

# ANTIMICROBIAL STEWARDSHIP (AMS) IN THE ERA OF MULTI-DRUG RESISTANCE

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*ESCMID Summer School 2015 (Istanbul, Turkey)*



# Learning objectives

- Know the drivers of bacterial resistance
- Understand the principles of AMS
- Understand the barriers to AMS

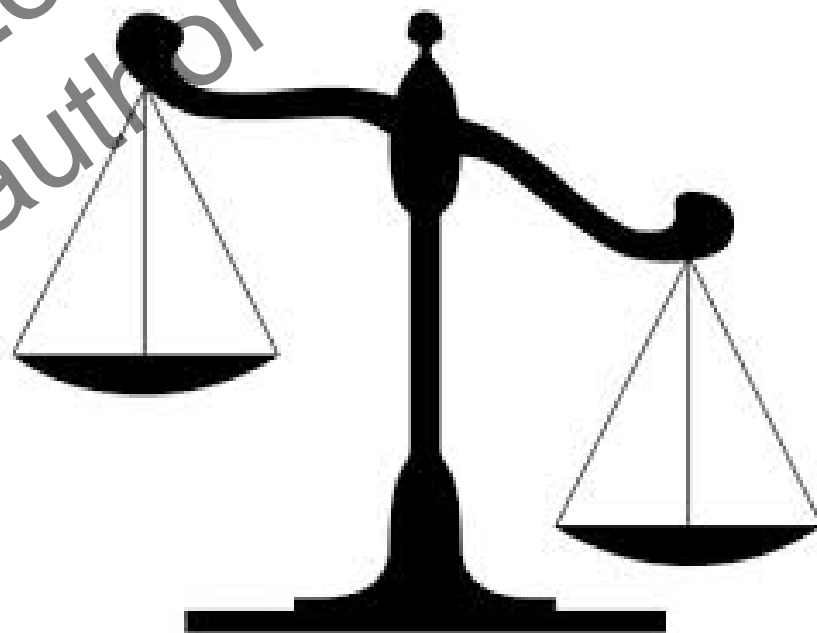
WHAT IS AMS ?

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# Definition - *Antimicrobial stewardship*

Prescription :

- The most efficient for the patient
- With as few side effects as possible: toxicity, *Clostridium difficile* infections and selection of resistance



# Not only the antibiotics

- Antifungals
- Antiparasitics
- Antivirals

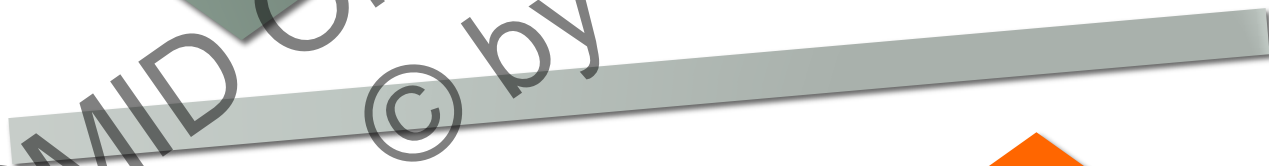
# Why is AMS important ?



# International crisis



Less  
antimicrobials



More  
resistance



# Burden of bacterial resistance

ECDC (2009)  
25 000 deaths/year in Europe



CDC (2013)





# Most recent estimates



Estimating the  
economic costs of  
antimicrobial resistance

Model and Results

- Enormous costs

- And very high number of deaths

Jirka Taylor, Marco Hafner, Erez Yerushalmi, Richard Smith, Jacopo Bellasio,  
Raffaele Vardavas, Teresa Bienkowska-Gibbs, Jennifer Rubin

# WHO



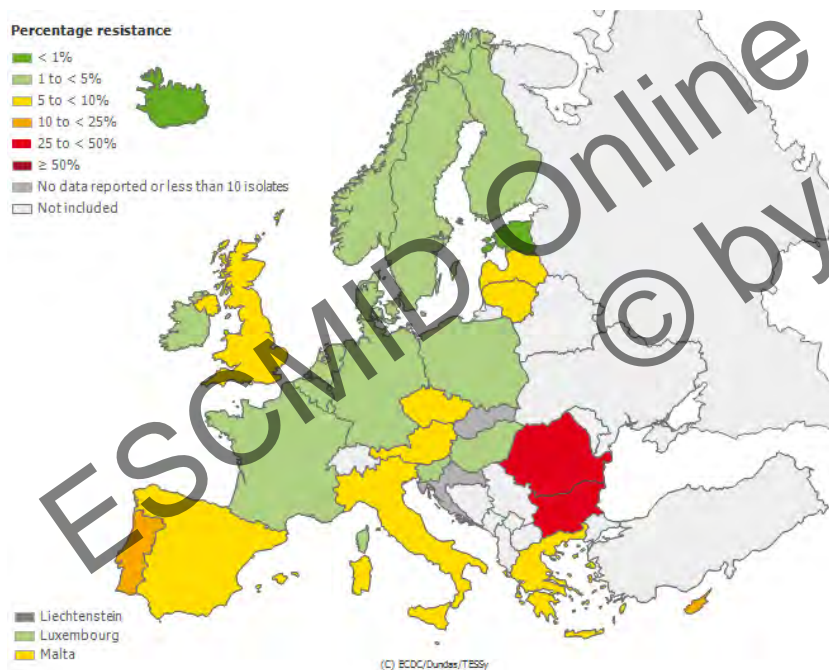
WHO **Global action plan on antimicrobial resistance** endorsed at the Sixty-eight World Health Assembly in May 2015

