

## ECDC DIRECTOR'S PRESENTATION

# European challenges on antimicrobial resistance from a *one health* perspective

Danish EU Presidency meeting, Copenhagen, 14 March 2012

Your Royal Highness Crown Princess Mary, Ministers, Distinguished guests, Ladies and Gentlemen,

I would like to thank the Danish EU Presidency for organising this very important conference on combating antimicrobial resistance, and to seize the opportunity to praise the Danish Government for being in the forefront regarding this serious issue.

I still recall taking part in the first Danish EU Presidency meeting dedicated to AMR some fifteen years ago. It was groundbreaking then, and the meeting today and tomorrow will be groundbreaking as well.

We are living in challenging times for public health. In Europe, and globally, attention is focused on the on-going effects of the financial crisis, widespread conflicts and environmental disasters.

It is more difficult than ever to get messages across concerning health, health protection, and on the fact that health is wealth.

In a couple of minutes, I will talk about the worrying trends of antimicrobial resistance, both in humans and in animals. But first, allow me to take a look back in history and to the very beginnings of medicine.

*'I will prescribe regimens for the good of my patients according to my ability and my judgment and **never do harm** to anyone.'*

This oath of Hippocrates I swore as young medical doctor. Today, I fear that it is sometimes forgotten, at least when we look at antibiotics and how they are prescribed.

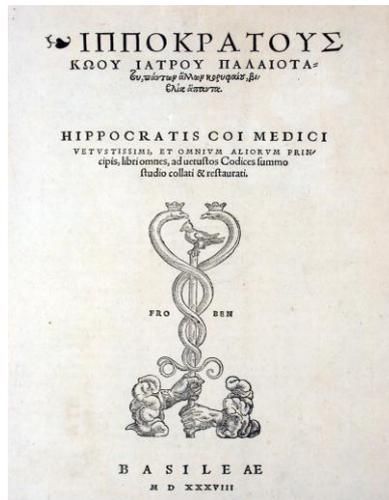
Antibiotics are not bad, *per se*, but they are often prescribed in the hope to offer a 'quick fix' for many infections. Long-term implications from antibiotics, such as antibiotic resistance are thus sacrificed out of convenience.

In a way I can understand that general practitioners do not always have the time, nor the energy, to think of alternative treatments. Especially when parents to young children insist to have antibiotics because they are concerned about being absent from work.

## Hippocratic oath

### Hippocratic oath

“  
I will prescribe regimens for  
the good of my patients  
according to my ability and  
my judgment and never do  
harm to anyone.”



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But let's go back to the pre-antibiotic era.

This is how children were treated for TB in the 1930s, **before** the discovery of antibiotics. It was called the "fresh air treatment".

## Fresh air treatment



The curve, on the next page, shows the huge decline in human mortality in the United States during the past century.

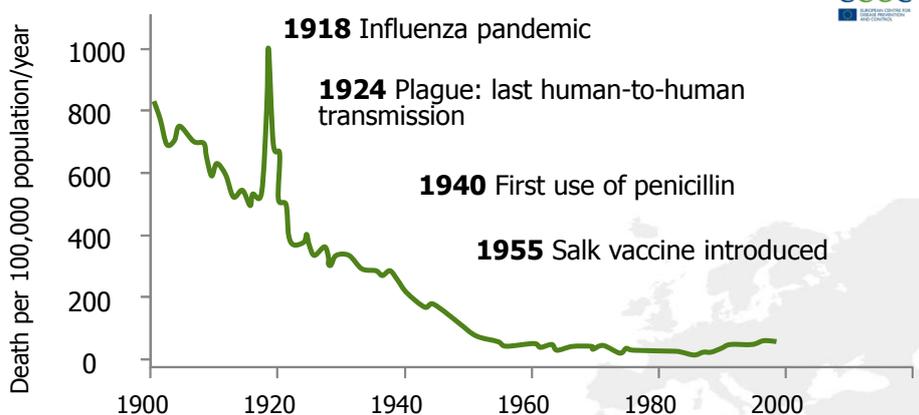
It is clear that there are two important discoveries in the history of medicine that contributed to this decrease:

- the discovery of antibiotics,
- and the development of vaccines.

