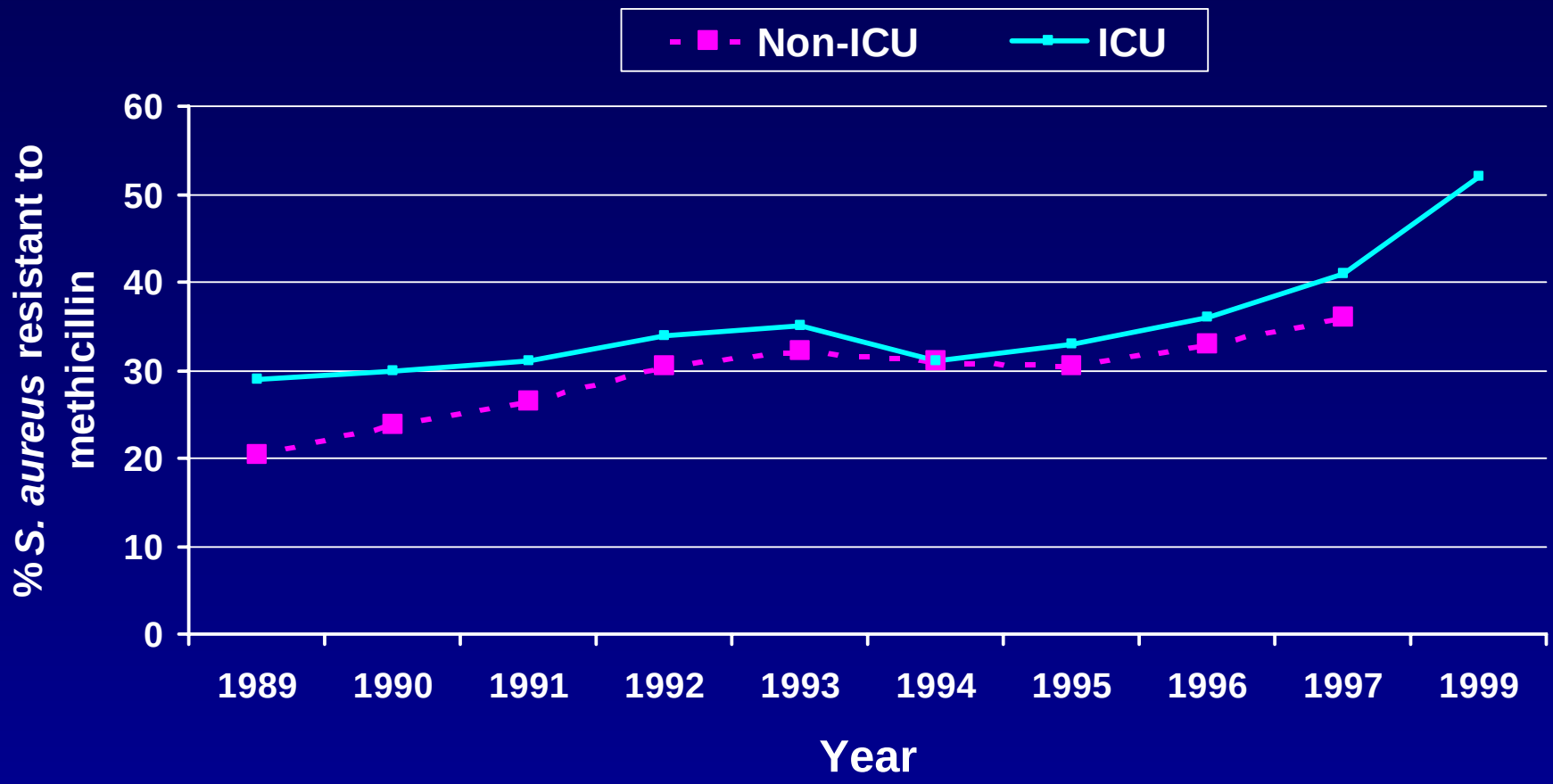
Controlling Antimicrobial Resistance

Barry M. Farr, MD, MSc
University of Virginia Health System
Charlottesville, VA

Rapid Increase in the Prevalence of Penicillin-resistant *Staphylococcus aureus*, Hammersmith Hospital, London

