Question 1

What gram-negative pathogen do you consider the most worrisome (emerging) at your hospital?

- Multidrug-resistant *Pseudomonas* spp.
- ESBL-producing *Klebsiella* and *E. coli*
- Imipenem-resistant *Klebsiella* spp.
- Multidrug-resistant *Acinetobacter* spp.
- Fluoroquinolone-resistant *Pseudomanas* spp.
- KPC

Case 1 and Question 2

- A 80 year old lady with confusion is transferred to your institution with confusion of 24 hours.
- UA demonstrates > 300 WBC/HPF with nitrates and leukoesterase.
- Antibiotics are started.
- Does she need isolation?

Case 1 and Question 2

- The LTC is known to have a problem with ESBLs and MRSA. Does that change your answer?

Risk Assessment

Table 2. Characteristics of the Multidrug-Resistant *Acinetobacter* Surveillance Culture Study Cohort

	Without MDR *Acinetobacter*	With MDR *Acinetobacter*	All
Patients	n = 1098	n = 13	N = 1111
Age, mean (95% CI) [range], y	56.4 (55.4-57.4) [17-102]	49.1 (39.4-58.8) [19-74]	56.3 (55.3-57.3) [17-102]
Women, No. (%), [95% CI]	527 (48.0) [45.0-51.0]	10 (76.9) [46.2-95.0]	537 (48.3) [45.4-51.3]
Paraplegia, No. (%) [95% CI]	12 (1.1) [0.6-1.9]	3 (23.1) [5.0-53.8]	15 (1.4) [0.8-2.2]
Admissions	n = 1210	n = 13	N = 1223
Admitted directly from a long-term care or rehabilitation facility, No. (%) [95% CI][a]	47 (3.9) [2.9-5.1]	6 (46.2) [19.2-74.9]	52 (4.3) [3.2-5.5]

Abbreviations: CI, confidence interval; MDR, multidrug-resistant.
[a]Of 13 patients with MDR *Acinetobacter*, 9 (69%) had been in a long-term care or rehabilitation facility within the preceding 6 months.

Maragakis , et al. JAMA. 2008;299::2513

How else can we identify patients at risk of MDROs?

- 96 patients with MDR ACIN at UMD and JHH were matched to 89 patients without ACIN infections and 90 patients with susceptible ACIN (1/2002–8/2004)
- Matched on unit and exposure time

Characteristic	OR	95% CI	*P*-value
LTCF within 30 days	13.2	1.3 - 132	0.03
Hemiplegia	6.9	1.1 - 45	0.04
Modified Apache III	1.03	1.00- 1.06	0.02

Wright MO, et al. *Infect Control Hosp Epidemiol*. 2004;25:167-8.

Case 1

What gram-negative pathogen would you worry about in this setting?

- Multidrug-resistant *Pseudomonas* spp.
- ESBL-producing *Klebsiella* and *E. coli*
- Imipenem-resistant *Klebsiella* spp.
- Multidrug-resistant *Acinetobacter* spp.
- Fluoroquinolone-resistant *Pseudomanas* spp.
- KPC

An *Acinetobacter* spp. Outbreak

- 12 isolates of multidrug-resistant Acinetobacter spp. over 8 weeks. All isolates were resistant to all antibiotics except polymixin B
- This represents a new resistance pattern
- Patients were in multiple units with a variety of underlying conditions

Maragakis LL, et al. JAMA. 2004;292:3006-11.

How Would You Define MDR?

1. Resistant to any 3 antibiotic classes
2. Resistant to all antibiotic classes except colistin
3. Resistant to cephalosporins, aminoglycosides, fluoroquinolones and beta-lactam combinations
4. Other

Is There A Role for Surveillance Cultures?

1. No
2. Yes, among contacts of cases
3. Yes among all patients
4. Yes among contacts of cases and healthcare workers

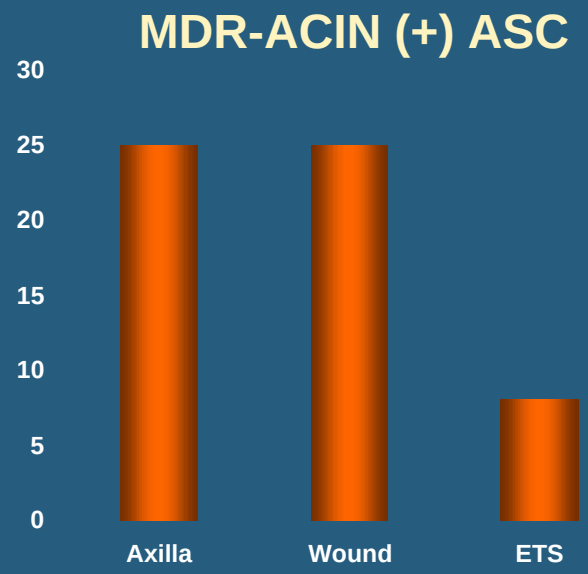
Is there a gram negative iceberg?

- Prospective cohort (2001–2004)—MICU/SICU at UMD. Peri-anal cultures on admission, weekly and on discharge
- 1806 patients admitted to ICU
  - 74 had ESBL producing *E. coli* on admission, 23 acquired ESBL and 14/23 PFGE were unique, 3 (13%) transmitted nosocomially
  - 27 acquired *K. pneumoniae*, 14 (52%) met our definition of patient-to-patient transmission. 6/27 (22%) had a subsequent ESBL
  - 8 acquired *K. oxytoca*, 1 (13%) was transmitted patient-to-patient

Harris AD, et al. Am J Infect Control. 2007;35:97-101.

The Acinetobacter iceberg

- 4-month prospective pilot study on 5 medical units at JHH
- Admission and weekly surveillance cultures for MDR-ACIN (Axilla, wound, sputum, endotracheal suction)
- 1601 admissions/transfers with 74%-94% compliance
- 7/1240 (0.006%) admission cultures and 5/470 (0.01%) weekly cultures grew MDR-ACIN
- 80% of patients with prior history had + culture



Maragakis , JAMA 2008.

Potential Prevention and Control Measures

- Infection Prevention/Control
  - Hand hygiene
  - Isolation and barrier precautions
  - Cohorting or separation of colonized/infected and non-colonized patients
  - Control of environmental or other potential sources
- Antibiotic stewardship/management

Isolation

What Type of Isolation Does Your Hospital Use for MDR-GNR?

1. No isolation beyond standard precautions
2. Contact precautions in open cubicle
3. Contact precautions in open cubicle using corner bed
4. Contact precautions in private room
5. Contact precautions in open cubicle using corner bed with nurse cohorting
6. Contact precautions in open cubicle with patient cohorting

Experience with Acinetobacter

Table 1. Methods for control and prevention of multidrug-resistant *Acinetobacter* infection.

Method	Comments
Point source control	Effective in the outbreak setting when a point source is identified
Standard precautions	Includes hand hygiene, correct and consistent glove use, and appropriate use of gowns and eye protection; reported compliance among healthcare personnel is often poor
Contact barrier precautions	Includes dedicated patient care equipment and gowns and gloves for health care personnel on entry to an isolation room
Environmental cleaning and disinfection	Widespread environmental contamination is often reported in the epidemic setting, and environmental reservoirs likely play a role in the endemic setting as well
Cohorting of patients	Grouping colonized and infected patients into a designated unit or part of a unit
Cohorting of health care personnel	Designating staff to care for only patients colonized or infected with the organism
Clinical unit closure	Required in some outbreak settings to interrupt transmission and allow for thorough environmental disinfection
Antimicrobial stewardship	Programs to promote judicious antimicrobial use and prevent emergence of resistance
Surveillance	Passive or active surveillance can identify infected or colonized patients so that interventions can be implemented

Maragakis and Perl CID 2008:46;1254

Contamination of Gowns, Gloves and Hands

TABLE 1. Frequency of Contamination of Gowns, Gloves, and Hands of Healthcare Workers (HCWs) after Caring for Patients Colonized or Infected with Specified Bacteria

Source of culture-positive sample	No. (% [95% CI]) of observations	
	Patients with MDR *Acinetobacter baumannii* carriage (n = 199)	Patients with MDR *Pseudomonas aeruginosa* carriage (n = 134)
Gloves	72 (36.2 [29.5–42.9])	9 (6.7 [2.5–11.0])
Gown	22 (11.1 [6.7–15.4])	6 (4.5 [1.0–8.0])
Gloves and/or gown	77 (38.7 [31.9–45.5])	11 (8.2 [3.6–12.9])
Hands[a]	9 (4.5 [1.6–7.4])	1 (0.7 [0–2.2])

NOTE. CI, confidence interval; MDR, multidrug-resistant.

[a] After removal of gloves and gown and before hand hygiene.

Morgan, D, et al. Infect Control Hosp Epidemiol. 2010;31:epub

Contamination of Gowns, Gloves and Hands

TABLE 3. Bivariate Analysis of Risk Factors for Detection of Multidrug-Resistant *Acinetobacter baumannii* on the Gowns and/or Gloves Worn by Healthcare Workers (HCWs) Caring for Patients with *A. baumannii* Carriage

Nature of HCW-patient contact	No. of observations	No. (%) of positive culture results (n = 77)	No. (%) of negative culture results (n = 122)	Proportion (%) of contacts that preceded detection of pathogen	P
Physical examination	18	11 (14.29)	7 (5.74)	11/18 (61)	.04
Wound dressing	16	15 (19.48)	1 (0.82)	15/16 (94)	<.01
Bathing and/or other form of hygiene	37	20 (25.97)	17 (13.93)	20/37 (54)	.03
Care or use of catheter and/or drain	36	16 (20.78)	20 (16.39)	16/36 (44)	.43
Care or use of endotracheal tube or tracheostomy site	78	37 (48.05)	41 (33.61)	37/78 (47)	.04
Checking vital signs	40	13 (16.88)	27 (22.13)	13/40 (33)	.37
Administering enteral medication	30	10 (12.99)	20 (16.39)	10/30 (33)	.51
Activity with intravenous pumps or lines	98	40 (51.95)	58 (47.54)	40/98 (41)	.54
Time in room of more than 5 minutes	125	64 (83.12)	61 (0.50)	64/125 (51)	<.01
Provider type					<.01
Physical, occupational, respiratory therapist	65	20 (25.97)	45 (36.89)	20/65 (31)	
Registered nurse	123	51 (66.23)	72 (59.02)	51/123 (41)	
Medical doctor or nurse practitioner	10	6 (7.79)	4 (3.28)	6/10 (60)	

Morgan, D, et al. Infect Control Hosp Epidemiol. 2010;31:epub

Independent Predictors of HCW Contamination

TABLE 4. Variables Found to Be Independently Predictive of Healthcare Worker Contamination with Multidrug-Resistant *Acinetobacter baumannii* by Means of Multiple Logistic Regression

Independent variable	aOR (95% CI)	*P*
Wound dressing	25.9 (3.1–208.8)	<.01
Care or use of endotracheal tube or tracheostomy site	2.1 (1.1–4.0)	.03
Time in room of more than 5 minutes	4.3 (2.0–9.1)	<.01
Physician or nurse practitioner, compared with therapist	7.4 (1.6–35.2)	.01
Nurse, compared with therapist	2.3 (1.1–4.8)	.03

NOTE. aOR, adjusted odds ratio; CI, confidence interval.

