Personalized approach of nosocomial infection management: 4-dimensional matrix

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Personalized approach of nosocomial infection ?

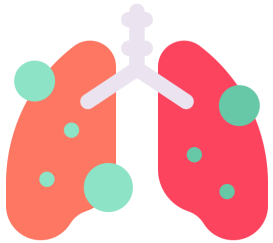
Q1. How do we manage nosocomial infection?

Nosocomial infection management

Risk of MDR

Culture

Targeted therapy



Nosocomial infection

Empiric

Deescalate

Escalate

Targeted therapy

2-3 days

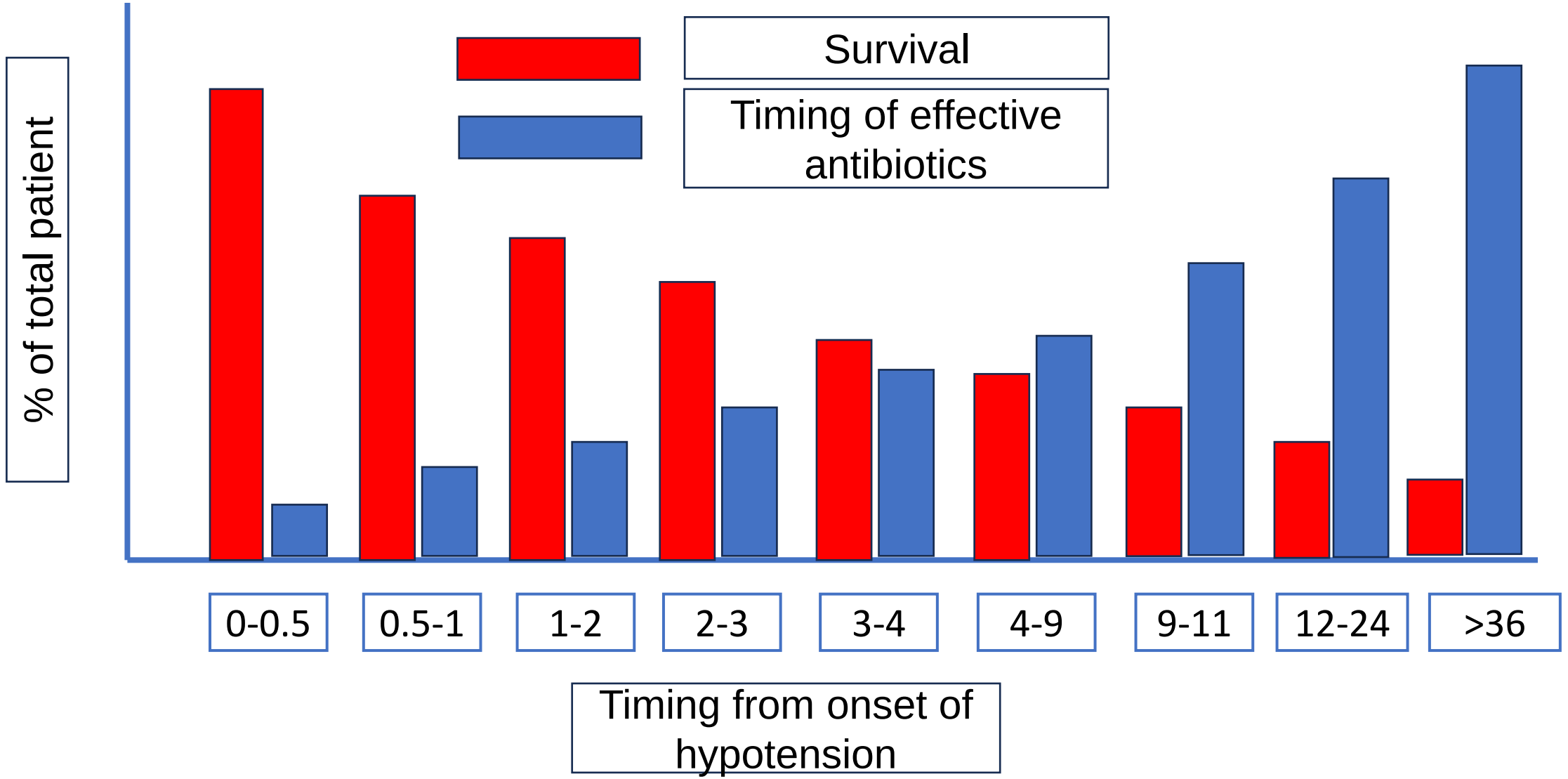
Severity of illness

Personalized approach of nosocomial infection ?

Q1. How do we manage nosocomial infection?

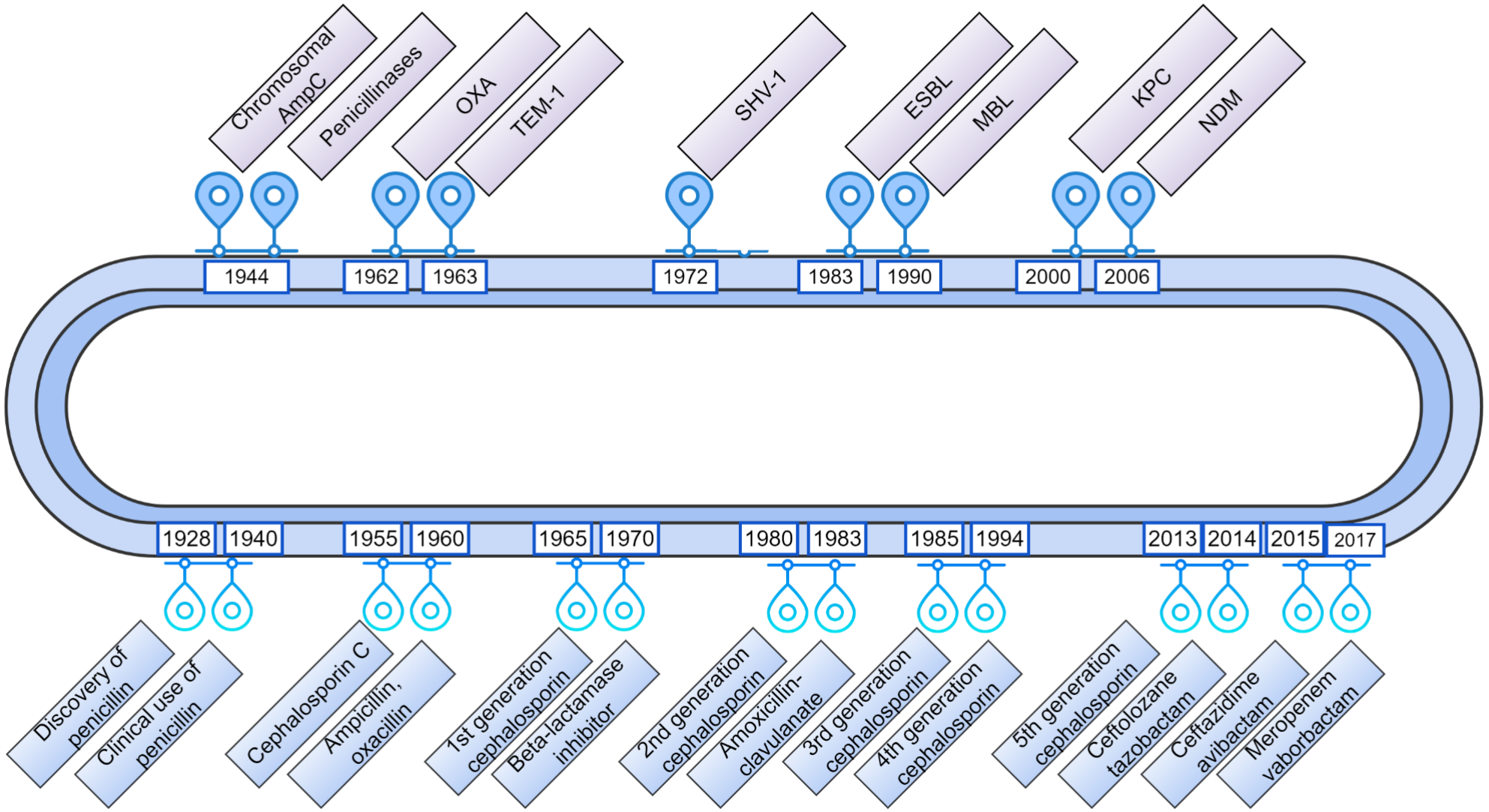
Q2. Why empirical therapy in nosocomial infection is important?

