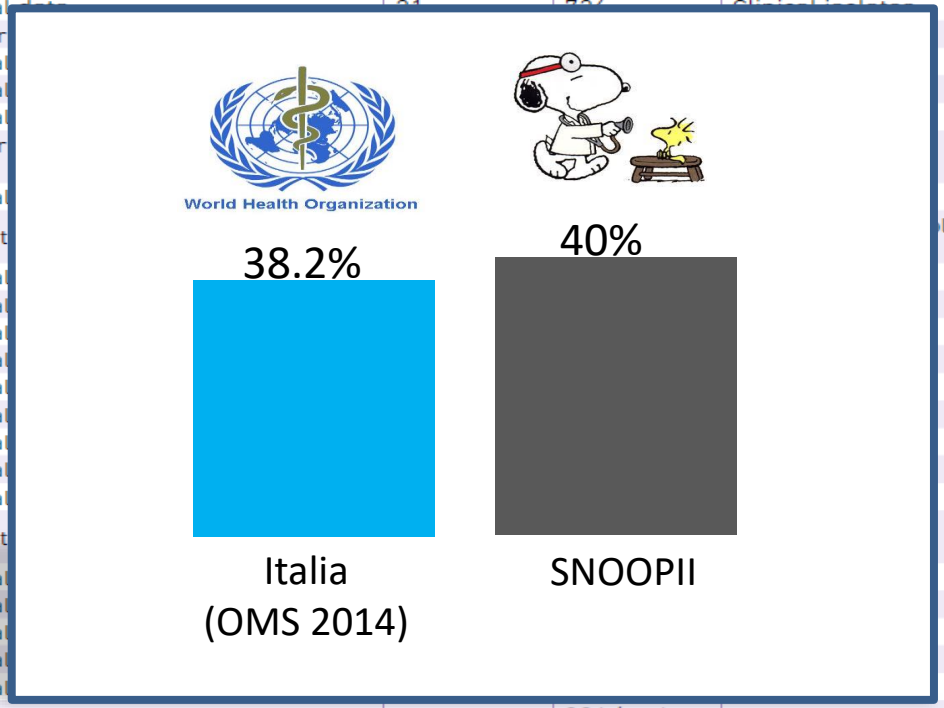
Countries, territories and other areas or groupings	Data sou…	Resistance (%)	No. tested	Type of surveillance, …	Period for data collection	Year of publication or report
Albania	National d…					2013
Andorra	No inform…					
Armenia	National d…					2013
Austria	National d…			…es	2011	2013
Azerbaijan	National d…					2013
Belarus	No inform… report[e]					
Belgium	National d…			…es	2011	2013
Bulgaria	National d…			…es	2011	2013
Croatia	National d…			…e	2012	2013
Cyprus	National d…			…es	2011	2013
Czech Republic	National d…			…es	2011	2013
Denmark	National d…			…es	2011	2013
Estonia	National d…			…es	2011	2013
Finland	National d…			…es	2011	2013
France	National d…			…es	2011	2013
Georgia	National d…			…e	2012	2013
Georgia	Publicatio…				2003–2004	2009
Germany	National d…			…es	2011	2013
Greece	National d…			…es	2011	2013
Hungary	National d…			…es	2011	2013
Iceland	National d…					2013
Ireland	National d…			…es	2011	2013
Israel	Publicatio…			…ng	2007–2008	2012
Israel	Publication (146)	5.4	298	Carrier screening		2010
Italy	National data	26.7	615	Invasive isolates	2011	2013



ANTIMICROBIAL RESISTANCE
Global Report on surveillance 2017

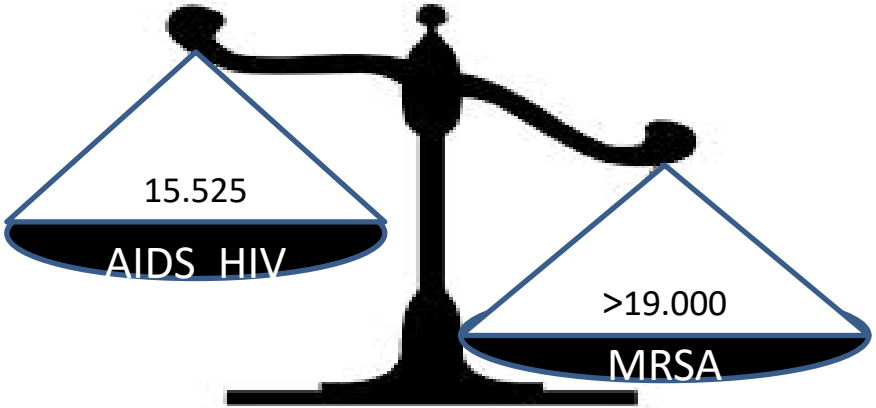
Stafilococco aureo: resistenza alla meticillina (MRSA)

Countries, territories and other areas or groupings	Data source[b, c, d]	Resistance (%)	No. tested isolates	Type of surveillance, population or samples[c]	Period for data collection	Year of publication or report
Albania	National				2011–2012	2013
Andorra	No infor					
Armenia	National					2013
Austria	National				2011	2013
Azerbaijan	National					2013
Belarus	No infor report[e]					
Belgium	National				2011	2013
Bosnia and Herzegovina	Publicat			logy	2006	2009
Bulgaria	National				2011	2013
Croatia	National				2012	2013
Cyprus	National				2011	2013
Czech Republic	National				2011	2013
Denmark	National				2011	2013
Estonia	National				2011	2013
Finland	National				2011	2013
France	National				2011	2013
Georgia	National					2013
Georgia	Publicat				2003–2004	2009
Germany	National				2011	2013
Greece	National				2011	2013
Hungary	National				2011	2013
Iceland	National				2011	2013
Ireland	National				2011	2013
Israel	Publication (69)	48.3	834 (entire period)	Blood isolates	(1997-)2004	2008
Italy	National data	38.2	1261	Invasive isolates	2011	2013



ANTIMICROBIAL RESISTANCE
Global Report on surveillance 2017

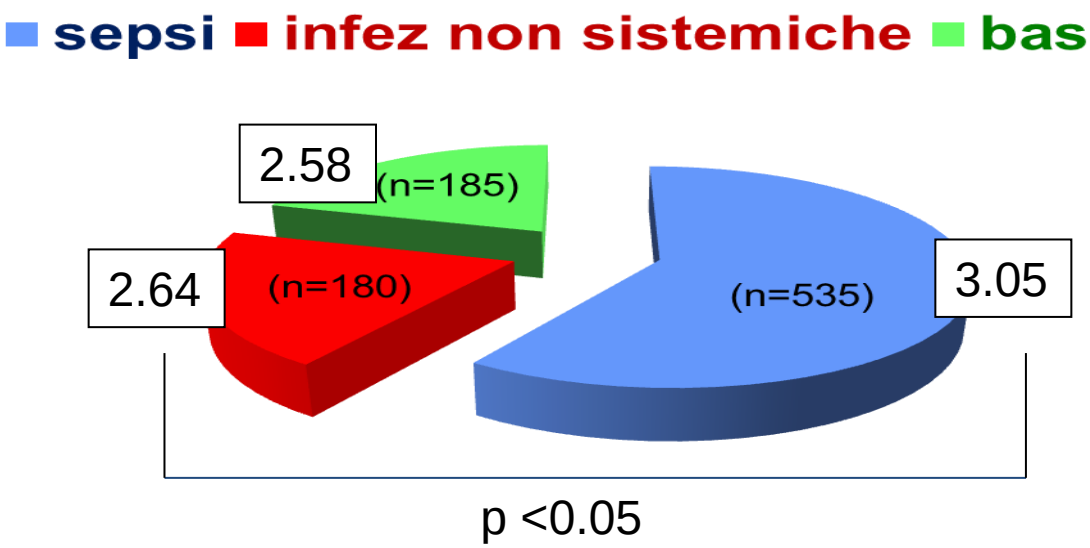
Negli USA le infezioni da MRSA causano un numero maggiore di morti rispetto a HIV ed AIDS



Dati relativi all'anno 2010 forniti da
Centers for Disease Control e Prevention

Kelland K *Antibiotic Resistance Catatrophic: UK Official*
www.medscape.com/viewarticle/780566_printnov 2013

Media delle comorbidità al ricovero per paziente



P value è < 0,05 confrontando sepsi con infezioni non sistemiche e basic, ma non tra questi ultimi due gruppi

Medicine
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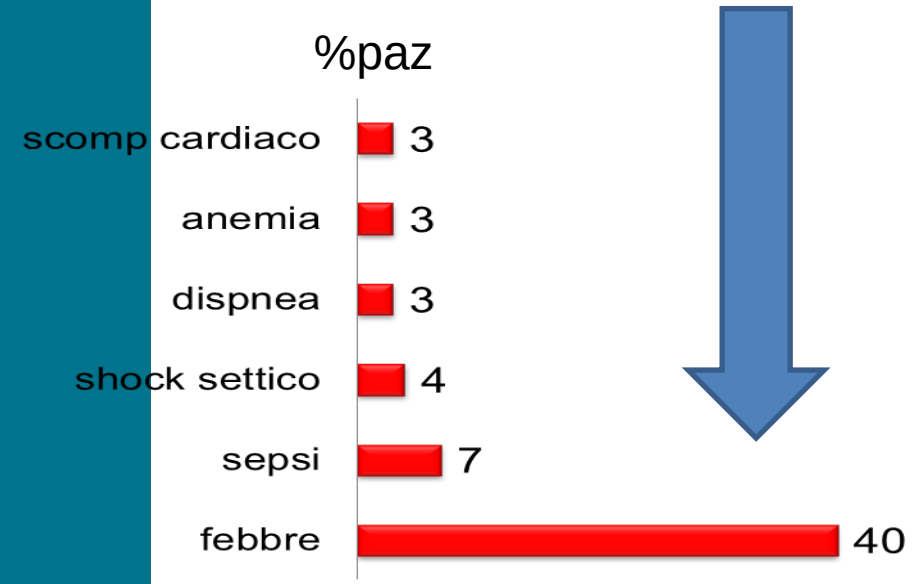
Clinical Features, Short-Term Mortality, and Prognostic Risk Factors of Septic Patients Admitted to Internal Medicine Units
Results of an Italian Multicenter Prospective Study
Antonino Mazzone, MD, Francesco Dentali, MD, Micaela La Regina, MD, Emanuela Foglia, MEcon, Maurizia Gambacorta, MD, Elisabetta Garagiola, MEng, Giorgio Bonardi, MD, Pierangelo Clerici, MD, Ercole Concia, MD, Fabrizio Colombo, MD, and Mauro Campanini, MD

Motivo dell'attuale ricovero – Sepsi



In altri termini…

Medicine
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Distribuzione batteri - Sepsi

Batteri	N.	%
E. coli	184	29,39%
Staphylococcus aureus	75	11,98%
Staphylococcus epidermidis	75	11,98%
Enterococcus faecalis	46	7,35%
Klebsiella pneumoniae	36	5,75%
Staphylococcus hominis	29	4,63%
Enterobacter cloacae	13	2,08%
Proteus mirabilis	10	1,60%
Streptococcus pneumoniae	10	1,60%
Pseudomonas aeruginosa	9	1,44%
Staphylococcus capitis	8	1,28%
Acinetobacter baumannii	7	1,12%
Candida albicans	7	1,12%
Staphylococcus haemolyticus	6	0,96%
Streptococcus mitis	6	0,96%
Staphyloccus capitis	5	0,80%
Streptococcus pyogenes	5	0,80%
Bacteroides fragilis	4	0,64%
Candida parapsilosi	4	0,64%
Gemella haemolysans	4	0,64%
Staphylococcus saprophyticus	4	0,64%
Streptococcus agalactiae	4	0,64%
Candida glabrata	3	0,48%
Candida tropicalis	3	0,48%
Klebsiella	3	0,48%
Klebsiella oxytoca	3	0,48%
Staphylococcus coag neg	3	0,48%
Staphylococcus warneri	3	0,48%
Streptococcus anginosus	3	0,48%
Streptococcus viridans	3	0,48%
Acinobacter	2	0,32%
Bacillus species	2	0,32%
Brucella	2	0,32%
Enterobacter asburiae	2	0,32%
Providencia stuartii	2	0,32%
Staphylococcus lugdunensis	2	0,32%
Staphylococcus xylosus	2	0,32%
Streptococcus mutans	2	0,32%
Acinetobacter	1	0,16%
Acinetobacter lwoffi	1	0,16%
Aeromonas hidrophila	1	0,16%
Candida non albicans	1	0,16%
Candida sake	1	0,16%
Candida spp	1	0,16%
Citrobacter Braakii	1	0,16%
Citrobacter freundii	1	0,16%
Corinebacterium species	1	0,16%
Enterobacte aerogenes	1	0,16%
Enterococcus	1	0,16%
Enterococcus avium	1	0,16%
Enterococcus casseliflavus	1	0,16%
Enterococcus cloacae	1	0,16%
Enterococcus gallinarum	1	0,16%
Enterococcus spp	1	0,16%
Fusobacterium Necrophorum	1	0,16%
Fusobacterium nucleatum	1	0,16%
Klebsiella planticola	1	0,16%
Kocuria varians	1	0,16%
Propionebacterium acnes	1	0,16%
Pseudomonas fluorescens	1	0,16%
Rothia mucillaginosa	1	0,16%
Salmonella	1	0,16%
Serratia marcescens	1	0,16%
Sphingomonas paucimobilis	1	0,16%
Staphylococcus cohnii	1	0,16%
Staphylococcus lentus	1	0,16%
Staphylococcus sanguinis	1	0,16%
Staphylococcus simulans	1	0,16%
Streptococcus aeruginosa	1	0,16%
Streptococcus gallolyticus	1	0,16%
Streptococcus group G	1	0,16%
Streptococcus oralis	1	0,16%
Streptococcus uberis	1	0,16%
Totale	**626**	**100,00%**

