RESISTANCE OF BACTERIA TO ANTIBIOTICS - URGENT PROBLEM OF CURRENT HEALTH CARE

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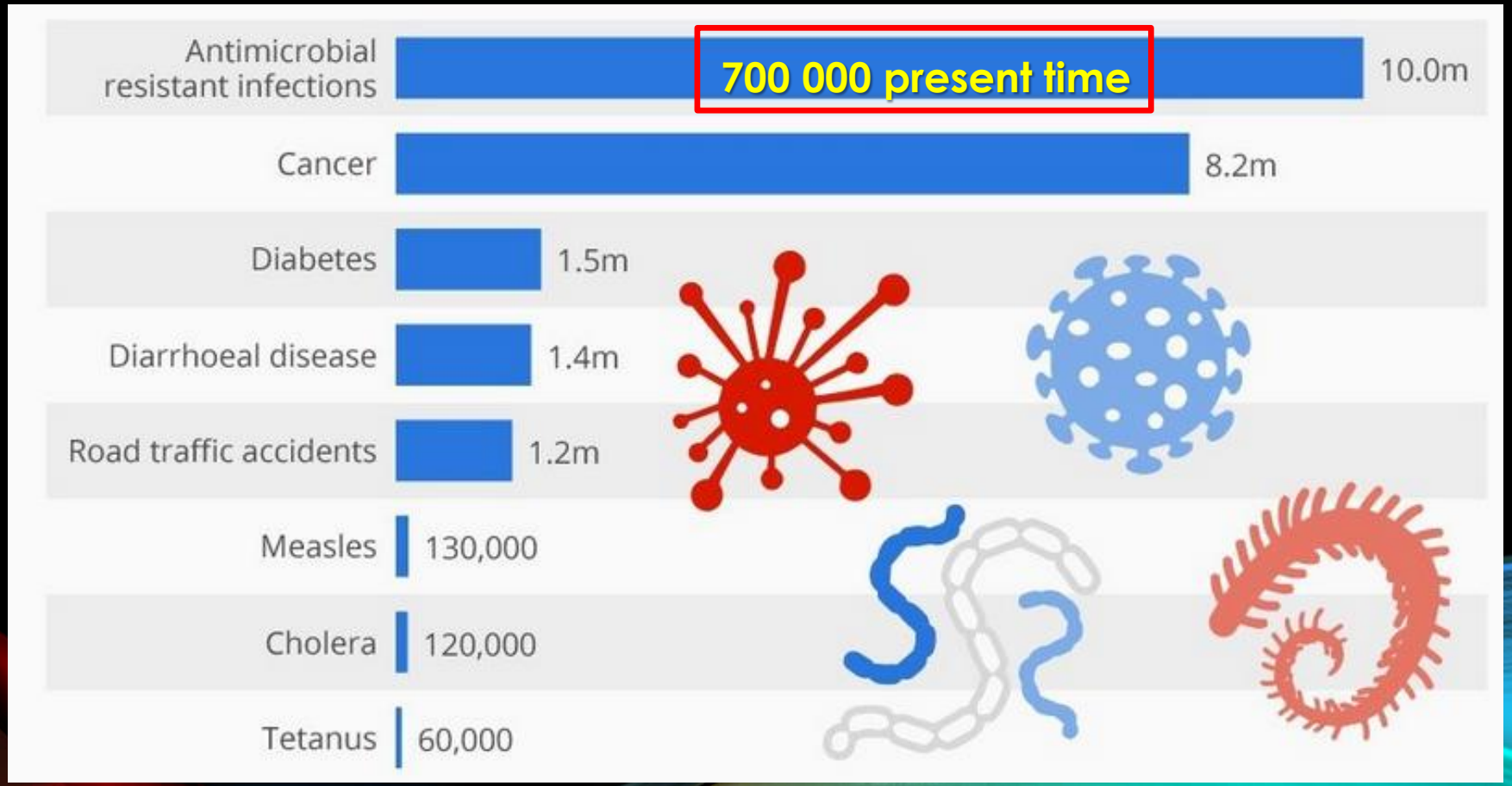
DEVELOPMENT OF ANTIBIOTIC RESISTANCE

