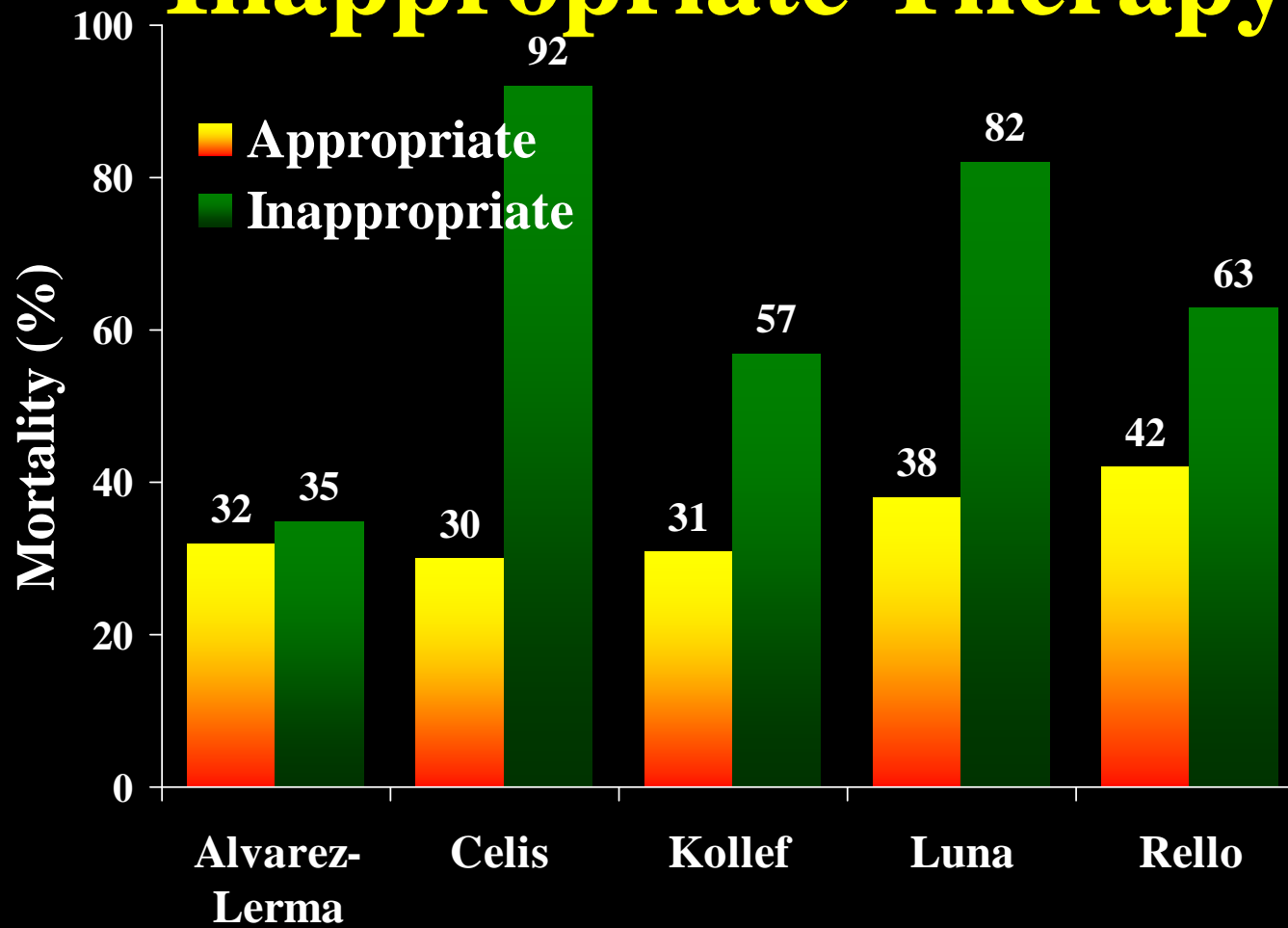


Determining Response to Therapy in VAP

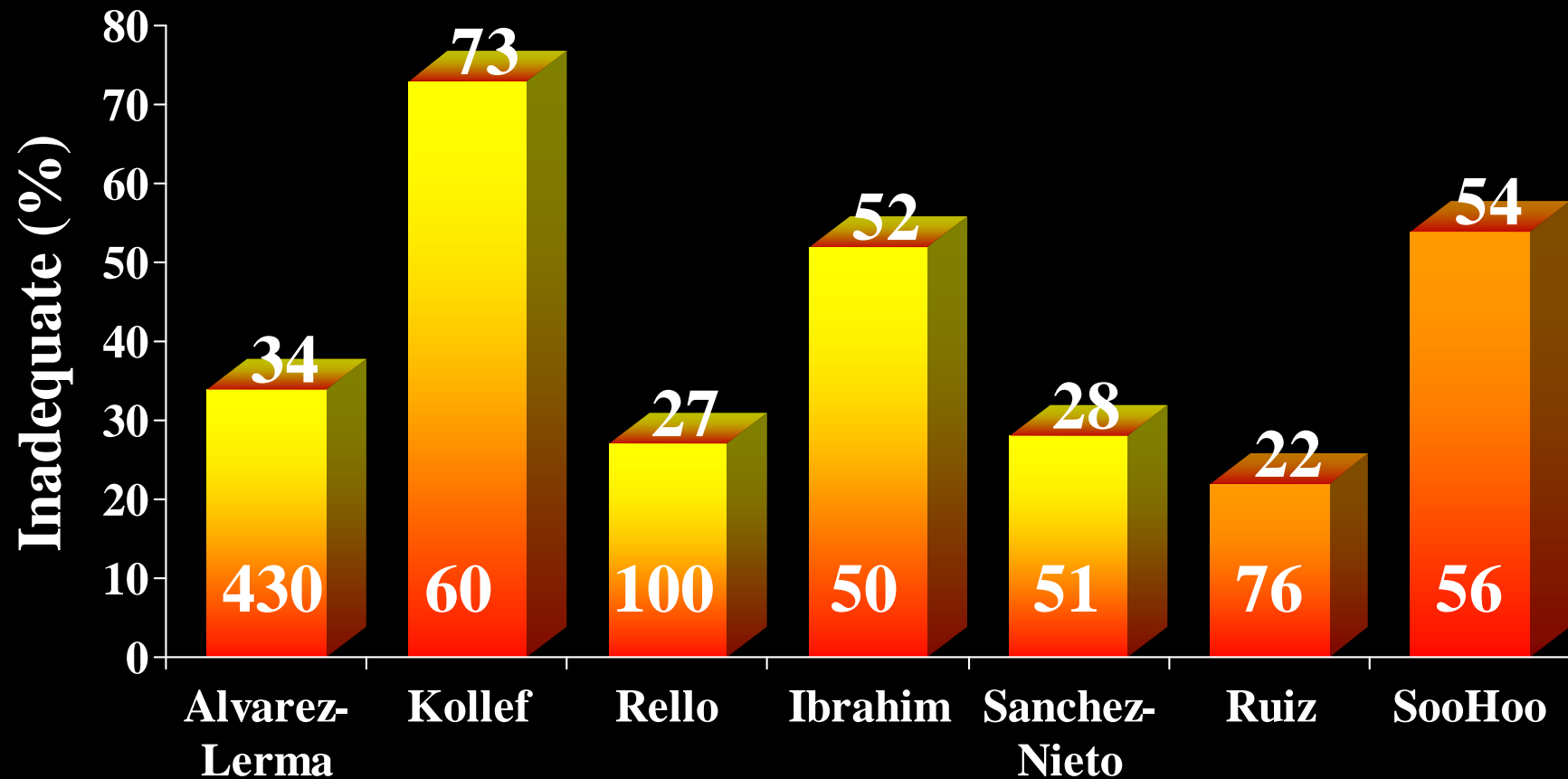
