Infection Prevention and Control "Building Capabilities"

2015

A TRADITION OF INDEPENDENT THINKING

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Resistance – New Challenges
Multidrug Resistant Organisms: Acute and Community Settings

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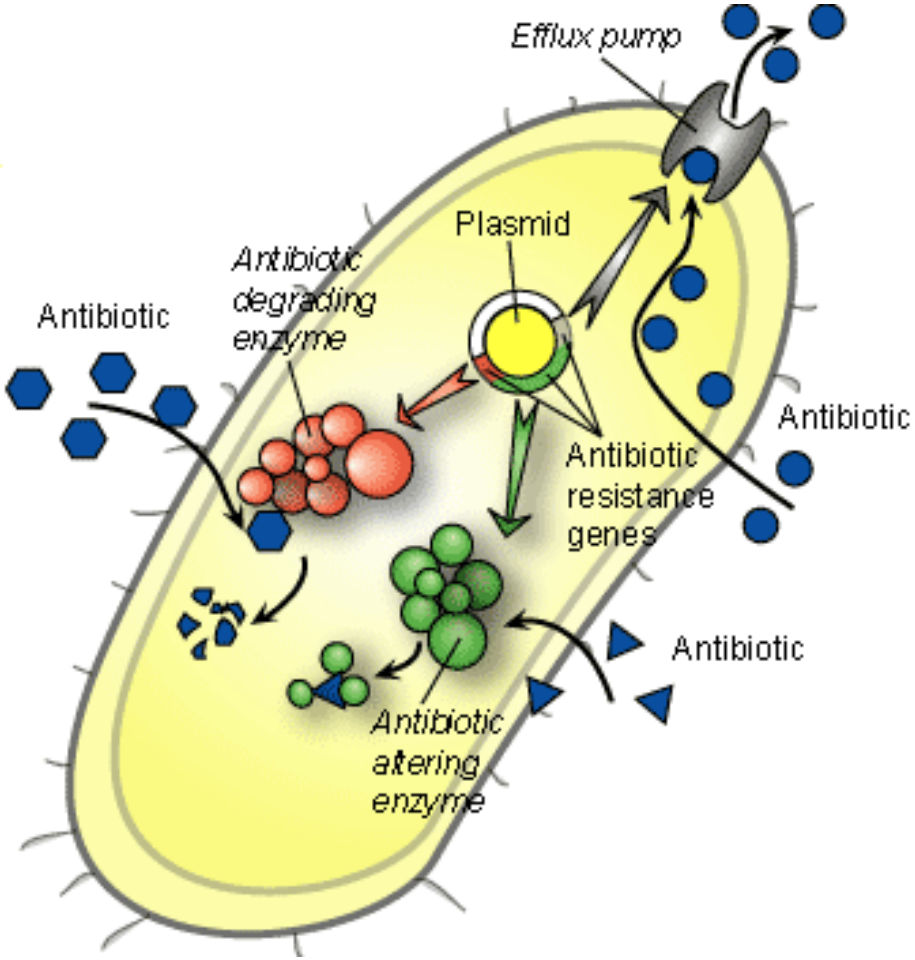
Talk outline

- What is a multidrug resistant organism (MDRO)?
- Why do we need to be worried about them?
- What rates of MDRO are present- Ireland and globally?
- What can be done to prevent their emergence and spread?

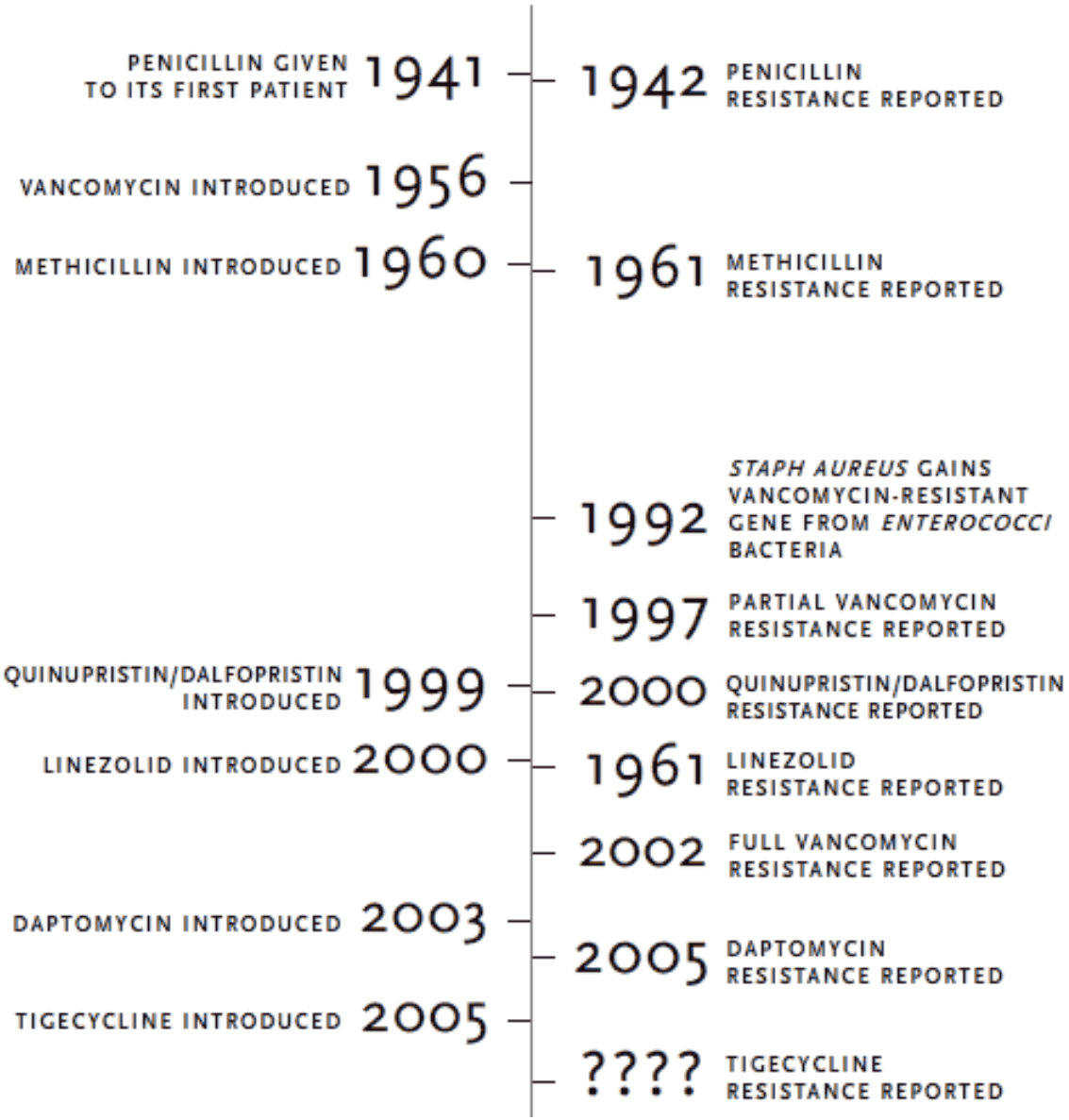
Multi-drug resistant organisms

- **MRSA**
- **VRE (Vancomycin resistant Enterococci)**
- **Linezolid resistant VRE**
- **Multi-resistant Gram negative bacteria (ESBLs, MDRKP, CRE)**
- **Penicillin resistant *Streptococcus pneumoniae***
- **Multi and extensively drug resistant TB**
- **Multi-drug resistant gonorrhoea…..**

