

Towards a strategy on the containment of antibiotic resistance in the WHO European Region



Presentation overview

- Background
- Seven-point regional strategic action plan
- World Health Day, 7 April 2011

Antimicrobial resistance globally



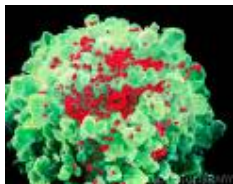
- Tuberculosis (TB)

- 440 000 new multidrug-resistant (MDR) TB cases annually
- 58 countries report extremely drug-resistant (XDR) TB
- In the WHO European Region, about 81 000 cases annually



- Malaria

- Emergence of artemisinin resistance, linked to the ongoing use of monotherapy
- In the WHO European Region, 167 autochthonous cases in 2009, target for elimination by 2015



- HIV

- Evidence of emerging resistance with the expanded use of antiretroviral therapy
- In the WHO European Region, HIV/AIDS programmes monitor resistance

- Antibiotic resistance is emerging for many infectious diseases caused by bacteria, including those acquired in health care settings

Antibiotic resistance in the WHO European Region

(Antibiotics are a class of antimicrobial drugs)

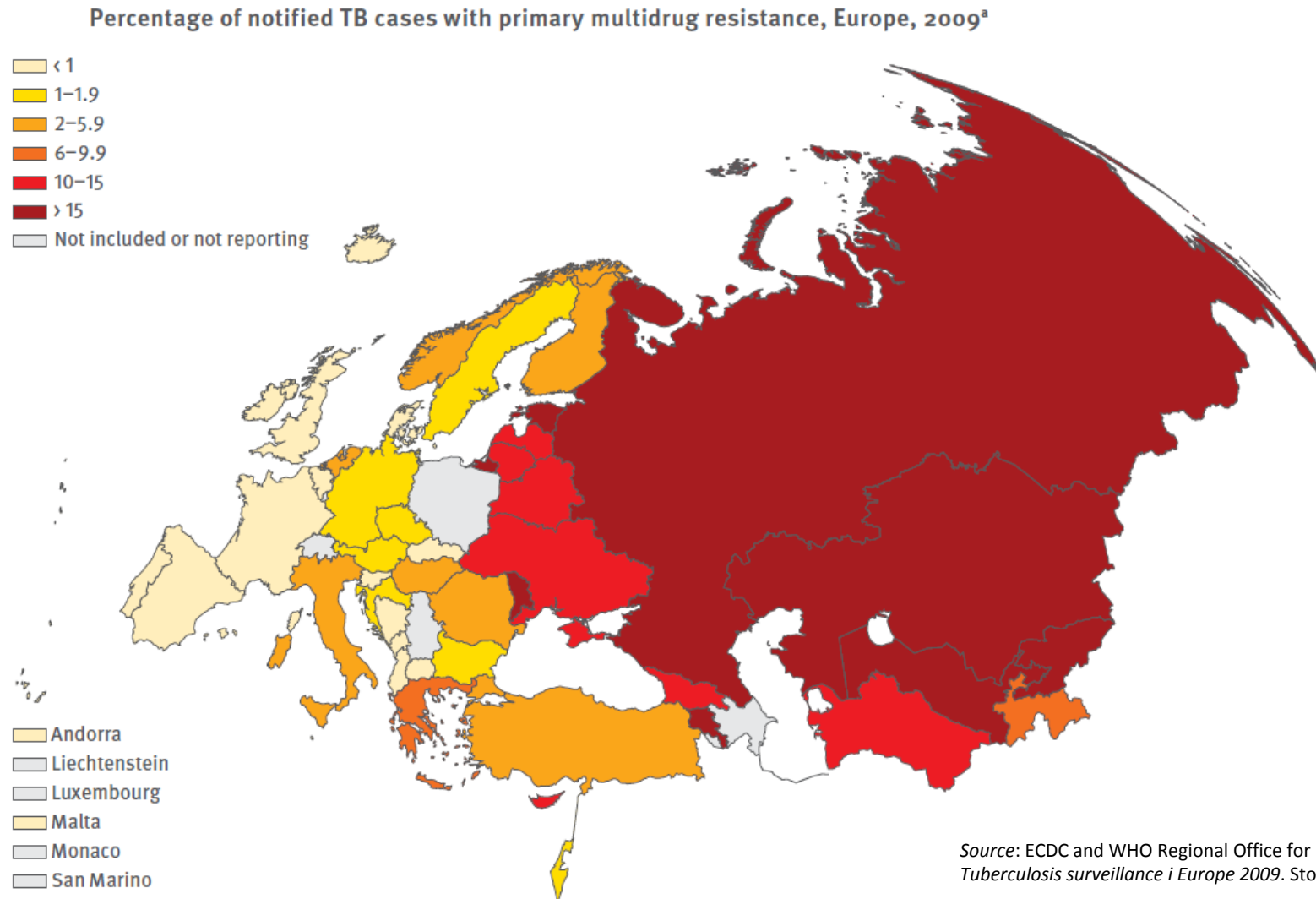
Most information comes from the European Union (EU), Iceland, Liechtenstein and Norway, representing about 55% of the total regional population of 900 million.

- In the EU (plus Iceland and Norway), 400 000 resistant hospital-acquired bacterial infections every year
- 25 000 people die from these infections every year
- 2.5 million extra hospital days annually, costing more than €900 million.
- 81 000 cases of MDR or XDR TB annually

Source: ECDC and European Medicines Agency. The bacterial challenge: time to react. A call to narrow the gap between multidrug-resistant bacteria in the EU and the development of new antibacterial agents. Stockholm, ECDC, 2009.

Tuberculosis

Proportion of TB cases with primary resistance, 2009
(actual detection rate is 34%)



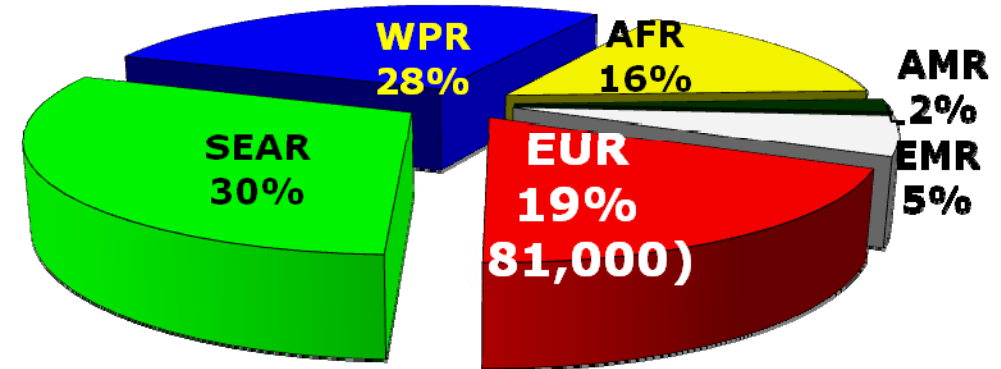
Source: ECDC and WHO Regional Office for Europe.
Tuberculosis surveillance in Europe 2009. Stockholm, ECDC.

^a Data from Kosovo (in accordance with Security Council Resolution 1244 (1999)) is not included in the figures reported for Serbia

Estimated MDR-TB prevalence in European Region countries (with these 15 countries being among those with the highest rates globally)

	New (%)	Re-treated (%)
Azerbaijan	22.3	55.8
Republic of Moldova	19.4	50.8
Tajikistan	16.5	61.6
Ukraine	16.0	44.3
Russian Federation	15.8	42.4
Estonia	15.4	42.7
Kazakhstan	14.2	56.4
Uzbekistan	14.2	49.8
Kyrgyzstan	12.5	42.1
Belarus	12.5	42.1
Bulgaria	12.5	42.1
Latvia	12.1	31.9
Armenia	9.4	43.2
Lithuania	9.0	47.5
Georgia	6.8	27.4

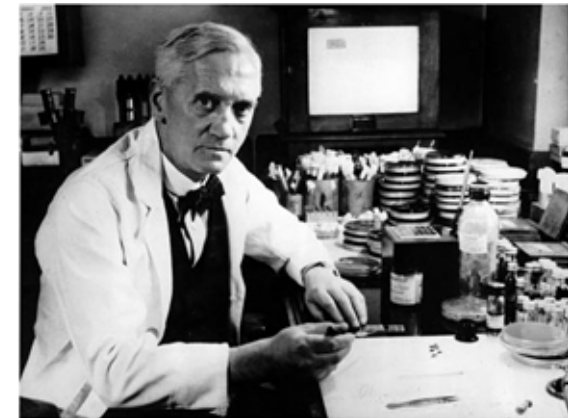
**MDR-TB burden
global estimates for 2008**



Globally 440 000 cases estimated

The main cause of antibiotic resistance

- Antibiotic resistance is a natural adaptation of microorganisms to products that try to stop their growth
- Use of antibiotics will lead to resistance, as was predicted by Alexander Fleming
- **Especially the overuse and misuse of antibiotics** in humans and livestock and poor infection prevention and control are responsible for the emergence and spread of antibiotic resistance
- Important link between the use of antibiotics in livestock and resistance to bacteria affecting humans

