

Novine u antimikrobnoj terapiji

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Značaj antimikrobnih lekova u medicini

Antimikrobni lekovi su jedna od najčešće propisivanih grupa lekova

Mortalitet (1900)

- TBC
- pneumonia
- dijareja
- bolesti srca
- bolesti jetre
- povrede
- mozdani udar
- kancer
- bronchitis
- Difterija

Prosečna starost 52 god.



Mortalitet (2000)

- Bolesti srca
- Kancer
- Moždani udar
- Hronične plućne bolesti
- Povrede
- Pneumonija
- Dijabetes
- Suicid
- Hronične bolesti bubrega
- Hronične bolesti jetre

Prosečna starost 76 god.

Antimikrobna rezistencija (AMR)

- AMR- jedan od 10 najvažnijih globalnih problema javnog zdravlja
- AMR potencijalno veći značaj od masovnih nezaraznih bolesti
- AMR je višedimenzionalni kompleksni izazov
- alarmantan nedostatak novih antibiotika

- zavisnost medicinskog progresa i infekcija MDR/XDR
- uzrok povećanog morbiditeta i mortaliteta
 - u 2019. 5miliona smrtnih slučajeva; 1,27miliona direktno povezanih
- **Značajno povećanje medicinskih troškova**
- Procenjuje se da bi do 2050. ukupni troškovi zdravstva za AMR mogli da se povećaju do 100 triliona dolara i do 10 miliona smrtnih slučajeva svake godine

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

E	<i>Enterococcus faecium</i>		E	<i>Enterococcus faecium</i>
S	<i>Staphylococcus aureus</i>		S	<i>Staphylococcus aureus</i>
C	<i>Clostridium difficile</i>	→	K	<i>Klebsiella pneumoniae</i>
A	<i>Acinetobacter baumannii</i>		A	<i>Acinetobacter baumannii</i>
P	<i>Pseudomonas aeruginosa</i>		P	<i>Pseudomonas aeruginosa</i>
E	Enterobacteriaceae		E	<i>Enterobacter spp.</i>

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 Vrsta analize: Urinokultura

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 Broj knjižice: [REDACTED]
 Datum izdavanja: [REDACTED]

BAKTERIOLOŠKI NALAZ

DMP

izolovani mikroorganizmi:
Klebsiella sp., 100.000/ml

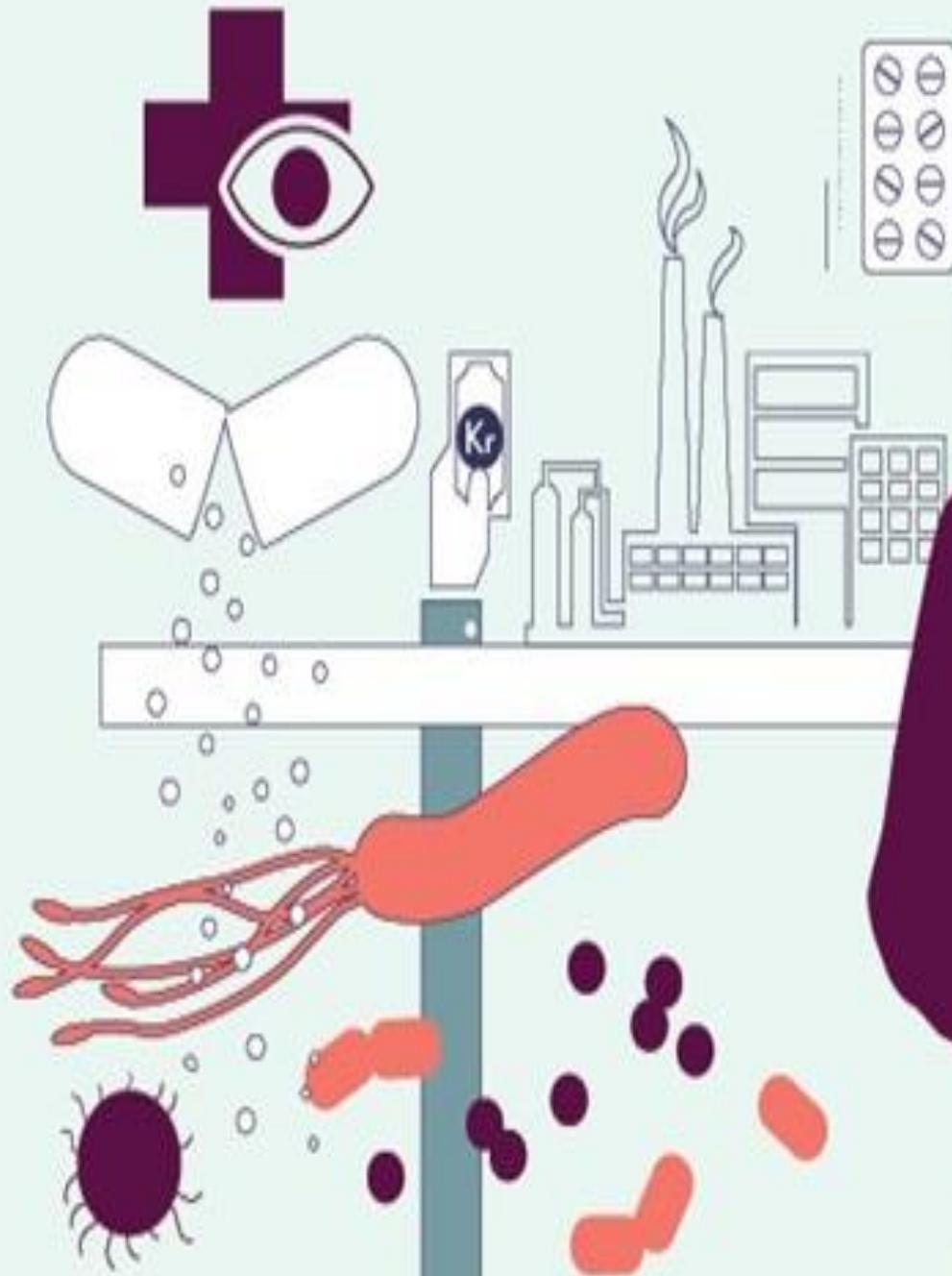
ANTIBIOGRAM ^[1]