Diseases that had previously been difficult to treat, and sometimes lethal, were now treatable or preventable, and many lives were saved.

## Human mortality in the US for the past century

### Human mortality, United States, 1900–2000



Adapted from: Aiello AE, Larson EL. *Lancet Infect Dis* 2002;2:103-10.



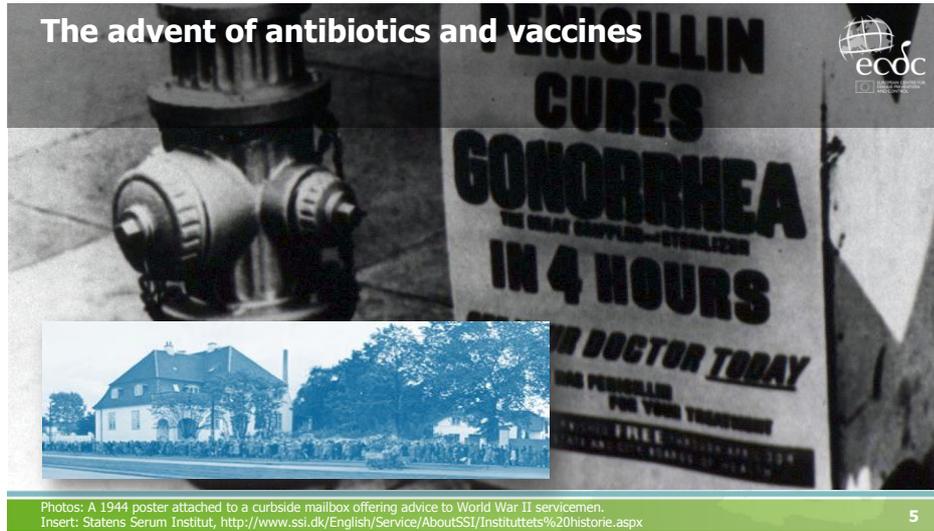
Since then, antibiotics have been fundamental in the treatment of many human infections such as gonorrhoea, pneumonia or tuberculosis.

Vaccines have also been fundamental in preventing many diseases. In the bottom picture, of the slide on the next page, you see hundreds of Danes queuing for vaccination at 'Statens Serum Institut' in Copenhagen. This institute, as several others in Europe, was pivotal in developing vaccines back in the early days.

But let's now continue focussing on antibiotics.

A few decades ago, it was easy to use antibiotics to treat human infections. But for the past decades, antimicrobial resistance has become a major public health threat!

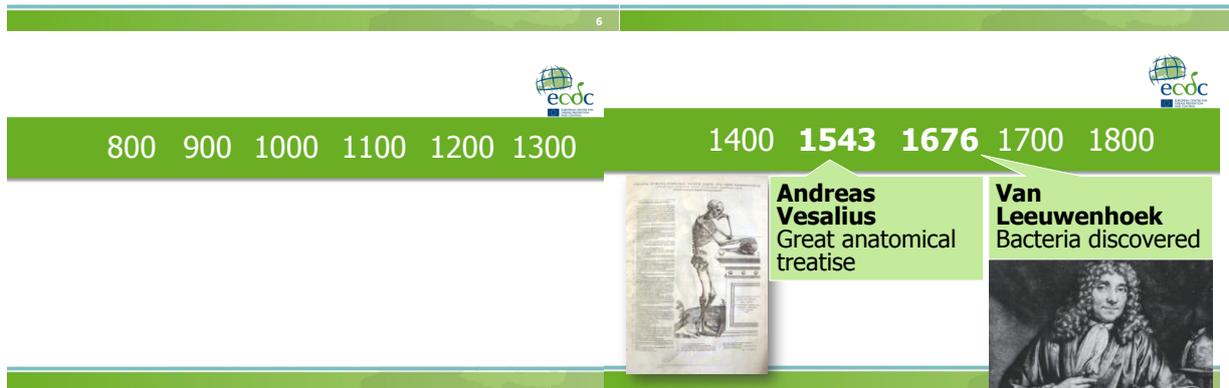
## Antibiotics and vaccines have been fundamental as treatment and prevention measures



This is an illustration of some important medical milestones.

