Multicenter Approach to Control Multidrug-Resistant Organisms

Yehuda Carmeli, M.D., M.P.H.
Division of Epidemiology,
Tel Aviv Sourasky Medical Center
& The Israeli Center for Antibiotic Resistance
Tel Aviv, Israel

ESCMID Online Lecture Library
© by author

Why Multicenter?

- Institutions in the same region share patients and organisms
- MDRO – can be transferred between institution
- Failure of one center may lead to reintroduction via patient transfer to centers that have succeeded in containment
- If interventions are not coordinated two adjacent hospitals may choose different target organisms and likely both will fail due to colonized patient transfer

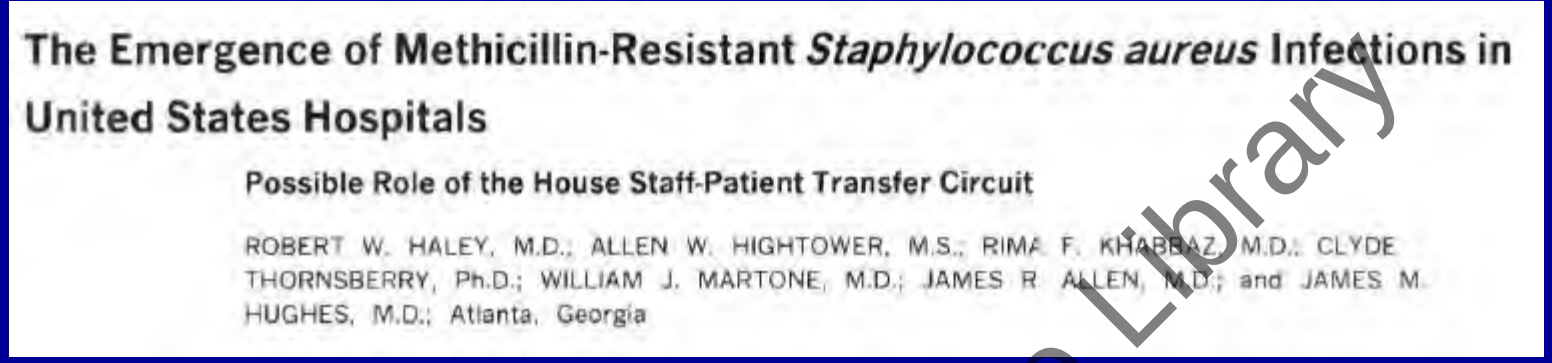
ESCMID Online Lecture Library
©by author

Inter-hospital transfer

- Inter-hospital transfer of patients was recognized as an important mode by which resistant organism spread
  - Late 1970's interstate spread of an single phage type MRSA strain traced to transfer of patient from affected hospital to another

Infection Control 1980

ESCMID Online Lecture Library
© by author



The Emergence of Methicillin-Resistant *Staphylococcus aureus* Infections in United States Hospitals

Possible Role of the House Staff-Patient Transfer Circuit

ROBERT W. HALEY, M.D.; ALLEN W. HIGHTOWER, M.S.; RIMA F. KHABBAZ, M.D.; CLYDE THORNSBERRY, Ph.D.; WILLIAM J. MARTONE, M.D.; JAMES R. ALLEN, M.D.; and JAMES M. HUGHES, M.D.; Atlanta, Georgia

- Analyzing the US outbreaks in the 70's
  - When an index patient was traced - it was a patient transfered from an affected hospital or nursing home
- Large teaching hospital more often affected by transfer
- Smaller hospitals may be affected by transfer but establishment is less likely

ANNALS of Internal Medicine
SEPTEMBER 1982 • VOLUME 97 • NUMBER 3

ESCMID Online Lecture Library ©by author

Citywide Clonal Outbreak of Multiresistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in Brooklyn, NY

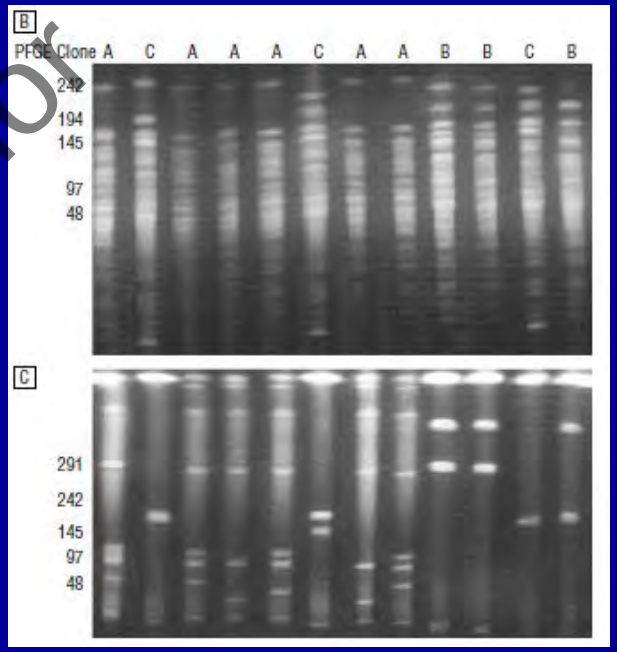
The Preantibiotic Era Has Returned

David Landman, MD; John M. Quale, MD; David Mayorga, MD; Adedeyo Adedeji, MD; Kalyani Vangala, MD; Jayshree Ravishankar, MD; Carlos Flores, MD; Steven Brooks, PhD

Table 4. Automated Ribotyping Results for 136 Imipenem-Resistant Isolates of *Pseudomonas aeruginosa*

Ribotype No.	No. (%) of Isolates*	No. of Hospitals†
1	26 (19)	12
2	20 (15)	10
3	17 (12)	5
4	6 (4)	4
5	5 (4)	3
6	5 (4)	3
7	4 (3)	4
8	4 (3)	3
9	4 (3)	2
10	3 (2)	3
11	3 (2)	2
12	2 (1)	2
13	2 (1)	1
14	2 (1)	1
15-47	33 (24)	1 Each

Several imipenem R PA clones affecting multiple hospitals



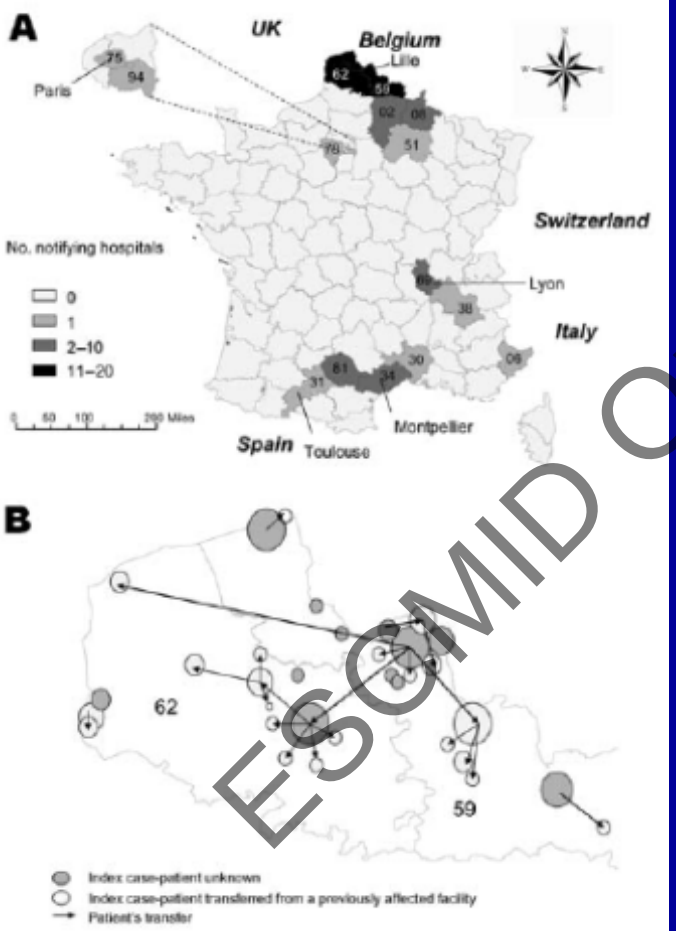
3 Acinetobacter clones affecting Multiple hospitals

Arch Intern Med 2002

ESCMID Online Lecture Library © by author

VEB-1 Extended-Spectrum β-Lactamase–producing *Acinetobacter baumannii*, France[1]