European Journal of Internal Medicine xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Predicting resistant etiology in hospitalized patients with blood cultures positive for Gram-negative bacilli

Falcone Marco[a,*], Tiseo Giusy[b], Dentali Francesco[c], La Regina Micaela[d], Foglia Emanuela[e], Gambacorta Maurizia[f], Garagiola Elisabetta[e], Bonardi Giorgio[g], Clerici Pierangelo[f], Colombo Fabrizio[h], Farcomeni Alessio[a], Concia Ercole[i], Corrao Salvatore[j], Campanini Mauro[k], Mazzone Antonino[g]

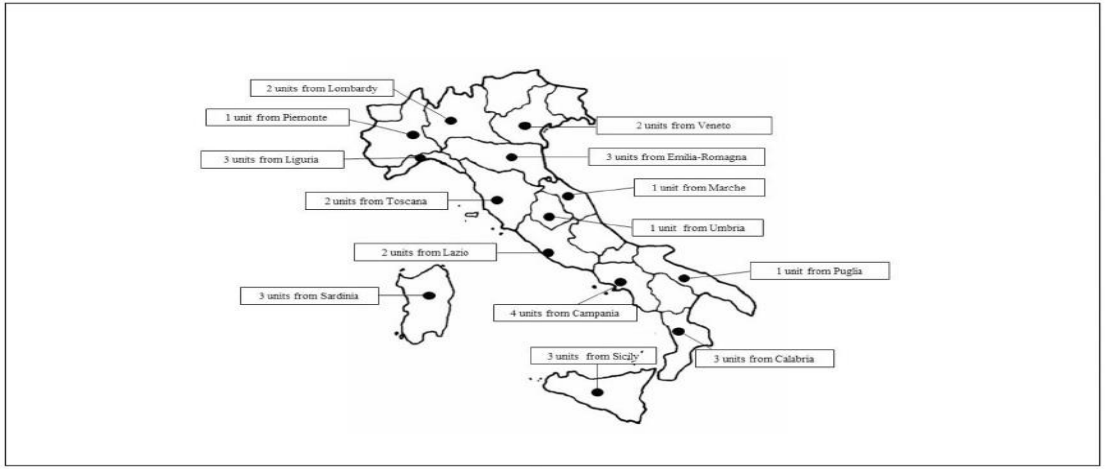
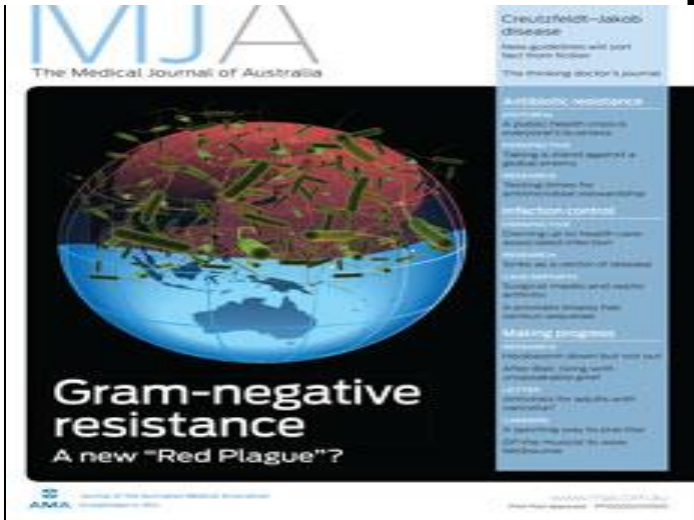
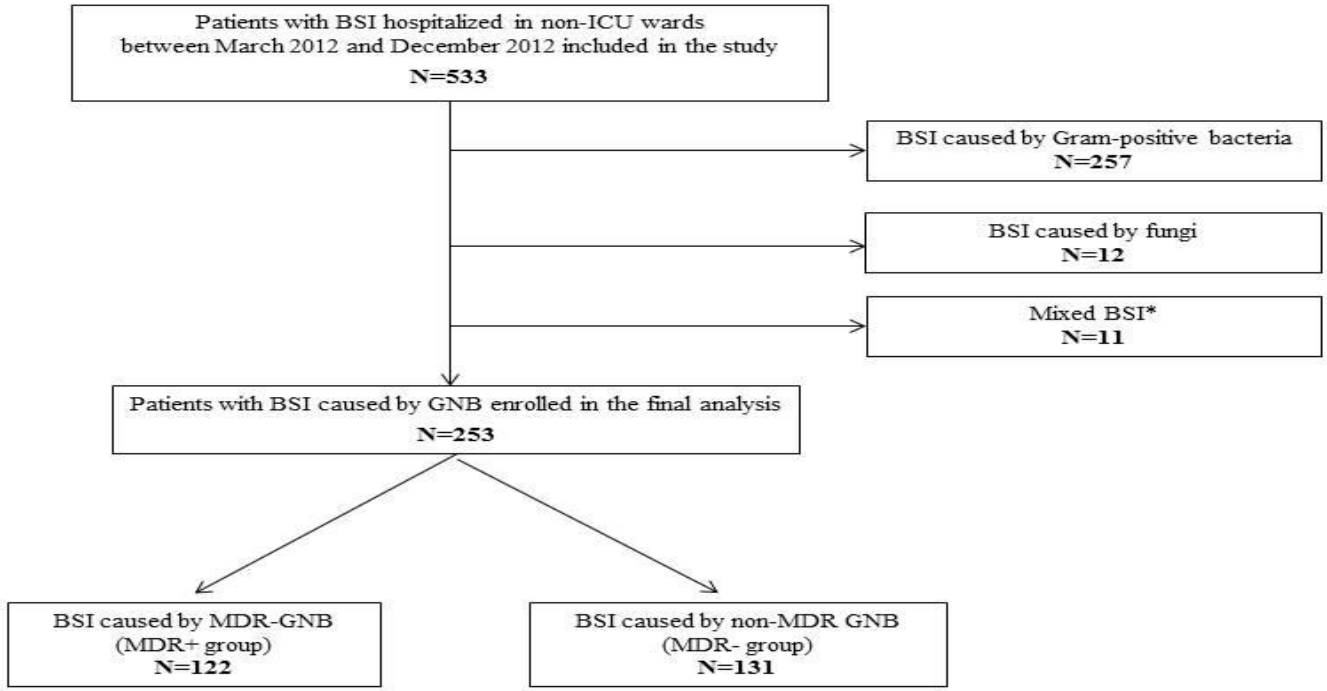


Fig. 1. Geographical distribution of the 31 Internal Medicine units from 14 different Italian regions participating to the study.



Study flow diagram



* Mixed etiology: 3 Gram-positive bacteria+fungi, 8 Gram-positive + Gram-negative bacteria

Falcone M… and Mazzone A 2018;EUR J INT MED 2018

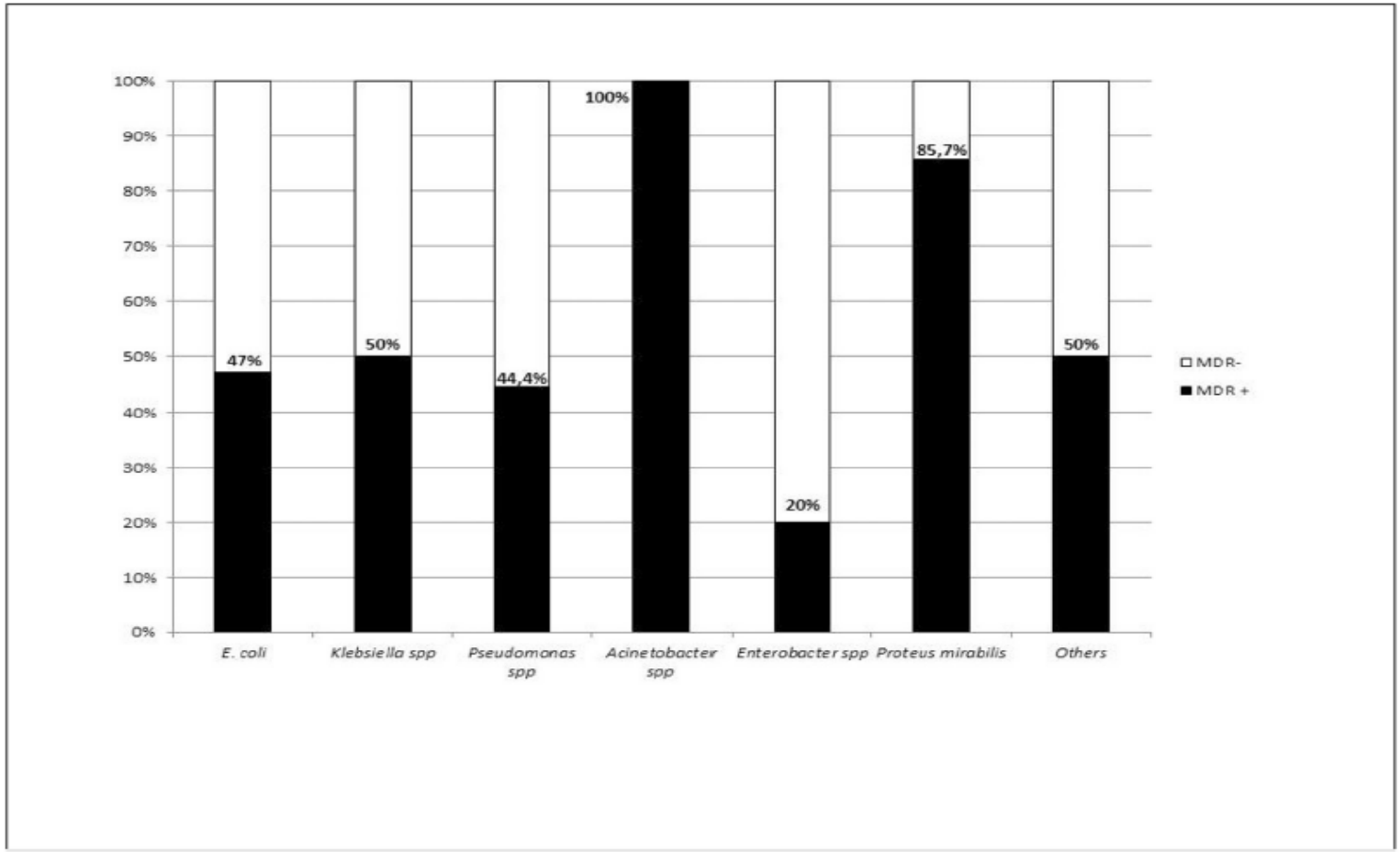


Fig. 3. Percentage of MDR organisms for each microbial species.

Etiology of bacteremia due to MDR Gram-negative bacilli and those caused by non MDR Gram-negative bacilli

	GNB MDR+ N= 122	GNB MDR- N= 131	p value
Escherichia coli	77 (63.1%)	87 (66.4%)	0.583
Klebsiella spp	19 (15.6%)	19 (14.5%)	0.812
Pseudomonas spp	4 (3.3%)	5 (3.8%)	0.817
Acinetobacter spp	7 (5.7%)	0	0.005
Enterobacter spp.	3 (2.5%)	12 (9.2%)	0.024
Proteus mirabilis	6 (4.9%)	1 (0.8%)	0.044
Bacteroides fragilis	1 (0.8%)	3 (2.3%)	0.349
Providencia stuartii	2 (1.6%)	0	0.141
Others*	3 (2.5%)	4 (3.1%)	0.773

BSI due to *Enterococcus* spp

	Survivors N= 31	Non-survivors N=10	p value
Demographic characteristics			
Age, years, median (IQR)	**69 (65-79)**	**84.5 (77.25-88)**	**0.009**
Gender, male	13 (41.9%)	7 (70%)	0.123
Hospitalization in the last 3 month	**11 (35.5%)**	**9 (90%)**	**0.003**
Community-acquired	9 (29%)	0	0.054
Healthcare associated	**10 (32.3%)**	**7 (70%)**	**0.035**
Nosocomial	12 (38.7%)	3 (30%)	0.619
Comorbid conditions			
Solid malignancy	6 (19.4%)	3 (30%)	0.479
COPD	7 (22.6%)	3 (30%)	0.635
Liver disease	4 (12.9%)	1 (10%)	0.807
Chronic kidney disease	7 (22.6%)	2 (20%)	0.864
Diabetes	11 (35.5%)	5 (50%)	0.413
SOFA score, median (IQR)	**2 (1-4)**	**12.5 (6-14.5)**	**<0.001**
Fever (>38° C)	28 (90.3%)	10 (100%)	0.307
Source of infection			
Genitourinary tract	9 (29%)	6 (60%)	0.077
Respiratory tract	8 (25.8%)	0	0.073
Gastrointestinal tract	8 (25.8%)	1 (10%)	0.294
Skin or soft tissue	4 (12.9%)	1 (10%)	0.807
CVC	1 (3.2%)	1 (10%)	0.387

MDR GNB versus non-MDR GNB

	GNB MDR+ N= 122	GNB MDR- N= 131	p value
Demographic characteristics			
Age, years, median (IQR)	80 (69-85)	74 (69-82)	0.492
Age ≥75 ys	78 (63.9%)	64 (48.9%)	0.016
Gender, male	60 (49.2%)	67 (51.1%)	0.755
Hospital admission in the last 3 month	71 (58.2%)	38 (28.6%)	<0.001
Antibiotic treatment in the last 3 months	67 (54.9%)	41 (30.8%)	<0.001
Way of acquisition			
Community-acquired	31 (25.4%)	61 (46.6%)	0.001
Healthcare associated	63 (51.6%)	43 (32.8%)	0.002
Nosocomial	28 (23%)	27 (20.6%)	0.652
Transfer from LTCF	12 (9.8%)	1 (0.7%)	0.001
Comorbid conditions			
Solid malignancy	40 (32.8%)	33 (24.8%)	0.183
Neutropenia	4 (3.3%)	3 (2.3%)	0.632
Cardiovascular disease	67 (54.9%)	81 (60.9%)	0.265
COPD	28 (22.9%)	32 (24.1%)	0.783
Liver disease	15 (12.3%)	30 (22.6%)	0.028
Chronic kidney disease	41 (33.6%)	31 (23.3%)	0.080
Diabetes	35 (28.7%)	46 (34.6%)	0.274
Charlson Comorbidity Index, median (IQR)	3 (2-5)	3 (2-5)	0.471

