

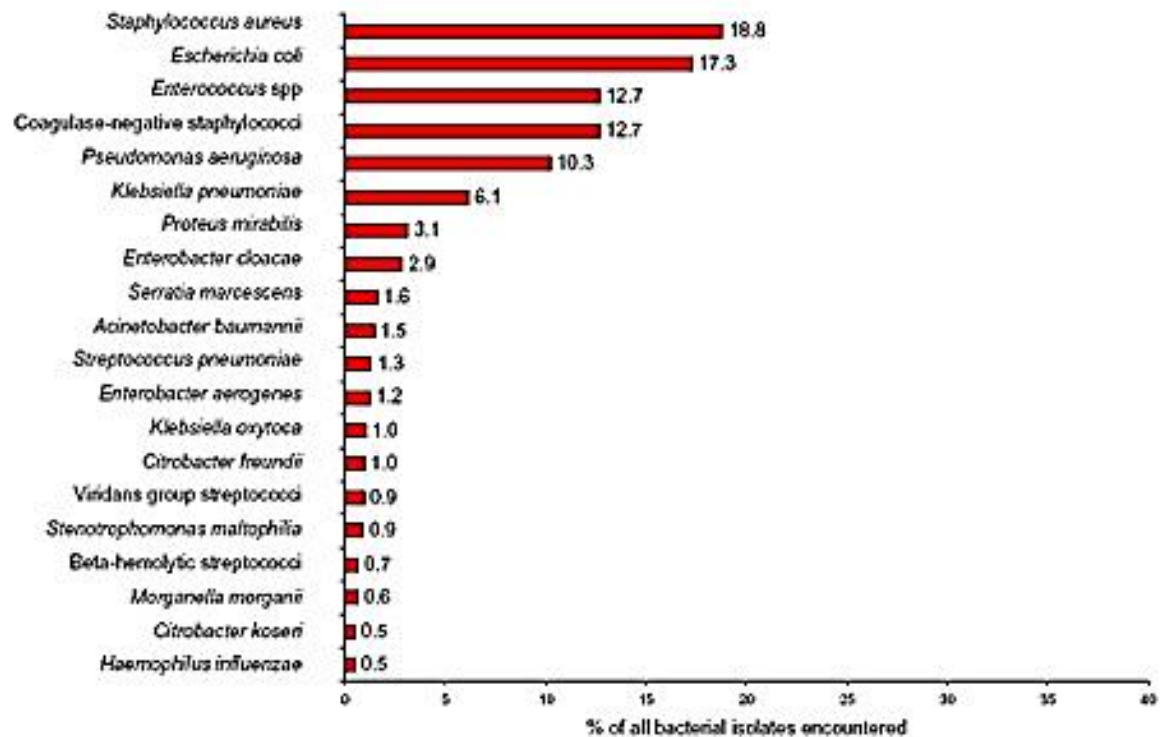
Changing Epidemiology of MDROs

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Disclosures: None

Frequency of Hospital Pathogens

Relative frequency of bacterial species/groups encountered in clinical specimens from inpatients



<http://www.microresistance.org/bacteriology.cfm>

Gram Positives (MRSA)

MRSA as a Key Hospital Pathogen

- 2009-10 CDC Data, National Healthcare Safety Network
- *S aureus*
 - #1 HAI pathogen
 - #1 VAP, SSI
 - #2 CLABSI
- Majority MRSA

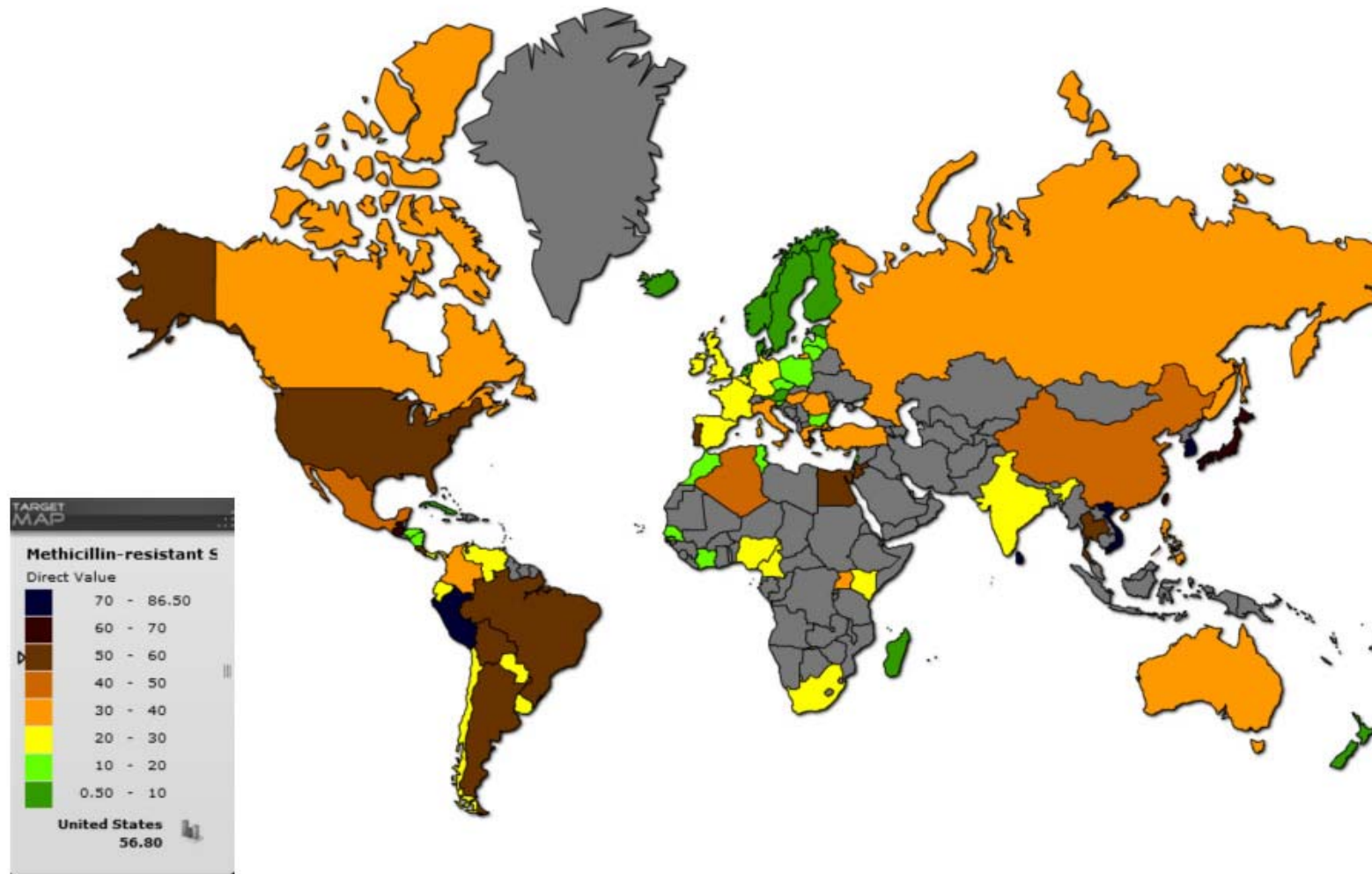
MRSA in ICUs

- US ICU Prevalence 8-20% ¹
- International ICU study: 1265 ICUs, 74 countries ²
 - 1 day point prevalence study (EPIC II)
 - 51% infected, 26% bacteremic
 - 15% *S aureus* (majority MRSA (65%))

