SCUOLA DI SPECIALIZZAZIONE IN MALATTIE INFETTIVE E TROPICALI

PANDORA ID - 24

TIME TO WEBINAR IN INFECTIOUS DISEASES

PROGETTO DI FORMAZIONE

Anno Accademico 23/24

STEWARDSHIP ANTIMICROBICA IN DIFFERENTI SETTING OSPEDALIERI E TERRITORIALI

21 Ottobre 2024 – Ore 16.00-19.00

Antimicrobial Stewardship in unità di terapia intensiva

Bruno Viaggi

Unit Infezioni Correlate all'assistenza del Paziente Critico
Dipartimento di Anestesia NeuroRianimazione AOU Careggi

Gruppo Tecnico Programma Lotta alla Sepsi
Coordinamento e Gruppo Tecnico AID
REGIONE TOSCANA

16.00-19.00	**STEWARDSHIP ANTIMICROBICA IN DIFFERENTI SETTING OSPEDALIERI E TERRITORIALI** Moderatore: Prof. Spinello Antinori (Milano)
16.00	**Antimicrobial stewardship in unità di terapia intensiva** Bruno Viaggi (Firenze)
16.20	**Discussione**
16.30	**Il ruolo dell'infettivologo in Pronto Soccorso e indicazioni di terapia empirica** Carlo Tascini (Udine)
16.50	**Discussione**
17.00	**Residenze per anziani: monitoraggio terapie antibiotiche e infection control** Marco Tinelli (Milano)
17.20	**Discussione**
17.30	**Antibioticoterapia e stewardship nella medicina territoriale** Mariagrazia Manfredi (Milano, OMCEOMI)
17.50	**Discussione**
18.00	.....
18.45	**Conclusioni e chiusura dei lavori**

Dichiarazione su potenziali conflitti di interesse
Consulenze, partecipazione advisory boards, speaker's bureau, contratti/contributi di ricerca e di eventi studio:

Abbott, Accelerate Diagnostics, Ada, Advanz Pharma, Alifax, Angelini, Becton Dickinson, Bellco, Biomerieux, Biotest, Cepheid, Correvio, Diasorin, Emmegi Diagnostica, Gilead, InfectoPharm, Menarini, MSD Italia, Nordic Pharma, Pfizer, Shionogi, Thermofischer Scientific, Viatris

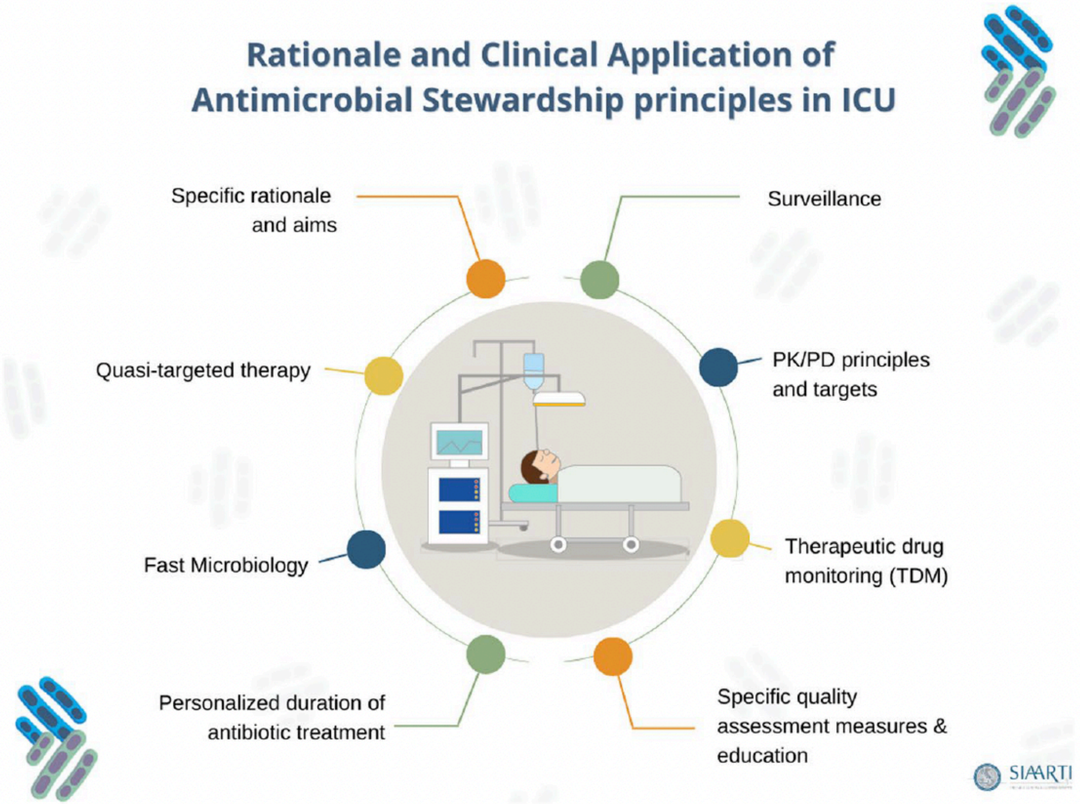
Cortegiani *et al. J Anesth Analg Crit Care* (2023) 3:11
https://doi.org/10.1186/s44158-023-00095-6

Journal of Anesthesia, Analgesia and Critical Care

ORIGINAL ARTICLE Open Access

Rationale and clinical application of antimicrobial stewardship principles in the intensive care unit: a multidisciplinary statement

Andrea Cortegiani[1,2*], Massimo Antonelli[3,4], Marco Falcone[5], Antonino Giarratano[1,2], Massimo Girardis[6], Marc Leone[7], Federico Pea[8,9], Stefania Stefani[10,11], Bruno Viaggi[12] and Pierluigi Viale[13,14]



Background: Antimicrobial resistance represents a major critical issue for the management of the critically ill patients hospitalized in the intensive care unit (ICU), since infections by multidrug-resistant bacteria are characterized by high morbidity and mortality, high rates of treatment failure, and increased healthcare costs worldwide

In the context of ASPs, all the following elements must be taken into account :

- Commitment by hospital leadership to provide human, financial resources.
- Identification of professionals responsible for program management and results.
- Appointment of a *reference pharmacist* to implement the use of antibiotics.
- Implementation of interventions (such as prospective audit, feedback, or pre-authorization)
- Monitoring the prescription of antibiotics and the impact of interventions.
- Effective communication with relevant figures, in relation to information on antibiotic use and the phenomenon of resistance.
- Educational pathways for prescribers, pharmacists, nurses, and patients, providing information on antibiotic adverse reactions, resistance, and optimal prescribing

Statement 1: Antimicrobial stewardship improves the management of antimicrobial therapy for critically ill patients in ICUs

FOR THIS REASON, THE QUALITY OF AN ANTIMICROBIAL STEWARDSHIP INTERVENTION CANNOT BE EVALUATED ONLY LOOKING AT COST SAVINGS, ESPECIALLY IN THE CONTEXT OF UNITS WITH PARTICULARLY SEVERE OR COMPLEX PATIENTS.

MOREOVER, IT IS IMPORTANT TO CONSIDER THAT PHARMACEUTICAL EXPENDITURE IN THE ICU SETTING IS INEVITABLY HIGHER THAN IN CONVENTIONAL WARDS, INCLUDING THAT OF NEW ANTIMICROBIAL DRUGS, DUE TO THE HIGHER PREVALENCE OF RISK FACTORS FOR INFECTIONS BY MDRO AND THE SEVERITY OF THE CLINICAL PRESENTATION

Cortegiani *et al. J Anesth Analg Crit Care* (2023) 3:11
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SIAARTI
PRO VITA CONTRA DOLOREM SEMPER

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1. Gatti M, et al. *Expert clinical pharmacological advice may make an antimicrobial TDM program for emerging candidate more clinically useful in tailoring therapy of critically ill patients. Crit Care* ***2022****; 26:178*
2. Dresser LD et a.l *Use of a structured panel process to define antimicrobial prescribing appropriateness in critical care. J Antimicrob Chemother* ***2018****; 73(1):246–249*

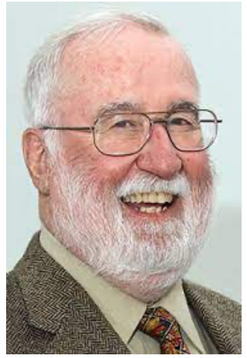
From the perspective of ensuring proper use of therapy, antimicrobial stewardship intervention is associated with a reasoned use of antibiotics and ***should not necessarily translate*** into a reduction in drug dosage or be strictly bound by the indications expressed in the various guidelines

Equilibrating SSC guidelines with individualized care

Vincent JL. et al. *Crit Care* **2021**; 25:397

When we forget the fundamental importance of individualized management, the ultimate result is that few interventions improve meaningful patient outcomes, especially mortality

"Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient. Without current best evidence, practice risks becoming rapidly out-of-date, to the detriment of patients." David Sackett



Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ*. **1996**;312:71–2

"Evidence based medicine is not "cookbook" medicine. (…) External clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patient at all and, if so, how it should be integrated into a clinical decision." David Sackett

Conclusion

Sepsis is clearly one instance where "one size does not fit all"

Twenty recommendations to individualize interventions in the early resuscitation of patients with sepsis

We recommend involving senior colleagues and consultants, especially since ***guidelines are most useful for non-experts***. Team work, communication and multidisciplinary teams are essential aspects. One of the most overarching recommendations is to seek for guidance from other colleagues and to clearly document the rationale for an intervention –be it recommended or not in the guidelines

Statement 2: Quasi-targeted therapy, based on rapid diagnosis using rapid microbiological diagnostic techniques, is the main pathogen-oriented antimicrobial treatment option in ICU