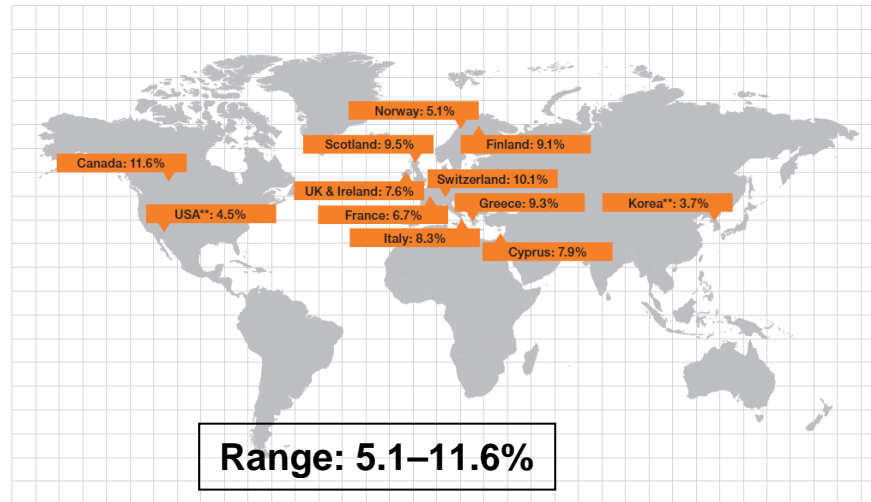


Alexander Fleming

Prevalence of hospital-acquired infections worldwide

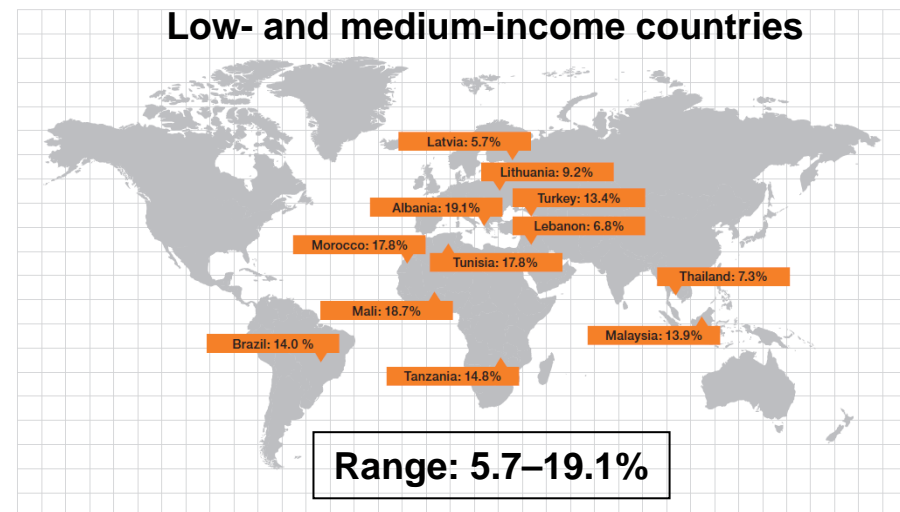
High-income countries

Figure 1 Prevalence of HCAI in developed countries*



* Systematic review conducted by WHO, 1995-2008
** Incidence

Figure 2 Prevalence of HCAI in developing countries*

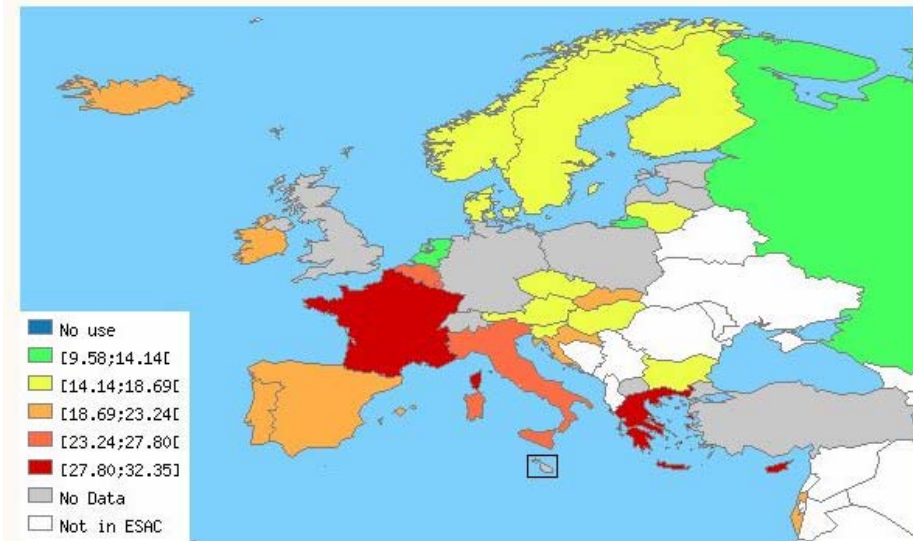


* Systematic review conducted by WHO, 1995-2008

Source: *The burden of health care-associated infection worldwide: a summary*. Geneva, World Health Organization, 2009.

European Surveillance of Antimicrobial Consumption (ESAC)

- Continual collection of comprehensive data on consumption of antimicrobial agents from ambulatory and hospital care
- ESAC III (2007–2010)
- North-south gradient

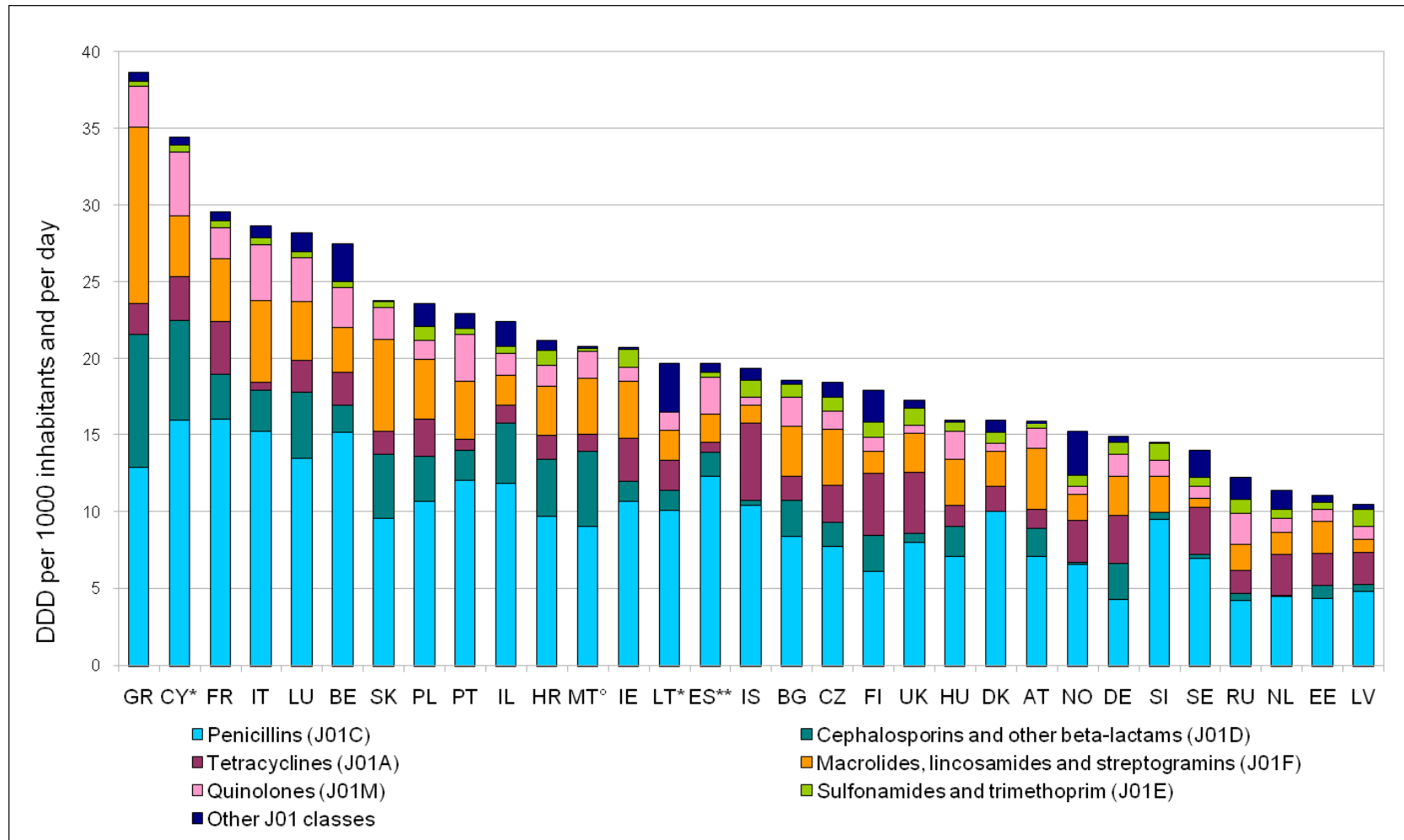


Defined daily doses per 1000 inhabitants per day

Source: ESAC, a project funded by the European Centre for Disease Prevention and Control.

