# Călătoriile germenilor multirezistenți

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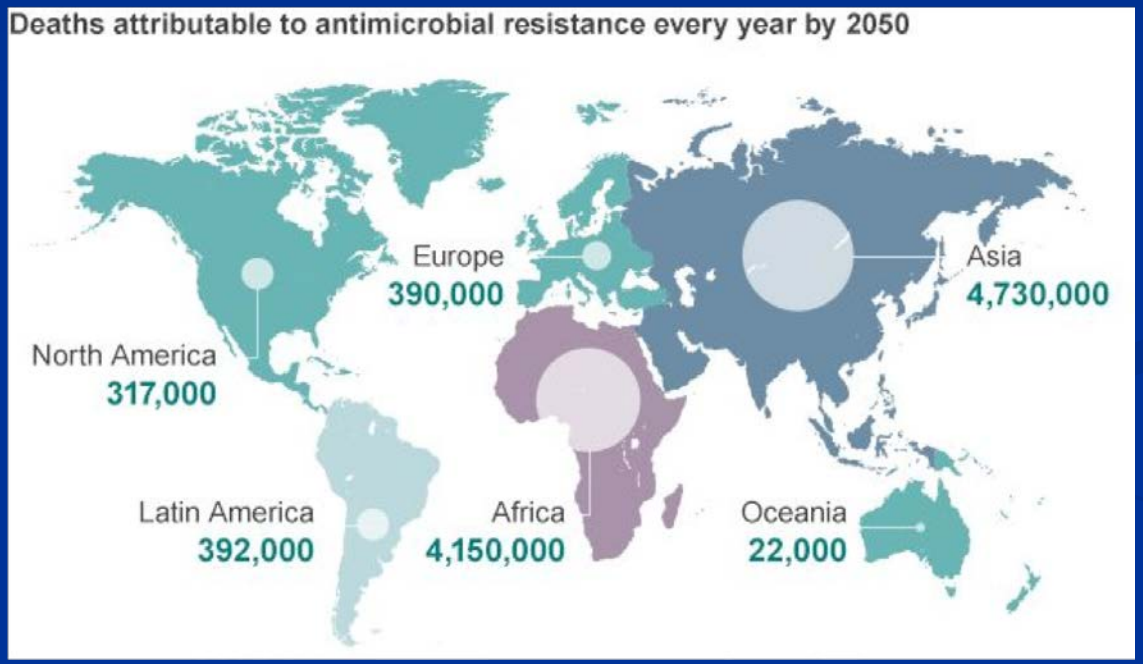
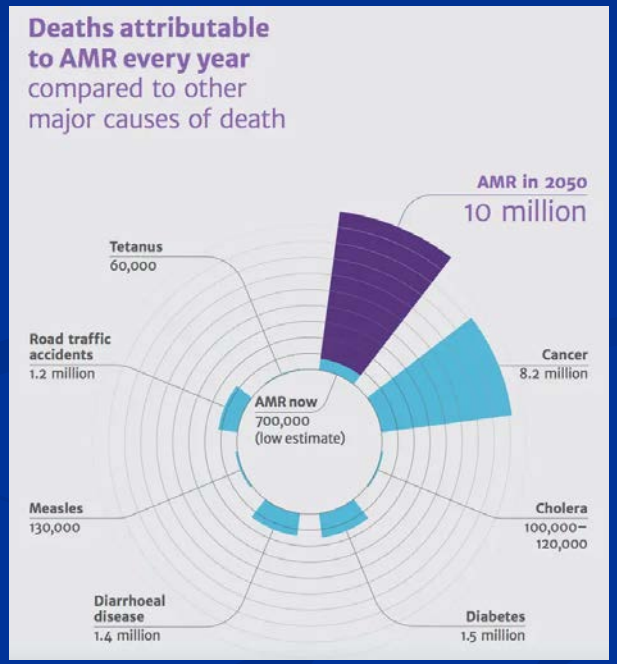
# "Pandemia silențioasă" de rezistență la antibiotice

- 2019 - 1.27 mil. DECESE cauzate de bacterii REZISTENTE la antimicrobiene;[1]