	I		I
	MIC		MIC
	µg/ml		µg/ml
BETALAKTAMI			
Ampicilin	R		
Amoxicilin/Clavulamski acid (KIU)*	R		
Amoxicilin/Clavulamski acid (NKIU)*	R		
Cefotaksim	R		
Cefiksim NKIU*	R		
Piperacilin/Tazobactam	R		
Cefazidim	R		
Cefepime	R		
SULFONAMIDI			
Cotrimoxazole	R		
KARBAPENEMI			
Imipenem	R		
Meropenem	R		
Ertapenem	R		
NITROFURANI			
Nitrofurantoin NKIU*	R		
KOLISTIN			
Colistin	R ¹⁶		
AMINOGLIKOZIDI			
Gentamicin	R		
Amikacin	R		
KVINOLONI			
Ciprofloksacin	R		
Levofloksacin	R		
NITROKSOLIN			
Nitroksolin NKIU*	S		
FOSFOMICIN			
Fosfomicin	S	I	

Kategorije osjetljivosti (S/I/R) određene su prema EUCAST protokolu (http://www.eucast.org/clinical_br)
 S – osjetljiv, standardni režim doziranja; I^{***} – osjetljiv, povećana izloženost; R – rezistentan
 I – Osjetljiv, povećana izloženost mikroorganizma antimikrobnom leku (doza, učestalost davanja, način primjene)

The most common carbapenemases at the Clinical Center of Niš

- OXA- 48 and NDM
- *Klebsiella spp.* 81% MDR, 7.9% XDR
- *Pseudomonas aer.*, 53% MDR, 19.2% XDR

