

ДАНИ ЗАВОДА
2023
28. СТРУЧНА КОНФЕРЕНЦИЈА

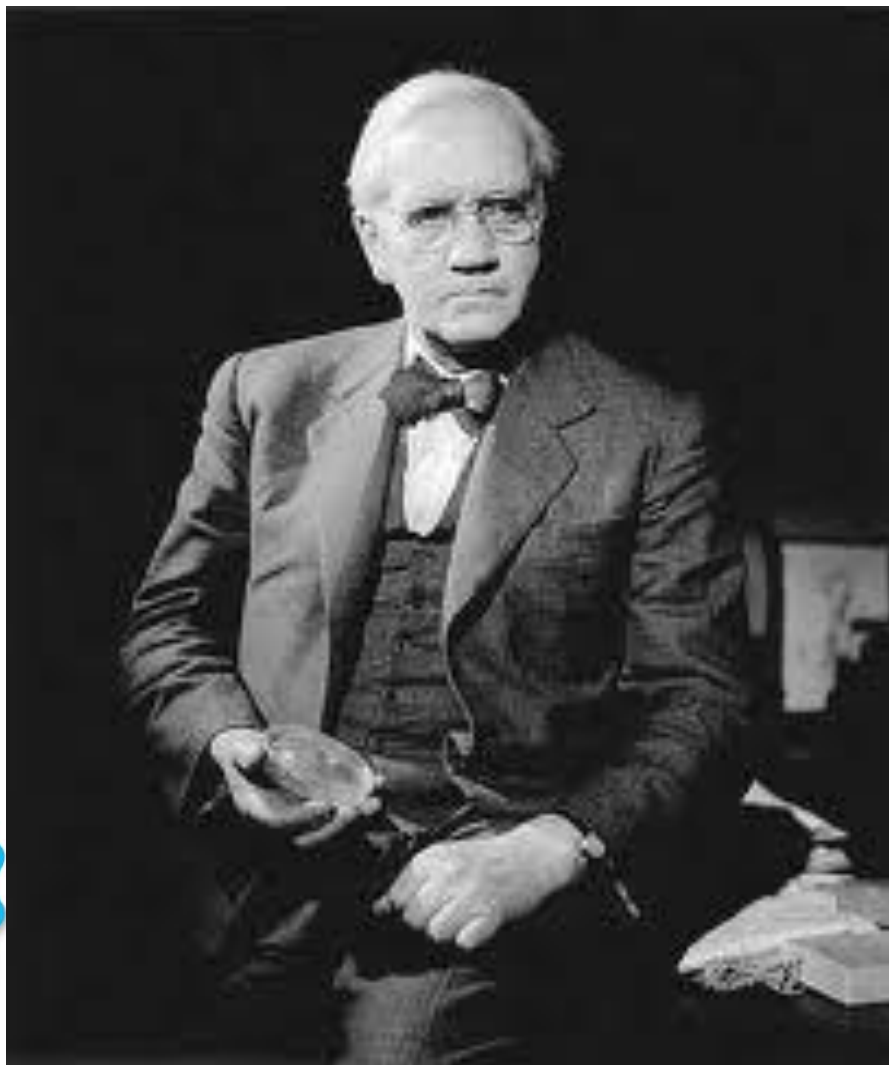
Upravljanje antibioticima kao način borbe protiv antimikrobne rezistencije

Vanredni Prof Goran Stevanović

Klinika za infektivne i tropske bolesti „Prof Dr Kosta Todorović“ Univerziteti Klinički Centar Srbije