1941	**<1%**
1946	**13%**
1947	**38%**
1948	**59%**

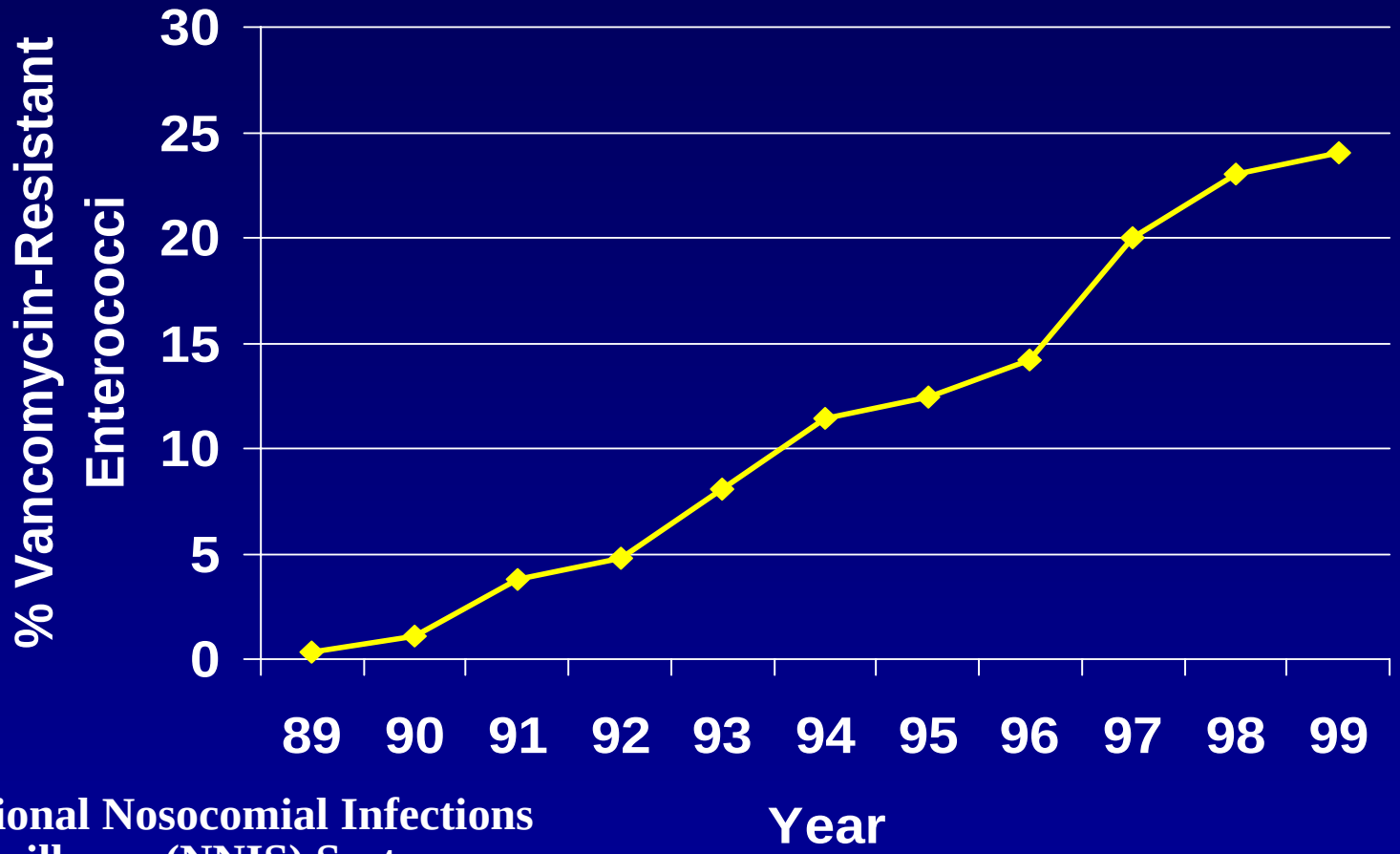
MRSA Isolates From ICUs vs Non-ICUs



ICU=intensive care unit

Fridkin. *Clin Chest Med*. 1999;20(2):303.

Percentage of Nosocomial Enterococci Reported as Resistant to Vancomycin, by Year



*National Nosocomial Infections Surveillance (NNIS) System Data, 1989-1999.

Genetic Mechanisms Of Developing Antibiotic Resistance

1. Random genetic mutation.
2. Plasmid swapping during conjugation.
3. Movement of transposons to plasmids/chromosomes.
4. Transduction by bacteriophages.
5. Transformation (acquisition of resistant genes from a recently killed cell and incorporation into a chromosome or plasmid).
6. Binary fission (replication) can share any of the above.

Mechanisms Of Developing Antibiotic Resistance

Natural Selection

Darwin C. *On the Origin of Species by Means of Natural Selection*, London, 1859.

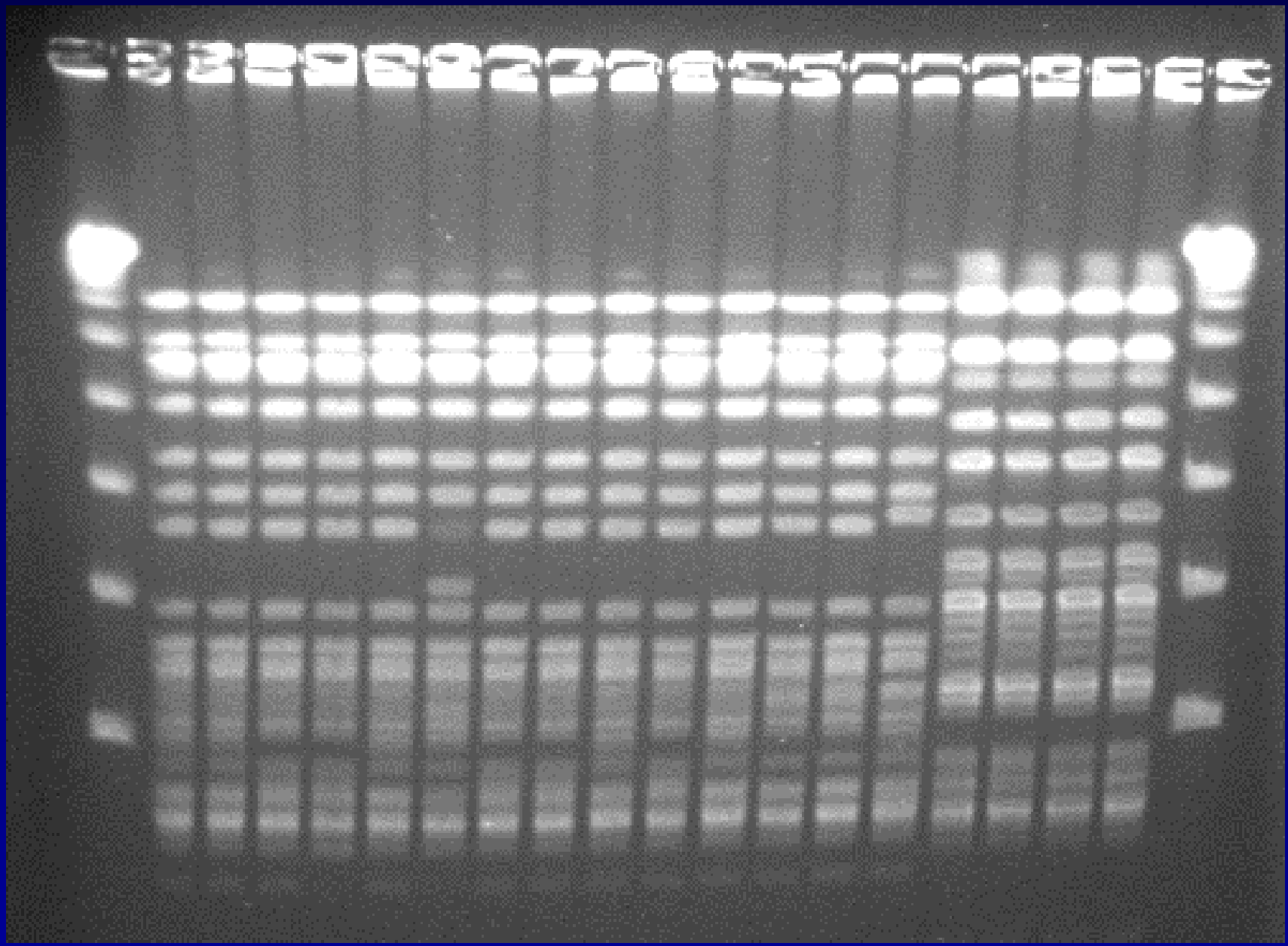
Antibiotic Exposure of Cases and Controls During Hospital VRE Outbreak

	Cases	Controls	p value
Vancomycin	46%	36%	0.219
Metronidazole	43%	21%	0.004
Clindamycin	31%	28%	0.755
Amp/sulbactam	27%	15%	0.073
Ticar/clav.	20%	14%	0.357
Imipenem	5%	4%	0.694
Ciprofloxacin	34%	24%	0.183
3rd gen. Ceph.	65%	50%	0.092
Aminoglycoside	45%	39%	0.492

VRE Incidence

Hospital Ward	Week 1	2	3	4
6th Floor				
ICU	0	0	0	0
Step-down Unit	0	0	0	0
5th Floor				
ICU	2	1	0	0
Step-down Unit	4	2	1	1
3rd Floor				
ICU	1	1	1	0
Step-down Unit	6	3	0	1

Byers KE, *et al.* *ICHE* 2001;22(3):140-147.