Morgan, D, et al. Infect Control Hosp Epidemiol. 2010;31:epub

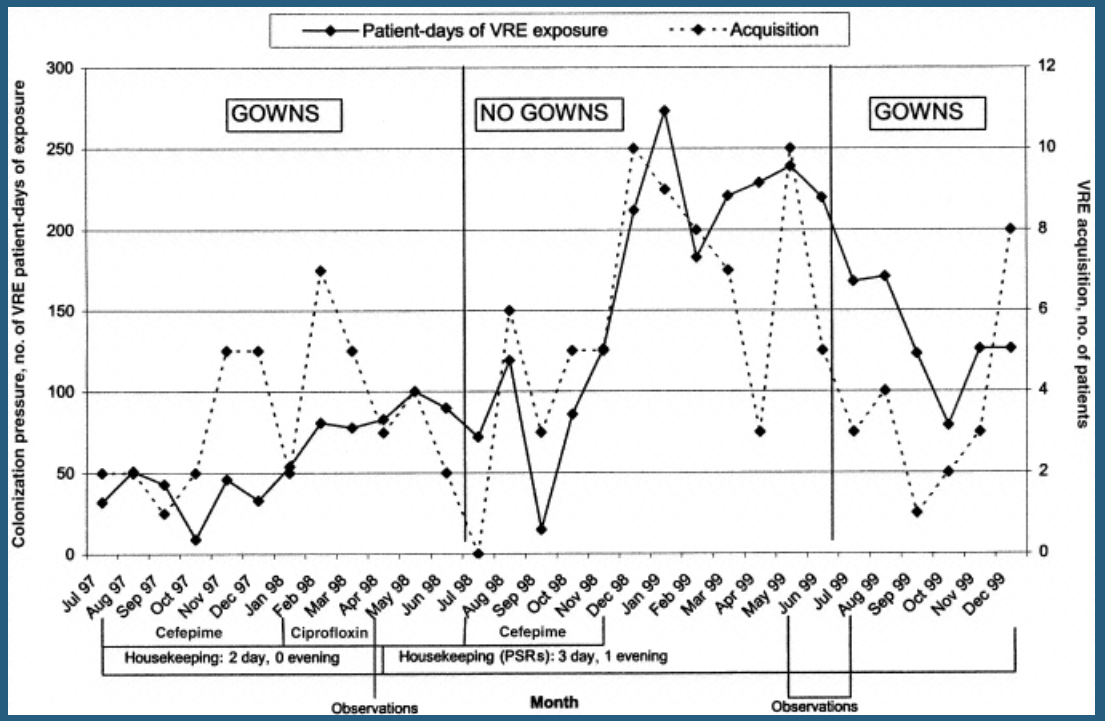
Isolation and Cohorting Measures

- Hospital and patient placement that increase the risk of acquiring VRE
  - Proximity to patient (p =0.0005)
  - Exposure to nurse caring for another patient with VRE (p =0.007)

Boyce et al, JCM 1994:32;1148-53

Preventing Transmission: Gowns + Gloves vs. Gloves Alone–2 Studies?

- JHH MICU-21% of patients at risk acquired VRE during the gown + glove period vs. 42% during the glove alone period (*P*=0.04)
  - VRE acquisition of 1.8 cases/100 days at risk with gowns + gloves compared to 3.78 cases with gloves alone (*P*=0.04, incidence rate ratio 0.48 (*P*=0.05, 95% CI 0.27-1.05)



Srinivasan A, et al. *Infect Control Hosp Epidemiol*. 2002;23:424-8; Puzniak LA, et al. *Clin Infect Dis*. 2002;35:18-25 .

Hand hygiene, and environmental and patient cleaning

What Would You Do About Hand Hygiene?

1. Review compliance data on affected unit
2. Review compliance data and increase observations
3. Review compliance and do hand cultures
4. Review compliance and do additional education
5. Review compliance, do hand cultures and do additional education

How do hands contribute?

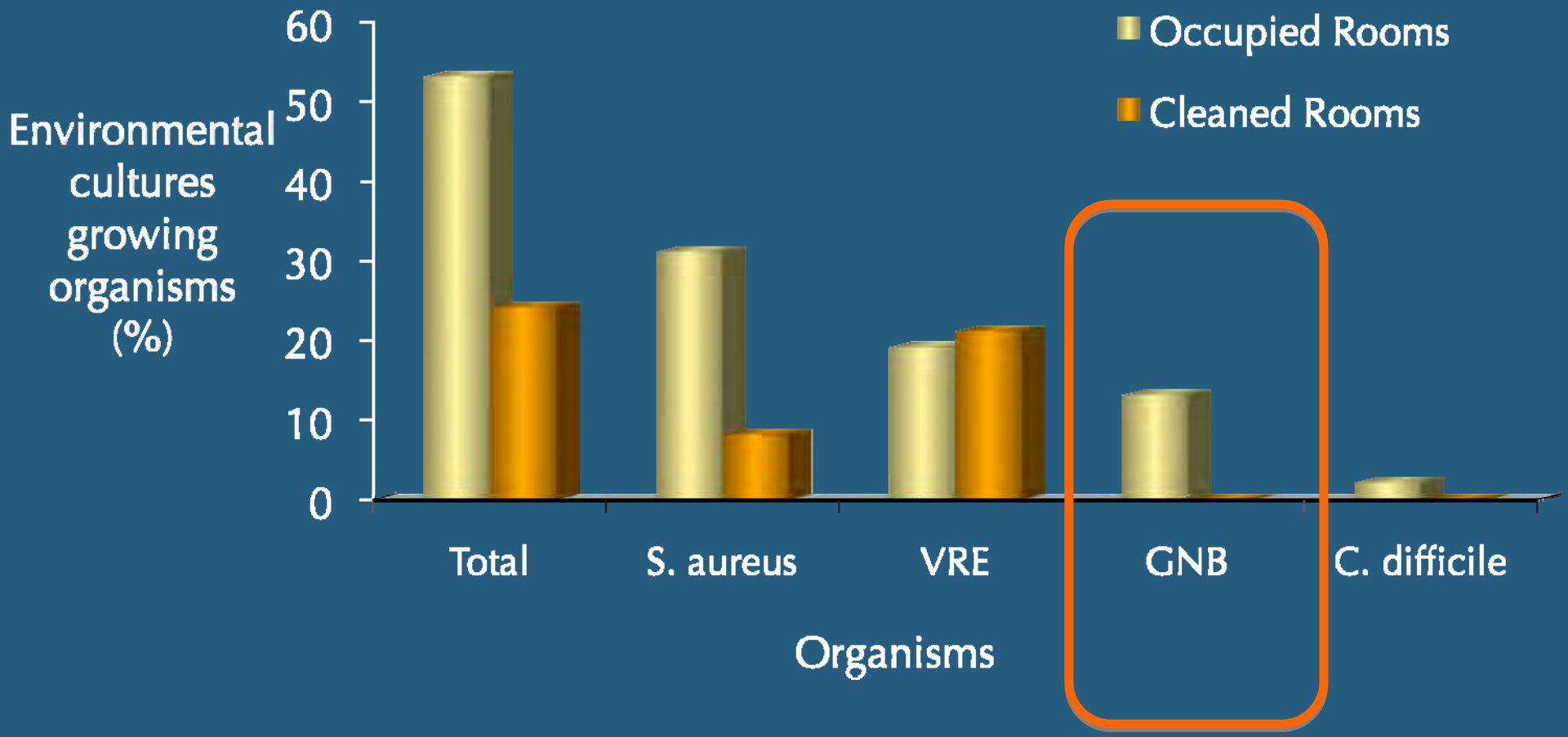
VRE can be recovered from hands 30 minutes after inoculation and after hand washing with bland soap

VRE transmission on hands

- 10.6% of sites not contaminated with VRE, grew the organism once touched with a contaminated hand
- Transfer highest for BP cuffs and antecubital fossa
- 39-46% of gloved hands acquired VRE
- 29% had pt strain on hands when gloves removed

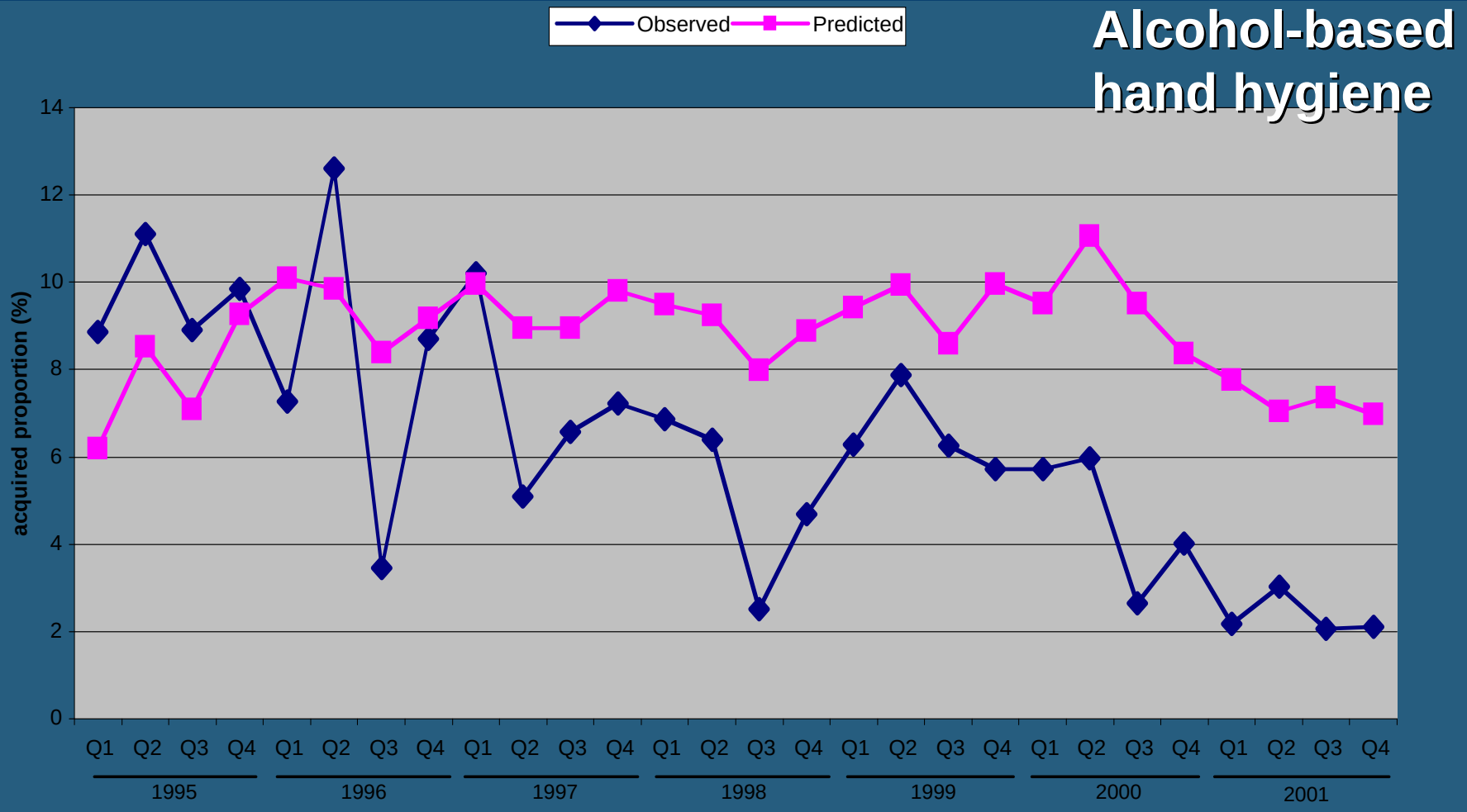
Bates et al., J Hosp Infect 1991, Duckro et al. Arch Intern Med 2005: 165:302, Ray et al. JAMA 2002;287:1400, Tenaorio etal. CID 2001;32:826-9