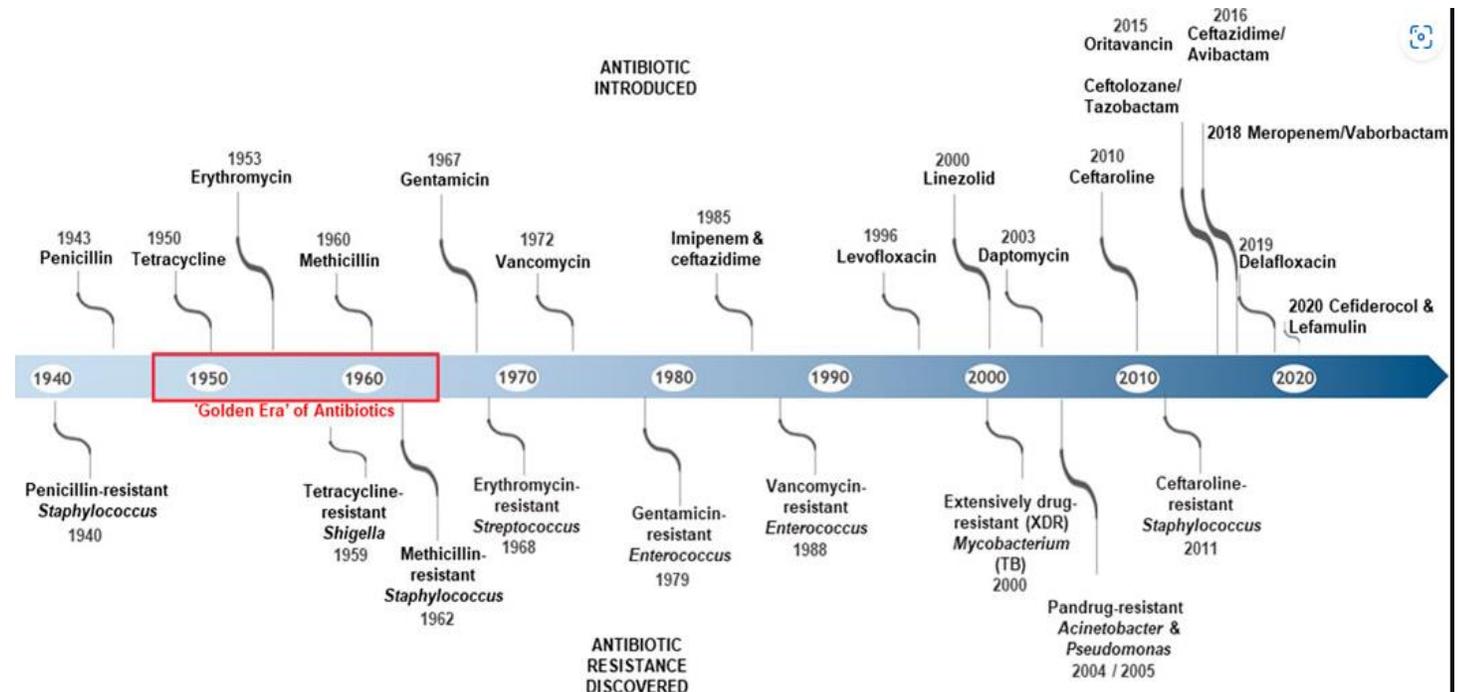


Da li postoji
rešenje?



Novi inovativni antimikrobni lekovi

- Ceftolozane/tazobactam
- Imipenem/relebactam
- Ceftazidime/avibactam
- Meropenem-vaborbactam
- Sulbactam-durlobactam
- Cefiderocol
- Plazomicin
- Eravacyclin
- Temocillin
- Lariocidin



New antibiotics-spectrum β -lactamase inhibition

Antibiotic	Enterobacteriaceae (e.g. <i>E. coli</i> , <i>Klebsiella</i> spp.)					<i>Pseudomonas</i> spp.		<i>Acinetobacter</i> spp.
	ESBL	AmpC	KPC	OXA-48	NDM	Efflux	AmpC	
Ceftolozane-tazobactam	Green	Yellow	Red	Yellow	Red	Green	Green	Red
Ceftazidime-avibactam	Green	Green	Green	Green	Red	Yellow	Green	Red
Meropenem-vaborbactam	Green	Green	Green	Red	Red	Red	Green	Yellow
Imipenem-relebactam	Green	Green	Green	Red	Red	Green	Green	Yellow
Aztreonam-avibactam	Green	Green	Green	Green	Green	Red	Yellow	Red
Eravacycline	Green	Green	Green	Green	Green	Red	Red	Green
Plazomicin	Green	Green	Green	Green	Red	Yellow	Yellow	Yellow
Cefiderocol	Green	Green	Green	Green	Green	Green	Green	Green

ESBL – Extended spectrum beta-lactamase

AmpC – Ambler class C beta-lactamase (the Amp probably stands for Ampicillin)

KPC – *Klebsiella pneumoniae* carbapenemase

OXA – Oxacillin carbapenemase number 48

NDM – New Delhi metallo-beta-lactamase

Unmet Medical Need povezana sa antimikrobnom rezistencijom

Clinical Infectious Diseases

SUPPLEMENT ARTICLE



Pathogen-Targeted Clinical Development to Address Unmet Medical Need: Design, Safety, and Efficacy of the ATTACK Trial

Richard R. Watkins,¹ Bin Du,² Robin Isaacs,³ and David Altarac³

Multidrug-resistant infections are rapidly increasing worldwide, and, unfortunately, few new antimicrobials capable of treating these infections are under development. The emergence of infections for which there are limited treatment options represents a critical unmet medical need.