# Worldwide increase in bacterial resistance, in all settings

*E. coli* C3G-R/I (2006)

Percentage resistance

- < 1%
- 1 to < 5%
- 5 to < 10%
- 10 to < 25%
- 25 to < 50%
- ≥ 50%
- No data reported or less than 10 isolates
- Not included

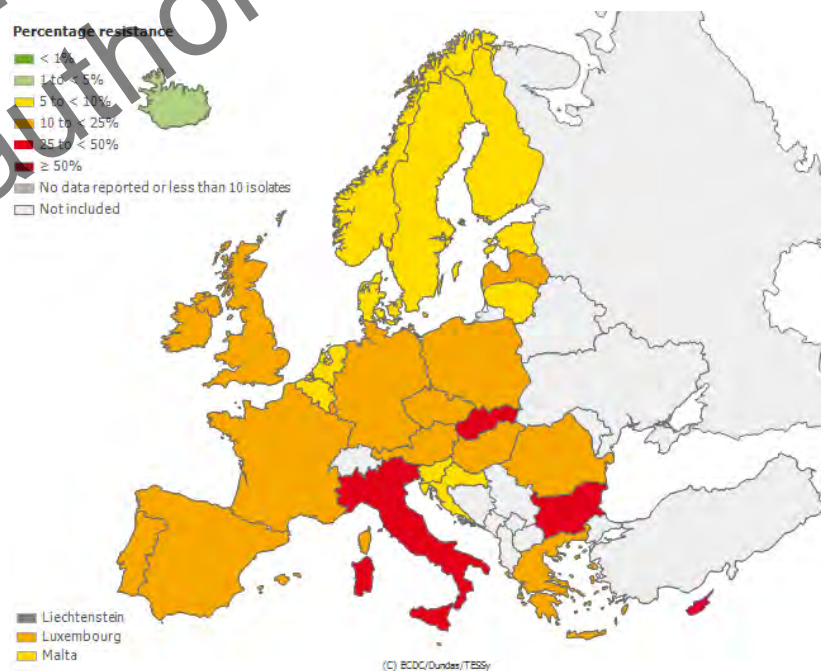


*E. coli* C3G-R/I (2013)

**ESBL**

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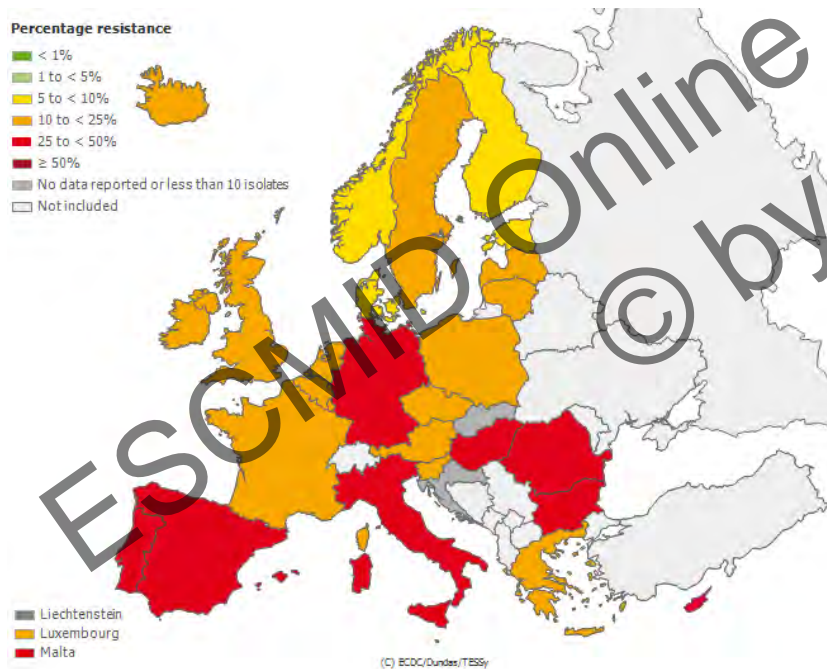


Data EARS-Net:

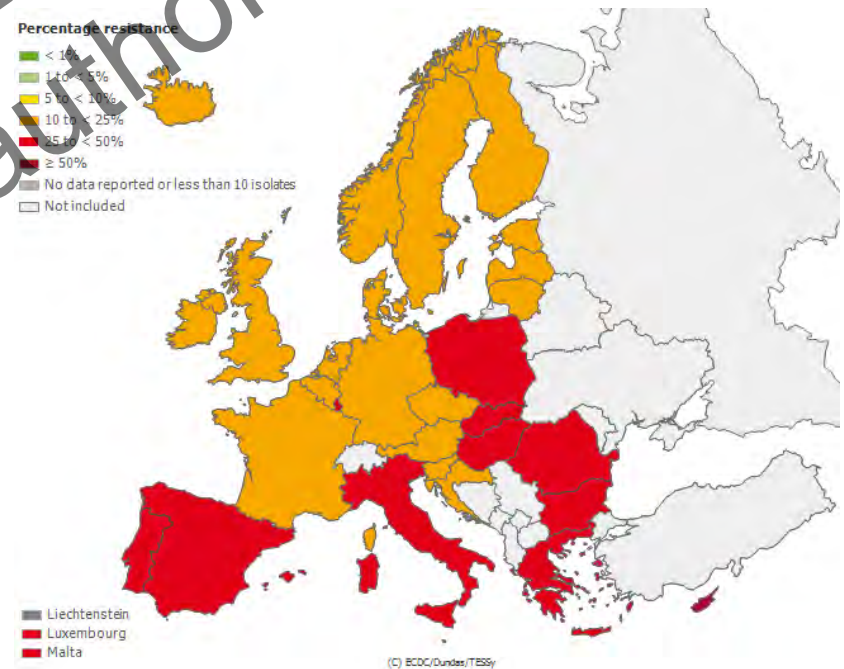
[http://www.ecdc.europa.eu/en/healthtopics/antimicrobial\\_resistance/database/](http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/)

# Fluoroquinolones

*E. coli* FQ-R/I (2006)



*E. coli* FQ-R/I (2013)



Data EARS-Net:

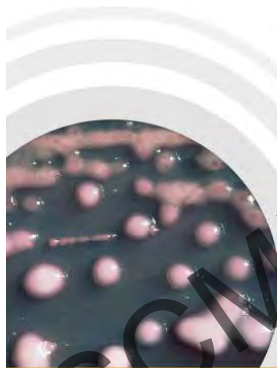
[http://www.ecdc.europa.eu/en/healthtopics/antimicrobial\\_resistance/database/](http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/)



# Carbapenemases: the next step...

Europe and beyond

*E. coli* carbap-R/I (2013)

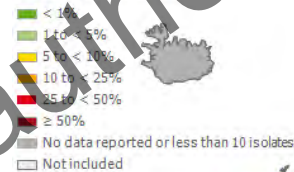


TECHNICAL REPORT

## Carbapenemase-producing bacteria in Europe

Interim results from the European survey on carbapenemase-producing *Enterobacteriaceae* (EuSCAPE) project 2013

Percentage resistance



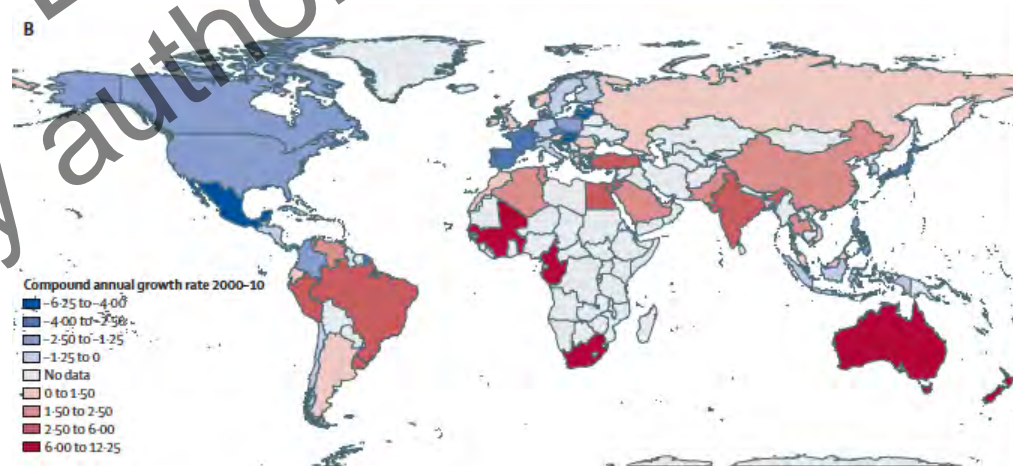
(C) ECDC/Ondas/TESSy

# Association between antibiotic use and resistance

- Any antibiotic taken has an impact on the microbiota
- Resistant bacteria spread to other living creatures and the environment
- Bacteria have remarkable adaptation capacities