1. What are (should be … g resistance of bacteria to antibioti…
2. What is the reason c… biotics ?

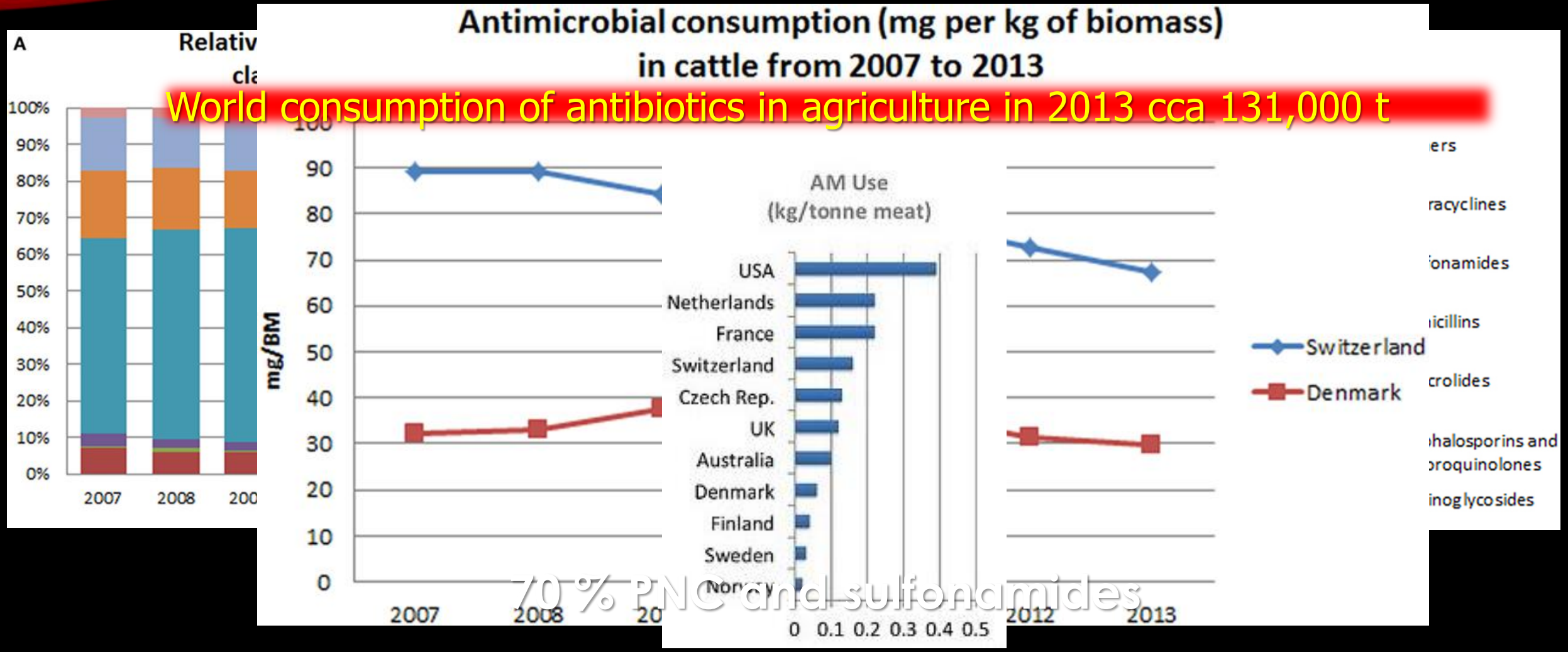
Ventola, 2015

DEATHS FROM DRUG-RESISTANT INFECTIONS TODAY VS 2050



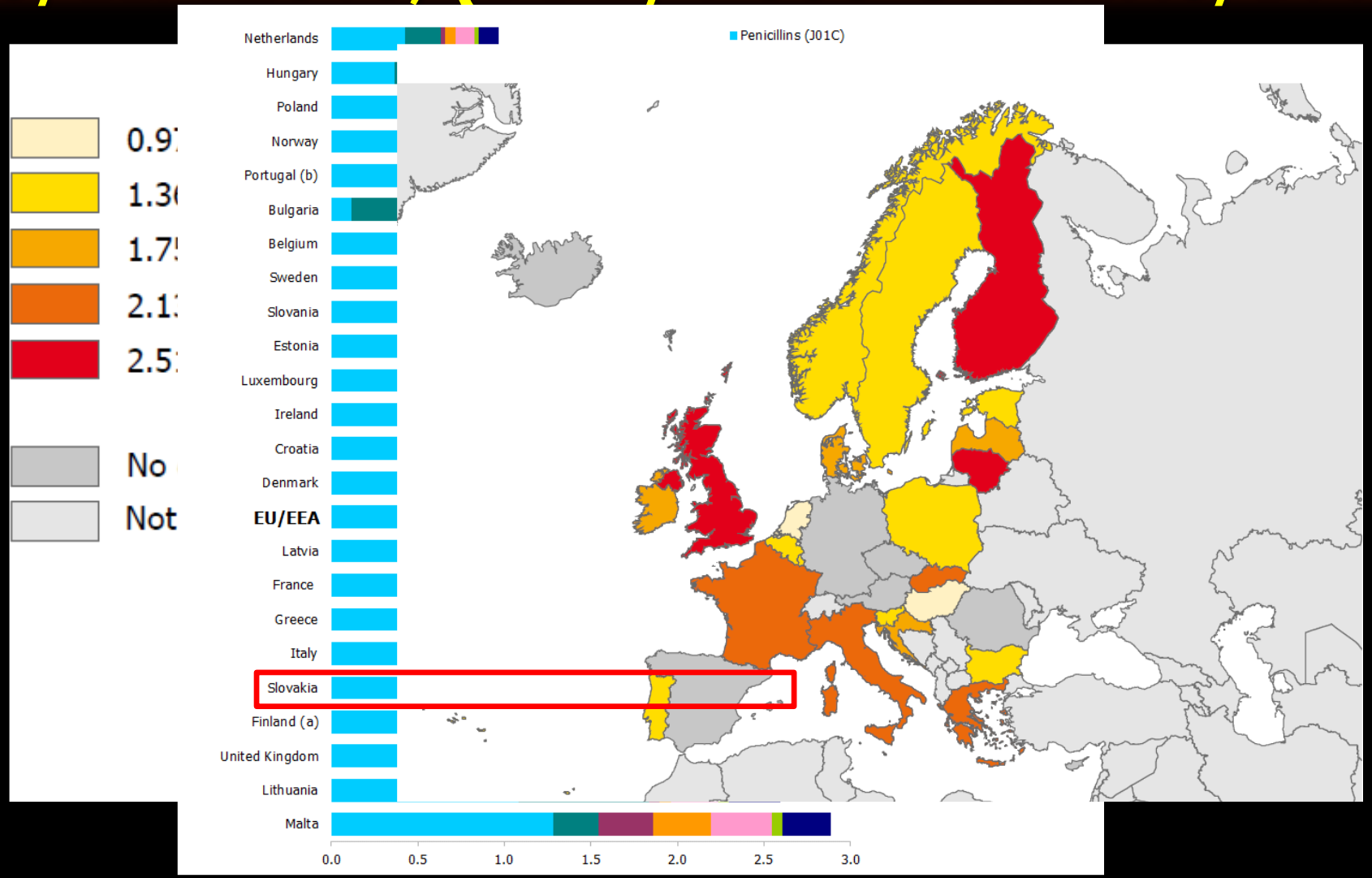
McCarthy, 2015

CONSUMPTION OF ANTIBIOTICS IN SELECTED COUNTRIES OF EUROPE



Carmo et al. 2017

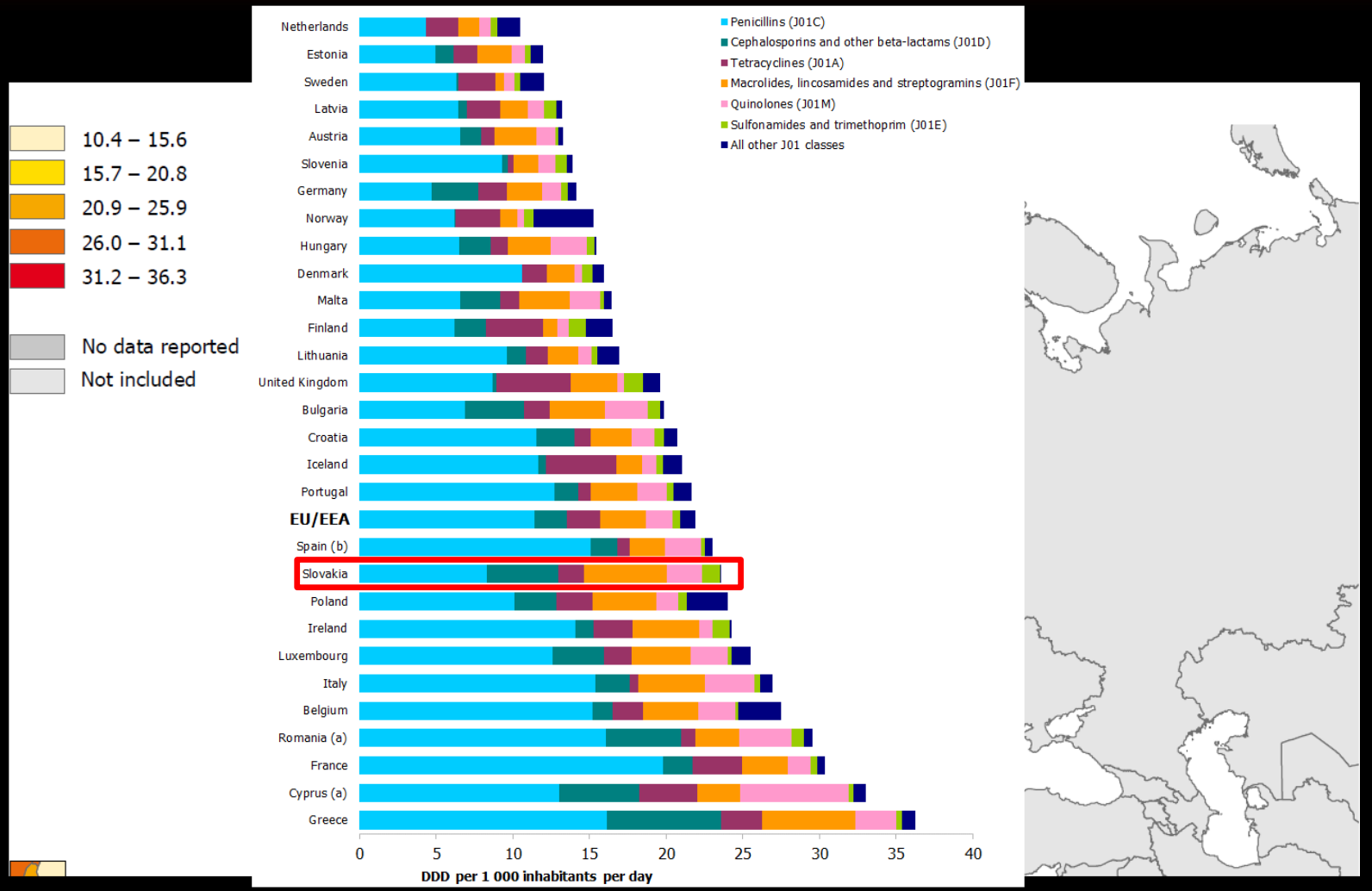
CONSUMPTION OF ANTIBIOTICS (J01) IN HOSPITALS IN EU/EEA 2016, (DDD/1 000 CITIZENS/DAY)



ECDC, 2016

CONSUMPTION OF ANTIBIOTICS (J01) IN COMMUNITY IN EU/EEA 2016, (DDD/1 000 CITIZENS/DAY)

Average: 21.9 DDD/1000
Min: 10.4 Netherlands
Max: 36.3 Greece



ECDC, 2016

EVALUATION OF ANTIBIOTIC RESISTANCE THREAT

URGENT

- *Clostridium difficile*
- Enterobacteria resistant to carbapenems

SERIOUS

- ESBL+ enterobacteria
- VRE (enterococci resist. to vankomycin)
- MRSA (*Staf. aureus* resist. to methicillin)
- Multiresistant *Acinetobacter spp.*
- *Campylobacter*

CONCERNING

- VRSA (*Staf. aureus* resist. to van)
- Strept. pyogenes resist. to ery
- *Neisseria gonorrhoeae*

