Μικροβιακή Αντοχή : Μία πρόκληση για την Κύπρο και τον κόσμο

Eirini Christaki
Lecturer of Internal Medicine
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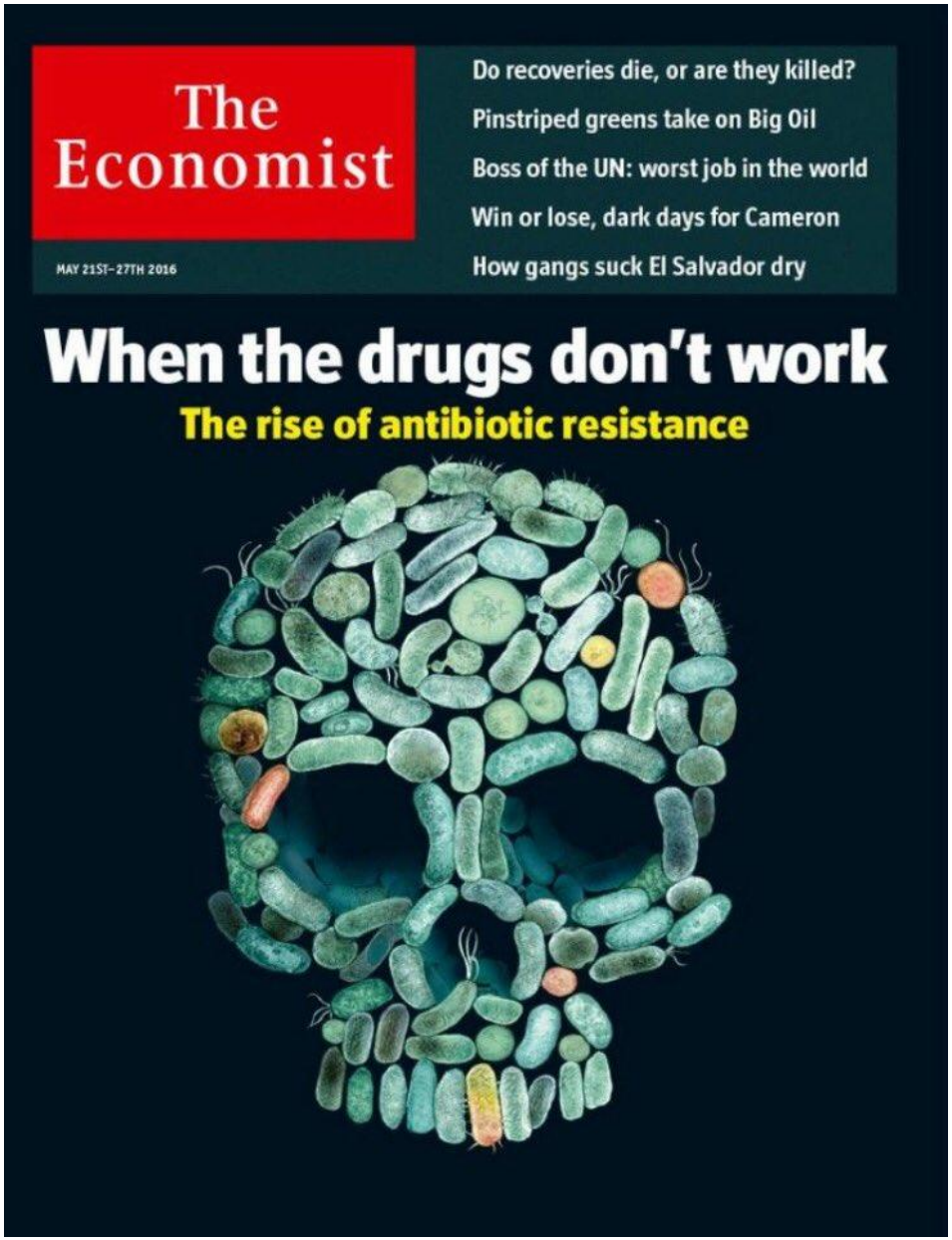

The Economist
MAY 21ST–27TH 2016
Do recoveries die, or are they killed?
Pinstriped greens take on Big Oil
Boss of the UN: worst job in the world
Win or lose, dark days for Cameron
How gangs suck El Salvador dry
When the drugs don't work
The rise of antibiotic resistance


Drug-resistant superbug may be more widespread than previously known
CNN
Home
Video
World
U.S.
Africa
Asia
Europe
Latin America
Middle East
President signs order to fight superbugs
By Saundra Young, CNN

Antimicrobial Resistance

WHO
2014

European Union
population 500m

25,000 deaths per year

2.5m extra hospital days

Overall societal costs
(€ 900 million, hosp. days)
Approx. €1.5 billion per year

Source: ECDC 2007

Thailand
population 70m

>38,000 deaths

>3.2m hospital days

Overall societal costs
US$ 84.6–202.8 mill. direct
>US$1.3 billion indirect

Source: Pumart et al 2012

United States
population 300m

>23,000 deaths

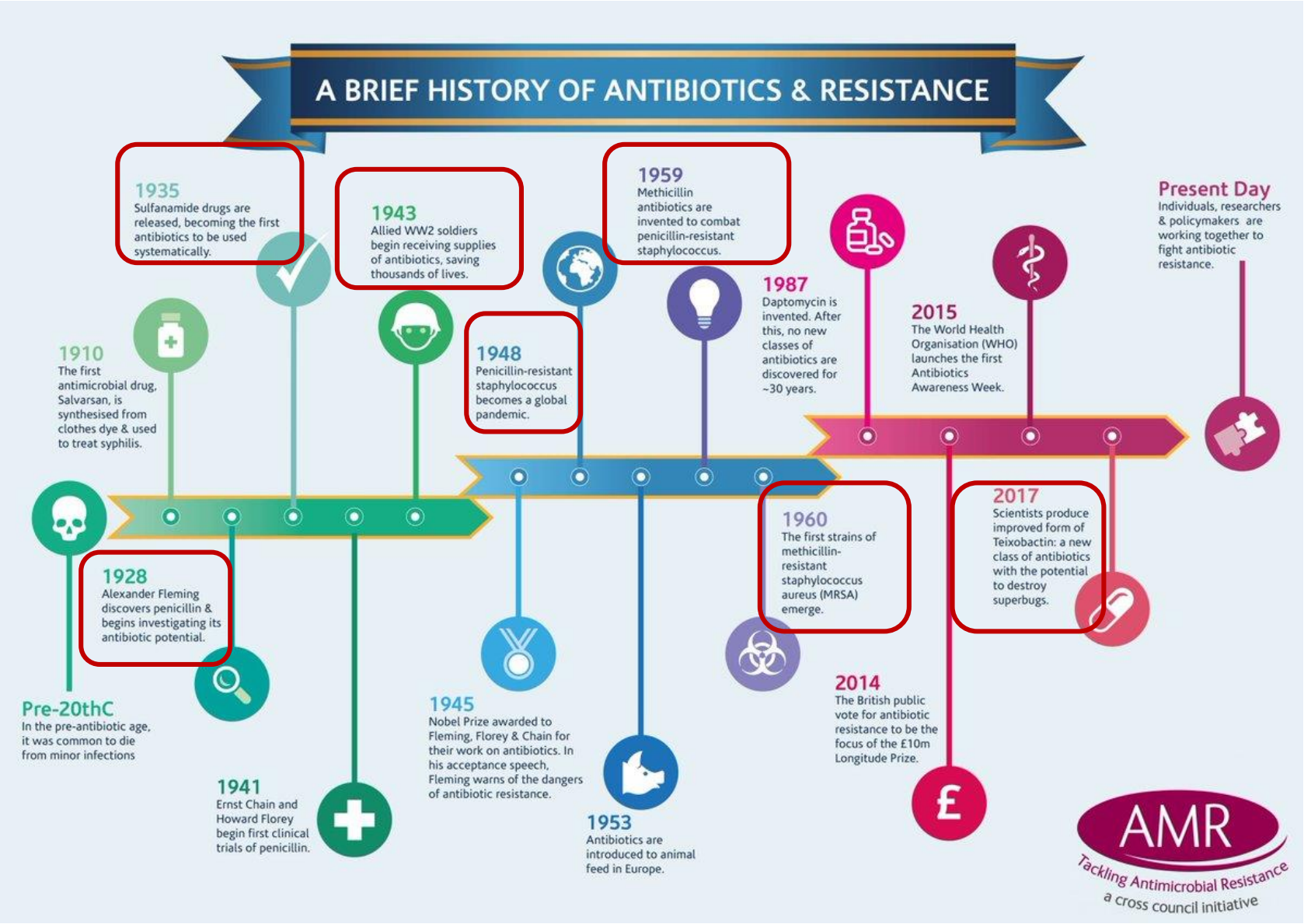
>2.0m illnesses

Overall societal costs
Up to $20 billion direct
Up to $35 billion indirect

Source: US CDC 2013

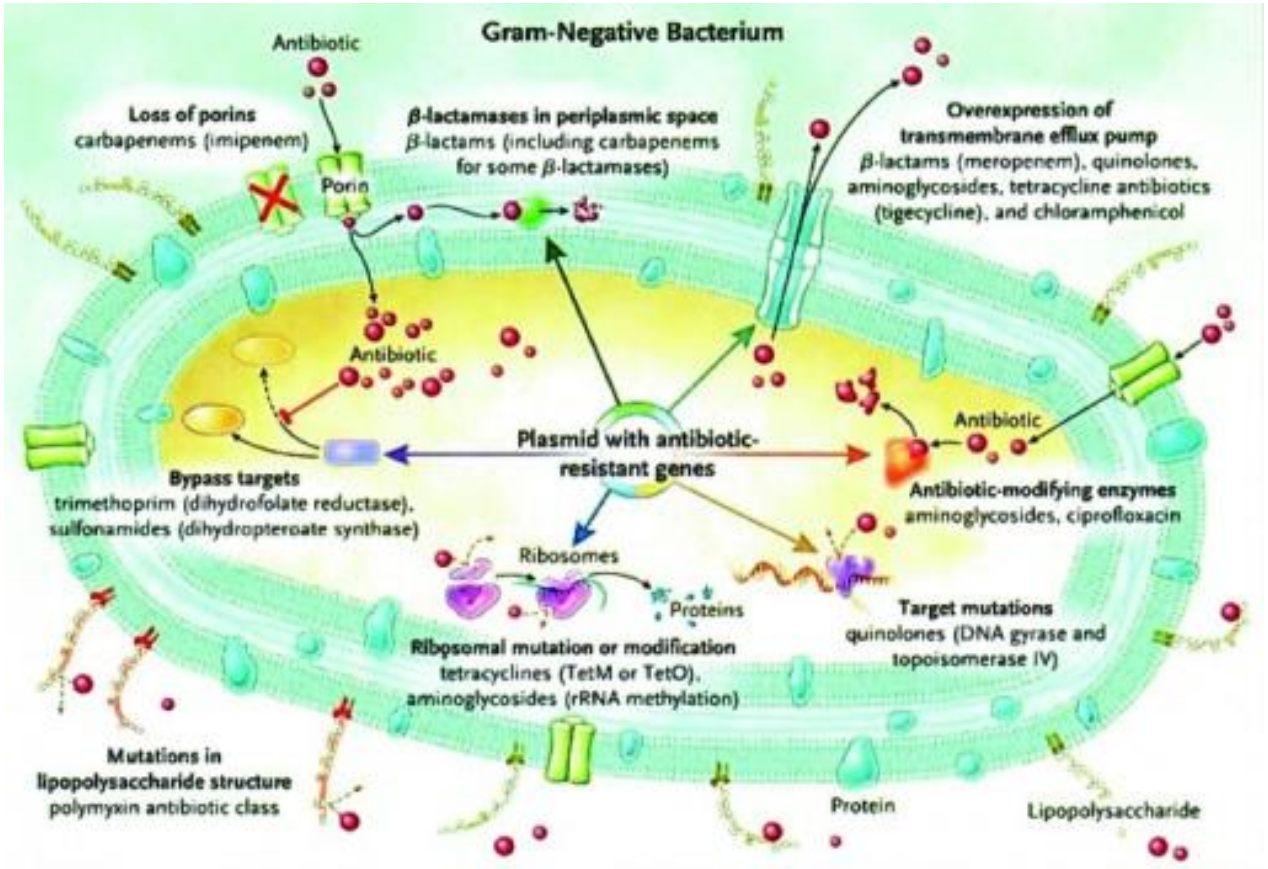
Antimicrobial Resistance

- **Antimicrobial Resistance (AMR):** the ability of microorganisms to become resistant to one or several antimicrobial agents used for therapy or prophylaxis;
- **Healthcare-Associated Infections (HAI):** all infections associated with patient care, in particular hospitals and long-term care facilities.