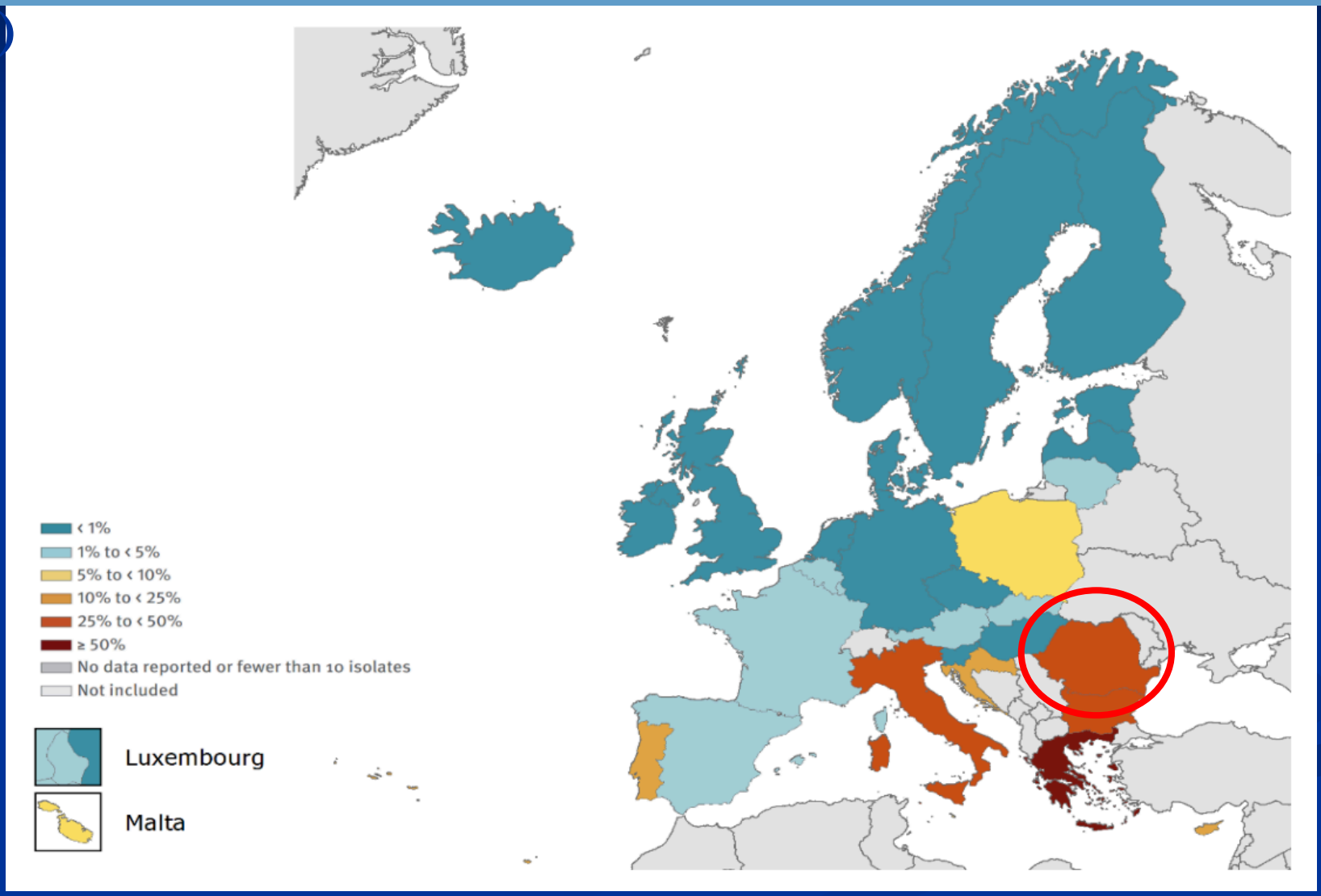


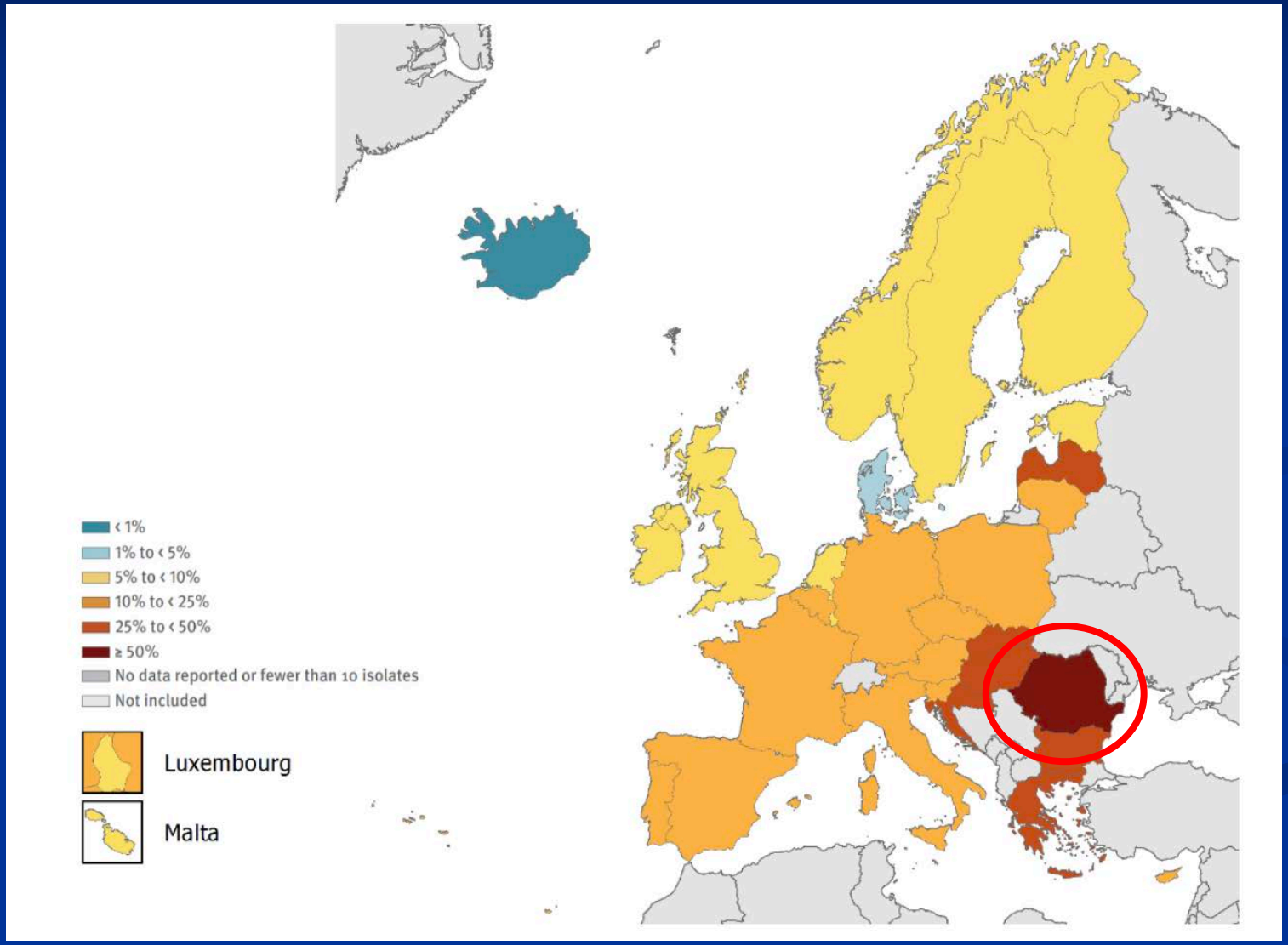

- comparativ, pandemia Covid-19 (mai 2022) - aprox. 527 mil. cazuri - 6.28 mil. DECESE;

[1]Murray, C. L. J. *et al. Lancet* 2022;

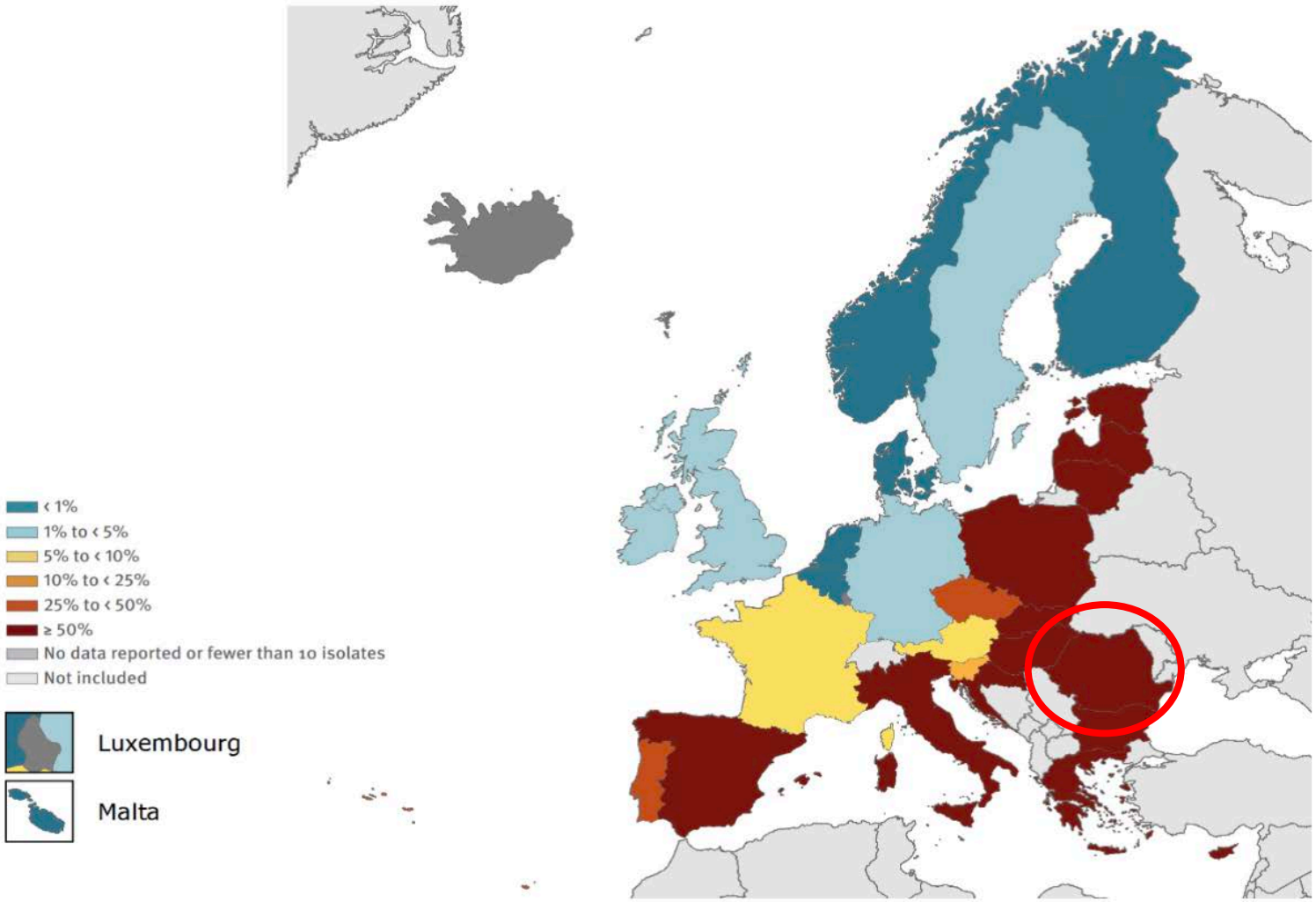
# Rezistența *Klebsiella pneumoniae* la carbapeneme (EARS Net, 2019)