In fact, these organisms can produce different types of carbapenemases, including KPC and NDM, which may lead to changes in effective antibiotic therapy, as the new antibiotics (CZA, MVB and IMR) are active agains KPC but not NDM

The integration of a molecular and a phenotypic approach is relevant, considering that there has been a change in the current epidemiology regarding carbapenemase-resistant Enterobacterales

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Since the biodiversity of the microbiota is restored rapidly when pharmacological pressure is suspended, it follows that a reduction in treatment time has a clear favorable role, both on the hospital system and on the individual patient

The gut microbiome has a high intrinsic resistance to colonization by pathogenic and/or multi-resistant germs. In contrast, UNDER CONDITIONS of dysbiosis, which occurs during exposure to antibiotics, the microbiota is much more prone to bacterial colonization, a condition that increases the risk of infection, disease, and pathogen spillover

Statement 3: "Short-term" antimicrobial therapy may reduce the chance of infection by multi-resistant bacteria

Risk stratification – the BIOSCORE

B Biomarkers <1h
Mono/dual approach
Pro-ADM
Link to SOFA

PCT

PPV
Think about value

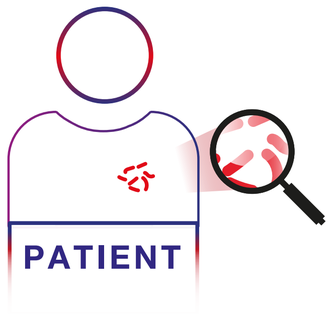
NPV
Advanced imaging
TC total body MdC TTE

"The role of stratification of the risk of infection"

A Microbiological Parameters

Colonization

Local epidemiology



C Scores
In terms of assistance in microbiological diagnostics

CRE

ESBL

C Scores
Critical patient severity

SOFA
PITT
CPISm

Tampone rettale PCR Arrow	Tampone rettale
Gene per Carbapenemasi KPC	Non rilevato
Gene per Carbapenemasi NDM	Non rilevato
Gene per Carbapenemasi IMP	Non rilevato
Gene per Carbapenemasi VIM	Non rilevato
Gene per Carbapenemasi OXA 48	Non rilevato
Gene per VanA	Non rilevato

ENVIRONMENT

Microbiological Theory — *Risks Related to Pathogen*

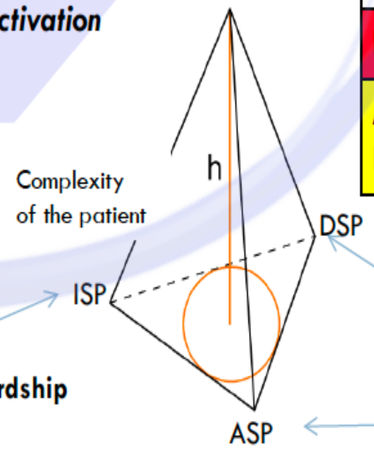
Ecological Theory — *Risks Related to Environment*

Immunological Theory — *Risks Related to Immune Deficiencies*

Genetic Theory — *Risks Related to Innate adapted immune activation*

BIOSCORE

HOST



Infection Prevention Stewardship

MICROBIOLOGY
FAST MICROBIOLOGY
(DIAGNOSTIC STEWARDSHIP)

TARGETED ANTIMICROBIAL THERAPY
(ANTIMICROBIAL STEWARDSHIP)

Risk stratification

SEVERITY SCORES
CLINICAL assessment: **CIS** SCORE **NEWS-qSOFA-SOFA-PSIS-SOFA2.0**

RISKS SCORES
RISK OF COMORBIDITIES
RISK OF IMMUNE DEFICIENCIES
RISK OF MDR INFECTION

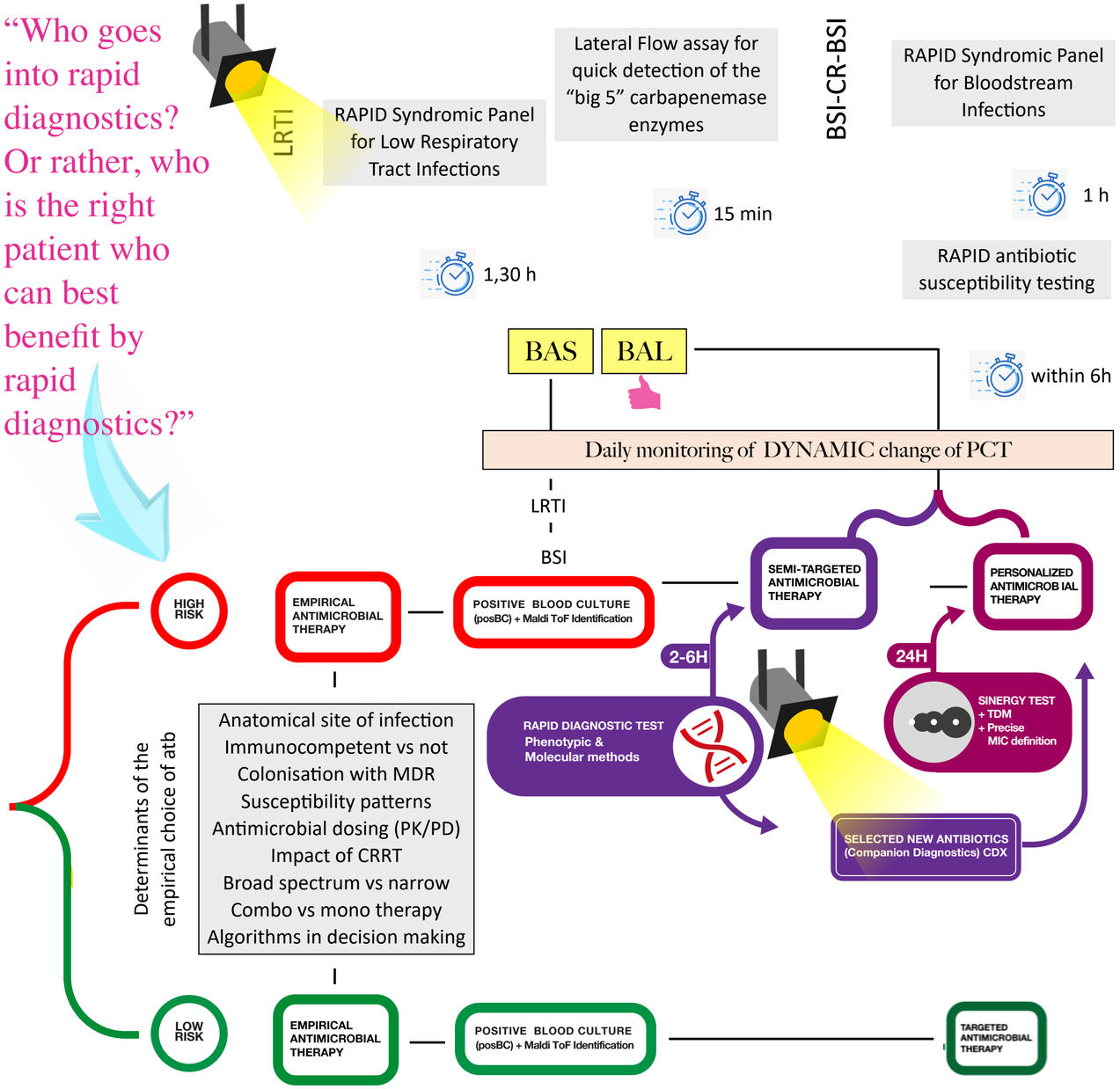
COLONIZATION OF MDR

BIOMARKERS (PCT, ProADM etc)

High Risk

Medium Risk
Low Risk

"Who goes into rapid diagnostics? Or rather, who is the right patient who can best benefit by rapid diagnostics?"



BIOFIRE® FILMARRAY® PNEUMONIA *PLUS* (PN*plus*) PANEL

1 Test. 34 Targets. ~1 Hour.

BACTERIA (Semi-Quantitative)

Acinetobacter calcoaceticus-baumannii complex
Enterobacter cloacae complex
Escherichia coli
Haemophilus influenzae
Klebsiella aerogenes
Klebsiella oxytoca
Klebsiella pneumoniae group
Moraxella catarrhalis
Proteus spp.
Pseudomonas aeruginosa
Serratia marcescens
Staphylococcus aureus
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

ATYPICAL BACTERIA (Qualitative)

Chlamydia pneumoniae
Legionella pneumophila
Mycoplasma pneumoniae

VIRUSES

Adenovirus
Coronavirus
Human metapneumovirus
Human rhinovirus/enterovirus
Influenza A virus
Influenza B virus
Middle East respiratory syndrome coronavirus (MERS-CoV)
Parainfluenza virus
Respiratory syncytial virus

ANTIMICROBIAL RESISTANCE GENES

Carbapenemases
IMP
KPC
NDM
OXA-48-like
VIM

ESBL
CTX-M

Methicillin Resistance
mecA/C and MREJ (MRSA)

"Who goes into rapid diagnostics? Or rather, who is the right patient who can best benefit by rapid diagnostics?"