CDC, 2015

MECHANISMS OF ANTIBIOTIC RESISTANCE

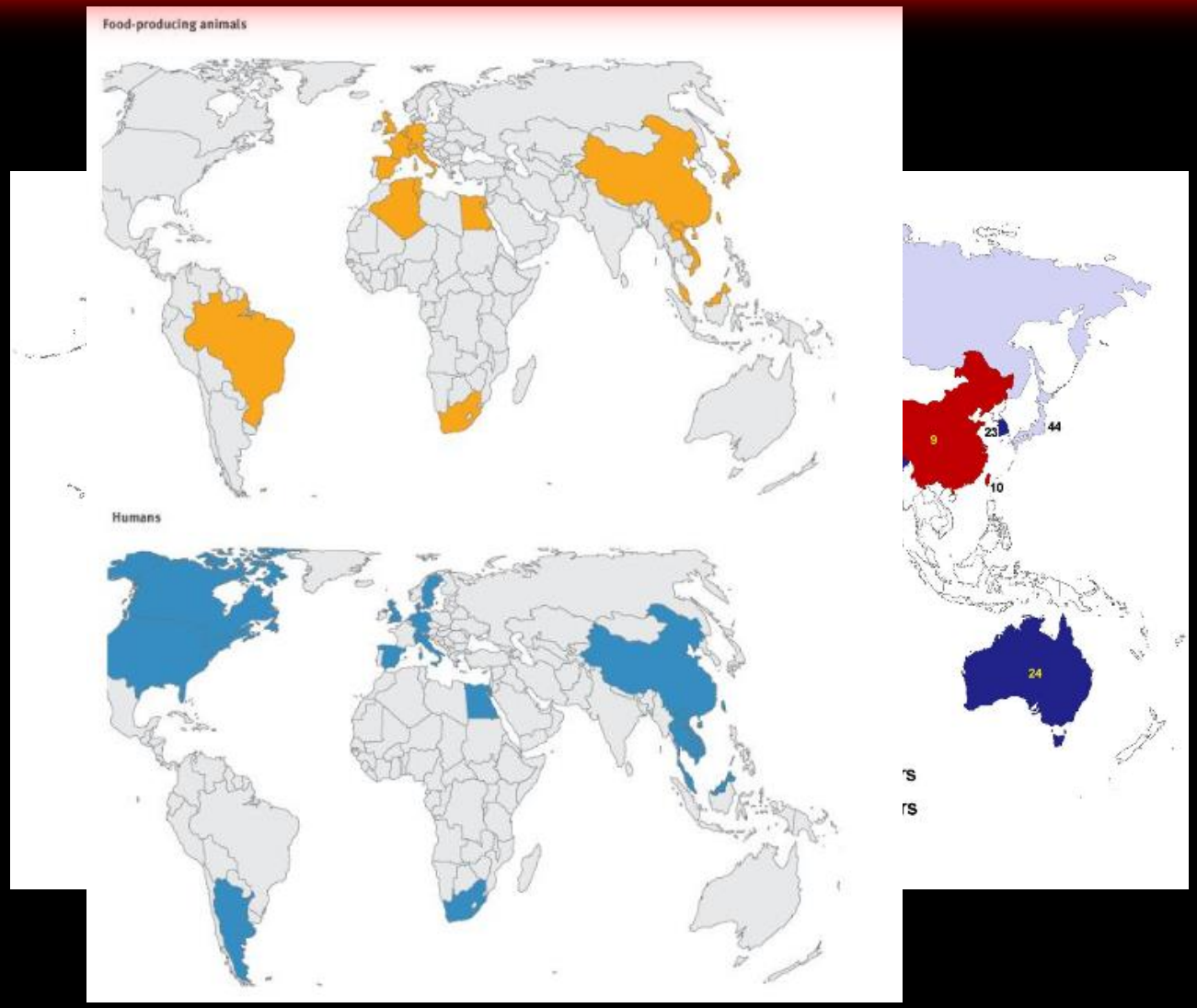
1. Modification of AB molecule
   - β-lactamase production
2. Changes in target site
   - MCR-1
3. Change of metabolic pathway
4. Reduced accumulation of antibiotic

1. ESβL (PNCs, extended-spectrum CEF -cefotaxim, ceftriaxon, ceftazidim, aztreonam)
   TEM, SHV, CTX-M
2. AmpC βL (PNCs, CEFs- cefalotin, cefazolin, cefoxitin, oxyiminocCEF-ceftizoxim,cefotaxim, ceftriaxon)
3. Carbapenemases (PNCs, oxyiminocCEF, cefamycins-cefoxitin, cefotaxim,ceftazidim, carbapenems)
   NDM-1 and others - VIM,IMP