# Rezistența *Pseudomonas aeruginosa* la carbapeneme (EARS Net, 2019)



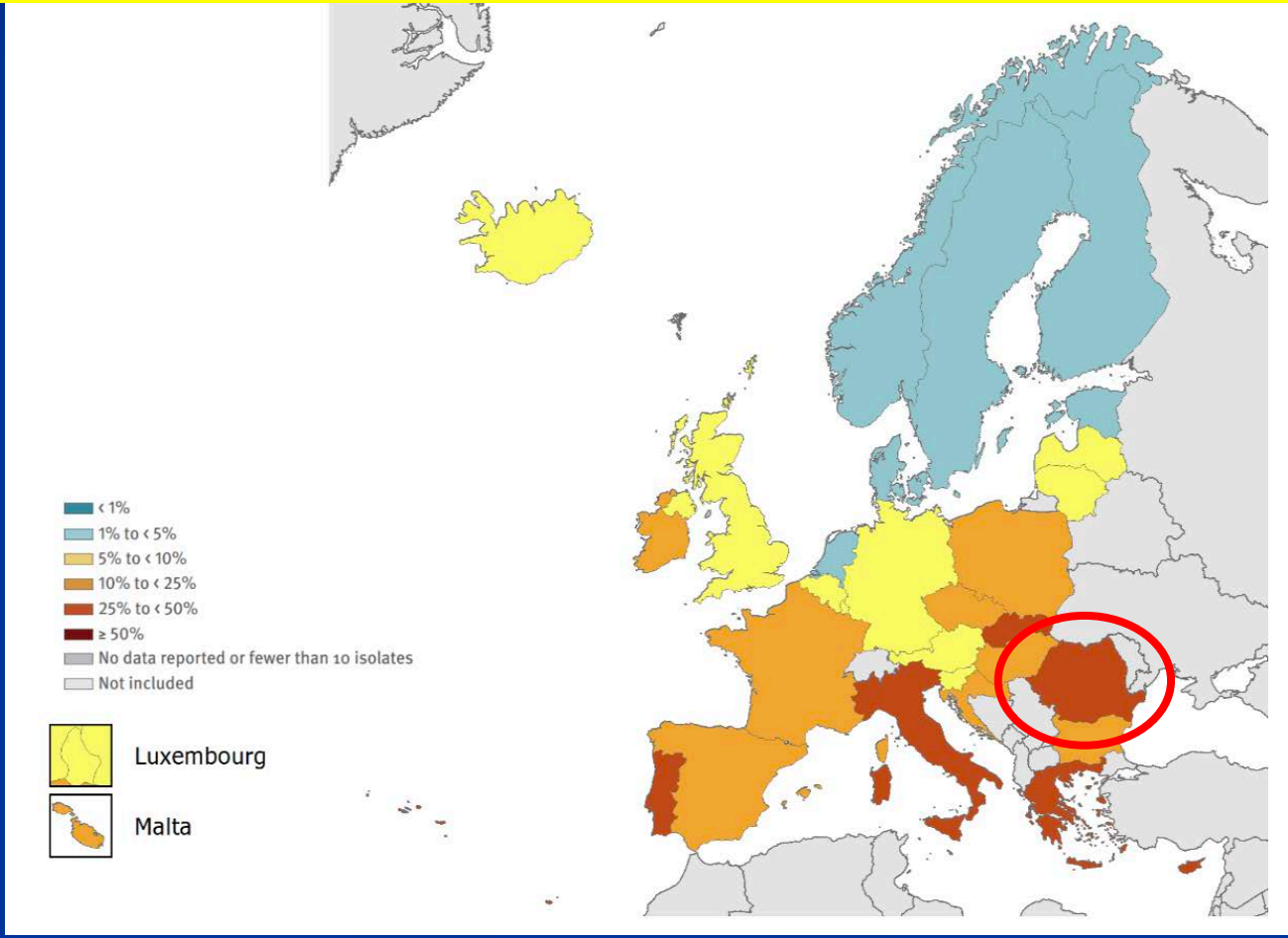
# Rezistența *Acinetobacter* la carbapeneme (EARS Net, 2019)