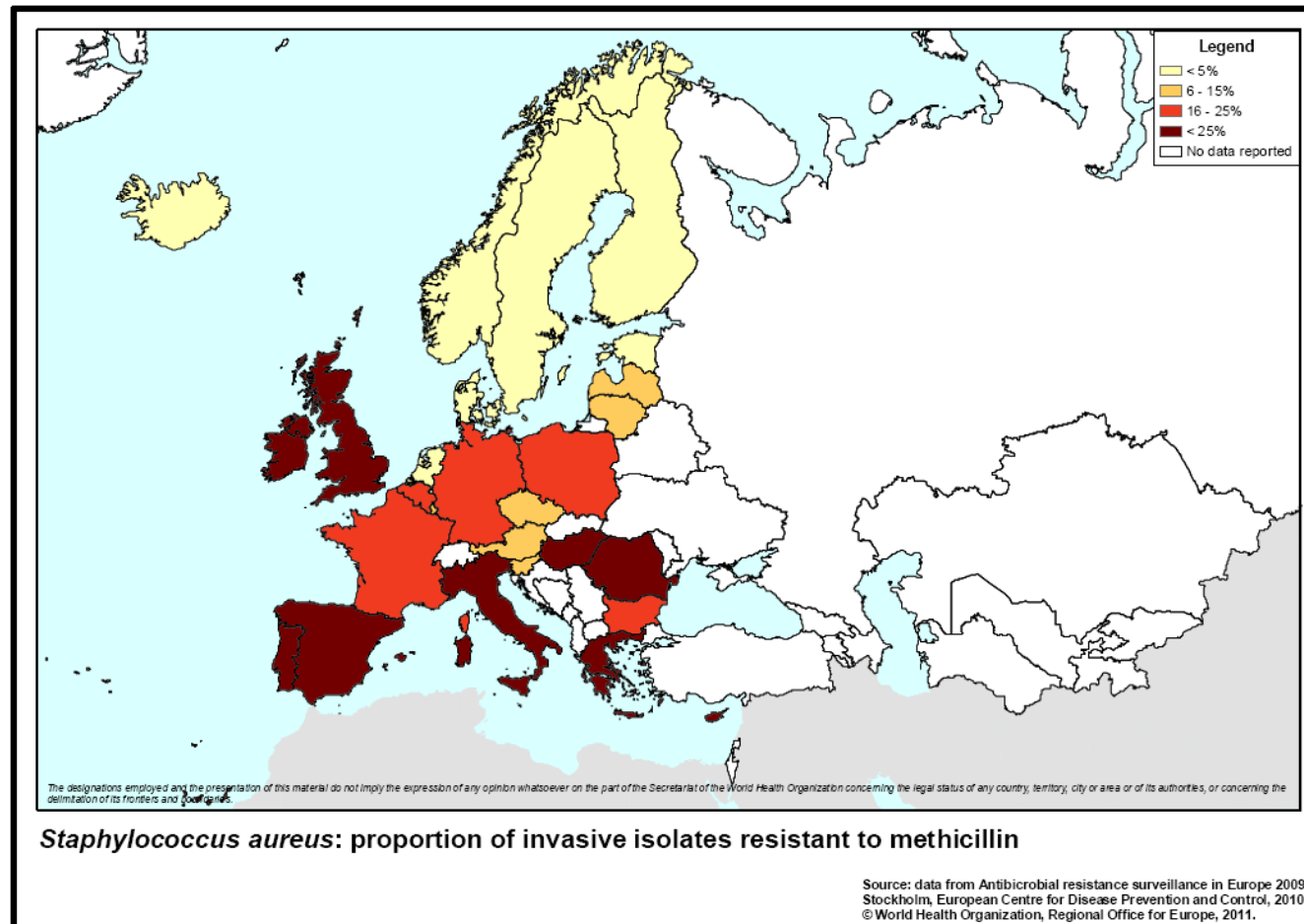
Total outpatient antibiotic use in 31 European countries, 2009

(defined daily doses per 1000 inhabitants per day)

