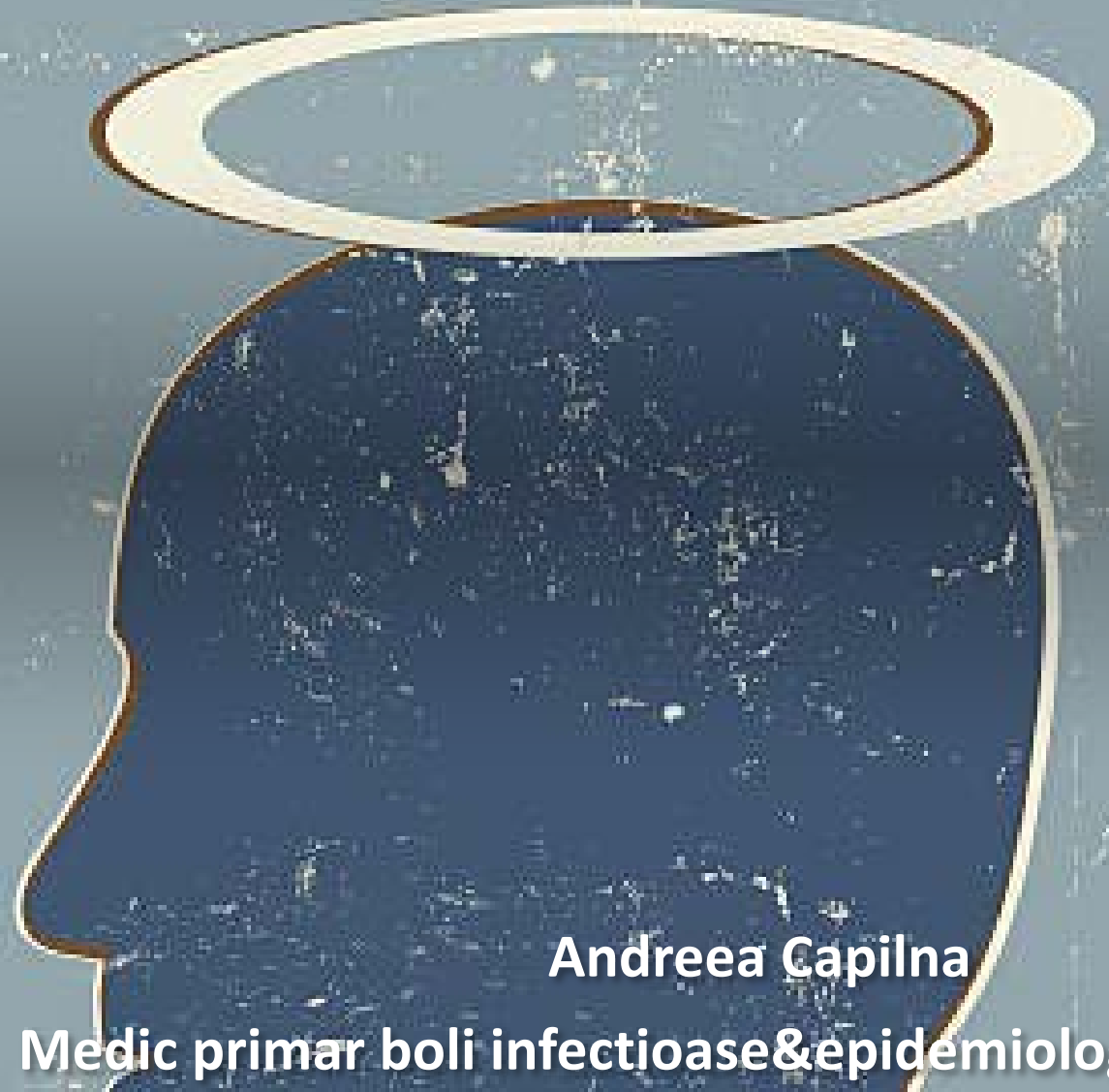


Antibioticele: aliat sau **inamic**?

TRIADA ADMINISTRARII



Andreea Capilna

Medic primar boli infectioase&epidemiologie

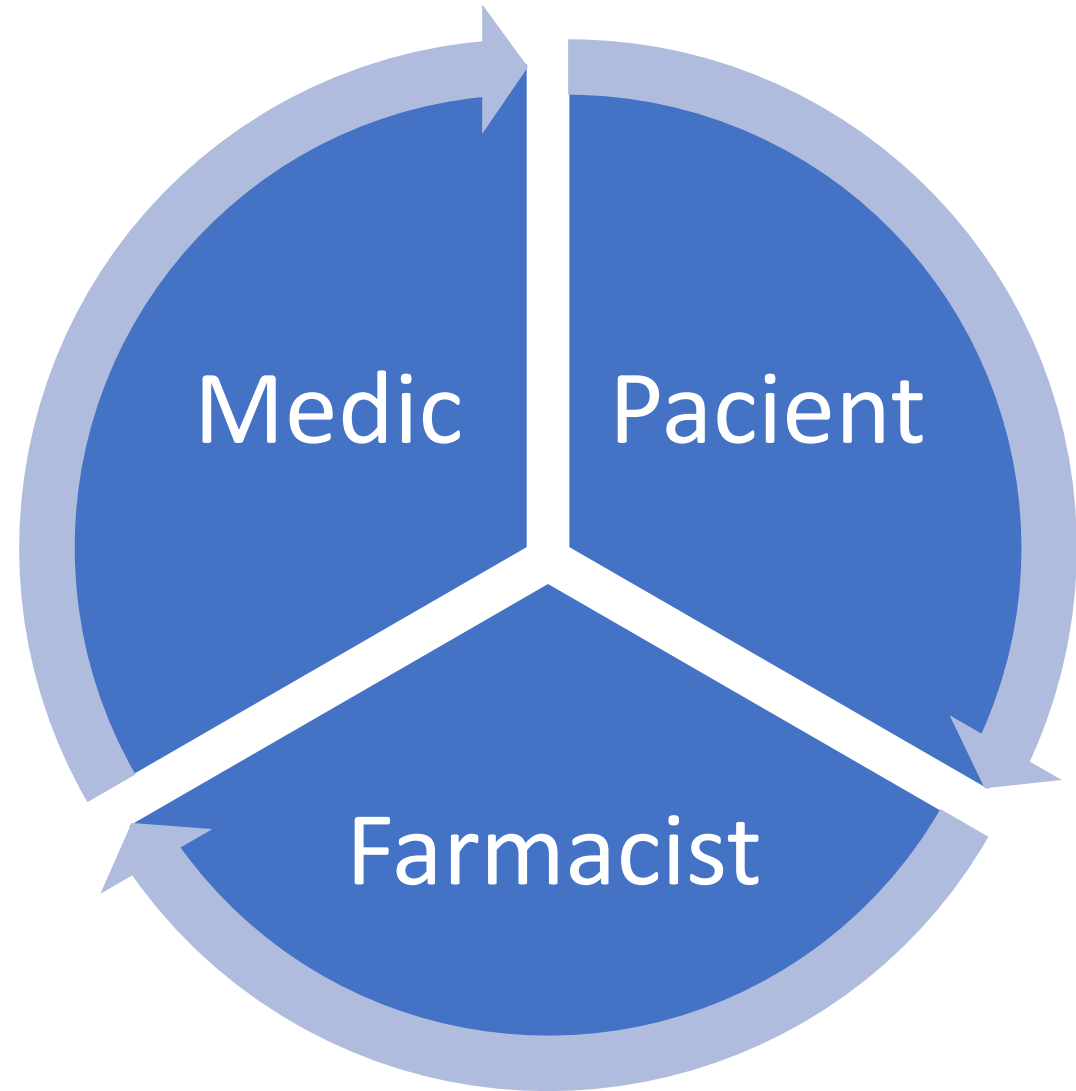




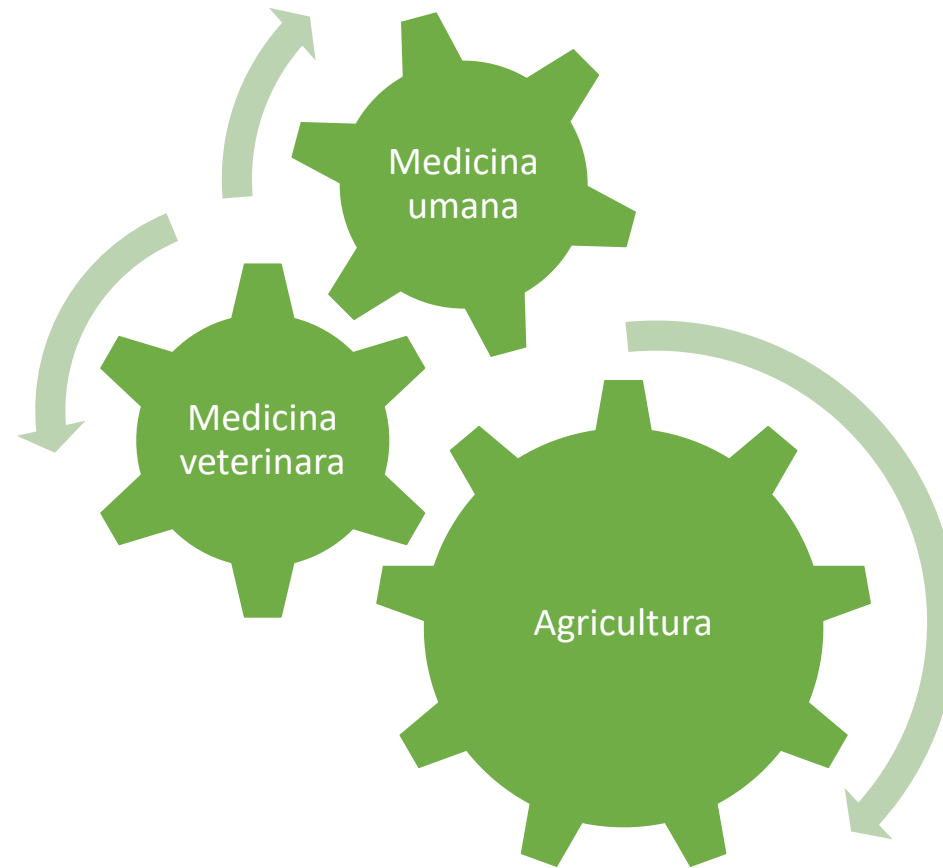
# Problema e universal valabila international mondial