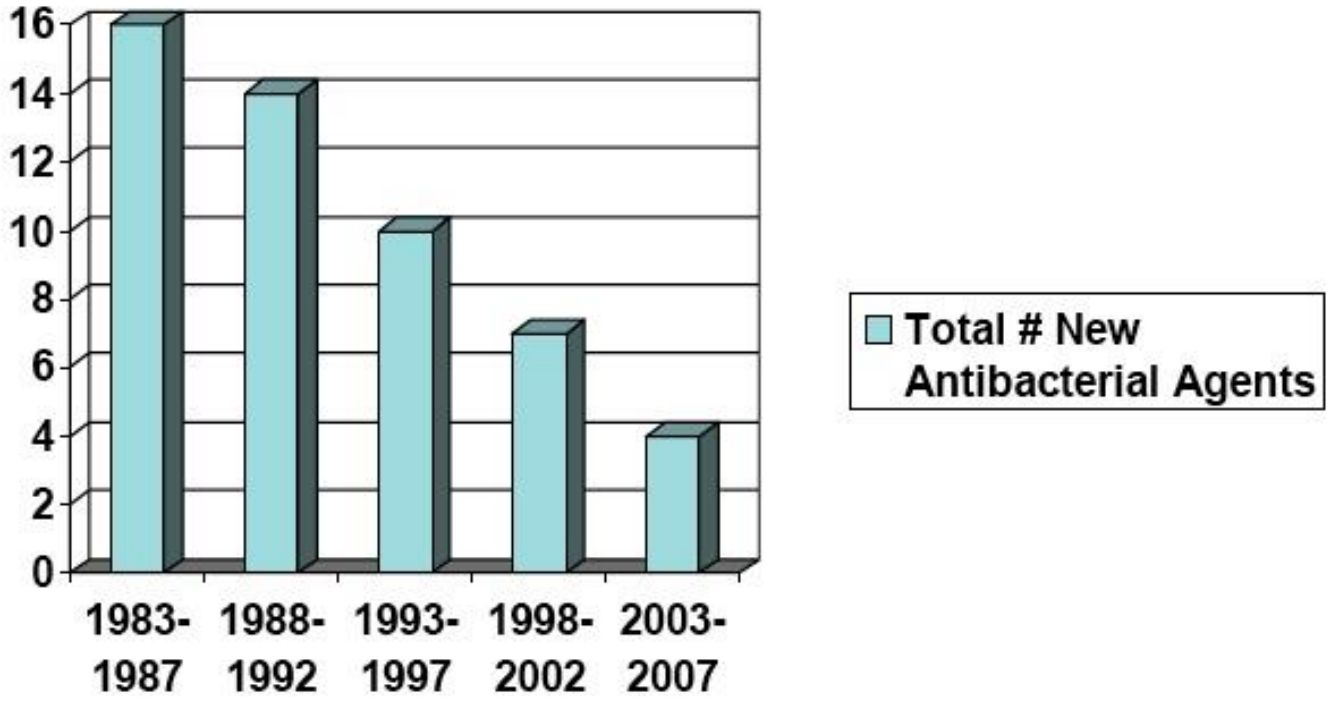
How do bacteria become resistant to antibiotics?



Why are MDROs an issue?



Antibacterial agents approved, 1983-2007



Spellberg, et. al., *CID* May 1 2004, Modified

March 11 2013

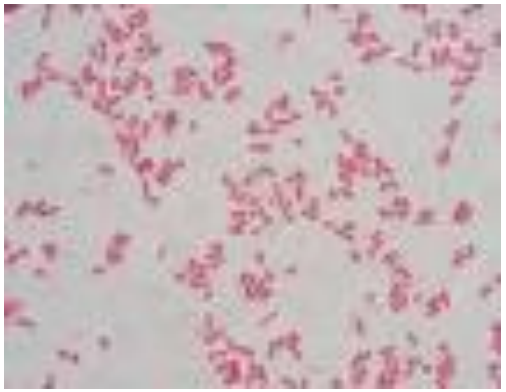
The chief medical officer, Dame Sally Davies, warns of a major increase in the number of bugs resistant to antibiotics. In a report published on Monday she says antibiotic-resistant bacteria with the potential to cause untreatable infections pose 'a catastrophic threat' to the population ranked alongside terrorism on a list of threats to the nation

MDROs discussed in this talk

- **ESBLs, MDRKPs, CRE/CPE**
- **VRE**

Enterobacteriaceae

- ***Enterobacteriaceae* family: *E coli*, *Klebsiella* spp, *Enterobacter* spp.**
- **Normal gut flora**
- **Common cause UTI in community**
- **Hospital acquired infections: UTI, pneumonia, intra-abdominal infections, wound infections, bloodstream infections**



What are ESBLs (extended spectrum beta-lactamases) ?

- **ESBLs are enzymes which confer resistance to beta-lactam antibiotics- ampicillin/amoxicillin, co-amoxiclav, all cephalosporins**

- **Produced by Gram negative bacteria eg. *E. coli, Klebsiella* spp., *Proteus* spp.**

- **Show the ability of Gram negative bacteria to develop new antibiotic resistance mechanisms in the face of the introduction of new antimicrobial agents**

Why do I need to know about ESBLs?

- **Incidence of resistance of Gram negative bacteria increasing**
- **Range of antibiotics available to treat these infections decreasing**
- **Infection caused by ESBL= more likely to have increased mortality, longer hospital stays and greater hospital costs**

Where do ESBLs come from?

- **Frequently plasmid encoded**
- **Plasmid= small DNA fragment that is capable of self replication and can be passed from one bacteria to another**
- **Plasmids containing enzymes for ESBL frequently carry genes encoding resistance to other antibiotics eg. aminoglycosides, quinolones**

Where are ESBLs found?

- **May live harmlessly in gut (similar to non-ESBL producing *E. coli*) but cause problems when enter urinary tract, bloodstream *etc*.**

What kind of infections do ESBLs cause?

- **Same range of infections as "regular" *E.coli, Klebsiella* spp. *Proteus* spp.**
- **Urinary tract infections**
- **Intra-abdominal infections**
- **Healthcare associated pneumonia**
- **Catheter related bloodstream infections**
- **Skin/ soft tissue (more unusual, these organisms tend to colonize rather than infect skin)**

Who is at risk of infections caused by ESBL-producing bacteria?

- Gut colonization
- Length of ICU stay
- Presence of central venous or arterial catheters
- Emergency abdominal surgery
- Presence of a gastrostomy or jejunostomy tube
-
- Low birth weight
- Prior administration of any antibiotic
- Prior residence in a long-term care facility (eg, nursing home)
- Severity of illness
- Presence of a urinary catheter
- Ventilatory assistance
- Undergoing haemodialysis

Can patients be cleared of ESBL carriage?

- Likely that patients will carry the ESBL producing organism for some time
- Persists in gut (will become part of normal flora)
- Sometimes strain lost naturally
- Use of antibiotics will not help

What do I tell patients/relatives?

- **Depends on whether colonized or infected**
- **Explain that patient has an infection which is resistant to many commonly used antibiotics**
- **Spread can be prevented through correct hand hygiene procedures**

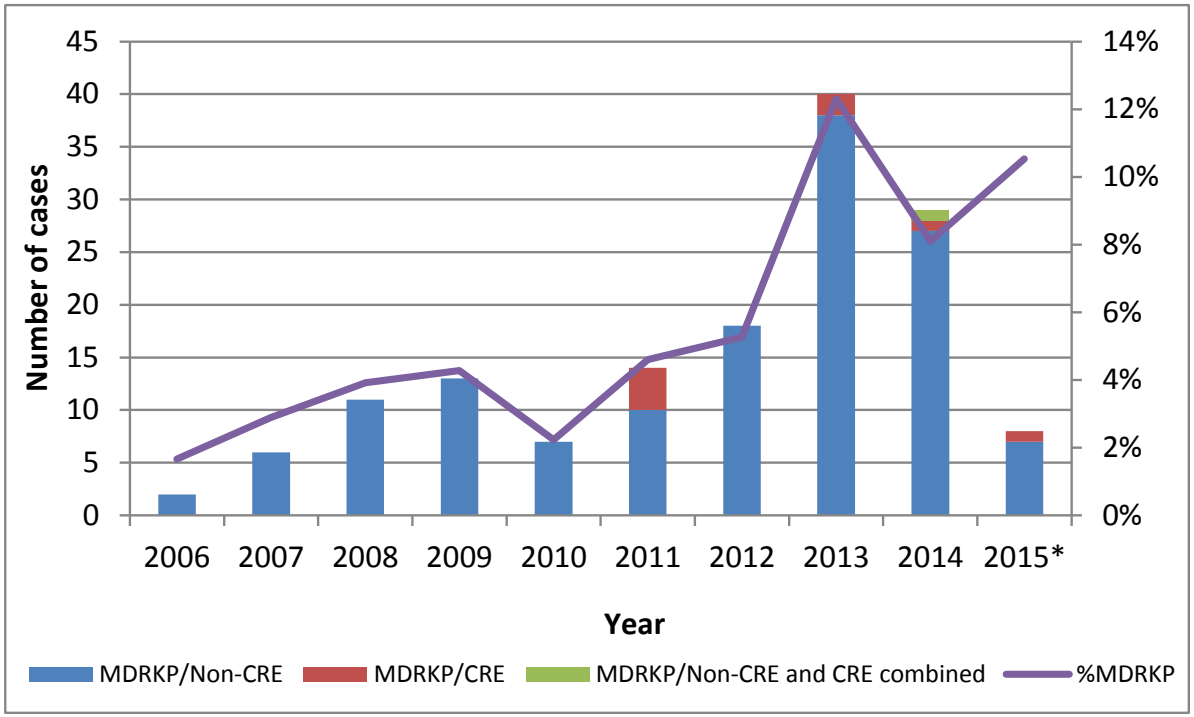
Treatment Options

- **Trimethoprim and nitrofurantion**
- **Ciprofloxacin**
- **Aminoglycosides**
- **Fosfomycin**
- **Pivmecillinam**
- **Cefepime**
- **Temocillin**
- **??piperacillin/tazobactam**
- **Carbapenems (ertapenem, meropenem)**

What is MDRKP?