Mortality increases 5-10% every hour until effective antibiotic is initiated



Crit Care Med 2006; **34**: 1589–96.

Discovery of beta-lactam and evolution of beta-lactamases



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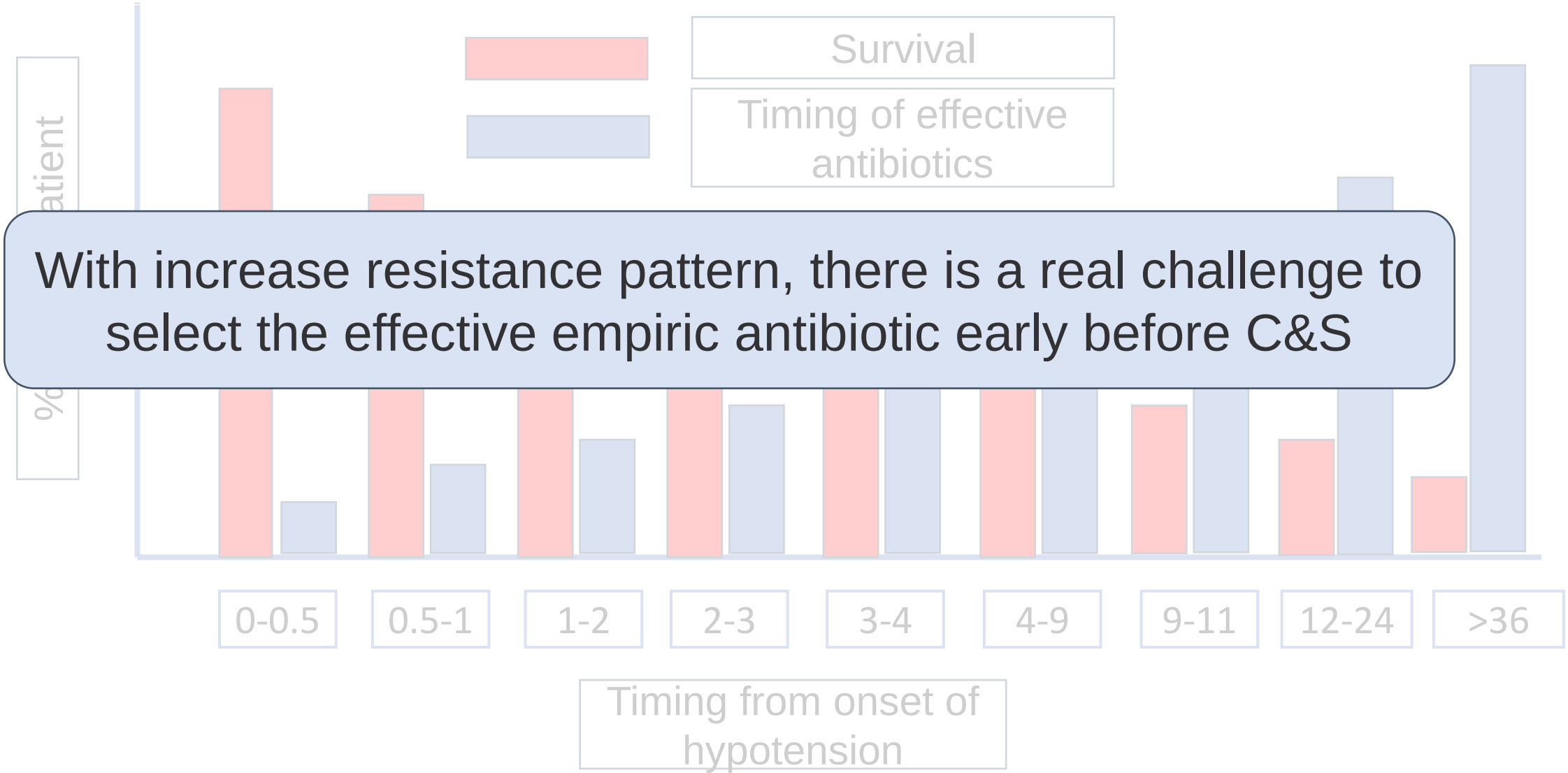


With increase resistance pattern, there is a real challenge to select the effective empiric antibiotic early before C&S

Crit Care Med 2006; **34**: 1589–96.

2016

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

ERJ open research

CrossMark click for updates

2018

CLINICAL SIGNPOST PNEUMONIA

Summary of the international clinical guidelines for the management of hospital-acquired and ventilator-acquired pneumonia

Guideline for VAP management

High risk for MDR

MRSA coverage + Two antipseudomonal from two separate classes

Guideline recommendation may be very aggressive for empiric antibiotic of nosocomial infection management

guidelines

AWaRe

Access. Watch. Reserve.

World Health Organization

WHO developed a framework based on three different categories – Access, Watch and Reserve

The WHO AWaRe (Access, Watch, Reserve) antibiotic book

Antimicrobial stewardship perspective

Access

- First or second choice
- Minimal potential of resistance

Watch

- Critically important
- High potential of resistance

Reserve

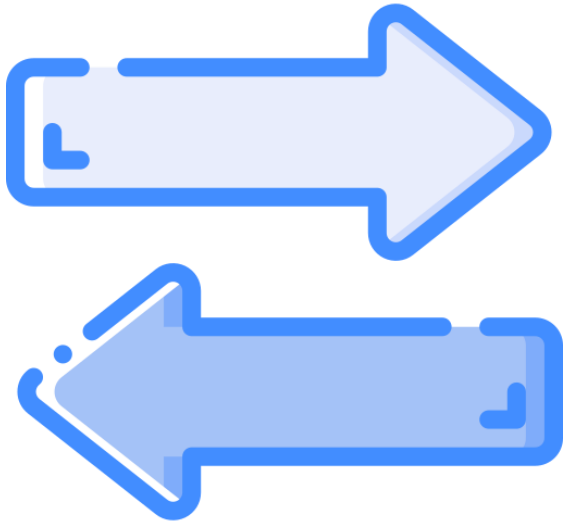
- Last resort
- Reserved for MDR infection

Access	Watch	Reserve
Ampicillin	Vancomycine	Colistin
Amikacin	Meropenem	Tigecycline
Cefazolin	Quinolones	Ceftazidime-avibactam

Antimicrobial therapy should be a trade off between conservative use of antibiotics and choice of effective therapy

Stewardship

Conservative use of antibiotic



Guideline

Choice of effective therapy

Personalized approach of nosocomial infection ?

Q1. How do we manage nosocomial infection?

Q2. Why empirical therapy in nosocomial infection is important?

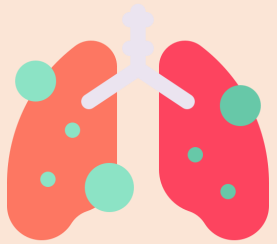
Q3. What is the concept of 4-Dimensional matrix?

Personalized approach for nosocomial infection management: 4-D matrix

Burden of MRSA & MDR-GNB

Guidelines recommendation

Risk of MDR



Site of infection

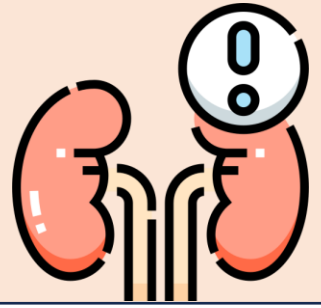
Type of pathogens

Efficacy of antibiotics

Choice from list

Optimal time for stopping

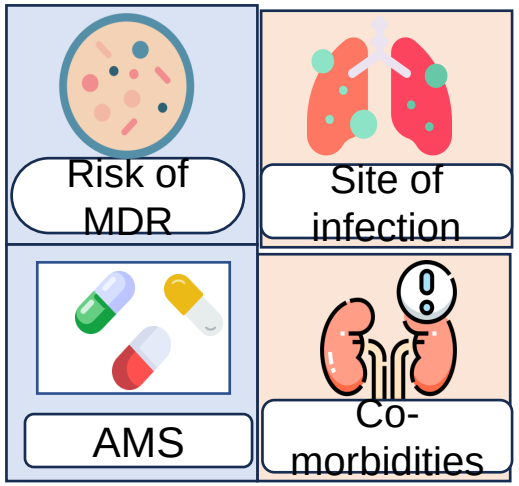
Antimicrobial stewardship



Comorbidities

Dose adjustment

Safety of antibiotics


Risk of MDR
Site of infection
AMS
Co-morbidities

Site of infection				
Co-morbidities				
Risk of MDR				
AMS				
Abx choice				

Personalized approach of nosocomial infection ?