LRTI

RAPID Syndromic Panel for Low Respiratory Tract Infections

1,30 h

Lateral Flow assay for quick detection of the "big 5" carbapenemase enzymes

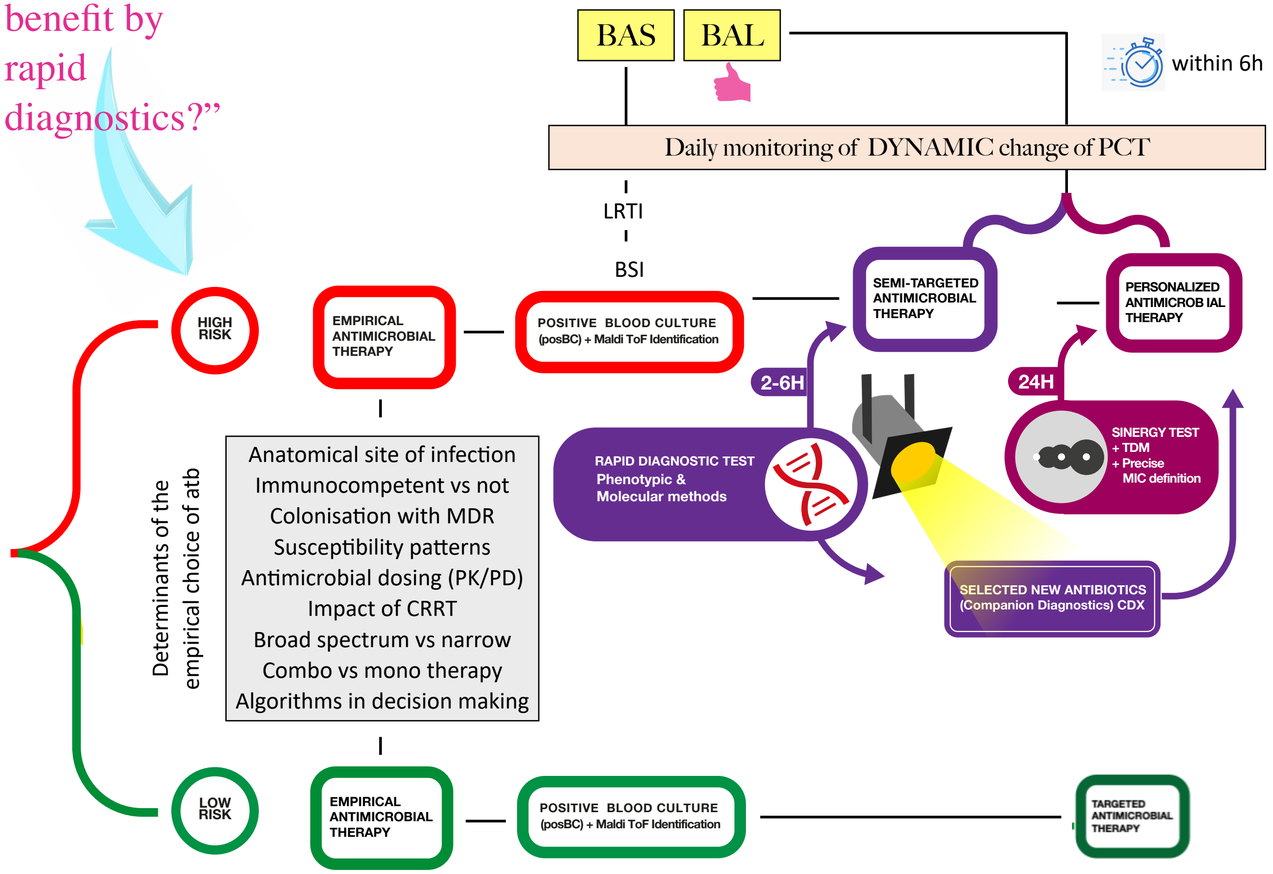
15 min

BSI-CR-BSI

RAPID Syndromic Panel for Bloodstream Infections

1 h

RAPID antibiotic susceptibility testing



Wide antimicrobial coverage for Gram-negative bloodstream infections, with 176 bug drug combinations.

ANTIMICROBIAL DRUG	MIC CALLING RANGE (µg/ml)	A. baumannii	C. freundii	C. koseri	E. cloacae	E. coli	K. aerogenes	K. oxytoca	K. pneumoniae	P. mirabilis	P. aeruginosa	
Amikacin	4 - 16	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Amoxicillin / Clavulanate	4/2 - 16/2			✓		✓		✓	✓	✓		5
Ampicillin	4 - 8					✓				✓		2
Aztreonam	1 - 16		✓	✓	✓	✓	✓	✓	✓		✓	8
Cefepime	0.125 - 64		✓	✓	✓	✓		✓	✓	✓	✓	8
Cefotaxime	0.125 - 4		✓	✓	✓	✓	✓	✓	✓	✓		8
Cefoxitin	8 - 16			✓		✓		✓	✓	✓		5
Ceftazidime	0.125 - 64		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Ceftazidime / Avibactam	0.25/4, 1/4 - 16/4		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Ceftazidime / Clavulanate	0.25/4 - 8/4					✓		✓	✓			3
Ceftolozane / Tazobactam	1/4 - 4/4				✓	✓	✓	✓	✓		✓	6
Ciprofloxacin	0.06, 0.25 - 1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Ertapenem	0.125 - 1		✓	✓	✓	✓	✓	✓	✓	✓		8
Gentamicin	2 - 4	✓	✓	✓	✓	✓	✓	✓	✓	✓		9
Imipenem	1 - 8	✓	✓	✓	✓	✓	✓	✓	✓		✓	9
Levofloxacin	0.25 - 1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Meropenem	0.125 - 8	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Meropenem / Vaborbactam	2/8 - 8/8		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Piperacillin	8 - 16		✓		✓	✓	✓	✓	✓	✓	✓	8
Piperacillin / Tazobactam	4/4 - 16/4		✓	✓	✓	✓	✓	✓	✓	✓	✓	9
Tigecycline	0.5 - 1			✓		✓						2
Tobramycin	2 - 4	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	10
Trimethoprim / Sulfamethoxazole	2/38 - 4/76	✓	✓	✓	✓	✓	✓	✓	✓	✓		9
TOTAL		8	17	19	18	23	17	21	21	18	14	176

System reports results with S/I/R interpretation according to CA-SFM 2019 and EUCAST 2021 Breakpoints

Coverage of *VITEK REVEAL® Gram negative PANEL*

Important message
test results in an average of ***5.5 hours*** from availability of a positive blood culture

Guidance by ***Molecular Antibiogram*** (*Enterobacterales*)

DIAGNOSTIC & ANTIMICROBIAL STEWARDSHIP

Antibiogr. molecolare	
CTX-M	RIL / No ril
KPC	RILEVATO
OXA-48	Non rilevato
IMP	Non rilevato
VIM	Non rilevato
NDM	Non rilevato

Antibiogr. molecolare	
CTX-M	RIL / No ril
KPC	RIL / No ril
OXA-48	RIL / No ril
IMP	RILEVATO (qualsiasi)
VIM	
NDM	

Antibiogr. molecolare	
CTX-M	RIL / No ril
KPC	RIL / No ril
OXA-48	RILEVATO
IMP	Non rilevato
VIM	Non rilevato
NDM	Non rilevato

Antibiogr. molecolare	
CTX-M	RILEVATO
KPC	Non rilevato
OXA-48	Non rilevato
IMP	Non rilevato
VIM	Non rilevato
NDM	Non rilevato

✓	CAZ-AVI MER-VAB IMI-REL FDC	FDC ATM + CAZ-AVI	CAZ-AVI FDC	Carbapenems TOL-TAZ CAZ-AVI
✗	Carbapenems TOL-TAZ	Carbapenems TOL-TAZ CAZ-AVI MER-VAB IMI-REL	Carbapenems MER-VAB IMI-REL	