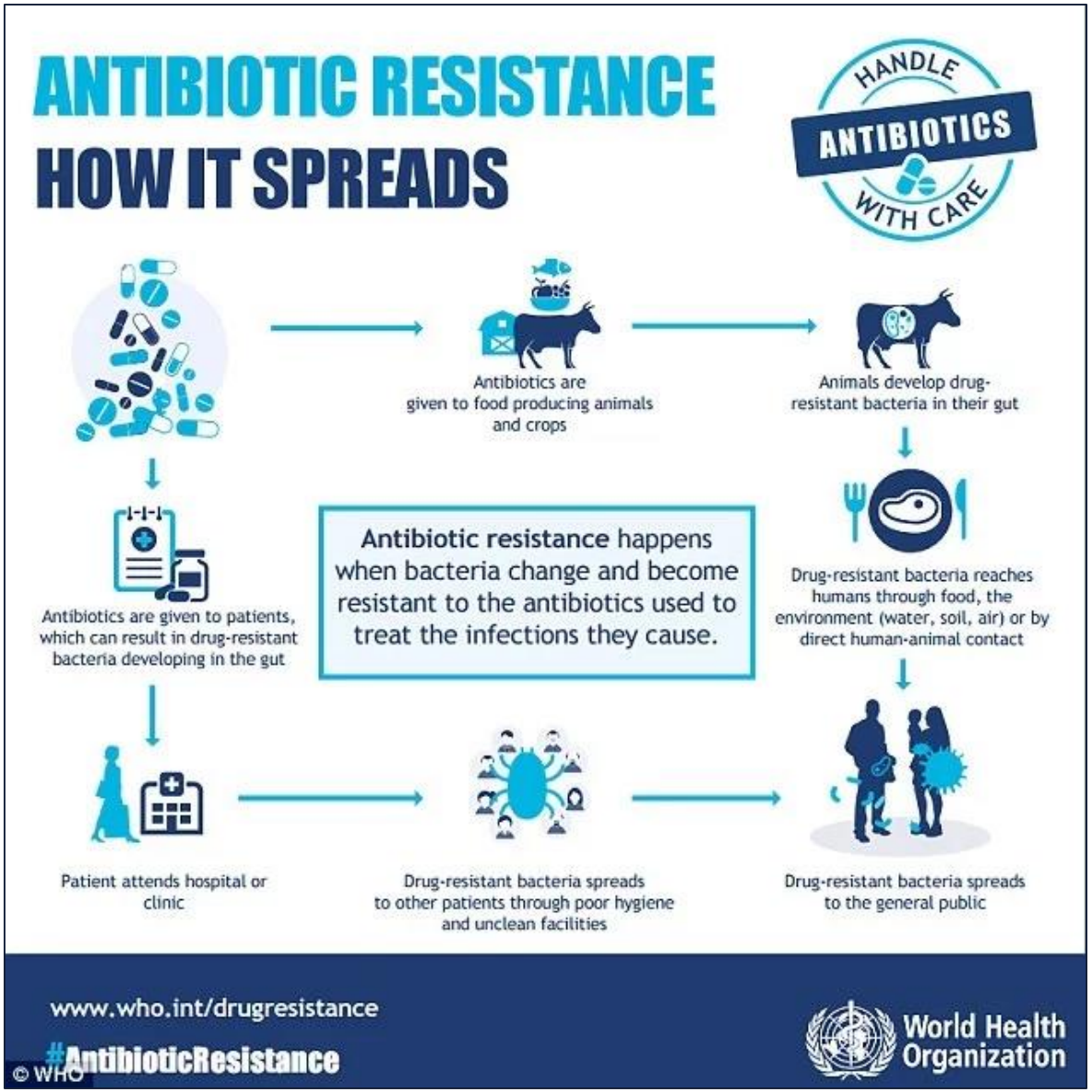
Graphic by Science and Technology Facilities Council, UK

Mechanisms of antimicrobial resistance



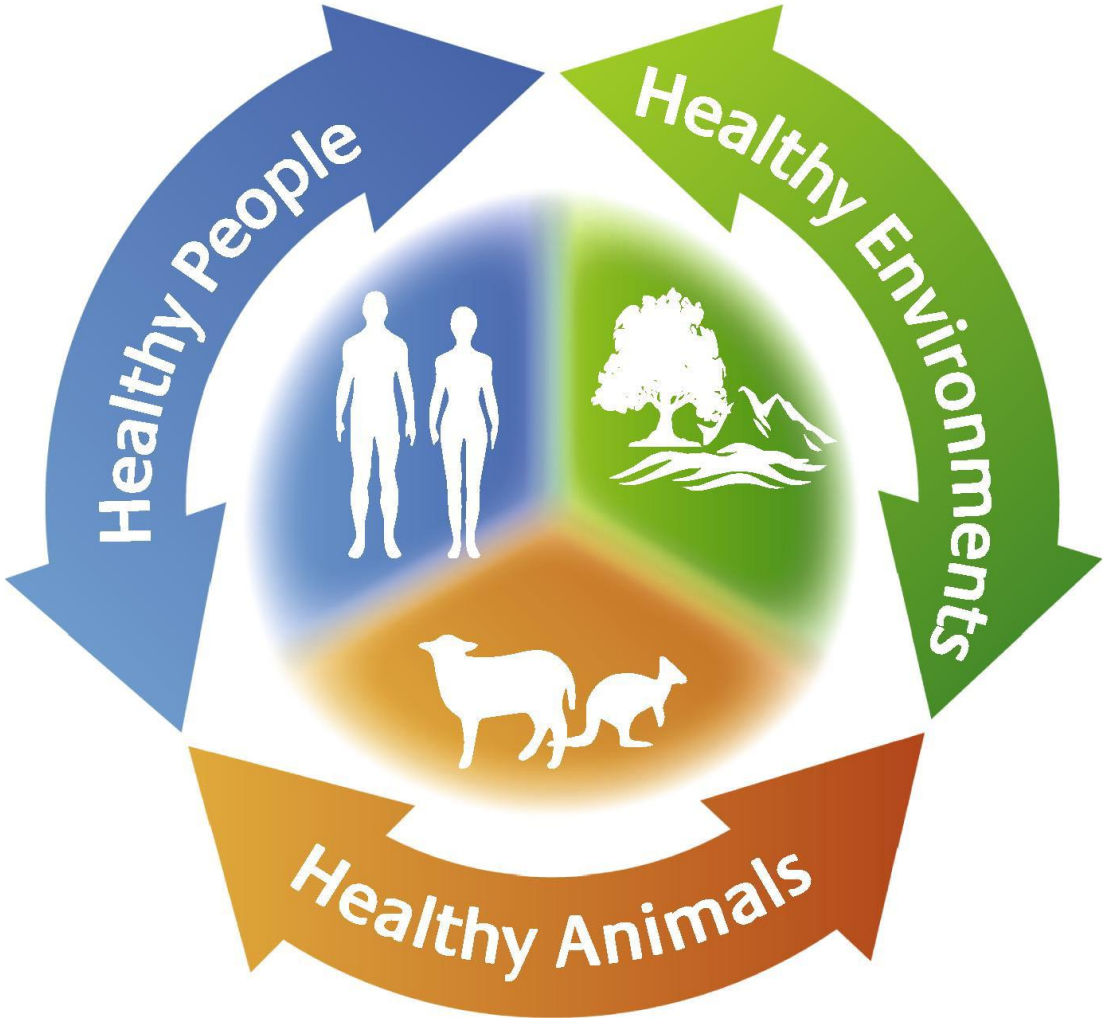
Pop-Vicas A, Opal SM - Virulence (2013)

- Κατάχρηση αντιμικροβιακών
- Μη σωστή χρήση αντιμικροβιακών
  - Ακαταλληλότητα
  - Υποδοσολογία
- Καθυστέρηση στην έγκαιρη διάγνωση
  - => Εμπειρική θεραπεία
  - => Αύξηση της διάρκειας χορήγησης αντιμικροβιακών
- Κατάχρηση αντιμικροβιακών στην κτηνοτροφία & αγροτική παραγωγή
- Ελλιπής συμμόρφωση με τα μέτρα πρόληψης λοιμώξεων στους χώρους παροχής υγείας



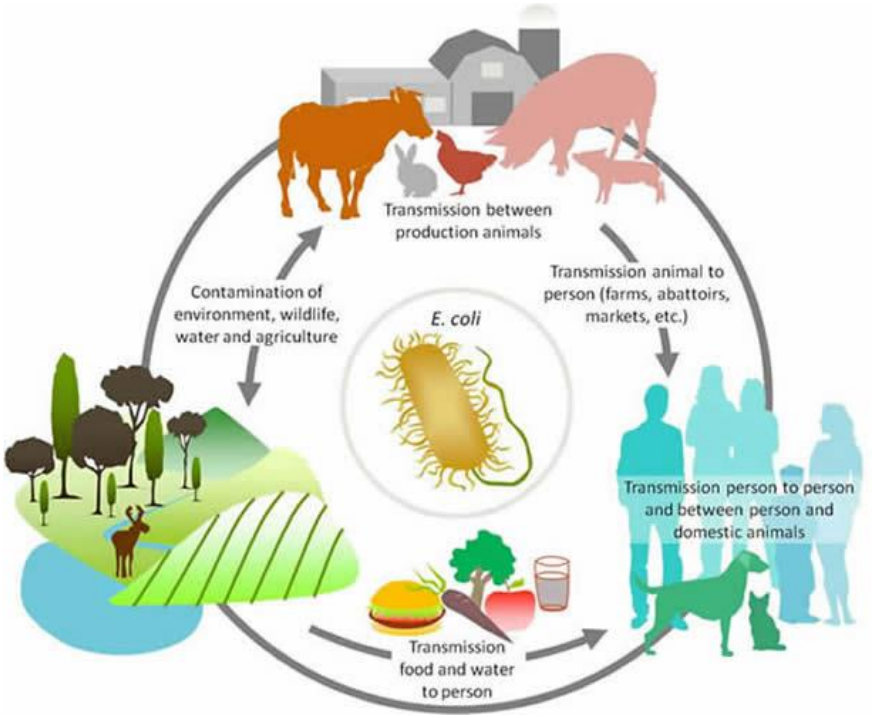
- Ανάπτυξη ανθεκτικών στελεχών μετά την έκθεση στα αντιμικροβιακά
- Μετάδοση ανθεκτικών παθογόνων (π.χ. νοσοκομειακές λοιμώξεις)
- Τροφική αλυσίδα

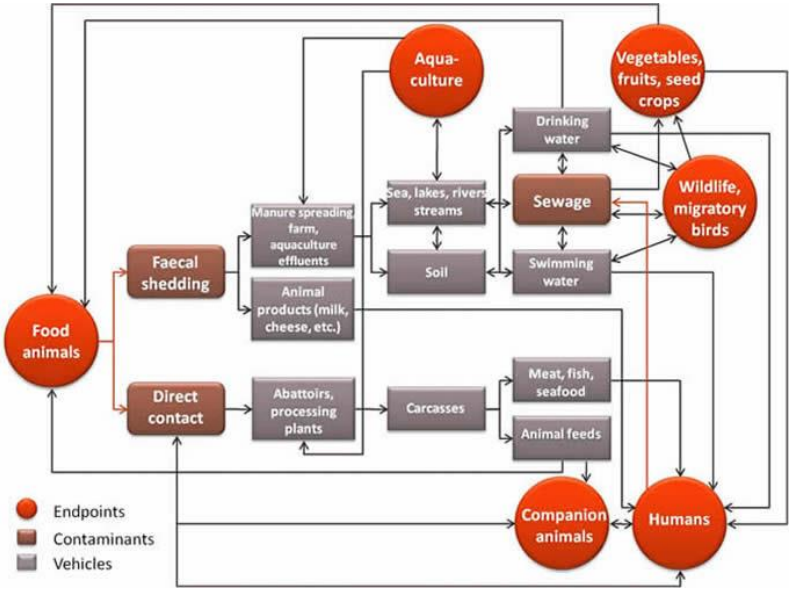
The One Health Triad



- 2/3 of emerging infectious diseases are zoonotic
- The interrelationship between environmental, animal and human health requires an interdisciplinary approach