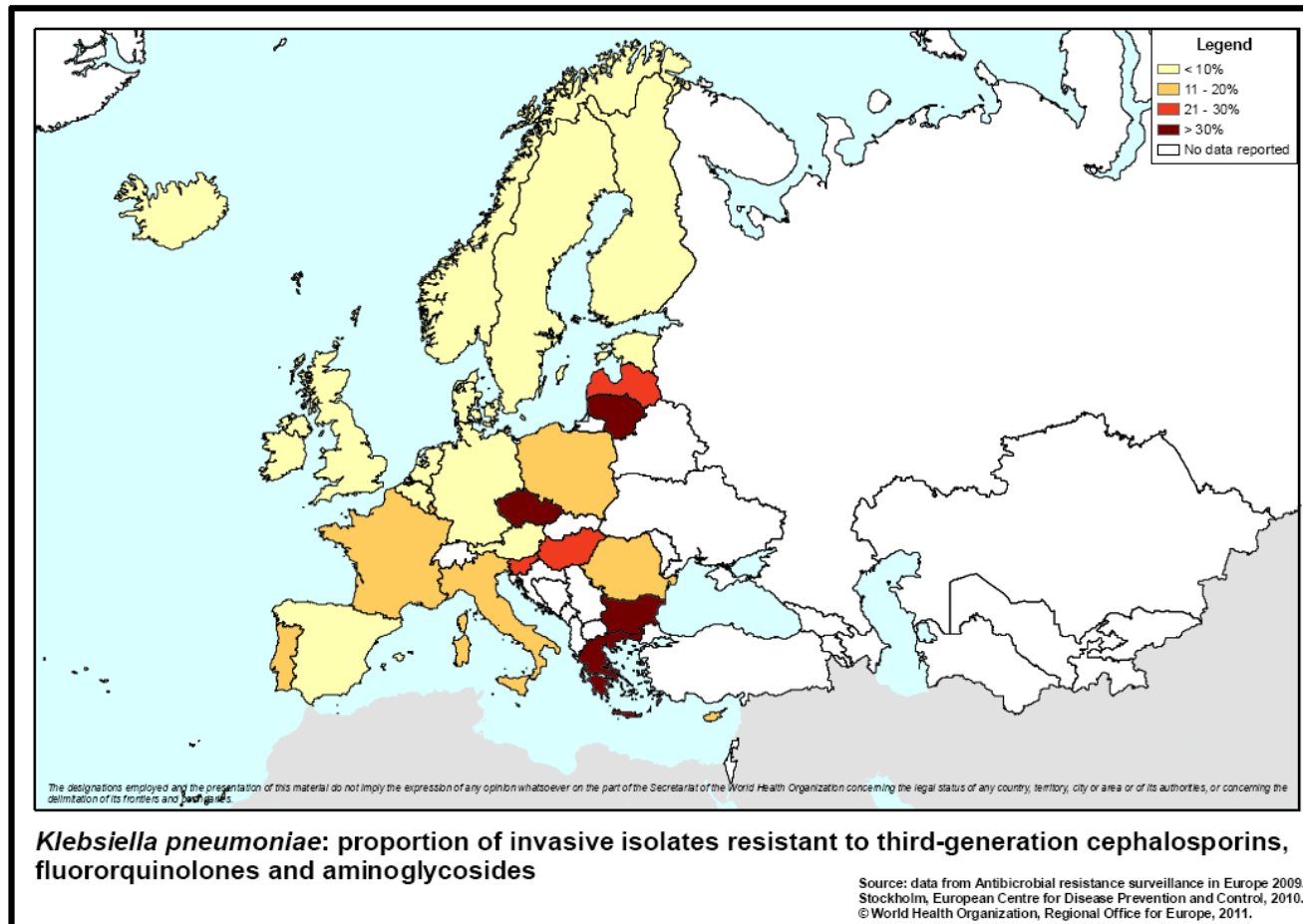


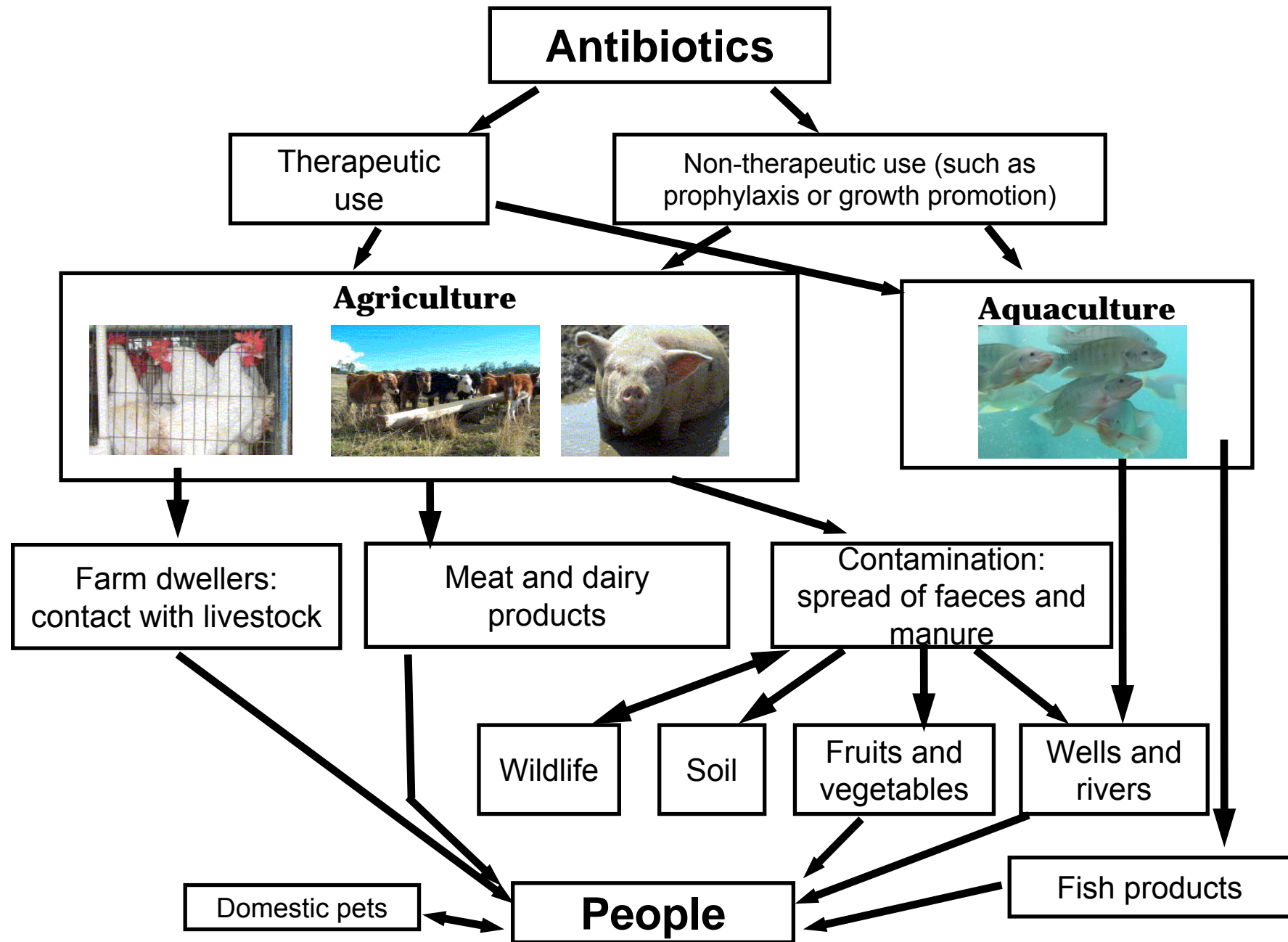
Courtesy of Herman Goossens, University of Antwerp, ESAC.

Resistance to methicillin among *Staphylococcus aureus* (MRSA) in the EU, Iceland and Norway, 2009



Multiantibiotic resistance to *Klebsiella pneumoniae* in the EU, Iceland and Norway, 2009



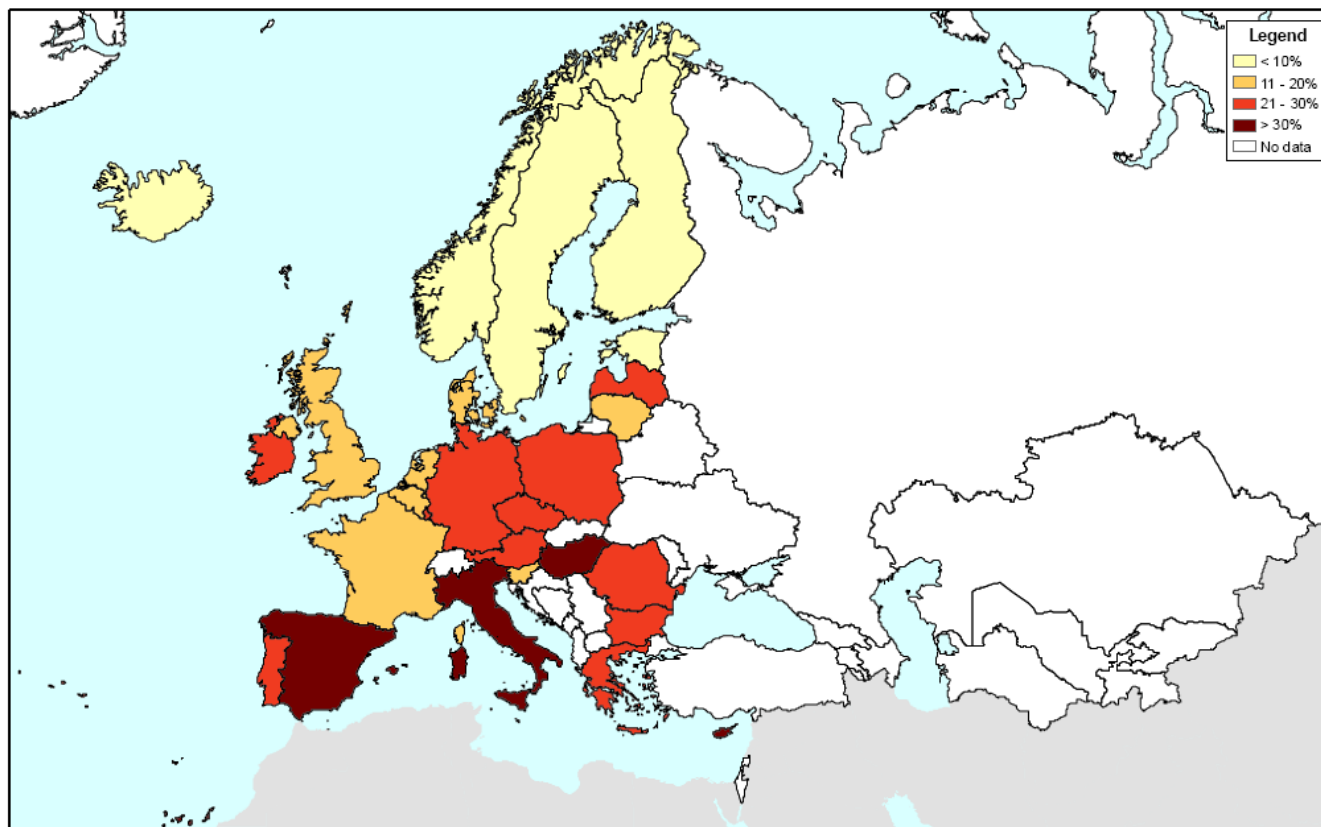


Antibiotic use in livestock production

- For therapeutic purposes
- For prophylaxis
- For growth promotion
 - Banned in the EU since 2006
- Use in livestock is substantial
 - Same antibiotic classes as in human medicine (some critical for human medicine, such as fluoroquinolones)
 - Seems to outweigh use for humans in some countries
 - Nordic countries have relatively low use owing to prudent-use policies



Resistance to fluoroquinolones among *Escherichia coli* in the EU, Iceland and Norway, 2009

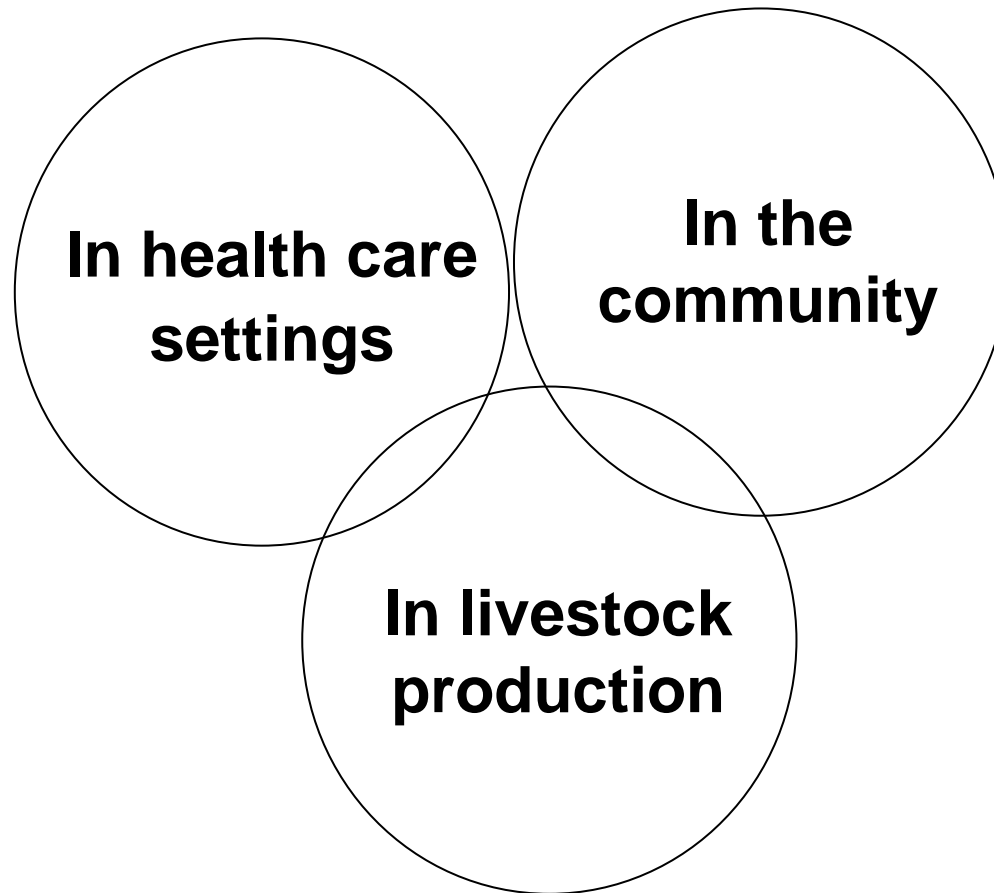


Escherichia coli: proportion of invasive isolates with resistance to fluoroquinolones

Source: data from Antimicrobial resistance surveillance in Europe 2009. Stockholm, European Centre for Disease Prevention and Control, 2010. © World Health Organization 2011.