Transmission Of Individual Clones Of VRE

Boyce, *J Cin Micro* 1994;32:1148.

Dembry, SHEA 1994 Abstract #28.

Edmond, *Clin Infect Dis* 1995;20:1126.

Handwerger, *Clin Infect Dis* 1993;16:750.

Livornese, *Ann Int Med* 1992;117:112.

Montecalvo, *Anti Ag Chemo* 1994;38:1363.

Rubin, *Infect Cont Hosp Epi* 1992;13:700.

Possible Control Measures

1) Antibiotic control

2) Prevention of spread

   a) hand hygiene for all patient contacts (Universal/Standard Precautions)

   b) identify colonized patients with active surveillance cultures and use barrier precautions to prevent spread

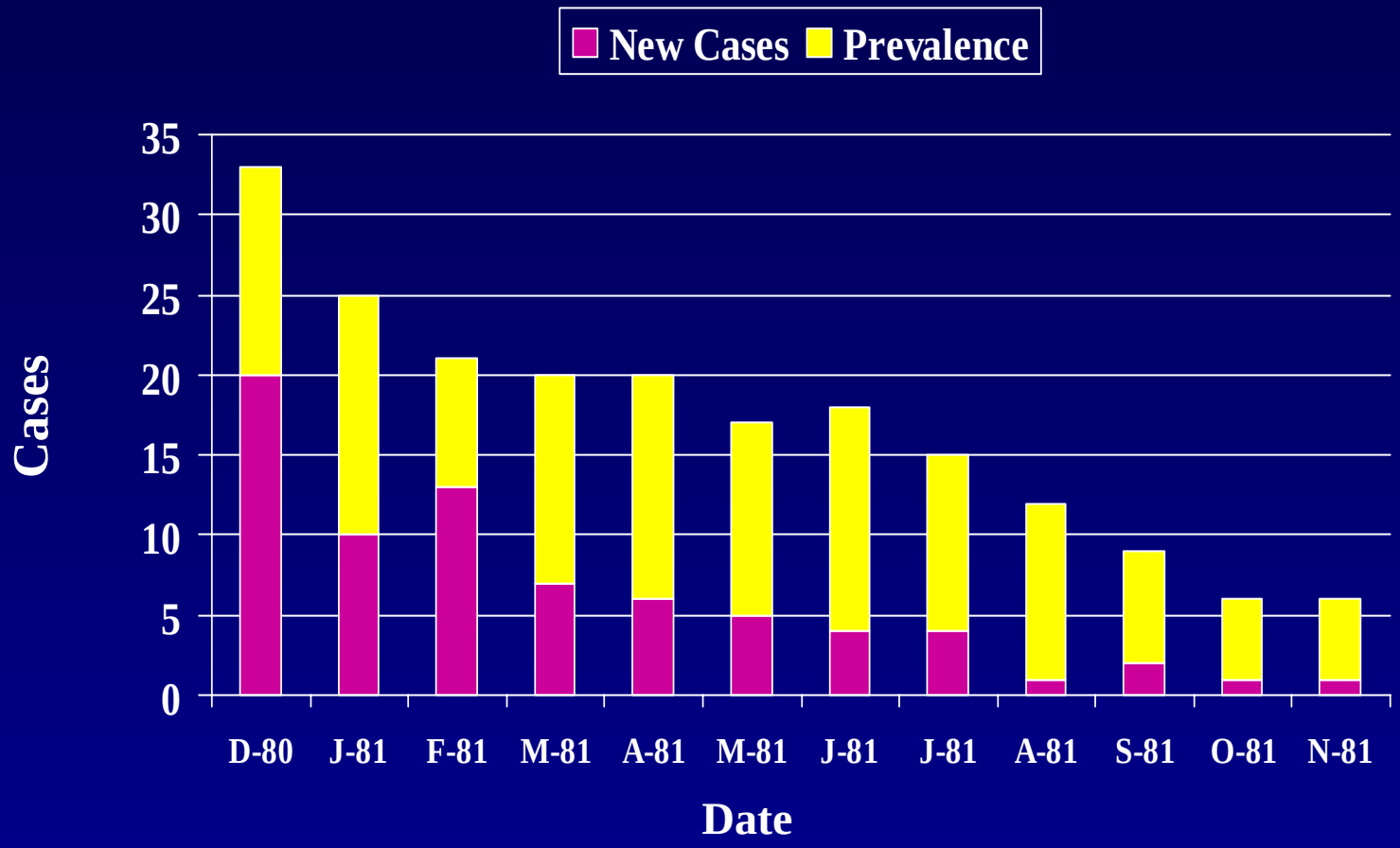
Failure to Control MRSA

- **Thompson *et al.* found that the prevalence of MRSA continued to increase** for 2.5 years **despite isolating patients known to have MRSA from routine clinical cultures**

	1977	1979	1980
Pneumonia	0%	19%	24%
Blood stream infection	0%	13%	40%
Surgical site infection	0%	27%	49%