- **MDRKP= Multi-drug resistant Klebsiella pneumoniae**
- ***Klebsiella pneumonia* that are ESBL positive and are resistant to ciprofloxacin and gentamicin**
- **Notifiable to HPSC**

Invasive MDRKP, including MDRKP/Non-CRE and MDRKP/CRE: distribution of cases by year, 2006-2015: HPSC most recent data



Carbapenems

- **Carbapenems are <u>invaluable</u> for the treatment of infection due to multi-resistant Gram negative bacteria**

- **Meropenem, ertapenem, doripenem, imipenem**

CRE

- ***Enterobacteriaceae*** **that have acquired enzymes that confer resistance to the carbapenem group of antibiotics**
- **Broadly resistant to beta lactam antibiotics**
- **These bacteria often have acquired mechanisms that confer resistance to other clinically important antibiotics eg. aminoglycosides, fluoroquinolones**
- **Few or no treatment options exist**

Emergence of CRE

- **Global spread of successful clones that follow patients**
- **First transferrable resistance described in Japan in 1990**
- **North Carolina in 1996- East Coast USA- spread throughout USA-Endemic in New York City**
- **Greek outbreaks in 2003…ongoing**
- **Importation from Indian subcontinent from 2008**
- **70% mortality in patients with bloodstream infection**

Treatment Options for CRE

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BRIEF REPORT

Infection with Panresistant *Klebsiella pneumoniae*: A Report of 2 Cases and a Brief Review of the Literature

Azza Elemam, Joseph Rahimian, and William Mandell
Section of Infectious Diseases, Saint Vincent's Hospital, New York, New York

Infections caused by carbapenemase-producing *Klebsiella pneumoniae* have been reported with increasing frequency, thereby limiting the choice of effective antimicrobial agents available to clinicians. This has prompted the increased use of polymyxins and tigecycline, but resistance to these agents is already emerging. We report 2 cases of infection with panresistant *K. pneumoniae*.

for 2 days. A urinalysis revealed nitrites and a white blood cell count >100 cells per high-power field. Her examination was notable for a temperature of 37.4°C and suprapubic tenderness. A urine culture showed >100,000 colony-forming units (cfu) per mL of a highly resistant, KPC-producing *K. pneumoniae* strain. The minimum inhibitory concentration (MIC) was 4 μg/mL for tigecycline and 96 μg/mL for polymyxin B. The patient's catheter was removed, and she began treatment with tigecycline and rifampin. She developed a rash, and the rifampin was discontinued. Her urinalysis results remained unchanged, and her urine culture again showed the presence of >100,000 cfu/mL of *K. pneumoniae*, which now had an MIC >8 μg/mL for tigecycline. Tigecycline was discontinued after 10 days of treatment, and the patient was discharged to home with persistent dysuria. She subsequently had spontaneous resolution of symptoms, although the last available urine culture

Journal of Antimicrobial Chemotherapy (2009) **64**, *Suppl. 1*, i29–i36
doi:10.1093/jac/dkp255

JAC

Has the era of untreatable infections arrived?

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Antibiotic resistance is a major public health concern, with fears expressed that we shortly will run out of antibiotics. In reality, the picture is more mixed, improving against some pathogens but worsening against others. Against methicillin-resistant *Staphylococcus aureus* (MRSA)—the highest profile pathogen—the range of treatment options is expanding, with daptomycin, linezolid and tigecycline all launched, and telavancin, ceftobiprole, ceftaroline and dalbavancin anticipated. There is a greater problem with enterococci, especially if, as in endocarditis, bactericidal activity is needed and the isolate has high-level aminoglycoside resistance; nevertheless, daptomycin, telavancin and razupenem all offer cidal potential. Against Enterobacteriaceae, the rapid and disturbing spread of extended-spectrum β-lactamases, AmpC enzymes and quinolone resistance is forcing increased reliance on carbapenems, with resistance to these slowly accumulating via the spread of metallo-, KPC and OXA-48 β-lactamases. Future options overcoming some of these mechanisms include various novel β-lactamase-inhibitor combinations, but none of these overcomes all the carbapenemase types now circulating. Multiresistance that includes carbapenems is much commoner in non-fermenters than in the Enterobacteriaceae, depending mostly on OXA carbapenemases in *Acinetobacter baumannii* and on combinations of chromosomal mutation in *Pseudomonas aeruginosa*. No agent in advanced development has much to offer here, though there is interest in modified, less-toxic, polymyxin derivatives and in the siderophore monobactam BAL30072, which has impressive activity against *A. baumannii* and members of the *Burkholderia cepacia* complex. A final and surprising problem is *Neisseria gonorrhoeae*, where each good oral agent has been eroded in turn and where there is now little in reserve behind the oral oxyimino cephalosporins, to which low-level resistance is emerging.

Keywords: β-lactamases, MRSA, *Escherichia coli*, *Acinetobacter baumannii*, *Neisseria gonorrhoeae*

BAD BUGS, NO DRUGS

As Antibiotic Discovery Stagnates ...
A Public Health Crisis Brews

IDSA
Infectious Diseases Society of America

July 2004

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VRE- Vancomycin Resistant Enterococci

- **Normal flora GIT**
- **Intrinsic resistance to many antibiotics (e.g. cephalosporins, quinolones)**
- **Very hardy and able to survive in the environment**

What kinds of infection are caused by VRE?

- Urinary tract infections
- Intra-abdominal infections
- Bloodstream infections
- Infective endocarditis
- NB: VRE does not cause diarrhoea

Risk factors for VRE

- Immunosuppression
- Haematological malignancies
- Organ transplantation
- Length of ICU stay
- Residence in a long-term care facility
- Proximity to another colonized or infected patient
- Hospitalization in a unit with a high prevalence of VRE
- Serious co-morbid conditions such as diabetes, renal failure, and high Acute Physiology and Chronic Health Evaluation (APACHE) II scores
- Prior exposure to antimicrobials including vancomycin, aminoglycosides, cephalosporins, clindamycin, metronidazole, and carbapenems

VRE- where did it come from?

- First encountered in clinical isolates in England and France in 1986, followed the next year by isolation of VRE in the United States
- In Europe, the rise of VRE was thought to arise from the use of a glycopeptide antibiotic avoparcin as a growth promoter in livestock
- In the US the predominance of VRE was in the hospital setting, believed to be due to the increasing use of the glycopeptide antibiotic vancomycin to treat MRSA

VRE resistance mechanisms spreading to MRSA….

