Torino, 31 gennaio 2014

Definizione di Antimicrobial Stewardship

Pierluigi Viale **Clinica di Malattie Infettive** **Policlinico S. Orsola – Malpighi**

KPC-producing *K. pneumoniae* of Clonal Complex 11

late 2008

The first reported cases of KPC-Kp ST258

early 2011

ST258, ST512

late 2012

ST512
ST258

THE EQUATION OF THE INFECTIOUS RISK

$$\frac{\text{BACTERIAL LOAD} \times \text{VIRULENCE}}{\text{HOST IMMUNITY}} + \text{DRUG RESISTANCE} = \text{INFECTIOUS RISK}$$

DEATHS

COSTS

SUPERBUGS

Infection control measures for Gram neg colonized patients

Courtesy E. Tacconelli & N. Petrosillo -ESCMID/SHEA guidelines

Multifaceted approaches

- Hand hygiene
- Physical separation of patients
- Education
- Detection/surveillance
- Environmental cleaning
- Cohort patients' and staff

- Antimicrobial stewardship

INFECTIOUS RISK CONTROL – A THREE PHASES ACTION

PREVENTION OF INFECTIONS

MANAGEMENT OF INFECTIONS

PREVENTION OF RESISTANCES

La Gestione del rischio infettivo in Emilia-Romagna il nuovo assetto organizzativo

DELIBERAZIONE DELLA GIUNTA REGIONALE 25 MARZO 2013, N. 318
Linee di indirizzo alle Aziende per la gestione del rischio infettivo: infezioni correlate all'assistenza e uso responsabile di antibiotici

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Dellit TH, et al. Clin Infect Dis 2007; 44:159-177*

Antimicrobial Stewardship: DEFINITIONS

An activity that optimizes antimicrobial management and includes selection, dosing, route and duration of antimicrobial therapy.

A marriage of infection control (Epidemiologist), and antimicrobial management (Infectious Diseases specialist) finalized to share the principles of the optimized treatment between the bench to bed side point of view and the hospital-wide vision

THE HISTORICAL PERIODS of ANTIMICROBIAL STEWARDSHIP

The MIDDLE AGE

COMPULSORY PROGRAMS

The REINASSANCE

SEMI-COMPULSORY PROGRAMS (post prescription reviews)

The NEXT FUTURE

SHARED NEW PARADIGMS for MANAGEMENT

PROBLEM-DRIVEN PROTOCOLS and PROGRAMS

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Dellit TH, et al. Clin Infect Dis 2007; 44:159-177*

6.
There are 2 core strategies, both proactive, that provide the foundation for an antimicrobial stewardship program. These strategies are not mutually exclusive.

A. **Prospective audit with intervention and feedback.** Prospective audit of antimicrobial use with direct interaction and feedback to the prescriber, performed by either an infectious diseases physician or a clinical pharmacist with infectious diseases training, can result in reduced inappropriate use of antimicrobials (A-I).

B. **Formulary restriction [illegible]authorization.** Formulary restriction and preauthorization requirement[illegible] immediate and significant reductions in antimicrobial use and cost (A-II[illegible] beneficial as part of a multifaceted response to a nosocomial outbreak o[illegible]-II). The use of preauthorization requirements as a means of controlli[illegible]bial resistance is less clear, because a long-term beneficial impact on re[illegible] not been established, and in some circumstances, use may simply shift to[illegible]e agent with resulting increased resistance (B-II).

The MIDDLE AGE

A marriage of infection control (Epidemiologist) and antimicrobial management (Infectious Diseases specialist) finalized to share the principles of the optimized treatment between the bench to bed side point of view and the hospital-wide vision

THE GOAL IS THE APPROPRIATENESS
of the prescriptions not only the costs saving

The REINASSANCE

The MULTIFACETED concept of APPROPRIATENESS

- RIGHT INDICATION (epidemiologically, microbiologically and PK/PD driven)
- RIGHT DAILY DOSE
- RIGHT MODALITY OF ADMINISTRATION
- RIGHT PRESCRIBER
- SHARED CRITERIA FOR DE-ESCALATION / INTERRUPTION
- IMPROVEMENT OF MICROBIOLOGICAL WORK UP

Transforming the hospital formulary in a true clinical instrument !

From the formulary to a shared management guidelines

How to lay out a stewardship program ?

-Hospital wide

-Drug directed

-Setting directed

-Disease directed

Antimicrobial stewardship programs- The devil is in the details

Cunha CB et al, Virulence 2013; 4:2, 147–149

Antimicrobial stewardship is a developing field, and every program must be tailored to its respective institution and each article has a distinctive focus and perspective.

Global impact of an educational antimicrobial stewardship programme on prescribing practice in a tertiary hospital centre. *Cisneros JM et al, Clin Microbiol Infect 2013 Feb 27*

Methodology of active intervention

The main activity of the program consists of a training program directed towards all antibiotic prescribers in the centre based on counselling interviews, carried out by a group of clinical experts who were selected by the PRIOAM operations team, and included 7 ID specialists, 6 critical-care specialists and 4 paediatricians.

PRIOAM advisors were selected from local leaders in the management of patients with infectious diseases in each area. Each advisor conducted counselling interviews in his/her area of responsibility.

The number of counselling interviews scheduled for each clinical department was proportional to its antimicrobial consumption: < 50 DDDs -> one per week,
50 to 100 DDD -> two per week
> 100 DDD -> 3 per week.

Global impact of an educational antimicrobial stewardship programme on prescribing practice in a tertiary hospital centre. *Cisneros JM et al, Clin Microbiol Infect 2013 Feb 27*

The advisor reviewed the antimicrobial treatment with the prescriber, examined the patient's clinical data and discussed the main aspects of the prescribed treatment and diagnosis of the infectious syndrome using a specific questionnaire.

Prescriptions were considered as 'appropriate' when all items of the questionnaire had been accomplished correctly. If one or more of them were incorrectly performed, the prescription was evaluated as 'inappropriate'.

To guarantee homogeneity, the PRIOAM team also coordinated monthly training meetings with these advisors, which also served to monitor the progress of the programme.