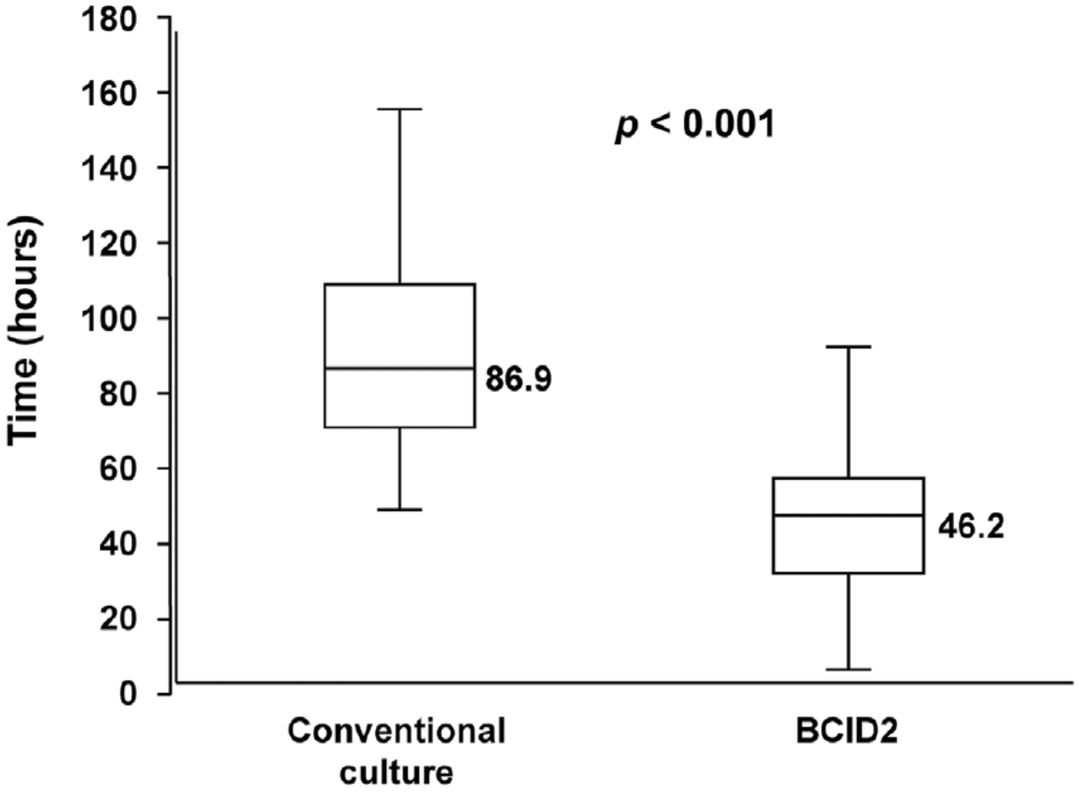
DIAGNOSTIC & ANTIMICROBIAL STEWARDSHIP

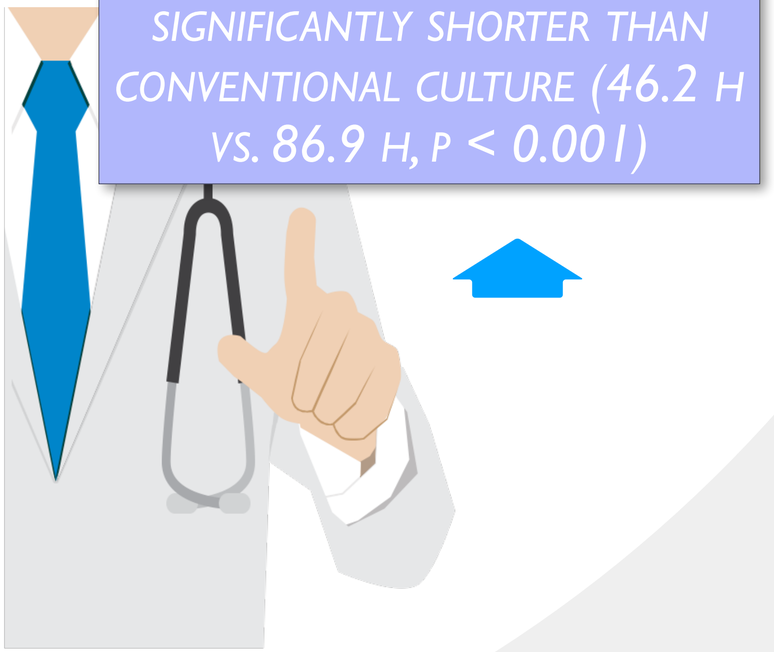
CAZ-AVI, Ceftazidime-Avibactam
MER-VAB, Meropenem-Vaborbactam
IMI-REL, Imipenem-Cilastatin-Relebactam
FDC, Cefiderocol
TOL-TAZ, Ceftolozane-Tazobactam

Gatti M, Viaggi B, Rossolini GM, Pea F, Viale P
Exp Rev Anti Infect Ther Sep **2021**
Infect Drug Resist Jun **2021**

Original Article Chen HY. et al. *J Microbiol* **2024**; 57:580-593

The real-world impact of the BioFire FilmArray blood culture identification 2 panel on antimicrobial stewardship among patients with bloodstream infections in intensive care units with a high burden of drug-resistant pathogens





THE TIME FROM BLOOD CULTURE COLLECTION TO OBTAINING BCID2 RESULTS WAS SIGNIFICANTLY SHORTER THAN CONVENTIONAL CULTURE (46.2 H VS. 86.9 H, P < 0.001)

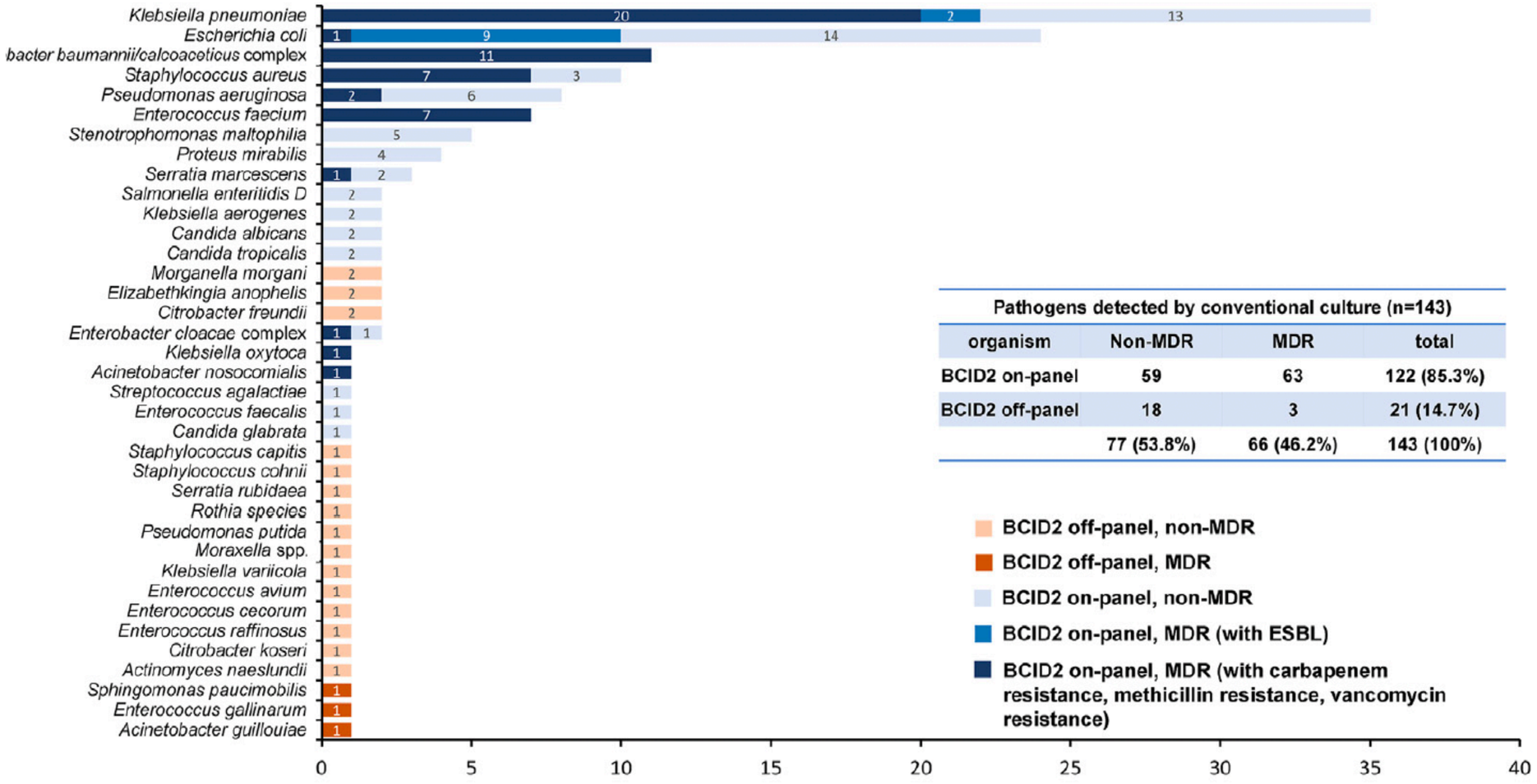
Methods: this retrospective observational study, conducted from July 2021 to August 2023, involved adult ICU patients with positive blood cultures who underwent BCID2 testing.

The ***concordance*** between BCID2 and conventional culture results was examined, and its ***impact on antimicrobial stewardship*** was assessed through a comprehensive retrospective review of patient records by intensivists

A total of 129 blood specimens from 113 patients were analysed

Among these patients, a high proportion of drug-resistant strains were noted, CRKP **57.1**%, CR AciBau **100**%, MRSA **70**%, and VRE **100**%

BCID2 DEMONSTRATED 100% CONCORDANCE IN GENOTYPE E PHENOTYPE CORRELATION IN ANTIMICROBIAL RESISTANCE (AMR) FOR CRKP, CARBAPENEM-RESISTANT ESCHERICHIA COLI, MRSA, AND VRE



Pathogens detected by conventional culture (n=143)

organism	Non-MDR	MDR	total
BCID2 on-panel	59	63	122 (85.3%)
BCID2 off-panel	18	3	21 (14.7%)
	77 (53.8%)	66 (46.2%)	143 (100%)

A TOTAL OF 40.5% OF PATIENTS RECEIVED INADEQUATE EMPIRICAL ANTIMICROBIAL TREATMENT. THE ANTIMICROBIAL REGIMEN WAS ADJUSTED OR CONFIRMED IN 55.4% OF PATIENTS FOLLOWING THE BCID2 RESULTS

