Antimicrobial Stewardship: Esperienza all'IRCCS – AOU San Martino-IST

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- Tutte le colleghe dell'UO dedicate alla stewardship

Direzione Sanitaria

- Alessandra Morando

Lo staff di SOFIA

Antimicrobial Stewardship

Antimicrobial Stewardship

Gestione dell'uso degli antibiotici

Perché?

World Health Organization

February 27th, 2017

GLOBAL PRIORITY LIST OF ANTIBIOTIC-RESISTANT BACTERIA TO GUIDE RESEARCH, DISCOVERY, AND DEVELOPMENT OF NEW ANTIBIOTICS

WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

http://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf?ua=1

Priority 1: CRITICAL[#]

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

* Enterobacteriaceae include: *Klebsiella pneumonia*, *Escherichia coli*, *Enterobacter* spp., *Serratia* spp., *Proteus* spp., and *Providencia* spp, *Morganella* spp.

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

*Mycobacteria* (including *Mycobacterium tuberculosis*, the cause of human tuberculosis), was not subjected to review for inclusion in this prioritization exercise as it is already a globally established priority for which innovative new treatments are urgently needed.

Priority 1: CRITICAL[#]

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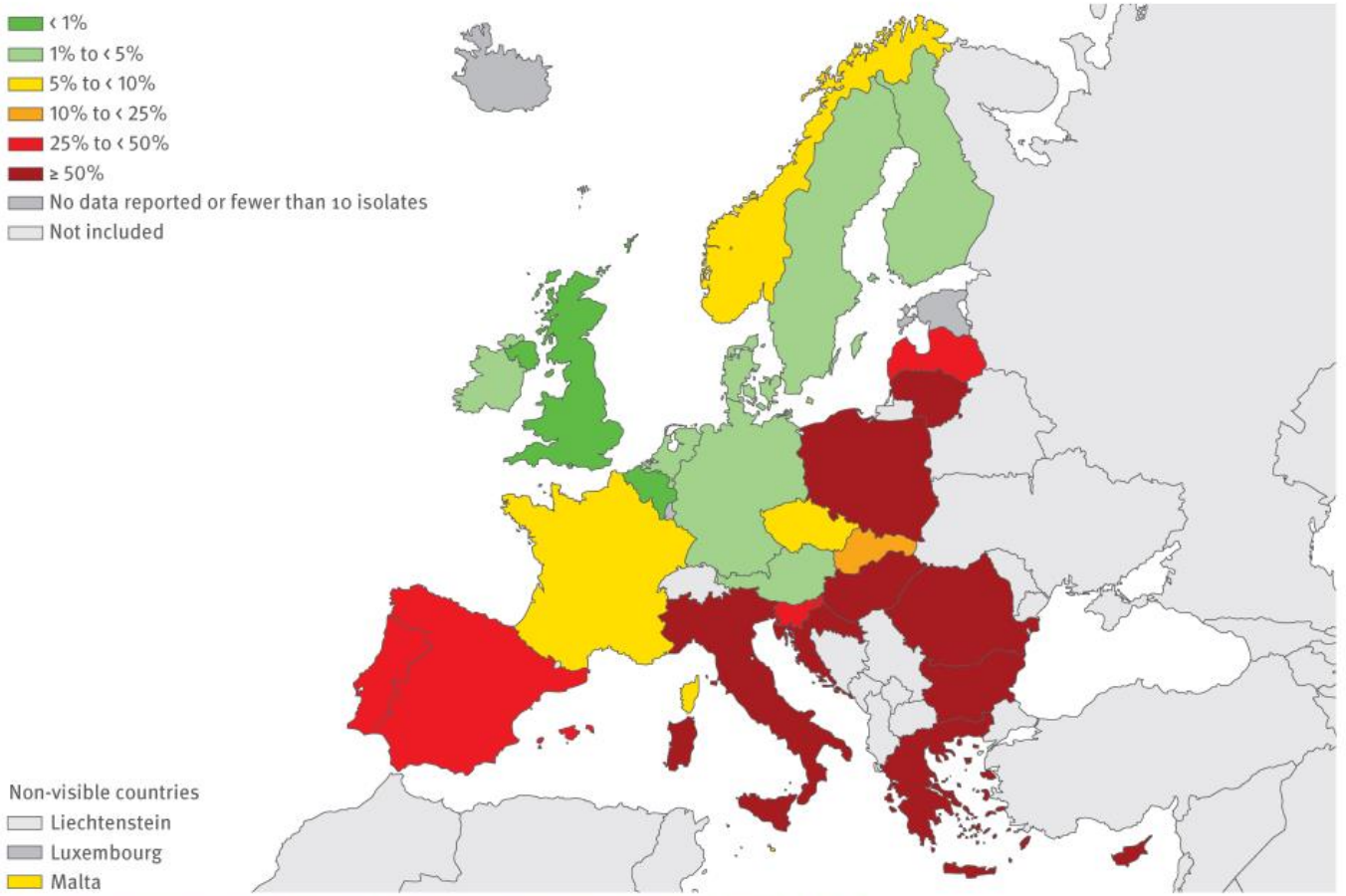
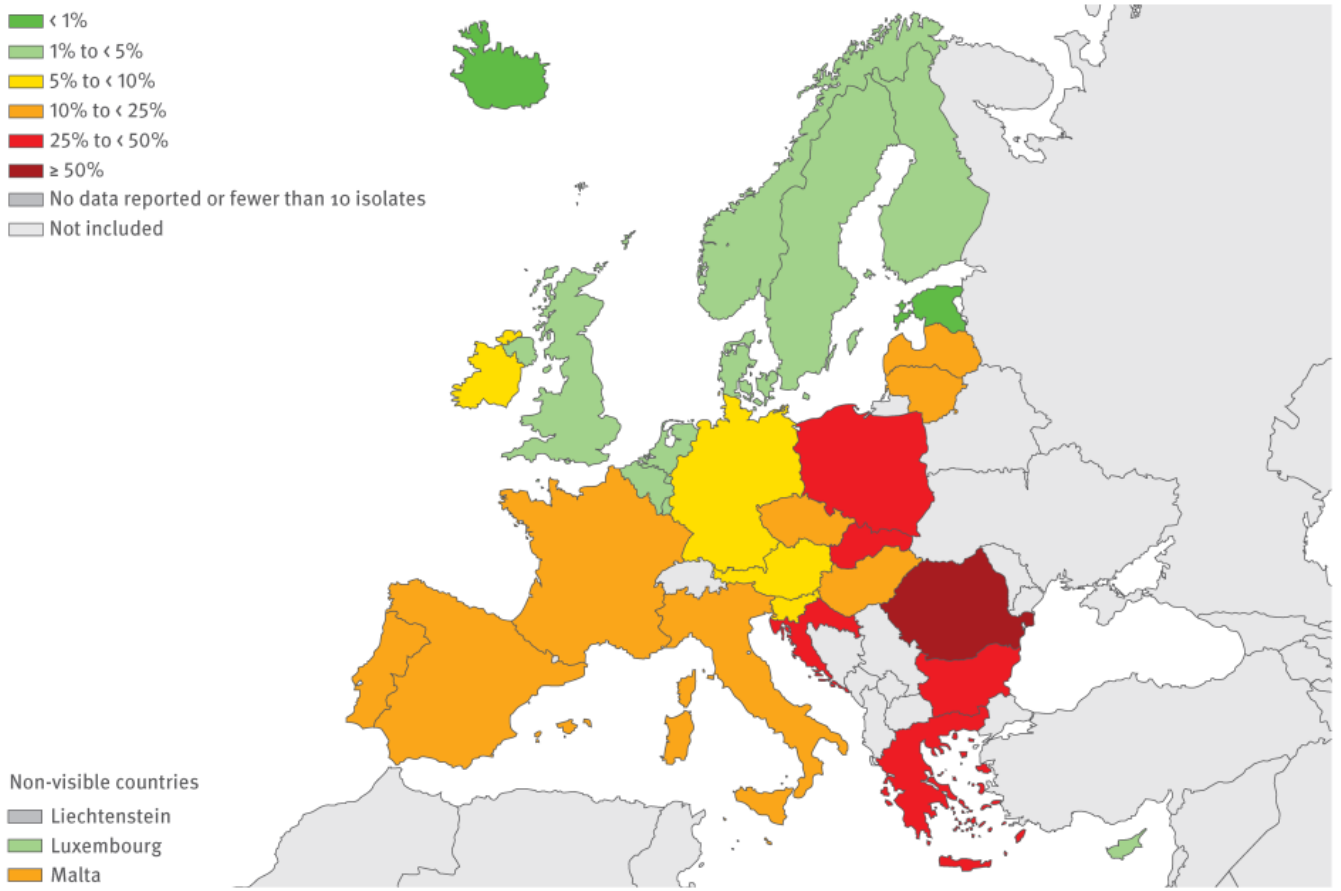
***Acinetobacter* spp.** Percentage (%) of invasive isolates with combined resistance to fluoroquinolones, aminoglycosides and carbapenems, by country, EU/EEA countries, 2015



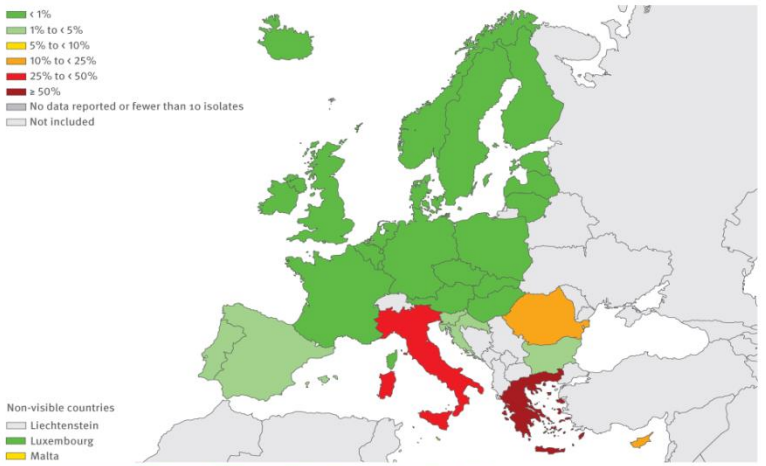
Source: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Stockholm: ECDC, 2017