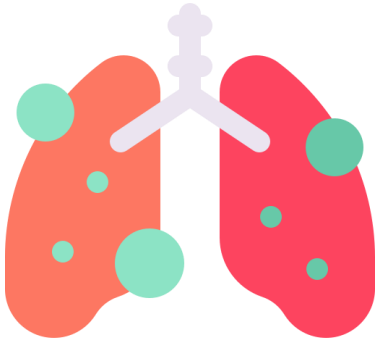
Q1. How do we manage nosocomial infection?

Q2. Why empirical therapy in nosocomial infection is important?

Q3. What is the concept of 4-Dimensional matrix?

Q4. How do we apply the personalized approach in clinical practice?

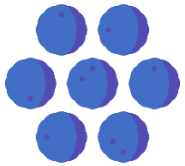
Personalized approach for nosocomial infection management



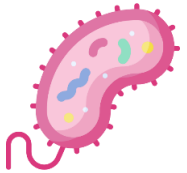
VAP/HAP

How the guideline assess the risk of MDR in VAP/HAP?

Patient risk: risk of MDR



Risk of MRSA



Risk of MDR:GNB

- Previous use of IV antibiotic in last 90 days

- 10-20% of staph isolates are MRSA
- Unknown prevalence of MRSA

Any of the following

- 20-25% of gram –ve isolates are MDR
- Septic shock at time of VAP
- ARDS preceding VAP
- RRT preceding VAP
- ≥ 5 days of hospitalization prior to VAP

Patient risk: risk of MDR

Risk of MRSA

- 10-20% of staph isolates are MRSA
- Unknown prevalence of MRSA

Risk of MDR:GNB

Any of the following

- 20-25% of gram –ve isolates are MDR
- Septic shock at time of VAP
- ARDS preceding VAP
- RRT preceding VAP
- ≥ 5 days of hospitalization prior to VAP

According to guideline, almost all patients acquired infection in the hospital will be at risk of MRSA and MDR-GNB

Guideline for VAP management

MRSA coverage

Vancomycin

OR

Linezolid

Two antipseudomonal from two separate classes

Piperacillin/taz

OR

Cephalosporin

OR

Carbapenem

Quinolones

OR

Aminoglycoside

OR

Colistin

Guideline for VAP management

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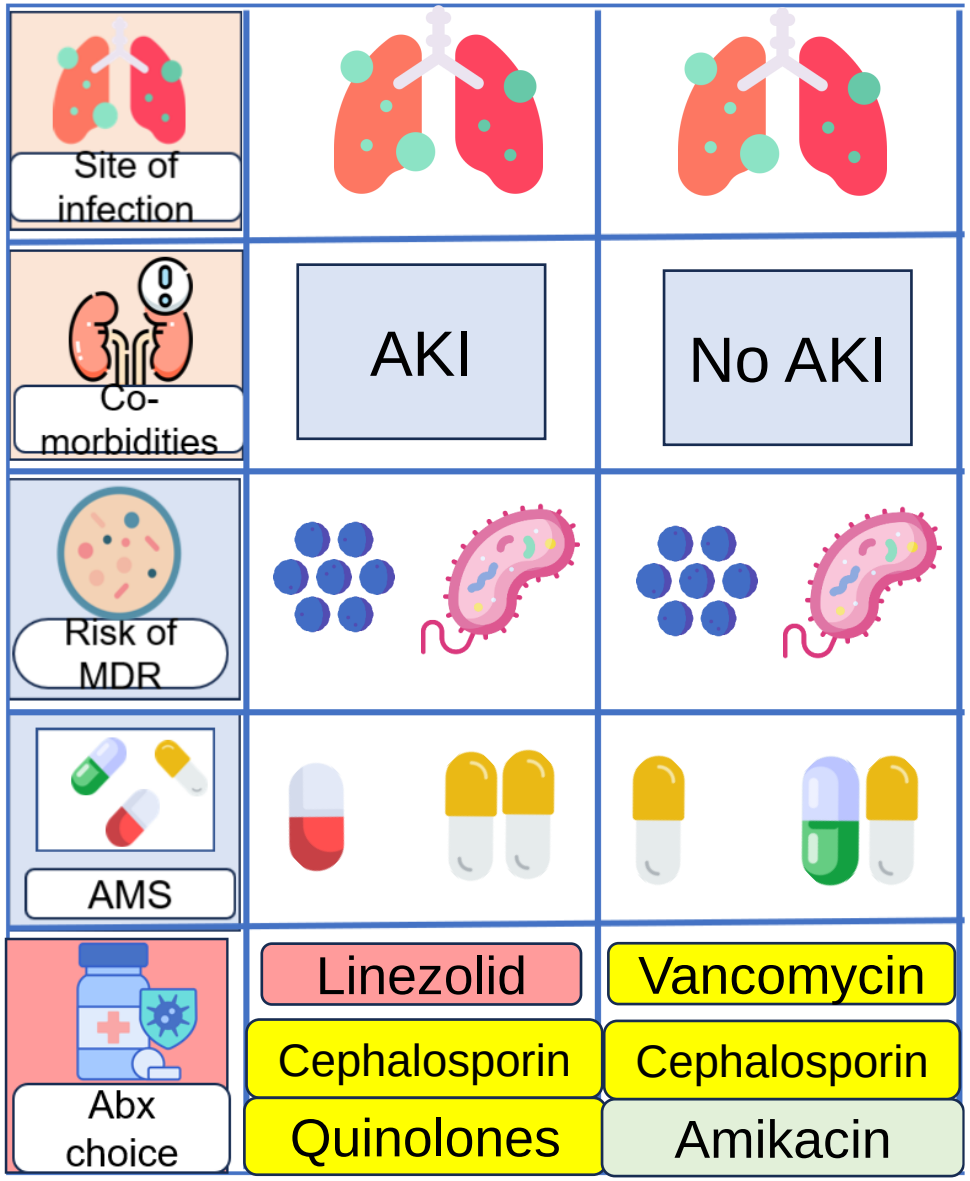
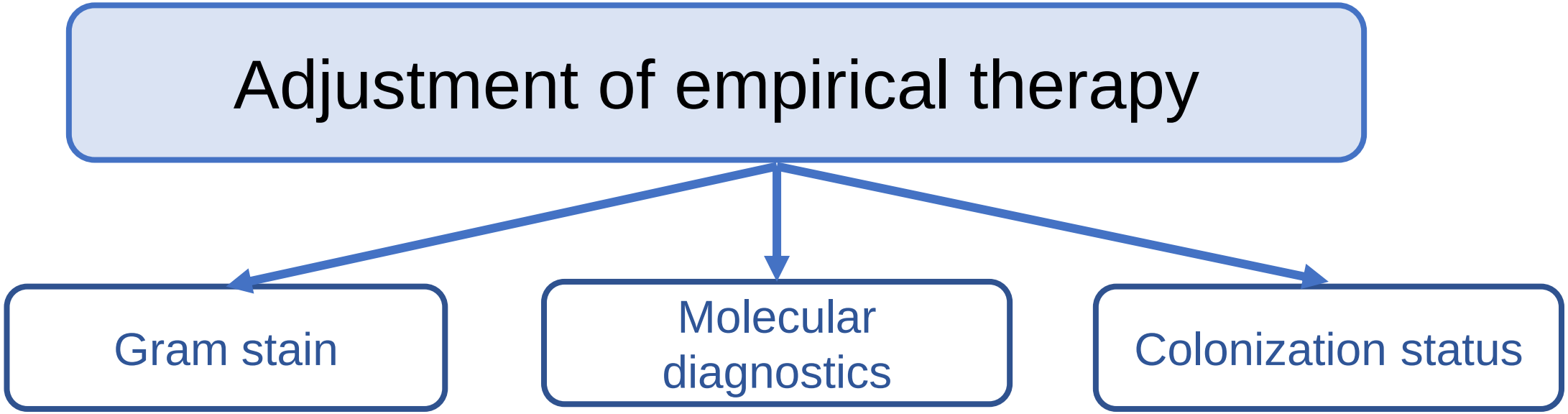
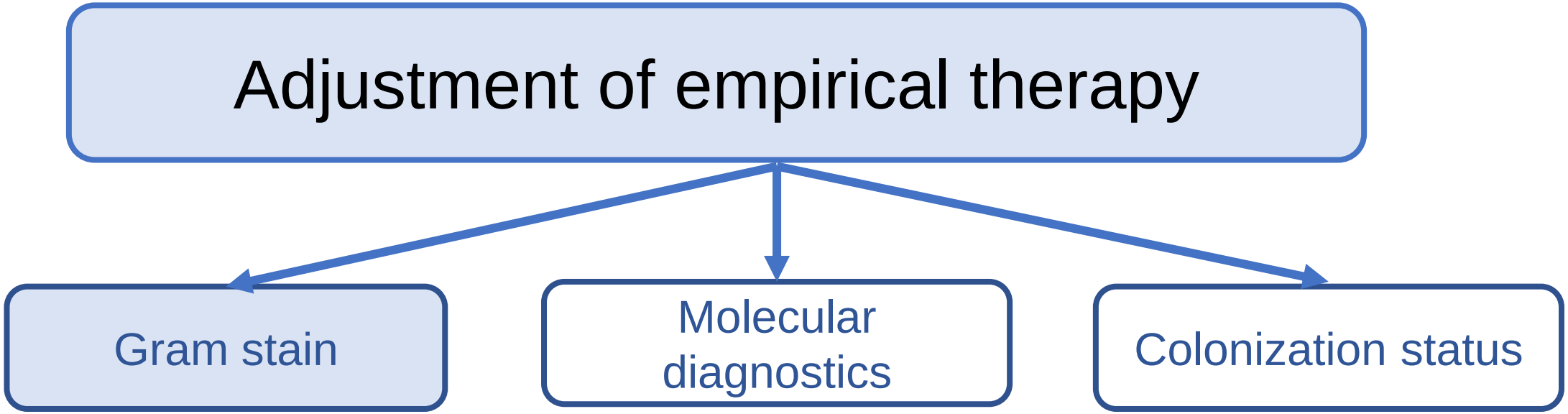
Personalized approach for VAP/HAP management using risk assessment of MDR by guideline



