


Satellite Symposium EAHP 2016
Austria Center Vienna



A multidisciplinary
approach to effective
antimicrobial stewardship

PP-TYG-EUR-0020, Date of preparation: March 2016

Working together for a healthier world 

Symposium objectives

- Provide an overview of current perspectives on antibacterial and antifungal stewardship
- Highlight areas where stewardship initiatives could be implemented or improved to ensure antimicrobial therapies are used appropriately
- Discuss the implications of responsible antimicrobial use in terms of cost-effectiveness and preservation of existing antimicrobial therapies

PP-TYG-EUR-0020, Date of preparation: March 2016

Agenda

Chairperson: Hayley Wickens (UK)

15:00	Welcome and introduction Hayley Wickens (UK)
15:00–15:20	The role of the pharmacist in antimicrobial stewardship programmes: UK point of view Hayley Wickens
15:20–15:40	The pharmacist's role in antimicrobial stewardship in Spain Jordi Nicolás (Spain)
15:40–16:00	Antifungal stewardship, where are we today? Patricia Muñoz (Spain)
16:00–16:20	Antimicrobial stewardship, an infectious disease specialist's view Matteo Bassetti (Italy)
16:20–16:30	Panel Q&A All, chaired by Hayley Wickens

PP-TYG-EUR-0020, Date of preparation: March 2016

Working together for a healthier world



Questions



- Questions will be taken during the Q&A session after the final presentation
- Please use a question card (located in the back of your programme booklet) or raise your hand for a microphone

A question card form with fields for Name, Address, Telephone, and Email. It also includes a section for 'Questions' and a Pfizer logo at the bottom right.

PP-TYG-EUR-0020, Date of preparation: March 2016

Working together for a healthier world



Housekeeping

- Please ensure all mobile phones are switched to silent



PP-TYG-EUR-0020, Date of preparation: March 2016

Working together for a healthier world



The role of the pharmacist in antimicrobial stewardship programmes: UK point of view

Dr. Hayley Wickens PhD FFRPS
Consultant Pharmacist, Anti-infectives
University Hospital Southampton NHSFT

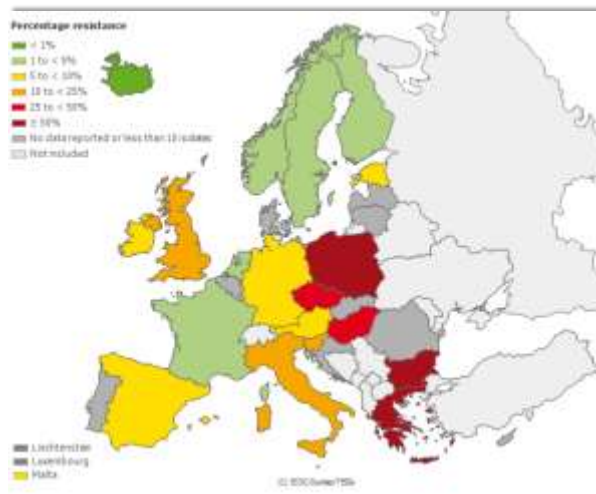
PP-TYG-EUR-0019, Date of preparation: March 2016

Disclosures

HW has received funding, honoraria and/or travel expenses for lectures, conference attendance or consultancy from a number of pharmaceutical companies and other organisations including Astellas, AstraZeneca, Basilea, Cubist, Forest, GSK, MSD, Novartis, Pfizer, Quintiles, Roche, Wyeth, UK Clinical Pharmacy Association and British Society for Antimicrobial Chemotherapy.

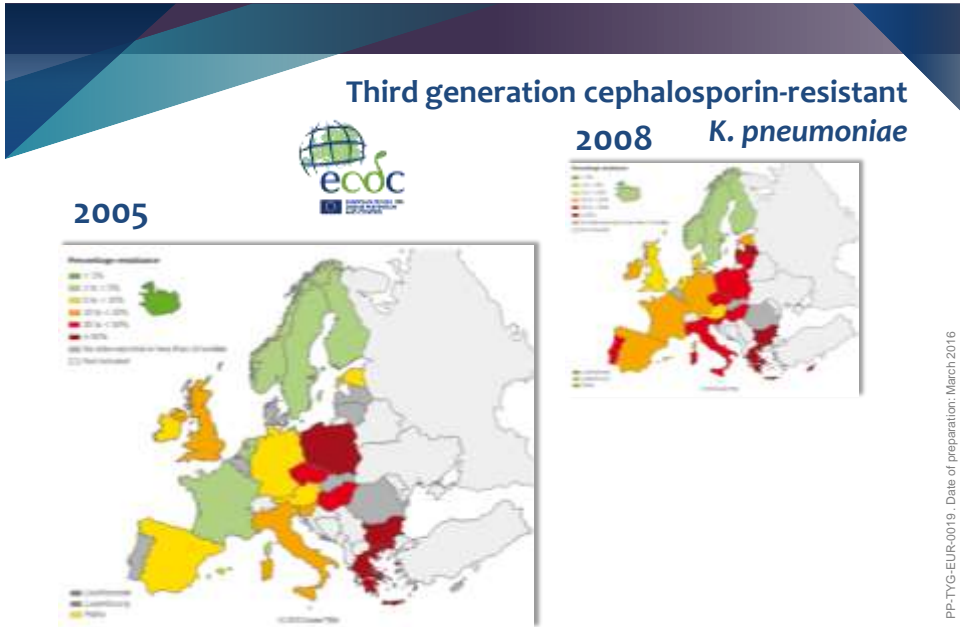
PP-TYG-EUR-0019 - Date of preparation: March 2016

Third generation cephalosporin-resistant *K. pneumoniae* (2005)

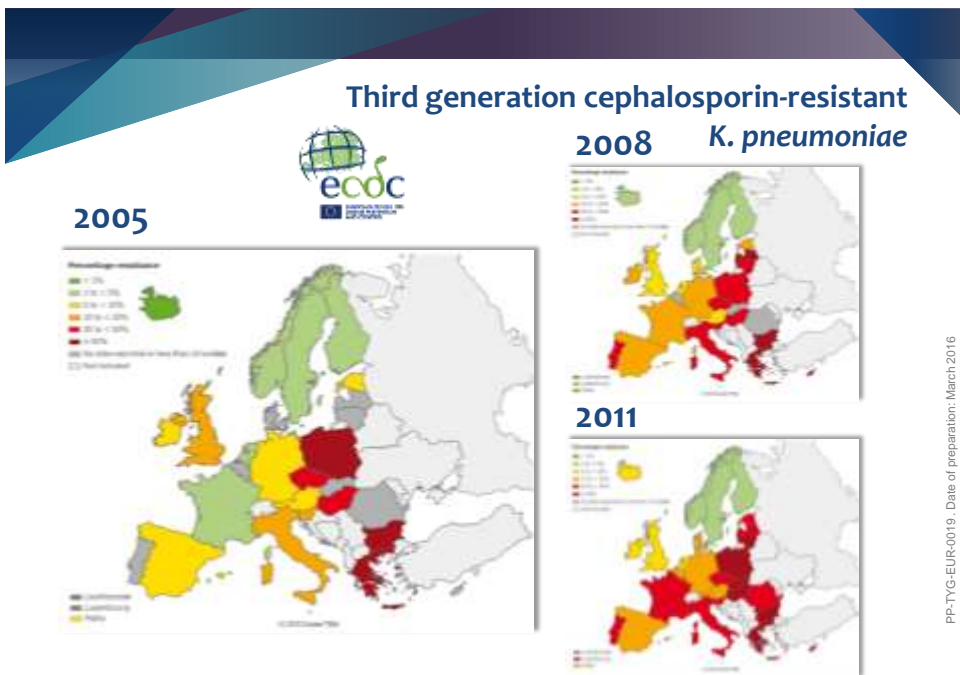


PP-TYG-EUR-0019 - Date of preparation: March 2016

ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]



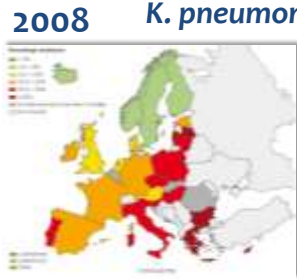
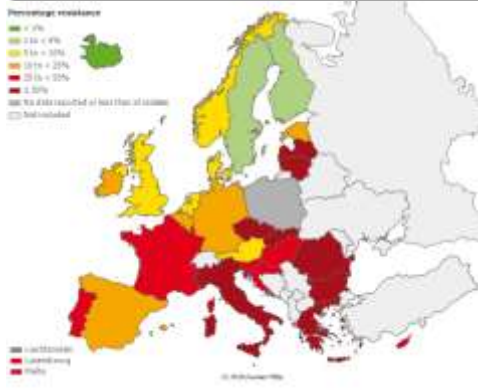
ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]



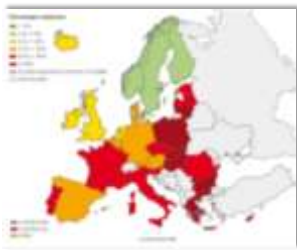
ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]

Third generation cephalosporin-resistant 2008 *K. pneumoniae*

2014



2011

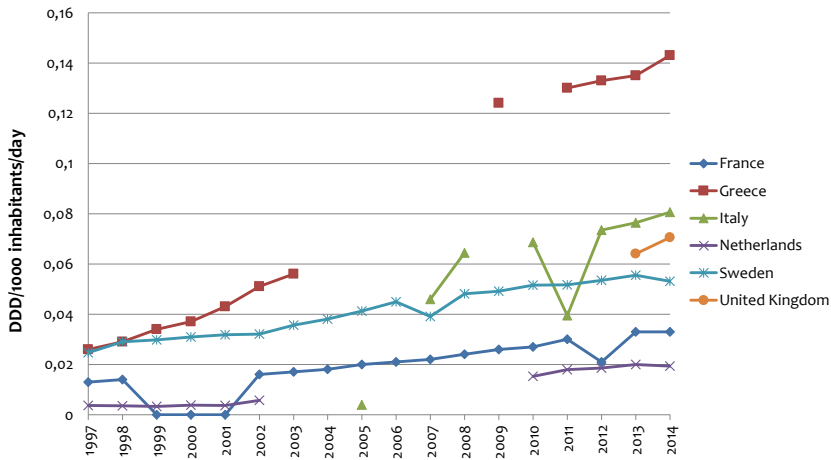


ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]

PP-TYG-EUR-0019 - Date of preparation: March 2016

Carbapenem use is increasing

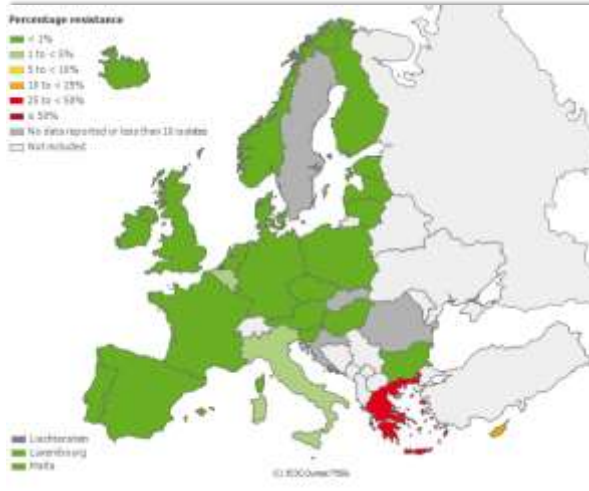
Hospital carbapenem use



DDD, defined daily dose.
 ECDC, antibiotic consumption. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/esac-net-database/Pages/trend-consumption-by-country.aspx [Accessed March 2016].

PP-TYG-EUR-0019 - Date of preparation: March 2016

Carbapenem-resistant *K. pneumoniae* in 2009



PP-TYG-EUR-0019 - Date of preparation: March 2016

ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]

Carbapenem-resistant *K. pneumoniae* 2010

2009



2010



PP-TYG-EUR-0019 - Date of preparation: March 2016

ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]

Carbapenem-resistant *K. pneumoniae*



2009



2010



2011



PP-TYG-EUR-0019 - Date of preparation: March 2016

ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]

Carbapenem-resistant *K. pneumoniae*



2014



2010



2011



PP-TYG-EUR-0019 - Date of preparation: March 2016

ECDC maps. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]

1

THE LANCET Infectious Diseases

Apocalypse Pig: The Last Antibiotic Begins to Fail

Emergence of plasmid-mediated colistin resistant MCR-1 in animals and human beings in China: a n and molecular biological study

MCR-1 was present:
in 15% of 523 samples of raw pork and chicken meat
in 21% of 804 pigs in slaughterhouses
In 1% of 1,322 samples from hospital patients with infections

PP-TYG-EUR-0019 - Date of preparation: March 2016

1. Liu Y, et al. Lancet Infect Dis. 2015;16(2):161–8. 2. National Geographic; Apocalypse pig. Available at: <http://phenomena.nationalgeographic.com/2015/11/21/mcr-gene-colistin/> [Accessed March 2016]

International Journal of Antimicrobial Agents

Early (2008–2010) hospital outbreak of *Klebsiella pneumoniae* producing OXA-48 carbapenemase in the UK

Claire P. Thomas^a, Luke S.P. Moore^{a,b,c}, Naik Elamin^a, Michel Doumith^a, Jiancheng Zhang^a, Sunil Maharjan^a, Marina Warner^a, Claire Perry^a, Jane F. Terton^a, Clare Johnston^a, Annette Jayson^a, Neil D.C. Duncan^a, Alison H. Holmes^{a,b}, David M. Livermore^{a,c}, Neil Woodford^d

ABSTRACT

OXA-48 carbapenemase is the most common carbapenemase. Pre-2007 reports were almost exclusively from Turkey, but subsequently its distribution has expanded. We report an early and prolonged outbreak in the UK of *Klebsiella pneumoniae* producing OXA-48 carbapenemase affecting a predominantly adult cohort in a West London hospital. Carbapenemase production was detected by the standard hedge test and confirmed by PCR for *bla*_{OXA-48}. Isolates were genotypically indistinguishable (PFGE) and exhibited sequence homology (MLST). Risk factors for acquisition were determined. Between January 2008 and April 2010, 202 *K. pneumoniae* isolates with reduced susceptibility to carbapenems were identified from 13 patients, comprising 12 inpatient cases and 1 out-patient. 9 were genotyped and 5 were sequenced. 7 were shown to be clonal and 4 cultured, including 2 with *bla*_{OXA-48} genes. 11 of whom died. Hedge tests were positive for all isolates and all had *bla*_{OXA-48}. PFGE showed close similarity to isolates from other patients (whom have patients' isolates were distinct), representing three distinct PFGE profiles and suggesting horizontal spread of *bla*_{OXA-48}. These patients had extensive antibiotic use in the preceding 12 months and all had healthcare contacts. Six major risk factors were found to confer with evidence that collectively brought the outbreak under control (contact with infection control personnel, attending, required intensive intensive care and antibiotic stewardship teams).

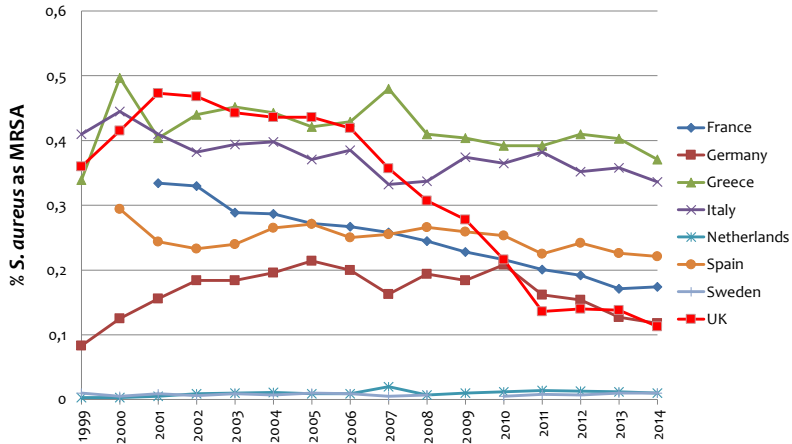
PP-TYG-EUR-0019 - Date of preparation: March 2016

Thomas C, et al. Int J Antimicrob Ag. 2013;42(6):531–36.