De fapt ne priveste pe toti la un loc si pe fiecare in parte

Ecuatia  
cererii si  
ofertei

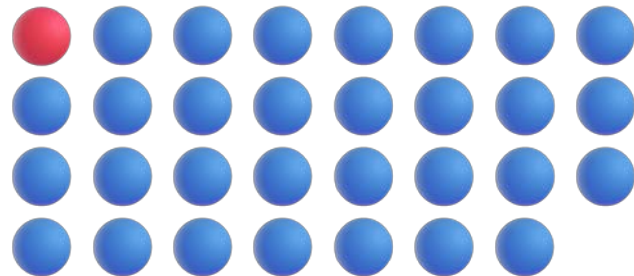


# Ecuatia utilizarii:



# Perspective

**1 din 31 dezvoltă o IAM**



IN USA

687.000 decese in spitale de acuti

**Majoritatea MDRB**

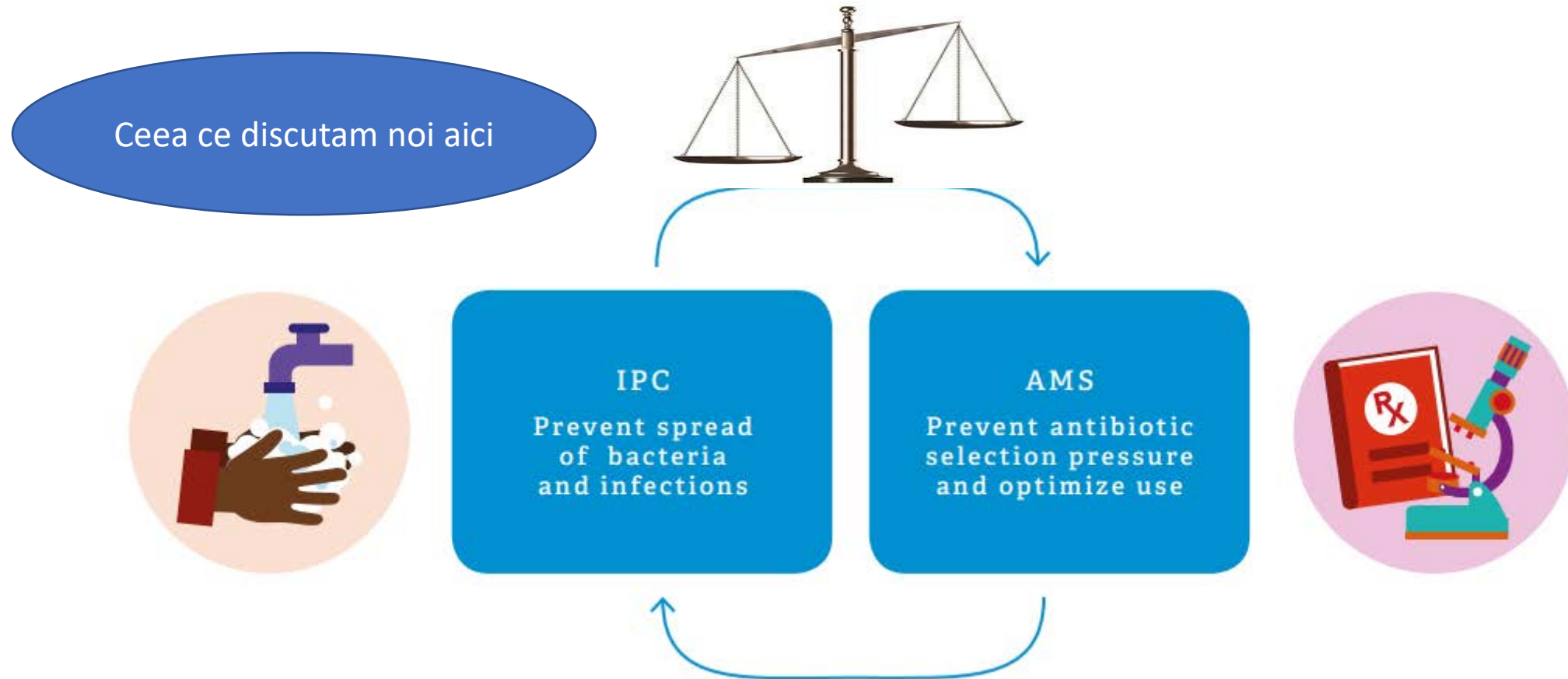
USA - approx. 72.000 decese / an

Echivalentul a:

Toledo (Spania), St Gallen (Elvetia),  
Bourges (Franta), Burnley (UK)



# Simplu si eficient, dar neaparat impreuna



A large pile of various colored capsules (red, white, blue, yellow) against a soft, warm background. The capsules are scattered across the frame, with a prominent blue and yellow capsule in the center foreground. The background is a soft, out-of-focus gradient of warm colors, suggesting a sunset or sunrise.

# Principiile Antibiotic Stewardship



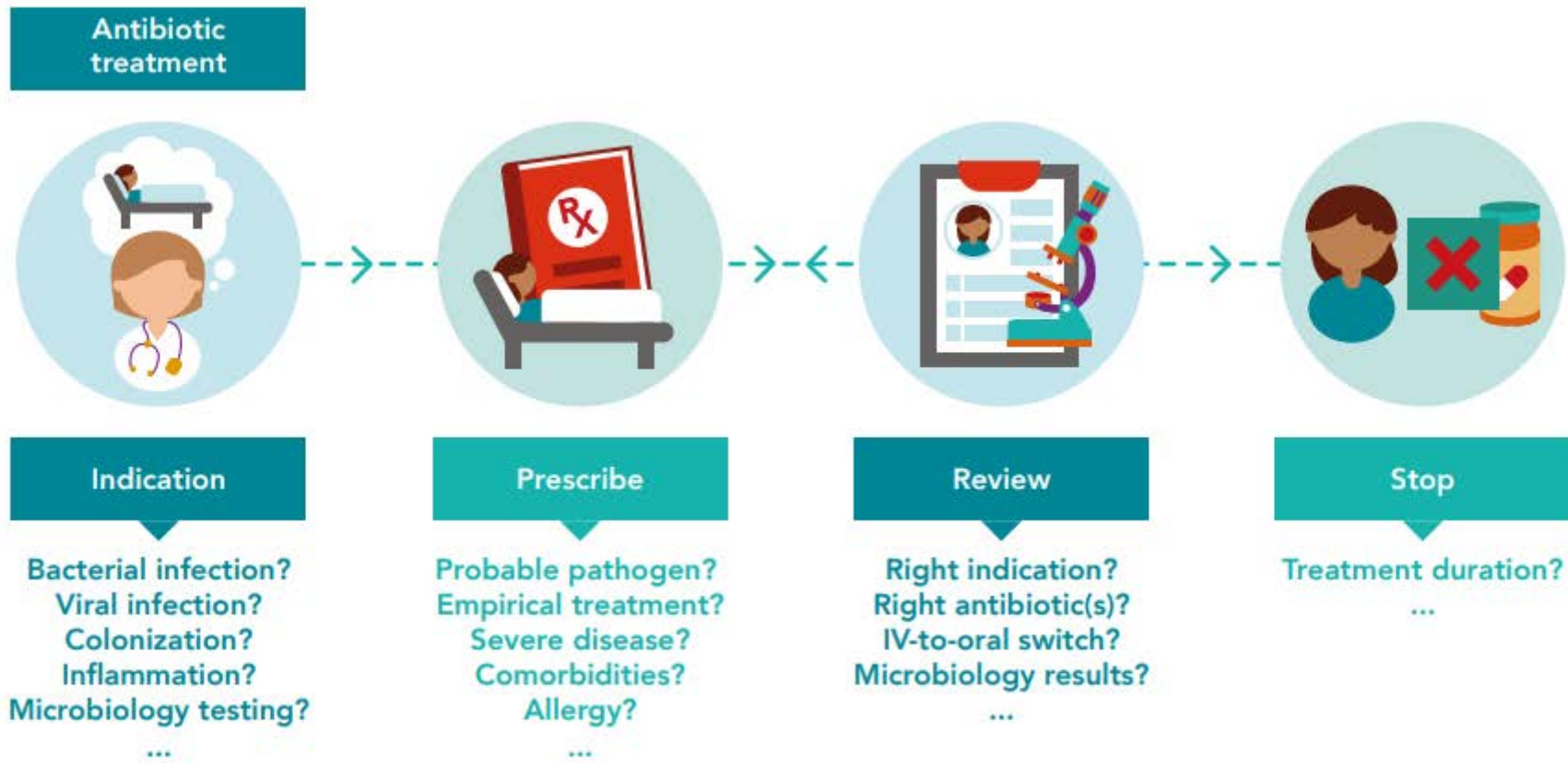
A scenic landscape of rolling green hills under a soft, hazy sky. A paved road winds through the hills, curving sharply in the foreground. The hills are covered in lush green grass, and the overall atmosphere is peaceful and natural.

Mai detaliat....