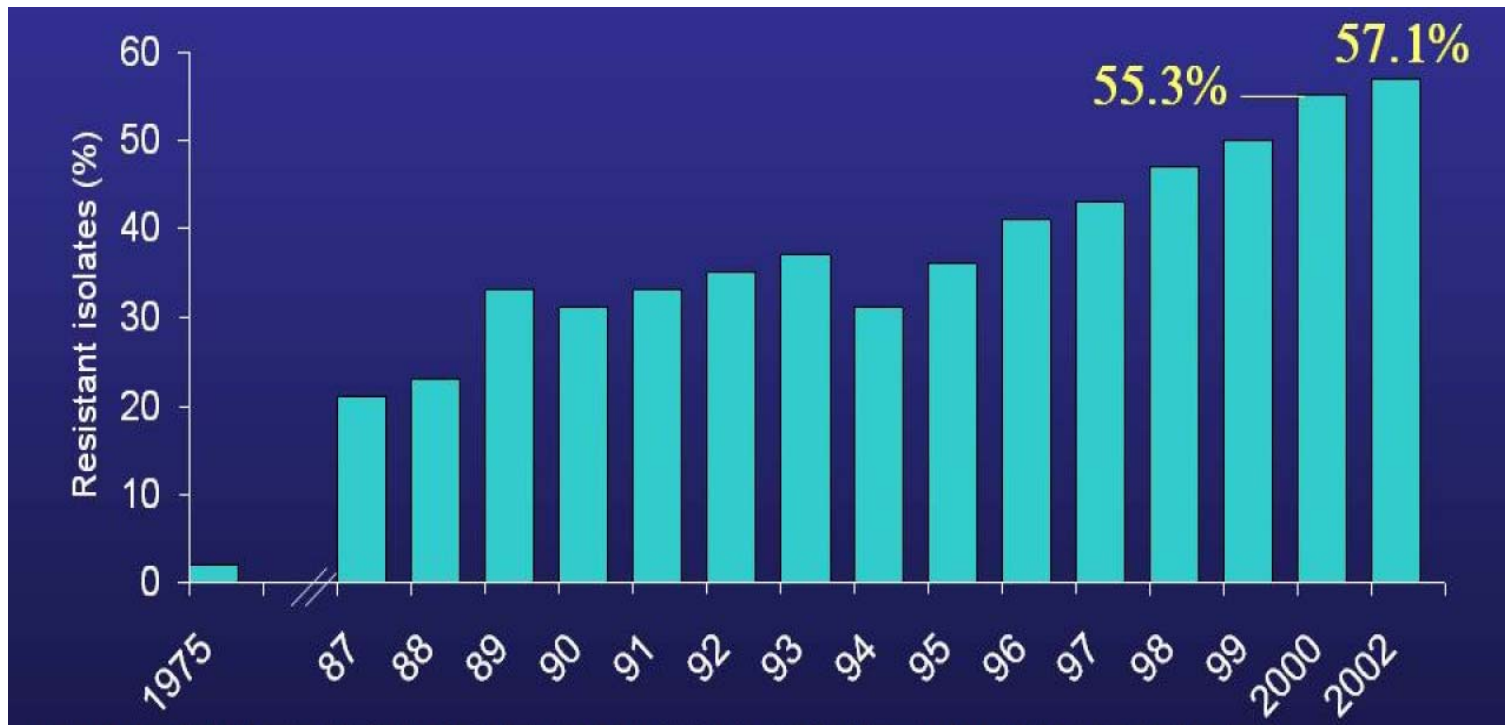
¹ Huang et al. JID 2007;195(3):330-8

² Vincent et al. JAMA 2009;302(21):2323-9

MRSA as a Proportion of *S. aureus* Isolates

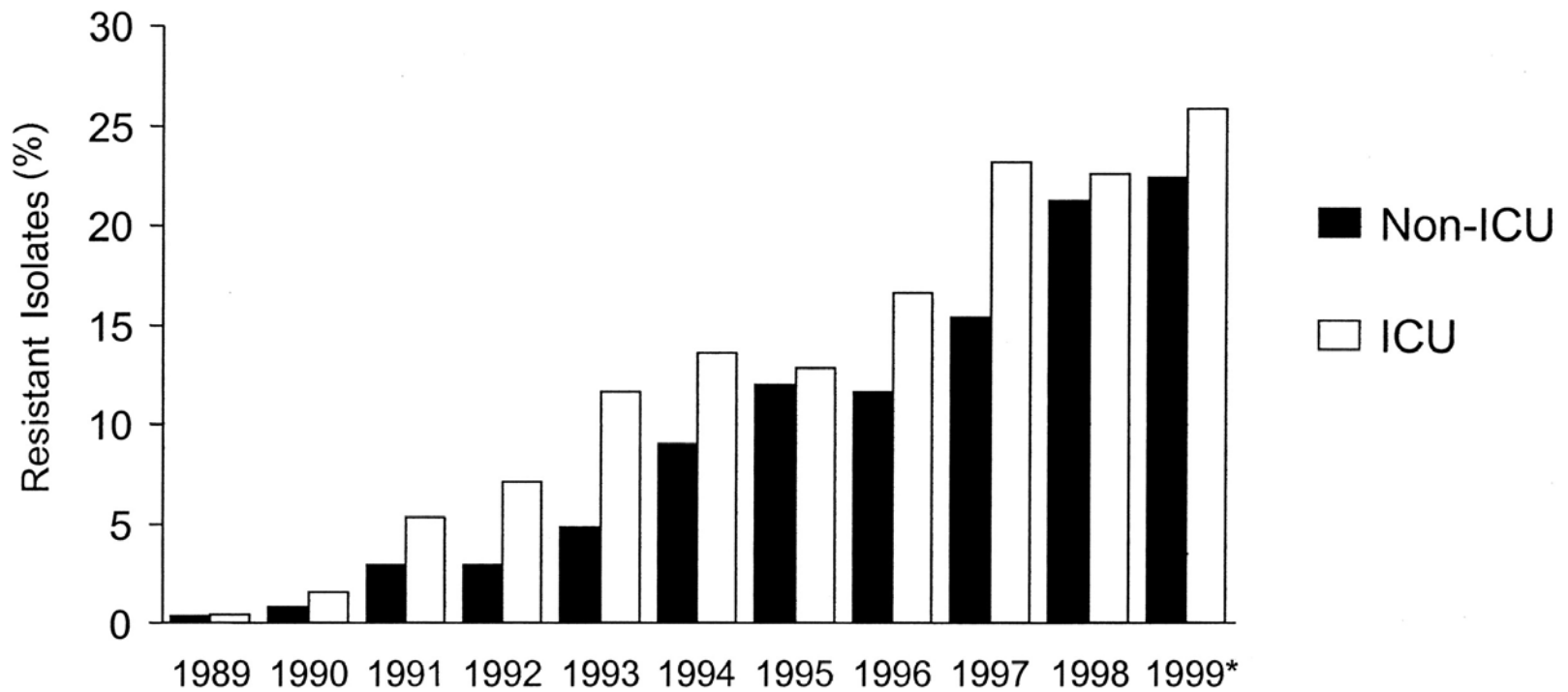


% MRSA Among *S. aureus*: US



CDC NNIS Data

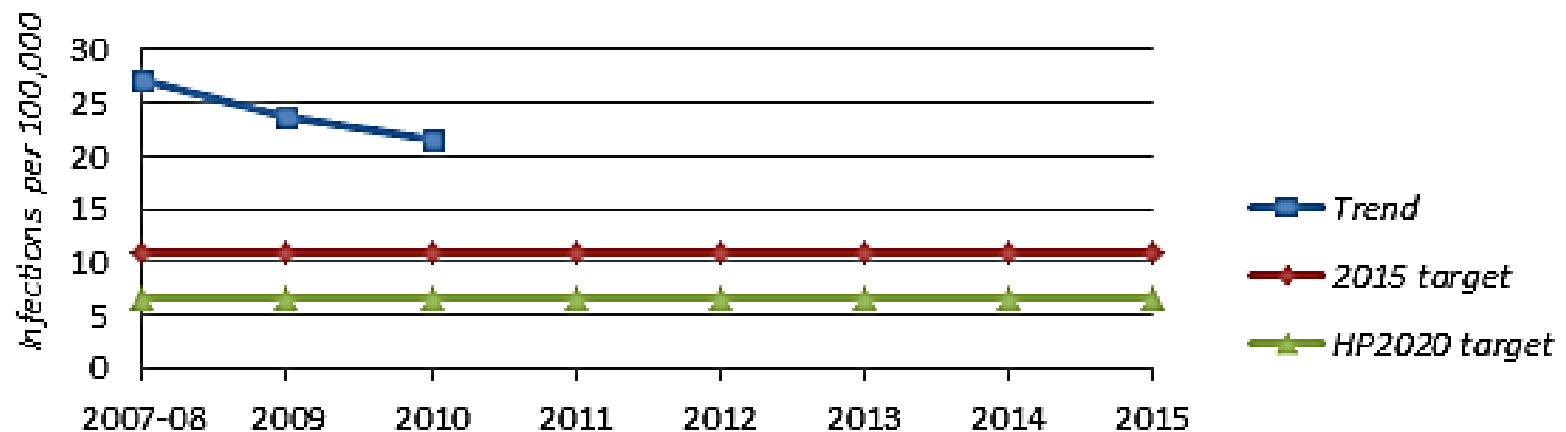
% VRE Among *Enterococci*: US



CDC NNIS Data

CDC's Winnable Battles

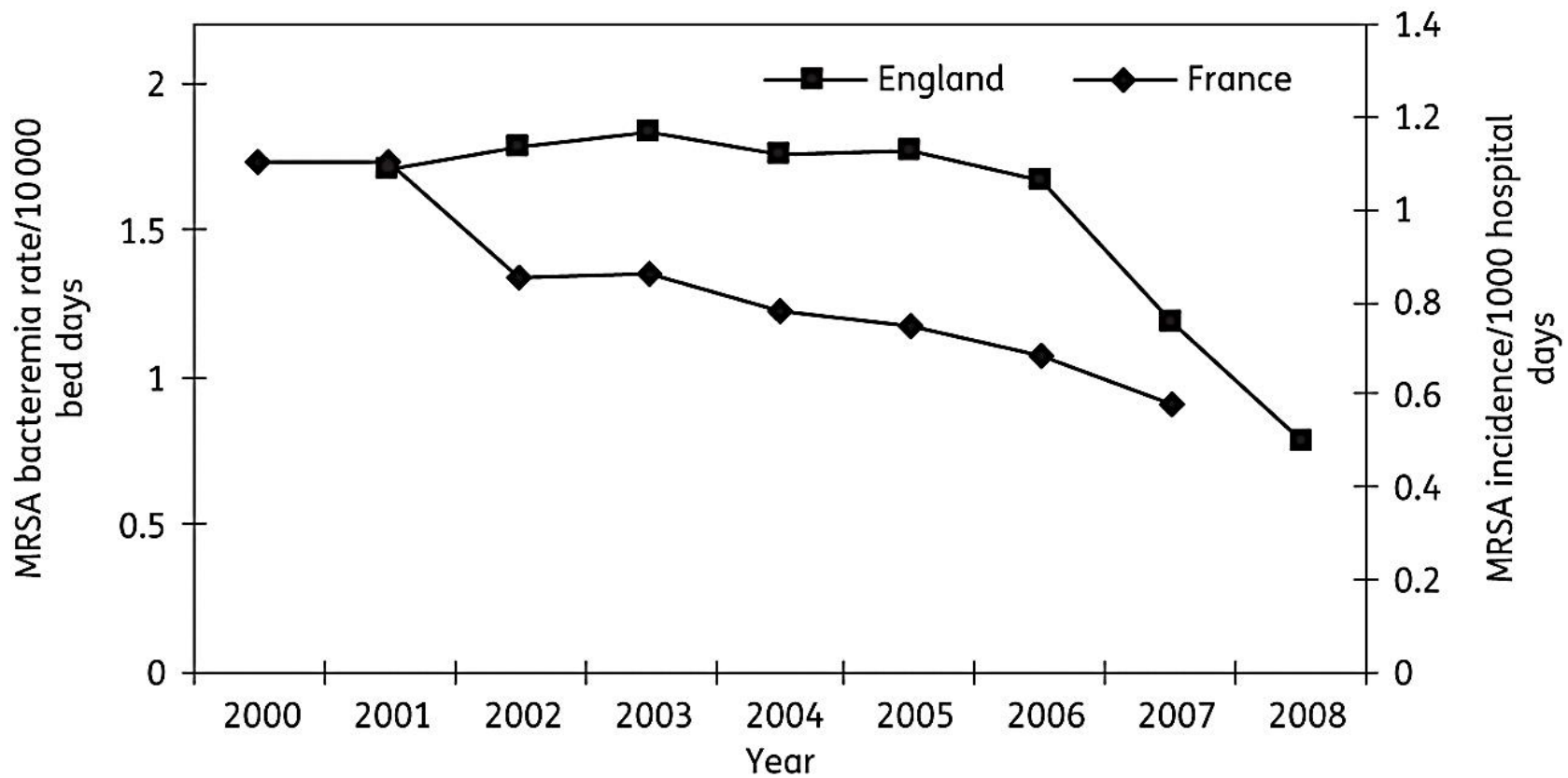
Trends in healthcare-associated invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections, 2007-2010



- 26% Reduction in hospital-associated MRSA invasive disease
- 30% Reduction in hospital-associated MRSA bacteremia

<http://www.cdc.gov/winnablebattles/targets/hai/index.html>

England & France: MRSA Trends



ICU vs Non-ICU HAI Infections

<i>Major site of infection</i>	<i>Well-baby nursery</i>	<i>High-risk nursery</i>	<i>Intensive care unit (adults and children)</i>	<i>Outside of intensive care units (adults and children)^a</i>	<i>Unadjusted total</i>	<i>Adjusted total^b</i>	<i>Percentage</i>
Urinary tract	1,413	2,418	102,200	424,060	530,091	561,667	32
Bloodstream	5,652	14,797	81,942	133,368	235,759	248,678	14
Pneumonia	1,785	4,400	100,689	129,519	236,393	250,205	15
Surgical site	21	967	28,725	244,385	274,098	290,485	22
Other	10,188	10,687	80,732	263,810	365,417	386,090	17
Total	19,059	33,269	394,288	1,195,142	1,641,758	1,737,125	100