Thompson RL, *Ann Intern Med* 1982;97:309

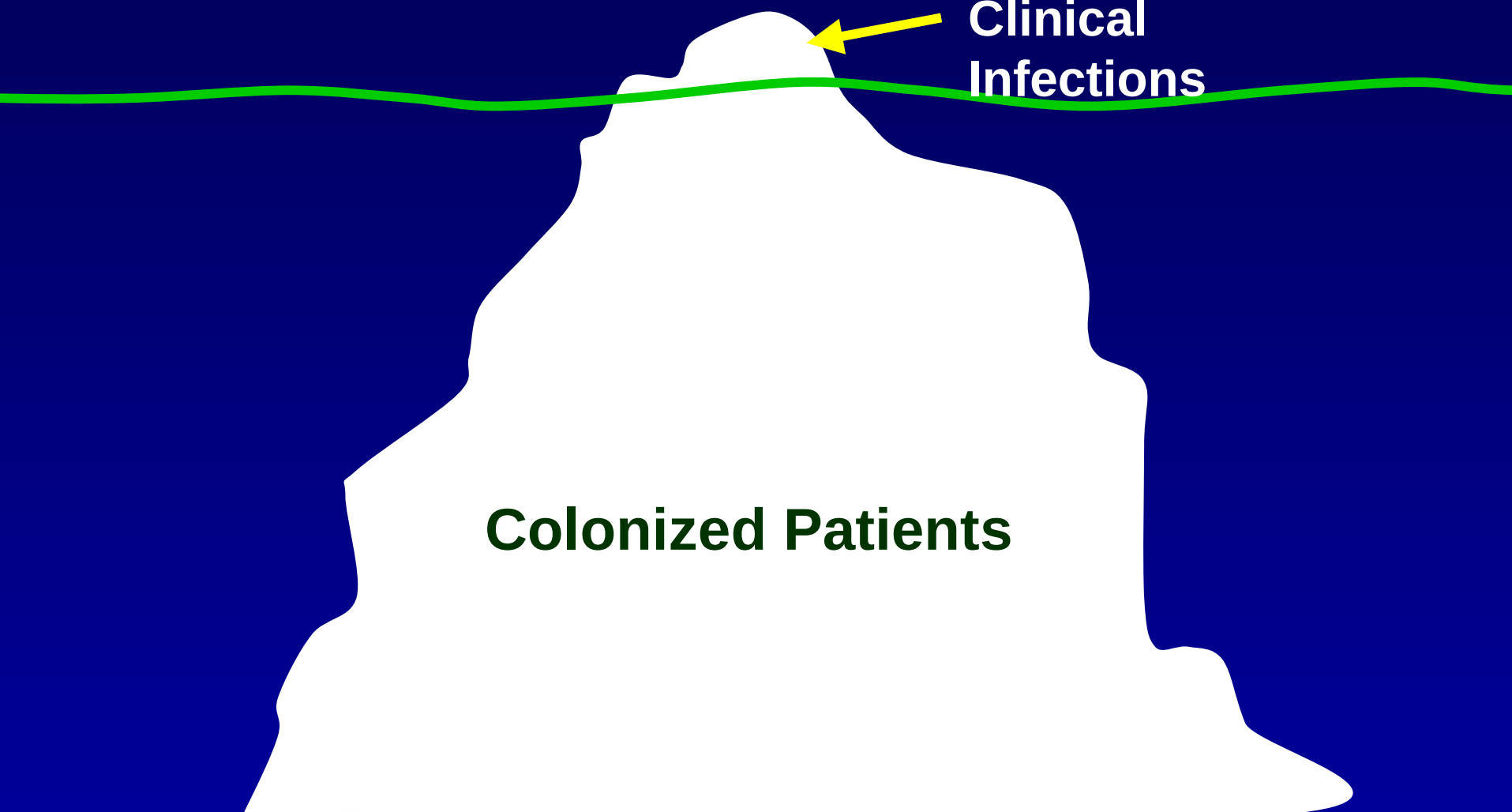
Control of MRSA Using Active Surveillance Cultures and Contact Precautions



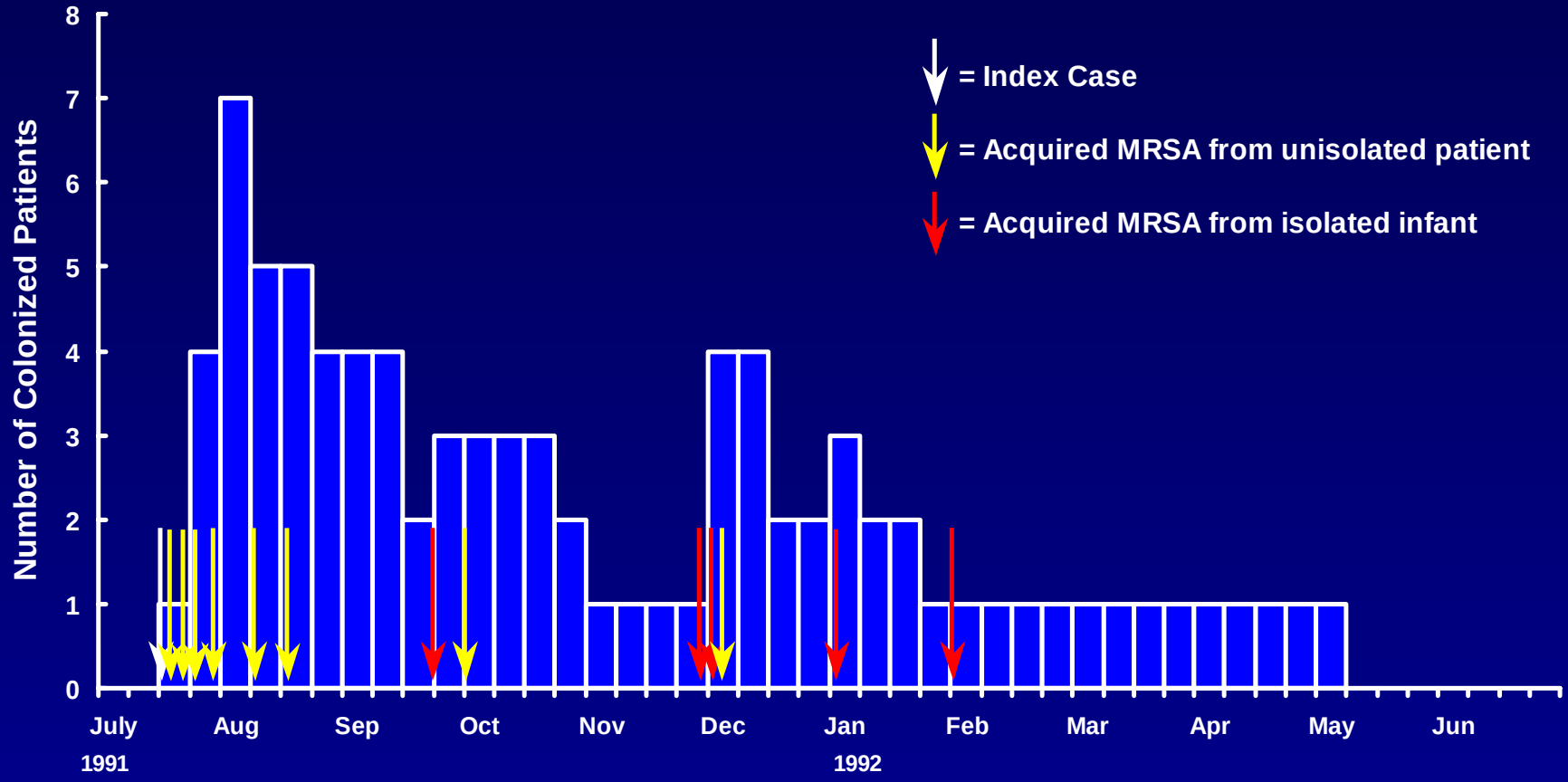
Incidence ($p < 0.002$) and Prevalence ($p < 0.001$)

Thompson RL, *Ann Intern Med* 1982;97:309

Reservoir for the Spread of Antibiotic Resistant Pathogens



Control of an MRSA NICU Outbreak Using ASC Without Antibiotic Control



Jernigan, *et al. Am J Epi* 1996;143

Rates of MRSA Transmission

	Source	
	Isolated	Unisolated
Transmissions	5	10
Patient-days	558	71.5
Rates	0.009	0.140

RR=15.6, 95% CI=5.3-45.6, p<0.0001

Jernigan, *et al. Am J Epi* 1996;143:496-504.