ONE HEALTH – The example of *Escherichia coli*





Ecl Lab, Universite de Montreal

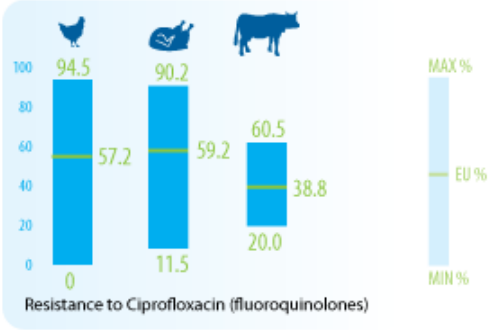
OVERVIEW OF RESISTANCE LEVELS IN EU

Based on the European Union Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2011

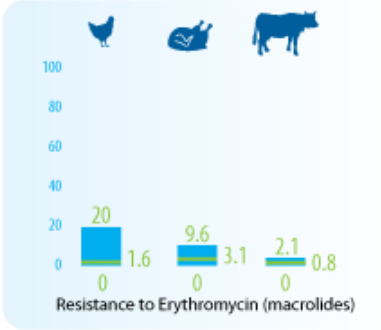
Monitoring
is a prerequisite for understanding the development and dissemination of antimicrobial resistance

ANIMALS

Campylobacter jejuni

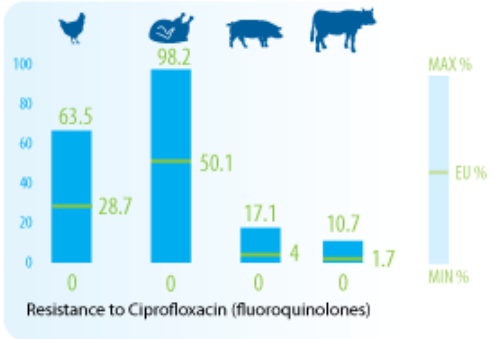


Resistance to Ciprofloxacin (fluoroquinolones)

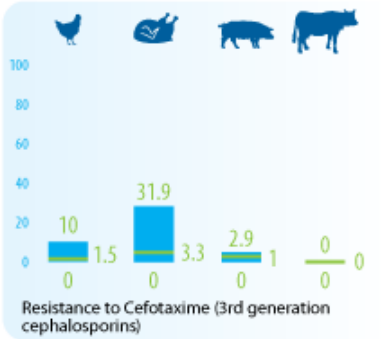


Resistance to Erythromycin (macrolides)

Salmonella



Resistance to Ciprofloxacin (fluoroquinolones)

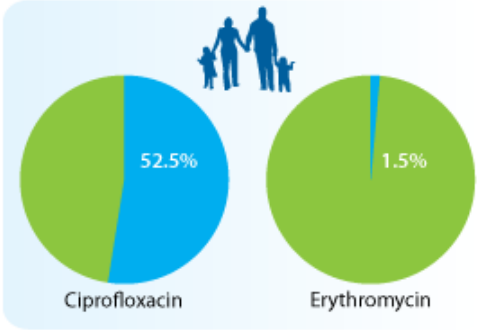


Resistance to Cefotaxime (3rd generation cephalosporins)

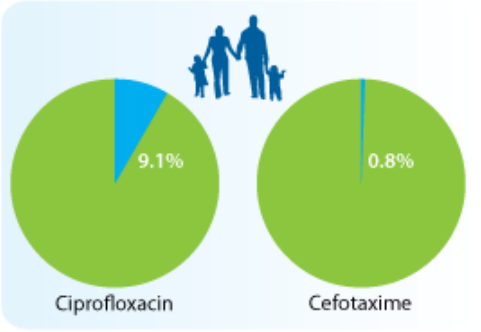
Interpretative criteria of resistance in humans and animals are different and generally result in higher levels in animals and food compared with humans.

HUMANS

Campylobacter jejuni



Salmonella
(all non-typhoidal serovars)

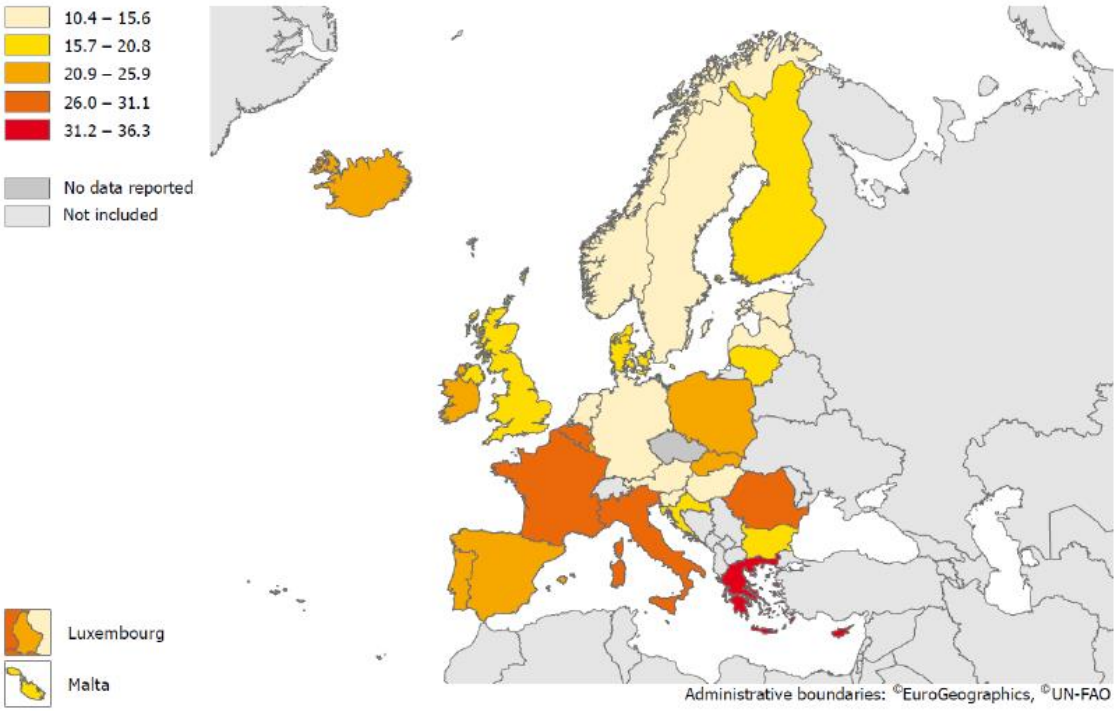


efsa
European Food Safety Authority

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

ECDC- Annual Epidemiological Report 2016 Antimicrobial Consumption

Figure 1. Consumption of antibacterials for systemic use (ATC group J01) in the community, EU/EEA countries, 2016, expressed as DDD per 1 000 inhabitants per day



Cyprus and Romania provided total care data, i.e. including the hospital sector.

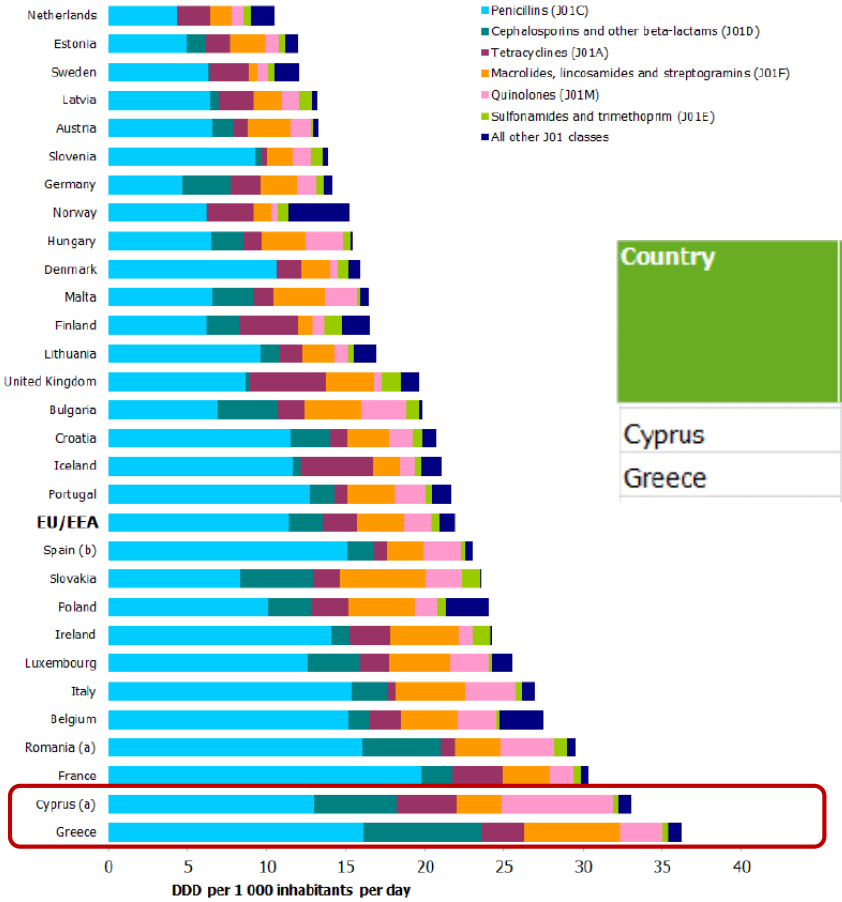
Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.

Population-weighted mean consumption of antibacterials for systemic use in the community was 21.9 DDD per 1 000 inhabitants per day, ranging from 10.4 in the Netherlands to 36.3 in Greece

Data retrieved from European Surveillance System (TESSy)

ECDC- Antimicrobial Consumption 2016

Figure 2. Consumption of antibacterials for systemic use (ATC group J01) and ATC group level 3 in the community, EU/EEA countries, 2016, expressed as DDD per 1 000 inhabitants per day



Country	2012	2013	2014	2015	2016	Trends in antimicrobial consumption, 2012–2016
Cyprus	29.7*	28.2*	26.1*	31.1*	33.0*	
Greece	32.5	32.2	35.1	36.1	36.3	

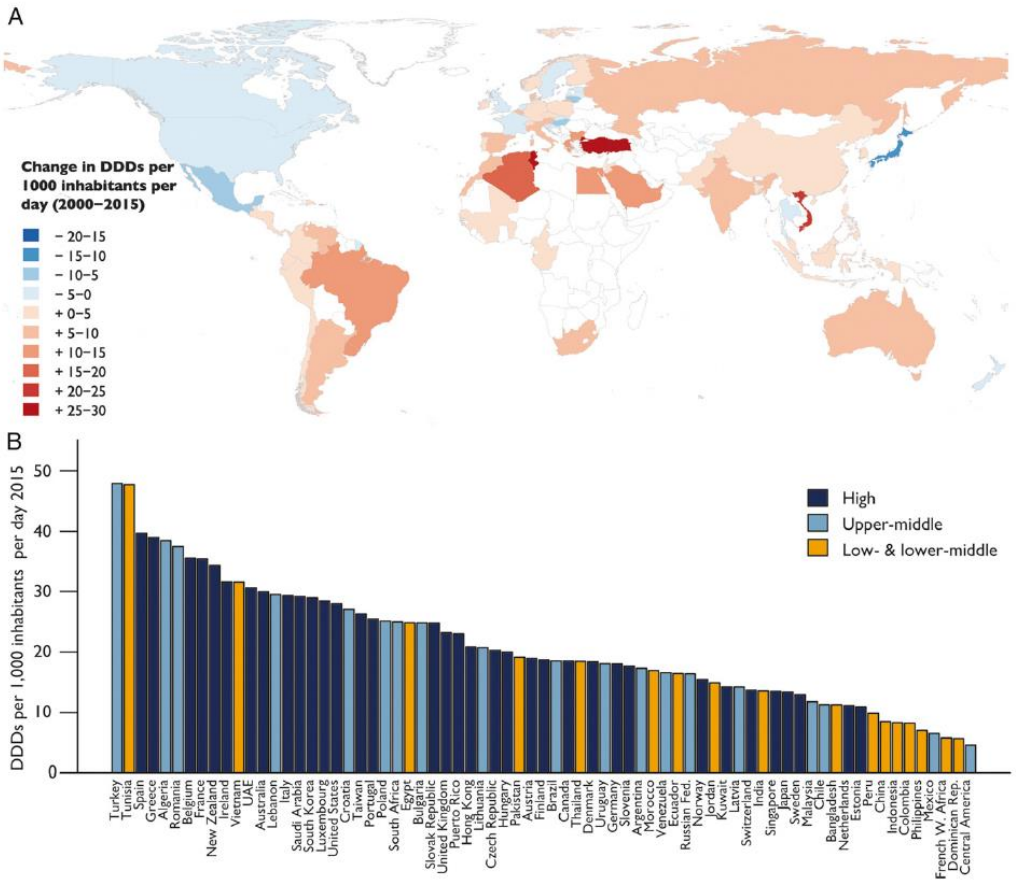
(a) Cyprus and Romania provided total care data (i.e. including the hospital sector).