Can we improve recognition of MDR burden during empiric therapy?


Adjustment of empirical therapy
Gram stain
Molecular diagnostics
Colonization status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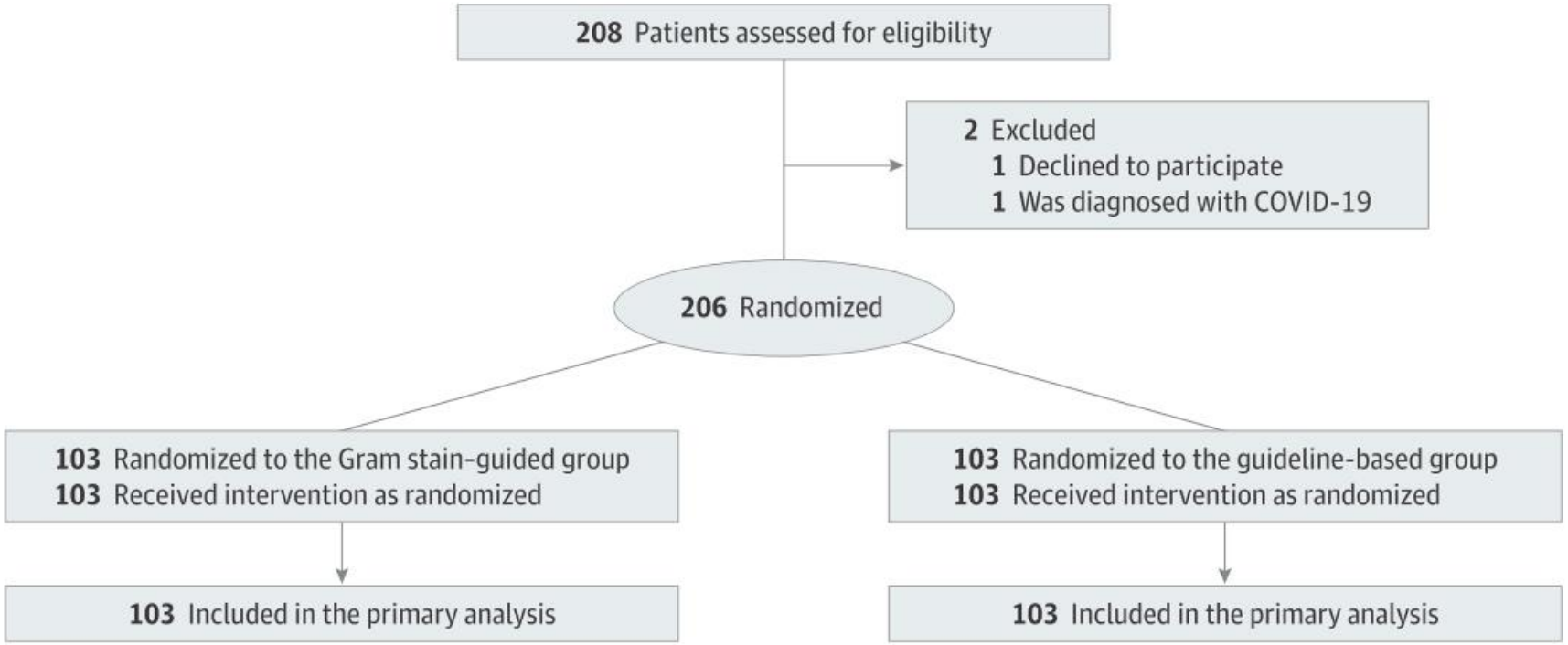
Original Investigation | Critical Care Medicine

Effect of Gram Stain-Guided Initial Antibiotic Therapy on Clinical Response in Patients With Ventilator-Associated Pneumonia

The GRACE-VAP Randomized Clinical Trial

Multicenter randomized controlled study



JAMA Network Open. 2022;5(4):e226136.

Original Investigation | Critical Care Medicine

Effect of Gram Stain–Guided Initial Antibiotic Therapy on Clinical Response in Patients With Ventilator-Associated Pneumonia

The GRACE-VAP Randomized Clinical Trial

Outcome	No. (%) Gram stain-guided group (n = 103)	Guideline-based group (n = 103)	*P* value
Primary outcome			
Clinical response rate	79 (76.7)	74 (71.8)	<.001[a]
Completion of antibiotic therapy within 14 d[b]	98 (95.1)	94 (91.3)	NA
Improvement or lack of progression of baseline radiographic findings[b]	85 (82.5)	78 (75.7)	NA
Resolution of signs and symptoms of pneumonia[b]	87 (84.5)	85 (82.5)	NA
Lack of antibiotic agent readministration[b]	85 (82.5)	85 (82.5)	NA
Secondary outcomes			
28-d mortality	14 (13.6)	18 (17.5)	.44
28-d ventilator-free days, median (IQR)	22 (15-24)	22 (18-25)	.21
28-d ICU-free days, median (IQR)	19 (15-22)	20 (16-23)	.42
Administration of antibiotic therapy			
Antipseudomonal agents	72 (69.9)	103 (100)	<.001
Anti-MRSA agents	63 (61.2)	103 (100)	<.001
Coverage rate of initial antibiotic therapy	89 (86.4)	95 (92.2)	.18
Escalation[b]	7 (6.8)	1 (1.0)	.03
De-escalation	67 (65.0)	79 (76.7)	.07
Antibiotic therapy days until de-escalation, median (IQR)	3 (2-4)	3 (2-4)	.22
Antibiotic therapy days, median (IQR)	8 (7-11)	8 (7-11)	.09

Multicenter randomized controlled study

Clinical response

Gram stain-guided

76%

Guideline-based guided

71%

P<0.001

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Multicenter randomized controlled study