Falcone M… and Mazzone A 2018;EUR J INT MED 2018

Multivariate analysis of risk factors for bacteremia due to MDR-GNB

	Multivariate analysis			
	OR	95.0% CI		p-value
		Lower	Upper	
Transfer from LTCF	9.013	1.089	74.579	***0.041***
Hospitalization in the last 90 days	2.882	1.580	5.259	***0.001***
Indwelling urinary catheter	2.315	1.202	4.459	***0.012***
Antibiotic therapy in the last 90 days	1.882	1.041	3.405	***0.036***
Age ≥75 ys	1.866	1.076	3.237	***0.026***

Falcone M… and Mazzone A 2018;EUR J INT MED 2018

SCORE

Variables	Score
Transfer from LTCF	+4
Hospitalization in the last 90 days	+2
Indwelling urinary catheter	+2
Antibiotic therapy in the last 90 days	+1
Age ≥75 ys	+1
Cut off for negative risk score: 0 (sensitivity 98%, specificity 6%, negative LR 0.10)	
Cut off for positive risk score: >6 (sensitivity 9%, specificity 99%, positive LR 11.8)	

SCORE = 0 (no item) → **Exclude MDR etiology with a good level of confidence**

SCORE 0-6 → **GREY ZONE (Clinical judgment, new rapide susceptibility test?)**

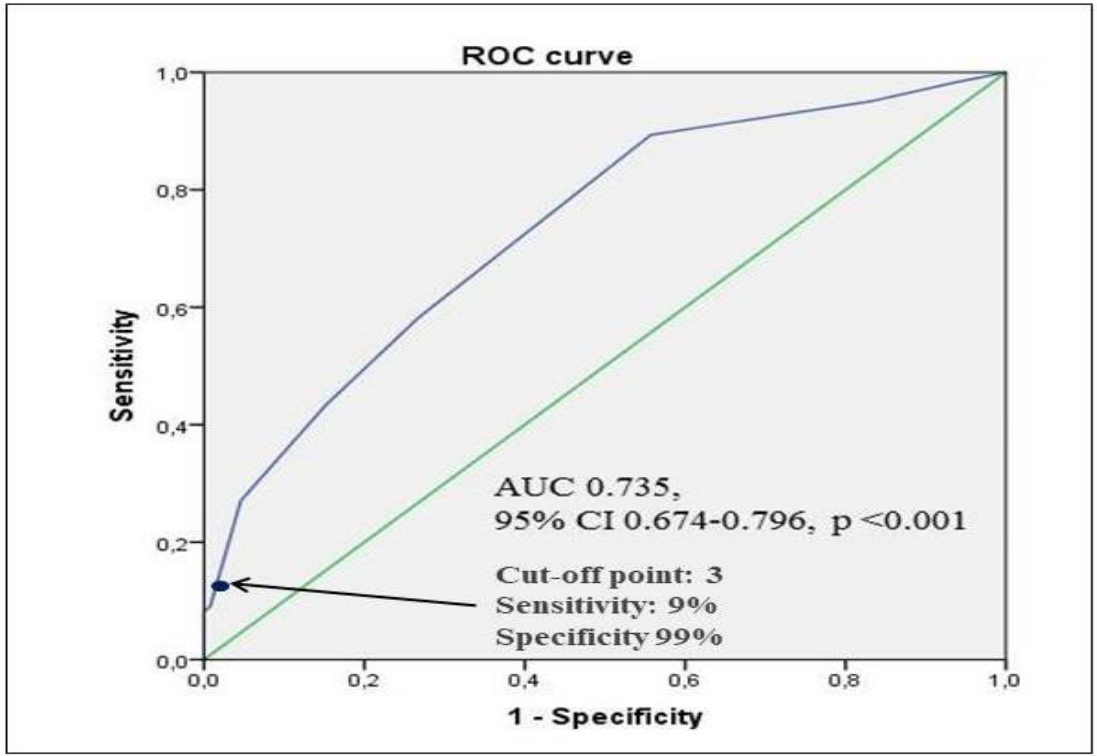
SCORE > 6 → **Evaluate broad spectrum therapy**

Percentage of GNB-MDR strains according to score

Score	Number of patients	MDR (%)
0	10	2 (20%)
1	18	4 (22.2%)
2	43	7 (16.3%)
3	76	38 (50%)
4	33	18 (54%)
5	34	20 (58.8%)
6	27	22 (81.5%)
7	2	1 (50%)
≥8	10	10 (100%)

Falcone M… and Mazzone A 2018;EUR J INT MED 2018

ROC curve of score for MDR etiology among patients with GNB bloodstream infection



Falcone M… and Mazzone A 2018:EUR J INT MED 2018

Early alert from the microbiology laboratory improves the outcome of elderly patients with *Enterococcus* spp. bloodstream infection: Results from a multicentre prospective study

M. Falcone[a,*], G. Tiseo[b], F. Dentali[c], E. Foglia[d], M. Campanini[e], F. Menichetti[a], A. Mazzone[f], on behalf of the FADOI (Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti) and GISA (Italian Group for Antimicrobial Stewardship)

[a] *Division of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy*
[b] *Department of Internal Medicine and Medical Specialties, 'Sapienza' University of Rome, Rome, Italy*
[c] *Department of Clinical Medicine, University of Insubria, Varese, Italy*
[d] *Centre for Research on Health Economics, Social and Health Care Management (CREMS), University Carlo Cattaneo–LIUC, Castellanza, Italy*
[e] *Internal Medicine Ward, Ospedale Maggiore della Carità, Novara, Italy*
[f] *Internal Medicine Ward, Ospedale Civile, Legnano, Italy*

In conclusion, BSI due to *Enterococcus* spp. in elderly patients is associated with a high risk of in-hospital mortality. Presence of a polymicrobial infection, age and SOFA score on the day of BSI were factors associated with increased mortality. Conversely, an early alert from the microbiology laboratory before obtaining blood cultures results can help clinicians to select appropriate antimicrobial therapy, thus improving patient survival. Rapid and efficacious communication from the microbiology laboratory to clinical units is crucial and should be implemented in hospital settings

Journal of Global Antimicrobial Resistance 18 (2019) 139–144

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

journal homepage: www.elsevier.com/locate/jgar

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Table 3
Cox regression analysis of risk factors for in-hospital mortality in patients with bloodstream infection due to *Enterococcus* spp.

Risk factor	HR (95% CI)	*P*-value
Polymicrobial infection	9.100 (1.295–63.949)	0.026*
Age	1.261 (1.029–1.546)	0.025*
SOFA score	1.244 (1.051–1.474)	0.011*
Alert from clinical microbiology laboratory	0.073 (0.007–0.805)	0.033*

HR, hazard ratio; CI, confidence interval; SOFA, Sequential Organ Failure Assessment.
* Statistically significant ($P \leq 0.05$).

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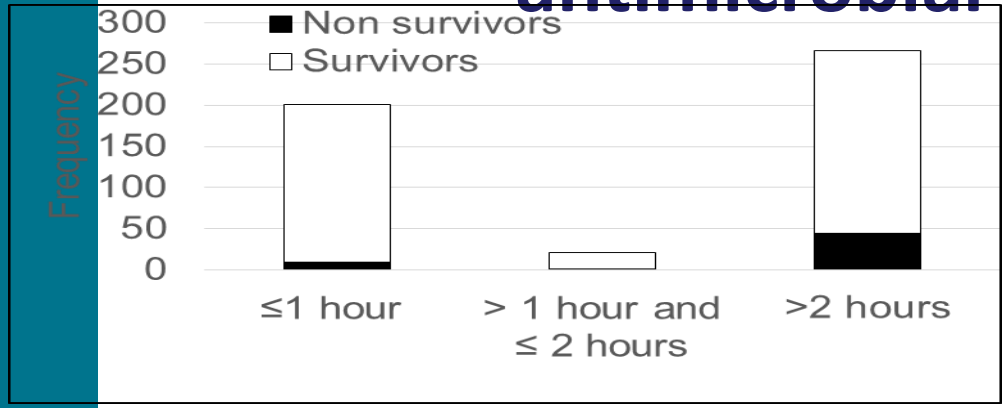
Time from sepsis recognition to adequate antimicrobial therapy

Time from sepsis diagnosis to adequate antimicrobial therapy	All patients (N=533)	Patients with sepsis (N=488)	Patients with septic shock (N=45)
≤1 hour	N (%) 214 (40.2%) Mortality **14 (6.5%)**	N (%) 201 (41.2%) Mortality **10 (5%)**	N (%) 13 (51.1%) Mortality **4 (30.8%)**
1 hour and ≤ 2 hours	N (%) 26 (4.9%) Mortality **2 (7.7%)**	N (%) 21 (4.3%) Mortality **1 (4.8%)**	N (%) 5 (11.1%) Mortality **1 (20%)**
>2 hours	N (%) 293 (54.9%) Mortality **59 (20.1%)**	N (%) 266 (54.5%) Mortality **45 (16.9%)**	N (%) 27 (60%) Mortality **14 (51.9%)**

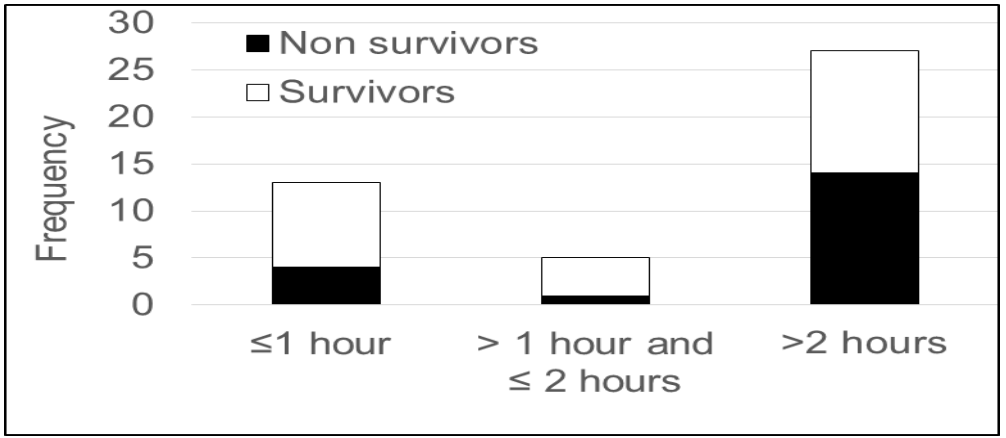
SNOOPII Study data

Time from sepsis recognition to adequate antimicrobial therapy



Patients with sepsis

Patients with septic shock



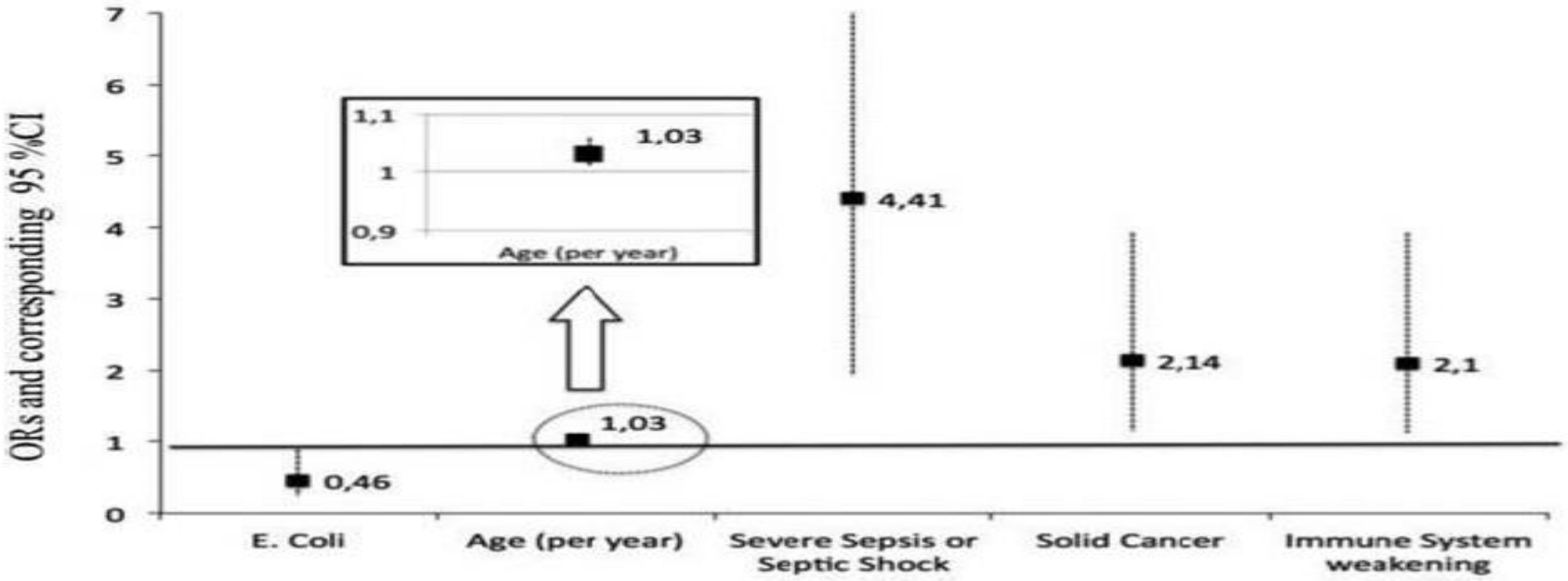


FIGURE 2. Independent predictors of in-hospital mortality at multivariate analysis. CI = confidence interval, ORs = odds ratios.