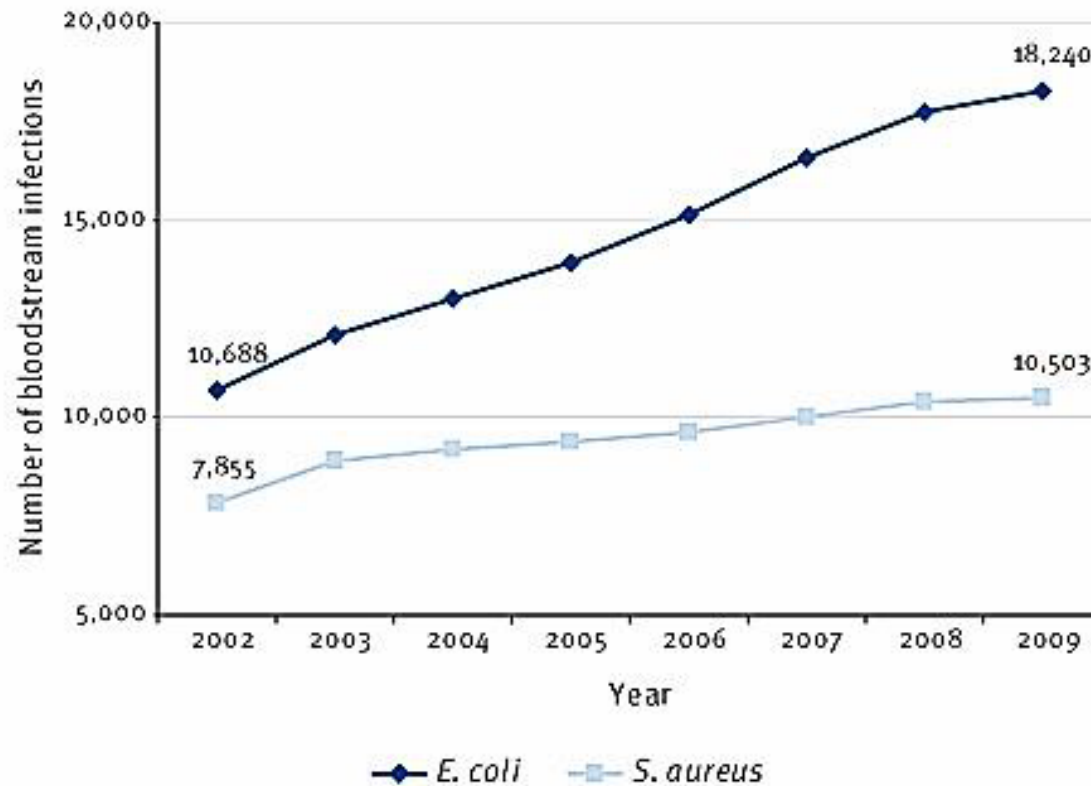
Pub Health Rep 2007; 122:160-6

Winning the Battle, Losing the War?

- Despite decrease in hospital-associated MRSA disease
- Increases in community and hospital prevalence
- Carriage associated with later invasive disease
- 86% of invasive disease is healthcare-associated
- *S. aureus* is still # 1 healthcare-associated infection pathogen

Kallen et al. JAMA 2010;304(6):641-8
Sievert et al. ICHE 2013;34(1):1-14

MRSA BSI: 22 European Countries



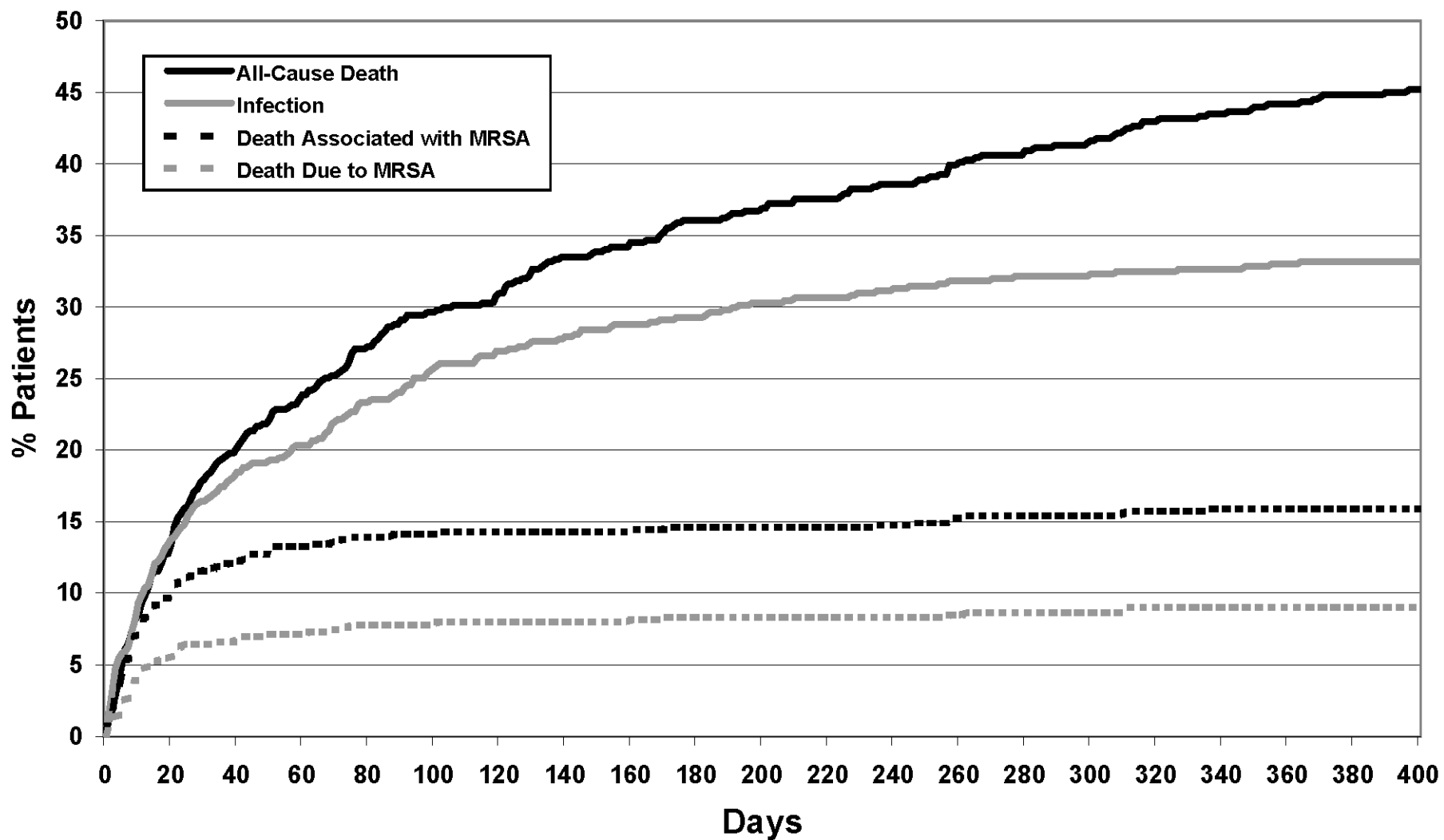
EARSS: European Antimicrobial Resistance Surveillance System;
EARS-Net: European Antimicrobial Resistance Surveillance
Network.