## Milestones in medical history

Milestones in medicine



Not much to report for 2000 years..

The 20th century contains the major milestones in modern medicine.

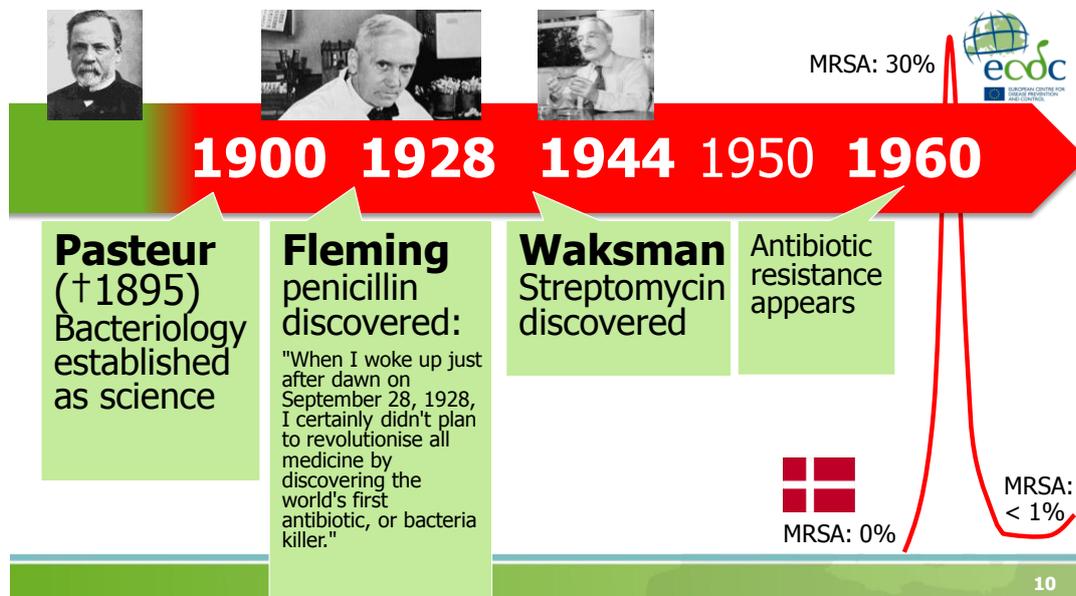
On such a large scale, it looks like the discovery of antibiotics and the following rise of resistance both happened in a split second of the world's history.

Denmark has been collecting and testing *Staphylococcus aureus* isolates from blood samples since the 1950s. The red tip of the curve indicates that MRSA increased rapidly in the mid-1960s, culminated at the end of the 1960s, before it gradually decreased to stay below 1% for two decades.

The good news is that Denmark showed, before any other country, that MRSA was not a curse and that it could be controlled through a combination of:

- increasing awareness about hospital hygiene, and;
- a more rational use of broad-spectrum antimicrobial agents.

### Major milestones in modern medicine



Let's now look at the current European MRSA data in some detail

So what is the current situation of antimicrobial resistance?