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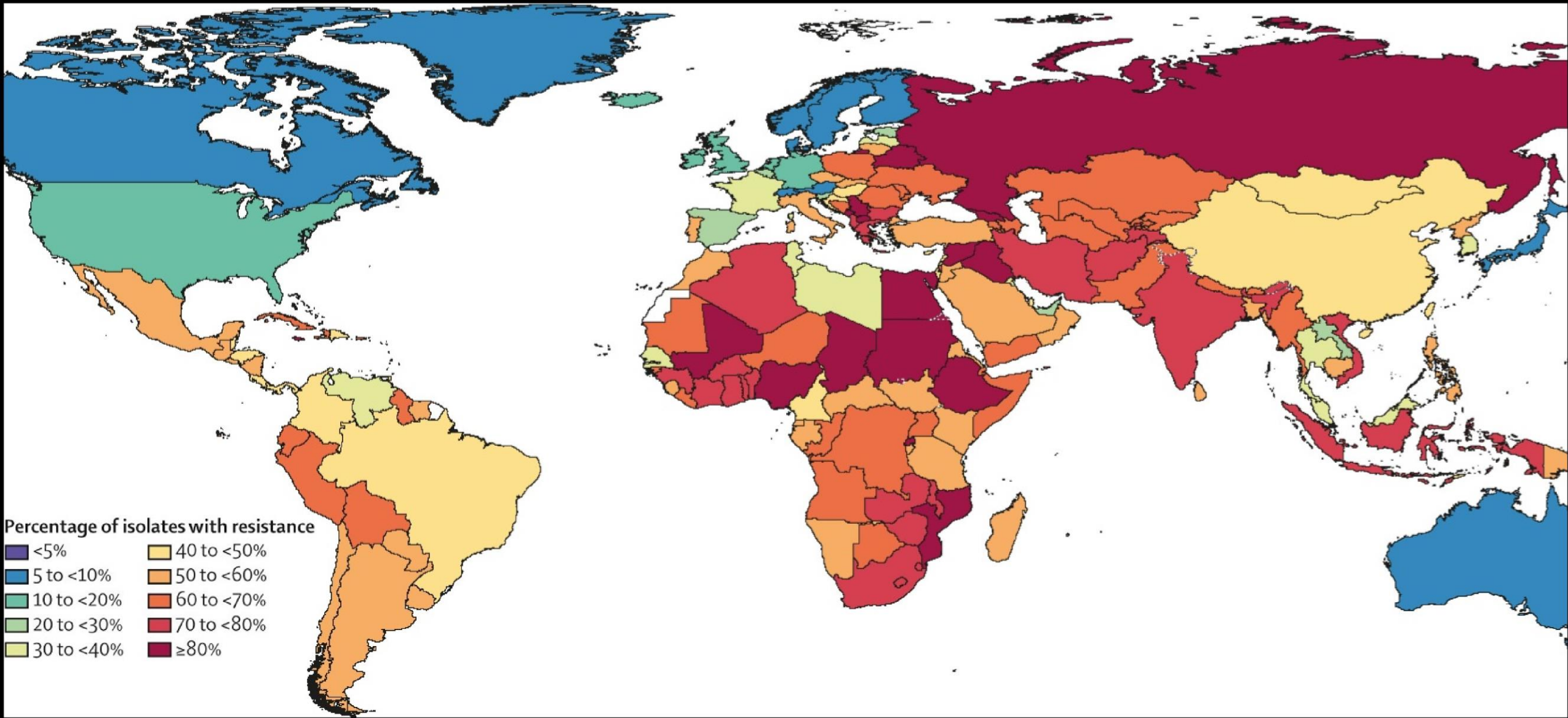
Sir Alexander Fleming



“Možda će doći vreme kada će biti moguće kupiti penicilin u svakoj prodavnici. Tada nastaje opasnost da neuki čovek može sebe lako da subdozira i da izlažuci svoje mikrobe ne-smrtonosnim količinama leka, njih nauči da budu rezistentni na penicilin.”

Predavanje u Nobel fondaciji, 1945





Procenjeno je da je u 2019 od infekcija uzrokovanim rezistentnim bakterijama umrlo 1,2 miliona ljudi.

AMR Worldwide

14,000 Patients Die of *C.difficile* infection annually in the **USA**.⁽¹⁾ The use of antibiotics was a major contributing factor in up to 85% of cases.⁽²⁾



23,000 Patients Die Each Year as a result of **antibiotic-resistant infections** in the **USA**.⁽¹⁾

2,000,000 Infections per year contain bacteria that are resistant to one or more antibiotics in the **USA**.⁽¹⁾

11,000 Estimated Deaths caused by methicillin-resistant *Staphylococcus aureus* (**MRSA**) each year in the **USA**.⁽³⁾



25,000 Patients Die Each Year as a result of antibiotic-resistant infections in **Europe**.⁽⁵⁾



400,000 Infections per year with the 6 most frequent multi-drug resistant (MDR) bacteria, in 4 types of infection, in **Europe**.⁽⁶⁾

