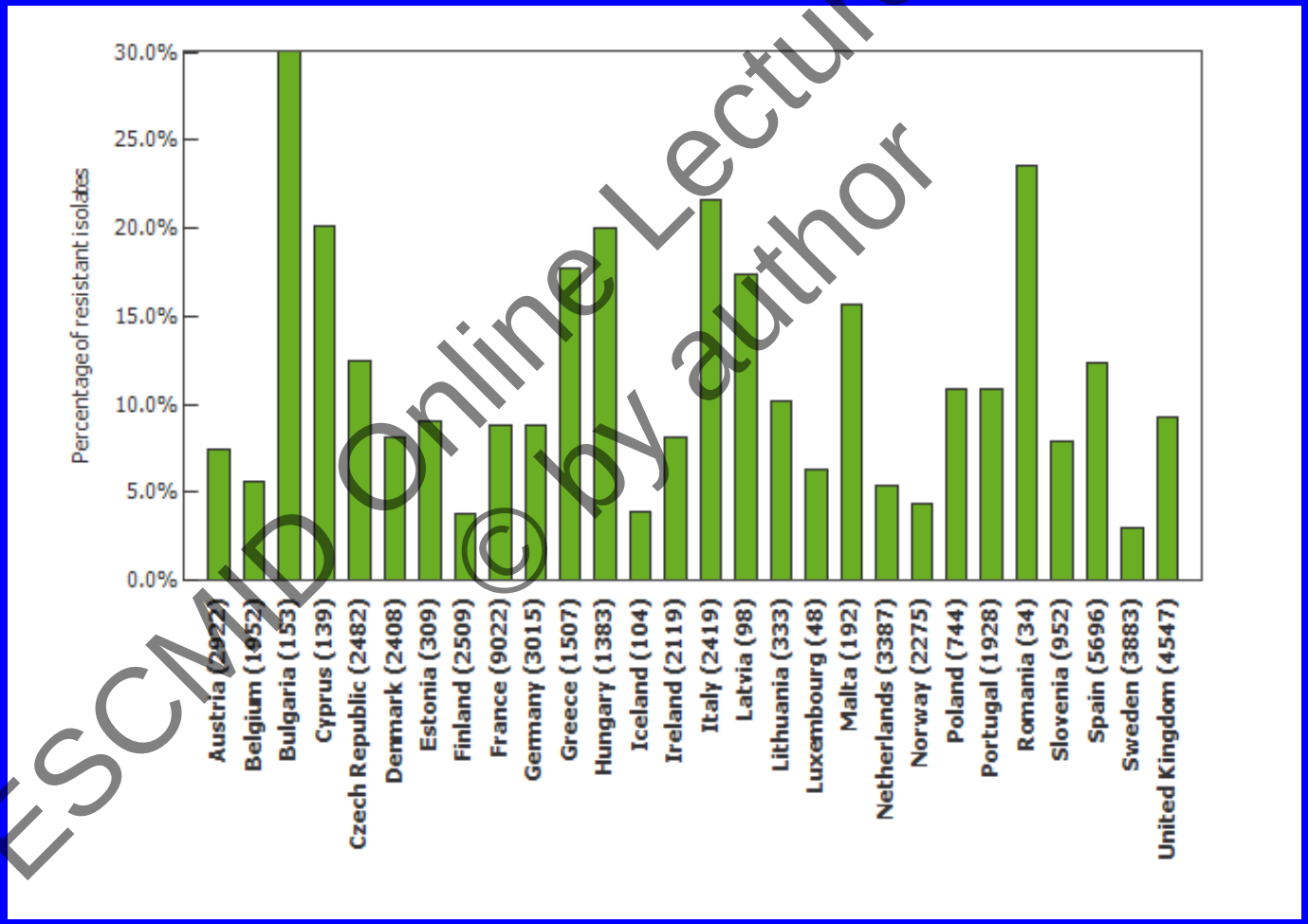
ESBL and KPC producers, Any news?

Yehuda Carmeli, MD, MPH
Division of Epidemiology,
Tel Aviv Sourasky Medical Center
& The Israeli Center for Antibiotic Resistance