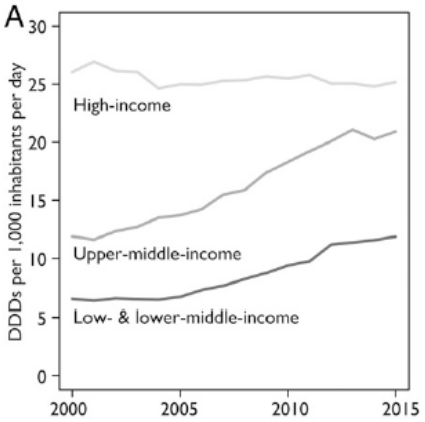
(b) Spain provided reimbursement data - i.e. not including consumption without a prescription and other non-reimbursed courses.

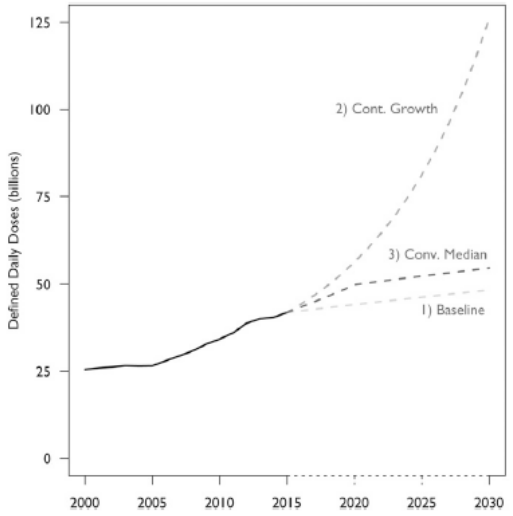
EU/EEA refers to the corresponding population-weighted mean consumption.

Global increase and geographic convergence in antibiotic consumption between 2000 and 2015

Eili Y. Klein[a,b,c,1], Thomas P. Van Boeckel[d], Elena M. Martinez[a], Suraj Pant[a], Sumanth Gandra[a], Simon A. Levin[e,f,g,1], Herman Goossens[h], and Ramanan Laxminarayan[a,f,i]







PNAS 2018

World Health Organization

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

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

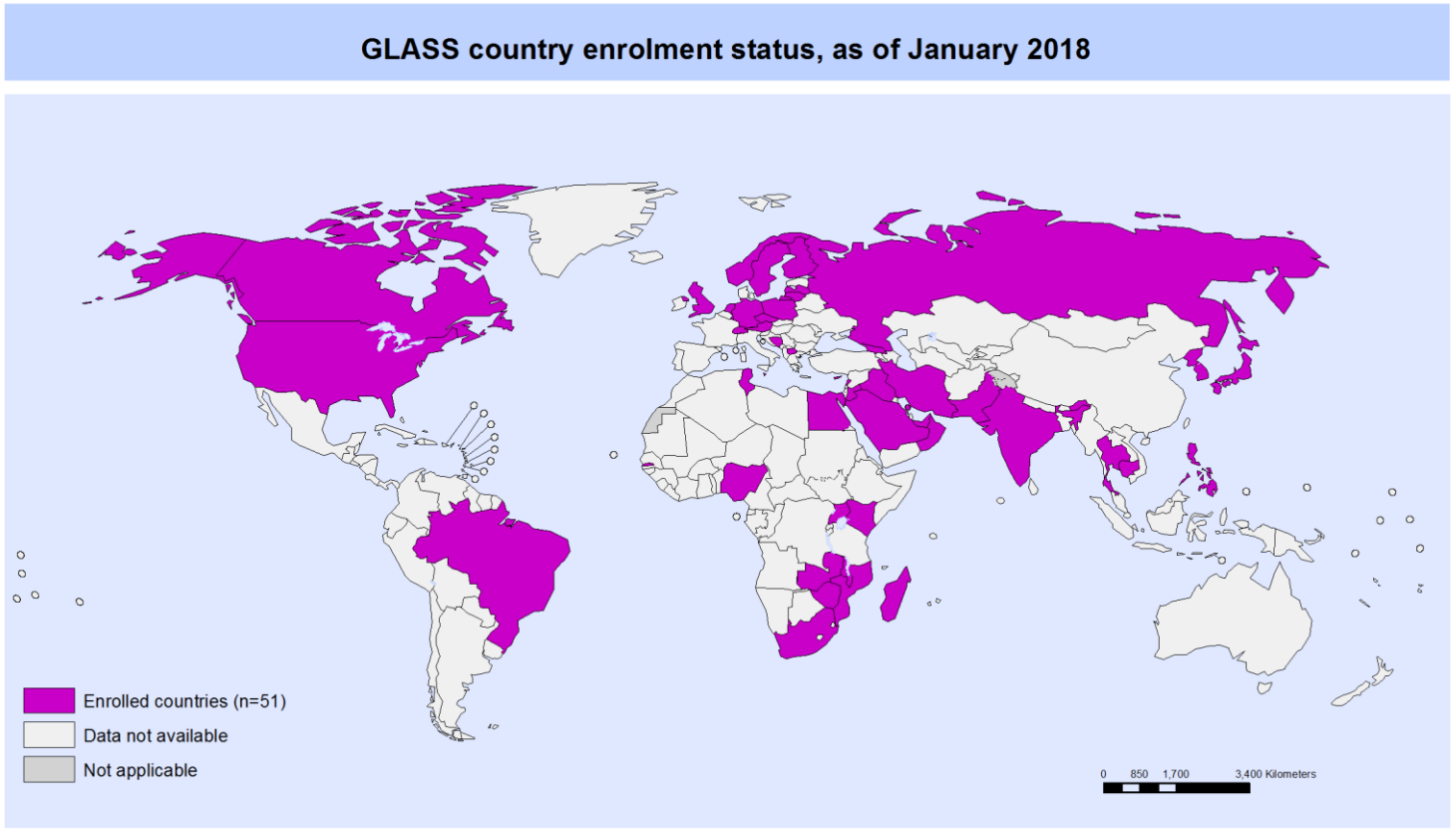
Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

GLASS | Global Antimicrobial Resistance Surveillance System (GLASS)



ResistanceMap

CDDEP Center for Disease Dynamics, Economics & Policy

About | Antibiotic Resistance | Antibiotic Use | Countries | Drug Resistance Index | Animal Use | Donate

Antibiotic Resistance

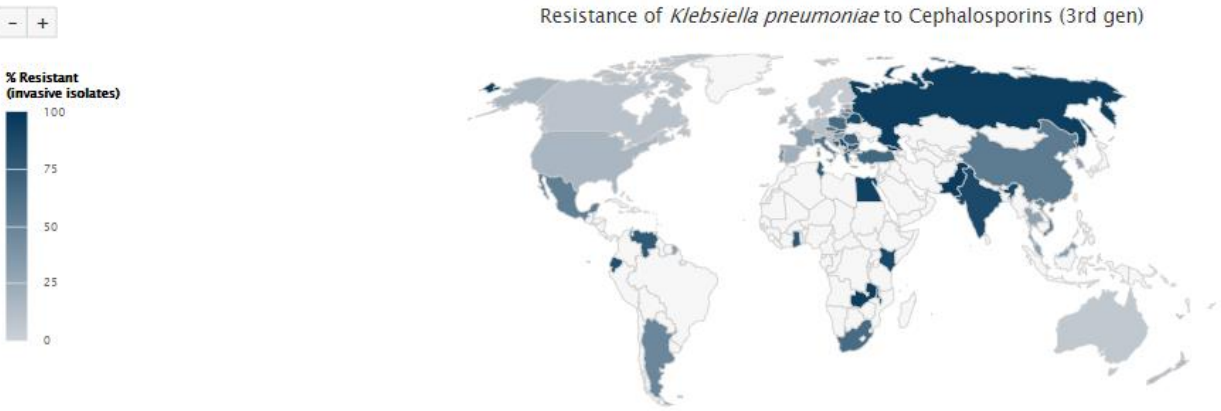
Map | Trend | Chart

Resistance of *Escherichia coli* to Fluoroquinolones

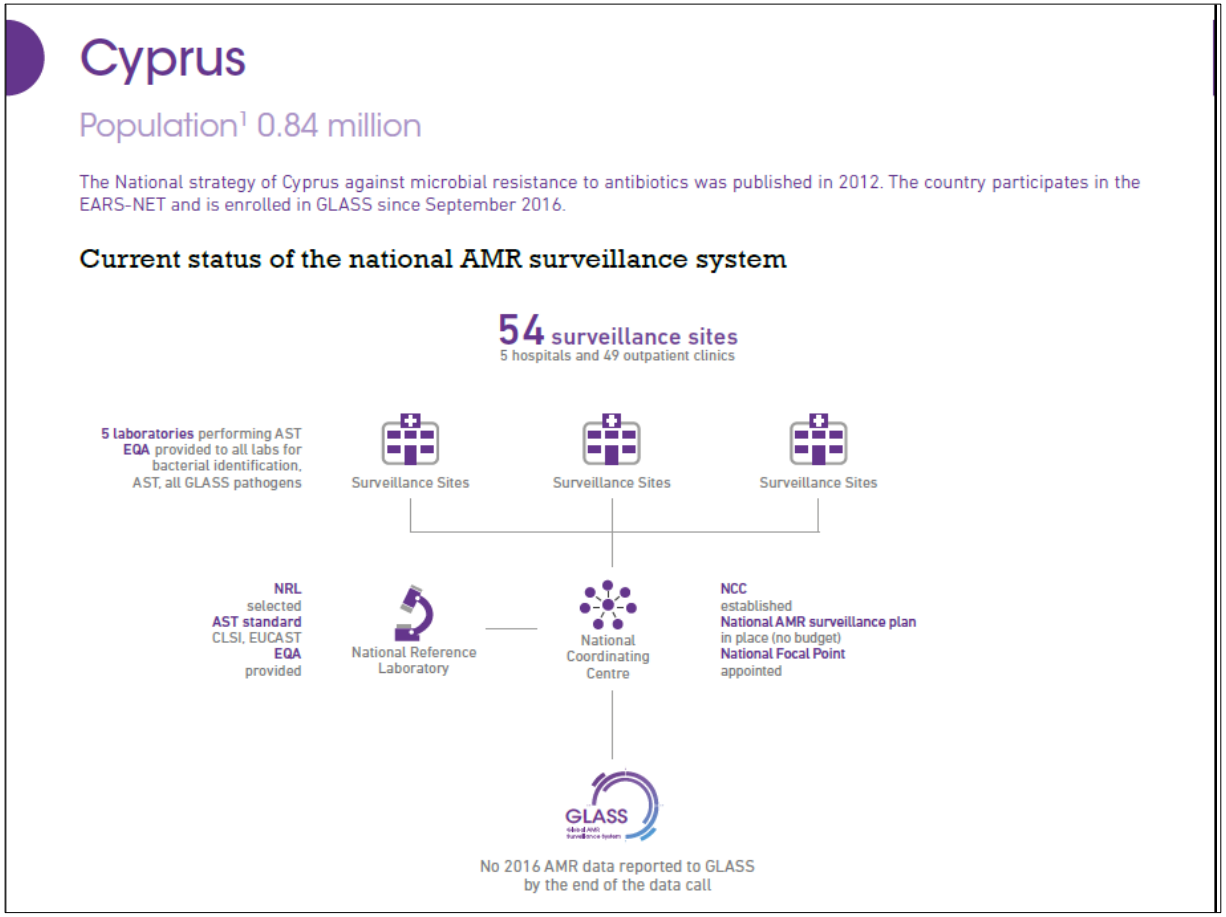
Antibiotic Resistance

Map | Trend | Chart

Resistance of *Klebsiella pneumoniae* to Cephalosporins (3rd gen)



GLASS | Global Antimicrobial Resistance Surveillance System (GLASS)