Use of antipseudomonal

Gram stain-guided

70%

Guideline-based guided

100%

P<0.001

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Original Investigation | Critical Care Medicine

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Multicenter randomized controlled study

Use of anti-MRSA

Gram stain-guided

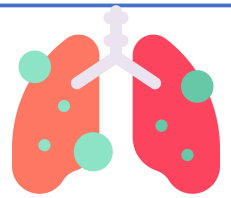
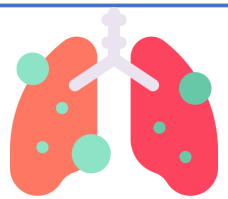
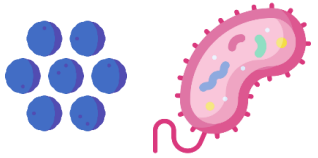
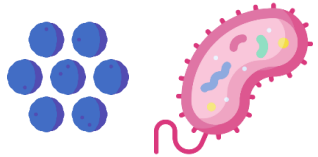
61%

Guideline-based guided

100%

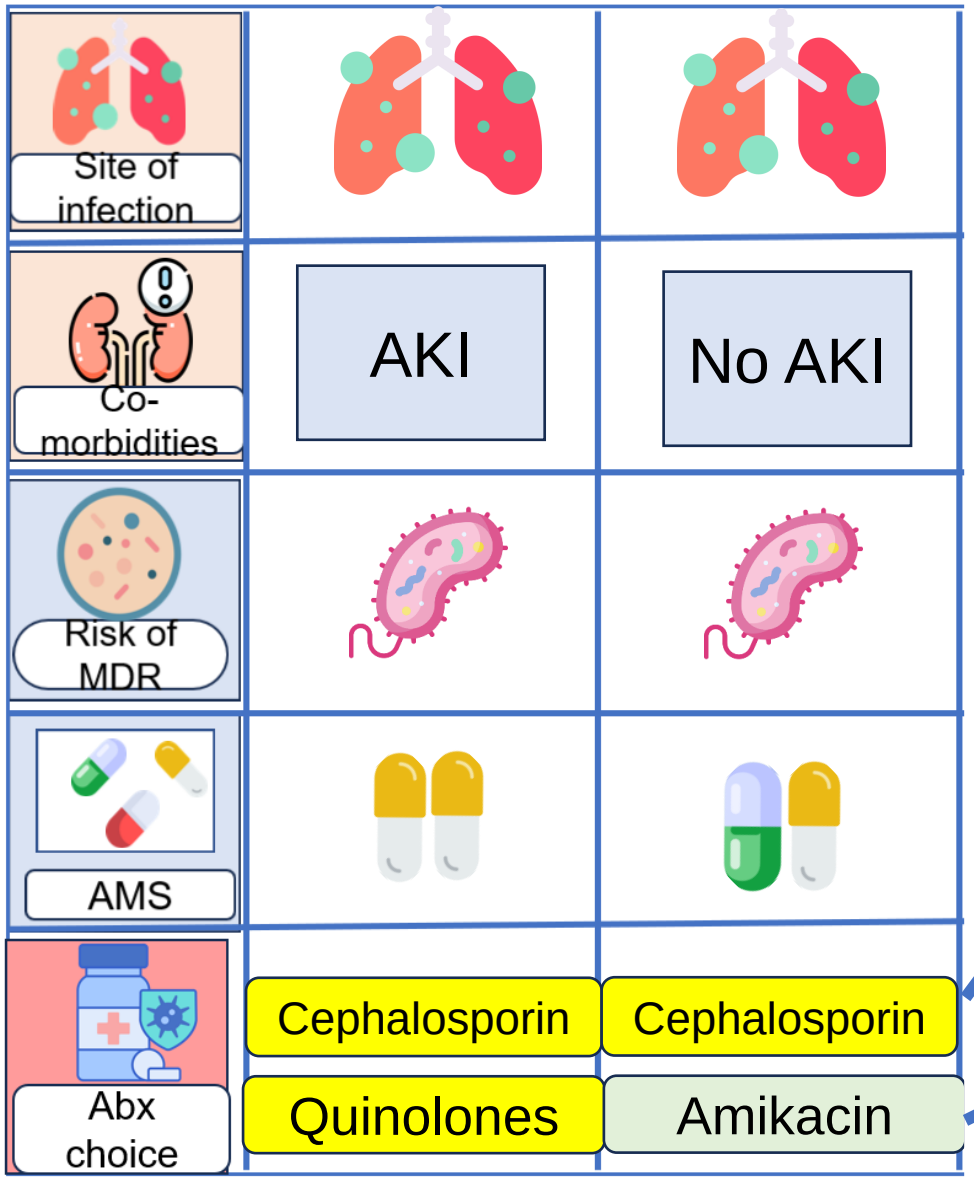
P<0.001

Personalized approach for VAP/HAP management using risk assessment of MDR by guideline

Site of infection		
Co-morbidities	AKI	No AKI
Risk of MDR		
AMS		
Abx choice	Linezolid Cephalosporin Quinolones	Vancomycin Cephalosporin Amikacin

Gram stain is negative for gram +ve

Personalized approach for VAP/HAP management using risk assessment of MDR by gram stain



Gram stain is negative for gram +ve

How can we improve the combination coverage for gram –ve?

Combined antibiogram: New concept

Traditional antibiogram reporting is the percent of pathogen that is susceptible to single drugs

Combination antibiogram determine likelihood that gram –ve will test susceptible to ≥1 agent

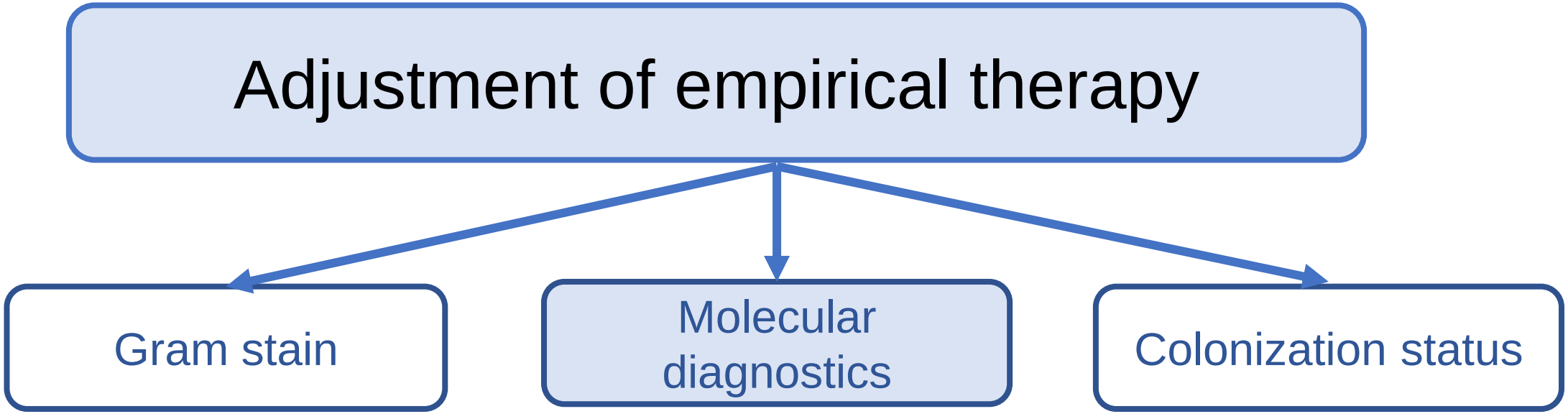
Combined antibiogram: New concept

TABLE 2. Percentage of All Gram-Negative Pathogens Isolated from Blood Cultures Susceptible to Combination Antimicrobial Therapy vs Monotherapy

