Résistance aux antibiotiques : une impasse thérapeutique ?
Implications nationales et internationales

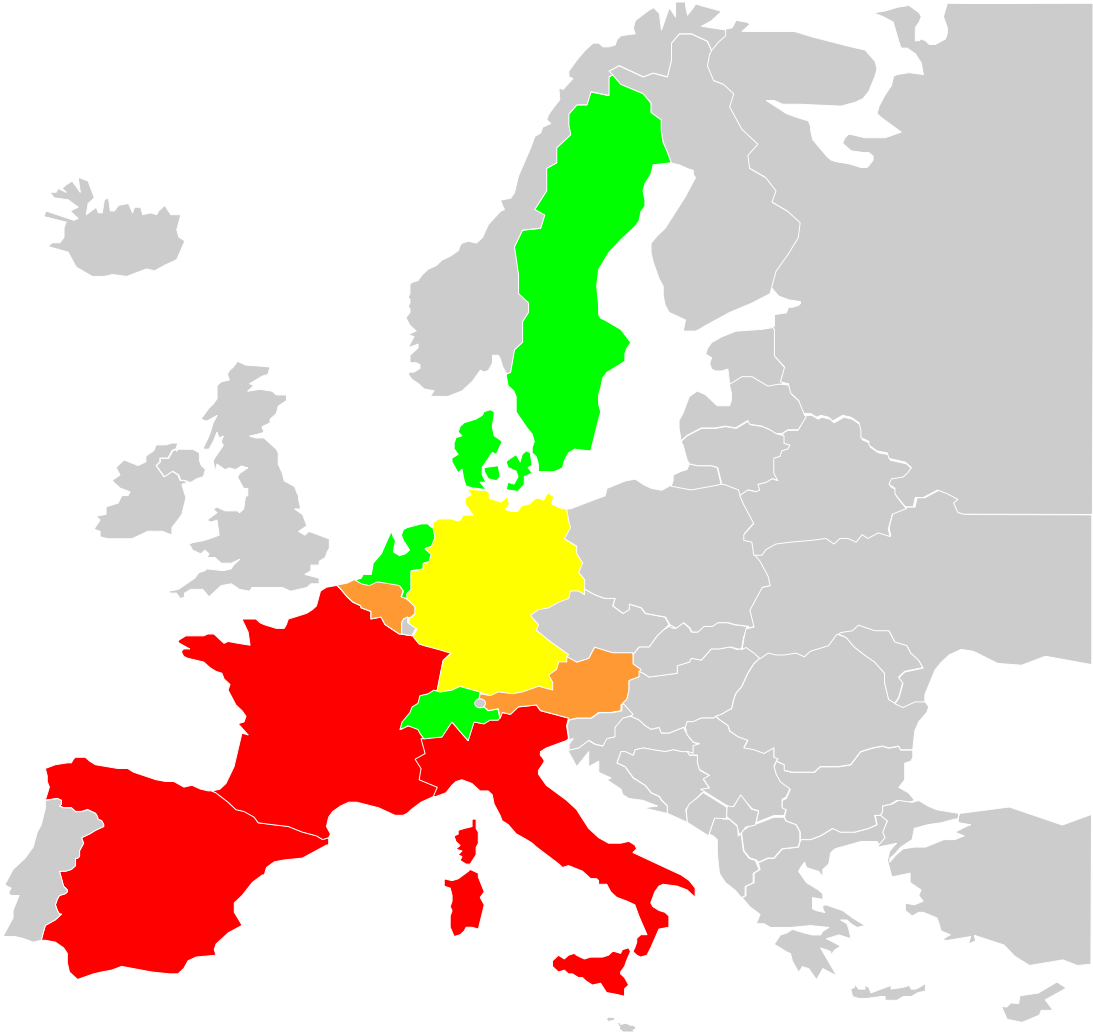
Stratégie et action européennes

Dominique L. Monnet, Senior Expert and Head of Disease Programme
Antimicrobial resistance and Healthcare-associated infections (ARHAI)
European Centre for Disease Prevention and Control

Paris, 21 November 2012

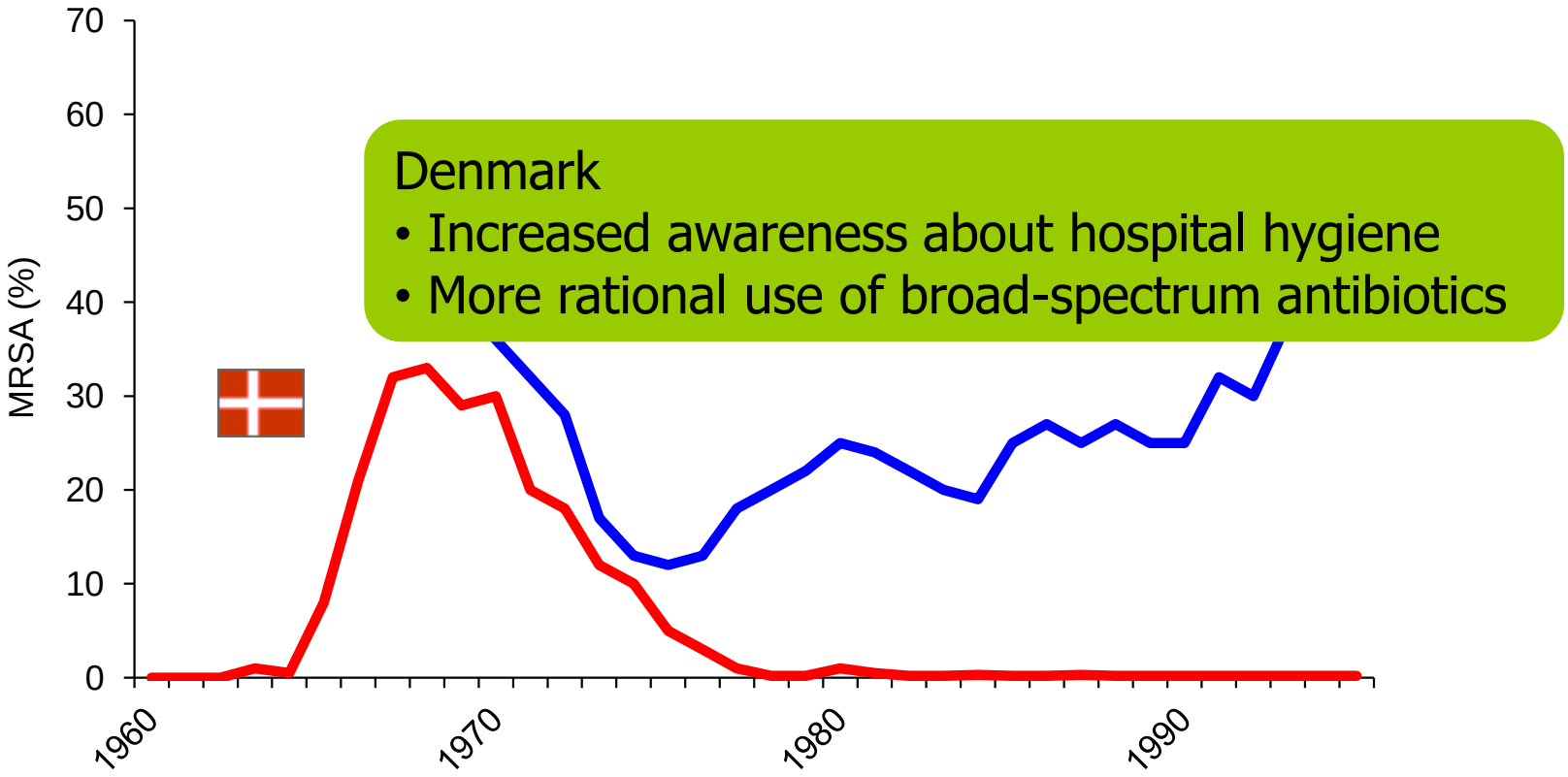
Methicillin-resistant *Staphylococcus aureus* (MRSA) in Europe, 1990-1991

- <3%
- 3 – 9%
- 10 – 29%
- >30%
- Did not participate



Source: Voss A, et al. Eur J Clin Microbiol Infect Dis 1994;13.50-55

Meticillin-resistant *Staphylococcus aureus* (MRSA) in one hospital in Paris (all isolates) and in Denmark (blood isolates), 1960-1995

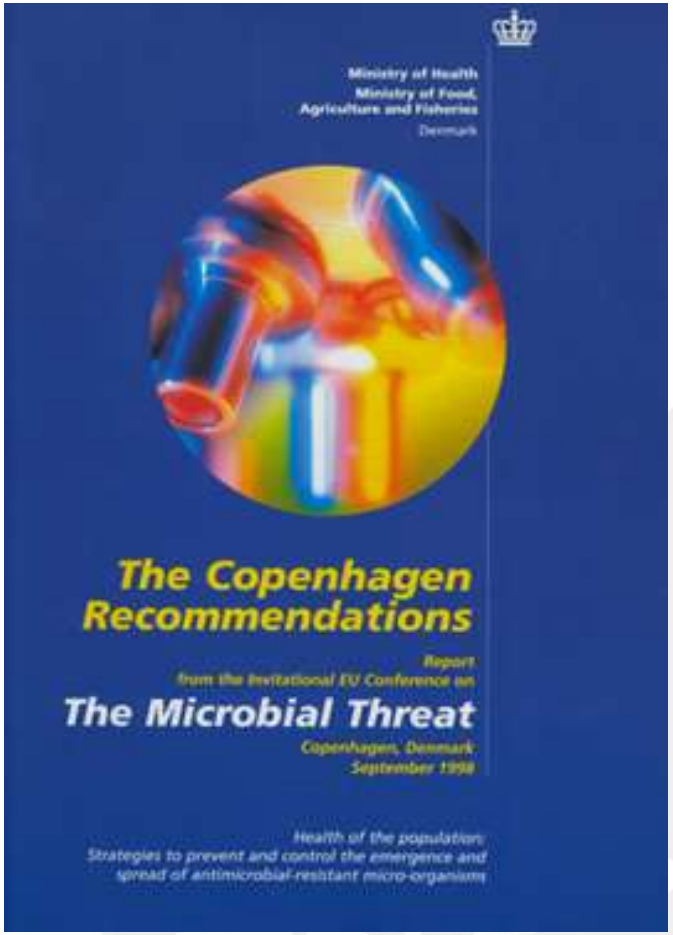


Source: Danish Staphylococcus Reference Laboratory (in DANMAP 1997);
Leclercq R. In: MRSA. Maurice Rapin Colloquia series, 1995.