The main driver of antimicrobial resistance

is “use” but especially overuse, misuse and underuse
Increasing evidence on the interconnections



Resistance under surveillance

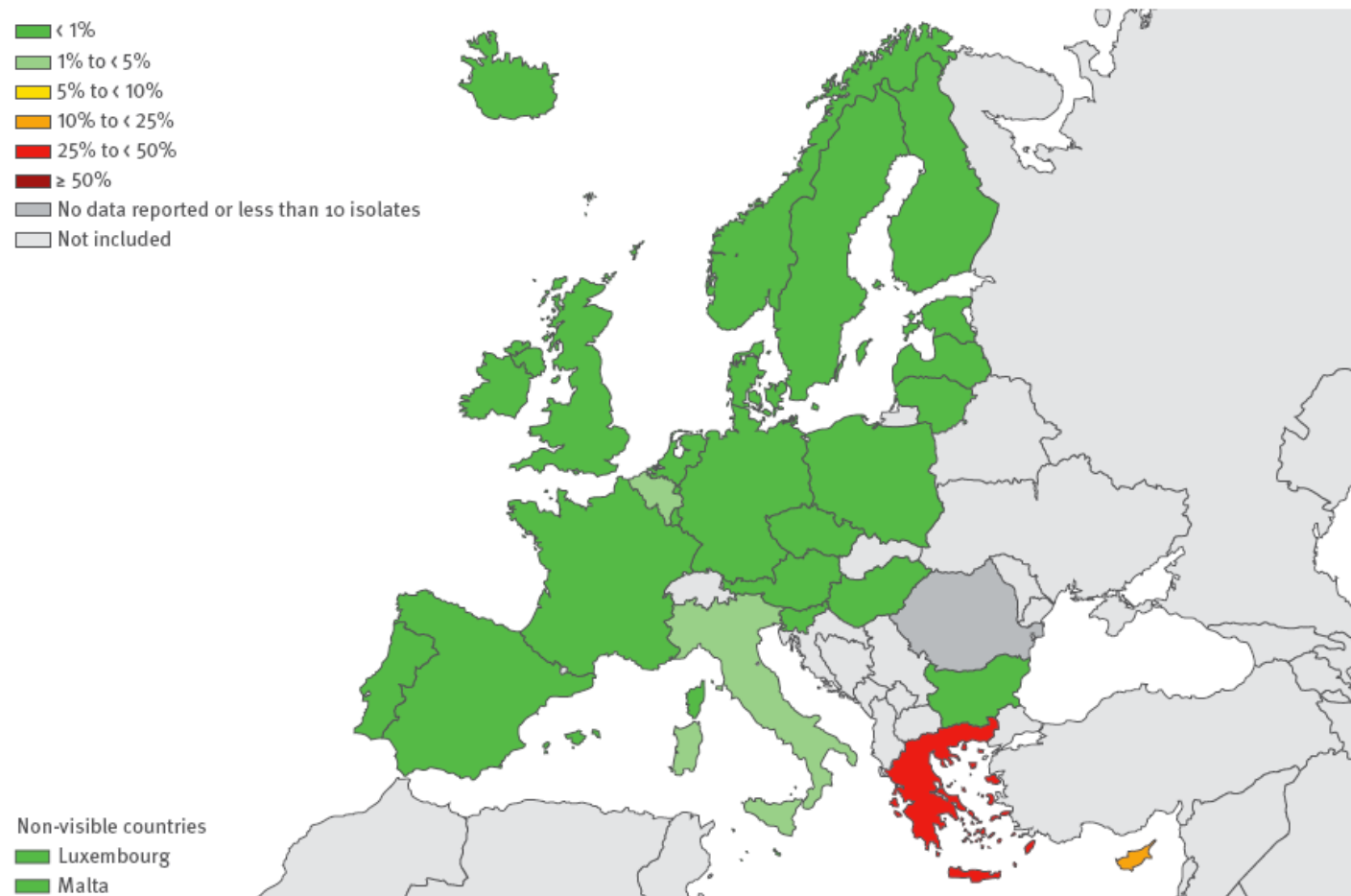
Emerging resistance mechanisms are new threats to last-resource antibiotics such as **carbapenems**

- Involves bacteria that have carbapenemase enzyme that make carbapenems inactive
- Well-known New Delhi metallo-beta-lactamase 1 or NDM-1
- Other types of carbapenemase exist (KPC, VIM, OXA-48)
- Often associated with travel history or transfer between hospitals
- *Klebsiella pneumoniae* most frequently involved
- In 2010, 13 countries reported 77 cases in the EU
- Hand hygiene and infection control can be very effective
- Are considered an **urgent public health** issue

Source: Eurosurveillance, 2010, 15(46).

Resistance to carbapenems among *Klebsiella pneumoniae* in the EU, Iceland and Norway, 2009

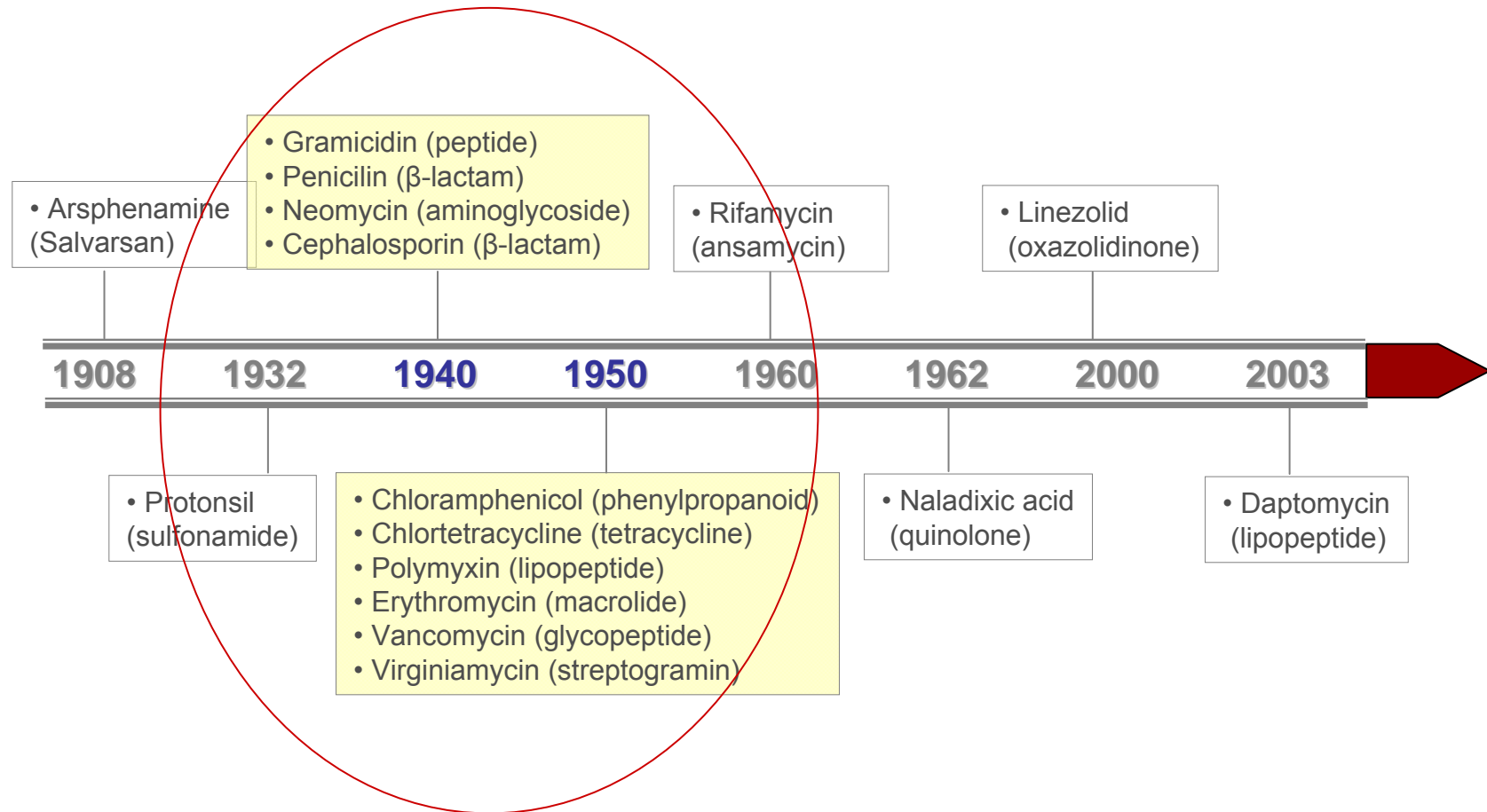
Figure 5.25: *Klebsiella pneumoniae*: proportion of invasive isolates resistant to carbapenems in 2009



Source: Antimicrobial resistance surveillance in Europe 2009. Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm, ECDC, 2010.