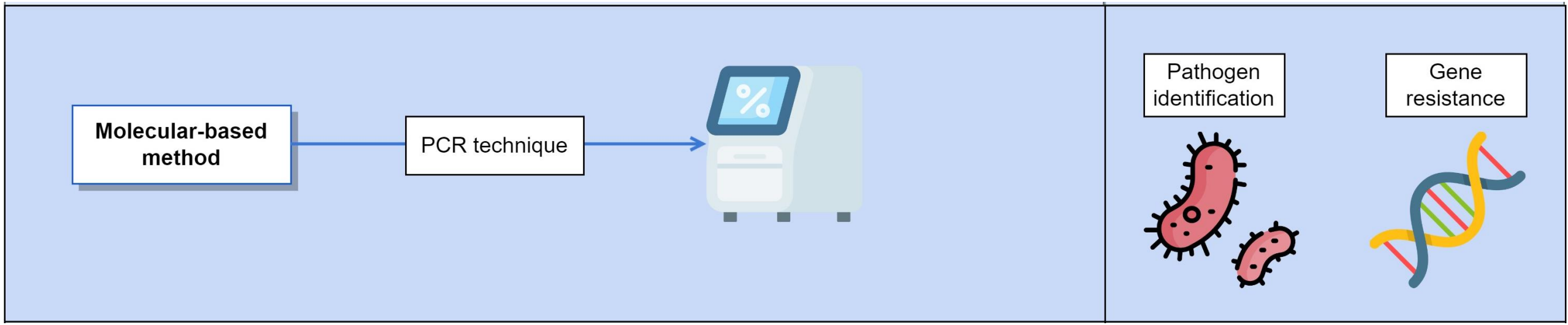
Therapy	Monotherapy, %	Gentamicin		Ciprofloxacin		Tobramycin		Amikacin	
		%	*P*	%	*P*	%	*P*	%	*P*
Imipenem	88.8	93.4	.007	92.1	.056	94.2	.001	95.8	<.001
Ceftazidime	69.2	84.4	<.001	81.3	<.001	84.6	<.001	92.6	<.001
Piperacillin-tazobactam	68.8	85.6	<.001	81.4	<.001	85.4	<.001	91.6	<.001

Combination antibiogram are useful in determining combined empiric antibacterial regimens for multidrug-resistant pathogens

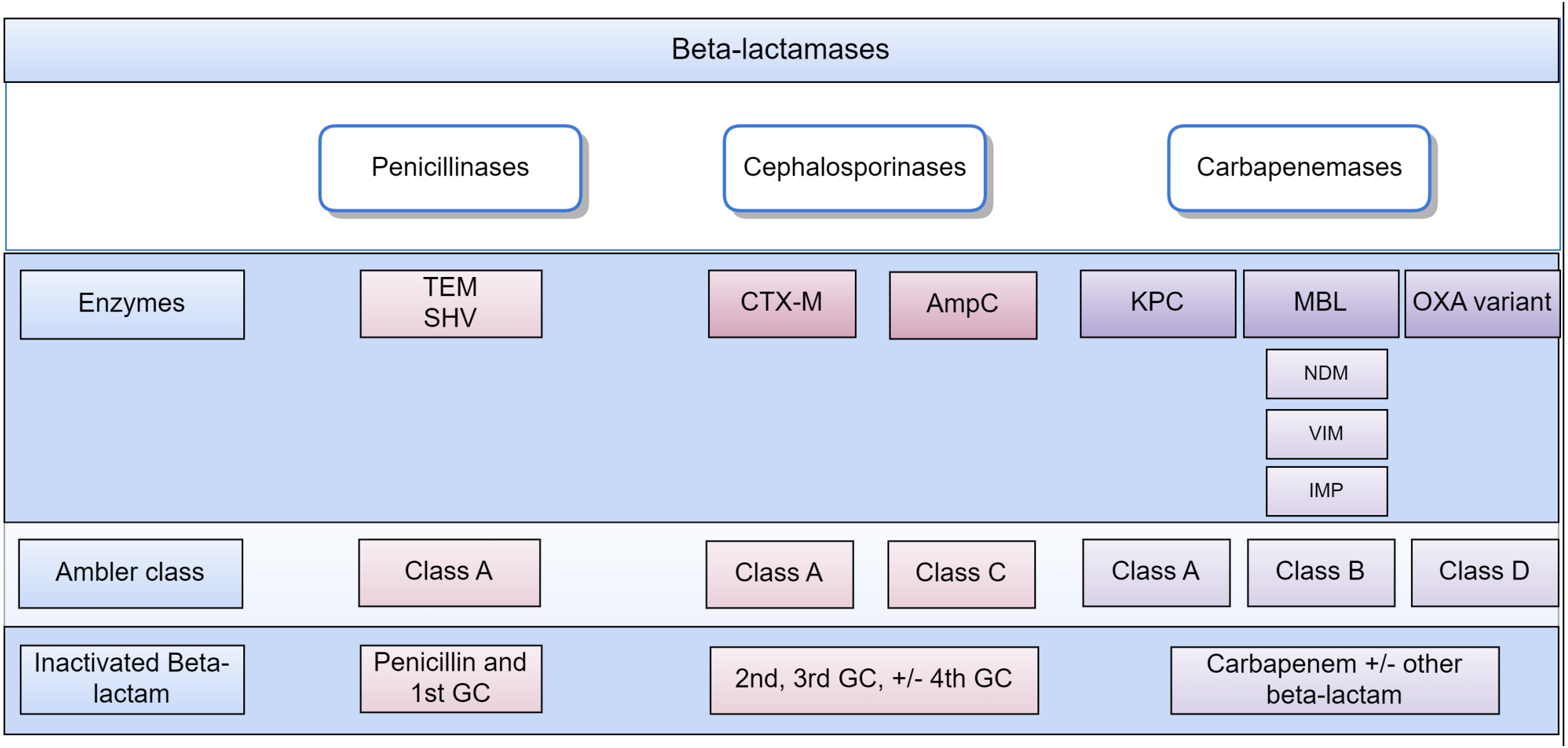
Antibiotics **2022**, *11*, 660.


Adjustment of empirical therapy
Gram stain
Molecular diagnostics
Colonization status

Molecular diagnostics



ß-lactamases classifications



Gene resistance and empirical antimicrobial therapy

Antibiotics	Enterobacterals					Pseudomonas aeruginosa				Acinetobacter baumanii	
	CTX-M	AmpC	KPC	OXA-48	MBL	AmpC	KPC	OXA-48	MBL	OXA-24 OXA-40	MBL
Ceftriaxone											
Cefipime											
Aminoglycosides											
Piperacillin-tazobactam											
Quinolones											
Ertapenem											
Carbapenems											
Tigecycline											
Polymixin, colistin											
Ceftazidime-avibactam											
Ceftolozane-tazobactam											
Meropenem-vaborbactam											
Imipenem-relebactam											
Cefiderocol											
Plazomicin											
Eravacyline											
Aztreonam-avibactam											
Cefepime-zidebactam											
Sulbactam-durlobactam											
Meropenem-nacubactam											
Meropenem-taniborbactam											