Medicine
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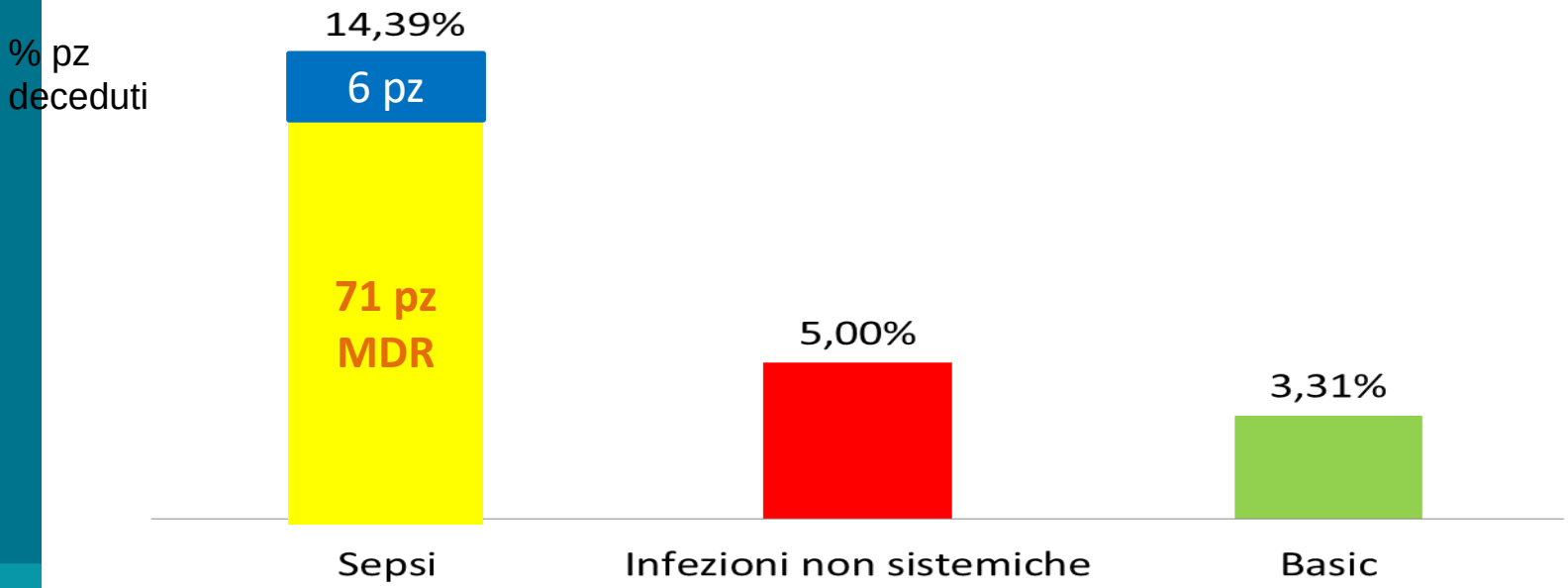
Mortalità


% pz deceduti
14,39%
6 pz
71 pz MDR
5,00%
3,31%
Sepsi
Infezioni non sistemiche
Basic

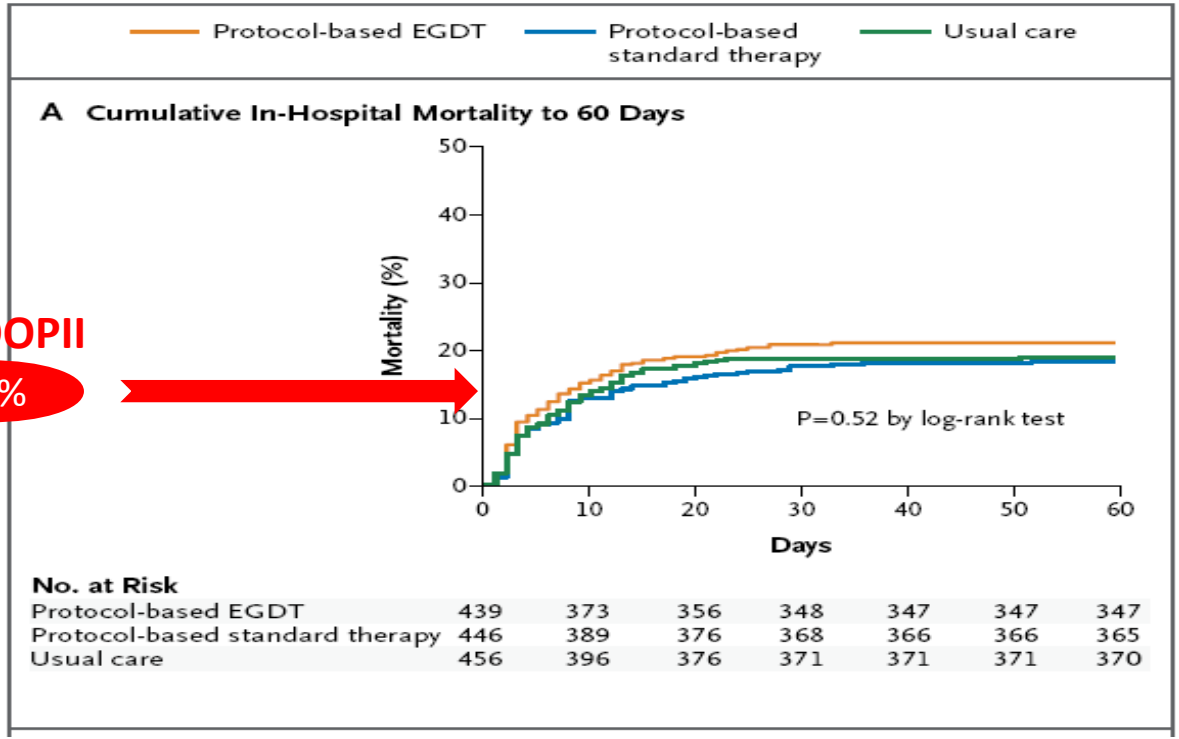
ORIGINAL ARTICLE

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

STUDIO SNOOPII

14%



NEJM 2014; 370:1683-93

ORIGINAL ARTICLE

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc., David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grieve, Ph.D., Rahi Jahan, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D., Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, D.M., and Kathryn M. Rowan, Ph.D., for the ProMISe Trial Investigators*

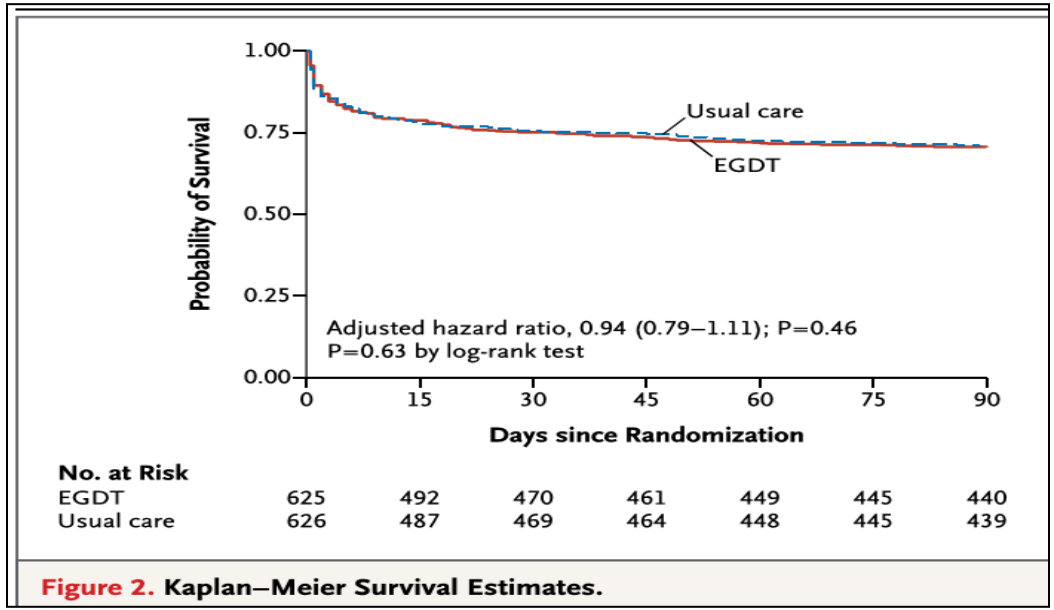


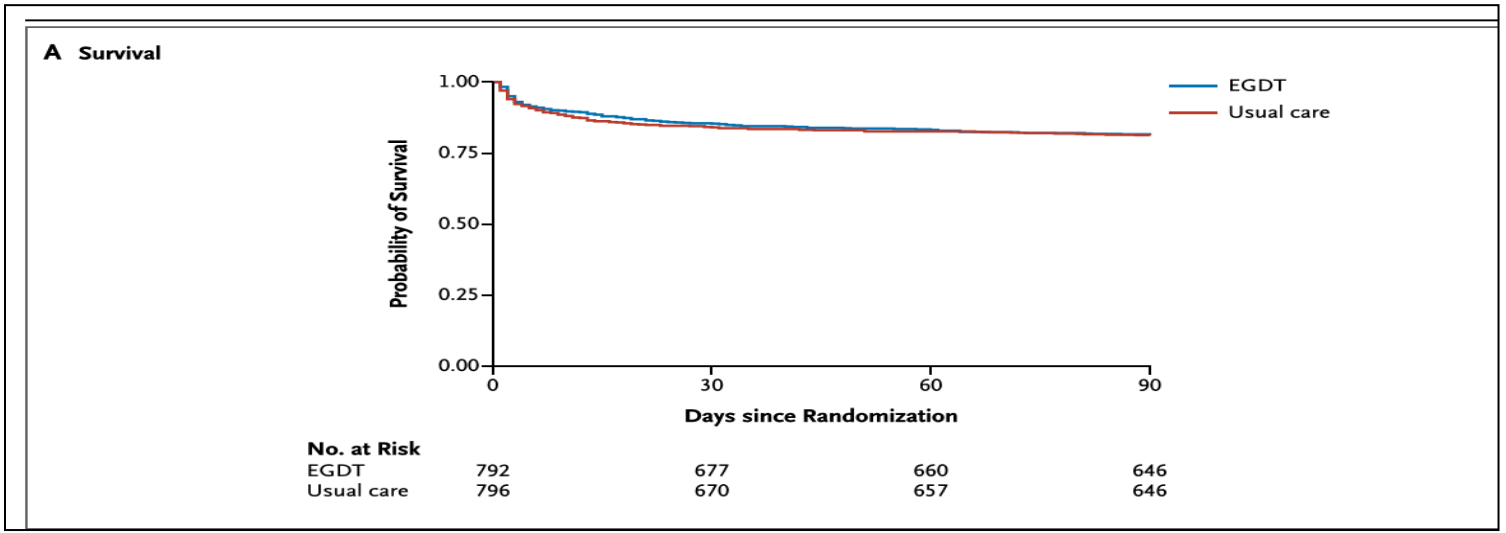
Figure 2. Kaplan–Meier Survival Estimates.

Mouncey PR et al. N Engl J Med 2015;372:1301-11

ORIGINAL ARTICLE

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*



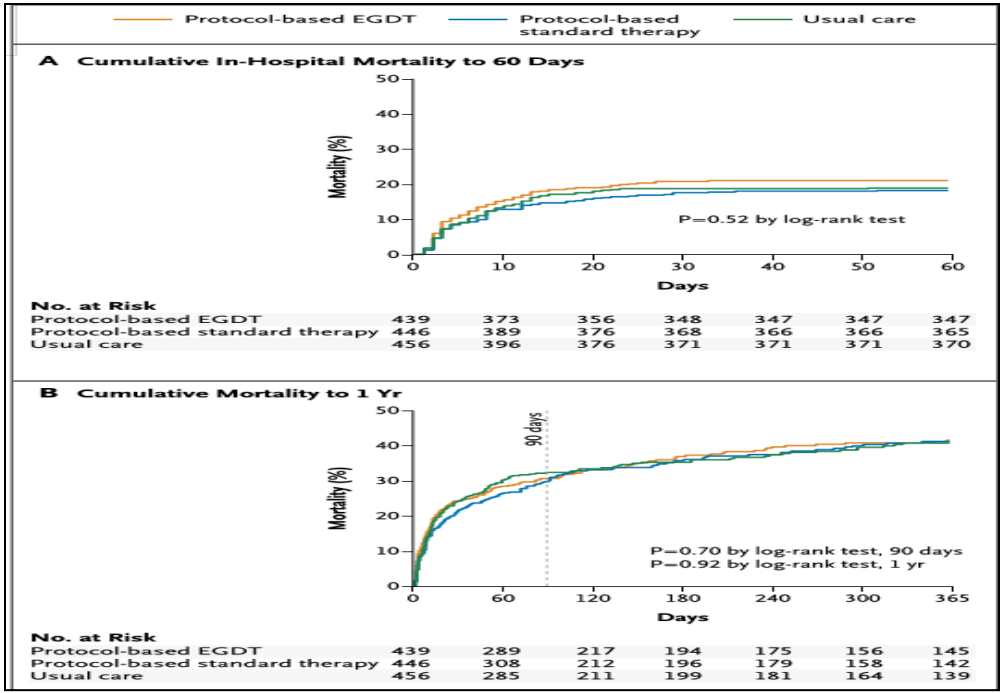
N Engl J Med 2014;371:1496-506

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*



N Engl J Med 2014;370:1683-93.

Time from sepsis recognition to adequate antimicrobial therapy

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

The ProCESS Trial — A New Era of Sepsis Management

Craig M. Lilly, M.D.