EU Conference on the Microbial Threat, 1998

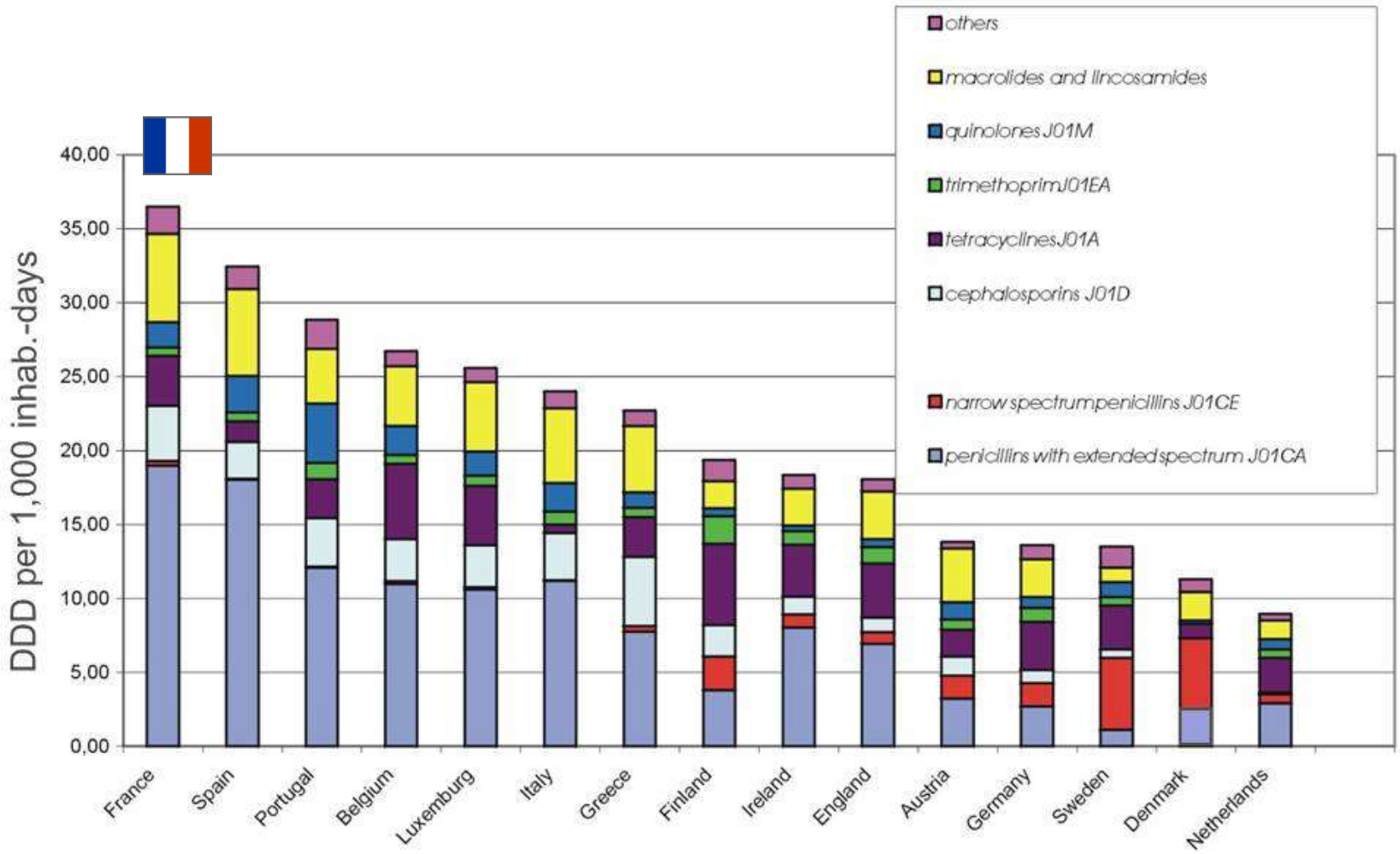
The Copenhagen Recommendations

- Antimicrobial resistance is a **major European and global problem**
- Set up **surveillance for antimicrobial resistance and consumption of antimicrobial agents**
- Pharmaceutical companies should be encouraged to develop **new antimicrobial agents**, but these will not solve the problem in the near future
- **Coordinated research** on antimicrobial resistance: high priority
- Encourage the adoption of a wide range of measures to promote **prudent use of antimicrobial agents**
- A way should be found to **review progress** with these recommendations and proposals



Available from: http://soapimg.icecube.snowfall.se/strama/Kopenhamnsmotet_1998.pdf

Antibiotic consumption in primary care, 15 EU countries, 1997



Source: Cars O, et al. Lancet 2001; 357: 1851-3

Community strategy against antimicrobial resistance, 2001

52001DC0333

Communication from the Commission on a Community Strategy against antimicrobial resistance /* COM/2001/0333 final Volume I */

COMMUNICATION FROM THE COMMISSION ON A COMMUNITY STRATEGY AGAINST ANTIMICROBIAL RESISTANCE

Executive Summary

The emergence and spread of antimicrobial resistance has become a major public health problem, within the Community and world-wide. Overuse and misuse of substances to kill or inhibit the growth of micro-organisms (including bacteria, viruses and fungae), and certain parasites (for example protozoa) have favoured the growth of resistant organisms. This so-called "antimicrobial resistance" can spread to other microbial populations. Infections by resistant organisms endanger the human population, animals and plants, including those not previously in contact with antimicrobial agents.

For the purposes of this Communication, the term "antimicrobial agent" encompasses a substance produced either synthetically or naturally by bacteria, fungae or plants, used to kill or inhibit the growth of micro-organisms, including bacteria, viruses and fungae, and parasites exhibiting the phenomenon of resistance (in particular protozoa). Antibiotics are substances with antibacterial effects.

Recent scientific opinions pointed out that prompt action is needed in the following areas: prudent use of antimicrobial agents, prevention of diseases, development of new products and methods of treatment and monitoring the situation.

Antimicrobial resistance is already addressed by the Community through various individual measures. The need is clear for an overall approach to this question, based on the provisions of Article 152 of the Treaty establishing the European Community which provides that a high level of health protection shall be ensured in the definition and implementation of all Community policies and activities.

On this basis, the Commission proposes to put in place a Community strategy on four key areas of action:

(1) Surveillance: Monitoring the evolution and the effects of interventions through the establishment/strengthening of accurate surveillance systems on antimicrobial resistance in the human and veterinary sector and the consumption of antimicrobial agents.

(2) Prevention of communicable diseases, and infection control to reduce the needs for antimicrobial agents. This includes the prudent use of antimicrobial agents which entails the need for improved product information for authorised antibacterial medicinal products and the promotion of educational and behavioural actions towards the professionals and the general public.

(3) Research and product development: New modalities for prevention and treatment of infections and continued support of research for new drugs and alternatives.

(4) International co-operation: Antimicrobial resistance does not respect frontiers. An effective strategy requires close co-operation and consultation between the Commission, the Member States and other involved parties, especially at international level.

The attached proposal for a Council Recommendation on the prudent use of antimicrobial agents plays an important part in the Community's multi-disciplinary and multi-faceted approach.

COMMUNICATION FROM THE COMMISSION ON A COMMUNITY STRATEGY AGAINST ANTIMICROBIAL RESISTANCE

(Text with EEA relevance)

Table Of Contents

15 action points

- Surveillance: 2 action points
  - Antimicrobial resistance (human+vet.)
  - Antimicrobial consumption (all sectors)
- Prevention: 8 action points, e.g.
  - AMR information for market authorisation (human+vet.)
  - Education campaigns
  - Prescription-only rule
  - Prevention programmes, incl. immunisation
  - Monitoring of residues in foods
  - Phase out antimicrobial growth promoters
- Research and product development (3 points)
- International cooperation (2 action points)

Commission Decisions 1999-2012 & Council Recommendations, 2001 & 2009

Avian influenza in humans

West Nile virus infection

2.5.4. *Serious imported diseases*

Cholera

Malaria

Plague

Viral haemorrhagic fevers

3. **SPECIAL HEALTH ISSUES**

3.1. **Nosocomial infections**

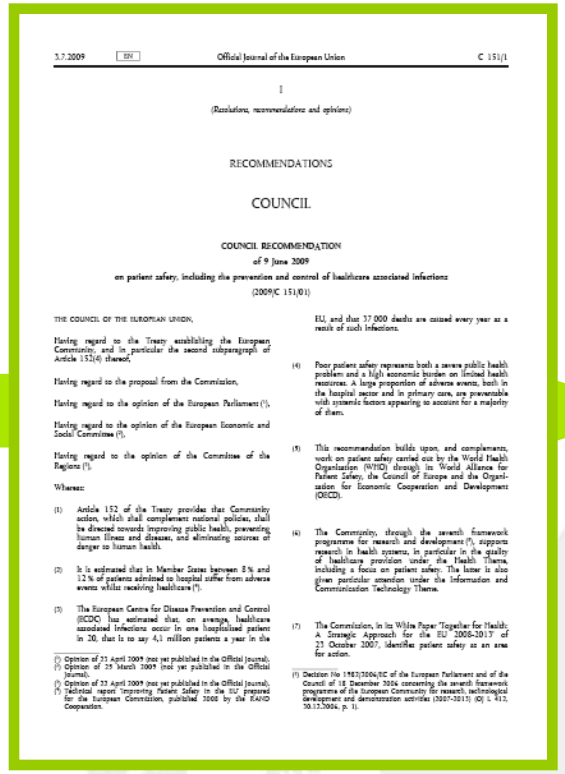
3.2. **Antimicrobial resistance'**

Commission Decision of 22 December 1999 on the communicable diseases to be progressively covered by the Community network under Decision No. 2119/98/EC (2000/96/EC).