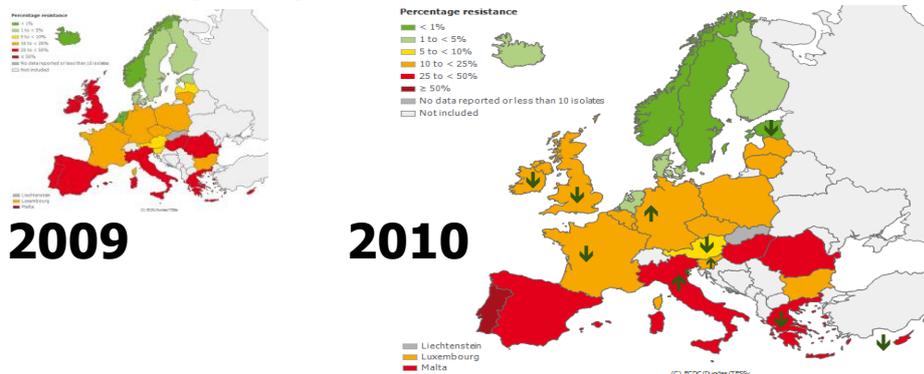
The slide below presents the latest data available for the EU. We see large variations among the countries, from less than 1% (*BRIGHT GREEN*) to more than 50% (*DARK RED*).

Now the good news is that in several European countries we see a declining trend of MRSA, if you compare the rates from 2009 and 2010.

So, since some countries in Europe were indeed able to decrease their rates of MRSA, thus confirming the early experience of Denmark, we are in other words able to change the trend.

**Trends for methicillin-resistant *Staphylococcus aureus***

***Staphylococcus aureus*:  
proportion of invasive isolates resistant to  
methicillin (MRSA); EU/EEA, 2009–2010**



↑ and ↓ indicate a significant increasing or decreasing trend for the period 2007 to 2010. These trends were calculated for laboratories that consistently reported between 2007 and 2010. Source: EARS-Net, 2011. 11

But the bad news is that we see increased resistance in other bacteria.

*Klebsiella pneumoniae* - a bacterium commonly found in hospital infections - is increasingly becoming resistant to multiple antibiotics as shown on this map.

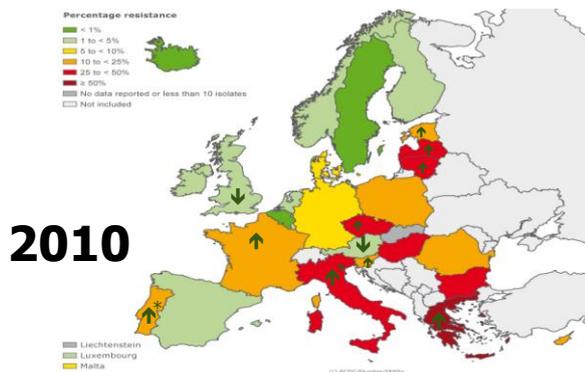
As a consequence, doctors in hospitals must increasingly rely on the type of antibiotics that should be seen as the last available resource to treat these patients, so-called last-line antibiotics.

***Klebsiella* bacteria has become resistant to multiple antibiotics**

***Klebsiella pneumoniae*:  
proportion of multidrug-resistant\* invasive  
isolates; EU/EEA, 2010**



\* Resistant to third-generation cephalosporins, fluoroquinolones and aminoglycosides



↑ and ↓ indicate a significant increasing or decreasing trend for the period 2007 to 2010. These trends were calculated for laboratories that consistently reported between 2007 and 2010. Source: EARS-Net, 2011. 12

And there is even worse news...

Due to the increased use of antibiotics and varying hospital infection control practices, *Klebsiella pneumoniae* is now even starting to show resistance to the main last-line class of antibiotics, known as carbapenems.

What is very worrisome here is the increase in carbapenem resistance that you can see when comparing these two maps from 2009 and 2010.