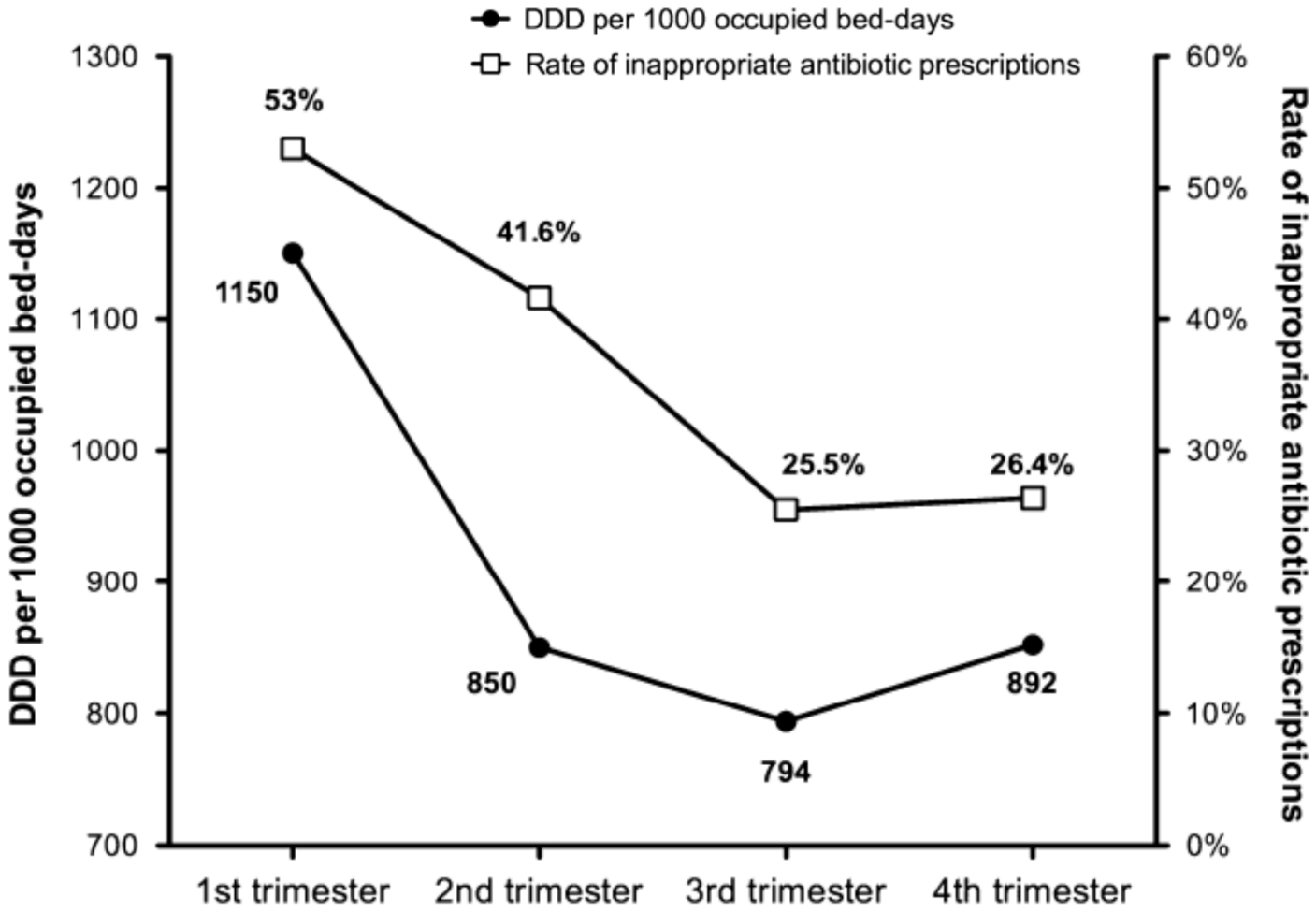
Global impact of an educational antimicrobial stewardship programme on prescribing practice in a tertiary hospital centre. *Cisneros JM et al, Clin Microbiol Infect 2013 Feb 27*

A total of 1206 CIs were performed during the first year of the programme. Interviews lasted approximately, 10 min, the equivalent of 201 working hours for the 1206 CIs.

The most frequently performed assessments were for empirical prescriptions (52.2%, n = 630), followed by targeted treatments (25.4%, n = 306) and surgical prophylaxis (22.4%, n = 270).

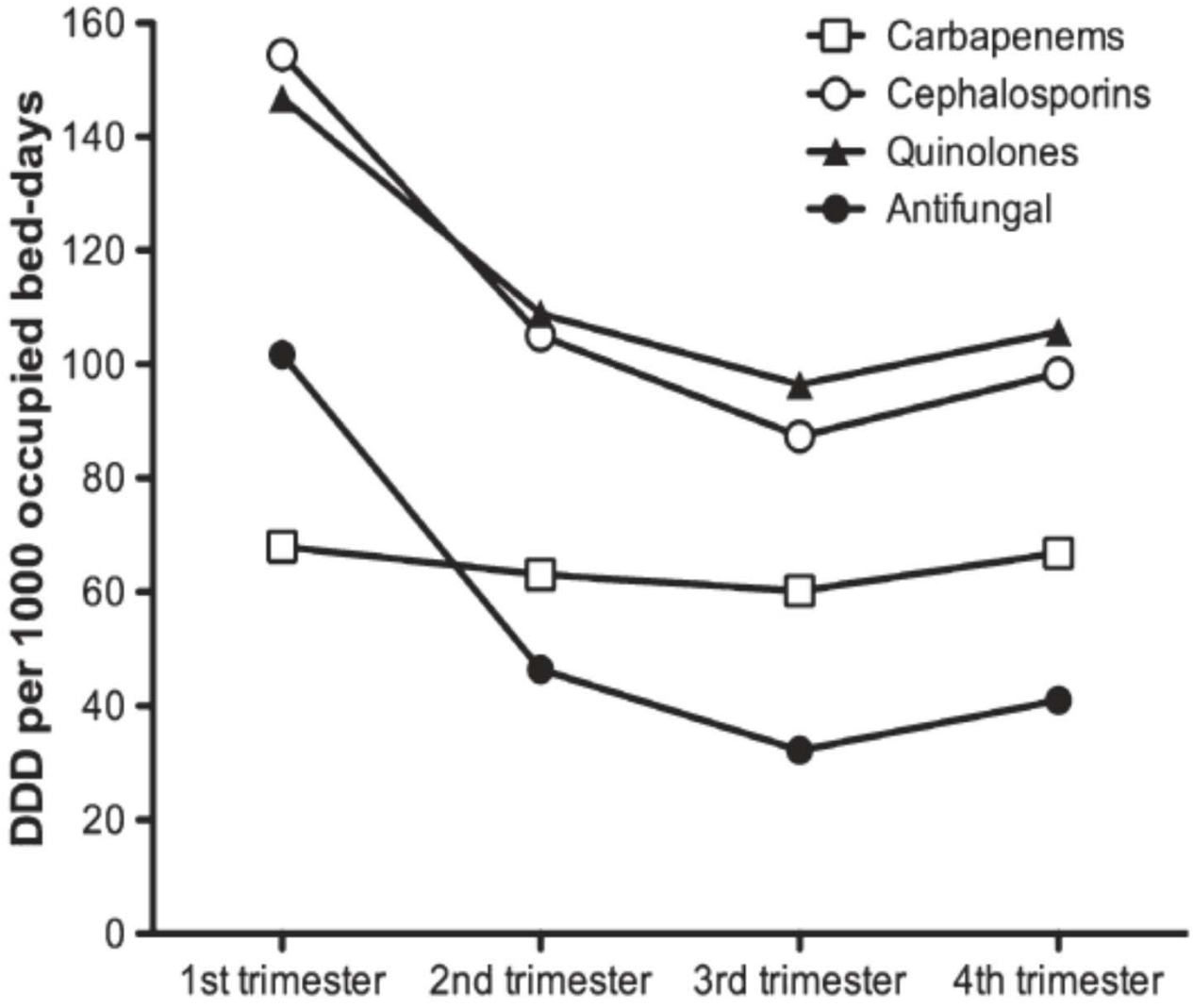
Global impact of an educational antimicrobial stewardship programme on prescribing practice in a tertiary hospital centre. *Cisneros JM et al, Clin Microbiol Infect 2013 Feb 27*