- Medic
- Pacient
- Farmacist

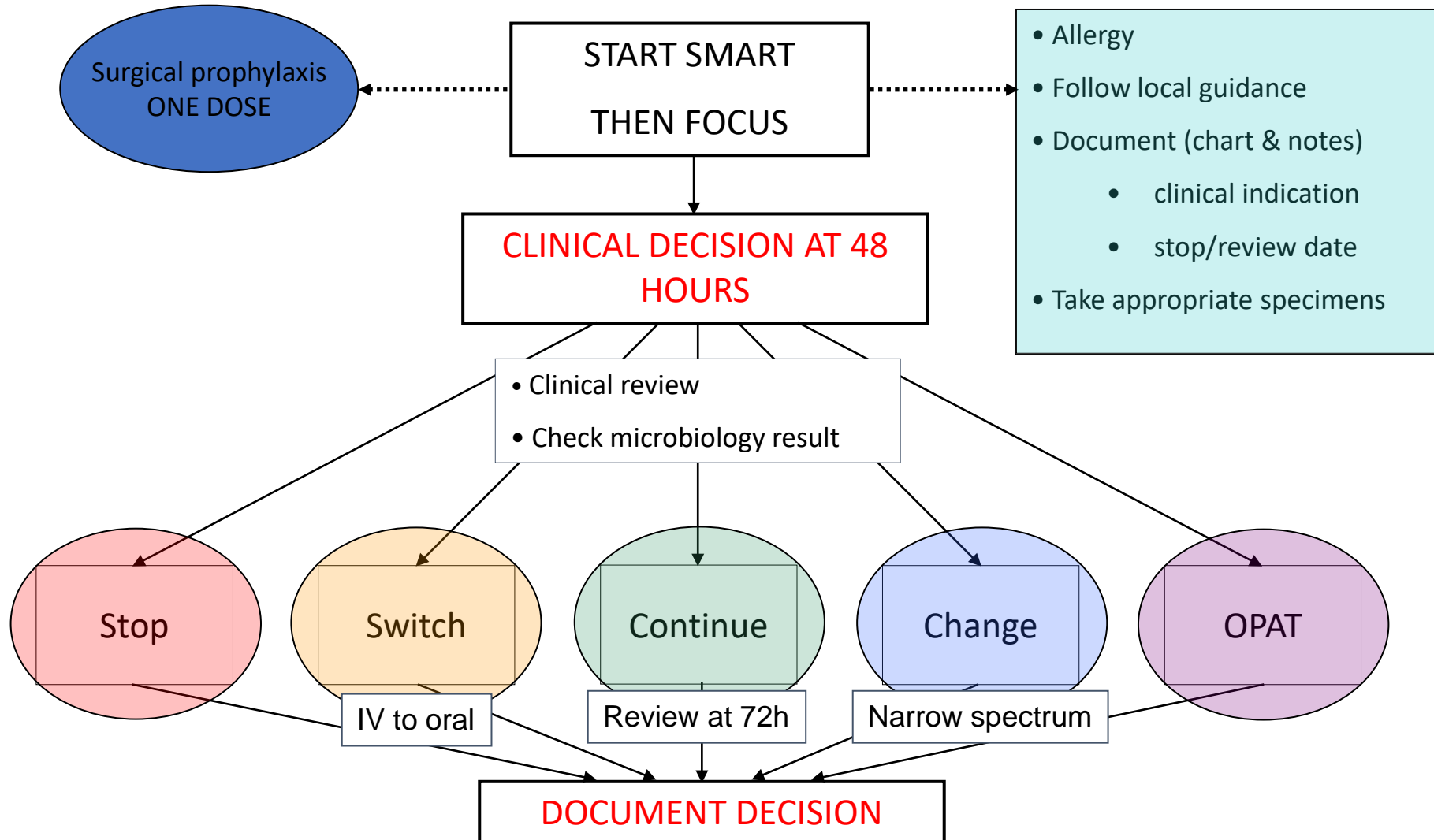


# Medic



Right Drug, Right Time, Right Dose, Right Duration.....

..... Every time



# Indicatie: intrebari existentiale

- **Infectie bacteriana vs virala**

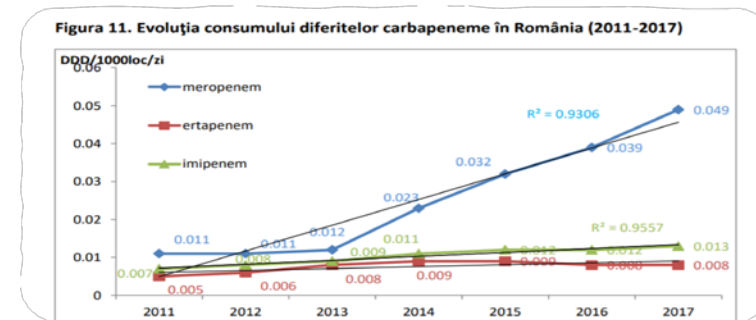
- HLG, PCR, clinica, context epidemiologic

- Exemplul pandemiei cu exces de : azitromicina / claritromicina (cand nu se gasea azitro → 2,5x consum anterior in 2021, 2022?), forexo, meropenem / imipenem

- 2011-2017

- 2021-2023???

- “antibioticele nu sunt anxiolitice”





# Colonizare vs contaminare vs infectie ?

## Definitii

- Contaminare
- Colonizare
- Infectie



Nu se trateaza cu antibiotic!!!  
(cu exceptia decolonizarii MRSA)

# Exemple colonizare

- Urocultura pozitiva pe sonda: NU se trateaza DECAT daca pacientul prezinta sindrom infectios, leucocitoza, sindrom inflamator, urina tulbure
- Ex bacteriologic pozitiv din ulcer de gamba: nu se trateaza decat daca exista sindrom infectios, leucocitoza, sindrom inflamator, CELULITA
- Colonizare bacteriana digestiva : nu se trateaza, nu exista beneficiu / eficienta
- Exudat nazal pozitiv fara leucocitoza, sindrom inflamator
  - Bactroban (Mupirocin) activ pe germeni G+
  - Prontoderm, octenisept: active pe G+ si G-



Alta problema majora: Saltul direct la atb de rezerva



# 1. Antibiotice de rezervă

- **Definiție:** medicamente de pe listele WHO ale medicamentelor esențiale cu un profil risc-beneficiu favorabil și o activitate dovedită împotriva agenților patogeni de "**prioritate critică**" sau de "**prioritate ridicată**" identificați de WHO, în special *Enterobacteriaceae* rezistente la carbapeneme.
- Antibioticele din categoria **Reserve** sunt **utilizate pentru tratarea infecțiilor multidrog-rezistente.**

# WHO global priority pathogens list of antibiotic-resistant bacteria

## Priority 1: CRITICAL

- • *Acinetobacter baumannii*, carbapenem-resistant
- • *Pseudomonas aeruginosa*, carbapenem-resistant
- • *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

•

## Priority 2: HIGH

- • *Enterococcus faecium*, vancomycin-resistant
- • *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant
- • *Helicobacter pylori*, clarithromycin-resistant
- • *Campylobacter spp.*, fluoroquinolone-resistant
- • *Salmonellae*, fluoroquinolone-resistant
- • *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant

•

## Priority 3: MEDIUM

- • *Streptococcus pneumoniae*, penicillin-non-susceptible
- • *Haemophilus influenzae*, ampicillin-resistant
- • *Shigella spp.*, fluoroquinolone-resistant

The WHO **AWaRe**  
(**A**ccess, **W**atch, **R**eserve)  
antibiotic book

**AWaRe**

**A**ccess, **W**atch, **R**eserve



## Community-acquired pneumonia

Page 2 of 2

### CURB-65 Severity Scoring System

**Signs & Symptoms (1 point each)**

- Presence of Confusion (new onset)
- Urea > 19 mg/dL (or > 7 mmol/L)\*
- Respiratory rate > 30/min
- Systolic BP < 90 mmHg (<12 kPa) or Diastolic BP ≤ 60 mmHg (<8 kPa)
- Age ≥ 65 years

**Score 0-1**  
• Consider outpatient treatment

**Score 2**  
• Consider inpatient treatment  
• Consider adding **daptomycin to beta-lactam** for atypical coverage  
• Perform microbiology tests

**Score ≥3**  
• Inpatient treatment (consider ICU)  
• Consider adding **daptomycin**  
• Perform microbiology tests

*Other considerations such as severe comorbid illnesses or inability to maintain oral therapy should be taken into account. CURB-65 has not been extensively validated in low-income settings.*

*\*The CURB-65 score, which does not require laboratory values for its calculation, can also be used; the score value interpretation is the same as for CURB-65*

### Rx Treatment

#### Antibiotic Treatment Duration

Treat for **5 days**

If severe disease, consider longer treatment and look for complications such as empyema, if patient not clinically stable at day 5

#### Severe Cases

All dosages are for normal renal function  
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

**First Choice**

**Cefotaxime 2 g q8h IV/IM**  
N0704

OR

**Ceftriaxone 2 g q24h IV (1 g q24h IM\*)**  
N0704

\*A larger volume would be painful to give as intramuscular injection

IF CURB-65 ≥2, CONSIDER ADDING

**Clarithromycin 500 mg q12h ORAL (or IV)**  
W01X1

*Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function*

**Second Choice**

**Amoxicillin+clavulanic acid 1 g+200 mg q8h IV**  
A01AD06  
• A higher daily dose can be considered: 1 g+200 mg q6h

IF CURB-65 ≥2, CONSIDER ADDING

**Clarithromycin 500 mg q12h ORAL (or IV)**  
W01X1

*Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function*

### Rx Mild to Moderate Cases

All dosages are for normal renal function  
Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated

**First Choice**

**Amoxicillin 1 g q8h ORAL**  
A01AD06

OR

**Phenoxymethylpenicillin (as potassium) 500 mg (800 000 IU) q6h ORAL**  
A01AD01

**Second Choice**

**Amoxicillin+clavulanic acid 875 mg+125 mg q8h ORAL**  
A01AD06

OR

**Doxycycline 100 mg q12h ORAL**  
A01AC06




## Manualul OMS **AWaRe** (**A**ccess, **W**atch, **R**eserve) privind utilizarea antibioticelor

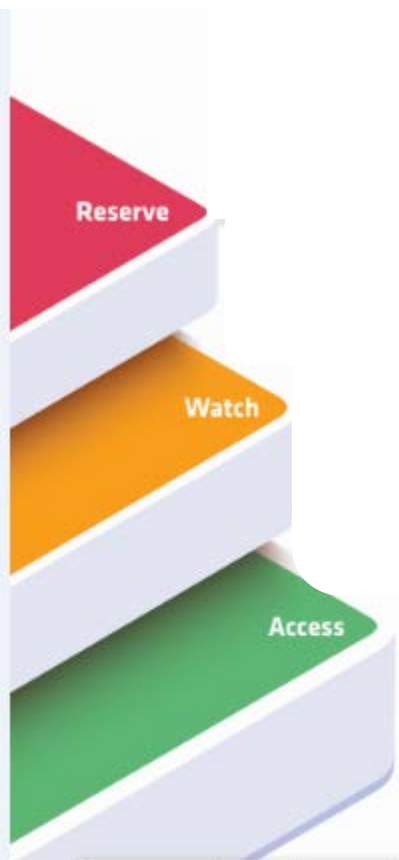
- ✓ Oferă îndrumări concise, bazate pe dovezi, privind
  - ✓ alegerea antibioticului
  - ✓ doza
  - ✓ calea de administrare
  - ✓ durata tratamentului

pentru mai mult de 30 dintre cele mai frecvente infecții clinice la copii și adulți, atât în asistența medicală primară, cât și în mediul spitalicesc.