# Worldwide increase of antibiotic use

- 2000-2010 international data
- + 36%, in particular broad-spectrum antibiotics
- Mainly Brazil, Russia, India, China and South Africa



Very few new antibiotics in the pipeline





# Impact of bacterial resistance

- Mortality
- Costs
- MDR/XDR bacteria infections jeopardize surgery, immunosuppressive treatments, intensive care management...
- Leads to increased use of broad-spectrum antibiotics: 'vicious' circle

# An alarming situation



- « ...a problem so serious that it threatens the achievements of modern medicine.  
A post-antibiotic era—in which common infections and minor injuries can kill—far from being an apocalyptic fantasy, is instead a very real possibility for the 21st century. »

# An alarming situation

- Professor Dame Sally Davies
- England's Chief Medical Officer

*« Antimicrobial resistance poses a catastrophic threat. If we don't act now, any one of us could go into hospital in 20 years for minor surgery and die because of an ordinary infection that can't be treated by antibiotics. And routine operations like hip replacements or organ transplants could be deadly because of the risk of infection. »*

# An alarming situation

- President Barack Obama took action in 2014
- Antibiotic Resistance National Action Plan released in March 2015
- More than \$1.2 billion funding

# 3 main strategies to curb resistance



All settings, all professionals

AMS



Infection control  
Environment



Vaccination

## One Health approach

DOES AMS REDUCE  
RESISTANCE ?

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# The evidence

- Yes, AMS reduces resistance, but not on its own
- ‘One health’ approach

# GENERAL PRINCIPLES OF AIMS

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# At the international level

- More and more initiatives
- Need for collaboration and global efforts
- Worldwide ESGAP survey including 660 hospitals in 2012: 58% had an existing AMS programme



# All settings: out- and inpatients, nursing homes

- Multifaceted comprehensive programmes
- Targeting professionals and the public

- Interesting resources:

<http://ecdc.europa.eu/en/eaad/Pages/Home.aspx>

<http://www.e-bug.eu>

# KEY COMPONENTS OF AN ASP

- Multidisciplinary team
- Institutional support
- Ability to monitor antibiotic use and bacterial resistance
- Guidelines
- Educational measures
- Restrictive measures

# Some AMS measures

## Structural measures

- Antibiotic order form
- Availability of expert advice
- Guidelines
- Computerised decision support systems
- Rapid diagnostic tests

## Educative measures

- Education
- Audits and feedback

# Some AMS measures

## Restrictive measures

- Restrictive prescribing
- Review of prescriptions
- Systematic expert advice in some cases (MDR, blood cultures, reserve antibiotics...)

## Monitoring

- Antibiotic use
- And resistance
- With feedback and benchmarking

# Final objective: appropriate antibiotic prescriptions

No unnecessary prescriptions

- Better diagnosis

No inappropriate prescriptions

- Choice of the molecule
- Dose
- Route of administration
- Duration

# BARRIERS TO ASP

## BARRIERS

- Funding
- Lack of IT support
- Lack of institutional support

## POTENTIAL SOLUTIONS

- Convince
  - International literature
  - Sensitive/high-priority area:
    - ✦ Patient safety
    - ✦ Healthcare-acquired infections / bacterial resistance / *C. difficile*
    - ✦ Costs
  - National association / lobbying
- Monitor your process and outcome measures to demonstrate success +++

# BARRIERS TO ASP

## BARRIERS

- Opposition from prescribers
- Where to start ?

## POTENTIAL SOLUTIONS

- « Low-hanging fruits »
- Mix restrictive and educative measures
- Build on successes, progressively
- Don't reinvent the wheel, share ideas
- Many tools on the ESGAP website



# COMMON MISTAKES

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# 1. CHANGING BEHAVIOUR

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# The Biggest Error We Make in Trying to Change Behavior

## Assuming knowledge changes behavior

- Our instinct to create change (esp. in medicine)