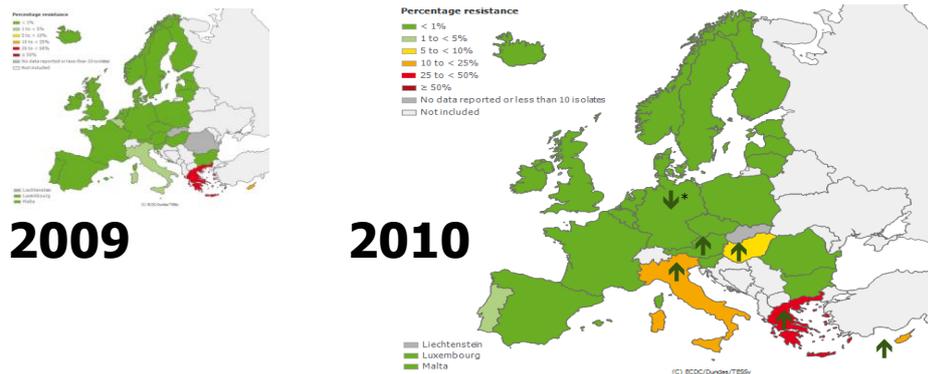
And this data most likely only represents the tip of the iceberg since localised outbreaks are also reported in the countries shown in green.

You may have heard of the outbreak, a year ago, of carbapenem-resistant *Klebsiella* at the Maasstad Hospital in the Netherlands.

More than 100 patients were infected, resulting in the death of 3 patients and with an additional 10 patients for whom infection probably contributed to their deaths. The Dutch health inspectorate concluded that doctors in this hospital had failed in controlling the outbreak and took disciplinary actions.

### Emergence in the EU of carbapenem-resistant *Klebsiella* bacteria

***Klebsiella pneumoniae*:  
proportion of invasive isolates resistant to carbapenems; EU/EEA, 2009–2010**



↑ and ↓ indicate a significant increasing or decreasing trend for the period 2007 to 2010. These trends were calculated for laboratories that consistently reported between 2007 and 2010. Source: EARS-Net, 2011.

I am personally most concerned about antimicrobial resistance in healthcare-associated infections and the threat they pose to patient safety.

## Antimicrobial resistance: a threat to patient safety

Options for treating patients infected with highly resistant bacteria are limited to antibiotics that are old and with limitations and toxic side-effects. All this leads to longer hospital stays, increased suffering, and even to death; and of course to increased costs.

In 2009, ECDC and EMA estimated that each year 25,000 Europeans die as a direct consequence of a multidrug-resistant infection. Not only does antimicrobial resistance have a significant human impact, but it also has large economic consequences.

In the same joint report the **economic impact** was estimated at € 1.5 billion per year. This estimation, though still valid, is likely to be an underestimation. We think the real costs of treating a patient with a multidrug-resistant infection are much higher than this.

## Costs of antimicrobial resistance

### Human and economic impact of antimicrobial resistance\*



Each year, **25 000 deaths** in EU countries are directly attributable to multidrug-resistant infections.

Extra in-hospital costs	Extra outpatient costs	Productivity losses due to absence from work	Productivity losses due to patients who died from their infection	TOTAL
€ 927.8 million	€ 10 million	€ 150.4 million	€ 445.9 million	<b>€ 1.5 billion</b>

\* Estimates for five common multidrug-resistant bacteria (EU Member States, Norway, and Iceland; 2007)

Source: The bacterial challenge: time to react. Joint report, ECDC and EMA, Stockholm, 2009. Available online at: [http://ecdc.europa.eu/en/publications/Publications/Forms/ECDC\\_DispForm.aspx?ID=444](http://ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DispForm.aspx?ID=444)

And there is one thing that we must not forget: there is always a patient and a personal story behind the statistics.

Last year, ECDC worked together with Euronews to produce a film that tells the story of patients suffering with multidrug-resistant bacteria.

In this film we hear the story of Paolo from Italy who, while on holiday, developed a complicated urinary tract infection from multidrug-resistant *E. coli* isolate, resistant to many antibiotics.

### A personal story behind the statistics



Paolo's *E. coli* was resistant to third-generation cephalosporins as well as to fluoroquinolones. The two maps here below show the resistance profile of the two antibiotics in question. We see that, with the exception of a few countries, resistance to these classes of antibiotics is already high in Europe.

In addition, as indicated by the arrows, it is still increasing in many European countries.