Richard G. Wunderink MD

**Northwestern University Feinberg School of Medicine
Chicago, IL**

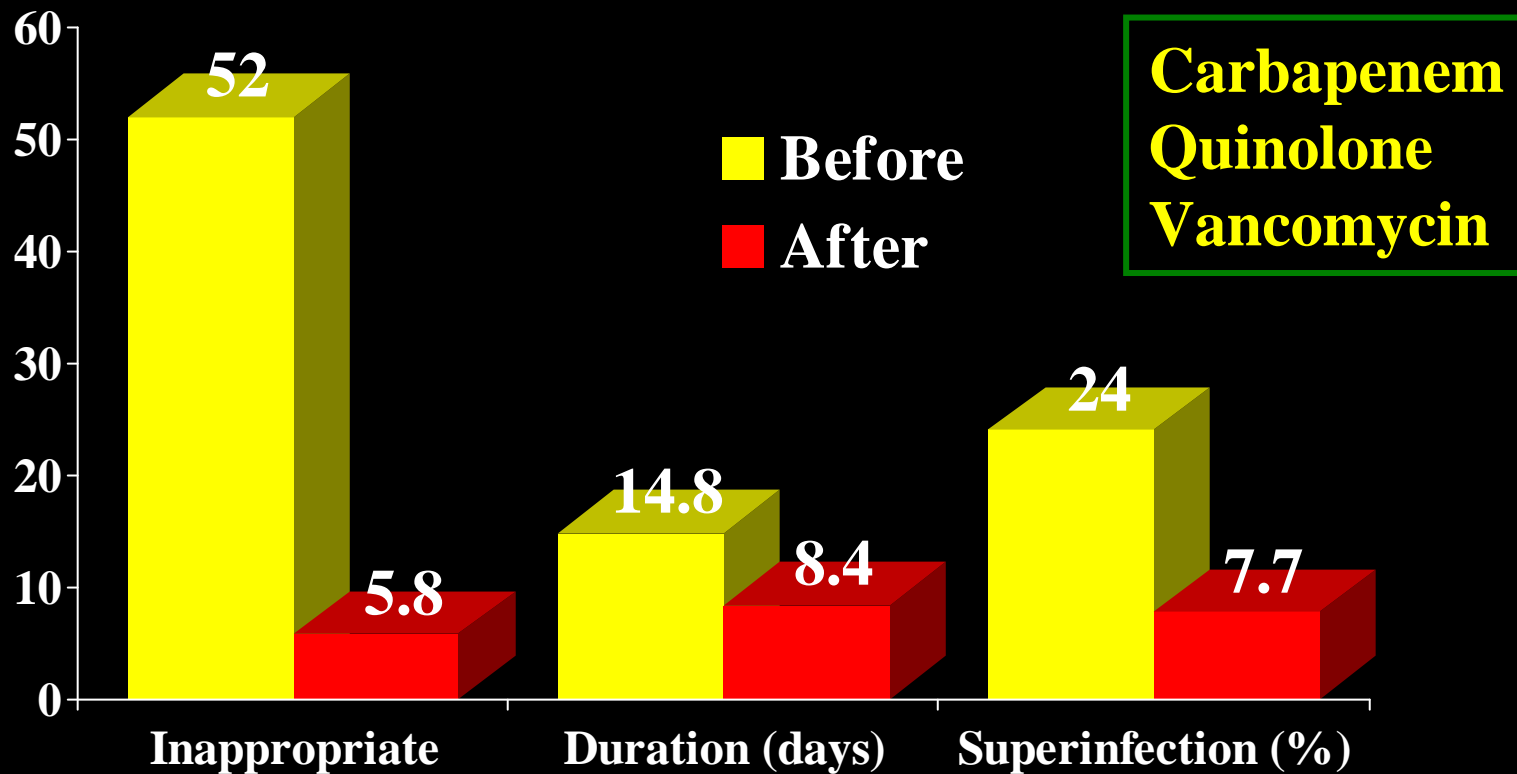