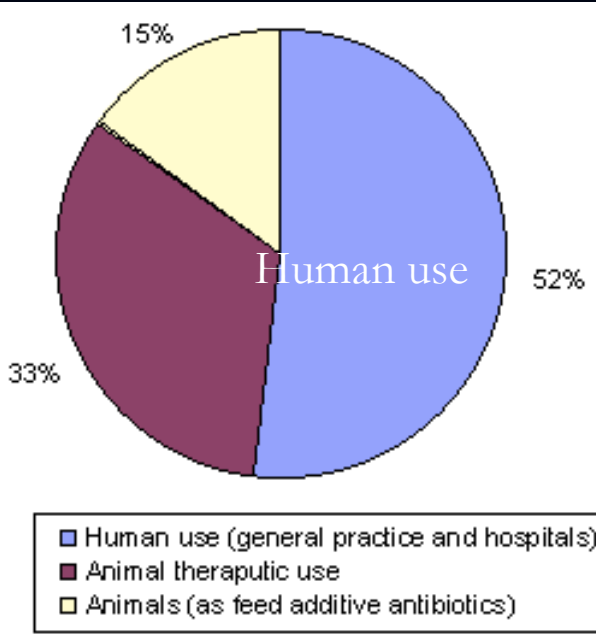
SPREAD AWARENESS
STOP RESISTANCE

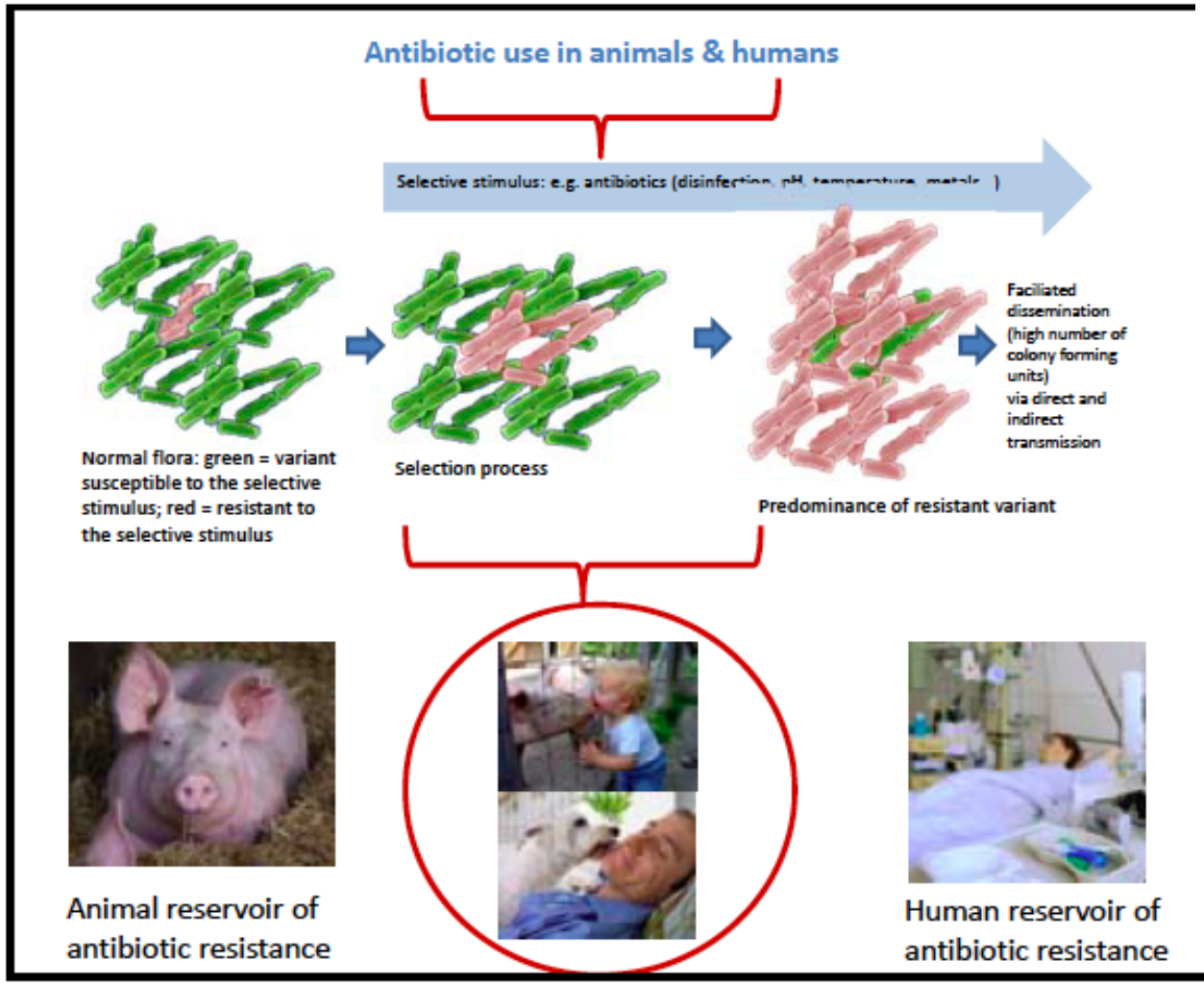
HANDLE ANTIMICROBIALS WITH CARE

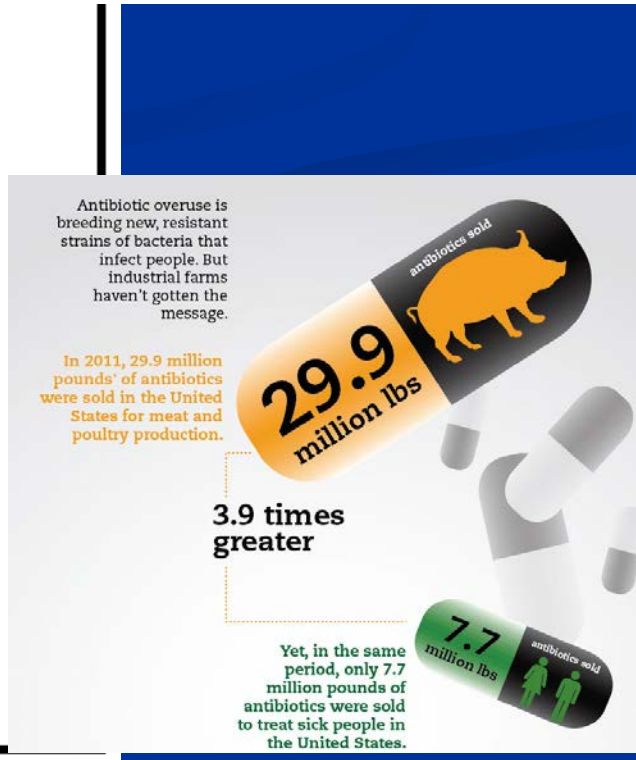
# MRSA în statele membre ale UE/EEA (EARS-Net 2019)