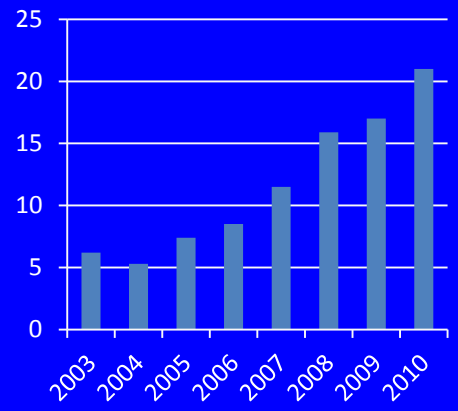
Prevalence of ESBLs

3GC resistant E. coli 2010 – EARS-net

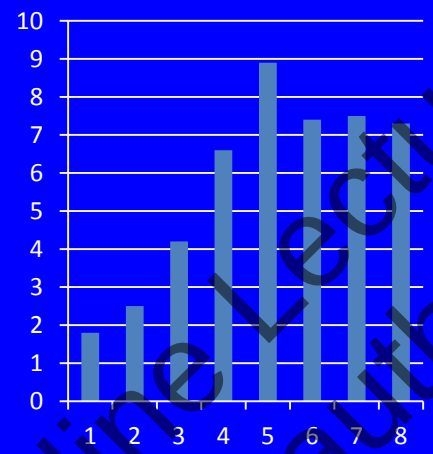


Trend in 3GC resistant E. coli EARS-net 2003-2010

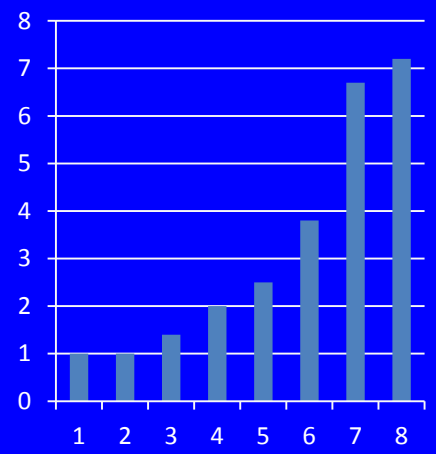
Italy



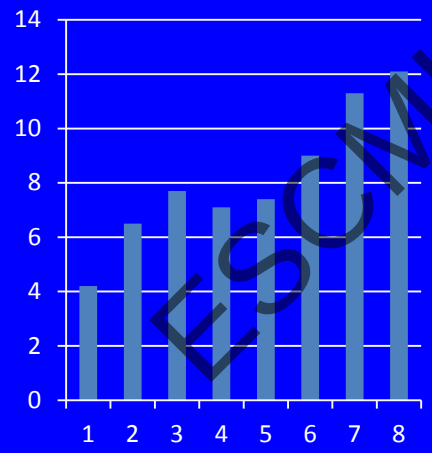
Austria



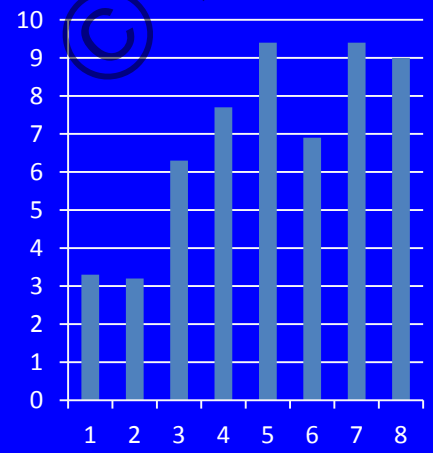
France



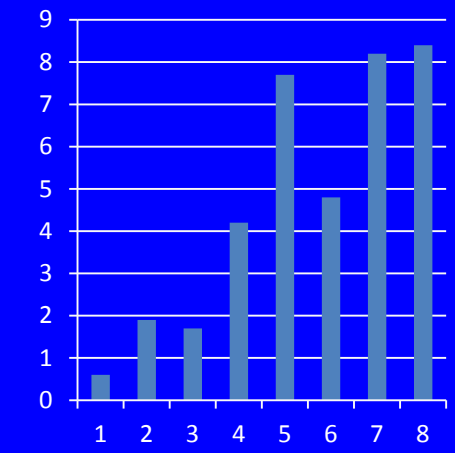
Spain



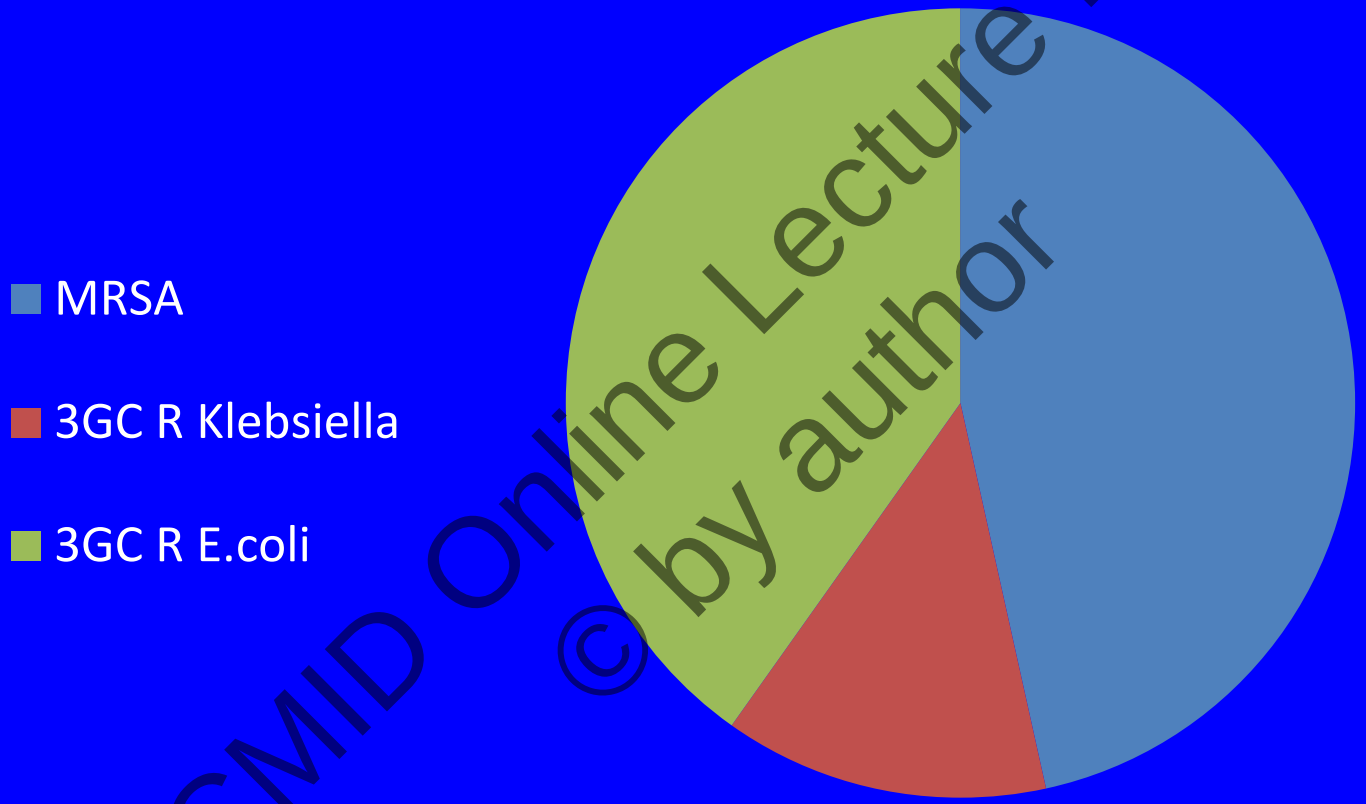
UK



Germany



3GC resistant enterobacteria bacteremia surpasses MRSA



Adapted according to E. Taconelli ECCMID 2012
Using the EARS-net data 2010 for:
Austria, France, Germany, Italy, Spain, UK (similar effect in all)

Carriage in the community

Thailand

- 445 healthy volunteers from 3 provinces
- 29 -51% carriers of CTX-M ESBL
- 92% E. coli
- Various CTX-M groups
- No association with age, gender, food consumption, or personal antibiotic use
- The highest carriage rate in the province with highest over the counter sales of antibiotics

Luvsansharav OU. JMM 2011

Rectal Carriage of Extended-Spectrum Beta-Lactamase-Producing Gram-Negative Bacilli in Community Settings in Madagascar

Perlinot Herindrainy[1☯], Frédérique Randrianirina[2☯], Rila Ratovoson[2], Elisoa Ratsima Hariniana[2], Yves Buisson[1], Nathalie Genel[3], Dominique Decré[3], Guillaume Arlet[3], Antoine Talarmin[2], Vincent Richard[2*]

- 484 patients attending outpatient clinics enrolled
  - Patients with fever, recent antibiotic treatment (3 months) or hospitalization (12 months) were excluded
  - Median age 28 (IQR 9-40)
- 10% ESBL carriers
  - no age or gender difference
- Only identifiable risk factors low socioeconomic class (by education, employment , number of rooms in the house, having a mobile phone)

PlosOne

Faecal carriage of multidrug-resistant Gram-negative bacilli during a non-outbreak situation in a French university hospital

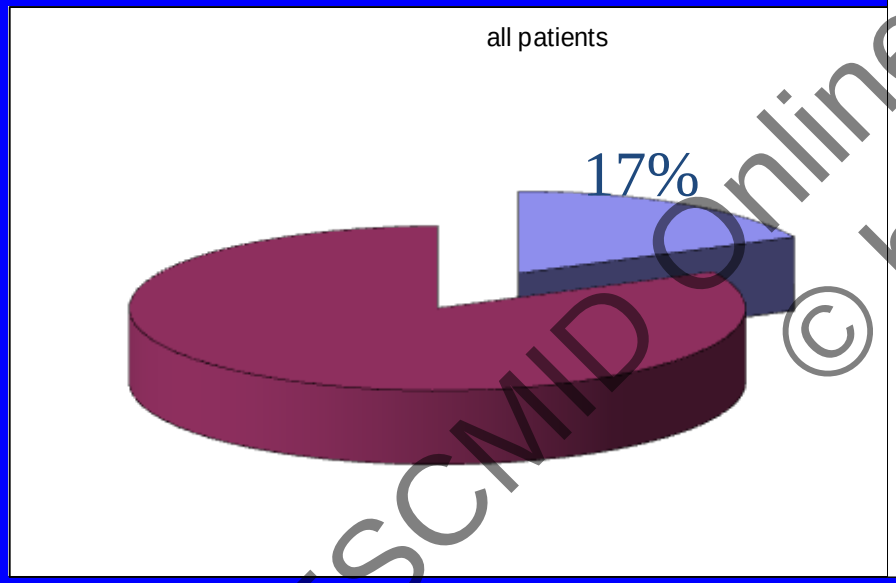
Laure Vidal-Navarro[1], Caroline Pfeiffer[1], Nicole Bouziges[1,2], Albert Sotto[1,3] and Jean-Philippe Lavigne[1,2*]