Indeed, septic shock was recognized early in a majority of the patients; 76% of the patients received antimicrobial agents by the time they underwent randomization, which occurred a mean of approximately 3 hours after patients' arrival in the emergency department. The rate of intravenous antimicrobial administration 6 hours after randomization was approximately 97%, a finding that suggests that notification that septic shock is present encourages the administration of antibiotics. A study that attributed in-

NEJM 2014; 370:1750-51

Impact of early antimicrobial therapy on mortality

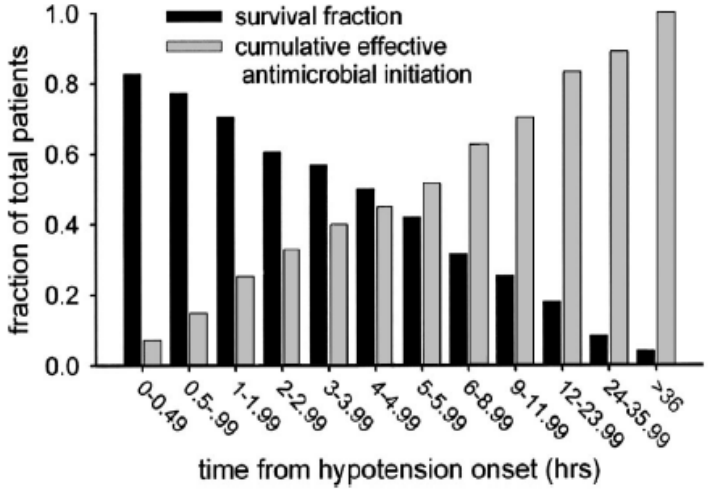


Figure 1. Cumulative effective antimicrobial initiation following onset of septic shock-associated hypotension and associated survival. The x-axis represents time (hrs) following first documentation of septic shock-associated hypotension. *Black bars* represent the fraction of patients surviving to hospital discharge for effective therapy initiated within the given time interval. The *gray bars* represent the cumulative fraction of patients having received effective antimicrobials at any given time point.

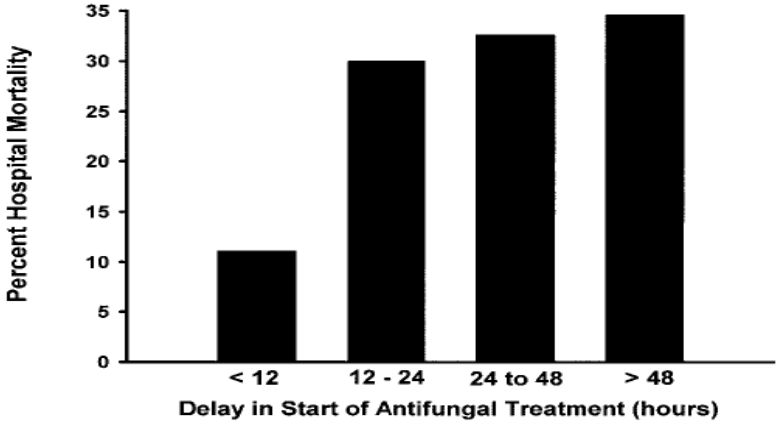


FIG. 1. Relationship between hospital mortality and the timing of antifungal treatment. The timing of antifungal therapy was determined to be from the time when the first blood sample for culture positive for fungi was drawn to the time when antifungal treatment was first administered to the patient.

Bacterial sepsis

Kumar et al., Clin. Care Med., 2006

Candidemia

Morrell et al., AAC, 2005

Timing emocoltura e somministrazione Antibiotico terapia

Ore tra sospetto sepsi e prima emocoltura positiva (effettuata durante il ricovero)	N.	%
< 1 ora	328	73,54%
tra 1 ora e 2 ore	0	0,00%
tra 2 ora e 3 ore	0	0,00%
tra 3 ore e 4 ore	0	0,00%
>4 ore	118	26,46%
Totale	**446**	**100,00%**

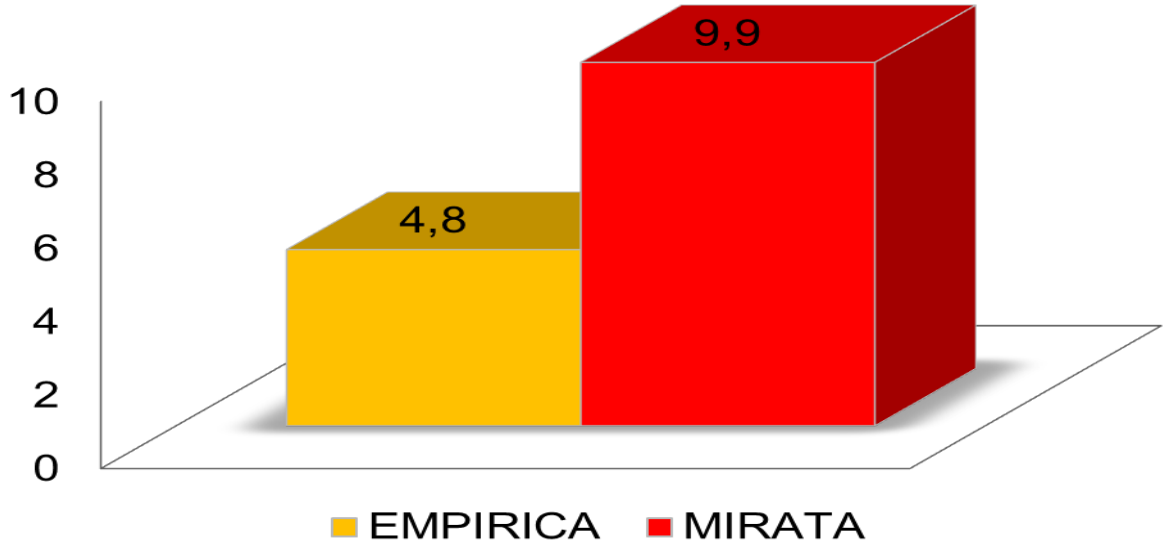
Sepsi

Il tempo tra il sospetto di sepsi e la prima emocoltura non è distribuito come una normale. Ci sono due fasce principali:

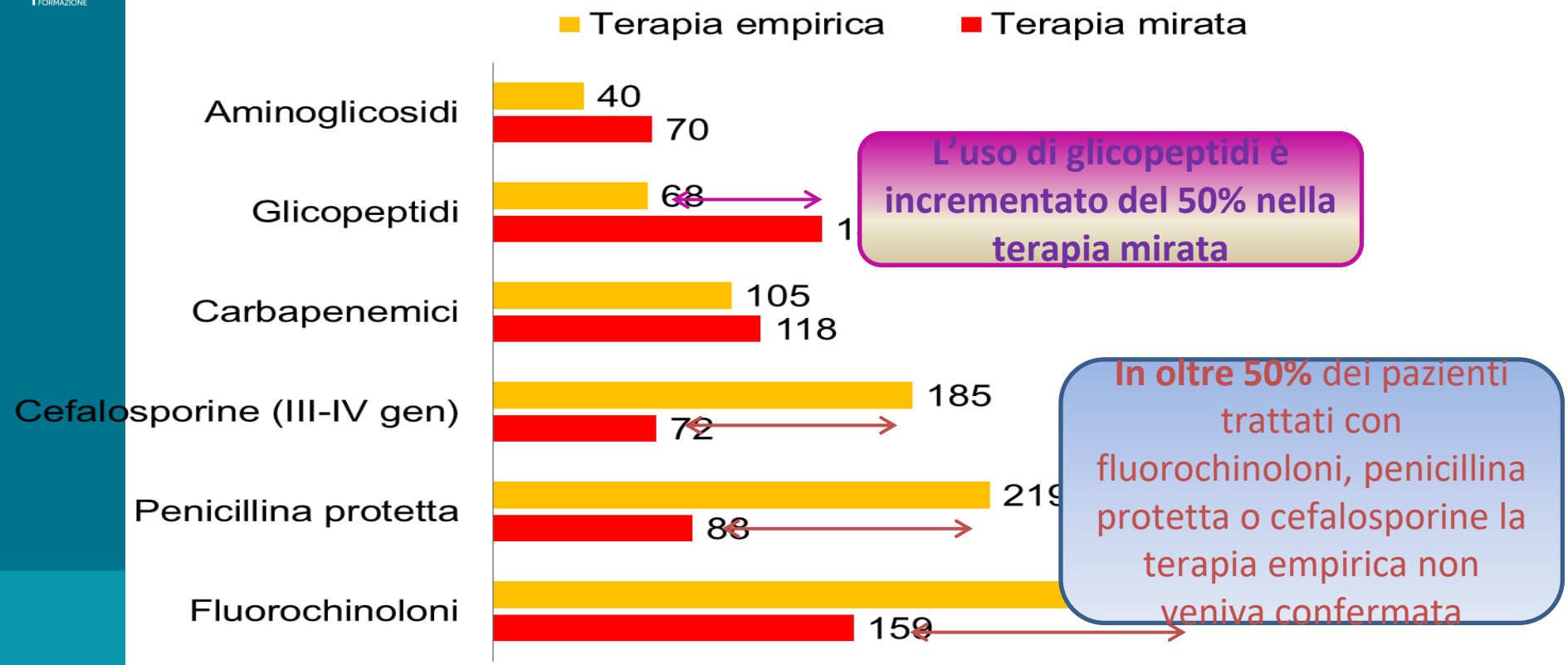
- richiesta di emocoltura in concomitanza con il sospetto di sepsi, per il 74% della popolazione
- richiesta di emocoltura dopo molte ore dal sospetto di sepsi, per il 26% della popolazione

Timing terapia antibiotica –Sepsi

Durata media (giorni) della terapia antibiotica empirica e mirata



Categorie di Antibiotici utilizzati-Sepsi



L'uso di glicopeptidi è incrementato del 50% nella terapia mirata

In oltre 50% dei pazienti trattati con fluorochinoloni, penicillina protetta o cefalosporine la terapia empirica non veniva confermata

QJM: An International Journal of Medicine, 2017, 369–373

doi: 10.1093/qjmed/hcw229
Advance Access Publication Date: 9 January 2017
Original paper

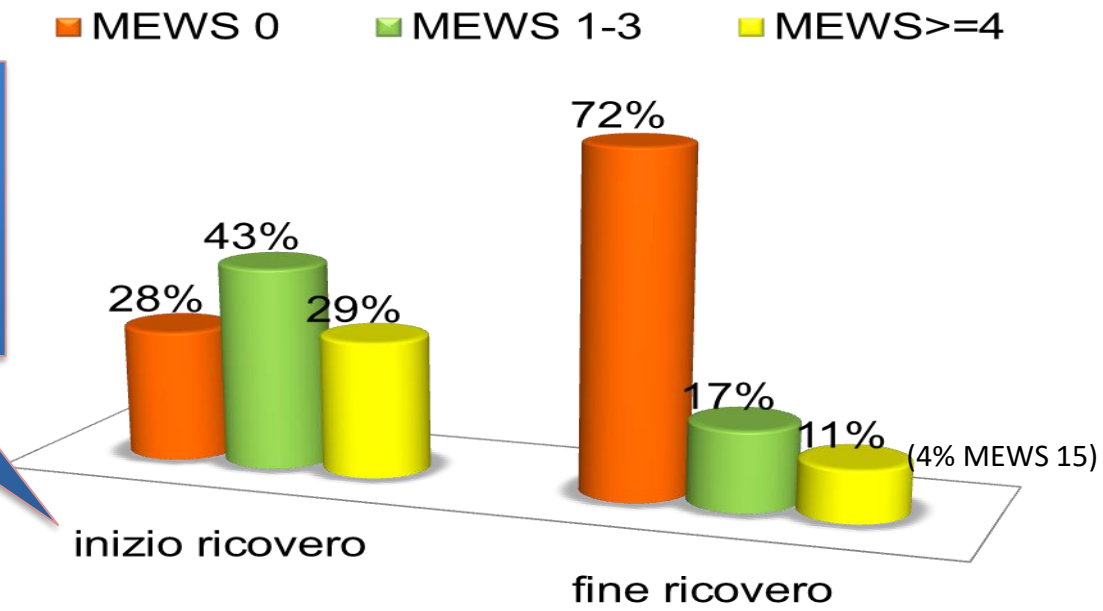
ORIGINAL PAPER

Evaluation of the threshold value for the modified early warning score (MEWS) in medical septic patients: a secondary analysis of an Italian multicentric prospective cohort (SNOOPII study)

D. Tirotta[1], M. Gambacorta[2], M. La Regina[3], T. Attardo[4], A. Lo Gullo[3,5], F. Panzone[6], A. Mazzone[7], M. Campanini[8] and F. Dentali[9]

MEWS – Sepsi

MEWS medio all'ingresso:
non deceduti =2.32
vs
deceduti =3.36



MEWS **è fallito** nel discriminare il **rischio** di **mortalità** a **breve termine** (sensibilità 34%, specificità 83.6%) in un'ampia coorte di pazienti settici ricoverati in UO di Medicina Interna

EMJ Online First, published on February 21, 2018 as 10.1136/emermed-2017-207120
Original article

qSOFA, SIRS and NEWS for predicting inhospital mortality and ICU admission in emergency admissions treated as sepsis

Robert Goulden,[1] Marie-Claire Hoyle,[1] Jessie Monis,[1] Darran Railton,[1] Victoria Riley,[1] Paul Martin,[1] Reynaldo Martina,[2] Emmanuel Nsutebu[1]

Table 2 Prognostic accuracy of scoring systems (95% CI) for predicting inhospital death and ICU admission in patients with suspected sepsis

	qSOFA	SIRS	NEWS
Inhospital death			
Sensitivity, %	37 (31 to 43)	80 (74 to 84)	74 (68 to 79)
Specificity, %	79 (77 to 81)	21 (19 to 23)	43 (41 to 46)
Positive predictive value, %	23 (19 to 28)	15 (13 to 17)	18 (16 to 21)
Negative predictive value, %	88 (86 to 90)	86 (82 to 89)	91 (88 to 93)
Positive likelihood ratio	1.78 (1.48 to 2.14)	1.01 (0.94 to 1.08)	1.30 (1.19 to 1.41)
Negative likelihood ratio	0.80 (0.72 to 0.88)	0.96 (0.75 to 1.25)	0.61 (0.55 to 0.61)
AUROC	0.62 (0.59 to 0.66)	0.49 (0.45 to 0.52)	0.65 (0.61 to 0.68)
ICU admission			
Sensitivity, %	36 (23 to 50)	85 (72 to 93)	77 (64 to 88)
Specificity, %	77 (75 to 79)	21 (19 to 23)	41 (39 to44)
Positive predictive value, %	5 (3 to 7)	3 (2 to 4)	4 (3 to 5)
Negative predictive value, %	98 (97 to 98)	98 (96 to99)	99 (97 to 99)
Positive likelihood ratio	1.57 (1.09 to 2.28)	1.08 (0.96 to 1.21)	1.32 (1.13 to 1.53)
Negative likelihood ratio	0.83 (0.68 to 1.02)	0.71 (0.37 to 1.36)	0.55 (0.33 to 0.90)
AUROC	0.59 (0.52 to 0.67)	0.54 (0.47 to 0.61)	0.64 (0.57 to 0.71)

All analyses except AUROC used thresholds of qSOFA ≥2, SIRS≥2 and NEWS≥5.
AUROC, area under the receiver operating characteristics curve; ICU, intensive care unit; NEWS, National Early Warning Score; qSOFA, quick Sequential Organ Failure Assessment; SIRS, Systemic Inflammatory Response Syndrome.