Analyze → Think → Change

- More effective way to create change

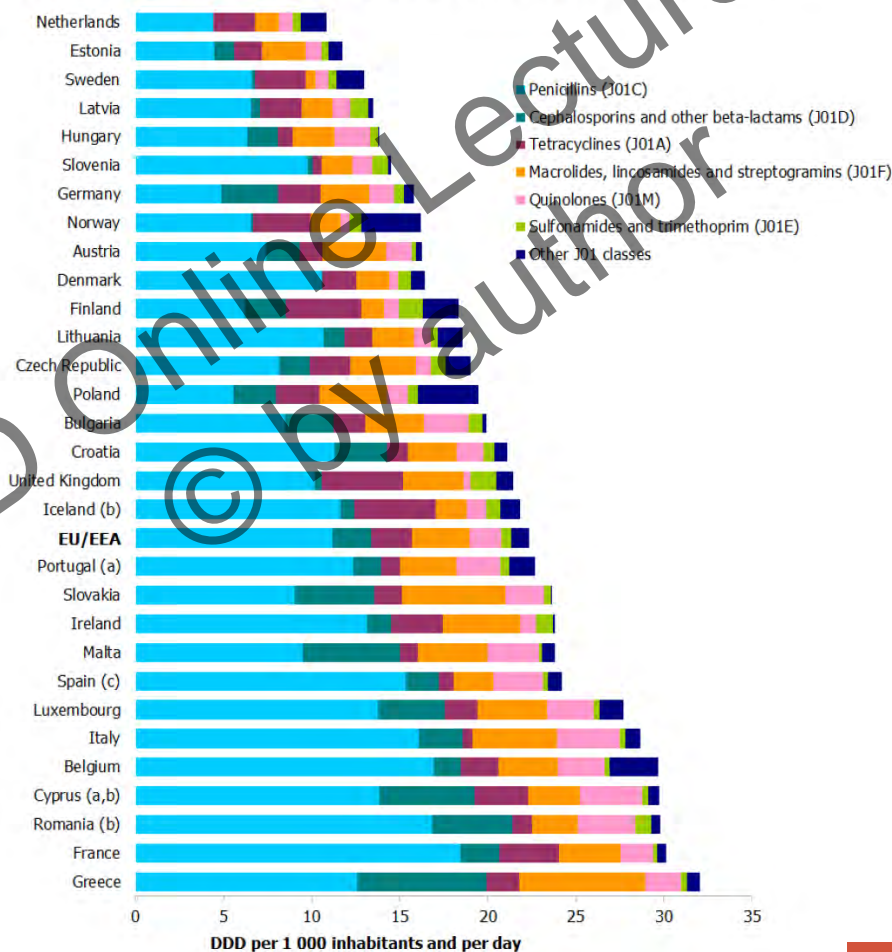
See → Feel → Change

# Goal = changing behaviour

- Behaviour change theories and strategies
- Cultural influence
- Quality improvement strategies
- No magic bullet

# Antibiotic prescribing = not a rational action

**Figure 1. Consumption of antibiotics for systemic use in the community by antibiotic group in 30 EU/EEA countries, 2013 (expressed in DDD per 1 000 inhabitants and per day)**



**REVIEW ARTICLE**

*‘We can never change the behaviour of any other human being, but we can facilitate for others to modify their own behaviour.’*

**Understanding and changing human behaviour—antibiotic mainstreaming as an approach to facilitate modification of provider and consumer behaviour**

CECILIA STÅLSBY LUNDBORG<sup>1</sup> & ASHOK J. TAMHANKAR<sup>1,2</sup>

*Charani E et al Behavior Change Strategies to Influence Antibiotic Prescribing in Acute Care: A Systematic Review. CID, October 2011;53(7):651–662*



Public Health  
England



Department  
of Health

# **Behaviour change and antibiotic prescribing in healthcare settings**

## **Literature review and behavioural analysis**

# Resistance to change





# Understanding the Determinants of Antimicrobial Prescribing Within Hospitals: The Role of “Prescribing Etiquette”

E. Charani,<sup>1</sup> E. Castro-Sanchez,<sup>1</sup> N. Sevdalis,<sup>2,3</sup> Y. Kyrtzia,<sup>1</sup> L. Dismright,<sup>1</sup> N. Shah,<sup>1</sup> and A. Holmes<sup>1</sup>

<sup>1</sup>The National Centre for Infection Prevention and Management, Hammermith Hospital; and <sup>2</sup>Department of Surgery and Cancer, and <sup>3</sup>Imperial Centre for Patient Safety and Service Quality, St Mary's Hospital, Imperial College London, United Kingdom

1. **Non-interference with the prescribing decisions of colleagues:** Reluctance to interfere with the prescribing decisions of colleagues. In the case of antimicrobial prescribing there is a reluctance to intercept antimicrobial prescriptions started by colleagues. This recognises the autonomous decision making process of prescribing.
2. **Accepted non-compliance to policy:** Deviations from policy recommendations are tolerated and put in the context of the prescriber's experience, expertise and the specific clinical scenario. This leads to hierarchy and expertise, and not policy as determinants of prescribing practice behaviours.
3. **Hierarchy of prescribing:** Prescribing as an activity is performed by junior doctors. But it is the senior doctors who decide what is prescribed.

**Keywords.** prescribing etiquette; antimicrobial prescribing; prescribing behavior.

## National cultural dimensions as drivers of inappropriate ambulatory care consumption of antibiotics in Europe and their relevance to awareness campaigns

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*Received 12 July 2011; returned 2 November 2011; revised 7 November 2011; accepted 26 November 2011*

**Objectives:** European countries exhibit significant geographical differences in antibiotic consumption per capita within ambulatory care, especially inappropriate use for colds/flu/sore throat (CFSt). One potential explanation could be national cultural differences resulting in varying perceptions and, therefore, influences.