NOVEL GENES OF ANTIBIOTIC RESISTANCE

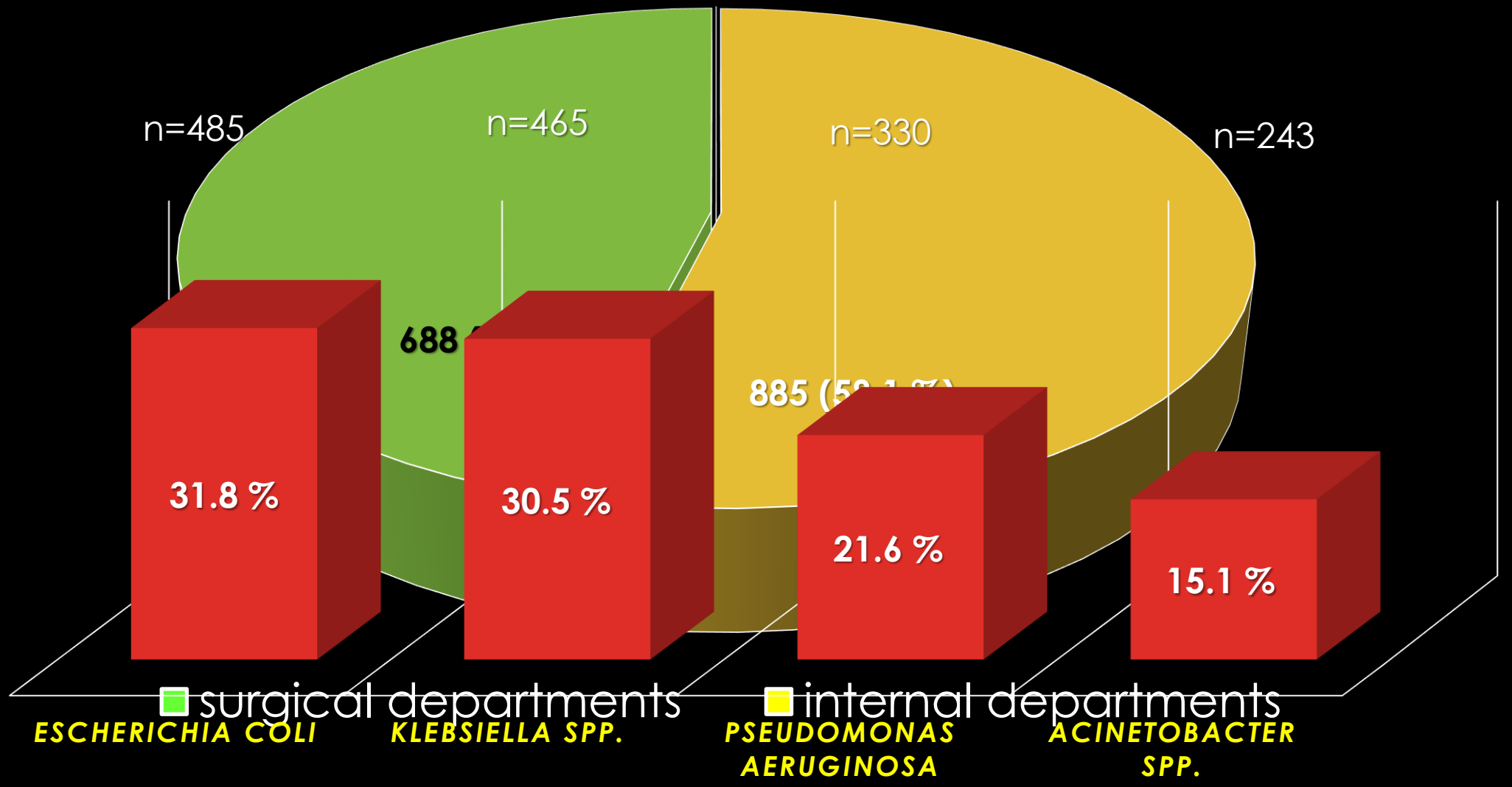
NDM-1
MCR-1
Kl. Pneumonica - 2008
Escherichia coli - 2015

Escherichia coli
Salmonella enterica,
Acinetobacter baumanii
Klebsiella pneumonia,
Enterobacter spp.
Shigella spp.
Citrobacter spp.