Hand imprint cultures after contact with environmental surfaces



Bhalla A, et al. Infect Control Hosp Epidemiol. 2004;25:164-7.

MRSA control programs in ICUs



Lucet et al. Intensive Care Med 2005; 31: 1051-1057

What Would You Do Next?

1. Culture environmental sites
2. Close the unit
3. Culture healthcare workers

Maragakis LL, et al. *JAMA*. 2004;292:3006-11.

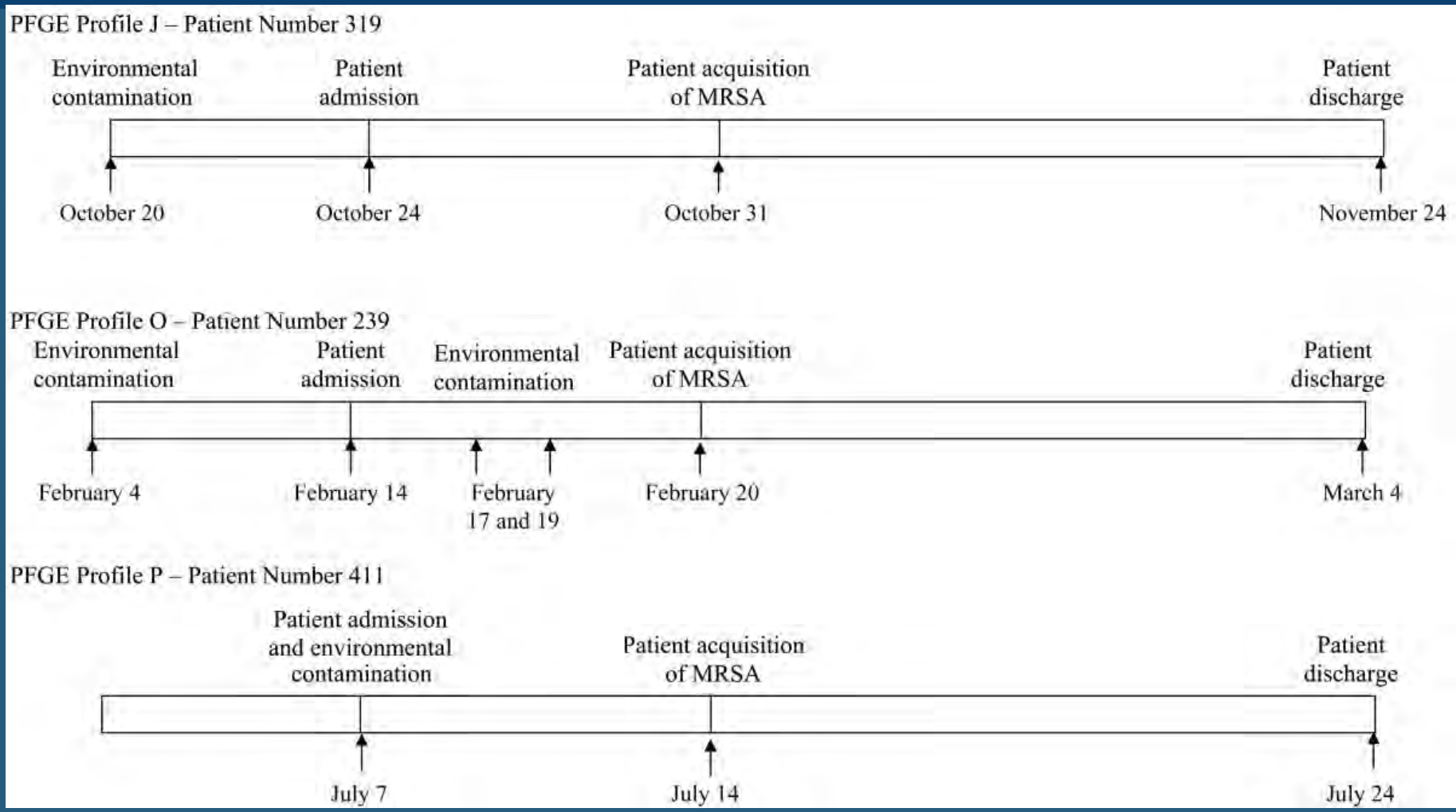
The Outbreak Continues

- PFGE of all isolates demonstrated identical strains
- Environmental isolates of multidrug resistant *Acinetobacter* spp. were identified in the patient area and from the pulsed lavage machine
- Environmental isolates matched patient isolates by PFGE

PFGE = pulsed field gel electrophoresis

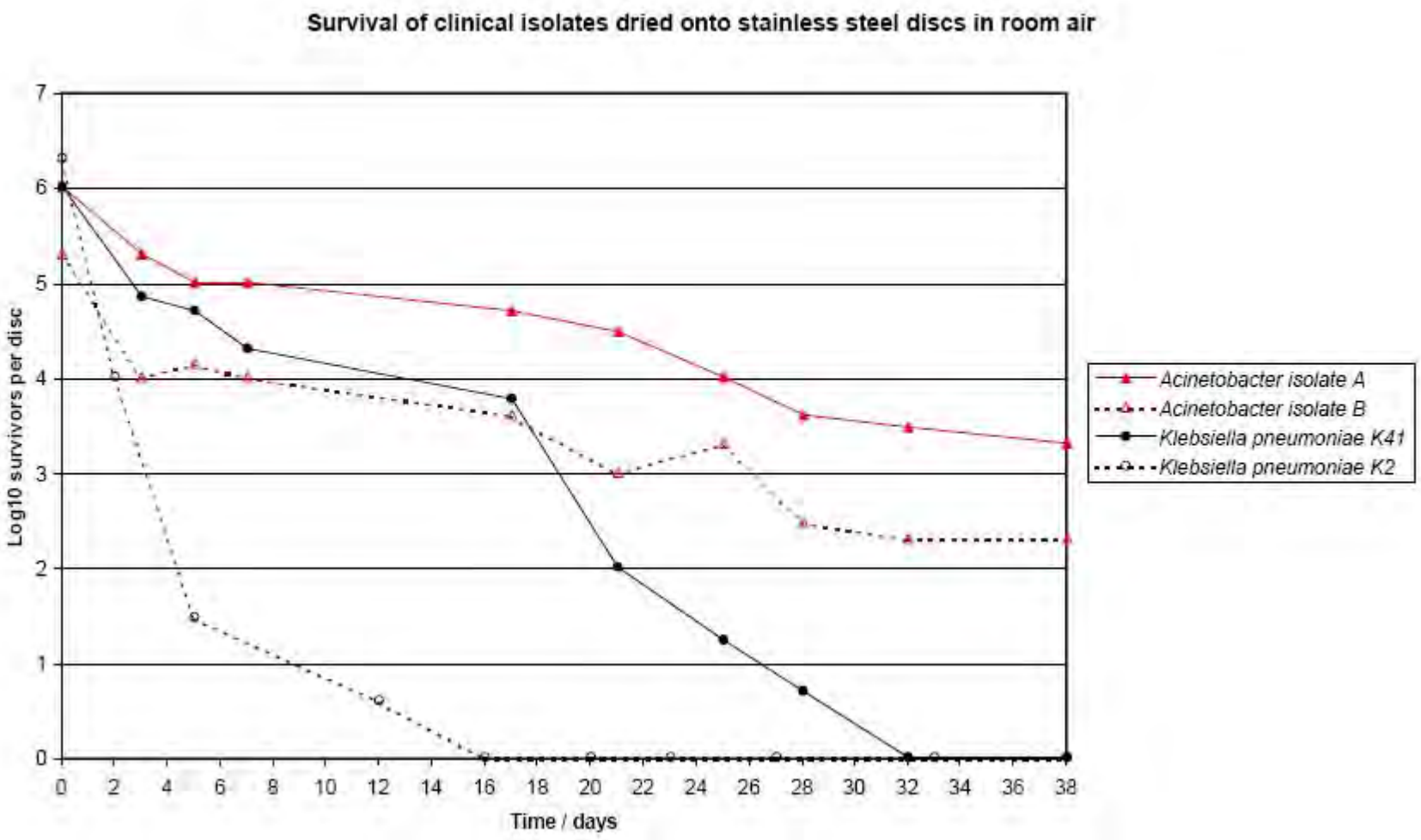
Maragakis LL, et al. *JAMA*. 2004;292:3006-11.