MRSA is stable or decreasing



MRSA as a proportion of *S. aureus* isolates



ECDC tables. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/table_reports.aspx [Accessed March 2016].

PP-TYG-EUR-0019 - Date of preparation: March 2016

The antibiotic pipeline dries up...

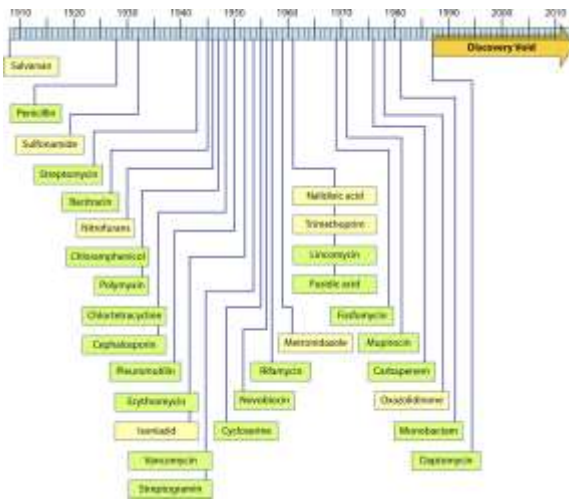


Illustration of the “discovery void.” Dates indicated are those of reported initial discovery or patent

In 1980, 20 major companies had antibiotic R&D programmes

Now there are four

Silver LL. *Clin Microbiol Rev.* 2011;24:71-109

PP-TYG-EUR-0019 - Date of preparation: March 2016

All antibiotic use drives resistance

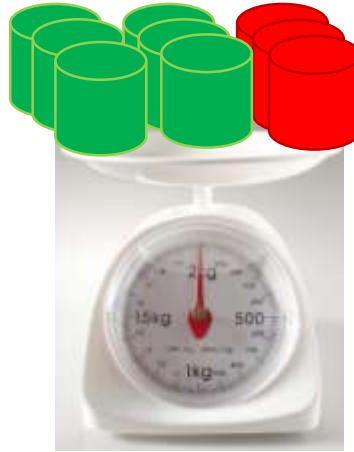


Image source: https://commons.wikimedia.org/wiki/File:Kitchen_scale_20101110.jpg

PP-TYG-EUR-0019 - Date of preparation: March 2016

ANTIMICROBIAL STEWARDSHIP

PP-TYG-EUR-0019 - Date of preparation: March 2016

What is antimicrobial stewardship?

“...an activity that includes appropriate selection, dosing, route, and duration of antimicrobial therapy”

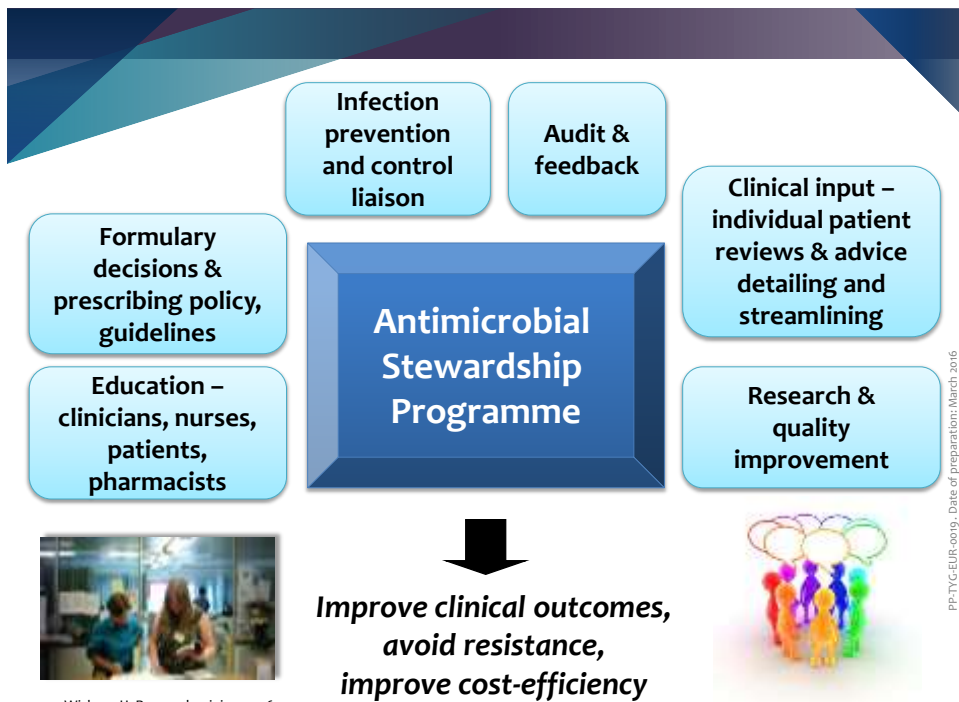
“...to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use”



UK Five Resistar 2013 to 2018
 2 **optimising prescribing practice** through implementation of antimicrobial stewardship programmes that promote rational prescribing and better use of existing and new rapid diagnostics (supports strategic aims i and ii),

PP-TYG-EUR-0019 - Date of preparation: March 2016

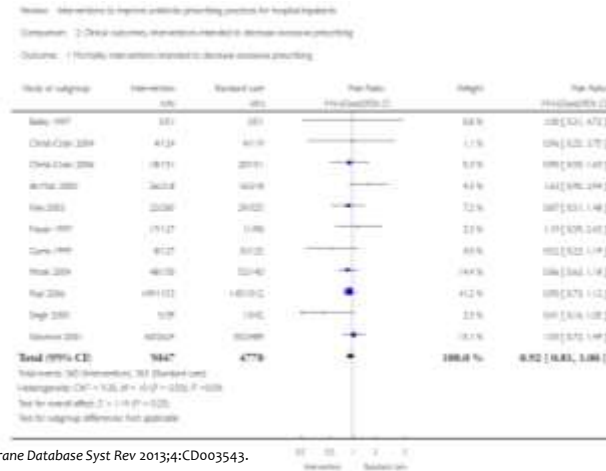
Dellit TH, et al. *CID* 2007;44:159-177.
 UK five year antimicrobial resistance strategy 2013 to 2018. Available at: <https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018> [Accessed March 2016]



PP-TYG-EUR-0019 - Date of preparation: March 2016

A win-win: stewardship interventions can reduce antibiotic prescribing without harming patients

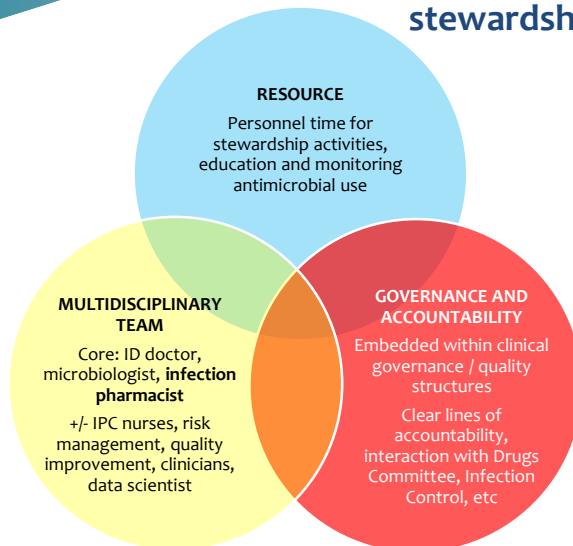
Clinical outcomes, interventions intended to decrease excessive prescribing
Mortality, interventions intended to decrease excessive prescribing



Davey P, et al. Cochrane Database Syst Rev 2013;4:CD003543.

PP-TYG-EUR-0019 - Date of preparation: March 2016

Key components of an antimicrobial stewardship programme



ID, infectious diseases; IPC, infection prevention and control.

Practical guide to antimicrobial stewardship in hospitals. Available at: <http://bsac.org.uk/wp-content/uploads/2013/07/Stewardship-Booklet-Practical-Guide-to-Antimicrobial-Stewardship-in-Hospitals.pdf> [Accessed March 2016]

PP-TYG-EUR-0019 - Date of preparation: March 2016

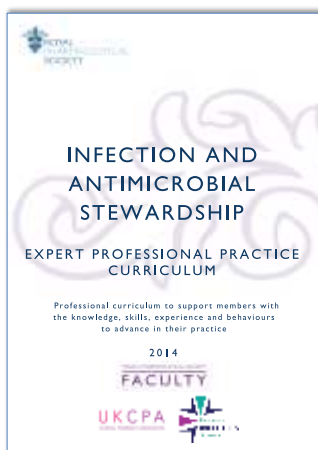
Developing the English antimicrobial pharmacy workforce

- Department of Health Hospital Pharmacy Initiative
 - £12M pump-prime funding
 - Available 2003–06
 - Non-recurring
- 63% employed new staff
- 23% expanded current roles
- 106 antibiotic pharmacy posts created
 - 50 on fixed-term contracts
- Specialist roles (2011 survey)
 - 187 in 120 organisations (↑ from 141/125 in 2005)
 - Consultant grade pharmacist roles now available
 - Independent prescribing
- MSc Infection Management for Pharmacists (Imperial College London)

PP-TYG-EUR-0019 - Date of preparation: March 2016

Wickens HJ, Jacklin A. *J Antimicrob Chemother* 2006;58(6):1230-7
 Wickens HJ et al. *J Antimicrob Chemother* 2013;68(11):2675-81

Competency framework for infection specialist pharmacists



- Developed by the **UK Clinical Pharmacy Association Pharmacy Infection Network**
- Endorsed by the **Royal Pharmaceutical Society**
- For training, competency assessment and revalidation of specialist infection pharmacists

PP-TYG-EUR-0019 - Date of preparation: March 2016

Royal Pharmaceutical Society. <http://bsac.org.uk/wp-content/uploads/2014/10/Professional-Curriculum-Infection-and-Antimicrobial-Stewardship.pdf> [Accessed March 2016]; Sneddon J, Gilchrist M, Wickens H. *J Antimicrob Chemother* 2015;70(5):1277–80



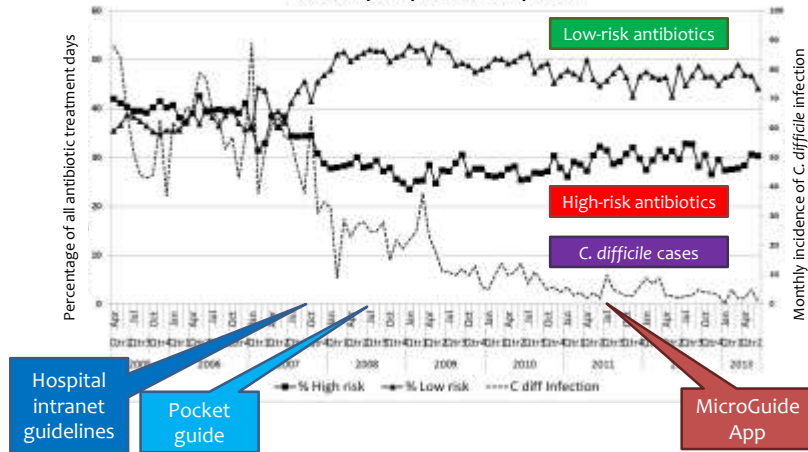
STEWARDSHIP IN ACTION – PHARMACIST-LED PROJECTS AT UHS

PP-TYG-EUR-0019 - Date of preparation: March 2016

UHS, University Hospital Southampton.

Outcomes: Campaign to promote 'low-risk' antibiotics in hospital

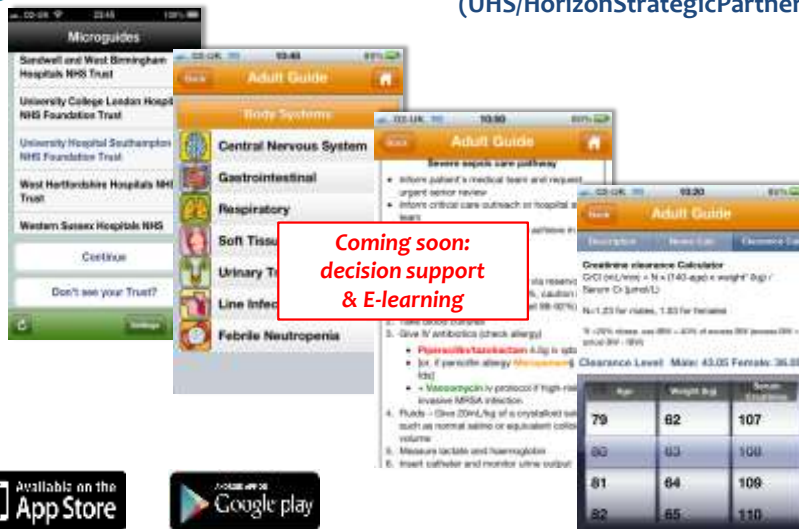
Trends in prescribing of high-risk and low-risk antibiotics versus *Clostridium difficile* incidence in University Hospital Southampton



PP-TYG-EUR-0019 - Date of preparation: March 2016

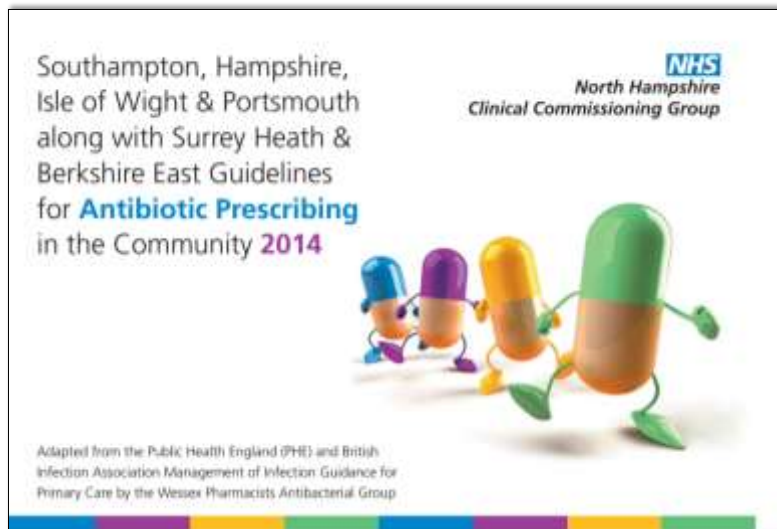
Wickens H. Personal communication. 2016.