VAP Mortality and Inappropriate Therapy



Inappropriate Initial Antimicrobial Therapy



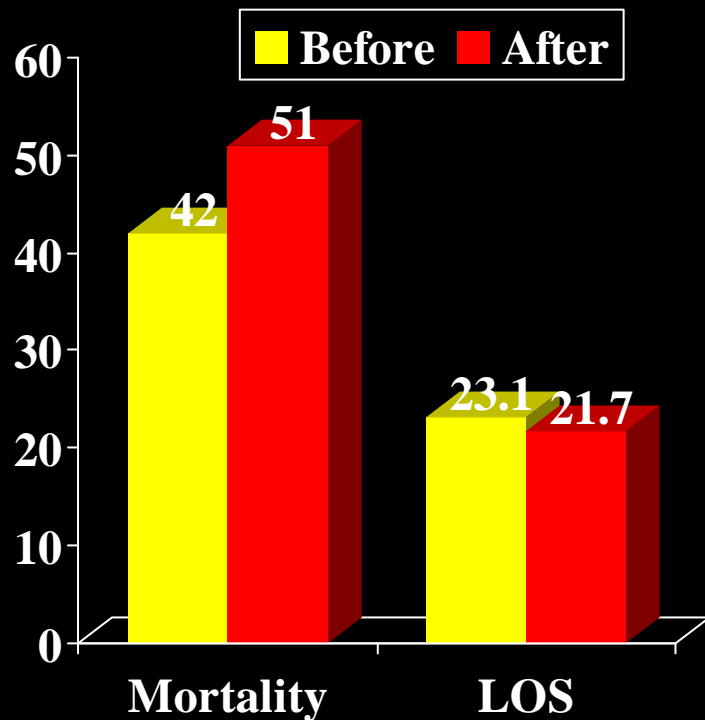