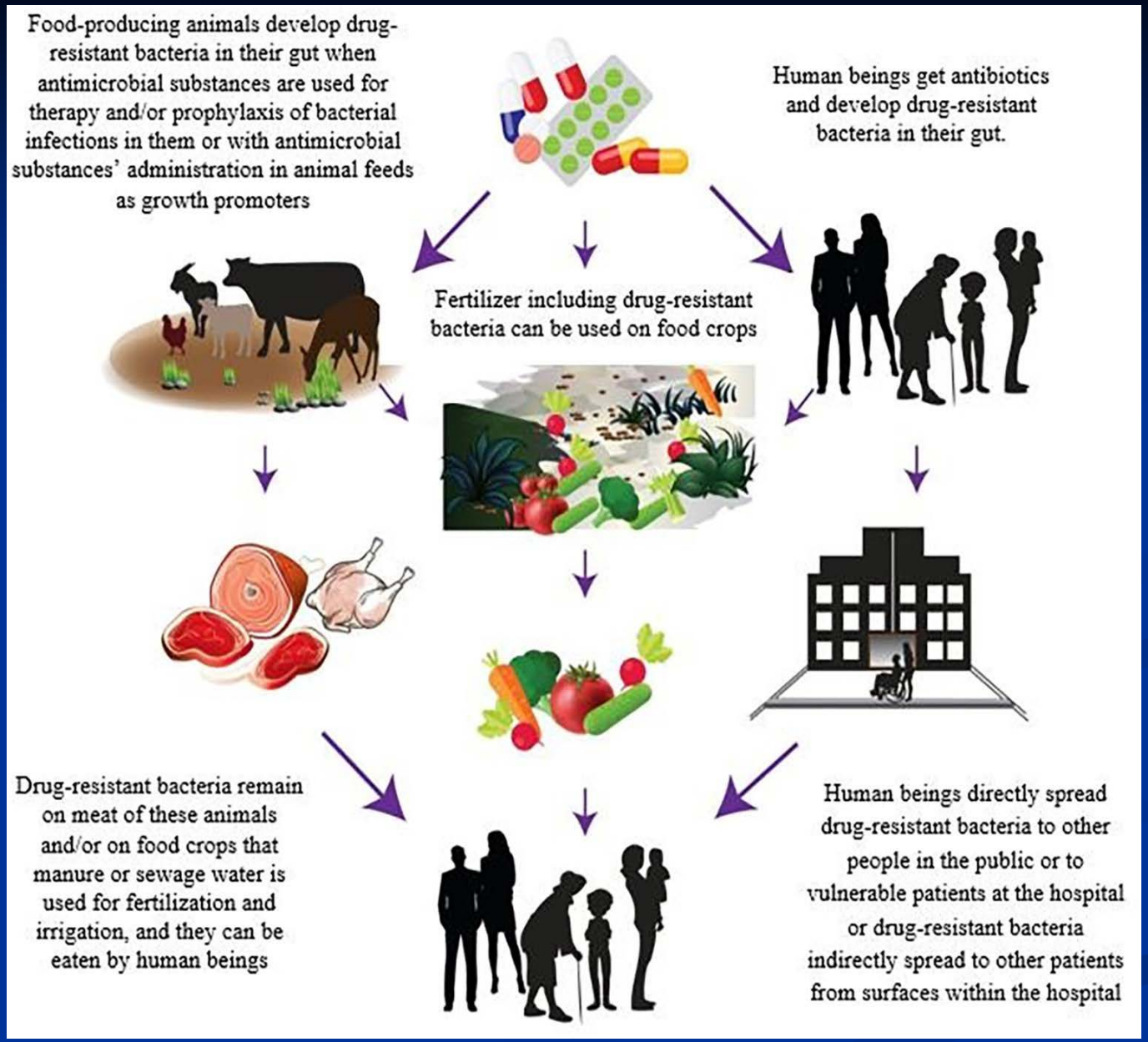


# Utilizarea de antibiotice animale/oameni



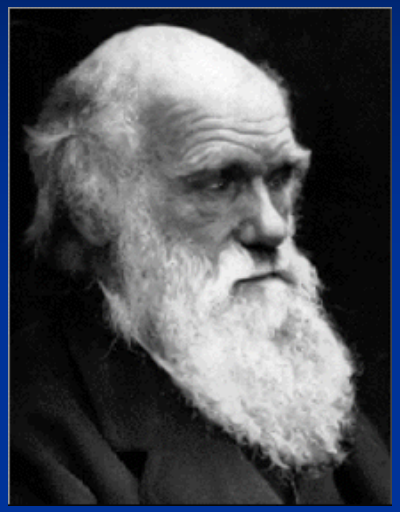





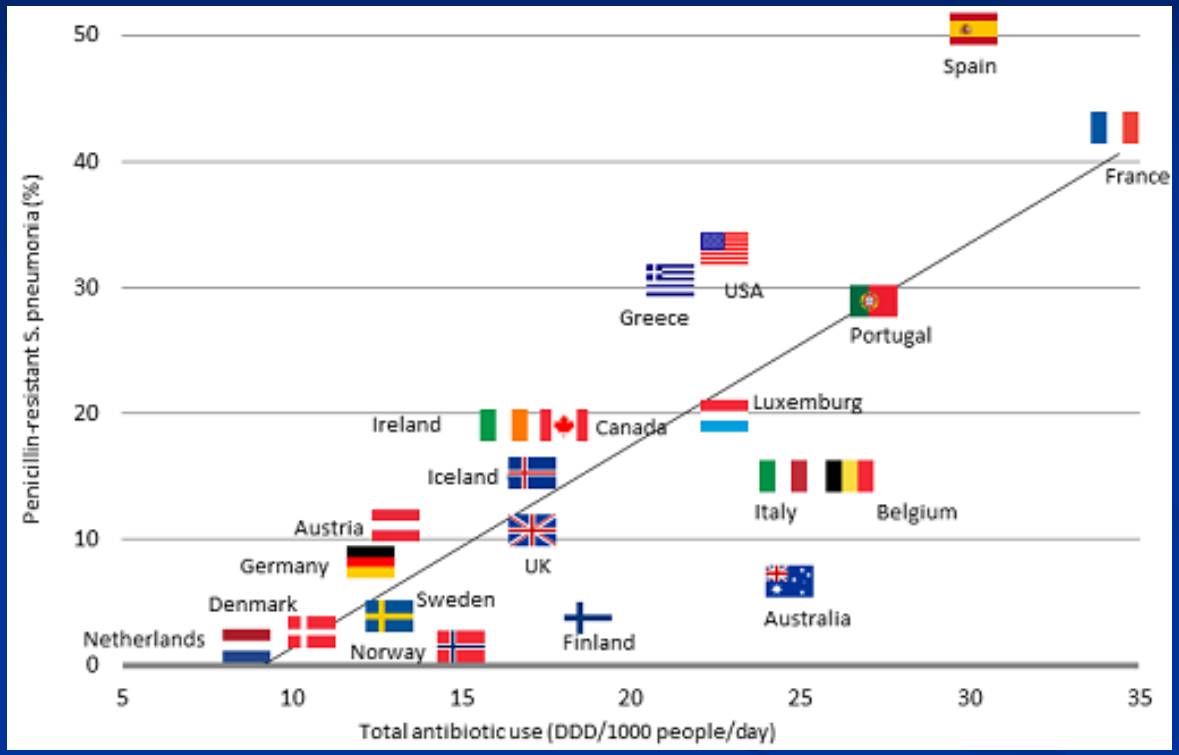

Perez-Rodriguez F, Mercanoglu Taban B Front. Microbiol. 2019 | https://doi.org/10.3389/fmicb.2019.02091

# Antimicrobials use and resistance



Resistant bacteria survive, those susceptible most likely die.

*"Natural Selection"*




Antimicrobial Resistance in G7 Countries and Beyond; Albrich et al 2004

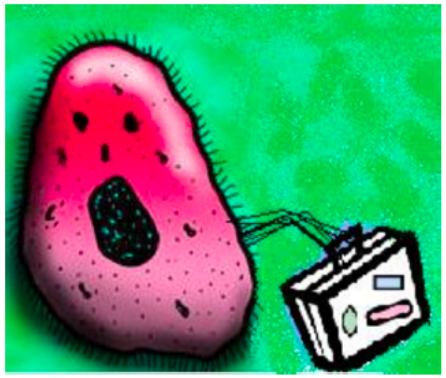

Failure of MDRO prevention and control
lack of compliance with hand hygiene
lack of education
non-prudent use of antibiotics
too low healthcare staffing levels
lack of financial ressources
lack of diagnostics, typing & screening
lack of isolation capacity
wrong or incompletely implemented MDRO prevention bundles
delayed begin of bundle implementation
lack of outbreak control
transfer of patients between healthcare institutions
density of healthcare-usage & healthcare facilities
sources for MDRO outside healthcare facilities

# Tourists on holiday "pick up" antibiotic resistant genes

Related Stories

**Back from vacation? Your gut bacteria picked up souvenirs, too**

Meredith Knight | July 31, 2016 | Genetic Literacy Project



The dreaded traveler's diarrhea is the most common illness associated with vacationing or working abroad.

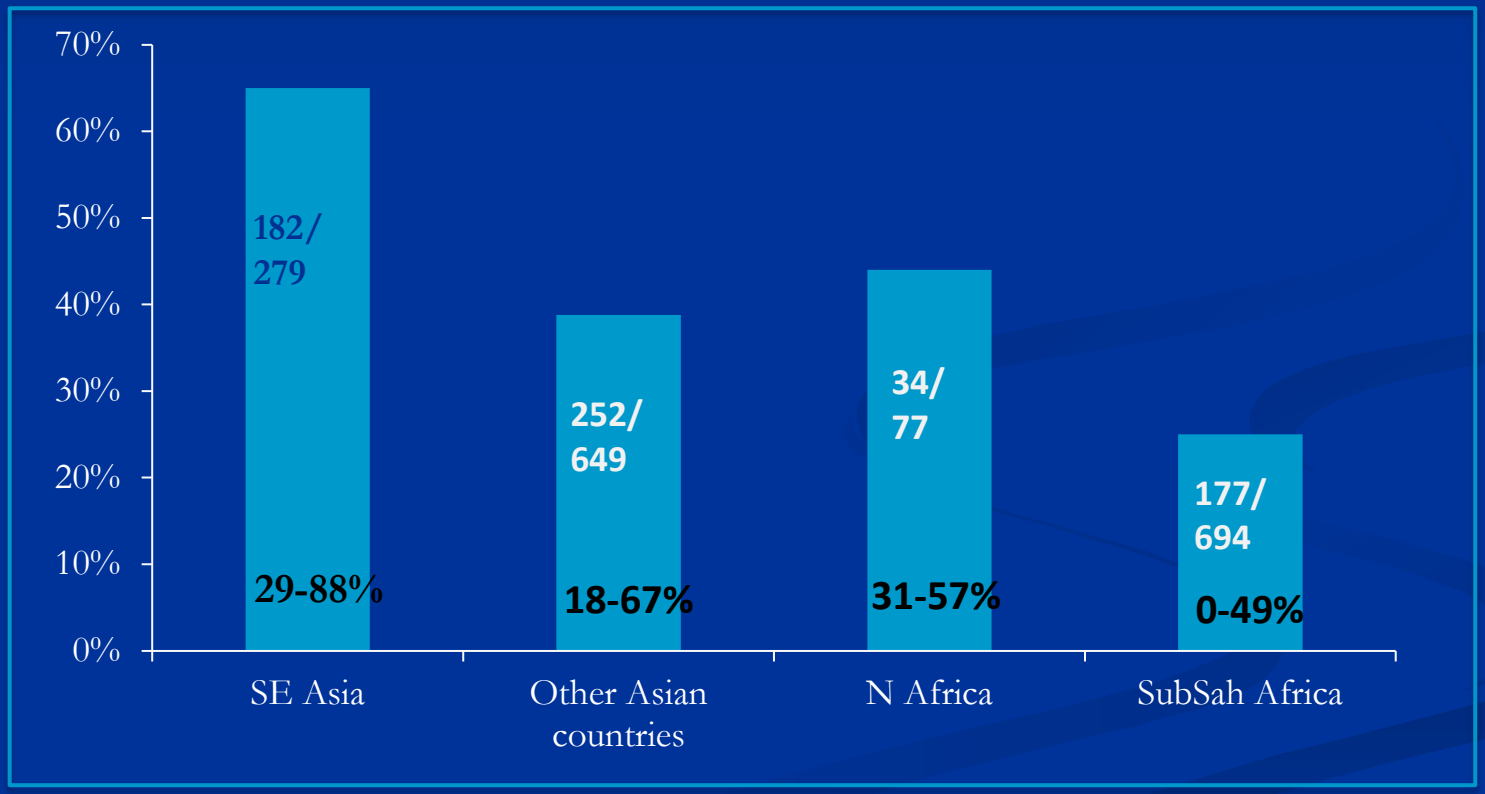
It's so common the CDC estimates 30 to 70 percent of travelers are affected, depending on where they go. Most cases are caused from food or water contaminated with locale-specific bacteria. Those bacteria cause the adverse reaction in our guts. They can also carry antibiotic resistance genes. And it turns out we can pick up those bugs very quickly—just 48 hours according to new research presented at the American Society for Microbiology meeting.