Discovery of antibiotics

The end of an era? **Few new classes over the past 50 years**



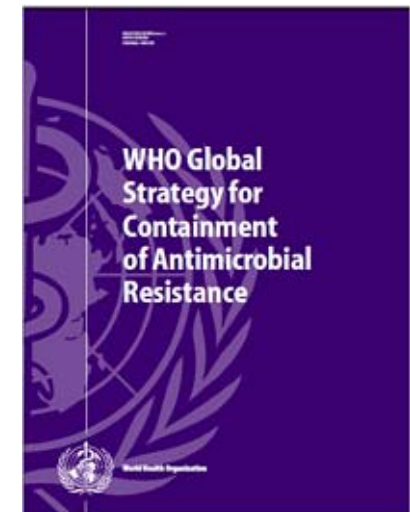
Source: Wright GD. The antibiotic resistome: the nexus of chemical and genetic diversity. *Nature Reviews Microbiology*, 2007, 5:175–186.

In addition, in many countries:

- Many health care systems are in transition in eastern Europe
- Many countries lack national surveillance systems on resistance
- Lack of laboratory capacity, and standards not uniform
- Over-the-counter sales of antibiotics
- Excessive prescription of antibiotics for infections that are not bacterial
- Use of antibiotics for healthy animals in many countries
- Using antibiotics as a growth promoter only banned in EU countries
- Poor infection control and hand-hygiene standards
- Lack of awareness on the emergence of antibiotic resistance, and the urgent need for action is not recognized
- Lack of training in the prudent use of antibiotics in medical and health-related faculties

Justification

- **World Health Assembly resolutions** 1984, 1998, 2001, 2005
- **WHO Global Strategy for Containment of Antimicrobial Resistance** published in 2001
- Strategy to combat antimicrobial resistance for EU countries (2001)
- Strong development of surveillance, guidance and tools in the EU by the ECDC and European Food Safety Authority
- Member States in transition require support and guidance
- **Need for a coherent and operational regional strategy**



Seven objectives in the WHO European strategy

1. Promote national coordination
2. Strengthen the surveillance of antibiotic resistance
3. Promote the rational use of antibiotics, including surveillance of antibiotic consumption
4. Improve infection control and the stewardship of antibiotic use in health care settings
5. Promote the surveillance, prevention and control of antibiotic resistance in the food chain
6. Promote research and innovation on new antibiotics
7. Improve awareness on antibiotic use and the risk of increasing resistance

1. National coordination

- Many actors involved who need to work together
- All inclusive and intersectoral: clinicians, epidemiologists, pharmacists, veterinarians and microbiologists
- Develop a national plan of action
- Guidance on antibiotic stewardship, regulations, information, awareness, training etc.
- Involving universities, ensure that the curriculum includes the prudent use of antibiotics (only prescribe when they are needed!)

1. Good practices

National antibiotics working groups such as Strama in Sweden and SWAB (Dutch Working Party on Antibiotic Policy) in the Netherlands:

- Provide analysis on antibiotic resistance
- Provide training programmes on prudent use
- Provide guidelines on antibiotic use
- Provide advice on national regulations when needed

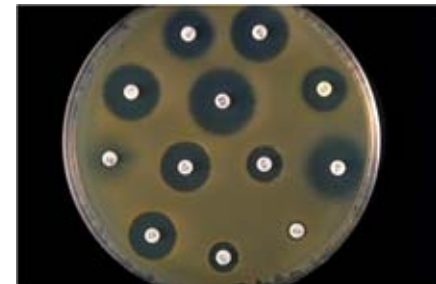
2. Surveillance of resistance

“If you do not know where you are going, any road can take you there.” (Lewis Carroll)

- Establish surveillance of the resistance to selected antibiotics in priority invasive bacteria in each country
- Establish a network of national clinical laboratories
- Promote European laboratory standards (European Committee on Antimicrobial Susceptibility Testing (EUCAST))
- Publish annual national and regional analysis and report

2. Good practices

- Well-established surveillance network in the EU: EARS-NET (European Antimicrobial Resistance Surveillance Network) managed by the ECDC
- Includes over 900 public health laboratories serving 1400 hospitals in the EU (27 countries), Iceland and Norway
- National software available through WHO and called WHONET
- Includes antibiotic resistance testing for seven major invasive pathogens:
 - *Streptococcus pneumoniae*
 - *Staphylococcus aureus*
 - *Escherichia coli*
 - *Enterococcus faecalis*
 - *Enterococcus faecium*
 - *Klebsiella pneumoniae*
 - *Pseudomonas aeruginosa*



3. Promote the rational use of antibiotics, including surveillance of antibiotic consumption

- Ban over-the-counter sales
- Reduce or eliminate incentives to use antibiotics
- Improve the quality of drugs
- Promote and change prescribing habits
- Improve the review of hospital infections and antibiotic use
- Adapt a university curriculum and promote the prudent use of antibiotics

3. Good practices

- The Belgium Antibiotic Policy Coordination Committee (BAPCOC) has promoted national campaigns on the prudent use of antibiotics **together** with concrete action and regulations
- Steady decline of 6.2% in antibiotic use in ambulatory care every year since the campaigns were organized
- Similar campaigns and results have been achieved in France, Poland, Spain, the United Kingdom and other countries

4. Improve infection control and the stewardship of antibiotics use in health care settings

- Need to develop and implement national guidelines on preventing and controlling infection
- Multidisciplinary hospital committees need to be in place to improve the surveillance of hospital-acquired infections and guide antibiotic therapy or prophylaxis
- For many interventions, prophylaxis can be as brief as 24 hours
- Need to involve the private and public sectors
- Promote hand hygiene and compliance

4. Good practices

Improved hand hygiene
(from University of Geneva Hospital)



Rationale

- Prevents cross-infection in hospitals
- Decreases hospital-acquired infections, including infections caused by resistant bacteria

Input

- Hospital campaign on hand hygiene and direct observation of compliance and performance feedback

Outcome

- During a three-year period, hand hygiene improved from 48% to 66%
- During the same period, transmission of methicillin-resistant *Staphylococcus aureus* decreased to less than half, from 2.16 to 0.93 per 10 000 patient-days
- The prevalence of hospital-acquired infections decreased from 16.9% to 9.9%

Pittet et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *Lancet* 2000;356:1307-12

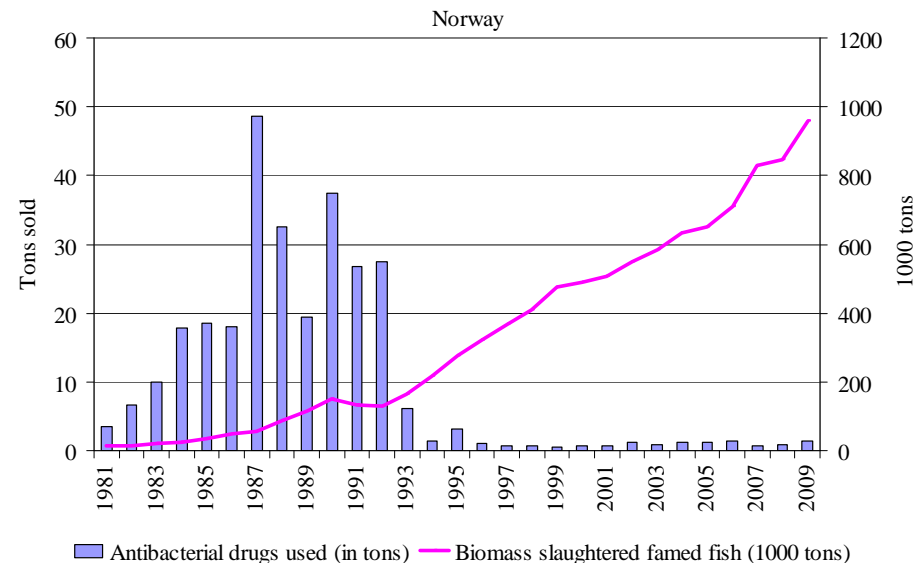
5. Promote the surveillance, prevention and control of antibiotic resistance in the food chain

- Antibiotics in animals only to be used when prescribed by a veterinarian
- Eliminate the use of antibiotics as a growth promoter
- Critically important antibiotics for use in human medicine only to be used in animals when justified
- Improve animal health through disease prevention, vaccination, hygiene and biosecurity measures
- Surveillance of antibiotic use in livestock
- Integrated (animal and human) surveillance of selected foodborne bacteria
- Improve awareness of antibiotic resistance from a food safety perspective



5. Good practices

- A ban on the use of antibiotics in the EU (2006) as a growth promoter has not led to any animal harm or production loss, as shown in Denmark
- Several countries such as Denmark, Finland, Norway and Sweden have reduced the use of antibiotics in animals by providing guidelines on prudent use and disease prevention
- In Norway, using vaccines and improving environmental conditions in salmon production has significantly reduced antibiotics use



Source: *Tackling antibiotic resistance from a food safety perspective in Europe*. Copenhagen, WHO Regional Office for Europe, 2011.