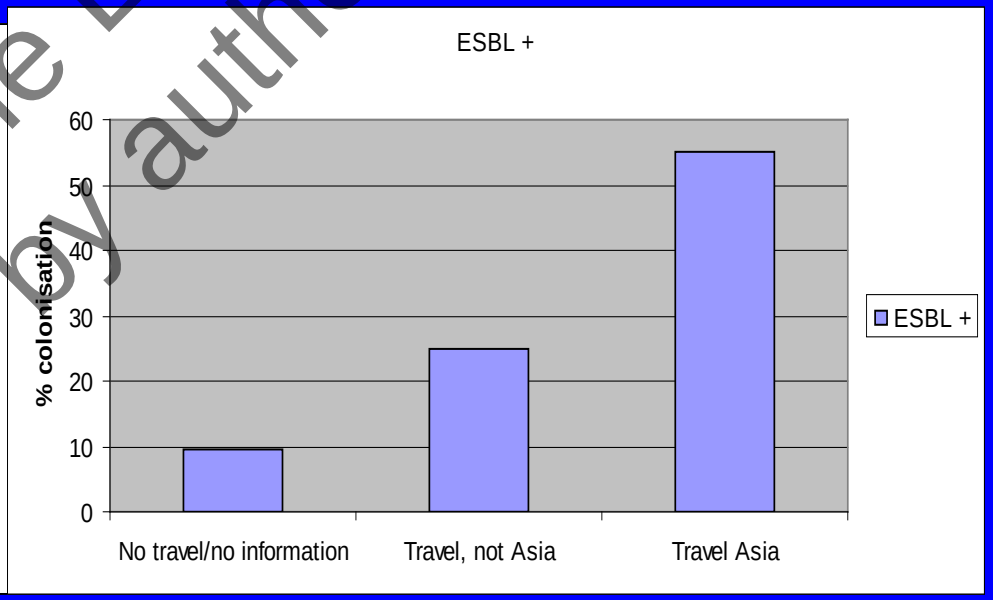
- Stool samples collected on admission from patients admitted with diarrhea
- 16% ESBL producers; 6% CTX-M
  - 90% previous hospitalization or nursing home
- 63% of all CTX-M strains were E. coli ST131

JAC 2010

Norway

- Stool submitted for Entero-pathogens were screened for ESBL



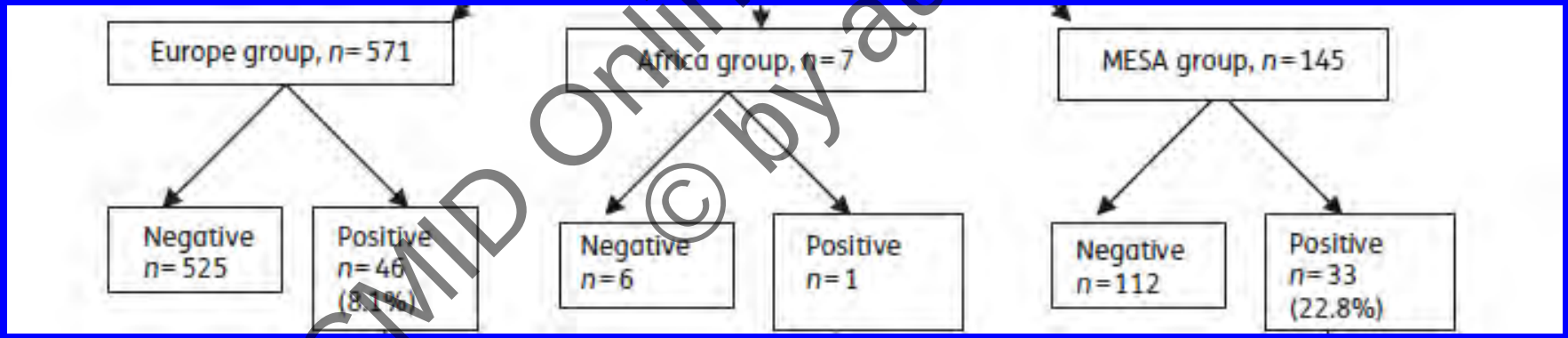


Jorgensen S. ECCMID 2012

High community faecal carriage rates of CTX-M ESBL-producing *Escherichia coli* in a specific population group in Birmingham, UK

Nimal H. Wickramasinghe[1], Li Xu[2,3], Andrew Eustace[2], Sahida Shabir[2], Tranprit Saluja[4] and Peter M. Hawkey[2,3]*

Stool submitted for other reason to the microlab
Origin determined by name using software OriginsInfo



JAC 2012

ESBL in the food chain

Fecal Carriage of Extended-Spectrum β-Lactamase-Producing *Enterobacteriaceae* in Swine and Cattle at Slaughter in Switzerland

N. GESER,[1] R. STEPHAN,[1] P. KUHNERT,[2] R. ZBINDEN,[3] U. KAEPPELI,[1] N. CERNELA,[1] AND H. HAECHLER[1]*

- 15.2% of the porcine and 17.1% of the bovine fecal samples yielded ESBL producers.
- Of the 21 isolated strains, 20 were Escherichia coli.
- High clonal diversity
- All had CTX-M enzymes
  - predominantly group 1

J food protection 2011

Cephalosporin resistance mechanisms in *Escherichia coli* isolated from raw chicken imported into the UK

Hiran Dhanji[1]*, Niamh M. Murphy[2], Michel Doumith[1], Sema Durmus[2], Susanne Surman Lee[2], Russell Hope[1], Neil Woodford[1] and David M. Livermore[1]

- Cephalosporin resistant E. coli found in 30% of batches of imported raw chicken
- No CTX-M 15 and no ST131 found
- Unrelated ESBLs to common ESBLs from humans in the UK

Table 1. Phylogenetic groups and major resistance mechanisms of 141 oxyimino-cephalosporin-resistant *E. coli* isolated from raw chicken

	Resistance gene(s) detected			
Phylogenetic group	CTX-M-2 (n=42)	CTX-M-8 (n=38)	CMY-type AmpC (n=59)	CTX-M-2+CMY-type AmpC (n=2)
A (n=21)	5	15	0	1
B1 (n=65)	14	9	42	0
B2 (n=5)	3	0	2	0
D (n=50)	20	14	15	1

JAC 2010

Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains

M. A. Leverstein-van Hall[1,2], C. M. Dierikx[3], J. Cohen Stuart[1], G. M. Voets[1], M. P. van den Munckhof[1], A. van Essen-Zandbergen[3], T. Platteel[1,4], A. C. Fluit[1], N. van de Sande-Bruinsma[2], J. Scharinga[1], M. J. M. Bonten[1,5] and D. J. Mevius[3,6]; on behalf of the national ESBL surveillance group*