- **In 2002 the threat of VRE colonization and infections increased when the first patient case of VRE transmitting resistance genes to methicillin-resistant *Staphylococcus aureus* (MRSA) to form a vancomycin-resistant *Staphylococcus aureus* (VRSA) isolate was reported**

VRE- Vancomycin Resistant Enterococci

- GIT colonization may persist for a very long time
- Decolonization strategies not effective
- Antibiotics will not decolonize

Treatment options for VRE

- **Nitrofurantion**
- **Fosfomycin**
- **Linezolid**
- **Tedizolid**
- **Daptomycin**
- **Tigecycline**

- **Outbreaks of Linezolid resistant VRE recently reported in Irish hospitals….**

Environmental reservoirs a problem with VRE

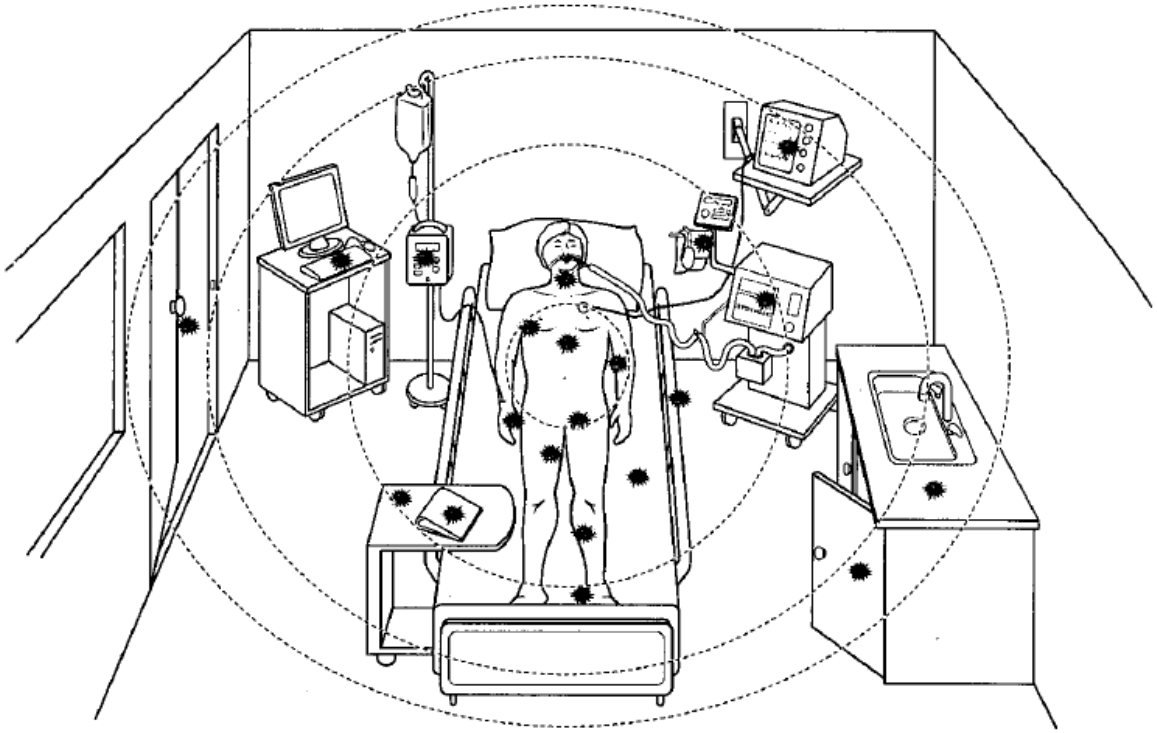


Figure 1. Patient and environmental sources of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE) in an intensive care unit room. *Expanding circles* highlight the patient as the major reservoir and epicenter for MRSA and VRE. *Splotches* represent locations where MRSA and VRE are commonly found.

How can infections with ESBLs, MDRKP, CRE and VRE be spread?

- **Most important mode of transmission via transient carriage on the hands of healthcare workers**
- **Environmental cleaning (especially VRE)**
- **Prudent use of antibiotics to prevent emergence of new strains (antimicrobial stewardship)**

What levels of antimicrobial resistance are present in Ireland?

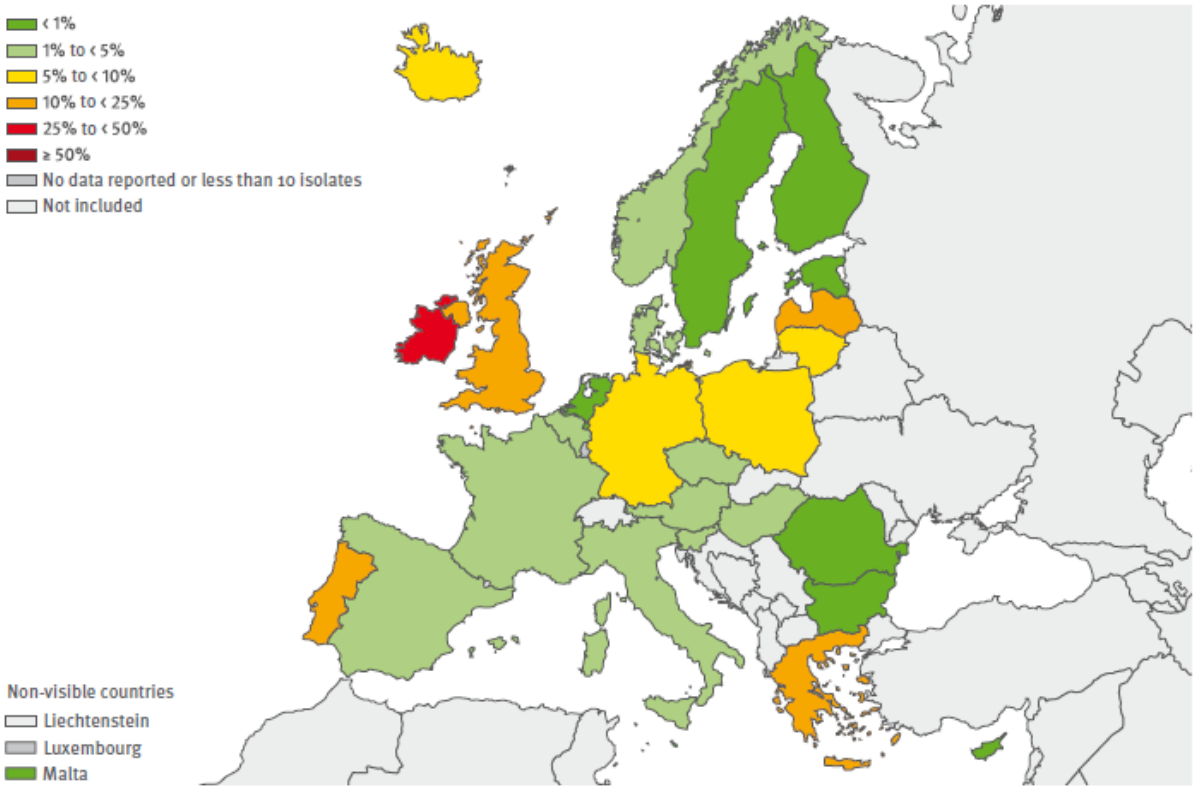
How do we compare to other countries?

EARS-net

- **EU Surveillance network for antimicrobial resistance**
- **Key pathogens**
- **Began 1999**
- **Excellent participation by Irish laboratories**