Pseudomonas aeruginosa. Percentage (%) of invasive isolates with combined resistance (resistance to three or more antimicrobial groups among piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems), by country, EU/EEA countries, 2015



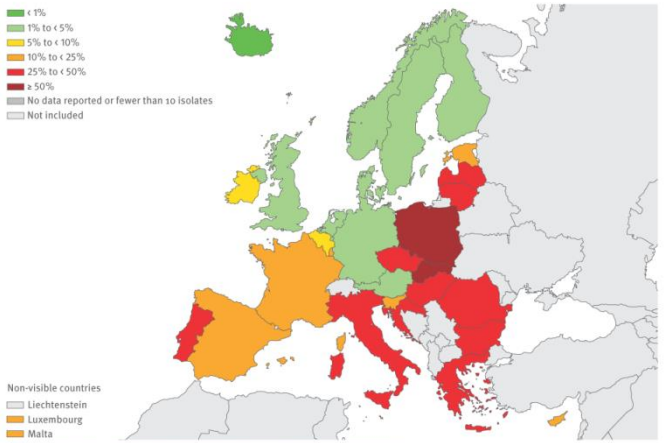
Source: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Stockholm: ECDC, 2017

Klebsiella pneumoniae. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2015



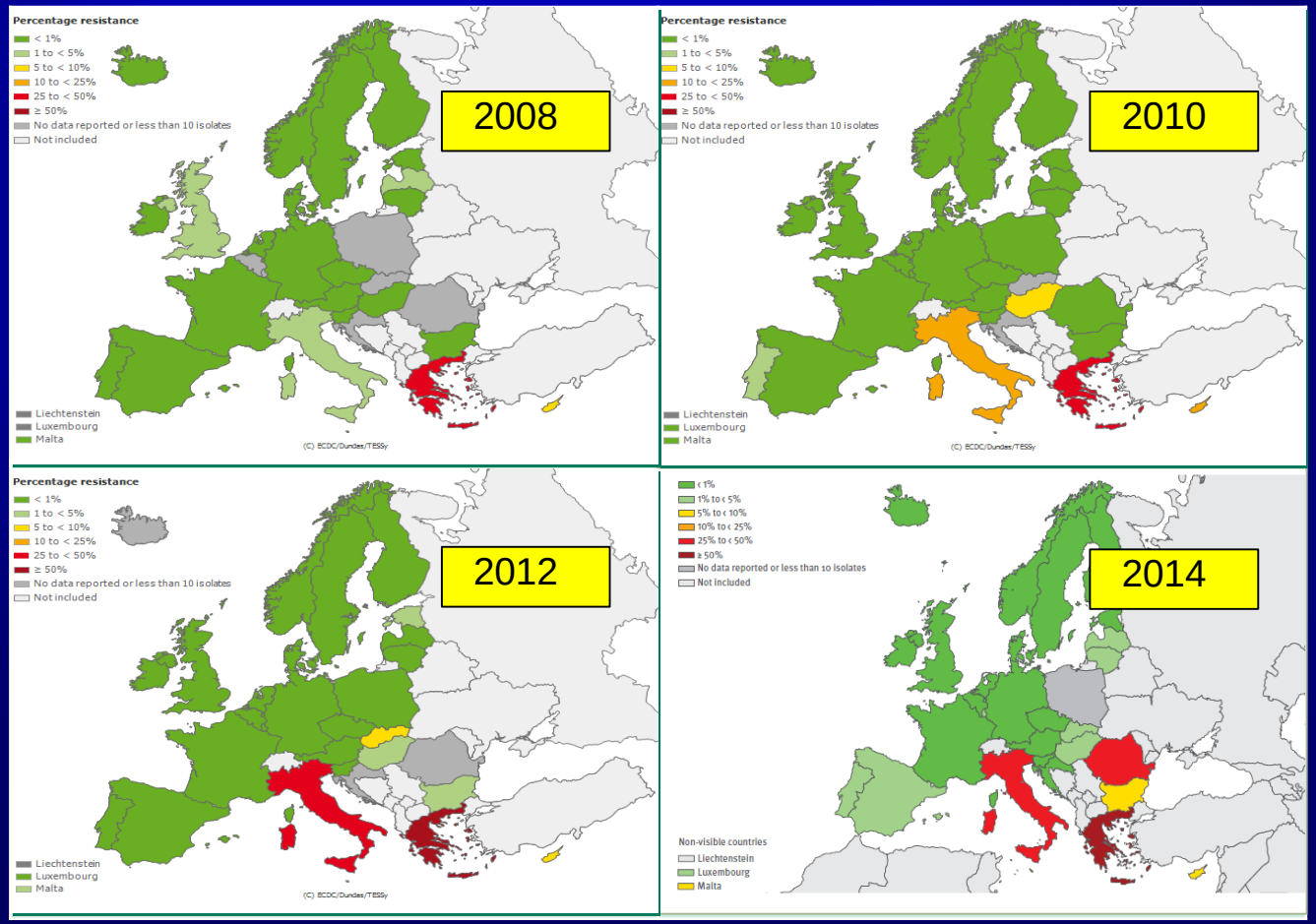
Source: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Stockholm: ECDC, 2017