MRSA Carriage and Infection

- Carriage strongly associated with later invasive disease ¹
- 33% of patients in an academic center → invasive disease within 1 year of discharge
 - 26% Diabetes
 - 13% Immunosuppressed
 - 7% Renal Disease
- Increased risk surrounding hospitalizations, devices

¹ Huang et al. PLoS ONE 2011;6(9):e24340

Days from MRSA Detection Until Infection or Death



Types of Infectious Sequelae

PRE-DISCHARGE

44% Lung Infections
19% Soft Tissue Infection
16% Disseminated/Unknown
7% Surgical Site Infection
5% Bloodstream/Vascular
1% Bone & Joint
1% Urinary Tract

26% Associated Bacteremia

POST-DISCHARGE

31% Lung Infections
31% Soft Tissue Infection
9% Disseminated/Unknown
5% Surgical Site Infection
8% Bloodstream/Vascular
9% Bone & Joint
5% Urinary Tract

26% Associated Bacteremia

No Good Immunity

- 3 medical centers
- Identified patients with serial MRSA cultures
 - Repeat Unrelated Bacteremia
 - Nares then Bacteremia
- Isolates genetically typed by PFGE
- Very high strain diversity

No Good Immunity

Serial Isolates: PFGE Patterns

	# Pts	Indistinguishable Strain Type	Same PFGE Type*	Different PFGE Type
Sterile-Sterile	37	28 (72%)	34 (87%)	5 (13%)
Bacteremia-Bacteremia	34	26 (72%)	31 (86%)	5 (14%)
Nonsterile-Sterile	29	22 (73%)	30 (100%)	0 (0%)
Nares-Bacteremia	27	20 (71%)	28 (100%)	0 (0%)

* Strains differ by ≤ 3 bands by PFGE

Vaccines in Clinical Trials

Candidate	Sponsor	Rationale	Status
StaphVAX	Nabi Biopharmaceuticals	CP5, CP8	Phase III Failed ¹
Veronate	Inhibitex	Cell Wall Adhesins	Phase III Failed
v710	Merck	Monovalent Iron Surface Determinant B	Phase III Failed ²
SA3Ag	Pfizer/Wyeth	Tri-valent CP5, CP8, rClfAm	Phase I Passed
Pentastaph	GSK (Nabi)	CP5, CP8, cell wall antigen 336, PVL and α toxin	Phase 1 Passed

¹ Shinefield et al. NEJM 2002;346(7):491-6.

² Fowler et al. JAMA 2013;309(13):1368-78

MRSA Transmission

- Patients who are colonized shed as much as those infected ¹
 - Patient skin
 - Environmental burden
 - HCW hands after contact
- Need to address the carrier state

¹ Chang et al. CID 2009;48:1423-8

Strain-Dependent Effects

- Evidence for competitive transmission, but not yet certain for development of infection
- Community-type strains (PVL, MEC IV)
 - Concern for higher necrosis, transmission
 - No evidence of increased severity as HAI ¹
- MSSA protects against MRSA nasal acquisition ²
- VSE does not protect against VRE rectal acquisition ²

¹ Lessa et al. CID 2012 Jul;55(2):232-41

² Huang et al. Crit Care 2011, 15(5):R210.

Emerging Gram Negatives

Resistance in Enterobacteriaceae

- Beta-lactamases 1950-60s
- Cephalosporinases 1970s
- ESBLs 1980s
- Carbapenemases 1990-2000s
 - Carbapenems introduced mid-1980s
 - Susceptibility limited to tigecycline, polymixins, occasional aminoglycoside
 - Strains resistant to all available antibiotics reported

Carbapenemases

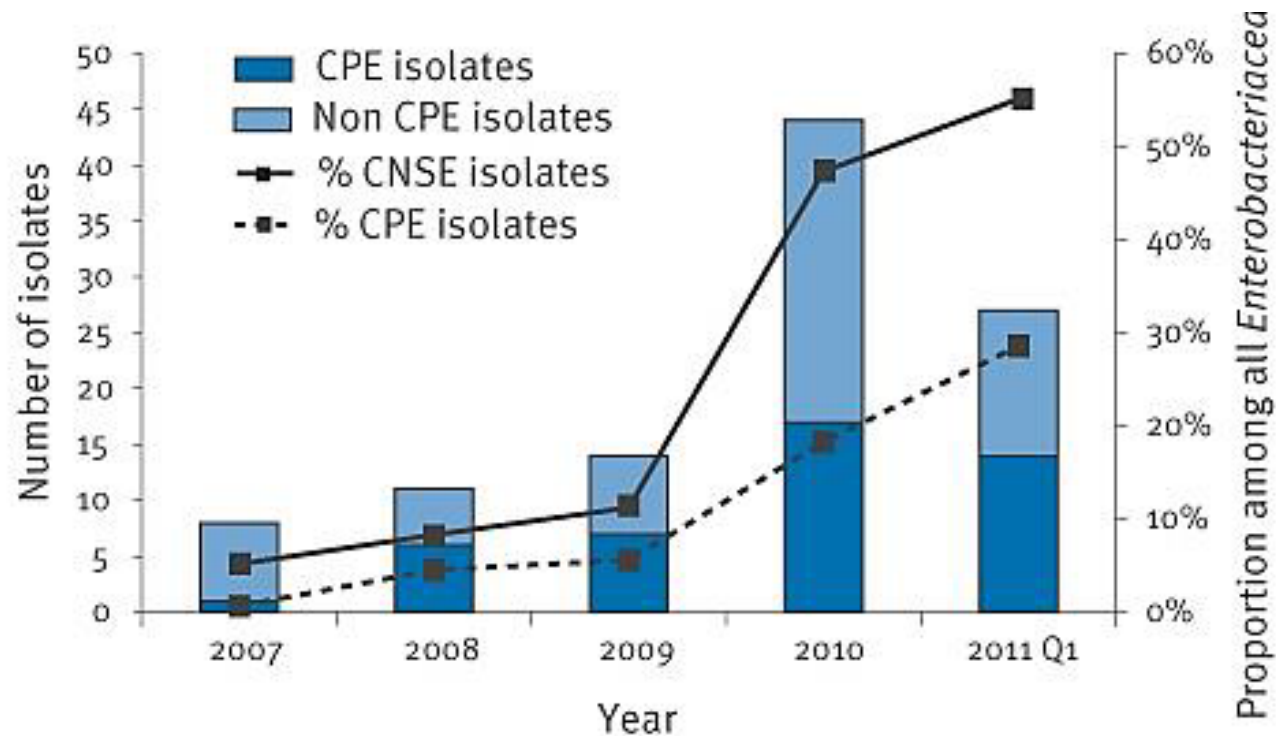
- IMP (imipenemase) ~1990
- VIM (verona integron) late 1990s
 - Outbreaks in Greece, Spain 2003+
- KPCs (ST 258) 2001 (N. Carolina)
 - Endemic NY, east coast early 2000s
 - US, Israel, Greece, Italy, Poland, France, China, L. America
- NDM-1 2008
 - India → Europe, US
- OXA-48 2009

European CRE Experience

Country	Stage	Epidemiological scale	Documented introduction from abroad	Dominant class
Greece	5	Endemic	Yes	KPC/VIM
Israel ^a				KPC
Italy	4	Interregional spread	Yes	KPC
Poland				
France	3	Regional spread	Yes	KPC
Germany				OXA-48/VIM
Hungary				KPC
Belgium	2b	Independent hospital outbreaks	Yes	VIM
Spain				KPC/VIM/IMP
England and Wales				NDM
Cyprus	2a	Single hospital outbreak		VIM
Netherlands			Yes	KPC
Norway			Yes	KPC
Scotland				KPC
Sweden			Yes	KPC
Bosnia Herzegovina	1	Sporadic occurrence	Yes	KPC
Denmark				KPC/VIM
Finland			Yes	KPC
Croatia				VIM
Czech Republic			Yes	VIM/KPC
Ireland				KPC
Lithuania				?
Latvia				?
Malta				?
Portugal				KPC
Romania				?
Switzerland		KPC		