Linking the Environment to Infection

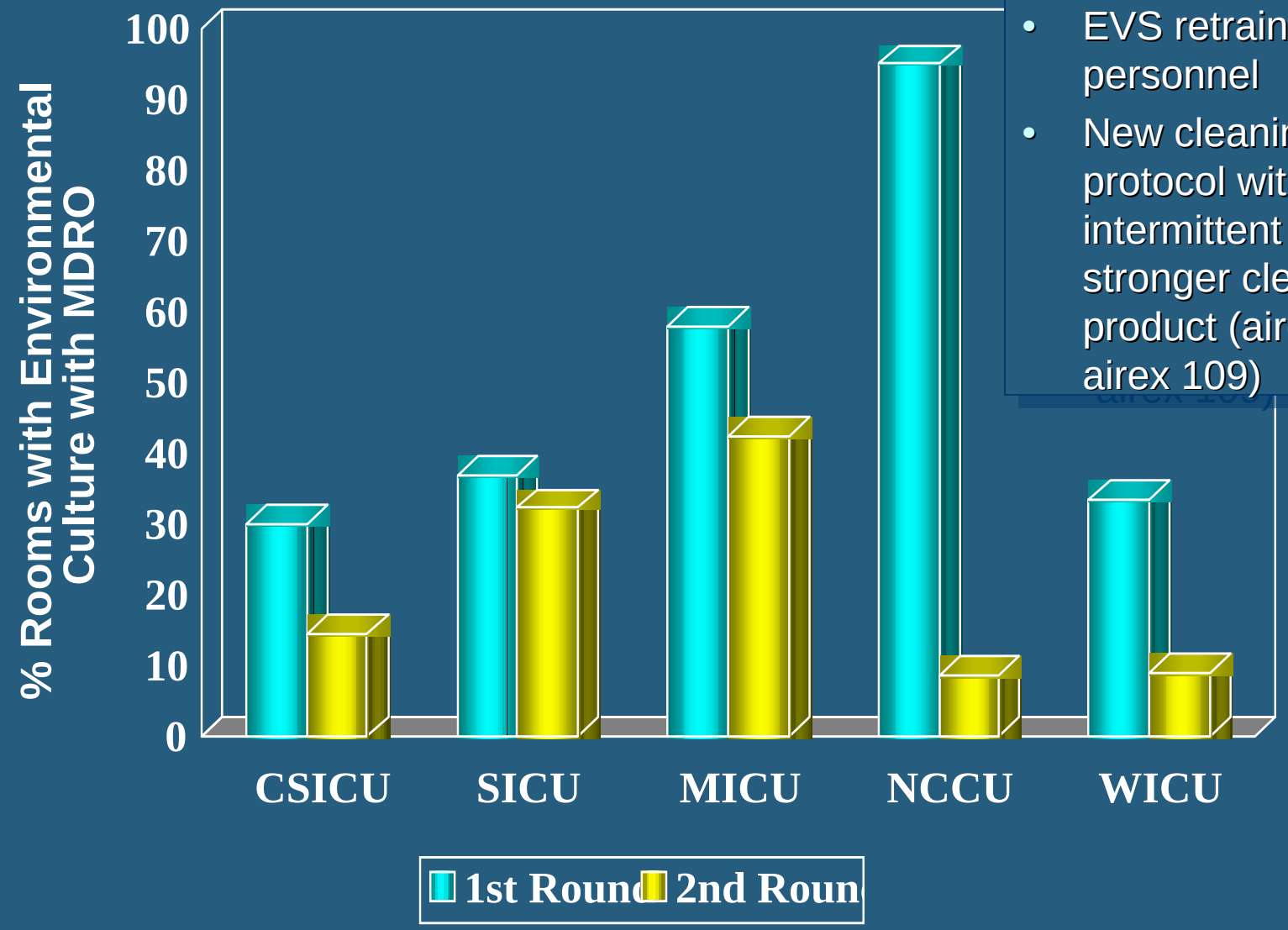


Hardy et al. Infection Control and Hospital Epidemiology 2006;27:127-132

Environmental Survival of Gram Negative Bacilli

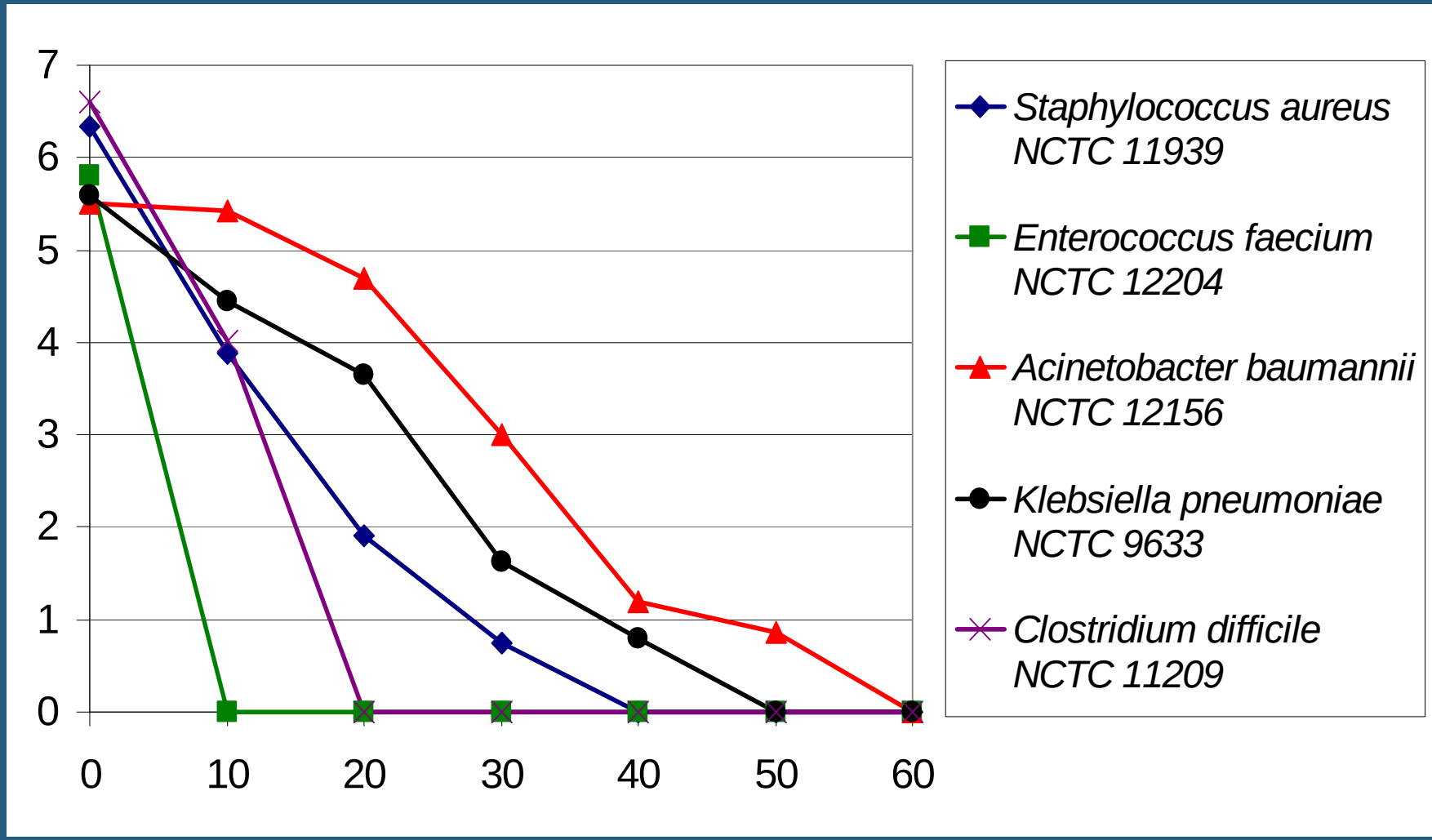


Enviromental cleaning in ICUs



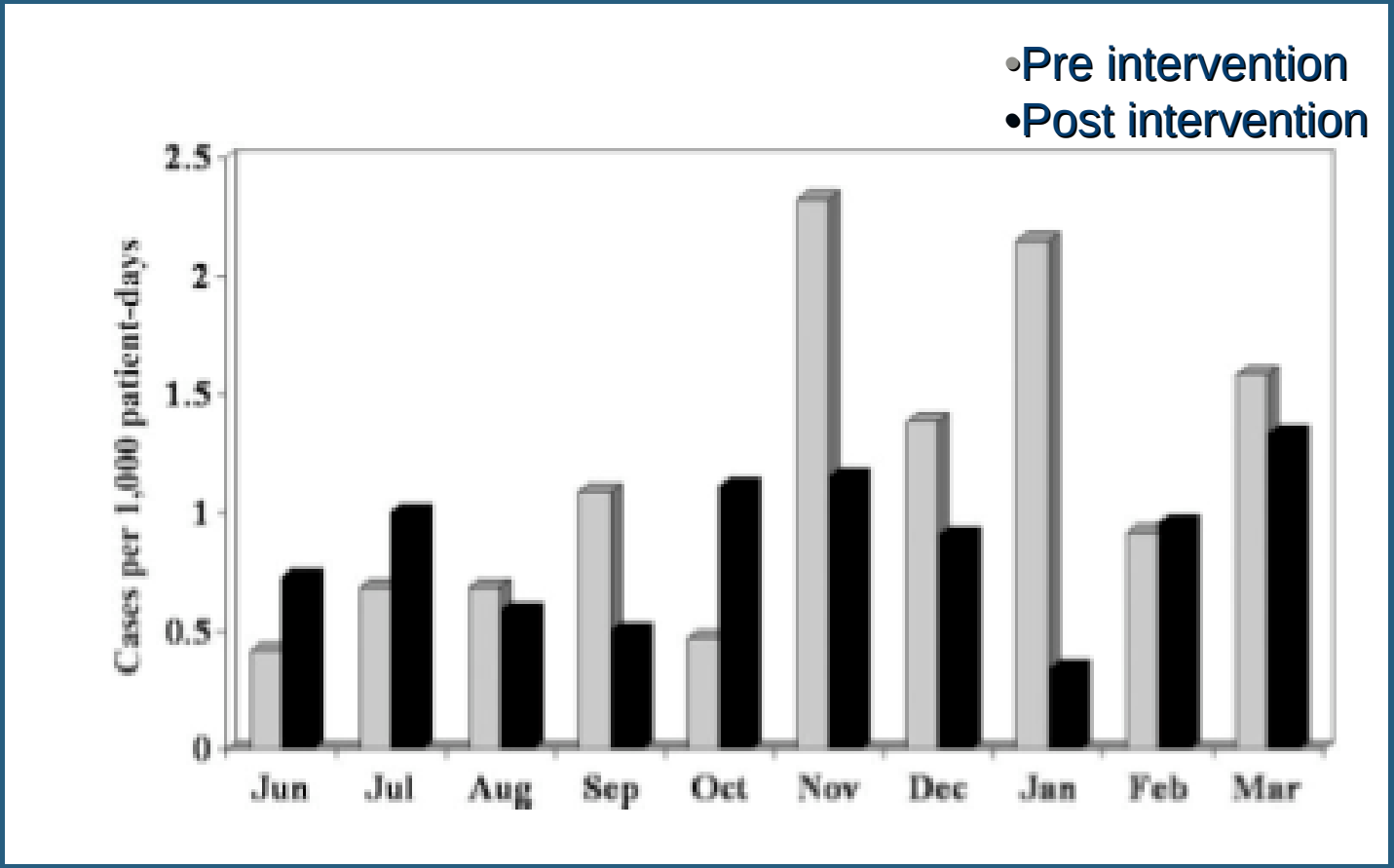
- EVS retraining of personnel
- New cleaning protocol with intermittent use of a stronger cleaning product (airex 44 vs. airex 109)

Cleaning with hydrogen peroxide



French GL, etal. 44th ICAAC,, 2004; Rogers JV, Sabourin CL, etal. J Appl Microbiol 2005;99:739-748; Bates CJ, Pearse R. J Hosp Infect 2005;61:364-366; Cabinet bio-decontamination trial. Centre for Applied Microbiology and Research (CAMR) , Porton Down. March 1995.