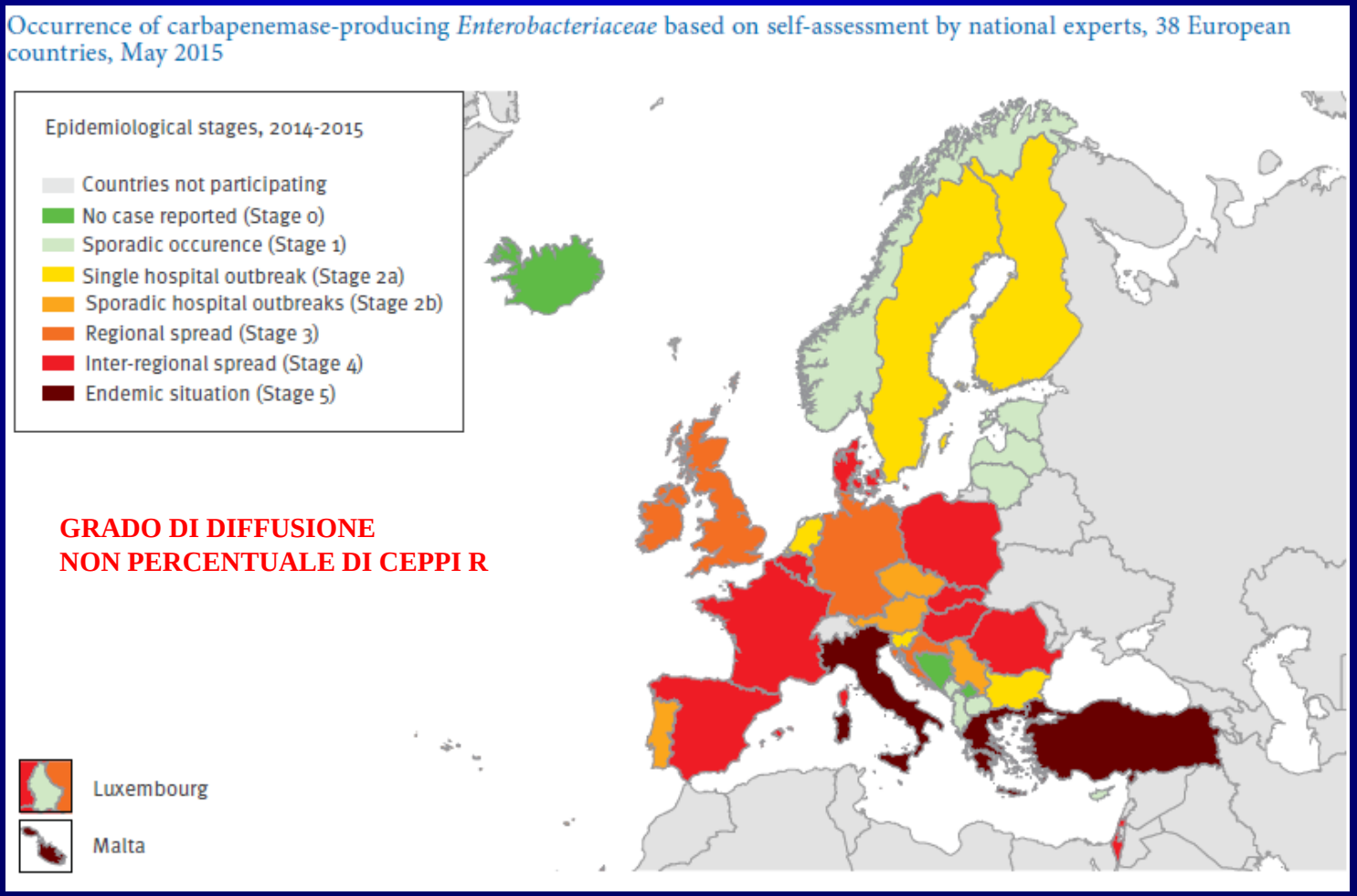
Klebsiella pneumoniae. Percentage (%) of invasive isolates with combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides, by country, EU/EEA countries, 2015



Source: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2015. Stockholm: ECDC, 2017

Proportion of CRKP in Europe





Albiger et al. Euro Surveill 2015

frontiers in Microbiology

REVIEW
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Global Dissemination of Carbapenemase-Producing *Klebsiella pneumoniae*: Epidemiology, Genetic Context, Treatment Options, and Detection Methods