### Resistance profile of the two third-generation antibiotics

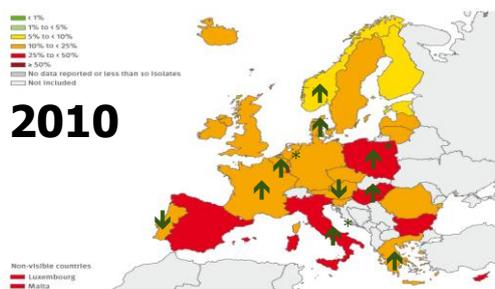
***Escherichia coli*: proportion of invasive isolates resistant to third-generation cephalosporins or to fluoroquinolones; EU/EEA, 2010**



**Resistant to third-generation cephalosporins**



**Resistant to fluoroquinolones**



↑ and ↓ indicate a significant increasing or decreasing trend for the period 2007 to 2010. These trends were calculated for laboratories that consistently reported between 2007 and 2010. Source: EARS-Net, 2011.

So far, I have only spoken about resistance in humans.

So what is the situation like in animals?

Today on the 14<sup>th</sup> of March, the European Food Safety Authority (EFSA) and ECDC are publishing a report showing that resistance to several antimicrobials was commonly detected in zoonotic bacteria.

The report makes an important contribution to current work being carried out at EU-level to fight antimicrobial resistance.

This slide presents one of the many results in the report, namely the percentage of ciprofloxacin and nalidixic acid resistance in indicator *E. coli* isolated from chicken:

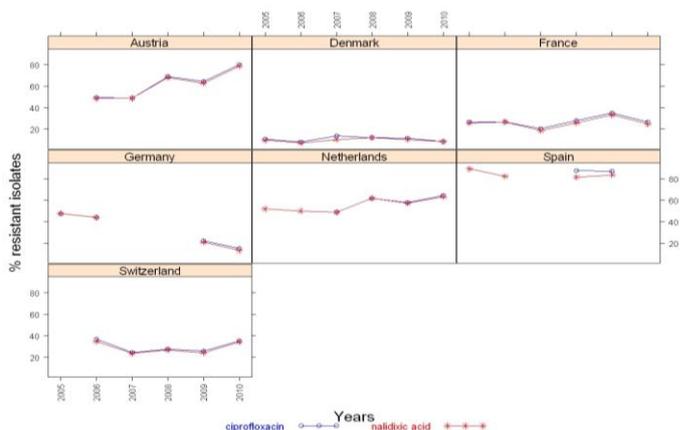
The graph indicates a low percentage of resistance in *E. coli* from, for example, Denmark and a much higher percentage in *E. coli* from several other countries.

Is this resistance, observed in food animals, relevant to antimicrobial resistance in humans?

I can assure you that that this is the case, as the next speaker in the programme, Professor Jan Kluytmans, will certainly point out.

### Percentage of ciprofloxacin and nalidixic acid resistance in indicator *E. coli* isolated from chicken

#### Trends in ciprofloxacin and nalidixic acid resistance in indicator *Escherichia coli* from chicken, 2005–2010, quantitative data



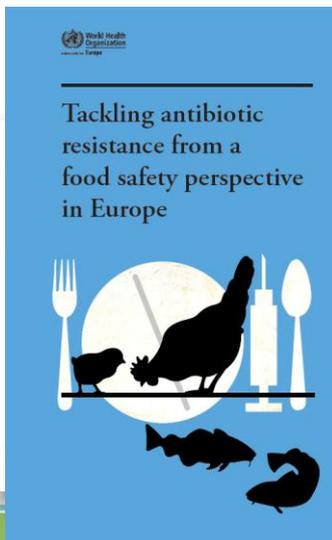
Source: EFSA and ECDC. EU summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food 2010, published 14 March 2012 18

And the issue of the relation of AMR in food animals and in humans is not only on our agenda, but also on WHO/Europe's 'plate'.