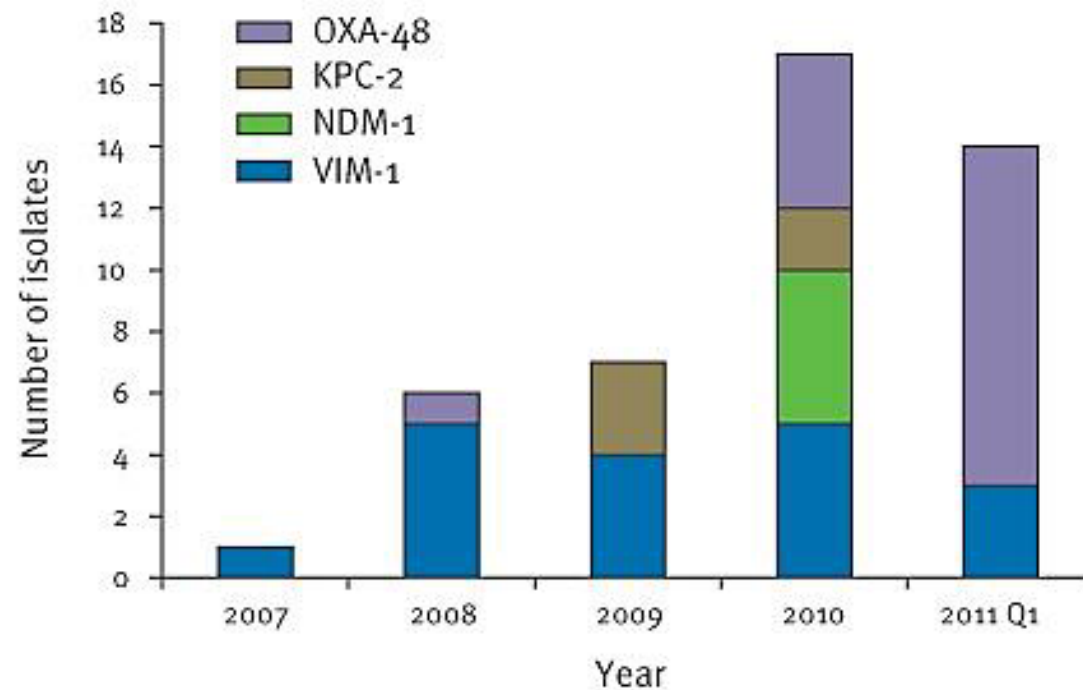
Grundmann H et al. Euro Surveill. 2010 Nov 18;15(46).

Belgium: Emergence of CRE



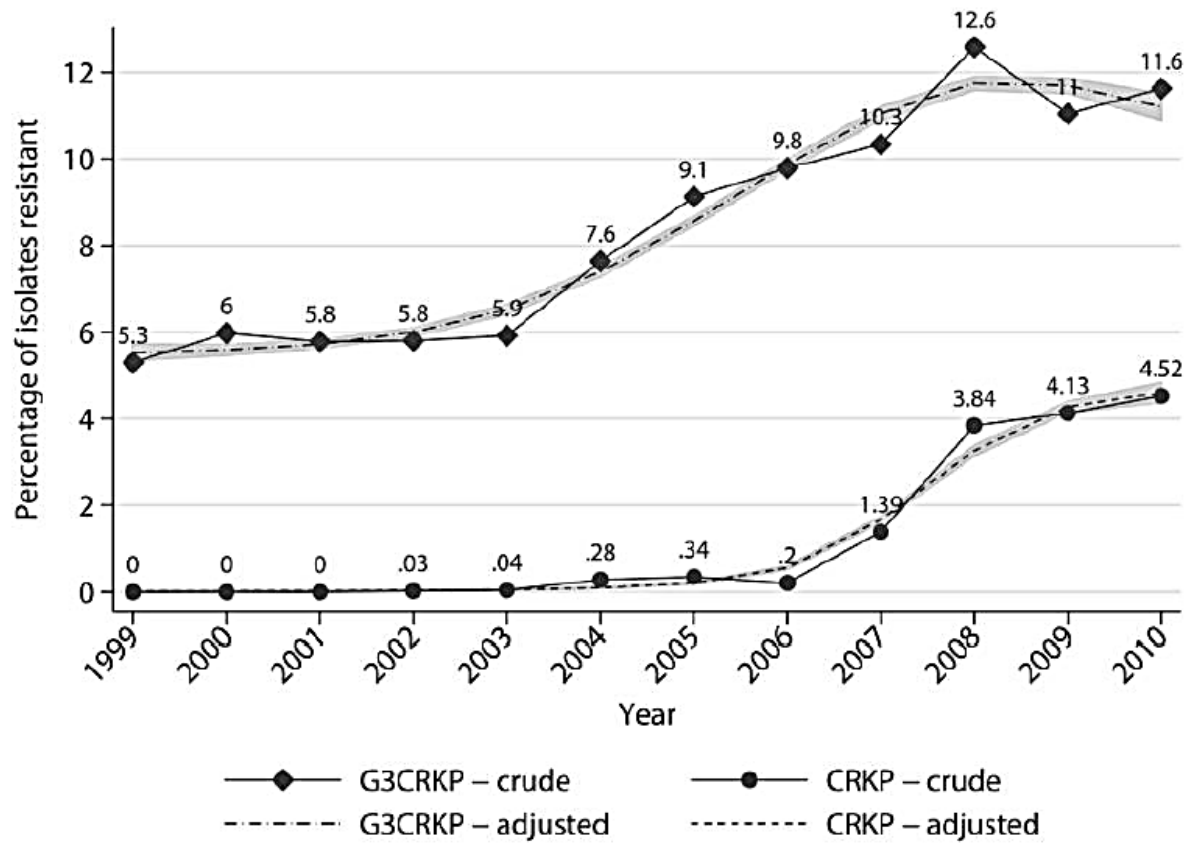
CNSE: carbapenem-non-susceptible *Enterobacteriaceae*;
CPE: carbapenemase-producing *Enterobacteriaceae*;
Q1: first quarter.