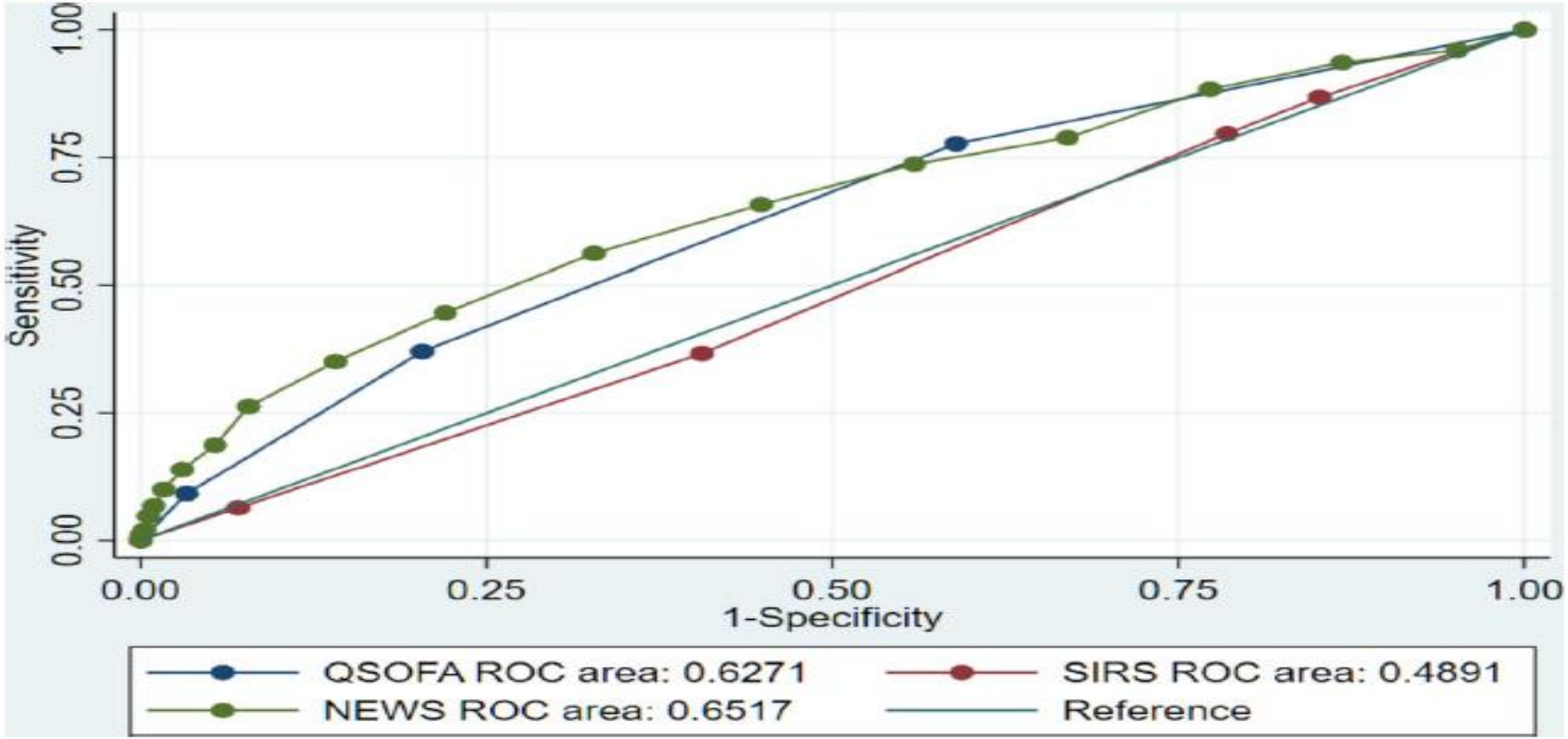


Figure 1 ROC curves of qSOFA, SIRS and NEWS for predicting inhospital death. NEWS, National Early Warning Score; qSOFA, quick Sequential Organ Failure Assessment; ROC, receiver operating characteristics curve; SIRS, Systemic Inflammatory Response Syndrome.

CHEST

A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality

A Systematic Review and Meta-Analysis

Q1 Q19 Q2 Q3 Rodrigo Serafim, MD; Jose Andrade Gomes, MD; Jorge Salluh, MD, PhD; and Pedro Póvoa, MD, PhD

CONCLUSIONS: The SIRS was significantly superior to the qSOFA for sepsis diagnosis, and the qSOFA was slightly better than the SIRS in predicting hospital mortality. The association of both criteria could provide a better model to initiate or escalate therapy in patients with sepsis.

SYSTEMATIC REVIEW REGISTRATION: PROSPERO CRD42017067645.

CHEST 2017; ■(■):■-■

KEY WORDS: qSOFA; sepsis diagnosis; SIRS criteria

CHEST

A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality

A Systematic Review and Meta-Analysis

Rodrigo Serafim, MD; Jose Andrade Gomes, MD; Jorge Salluh, MD, PhD; and Pedro Póvoa, MD, PhD

Study or Subgroup	qSOFA Mean	qSOFA SD	qSOFA Total	SIRS Mean	SIRS SD	SIRS Total	Weight	Std. Mean Difference IV, Random, 95% CI
April, 2017	0.66	2.61	214	0.65	2.61	214	0.7%	0.00 (–0.19 to 0.19)
Churpek, 2017	0.69	1.34	30,677	0.65	1.34	30,677	31.9%	0.03 (0.01 to 0.05)
Finkelsztein, 2017	0.74	0.47	152	0.59	0.5	152	0.5%	0.31 (0.08 to 0.53)
Freund, 2017	0.8	1.59	879	0.65	0.83	879	2.8%	0.12 (0.02 to 0.21)
Park, 2017	0.733	1.54	1,009	0.599	1.46	1,009	3.2%	0.09 (0.00 to 0.18)
Raith, 2017	0.607	0.88	184,875	0.58	0.88	184,875	42.6%	0.03 (0.02 to 0.04)
Williams, 2017	0.73	0.48	8,871	0.72	0.48	8,871	18.3%	0.02 (–0.01 to 0.05)
Total (95% CI)			**226,677**			**226,677**	**100.0%**	**0.03 (0.02 to 0.05)**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 11.39$, df = 6 ($P = .08$); $I^2 = 47\%$
Test for overall effect: Z = 4.12 ($P < .0001$)

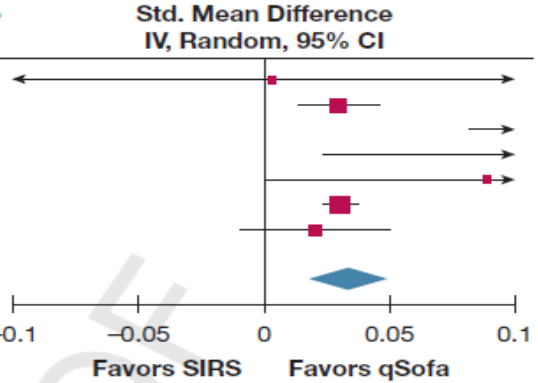


Figure 2 – ***Forest plot of mortality.*** *Effects measure = risk ratio; analysis model = random effects; statistical method = I^2 heterogeneity. The "diamond" at the bottom represents the 95% CI. IV = initialization vector; qSOFA = quick Sepsis-related Organ Failure Assessment; SIRS = systemic inflammatory response syndrome; Std = standard.*

CHEST

A Comparison of the Quick-SOFA and Systemic Inflammatory Response Syndrome Criteria for the Diagnosis of Sepsis and Prediction of Mortality

A Systematic Review and Meta-Analysis

Rodrigo Serafim, MD; Jose Andrade Gomes, MD; Jorge Salluh, MD, PhD; and Pedro Póvoa, MD, PhD

Study or Subgroup	SIRS Mean	SIRS SD	SIRS Total	qSOFA Mean	qSOFA SD	qSOFA Total	Weight	Std. Mean Difference IV, Random, 95% CI
Churpek, 2017	0.88	0.45	30,677	0.38	0.45	30,677	14.4%	1.11 (1.09 to 1.13)
Donnelly, 2017	0.54	0.02	2,593	0.12	0.26	2,593	14.3%	2.28 (2.21 to 2.35)
Dorsett, 2017	0.39	0.5	152	0.16	0.38	152	14.2%	0.52 (0.29 to 0.75)
Freund, 2017	0.74	0.45	879	0.25	0.45	879	14.3%	1.09 (0.99 to 1.19)
Raith, 2017	0.86	0.11	184,875	0.54	0.11	184,875	14.4%	2.91 (2.90 to 2.92)
Siddiqui, 2017	0.62	0.47	58	0.42	0.51	58	14.0%	0.41 (0.04 to 0.77)
Williams, 2017	0.47	0.48	8,871	0.1	0.34	8,871	14.4%	0.89 (0.86 to 0.92)
Total (95% CI)			**228,105**			**228,105**	**100.0%**	**1.32 (0.40 to 2.24)**

Heterogeneity: Tau² = 1.53; Chi² = 43948.08, df = 6 ($P < .00001$); I² = 100%
Test for overall effect: Z = 2.81 ($P = .005$)

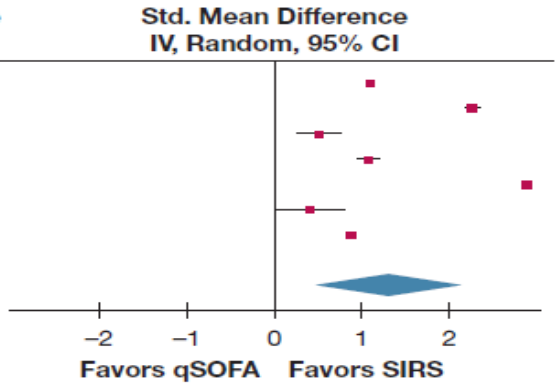
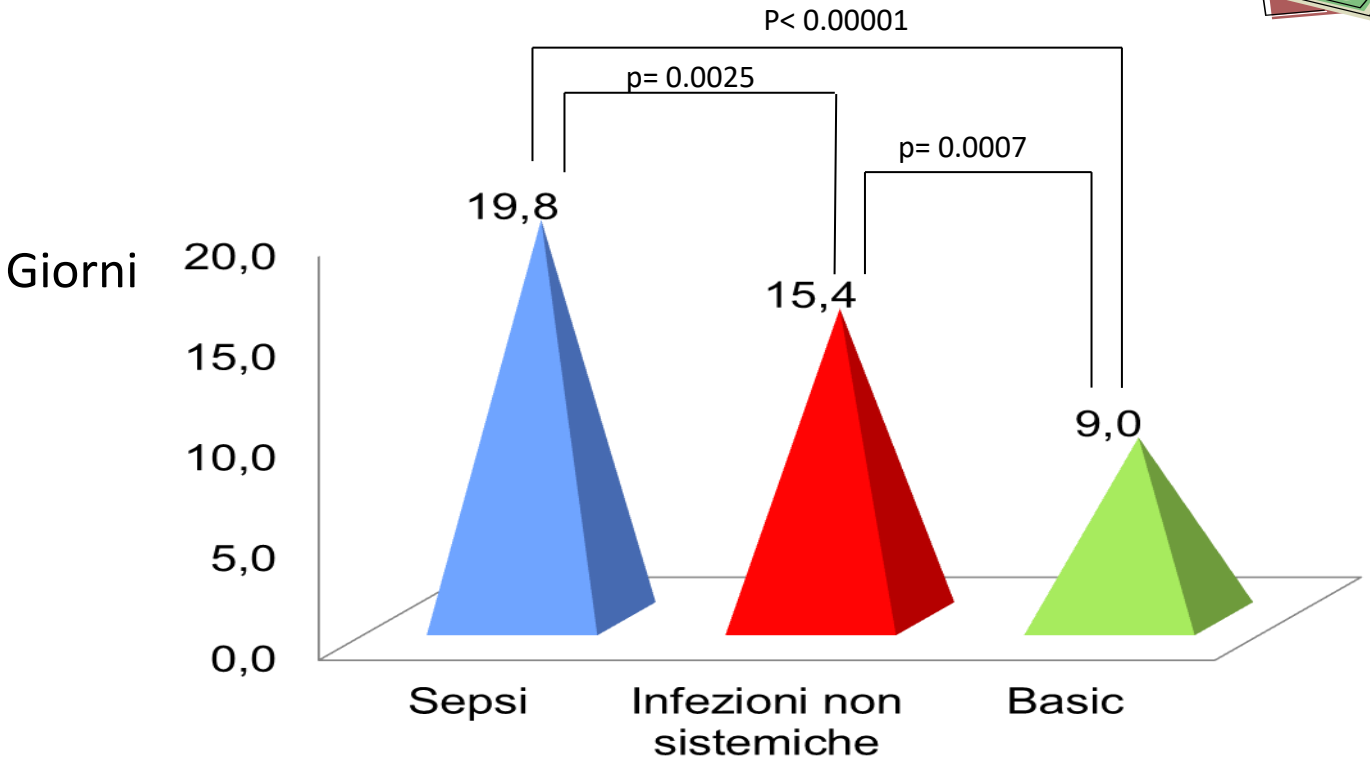