Last year, WHO/Europe published a report on tackling antibiotic resistance from a food safety perspective and its strategic action plan on antibiotic resistance. And just last week, WHO published its report on the evolving threat of AMR.

### Reports on antimicrobial resistance

WHO reports and European strategic action plan on AMR



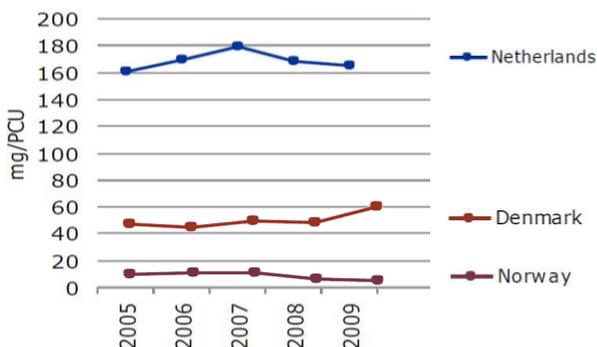
Source: WHO, 2012; WHO Regional Office for Europe, 2011.

Last year, the European Medicines Agency (EMA) published the first report on its European Surveillance of Veterinary Antimicrobial Consumption (ESVAC).

Data on the sales of veterinary antibiotics from 9 countries were presented, three of which we have selected for this slide.

### Sales of veterinary antibiotics

Sales of veterinary antimicrobial agents (mg per population correction unit) in NL, DK, NO in 2005–2009



Source: European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), EMA, 2012.

These first results showed that there were **large variations** depending on the country, with a very high consumption in the countries at the top of the graph, such as the Netherlands; to a much lower consumption in the countries at the bottom of the graph, such as Denmark or Norway.

We have similar data regarding human consumption of antibiotics.

The map here below shows the total consumption of antibiotics in humans in the community (i.e. outside of hospitals). \*

As with animals, antibiotic consumption in humans varies widely depending on the EU country.

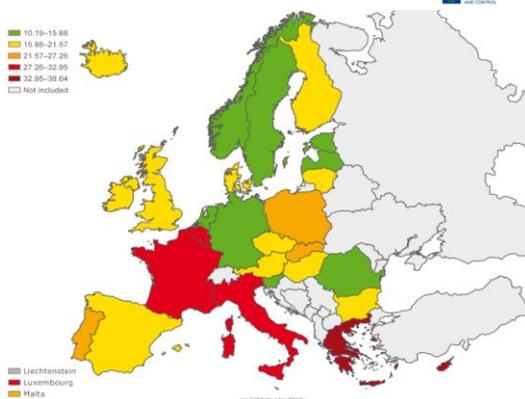
There is a four-fold difference between:

- countries in southern and eastern Europe, usually reporting the highest consumption, and;
- countries from northern Europe that report a much lower consumption.

### Antibiotic consumption in EU/EEA countries in humans, 2009



For Cyprus and Lithuania: total consumption (both community and hospital sector).  
For Spain: reimbursement data that do not include over-the-counter sales without a prescription.



Source: ESAC, 2010

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*\*(expressed in Defined Daily Doses per 1 000 inhabitants and per day)*

The problems of high antibiotic consumption levels in both humans and animals, and of AMR, cannot be solved in isolation. **Animals and humans are one health.**

The European Commission advocates for the '*One health*' aspect in order to tackle AMR. As Commissioner for Health, John Dalli, has just mentioned in his video message, the Commission has launched an '*Action Plan against the rising threats from Antimicrobial Resistance*' that embraces this holistic approach.

We need healthy animals in order to have healthy humans.

But equally important, **prudent use of antibiotics** is crucial, **not only in humans but also in animals!**




**Humans + Animals = One Health**

**Prudent use of antibiotics.  
We are all responsible!**

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So how can we make sure that no further harm is done?

Firstly, Prudent use of antibiotics

- Take them only when needed and only with the correct dose, dose intervals and duration.
- And only upon prescription.