- 94% of chicken meat-E. coli ESBL phenotype

Poultry-associated ESBL genes	Poultry $n = 35$	Poultry meat samples[a] $n = 81$	Human[a] $n = 409$
$bla_{CTX-M-1}$ (%)	49	49	24
bla_{TEM-52} (%)	29	26	6
bla_{SHV-12} (%)	0	16	4
bla_{SHV-2} (%)	11	4	0.4
$bla_{CTX-M-2}$ (%)	9	4	0.2
bla_{TEM-20} (%)	3	1	0
Total (%)	100	100	35

The number of isolates analysed by array among meat and human isolates was 81 and 409, respectively. The number of isolates analysed by sequencing among poultry, meat and human isolates was 35 (100%), 81 (100%) and 208 (51%), respectively.
[a]Percentages are extrapolations based on array results and sequence results. For calculation of the percentages see also Fig. 1. For example percentage of $bla_{CTX-M-1}$ in human isolates = 0.64 × 0.85 × 0.34 = 24%.

TABLE 2. The proportion of human extended-spectrum beta-lactamase (ESBL) -positive *Escherichia coli* isolates that is genetically related to ESBL-positive poultry isolates on the level of gene, plasmid and strain genotype[a]

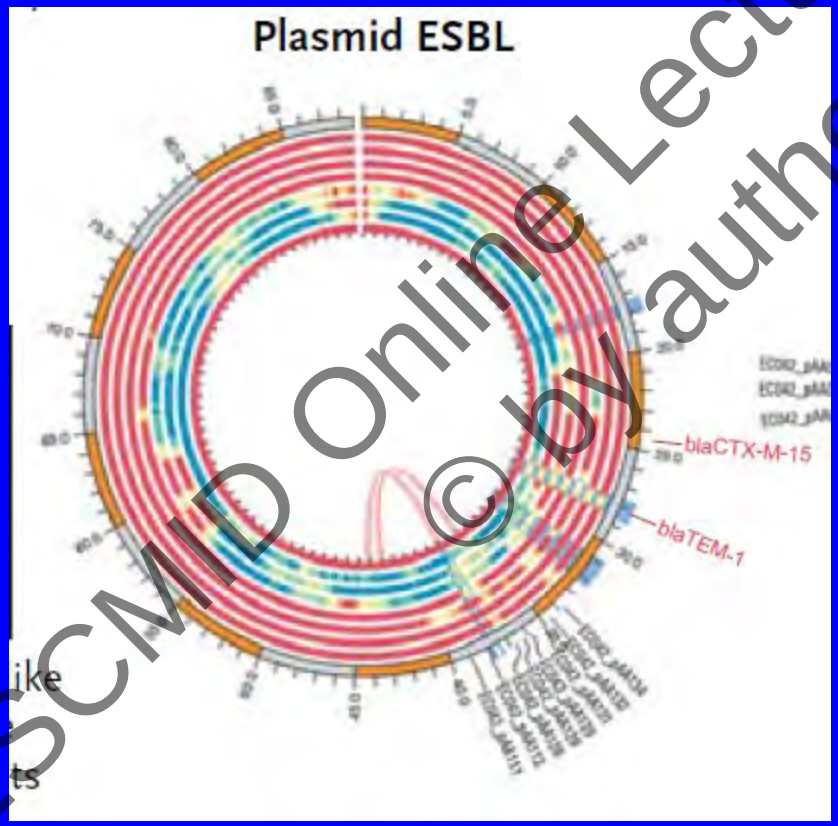
Level of genetic typing	% of human isolates with poultry associated genetic element[a]
ESBL genes ($bla_{CTX-M-1}$, bla_{TEM-52}, bla_{SHV-12}, bla_{SHV-2} and $bla_{CTX-M-2}$)	35% (see Table 1)
$bla_{CTX-M-1}$ and bla_{TEM-52} genes	30% (23.7% $bla_{CTX-M-1}$; 6.2% bla_{TEM-52})
$bla_{CTX-M-1}$ and bla_{TEM-52} genes on IncI1 plasmid	20% (14.2% $bla_{CTX-M-1}$; 6.2% bla_{TEM-52})
$bla_{CTX-M-1}$ and bla_{TEM-52} genes on IncI plasmid belonging to complex CC7 or CC3 and CC5 resp.	19% (12.6% $bla_{CTX-M-1}$; 6.2% bla_{TEM-52})
$bla_{CTX-M-1}$ and bla_{TEM-52} genes on IncI plasmid belonging to complex CC7 or CC3 and CC5 resp. in a poultry-associated MLST strain (ST10, ST58 or ST117)	11% (9.5% $bla_{CTX-M-1}$; 2.0% bla_{TEM-52})

MLST, multi-locus sequence typing.
For example percentage of bla_{TEM-52} genes on IncI1 plasmid belonging to complex CC5 in to poultry identical MLST strains = 0.84 (row A) × 0.09 (row B) × 0.82 (row C) × 1 (row D) × 1 (row E) × 0.33 (row F) = 2.0%.
[a]Percentages are extrapolations based on array results, sequence results and results of plasmid characterization and strain typing. For calculation of the percentages see Fig. 1.