MicroGuide (UHS/HorizonStrategicPartners)



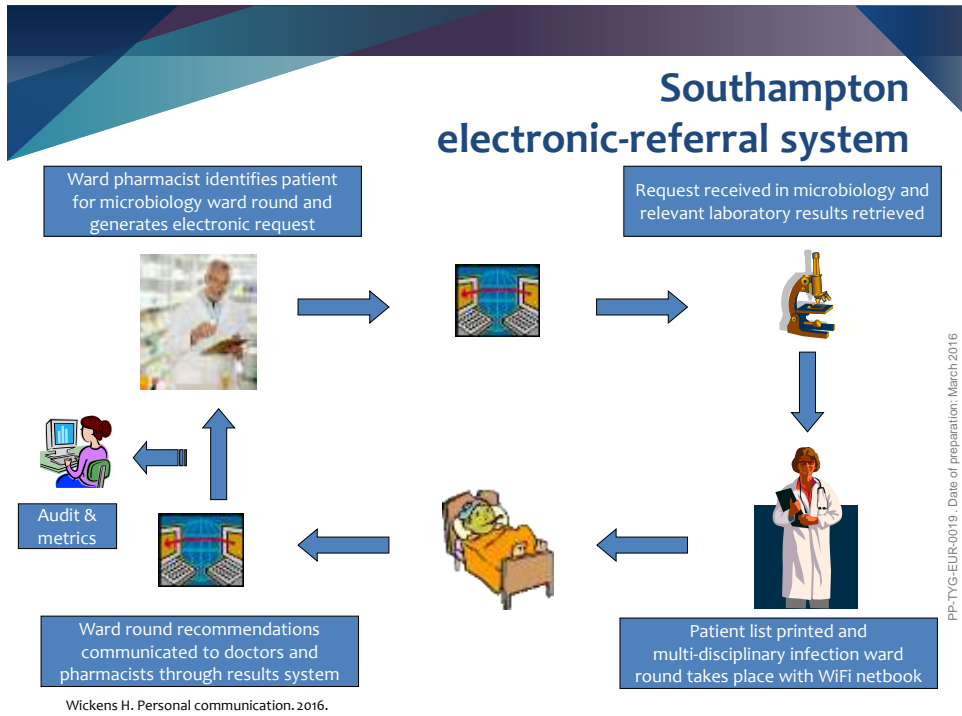
MicroGuide. Available at: <https://itunes.apple.com/gb/app/microguide/id447171786?mt=8> [Accessed March 2016]

PP-TYG-EUR-0019 - Date of preparation: March 2016



NHS. Antibiotic prescribing in the community 2014. <http://www.nhsantibioticguidelines.org.uk/> [Accessed March 2016]

PP-TYG-EUR-0019 - Date of preparation: March 2016



The next generation

University Hospital Southampton NHS Foundation Trust
13 November 2015 · 46

Our pharmacy team has been out and about today, raising awareness for European Antibiotic Awareness Day. They've visited wards to discuss our local antibiotic prescribing data with clinicians, and to encourage both staff and patients to sign up for Public Health England's Antibiotic Guardian campaign (<https://www.antibioticguardian.com>)

For more information about European Antibiotic Awareness Day visit https://www.facebook.com/EAAD_EU

@ECDC_EU · 13 Nov 2015

Our pharmacy team has been out and about today, raising awareness for European Antibiotic Awareness Day

Wickens H. Personal communication. 2016.

PP-TYG-EUR-0019 - Date of preparation: March 2016



Summary

- Evolution in action – the rise of antimicrobial resistance
- What is antimicrobial stewardship?
- Examples of stewardship projects led by pharmacists in the UK

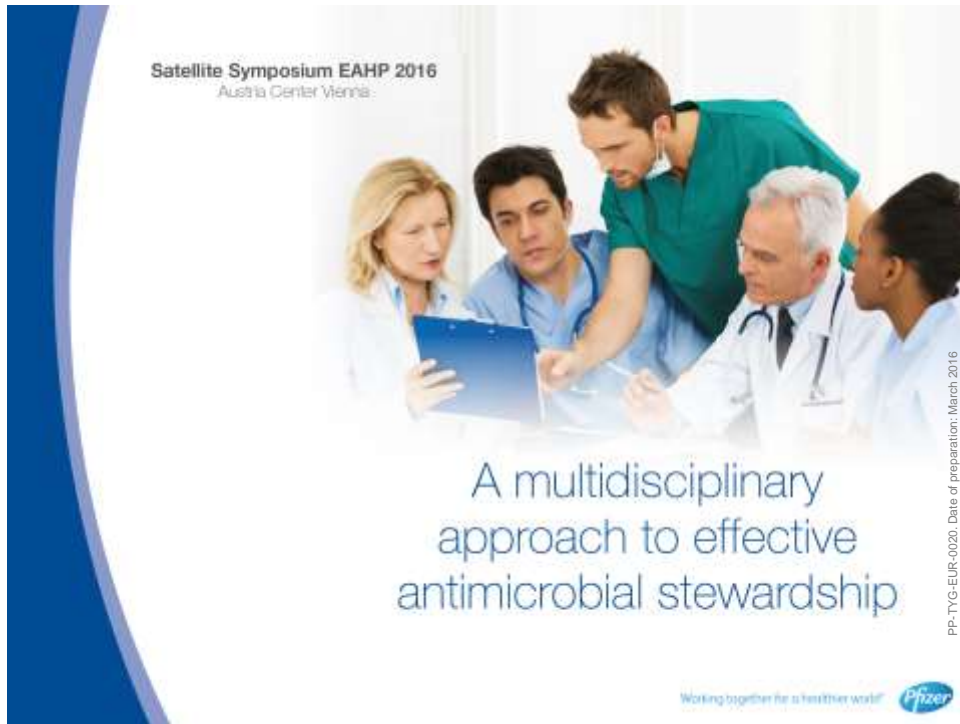
PP-TYG-EUR-0019 - Date of preparation: March 2016



Acknowledgements

- Dr. Kieran Hand, UHS
- Horizon Strategic Partners
- UHS Antimicrobial Stewardship Team

PP-TYG-EUR-0019 - Date of preparation: March 2016



A multidisciplinary approach to effective antimicrobial stewardship

The pharmacist's role in antimicrobial stewardship in Spain



Dr. Jordi Nicolás Picó
Servei de Farmàcia
Hospital Universitari Mútua de Terrassa



PP-TYG-EUR-0022. Date of preparation: March 2016



Financial disclosures

- As speaker
 - MSD, Pfizer
- As consultant
 - Gilead, MSD, Abbvie
- Research grants
 - MSD

PP-TYG-EUR-0022. Date of preparation: March 2016



Summary

- Resistance in Europe and in Spain
- Antimicrobial stewardship programmes in Spain
- The pharmacist's role in antimicrobial stewardship in Spain

PP-TYG-EUR-0022. Date of preparation: March 2016



SMARTNEWS *Keeping you current*

Superbugs Could Become a Top Cause of Death by 2050

If left unchecked, antibiotic-resistant bacteria could kill more people than cancer by 2050



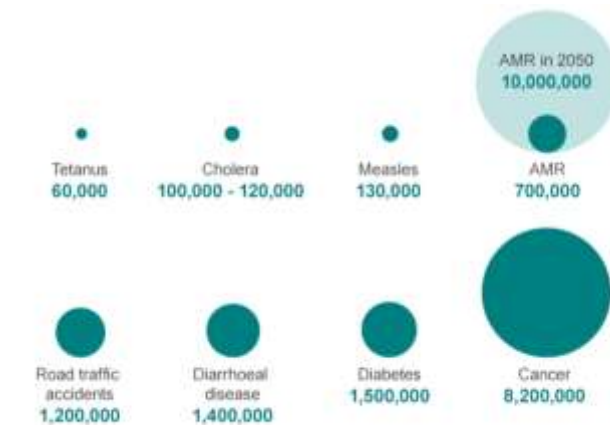
PP-TYG-EUR-002. Date of preparation: March 2016



Available at: <http://www.bbc.co.uk/news/health-30416844>
[Accessed March 2016]



Deaths attributable to antimicrobial resistance every year compared to other major causes of death



Source: Review on Antimicrobial Resistance 2014

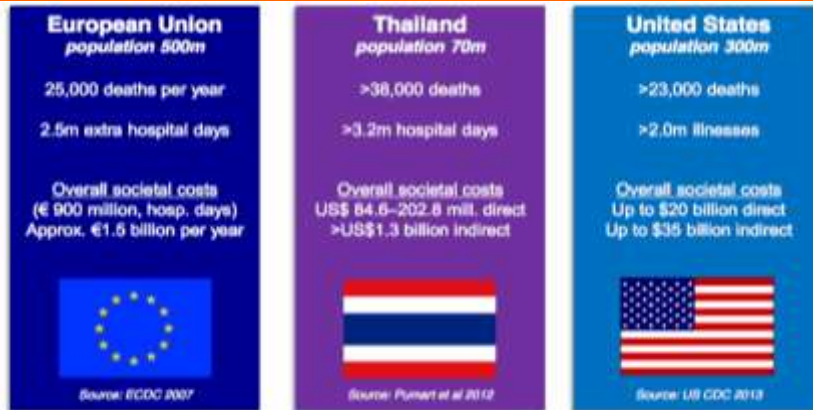
PP-TYG-EUR-002. Date of preparation: March 2016



Available at: <http://www.bbc.co.uk/news/health-30416844>
[Accessed March 2016]



Estimates of burden of resistance



Global information is insufficient to show complete disease burden impact and costs

1. WHO (2014) Antimicrobial resistance. Global report on Surveillance. Available at: www.who.int/drugresistance/documents/surveillance-report/en/ [Accessed February 2016]; 2. WHO (2014) Antimicrobial resistance slide set. Available at: www.who.int/drugresistance/documents/AMR_report_Web_slide_set.pdf [Accessed February 2016]



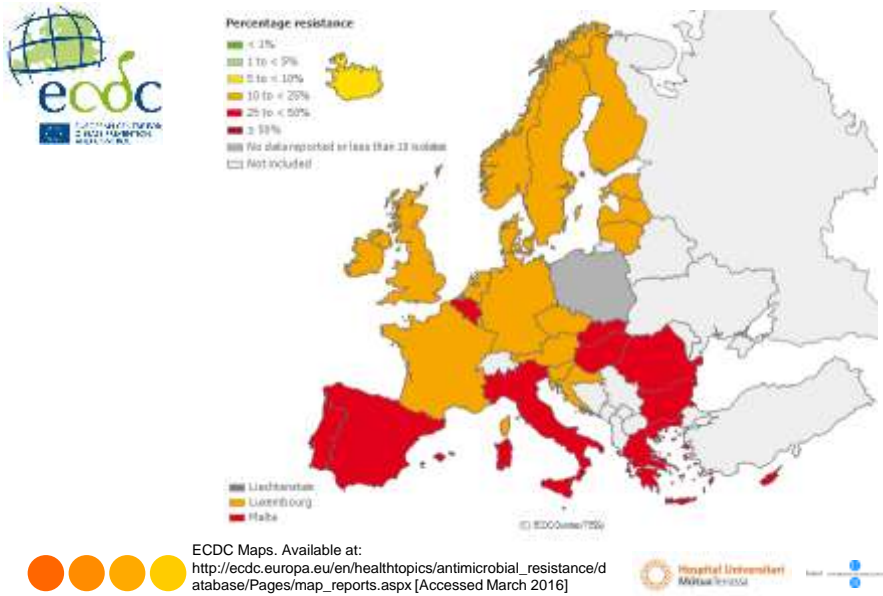
PP-TYG-EUR-002. Date of preparation: March 2016

Escherichia coli

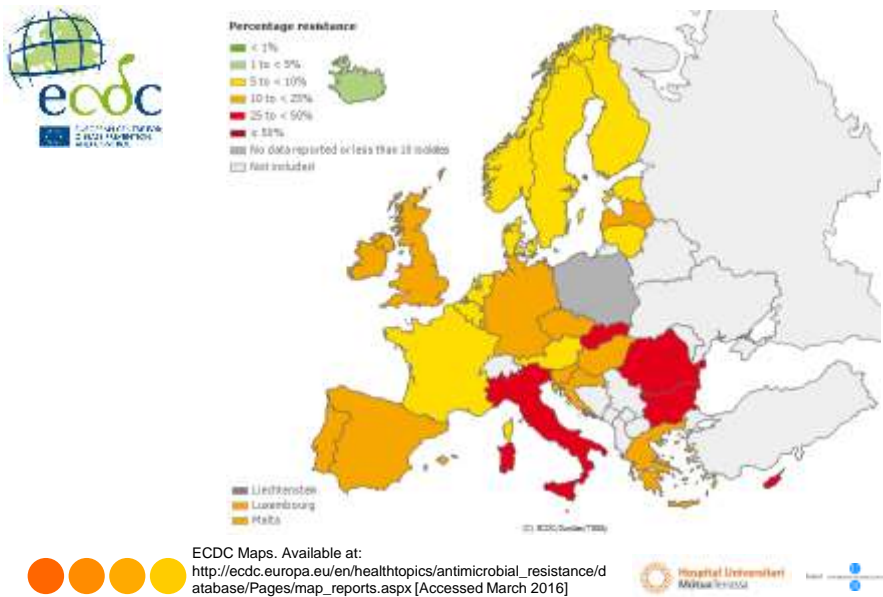


PP-TYG-EUR-002. Date of preparation: March 2016

Proportion of fluoroquinolone-resistant *E. coli* isolates in participating countries in 2014



Proportion of third generation cephalosporin-resistant *E. coli* isolates in participating countries in 2014

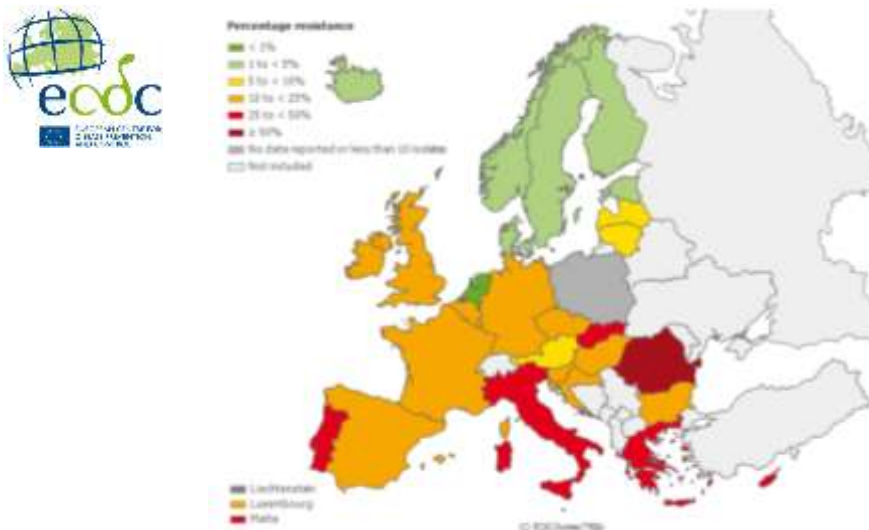


Staphylococcus aureus

PP-TYG-EUR-0022. Date of preparation: March 2016



Proportion of MRSA isolates in participating countries in 2014



PP-TYG-EUR-0022. Date of preparation: March 2016



MRSA, methicillin-resistant *S. aureus*.
 ECDC Maps. Available at:
http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/databse/Pages/map_reports.aspx [Accessed March 2016]

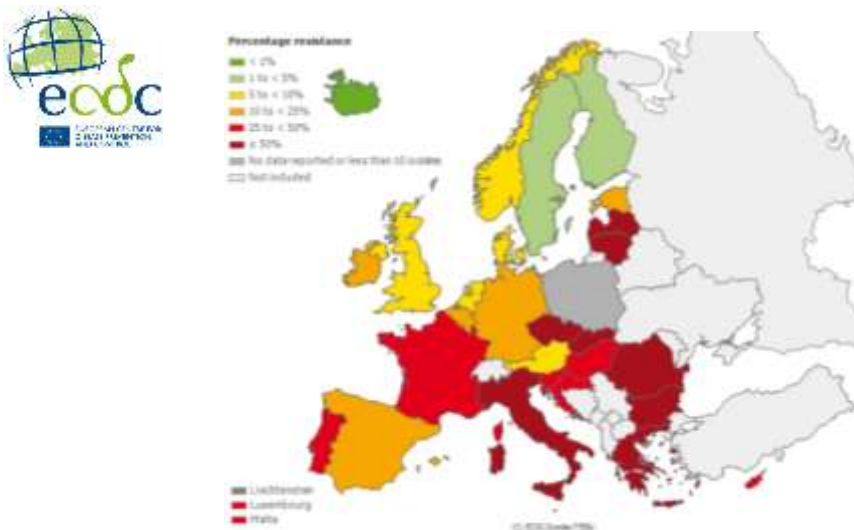


Klebsiella pneumoniae

PP-TYG-EUR-0022. Date of preparation: March 2016



Proportion of third generation cephalosporin-resistant *Klebsiella pneumoniae* isolates in participating countries in 2014