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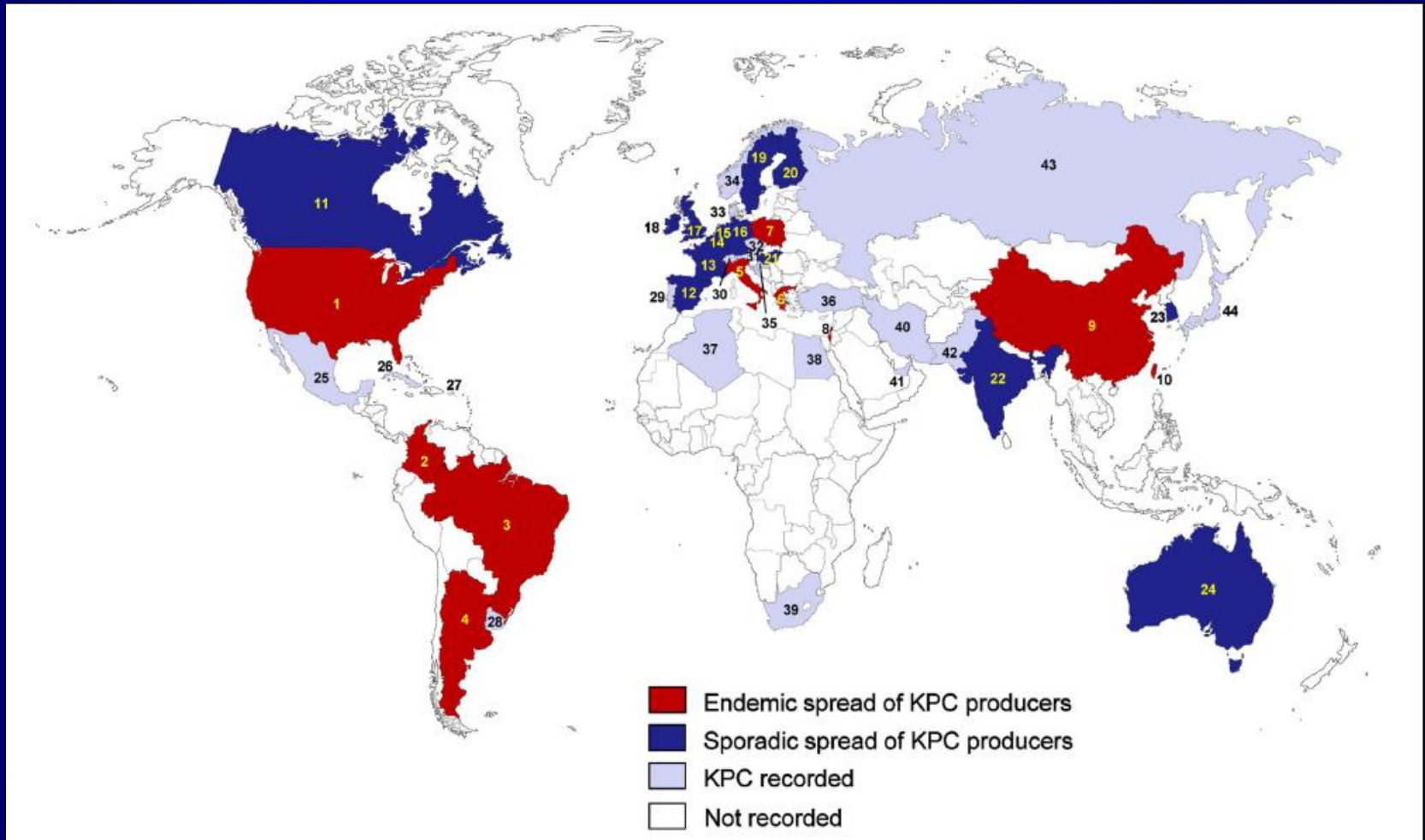
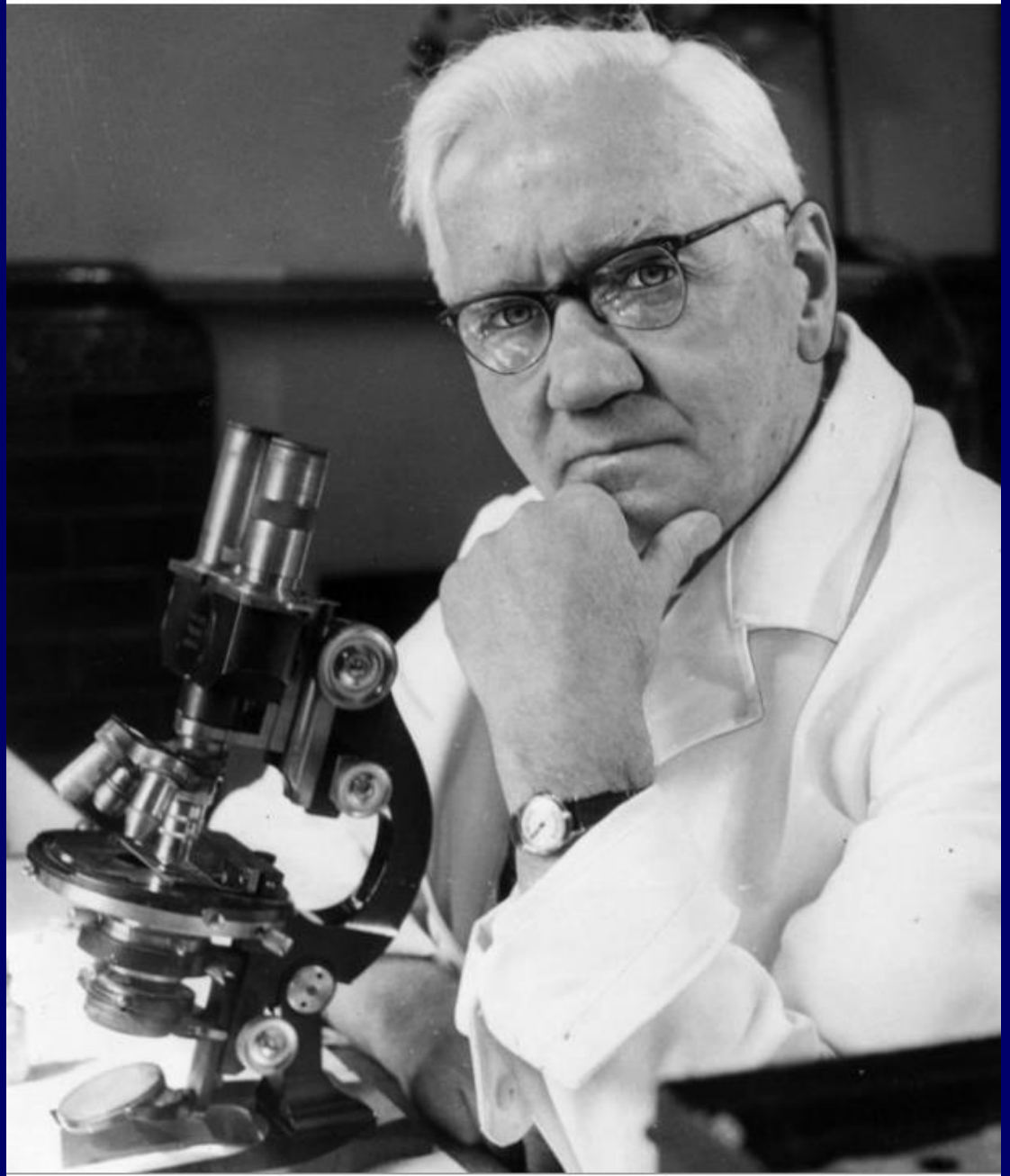