rates of inappropriate antimicrobial use



Global impact of an educational antimicrobial stewardship programme on prescribing practice in a tertiary hospital centre. *Cisneros JM et al, Clin Microbiol Infect 2013 Feb 27*

Evolution of the consumption by class of antibiotics



A marriage of infection control (Epidemiologist) and antimicrobial management (Infectious Diseases specialist) finalized to share the principles of the optimized treatment between the bench to bed side point of view and the hospital-wide vision

RUN FOR THE APPROPRIATENESS

The S. Orsola-Malpighi Stewardship program

Checking the quality instead of the quantity

The S. Orsola-Malpighi Teaching Hospital

2012

Beds number : 1.425 DO + 155 DH/DS

N. of discharged pts = 71.303
- Day Hospital: 20,5%
- Medical DRG : 62,2%
- Surgical DRG : 37,8%
- % complicated DRG: 42,7%

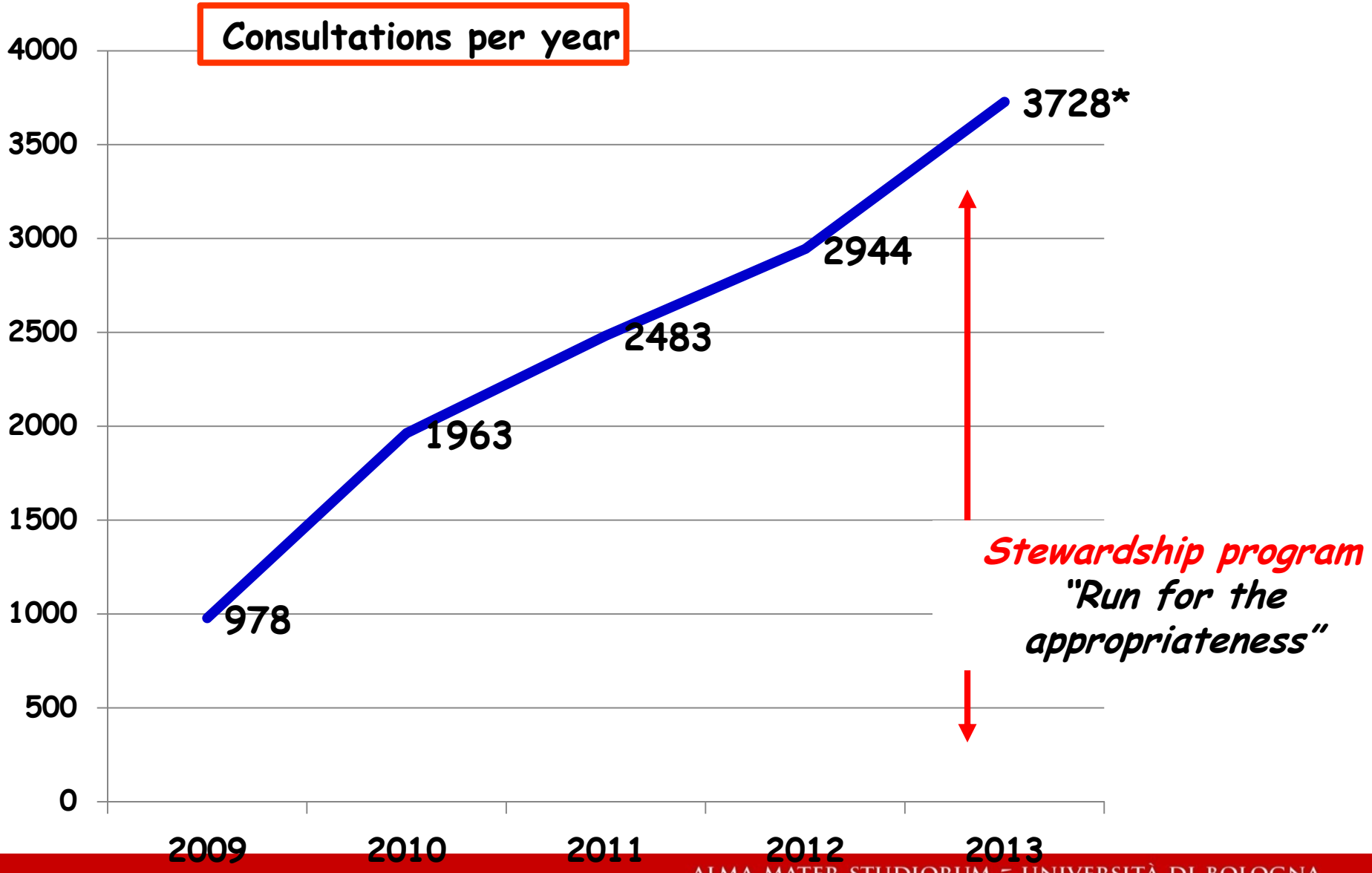
Surgical activity
- N. of interventions 32.771
- General Surgery 21.7%
- Cardio Surgery 5.2%
- Specialized Surgery 73.1%

Transplant Activity	2009	2010	2011	2012
LIVER	71	78	65	77
KIDNEY	63	66	60	84
HEARTH	27	23	28	19
LUNG	3	1	5	3
BOWEL	1	3	2	2
MULTI	2	6	7	3
OVERALL	167	177	168	186
HSTC	167	167	177	169
OVERALL	334	344	335	355