Secondly, resistance to antibiotics will not be brought under control without paying attention to infection control practises, and especially to hand hygiene in healthcare settings.

Finally, we would also need to develop new antibiotics.

### Main actions to prevent and control antimicrobial resistance

#### Main actions to prevent and control AMR



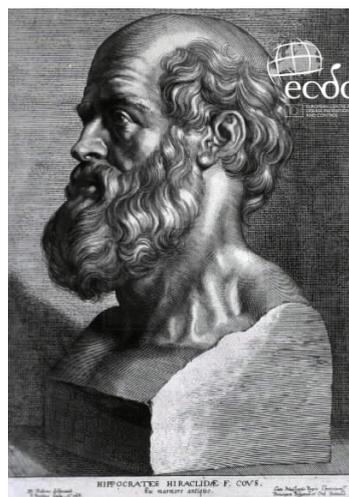
**Prudent use of antimicrobials**



**Infection control**



**New antibiotics**



During the week of 18 November each year, the European Antibiotic Awareness Day takes place in the whole of the EU.

This European health initiative coordinated by ECDC aims to support EU Member States in their efforts to promote **prudent use of antibiotics**. And last year, the initiative took place for the 4<sup>th</sup> consecutive year with 37 European countries participating.

Here you see the dedicated European Antibiotic Awareness Day banner on the Commission's Berlaymont building in Brussels.

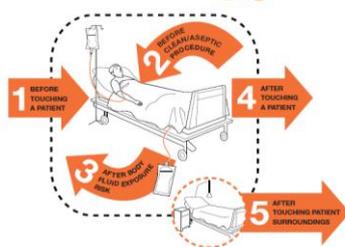


Regarding **infection control**, WHO has been very active in promoting **hand hygiene** worldwide.

**WHO first global patient safety challenge: 'Clean care is safer care' in Europe, 2005–2011**



**Your 5 Moments for Hand Hygiene**



European countries that have pledged their **support** to implement hand hygiene and other actions as a mean of combating healthcare-associated infection (HAI).



Source: WHO, 2009

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So my **take home message** for today is that antimicrobial resistance is one of the most serious global health challenges that we face.

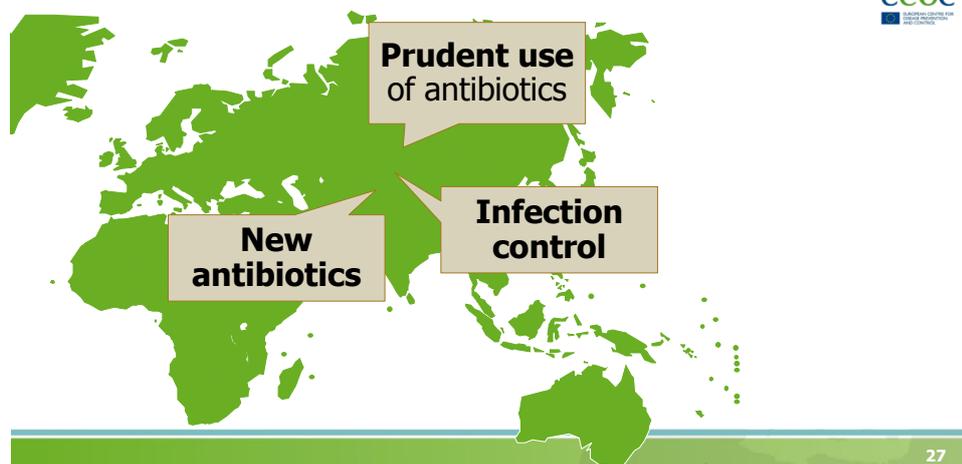
We need to focus on the solutions, in other words on:

- prudent use of antibiotics;
- infection control, and;
- on the development of new antibiotics.

This is a responsibility for everybody – patients, doctors, nurses, veterinarians, policy makers, you and me ...

## Take home message on antimicrobial resistance

### Antimicrobial resistance: three messages



Thank you for your attention today.