C. difficile after cleaning with hydrogen peroxide



Boyce et al. 2008 ICHE:29(8):1-8

Antibiotic Stewardship

Do You Have An Antibiotic Management Program?

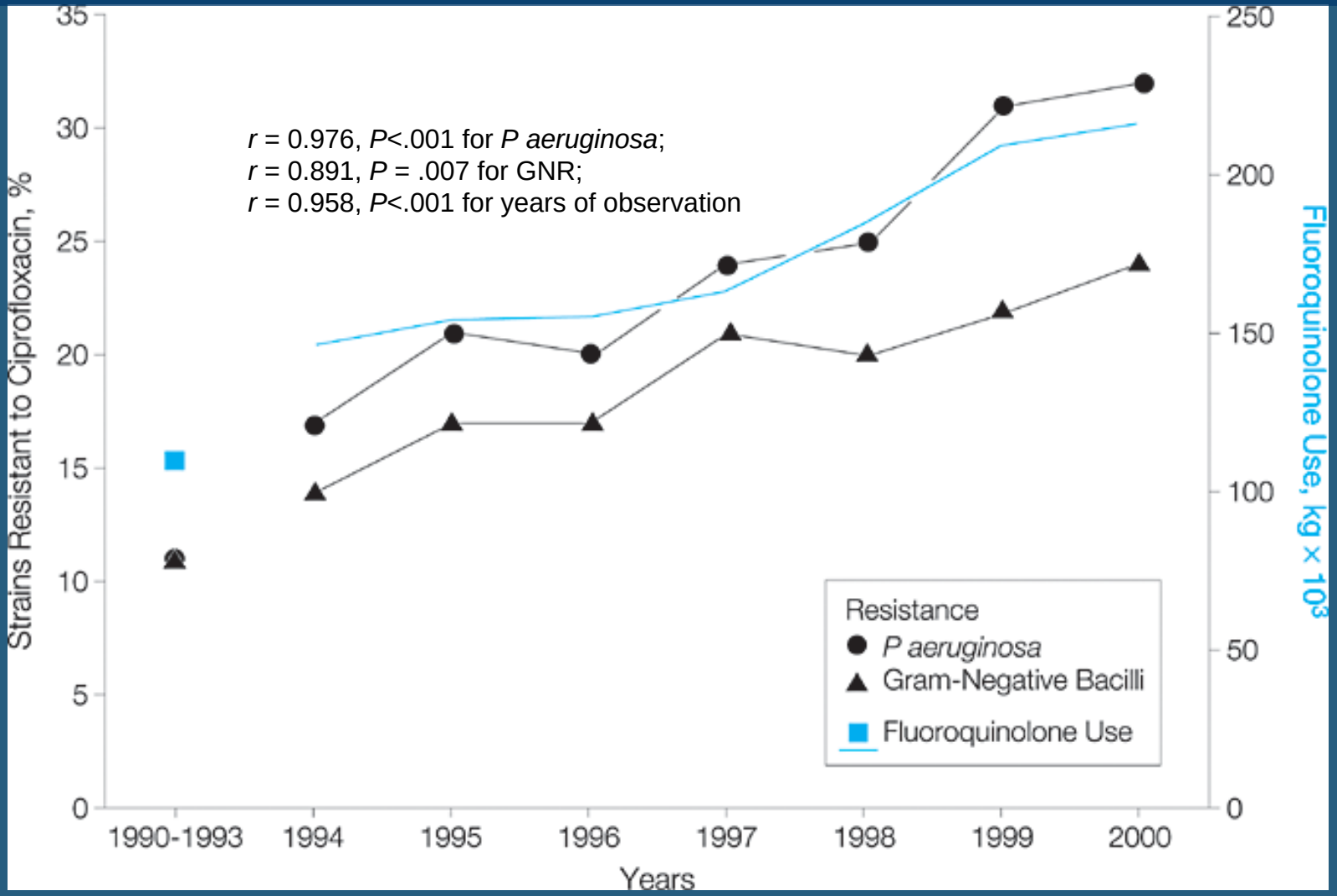
- If yes what?

1. Formulary limitations/restrictions
2. Antimicrobial stewardship programs
3. Selective reduction of implicated agents
4. Antimicrobial cycling
5. Early discontinuation
6. Other

If You Have Restriction Which Antibiotics with GN Activity Are Restricted?

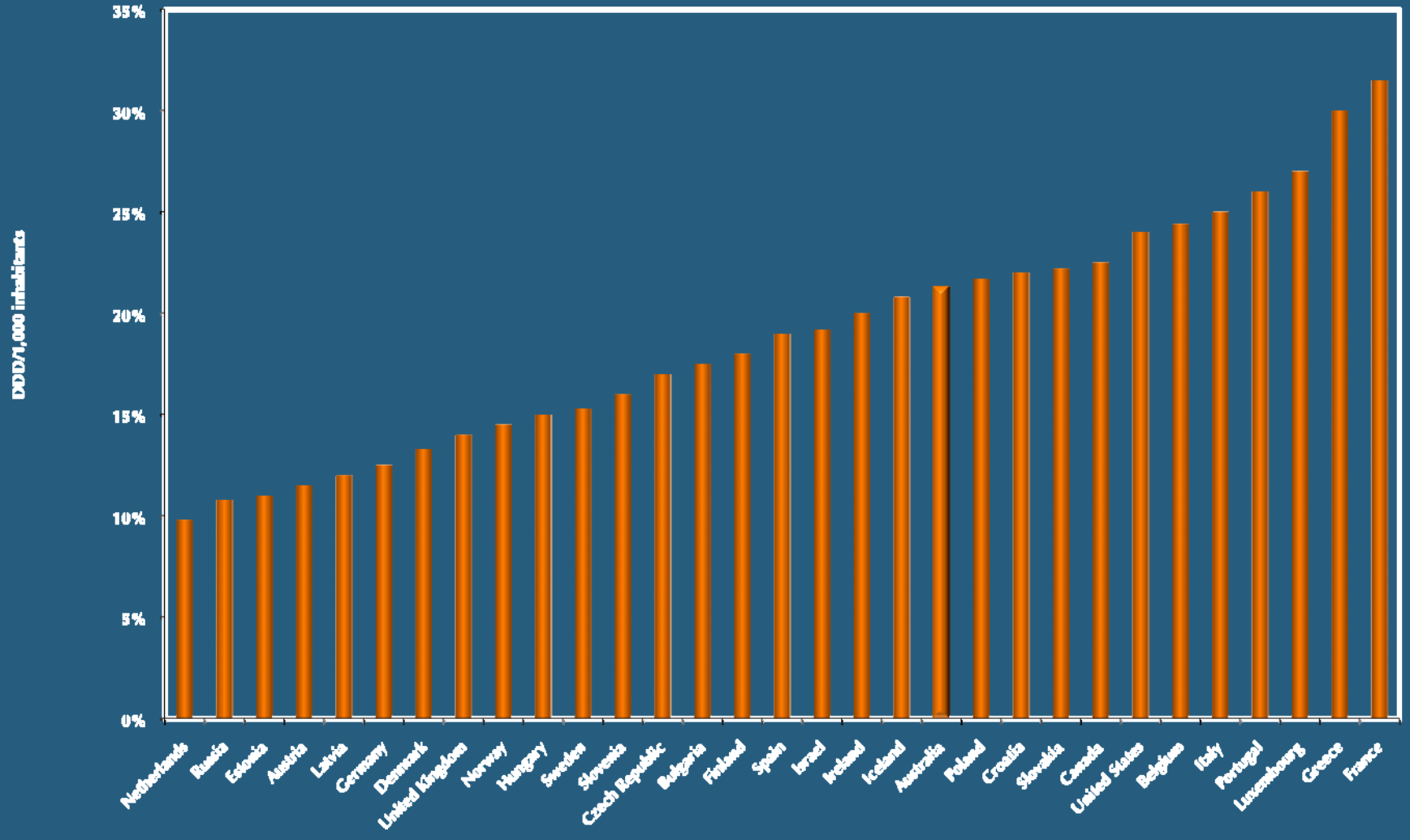
1. Fluoroquinolones
2. Tazobactam/pipericillin
3. 3rd generation Cephalosporins
4. 4th generation Cephalosporins
5. Carbapenems
6. Amikacin