S. Orsola-Maplighi Teaching Hospital – the ID consultant team

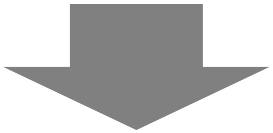
Four Seniors + 3 Fellows

Daily Consultation in TX Center / Cardio Surgery / ICUs / Hospitalwide on demand



The change

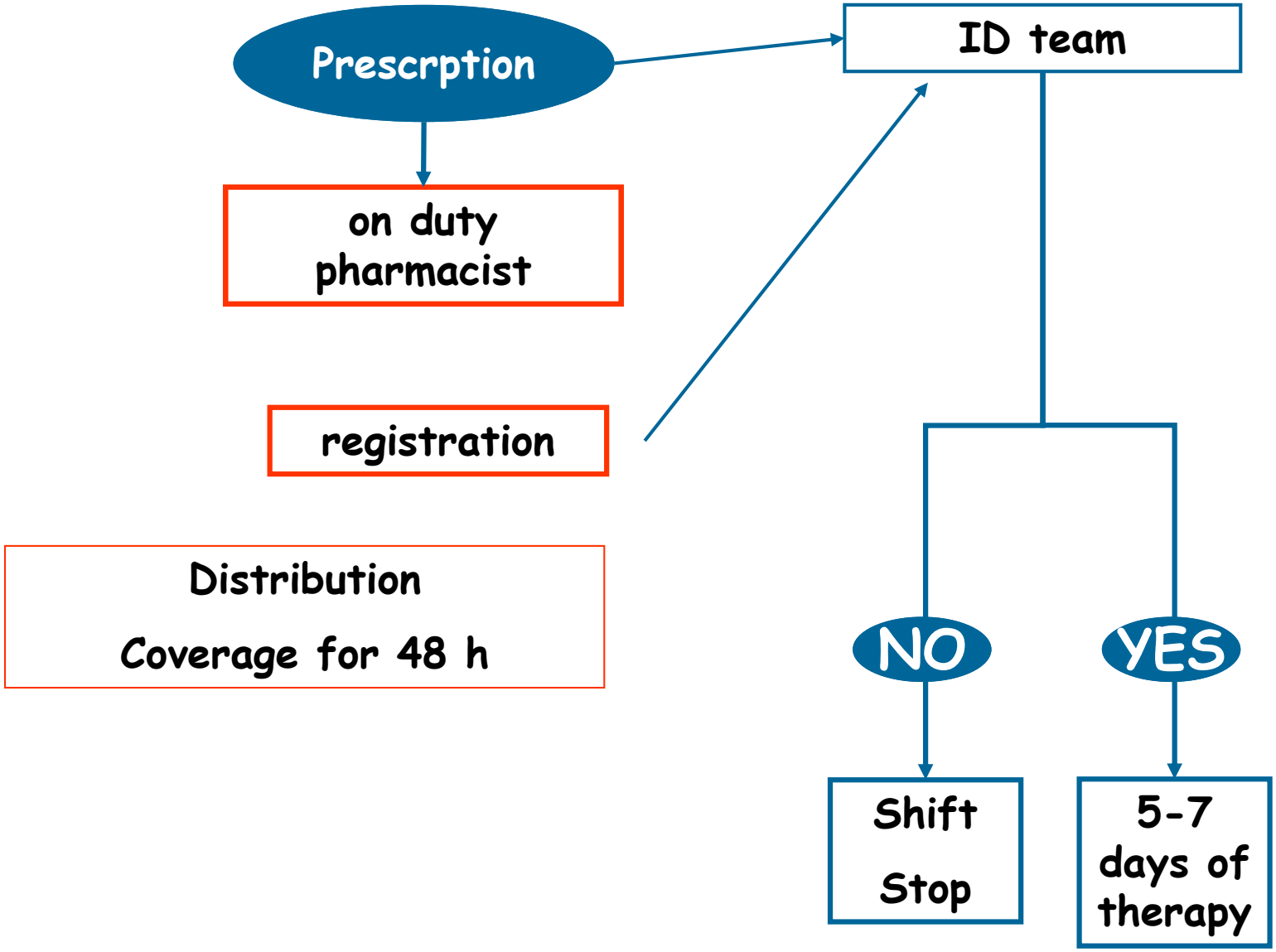
- Formulary restrictions
- Preauthorization requirements
- Retrospective Audits
- Diffusion of international and local guidelines



Run for the appropriateness

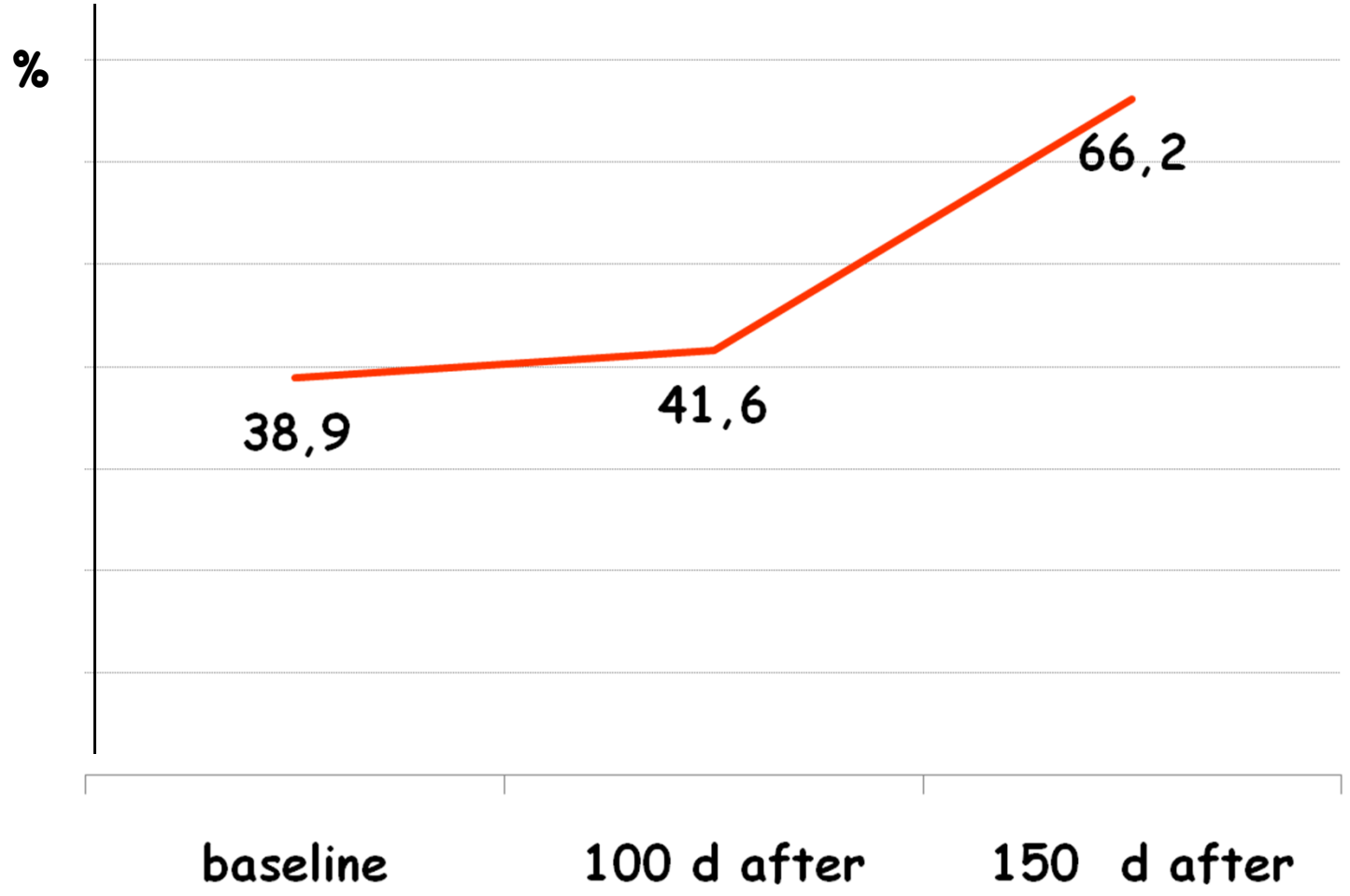
- Shared definitions of appropriateness
- No pre defined restrictions but …
- "Real time" evaluation of any prescription by the ID consultant team