6. Promote research and innovation on new drugs and tools

- Contradiction: develop new drugs but then only use them very carefully
- The high cost of research and development needs to be leveraged by “push” and “pull” incentives
- Governments need to be involved to create incentives and innovation for research

6. Good practices

- Promote research on new antibiotics such as that undertaken by ReAct (Action on Antibiotic Resistance) and EU presidencies
- European Observatory on Health Systems and Policies report: *Policies and incentives for promoting innovation in antibiotic research*



7. Improve awareness of antimicrobial use and resistance

- Collaboration and involvement with patient safety groups
- Establish national and international partnerships
- Sustainable campaigns linked to policy guidance and regulations
- Promote hand hygiene and information on infections etc. at schools (www.e-bug.eu)
- Promote European Antibiotic Awareness Day on 18 November every year

7. Good practices



DG SANCO, DG Research

WHONET

EFMA European Federation of Medical Associations



European Surveillance of Antimicrobial Consumption

ReAct Action on Antibiotic Resistance



Improving Patient Safety in Europe

CDC



Antibiotic Resistance Surveillance & Control in the Mediterranean Region



European Union Invasive Bacterial Infections Surveillance Network

APUA Alliance for the Prudent Use of Antibiotics

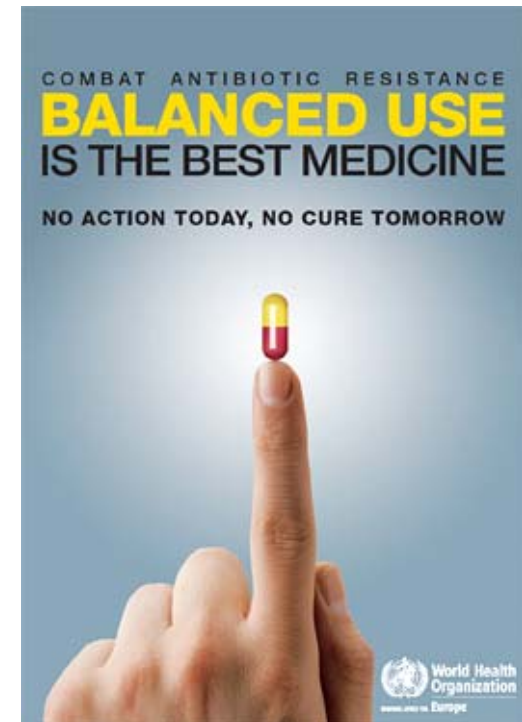
ESCMID *European Society of Clinical Microbiology and Infectious Diseases*

ARPEC: Antibiotic Resistance and Prescribing in European Children

World Health Day, 7 April 2011

- Global event on antimicrobial resistance
- “No action today, no cure tomorrow”

- All country offices
- Events with Regional Office involvement:
 - Moscow
 - Kiev
 - London
 - Strasbourg
 - Rome
 - Copenhagen



Everyone needs to get involved: WHO Regional Office for Europe communication strategy with five focus groups

- Health professions, pharmacists and veterinarians who prescribe the right antibiotic, for the right purpose and at the right dose and right time
- The public should know more about antibiotics and when to use them and when not
- Veterinarians and farmers need to use antibiotics prudently
- Pharmaceutical industry to develop new drugs
- Policy-makers to develop and implement national action plans

Conclusions

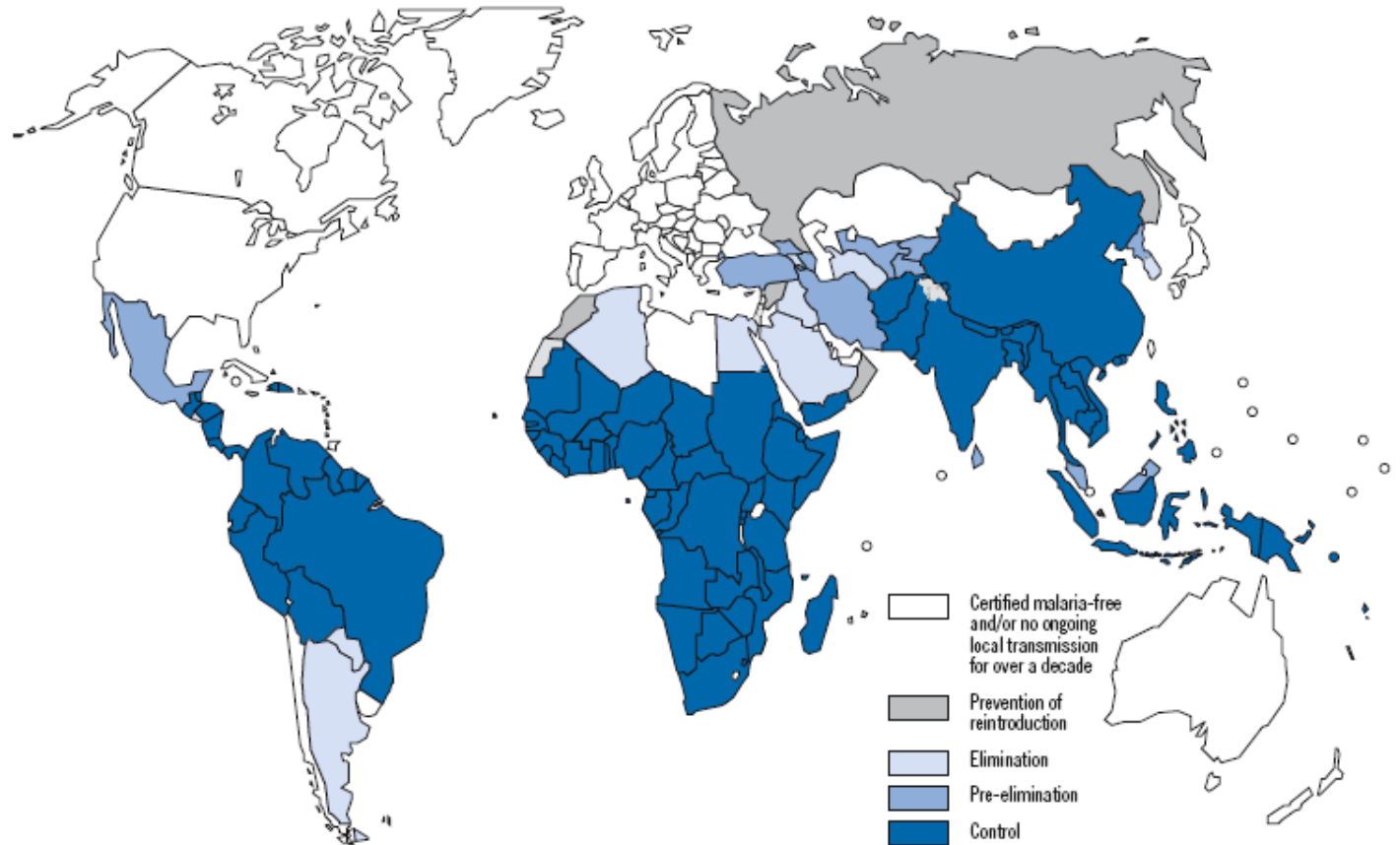
- Antibiotic resistance is becoming a public health emergency of yet unknown proportions
- All 53 WHO European Member States should gradually implement the regional comprehensive action plan
- World Health Day and the European Antibiotic Awareness Day are excellent opportunities to increase awareness on the need for **ACTION**