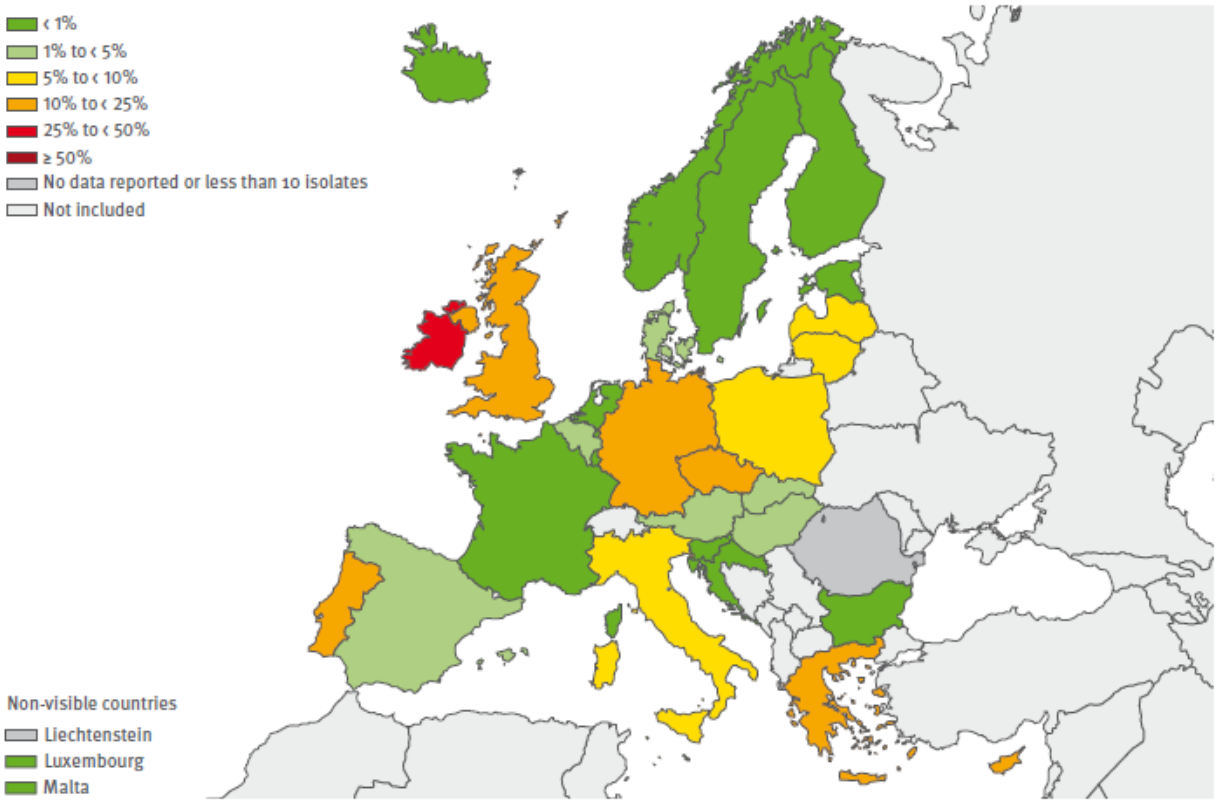
VRE 2010

Figure 5.12: *Enterococcus faecium*: proportion of invasive isolates resistant to vancomycin in 2010



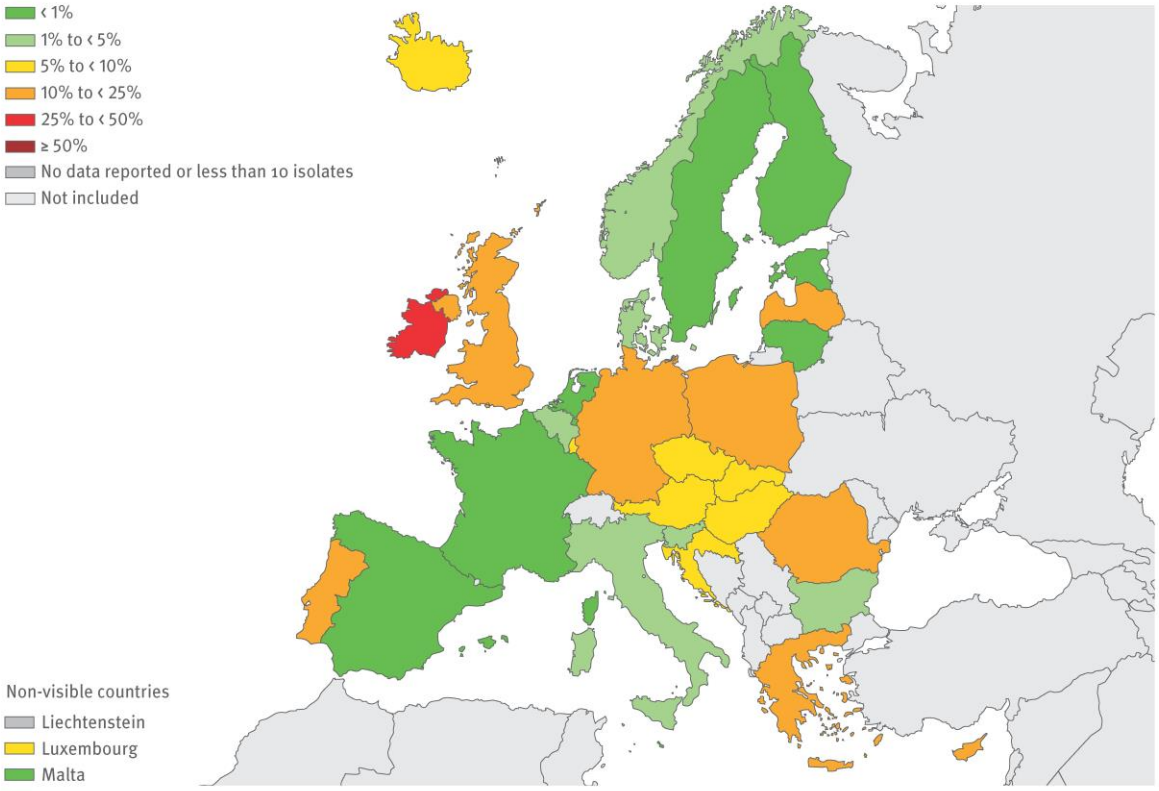
VRE 2012

Figure 3.46. *Enterococcus faecium*. Percentage (%) of invasive isolates resistant to vancomycin, by country, EU/EEA countries, 2012



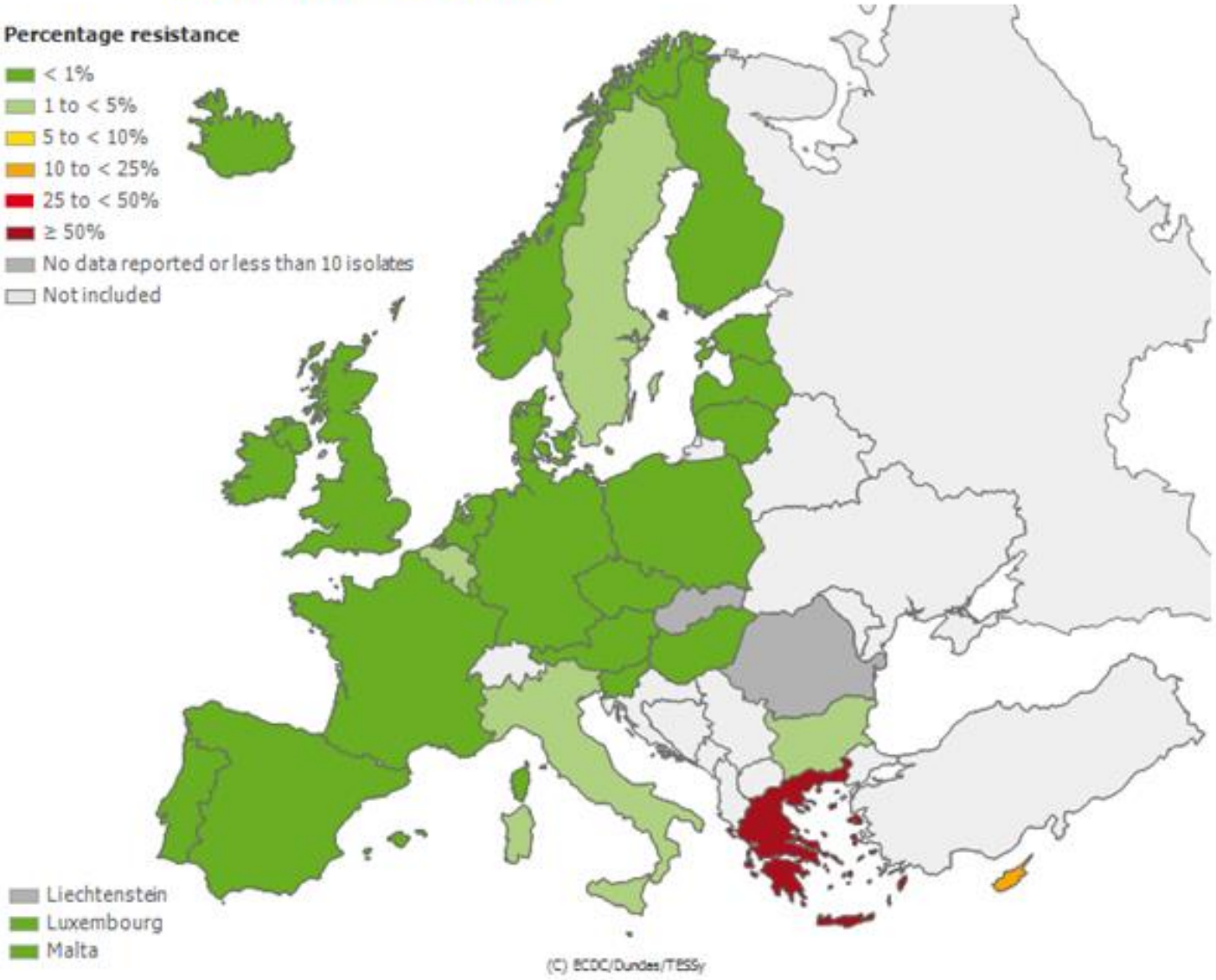
VRE 2013

Enterococcus faecium. Percentage (%) of invasive isolates resistant to vancomycin, by country, EU/EEA countries, 2013