Inappropriate Antibiotics for VAP



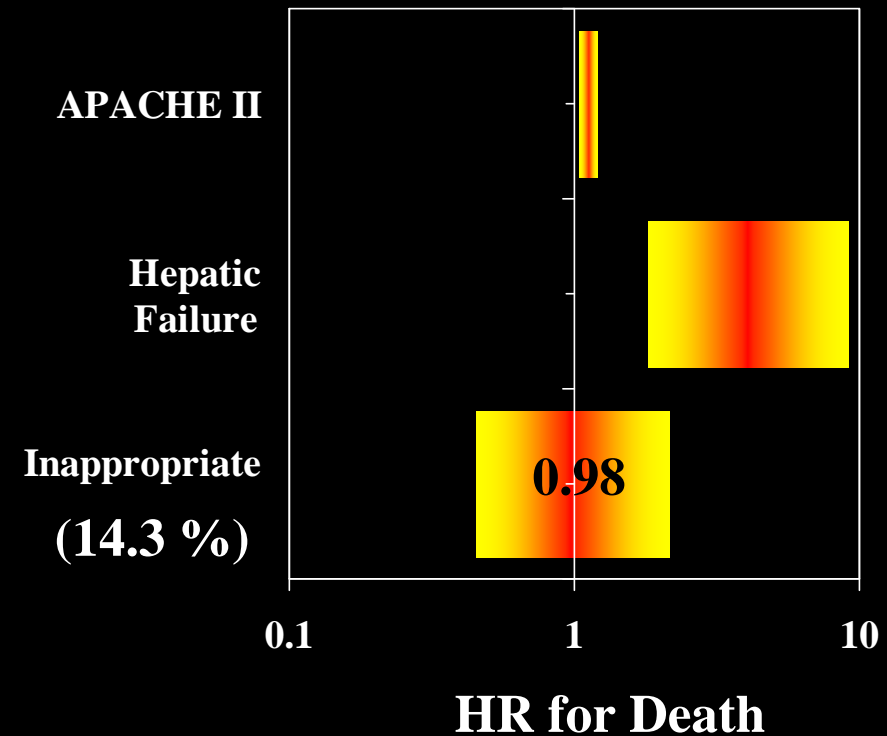
Ibrahim, Crit Care Med, 2001

Why discuss response?