Control of 2 MRSA NICU Outbreaks Using ASC and Barrier Precautions Without Antibiotic Control

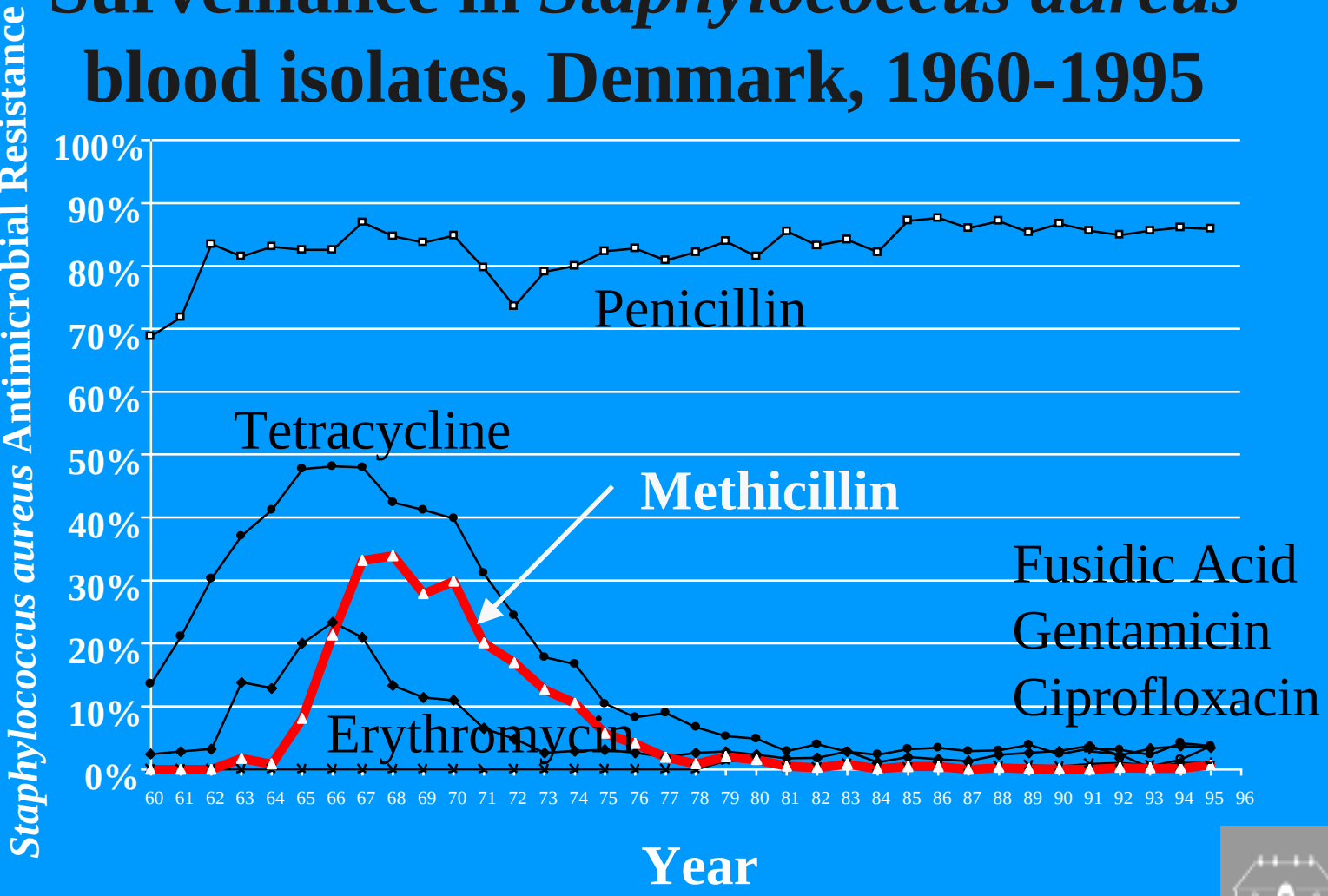
First outbreak in a 50-bed NICU controlled over several months

- **32 colonized over 5 weeks**
- **5 colonized infants (16%) became infected and one died of MRSA BSI.**

2nd outbreak of 14 colonized and 4 infected (29%) (with another death due to MRSA BSI) controlled in less than one month.

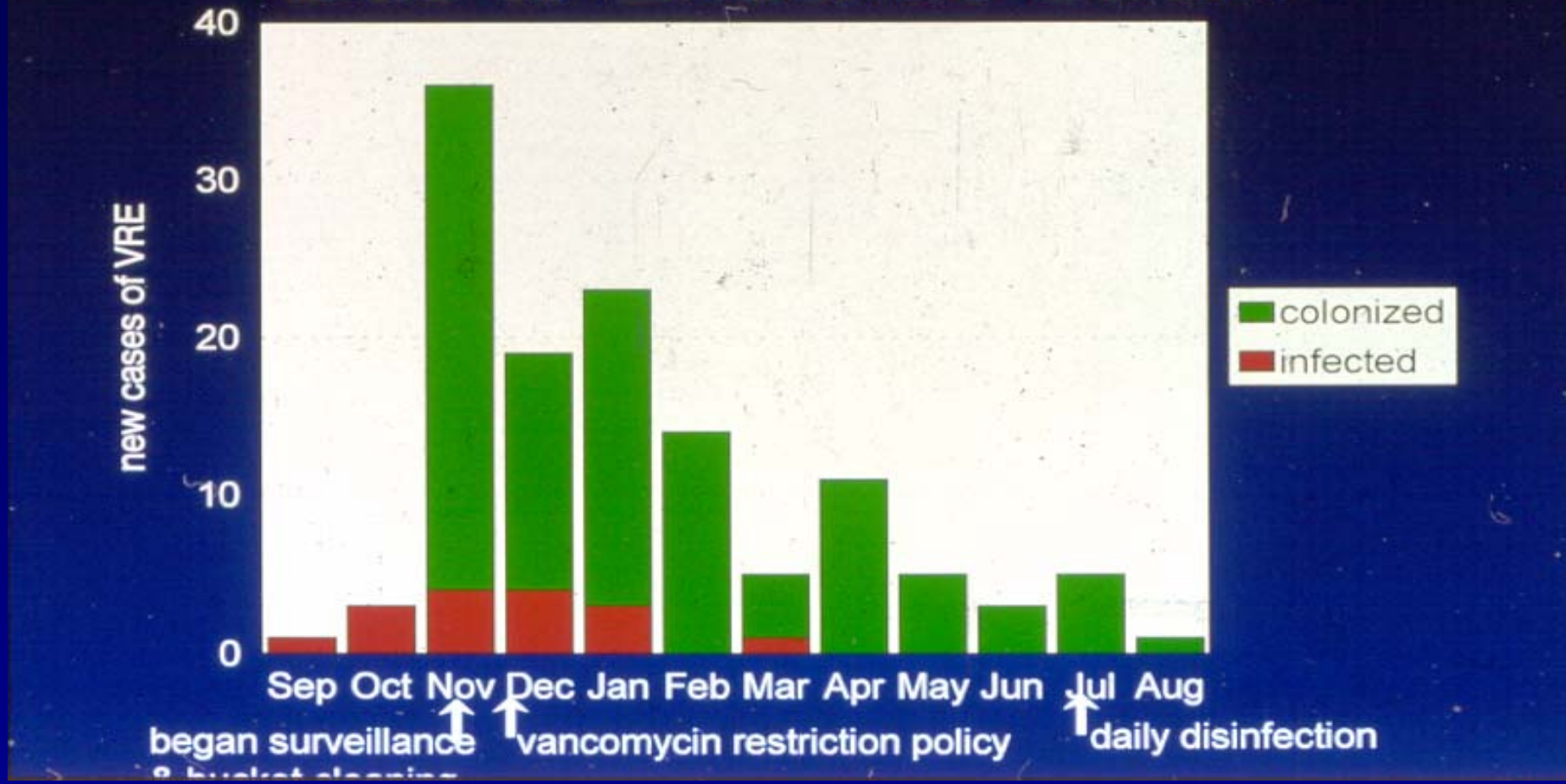
Back NA, *et al. ICHE 1996;17:227-231*.