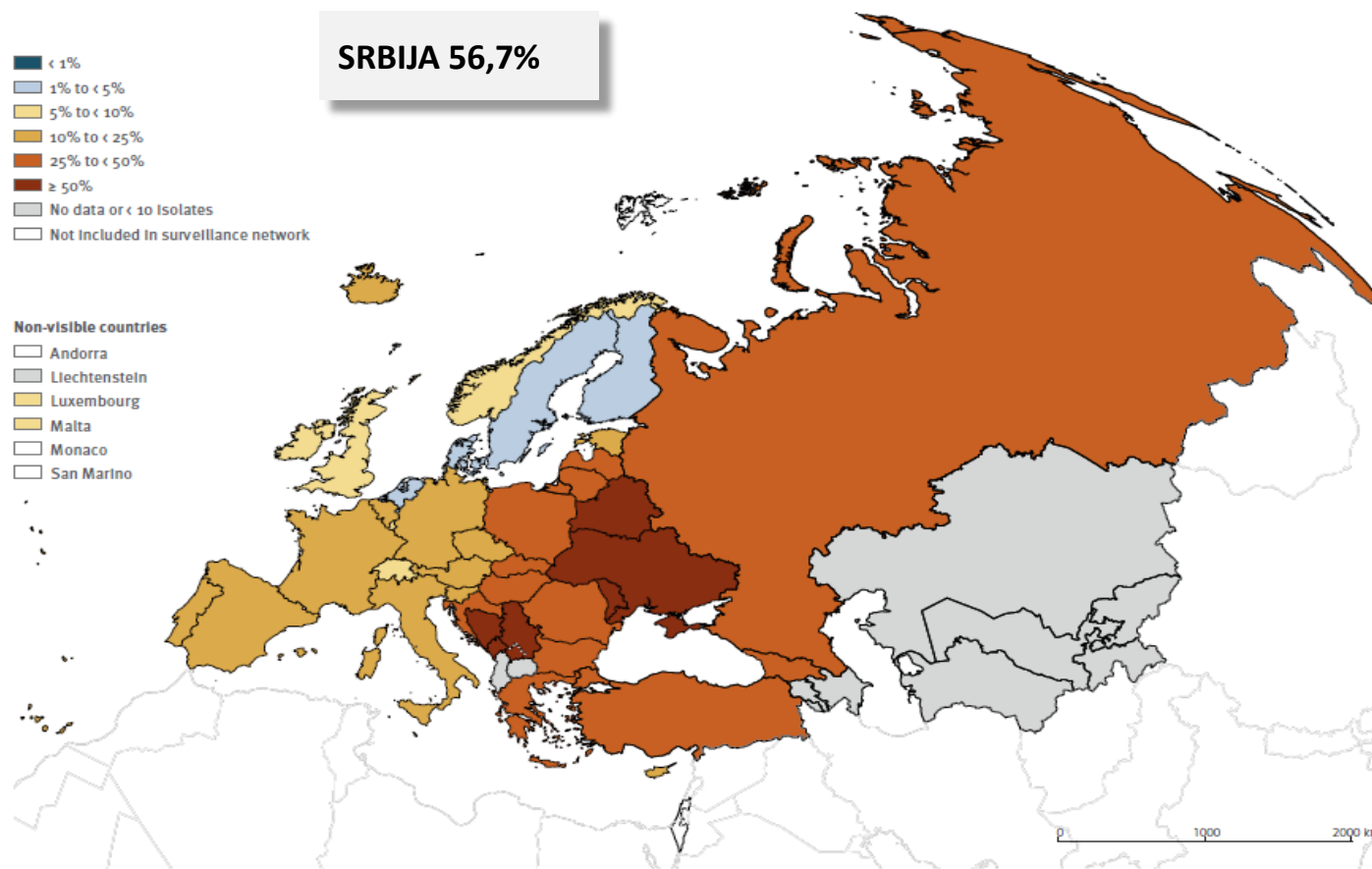
480,000 People Infected by drug-resistant TB strains in 2013 **Worldwide**.⁽⁴⁾

1 Child Dies Every 9 Minutes from an infection caused by antibiotic-resistant bacteria in **India**.⁽⁷⁾



Pseudomonas aeruginosa - procenat invazivnih izolata rezistentnih na karbapeneme, po zemljama, SZO Evropski region

Fig. 6 *P. aeruginosa*: percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country/area, WHO European Region, 2020



Rezistencija na karbapeneme kod izolata *P. aeruginosa* u većini zemalja EU je <25%, dok je u Bugarskoj, Grčkoj, Mađarskoj, Poljskoj, Slovačkoj i Hrvatskoj od 25-50%. Među zemljama CAESAR mreže u većini zemalja rezistencija je >50%.