**Methods:** Publicly available data on the proportions of respondents in the 2009 Eurobarometer survey who had taken antibiotics for CFSt were tested for association against country scores derived from the Hofstede cultural dimension model. They were also correlated with knowledge of respondents about various key antibiotic facts.

**Results:** The Eurobarometer dataset incorporated 26 259 responses from all European Union (EU) countries except Cyprus. Using multiple regression, uncertainty avoidance and masculinity were identified as the two national cultural dimensions significantly associated with the use of antibiotics for CFSt ( $R$ -adjusted=0.45;  $P<0.001$ ). After controlling for these cultural influences, individuals who stated they had received information about antibiotics in the previous year were also more likely to correctly answer antibiotic-related questions ( $r=0.721$ ;  $P<0.001$ ). The use of antibiotics for CFSt was found to be inversely correlated with respondents' knowledge that antibiotics are ineffective against viruses ( $r=-0.724$ ;  $P<0.001$ ) and that misuse will render them ineffective in the longer term ( $r=-0.775$ ;  $P<0.001$ ).

**Conclusions:** National cultural dimensions, especially uncertainty avoidance and masculinity, appear to have a very significant impact on inappropriate antibiotic use within European countries. Nevertheless, their influence can be reduced by making EU citizens more knowledgeable about antibiotics through appropriate messages and targeted campaigns.