Thierry Naas,*2 Bruno Coignard,†2 Anne Carbonne‡, Karine Blanckaert,‡ Odile Bajolet,§ Claude Bernet,¶ Xavier Verdeil,# Pascal Astagneau,‡ Jean-Claude Desenclos,† and Patrice Nordmann,* on behalf of the French Nosocomial Infection Early Warning, Investigation and Surveillance Network



Within 15 months 53 hospitals:
275 clonally related VEB producing
A. baumannii
Inter-hospital spread associated with patients transfer
Regional intervention:
Recommendation for surveillance
Contact precaution and ABX use
Reporting to health authorities
Information exchange between hospitals
Limiting patient transfer

EID 2006

ESCMID Online Lecture Library
© by author

Quantifying Interhospital Patient Sharing as a Mechanism for Infectious Disease Spread

- Orange County 2005 data (32 hospitals)
- 320,000 admissions
- 29% at least two admissions
  - median interval 53d
  - 75% more than 1 hospital
  - 94% indirect (not same day)
- 6 hospitals to readmitted pts to >50% of the hospitals
- 28 hospitals shared at least one patient

Huang S. ICHE 2010

ESCMID Online Lecture Library © by author

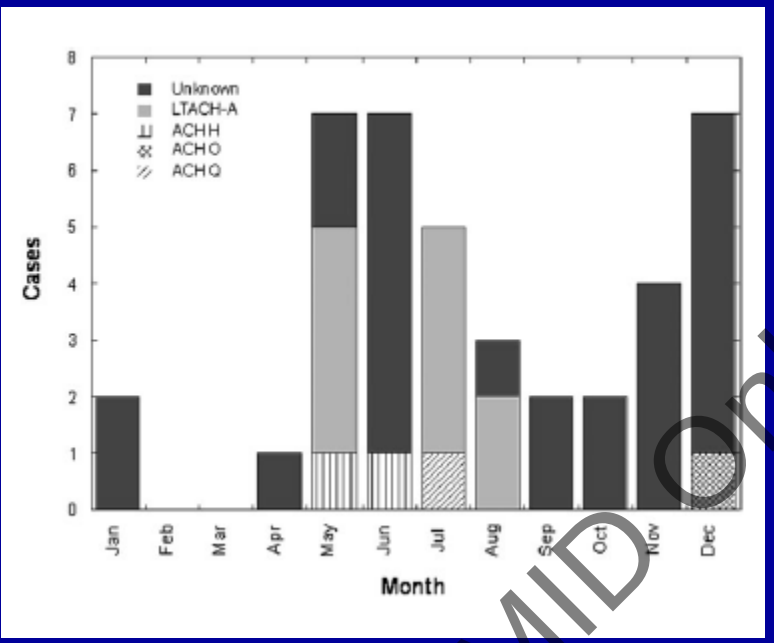
Analyzing C. difficile patients transfer

- Within 12 weeks
- 25% readmitted
- 41% of readmissions to another hospital
- 30% direct (same day) transfer

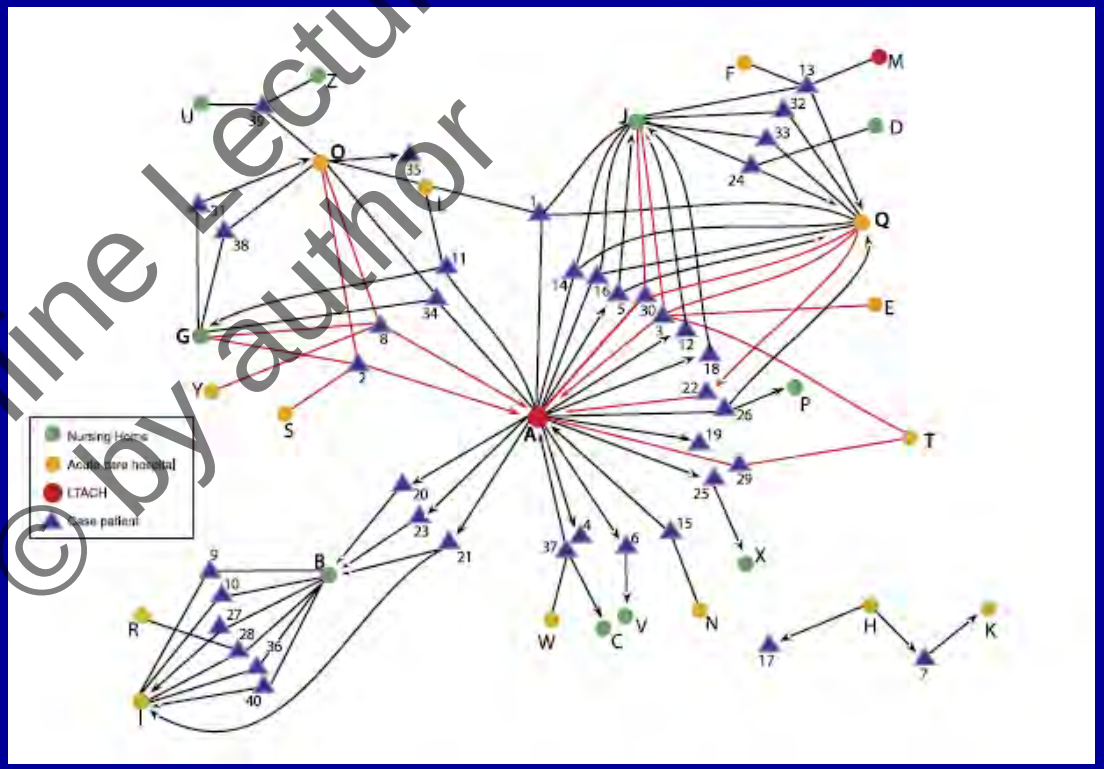
ESCMID Online Lecture Library
© by author

Emergence and Rapid Regional Spread of *Klebsiella pneumoniae* Carbapenemase–Producing *Enterobacteriaceae*

Sarah Y. Won,[1,2] L. Silvia Munoz-Price,[3] Karen Lolans,[4] Bala Hota,[4,5] Robert A. Weinstein,[4,5] and Mary K. Hayden[4] for the Centers for Disease Control and Prevention Epicenter Program



Rapid spread various institutions



Network graph illustrate the central role of LTAC (red)

CID 2011

ESCMID Online Lecture Library
© by author

CONTROL OF VANCOMYCIN-RESISTANT ENTEROCOCCUS IN HEALTH CARE FACILITIES IN A REGION

BELINDA E. OSTROWSKY, M.D., M.P.H., WILLIAM E. TRICK, M.D., ANNETTE H. SOHN, M.D., STEPHEN B. QUIRK, M.P.P., STACEY HOLT, M.M.SC., LORETTA A. CARSON, M.S., BERTHA C. HILL, B.S., MATTHEW J. ARDUINO, PH.D., MATTHEW J. KUEHNERT, M.D., AND WILLIAM R. JARVIS, M.D.

- Mid 90's 63 cases of VRE reported to the CDC from Siouxland region (Iowa, S. Dakota, Nebraska)
  - 135,000 population
  - 4 acute care facilities
  - 28 LTCFs

ESCMID Online Lecture Library © by author

NEJM 2001

TABLE 1. GUIDELINES FOR THE CARE OF PATIENTS WITH VANCOMYCIN-RESISTANT ENTEROCOCCI WHO ARE IN ACUTE CARE AND LONG-TERM CARE FACILITIES.*

INTERVENTION	ACUTE CARE FACILITY	LONG-TERM CARE FACILITY
Screening on admission	High risk population	High risk population
Room assignment	Private or with other carriers	Private or with other carriers Allow exceptions
education		
communication	Flagging carriers	Flagging carriers

TABLE 3. PREVALENCE OF COLONIZATION WITH VANCOMYCIN-RESISTANT ENTEROCOCCI AMONG PATIENTS OR RESIDENTS OF 30 ACUTE CARE AND LONG-TERM CARE FACILITIES IN THE SIOUXLAND REGION IN JULY AND AUGUST 1997, OCTOBER 1998, AND OCTOBER 1999.*