Commission Implementing Decision of 8 August 2012 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases…

COUNCIL

Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC)



3.7.2009 EN Official Journal of the European Union C 151/1

I

(Resolutions, recommendations and opinions)

RECOMMENDATIONS

COUNCIL

COUNCIL RECOMMENDATION

of 9 June 2009

on patient safety, including the prevention and control of healthcare associated infections

(2009/C 151/01)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular the second subparagraph of Article 152(4) thereof,

Having regard to the proposal from the Commission,

Having regard to the opinion of the European Parliament (1),

Having regard to the opinion of the European Economic and Social Committee (2),

Having regard to the opinion of the Committee of the Regions (3),

Whereas:

(1) Article 152 of the Treaty provides that Community action, which shall complement national policies, shall be directed towards improving public health, preventing human illness and diseases, and eliminating sources of danger to human health.

(2) It is estimated that in Member States between 8 % and 12 % of patients admitted to hospital suffer from adverse events whilst receiving healthcare (4).

(3) The European Centre for Disease Prevention and Control (ECDC) has estimated that, on average, healthcare associated infections occur in one hospitalised patient in 20, that is to say 4,1 million patients a year in the EU, and that 37 000 deaths are caused every year as a result of such infections.

(4) Poor patient safety represents both a severe public health problem and a high economic burden on limited health resources. A large proportion of adverse events, both in the hospital sector and in primary care, are preventable with systemic factors appearing to account for a majority of them.

(5) This recommendation builds upon, and complements, work on patient safety carried out by the World Health Organisation (WHO) through its World Alliance for Patient Safety, the Council of Europe and the Organisation for Economic Cooperation and Development (OECD).

(6) The Community, through the seventh framework programme for research and development (5), supports research in health systems, in particular in the quality of healthcare provision under the Health Theme, including a focus on patient safety. The latter is also given particular attention under the Information and Communication Technology Theme.

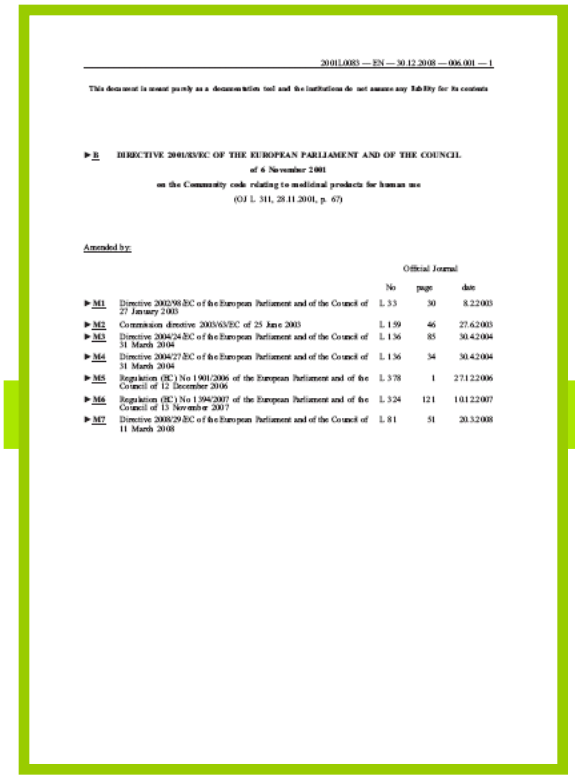
(7) The Commission, in its White Paper 'Together for Health: A Strategic Approach for the EU 2008-2013' of 23 October 2007, identifies patient safety as an area for action.

(1) Opinion of 23 April 2009 (not yet published in the Official Journal).
(2) Opinion of 25 March 2009 (not yet published in the Official Journal).
(3) Opinion of 23 April 2009 (not yet published in the Official Journal).
(4) Technical report 'Improving Patient Safety in the EU' prepared for the European Commission, published 2008 by the RAND Corporation.

(5) Decision No 1982/2006/EC of the European Parliament and of the Council of 18 December 2006 concerning the seventh framework programme of the European Community for research, technological development and demonstration activities (2007-2013) (OJ L 412, 30.12.2006, p. 1).

Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare associated infections (2009/C 151/01)

Directive on medicinal products,2001 & Regulation on additives for use in animal nutrition, 2003



2001L0083 — EN — 30.12.2008 — 006.001 — 1

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►B DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 November 2001

on the Community code relating to medicinal products for human use

(OJ L 311, 28.11.2001, p. 67)

Amended by:

		Official Journal		
		No	page	date
►M1	Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003	L 33	30	8.2.2003
►M2	Commission directive 2003/63/EC of 25 June 2003	L 159	46	27.6.2003
►M3	Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004	L 136	85	30.4.2004
►M4	Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004	L 136	34	30.4.2004
►M5	Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006	L 378	1	27.12.2006
►M6	Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007	L 324	121	10.12.2007
►M7	Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008	L 81	51	20.3.2008

Photo: Keith Weller.

Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Consolidated 30/12/2008)

Regulation EC (EC) No 1831/2003 of the European Parliament and the of the Council of 22 September 2003 on additives for use in animal nutrition

What is the role of ECDC in its Founding Regulation?

… to identify, assess and communicate current and emerging health threats to human health from communicable diseases.

— ECDC Founding Regulation (851/2004), Article 3

- EU-level disease surveillance and epidemic intelligence
- Scientific opinions and studies
- Early Warning System and response
- Technical assistance and training
- Communication to scientific community
- Communication to the public

Council Conclusions, 2008, 2009 & 2012

COUNCIL OF
THE EUROPEAN UNION

EN

Council Conclusions on Antimicrobial Resistance (AMR)

2876th EMPLOYMENT, SOCIAL POLICY, HEALTH AND CONSUMER AFFAIRS Council meeting

Luxembourg, 10 June 2008

The Council adopted the following conclusions:

"The Council of the European Union

1. **RECALLS** that Article 152 of the Treaty establishing the European Community states that Community action in the field of public health is to complement national policies and be directed to ensure a high level of human health protection. This Community action shall fully respect the responsibilities of the Member States for the organisation and delivery of health services and medical care.

2. **RECALLS** the Council Recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine[1].

3. **NOTES** that the first Report[2] from the Commission on the basis of Member States reports on the implementation of the Council Recommendation showed that most Member States had taken a variety of actions, as requested by the recommendation, however there remained numerous areas where only limited action had been undertaken.

[1] doc. 14771/01
[2] doc. 5457/06 Report from the Commission to the Council on the basis of Member States' reports on the implementation of the Council recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine (ref(2003) 1745)

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EN

COUNCIL OF
THE EUROPEAN UNION

EN

Council Conclusions on innovative incentives for effective antibiotics

2980th EMPLOYMENT, SOCIAL POLICY, HEALTH AND CONSUMER AFFAIRS Council meeting

Brussels, 1 December 2009

"The Council adopted the following conclusions:

Nota bene: In this document, the term "antibiotics" encompasses medicinal products produced either synthetically or naturally used to kill or inhibit the growth of bacteria as well as those with alternative mechanisms of action e.g. effect on bacterial virulence. In this context, alternative methods for prevention and control of infections should also be taken into account.

1. **RECALLS** the Community Strategy against antimicrobial resistance (COM(2001) 0333).

2. **RECALLS** the Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine[1].

3. **RECALLS** the Council Conclusions on antimicrobial resistance of 10 June 2008[2].

4. **RECALLS** the Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare associated infections[3].

5. **RECALLS** the WHO report (2004) Priority Medicines for Europe and the World[4]

[1] OJ L 34, 5.2.2002, p. 13.
[2] 9637/08.
[3] OJ C 151, 3.7.2009, p. 1.
[4] http://whqlibdoc.who.int/hq/2004/WHO_EDM_PAR_2004.7.pdf.

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Council conclusions on
the impact of antimicrobial resistance in the human health sector and in the veterinary sector – a "One Health" perspective

3177th EMPLOYMENT, SOCIAL POLICY, HEALTH and CONSUMER AFFAIRS Council meeting

Luxembourg, 22 June 2012

The Council adopted the following conclusions:

"The Council of the European Union

1. **RECALLS** the Council conclusions of 10 June 2008 on antimicrobial resistance (AMR)[1].

2. **RECALLS** the Council conclusions of 23 November 2009 on innovative incentives for effective antibiotics[2].

3. **RECALLS** the Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine[3], including the reports of December 2005 and April 2010 from the Commission to the Council on its implementation[4].

4. **RECALLS** the Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare associated infections[5].

5. **ACKNOWLEDGES** the Scientific Opinion of October 2009 of the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA), the European Medicines Agency (EMA) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) on antimicrobial resistance focused on zoonotic infections[6].

[1] 9637/08
[2] OJ C 302, 12.12.2009, p. 10
[3] OJ L 34, 5.2.2002, p.13
[4] 5427/06 [COM(2005)684 final] and 8493/10 [COM(2010)341 final]
[5] OJ C 151, 3.7.2009, p.1
[6] EFSA Journal 2009; 7(11):1372.
http://ec.europa.eu/health/scientific_committees/emerging/docs/ssc_o_026.pdf
EMEA/CVMP/44759/2009

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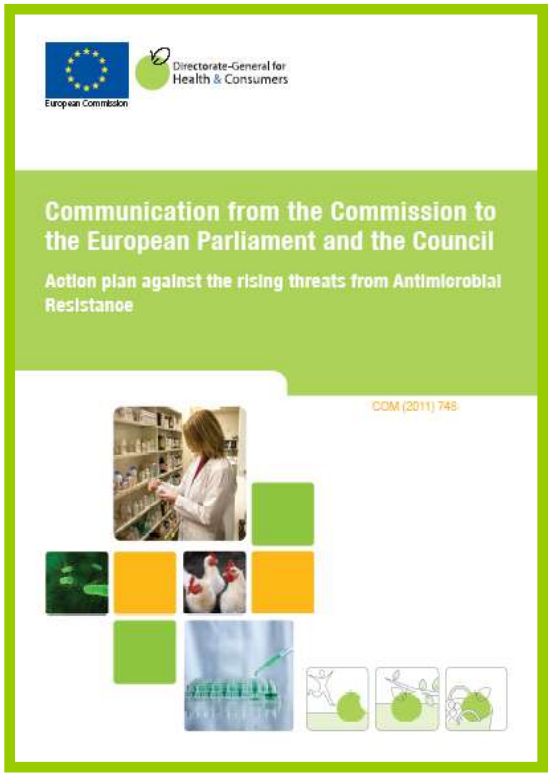
Council Conclusions on Antimicrobial Resistance (AMR) (10 June 2008)