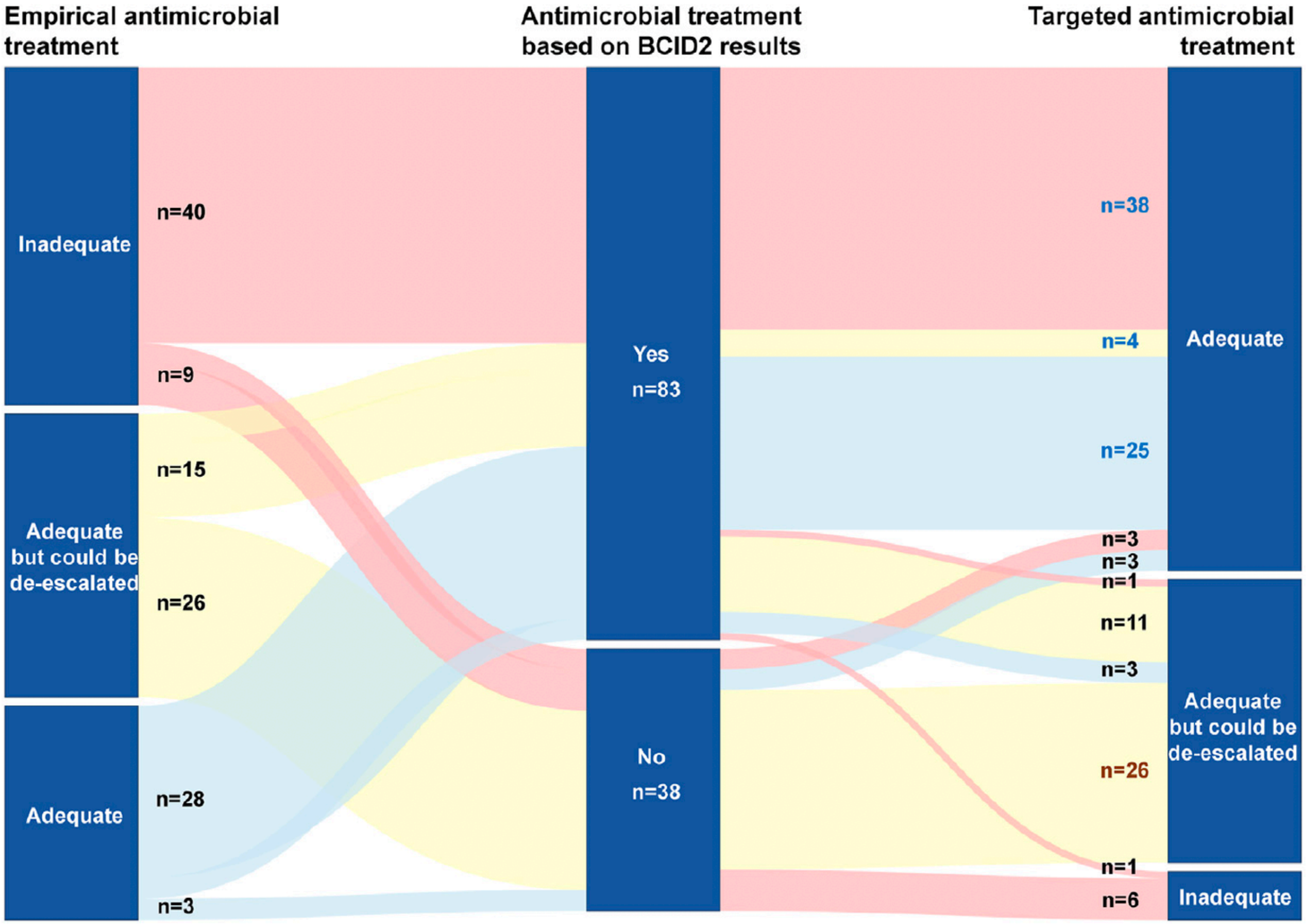


Fig. 5. Sankey diagram of the real-world antimicrobial behavior transitioning from empirical to targeted therapy, guided by the FilmArray® Blood Culture Identification Panel 2 (BCID2) panel. The first column compares the adequacy of empirical antimicrobial treatment to conventional blood culture results with antimicrobial susceptibility testing (AST). The second column represents real-world antimicrobial behavior based on BCID2 results. The third column assesses the adequacy of targeted antimicrobial treatment compared to conventional blood culture results with AST. AST, antimicrobial susceptibility testing.

Chen HY. et al. *J Microbiol* **2024**; 57:580-593

2600 ptz
333 ICUs in 52 countries

78% HA-BSI
Were ICU-acquired

Tabah A. et al. Epidemiology and outcomes of hospital-acquired bloodstream infections in intensive care unit patients: the EUROBACT-2 international cohort study. *Intensive Care Med* **2023;49**:178e90

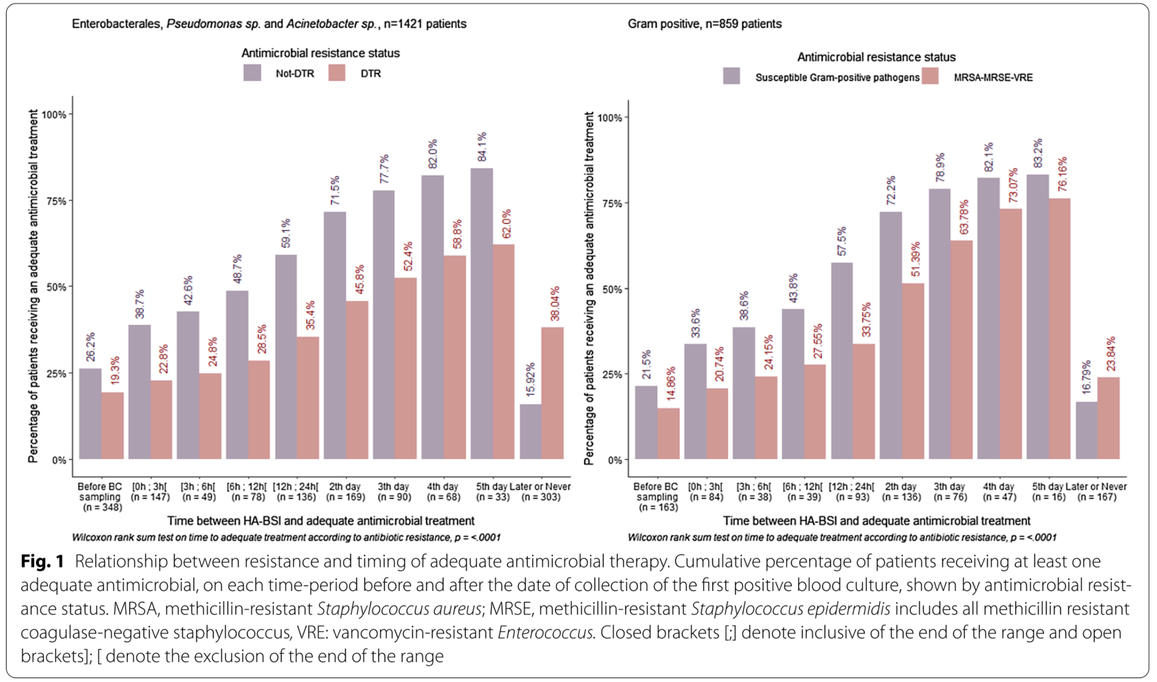


Fig. 1 Relationship between resistance and timing of adequate antimicrobial therapy. Cumulative percentage of patients receiving at least one adequate antimicrobial, on each time-period before and after the date of collection of the first positive blood culture, shown by antimicrobial resistance status. MRSA, methicillin-resistant *Staphylococcus aureus*; MRSE, methicillin-resistant *Staphylococcus epidermidis* includes all methicillin resistant coagulase-negative staphylococcus, VRE: vancomycin-resistant *Enterococcus*. Closed brackets [;] denote inclusive of the end of the range and open brackets]; [denote the exclusion of the end of the range

EARLY MICROBIOLOGICAL DIAGNOSIS THROUGH MOLECULAR RAPID DIAGNOSTIC TESTING MAY PLAY A CRUCIAL ROLE IN INITIATING TIMELY AND APPROPRIATE ANTIMICROBIAL TREATMENT

MONITORING AS DRUG-RESISTANT PATHOGENS ARE RAPIDLY RISING IN THE ICU, THE RECOMMENDED PRACTICE FOR ANTIMICROBIAL THERAPY BEFORE FINALIZING AST IN THE ICU IS TO PRESCRIBE EMPIRICAL ANTIBIOTICS BASED ON LOCAL MICROBIOLOGIC DATA AND RISK FACTORS ASSOCIATED WITH MULTIDRUG-RESISTANT (MDR) BACTERIA. HOWEVER, NO SINGLE ALGORITHM CAN BE USED TO PERFECTLY PREDICT MDR INFECTION. CONSEQUENTLY, THE EUROBACT-2 STUDY REPORTED THAT ANTIMICROBIAL THERAPY WAS CONSIDERED ADEQUATE IN ONLY 51.5% WITHIN 24 H OF BLOOD CULTURE SAMPLING, AND ANTIMICROBIAL RESISTANCE LEAD TO A LONGER DELAY

Difficult-to-treat resistance (DTR) was present in *23.5*% and pan-drug resistance in *1.5*%. Antimicrobial therapy was deemed adequate within 24 h for *51.5*%. Antimicrobial resistance was associated with longer delays to adequate antimicrobial therapy. Source control was needed in *52.5*% but not achieved in *18.2*%

Cortegiani *et al. J Anesth Analg Crit Care* (2023) 3:11
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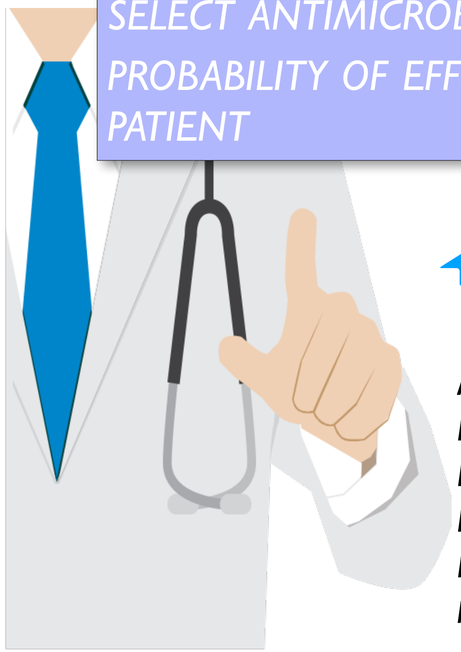
THIS PROVIDES AN INFORMATION BASE FROM WHICH TO PERFORM EMPIRICAL CLINICAL REASONING IN ORDER TO SELECT ANTIMICROBIAL THERAPY, THAT HAS THE HIGHEST PROBABILITY OF EFFICACY WHEN USED IN THE CRITICAL PATIENT



MONITORING LOCAL EPIDEMIOLOGY IS ESSENTIAL TO PROVIDE THE INTENSIVIST WITH BASIC INFORMATION REGARDING MOST LIKELY CAUSES OF INFECTIONS AND THE POSSIBLE PATTERNS OF RESISTANCE

Statement 4: Surveillance data lead to more rational choices of empirical therapy

ARS TOSCANA agenzia regionale di sanità — Regione Toscana

L'ANTIBIOTICO-RESISTENZA E L'USO DI ANTIBIOTICI IN TOSCANA NEL 2023

To overcome the lack of representativeness in regional and national territories of the EARS-NET surveillance system, the use of network services was promoted by some Italian regions (i.e., ARS Toscana)