TYPE OF FACILITY	COLONIZATION WITH VRE			1998 VERSUS 1997		1999 VERSUS 1998		1999 VERSUS 1997†	
	1997	1998	1999	RELATIVE RISK (95% CI)	P VALUE	RELATIVE RISK (95% CI)	P VALUE	RELATIVE RISK (95% CI)	P VALUE
	no. of patients (%)								
All	40 (2.2)	26 (1.4)	9 (0.5)	0.6 (0.4–1.1)	0.08	0.4 (0.2–0.8)	0.005	0.2 (0.1–0.5)	<0.001
Acute care	10 (6.6)	9 (5.5)	0	0.8 (0.4–2.0)	0.67	0	0.002	0	<0.001
Long-term care	30 (1.7)	17 (1.0)	9 (0.5)	0.6 (0.3–1.0)	0.05	0.6 (0.2–1.3)	0.14	0.3 (0.2–0.7)	0.001

ESCMID Online Lecture Library © by author

NEJM 2001

Persistent colonization and the spread of antibiotic resistance in nosocomial pathogens: Resistance is a regional problem

David L. Smith*†‡, Jonathan Dushoff§, Eli N. Perencevich¶, Anthony D. Harris¶, and Simon A. Levin‖

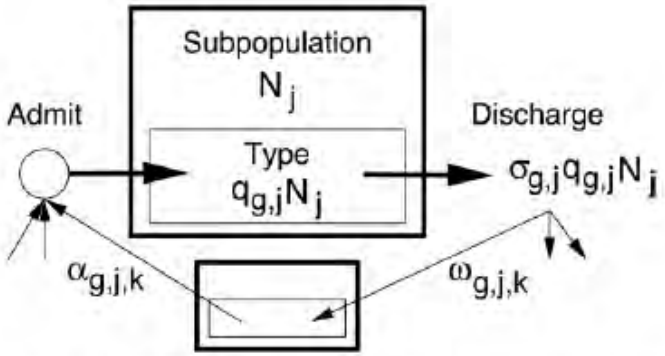
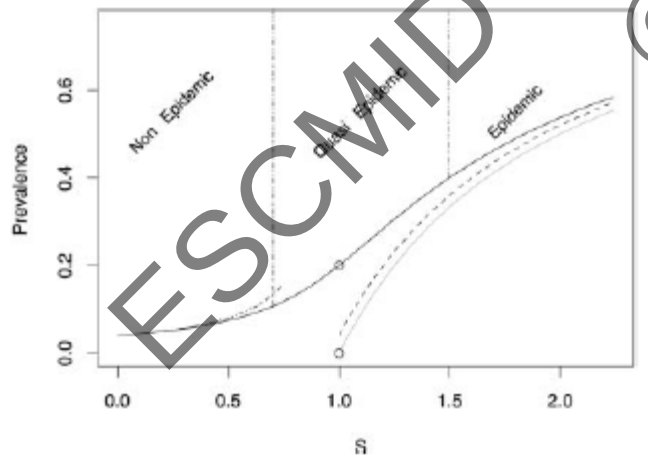


Fig. 1. A diagram of the general model. Individuals move among subpopulations, such as hospitals, LTCFs, and the community. The subpopulation is assumed to be well mixed with respect to the transmission of ARB. The population is also classified by group, based on some epidemiologically important difference. The size of the population at each location, N_j, and the proportion of each group, $q_{g,j}$, are constant by assumption. The admission rate is equal to the discharge rate, $\sigma_{g,j}q_{g,j}N_j$. The portion of discharged individuals from subpopulation j that move to k is $\omega_{g,j,k}$. The portion of admitted individuals to subpopulation j that are from k is



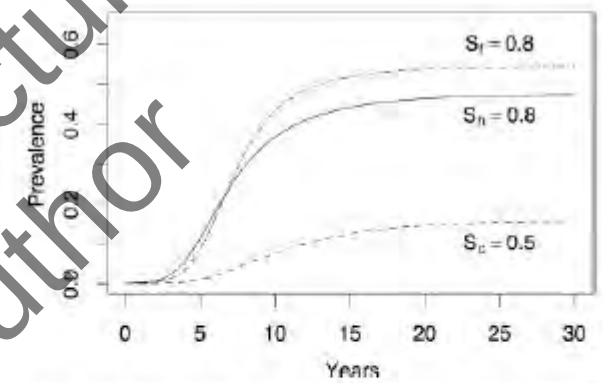
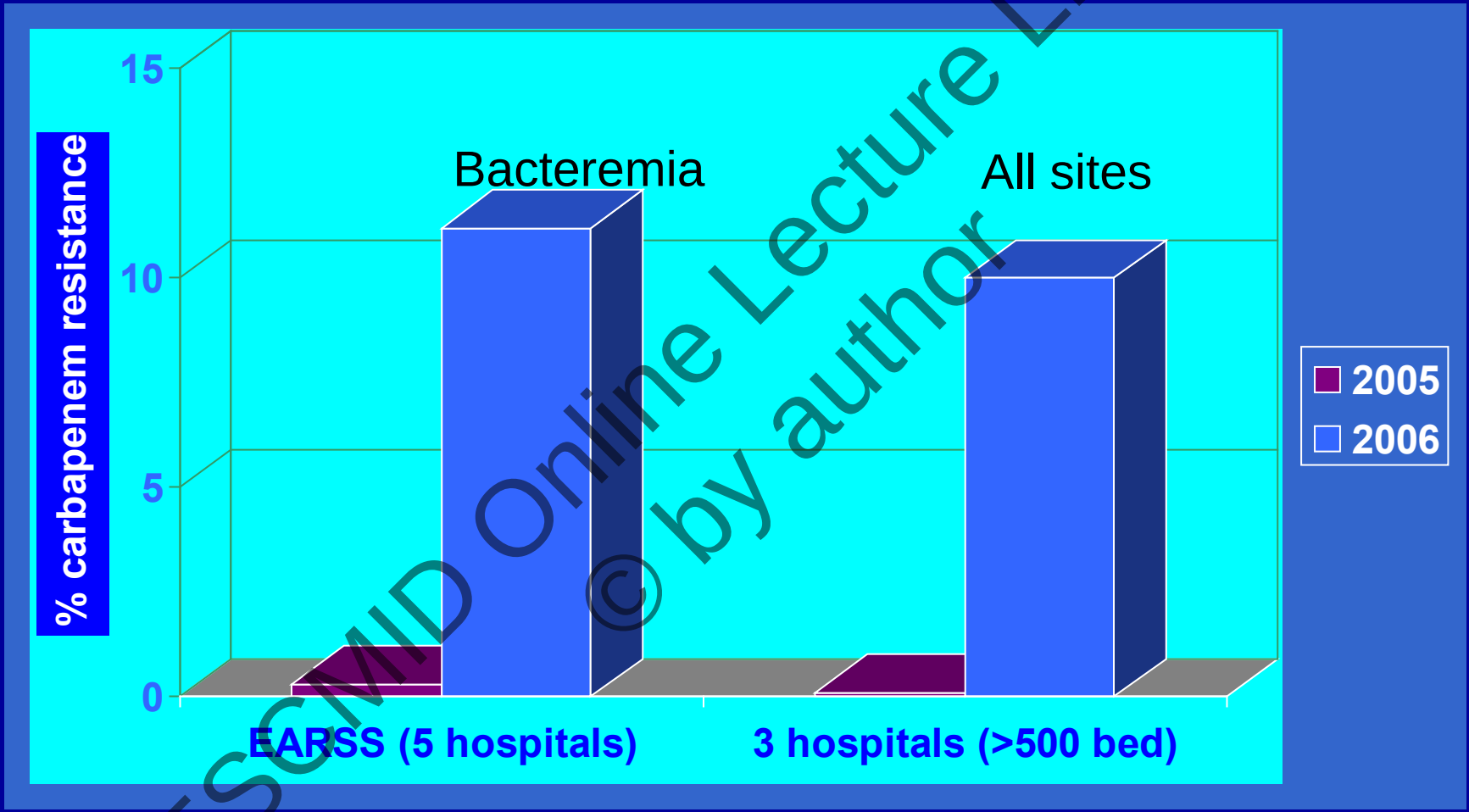


Fig. 5. LTCFs (dashed–dotted trace) may be the most important type of institution in health-care networks because LTCF patients are frequently hospitalized and receive a similar level and type of care as hospitalized patients. Single-stay reproductive numbers for the hospital and community are identical to those in Figs. 3*a* and 4. In this simulation, the single-stay reproductive numbers in the LTCF and hospital are identical, but the closed-population reproductive rate for the LTCF is much lower than the hospital because of the longer LOS. Compared with earlier simulations, prevalence increases faster and reaches a higher equilibrium in hospitals (solid trace) and the community (dashed trace).