Antimicrobial Resistance Surveillance in *Staphylococcus aureus* blood isolates, Denmark, 1960-1995



Source: DANMAP Report, 1997.

Incidence of Nosocomial VRE Due to Endemic Strain



Byers KE et al. ICHE 2001;22:140-7.

Conditional Logistic Regression Analysis

Variable	OR	P
Proximity to unisolated VRE patients	2.04*	0.0014
History of major trauma	9.27	0.020
Metronidazole therapy	3.04	0.040

* Per exposure-unit

Byers KE et al. ICHE 2001;22:140-7.

VRE Prevalence in 32 Healthcare Facilities, Siouxland, 1997 vs 1999

Facility	Number (%) VRE-Colonized		Relative Risk	p-value
	1997	1999		
All	40 (2.2)	9 (0.5)	0.23	<0.001
Acute Care	10 (6.6)	0	0	<0.001
Long-Term Care	30 (1.8)	9 (0.5)	0.31	0.001

Ostrowsky BE, *et al.*, NEJM 2001;344:1427-1433.

Excess Cost of MRSA Infection

MRSA infections cost significantly more than MSSA infections.

Engelmann J et al, ICAAC 2001 abst. K-2056, p. 441.

Cosgrove SE et al, ICAAC 2001 abst. K-1221, p. 415.

Abramson, *ICHE* 1999;20:408.

Wakefield, *AJIC* 1988;16:185-192.

Cheng, *J Hosp Infect* 1988;12:91-101.

Comparison of Primary MSSA and MRSA Nosocomial Bloodstream Infections

	MSSA	MRSA	P-value
Attributable excess length of stay median, days	4	12	0.023
Attributable total cost median	$9,661	$27,083	0.043
Attributable variable direct cost median	$4,989	$14,783	0.043

Abramson MA, *ICHE* 1999;20:408-11.

Attributable Mortality of MRSA Bacteremia

- Association with death was almost two-fold higher for MRSA bloodstream infections than for MSSA BSI (OR=1.9, 95% CI, 1.5,2.4, $p < 0.001$) after adjustment for severity of illness in a recent meta-analysis.

Cosgrove. SHEA 2001. Abstract #96.

Cost Benefit Analysis of Controlling MRSA

Compared: Excess costs generated by MRSA infection with the costs of control program (surveillance cultures and isolation).

Concluded: That control measures cost less than the infections and that this would remain so even if infection rates had declined by only 14%.

Chaix, *et al. JAMA* 1999;282:1745.

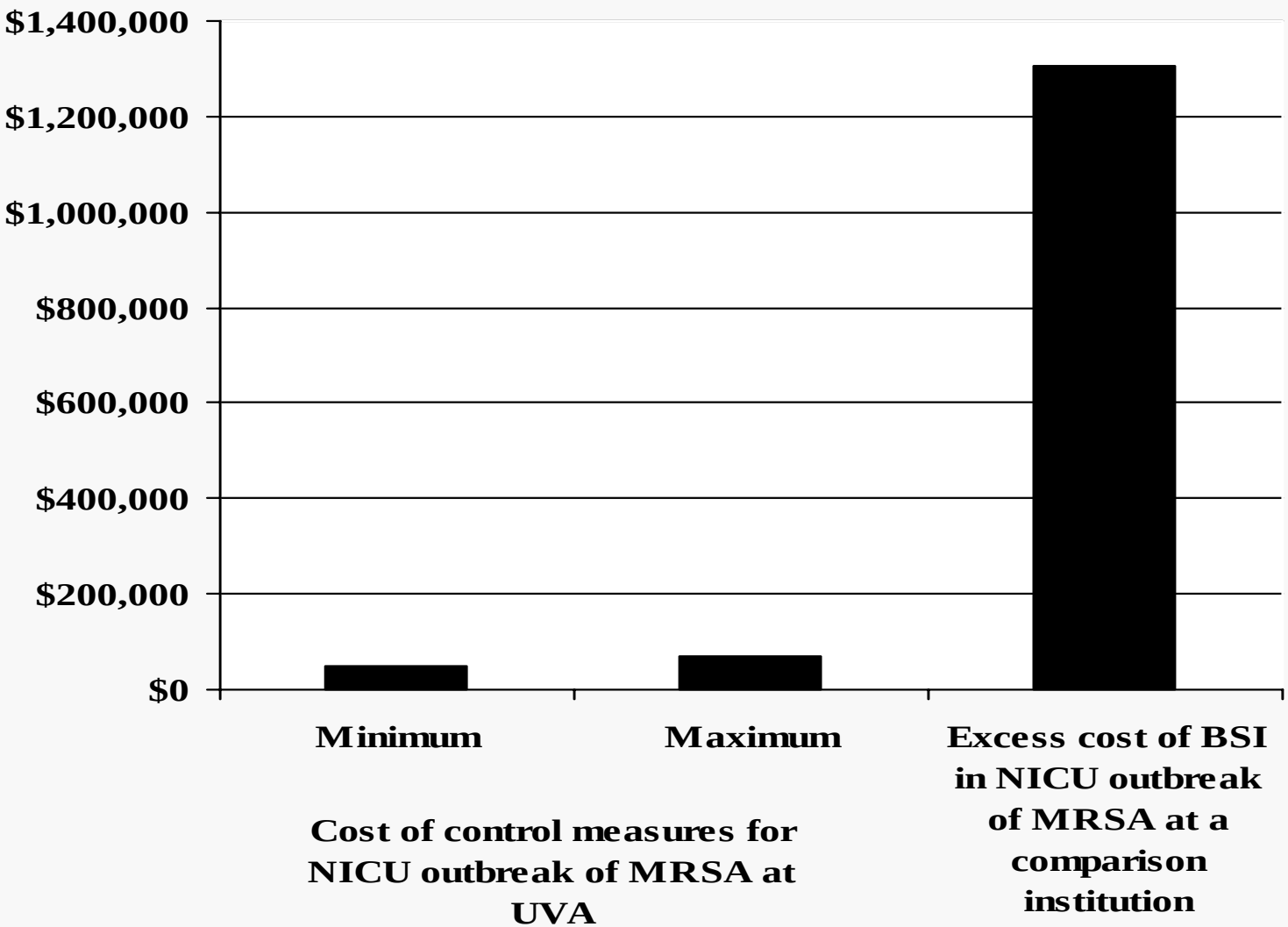
Cost Benefit Analysis of Controlling MRSA