Thank you
www.euro.who.int

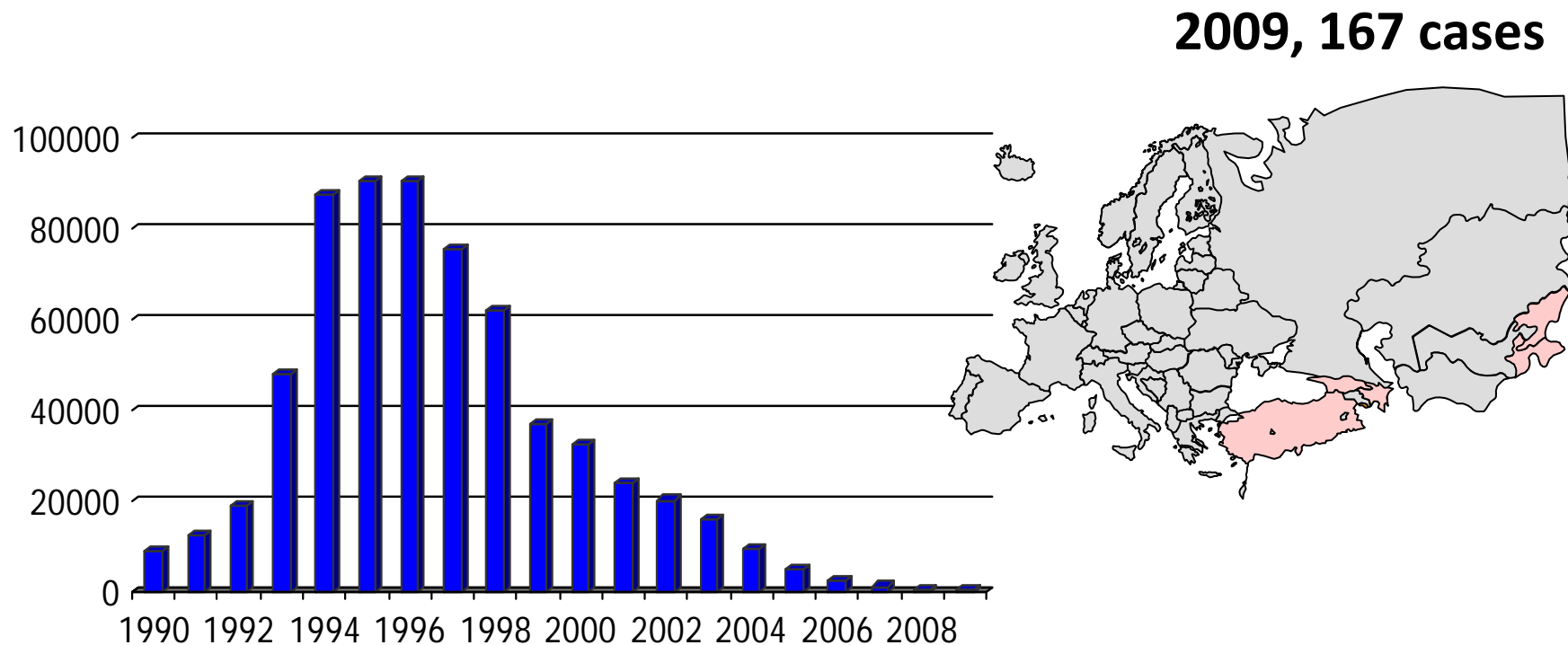
Global malaria situation

Fig. 3.1 Malaria-free countries and malaria-endemic countries in phases of control, pre-elimination, elimination and prevention of reintroduction, end 2007



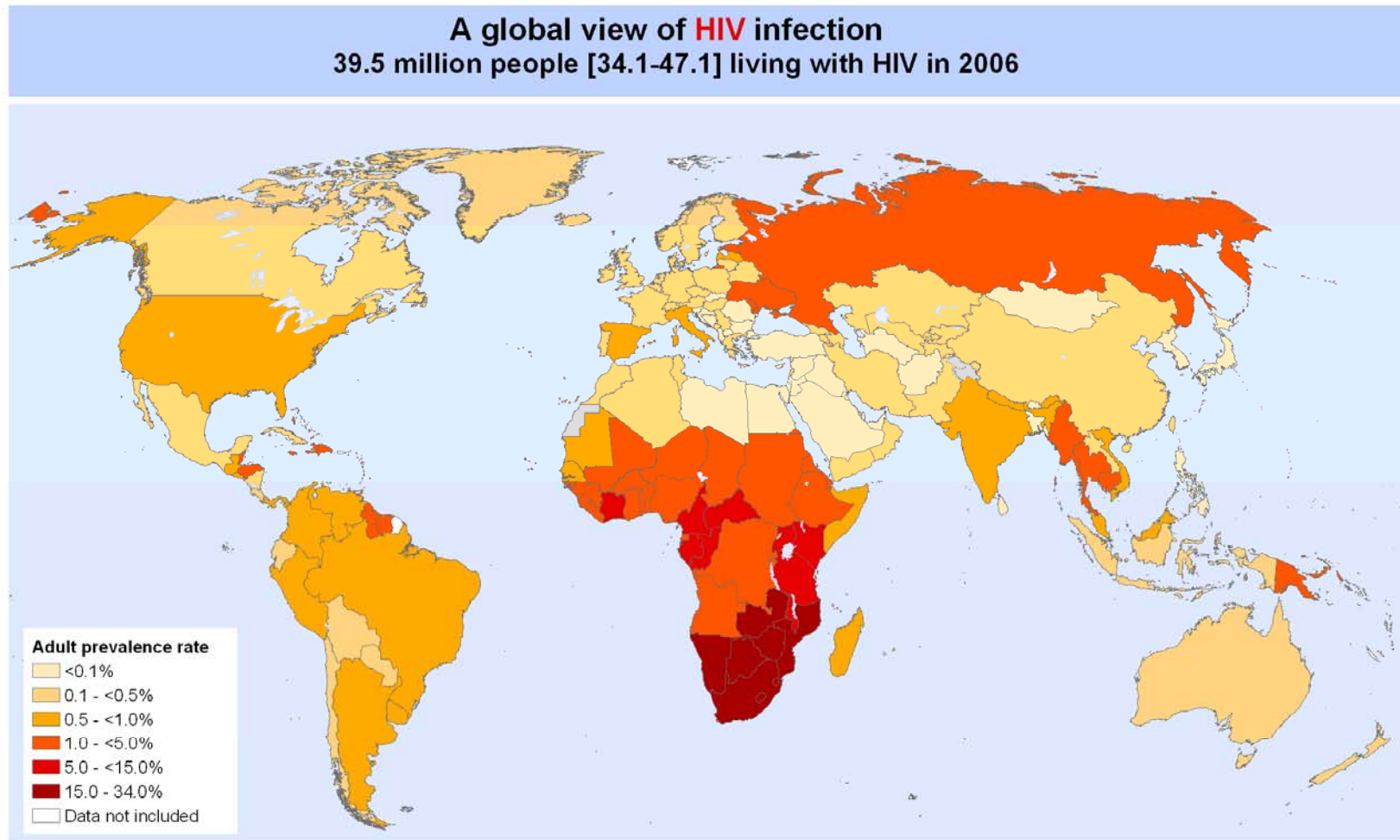
* China, Indonesia, Philippines, Solomon Islands, Sudan, Vanuatu and Yemen have subnational elimination programmes.

Malaria elimination by 2015: reachable target for the WHO European Region



Number of locally acquired cases of malaria in the Region, 1990–2009

In industrialised world between 5-20% resistance to at least one ARV drug



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO / UNAIDS
Map Production: Public Health Mapping and GIS
Communicable Diseases (CDS)
World Health Organization

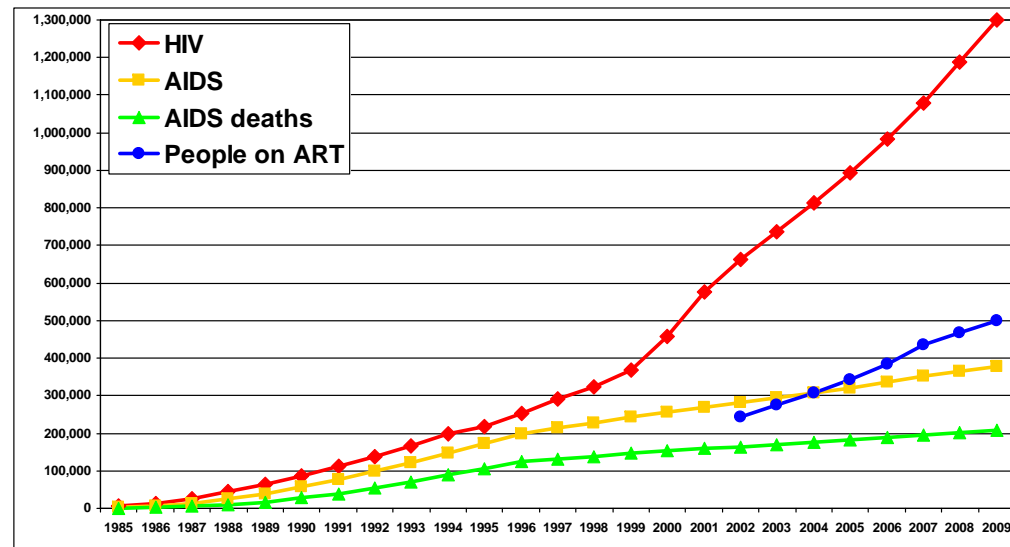


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HIV/AIDS

- In the European Region only multi-drug anti-retroviral treatment (ARV) is used, this largely prevents clinical resistance. Surveillance of resistance is part of programme monitoring
- Many patients not yet on Anti-retroviral treatment

Cumulative number of reported cases and deaths in European Region, 1985–2009



Resistance threatening MDG4 child mortality

Pneumonia: “the forgotten killer of children”

World wide: 29% of infections are pneumonia (19%) and blood stream infections (10%) (2004)

CEE/CIS : 21% (pneumonia 13% and blood stream infections 8%) (2004)

- Caused mainly by 2 bacteria both have a vaccine (*H.Influenzae*, *S.pneumoniae*)
- Vaccination is effective prevention but expensive
- Hand hygiene are cheap preventive measures for many infectious diseases
- Use of antibiotics is needed but threatened by resistance
- Estimates on ANTIBIOTIC resistance are as high as 70%