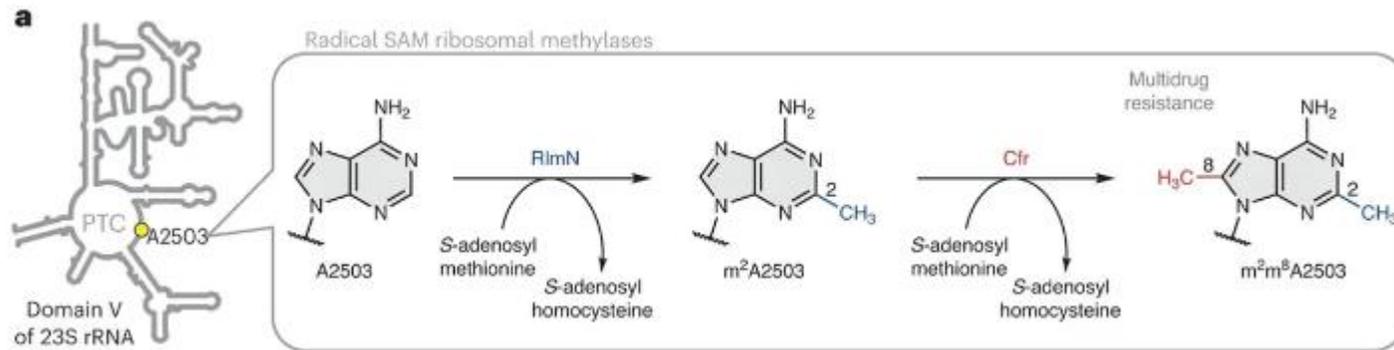
Development of novel antimicrobials or alternatives is a prime example of unmet medical need, given the lack of therapeutic options to address antimicrobial resistance (AMR).

There is a crucial need for novel antibiotics to stem the tide of antimicrobial resistance, particularly against difficult to treat gram-negative pathogens like ***Acinetobacter baumannii***.

An innovative approach to addressing antimicrobial resistance may be pathogen-targeted development programs.