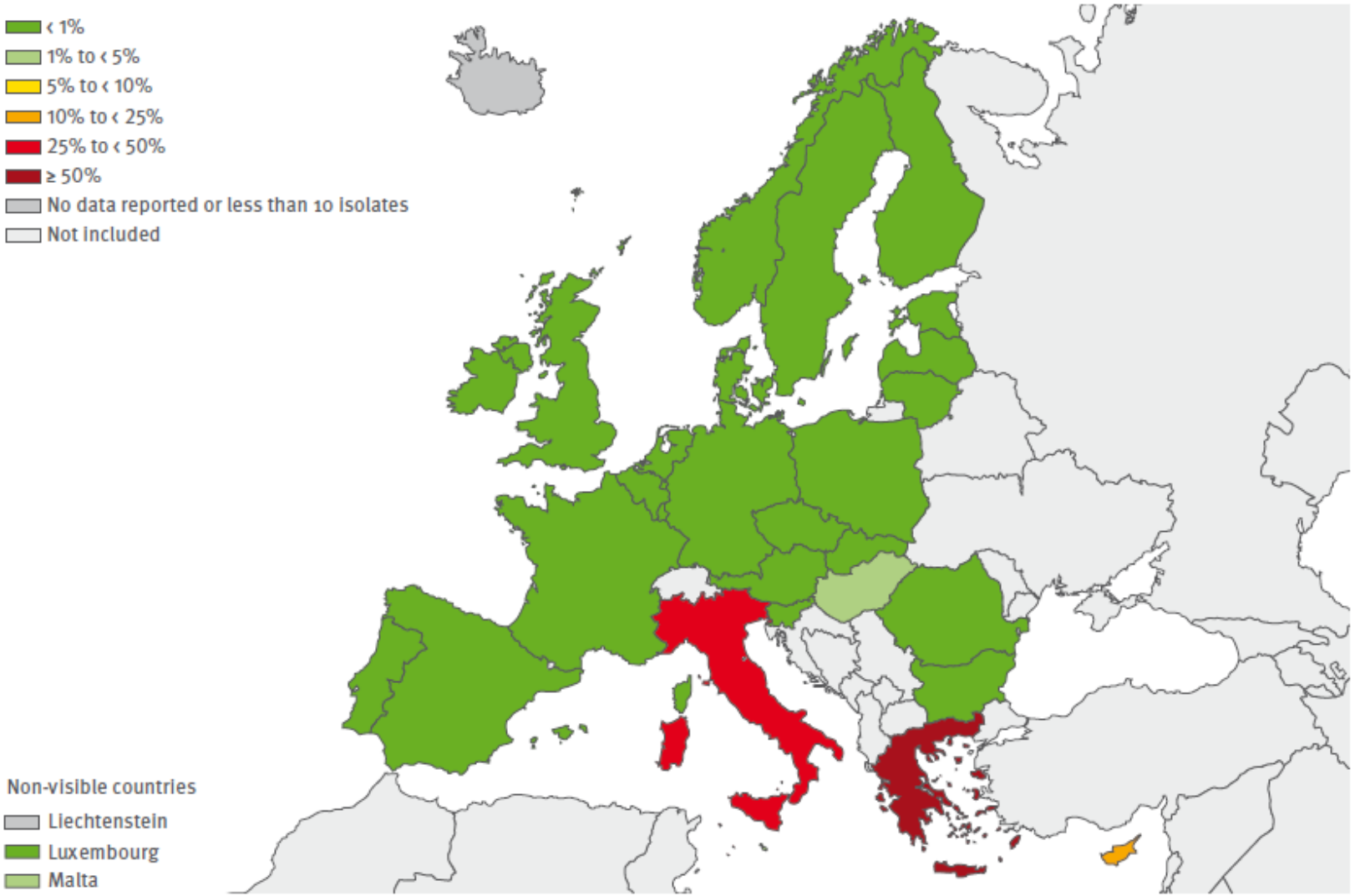
Source: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2013. Stockholm: ECDC, 2014

Proportion of Carbapenems (R+I) resistant Klebsiella pneumoniae isolates in participating countries in 2009



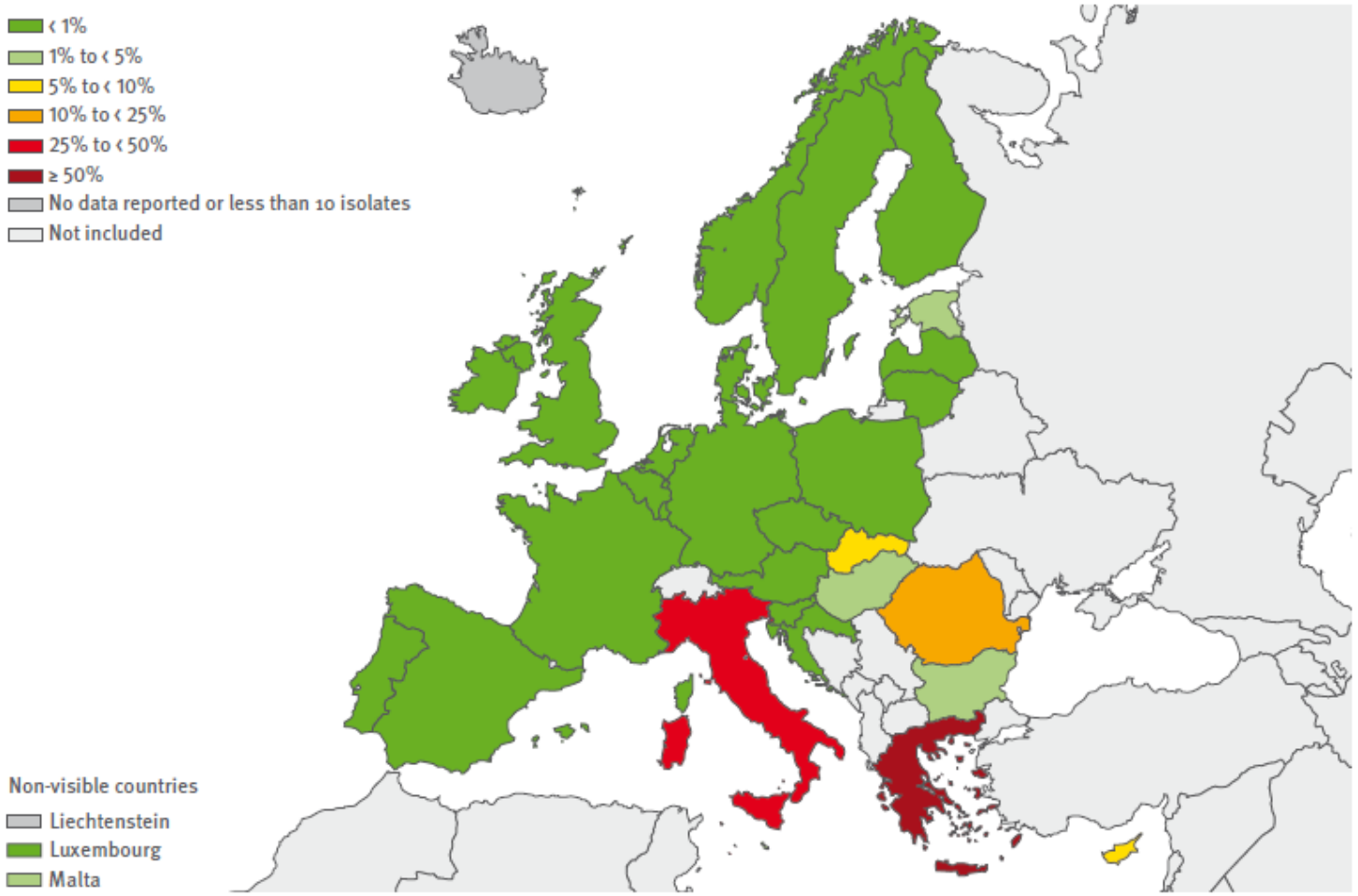
Carbapenem resistant *Klebsiella pneumoniae* 2011

Figure 4.12: *Klebsiella pneumoniae*: percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2011