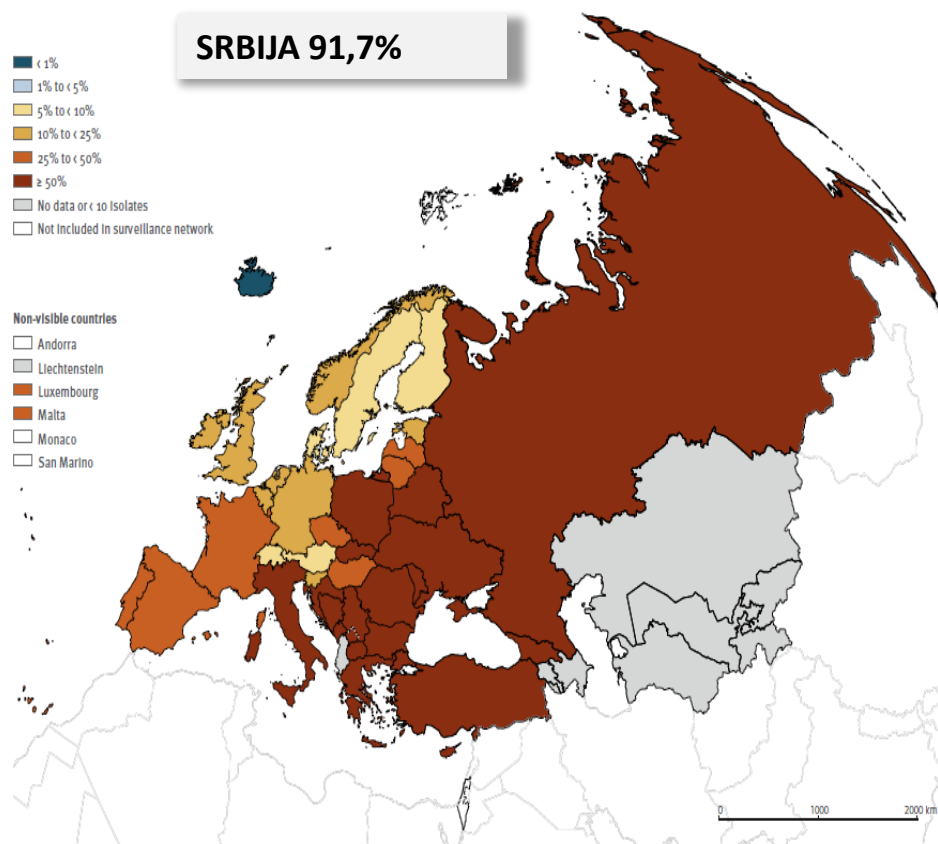
Note: data for Serbia and Kosovo (All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)) were combined for this map. Data for the United Kingdom for 2020 do not include Scotland and Wales.

Data sources: 2020 data from the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR, ©WHO 2021. All rights reserved.) and 2020 data from the European Antimicrobial Resistance Surveillance Network (EARS-Net, ©ECDC 2021).
Map production: ©WHO



Klebsiella pneumoniae - procenat invazivnih izolata rezistentnih na III gen. cefalosporina, po zemljama, SZO Evropski region

Fig. 4 *K. pneumoniae*: percentage of invasive isolates resistant to third-generation cephalosporins (cefotaxime/ceftriaxone/ceftazidime), by country/area, WHO European Region, 2020

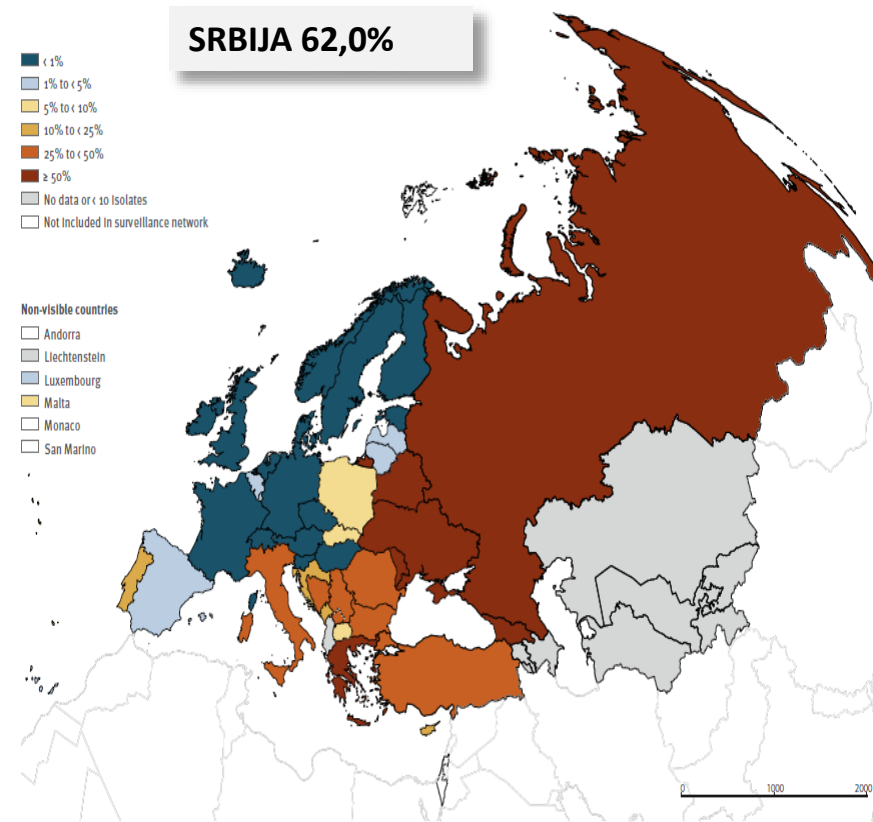


Rezistencija na 3. gen. cefalosporina kod izolata *K. pneumoniae* među evropskim zemljama je > 50% u Bugarskoj, Grčkoj Italiji, Poljskoj, Rumuniji, Slovačkoj i Hrvatskoj, kao i u svim ostalim zemljama CAESAR mreže izuzev Švajcarske i V. Britanije.