Documenti ARS Toscana

maggio 2024 122

Cortegiani *et al. J Anesth Analg Crit Care* (2023) 3:11
https://doi.org/10.1186/s44158-023-00095-6

Journal of Anesthesia, Analgesia and Critical Care

ORIGINAL ARTICLE Open Access

Rationale and clinical application of antimicrobial stewardship principles in the intensive care unit: a multidisciplinary statement

Andrea Cortegiani[1,2*], Massimo Antonelli[3,4], Marco Falcone[5], Antonino Giarratano[1,2], Massimo Girardis[6], Marc Leone[7], Federico Pea[8,9], Stefania Stefani[10,11], Bruno Viaggi[12] and Pierluigi Viale[13,14]

FOR EXAMPLE, IN CASES OF MORE SEVERE PATIENTS, IT IS NECESSARY TO ASSESS THE INAPPROPRIATENESS OF TREATMENT FROM THE POINT OF VIEW OF THE TIME OF DRUG EXPOSURE, THE NUMBER OF TIMES UNDER/ OVER TREATMENT OCCURRED, AND WHETHER OR NOT THE THERAPEUTIC TARGET WAS REACHED (USE OF THE PK/ PD PARAMETER OPTIMIZATION MODE OR NOT)

Statement 6: Effective antimicrobial stewardship in ICU involves *specific indicators* and appropriate training

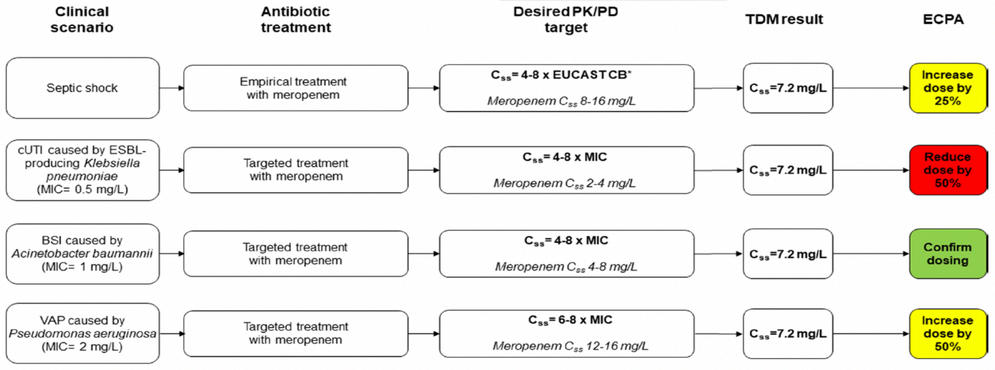
Statement 5: In the critical patient, antibiotics *should be* administered in a manner defined according to the pharmacokinetic-pharmacodynamic (PK/PD) targets of each drug class and site of infection

Research | Open access | Published: 14 June 2022

Expert clinical pharmacological advice may make an antimicrobial TDM program for emerging candidates more clinically useful in tailoring therapy of critically ill patients

Milo Gatti, Pier Giorgio Cojutti, Michele Bartoletti, Tommaso Tonetti, Amedeo Bianchini, Stefania Ramirez, Giacinto Pizzilli, Simone Ambretti, Maddalena Giannella, Rita Mancini, Antonio Siniscalchi, Pierluigi Viale & Federico Pea

Critical Care **26**, Article number: 178 (2022) | Cite this article



*EUCAST clinical breakpoint for *Enterobacterales*, *Pseudomonas spp*, and *Acinetobacter spp* = 2 mg/L

Fig. 1 Algorithms for optimizing meropenem dosing schedule according to different scenarios of empirical or targeted therapy. Dosing adjustments are implemented according to Table 1

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AN EFFICIENT ANTIMICROBIAL STEWARDSHIP PROGRAM, CARRIED OUT IN AN INTENSIVE CARE SETTING, REQUIRES THE IMPLEMENTATION OF EDUCATIONAL PATHWAYS FOR HEALTHCARE PERSONNEL TO IMPROVE ANTIMICROBIAL PRESCRIBING PRACTICE AND INFECTION CONTROL

IN THE STATEMENTS, THE IMPORTANCE OF EARLY THERAPEUTIC INTERVENTION IS EMPHASIZED, WHICH IS ACHIEVED THROUGH THE USE OF RAPID DIAGNOSTIC TECHNIQUES AND THE SHARING OF DIAGNOSTIC ALGORITHMS ENABLING FASTER PATHOGEN IDENTIFICATION

Journal of *Clinical Medicine* *J. Clin. Med.* **2022**, *11*, 4409. https://doi.org/10.3390/jcm11154409 MDPI

Article

Effectiveness of a Multifaced Antibiotic Stewardship Program: A Pre-Post Study in Seven Italian ICUs

Giulia Mandelli [1], Francesca Dore [1,2,*], Martin Langer [2,3], Elena Garbero [1,2], Laura Alagna [4], Andrea Bianchin [5], Rita Ciceri [2,6], Antonello Di Paolo [7], Tommaso Giani [8,9], Aimone Giugni [2,10], Andrea Gori [4,11,12], Ugo Lefons [13], Antonio Muscatello [4], Carlo Olivieri [2,14], Angelo Pan [15], Matteo Pedeferri [2,16], Marianna Rossi [17], Gian Maria Rossolini [8,9], Emanuele Russo [18], Daniela Silengo [2,19], Bruno Viaggi [2,20], Guido Bertolini [1] and Stefano Finazzi [1,2]

To improve patients' safety and outcomes while maintaining the efficacy of antimicrobials, ***complex interventions*** are needed involving infection control and appropriate pharmacological treatments in antibiotic stewardship programs. We conducted a ***multicenter pre-post study*** to assess the impact of a stewardship program in seven Italian intensive care units (ICUs)

Phases of the Project

- ***Definition of the indicators:*** The study board designed all indicators to measure several dimensions related to the management of infections in ICUs (resistance patterns of the isolated microorganisms to drug classes, appropriateness of drug use, clinical decisions)
- ***Plenary session:*** A kick-off meeting was organised with representatives of the ICUs (nurses, intensivists, microbiologists, infectious disease specialists, pharmacists/pharmacologists) to share the objectives of the project, to describe its phases, and to recall and discuss standard strategies for infection control in the ICU and what is known to limit the emergence of antimicrobial resistance

- ***On-site visits and follow up:*** All ICUs were visited between October 2018 and February 2019 by experienced members of the study board
- ***Final evaluation of the results***

Each ICU was visited by a multidisciplinary team involving clinicians, microbiologists, pharmacologists, infectious disease specialists, and data scientists.

Interventions ***were targeted*** according to the characteristics of each unit. The effect of the program was measured with ***a panel of indicators*** computed with data from the Margherita Tre electronic health record

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Outcomes

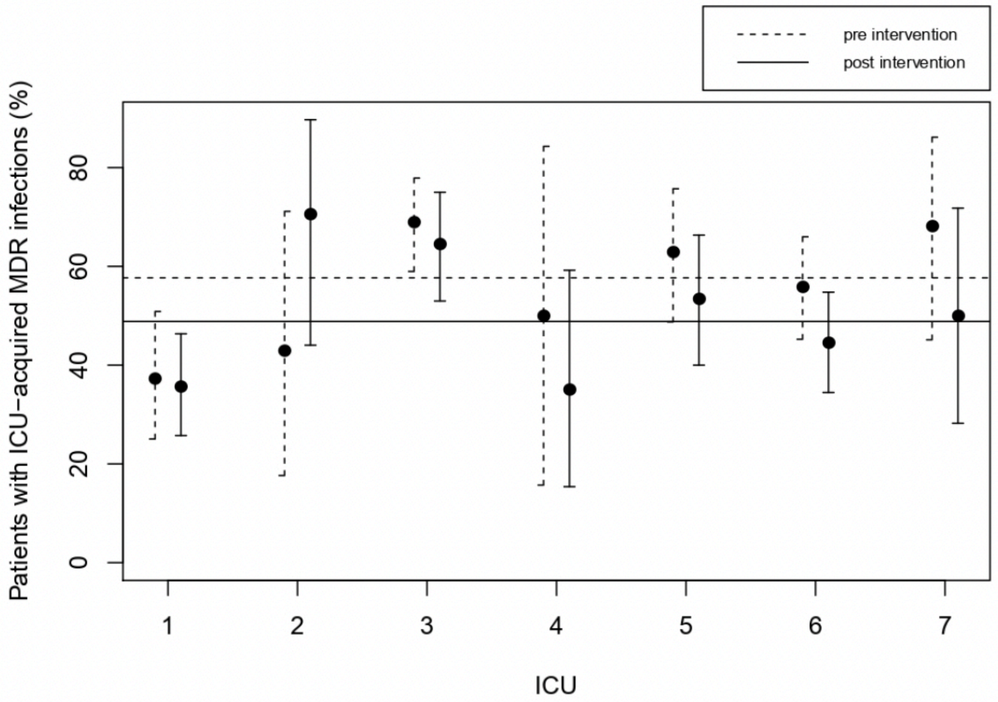

Table 2. Endpoints with % pre-/post- (aggregated) and *p*-values for all indicators. Significant levels are indicated as * $p < 0.05$, *** $p < 0.001$.