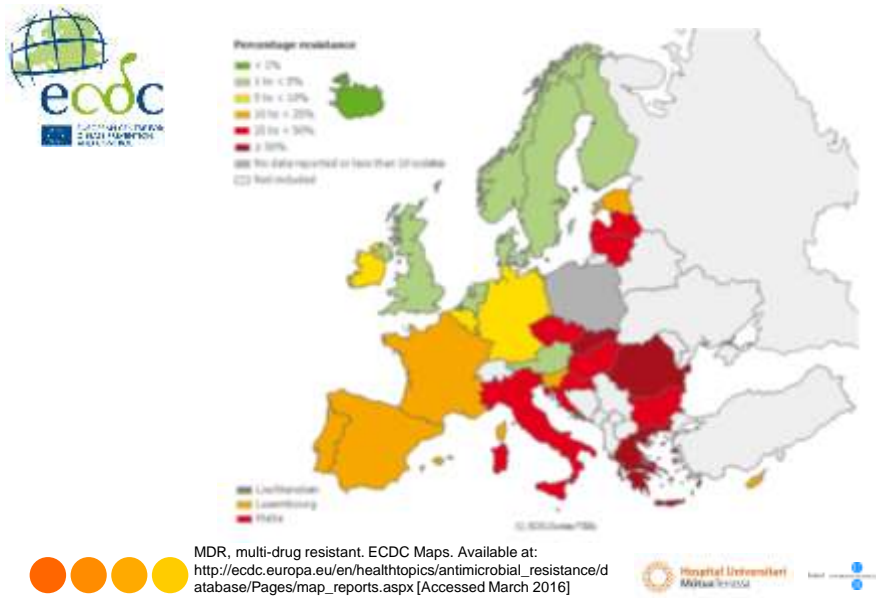
PP-TYG-EUR-0022. Date of preparation: March 2016



ECDC Maps. Available at:
http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016]



MDR *K. pneumoniae* isolates in participating countries in 2014 (Resistant to third generation cephalosporins, fluoroquinolones and aminoglycosides)



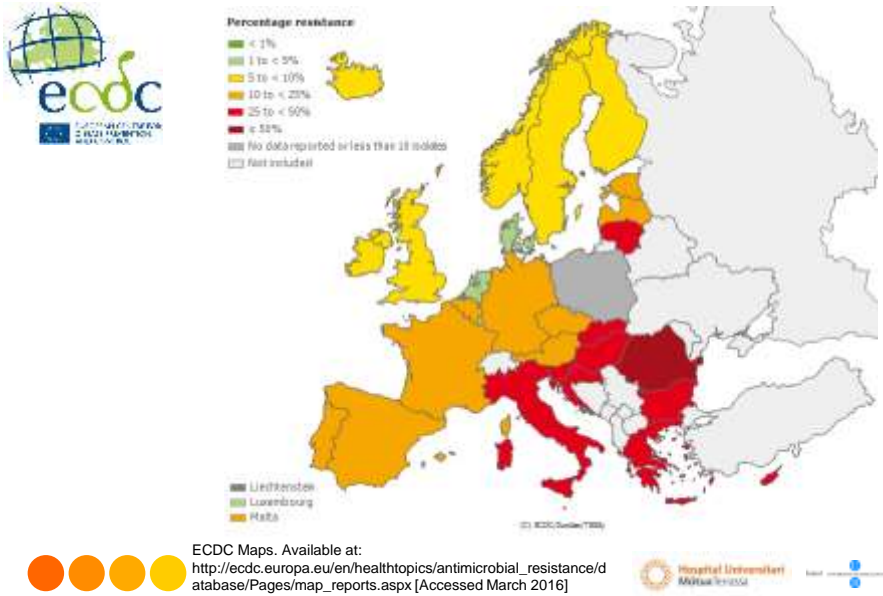
PP-TYG-EUR-0022. Date of preparation: March 2016

Pseudomonas aeruginosa

PP-TYG-EUR-0022. Date of preparation: March 2016

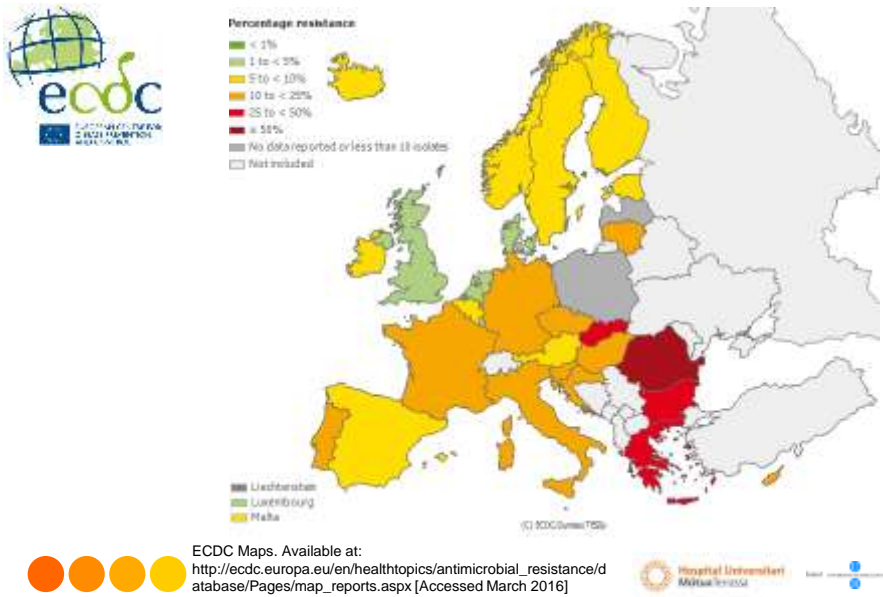


Proportion of carbapenem-resistant *Pseudomonas aeruginosa* isolates in participating countries in 2014



PP-TYG-EUR-002. Date of preparation: March 2016

Proportion of ceftazidime-resistant *Pseudomonas aeruginosa* isolates in participating countries in 2014



PP-TYG-EUR-002. Date of preparation: March 2016



Emergence of New Delhi Metallo-Beta-Lactamase (NDM-1) and *Klebsiella pneumoniae* carbapenemase (KPC-2) in South Africa

PP-TYG-EUR-0022, Date of preparation: March 2016



Brink AJ, et al. J Clin Oncol 2012;50:525-7



PP-TYG-EUR-0022, Date of preparation: March 2016



Available at: <http://www.who.int/world-health-day/2011/en/> [Accessed March 2016]



WHO Health Day 2011

The World Health Organization's policy package to combat antimicrobial resistance

- Commit to a comprehensive, financed national plan with accountability and civil society engagement
- Strengthen surveillance and laboratory capacity
- Ensure uninterrupted access to essential medicines of assured quality
- Regulate and promote rational use of medicines, including animal husbandry, and ensure proper patient care
- Enhance infection prevention and control
- Foster innovations and research and development for new tools

PP-TYG-EUR-0022. Date of preparation: March 2016



Available at: <http://www.reactgroup.org/uploads/publications/other-publications/WHO-Policy-Package-to-Combat-Antimicrobial-Resistance.pdf> [Accessed March 2016]



AMS survey in Spain

• n=71



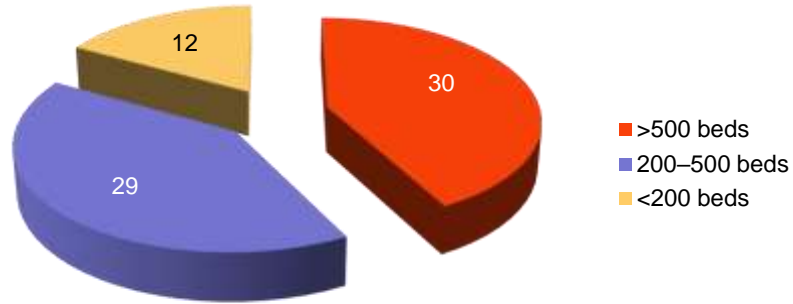
PP-TYG-EUR-0022. Date of preparation: March 2016



J. Nicolas. Personal Communication.



Hospitals

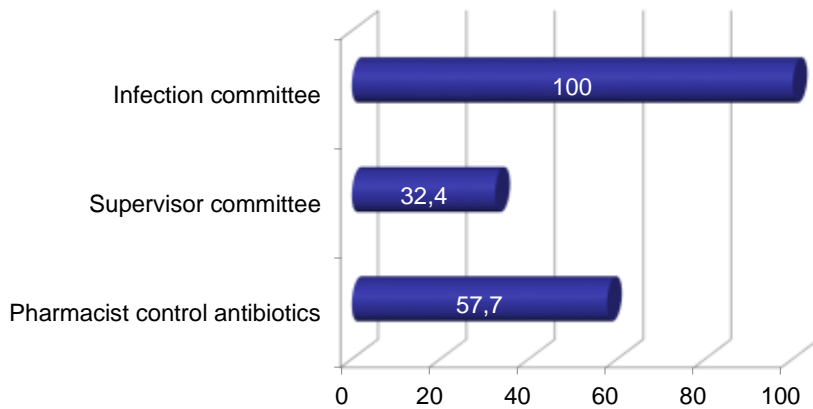


PP-TYG-EUR-0022. Date of preparation: March 2016

●●●● J. Nicolas. Personal Communication.



Basic structure

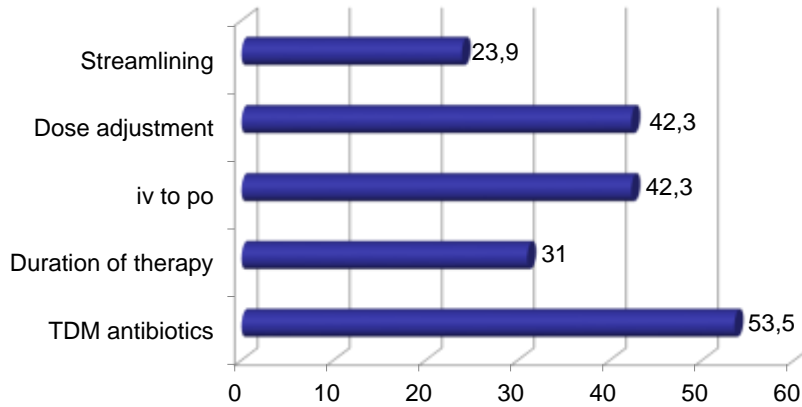


PP-TYG-EUR-0022. Date of preparation: March 2016

●●●● J. Nicolas. Personal Communication.



Antimicrobial stewardship activities



PP-TYG-EUR-0022. Date of preparation: March 2016

●●●● TDM, therapeutic drug monitoring.
J. Nicolas. Personal Communication.



Antimicrobials related to AMS

- Antibiotics for Gram-positive resistant organisms
- Antibiotics for Gram-negative resistant organisms
- Some control of antifungal agents

PP-TYG-EUR-0022. Date of preparation: March 2016





Self-assessment of patterns of antibiotic use in a university hospital

- Antibiotic de-escalation was recognized as usual practice in 20%
- Treatment duration was adjusted in 45%
- Antibiotic dose was adjusted according to site of infection and underlying conditions in 65%
- Antibiotic was chosen according to hospital guidelines in 42%

PP-TYG-EUR-0022. Date of preparation: March 2016



Gomez J, et al. *Enferm Infecc Microbiol Clin.* 2014;32(8):507–10.



Programs for optimizing the use of antibiotics (PROA) in Spanish hospitals: GEIH-SEIMC, SEFH and SEMPSPH consensus document



PP-TYG-EUR-0022. Date of preparation: March 2016



Rodriguez-Bano J, et al. *Farm Hosp.* 2012;36(1):33.e1-30.



Objectives of the PROA document

- To improve clinical results of patients with infections
- To minimize adverse events associated with the use of antimicrobials, including the emergence and spread of antibiotic resistance
- To ensure use of the most cost-effective treatments

PP-TYG-EUR-0022. Date of preparation: March 2016



PROA, Programs for optimizing the use of antibiotics
Rodríguez-Bano J, et al. Farm Hosp. 2012;36(1):33.e1-30.



Recommendations for implementation

- Multidisciplinary antibiotic teams should be formed under the auspices of the Infection Committees
- The PROA needs to be considered as part of institutional programs and the strategic objectives of the hospital
- The PROA should include specific objectives based on:
 - measurable indicators
 - activities aimed at improving the use of antimicrobials

PP-TYG-EUR-0022. Date of preparation: March 2016



PROA, Programs for optimizing the use of antibiotics
Rodríguez-Bano J, et al. Farm Hosp. 2012;36(1):33.e1-30.



National plan for antimicrobial resistance



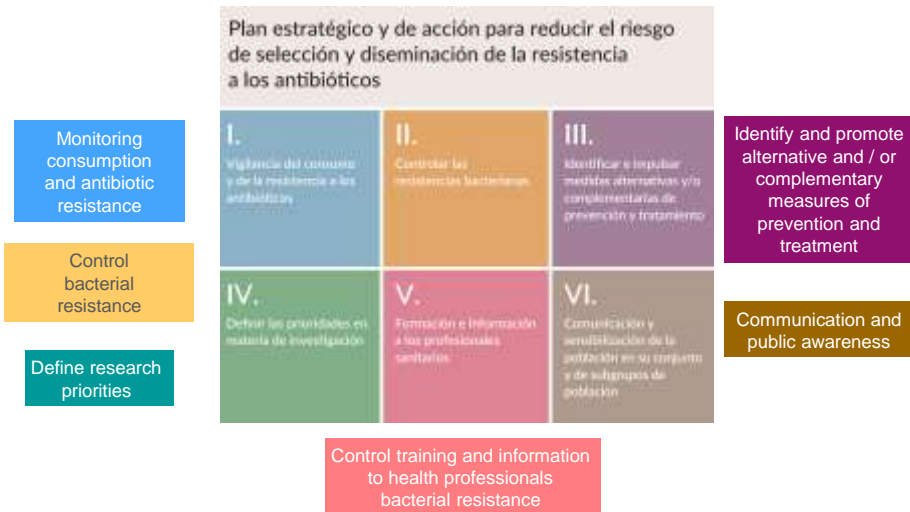
PP-TYG-EUR-002. Date of preparation: March 2016



Available at: www.aemps.gob.es/publicaciones/publica/plan-estrategico-antibioticos/v2/docs/plan-estrategico-antimicrobianos-AEMPS.pdf [Accessed March 2016]



Strategy and action plan to reduce the risk of selection and spread of antibiotic resistance



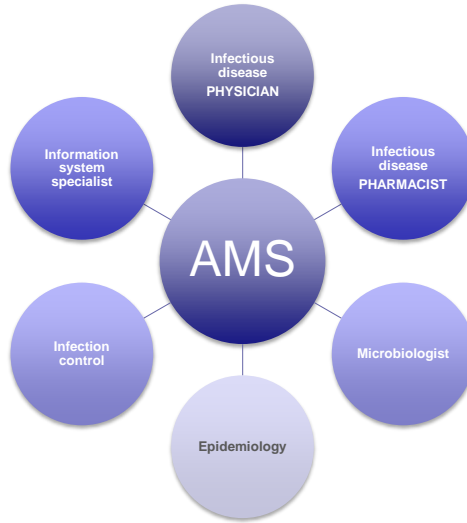
PP-TYG-EUR-002. Date of preparation: March 2016



Available at: www.aemps.gob.es/publicaciones/publica/plan-estrategico-antibioticos/v2/docs/plan-estrategico-antimicrobianos-AEMPS.pdf [Accessed March 2016]



AMS: Global solution



PP-TYG-EUR-0022, Date of preparation: March, 2016



Dellit TH, et al. *Clin Infect Dis.* 2007;44:159–77.



...the program (AMS) is usually directed by an infectious diseases physician or codirected by an infectious diseases physician and a clinical pharmacist with infectious diseases training (A-III).¹

...The essential core must consist of an infectious disease or clinical infectious disease expert, an expert clinical pharmacist in antimicrobials, and an expert microbiologist in antimicrobial resistance³

...infectious-disease physicians and pharmacists could improve antibiotic prescribing patterns....