CMI 2011

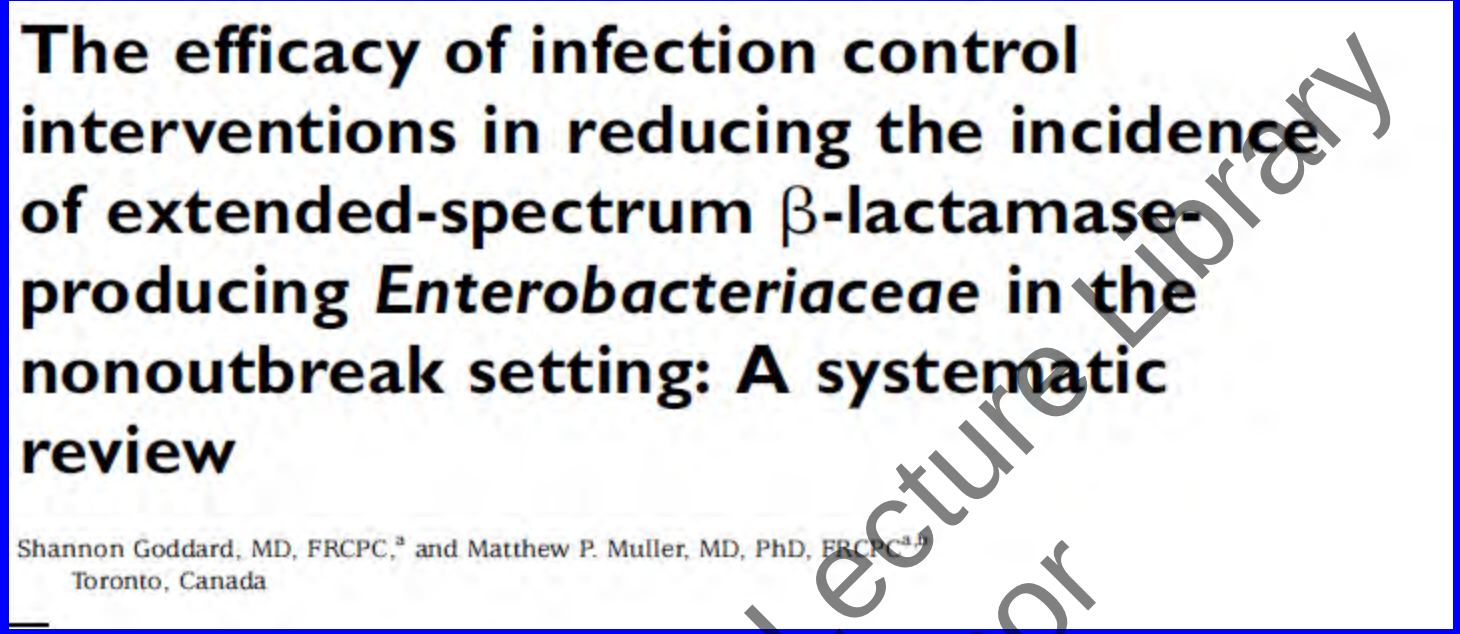
ORIGINAL ARTICLE

Origins of the *E. coli* Strain Causing an Outbreak of Hemolytic–Uremic Syndrome in Germany



Rasko DA. NEJM 2011

Transmission and control of ESBL



The efficacy of infection control interventions in reducing the incidence of extended-spectrum β-lactamase-producing *Enterobacteriaceae* in the nonoutbreak setting: A systematic review

Shannon Goddard, MD, FRCPC,[a] and Matthew P. Muller, MD, PhD, FRCPC[a,b]
Toronto, Canada

- No high quality studies identified
- No conclusions can be drawn
- Recommendation to fund prospective controlled studies

AJIC 2011

Orally administered colistin leads to colistin-resistant intestinal flora and fails to prevent faecal colonisation with extended-spectrum β-lactamase-producing enterobacteria in hospitalised newborns

Volker Strenger[a,*], Tanja Gschliesser[a], Andrea Grisold[b], Gernot Zarfel[b], Gebhard Feierl[b], Lilian Masoud[b], Martin Hoenigl[c], Bernhard Resch[a], Wilhelm Müller[a], Berndt Urlesberger[a]

- 18 month (2005-2007) NICU in Graz Austria
- Routine SDD for NEC prophylaxis - oral gentamicin or colistin
- ESBL carriage 4.5% of neonates
  - ESBL transmission occurred similarly under both regimens
  - Colistin resistant Klebsiella spp. higher among colistin recepients
  - Colistin resistance emerged within susceptible clones

Int J Antimicrob Agents 2011

E. Coli ESBL transmission in hospitals

- ICU study in the US
  - 1806 patients admissions
  - 74 ESBL on admission
  - 23 detection during ICU stay
    - molecular typing suggested only 3 transmissions
- Study in Basel, Switzerland
  - 99 patients with ESBL detected (index patients)
  - 133 patients who had close contact (average 4.3D) were screened
  - 7 (5.4%) positive with similar ESBL type
  - only 2 (1.7%) similar PFGE
- MOSAR – rehabilitation center
  - 492 patients admitted
  - 52 ESBL E. coli on admission
  - 59 detected during stay with similar PFGE and enzyme
  - average stay at detection 19d

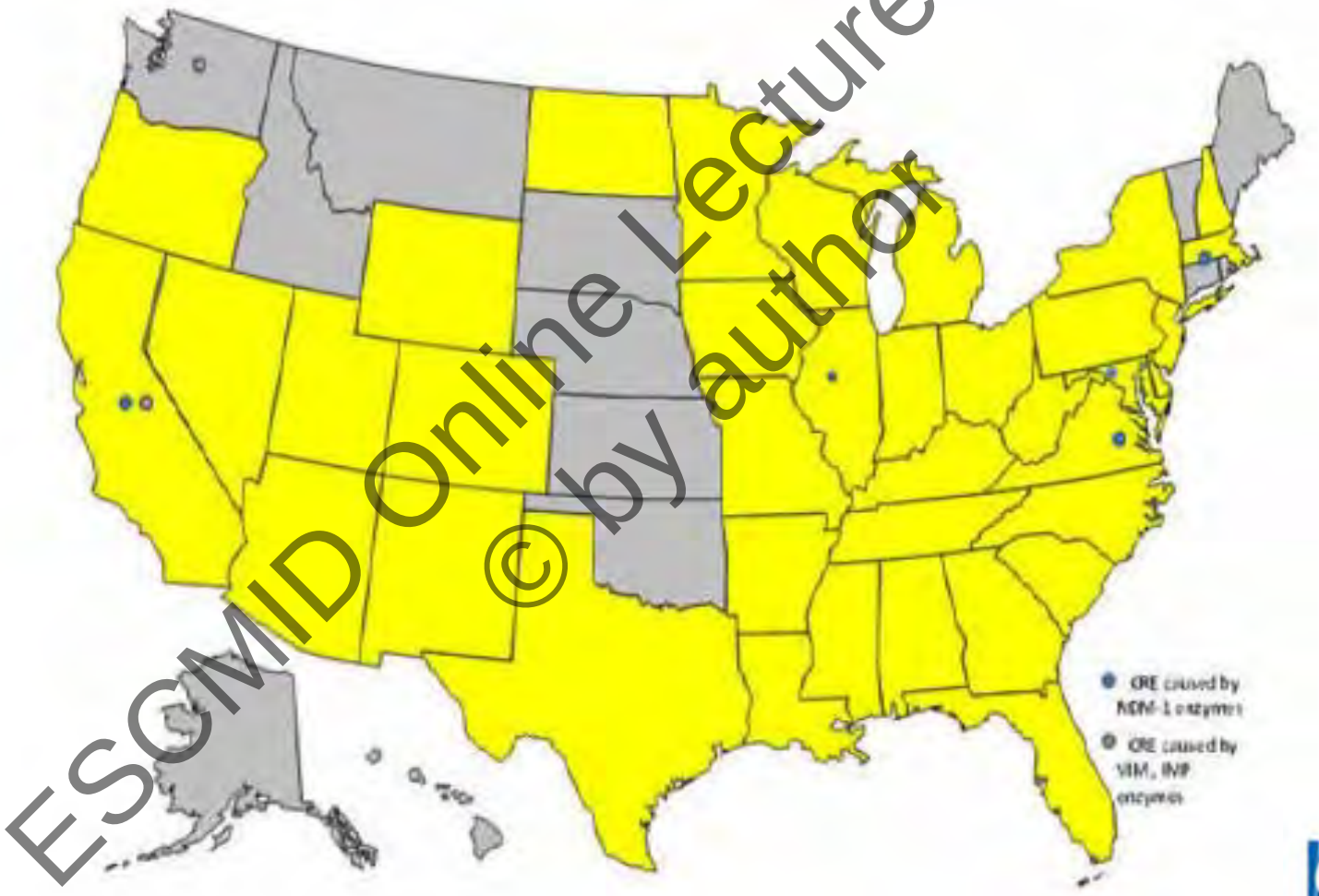
Harris A. AJIC 2007; Tschudin-Sutter S. ECCMID 2012; Adler A. Submitted