Note: data for Serbia and Kosovo (All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)) were combined for this map. Data for the United Kingdom for 2020 do not include Scotland and Wales.
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Klebsiella pneumoniae - procenat invazivnih izolata rezistentnih na karbapeneme, po zemljama, SZO Evropski region

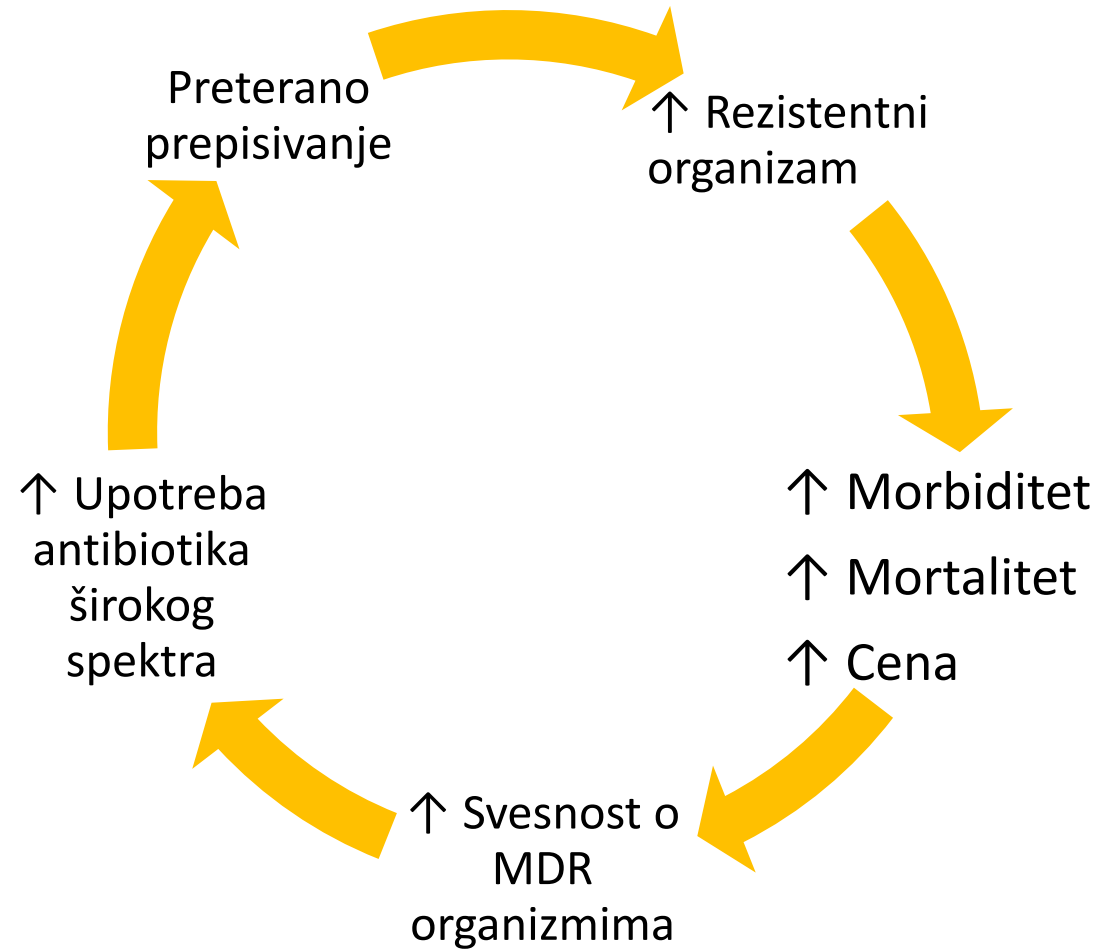
Fig. 5 *K. pneumoniae*: percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country/area, WHO European Region, 2020



Među evropskim zemljama, visok nivo rezistencije na karbapeneme kod izolata *K. pneumoniae* zabeležen je u Rumuniji (48,3%) i u Grčkoj (66,3%). Među zemljama CAESAR mreže, visok nivo rezistencije zabeležen u BiH.

Note: data for Serbia and Kosovo (All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)) were combined for this map. Data for the United Kingdom for 2020 do not include Scotland and Wales.
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Map production: ©WHO.

Rezistencija i propisivačka praksa





Multirezistentni mikroorganizmi (MDROs): “ESCAPE”

E*nterococcus faecium* (VRE)

S*taphylococcus aureus* (MRSA)

C*lostridium difficile*

A*cinetobacter baumannii*

P*seudomonas aeruginosa*

E*nterobacteriaceae* (ESBLs)

**Karbapenem rezistentne
Enterobacteriaceae su u
usponu!**





Faktori rizika za MDRO

- Prethodno izlaganje antibioticima
- Ranije MDRO ili kontakt sa drugim kolonizovanim pacijentima
- Skorašnji ili produženi boravak u bolnici
- Boravak u ustanovama produžene nege
- Imunosupresivne bolesti i/ili terapije
- Dijaliza
- Komorbiditeti/Invalidnost (zavisnost od kontaktne nege)
- Visoka učestanost antibiotske rezistencije u sredini

Drinka P, et al. JAMDA 2011; June editorial: 321-325.
Muto CA, et al. Infect Control Hosp Epidemiol 2002;23:429-435.
Muto CA, et al. Infect Control Hosp Epidemiol 2003;24:362-386.
Ostrowsky et al. N Engl J Med 2001;344:1427-1433.