Council Conclusions on innovative incentives for effective antibiotics (1 December 2009)

Council Conclusions on the impact of antimicrobial resistance in the human health sector and in the veterinary sector –a "One Health" perspective (22 June 2012)

European Commission action plan to combat AMR, 2011



Communication from the Commission to the European Parliament and the Council. Action plan against the rising threats from Antimicrobial Resistance (COM (2011) 748)

Based on preparatory work

- Staff working paper 2009 and public consultation
- Council conclusions on AMR
- EP resolutions on AMR

Holistic approach

- public health
- consumer safety
- food safety
- non therapeutic use
- environment
- animal health & welfare

Objective: combat the rising threat of AMR

- to reduce and prevent the spread of AMR
- to preserve the ability to treat and prevent microbial infections

European Commission action plan to combat AMR, 2011: overall aims

- To mitigate the risk of developing AMR in humans from the use of antimicrobials both in humans and animals by effectively ensuring across the EU their **appropriate use**, and promoting **microbiological diagnosis** as the means to determine, to the extent possible, the need for antimicrobials
- To put in place effective ways to **prevent microbial infections** and their spread
- **To develop effective antimicrobials** or alternatives for treatment of human and animal infections
- To join forces with **international partners** to contain the risks of spreading AMR form international trade and travel and via the environment
- To reinforce **research** to develop the scientific basis and innovative means to combat AMR
- To improve **communication, education and training**

Reports on implementation of Council Recommendations & Eurobarometer, 2010-2012


SECOND REPORT FROM THE COMMISSION TO THE COUNCIL

ON THE BASIS OF MEMBER STATES' REPORTS ON THE IMPLEMENTATION OF THE COUNCIL RECOMMENDATION (2002/77/EC) ON THE PRUDENT USE OF ANTIMICROBIAL AGENTS IN HUMAN MEDICINE

(Text with EEA relevance)

EN EN


EUROBAROMETER

Antimicrobial Resistance

Fieldwork: November - December 2009

Publication: April 2010

Report


EUROPEAN COMMISSION

REPORT FROM THE COMMISSION TO THE COUNCIL

on the basis of Member States' reports on the implementation of the Council Recommendation (2009/C 151/01) on patient safety, including the prevention and control of healthcare associated infections

(Text with EEA relevance)

EN EN

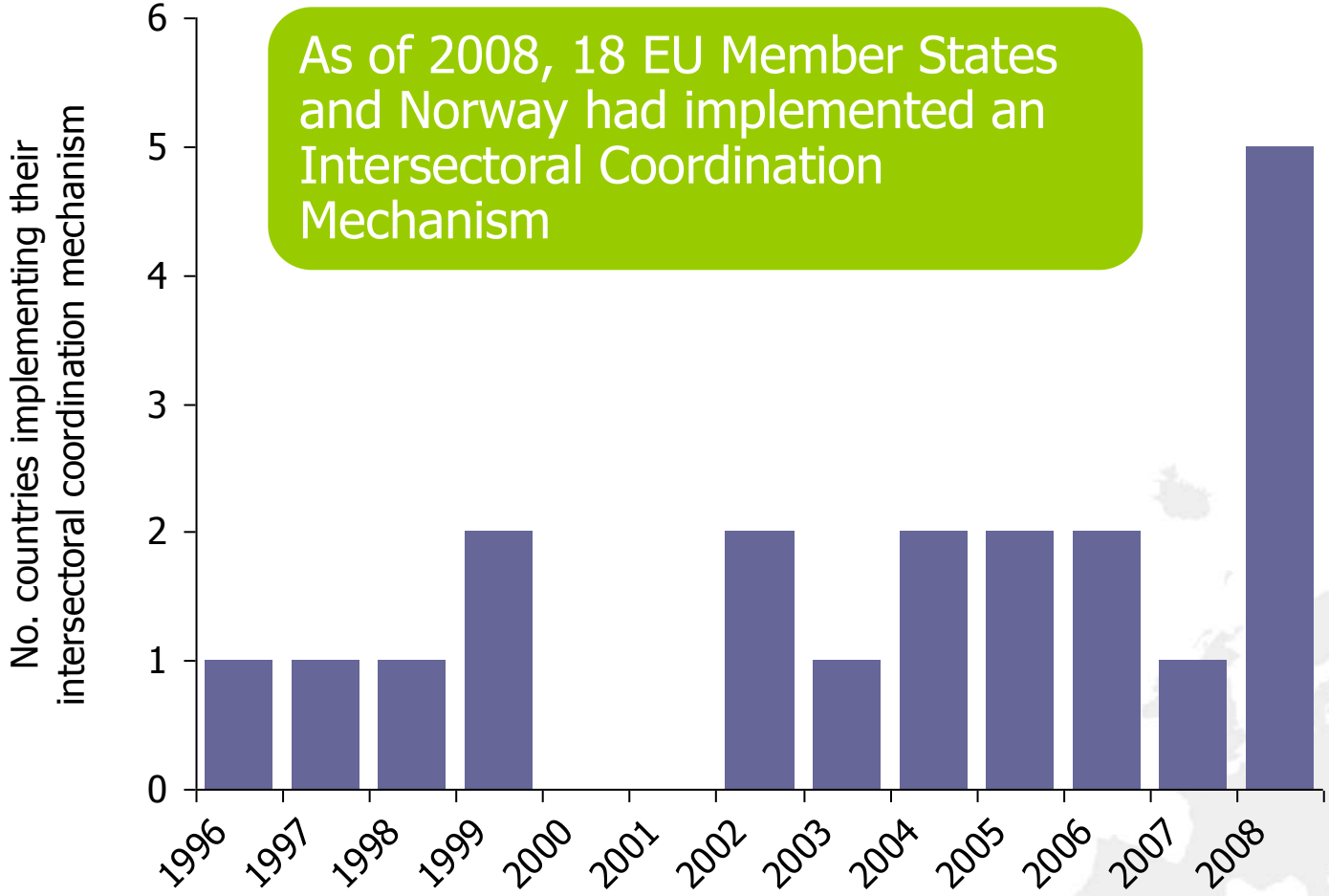
2nd report from the Commission to the Council on the basis of Member States' reports on the implementation of the Council Rec.ommendation 2002/77/EC

Special Eurobarometer 338 "Antimicrobial resistance"

(9 April 2010)

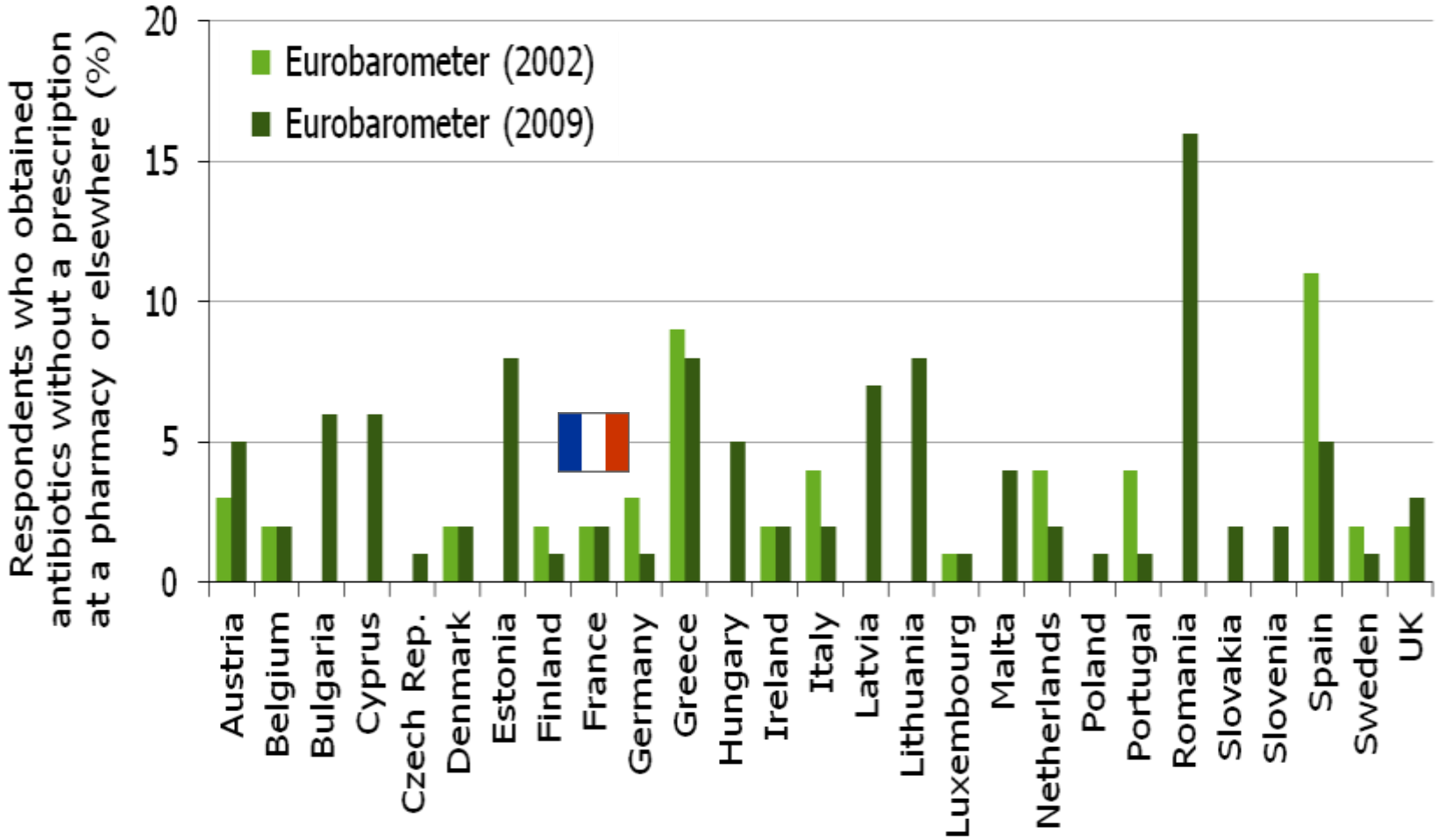
1st report from the Commission to the Council on the basis of Member States' reports on the implementation of the Council Rec.ommendation 2009/C 151/01

Implementation of National Intectoral Coordination Mechanisms on AMR



Adapted from: European Commission, Directorate - General Health and Consumers, 2010.