ESCMID Online Lecture Library
© by author

PNAS 2004

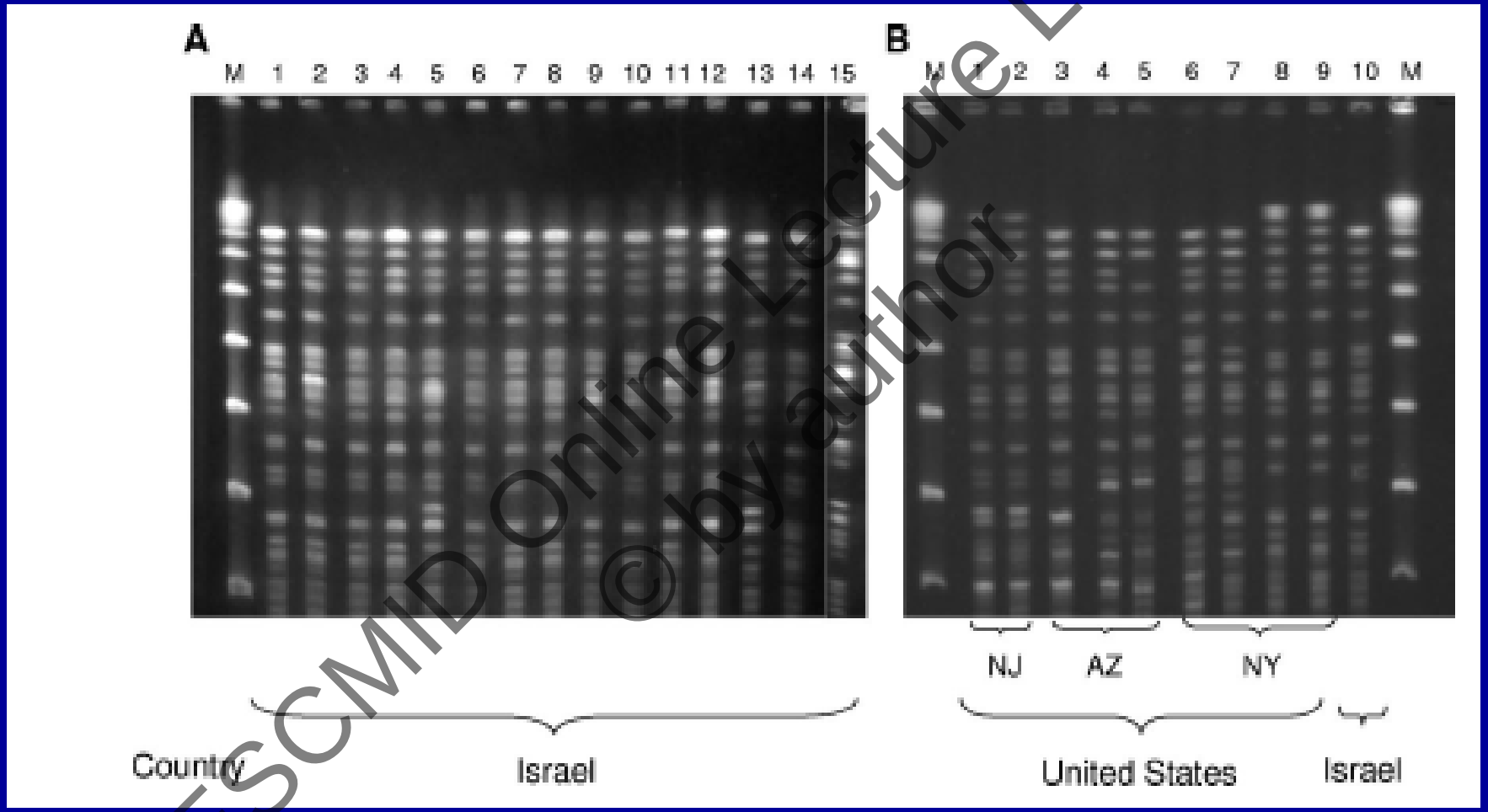
Nationwide emergence of carbapenem-resistant Kpn - Israel



ESCMID Online Lecture Library
© by author

Incidence: 60-100 cases per 1,000 hospital beds/year
Total number of cases: ~1000 (per 7 million population) mortality 44%

Genetic relatedness to US outbreak strains

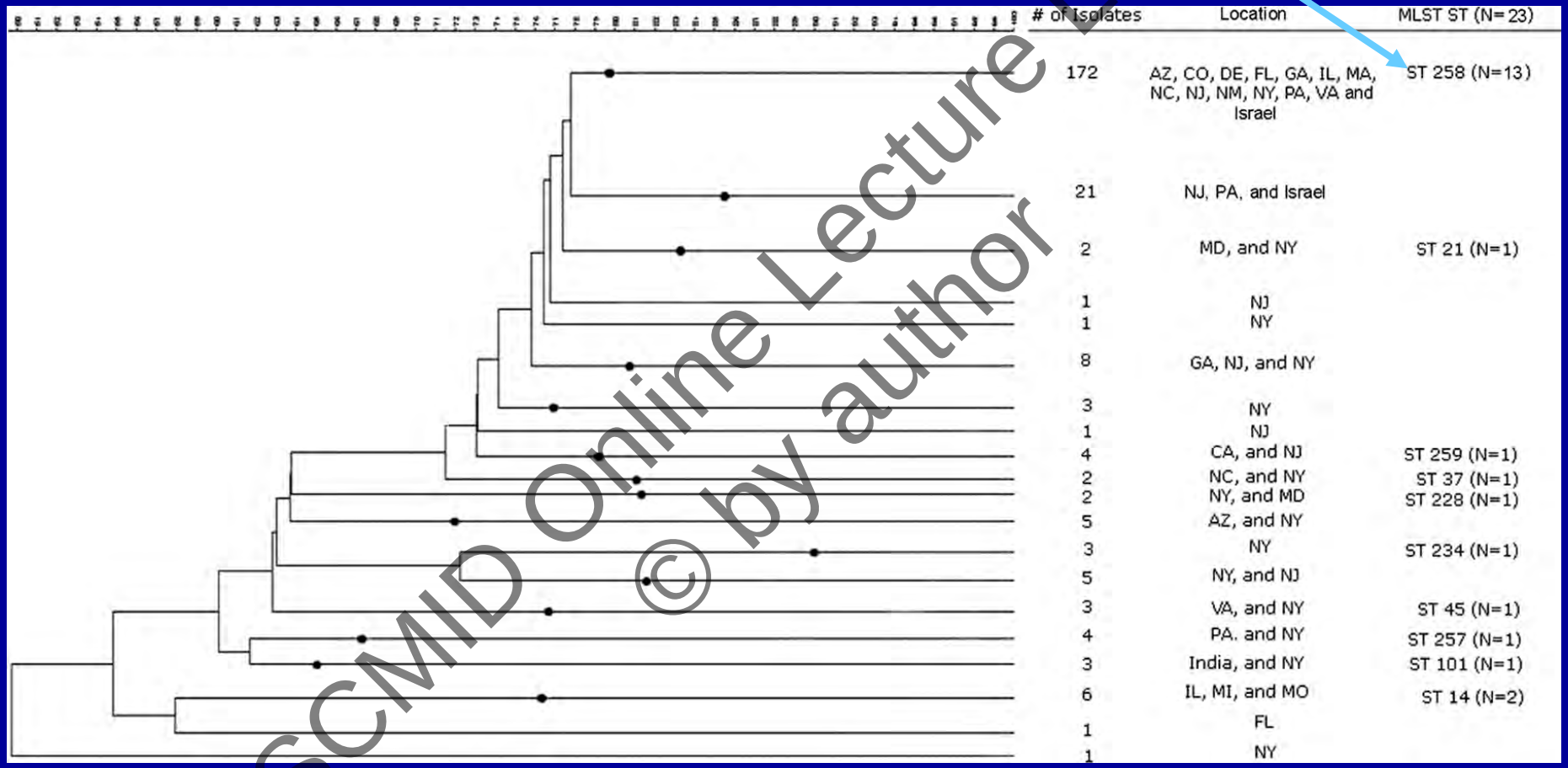


ESCMID Online Lecture Library
© by author

Navon-Venezia S. AAC 2009

Dendrogram of the CDC's KPC-producing *K. pneumoniae* PFGE database (n = 248)