ESBLs

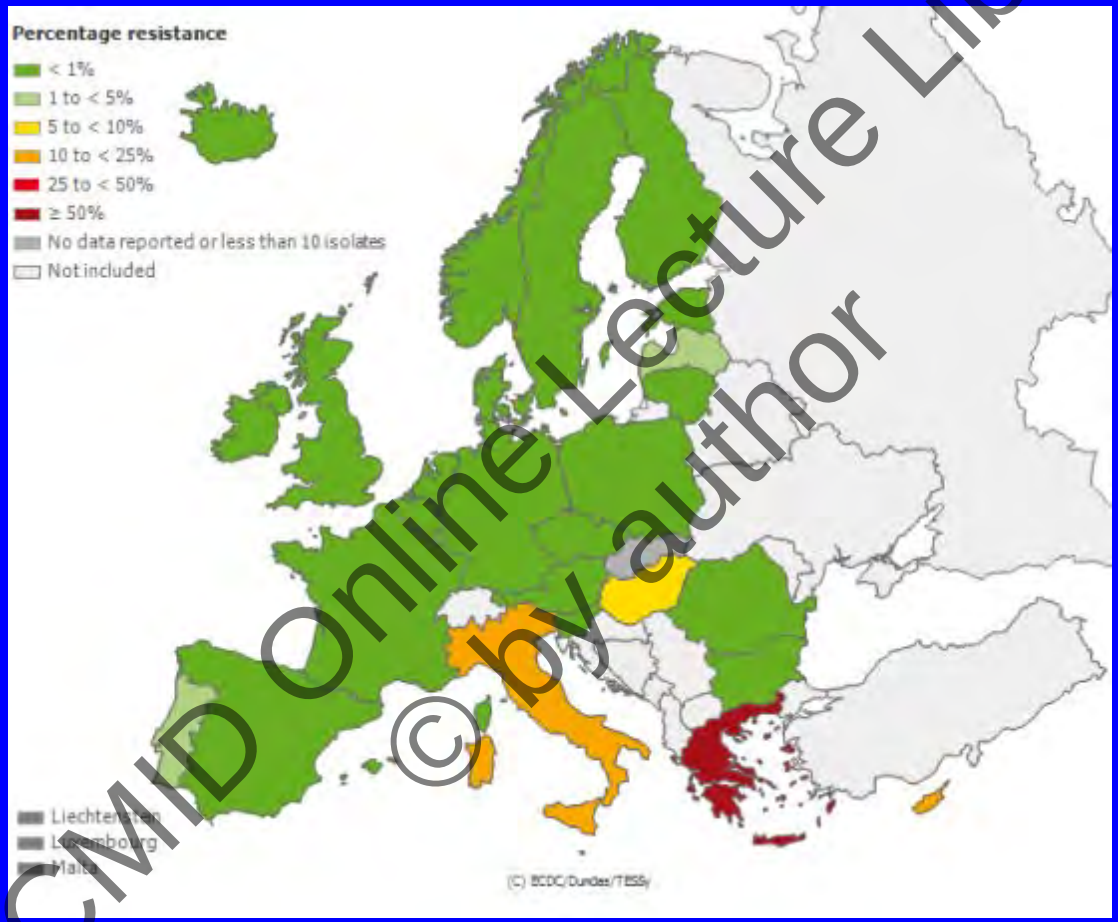
- Continue to rise, becoming the most common MDR cause for serious infections
- Common in the community
- Enters via the food chain, immigration and tourism
- Transmission in hospitals of ESBL-E. coli is variable
- Effectiveness and usefulness of interventions to limit the spread are not well defined and should be individualized to the local epidemiology

KPC

2011 Location of Carbapenem-Resistant *Enterobacteriaceae* (CRE) caused by KPC enzyme; CRE caused by other enzymes noted



Carbapenem resistant Klebsiella 2010



1200 episodes of bacteremia reported

Containment of a Country-wide Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* in Israeli Hospitals via a Nationally Implemented Intervention

Mitchell J. Schwaber,[1] Boaz Lev,[2] Avi Israeli,[2] Ester Solter,[1] Gill Smollan,[1] Bina Rubinovitch,[1] Itamar Shalit,[1] Yehuda Carmeli,[1] and the Israel Carbapenem-Resistant Enterobacteriaceae Working Group[a]