FIGURE 1 | Epidemiological features of KPC-producing *Klebsiella pneumoniae*. (1) USA; (2) Colombia; (3) Brazil; (4) Argentina; (5) Italy; (6) Greece; (7) Poland; (8) Israel; (9) China; (10) Taiwan; (11) Canada; (12) Spain; (13) France; (14) Belgium; (15) Netherlands; (16) Germany; (17) UK; (18) Ireland; (19) Sweden; (20) Finland; (21) Hungary; (22) India; (23) South Korea; (24) Australia; (25) Mexico; (26) Cuba; (27) Puerto Rico; (28) Uruguay; (29) Portugal; (30) Switzerland; (31) Austria; (32) Czech Republic; (33) Denmark; (34) Norway; (35) Croatia; (36) Turkey; (37) Algeria; (38) Egypt; (39) South Africa; (40) Iran; (41) United Arab Emirates; (42) Pakistan; (43) Russia; (44) Japan.



Warning from the father of antibiotics

ALEXANDER FLEMING

Penicillin

Nobel Lecture, December 11, 1945

But I would like to sound one note of warning. Penicillin is to all intents and purposes non-poisonous so there is no need to worry about giving an

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. Here is a hypothetical illustration. Mr. X. has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs. X gets pneumonia and is treated with penicillin. As the streptococci are now resistant to penicillin the treatment fails. Mrs. X dies. Who is primarily responsible for Mrs. X's death? Why Mr. X whose negligent use of penicillin changed the nature of the microbe. *Moral:* If you use penicillin, use enough.

Il concetto delle infezioni correlate alle pratiche assistenziali

- Fa
- Cl
- Tr
- Cl che (leucemie)
- Terapie intensive che tengono in vita malati un tempo senza speranza

Tutte procedure che si associano di per sé e indipendentemente dalle buone o cattive pratiche assistenziali ad un intrinseco aumentato rischio di infezione

A SUPPLEMENT BY MEDIAPLANET DISTRIBUTED WITHIN THE INDEPENDENT

NOVEMBER 2015 GLOBALHEALTHACTION.CO.UK

MEDIA PLANET

THE HISTORY

A world antib

E' **possibile curare le leucemie, fare i trapianti, guarire i tumori, fare alta chirurgia, usare le terapie immunosoppressive senza antibiotici?**

Pre-antibiotic age

In a world before antibiotics, as recently as the 1930s, people often died from infections like pneumonia or meningitis. Simple medical procedures and operations were risky due to the chance of infection.