**Back from vacation?**
**Your gut bacteria picked up souvenirs, too**


**CDC: 30 to 70 percent of travelers are affected, depending on where they go.**

# Genes picked up by the bacteria in the traveler's guts depended on where they went on vacation

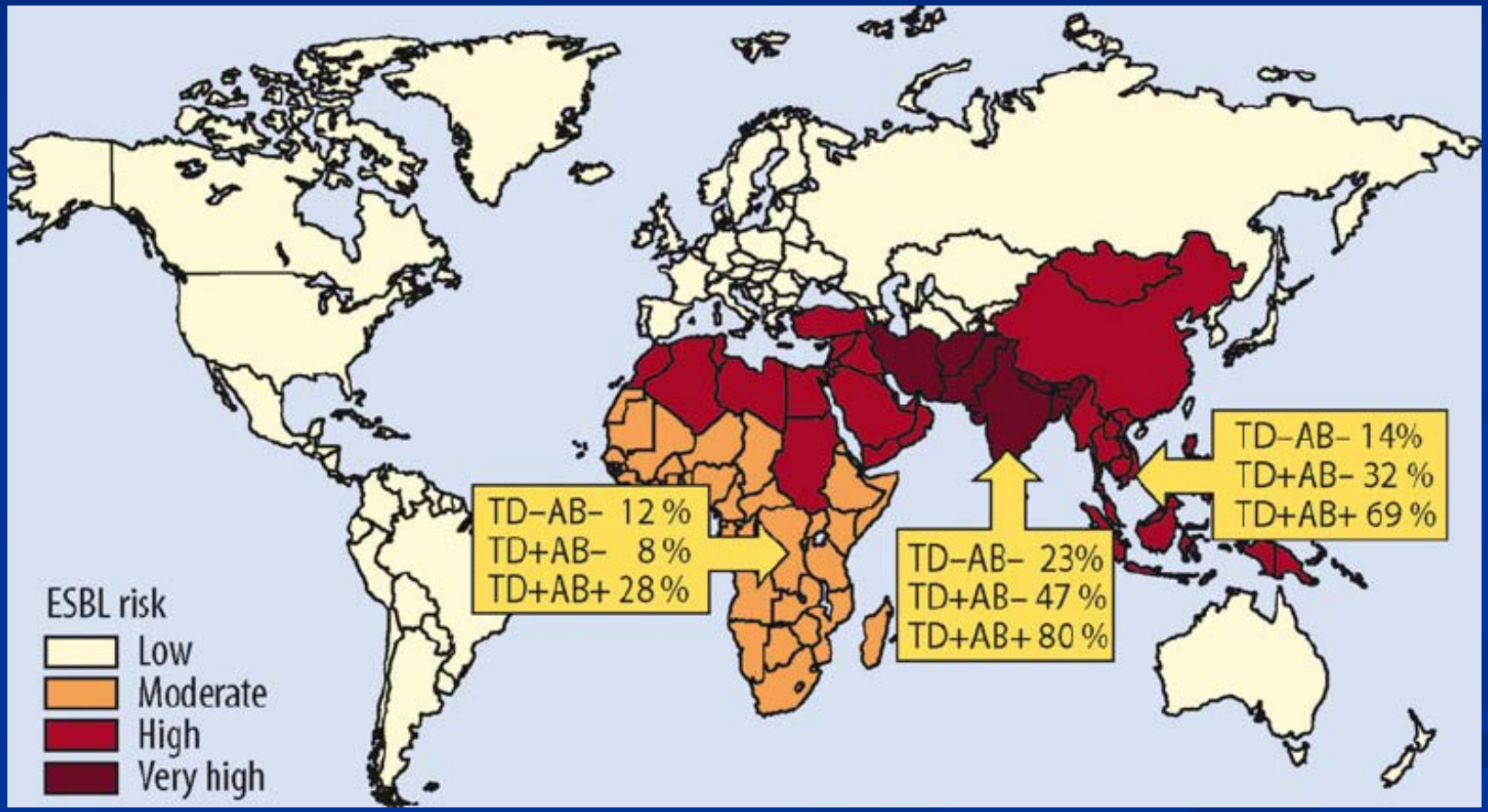
**Proportion of travelers who acquired MDR Enterobacteria by travel destination**




South and Central America (0–33%)
North America, Europe and Oceania was rare.

Hassing et al Eurosurveillance 2015

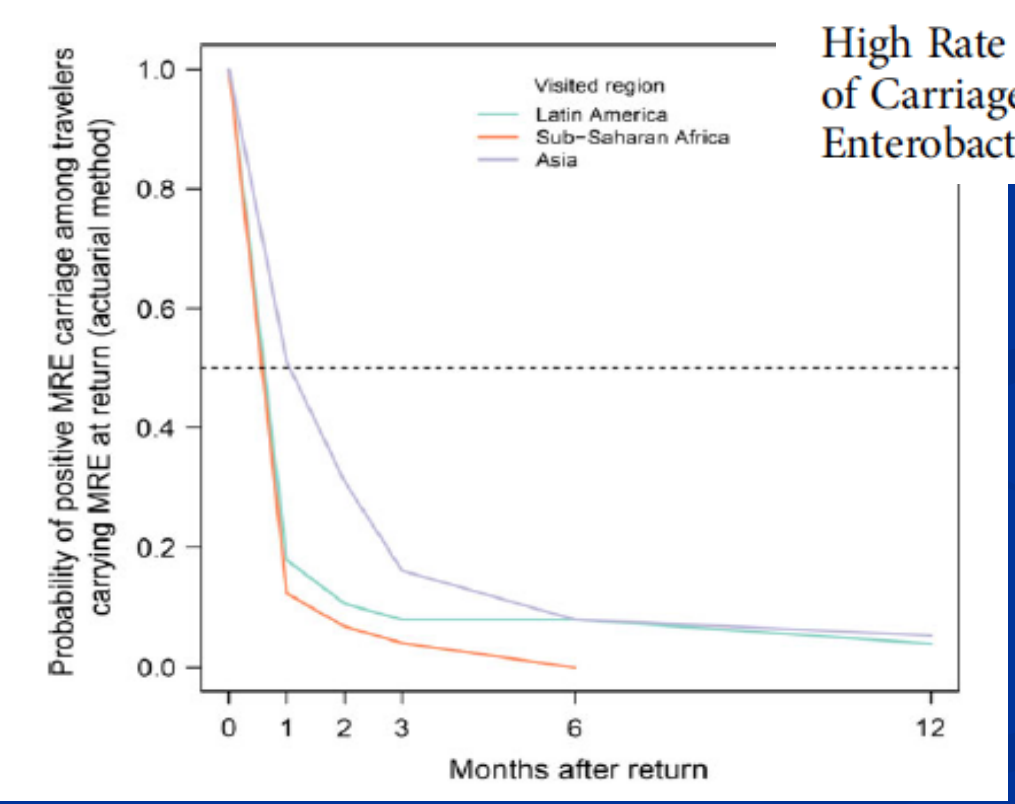
# World map indicating the risk levels of contracting extended-spectrum beta-lactamase–producing Enterobacteriaceae




Kantele Clin Infect Dis 2015

# How long does the carriage last?

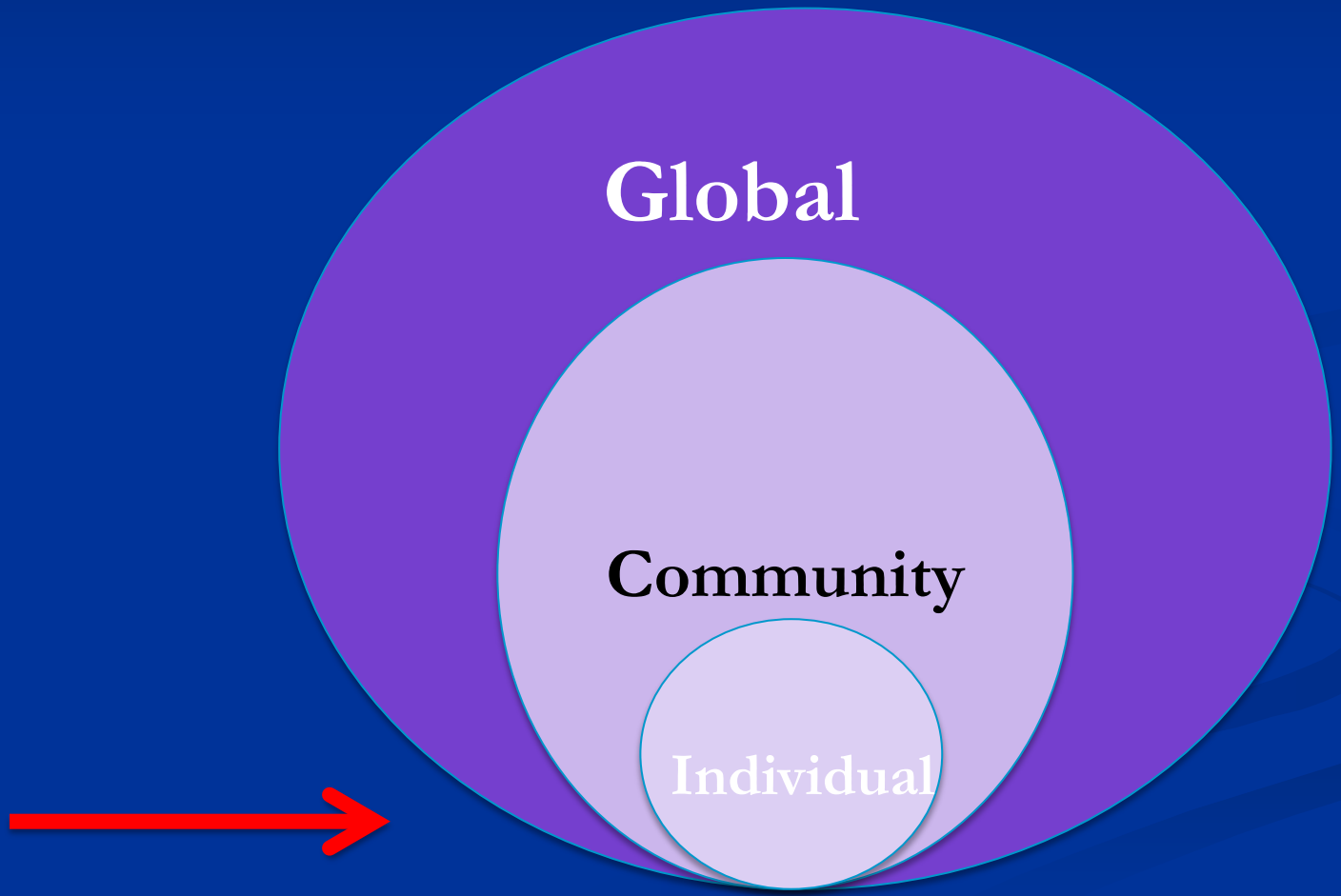
Survival curve representing multidrug-resistant *Enterobacteriaceae* (MRE) carriage rates among travelers during follow-up, according to the travel destination