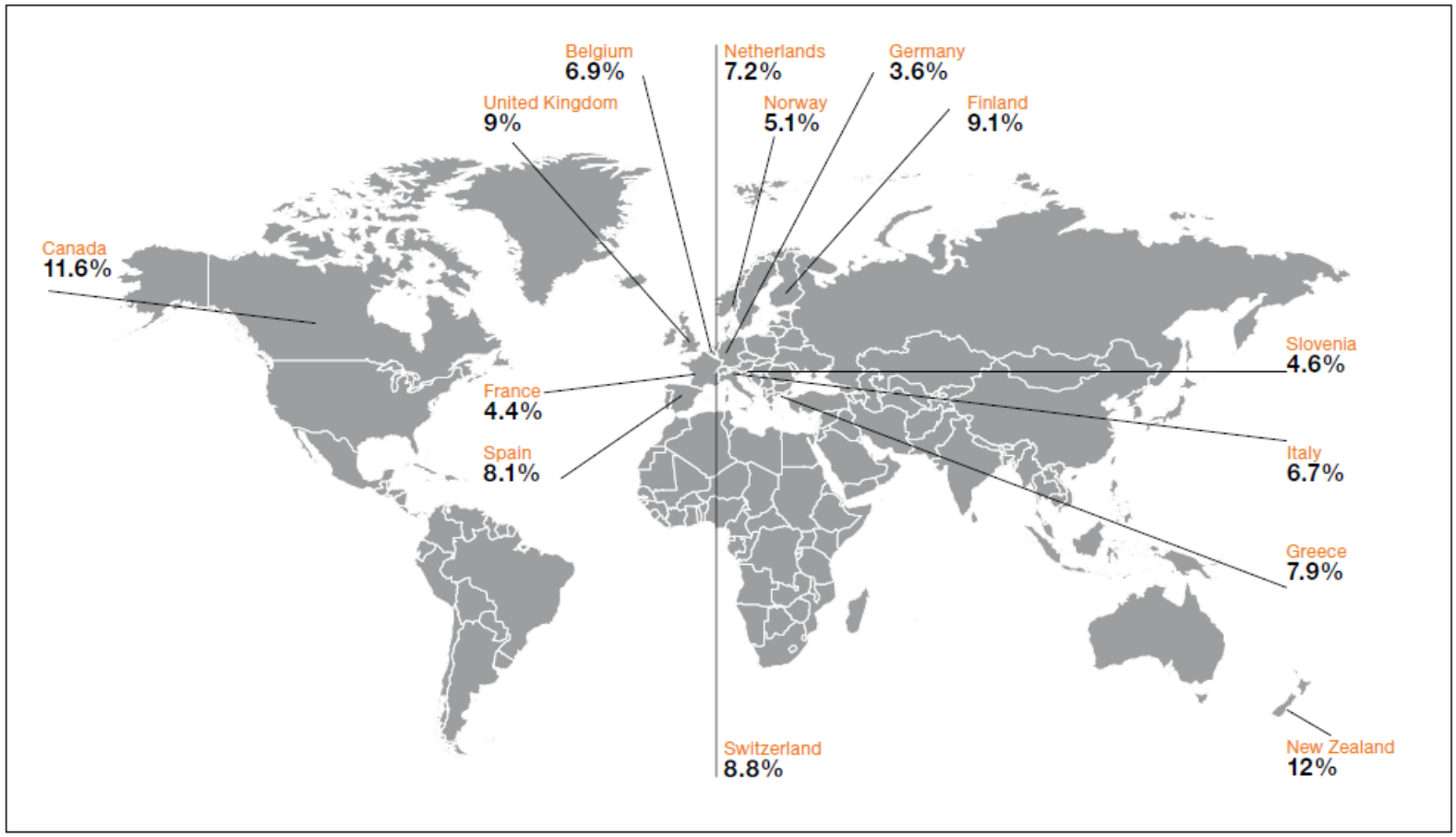


Antimicrobial Resistance in Healthcare-associated infections (HAIs)

- 70% are caused by pathogens that are resistant to at least one antimicrobial
- Infections due to multi-drug resistant pathogens cause approximately 25,000 deaths/year in Europe
  - In addition to these avoidable deaths, extra healthcare costs and productivity losses are estimated to be at least EUR 1.5 billion
- Cost of antimicrobial resistance in US – 5 billion

The bacterial challenge: time to react. Stockholm: ECDC; 2009

Prevalence of healthcare-associated infections



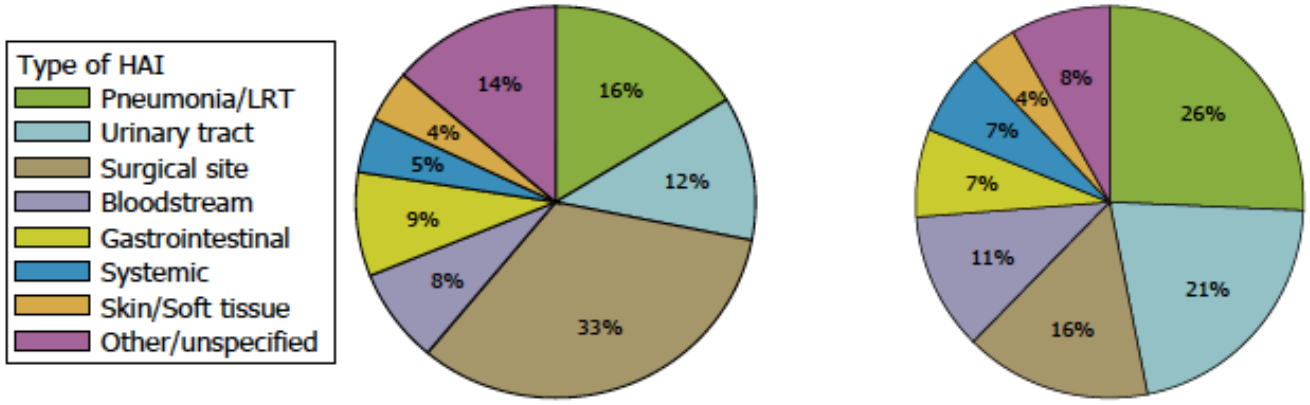
ECDC SURVEILLANCE REPORT

Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals

2011–2012

- 29 countries, 947 acute care hospitals, N: 231,459 patients
- Prevalence of patients with at least one HAI - 6% (2.3%-10.8%)
  - Adjusted based on average daily number of occupied beds/country - 5.7%, (CI 4.5-7.4%)
- 23% HAI upon admission (54% associated with previous stay at the same hospital)

Figure 1. Distribution of HAI types by presence of HAI on admission, HAI present on admission (left) HAI onset during hospitalisation (right)



HAI observed and predicted prevalence by country

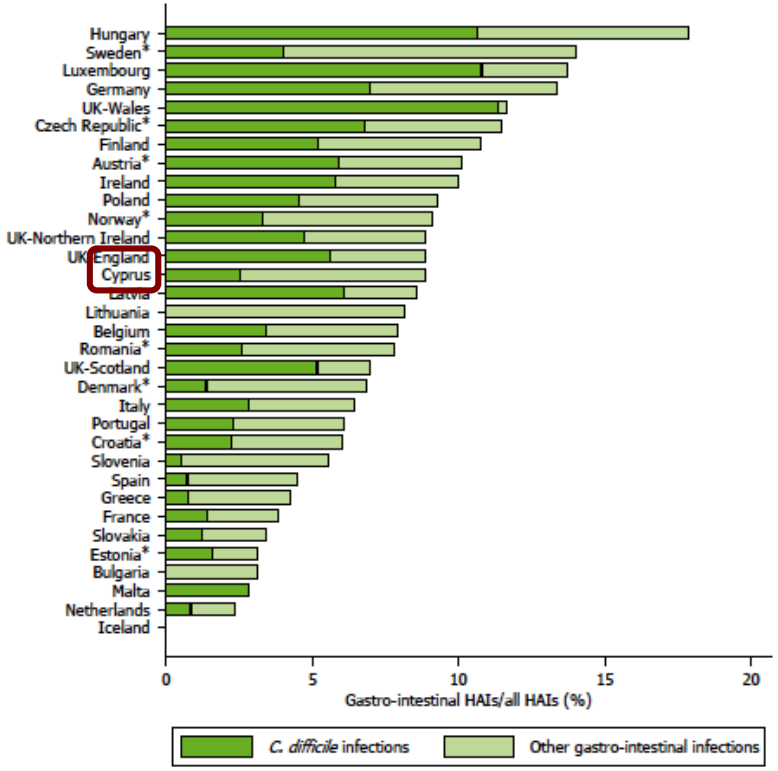
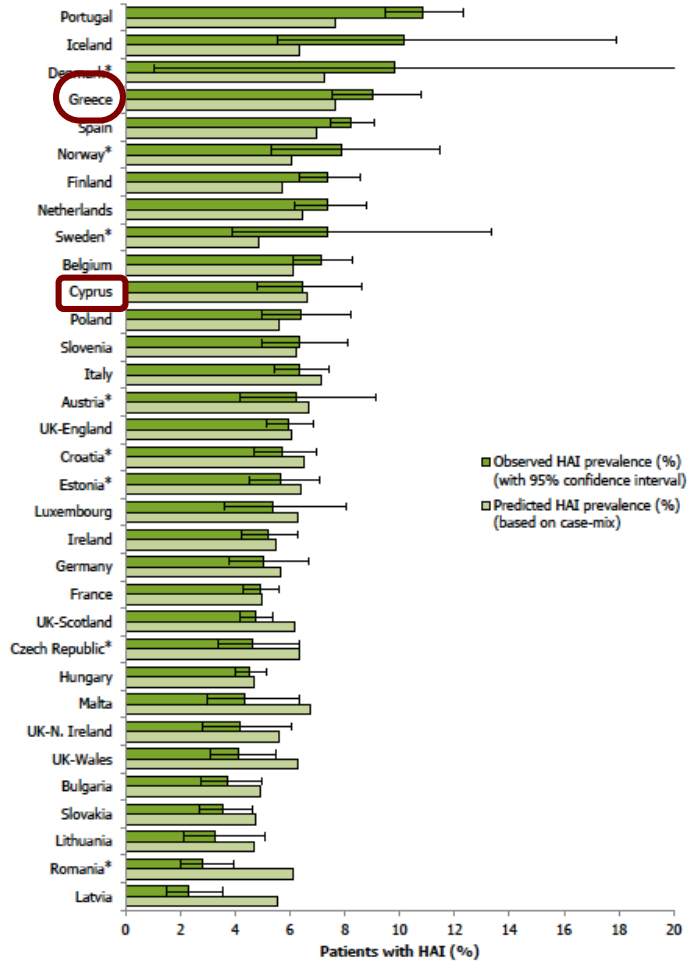


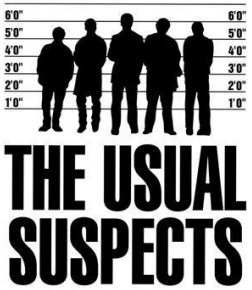
Figure 2. **Observed HAI prevalence with 95% confidence intervals and predicted HAI prevalence based on case mix and hospital characteristics, by country, ECDC PPS 2011–2012**



Most Important HAIs

- Health care-associated urinary tract infection (UTI)
  - Catheter-Associated Urinary Tract Infections (CAUTI)
- Health care-associated bloodstream infection (BSI)
  - Central Line-Associated Bloodstream Infections (CLABSI)
- Hospital-acquired pneumonia (HAP)
  - Ventilator-Associated Pneumonia (VAP)
- Surgical Site Infection (SSI)
- Clostridium difficile infection (CDI)

The microorganisms



- Enterococcus faecium
- **Staphylococcus aureus**
- **Klebsiella pneumoniae**
- **Acinetobacter baumanii,**
- **Pseudomonas aeruginosa**
- Enterobacter species