Antibiotic age

Since the 1940s our antibiotics have allowed us to fight infections and save millions of lives. But they are becoming ineffective against many infections because we aren't using them properly.

tant'
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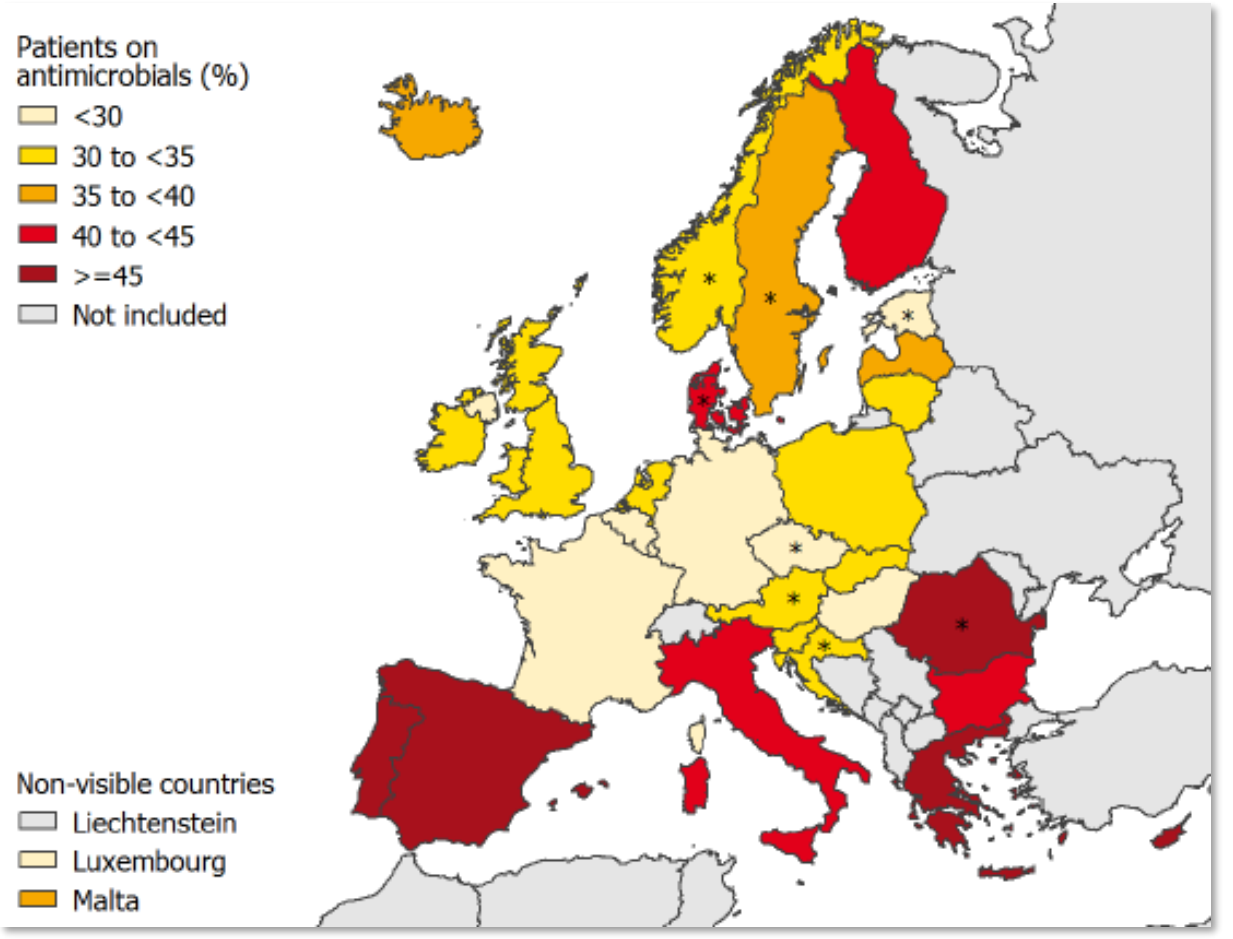
treatments will again become increasingly dangerous. Setting broken bones, basic operations, even chemotherapy all rely on access to antibiotics that work. Antibiotic resistance is one of the biggest threats facing us today but we have a chance to fight back. Find out how at:
antibioticguardian.com

Effetti indesiderati degli antibiotici

- Gli antibiotici sono gli unici farmaci il cui cattivo uso si riflette non solo sul paziente ma soprattutto sugli altri pazienti, su noi stessi e sulle generazioni future
- Induzione di resistenza
- Elezione di patogeni (*Clostridium difficile*)
- L'uso o il maluso degli antibiotici induce resistenza

Factors affecting different infection prevalence and rates of antimicrobial resistance across Europe



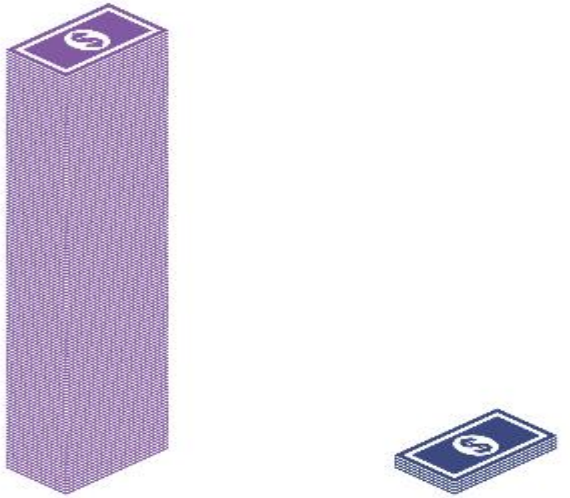
HAI-NET PPS 2011-12

Percentage of patients on antimicrobials
HAI PPS survey

ANTIMICROBIAL R&D IS NOT ATTRACTIVE TO VENTURE CAPITALISTS

Less than 5%

of venture capital investment in pharmaceutical R&D between 2003 and 2013 was for antimicrobial development.