Fluoroquinolone use and resistance rates in *P. aeruginosa* and GNR

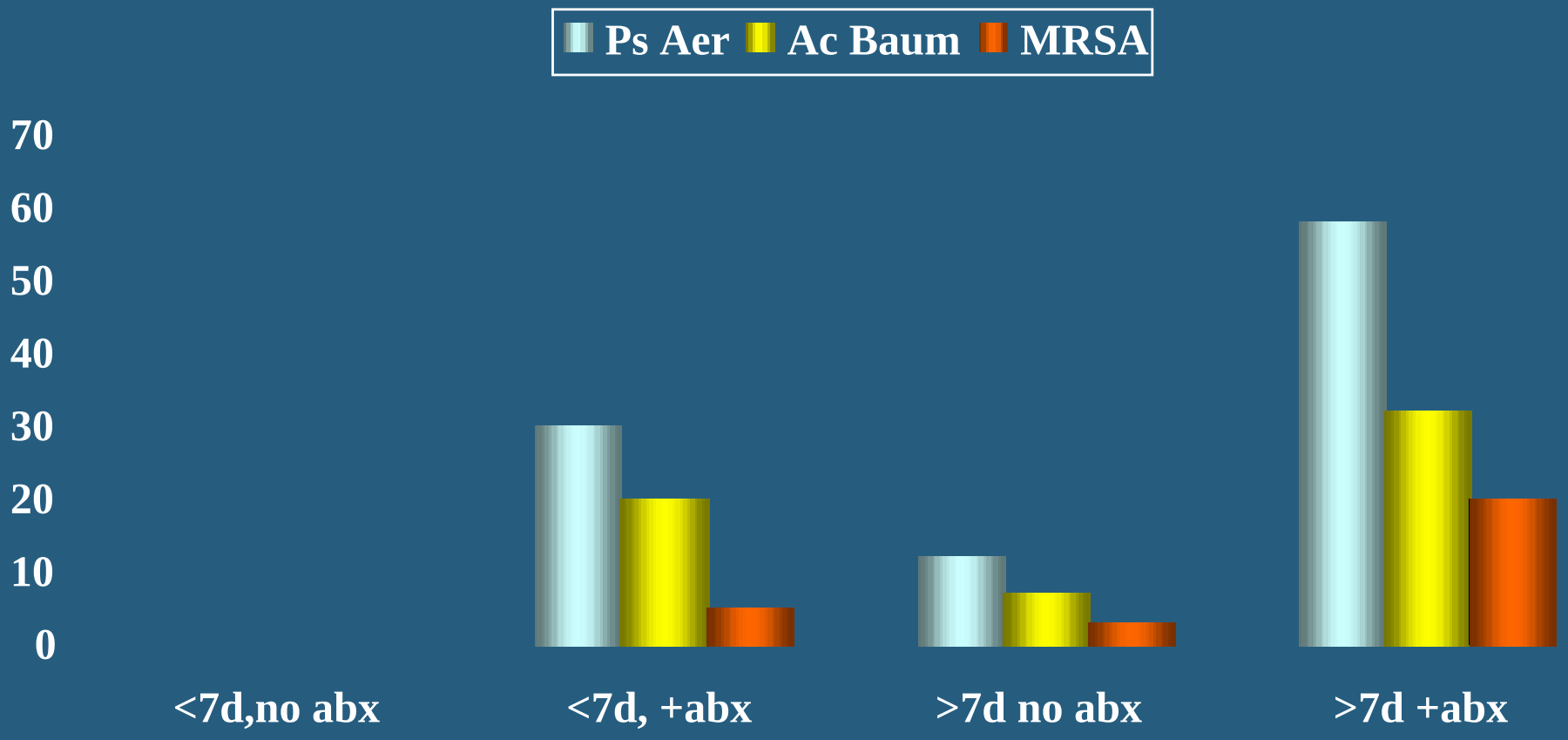


Neuhauser MM, et al. JAMA. 2003;289:885-8.

Worldwide antibiotic use



Antibiotic resistance in the ICU



Trouillet JL et al. Am J Resp Crit Care Med 1998;157:531-9

Impact of Antimicrobial Formulary Interventions on ESBL *E. coli* and *Klebsiella spp.*

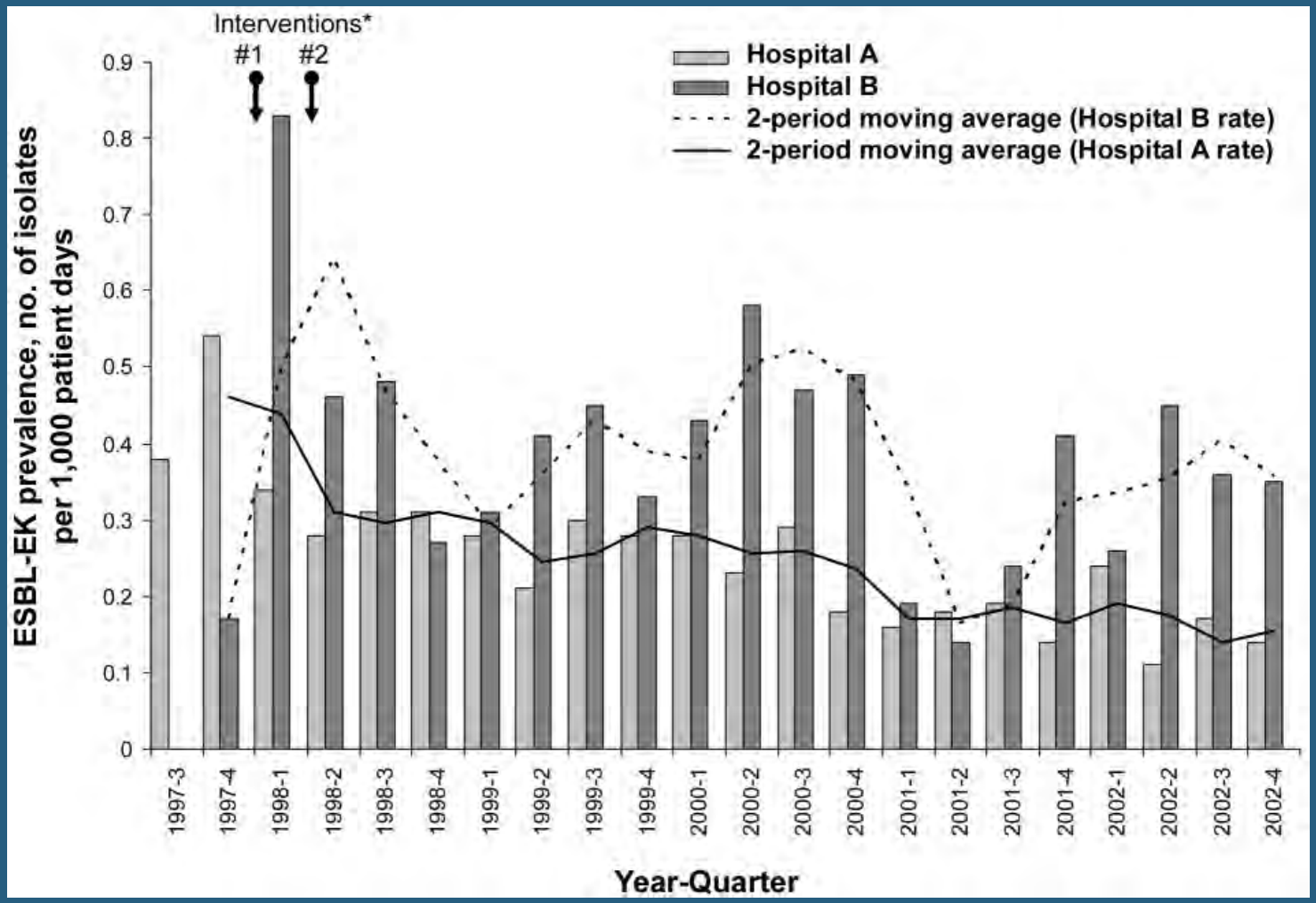
- Quasi-experimental design to evaluate the impact of antimicrobial interventions (ie, restriction of ceftazidime & ceftriaxone) to interrupt spread of ESBL in 2 hospitals (625 beds and 344 beds) over 5-years (7/1/1997–12/31/2002).

- Post-intervention, ceftriaxone use decreased 86% at Hospital A & 95% at Hosp B. Ceftazidime use decreased 95% at Hospital A & 97% at Hospital B.

- ESBL prevalence decreased 45% at Hospital A (*P*<.001), & 22% at Hospital B (*P*=.36). ESBL-EK-infected patients at Hospital B were more likely to have resided in a LTCF (adjusted OR, 3.77 [95% CI, 1.70-8.37]), be older (adjusted OR, 1.04 [95% CI, 1.01-1.06]), and have a decubitus ulcer (adjusted OR, 4.13 [95% CI, 1.97-8.65]).

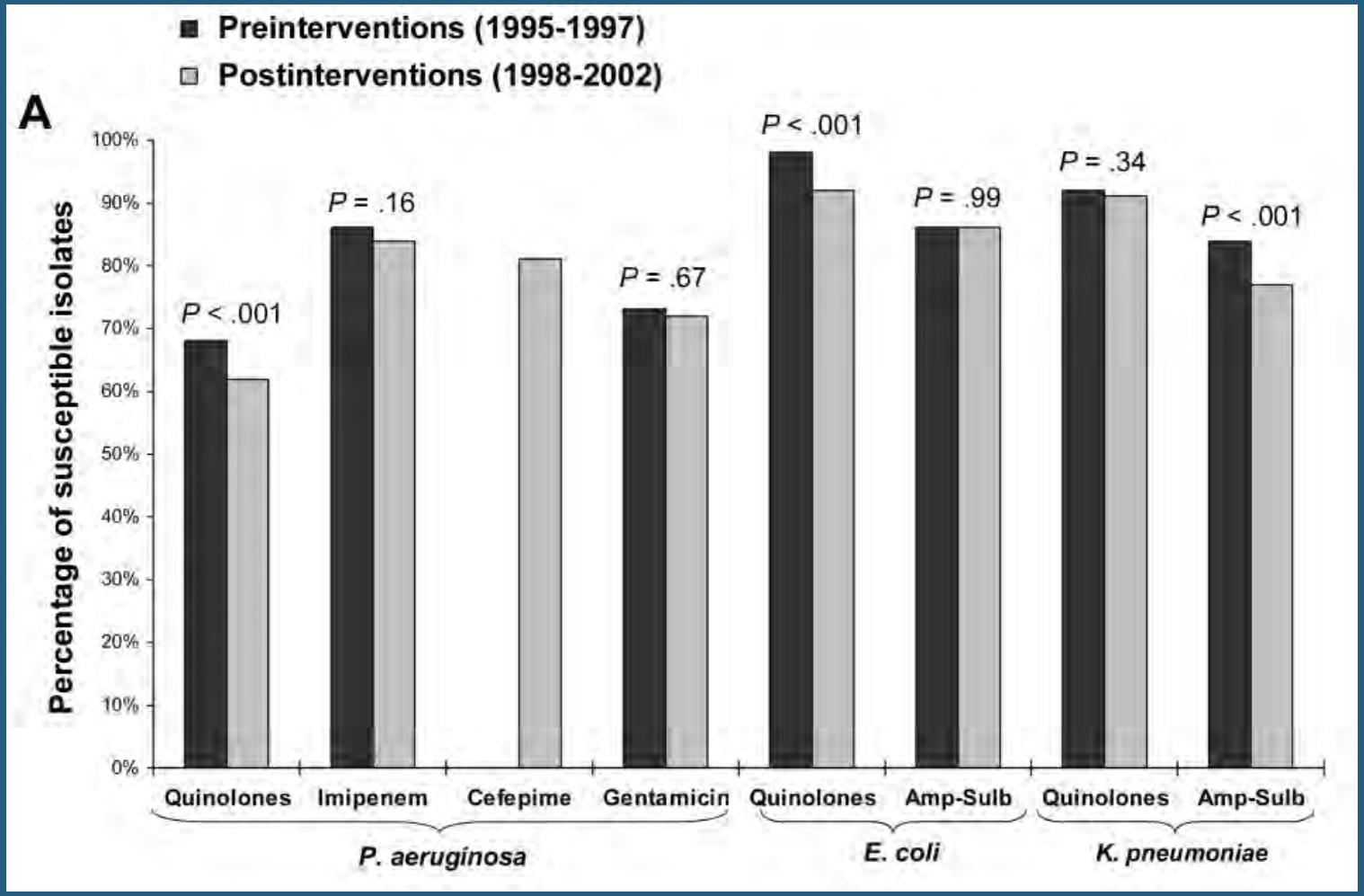
Lipworth AD, et al. Infect Control Hosp Epidemiol. 2006;27:279-86.