Run for the appropriateness



"Run for the appropriatenss" project

Appropriateness trend – first prescriptions by others than ID

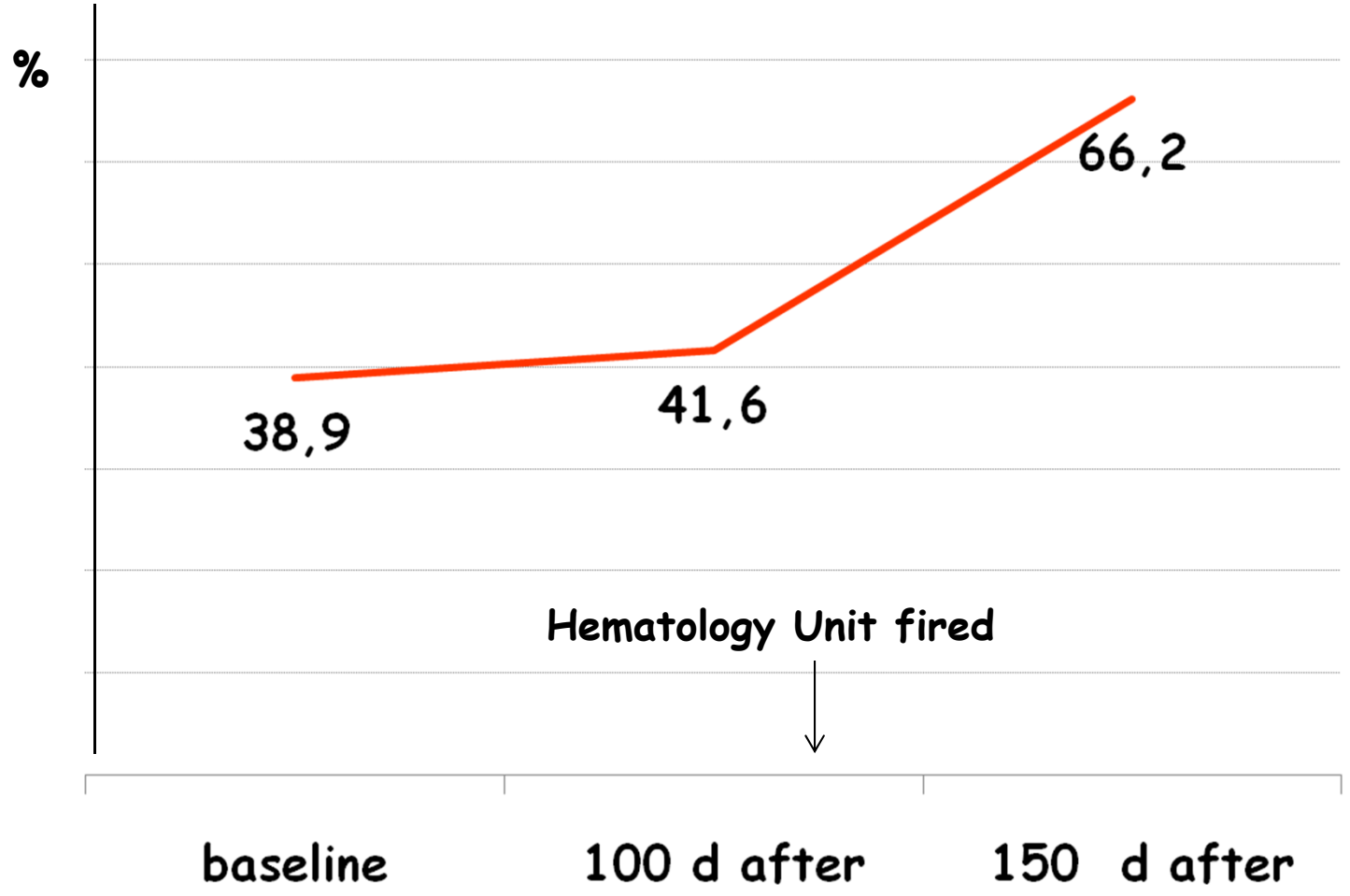


Consumi (DDD/100ggdd) e costi: 10m 2013 vs 2012

Gruppo terapeutico	Farmaco	DDD	VAR% DDD	VAR COSTI	VAR% costi
	DAPTOMICINA	0,88	50,2 %	60.990	47,9 %
	LINEZOLID	0,65	32,7 %	59.792	29,8 %
	MEROPENEM	1,80	-38,7 %	-61.836	-40,9 %
	TIGECICLINA	0,42	-44,3 %	-124.155	-45,5 %
ANTIBATTERICI PER USO SISTEMICO		**3,74**	**-21,4 %**	**-65.209**	**-8,7 %**
	AMFOTERICINA	1,20	-8,1 %	-45.660	-10,1 %
	CASPOFUNGIN	0,25	8,7 %	21.180	6,2 %
	VORICONAZOLO	0,24	5,0 %	2.036	1,9 %
ANTIMICOTICI PER USO SISTEMICO		**1,68**	**-4,3 %**	**-22.444**	**-2,5 %**
Totale farmarci sorvegliati		**5,42**	**-16,7 %**	**-87.653**	**-5,3 %**

"Run for the appropriatenss" project

Appropriateness trend – first prescriptions by others than ID



S. Orsola-Malpighi Teaching Hospital – today looking at the future

NEW PARADIGMS OF MANAGEMENT FOR SPECIFIC PROBLEMS

- SESPIS TEAM

observational phase ongoing / interventional phase planned form March 2014

- PNEUMONIA TASK FORCE

ongoing

- BUNDLE FOR THE MANAGEMENT OF CANDIDEMIA

observational phase ongoing

- BD GLUCAN DRIVEN DE-ESCALATION OF EMPIRICAL ANTIFUNGAL TX

under submission to Ethical Committee

- AMBIHOW PROTOCOL

enrollment ongoing

- SCORE /CTPA DRIVEN ANTIMOLDS Tx FOR POSSIBLE INFECTIONS

multidisciplinary discussion ongoing

- CORRECT PCT USE

ongoing (40% reduction of requests)