Empiric therapy based on molecular test

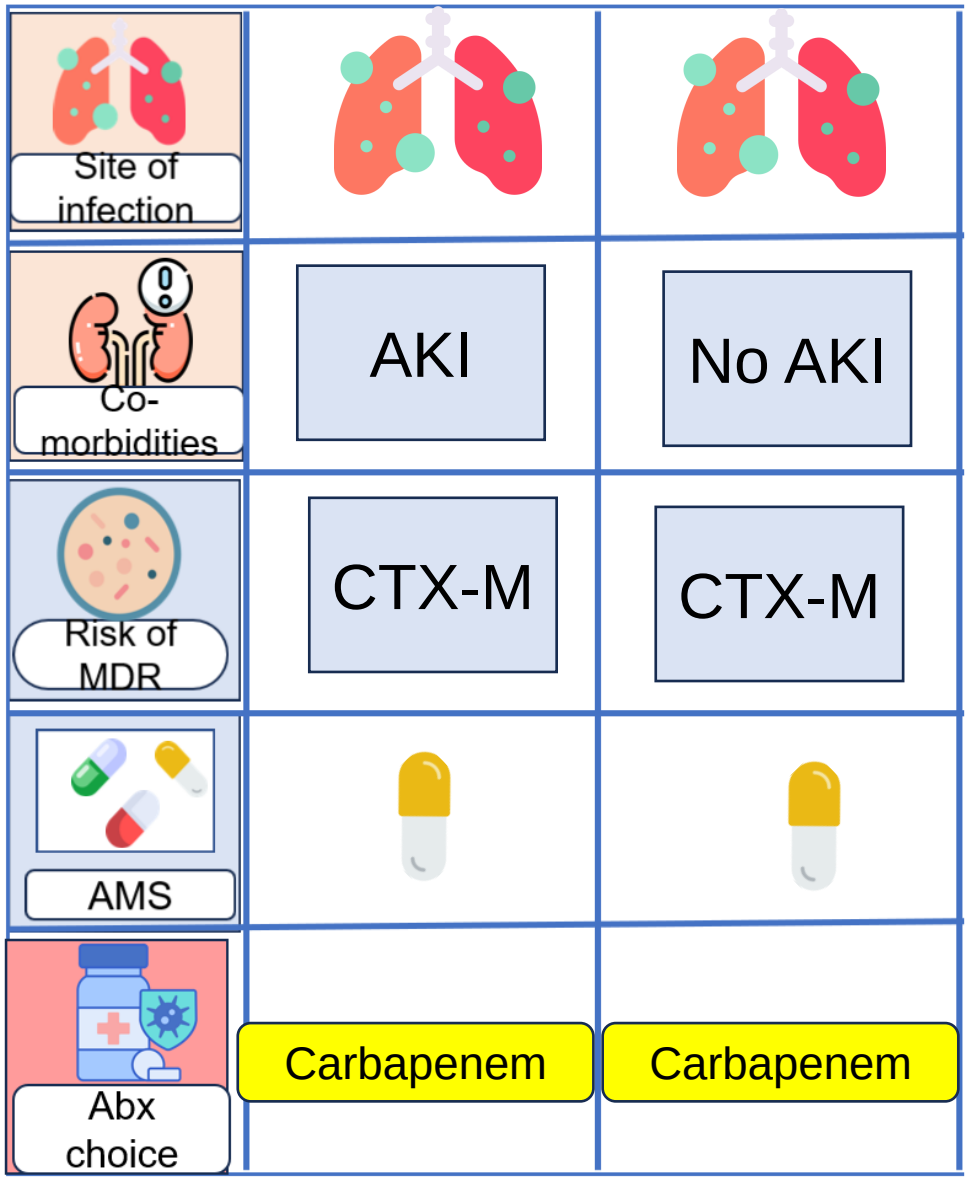
PCR-based

Type of pathogen	Resistant gene	
Klebsiella	CTX-M	Detected
	KPC	Not-detected
	OXA-48	Not-detected
	NDM	Not-detected
	VIM	Not-detected
	IMP	Not-detected

Interpretation of PCR

Antibiotic	Status
Amox-clav	R
Ceftriaxone	R
Cefepime	?
Piperaz/taz	?
Cipro	?
Aminoglycosides	S
Ertapenem	S
Meropenem	S
Colistin	S
tigecycline	S

Personalized approach for VAP/HAP management using risk assessment of MDR by molecular diagnostics



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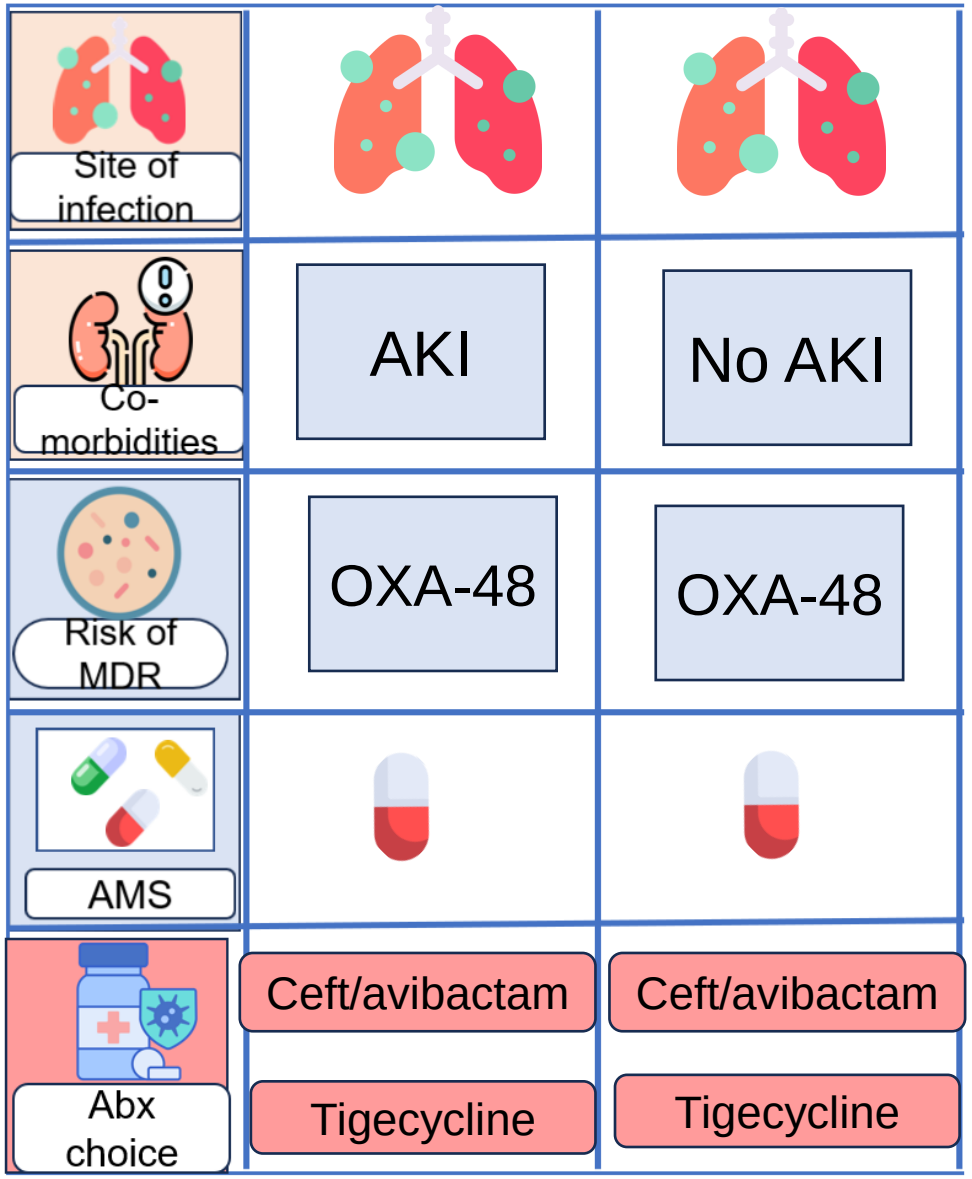
Interpretation of PCR

Antibiotic	Status
Ceftriaxone	R
Cefepime	R
Piperaz/taz	R
Ertapenem	R
Meropenem	R
Cipro	?
Aminoglycosides	?
Colistin	?
tigecycline	S
Ceft/avi	S

Personalized approach for VAP/HAP management using risk assessment of MDR by molecular diagnostics



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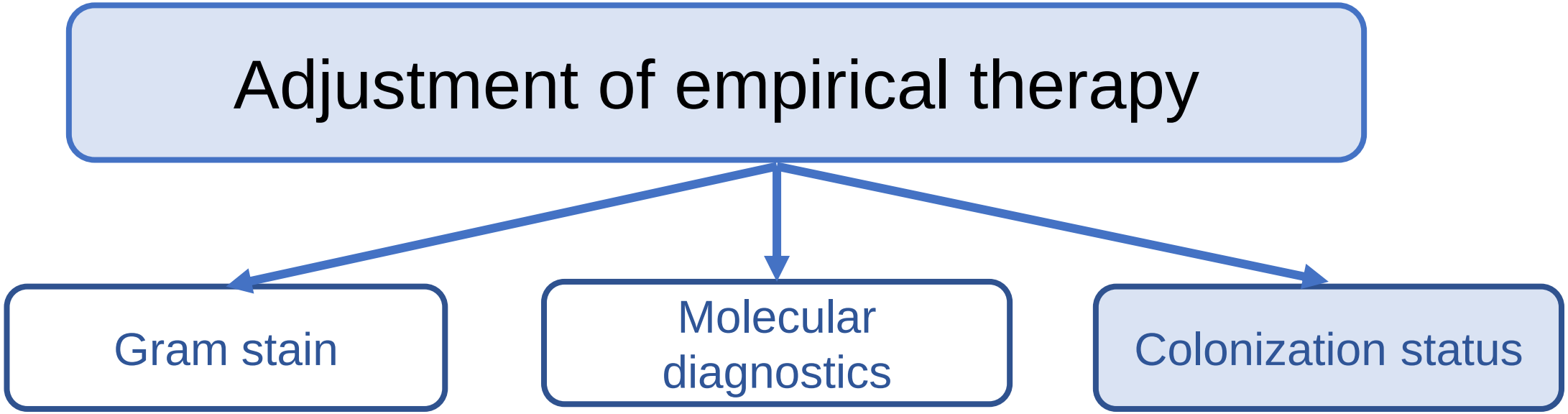
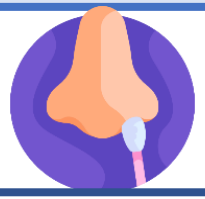
	VIM	Not-detected
	IMP	Not-detected