... Pharmacy leader: Identify a single pharmacy leader who will co-lead the programme...²

PP-TYG-EUR-0022, Date of preparation: March, 2016



1. Dellit TH, et al. *Clin Infect Dis.* 2007;44:159–77; 2. CDC. Available at: <http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html>;
 3. Rodriguez-Bano J, et al. *Farm Hosp.* 2012;36(1):33.e1-30; 4. Report to the president. Available at: https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_earb_report_sept2014.pdf



What is the pharmacist's role?



PP-TYG-EUR-0022. Date of preparation: March 2016



Strategies

- Formulary restriction
- Prospective audit with intervention and feedback



PP-TYG-EUR-0022. Date of preparation: March 2016



ASHP: Statement on the Pharmacist's Role in Antimicrobial Stewardship and Infection Prevention and Control

- To ensure the optimal use of antimicrobial agents throughout the health system
- To prevent or reduce the transmission of infections
- To provide education and information about antimicrobial stewardship and infection prevention

PP-TYG-EUR-002: Date of preparation: March 2016



Available at:

<http://www.ashp.org/doclibrary/bestpractices/specificantimicrob.aspx> [Accessed March 2016].



To ensure the optimal use of antimicrobial agents

- To ensure that the prophylactic, empirical, and therapeutic use of antimicrobial agents result in optimal patient outcomes
 - Optimal dose, quick start, monitor, de-escalation, sequential therapy
- Participation in an infectious disease committee
 - To ensure that the number and types of antimicrobial agents available are appropriate for the patient population served
- Participation in an antimicrobial stewardship programme
- Generating and analyzing quantitative data on antimicrobial drug use to perform clinical and economic outcome analyses
- Facilitating safe medication management practice for antimicrobial agents by utilizing efficient and effective systems to reduce potential errors and adverse drug event

PP-TYG-EUR-002: Date of preparation: March 2016



Available at:

<http://www.ashp.org/doclibrary/bestpractices/specificantimicrob.aspx> [Accessed March 2016].



Barriers to stewardship

- Clinical pharmacist with infectious diseases training
- Resources

PP-TYG-EUR-0022. Date of preparation: March 2016



J. Nicolas. Personal Opinion.



Activities

- Broad spectrum antibiotic review >2–3 days
- Antibiotic treatment >10 days
- Surgical prophylaxis (correct antibiotic, optimal dose, right duration, right time)
- Positive cultures
- Sequential therapy
- TDM

PP-TYG-EUR-0022. Date of preparation: March 2016



TDM, therapeutic drug monitoring
J. Nicolas. Personal Opinion.





Available at: <http://www.mondragon-health.com/?p=8284>
[Accessed March 2016]



Roundtable discussion

Moderator Dr. Sara Cobo

10:00-10:30h: Computerized systems to support PROA. **Dr. Jordi Nicolás** Hospital Universitario Mútua de Terrassa (AFINF SEFH)

10:30-11:00h: Clinical indicators and quality. **Dr. José Ramón Paño Pardo** Hospital Universitario Miguel Servet

11:00-11:30h: Consumption of antibiotics in ICUs and de-escalation. **Dr. Rafael Zaragoza** Hospital Universitari Dr Peset (SEMICYUC)

11:30-12:00h: Break/coffee

Roundtable discussion

Moderator Dr. Jordi Nicolás

12:00-12:30h: Surgical antibiotic prophylaxis audit. **Dr. Miquel Pujol** Hospital Universitari Bellvitge (SEIMC)

12:30-13:00h: Results of application of the PROA on antifungals. **Dr. Carmen Rodríguez** Hospital Universitario Gregorio Marañón

13:00-14:00h: Plenary session: Use of ATB in the community. Interventions on primary prescribing. **Dr. Philip Howard** NHS

14:00-15:00h: Lunch

Roundtable discussion

15:00-15:30h: Educational interventions to improve hospital prescription. **Dr. Esther Calbo**. Hospital Universitari Mútua de Terrassa

15:30-16:00h: Organizing and prioritizing activities in the PROA. **Dr. Javier Murillas**. Hospital Universitari Son Espases.

16:00-17:30h: Workshops

17:30-18:00h: Debate workshops

18:00: Conclusions of the course



Available at: <http://60congreso.sefh.es/images/60-congreso-programa-cientifico.pdf> [Accessed March 2016]



PP-TYG-EUR-0022. Date of preparation: March 2016

PP-TYG-EUR-0022. Date of preparation: March 2016



Thank you
jnicolas@mutuaterrassa.cat



PP-TYG-EUR-0022. Date of preparation: March 2016



Satellite Symposium EAHP 2016
Austria Center Vienna

A multidisciplinary approach to effective antimicrobial stewardship

PP-TYG-EUR-0020. Date of preparation: March 2016

Working together for a healthier world® Pfizer

Thursday 17th March 2016, Vienna, Austria

A multidisciplinary approach to effective antimicrobial stewardship

Antifungal stewardship, where are we today?

Patricia Muñoz, MD. Ph.D.

Hospital General Universitario Gregorio Marañón

Department of Medicine. Universidad Complutense of Madrid. Spain

pmunoz@hggm.es



Hospital General Universitario
Gregorio Marañón



ESCMID
Collaborative Centres
and Observerships



PP-TYG-EUR-0021. Date of preparation: March 2016

Conflict of interest disclosures

Within the last 12 months:

Consultant and/or speaker for Astellas, Gilead,
Merck, Novartis and Pfizer

PP-TYG-EUR-0021. Date of preparation: March 2016

Antifungal stewardship?

■ Concept and justification

Definition of ABS
Use of antimicrobials
Are AF different?

■ Data from the literature

■ Our experience

ABS, antibiotic stewardship; AF, antifungals

Use of antifungals

■ Even more difficult than antibacterials

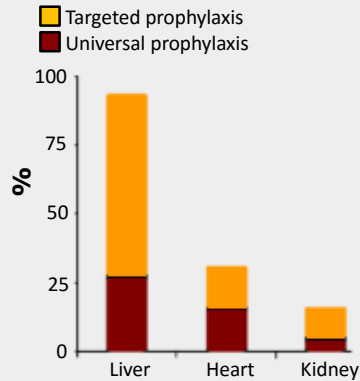
- Different types of patients
- Unspecific clinical presentation
- Microbiology: poor sensitivity
- Very high mortality
- Impact of early therapy
- New drugs are less toxic

Increase
empirical
therapy

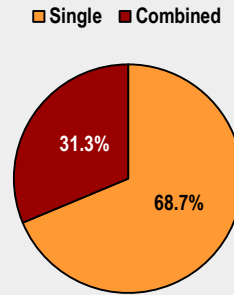
Prophylaxis

Poor compliance with antifungal drug use guidelines by transplant physicians

Antifungal prophylaxis in solid organ transplantation



First-line antifungal treatment regimen for IA



COMIT Study Group



IA, invasive aspergillosis
Muñoz et al. *Clin Transplant* 2012;26:87-96.

PP-TYG-EUR-0021. Date of preparation: March 2016

Using propensity scores to assess candidemia-attributable mortality in critically-ill patients

Empirical

Low PPV

Characteristics of the study patients according to infection status

	Without candidemia (number = 1,069)	With candidemia (number = 38)	P value
Age, years, mean (SD)	60.0 ± 17.1	59.0 ± 17.9	0.706
Male/female (%)	67.4/32.6	63.2/36.8	0.583
APACHE II score at ICU admission, mean SD	18.3 ± 7.0	20.1 ± 6.5	0.131
SOFA score at ICU admission	7 (4 to 9)	8.5 (7 to 10)	0.004
ICU level			0.001
Hospital			0.436
ICU mortality			0.001
Overall mortality			0.001
Risk factors			
Urinary catheter			0.387
Central venous catheter			0.193
Mechanical ventilation			0.097
Broad-spectrum antibiotics			0.046
Empiric/pre-emptive antifungal treatment	180 (16.8)	2 (5.3)	0.032
Arterial catheter	846 (79.5)	37 (97.4)	0.001
Enteral nutrition	825 (77.2)	26 (68.4)	0.225
Total parenteral nutrition	428 (40.4)	27 (71.1)	<0.001
Corticosteroids	300 (28.5)	12 (31.6)	0.679
Renal replacement therapy	126 (12.0)	15 (39.5)	<0.001

180 x €5000 = €900,000



€5000 is an estimate of the median cost of candins in Europe. Personal opinion P. Muñoz

González de Molina et al. *Crit Care* 2012;16:R105.

PP-TYG-EUR-0021. Date of preparation: March 2016

Implications for antimicrobial stewardship: antifungal therapy in candidemic patients

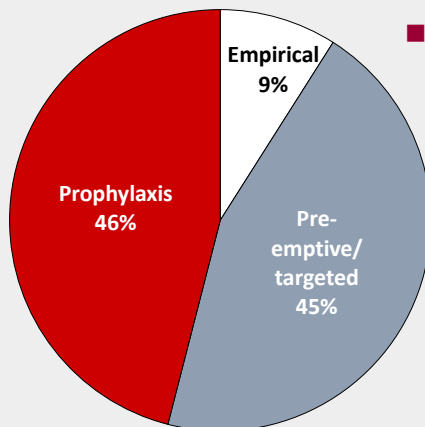
Targeted

- Candidemic patients treated with fluconazole (36%) or candins (64%)¹
- De-escalation with susceptible strains: **39%!²**
 - **24% if non-albicans**
 - Data available day +5

PP-TYG-EUR-0021, Date of preparation: March 2016

Adherence to recommendations for the use of antifungal agents: treatments

Consequences



■ **Inappropriate** antifungal use = **34%**

- **Survival** at 12 weeks was higher if appropriate therapy used (81% appropriate vs 68% inappropriate)

PP-TYG-EUR-0021, Date of preparation: March 2016

Retrospective study

Study of incidence and factors involved with inappropriate use of antifungals (Thailand)

■ Thai tertiary care centre

- Incidence of **inappropriate** antifungal use = **74%** (in 42 of 57 patients)
- Isolation of *Candida* species from **urine** ($p=0.004$) was a risk factor
- Receipt of an **infectious disease consultation** ($p=0.004$) was protective

Prospective study

Antifungal stewardship?

- Concept and justification
 - It seems to be necessary
- Examples from the literature
- Our experience

Antimicrobial stewardship: cost analysis before, during and after a 7-year program

■ Active AF stewardship 2001–2008 (US)

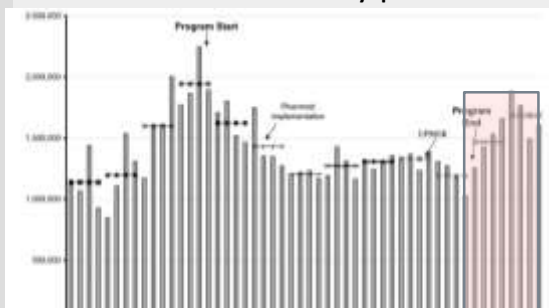
- Expenditure reduced **37%** (\$1 million USD/year in the first 3 years)
 - **AF**: 50% budget (\$3.7 million USD)
 - **REDUCTION**: **60.7%**
- Most effective in cancer center, medical and surgical ICUs and transplant units



PP-TYG-EUR-0021, Date of preparation: March 2016

Antimicrobial stewardship: cost analysis before, during and after a 7-year program

Antimicrobial costs by quarter



Increase = 41%

Therefore, programme was restarted

- Programme terminated due to dissatisfaction with the preauthorization requirements
- ID physicians provide antifungal stewardship when deciding on appropriate therapy: similar effect?



PP-TYG-EUR-0021, Date of preparation: March 2016

Impact of education and an antifungal stewardship programme for candidiasis

- Education, dose adjustment tool, antifungal prescription forms, and prescription-control strategies
- Led to **59%** reduction in antifungal prescriptions
- **Inappropriate antifungal use:** decreased from **71% to 24%**
- Reduction in *C. glabrata* and *C. krusei*

PP-TYG-EUR-0021, Date of preparation: March 2016

Compliance with the Comprehensive Care Bundle for candidemia*

	Control group (n=37)	Antimicrobial stewardship intervention group (n=41)	p value
All bundle elements successfully completed	15 (40.5)	32 (78.0)	0.0016
Patients with more than one element not completed successfully	9 (24.3)	1 (2.4)	0.0108
Completion of individual elements			
Appropriate therapy after culture and susceptibility results	32 (86.5)	41 (100)	0.0488
Intravenous catheter removed	32 (86.5)	39 (95.1)	0.3494
Blood cultures every 48 hours until negative	29 (78.4)	35 (85.4)	0.6118
Appropriate duration of therapy	25 (67.6)	40 (97.6)	0.0012
Ophthalmologic examination performed	28 (75.7)	40 (97.6)	0.0108

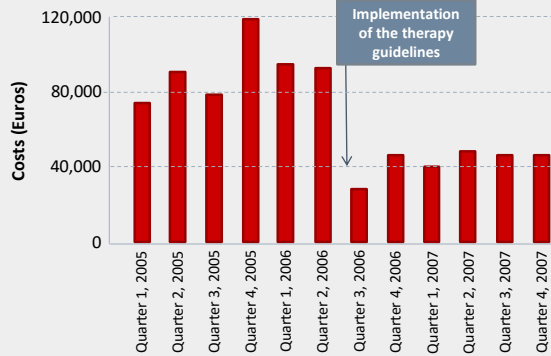
*Data are no. (%) of patients

- Fewer excess total days of therapy (5 versus 83 total antifungal days)
- Similar clinical outcome

PP-TYG-EUR-0021, Date of preparation: March 2016

Implementation of local guidelines

■ 50% reduction

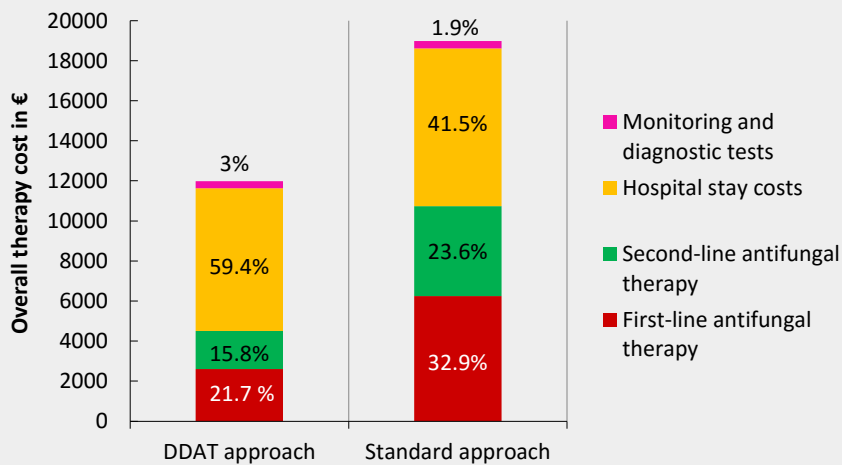


PP-TYG-EUR-0021, Date of preparation: March 2016



Swoboda et al. *Chemotherapy* 2009;55:418–24.

Contribution of different cost components to the overall therapy cost



PP-TYG-EUR-0021, Date of preparation: March 2016



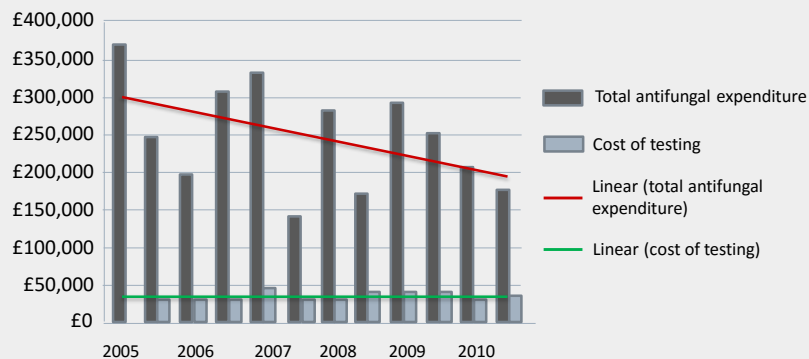
DDAT, diagnostic-driven antifungal therapy
 Martín-Peña et al. *Antimicrob Agents Chemother* 2013;57:4664–72.