S. Orsola-Malpighi Teaching Hospital

SEPSIS TEAM

Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department

Gaieski DF et al, Crit Care Med 2010; 38:1045-1053

Table 6. In-hospital mortality: Time from triage to appropriate antibiotics

				Adjusted			
Cutoffs	Number	Mortality, %	Difference, %	OR	95% CI	*p*	Probability of Death
≤1 hr	41	19.5	13.7	0.30	0.11–0.83	.02	.13 vs. .29
>1 hr	220	33.2					
≤2 hrs	124	28.2	5.4	0.54	0.29–1.03	.06	.22 vs. .31
>2 hrs	137	33.6					
≤3 hrs	172	27.9	9.2	0.53	0.27–1.01	.05	.23 vs. .34
>3 hrs	89	37.1					
≤4 hrs	200	28.5	10.8	0.62	0.31–1.24	.18	.25 vs. .34
>4 hrs	61	39.3					
≤5 hrs	218	30.7	1.8	0.82	0.37–1.79	.62	.27 vs. .29
>5 hrs	43	32.6					

The epidemiology of adults with severe sepsis and septic shock in Scottish emergency departments. *Gray A et al, Emerg Med J 2012 Jun 29*

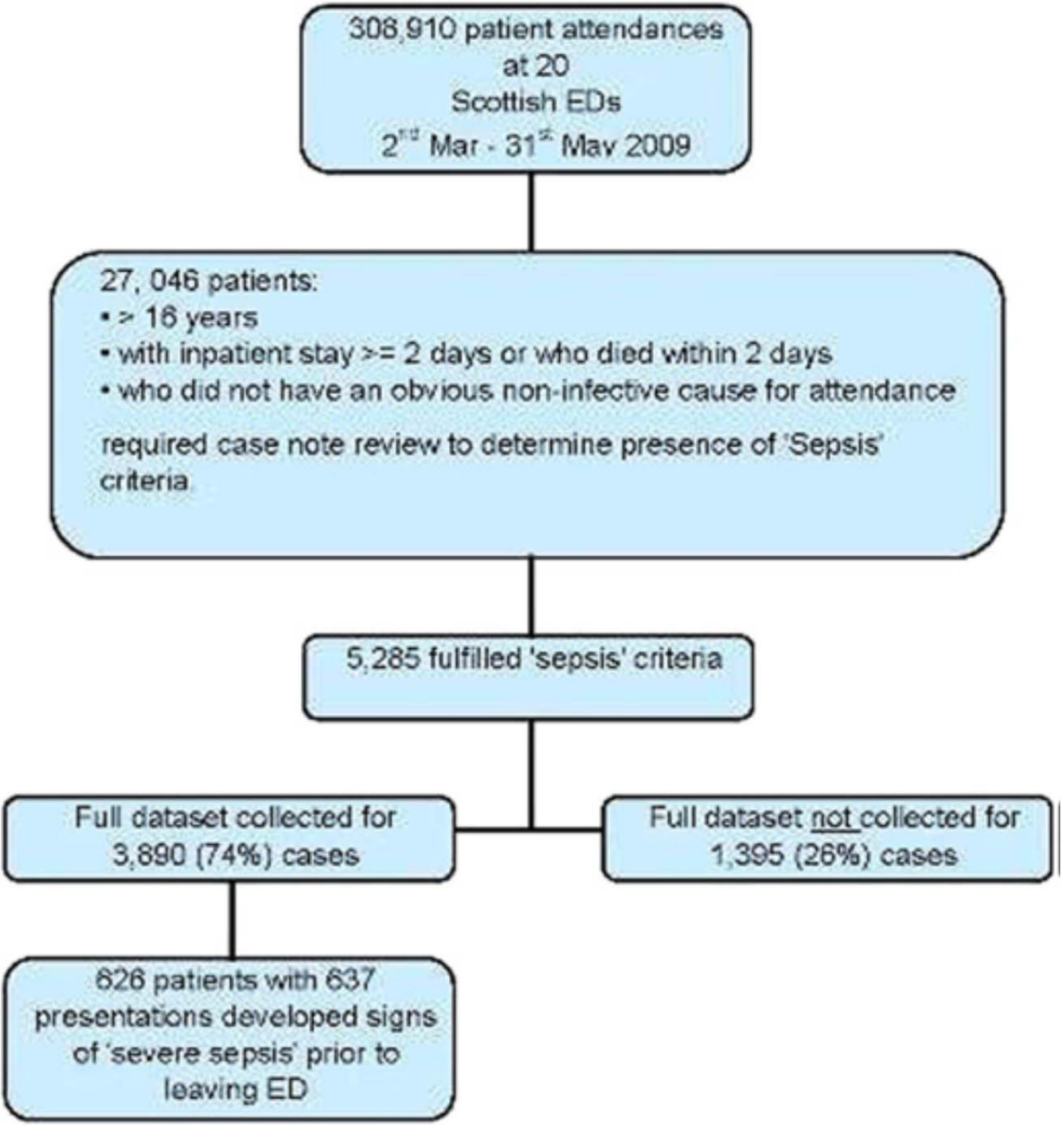
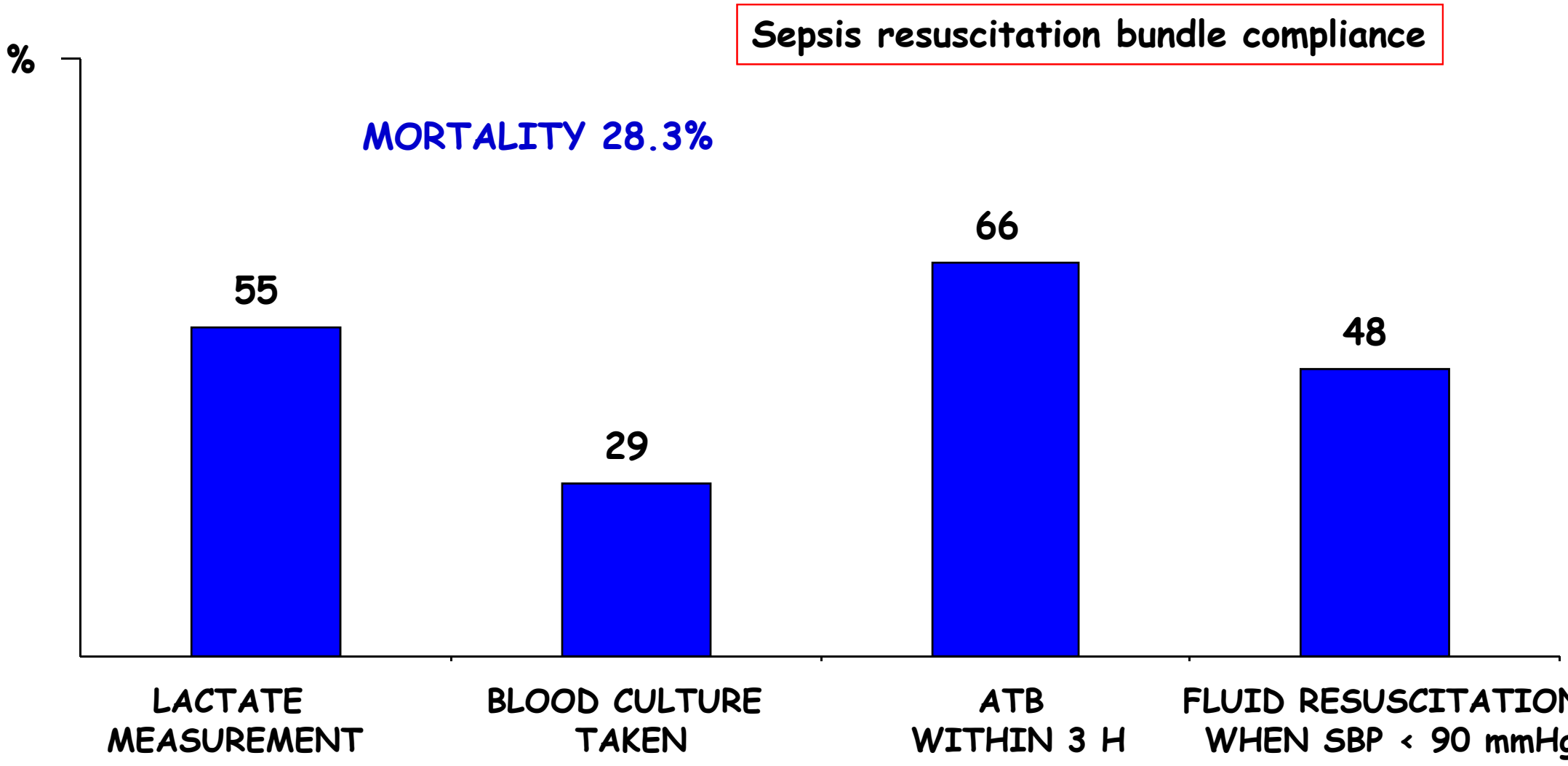