## Sistemul **Access**, **Watch**, **Reserve** (AWaRe)

Minim **60%** din totalul antibioticelor prescrise la nivel național să fie antibiotice de **Access**

Clasa	Simbol	Nr total molecule	Tip antibiotice	Portofoliul Antibiotice	
				Injectabile	Orale
Acces (acces)		48	antibiotice de primă intenție potențial scăzut de a dezvolta rezistență	Amoxicilină/acid clavulanic Ampicilină Ampicilină/sulbactam Benzilpenicilină Benzatin-benzilpenicilină Cefazolină Oxacilină	Amoxicilină Ampicilină Cefadroxil Doxiciclină Oxacilină Tetraciclină
Watch (de supravegheat)		110	antibiotice cu spectru mai larg antibiotice de importanță clinică potențial crescut de a dezvolta rezistență	Cefuroximă Cefotaximă Ceftazidimă Ceftriaxonă Ertapenem Imipenem/cilastatin Meropenem Piperacilină/tazobactam Vancomicină	Levofloxacină Cefiximă Ciprofloxacină Claritromicină Eritromicină Rifampicină
Reserve		22	antibiotice pentru germeni MDR (multidrogrezistenți) antibiotice de ultimă instanță	Colistină Tigeciclină	





# Antibiotice de rezervă

!!! Noile antibiotice sunt de fapt “reinventate”, pt ca tot e la moda.....

aztreonam

carumonam

cefiderocol

ceftaroline

ceftazidime + avibactam

ceftobiprole

ceftolozane + tazobactam

colistin (injection)

colistin (oral)

linezolid

meropenem + vaborbactam

minocycline (injection)

omadacycline

oritavancin

plazomicin

polymyxin B (injection)

polymyxin B (oral)

tedizolid

dalbavancin

dalfopristin + quinupristin

daptomycin

eravacycline

faropenem

fosfomicin (injection)

iclaprim

imipenem + cilastatin + relebactam

lefamulin

telavancin

tigecycline

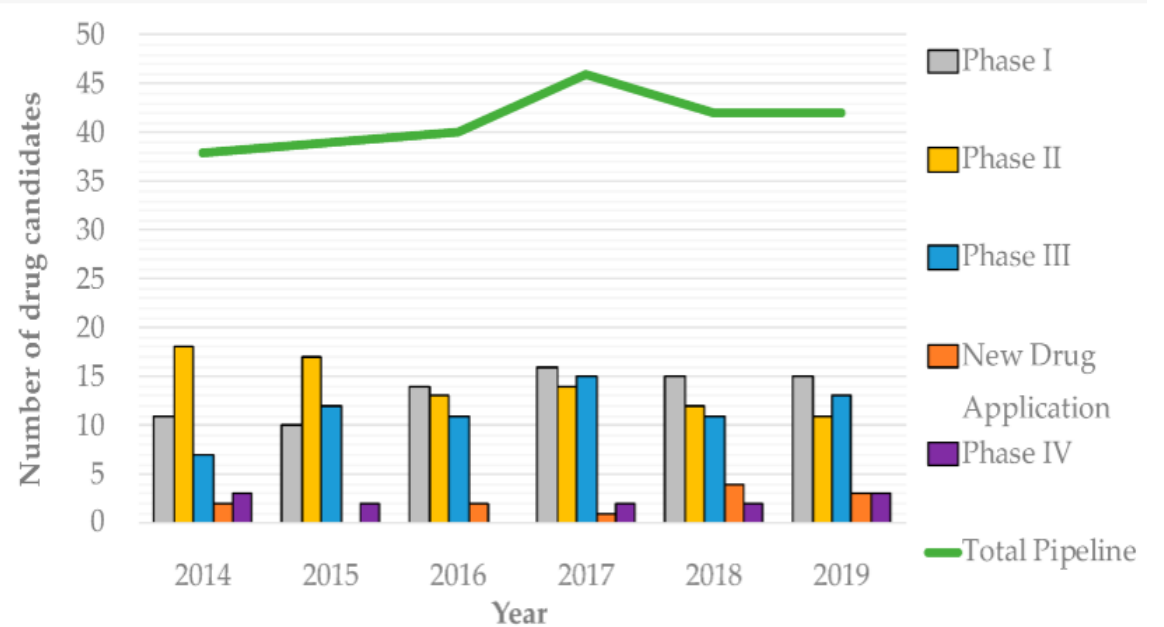


# Vistieria e săracă....

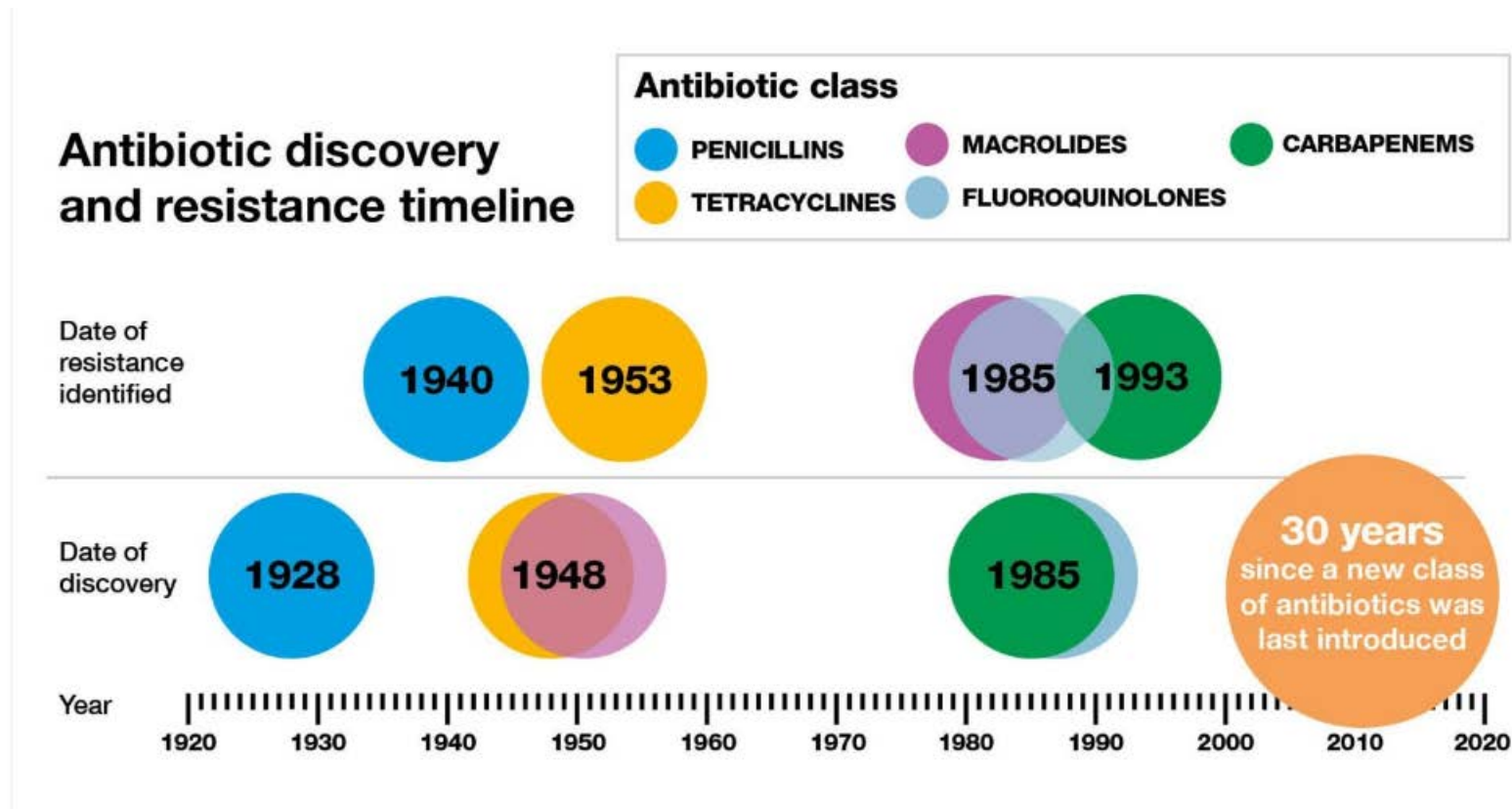
## The Antibiotic Pipeline is Dry....



**Figure 1.** Evolution of the total antibiotic pipeline and the antibiotic pipeline by stage of development, which includes: Clinical Trials ranging from Phase I, to evaluate safety; Phase II, to access effectiveness and safety; Phase III, to gather statistically significant data on safety, effectiveness and benefits-versus-risk; submission of a New Drug Application, for marketing approval; and lastly, Phase IV for post-marketing surveillance.



# Dezvoltarea de noi antibiotice



Nicio clasa noua de antibiotice nu a fost descoperita din 1987

Altfel spus, din 1987 nu s-a mai elaborat nici o clasa noua de antibiotice!!