Antibiotics obtained without a prescription EU Member States, 2002 & 2009



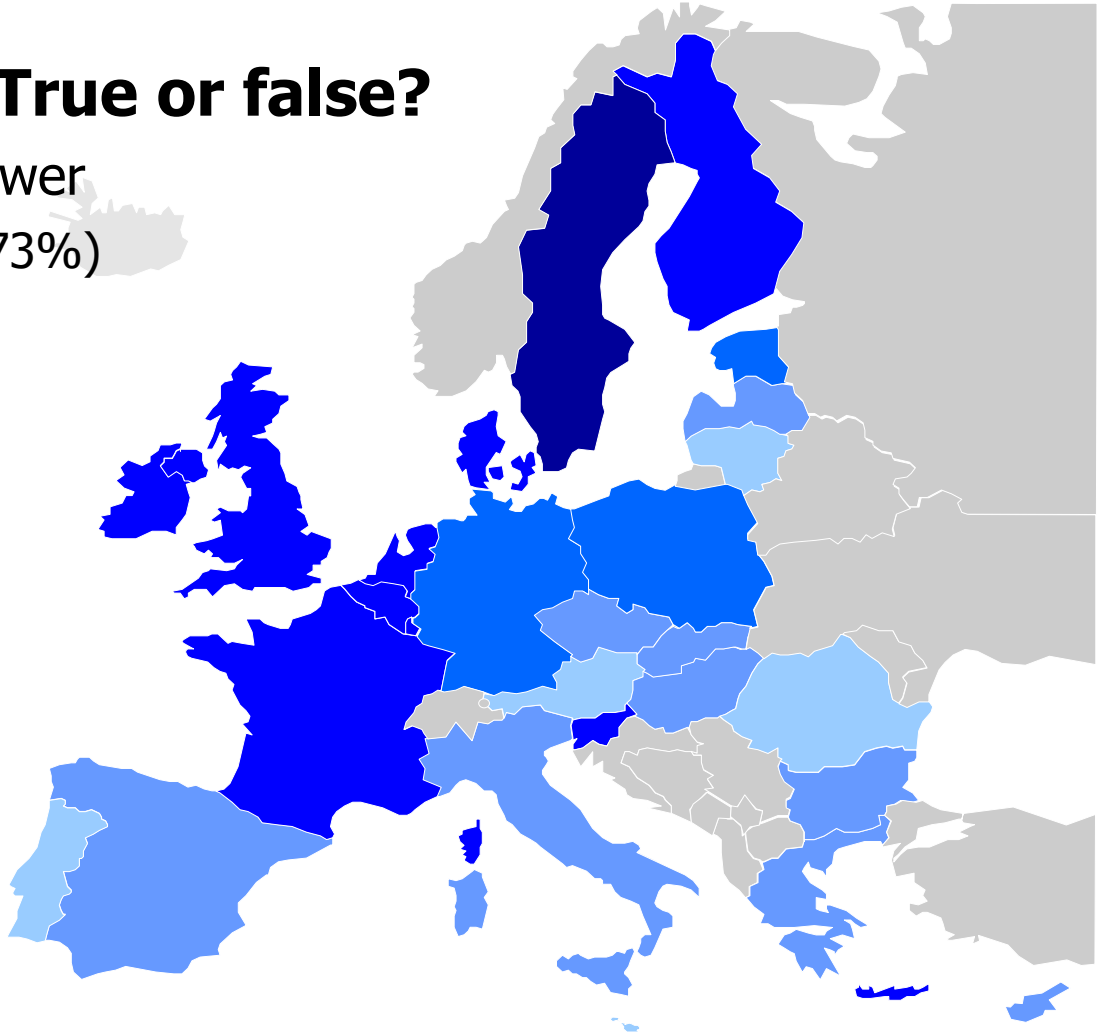
Source: European Commission, Eurobarometer. In: Lancet Infect Dis 2012 Mar;12(3):182-3.

Eurobarometer Opinion Poll, November-December 2009

Antibiotics kill viruses. True or false?

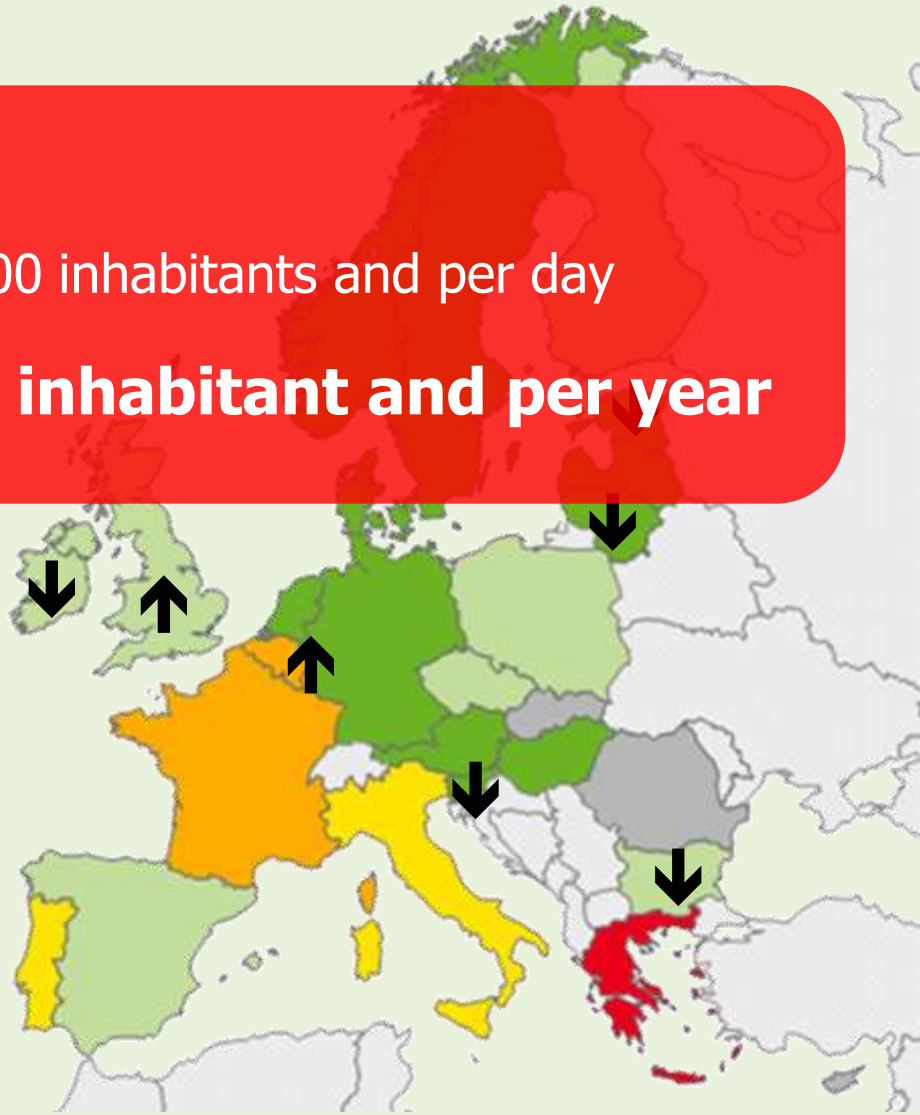
% respondents with correct answer (i.e., "false"): 36% (range: 14 – 73%)

- 61 – 73%
- 41 – 60%
- 31 – 40%
- 21 – 30%
- 14 – 20%



Source: Special Eurobarometer 338 / 72.5 "Antimicrobial resistance", Nov.-Dec. 2009.

Consumption of antibiotics for systemic use (ATC group J01) in the community*; EU/EEA, 2010



No data reported
Not included

Liechtenstein
Luxembourg
Malta

France

4.8 packages per 1,000 inhabitants and per day

1.8 package per inhabitant and per year

*in Defined Daily Doses
per 1000 inhabitants and per day

0	16.72 to < 22.38	28.04 to < 33.71
11.06 to < 16.72	22.38 to < 28.05	33.71 to < 39.37

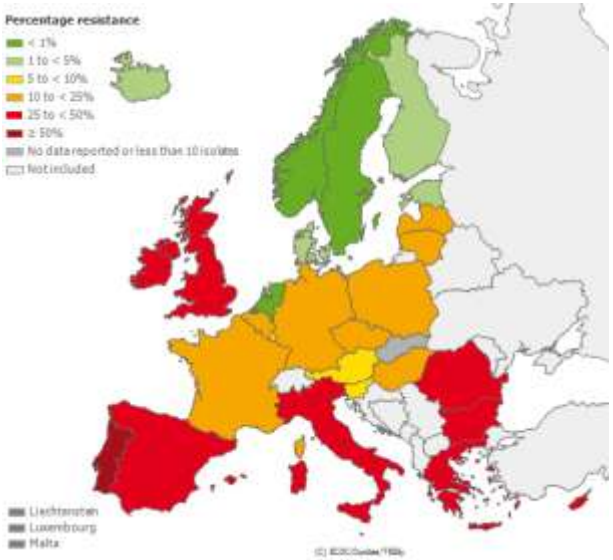
Greece and Iceland:
includes both community and hospital sector

Spain: reimbursement data that do not include over-the-counter sales without a prescription