Upravljanje antibioticima

-Antimicrobial Stewardship-

- Set usklađenih intervencija koje imaju za cilj unapređenje i praćenje pravilne upotrebe antibiotika putem promocije odabira optimalnog leka, njegove doze, trajanja terapije i puta primene.
- *Pravi lek, prava doza, pravo vreme, pravo trajanje.*



Infect Control Hosp Epidemiol 2014; 35: 1444-1451





Clinical Infectious Diseases

IDSA GUIDELINE

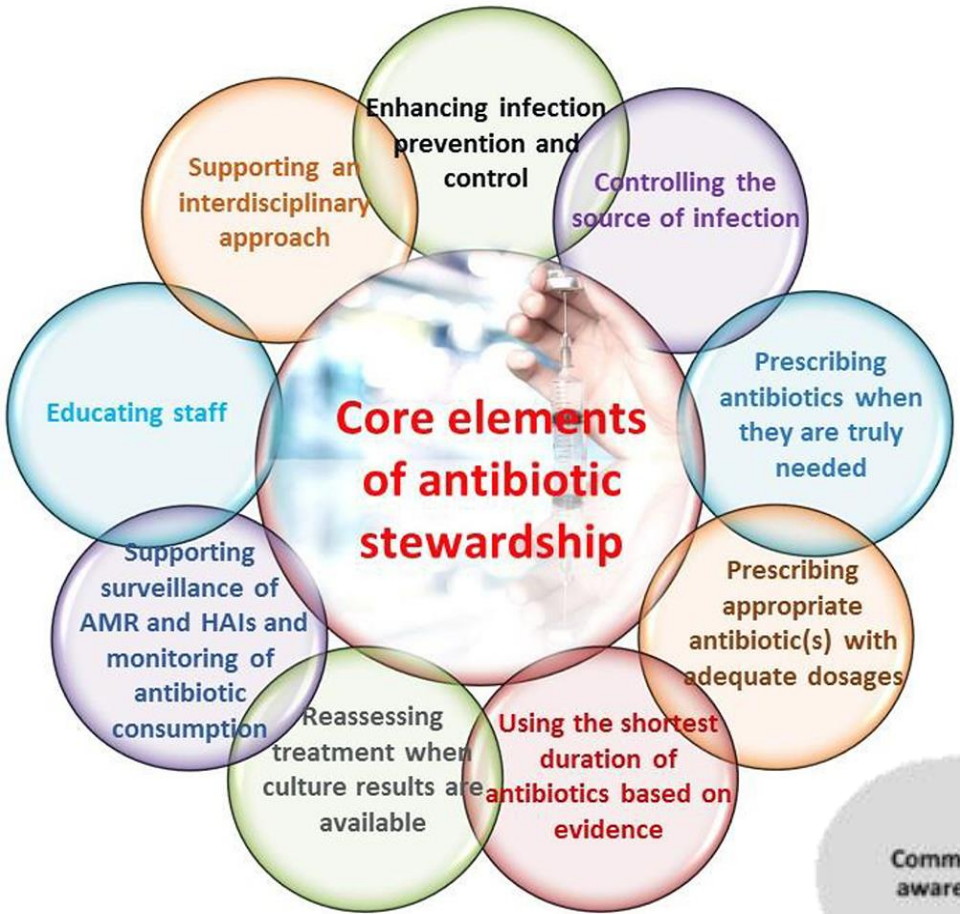


Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

May 2016

Clinical Infectious Diseases 2016;62 (10):e51-e77





Mathew, Philip & Ranjalkar, Jaya & Chandy, Sujith. (2020). Challenges in Implementing Antimicrobial Stewardship Programmes at Secondary Level Hospitals in India: An Exploratory Study. *Frontiers in Public Health*. 8. 493904. [10.3389/fpubh.2020.493904](https://doi.org/10.3389/fpubh.2020.493904)

Philip M, Jaya R, John CS. Challenges in Implementing Antimicrobial Stewardship Programmes at Secondary Level Hospitals in India: An Exploratory Study. *Frontiers in Public Health*. 2020;8. <https://www.frontiersin.org/articles/10.3389/fpubh.2020.493904>. DOI=10.3389/fpubh.2020.493904