# Group dynamic

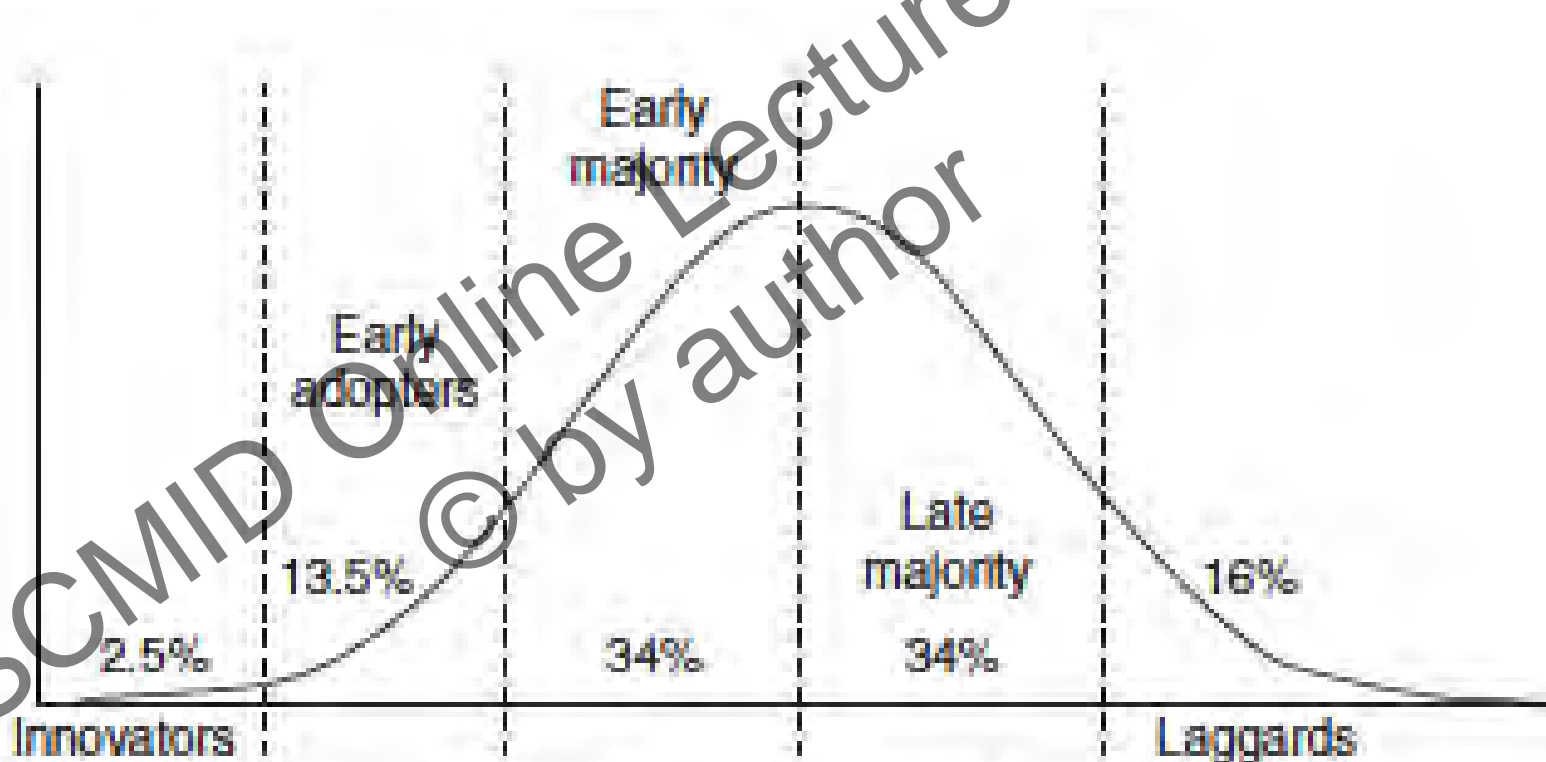


Fig. 1. Rogers's adoption/innovation bell curve (reproduced)

## Program Implementation

### Overall concepts

Envision the problem within the larger healthcare system  
Engage collaborative multidisciplinary teams centrally (stages 1-3) and locally (stage 4)

#### 1. Summarise the evidence

Identify interventions associated with improved outcomes  
Select interventions with the largest benefit and lowest barriers to use  
Convert interventions to behaviours

#### 2. Identify local barriers to implementation

Observe staff performing the interventions  
“Walk the process” to identify defects in each step of implementation  
Enlist all stakeholders to share concerns and identify potential gains and losses associated with implementation

#### 3. Measure performance

Select measures (process or outcome)  
Develop and pilot test measures  
Measure baseline performance

#### 4. Ensure all patients receive the interventions

Implement the “four Es” targeting key stakeholders from front line staff to executives

##### Engage

Explain why the interventions are important

##### Educate

Share the evidence supporting the interventions

##### Execute

Design an intervention “toolkit” targeted at barriers, standardisation, independent checks, reminders, and learning from mistakes

##### Evaluate

Regularly assess for performance measures and unintended consequences

## 2. LACK OF PLANNING

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# Think and plan !

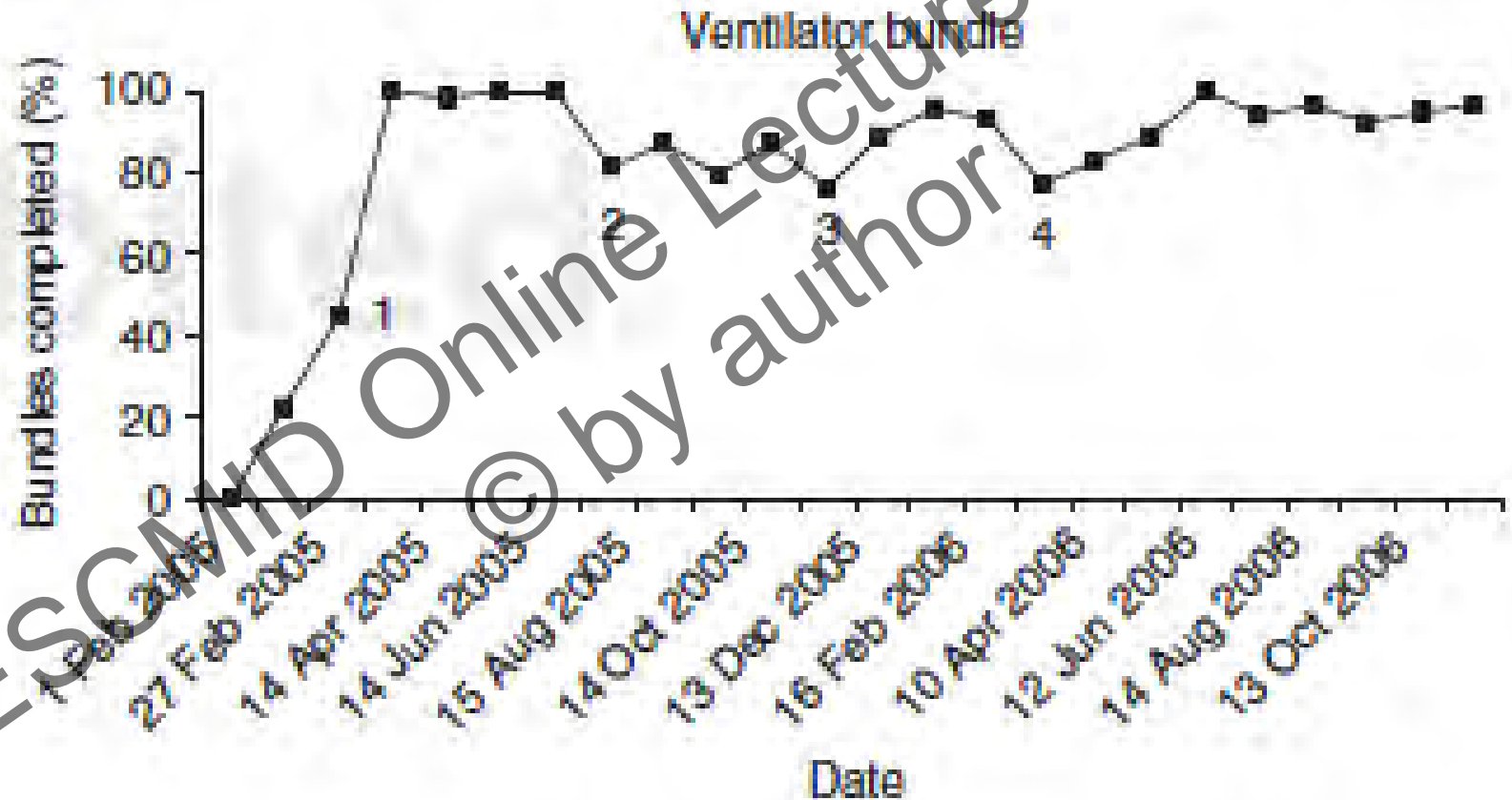
- Action is good
- But planning, monitoring and assessing are crucial steps