Adjustment of empirical therapy
Gram stain
Molecular diagnostics
Colonization status

Colonization status: Swab



Nasal swab (MRSA PCR)

Objective	MRSA detection
If -ve	Discontinue anti-MRSA
Negative predictive value	95%

CLINICAL REPORT

Effect of rapid methicillin-resistant *Staphylococcus aureus* nasal polymerase chain reaction screening on vancomycin use in the intensive care unit

Retrospective study

Table 3. Primary and Secondary Outcomes

Outcome	Preprotocol Group (*n* = 137)	Postprotocol Group (*n* = 281)	*P* Value
Primary outcome			
Vancomycin duration, median (IQR), days	2.59 (1.68-4.55)	1.44 (0.91-2.08	<0.01
Secondary outcomes			
Vancomycin duration, median (IQR), days			
Extracorporeal membrane oxygenation (34 patients)	3.78 (2.17-7.66)	1.76 (1.02-2.39)	<0.01
Immunocompromise (90 patients)	2.50 (1.92-3.30)	1.73 (0.93-2.84)	0.26
Mechanical ventilation (124 patients)	2.48 (1.67-4.59)	1.55 (0.97-2.27)	<0.01
Vasopressors (78 patients)	2.68 (1.71-5.23)	1.35 (0.89-2.23)	<0.01
Hospital length of stay, median (IQR), days	19.3 (12.3-33.9)	16.1 (8.9-31.6)	0.09
ICU length of stay, median (IQR), days	9.8 (4.76-18.67)	8.25 (3.96-17.94)	0.23
In-hospital mortality, No. (%)	43 (31)	62 (23)	0.06
ICU readmission due to pneumonia, No. (%)	1 (1)	4 (1.4)	0.54
Rate of acute kidney injury, No. (%)[a,b]	31 (24)	33 (13)	0.01
Resumption of vancomycin at 3 days, No. (%)	9 (6.6)	22 (8)	0.65
Resumption of vancomycin at 7 days, No. (%)	21 (15)	44 (16)	0.93
Vancomycin levels (random or trough) obtained per patient, median	1	0	<0.01
Trough	1	0	
Random	0	0	
No levels (random or trough) obtained, No. (%)	26 (19)	149 (53)	<0.01

Vancomycin duration

Pre-protocol group

Post-protocol group

2.5 days

1.4 days

P<0.01

Am J Health-Syst Pharm. 2021;78:2236-2244

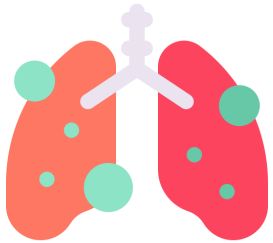
Site of infection				
Co-morbidities				
Risk of MDR				
AMS				
Abx choice				

Nosocomial infection management

Risk of MDR

Culture

Targeted therapy



Nosocomial infection

Empiric

Deescalate

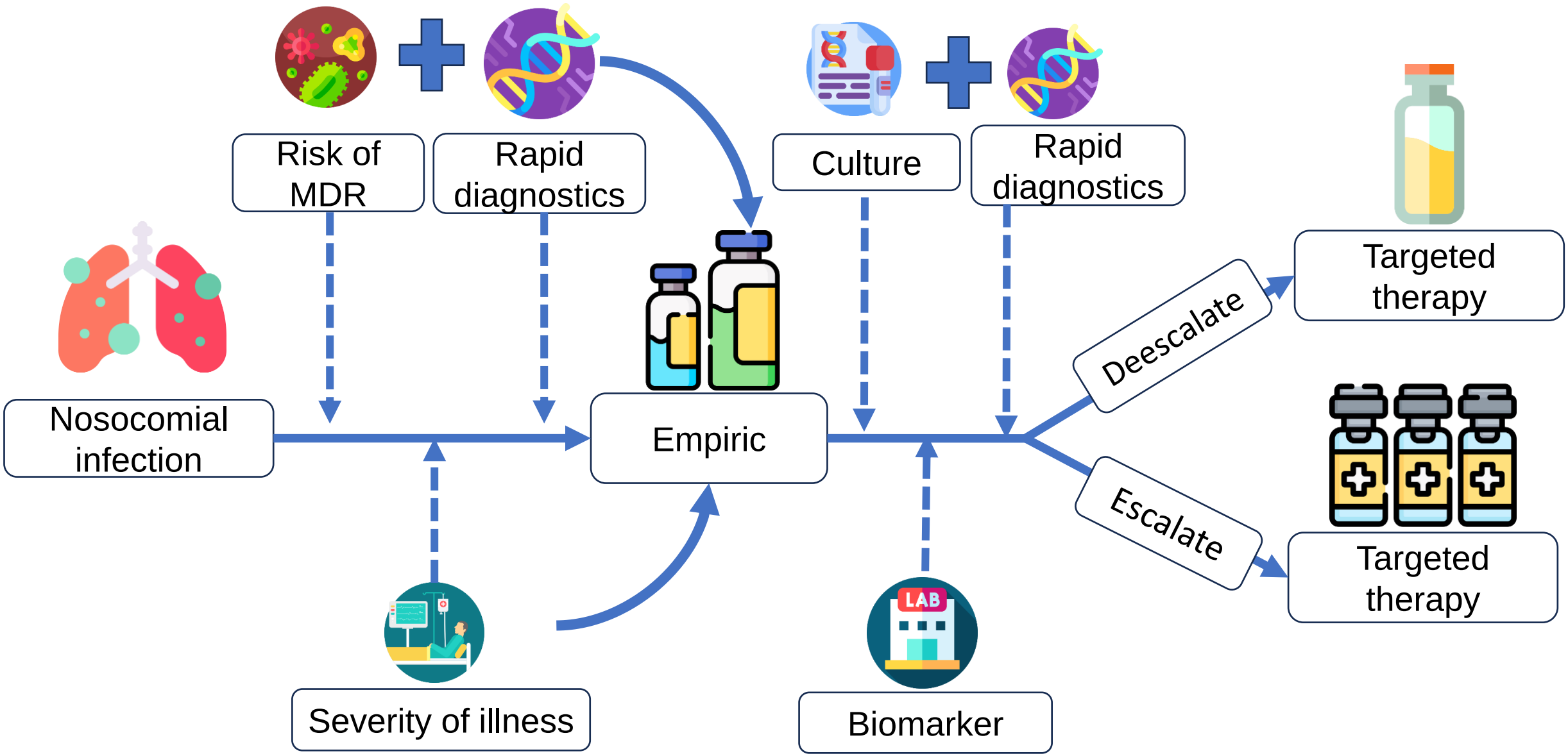
Escalate

Targeted therapy

2-3 days

Severity of illness

Nosocomial infection management



Summary

Extremely drug-resistant infections have become a fact of life in global clinical practice.

Early effective antibiotic therapy is the most important factor to improve survival in nosocomial infection

The current guidelines propose aggressive management for empiric antimicrobial therapy

On the other hand, most of AMS intervention is based on restrictive interventions

Personalized approach of nosocomial infection is based on the considering multi-dimensional factors to tailor management

Summary

Site of infection, co-morbidities, burden of MDR, and AMS should be considered during antimicrobial prescription .

Early identification of MDR burden can be improved using gram stain, colonization status, and molecular diagnostics

Thank You

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