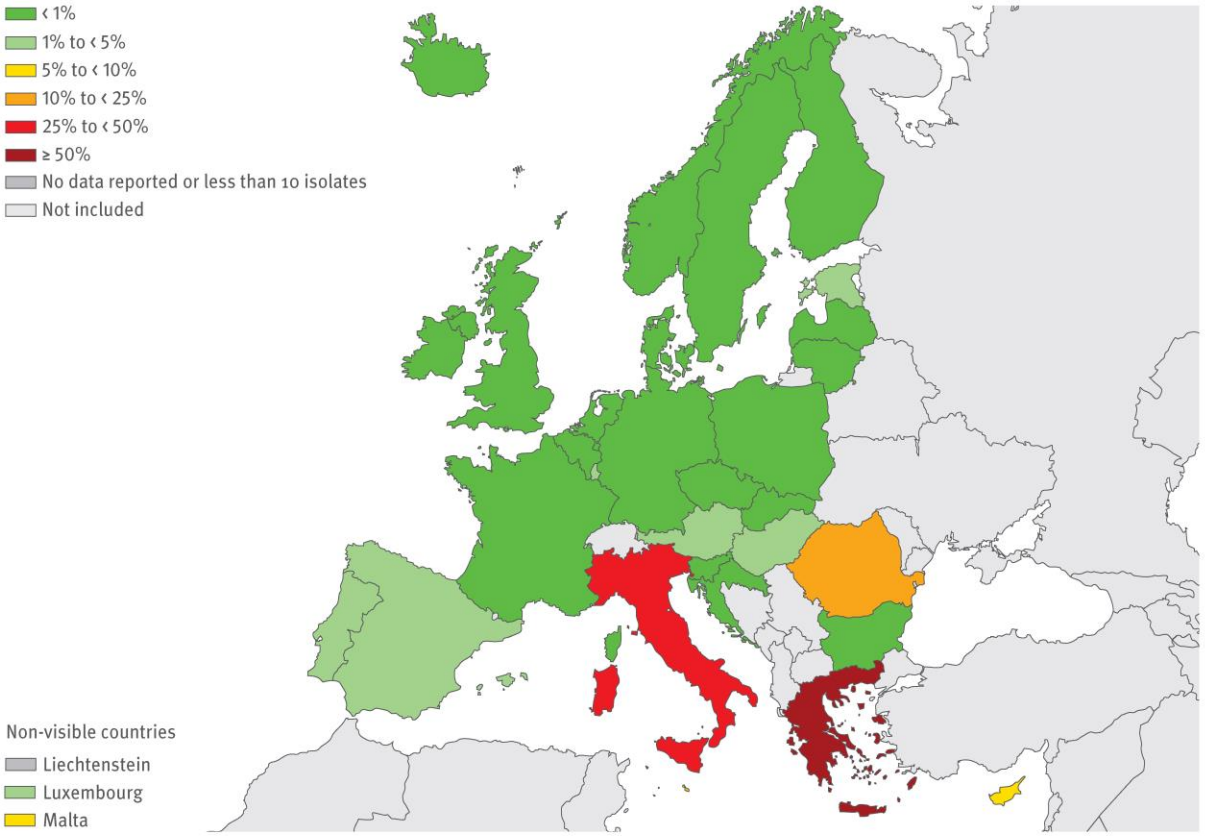
2012…

Figure 3.13. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2012



CRE 2013

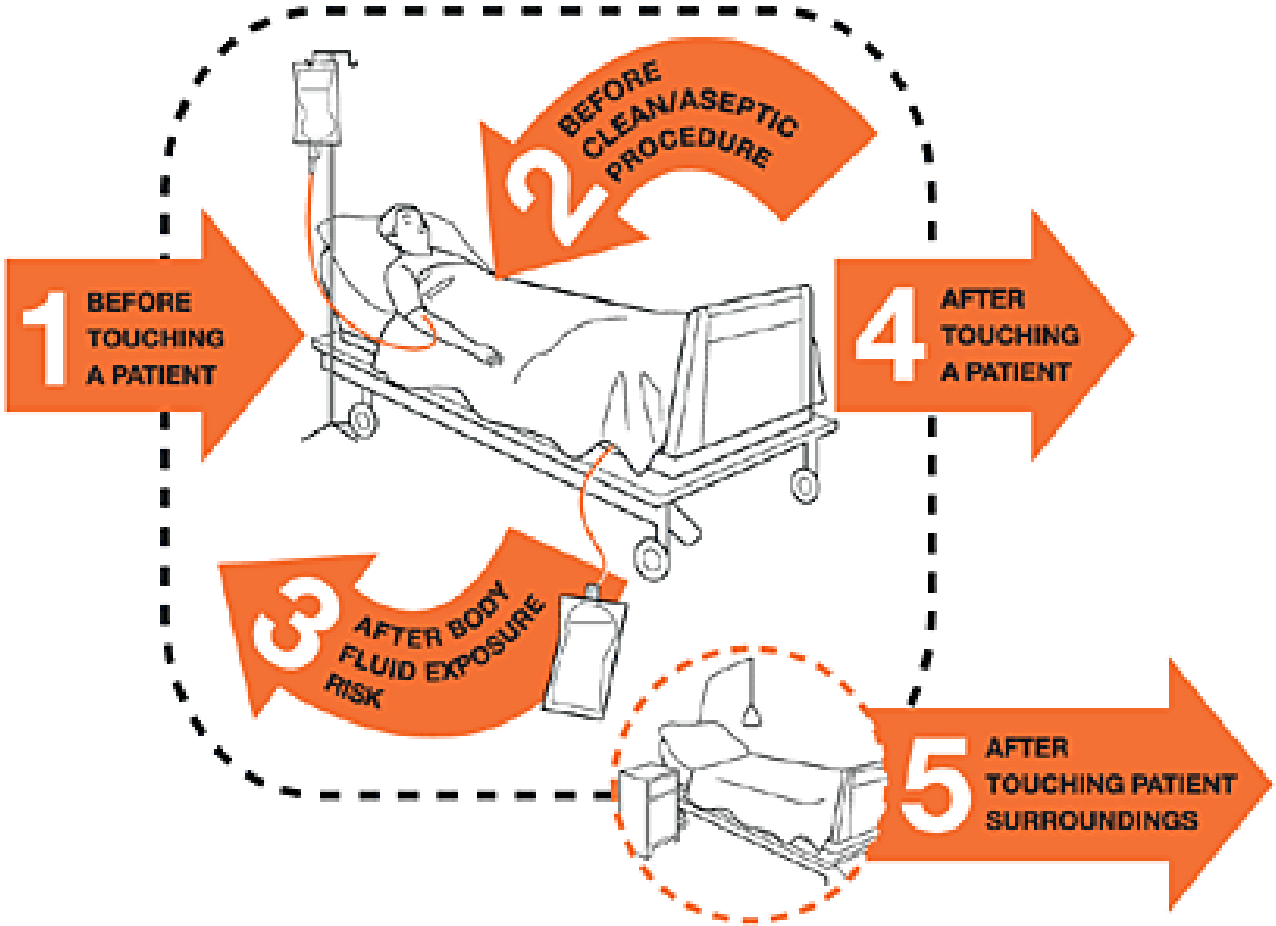
Klebsiella pneumoniae. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2013

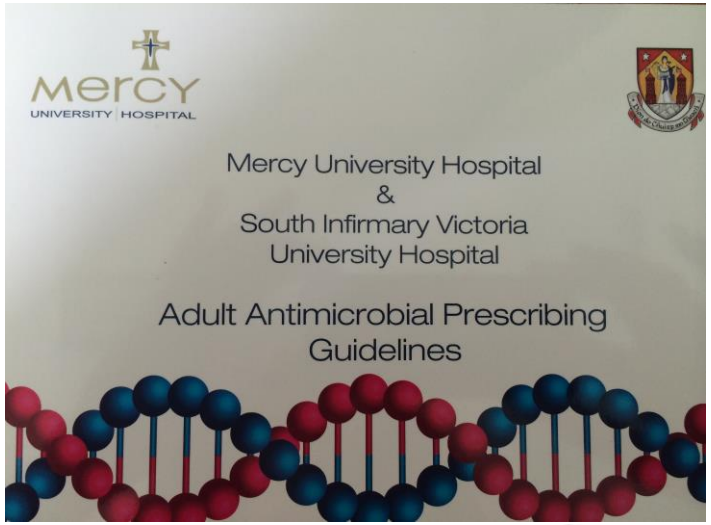


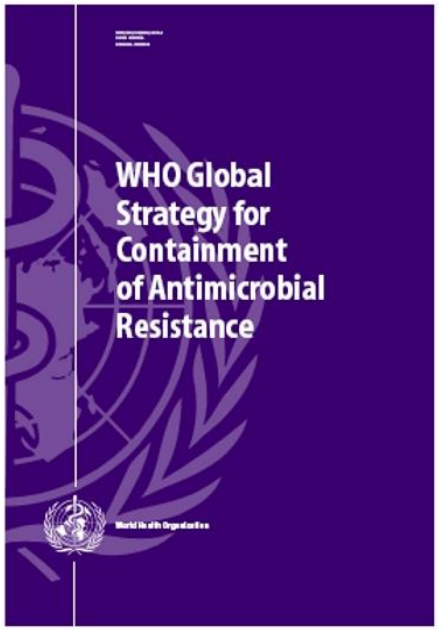
Source: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2013. Stockholm: ECDC, 2014

What can be done?