Impact of Antimicrobial Formulary Interventions on ESBL *E. coli* and *Klebsiella spp.*



Lipworth AD, et al. Infect Control Hosp Epidemiol. 2006;27:279-86.

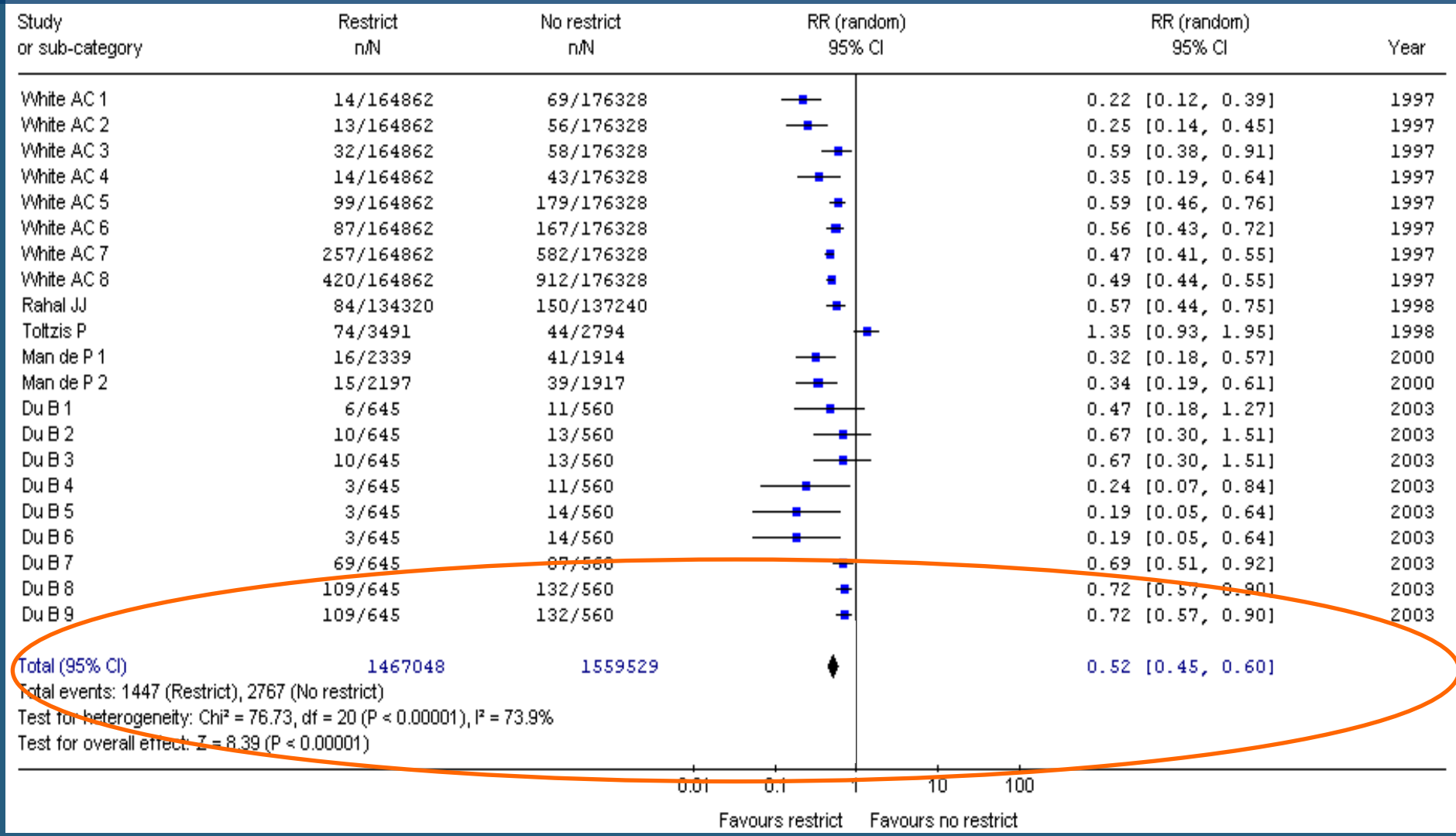
Changes in Antimicrobial Susceptibility After an Antimicrobial Intervention



Lipworth AD, et al. *Infect Control Hosp Epidemiol*. 2006;27:279-86.

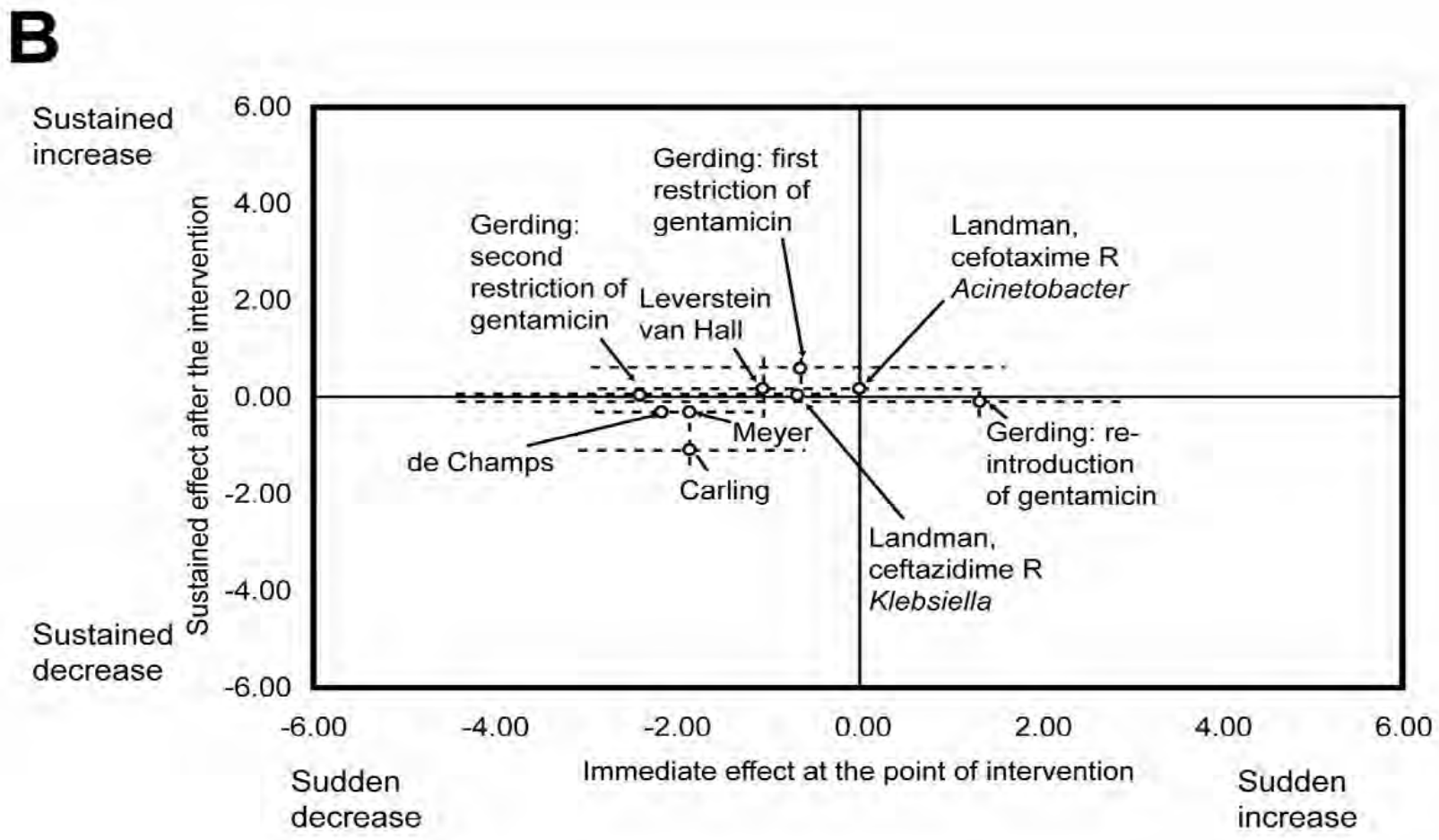
Meta-analysis: Effect of Antimicrobial Restriction

Review: Cephalosporin restriction in controlling cephalosporin resistance
Comparison: 01 Restrict
Outcome: 01 Antibiotic resistant ESBL Enterobacteriaceae



Ng & Tambyah 2nd APSIC

Do These Approaches Work? Effects for MDR-GNR



Davey P, et al. Systematic Review of Antimicrobial Drug Prescribing in Hospitals. Emerging Infectious Diseases .2006;12:211-216.

What Other Potential Control Measures Would You Institute

- Hand hygiene
- Isolation and barrier precautions
- Cohorting or separation of colonized/infected and non-colonized patients
- Control of environmental (cleaning) or other potential sources
- Antibiotic stewardship/management

Audience Response Question 3

Do antimicrobial interventions decrease resistance among gram-negative-R MDROs?

- No
- Yes, *Acinetobacter*
- Yes, ESBLs
- Yes, fluoroquinolone-R *P. aeruginosa*
- Yes, carbapenem-R *Acinetobacter*
- Yes, all gram-negative-Rs
- I don’t know and am tired!

Saurina G, et al. *J Antimicrob Chemother.* 2000;45:895-8.

Source control with chlorhexidine

- 6 ICUs in 4 centers
- Quasi experiemental design
- MRSA acquision decreased 32% (5.04 cases / 1000 eligible pt days vs 3.44, p=0.046)
- VRE acquisition decreased 50% (4.35 cases / 1000 eligible pt days vs 2.19 cases, p=0.008)
- Incident BSI decreased 21% (10.92 cases per 1000 pt days vs 8.66 cases, p=0.046)
- Progression to VRE bacteremia among VRE colonized patients (RR 3.35; 95% CI 1.13-9.87; P=0.035).