Source: ESAC-Net, 2012

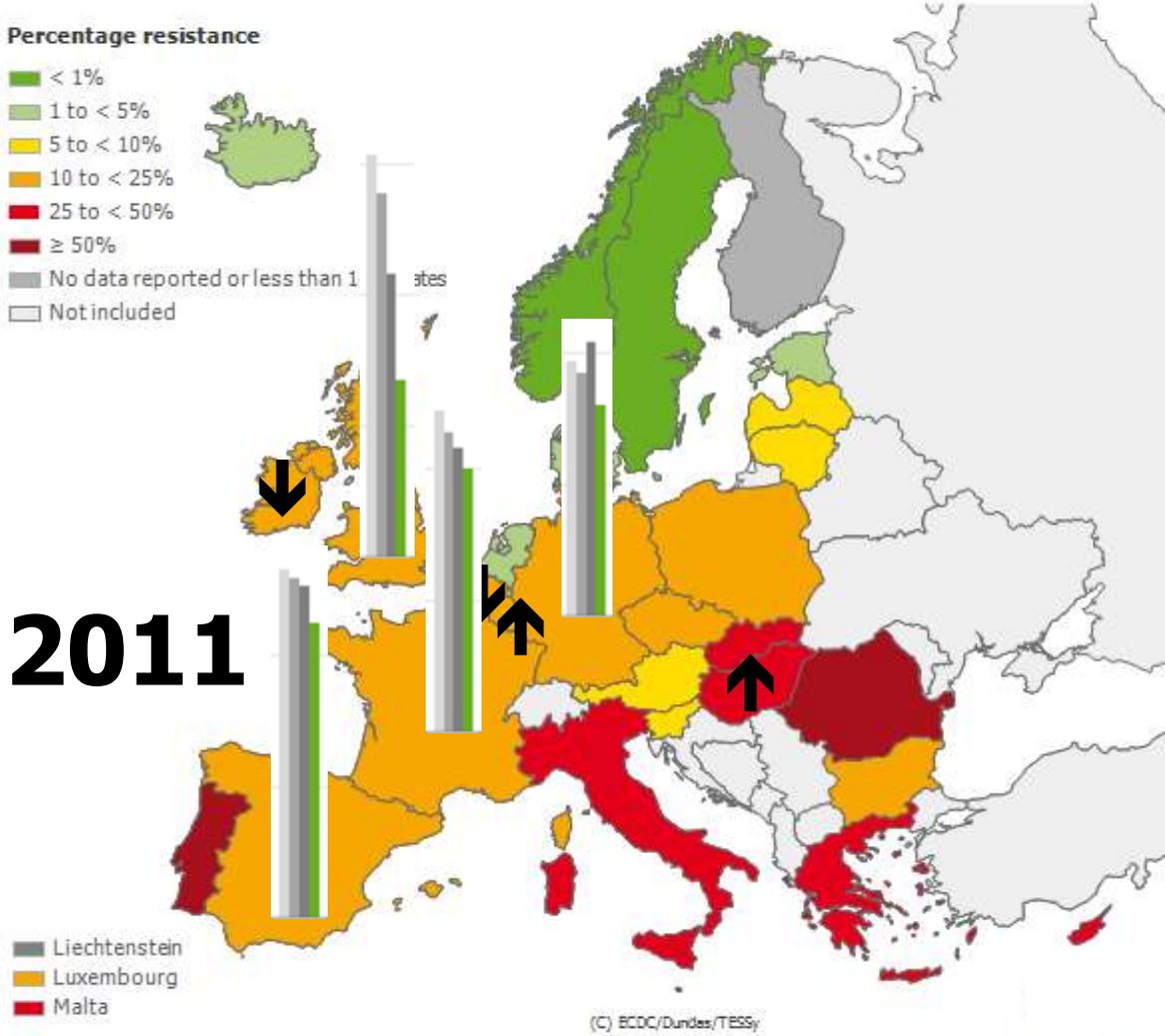
The symbols ↑ and ↓ indicate a continuous increase or decrease for the period 2008-2010, respectively. These trends were reported only for countries that consistently reported during 2008-2010.

Staphylococcus aureus: percentage of invasive isolates resistant to meticillin (MRSA); EU/EEA, 2008–2011



2008

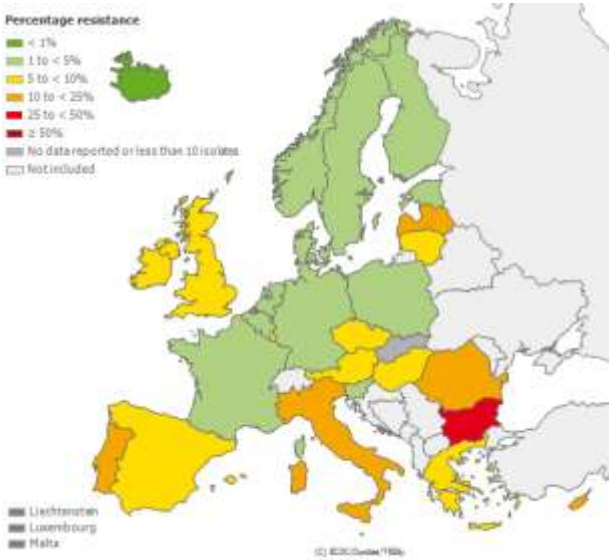
2011



Source: EARS-Net, 2012

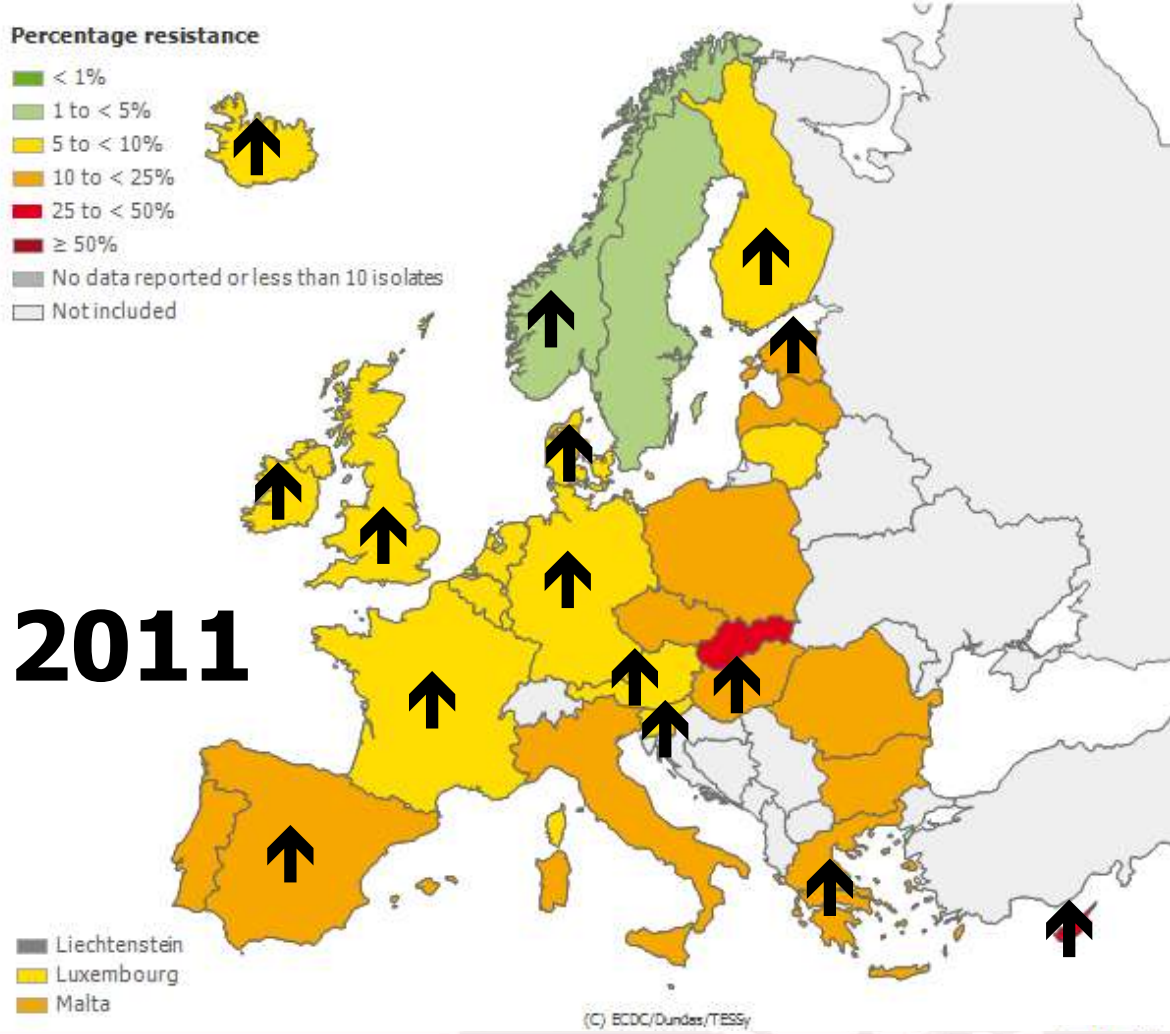
The symbols ↑ and ↓ indicate a significant increasing or decreasing trend for the period 2008-2011, respectively. These trends were calculated on laboratories that consistently reported during 2008-2011.

Escherichia coli: percentage of invasive isolates resistant to third-generation cephalosporins; EU/EEA, 2008–2011