Very high NPV of negative PCR + EIA

“Our results suggest screening has a role in high-risk populations. The high NPV allows empiric antifungal agents to be safely withheld in febrile patients and in this combined diagnostic strategy the post-test probability of not having IA for a patient consistently negative by PCR and EIA is 99.6%.”

PP-TYG-EUR-0021, Date of preparation: March 2016

Impact on antifungal expenditure



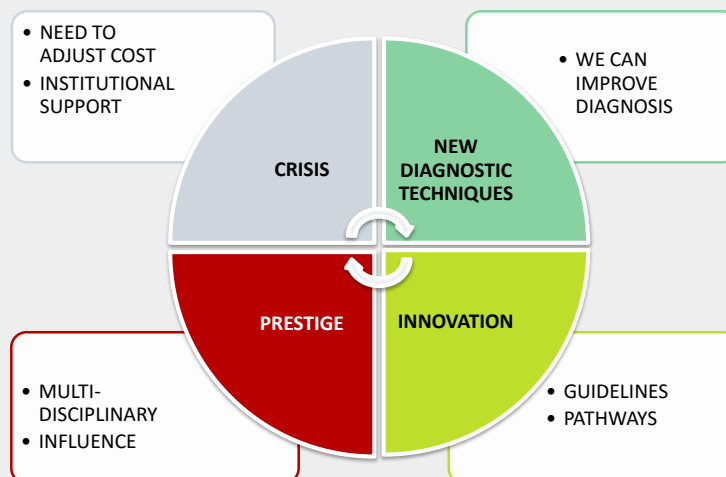
PP-TYG-EUR-0021, Date of preparation: March 2016

Antifungal stewardship?

- Concept and justification
- Data from the literature
 - It seems to be feasible
- Our experience in a general hospital

PP-TYG-EUR-0021. Date of preparation: March 2016

Opportunities/urgency



PP-TYG-EUR-0021. Date of preparation: March 2016

Must have



- **Leadership**
 - **ID physician** (30–50% dedication)
 - **Pharmacist trained in ID** (20–30% dedication)
 - **Microbiology** (10% dedication)
- **Institutional support**
 - Medical director, ID chief, infection control, quality, ethics committee
- **Prescriber's acceptance**

PP-TYG-EUR-0021, Date of preparation: March 2016

Choices

Compulsory vs non-compulsory

■ ACTIVE MEASURES


- Bedside advice
- On-site education
- Multidisciplinary groups
- Communication, communication, communication
- **RESOURCES, TIME**

■ PASSIVE MEASURES

- Automatic stop orders
- Order forms
- Limited formularies
- Education
- Restricted industry contact
- Restricted susceptibility reports

PP-TYG-EUR-0021, Date of preparation: March 2016

Methods: first steps toward AF stewardship

- ✓ **Setting:** 1,550-bed tertiary teaching center serving a population of approximately 715,000 inhabitants¹ 
 - Approximately 1,500 patients per year receive systemic AFs, with a cost of ~**€3,000,000**¹
- 1. Identified the **main AF prescribing departments:** Hematology, ICUs, Oncology, Nephrology, Gastroenterology, Pediatrics, Transplant units²
- 2. Conducted **surveys to evaluate physicians' knowledge** on the diagnosis and management of invasive fungal infections and **AF prescribing practices: EDUCATION**²
- 3. Created a **Collaborative Group on Mycoses (COMIC)**
 - ✓ At least: pharmacists, clinical microbiologists, ID consultants and physicians from the top AF prescribing departments²

Identify knowledge gaps

- **Knowledge survey (20 questions, score 0–10)**
 - Members of most prescribing departments (physicians of differing seniority)
 - Mean score of correct responses was **5.16 ± 1.73**
 - **<35%** correct answers in:
 - **Candida:** meaning of respiratory cultures, percentage of fluconazole resistance, indications for prophylaxis and empirical therapy, de-escalation
 - **Aspergillus:** indications of L-AmB, GM use, antifungal combinations, initial therapy of aspergillosis!



RESEARCH ARTICLE
Open Access

How much European prescribing physicians know about invasive fungal infections management?

Maricela Valerio^{1,2}, Antonio Vera^{3,4,5}, Emilio Bouza^{1,2,3}, Nanna Reiter⁶, Perikaj Vake⁷, Marcel Hochreiter⁸, Nicoletta Giannella⁹, Patricia Muñoz^{1,2,3} and on behalf the CORMIC study group (Collaborative group on Mycosis)

Percentage of adequate answers regarding department and physician category				
Question	Adequate answer	Overall N=121	Medical n=62	ICU N=52
Which do you think is the percentage of fluconazole resistance in <i>Candida</i> strains isolated from blood cultures at your hospital?	Less than 5%	24	19.4	28.8
In which of the following scenarios would you choose L-AmB as your first choice?	In unspecified invasive filamentous fungal infection	471	51.6	44.2
Regarding the treatment with azoles and candins, which of the following statements is true	Candins can be used as empirical treatment before knowing the yeast antifungal susceptibility	67.8	64.5	75
When isolating <i>Aspergillus</i> spp. in a respiratory sample, you would consider	Treatment in patients who fulfilled the criteria of proven or probable invasive aspergillosis	52.1	74.2	26.9
Which of the following statements regarding the galactomannan test is false	It can only be performed in serum samples	42	50.8	35.3

Hospital General Universitario Gregorio Marañón

L-AmB, liposomal amphotericin B
Valerio et al. *BMC Infectious Diseases* 2015;15:80

PP-TYG-EUR-0021, Date of preparation: March 2016

Survey

Journal of Antimicrobial Chemotherapy

Evaluation of antifungal use in a tertiary care institution: antifungal stewardship urgently needed

Maricela Valerio^{1,2}, Carmen Escobedo³, Rodrigo Escobedo⁴, Patricia Muñoz^{1,2,3}, Antonio Vera⁵, María Serrano⁶ and Emilio Bouza^{1,2,3} as behalf of the CORMIC study group (Collaborative Group on Mycosis)

Feature	Question	Answer	Points
Indication	Did the patient need an antifungal?	Yes	2
		No	0
Selection	Did the antifungal cover the suspected fungi and was it the first option recommended by the guidelines?	It covered the suspected fungi and was the first option	2
		It covered the suspected fungi but was the alternative option	1
		It did no cover the suspected fungi	0
Dosage	Was the dosage correct according to the body weight, hepatic and renal function, and potential interactions with other drugs?	Yes	1
		No	0
Microbiological adjustment	Was the antifungal adjusted after microbiological results (identification of microorganism, antifungal susceptibility tests and indirect tests) become available?	Yes	2
		No	0
Administration route	Was the intravenous route switched to the oral route when possible?	Yes	1
		No	0
Duration	Was the duration of therapy correct according to the guidelines?	Yes	2
		No	0

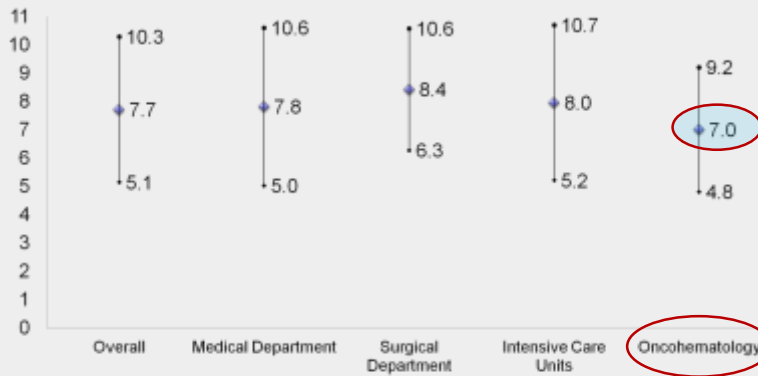
Total score (from 0 to 10)
Both low and high doses were considered incorrect. Adjustment for renal and hepatic failure and drug-to-drug interactions were also addressed. At the time of the study, monitoring of serum voriconazole and posaconazole was not available. Durations that were too short and too long were considered incorrect.

If any defect: classified as inappropriate

Valerio M, *JAC* 2014; 69(7):1993-9.

PP-TYG-EUR-0021, Date of preparation: March 2016

Mean scores for adequacy of AF use by department



PP-TYG-EUR-0021, Date of preparation: March 2016

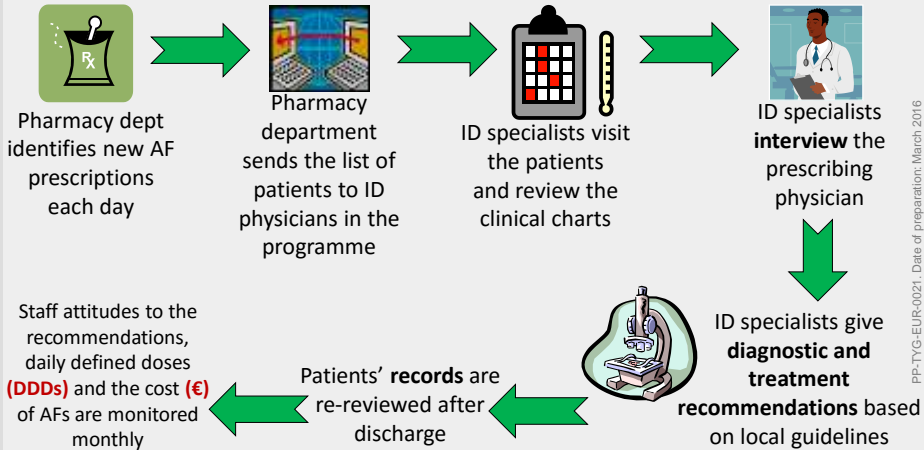
Methods: AF stewardship structure



PP-TYG-EUR-0021, Date of preparation: March 2016

Methods: bedside intervention

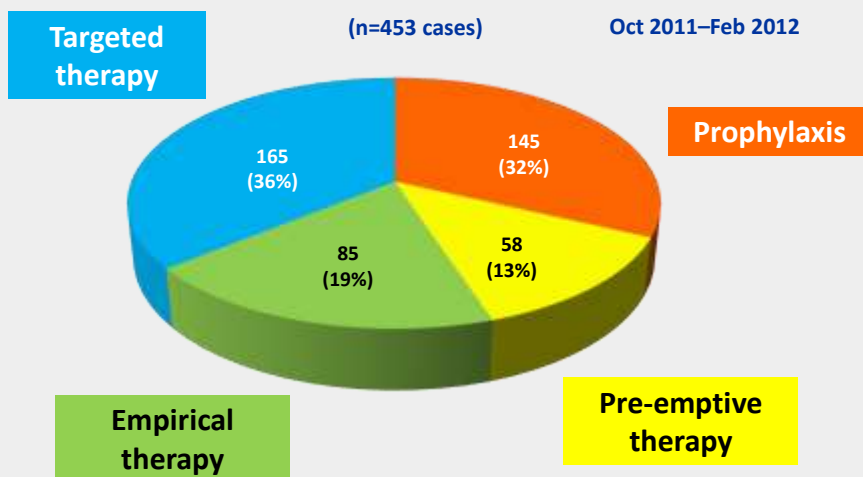
■ Ongoing intervention since Oct 2011



Muñoz P. Mycoses. 2015 Jun;58 Suppl 2:14-25

PP-TYG-EUR-0021. Date of preparation: March 2016

Results overview: reasons for prescribing AFs

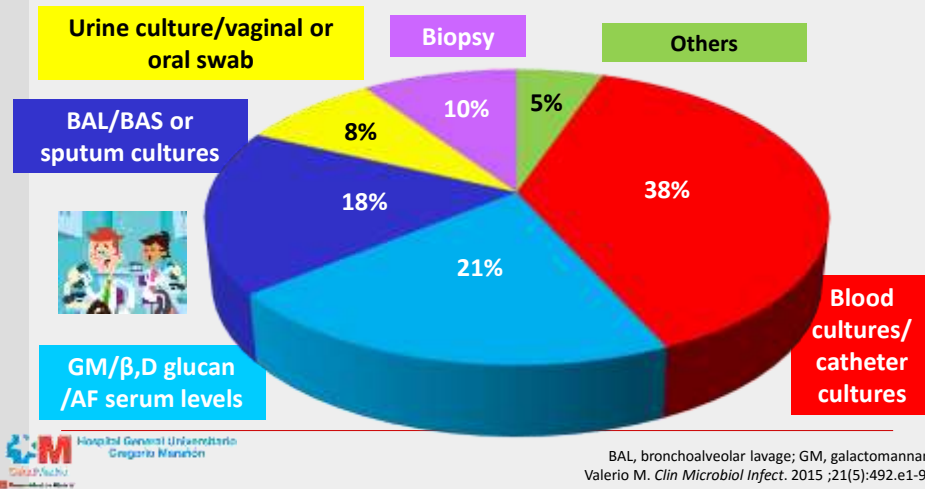


Valerio et al. ICAAC 2013; Poster No. 1610
P. Munoz, personal communication.

PP-TYG-EUR-0021. Date of preparation: March 2016

Results: diagnostic advice

Diagnostic recommendations: **67%** cases



PP-TYG-EUR-0021. Date of preparation: March 2016

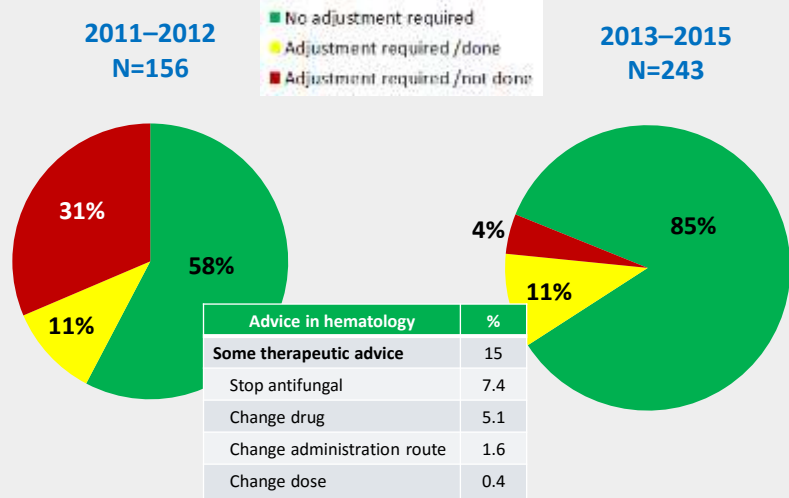
Bedside intervention: therapeutic advice

Therapeutic advice at initial visit, n (%)	
No change required	310 (68.4)
De-escalate the antifungal	79 (17.4)
Stop the antifungal	32 (7.1)
Escalate the antifungal	14 (3.1)
Modify the dose	12 (2.6)
Switch drug due to toxicity	2 (0.4)
Add a second antifungal	1 (0.2)

Evaluation of antifungal use at discharge, n (%)	
Inadequacy in any aspect of antifungal use	203 (44.8)
Indication	20 (4.4)
Drug choice	109 (24.1)
Dosage	17 (3.8)
Adjustment to microbiology results	84 (18.5)
Sequential therapy	30 (6.6)
Length of therapy	129 (28.5)

PP-TYG-EUR-0021. Date of preparation: March 2016

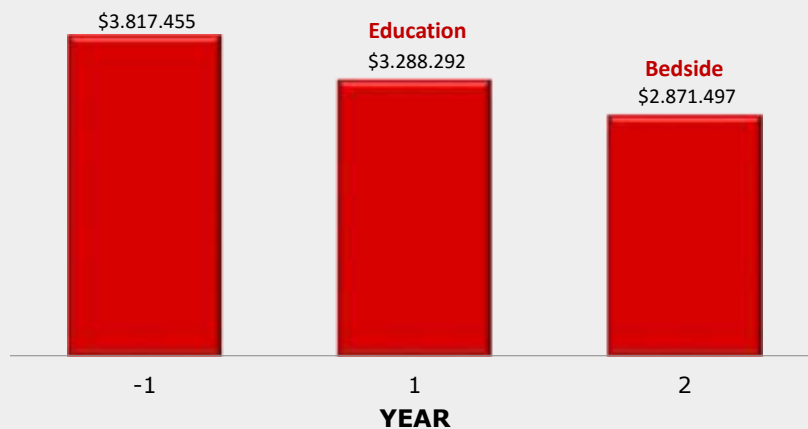
Bedside intervention in hematology (5 years!)