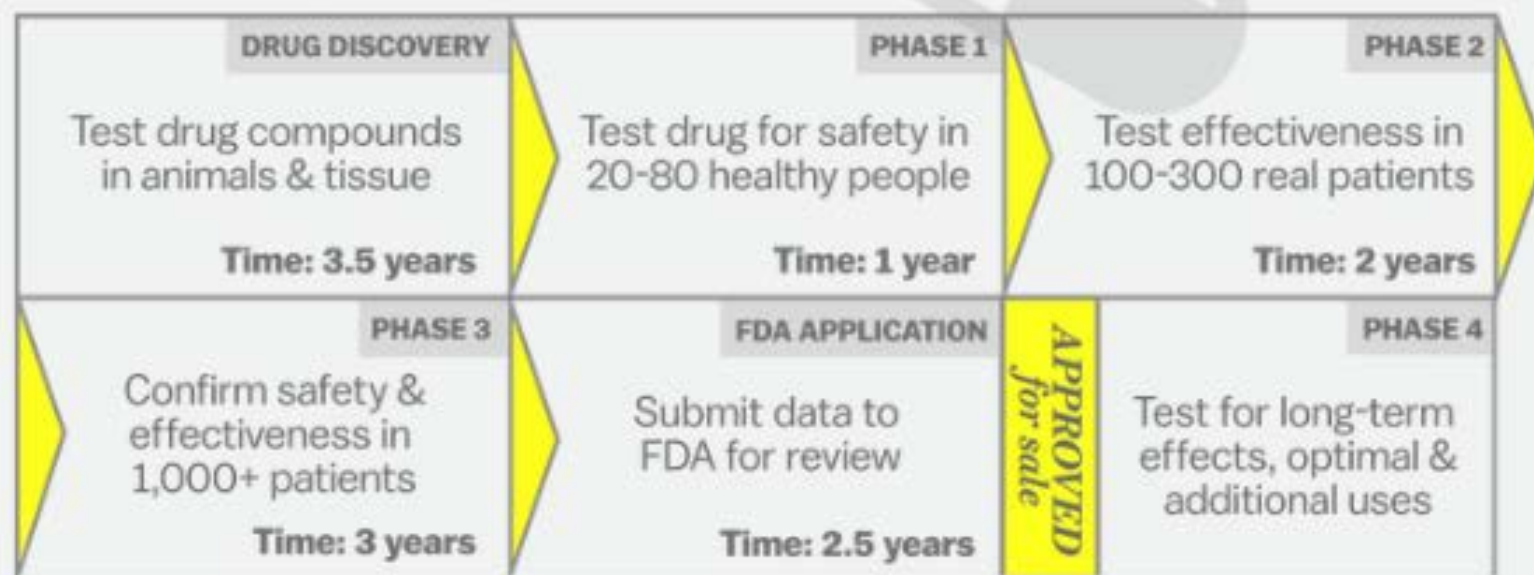




# *From the lab to the pharmacy*

**V**

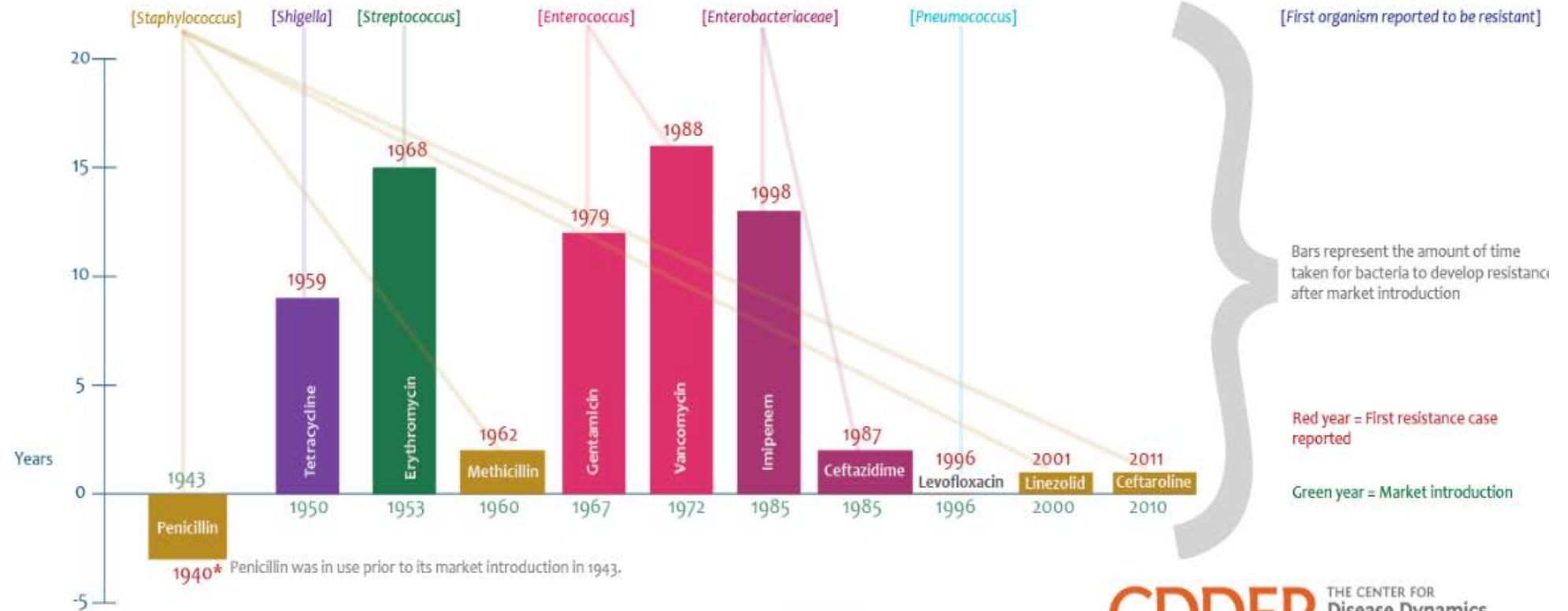
The FDA's drug-approval process (on average)



Total cost: **\$100 million to \$1 billion** Total time: **Approximately 12 years**

Success rate: **Five of 5,000 compounds reach human tests; One is approved**

# Istoria primelor cazuri de rezistența bacteriană



Data source: Antibiotic Resistance Threats in the United States, 2013.  
US Centers for Disease Control and Prevention (CDC).



# Acronym minefield

CRE

MDR-GNR

CPC

ESBL

MDR-GNB

CRO

NDM

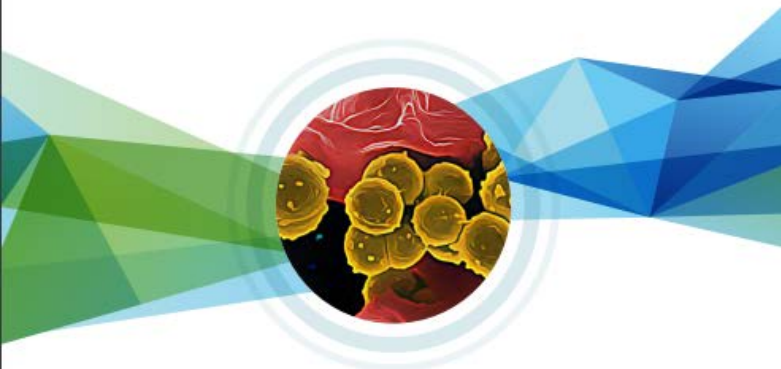
CPE

CRC

KPC

CRAB

# Rezistența la antimicrobiene (AMR)



## Antimicrobial resistance surveillance in Europe

2022

2020 data

- România - locul 3 în UE
- Niveluri crescute ale AMR în comparație cu majoritatea țărilor europene
- **AMR este o problemă europeană și globală**

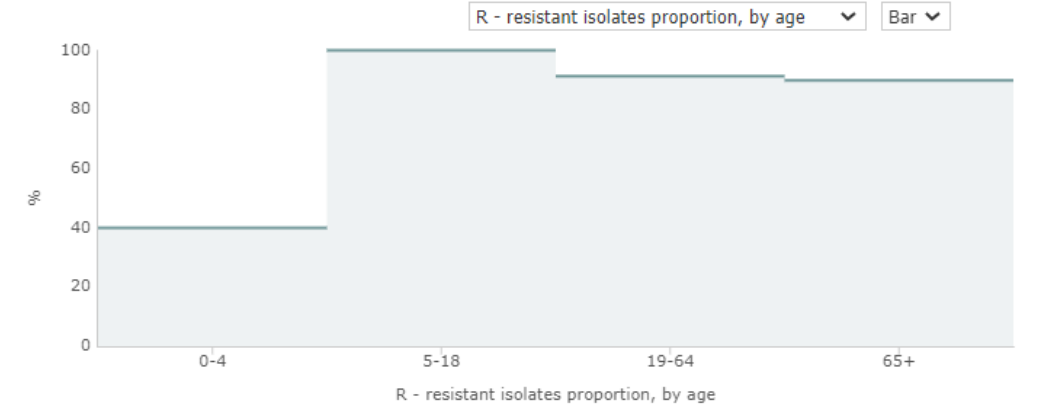
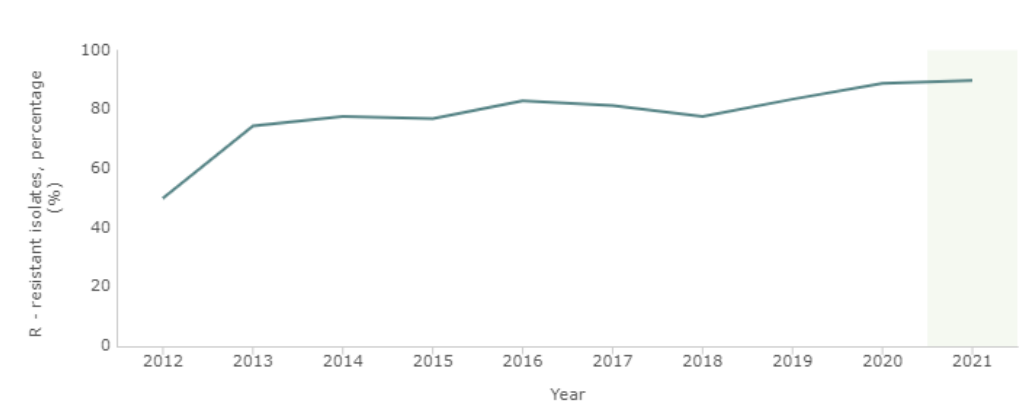
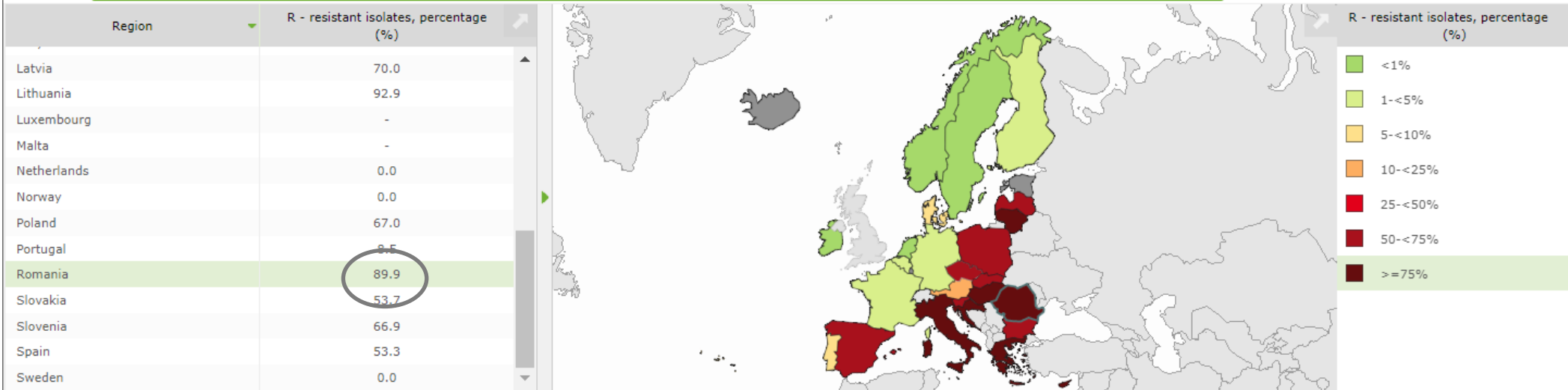