Belgium: CRE Resistance Mechanisms

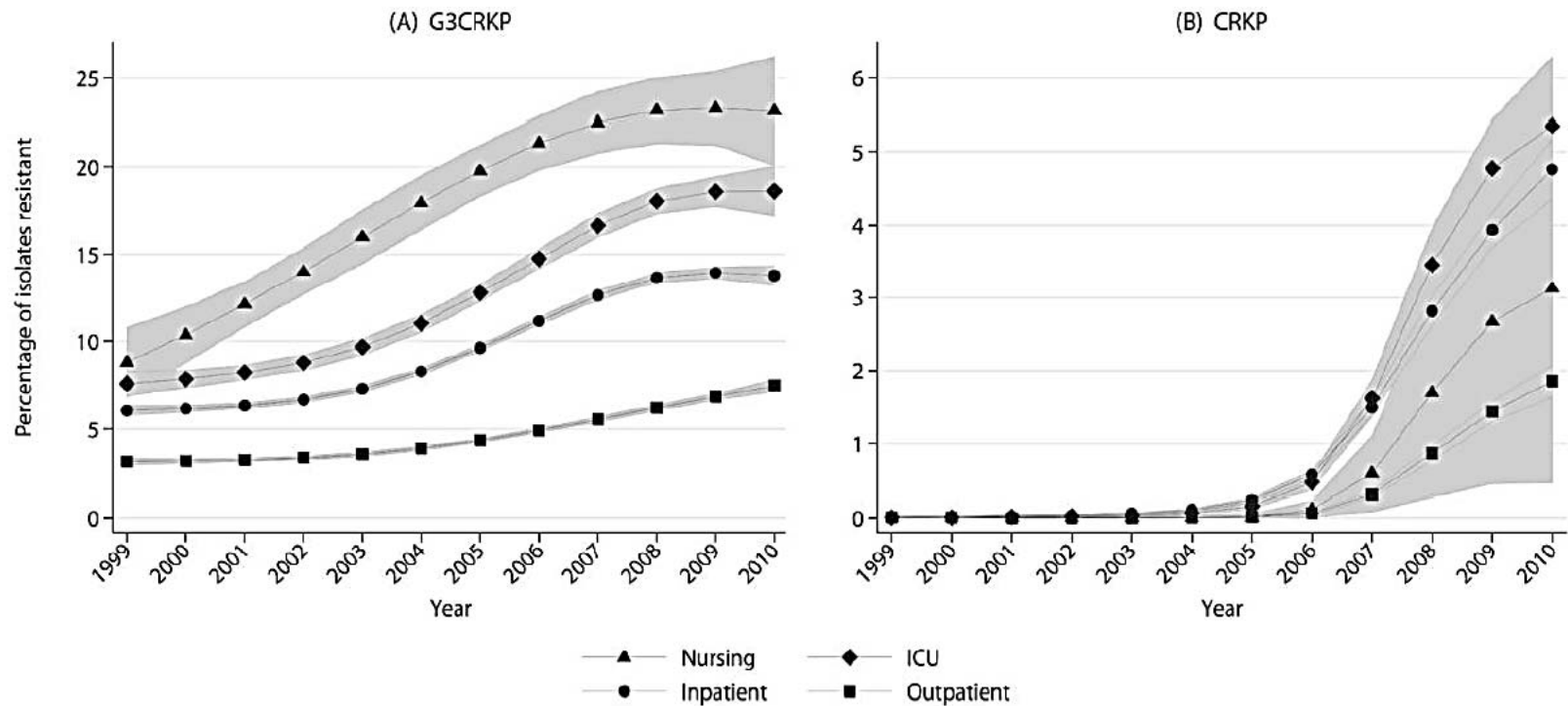


KPC: *Klebsiella pneumoniae* carbapenemase; NDM: New Delhi metallo-beta-lactamase; OXA: oxacillinase; Q1: first quarter; VIM: Verona integron-encoded metallo-beta-lactamase.

US Trends in CRE



US Trends in CRE



Outpatient < non-ICU (2x) < ICU (3x) < Long term care (4x)

Predictors of MDR Enterobacteriaceae

- ESBL ¹
 - Recent hospitalization, transfer from acute care facility
 - Multiple comorbidities, urinary catheter
- CRE ²
 - 7-fold risk if from LTAC and SNF with ventilator beds
 - Antibiotics, urinary catheter
 - History of CRE, other MDROs
 - Most usually on contact precautions already