Majumder MAA, Rahman S, Cohall D, et al. Antimicrobial Stewardship: Fighting Antimicrobial Resistance and Protecting Global Public Health. *Infect Drug Resist*. 2020;13:4713-4738 <https://doi.org/10.2147/IDR.S290835>



Upravljanje -Stewardship-

- Upravljanje **NIJE SAMO** ograničenje neadekvatne upotrebe antibiotika
 - Optimalizacija izbora antibiotika
 - Doziranje
 - Put primene
 - Trajanje terapije





Tim za upravljanje antibioticima

- Infektolog
- Klinički farmakolog sa obukom iz oblasti infektivnih bolesti
 - Bolnički farmaceut sa **obukom iz oblasti** infektivnih bolesti
- Mikrobiolog
- Član tima zadužen za kontrolu infekcija
- Bolnički epidemiolog
- IT specijalista/tehničar
- Ordinirajući lekar



Ciljevi Programa Upravljanja Antibioticima (PUA)

- **Poboljšanje** ishoda lečenja
- **Prilagođavanje** antibiotske terapije prema pacijentu
- **Minimalizovanje** razvoja rezistencije na nivou pacijenta, bolnice i sredine (naselje, grad)



Ciljevi Programa Upravljanja Antibioticima (PUA)

- **Rezervni** lekovi koji su efikasni protiv MDRO za lečenje infekcija uzrokovanih rezistentnim patogenima
- **Edukacija** o pravilnoj upotrebi antibiotika
- **Redukovanje** troškova za antibiotike



Metode upravljanja

- Edukacija
- Vodiči i kliničke smernice
- Formulari za potraživanje antibiotika (Prethodno pripremljeni set)
- Optimalizacija doze
- Konverzija sa parenteralne na oralnu
- Usmeravanje ili deeskalacija terapije





Usvojen 2017 od strane EC

In hospitals, the elements of antimicrobial stewardship programmes should include:

- ▶ An antimicrobial committee or similar formal organisational structure with senior management support.

Infectious disease specialists should:

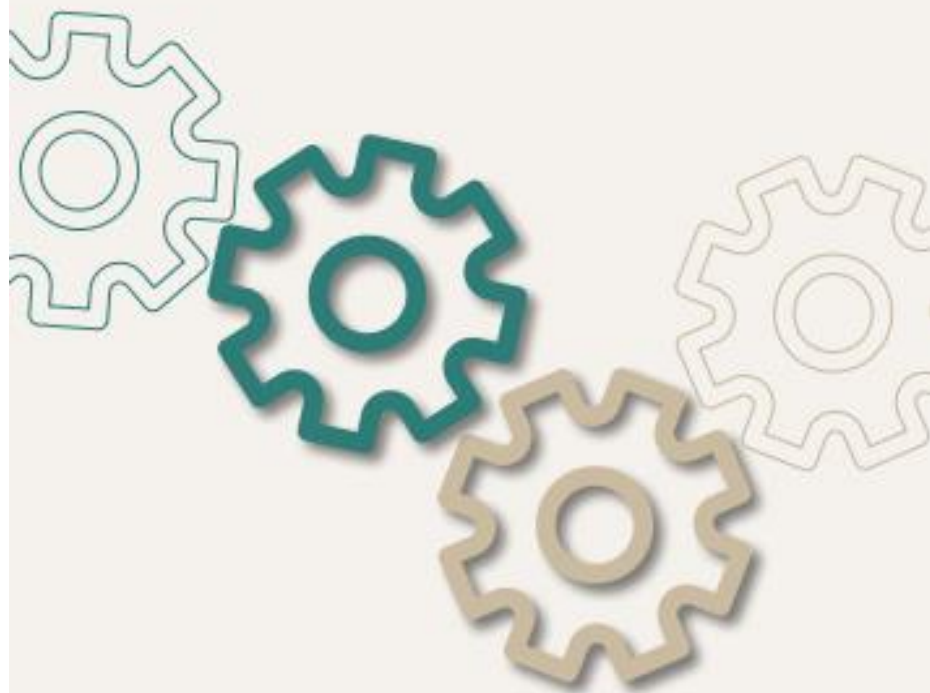
- ▶ Be available for consultation on diagnostic evaluation and treatment of infectious diseases including difficult-to-treat pathogens and complicated infections, as well as appropriate antimicrobial use.
- ▶ As full members of the antimicrobial stewardship team, take on responsibilities that include coordination, planning, post-prescription review and feedback.



- ▶ Be available for consultation on diagnostic evaluation and treatment of infectious diseases including difficult-to-treat pathogens and complicated infections, as well as appropriate antimicrobial use.
- ▶ As full members of the antimicrobial stewardship team, take on responsibilities that include coordination, planning, post-prescription review and feedback.