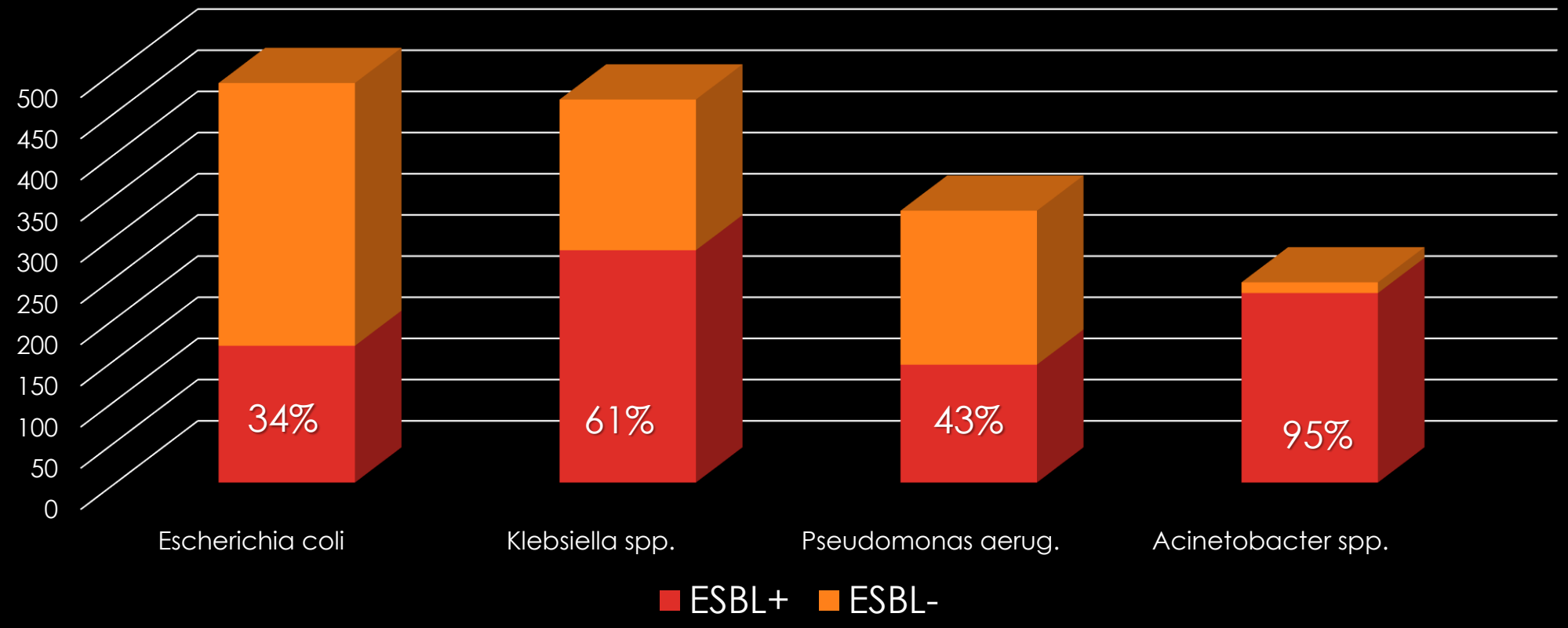


ECDC, 2016

ISOLATION OF 1523 STRAINS FROM WORK PLACES IN L. PASTEUR UNIVERSITY HOSPITAL



ESBL PRODUCTION IN EXAMINED BACTERIA



DETECTION OF BL IN PHENOTYPE AND GENOTYPE

Beta-lactamase	Number (%)
AmpC	623 (40.9)
TEM ESBL	480 (31.5)
CTX-M ESBL	398 (26.1)
SHV ESBL	102 (6.6)

ISOLATION OF *NDM-1 KL. PNEUMONIAE* IN UNLP

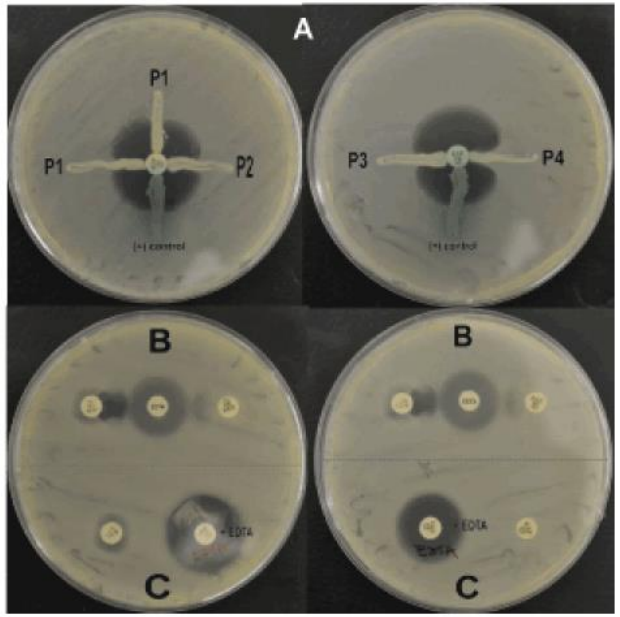


Figure 1: Phenotypic detection of carbapenemases in a *K. pneumoniae* NDM-1 strain isolated from a nasal wash specimen. (A) Modified Hodge test, using IPM, for detection of carbapenemase, performed by the CLSI reference method (P1, P2, P3, P4). (B) EDTA-IMP, CAZ double disc synergy test for MBL. (C) Carbapenem-EDTA combined disc diffusion test for MBL. The *K. pneumoniae* isolate was inoculated to the surface of a MHA plate. Discs containing 10μg/mL IMP and 30μg/mL CAZ plus 10μl of 0.5 M EDTA (pH 7.8) was placed on the agar.

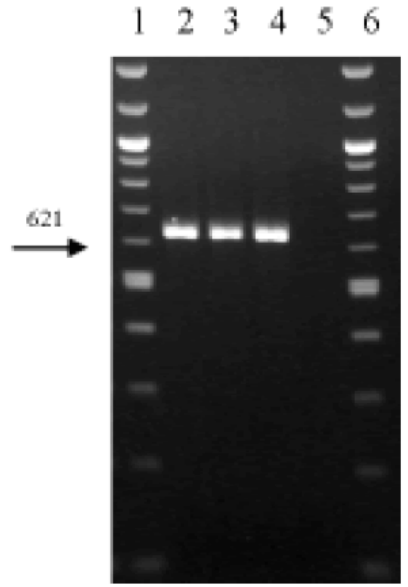


Figure 2: PCR results of detection the *bla*$_{NDM}$*-1* gene from *K. pneumoniae* isolates Lane 1. and 6. –100bp DNA Ladder (BioLabs), lane 2-P1, lane 3-P2, lane 4-P3, lane 5-P4 (negative for gene NDM-1)

Lovayová V., Vargová L., Habalová V., Pastvová L., Čurová K., Siegfried L.
New Delhi Metallo-Beta-Lactamase (NDM-1) Producing *Klebsiella pneumoniae* in Slovakia, 2014

NEW DEFINITIONS OF ACQUIRED RESISTANCE TO ANTIBIOTICS

Multiresistance (MDR)
Acquired resistance to at least 1 AB in ≥ 3 defined groups of antibiotics effective for given species (genus, family) of bacteria

Polyresistance (XDR)
Acquired resistance to at least 1 AB in all but two or fewer antimicrobial groups effective for given species (genus, family) of bacteria

Panresistance (PDR)
Acquired resistance to all AB in all defined categories of AB effective for given species (genus, family) of bacteria

Magiorakos et al., 2012

NEW ANTIBIOTICS 2010-2015

G-

Ceftolozane-taz

(IAI E.cloacae, E.coli, Klebsiella,

stellatus, Strept. salivarius)