2008

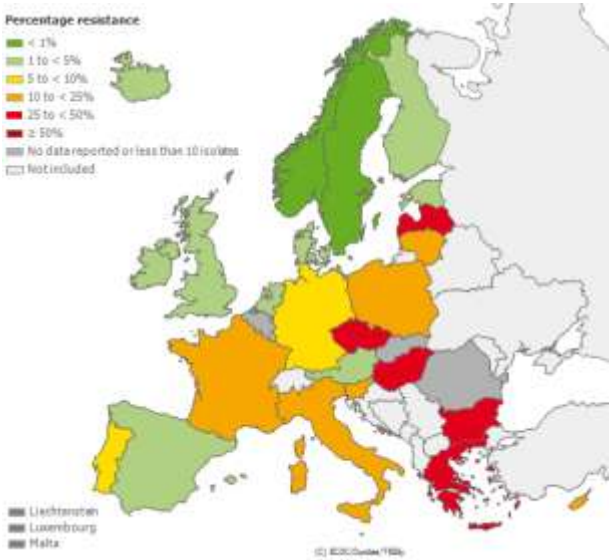
2011



Source: EARS-Net, 2012

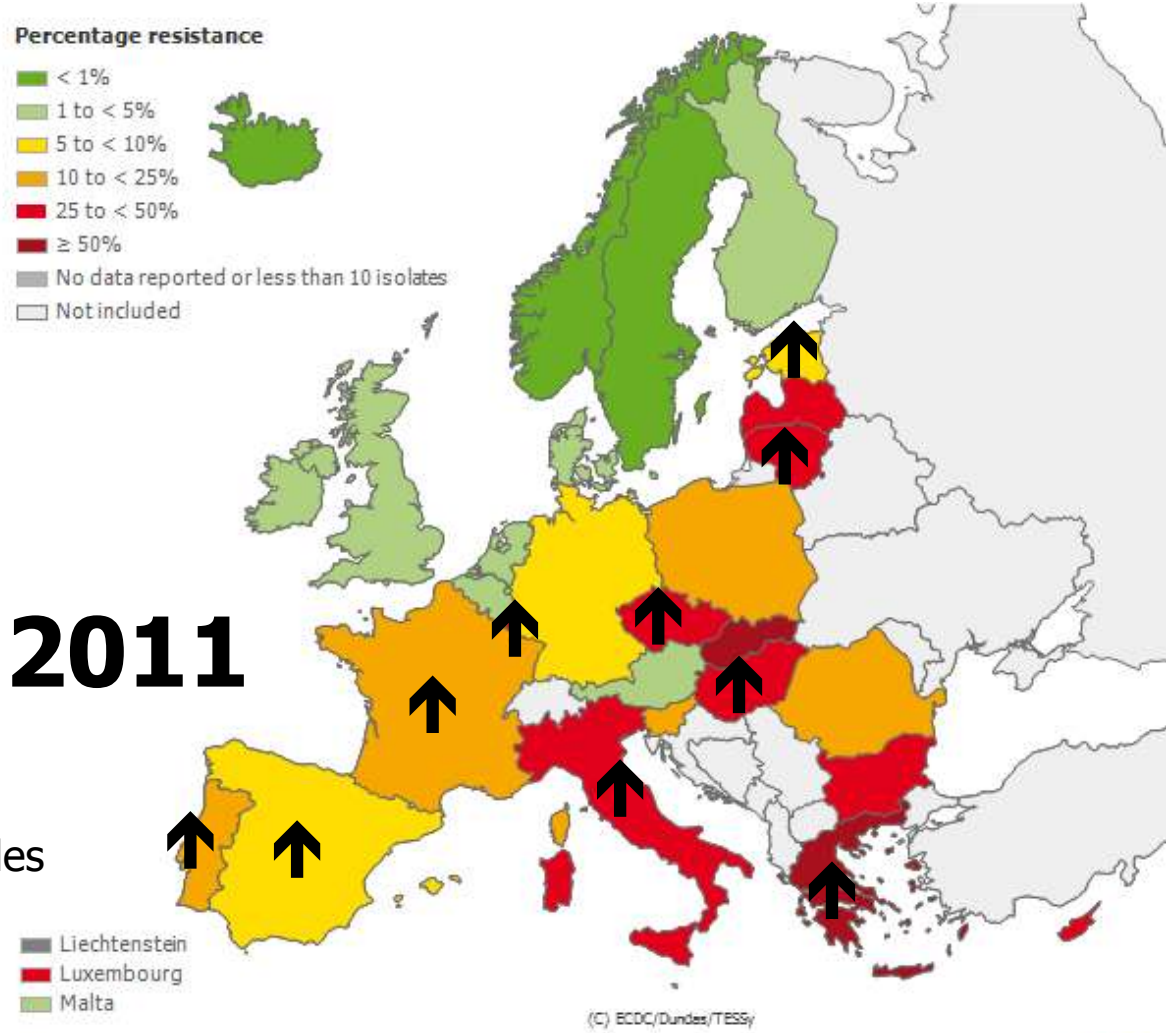
The symbols ↑ and ↓ indicate a significant increasing or decreasing trend for the period 2008-2011, respectively. These trends were calculated on laboratories that consistently reported during 2008-2011.

Klebsiella pneumoniae: percentage of invasive isolates with combined resistance*; EU/EEA, 2008–2011



2008

2011

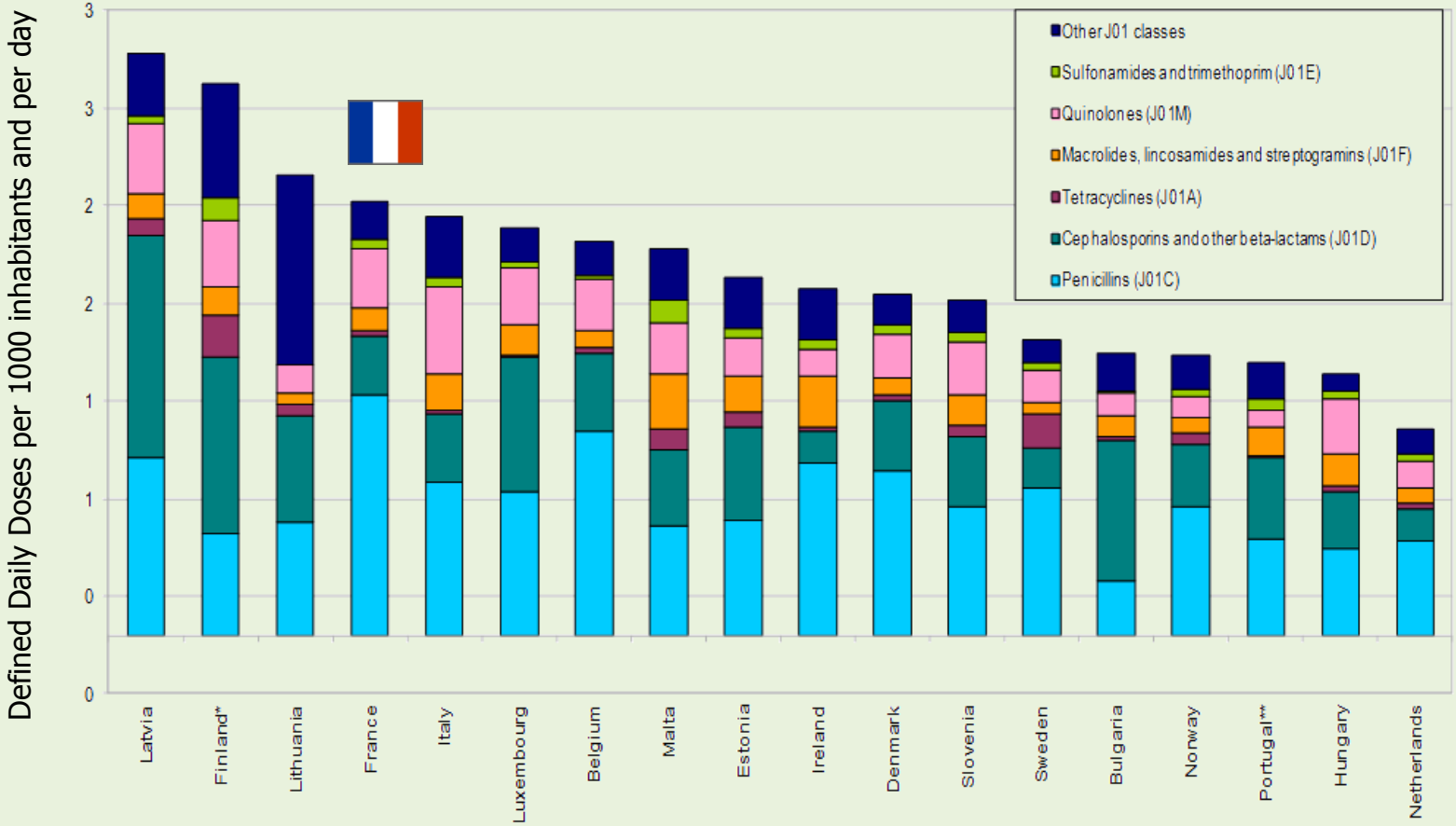


*Combined resistance: resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides

Source: EARS-Net, 2012

The symbols ↑ and ↓ indicate a significant increasing or decreasing trend for the period 2008-2011, respectively. These trends were calculated on laboratories that consistently reported during 2008-2011.

Consumption of antibiotics for systemic use (ATC group J01) in the hospital sector; EU/EEA, 2010

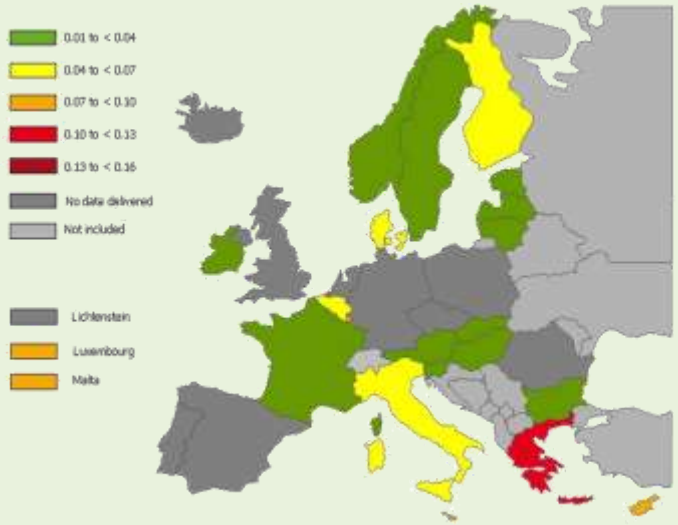


* Finland: data include consumption in remote primary health care centres and nursing homes.