Personal data. Hospital General Universitario Gregorio Marañón. Madrid. Spain

PP-TYG-EUR-0021. Date of preparation: March 2016

Annual cost of antifungals (\$ USD)



~Half a million USD per year



Valerio M. Clin Microbiol Infect. 2015 ;21(5):492.e1-9.

PP-TYG-EUR-0021. Date of preparation: March 2016

IFIs are hard to prove and to exclude: biomarkers



T2 MR

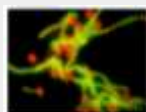


Behavioural vs technical changes

Aspergillus PCR

glucan

CAGTA

Aspergillus
antigen (GM)

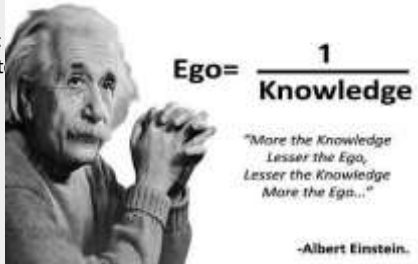
Some of our recent references in the field

- **Knowledge surveys:** room for improvement. Valerio M, et al. *Enf Infect Microbiol Clin* 2015;33(4):221–7 and Valerio M, et al. *BMC Infect Dis* 2015 21;15(1):80
- **Antifungal use audit:** identifies how AF are used and targets for intervention. Valerio M, *JAC* 2014;69(7):1993–9
- **Non-restrictive bed-side intervention:** safe and very cost-effective. Valerio M, et al. *CMI* 2015;21(5):492.e1-9
- **Combination of *Candida* biomarkers:** help for stopping antifungals. Martínez-Jiménez MC, et al. *Med Mycol.* 2014;52(3):270-5; Martínez-Jimenez MC *JAC* 2015;70(8):2354–61 and Martínez-Jimenez MC *JAC* 2015;70(11):3107–15
- **Monitoring AF levels:** Guinea J, et al. *Med Mycol.* 2016. Epub ahead of print. doi: 10.1093/mmy/myv099
- **A review:** Muñoz P. *Mycoses.* 2015;58(Suppl 2):14–25

Multidisciplinary interventions

Pharmacy department

- AF alerts, prescription tools, interactions, iv fluconazole to po
- Monitor cost: overall and at unit level
- Price negotiation!
- Expert pharmacists: audit of agreed prot



Hematologists

- More diagnostic work-up
- Share knowledge
- Accept AFS team decisions

neumologist, radiologists...

ID physicians

- Daily bedside intervention
 - Prescribing etiquette:
 - Different healthcare models
 - Perceived loss of autonomy, local leaders in charge
- Consultation

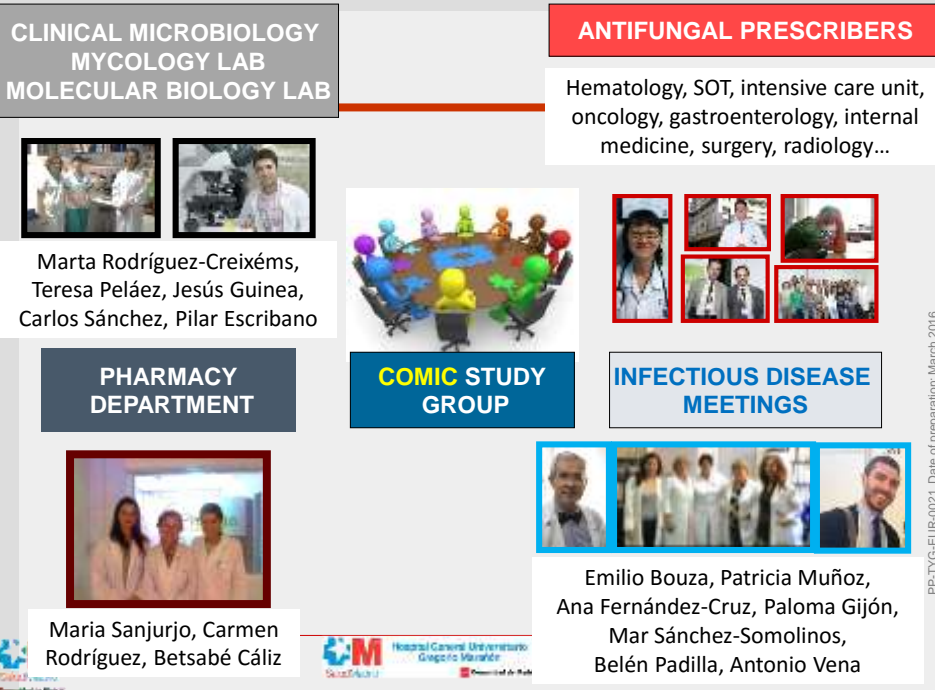
Clinical microbiology

- Rapid turnover of lab results (streamlining)
- Help clinicians with diagnostic investigations
- TDM
- New diagnostic tools




Dx, diagnostics; TDM, therapeutic drug monitoring
Muñoz P. Personal opinion

PP-TYG-EUR-0021. Date of preparation: March 2016




PP-TYG-EUR-0021. Date of preparation: March 2016

Satellite Symposium EAHP 2016
Austria Center Vienna



A multidisciplinary
approach to effective
antimicrobial stewardship

PP-TYG-EUR-0020, Date of preparation: March 2016

Working together for a healthier world 

Antimicrobial stewardship, an infectious disease specialist's view

Matteo Bassetti, MD, PhD
Infectious Diseases Division
Santa Maria Misericordia University Hospital
Udine, Italy



PP-TYG-EUR-0018, Date of preparation: March 2016

Disclosures

- Research grants
 - Astellas, Pfizer, MSD, Gilead
- Advisor/consultant
 - AstraZeneca, Astellas, Bayer, Cubist, Pfizer, MSD, Gilead, Angelini, Vifor, Shionogi, Novartis, Trius
- Speaker/chairman
 - AstraZeneca, Astellas, Pfizer, MSD, Gilead, Angelini, Vifor, Shionogi, Novartis

PP-TYG-EUR-0018, Date of preparation: March 2016

Brief history of antimicrobials

- Alexander Fleming discovered that *Penicillium* kills bacteria in 1928
- Fleming was convinced that the observation could never lead to therapeutic agents
- Florey and Chain resurrected the work, isolated penicillin, and by World War II were treating millions with antibiotics
- The age of antibiotics changed the landscape of modern medicine and antibiotics are one of the key medical interventions that have impacted human health



Alexander Fleming



Ernst Chain

Howard Florey

PP-TYG-EUR-0018, Date of preparation: March 2016

Alexander Fleming

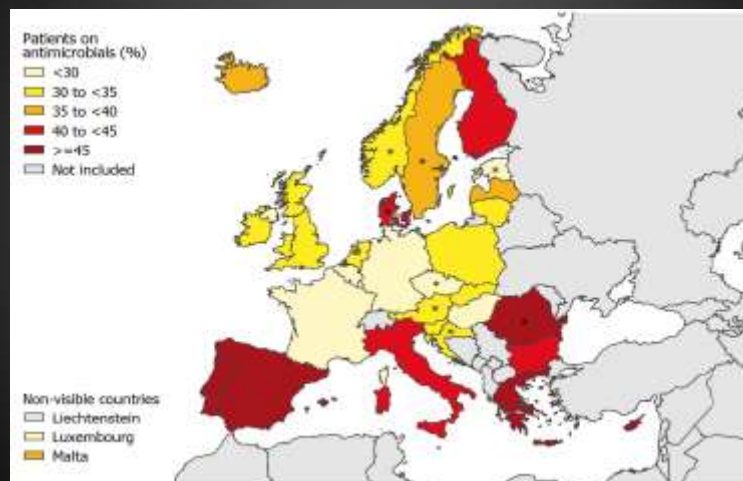


“It is not difficult to make microbes resistant to penicillin...The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.”

Fleming A. Nobel Lecture, 1945.

PP-TYG-EUR-0018. Date of preparation: March 2016

Antimicrobial use 2013



European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC, 2013.

*PPS data representation was poor in Austria, Croatia, Czech Republic, Estonia, Norway and Romania. Representation was very poor in Denmark and Sweden.

PP-TYG-EUR-0018. Date of preparation: March 2016

Klebsiella pneumoniae resistant to...

Third generation cephalosporins (2014)



Fluoroquinolones (2014)



Aminoglycosides (2014)



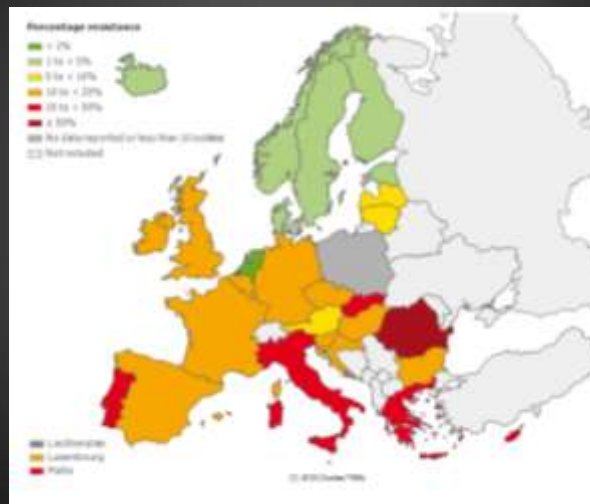
Carbapenems (2014)



ECDC maps, 2014. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016].

PP-TYG-EUR-0018. Date of preparation: March 2016

MRSA 2014



ECDC maps, 2014. Available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/map_reports.aspx [Accessed March 2016].

MRSA. Methicillin-resistant *Staphylococcus aureus*.

PP-TYG-EUR-0018. Date of preparation: March 2016

A growing problem

- Resistance in clinically important pathogens has reached alarming rates
- Bacterial resistance exerts a significant impact on clinical outcomes:
 - No longer confined to the hospital setting alone
 - Will continue to worsen if not addressed
 - Limited antimicrobial options on the immediate horizon



PP-TYG-EUR-0018, Date of preparation: March 2016

IDSA Public Policy. *Clin Infect Dis* 2011;52(Suppl 5):S397-428.

The BUGS 'perfect storm'

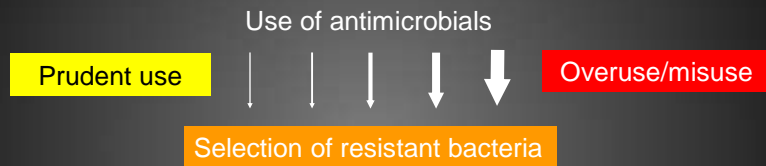
- MRSA
- VRE
- MDR *A. baumannii*
- MDR *P. aeruginosa*
- ESBL(+) *E. coli*
- ESBL(+) *K. pneumoniae*
- Carbapenemase(+) *K. pneumoniae*
- Penicillin/macrolide resistant *S. pneumoniae*
- MDR *M. tuberculosis*

PP-TYG-EUR-0018, Date of preparation: March 2016

ESBL, Extended-Spectrum Beta-Lactamases; MDR, multidrug resistant; MRSA, Methicillin-resistant *Staphylococcus aureus*; PR, penicillin resistant; VRE, Vancomycin-resistant Enterococcus.

IDSA Public Policy. *Clin Infect Dis* 2011;52(Suppl 5):S397-428.

Selection of antimicrobial resistance



- Once established, resistance is not always reversible
- There is a continuing need for new antimicrobial agents active against resistant pathogens

Hamilton-Miller JMT. *Int J Antimicrob Agents* 2004;23:209-12.

PP-TYG-EUR-0018. Date of preparation: March 2016

Rationale for antibiotic optimization: Balancing the needs of the patient and society

Inappropriate antibiotic therapy associated with higher mortality¹



Indiscriminate use of broad-spectrum antibiotics driving resistance

- The most important decision in antibiotic treatment is the choice between present and future patients

1. Shorr AF, et al. *Crit Care Med* 2011;39:46-51; 2. Richards GA. *Clin Microbiol Infect* 2005;11(Suppl):18-22.

PP-TYG-EUR-0018. Date of preparation: March 2016

What are the goals of antibiotic stewardship?

Optimize clinical outcomes while minimizing unintended consequences of antibiotic use



Comprehensive infection control to limit emergence and transmission of resistance



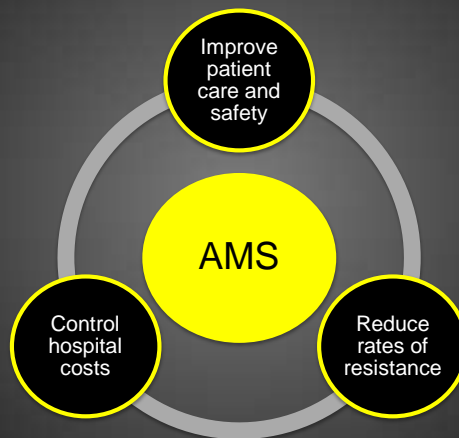
- Toxicity
- Selection of pathogenic organisms
- Emergence of resistance

Reduce healthcare costs without adversely impacting quality of care

Dellit TH, et al. *Clin Infect Dis* 2007;44:159-77.

PP-TYG-EUR-0018, Date of preparation: March 2016

Balancing the antibiotic needs of the patient with antibiotic effectiveness for society



CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available at <http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html>. [Accessed February 2016].

AMS, antimicrobial stewardship.

PP-TYG-EUR-0018, Date of preparation: March 2016

Improving patient outcomes

Clinical outcomes: comparing a stewardship program* to usual practice¹

Outcome	Stewardship program (n=96)	Usual practice (n=95)	Relative risk (95% CI)
Appropriate antimicrobial	90%	32%	2.8 (2.1–3.8)
Cure	91%	55%	1.7 (1.3–2.1)
Failure	5%	31%	0.2 (0.1–0.4)
Resistance	1%	9%	0.13 (0.02–1.0)

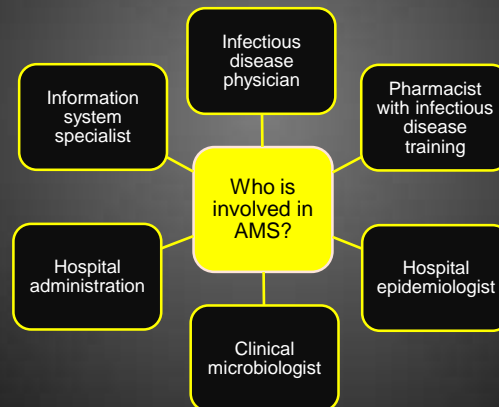
- Antimicrobial stewardship programs have shown that appropriate initial antibiotic use leads to decreased mortality,² improved infection cure rates, reduced resistance³ and reduced surgical infection rates¹

1. Fishman N. *Am J Med* 2006;119:S53–61; 2. Shorr AF, et al. *Crit Care Med* 2011;39:46–51; 3. Davey P, et al. *Cochrane Database of Systematic Reviews* 2013;4; Art. No.: CD003543.

*AMS program at the Hospital of the University of Pennsylvania, Philadelphia, PA, USA. AMS, antimicrobial stewardship; CI, confidence interval.