Ceftazidime-avi

G+

Fidaxomicin

Ceftaroline

Dalbavancin

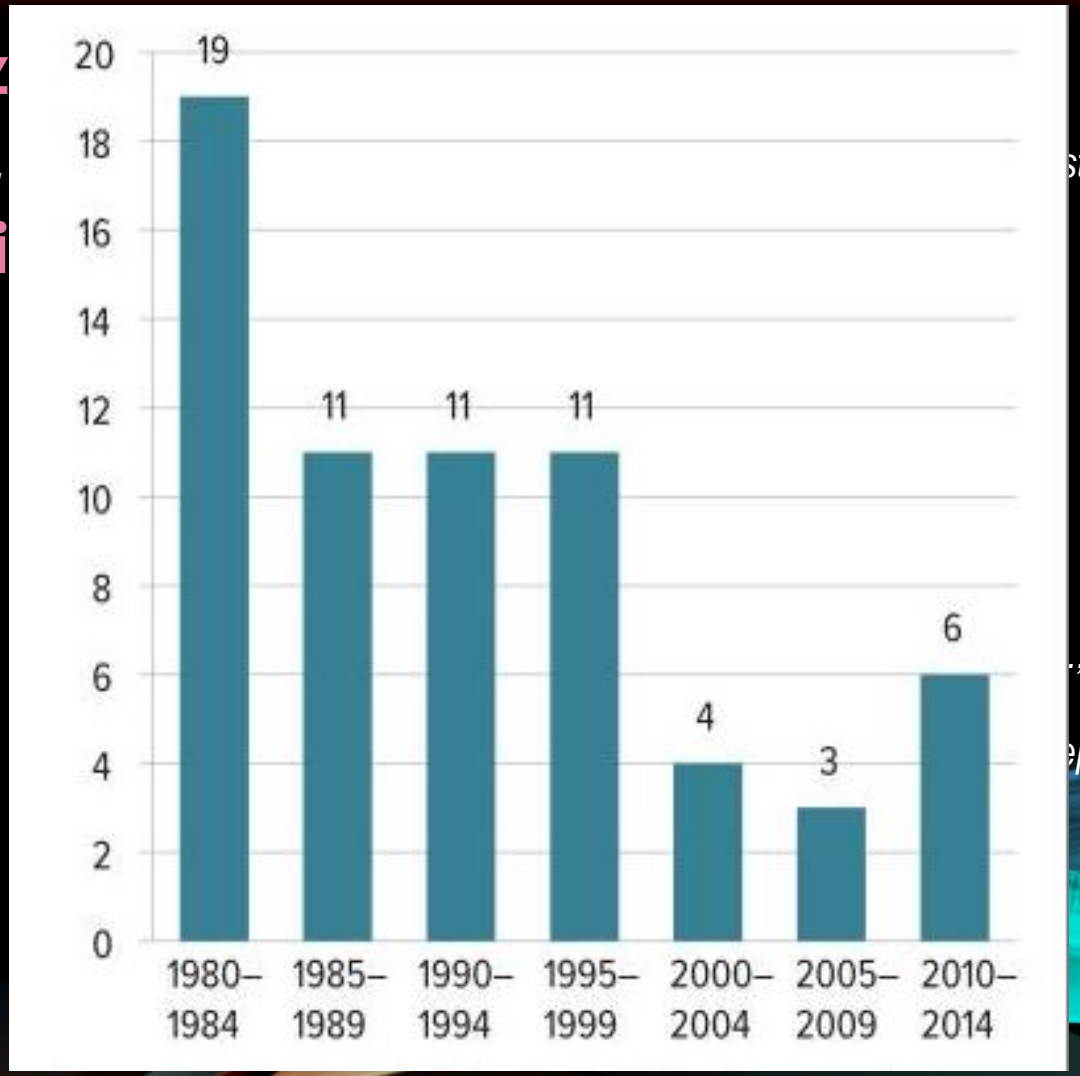
Tedizolid

., enterococci)

Oritavancin

eptococci)