Total venture capital investment

$38bn

Antimicrobial venture capital investment

$1.8bn

Source: Renwick MJ, Simpkin V, Mossialos E, International and European Initiatives Targeting Innovation in Antibiotic Drug Discovery and Development, The Need for a One Health – One Europe – One World Framework, Report for the 2016 Dutch Presidency of the European Union.

Review on Antimicrobial Resistance

Come contrastare le resistenze

- Antimicrobial stewardship: usare meglio i vecchi antibiotici e usarne meno
- Migliorare la diagnostica per fare terapie meno empiriche e più mirate
- Bloccare la trasmissione intraospedaliera
- Ricerca e Sviluppo su resistenze e nuovi antibiotici
- Diffondere la cultura delle infezioni e degli antibiotici

Attività

- IRCCS San Martino –IST
  - Nel 2012, allarme dei clinici infettivologi a seguito dell'evidenza clinica delle dimensioni del fenomeno KPC-Kp
  - Intervento DS e Infection Control: inizio screening e isolamento portatori e screening dei contatti (esempio Emilia-Romagna)
- Altri ospedali della Regione
  - Interventi simili vengono progressivamente iniziati in tutti gli altri ospedali della Regione per spinta degli infettivologi clinici

Metodologia del nostro intervento

- UOC Igiene: infection control
  - Corsi aggiornamento
  - Studi di prevalenza (Specializzandi in Igiene e in Malattie Infettive)
  - Interventi sul campo (Infection Control Nurses)
- US Microbiologia: sorveglianza
- Clinica Malattie Infettive e UOC Farmacia:
  - Antimicrobial Stewardship
    - Interventi persuasivi
    - Interventi restrittivi

Antimicrobial Stewardship

Fase persuasiva

- (Giugno 14-Dicembre 16)

- 20 pomeriggi di approfondimento mirati sulle varie specialità/discipline/Dipartimenti
- Approccio multidisciplinare (farmacisti, farmacologi, microbiologi, igienisti e infection control, allergologi, infettivologi)
- Circa 300 partecipanti (pochi), nonostante obbligatorietà sancita dalla DS
- Discussione di scelte, indicazioni, stopping rules

Fase semi-restrittiva

- Basato sul sistema computerizzato di personalizzazione della prescrizione del farmaco in ospedale (SOFIA® e MARIO®)
- Gli antibiotici controllati non sono disponibili in reparto (non dovrebbero)
- Nulla osta infettivologico motivato nel percorso prescrittivo computerizzato per alcuni antibiotici cruciali come salva-vita, di alto costo o forti induttori di resistenze
- All'atto della prescrizione è prevista la fornitura del farmaco per 48 ore massimo
- Entro tale tempo l'infettivologo valuta se concedere o meno il nulla osta per la prosecuzione della terapia antibiotica e per quanto tempo (rivalutazione)
- Se il nulla osta è negato, la fornitura di farmaco da parte della farmacia viene automaticamente interrotta
- Contatto con il reparto per spiegare l'eventuale stop e/o terapia alternativa.

Antibiotici sottoposti a restrizione

- meropenem,
- ertapenem,
- vancomicina,
- teicoplanina,
- daptomicina,
- tigeciclina
- ceftolozano-tazobactam
- dalbavancina
- colistina,
- linezolid,
- echinocandine,
- AmB lipidiche
- voriconazolo
- posaconazolo
- isavuconazolo

Risultati preliminari

- Periodo pre-intervento: maggio 2014-Aprile 2015
- Periodo post-intervento: maggio 2015-Aprile 2016

- INTERVENTI INFETTIVOLOGO TRAMITE SOFIA®
- Numero interventi: 6689
- Approvazioni/variazioni lunghezza terapia: 6217 (93%)
- Sospensioni entro 48/72 h: 86 (1%)
- Terapie valutate oltre 48/72 h: 386 (6%)

- Degenza nei reparti inclusi nello studio:
- Giornate di degenza: 306345 (pre) → 305866 (post)

Antibatterici

- DDD (N°/1000 patient/days):
  - 168700 (550.7) → 163716 (535.3)
  - Δ = - 4984

Antifungini

- DDD: (N°/1000 patient/days):
  - 8244 (26.9) → 8606 (28.1)
  - Δ = + 362

Antibatterici sottoposti a restrizione

- DDD (N°/1000 patient/days):
  - 28442 (92.8) → 26902 (88.0)
  - Δ = - 1540

Antibatterici non sottoposti a restrizione

- DDD (N°/1000 patient/days):
  - 140259 (457.8) → 136815 (447.3)
  - Δ = - 3444

Grazie per l’attenzione