- **Awareness and communication**
- **Antimicrobial stewardship**
- **Infection prevention and control**







EUROPEAN ANTIBIOTIC AWARENESS DAY

A European Health Initiative

Department of Health
Advisory Committee on Antimicrobial Resistance
and Healthcare Associated Infection (ARHAI)

Get better without using antibiotics

This leaflet explains the need to get the right treatment for common illnesses such as colds and coughs without encouraging antibiotic resistance.

ANTIMICROBIAL STEWARDSHIP:

"START SMART - THEN FOCUS"

University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

An Ongoing National Intervention to Contain the Spread of Carbapenem-Resistant Enterobacteriaceae

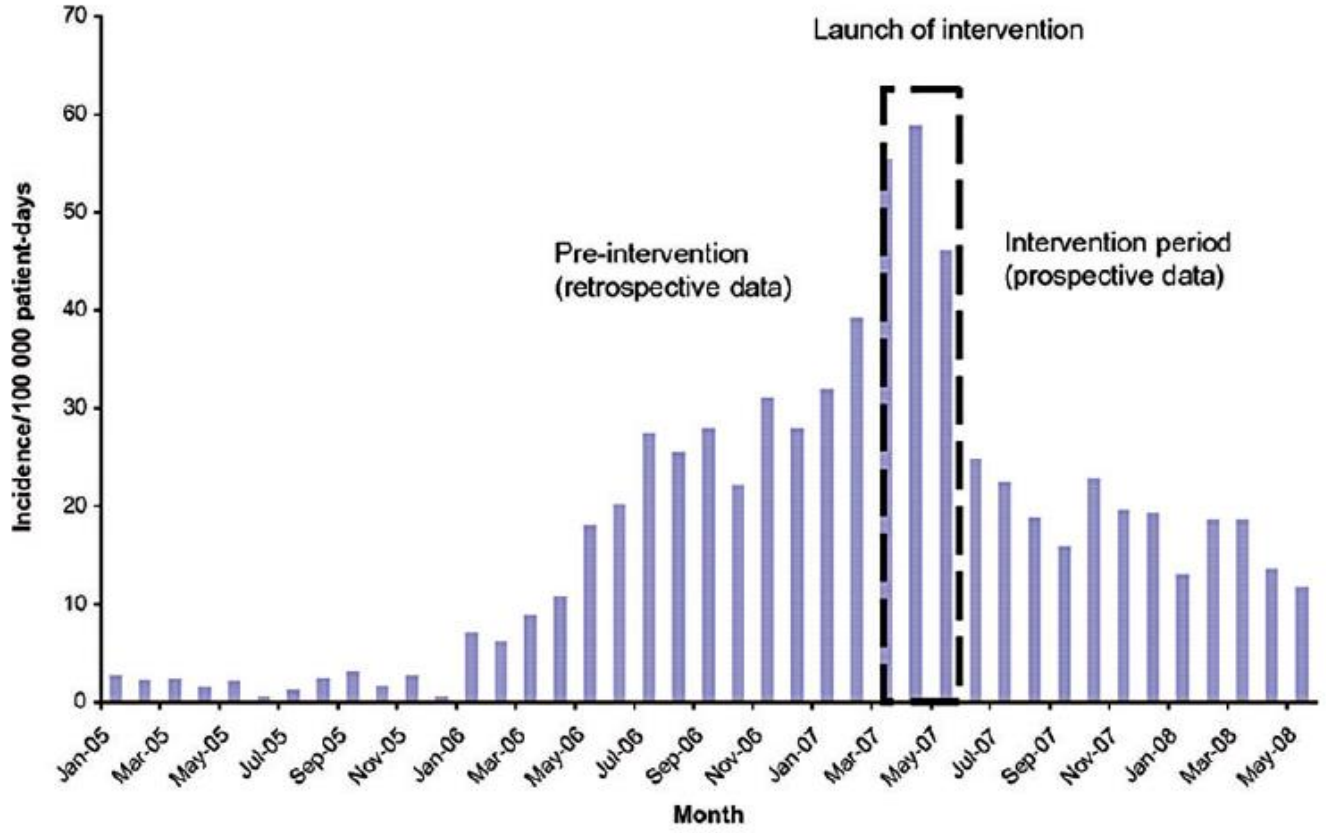
Mitchell J. Schwaber and Yehuda Carmeli

National Center for Infection Control, Tel Aviv, Israel

Clinical Infectious Diseases 2014;58(5):697–703

- **Nationwide spread of CRE in Israel 2006- failure to contain a local levels**
- **Acquisition rate of 55.5 cases per 100,000 patient days**
- **National intervention for CRE containment**

Acquisition rate now 4.8 cases per 100,000 patient days..



What worked?

TABLE 1. Compliance with Infection Control Guidelines in 13 Post-Acute Care Hospitals as Noted on 3 Site Visits

Variable	2008	2010	2011	*P*
Infection control consultant	62	85	92	.055
Hand hygiene[22]				
Presence of ABHR in each room	85	92	100	.146
ABHR at site of care	15	54	85	<.001
Presence of antiseptic soap	15	92	85	<.001
Presence of sink in each room	23	31	46	.164
Paper towel availability	69	85	100	.032
Compliance audits	0	46	77	<.001
Appropriate use of barrier precautions in context of standard precautions[23]				
Gloves	31	69	92	.001
Gowns	54	77	77	.208
Masks	38	62	69	.118
CRE prevention program				
Placement of colonized patients in single rooms or cohorting	77	85	100	.082
Use of gown and gloves in contact isolation	46	92	100	.001
Designated medical equipment	92	100	100	.221
Admission screening cultures	15	69	77	.002
Contact screening	38	77	100	.001
Discontinuation of isolation per standard protocol	15	46	100	<.001
Total infection control score (average, out of possible 16)	6.8	11.6	14.0	<.001

NOTE. Data are percentage of compliant hospitals ($n = 13$), unless otherwise indicated. ABHR, alcohol-based hand rub; CRE, carbapenem-resistant Enterobacteriaceae.

TABLE 2. Israeli National Guidelines for the Care of Patients with Carbapenem-Resistant Enterobacteriaceae in Acute Care versus Post-Acute Care Hospitals

Variable	Acute care hospitals	Post-acute care hospitals	
		Skilled nursing/chronic ventilated/subacute wards	Rehabilitation wards
Room assignment	Private or cohorting with other CRE carriers	Private or cohorting with other CRE carriers	No regulation regarding room assignment
Dedicated nursing staff for CRE carriers	Required	Not required	Not required
Use of gloves and gowns in care of CRE carriers	Mandatory on room entrance	Mandatory on room entrance	According to standard precautions
Admission CRE screening of high-risk groups[a]	Required	Required	Not required, except in outbreak setting
CRE screening of patient contacts	Required	Required	Required
Participation in group activities	Prohibited	Allowed	Allowed
Standard protocol for discontinuation of contact isolation	Yes	Yes	Yes
Regular mandatory census reporting to NCIC	Yes	Yes	Yes

NOTE. CRE, carbapenem-resistant Enterobacteriaceae; NCIC, National Center for Infection Control.

[a] High-risk groups were defined as patients transferred from other facilities or patients with earlier hospitalization within the previous 6 months.

Take home messages

- **MDRO rates a major concern in Irish healthcare and globally**
- **Antimicrobial resistance a real threat to how we all practice medicine**
- **Stewardship and adherence to infection prevention and control practices our best (only) means to limit the spread**

Video

Video Link

- https://www.youtube.com/watch?v=Q7HFCrvcOBM

Thank you!

Questions…….