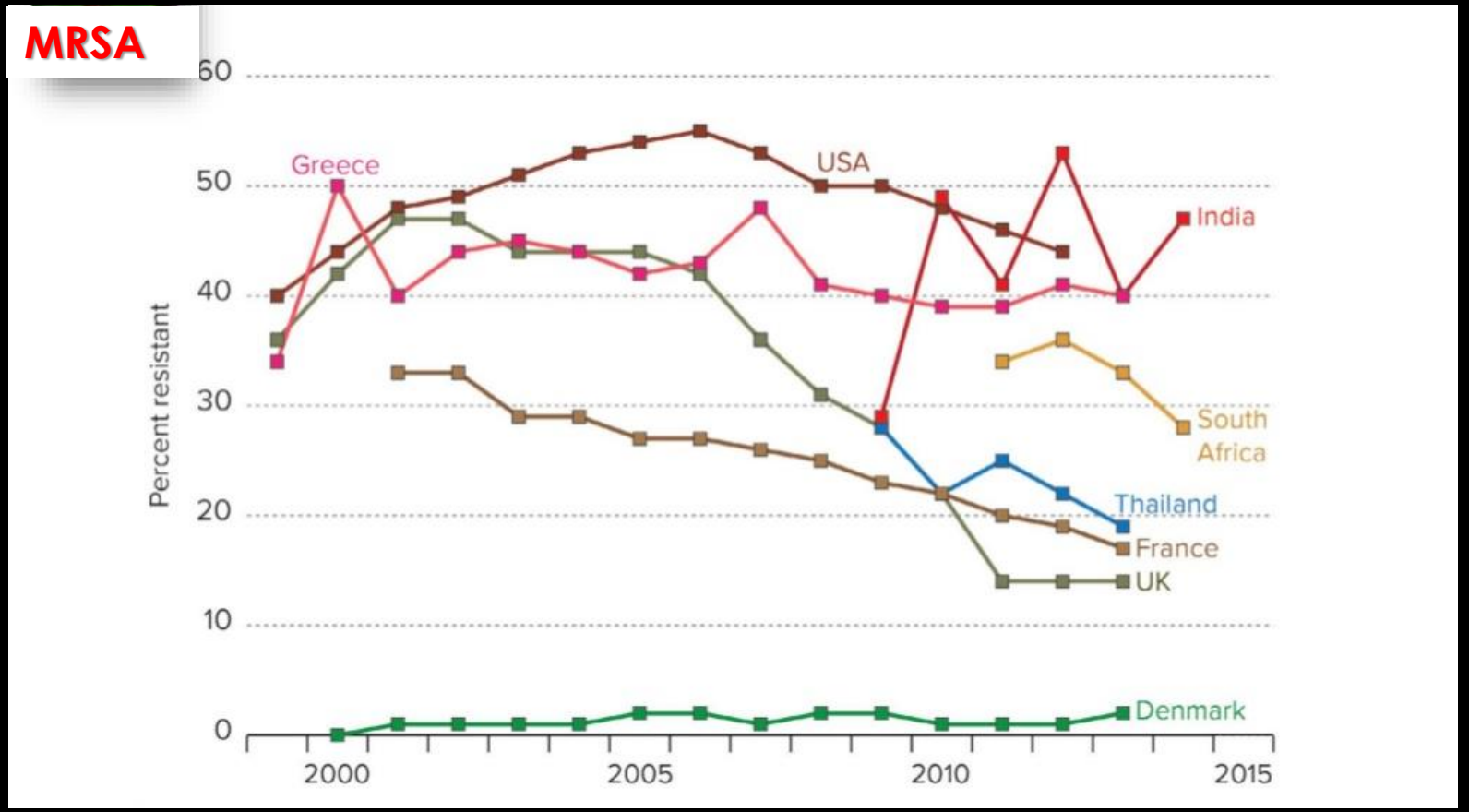
Bedaquiline



Ventola, 2015

CONCLUSION

GLOBÁLNY TREND VÝSKYTU MRSA



Percentuálny výskyt *Staphylococcus aureus* rezist. proti meticilínu 1999-2014

CDDEP, 2015

1 Public Awareness

- Public health programs across the countries

2 Prevent the spread of infection

- Expansion of the access to clean water and appropriate sanitation
- Reduction of infection in hospitals and care settings

3 Reduction of antibiotic use in agriculture

- Restriction on the use of highly critical antibiotics in farming
- Prevention of antibiotic dissemination into environment

4 Global surveillance

- Major surveillance programs including USA Global Health Security Agenda, UK Fleming Fund, WHO Global AMR Surveillance System
- Easy data accessibility around the world

5 Rapid new diagnostics

- Support research and innovation in this area

6 Use of alternative antimicrobials

- Vaccines
- Bacteriophage therapy, engineered bacteria, antimicrobial peptides

7 Recognition of researchers in infectious disease

- Clear career paths and rewards for scientists in the field

8 Global Innovation Fund

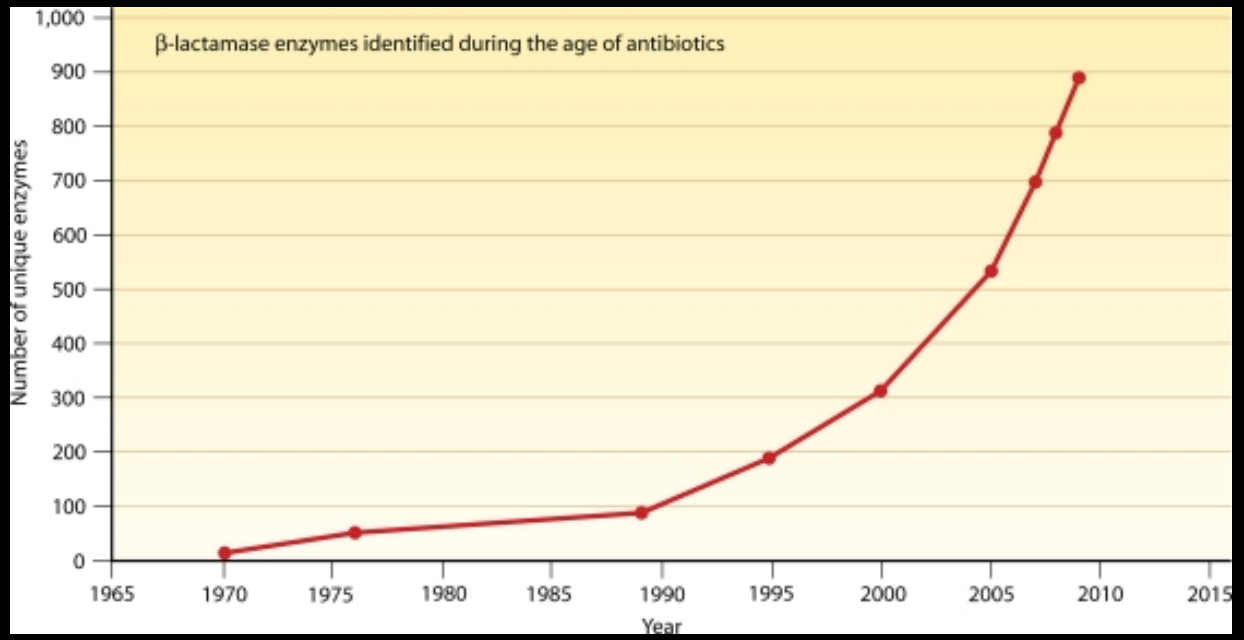
- Link and expand major initiatives
- Fund different projects (e.g. R&D that might lack commercial imperative)

9 Better investment for new drugs

- Governments should find new ways to reward innovation
- Link between profit and volume of sales should be reduced

10 Global Coalition for real action

- Joint efforts from G20 and UN are needed


β-lactamase enzymes identified during the age of antibiotics
Number of unique enzymes
1,000
900
800
700
600
500
400
300
200
100
0
1965
1970
1975
1980
1985
1990
1995
2000
2005
2010
2015
Year