High Rate of Acquisition but Short Duration of Carriage of Multidrug-Resistant Enterobacteriaceae After Travel to the Tropics

Ruppe E et al Clin Infect Dis 2015

# MDR/ESBL colonization: three levels of significance

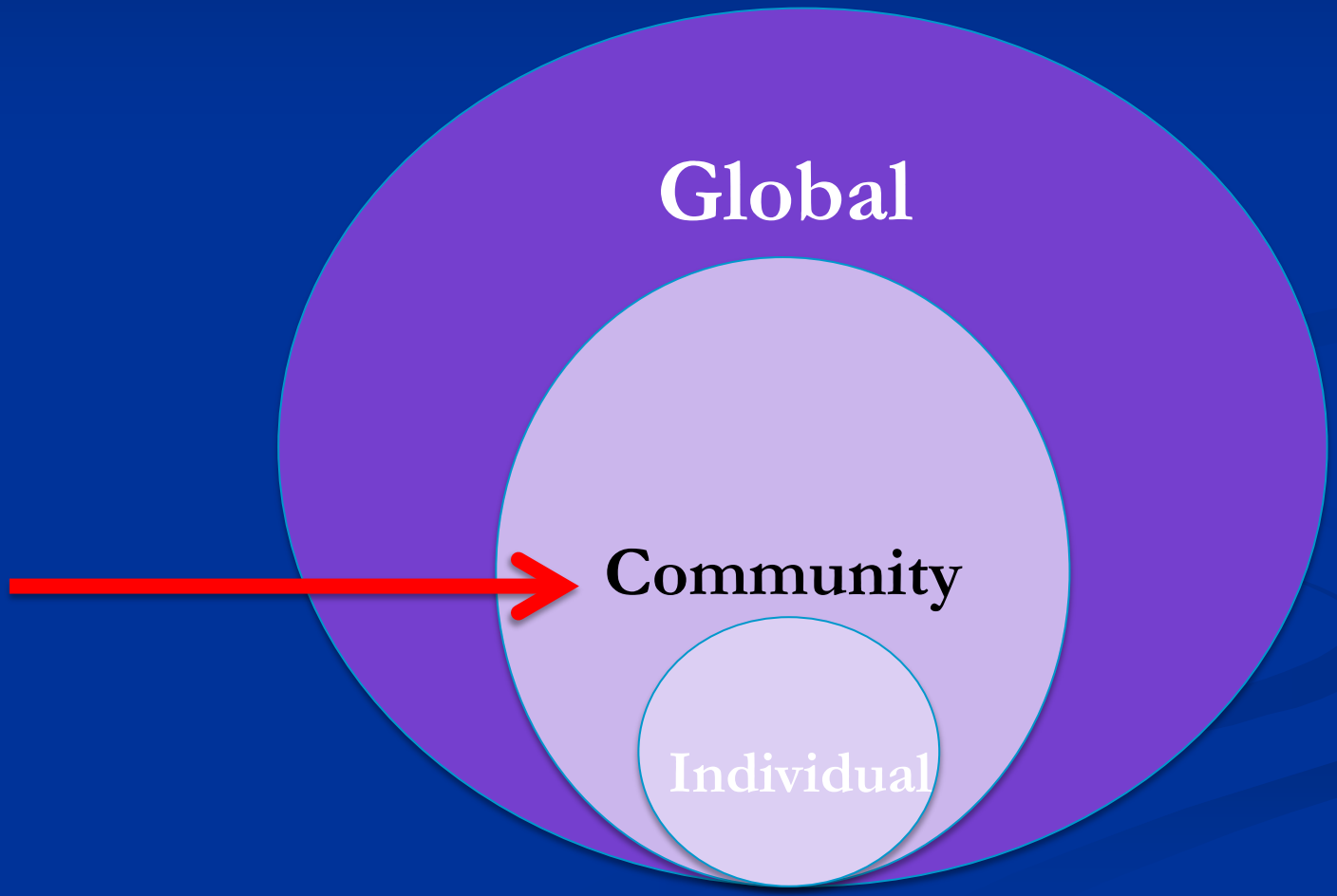


# MDR/ESBL colonization: Individual level

- Usually asymptomatic
- Risk of infection:
  - generally low (1%?)
  - higher (10%?)
    - the longer the colonization lasts
    - for severely ill
    - for hospitalized patients, particularly if antibiotics/intensive care
- Infections:
  - urinary tract infections → life threatening septicemia
  - more difficult to treat
  - increased mortality

*Schechner 2013*

# MDR/ESBL colonization: three levels of significance



# The globalisation of AMR

- Infected by a resistant pathogen
  - may make treatment more difficult (if warranted)
- Colonised by a resistant pathogen
  - may cause infection at future date
  - may pass its genes to susceptible flora
- Transient passage of a resistant pathogen
  - may pass its genes to susceptible flora

# Who are the enemies?

**Running out of artillery:**
**the fight against CREs and other resistant Gram-negative bacteria**

| Pathogen | Established problems | Emerging threats |
|---|---|---|
| *E. faecium* | VRE, HLGR, Amp-R | Lin-R, Dap-R, Tig-R |
| *S. aureus* | MRSA (ha/ca) | Van-R, Lin-R, Dap-R |
| ***Klebsiella*** | **ESBLs** | **Carbapenemases, Col-R** |
| ***Acinetobacter*** | **MDR, Carbapenemases** | **Tig-R, Col-R** |
| ***Pseudomonas*** | **MDR, except Col** | **Carbapenemases, Col-R** |
| ***Enterobacter*** | **AmpC, ESBLs** | **Carba-R, Carbapenemases** |
| ***E. coli*** | **Cip-R, ESBLs** | **Carbapenemases** |

## Antibiograma - Metoda difuzimetrica

| | |
|---|---|
| Denumire organism | **Klebsiella pneumoniae** |
| Betalactamaza | |
| ESBL | |
| Carbapenemaza | |
| MBL | |
| Rezistenta inductibila Clindamicina | |

| Antibiotic | Valoare | UM | Caracteristica |
|---|---|---|---|
| Cefiderocol | 6 | mm | R |