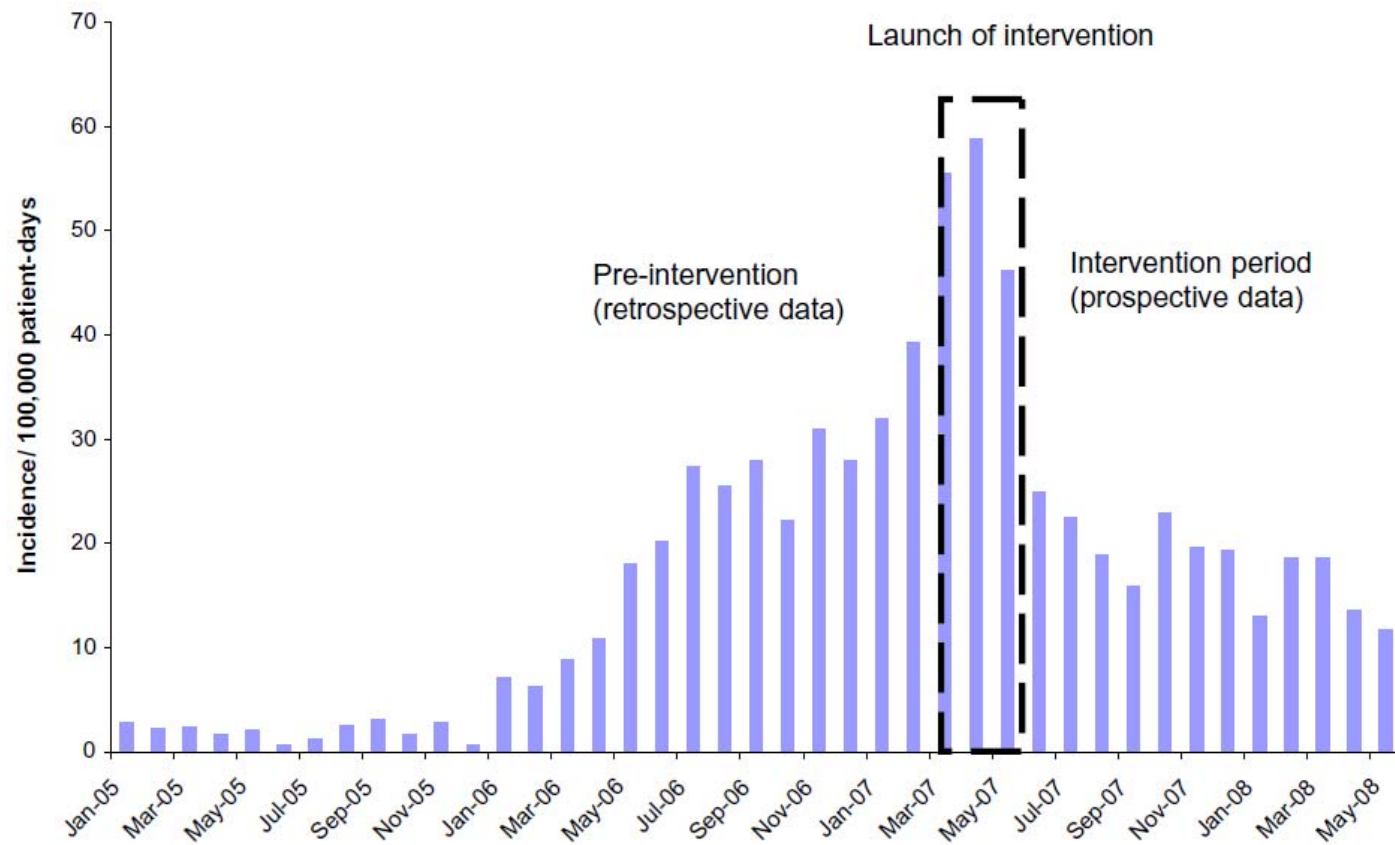
¹ Johnson et al. ICHE 2013;34(4):385–92

² Prabaker et al. ICHE 2012;33(12):1193-99

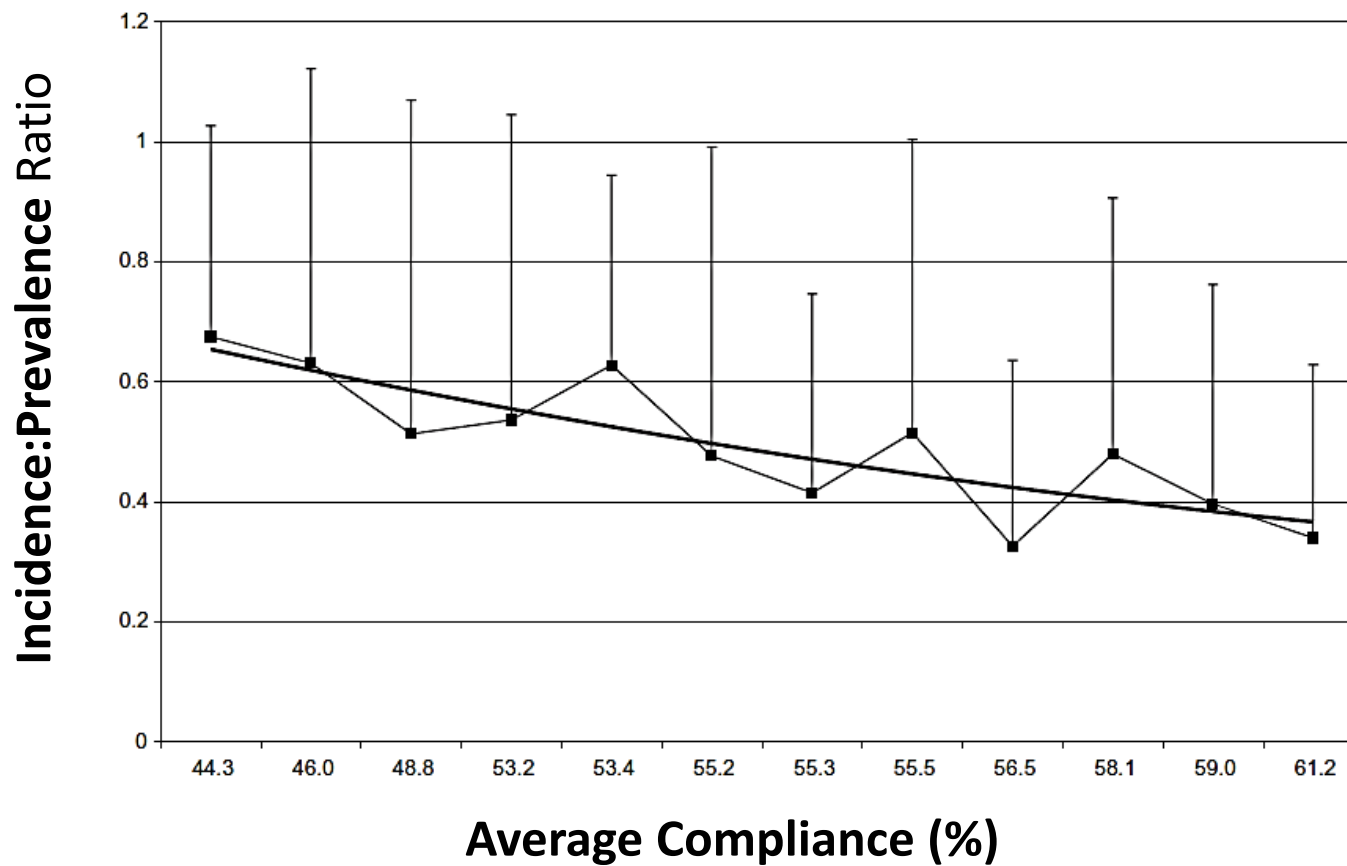
Israel: National Response to CRE

- 2006: Multiple hospital outbreaks of KPC
- 2007: National spread → task force for action
- National mandate
 - Daily report of CRE carriers, status, disposition
 - Daily report of contact precaution adherence for each CRE patient
 - Dedicated nursing for CRE patients
 - Task force for Antibiotic Resistance and Infection Control
 - Site visits for enforcement

Israel: CRE Incidence



Reduction in CRE by Compliance with Contact Precautions



Schwaber et al. CID 2011;52(7):848–855

US CDC Recommendations for CRE


- Laboratory alert
- Contact precautions, including on readmissions
 - Single room, gown/gloves, dedicated equipment
- Dedicated nursing
- Low threshold for rectal screening of same-ward patients
- Consider chlorhexidine bathing
- Report importation from India (possible NDM-1)
- Notification to transferring facilities

ICU Knowledge of GNR MDROs

TABLE 3. Healthcare Professionals' Knowledge of the Activity of Antimicrobial Agents

Question (correct answer)	Participants with correct response, %			
	ID HCP (n = 43)	ICU HCP (n = 120)	Adult ICU (n = 55)	Pediatric ICU (n = 65)
Carbapenem agents are ineffective for GNB expressing extended-spectrum β -lactamases (false)	98 ^a	64	64	65
Tigecycline is an option for hospital-associated pneumonia caused by MDR <i>Pseudomonas aeruginosa</i> (false)	83 ^a	25	36 ^b	15
Carbapenem-resistant <i>Klebsiella</i> species are usually susceptible to quinolone agents (false)	86 ^a	37	58 ^b	19
Quinolone agents exhibit concentration-dependent killing (true)	60 ^a	28	33	25
Correct answers per respondent, mean	3.3	1.5	1.9	1.2

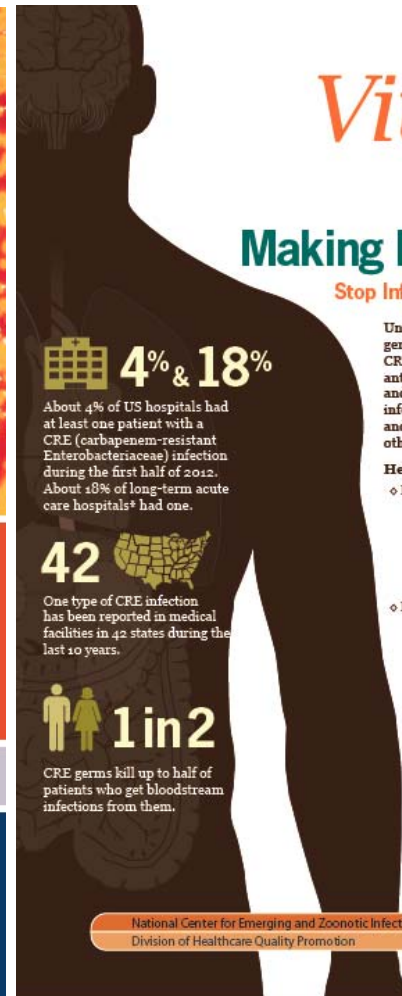

US (CDC) Materials



Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

2012 CRE Toolkit

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion



VitalSigns™

CDC
March 2013

Making Health Care Safer

Stop Infections from Lethal CRE Germs Now

Untreatable and hard-to-treat infections from CRE germs are on the rise among patients in medical facilities. CRE germs have become resistant to all or nearly all the antibiotics we have today. Types of CRE include KPC and NDM. By following CDC guidelines, we can halt CRE infections before they become widespread in hospitals and other medical facilities and potentially spread to otherwise healthy people outside of medical facilities.

Health Care Providers can


- ◊ Know if patients in your facility have CRE.
 - Request immediate alerts when the lab identifies CRE.
 - Alert the receiving facility when a patient with CRE transfers, and find out when a patient with CRE transfers into your facility.
- ◊ Protect your patients from CRE.
 - Follow contact precautions and hand hygiene recommendations when treating patients with CRE.
 - Dedicate rooms, staff, and equipment to patients with CRE.
 - Prescribe antibiotics wisely.
 - Remove temporary medical devices such as catheters and ventilators from patients as soon as possible.

*Long-term acute care hospitals provide complex medical care, such as ventilation or wound care, for long periods of time.

→ See page 4
Want to learn more? Visit

www.cdc.gov/vitalsigns

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion



 **4% & 18%**

About 4% of US hospitals had at least one patient with a CRE (carbapenem-resistant Enterobacteriaceae) infection during the first half of 2012. About 18% of long-term acute care hospitals* had one.

42 

One type of CRE infection has been reported in medical facilities in 42 states during the last 10 years.

 **1 in 2**

CRE germs kill up to half of patients who get bloodstream infections from them.

Questions?