"The high levels of AMR for several important antibiotic-bacterium combinations reported in 2020 show that AMR remains a serious challenge in the EU/EEA."

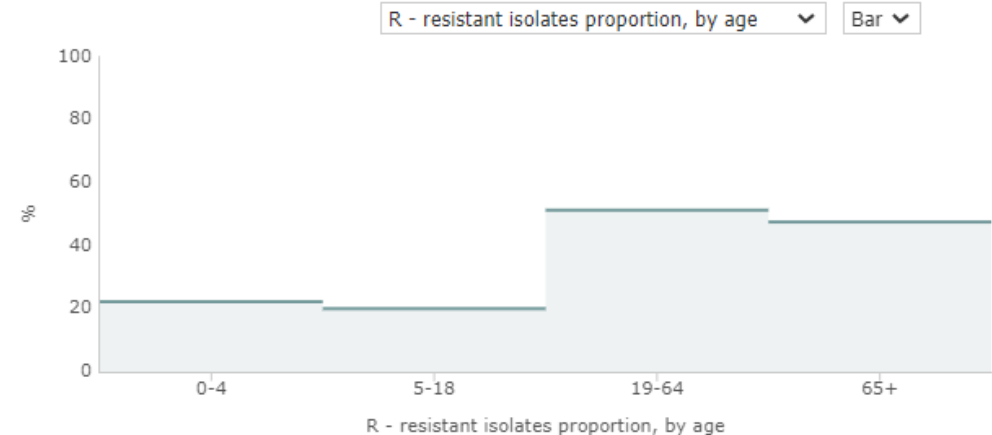
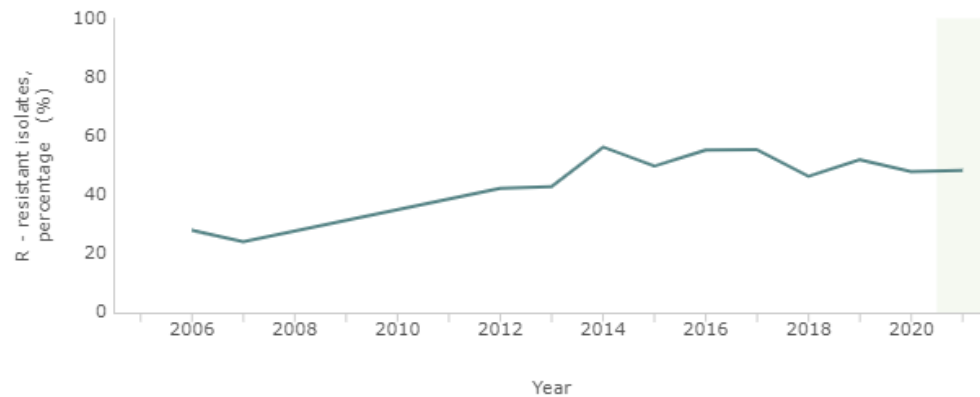
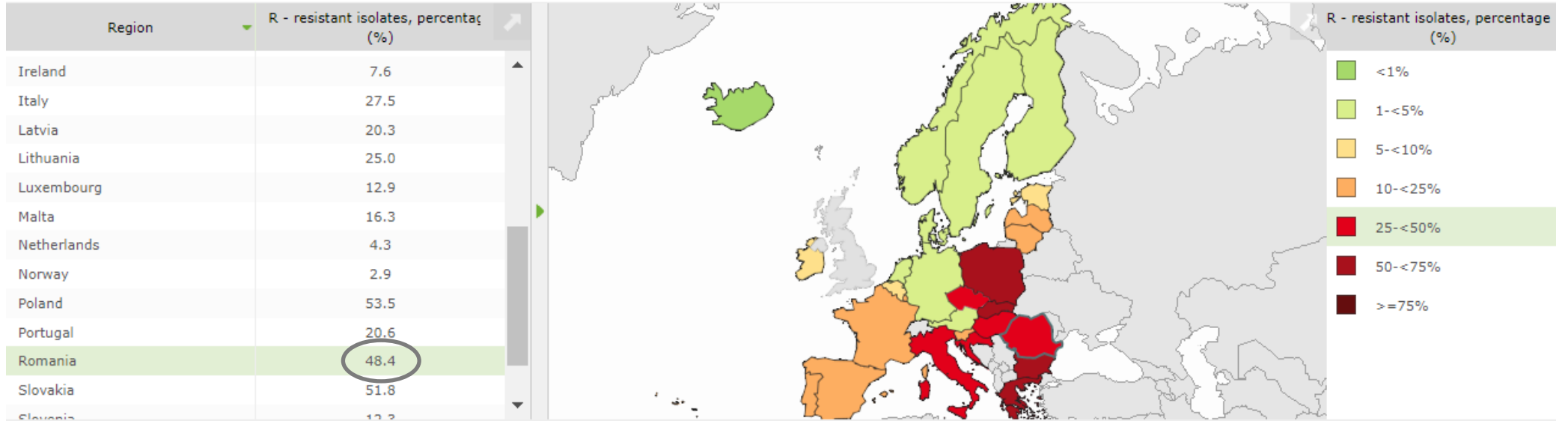
2022 - Latest ECDC report (European Centre for Disease Prevention and Control)



Antimicrobial resistance | Acinetobacter spp. | Combined resistance (fluoroquinolones, aminoglycosides and carbapenems) | R - resistant isolates, percentage | 2021



Antimicrobial resistance ▾  
 Klebsiella pneumoniae ▾ Combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycoside) ▾  
 R - resistant isolates, percentage ▾ 2021 ▾





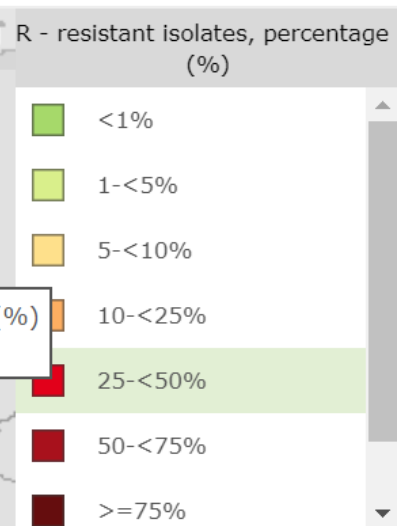
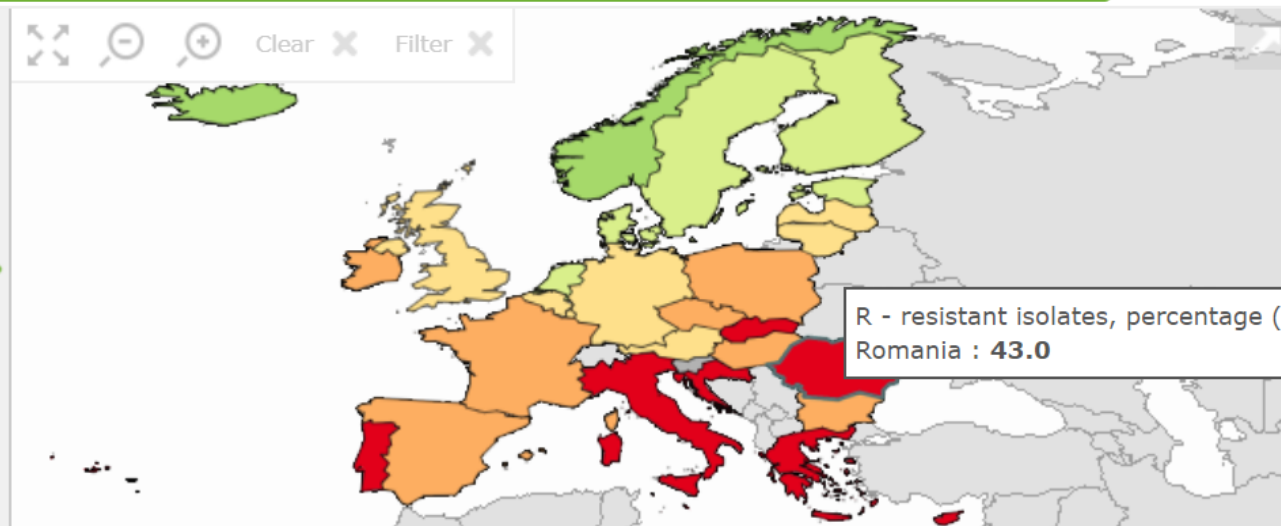
# Surveillance Atlas of Infectious Diseases