Predominance of a single clone - ST258

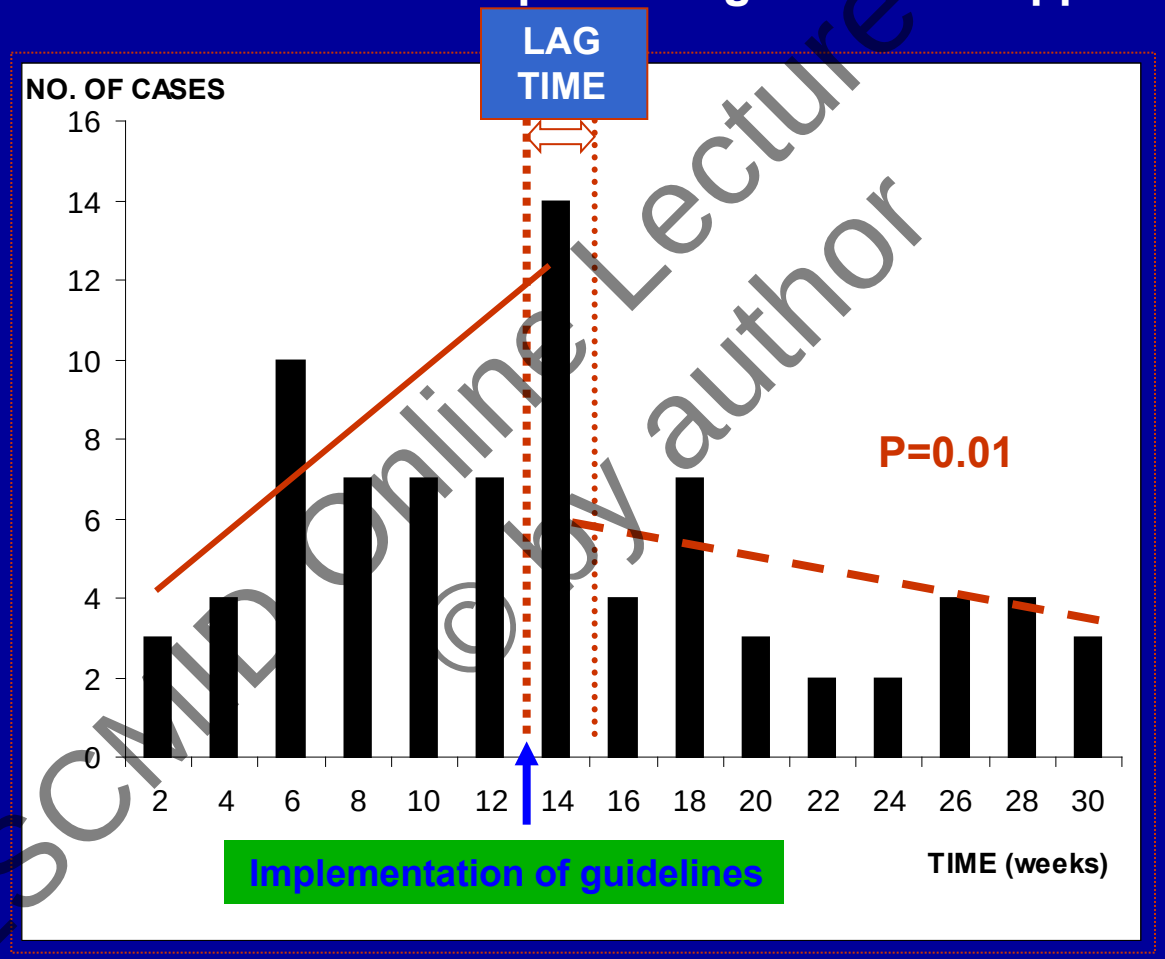


ESCMID Online Lecture Library © by author

Kitchel et al, AAC, 2009

One hospital's experience –moving from single room contact to cohorting and dedicated staff

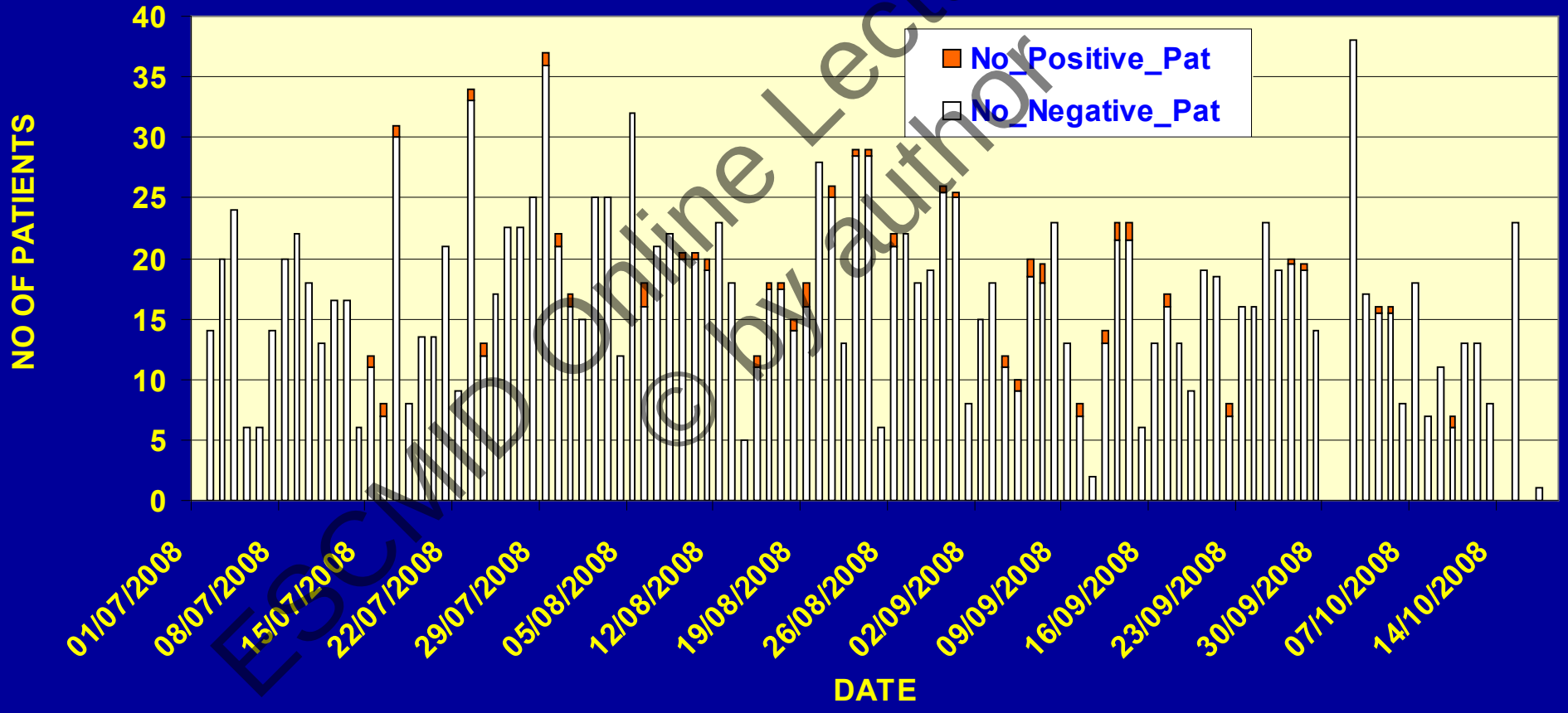
Incidence of KPC-producing *Klebsiella* spp.