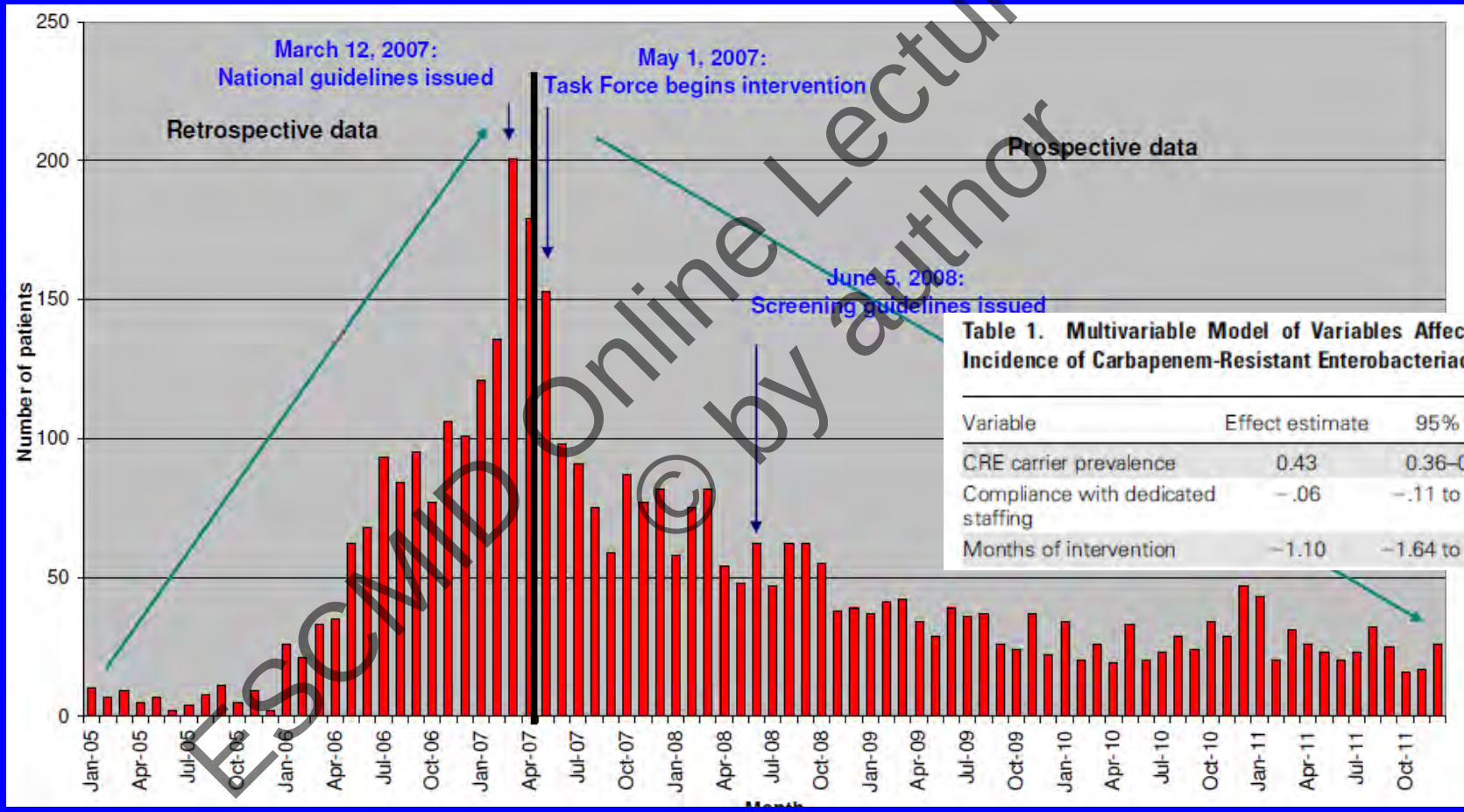


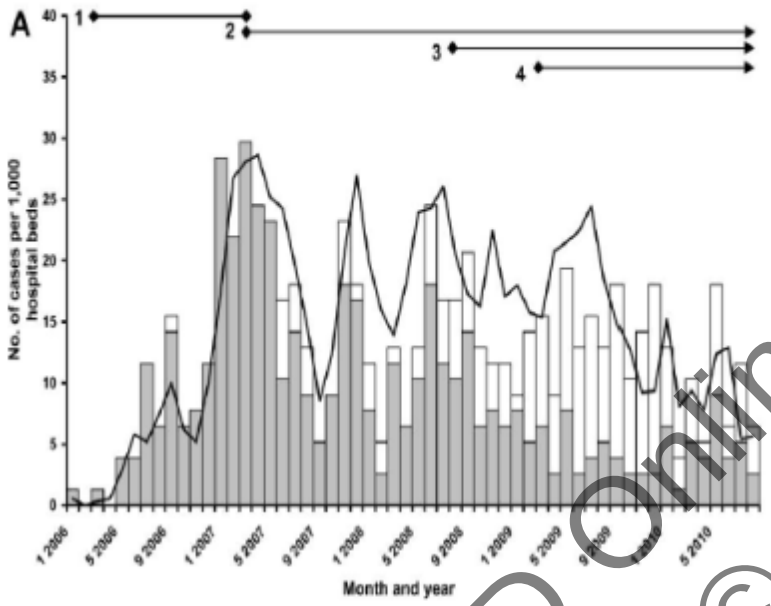
Table 1. Multivariable Model of Variables Affecting Monthly Incidence of Carbapenem-Resistant Enterobacteriaceae (CRE)

Variable	Effect estimate	95% CI	*P*
CRE carrier prevalence	0.43	0.36–0.50	<.001
Compliance with dedicated staffing	−.06	−.11 to −.01	0.02
Months of intervention	−1.10	−1.64 to −0.56	<.001

CID 2011

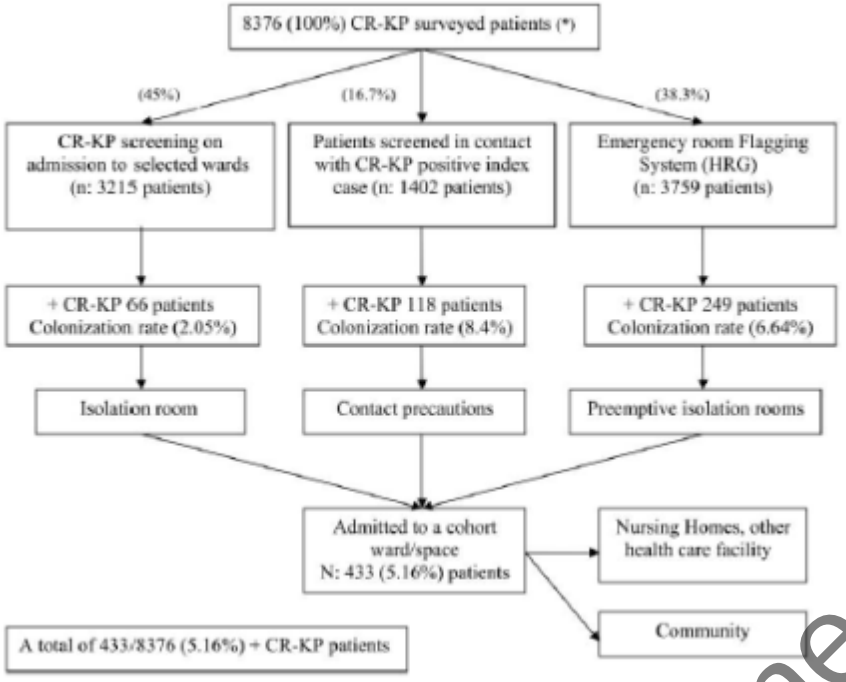
TABLE 1. Interventions Undertaken to Curtail the Epidemic Spread of Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP)

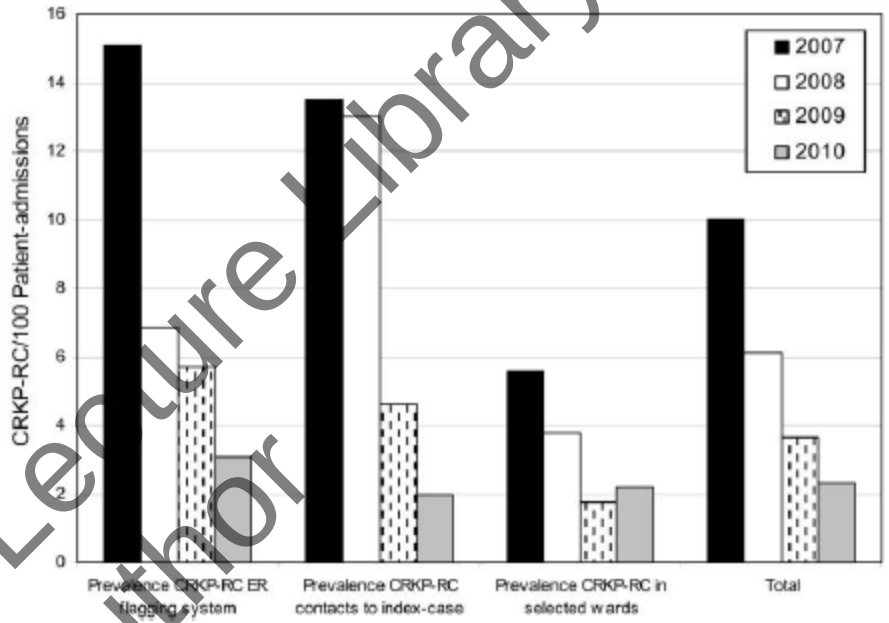
Intervention	Description	Date begun
Intervention 1	Single-room isolation and contact precautions	March 2006
Intervention 2	Cohorting of patients and nursing staff, screening of patients in the same room as newly identified carriers of CRKP ("snow ball" active surveillance), and local protocol for continued cohorting of returning patients	March 2007
Intervention 3	Weekly active surveillance in the intensive care unit	August 2008
Intervention 4	Active surveillance of patients on admission to the emergency department	March 2009