Antimicrobial resistance ▾ Staphylococcus aureus ▾ Meticillin (MRSA) ▾ R - resistant isolates, percentage ▾

2018 ▾



Region	R - resistant isolates, percentage (%)
Austria	6.4
Belgium	9.1
Bulgaria	17.6
Croatia	26.4
Cyprus	40.2
Czechia	13.6
Denmark	1.7
Estonia	3.3
Finland	2.0



age 100

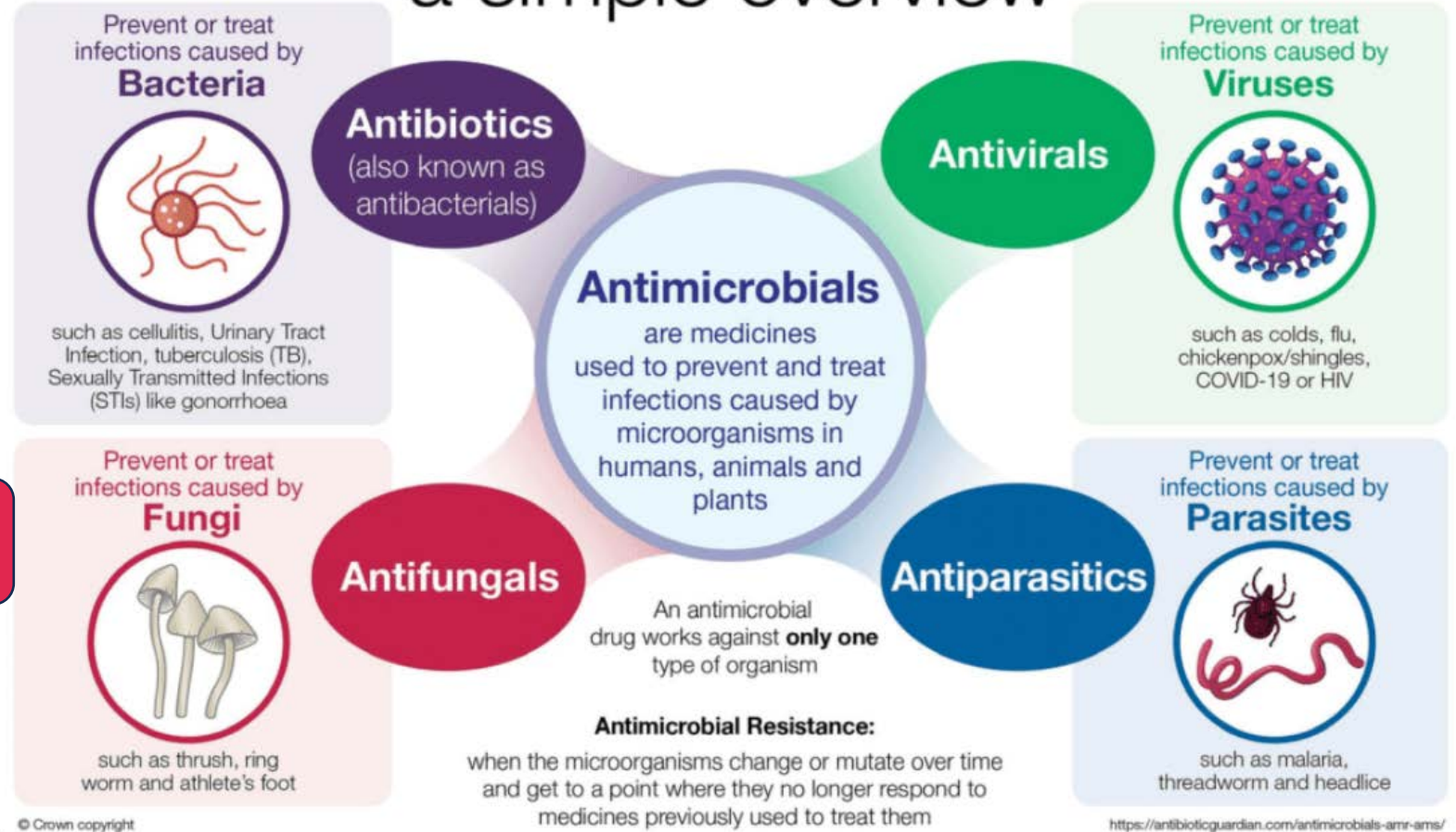
100

R - resistant isolates proportion, by gender ▾

# La ce se referă antimicrobial stewardship?



## Antimicrobials: a simple overview



Nu mai prescrieti fluconazol din start!!!







Centers for Disease ...



**NEW CDC DATA**

**MORE THAN HALF OF ANTIBIOTIC PRESCRIBING FOR SELECTED EVENTS IN HOSPITALS WAS NOT CONSISTENT WITH RECOMMENDED PRESCRIBING PRACTICES**



**ANTIBIOTIC PRESCRIBING WAS NOT SUPPORTED IN:**



with community-acquired pneumonia



with urinary tract infections



prescribed fluoroquinolone treatment



prescribed intravenous vancomycin antibiotic

**HOSPITAL PRESCRIBERS & PHARMACISTS CAN IMPROVE PRESCRIBING:**



Optimize antibiotic selection



Re-assess antibiotic treatment when the results of diagnostic testing are available



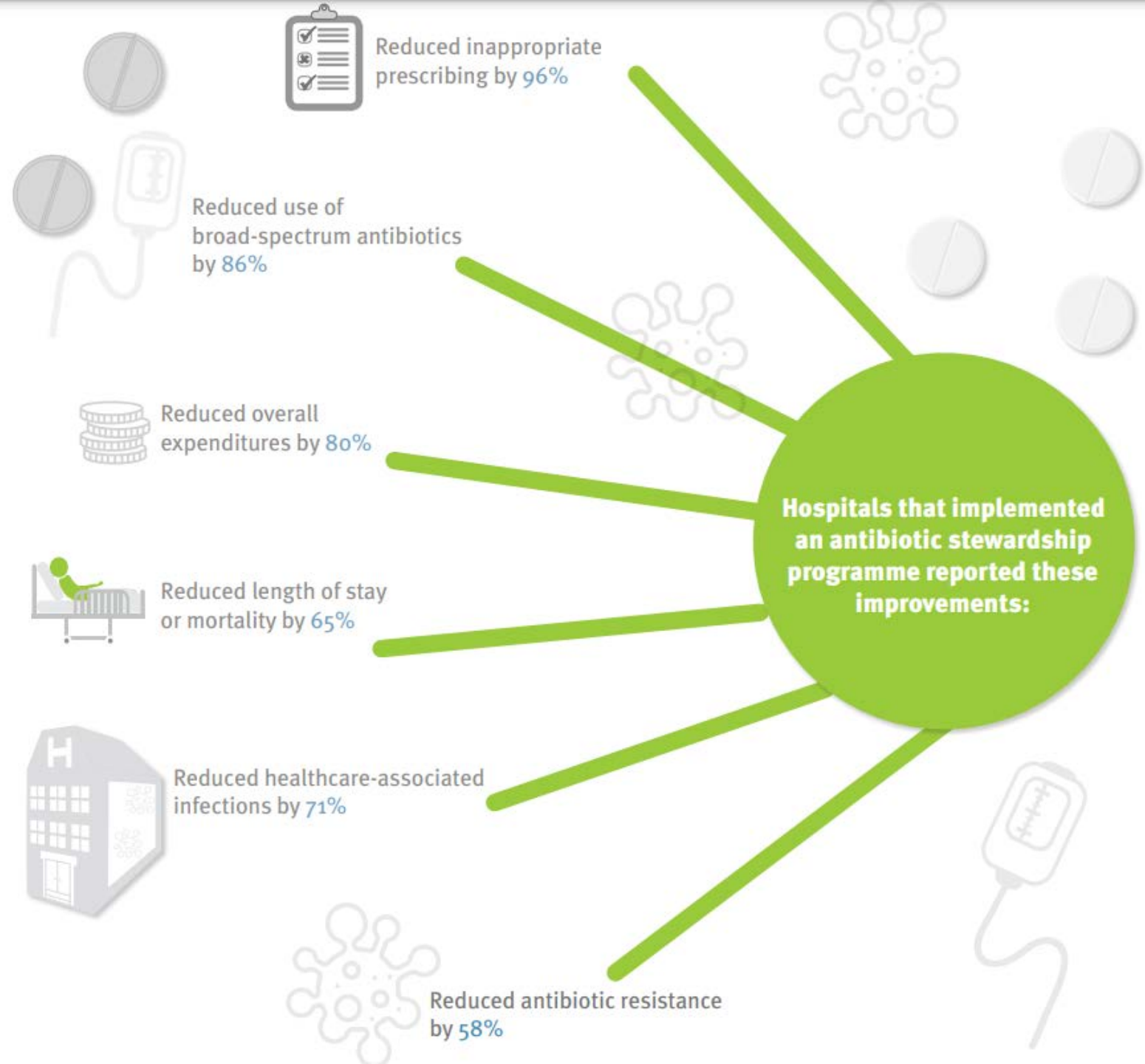
Use the shortest effective duration of therapy

FIND RESOURCES ON HOW TO IMPROVE HOSPITAL ANTIBIOTIC USE AND HELP FIGHT ANTIBIOTIC RESISTANCE:  
<https://bit.ly/HospitalCoreElements>



# Antibiotic stewardship

Spitalele care au **implementat** un program de antibiotic stewardship au raportat **îmbunătățiri**:



Reduced inappropriate prescribing by 96%

Reduced use of broad-spectrum antibiotics by 86%

Reduced overall expenditures by 80%

Reduced length of stay or mortality by 65%

Reduced healthcare-associated infections by 71%

Reduced antibiotic resistance by 58%

Hospitals that implemented an antibiotic stewardship programme reported these improvements:





**1**  
**Italy**  
A four-year infection control programme decreased the incidence of infections and colonisation caused by carbapenem-resistant bacteria in a teaching hospital. The programme included antibiotic stewardship measures targeting carbapenem use.