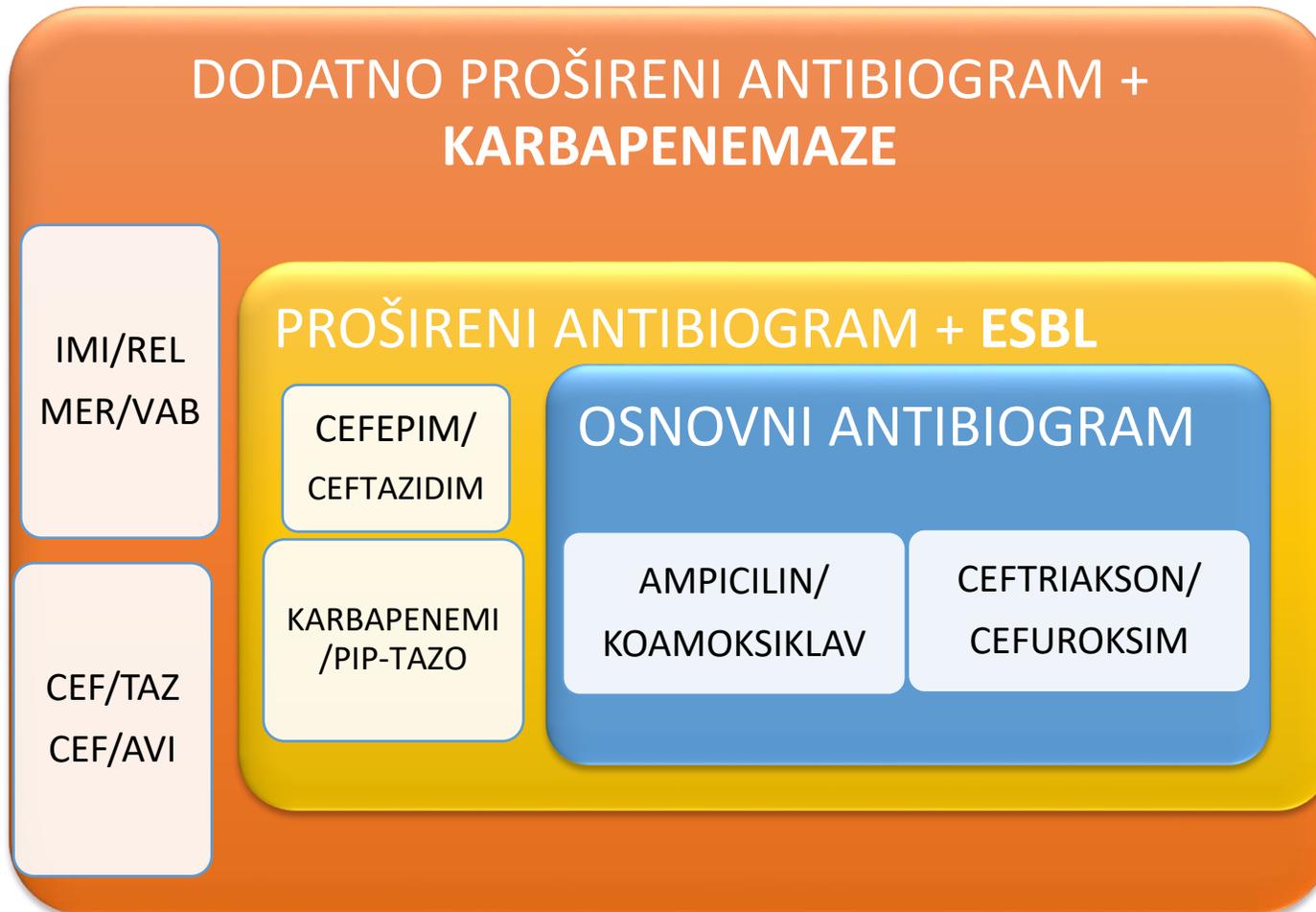
Sulbactam-durlobactam (SUL-DUR) is a β -lactam/ β -lactamase inhibitor combination antibiotic that is being developed to specifically target drug-resistant ABC.

Cresomycin: A New Hope in the Fight Against Antibiotic-Resistant Superbugs

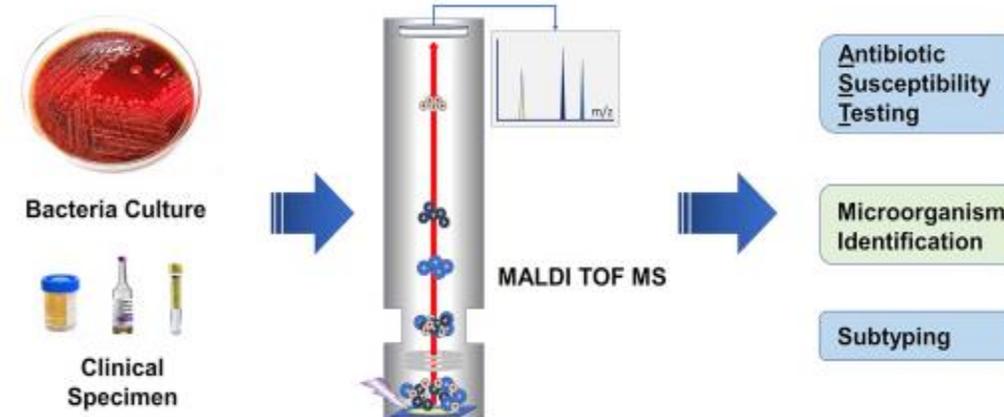


- **Cresomicin** - novi potencijalni antibiotik dizajniran za MDR bakterije
- zaobilazi uobičajeni mehanizam koji bakterije koriste da bi dobile prednost protiv antimikrobnih jedinjenja.
- efikasan protiv gram-pozitivnih i gram-negativnih bakterija, *Staph. aureus*, *E. coli* i *P. aeruginosa*, *MDR* i *XDR*
- Molekul odbacuje metil grupe u ribozomima otpornim na lekove koji sprečavaju vezivanje drugih antibiotika.