- **Clostridium difficile**

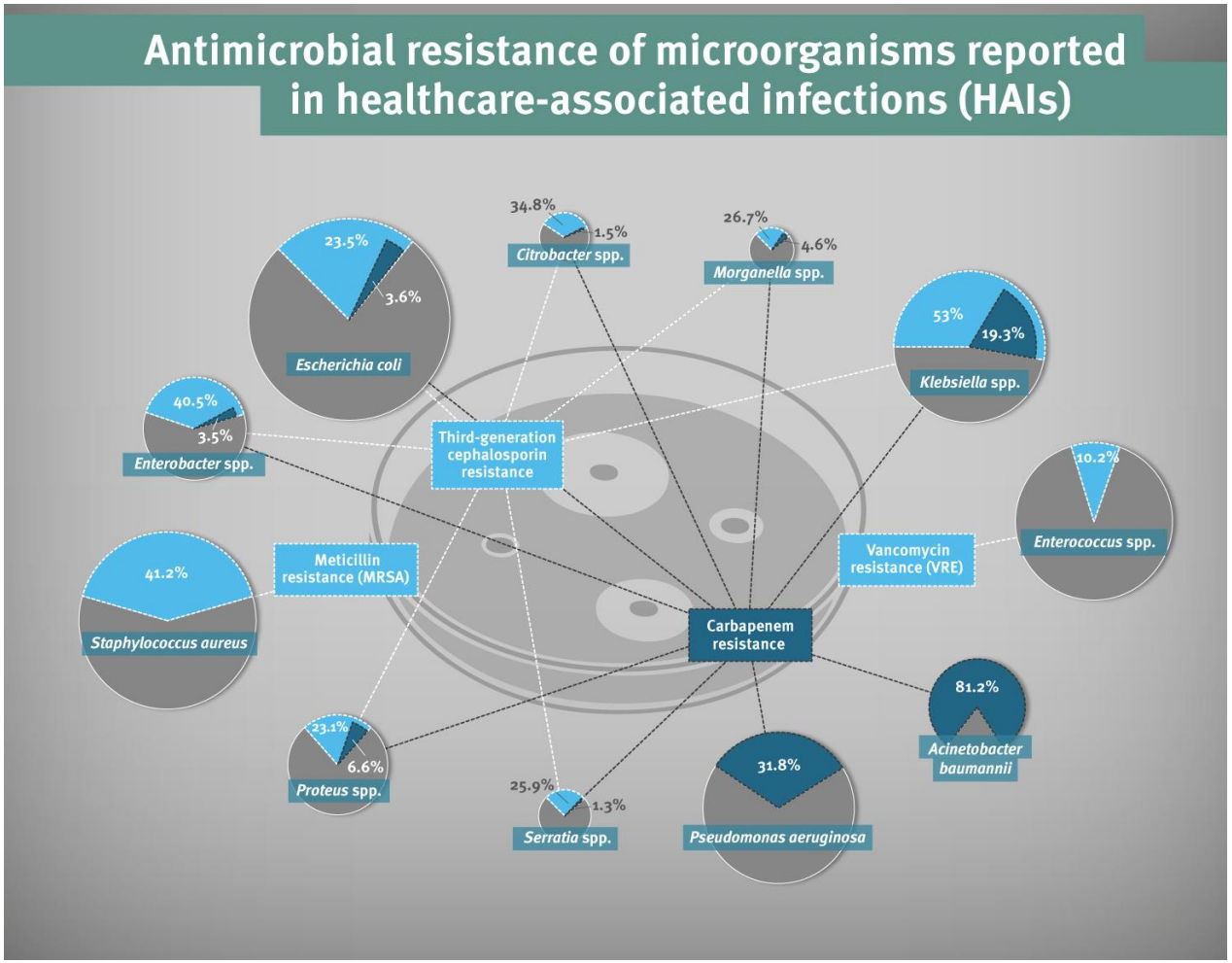
- cause the majority of hospital infections
- and effectively "escape" the effects of antibacterial drugs

Bad Bugs, No Drugs: No ESKAPE! An Update from the Infectious Diseases Society of America

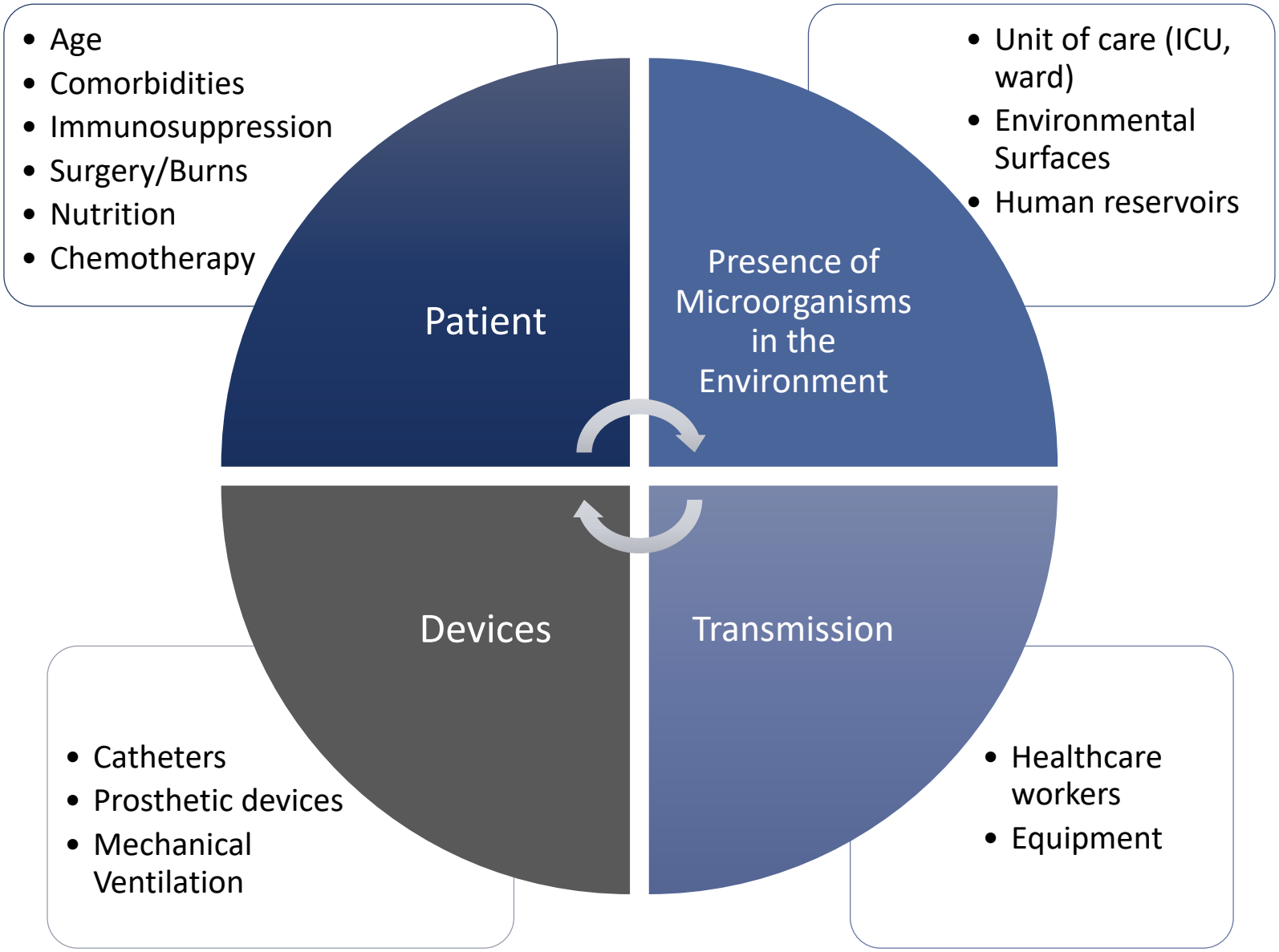
Helen W. Boucher,[1] George H. Talbot,[2] John S. Bradley,[3,4] John E. Edwards, Jr,[5,6,7] David Gilbert,[8] Louis B. Rice,[9,10] Michael Scheld,[11] Brad Spellberg,[5,6,7] and John Bartlett[12]

Rice LB. J Infect Dis 2008; 197:1079–81.

Antimicrobial Resistance in Healthcare-associated infections (HAIs)



ECDC PPS Study 2011.


Age
Comorbidities
Immunosuppression
Surgery/Burns
Nutrition
Chemotherapy
Unit of care (ICU, ward)
Environmental Surfaces
Human reservoirs
Patient
Presence of Microorganisms in the Environment
Devices
Transmission
Catheters
Prosthetic devices
Mechanical Ventilation
Healthcare workers
Equipment

BMC Infectious Diseases

BioMed Central

Research article

Open Access

How long do nosocomial pathogens persist on inanimate surfaces? A systematic review

Axel Kramer*[1], Ingeborg Schwebke[2] and Günter Kampf[1,3]

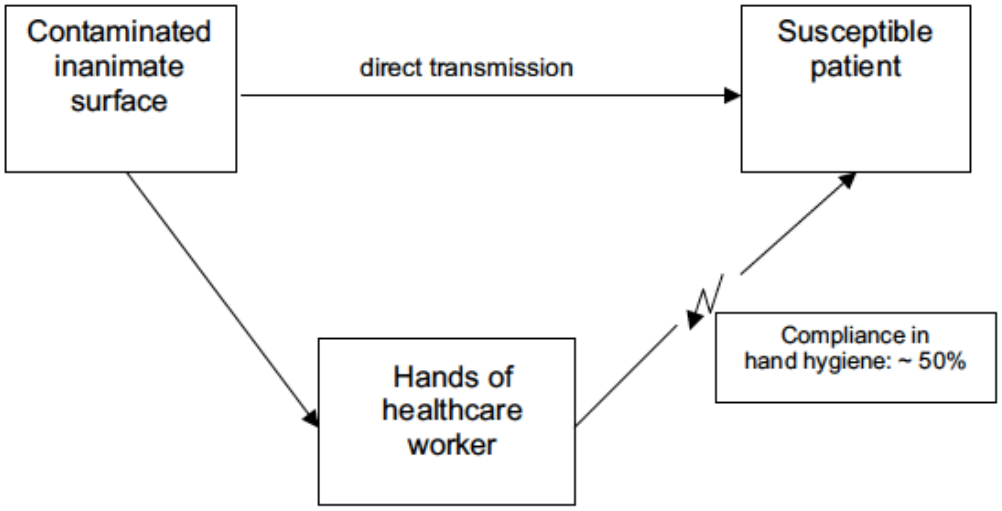
Pathogen	Duration of persistence
Acinetobacter spp.	3 days – 5 months
Clostridium difficile (spores)	5 months
Eschrrichia coli	1.5 hrs to 16 months
Enterococcus spp	5 days to 4 months
Klebsiella spp.	2 hrs to >30 months
Pseudomonas aeruginosa	6 hrs to 16 months (5 w on dry floor)
Staphylococcus aureus	7 days to 7 months

A single hand contact can result with a contaminated surface can result even to 100% transfer (i.e. Escherichia coli, S. aureus)

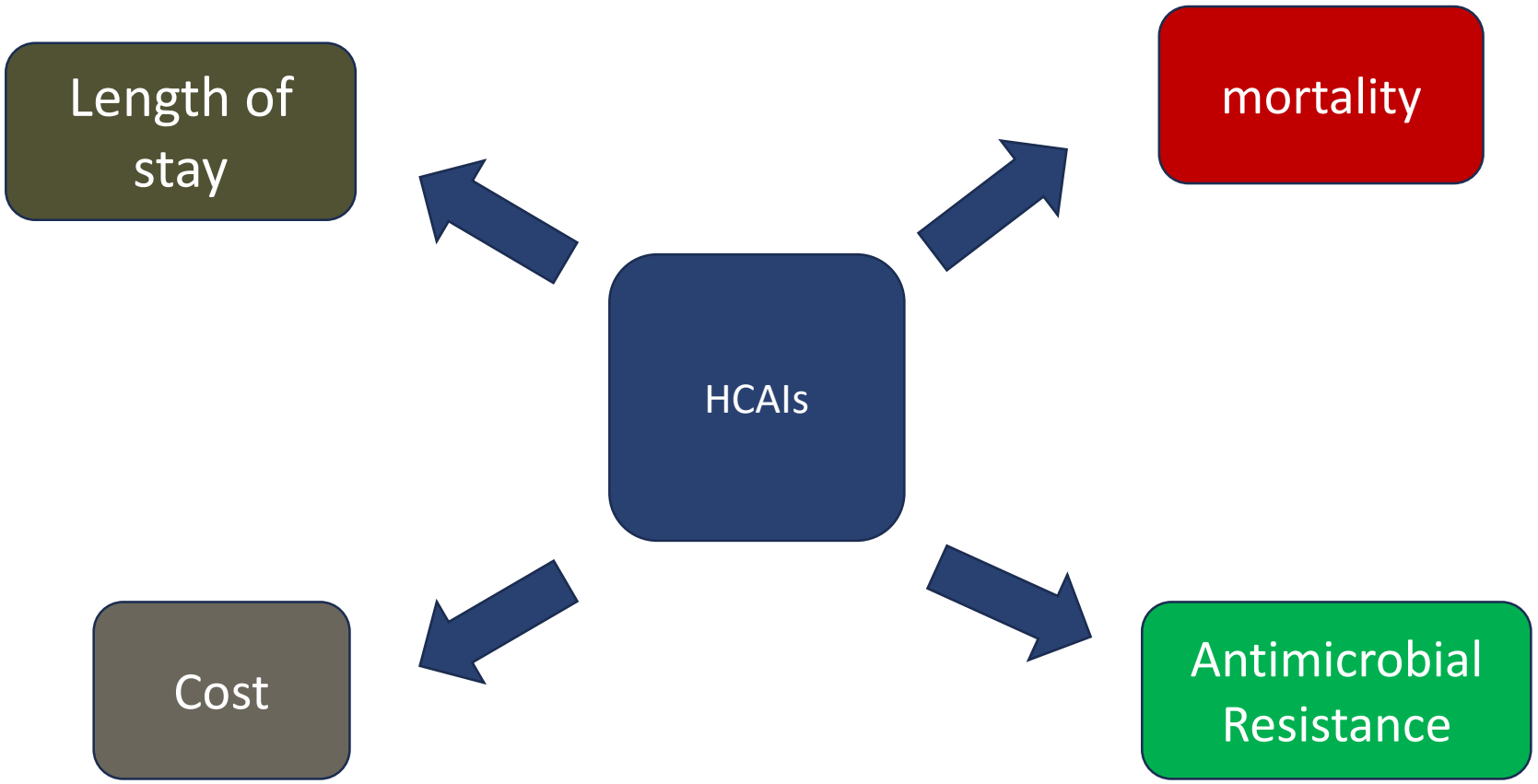
Kramer A. et al., BMC Inf Dis 2006

Transmission

Human reservoir:
1. Persons with acute or subclinical illness
2. Carriers
convalescent carriers
chronic carriers
intermittent carriers