**2**  
**Netherlands**  
Case audits for the reassessment of antibiotic use after 48 hours reduced antibiotic consumption and length of stay in a urology ward of an academic hospital, and also had a positive direct return on investment .

**3**  
**Spain**  
After only one year, education on guidelines combined with regular feedback led to a 26% improvement in the rate of appropriate treatments, and a 42% reduction of antibiotic consumption at a tertiary teaching hospital.

**4**  
**Sweden**  
Twice weekly audit and feedback in an internal medicine department led to an absolute 27% reduction of antibiotic use , especially of broad-spectrum antibiotics, as well as shorter antibiotic treatment durations and earlier switching to oral therapy.

**5**  
**Poland**  
Developing guidelines for antibiotic prescriptions and pre-authorisation approval for restricted antibiotics decreased total antibiotic consumption in a general paediatric ward.

# Calea de administrare

- iv vs po?
  - “pacientii, daca tot sunt internati, sa primeasca trat iv”
  - Pacient cu toleranta digestiva buna
  - Antibiotic cu biodisponibilitate inalta (ex metronidazole)
  - Alternative po (amoxi/ac clav, ampi/sulbactam, clinda, FQ, CFSP gen 2a, 3a, etc)
  - Switch iv → po cand:
    - Evolutie clinica si biologica buna
    - La 72 h de afebrilitate

## ✓ De ce?

- ✓ Risc mai mic de flebite / CLABSI/ septicemii
- ✓ Risc mai mic pentru personal de a se expune la produse biologice
- ✓ Consumuri materiale mai mici
- ✓ Comfort crescut al pacientului



# Dezescaladare

- Situația clinică
- Disponibilitatea datelor microbiologice
- APP
- Disponibilitatea medicației in spital...
- Evoluția pacientului
- Asumarea medicului....
- Mai ales conștientizarea ca:
  - Dușmanul binelui e prea binele
  - Less is more



# Adaptarea dozei de antibiotic (si nu numai ATB)

- Pacienți cu:
  - Insuficiență renală
  - Insuficiență hepatică
  - Greutate:
    - Cașexie
    - Obezitate
  - Vârstă
  - Gravitatea infecției



# Considerarea interacțiunilor medicamentoase

- Rolul farmacistului de spital
- Integrator al întregii condiții de prescripție a pacientului
- Clinician “neatent ” la acest aspect:
  - Grabă....
  - Prea multe...
  - Mai curând, lipsa reflexului de a integra toate tratamentele
  - Desconsiderare a importanței interacțiunilor medicamentoase
  - Lipsa preocupării în acest sens : pe vremea mea.....
- Din nou, **COLABORAREA MEDIC-FARMACIST**





Drug Interactions Checker > Search

# Drug Interaction Report

2 potential interactions found for the following 3 drugs:

- **fluconazole**
- **metronidazole**
- **Paracetamol (acetaminophen)**

Moderate

**fluconazole** ⇌ **metroNIDAZOLE**

Applies to: fluconazole, metronidazole

Using **fluconazole** together with **metroNIDAZOLE** can increase the risk of an irregular heart rhythm that may be serious and potentially life-threatening, although it is a relatively rare side effect. You may be more susceptible if you have a heart condition called congenital **long QT syndrome**, other cardiac diseases, conduction abnormalities, or electrolyte disturbances (for example, magnesium or potassium loss due to severe or prolonged **diarrhea** or **vomiting**). Talk to your doctor if you have any questions or concerns. Your doctor may be able to prescribe alternatives that do not interact, or you may need a dose adjustment or more frequent monitoring to safely use both medications. You should seek immediate medical attention if you develop sudden **dizziness**, lightheadedness, fainting, shortness of breath, or **heart palpitations** during treatment with these medications, whether together or alone. It is important to tell your doctor about all other medications you use, including **vitamins** and herbs. Do not stop using any medications without first talking to your doctor.



# Drug Interaction Report

1 potential interactions found for the following 2 drugs:

- amikacin
- ibuprofen

## Interactions between your drugs

**Moderate** ibuprofen ⇌ amikacin  
Applies to: ibuprofen, amikacin

[Amikacin](#) can sometimes cause kidney damage, and using it with [ibuprofen](#) may increase that risk, particularly if the latter is used chronically for prolonged periods. Talk to your doctor if you have any questions or concerns. Your doctor may already be aware of the risks, but has determined that this is the best course of treatment for you and has taken appropriate precautions and is monitoring you closely for any potential complications. Signs and symptoms of kidney damage may include [nausea](#), [vomiting](#), loss of appetite, increased or decreased urination, sudden weight gain or [weight loss](#), [fluid retention](#), swelling, shortness of breath, muscle cramps, tiredness, weakness, [dizziness](#), confusion, and irregular heart rhythm. Let your doctor know if you experience some or all of these problems during treatment. It is important to tell your doctor about all other medications you use, including [vitamins](#) and herbs. Do not stop using any medications without first talking to your doctor.

# Drug Interaction Report

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# Drug Interaction Report

2 potential interactions found for the following 2 drugs:

- fluconazole
- tacrolimus

**Major** fluconazole ⇌ tacrolimus  
Applies to: fluconazole, tacrolimus

**Fluconazole** may significantly increase the blood levels of **tacrolimus**. This may increase the risk of serious side effects such as kidney problems, diabetes, nervous system disorders, **hyperkalemia** (high potassium levels in the blood), **high blood pressure**, irregular heart rhythm, **heart failure**, infections, and various types of malignancies including **lymphoma** and **skin cancer**. You may need a dose adjustment if you have been taking tacrolimus and are starting treatment with fluconazole. Talk to your doctor if you have any questions or concerns. Your doctor may already be aware of the interaction, but has determined that this is the best course of treatment for you and has taken appropriate precautions and is monitoring you closely for any potential complications. Contact your doctor if you develop signs and symptoms of **infection** such as **fever**, chills, **diarrhea**, **sore throat**, muscle aches, shortness of breath, blood in phlegm, **weight loss**, red or inflamed skin, body sores, and **pain** or burning during urination. Also seek medical attention if you experience **frequent urination**, increased hunger or thirst, loss of appetite, confusion, tremor, **numbness** or tingling, **seizures**, vision changes, sudden **dizziness**, lightheadedness, fainting, shortness of breath, **heart palpitations**, and chest pain. It is important to tell your doctor about all other medications you use, including **vitamins** and herbs. Do not stop using any medications without first talking to your doctor.

# Situatie reala, pacient real

## Your Drugs

**Tigecycline**

• Tygacil



**Metronidazole**



**Vancomycin**



**Amiodarone**



**Propofol**



**Enoxaparin**



**Pantoprazole**



**Norepinephrine**



**Furosemide**



[Clear All](#)

## **SERIOUS**

Potential for serious interaction; regular monitoring by your doctor required or alternate medication may be needed.

### **Propofol + Norepinephrine**

Propofol increases levels of Norepinephrine by slowing drug metabolism.



## **MONITOR CLOSELY**

Significant interaction possible (monitoring by your doctor required).

### **Metronidazole + Amiodarone**

Metronidazole will increase the level or effect of Amiodarone by altering drug metabolism.

### **Norepinephrine + Furosemide**

Norepinephrine and Furosemide both decrease potassium levels in the blood.

## **MINOR**

Interaction is unlikely, minor, or nonsignificant.

### **Norepinephrine + Furosemide**

Norepinephrine , Furosemide Mechanism: additive drug effects.

Additional Information: Low potassium (hypokalemia).

Last but not least:  
The Microbiology lab  
(&team)



# Reflex

- De a solicita **examen bacteriologic**
  - !!! Proceduri de recoltare, care să fie aplicate prompt (și iarăși revenim la reflex)
- De a-l urmări, ca rezultat
- De a ține cont de rezultat
- De a aplica
- De a adapta



# Medic – erori / push de prescriere

- deficit de cunoștințe ale clinicianului;
- acces limitat la teste clinice sau microbiologice;
- acces limitat la antimicrobiene;
- teamă pentru prescrierea unor antibiotice cu spectru tintit
- teama de responsabilitate medico - legala
- comunicare limitată / absenta între medici;

# Cauze ale abuzului de antibiotic (2)

- infrastructură și/sau suport administrativ limitate pentru aplicarea politicii de ATBterapie
- acces limitat la date / informatii/ ghiduri despre prescrierea ATB & lipsa informatiilor despre rezistenta in comunitate;
- lipsa de informare?
- acceptarea limitată de către public/pacient sau, din contra, CEREREA DE PRESCRIERE a ATB
- accesul public la antimicrobiene fără prescripție medicală în comunitate
- !!!!!!!!!!! SI ANTIFUNGICELE – **FLUCONAZOLUL**- SUNT IN ACEEASI CATEGORIE



# Take home messages (spuse popular, dar franc si din suflet)

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- Nu avem multe antibiotice disponibile
- Microbii sunt mai inteligenti decat credeam (uneori, mai inteligenti si mai rapizi decat noi – si sigur mai intelepti)
- Depinde doar de noi toti ce lasam stramosilor nostri
- Dezinteresul ne va afecta pe noi toti, incepand cu “EU”
- Antibiotic stewardship: vital, dar valabil pt toti
- Baza unui tratament antibiotic corect o reprezinta documentarea bacteriologica
- Conducerea unui tratament antibiotic este similara cu cea a unei masini: necesita atentie permanenta si adaptare din mers
- Antibioticele de rezerva trebuie sa ramana DE REZERVA
- Pacientii trebuie si ei informati si invatati ce au de facut; lautarescul nu ajuta, iar antibioticele nu sunt anxiolitice
- E o munca de echipa, in care rolul fiecaruia dintre noi (medici, producatori, farmacisti, consumatori) este de egala importanta



**Fiti proactivi, nu va multumiti sa va faceti  
strict treaba pt care veniti la munca.**

**Implicati-va, fiecare dintre voi!!!**


**Beneficiul e al tuturor!**



- Şi eliberaţi
- Şi folosiţi



**KEEP  
CALM  
AND  
PRESCRIBE  
ANTIBIOTICS  
APPROPRIATELY**

- 
- Mulțumesc pentru atenție!
  - Voi fi onorată sa îmi puneți întrebări