ESCMID Online Lecture Library
© by author

Schechner, unpublished

Targeted screening for CRE upon admission



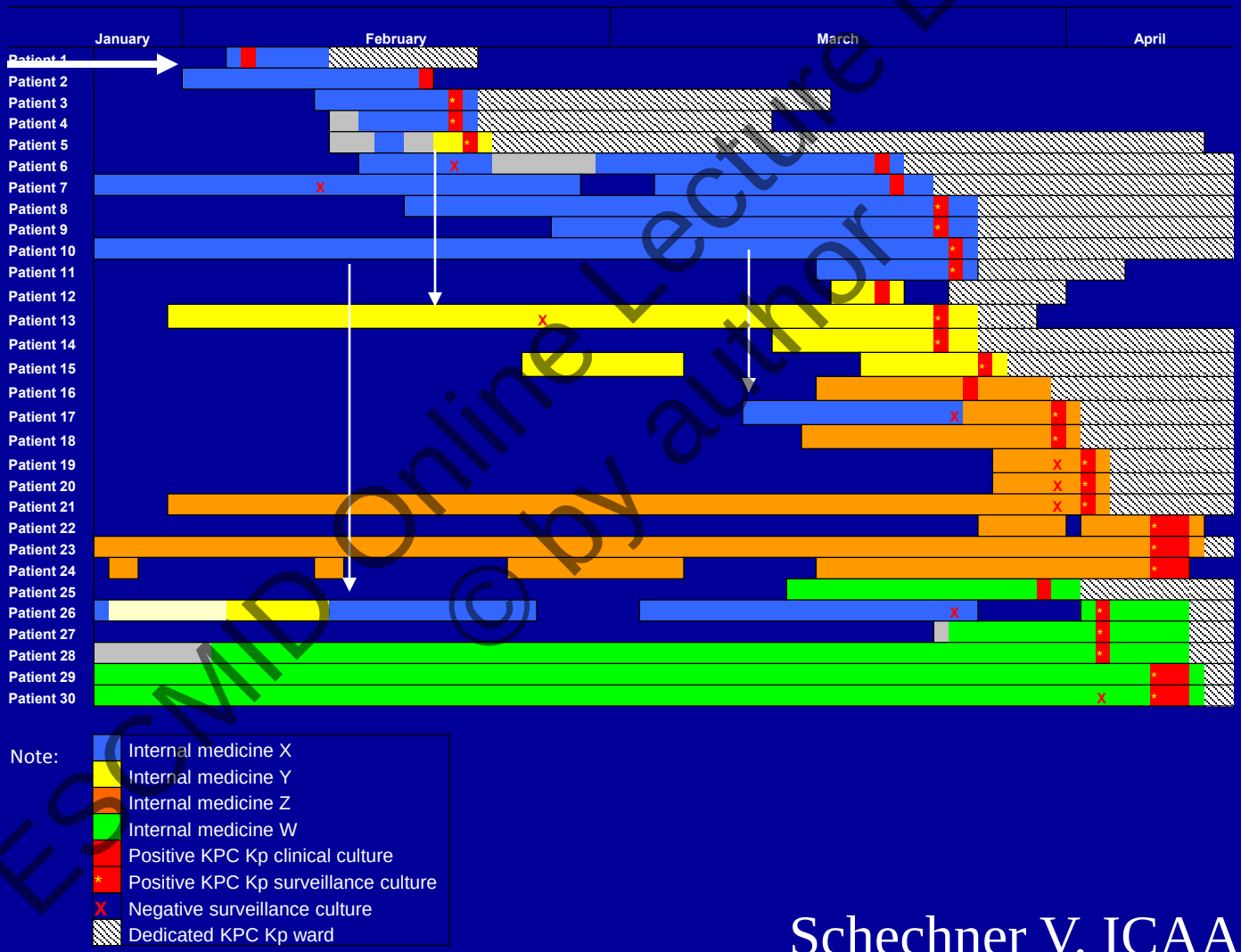
ESCMID Online Lecture Library © by author

Tale of one outbreak

- 2.4 patient A admitted (recent previous hosp elsewhere) to Tel Aviv Medical Center (multi-patient room)
- 2.5 urine culture taken
- 2.6 suspected carbapenem resistance –but requires further testing
  - pt isolated in single patient room
- 2.7 technical problem with confirmation
  - test needs to be repeated
- 2.8, 2.9 – weekend
- 2.10 carbapenem resistance confirmed
  - patient cohorted in a dedicated ward
  - Screen culture taken from 10 patients – all negative

ESCMID Online Lecture Library © by author

Figure: The movement of KPC Kp through 30 patients in 4 different wards



ESCMID Online Lecture Library © by author

Schechner V. ICAAC 2008

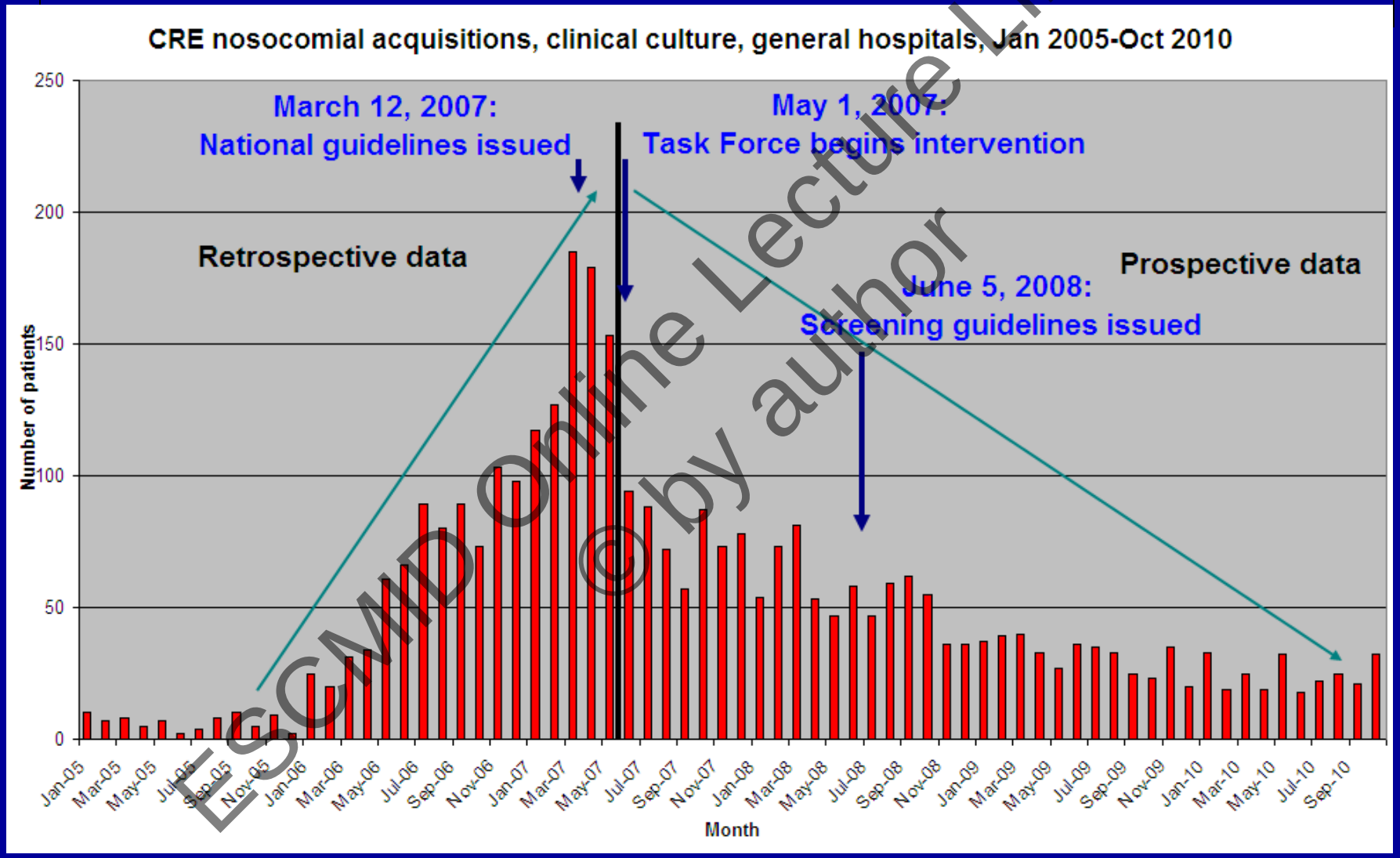
Consequences of not acting immediately

- Admission of an unidentified carrier of KPC Klebsiella and 5 days delay until cohorting led to a difficult to control outbreak, involving 30 patients (6 clinical infections) in 4 wards[1]
- Transfer overseas of a known carrier, but failure to isolate immediately, resulted in 9 additional clinical cases