Kramer A. et al., BMC Inf Dis 2006


Length of stay
mortality
HCAIs
Cost
Antimicrobial Resistance

Healthcare-associated infections and Outcomes - Mortality

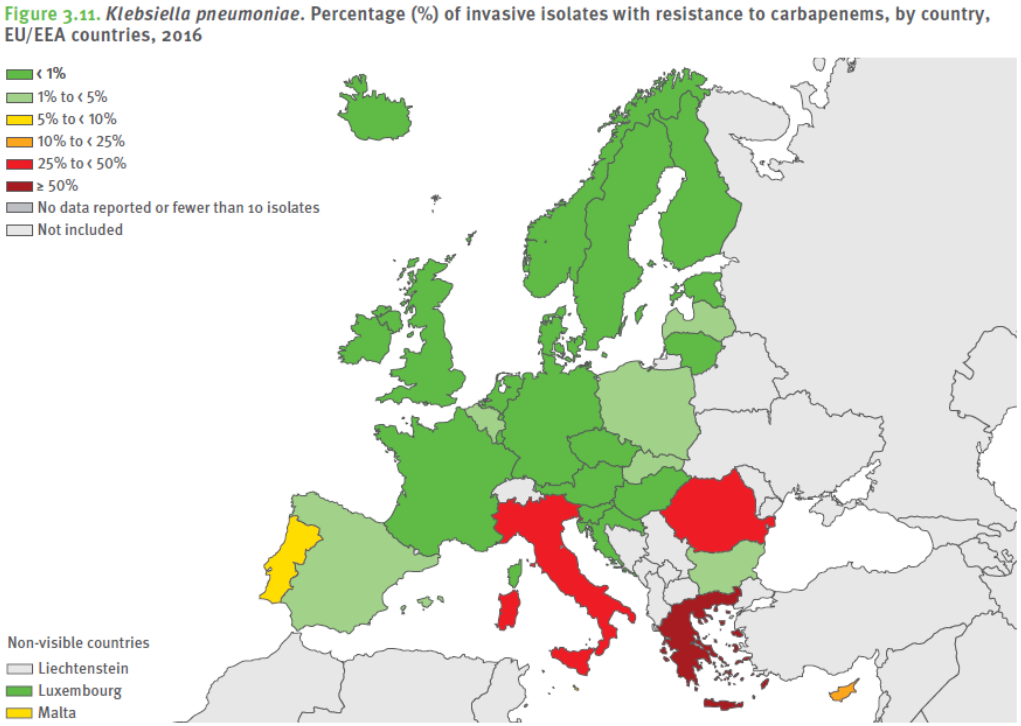
- USA
  - Approximately 90,000 deaths
  - CLABSI:12.3-35%, VAP:14.4%, CAUTI:2.3%, SSI:2.8%

Klevens RM, et al. Public HealthRep 2007;122(2):160-6.

Pittet D, Harbarth S. Lancet1998;352(9122):83-4.

- Europe (ECDC)
  - 37.000 deaths/year attributed to HAI
  - HAIs contribute additionally to 110.000 deaths/year

Carbapenem resistant Klebsiella pneumoniae



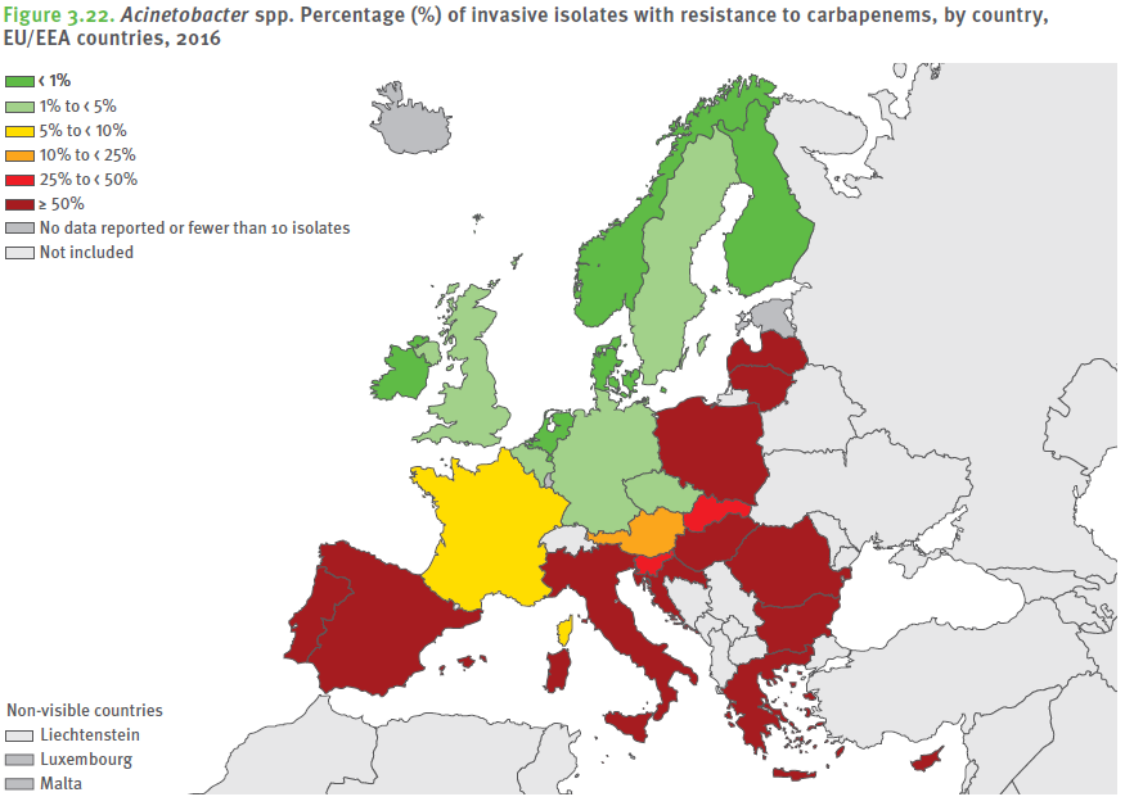
<u>Cyprus</u>

- **Klebsiella pneumoniae**
  - Carbapenem resistance (All invasive isolates)
    - 2014: **5%**
    - 2016: **10.7%**

ECDC

European Antimicrobial Resistance Surveillance Network (ERAS-Net) 2016 Report

Multidrug resistant Acinetobacter baumanii



<u>Cyprus</u>

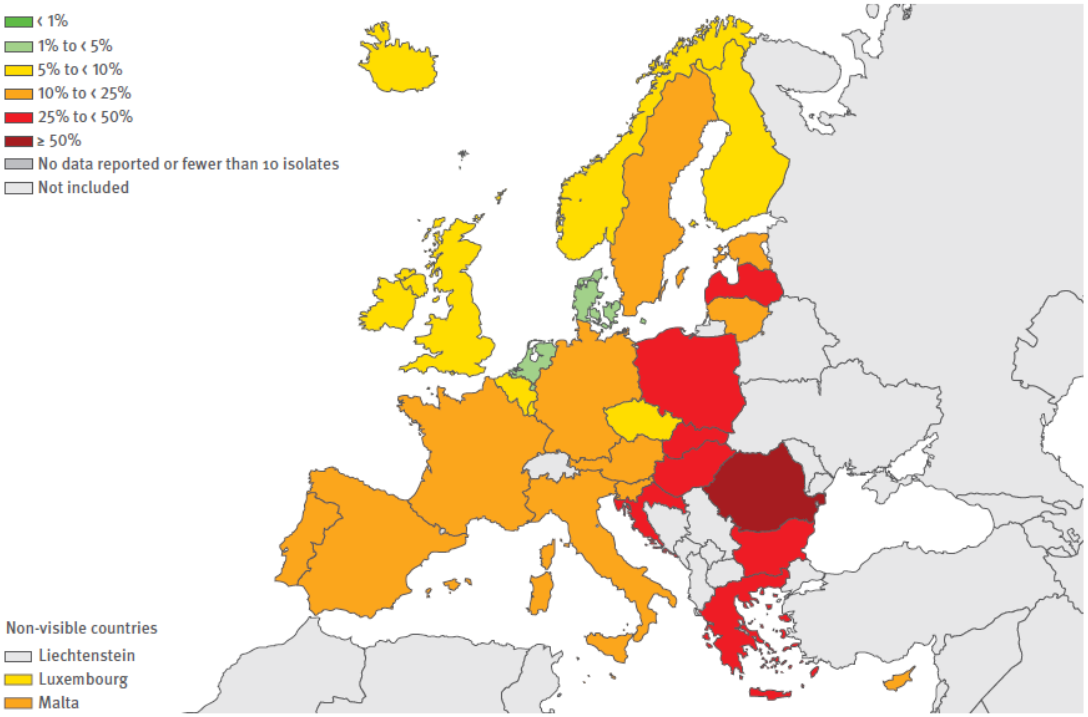
- **Acinetobacter baumannii**
  - Carbapenem resistance (All invasive isolates)
    - 2014: **77.6%**
    - 2016: **71.4%**

ECDC

European Antimicrobial Resistance Surveillance Network (ERAS-Net) 2016 Report

Multidrug resistant Pseudomonas aeruginosa

Figure 3.17. *Pseudomonas aeruginosa*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2016



Cyprus

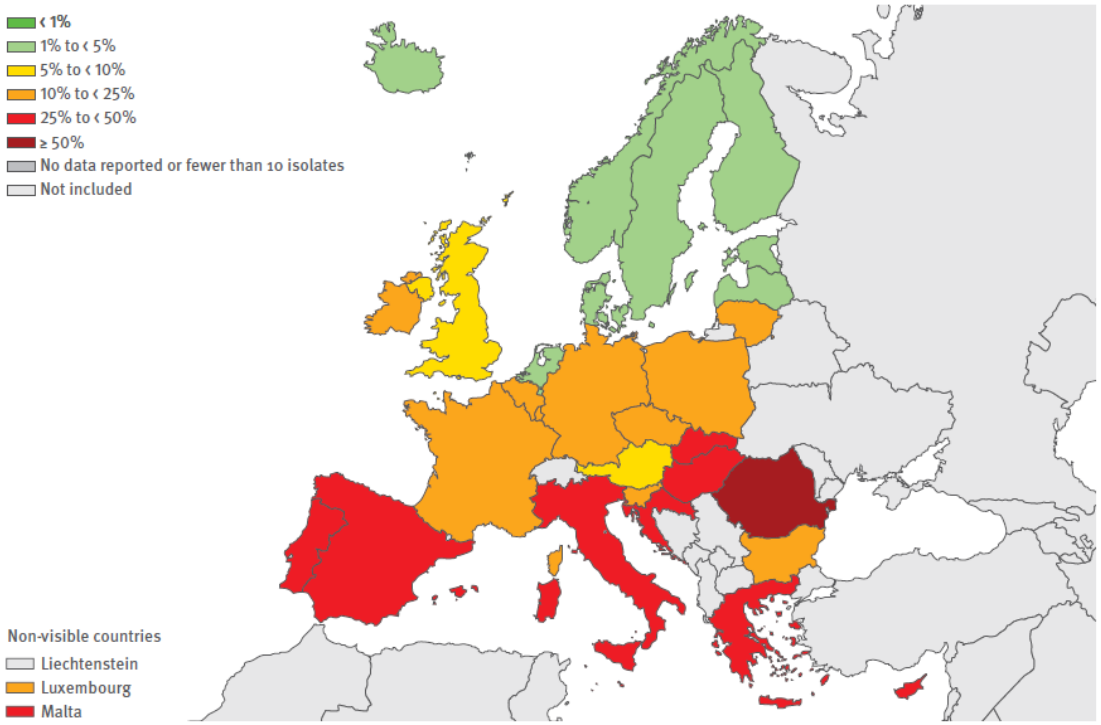
- **Pseudomonas aeruginosa**
  - Carbapenem resistance (All invasive isolates)
    - 2014: **33.3%**
    - 2016: **18.8%**