Antimicrobial stewardship interventions: a practical guide



ANTIMICROBIAL STEWARDSHIP PROGRAMMES

IN HEALTH-CARE FACILITIES IN LOW- AND

MIDDLE-INCOME COUNTRIES

A WHO PRACTICAL TOOLKIT





NATIONAL ANTIBIOTIC RESISTANCE CONTROL PROGRAMME FOR THE PERIOD 2019-2021

FEBRUARY 2019
REPUBLIC OF SERBIA

<https://www.who.int/teams/surveillance-prevention-control-AMR/national-action-plan-monitoring-evaluation/library-of-national-action-plans>

Evidence brief for policy

EVIPNet Europe

Number 11

Improving the appropriate use of antibiotics
in Serbian health-care settings



Nevenka PAVLOVIĆ
Goran STEVANOVIĆ
Bojana MATEJIĆ
Ljiljana MARKOVIĆ-DENIĆ
Ivana ČIRKOVIĆ

 World Health
Organization
European Region

Suggested citation. Pavlović N, Stevanović G, Matejić B, Marković-Denić LJ, Čirković I. Evidence brief for policy: improving the appropriate use of antibiotics in Serbian health-care settings. Number 11. Copenhagen: WHO Regional Office for Europe; 2023. Licence: [CC BY-NC-SA 3.0 IGO](https://creativecommons.org/licenses/by-nc-sa/3.0/).

Saveti stručnjaka: Uloga infektologa

- Poznavanje prirode infekcija uopšte i principa njihovog lečenja
- Kliničar sa iskustvom lečenja bolesnika
- Sposobnost prilagođavanja i brzog reagovanja sa nepotpunim informacijama
- Poznavanje i odluka o adekvatnim kliničkim kombinacijama antiinfektiva
- Infektološka konsultacija
 - Formalna i neformalna “kao forma ograničenja”
 - Konsultacije na licu mesta usmerene na zaokruživanje PUA tima
 - Konsultacije sa distance putem telemedicine (uskladjene video/audio tehnologije)





Saveti stručnjaka: Uloga mikrobiologa

- Pravilna analitika
 - Tačna
 - Brza
- Poznavanje prirode bakterija
- Praćenje fenotipskih karakteristika
 - Promena rezistencije tokom lečenja
- Relevantnost uzorka
 - Šta je uzorkovano
 - Na koji način
- Relevantnost izolata
 - Kolonizacija
 - Infekcija



Saveti stručnjaka: Uloga epidemiologa

- Izrada i poznavanje epidemiološke „karte“ mikroorganizama u ustanovi
- Poznavanje mera prevencije i najefikasnijeg suzbijanja širenja infekcija
- Poznavanje i kontrola mera bolničke higijene
- Poznavanje „šire“ mikrobiološke slike
- Nadzor nad patogenima od interesa
- Izveštavanje



Saveti stručnjaka: Uloga kliničkog farmakologa

- Poznavanje farmakokinetike i farmakodinamike
 - kod zdravih (registracione studije)
 - kod patoloških (i drugih posebnih) stanja
- Poznavanje interreakcija lekova
- Predlaganje najboljih farmakoloških kombinacija lekova

Ideal: Pristup svim medicinski značajnim podacima elektronski



Koristi od primene PUA

- Redukcija upotrebe antibiotika
- Redukcija troškova lečenja
- Smanjenje mortaliteta povezanog sa rezistencijom i/ili bolničkim infekcijama
- Potencijalno smanjenje rezistencije (potrebno vreme)
- Olakšanje rada JIL i ostalih odeljenja
- Manji stres na zaposlene
- Veće poverenje pacijenata (potrebno vreme)



Aiesh, B.M., Nazzal, M.A., Abdelhaq, A.I. et al. Impact of an antibiotic stewardship program on antibiotic utilization, bacterial susceptibilities, and cost of antibiotics. *Sci Rep* 13, 5040 (2023). <https://doi.org/10.1038/s41598-023-32329-6>

Gebretekle GB, Mariam DH, Mac S, et al. Cost–utility analysis of antimicrobial stewardship programme at a tertiary teaching hospital in Ethiopia. *BMJ Open* 2021;11:e047515. doi: 10.1136/bmjopen-2020-047515

Trotter NE, Slight SP, Karimi R, et al. The effect of digital antimicrobial stewardship programmes on antimicrobial usage, length of stay, mortality and cost. *Informatics in Medicine Unlocked* 2023;37, 101183, ISSN 2352-9148, <https://doi.org/10.1016/j.imu.2023.101183>





Uslov za uspeh

- Mobilizacija i zainteresovanost svih koji učestvuju u procesu brige o pacijentu
 - Podrška lekara kliničara (ordinirajućih lekara)
 - Podrška uprave ustanove
 - Velika upornost, entuzijazam i posvećenost članova tima
-
- **Znanje članova tima**
 - **Edukacija svih**





<https://ukhsa.blog.gov.uk/2015/12/10/health-matters-your-antimicrobial-resistance-toolkit/>