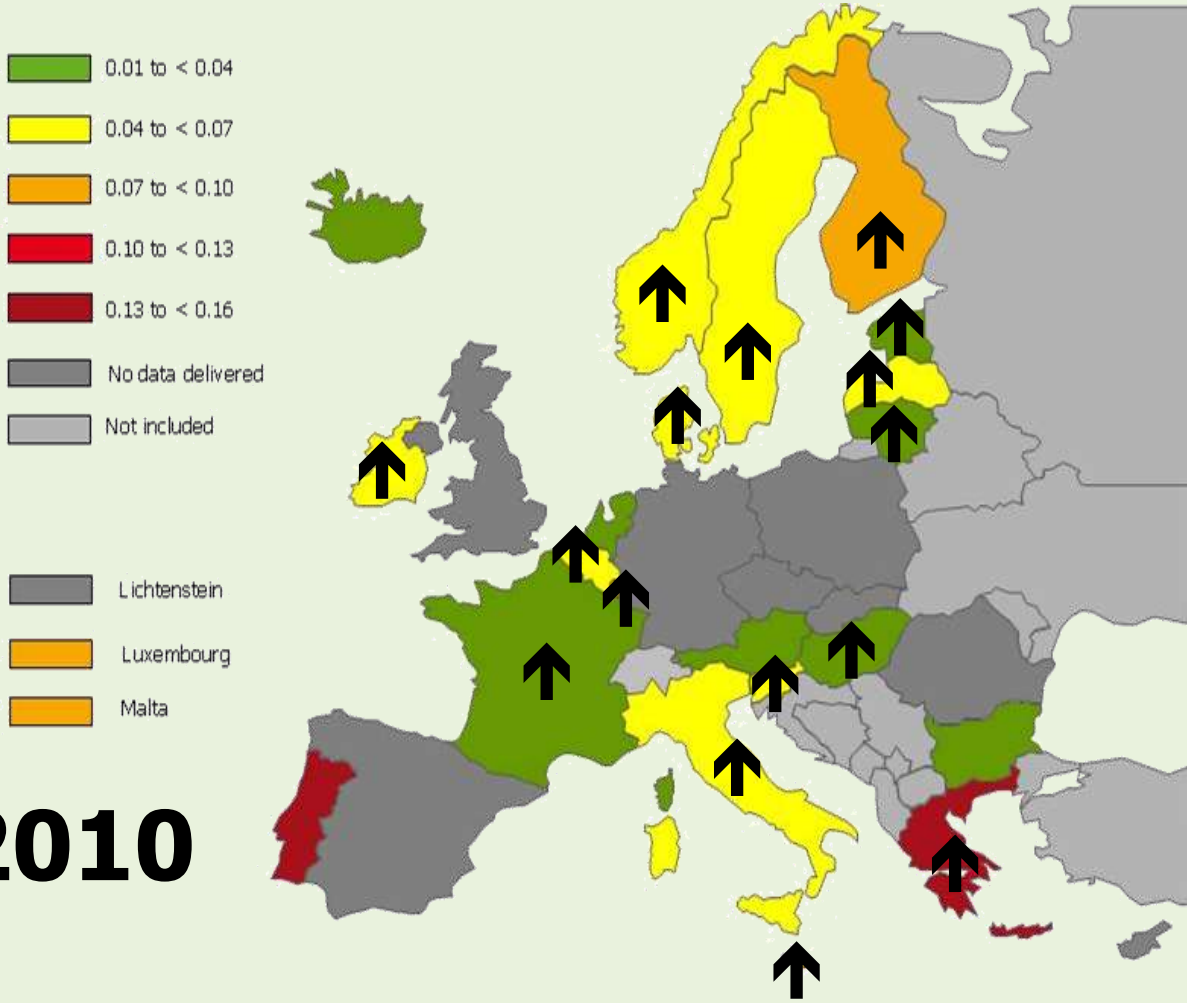
** Portugal: data only correspond to public hospitals

Source: ESAC-Net, 2012

Carbapenem consumption* (for the large majority in hospitals); EU/EEA, 2007–2010



2007



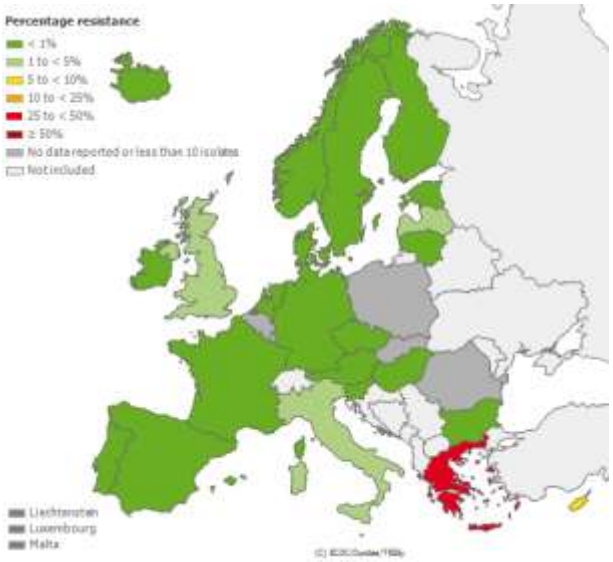
2010

*in Defined Daily Doses
per 1000 inhabitants and per day

Source: ESAC-Net, 2012

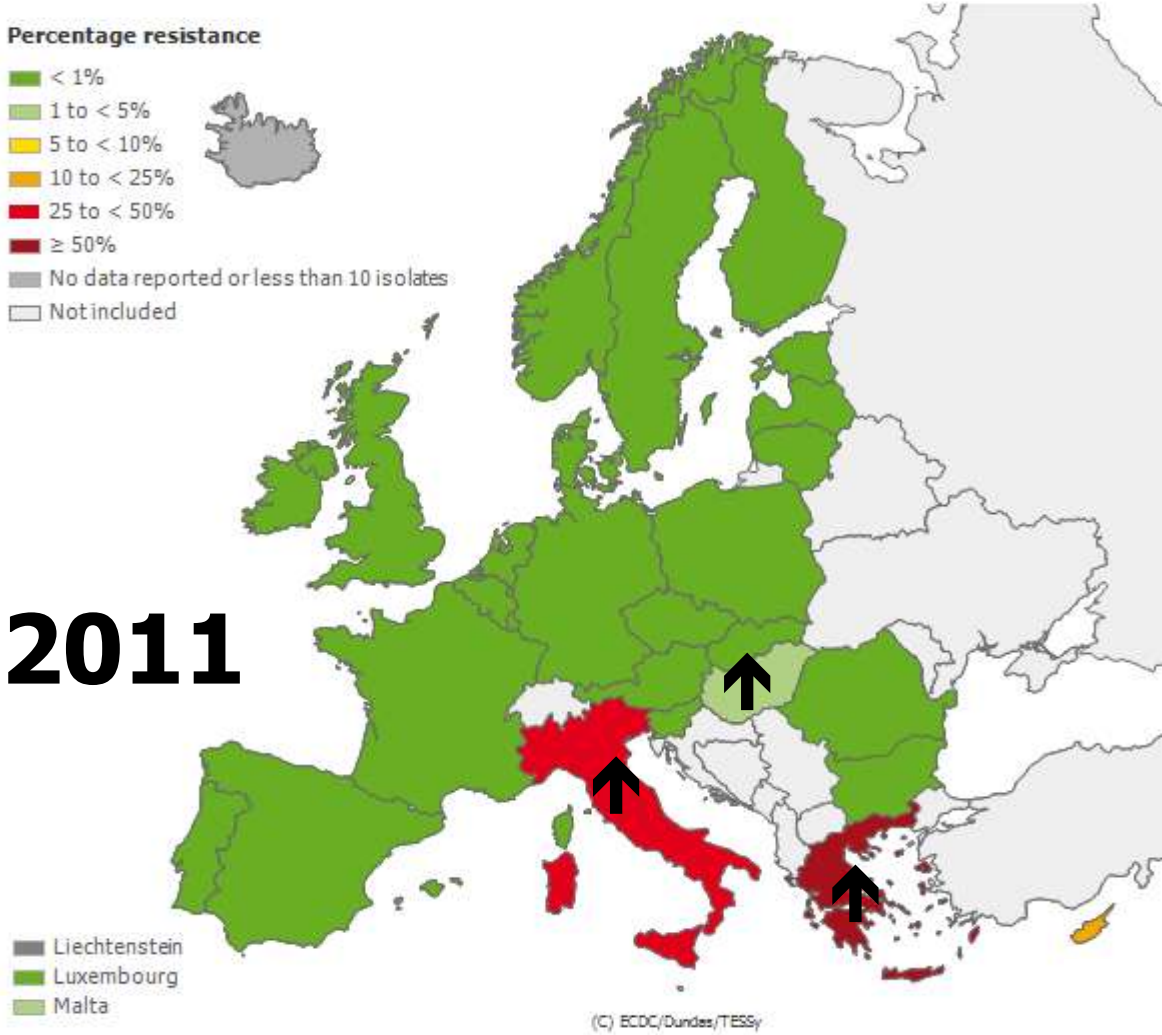
The symbols ↑ and ↓ indicate a significant increase or decrease between 2007 and 2010, respectively. These trends are indicated only for countries that reported relevant data for both 2007 and 2010.

Klebsiella pneumoniae: percentage of invasive isolates resistant to carbapenems; EU/EEA, 2008–2011



2008

2011



Source: EARS-Net, 2012

The symbols ↑ and ↓ indicate a significant increasing or decreasing trend for the period 2008-2011, respectively. These trends were calculated on laboratories that consistently reported during 2008-2011.

ECDC risk assessments: NDM-1 and carbapenemase-producing *Enterobacteriaceae*

Source: ECDC, 2010 & 2011.

Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) Programme

	EARS-Net	ESAC-Net	HAI-Net
Coordination	Coordination Group	Coordination Group	CG + Business Meet.
	Joint Annual Meeting of ARHAI Networks		
Ongoing surveillance	Interactive database & Annual report	Interactive database & Annual report	Interactive database & Reports
	Inter-agency report (2013)		
Epidemic intelligence	EPIS AMR-HAI		EPIS AMR-HAI
Point prevalence survey	Point prevalence survey of HAI and antimicrobial use in acute care hospitals		
Indicators		Antibiotic stewardship indicators	Infection control indicators
Ad-hoc studies / projects	**Carbapenemase survey (2013)**		HALT-2
Risk assessment : syst. reviews and guidance	Carbapenemase-producing *Enterobacteriaceae*	Perioperative proph. & Antibiotic stewardship prog.	Infection control prog.
Communication	European Antibiotic Awareness Day		Contribution to WHO Hand Hygiene Day
Training	Short course on prevention and control of MDROs		
			Infection control training needs

Main actions to prevent and control antibiotic resistance

Prudent use of antibiotics
(only when needed, correct dose, correct dose intervals, correct duration)

Infection control
(hand hygiene, screening, isolation)

New antibiotics
(with a novel mechanism of action, research, development)

European Commission action plan to combat AMR, 2011: 12 key actions

<u>*Human medicine*</u>

1. Appropriate use
4. Prevention infections
6. New antibiotics
9. Surveillance

<u>*Human + Veterinary*</u>

8. International cooperation
11. Research & Innovation
12. Communication, education

<u>*Veterinary medicine*</u>

2 & 3. Appropriate use
5. Prevention infections
7. Need for new antibiotics
10. Surveillance

18 November 2012

EUROPEAN ANTIBIOTIC AWARENESS DAY

A European Health Initiative

http://antibiotic.ecdc.europa.eu