	Pre-Intervention	Post-Intervention	*p*-Value	
Frequency of patients with MDR infections (*N*/*D*)	44.9% (315/701)	39.5% (305/772)	0.11	
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ICU acquired (*N*/*D*)	57.7% (203/352)	48.8% (189/387)	0.09	
Median (IQR) duration of empirical therapy (*D*)	5.6 days (1275)	4.6 days (1406)	<0.001	***
Median duration of prophylaxis (*D*)	2.3 days (589)	2.0 days (584)	0.06	
Inappropriateness of antibiotics by penetration into the site of infection (*N*/*D*)	2.3% (49/2117)	1.9% (49/2619)	0.26	
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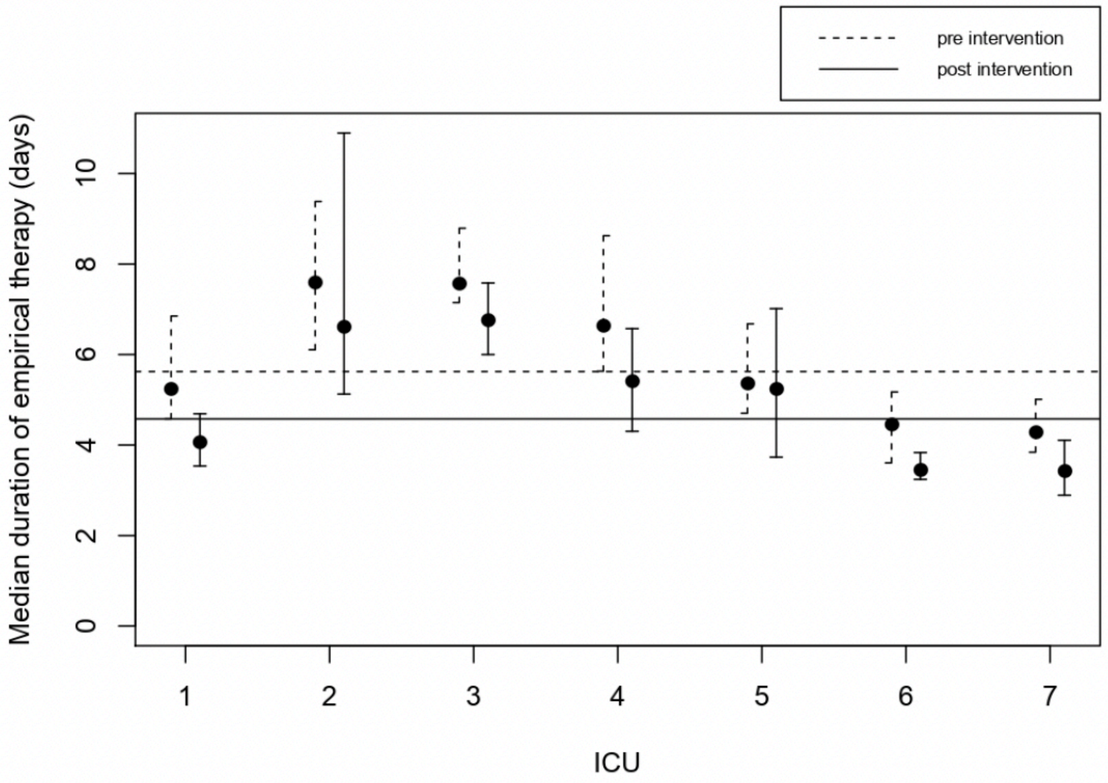

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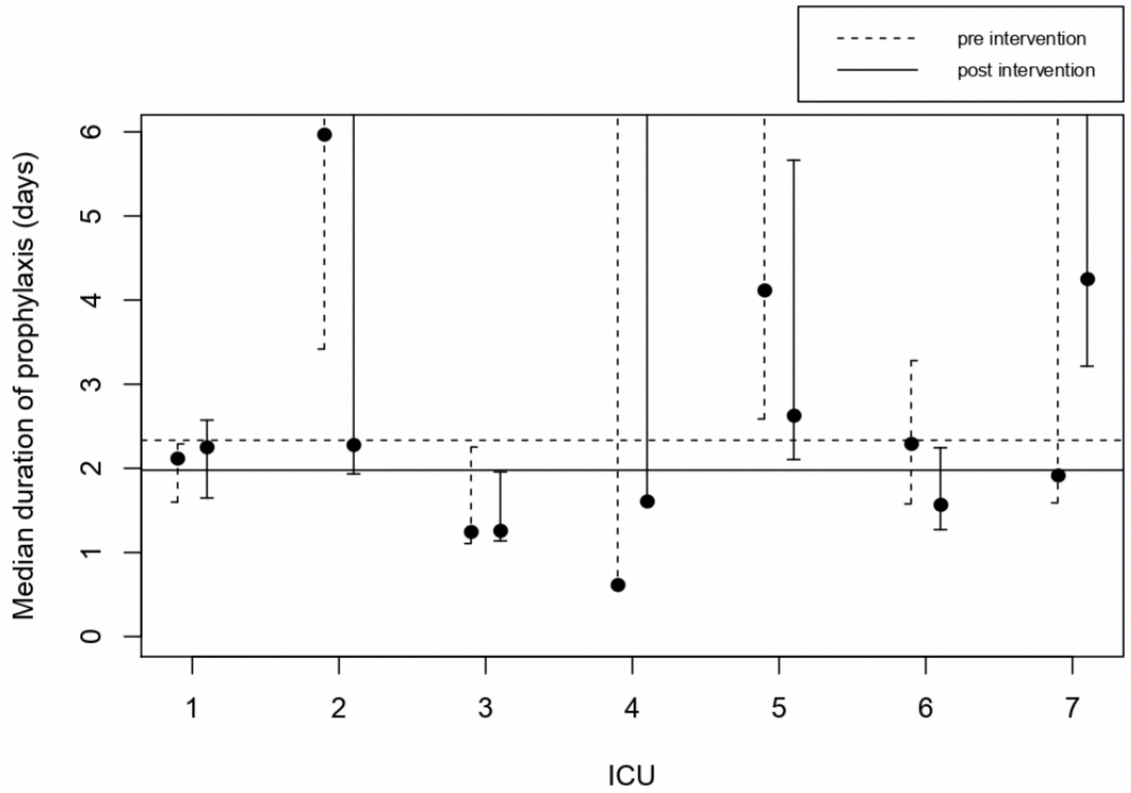

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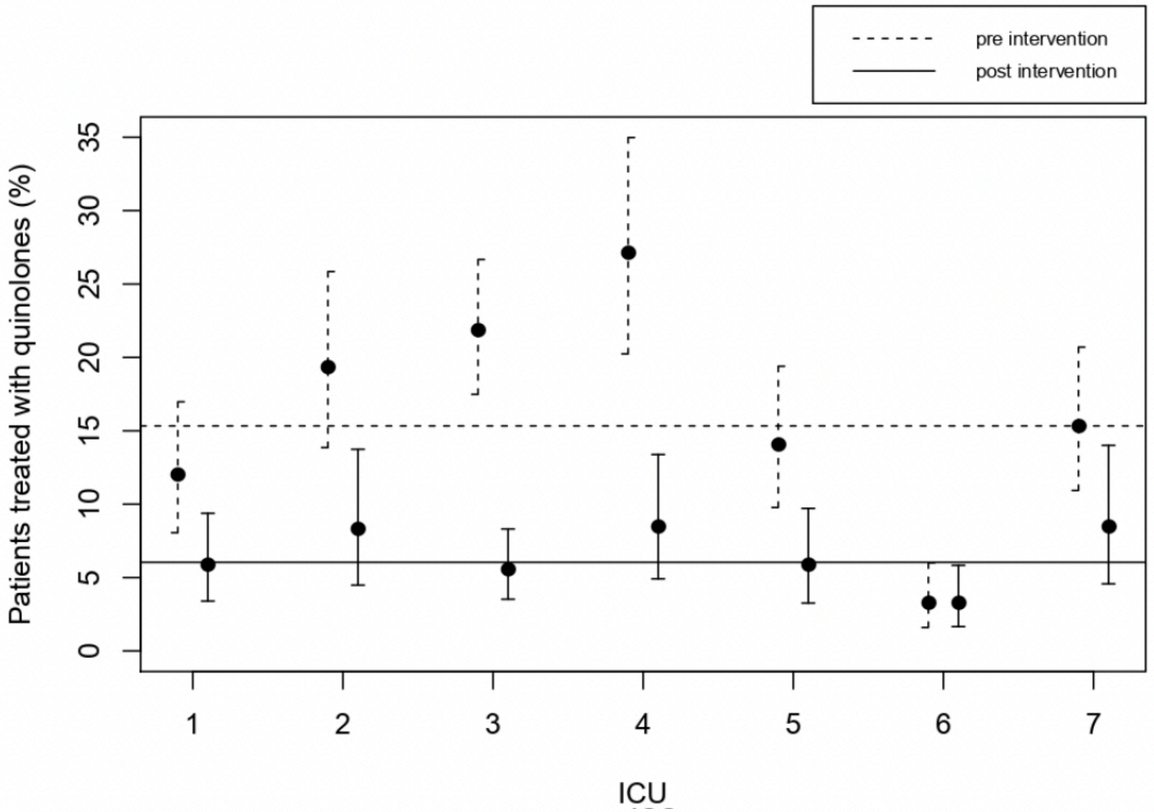

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1.5.1.2 Terapie mirate

Definizione:
La terapia con carbapenemico é inappropriata quando il germe é sensibile ad una cefalosporina o penicillina.