Table 1 Presumed source of infection

Source of infection	(n=)	%
Respiratory tract	411	64.5
Acute abdominal infection	55	8.6
Urinary tract	51	8.0
Skin/soft tissue	21	3.3
Other	12	1.9
Unknown source	87	13.7
Total	637	100.0%

The epidemiology of adults with severe sepsis and septic shock in Scottish emergency departments. *Gray A et al, Emerg Med J 2012 Jun 29*



SEPSIS TEAM for patients admitted to ED with a diagnosis ≥ severe sepsis

STUDY ARM

ED EVALUATION

↓

Severe sepsis/septic shock diagnosis

→ RESUSCITATORY BUNDLE

\+

ID EVALUATION (within 20')

↓

DIAGNOSTIC and

THERAPEUTIC MANAGEMENT

CONTROL ARM

ED EVALUATION

↓

Severe sepsis/septic shock diagnosis

→ RESUSCITATORY BUNDLE

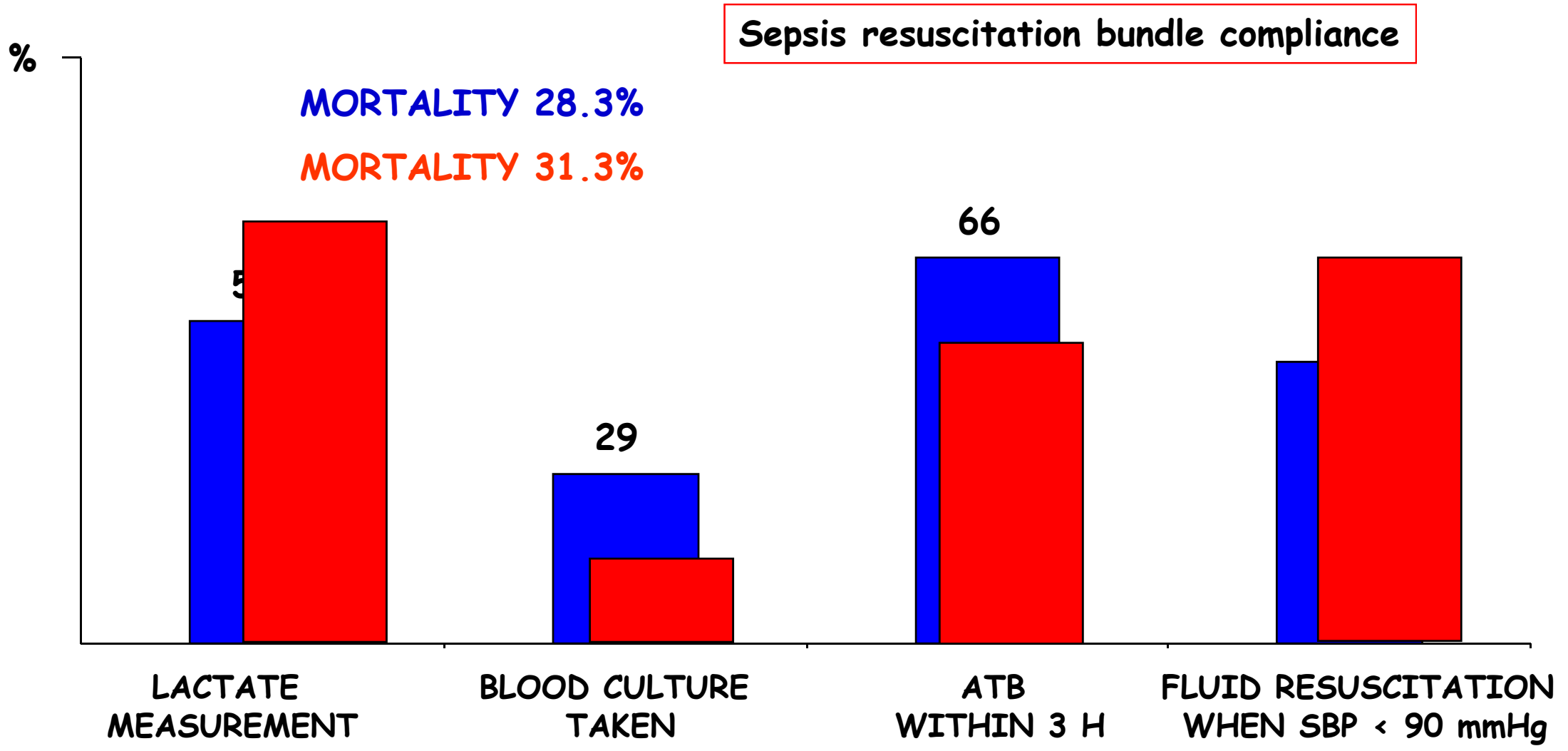
\+

DIAGNOSTIC and

THERAPEUTIC MANAGEMENT

SEPSIS TEAM for patients admitted to ED with a diagnosis ≥ severe sepsis

obsevational phase: The first 100 cases



S. Orsola-Malpighi Teaching Hospital

PENUMONIA TASK FORCE

An Infectivologist / Pneumologist connection finalized to …

Standardize antimicrobial approach

Guarantee an Early Respiratory Support

Avoid unnecessary days of therapy

Reduce Length of Hospital Stay

What Are the Potential Cost Savings Associated with Decreased Length of Stay with CAP?