# Measuring the impact of an AMS programme

| Indicators Measures | Quality                     | Accountability                                     | Research  |
|---------------------|-----------------------------|--|---|
| Objective           | Improving practices         | Public benchmarking                                | Knowledge   |
| Measures            | Few<br>Easy to collect      | Few<br>Complex collection<br>Valid<br>Reproducible | Many<br>Complex collection<br>Valid<br>Reproducible |
| Period of time      | Short<br>Real time feedback | Long<br>Delayed feedback                           | Long<br>Delayed feedback                            |

# How to measure to bring about change ?



Few measures (20/month), run chart, real time feedback



# Measuring the impact of an AMS programme

- Accurate definition of numerators/denominators
- Structure/activity measures
- Process measures (surrogate markers):
  - IV-oral switch
  - Review of antibiotic prescriptions
  - Expert advice for bacteremia
  - Prescription compliant with guidelines...
- Outcome measures : influenced by many factors
  - Antibiotic use
  - Bacterial resistance
  - *C. difficile* infections
  - *S. aureus* bacteremia mortality rate
  - SSIs rate...
- Balancing measures:
  - Readmission rate for infections

# Possible quality indicators for antimicrobial drug use

| <i><b>Indicator</b></i> | <b>Drug oriented</b>   | <b>Disease oriented</b>  | <b>Patient oriented</b>  |
|-------------------------|--|--|--|
| <b>Structure</b>        | - Presence of an antimicrobial management team   | - Systematic ID advice for bacteremia                          | - Systematic weekly ward round in ICUs   |
| <b>Process</b>          | - Clinical indication for all antibiotic prescriptions<br>- Systematic day 3 reassessment<br>- IV-oral switch criteria | - One dose only for surgical prophylaxis                       | - Compliance to guidelines for ICU patients                                    |
| <b>Outcome</b>          | - Antibiotic consumption in DDDs and euros<br>- % IV/oral for some antibiotics: FQ                                     | - % <i>Clostridium difficile</i> colitis<br>- Resistance rates | - Incidence of VAP in ICU patients/<br>number of patients between VAP episodes |

# CONCLUSIONS

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# Have courage !

- Implementing an AMS programme is a long journey
- Implement progressively
- Start with easy things, with early adopters colleagues
- Assess your actions

# References for further reading

- ESGAP : <https://www.escmid.org/index.php?id=140> and <http://esgap.escmid.org>
- WHO : <http://www.who.int/drugresistance/en/>
- ECDC : [http://ecdc.europa.eu/en/healthtopics/antimicrobial\\_resistance/Pages/index.aspx](http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/Pages/index.aspx)
- CDC : <http://www.cdc.gov/drugresistance/>
- UK: <https://www.gov.uk/government/collections/antimicrobial-resistance-amr-information-and-resources>
- Australia : <http://www.safetyandquality.gov.au/our-work/healthcare-associated-infection/antimicrobial-stewardship/>
- Practical guide (D. Nathwani et al.): <http://www.biomerieux-industry.com/node/886>

# You like AMS... join ESGAP!

https://www.escmid.org/research\_projects/study\_groups/antibiotic\_policies/esgap\_membership\_application/ — ESCMID: ESGAP membership application

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- Antibiotic Policies**
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  - ABC Calc (AMC Tool)
  - Executive Committee
  - Mission & Objectives
  - Links
  - Statutes & Membership
  - Newsletters
- ESGAP membership application**
- Biofilms
- Bloodstream Infections and Sepsis
- Brain Infections
- Clinical Parasitology
- Clostridium difficile
- Critically Ill Patients
- Elderly Infections
- Epidemiological Markers
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- Forensic/Postmortem Microbio
- Fungal Infection
- Immunocompromised Hosts
- Implant Infections
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