Climo et al. SHEA 2007

CHG skin decontamination in ICU patients

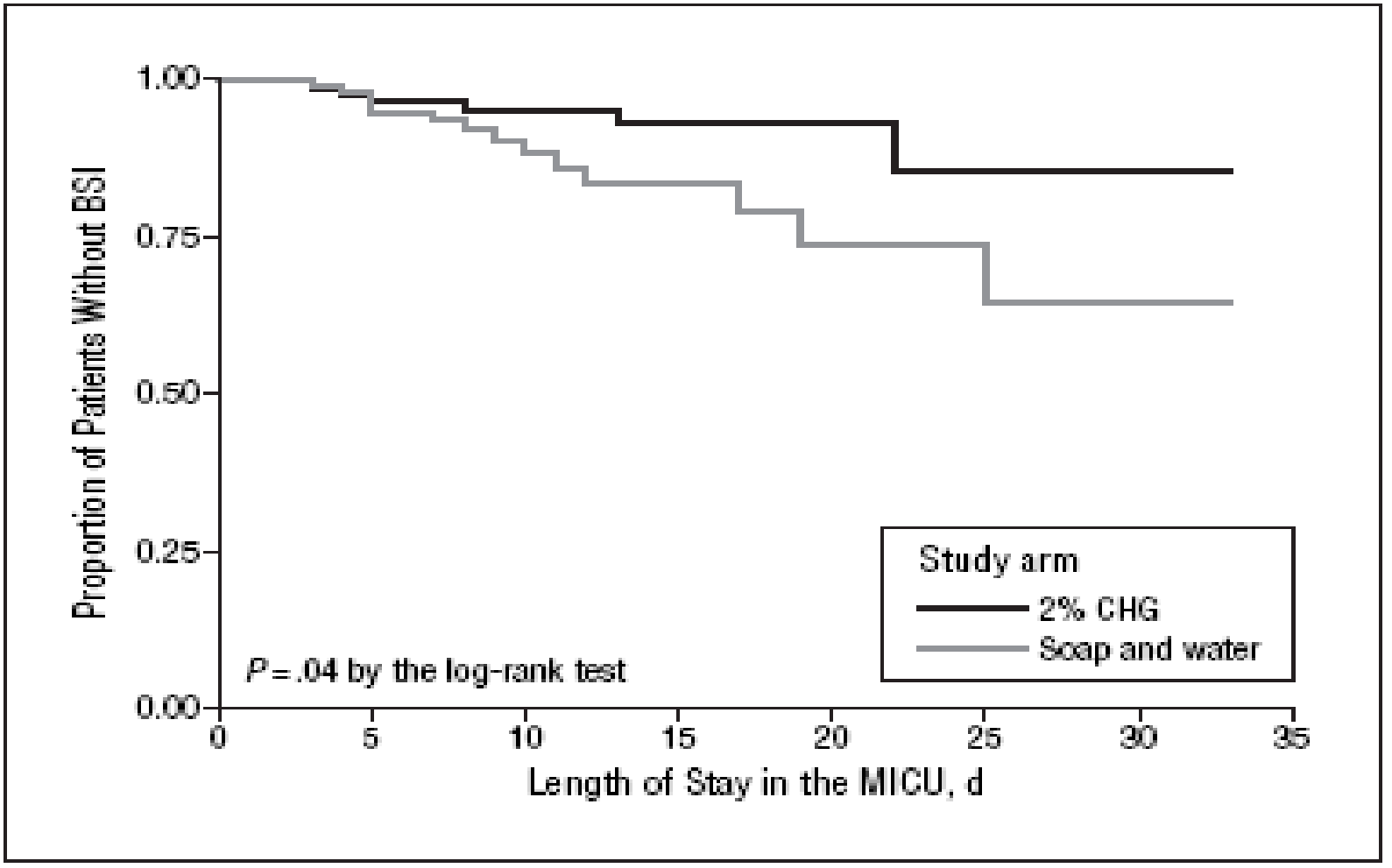
- Prospective, sequential group, single arm trial compared soap/water baths to cloths impregnated with 2% CHG in 1787 MICU pts
- 21 bed MICU
- 2004-6
- Outcomes: VAP, CLA-BSI

TABLE 1. Comparison of Nosocomial Infection Rates in the Medical Intensive Care Unit during 2 Study Periods

	Soap-and-water period		Chlorhexidine gluconate period		
Type of infection or culture	No. of cases	Rate	No. of cases	Rate	*P*
CVC-associated BSI	19	5.31[a]	2	0.69[a]	.006
Contaminated blood culture	47	6.99	23	4.1	.04
Secondary BSI	3	0.45	4	0.71	.48
CDI	6	0.89	2	0.36	.26
VAP	13	5.55[b]	10	6.33[b]	.76
UTI	20	2.97	13	2.32	.78
Clinical culture with drug-resistant bacteria					
Imi-res *A. baumannii*	7	1.04	2	0.36	.18
MRSA	11	1.63	8	1.43	.77
VRE	6	0.89	3	0.53	.47
Total	24	3.57	13	2.32	.21

Popovich et al. ICHE 2009;959-6

Effectiveness of CHG Bathing to Reduce Catheter-Associated BSI in MICU



Arch Intern Med 2007; 167:2073

CHG skin decontamination in trauma

- Prospective, sequential group, single arm trial compared soap/water baths to cloths impregnated with 2% CHG in 286 severely injured patients
- Single trauma center

Table 3. Outcome Variables Associated With Method of Bathing

Variable	Mean (SD) Without Chlorhexidine (n=253)	Mean (SD) With Chlorhexidine[a] (n=286)	*P* Value
Mechanical ventilation, d	10.3 (7.9)	9.5 (8.5)	.26
ICU length of stay, d	12.5 (12.7)	10.9 (15.2)	.19
Hospital length of stay, d	18.7 (14.3)	15.8 (11.8)	.01
Maximum MODS score	4.1 (3.5)	3.6 (3.1)	.08
Mortality, No. (%)	17 (6.7)	16 (5.6)	.72

Evans et al Arch Surg 2010:145 (3);240-6

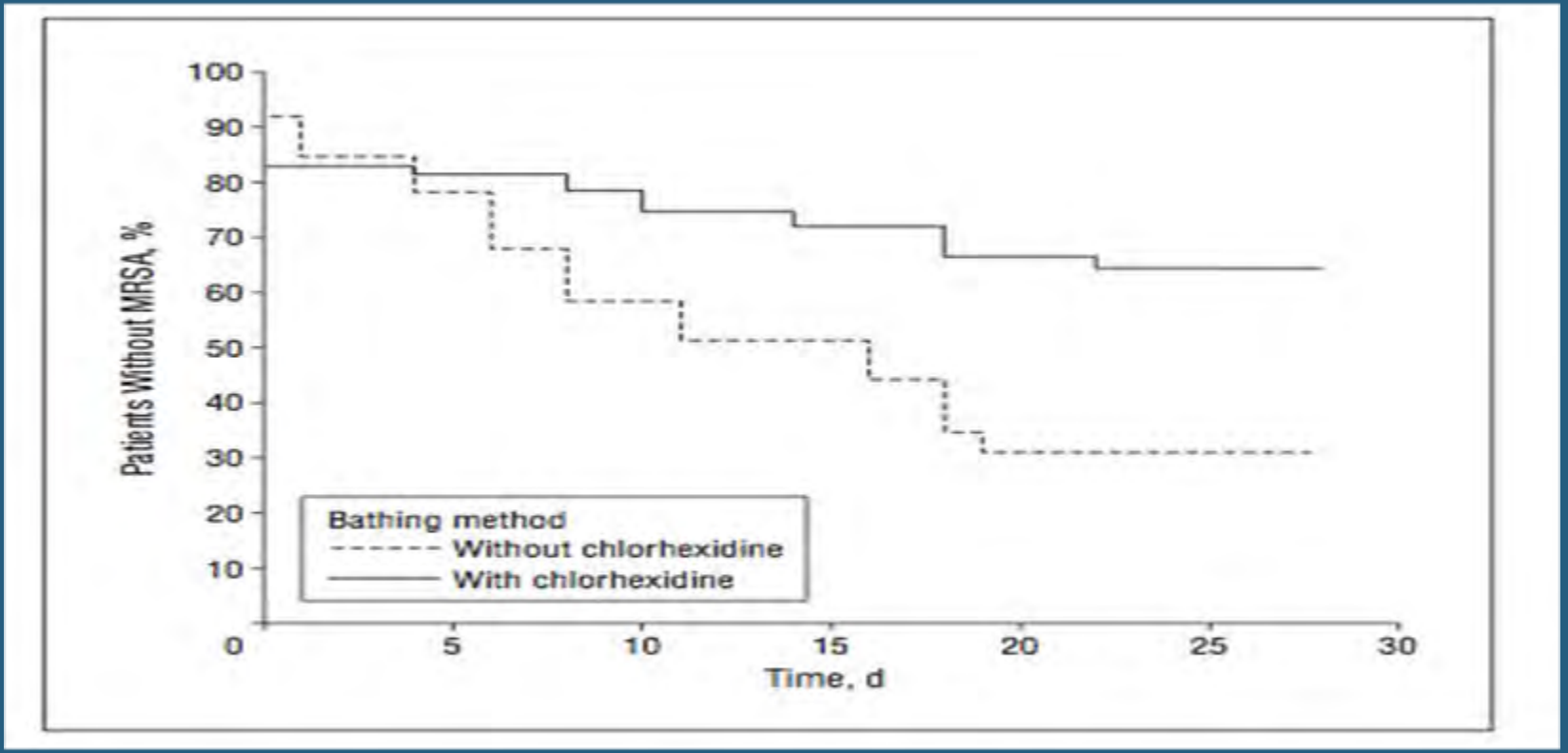
CHG skin decontamination in trauma

Table 4. Comparison of Infection Incidence by Method of Bathing

Infection	No. (No. per 1000 Device-Days) Without Chlorhexidine	With Chlorhexidine[a]	Difference (95% CI)	*P* Value
CRBSI	15 (8.4)	4 (2.1)	6.2 (1.6 to 1.9)	.01
UTI	14 (7.1)	12 (6.5)	0.6 (–4.5 to 5.7)	.82
VAP	38 (21.6)	33 (16.9)	4.7 (–4.2 to 13.6)	.30
Secondary BSI	6 (3.0)	5 (2.5)	0.5 (–2.7 to 3.8)	.76

Evans et al Arch Surg 2010:145 (3);240-6

CHG skin decontamination in trauma



Evans et al Arch Surg 2010:145 (3);240-6