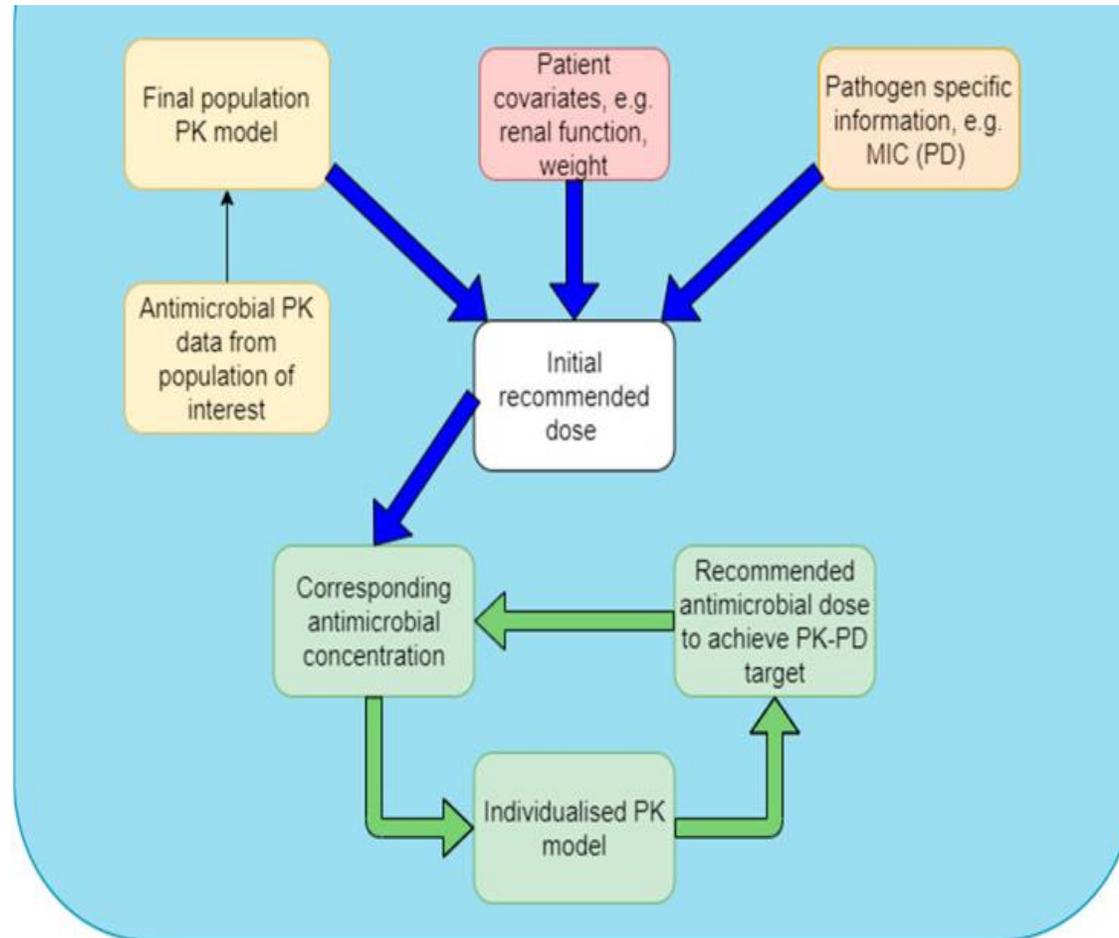
ULOGA MIKROBIOLOŠKE LABORATORIJE TESTIRANJE BETA-LAKTAMSKIH ANTIBIOTIKA-ETAPE



Detekcija karbapenemaza brzim testovima



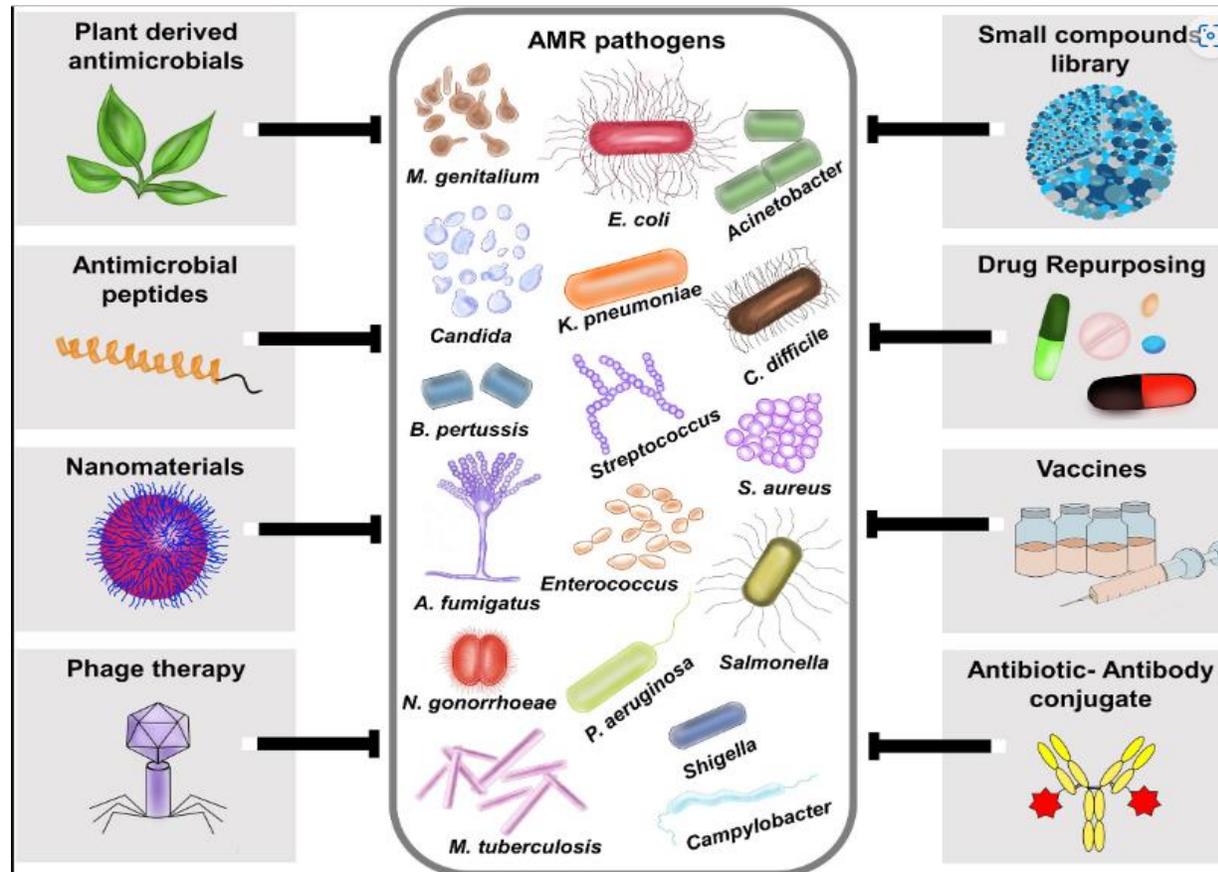
Budućnost u optimalnom doziranju antibiotika -AI



Farmakokinetički kalkulatori za individualizaciju doziranja antibiotika su značajni alati za primenu personalizovane medicine,

- režimi doziranja prilagođeni potrebama i individualnim karakteristikama svakog pacijenta,
- maksimizirajući efikasnost i minimizirajući toksičnost.

Different therapeutic strategies for combating antimicrobial resistant pathogens



AMR pathogens depicted in the figure is based on the [CDC, 2019](https://www.cdc.gov/drugresistance/biggest-threats.html) antibiotic resistance threats report, which categorized the AMR pathogens into urgent threats, serious threats, concerning threats and watch list <https://www.cdc.gov/drugresistance/biggest-threats.html>

“Borba protiv antimikrobne otpornosti: odsustvo akcije danas, nedostatak antibiotika sutra”

mikrobiologija

- Sistem aktivnog nadzora
- Fenotipska i genotipska detekcija karbapenemaza

klinika

- Upravljanje antibioticima
- Racionalna upotreba antibiotika
- Ograničavanje upotrebe invazivnih uređaja

epidemiologija

- Dobre smernice za kontrolu infekcije
- Kontakt mere prevencije i higijene ruku
- Monitoring lokalne flore

Zaključak

- Antimikrobni lekovi su među najmoćnijim alatima za unapredjenje zdravstvenih ishoda
- postoji potreba za inovativnim antibioticima zbog razvoja AMR
- brza mikrobiološka dijagnostika i poznavanje lokalne bakterijske osetljivosti/ mehanizama rezistencije /fenotipska i genotipska detekcija karbapenemaza osnova antimikrobne terapije
- Upravljanje antibioticima zahteva multidisciplinarni pristup i kontinuiranu akciju