Si considerano solo gli antibiogrammi (funghi esclusi) con referto visionato nei tre giorni precedenti o nei primi tre giorni di terapia.

$$\text{Percentuale} = \frac{\text{Numero di terapie mirate inappropriate secondo definizione}}{\text{Numero di terapie mirate con germe identificato e antibiogramma}} \times 100 \qquad (12)$$

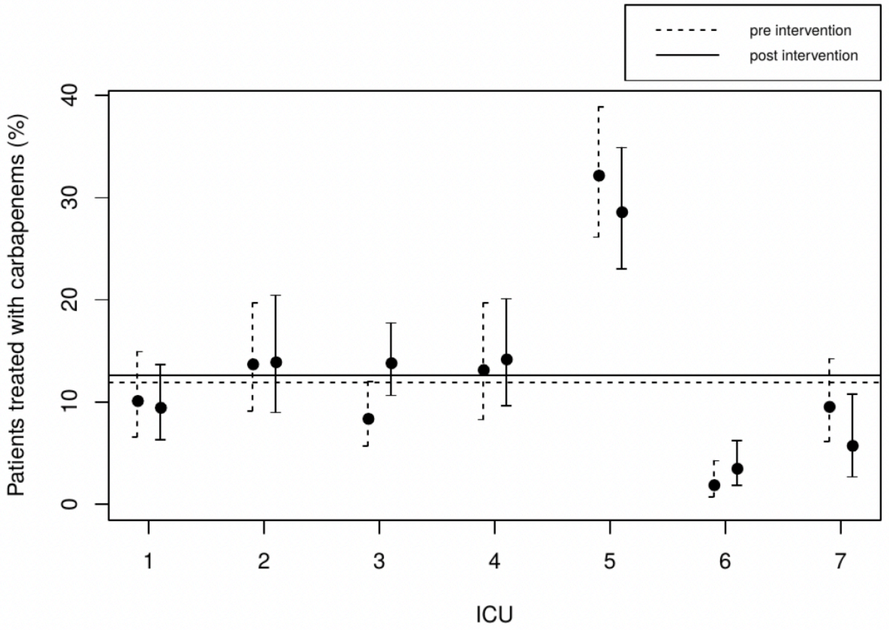
Numeratore	25 terapie
Denominatore	57 terapie
Indicatore	43.86%
Intervallo di confidenza (80%)	(34.85,53.21)

ATTENZIONE: Per questo indicatore si sono considerati i dati di tutti i centri dal momento che i dati per singolo centro sono pochi.

Elenco pazienti con terapia mirata di carbapenemico inappropriata:

Codice centro	Codice Paziente	Molecola
IT512	610	MEROPENEM TRIIDRATO
IT512	647	MEROPENEM TRIIDRATO
IT512	688	MEROPENEM TRIIDRATO
IT512	717	MEROPENEM TRIIDRATO

e. Use of carbapenems



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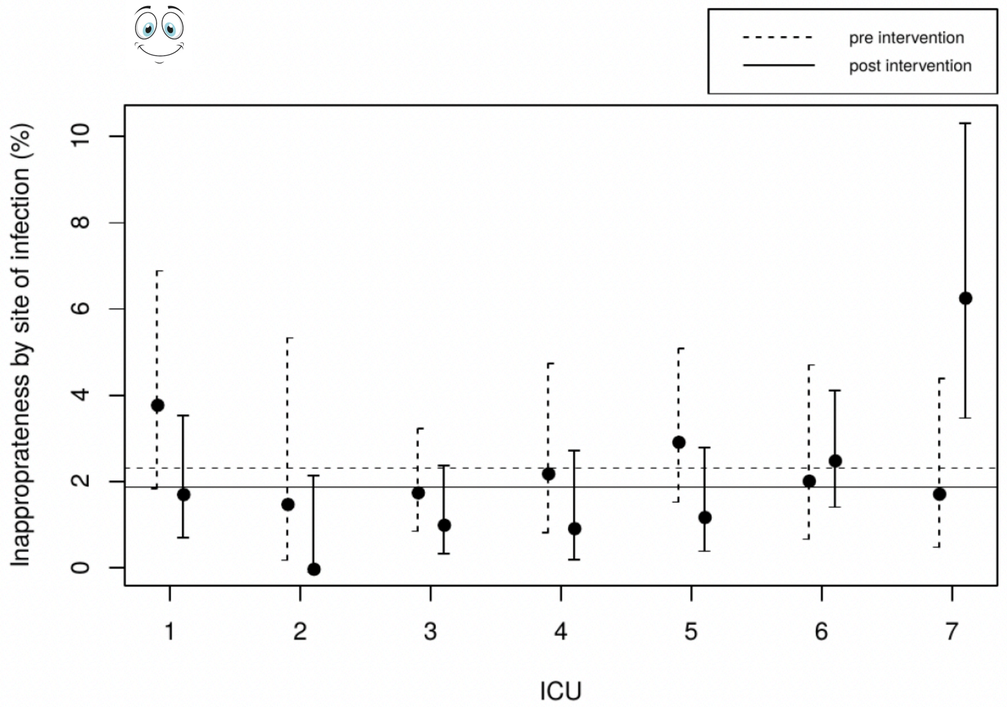
EHR= Electronic Health Record

b. Inappropriateness of antibiotics by penetration into the site of infection



THE FEASIBILITY AND THE SUCCESS OF THIS MULTICENTER ASP SHOULD NOW ENCOURAGE HEALTHCARE POLICY MAKERS TO CONSIDER THAT "WHERE THERE'S A WILL, THERE'S A WAY"

OUR ASP ADOPTED A MULTIDISCIPLINARY APPROACH INVOLVING CLINICIANS, MICROBIOLOGISTS, PHARMACOLOGISTS, INFECTIOUS DISEASE SPECIALISTS, AND DATA SCIENTISTS. IT SUCCESSFULLY REDUCED ANTIBIOTIC CONSUMPTION AND MDR, WITHOUT RISKING PATIENT SAFETY. SIMPLE INDICATORS, WHICH CAN EASILY BE UPDATED TO THE NEWER DRUGS AND DIFFERENT PATIENT POPULATIONS, WERE AUTOMATICALLY COMPUTED FROM COMMON EHR, HELPING TO MONITOR ASP DATA

Antibiotic stewardship in sepsis management: toward a balanced use of antibiotics for the severely ill patient

Jan J. De Waele & Sofie Dhaese

To cite this article: Jan J. De Waele & Sofie Dhaese (2019) Antibiotic stewardship in sepsis management: toward a balanced use of antibiotics for the severely ill patient, Expert Review of Anti-infective Therapy, 17:2, 89-97, DOI: 10.1080/14787210.2019.1568239

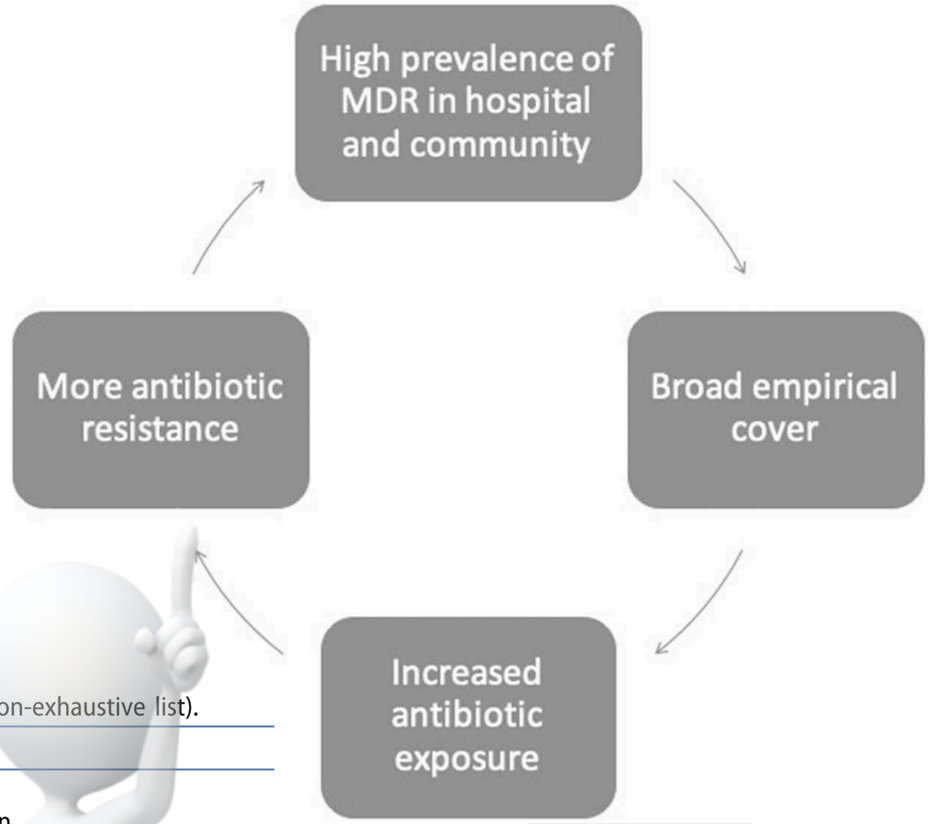


Table 2. Examples of possible actions and interventions in the context of antimicrobial stewardship aimed at balanced antibiotic use (non-exhaustive list).

Domain	Possible actions or interventions*
Optimized risk assessment for MDR involvement	• 'Antibiotic history'-taking before deciding on empirical therapy • Personal EMR review for recent hospitalization or known MDR colonization
Informed empirical therapy	• Use of surveillance cultures • Up-to-date information on local susceptibility patterns and microbiological epidemiology trends • 24/7 availability of direct examination of clinical samples and clinical microbiology consultation
Rapid diagnostics to rule in or rule out MDR involvement	• Use of molecular biological techniques to identify MRSA and other MDR pathogens • Direct antibiogram on clinical samples
Optimized dosing	• Prolonged infusion of beta-lactam antibiotics • Availability of therapeutic drug monitoring
Early discontinuation in unconfirmed infection	• Complete microbiological work-up at initiation of antibiotics • Regular discussion with clinical microbiologist • Adequate documentation of diagnostic certainty with details at the start of antibiotics
Watchful waiting in non-septic shock patients without obvious infection	• Antibiotic withholding and repeated clinical re-evaluation in patients without septic shock and uncertain infection diagnosis

Legend. MDR = multidrug resistance; EMR = electronic medical records; MRSA = methicillin-resistant *Staphylococcus aureus*.

bruno.viaggi@gmail.com