Successful antimicrobial stewardship involves a multidisciplinary approach

- Antimicrobial stewardship is an inter-professional effort,¹ involving multidisciplinary collaboration from various core members²



1. Moody J, et al. *Am J Infect Control* 2012;40:94–5; 2. Dellit TH, et al. *Clin Infect Dis* 2007;44:159–77.

AMS, antimicrobial stewardship.

Evaluation of stewardship strategies

Tactic	Comment	Level of evidence
Education	Essential but needs active intervention	A-III
Guidelines and clinical pathways	Can improve antibiotic utilization	A-I
Antimicrobial cycling	Insufficient data	C-II
Antimicrobial order forms	Can be an effective component	B-II
Combination therapy	Insufficient data	C-II
Streamlining or de-escalation	Can be an effective component	A-II
Dose optimization	Is an important component	A-II
IV to PO switch	Can be an effective component	A-III

Dellit TH, et al. *Clin Infect Dis* 2007;44(2):159-77.

IV, intravenous; PO, oral administration.

PP-TY6-EUR-0018, Date of preparation: March 2016

Antibiotic stewardship in Europe

- A pan-European survey to investigate antibiotic policy criteria in 170 hospitals from 32 countries

Conclusions:

- 57% of European hospitals surveyed have a written antibiotic policy
 - 1/5 of the teaching hospitals did not
- Hospitals in Northern and Western Europe are most likely to convene antibiotic committees
- Policies and practices relating to antibiotic stewardship vary considerably across Europe
- New stewardship initiatives are necessary to achieve harmonization of recommended practices

Bruce J, et al. *J Antimicrob Chemother* 2009;64:853-60.

PP-TY6-EUR-0018, Date of preparation: March 2016

The worldwide situation

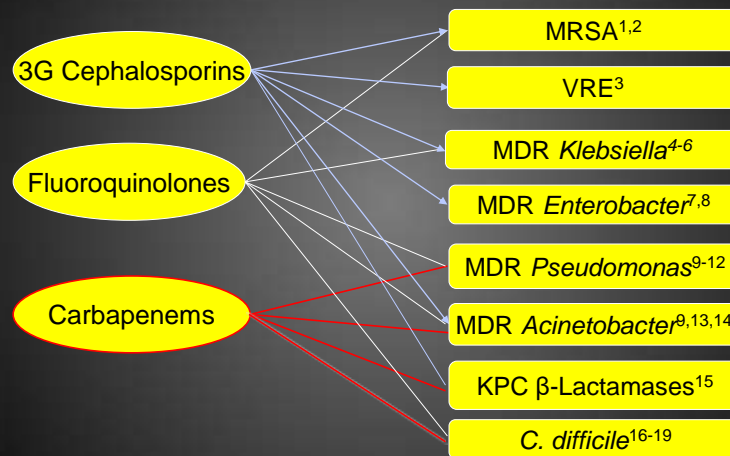
- An international cross-sectional survey of antimicrobial stewardship programs in hospitals
- Internet-based survey in 2012: 43 questions
- Answers from 660 hospitals in 67 countries:
 - National stewardship program 52%
 - Local stewardship program 58%
 - Country AMS program (Europe) 81%

Howard P, et al. *J Antimicrob Chemother* 2014;70:1245–55.

AMS, antimicrobial stewardship.

PP-TYG-EUR-0018. Date of preparation: March 2016

An additional point to consider when selecting antimicrobial coverage: collateral damage



MDR, multidrug resistant; MRSA, Methicillin-resistant *Staphylococcus aureus*; VRE, Vancomycin-resistant *Enterococcus*; KPC, *Klebsiella pneumoniae* Carbapenemase. 1. Gade ND, et al. *J Lab Physicians* 2013;5:109–12. 2. Kim ES, et al. *PLoS One* 2014;8:e114127. 3. Fridkin S, et al. *Ann Intern Med* 2001;135:175–83. 4. Lautenbach E, et al. *Clin Infect Dis* 2001;33:1288–94. 5. Paterson DL, et al. *Clin Infect Dis* 2000;30:473–78. 6. Quale JM, et al. *Clin Infect Dis* 2002;35:834–41. 7. Saurina G, et al. *J Antimicrob Chemother* 2000;45:895–8. 8. Souli M, et al. *Clin Infect Dis* 2008;46:847–54. 9. Landman D, et al. *Arch Intern Med* 2002;162:1515–20. 10. Cao B, et al. *J Hosp Infect* 2004;57:112–8. 11. Lepper PM, et al. *Antimicrob Agents Chemother* 2002;46:2920–5. 12. Mentzelopoulos SD, et al. *Int Care Med* 2007;33:1524–32. 13. Manikall VM, et al. *Clin Infect Dis* 2000;31:101–8. 14. Lee SO, et al. *Antimicrob Agents Chemother* 2004;48:224–8. 15. Arnold R, et al. *South Med J* 2011;104:40–45. 16. Lai KK, et al. *Infect Control Hosp Epidemiol* 1997;18:628–32. 17. Nelson DE, et al. *Infect Control Hosp Epidemiol* 1994;15:88–94. 18. Yip C, et al. *Infect Control Hosp Epidemiol* 2001;22:572–5. 19. Gaynes R, et al. *Clin Infect Dis* 2004;38:640–5.

PP-TYG-EUR-0018. Date of preparation: March 2016

Summary of antimicrobial stewardship

Summary of the antibiotic care bundle¹

Right drug
 Right time
 Right dose
 Right duration

+

Infection control

'A 'post-antibiotic era' is difficult to contemplate but might become a reality unless the threat of progressive antibiotic resistance is taken seriously.'²

1. Fishman N. *Am J Med* 2006;119:S53–61.
 2. Opal SM, et al. *JAMA* 2009;302:2367-8.

PP-TYG-EUR-0018, Date of preparation: March 2016

Recent experience of AMS in South Africa

'5 main' interventions	
1	Cultures not done prior to commencement of empiric antibiotics
2	More than 4 antibiotics at the same time
3	More than 7 days of antibiotic treatment
4	More than 14 days of antibiotic treatment
5	Double-redundant antibiotic cover

Adrian Brink. Personal communication from the authors, 2016.

PP-TYG-EUR-0018, Date of preparation: March 2016

Role of infectious diseases specialist in stewardship

- Cohort study in an ICU over 4 years (2001–2004)
- Patients with a possible or definite diagnosis of infection who received antimicrobial treatment
- Analysis of the appropriateness of antimicrobial therapy prescription before (P1) and after (P2) the implementation (January 1, 2003) of a systematic ID specialist consultation program

PP-TYG-EUR-0018, Date of preparation: March 2016

Ranieri E, et al. *Am J Infect Control* 2008;36:283-90.

ICU, intensive care unit; ID, infectious disease.

To ID or not to ID?

	P1 (no ID)	P2 (with ID)	P
Infections	205	197	
Appropriate therapy	141 (68.8%)	165 (83.7%)	0.0004
Adherence to the local guidelines for empirical antimicrobial therapy	63.4%	83.8%	<0.0001

- Shorter duration of antibiotic treatment ($P<0.0001$), mechanical ventilation ($P<0.0001$), ICU stay ($P<0.0001$), and reduced in-hospital mortality ($P=0.006$)

PP-TYG-EUR-0018, Date of preparation: March 2016

Ranieri E, et al. *Am J Infect Control* 2008;36:283-90.

ICU, intensive care unit; ID, infectious disease; P1, prescription before implementation; P2, prescription after implementation.

Stewardship in my region and Udine hospital

Region

- Local guidelines CRE, *Acinetobacter*, *C. difficile*
- Local guidelines for UTI, pneumonia, SSTI, bacteremia

Udine hospital

- Antibiotic prophylaxis (drug, dose: when and how, duration)
- Internal guidelines/pathways for all infections:
 - Local epidemiology
 - PK/PD
 - De-escalation
 - Duration
 - IV/PO

PP-TYG-EUR-0018. Date of preparation: March 2016

Bassetti M. Personal communication, 2016.

CRE, Carbapenem-resistant Enterobacteriaceae; UTI, urinary tract infection; SSTI, skin and soft tissue infection; PK, pharmacokinetic; PD, pharmacodynamic; IV, intravenous; PO, oral administration.



Vademecum per la gestione delle infezioni correlate con le pratiche assistenziali presso l'A.O.U. Santa Maria della Misericordia

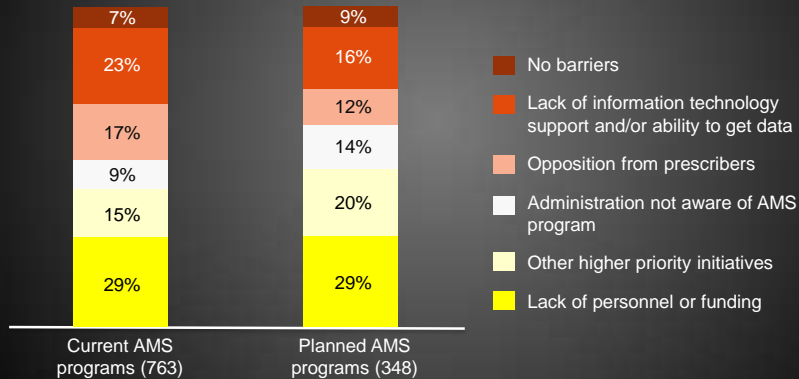
a cura di

Matteo Bassetti, Barbara Cadeo, Claudio Scarparo, Assunta Sartor, Roberto Cocconi, Federico Pea, Maria Grazia Troncon, Adriana Cecchi, Alessandra Tonizzo

PP-TYG-EUR-0018. Date of preparation: March 2016

Bassetti M. Personal communication, 2016.

Barriers to implementation of antimicrobial stewardship programs*



Howard P, et al. *J Antimicrob Chemother* 2014;70:1245-55.

*Based on responses from 660 hospitals in 67 countries from a survey in which 43 questions were disseminated worldwide in 2012. AMS, antimicrobial stewardship.

PP-TYG-EUR-0018. Date of preparation: March 2016

In summary

- Antimicrobial stewardship is a growing activity responding to a growing need
- In Europe there are still very clear-cut opportunities for improvement in antimicrobial stewardship
- A well-respected leader and a multidisciplinary group is necessary to start a stewardship program
- A yearly working plan should be written and discussed in all institutions with clear-cut objectives

PP-TYG-EUR-0018. Date of preparation: March 2016

In summary

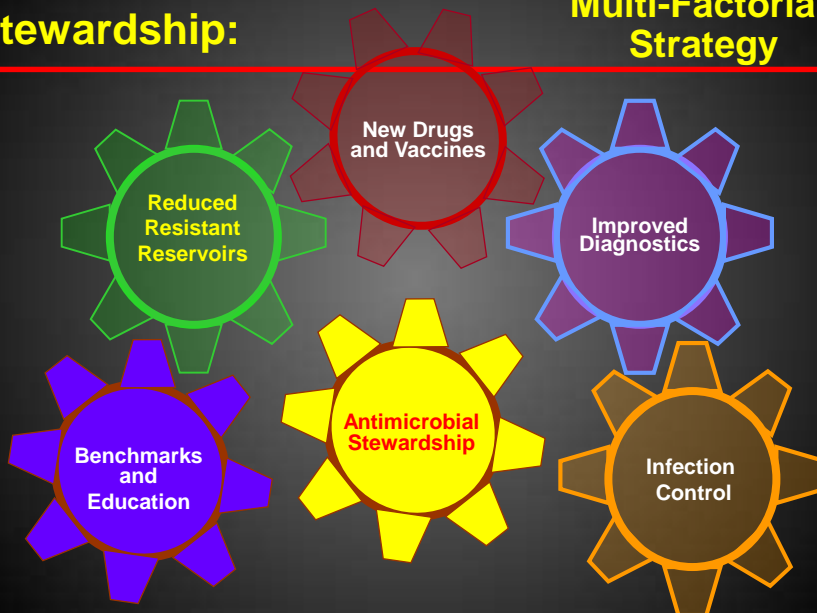
- Interventions may be divided into educational and other interventions, including restrictive
- Responsibility for intervention must be clarified at the beginning
- The selection of metrics is essential and should be the responsibility of different team members
- The impact of stewardship on the evolution of MDR infections should be estimated
- An estimation of the economic impact of the project is better than no estimation at all
- A yearly report is required

PP-TYG-EUR-0018, Date of preparation: March 2016

MDR, multi-drug resistant.

Antibiotic Stewardship:

A Multi-Factorial Strategy



PP-TYG-EUR-0018, Date of preparation: March 2016

Adapted from Fishman N. *Am J Med* 2006;119:S53-61.

H | T | I | D | E

Hot Topics in Infectious Diseases

Register at:
www.htide.net

PP-TY6-EUR-0018, Date of preparation: March 2016

Satellite Symposium EAHP 2016
Austria Center Vienna



A multidisciplinary
approach to effective
antimicrobial stewardship

Working together for a healthier world



Q&A

PP-TYG-EUR-0020. Date of preparation: March 2016

Working together for a healthier world! 

Questions



- Please use a question card (located in the back of your programme booklet) or raise your hand for a microphone

<p>Satellite Symposium EASP 2016 Austria Center Vienna A multidisciplinary approach to effective antimicrobial stewardship Thursday 17th March 2016 • 15:00-16:30 • 1416</p> <p>Question card</p>	
Name:	_____
Question for:	_____
Question:	_____ _____ _____
<p>Please give this question card to a member of the meeting staff.</p>	
<p>How Pfizer Works 100 Years of Innovation 130 Countries Sustained Commitment to Quality</p>	<p>Working together for a healthier world! </p>

PP-TYG-EUR-0020. Date of preparation: March 2016

Working together for a healthier world! 

Don't forget

- Please complete the evaluation form inside your programme booklet
- Your feedback is important to us

Satellite Symposium EAHF 2016
Audi Center Vienna

A multidisciplinary approach to effective antimicrobial stewardship
Tuesday 17 March 2016, 13:30-16:30

Guest feedback

Thank you for your time in completing this short evaluation questionnaire. Your answers provide valuable feedback and will be used to identify future Programme Improvement opportunities. Please circle the most appropriate answer for the question using the scale below where 1 is your best answer.

	Yes	No
How would you rate the symposium overall?	1 2 3 4 5	
How relevant or useful was the programme to you?	1 2 3 4 5	
How would you rate the quality of the programme content on learning knowledge in this area?	1 2 3 4 5	
How would you rate the programme format?		
Style	1 2 3 4 5	
Time	1 2 3 4 5	
Attention	1 2 3 4 5	
How well you manage programme after attending the symposium? Please tick all that apply.		
I will undertake practice and/or processes	<input type="checkbox"/>	<input type="checkbox"/>
I will actively seek to contribute	<input type="checkbox"/>	<input type="checkbox"/>
I will change management and/or treatment of my patients	<input type="checkbox"/>	<input type="checkbox"/>
I will not make any changes to my practice	<input type="checkbox"/>	<input type="checkbox"/>
Do you intend to share the content of this symposium with a colleague? Please tick one option.		
No (I do not intend to share the content) or I will do so in the future	<input type="checkbox"/>	<input type="checkbox"/>
Yes (I intend to share the content) or I have already done so	<input type="checkbox"/>	<input type="checkbox"/>
No	<input type="checkbox"/>	<input type="checkbox"/>

Please give the questionnaire back to a member of the meeting staff.

For further information contact: antimicrobial@pfizer.com or www.pfizer.com

Working together for a healthier world!

PP-TYG-EUR-0020, Date of preparation: March 2016



Satellite Symposium EAHF 2016
Audi Center Vienna

A multidisciplinary approach to effective antimicrobial stewardship

Thank you

PP-TYG-EUR-0020, Date of preparation: March 2016

Working together for a healthier world!

Satellite Symposium EAHP 2016
Austria Center Vienna



A multidisciplinary approach to effective antimicrobial stewardship

PP-TYG-EUR-0020, Date of preparation: March 2016

Working together for a healthier world®