ECDC

European Antimicrobial Resistance Surveillance Network (ERAS-Net) 2016 Report

Methicillin-resistant S. aureus (MRSA)

Figure 3.25. *Staphylococcus aureus*. Percentage (%) of invasive isolates with resistance to meticillin (MRSA), by country, EU/EEA countries, 2016



Cyprus

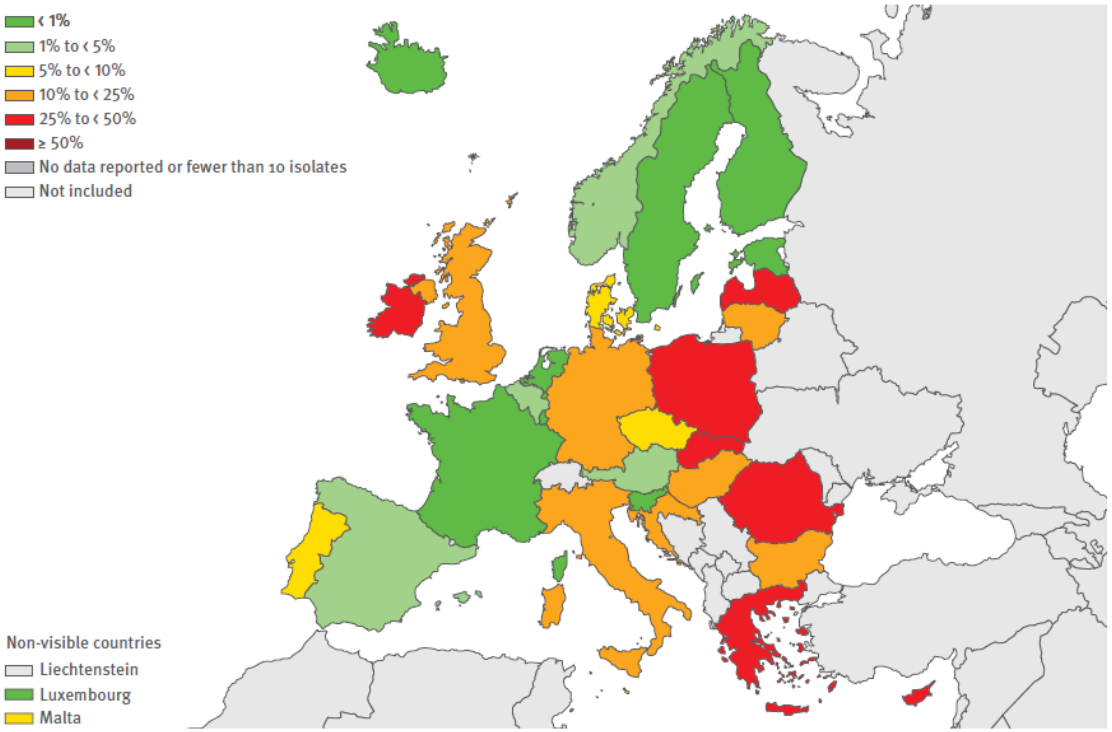
- **MRSA**
  - (All invasive isolates)
    - 2014: **36%**
    - 2016: **38.8%**

ECDC

European Antimicrobial Resistance Surveillance Network (ERAS-Net) 2016 Report

Vancomycin-resistant Enterococcus (VRE)

Figure 3.28. *Enterococcus faecium*. Percentage (%) of invasive isolates with resistance to vancomycin, by country, EU/EEA countries, 2016



Cyprus

- **VRE**
  - (All invasive isolates)
    - 2014: **40%**
    - 2016: **46.3%***

*Υψηλότερο ποσοστό μεταξύ των Ευρωπαϊκών χωρών

ECDC

European Antimicrobial Resistance Surveillance Network (ERAS-Net) 2016 Report

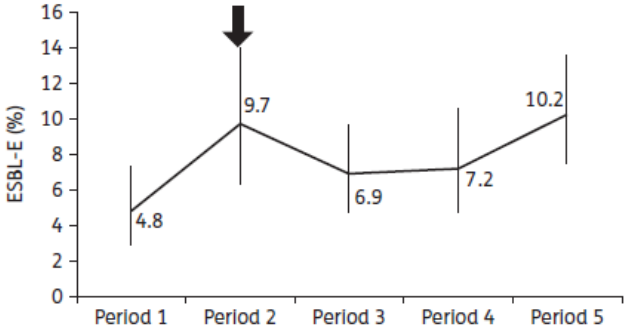
Birgy et al. BMC Infectious Diseases 2012, 12:315
http://www.biomedcentral.com/1471-2334/12/315

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Community faecal carriage of extended-spectrum beta-lactamase-producing *Enterobacteriaceae* in french children

André Birgy[1], Robert Cohen[2], Corinne Levy[2], Philippe Bidet[1], Céline Courroux[1], Mohamed Benani[2], Franck Thollot[3] and Edouard Bingen[1,4*]



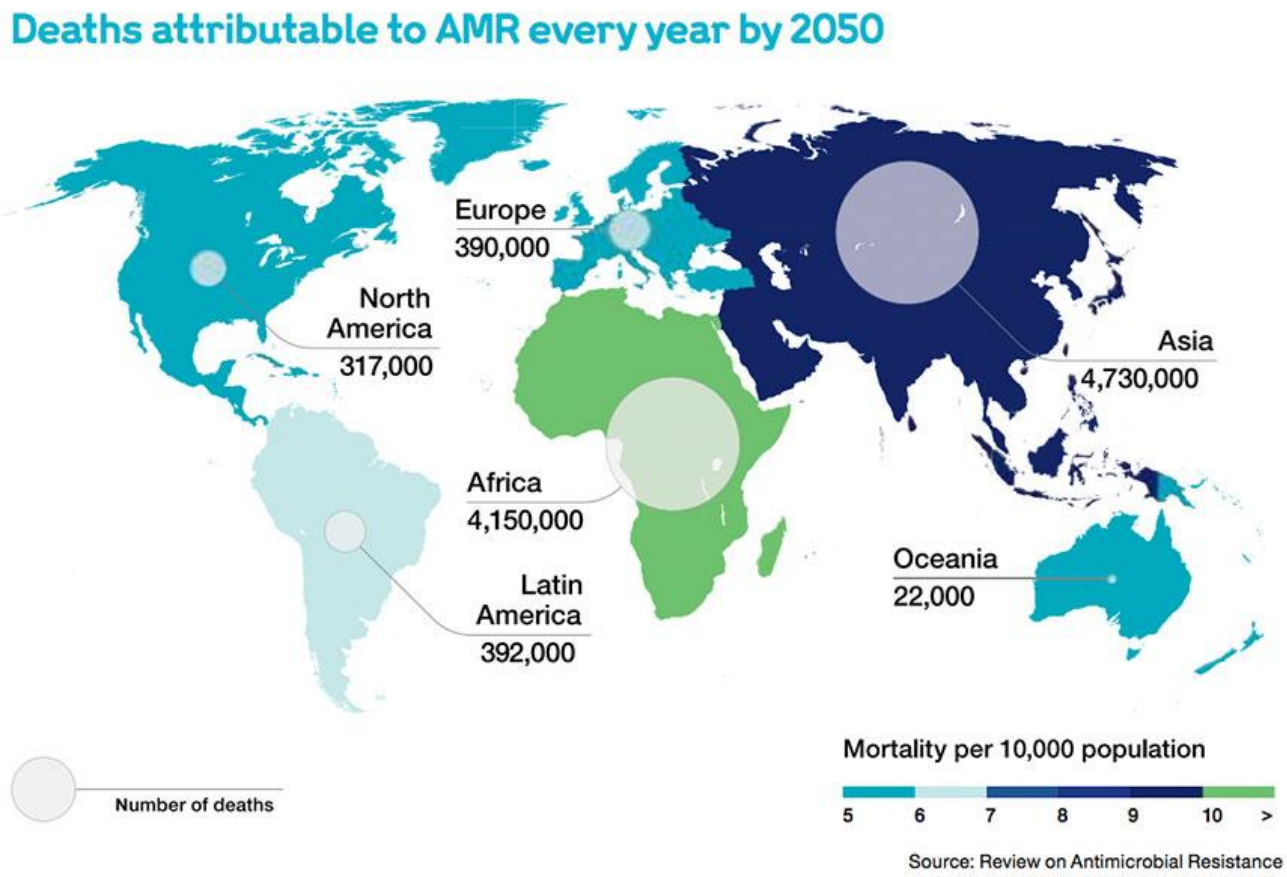
J Antimicrob Chemother 2016; **71**: 2949–2956
doi:10.1093/jac/dkw219 Advance Access publication 20 June 2016

Journal of Antimicrobial Chemotherapy

ESBL-producing *Escherichia coli* ST131 versus non-ST131: evolution and risk factors of carriage among French children in the community between 2010 and 2015

André Birgy[1–3], Corinne Levy[4–6], Philippe Bidet[1–3], Franck Thollot[4,7], Véronique Derkx[4], Stéphane Béchet[4], Patricia Mariani-Kurkdjian[3], Robert Cohen[4–6,8] and Stéphane Bonacorsi[1–3]*

Conclusions: Between 2010 and 2015, the carriage of ESBL-E in community children doubled because of the massive expansion of the *E. coli* ST131 clonal group. The risk for carrying ST131 was associated with previous hospitalization, but not, contrary to the counterpart, antibiotic treatment, daycare attendance or travel history.



Sustaining global action on antimicrobial resistance
United Nations Foundation and Wellcome Charitable Trust

GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE

Five strategic objectives:

1. Improve awareness and understanding
2. Strengthen the knowledge through surveillance and research
3. Reduce the incidence of infection
4. Optimize the use of antimicrobial medicines
5. Ensure sustainable investment

ANTIBIOTIC RESISTANCE
WHAT YOU CAN DO

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

1. Only use antibiotics when **prescribed** by a certified health professional
2. Always take the **full prescription**, even if you feel better
3. **Never use left over** antibiotics
4. **Never share** antibiotics with others
5. **Prevent infections** by regularly washing your hands, avoiding contact with sick people and keeping your vaccinations up to date

www.who.int/drugresistance
#AntibioticResistance

World Health Organization

ANTIBIOTIC RESISTANCE
WHAT CAN HEALTH WORKERS DO?

HANDLE ANTIBIOTICS WITH CARE

Antibiotic Resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

- ✓ Are your **hands, instruments & environment clean**?
- ✓ Do you **only prescribe & dispense antibiotics when** they are **needed**, according to current guidelines?
- ✓ Do you **report drug-resistant infections** to surveillance teams?
- ✓ Do you **talk to patients** about **how to take antibiotics correctly, antibiotic resistance** & the **dangers of misuse**?
- ✓ Do you talk to patients about **preventing infections** (e.g. vaccination, hand washing, safer sex, covering nose & mouth when sneezing)?

AntibioticResistance www.who.int/waaw

World Health Organization

ANTIBIOTIC RESISTANCE
WHAT THE AGRICULTURE SECTOR CAN DO

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

1. Ensure that antibiotics given to animals—including food-producing and companion animals—are **only used to control or treat** infectious diseases and under veterinary supervision
2. **Vaccinate** animals to reduce the need for antibiotics and **develop alternatives** to the use of antibiotics in plants
3. Promote and apply **good practices** at all steps of production and processing of foods from animal and plant sources
4. Adopt **sustainable systems** with improved hygiene, biosecurity and stress-free handling of animals
5. Implement **international standards** for the responsible use of antibiotics and guidelines, set out by OIE, FAO and WHO

www.who.int/drugresistance
www.oie.int/antimicrobial-resistance
www.fao.org/antimicrobial-resistance
#AntibioticResistance

Food and Agriculture Organization of the United Nations
OIE WORLD ORGANISATION FOR ANIMAL HEALTH
World Health Organization

ANTIBIOTIC RESISTANCE
WHAT POLICY MAKERS CAN DO

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

1. Ensure you have a robust **national action plan** to tackle antibiotic resistance
2. Improve **surveillance** of antibiotic-resistant infections
3. Strengthen **infection prevention** and control measures
4. **Regulate and promote** the appropriate use of quality medicines
5. Make information on the **impact** of antibiotic resistance available

www.who.int/drugresistance
#AntibioticResistance

World Health Organization

Thank you for your attention

Illustration by Hvass & Hannibal