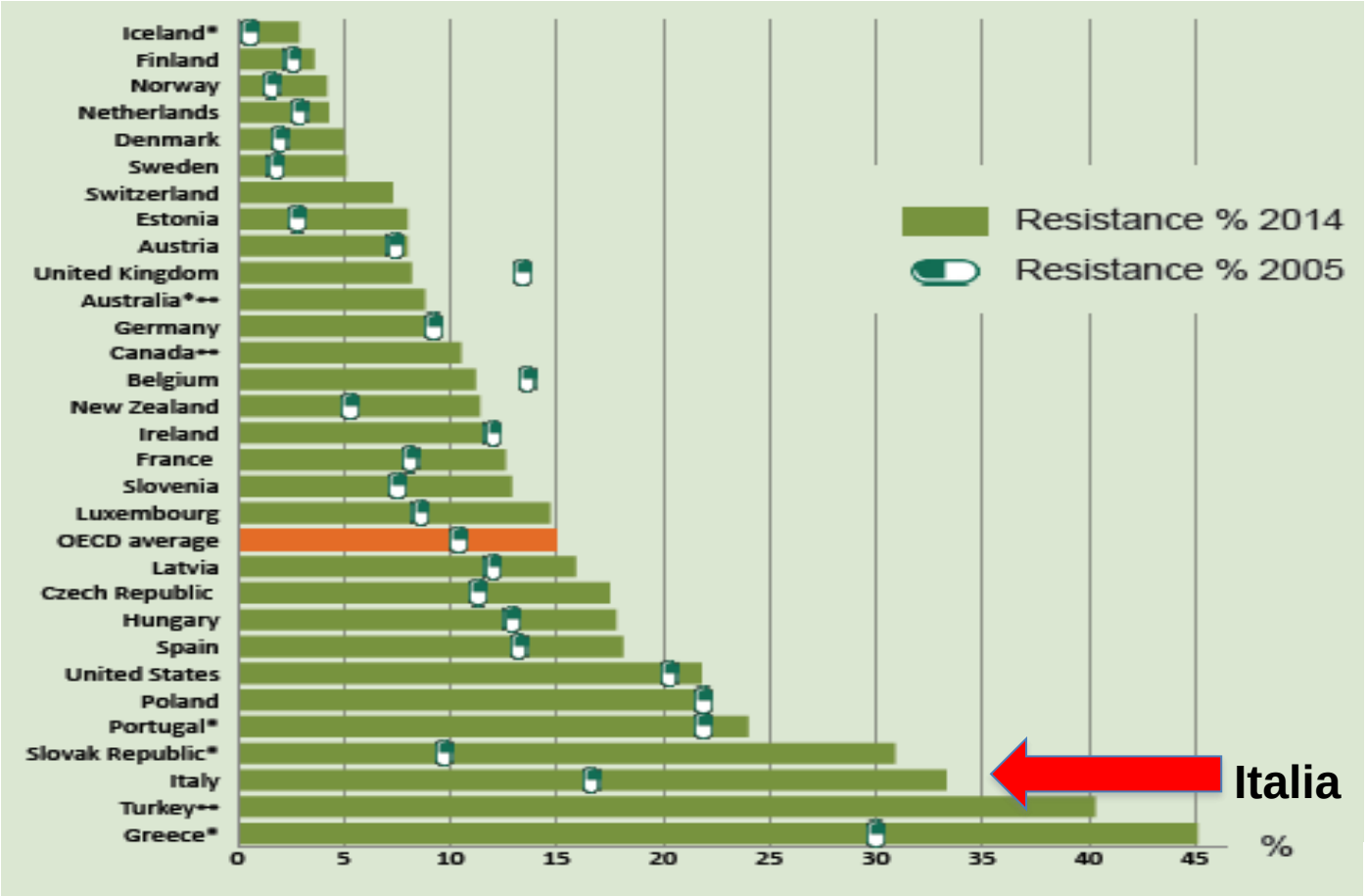
Figure 3 – *Forest plot of sensitivity for* ***diagnosis of sepsis****. Effects measure = risk ratio; analysis model = random effects; statistical method =* I^2 *heterogeneity. The "diamond" at the bottom represents the 95% CI. See Figure 2 legend for expansion of abbreviations.*

Media giornate di degenza



Costi del percorso del paziente

Antibiotico-resistenza, Europa



OECD 2016

The domino effect of the ESBL pandemic

Dissemination of Enterics producing ESBLs

↓

Carbapenem Overuse

↓

Dissemination of Carbapenem R Gram-negatives

Idea: Gianni Rossolini

Decalogo GISA: azioni prioritarie

Prevenzione primaria e secondaria delle infezioni

- **Vaccinazioni nell'adulto e nell'ospite immunocompromesso**
- **Profilassi antibiotica in chirurgia e nei pazienti a rischio**

Controllo della diffusione delle infezioni e dell'AMR

- **Infection control**

Prevenzione dell'antibiotico-resistenza

- **Controllo dell'uso degli antibiotici negli animali e nel cibo**
- **Uso appropriato degli antibiotici nell'uomo (ASP)**

www.antimicrobialstewardship.net

Prevenzione delle infezioni batteriche: Vaccinazioni per adulti ed immunocompromessi

Influenza, inattivato (R)

Pneumococco 13/23 (R)

- **Adulti > 65 anni**
- **Adulti > 19 anni in base a patologie od altre indicazioni:**
  Insufficienza renale, cardiopatie e malattie polmonari croniche, alcolismo, epatopatie croniche, Diabete, personale sanitario, MSM
- **HIV/AIDS**
- **Tumori**
- **Trapianto di midollo osseo**
- **Trapianto di organo solido**
- **Malattie infiammatorie croniche o terapie immunosoppressive**
- **Asplenia, anemia falciforme, impianti cocleari, liquorrea**

R: raccomandato

Infection control: le buone pratiche assistenziali

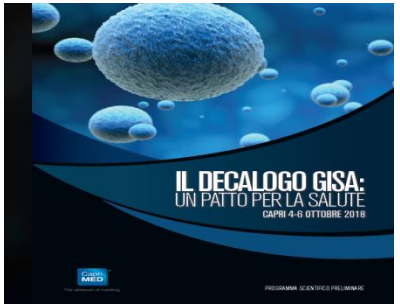
- **Il controllo delle infezioni è una priorità chiave per il sistema sanitario a livello nazionale e regionale**
- Campagne di informazione rivolte agli amministratori ospedalieri per aumentare la conoscenza del problema e definire **delle competenze di base sul controllo delle infezioni e l'antibiotico-resistenza per tutto il personale sanitario e di assistenza**
- Migliorare i progetti del Ministero della Salute: igiene delle mani, aderenza alle misure di prevenzione e controllo, controllo dell'MRSA, sorveglianza di *C. difficile* e CRE.
- Implementare un diffuso utilizzo dei programmmi di sorveglianza CCM delle infezioni del sito chirurgico e delle infezioni in Terapia Intensiva

www.antimicrobialstewardship.net

Il metodo più efficace per prevenire la trasmissione delle infezioni

Antimicrobial stewardship

- ***Migliorare l'outcome del paziente***
- ***Limitare l'insorgenza di resistenze***
- ***Diminuire gli eventi avversi (C. difficile)***
- ***Contenere i costi***



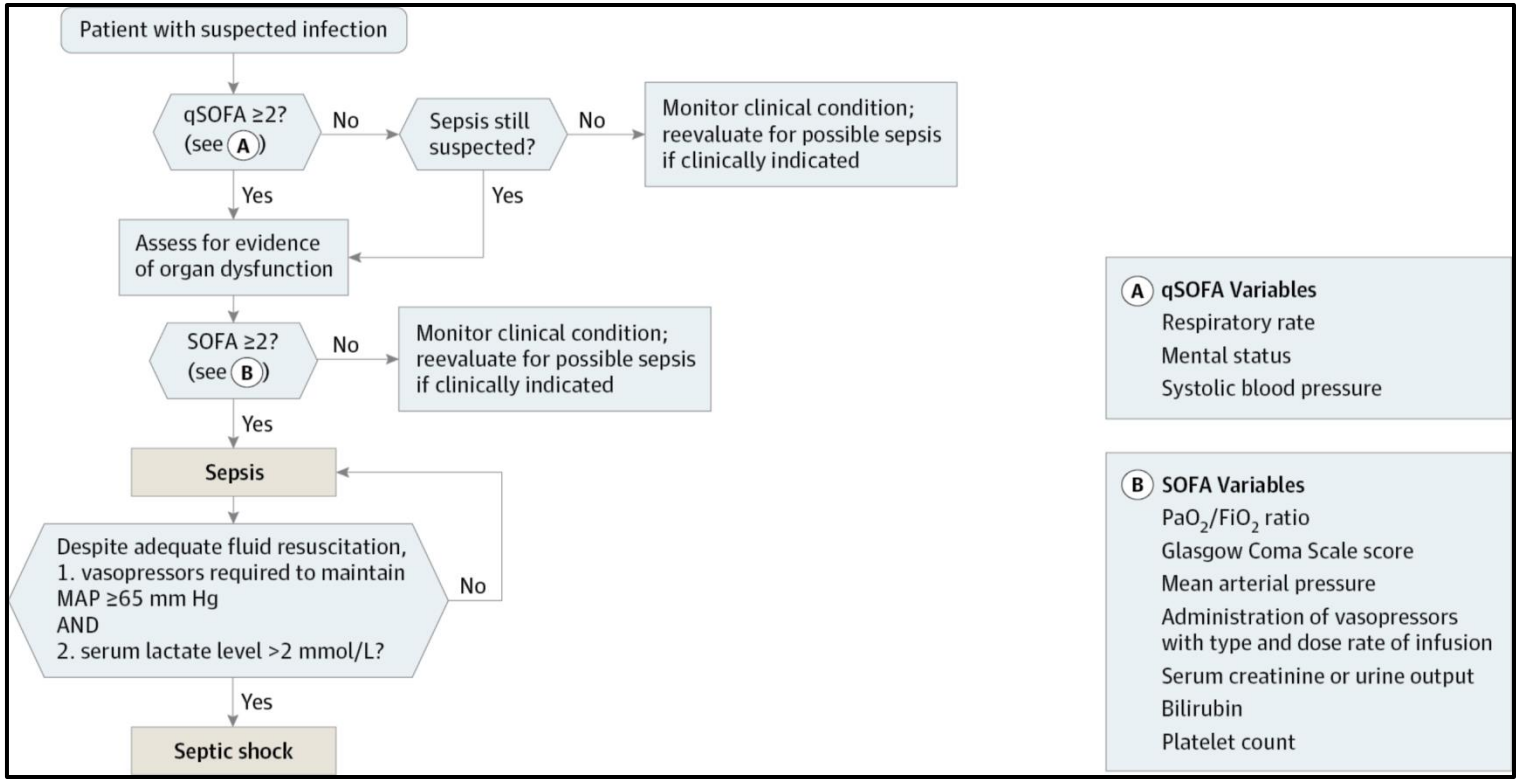
Precauzioni da contatto

Pazienti con infezione/colonizzazione e da MDR

MRSA, VRE, *C. difficile*, CRE

Sovracamici e guanti; presidi dedicati

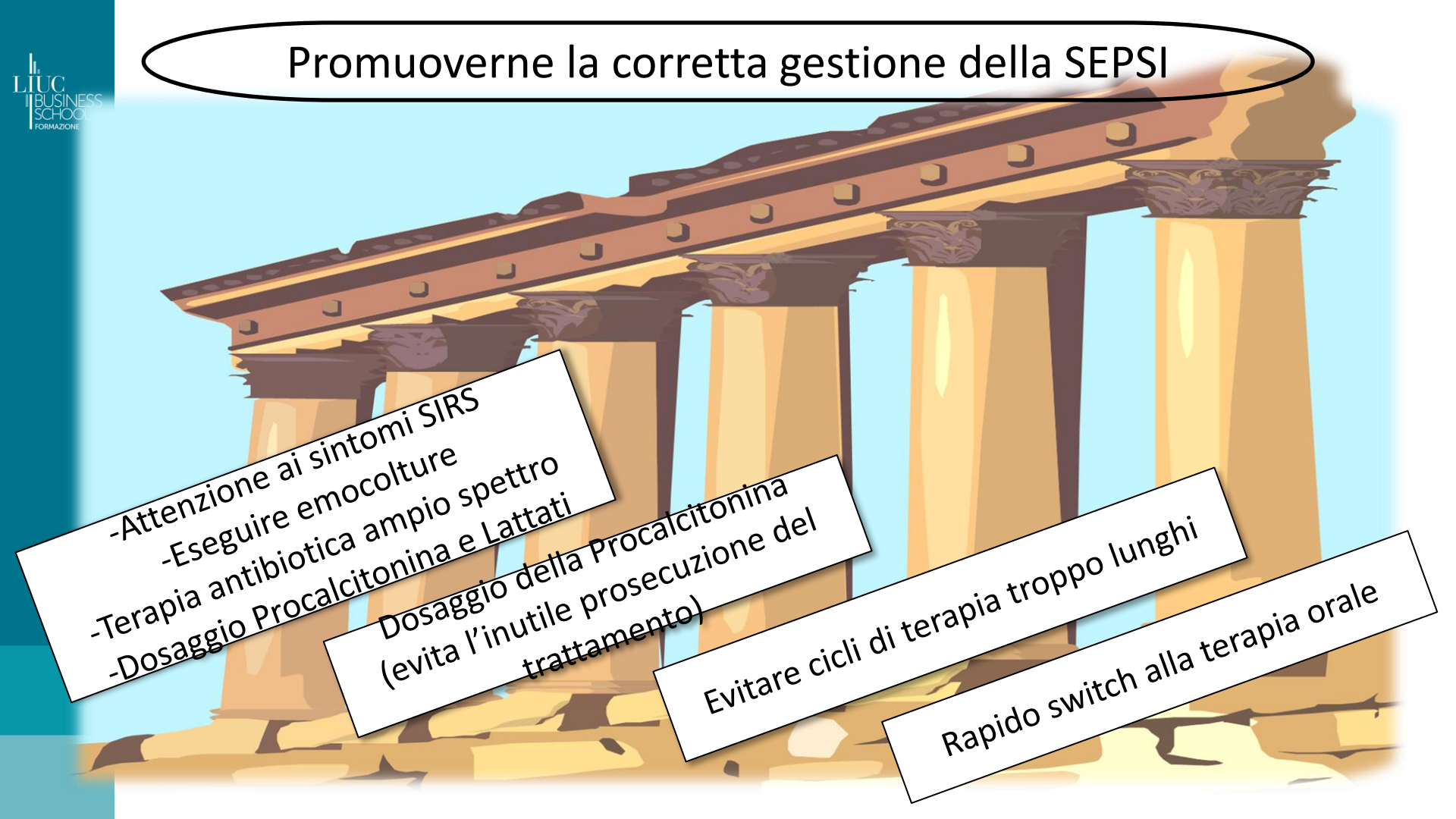
New sepsis definition



Singer M et al. JAMA. 2016;315:801-10.