## Antibiograma - Metoda CMI

| | |
|---|---|
| Denumire organism | **Klebsiella pneumoniae** |
| Betalactamaza | |
| ESBL | **Pozitiv** |
| Carbapenemaza | |
| MBL | **Pozitiv** |
| Rezistenta inductibila Clindamicina | |

| Antibiotic | Valoare | UM | Caracteristica |
|---|---|---|---|
| Amikacin | >16 | µg/ml | R |
| Ampicillin/Sulbactam | >8/4 | µg/ml | R |
| Ceftazidime/Avibactam | >8/4 | µg/ml | R |
| Ceftazidim | >32 | µg/ml | R |
| Ciprofloxacin | >1 | µg/ml | R |
| Colistin | >4 | µg/ml | R |
| Cefoxitin | >8 | µg/ml | R |
| Ceftriaxon | >2 | µg/ml | R |
| Ceftolozane/Tazobactam | >4/4 | µg/ml | R |
| Ertapenem | >0.5 | µg/ml | R |
| Gentamicin | >4 | µg/ml | R |
| Imipenem | >4 | µg/ml | R |
| Levofloxacin | >4 | µg/ml | R |
| Meropenem | >32 | µg/ml | R |
| Piperacillin/Tazobactam | >16/4 | µg/ml | R |
| Trimethoprim/Sulfamethoxazol | >4/76 | µg/ml | R |
| Tigecicline | =1 | µg/ml | |
| Aztreonam | >16 | µg/ml | R |
| Fosfomycin | >32 | µg/ml | R |

# Greșeli frecvente de prescriere a antibioticelor

1. LIPSA DIAGNOSTICULUI CLINIC
2. LIPSA DIAGNOSTICULUI BACTERIOLOGIC
3. INDICAȚII NEJUSTIFICATE
4. ALEGEREA GREȘITĂ A ANTIBIOTICELOR
5. GREȘELI ÎN SCHEMA TERAPEUTICĂ
6. ABUZ IN PROFILAXIA CU ANTIBIOTICE
7. PRESCRIEREA "DEFENSIVĂ" DE ANTIBIOTICE

Ghidul Angelescu de Terapie Antimicrobiană, 2018

# COLONIZARE sau INFECȚIE?

## COLONIZARE

- **Toleranța** organismului față de prezența bacteriilor;
- **Pacientul este ASIMPTOMATIC**;
- De regulă, **tratamentul antibiotic NU este necesar**;
- **Colonizarea este NORMALĂ***;
- **Orice corp străin** prezent în organism și care are legătură cu mediul exterior **se poate coloniza (*CVC, sonde urinare, drenaje externe*) sau ulcere, etc.**
- **Germeni SENSIBILI sau multi-REZISTENȚI;**

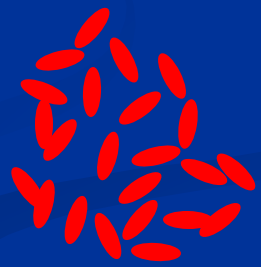
## INFECȚIE

- **Absența toleranței** organismului față de prezența bacteriilor (conflict imun);
- **Pacientul este SIMPTOMATIC**;
- De regulă, **este necesar un tratament antibiotic**;
- **Germeni SENSIBILI sau multi-REZISTENȚI;**

# The Power of Bacteria

## Age:

| | |
|---|---|
| Bacteria | 3,500,000,000 years |
| Eukaryotes | 1,800,000,000 years |
| Multicellulars | 580,000,000 years |
| Australopithecus | 4,000,000 years |
| Homo erectus | <2,000,000 years |
| Antibiotic use | 60 years |



## Numbers:

" The number of *E.coli* in the gut of each human being far exceed the number of people that now live or have ever inhabited the earth" !!!

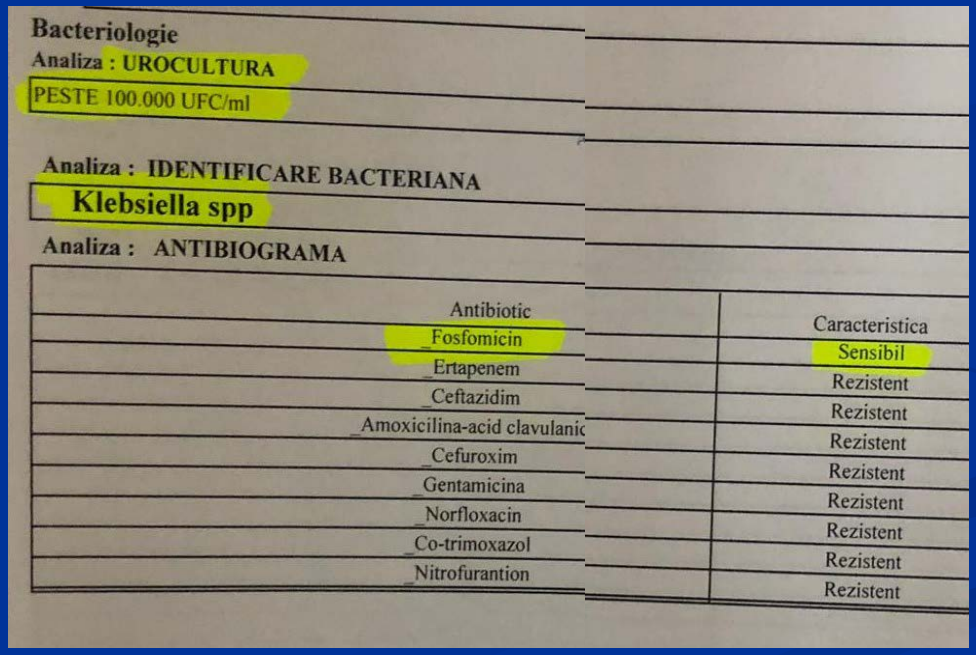
**They are ubiquitous and indestructible**

Gould SJ. Life's Grandeur; Vintage (Pub), 1997

# Colonizare sau infecție?

**Exemplul 2 - La nivelul tractului urinar**

- **pacient asimptomatic, urocultură pozitivă (corect recoltată și prelucrată < 2h** de la recoltare - de verificat întotdeauna!);



**Bacteriologie**

**Analiza : UROCULTURA**

PESTE 100.000 UFC/ml

**Analiza : IDENTIFICARE BACTERIANA**

**Klebsiella spp**

**Analiza : ANTIBIOGRAMA**

| Antibiotic | Caracteristica |
|---|---|
| _Fosfomicin | Sensibil |
| _Ertapenem | Rezistent |
| _Ceftazidim | Rezistent |
| _Amoxicilina-acid clavulanic | Rezistent |
| _Cefuroxim | Rezistent |
| _Gentamicina | Rezistent |
| _Norfloxacin | Rezistent |
| _Co-trimoxazol | Rezistent |
| _Nitrofurantion | Rezistent |

# Colonizare sau infecție?

**Exemplu clinic - La nivelul tractului urinar**

**Colonizare = BACTERIURIE ASIMPTOMATICĂ (BA) - diagnostic**

- **Urocultură semnificativă**

  ♀: **2 uroculturi** (aceeaşi tulpină) cu **≥ $10^5$ UFC/mL**

  ♂: **1 urocultură** (corect recoltată) cu **≥ $10^5$ UFC/mL**

- **FĂRĂ SIMPTOME/SEMNE DE INFECȚIE (! Aspectul și/sau mirosul modificat nu fac parte din tabloul clinic, fără alte simptome asociate)**

# Colonizare sau infecție?

**Exemplu clinic - La nivelul tractului urinar**

**NU** li se vor recolta **UROCULTURI** pacienților **ASIMPTOMATICI***, **chiar dacă**/cu atât mai mult cu cât ȘI **NU SE TRATEAZĂ**:

- **Vârstnici/instituționalizați**;
- **Diabet zaharat**, alte comorbidități;
- Pacienți cu patologie medulară;
- **Pacienți purtători de sondă urinară**;

**Excepții ***:

1. **GRAVIDE** (testare trimestrial);
2. **PROCEDURI UROLOGICE INVAZIVE** (**NU** montare/schimbare **sondă vezicală**!) - mai ales **TURP**, schimbare **sondă ureterală**;

# Colonizare sau infecție?

**Exemplu clinic - La nivelul tractului urinar**

**NU se TRATEAZĂ:**

- **Bacteriuria asimptomatică;**
- **Modificările din sumarul de urină + bacteriuria asimptomatică;**

**Excepții**:

1. **GRAVIDE** - testare trimestrial, **tratament 3-7 zile** (ex: *E.coli* sensibil – **amoxi-clavulanat**), ulterior urocultură lunar, până la naștere;
2. **PROCEDURI UROLOGICE INVAZIVE** (**NU** la înlocuire/montare **sondă vezicală**!) – mai ales **TURP**, schimbare **sondă ureterală**;

# What then ?

These data all give the same impression: R bacteria is like climate change: everyone is aware of the problem, we know that the disaster is possible but as the solutions are not obvious we do nothing, or not so much.

# Vă mulţumesc!