ESCMID Online Lecture Library
© by author

1 Schechner V. ICAAC/IDSA 2008, paper 3806
2 Morris M. ICAAC/IDSA 2008, paper 1015

Summary of intervention results to date:



ESCMID Online Lecture Library
© by author

Israeli Nationwide Intervention

- Task force
- To provide regional coordination and supervision
- National guidelines
- Strict isolation with dedicated staff
- Rapid identification of carriers by flagging, information transfer, and surveillance of high risk population
- Continuous root-cause analysis

ESCMID Online Lecture Library © by author

Laboratory algorithm – common language and definitions

Growth of CRE → MHT

MHT + → CPE: isolate and cohort

MHT - → Non-CP-producing CRE: isolate w/o cohorting

OR

KPC PCR + → CPE: isolate and cohort

KPC PCR - → MHT

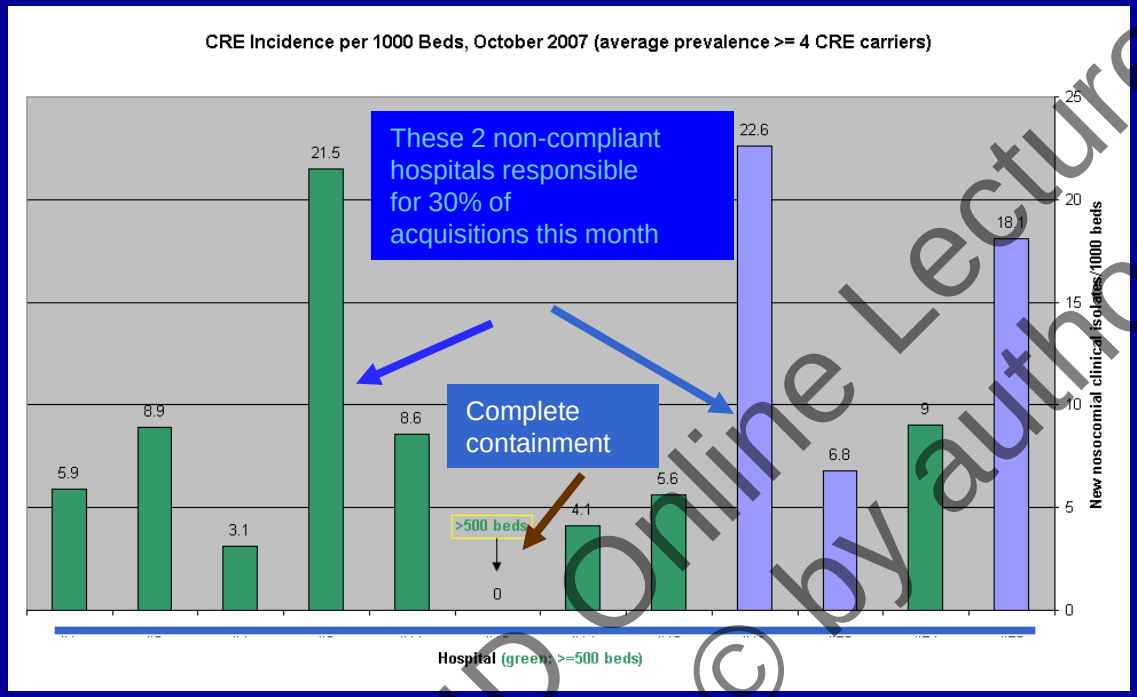
MHT + → CPE (not KPC): isolate and cohort

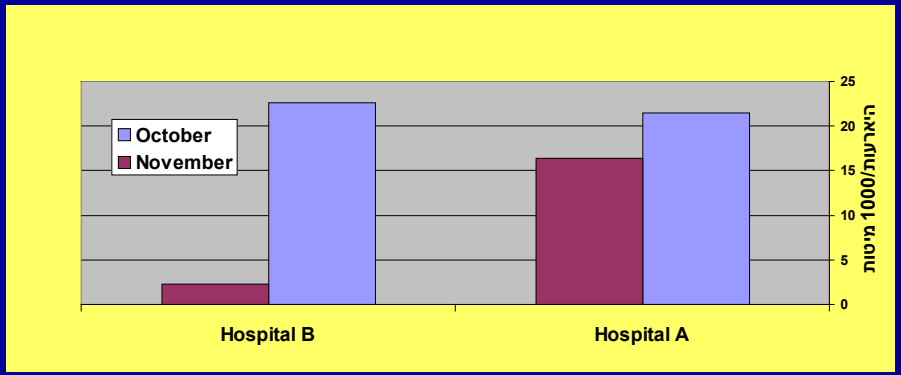
MHT - → Non-CP-producing CRE: isolate w/o cohorting

Once a CPE carrier, always a CPE carrier, until proven otherwise

ESCMID Online Lecture Library © by author

Assuring adherence to guidelines

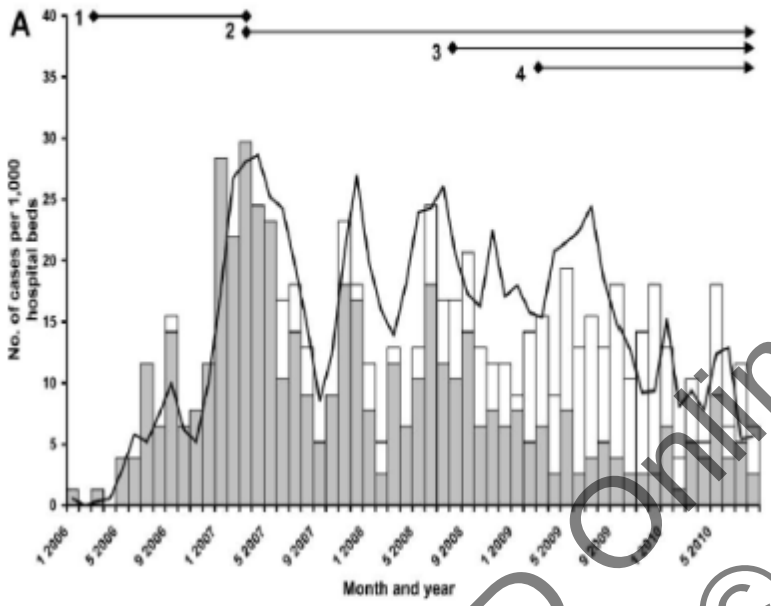




ESCMID Online Lecture Library © by author

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

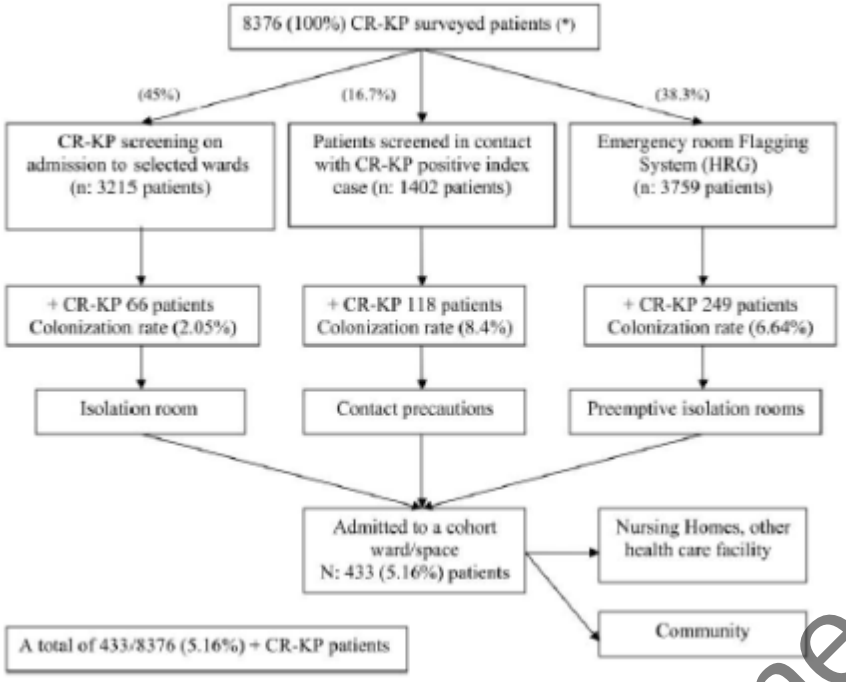
Intervention	Description	Date begun
Intervention 1	Single-room isolation and contact precautions	March 2006
Intervention 2	Cohorting of patients and nursing staff, screening of patients in the same room as newly identified carriers of CRKP ("snow ball" active surveillance), and local protocol for continued 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