A cost savings for each day of reduction in length of

Stay between $2,273 and $2,373 in 2009 USD

Economic benefit of a 1- day reduction in hospital stay for CAP

Kozma CM, et al. J Med Econ. 2010;13:719–27

Effect of a 3-Step Critical Pathway to Reduce Duration of Intravenous Antibiotic Therapy and Length of Stay in CAP. *Carratalà J et al, Arch Intern Med. 2012;172:922-928.*

Prospective, randomized trial. Enrolled patients (401 adults who required hospitalization for CAP) were randomly assigned to follow a 3-step critical pathway including early mobilization and use of objective criteria for switching to oral antibiotic therapy and for deciding on hospital discharge or usual care. Primary End Point: LOS.

The 3-steps of the critical pathway were (1) early mobilization of patients; (2) use of objective criteria for switching to oral antibiotic therapy; and (3) use of predefined criteria for deciding on hospital discharge.

Early mobilization was defined as movement out of bed with a change from the horizontal to the upright position for at least 20 minutes during the first 24 hours of hospitalization, with progressive movement each subsequent day during hospitalization, as described elsewhere.
Criteria for switching were ability to maintain oral intake; stable vital signs (considered as temperature 37.8°C, respiratory rate <24 breaths/min, systolic blood pressure > 90 mm Hg without vasopressor support for at least 8 hours); and absence of exacerbated major comorbidities (ie, heart failure, COPD) and/or septic metastases.
Predefined criteria for hospital discharge were meeting criteria for switching to oral antibiotic, baseline mental status, and adequate oxygenation on room air (PaO2 60 mm Hg or pulse oximetry >90%).

Effect of a 3-Step Critical Pathway to Reduce Duration of Intravenous Antibiotic Therapy and Length of Stay in CAP. *Carratalà J et al, Arch Intern Med. 2012;172:922-928.*

Characteristic	3-Step Critical Pathway Group (n = 200)	Usual Care Group (n = 201)
Sex, No. (%)		
Male	132 (66.0)	129 (64.2)
Age, mean (SD), y	71.5 (14.0)	69.7 (15.1)
Age group, y, No. (%)		
18-49	19 (9.5)	20 (10.0)
50-69	43 (21.5)	63 (31.3)
70-97	138 (69.0)	118 (58.7)
Alcohol consumption > 80 g/d, No. (%)[a]	28 (14.8)	40 (20.6)
Tobacco smoking, No. (%)[b]	38 (20.0)	48 (24.6)
Influenza vaccine[c]	113 (62.4)	102 (55.4)
Pneumococcal vaccine, 5 y[d]	36 (20.6)	48 (27.1)
Comorbid conditions, No. (%)	166 (83.0)	169 (84.1)
Oxygen saturation with room air, mean (SD), %[e]	90.6 (6.1)	90.8 (5.4)
Multilobar pneumonia, No. (%)	50 (25.0)	46 (22.9)
Severity risk class, No. (%)		
I, II, III	77 (38.5)	76 (37.8)
IV	88 (44.0)	92 (45.8)
V	35 (17.5)	33 (16.4)

Effect of a 3-Step Critical Pathway to Reduce Duration of Intravenous Antibiotic Therapy and Length of Stay in CAP. *Carratalà J et al, Arch Intern Med. 2012;172:922-928.*

Event	3-Step Critical Pathway Group (n = 200)	Usual Care Group (n = 201)	Difference (95% CI)[a]	*P* Value[b]
Primary end point: LOS, median (IQR), d				
Overall	3.9 (2.79 to 5.75)	6.0 (4.75 to 8.83)	−2.1 (−2.7 to −1.7)	<.001
IDIBELL–Hospital Universitari de Bellvitge	4.0 (2.83 to 5.75)	6.0 (4.62 to 8.88)	−2.0 (−2.7 to −1.3)	<.001
SCIAS–Hospital de Barcelona	3.7 (2.71 to 5.67)	6.3 (4.87 to 8.71)	−2.6 (−3.2 to −1.7)	<.001
Secondary end points				
Length of intravenous antibiotic therapy, median (IQR), d	2.0 (2.0 to 3.0)	4.0 (2.0 to 6.0)	−2.0 (−2.0 to −1.0)	<.001
Adverse drug reactions, No. (%)	9 (4.5)	32 (15.9)	−11.4 (−17.2 to −5.6)	<.001
Phlebitis	8 (4.0)	21 (10.4)	−6.4 (−11.5 to −1.4)	.02
Skin eruption	0	2 (1.0)	−1.0 (−2.4 to 0.4)	.50
Vomiting/diarrhea	0	4 (2.0)	−2.0 (−3.9 to −0.1)	.12
Allergy	1 (0.5)	1 (0.5)	0 (−1.4 to 1.4)	>.99
Transaminitis	0	3 (1.5)	−1.5 (−3.2 to 0.2)	.25
Medical complications, No. (%)	40 (20.0)	49 (24.4)	−4.4 (−12.6 to 3.8)	.34
Empyema	3 (1.5)	6 (3.0)	−1.5 (−4.4 to 1.4)	.50
Cardiac complication[c]	8 (4.0)	16 (8.0)	−4.0 (−8.6 to 0.7)	.14
Respiratory failure	15 (7.5)	8 (4.0)	3.5 (−1.0 to 8.1)	.14
Acute confusion	7 (3.5)	8 (4.0)	−0.5 (−4.2 to 3.2)	>.99
Renal failure	7 (3.5)	8 (4.0)	−0.5 (−4.2 to 3.2)	>.99
Nosocomial infection	2 (1.0)	3 (1.5)	−0.5 (−2.7 to 1.7)	>.99
Severe hyperglycemia	3 (1.5)	9 (4.5)	−3.0 (−6.3 to 0.3)	.14
Shock	2 (1.0)	3 (1.5)	−0.5 (−2.7 to 1.7)	>.99
Subsequent hospital admission (<30 d), No. (%)[d]	18 (9.1)	15 (7.5)	1.6 (−3.8 to 7.1)	.59
Overall case-fatality rate (<30 d), No. (%)	4 (2.0)	2 (1.0)	1.0 (−1.4 to 3.4)	.45