Compared: Excess costs generated by MRSA infection with the costs of control program (surveillance cultures and isolation).

Concluded: That control measures cost less than the infections and that this could prevent 8 to 41 nosocomial infections and save a tertiary care hospital from $20,062 to $462,067 per year.

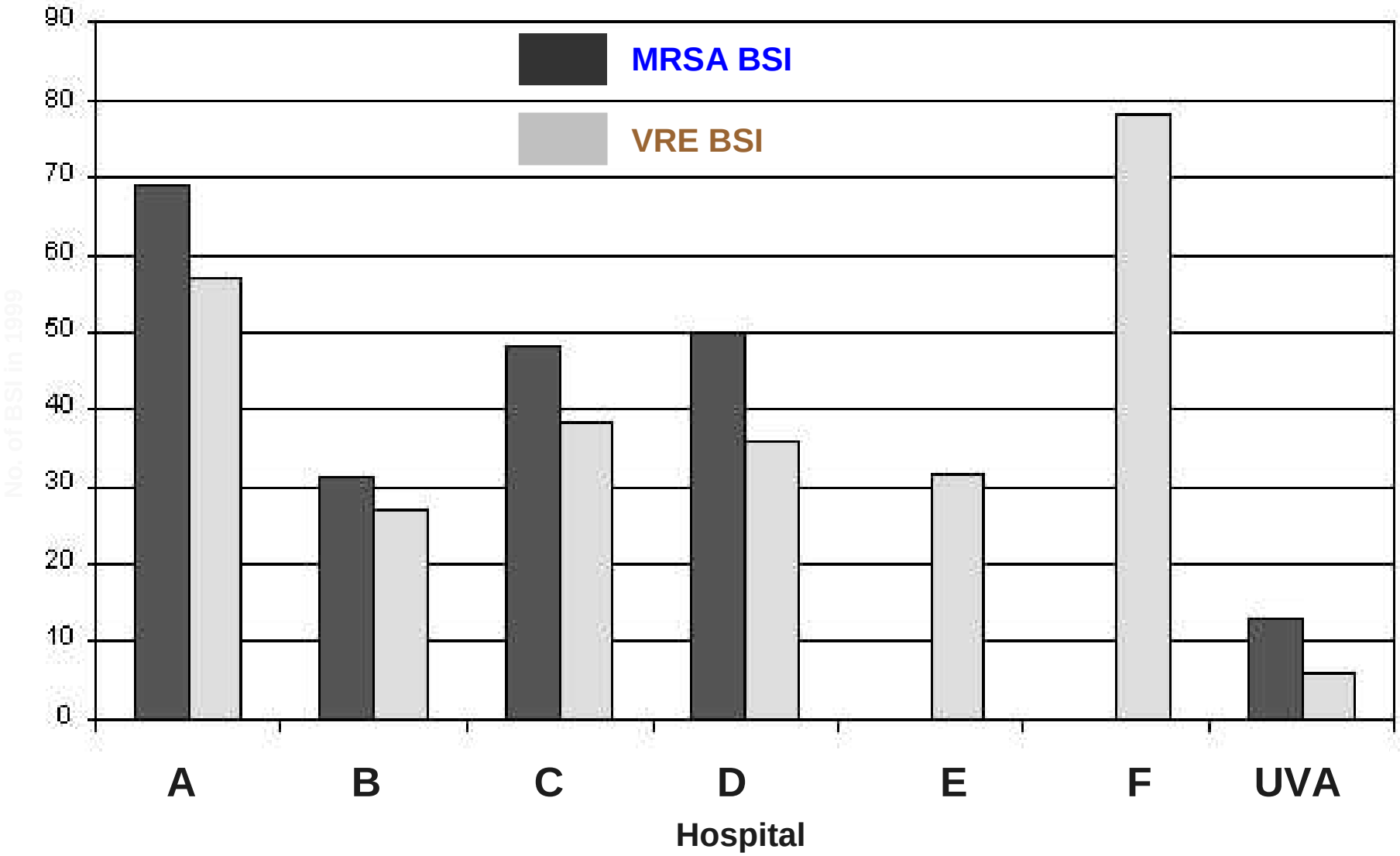
Jernigan JA, *et al. ICHE* 1995;16:686.