NEJM 2013; 369:840-51

Promuoverne la corretta gestione della SEPSI

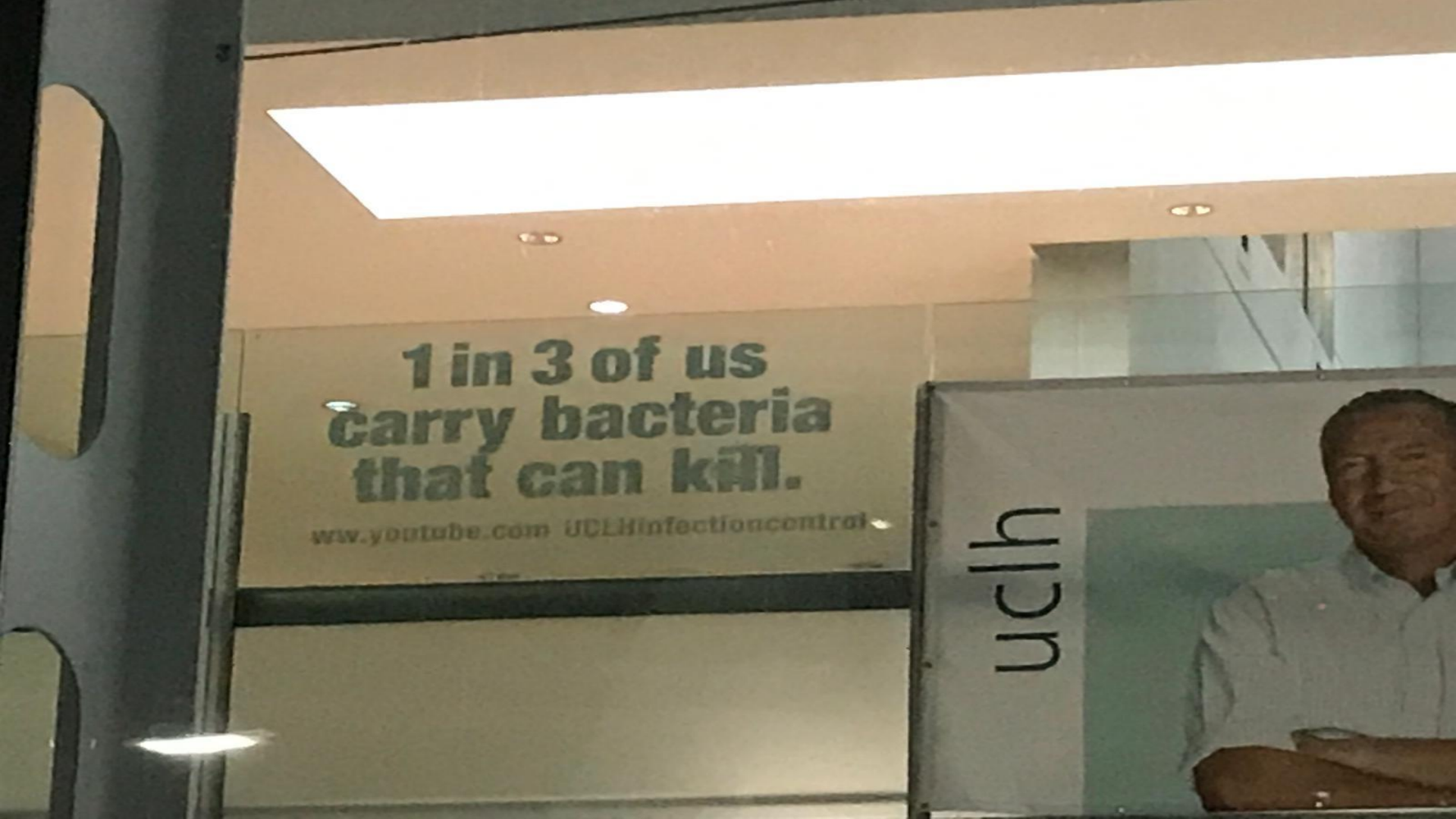


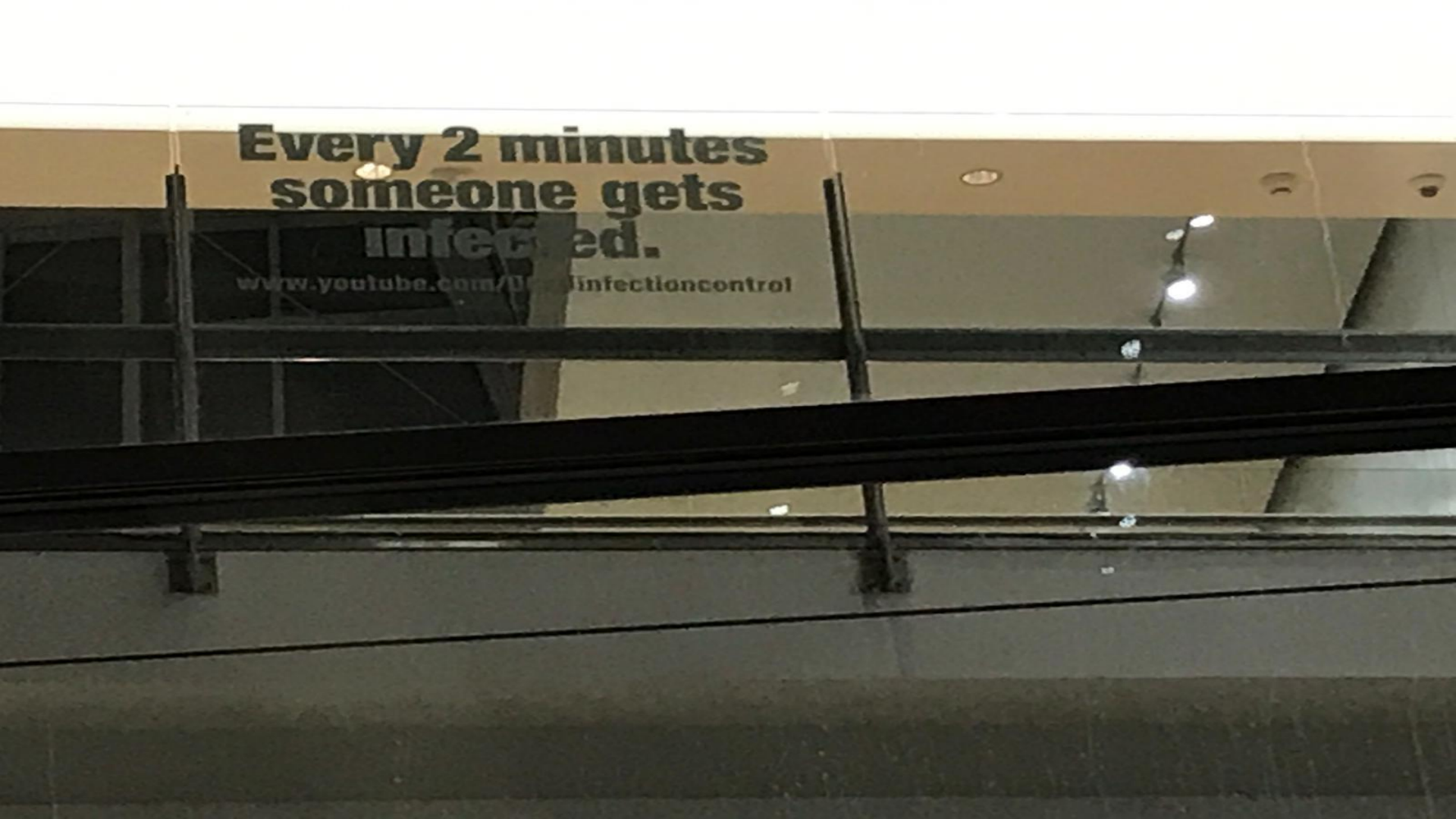
-Attenzione ai sintomi SIRS
-Eseguire emocolture
-Terapia antibiotica ampio spettro
-Dosaggio Procalcitonina e Lattati

Dosaggio della Procalcitonina (evita l'inutile prosecuzione del trattamento)

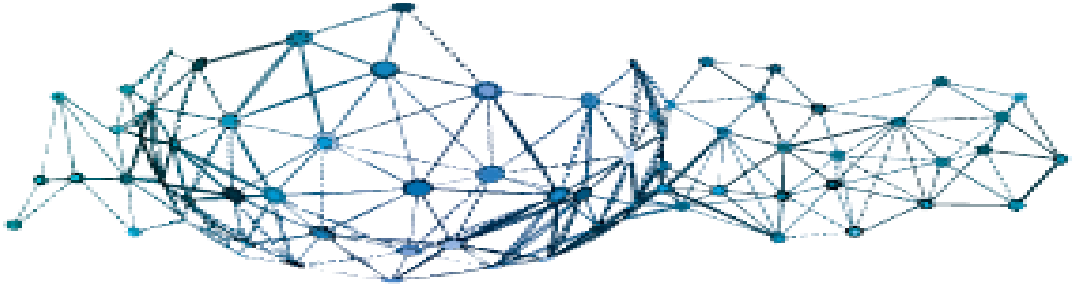
Evitare cicli di terapia troppo lunghi

Rapido switch alla terapia orale


1 in 3 of us
carry bacteria
that can kill.
www.youtube.com UCLHinfectioncontrol
uclh


Every 2 minutes
someone gets
infected.
www.youtube.com/u infectioncontrol

www.antimicrobialstewardship.net



G.I.S.A.

GRUPPO ITALIANO PER LA STEWARDSHIP ANTIMICROBICA

Presidente Onorario: Prof. Johnatan Cohen

Società Scientifica multidisciplinare, promuove la cultura dell'ASP intesa come <u>GOVERNO CLINICO DELLA TERAPIA ANTIMICROBICA</u> attraverso il confronto equo tra esperti e prescrittori.

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NuoveVoci STRADE

È la malinconia, quella emozione sana, molte volte allegra, qualche volta commovente, il fil rouge che unisce tutti i capitoli e che torna, nell'animo dell'autore, come un costante ritornello: la nostalgia di un tempo che non c'è più ma che, scaturita dai ricordi che sempre affollano la mente e il cuore, induce a sorridere e, a volte, anche a commuoversi. E siccome nella memoria, tempo e spazio spesso coincidono e si mescolano, i giorni felici dell'infanzia e dell'adolescenza si rispecchiano nel mare, nel cielo e nella sagoma delle Eolie ammirate dalla terrazza di casa, divenendo estasi e tormento, consolazione e rimpianto. "È la nostalgia a nutrire la nostra anima, non l'appagamento", diceva Arthur Schnitzler: come, dunque, non considerare conquiste della nostalgia l'umanità, l'umiltà, la capacità d'immedesimarsi nella persona che soffre che rendono Conitto il medico speciale che è? Ma Conitto è l'autore e la nostalgia è materia d'ispirazione per questo romanzo.

Cristina Masetti

In copertina:
foto di proprietà dell'Autore.

Antonino Mazzone nato a Naso (ME) nel 1956, si è formato presso l'Università degli Studi di Pavia, laureandosi in Medicina e Chirurgia, con lode. Specialista in Medicina Interna, Ematologia, Immunologia Clinica e allergologia, ha lavorato presso il Policlinico San Matteo di Pavia, da diciotto anni Primario Direttore della UO di Medicina Interna dell'Ospedale di Legnano. È stato Presidente della FADOI, Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti. Ha fondato la Fondazione FADOI che oggi è tra i primi per ricerca e formazione in ambito medico e infermieristico. Ha pubblicato oltre trecento lavori, molti su riviste Internazionali di alto prestigio. Nel 1971 ha vinto il primo premio Poesia città di Capo d'Orlando, dedicato a giovani studenti. Questa è la sua prima esperienza come scrittore di romanzi.

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Euro 14,50

Parte del ricavato dalla vendita di questo libro sarà destinato alla realizzazione e al sostegno dei laboratori solidali di scrittura *LetterariaMente*.

ANTONINO MAZZONE

LA MALINCONIA DEI NATI ALTROVE

STRADE

Antonino Mazzone

La malinconia dei nati altrove

Albatros