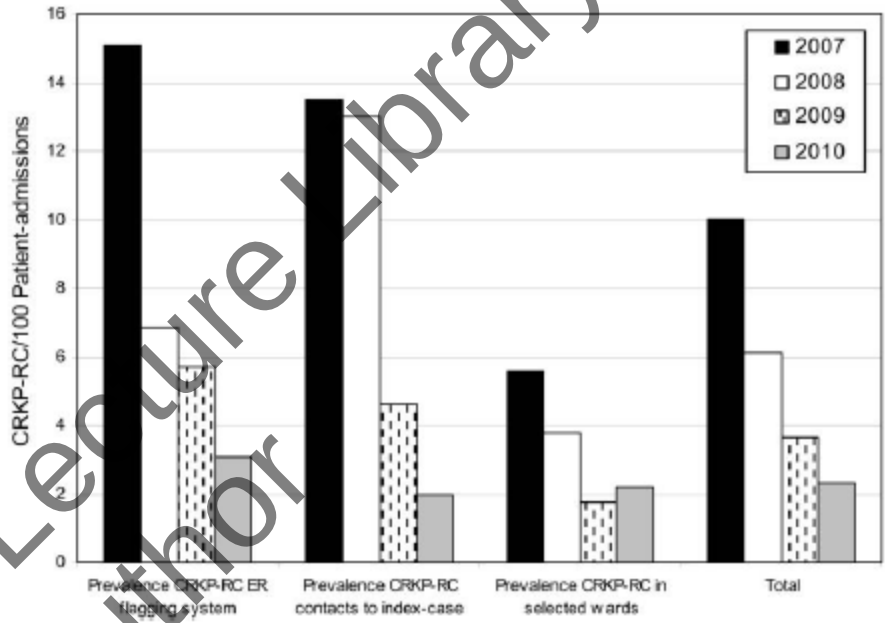


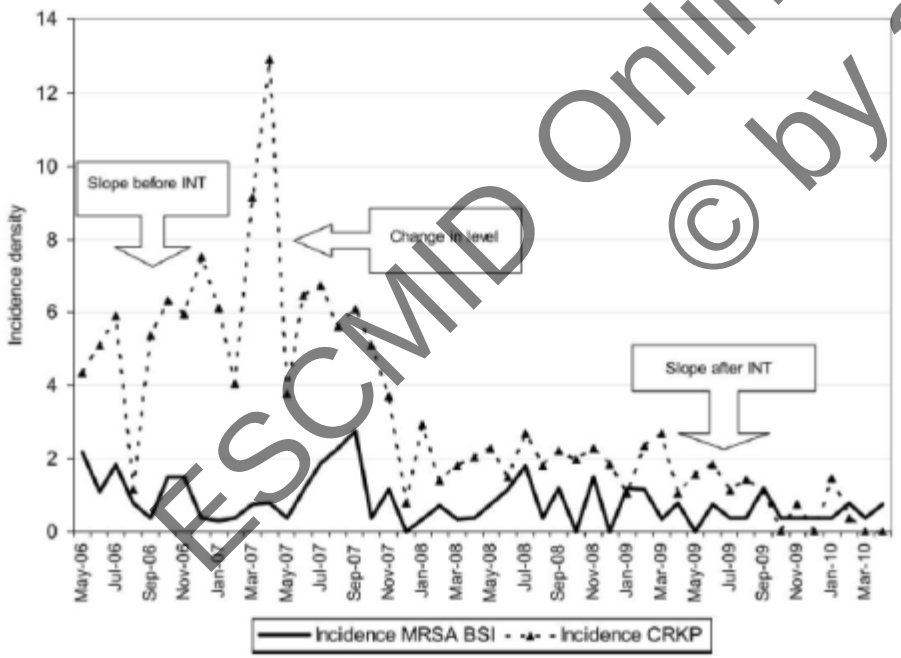
Intervention (period)	Incidence: No. of cases per 1,000 hospital beds, Mean	Median	Slope[a]	P[b]
Intervention 1 (Mar 2006–Mar 2007)	8.4	6.45	1.9	
Intervention 2 (Apr 2007–Aug 2008)	13.4	11.6	−0.7	<.001
Intervention 3 (Sep 2008–Mar 2009)	8.3	7.7	−0.8	.76
Intervention 4 (Apr 2009–Aug 2010)	4.3	3.8	−0.008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

ESCMID Online Lecture Library
© by author

Cohen M. ICHE 2011







ESCMID Online Lecture Library
© by author

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

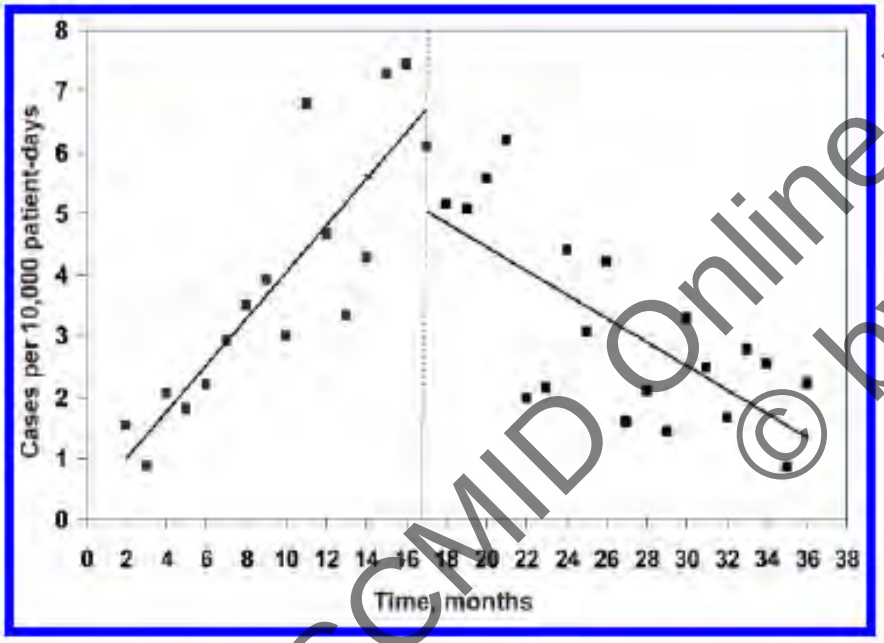


FIGURE 1. Scatterplots showing the change in the number of clinical cases of infection with carbapenem-resistant *Klebsiella pneumoniae* per 10,000 patient-days, before and after the intervention, implemented in month 17. Solid lines represent the linear regression fits across all cases.

>700 surveillance cultures/month

4% positivity on admission

Ben David D. et al. ICHE 2011

ESCMID Online Lecture Library
© by author

Interventions in 13 large LTCF (2913 beds)

	2008	2010	P
Infection control score	6.7	10.9	0.02
Strategies for prevention of CRKP			
cohorting patients	10	11	
dedicated medical equipment	12	13	
single-use gown	6	12	
admissions screening	2	9	
contact screening	5	10	

ESCMID Online Lecture Library © by author

Incidence of carbapenem resistant *K. pneumoniae* acquisitions

	Period I	Period II	Prevented fraction	P
Incidence of clinical acquisitions	5.2	2.4	53.7%	<0.001
Incidence of screening acquisitions	6.5	7.4		0.12
% identified by screening cultures	36.2%	69.9%		<0.001
Total incidence	**11.8**	**9.9**	**16.1%**	**0.01**

ESCMID Online Lecture Library © by author

Cross section prevalence studies

Type of ward	2008 (n=1004)	2010 (n=1027)	
Skilled nursing care	25.9%	15.6 %	
chronic mechanical ventilation	11.9%	10.9 %	
sub acute	9.6%	7.7 %	
Rehabilitation	2.5%	1.1 %	
TOTAL	**12.0%**	**8.3%**	

ESCMID Online Lecture Library © by author

Multicenter regional approach

- Is important to control MDRO
- Require inclusion of all healthcare facilities
- LTCF may serve as important reservoir and amplify MDRO
- Control in LTCFs is particularly challenging

ESCMID Online Lecture Library © by author