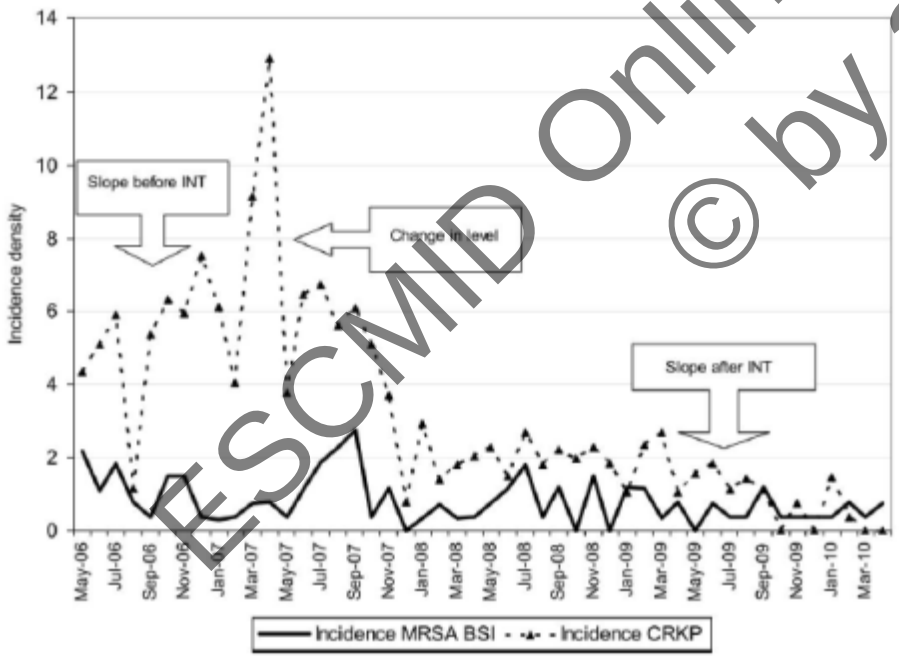


Intervention (period)	Incidence: No. of cases per 1,000 hospital beds, Mean	Median	Slope[a]	P[b]
Intervention 1 (Mar 2006–Mar 2007)	8.4	6.45	1.9	
Intervention 2 (Apr 2007–Aug 2008)	13.4	11.6	−0.7	<.001
Intervention 3 (Sep 2008–Mar 2009)	8.3	7.7	−0.8	.76
Intervention 4 (Apr 2009–Aug 2010)	4.3	3.8	−0.008	.27

Cohen M. ICHE 2011







Borer A. ICHE 2011

Potential Role of Active Surveillance in the Control of a Hospital-Wide Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* Infection

Active surveillance of high risk population and high risk areas, combined with contact isolation led to dramatic decrease in clinical cases

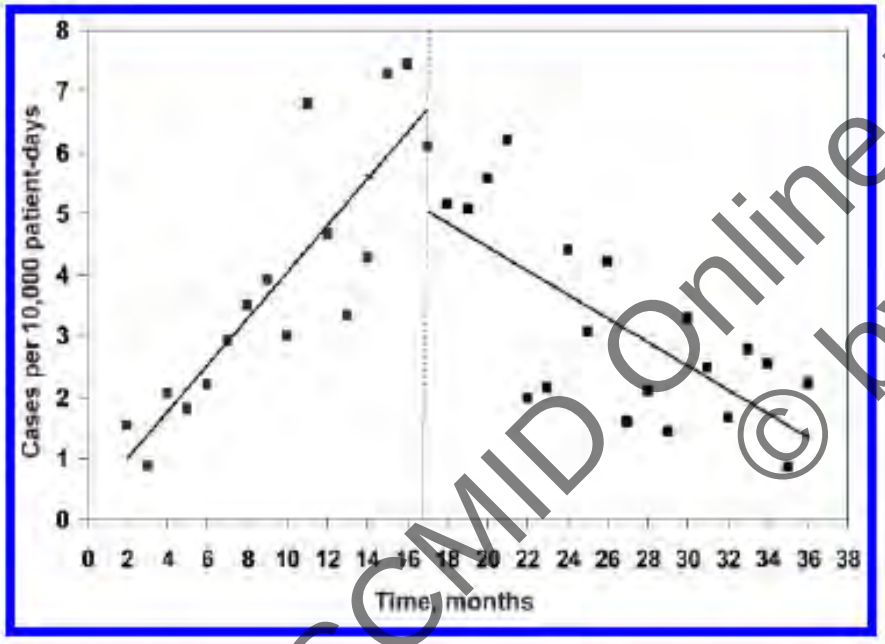


FIGURE 1. Scatterplots showing the change in the number of clinical cases of infection with carbapenem-resistant *Klebsiella pneumoniae* per 10,000 patient-days, before and after the intervention, implemented in month 17. Solid lines represent the linear regression fits across all cases.

>700 surveillance cultures/month
4% positivity on admission

Ben David D. et al. ICHE 2011

KPC

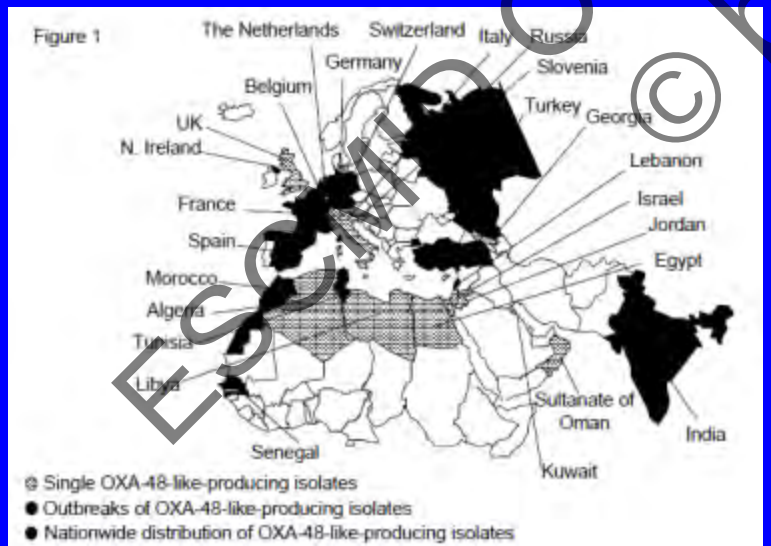
- Rapidly spreads within healthcare facilities
- No community transmission
- Success of multifaceted interventions which include
  - Rapid identification of carriers by flagging, information transfer, and surveillance of high risk population
  - Strict isolation with dedicated staff
  - Regional coordination and supervision
  - Continuous root-cause analysis

NDM

- Wide spread in India and Pakistan 2005-2010 went unnoticed
  - Detected when causing outbreaks in Europe traced to visitors to India and Pakistan
- Spread very likely by food and water
- 30-70% of water sources sampled around New Delhi found contaminated with NDM
- It is estimated that >100 millions Indians carry NDM

OXA-48

- Detected in mid 2000's in Turkey
  - Single plasmid spread
- Wide spread around the Mediterranean basin
  - epidemiology not well characterized but likely mainly community transmission
- Hospital outbreaks in Europe



Poirel L. JAC 2012 in press

Control of carbapenamses

- In Europe community spread is limited
- Importation by tourism may be important
- Prevention of spread in hospital is feasible
  - Requires structured multifaceted regional action
- In some parts of the world, carbapenamses are widely spreading in the community
  - Improved water system, sanitation and hygiene are likely the most important interventions