FIGURE



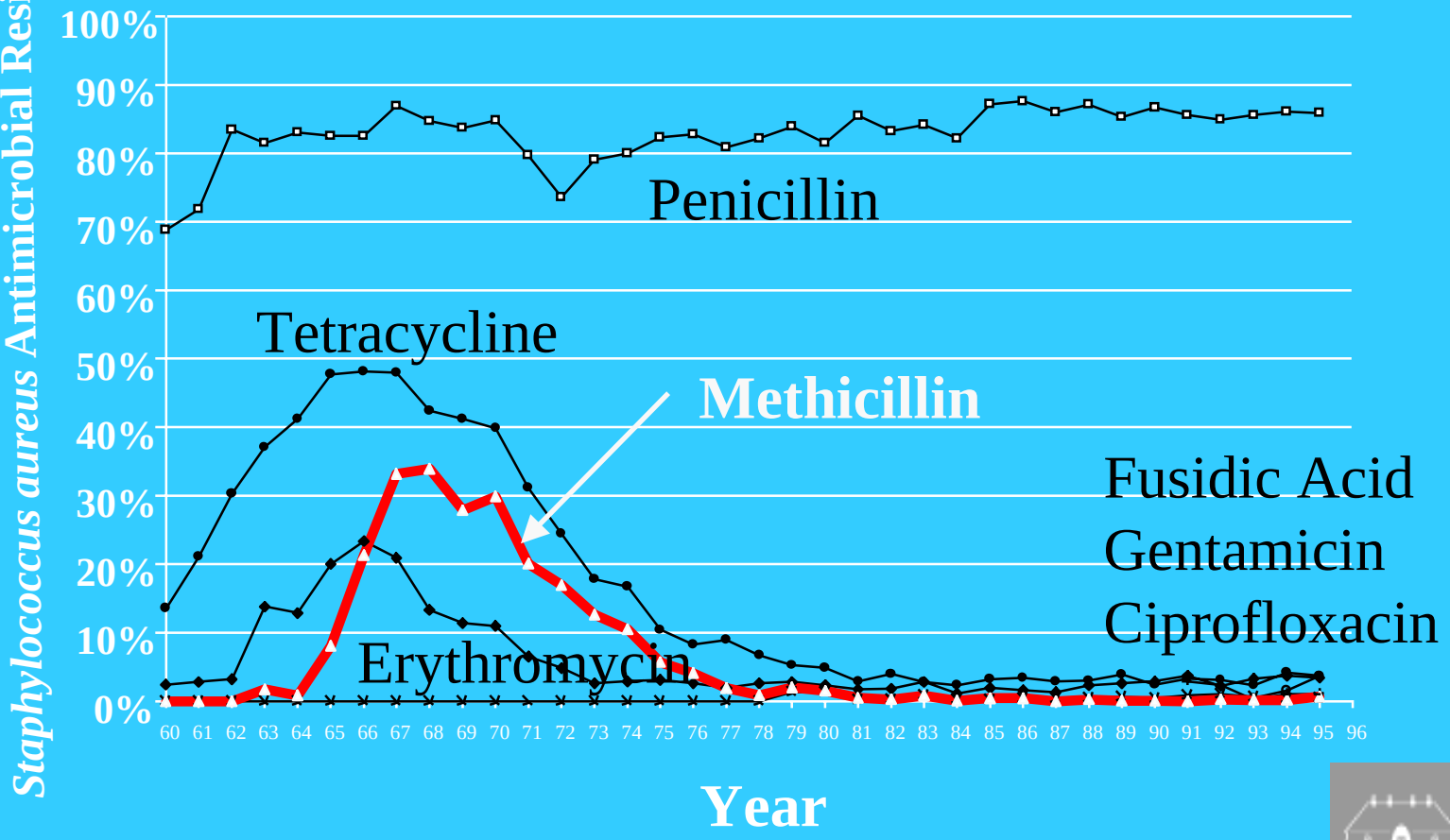
Karchmer TB et al, J Hosp Infect. In press.

VRE and MRSA Bacteremias at Hospitals of Comparable Size and Complexity, 1999



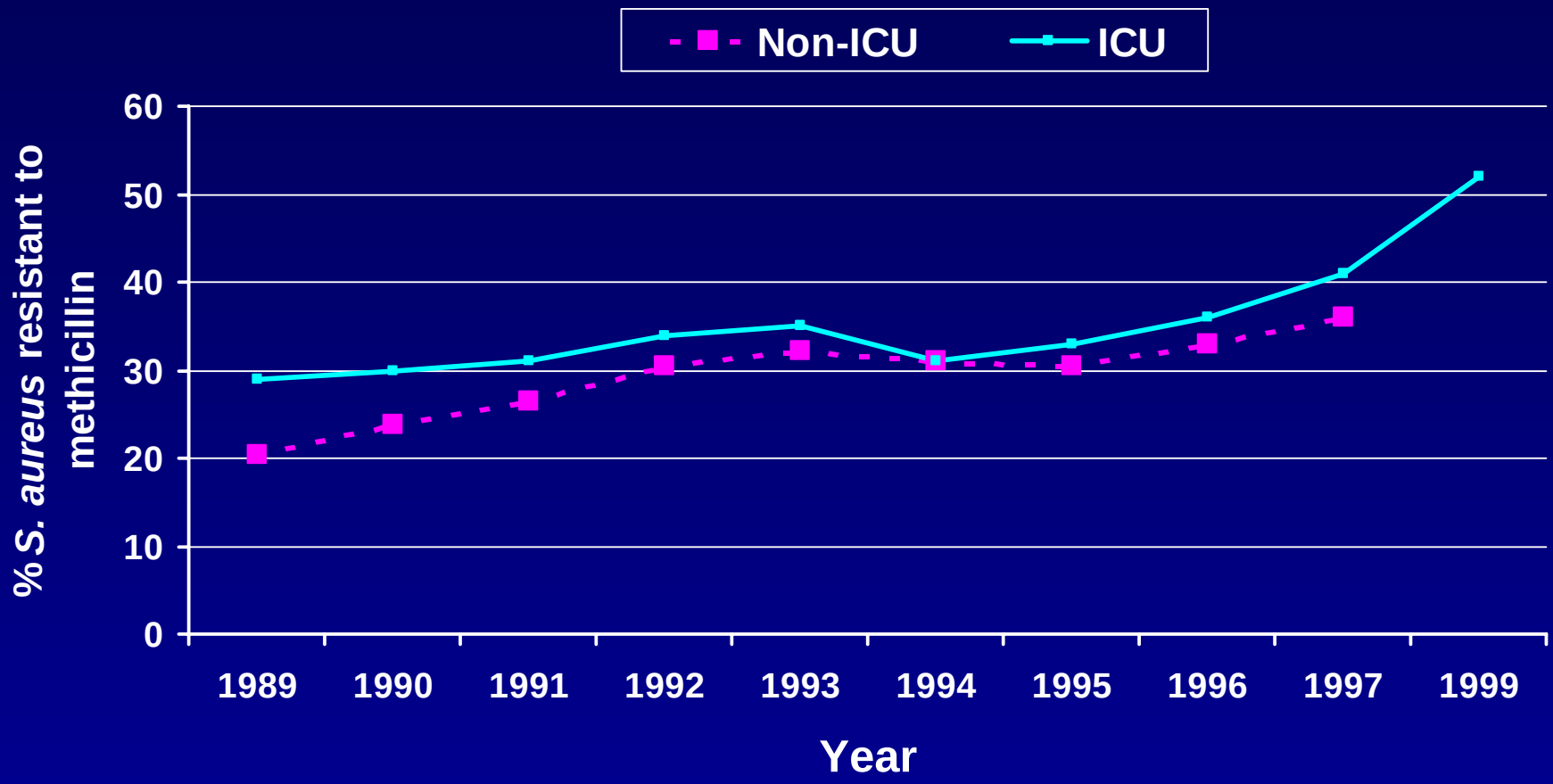
Calfee DP, et al. SHEA 2001, abstract 127, p 66.

Antimicrobial Resistance Surveillance in *Staphylococcus aureus* blood isolates, Denmark, 1960-1995



Source: DANMAP Report, 1997.

MRSA Isolates From ICUs vs Non-ICUs



ICU=intensive care unit

Fridkin. *Clin Chest Med*. 1999;20(2):303.