Mortality with Low Inappropriate Initial Antibiotic Rates



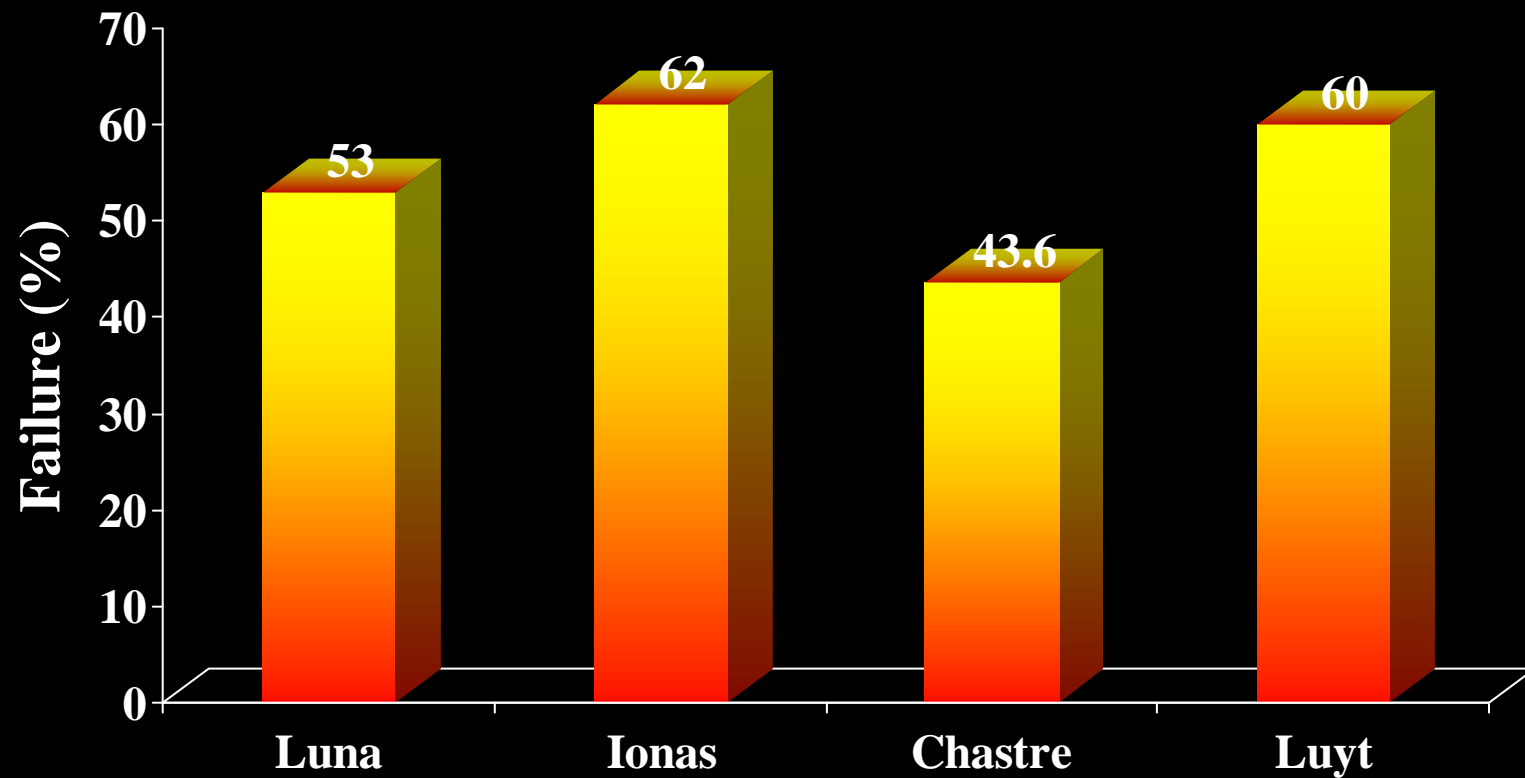
Ibrahim, Crit Care Med, 2001



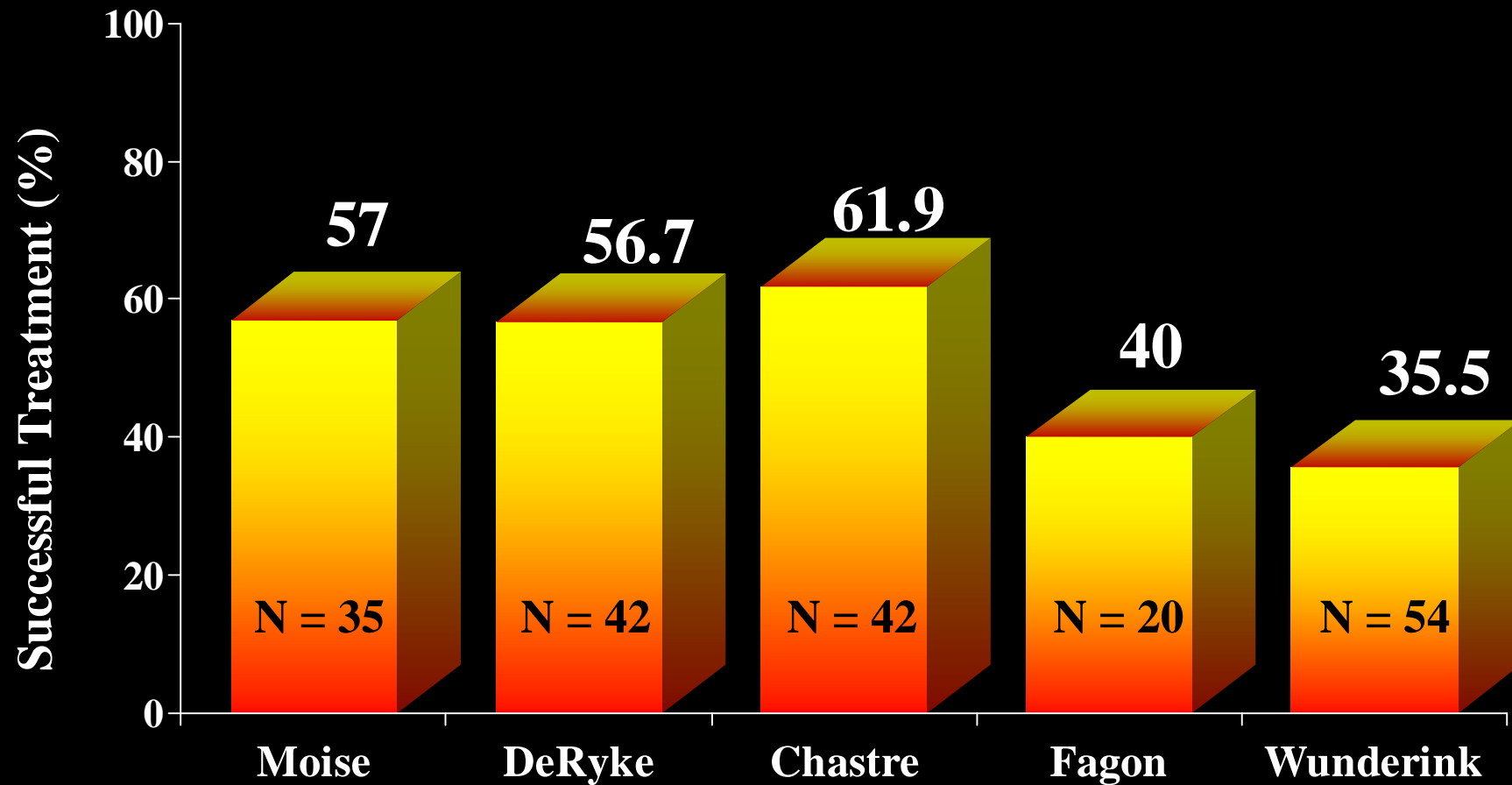
Fowler, Chest, 2003

Appropriate empiric
antibiotic therapy is
necessary but may not be
sufficient to improve
mortality of VAP

Treatment Failure in VAP

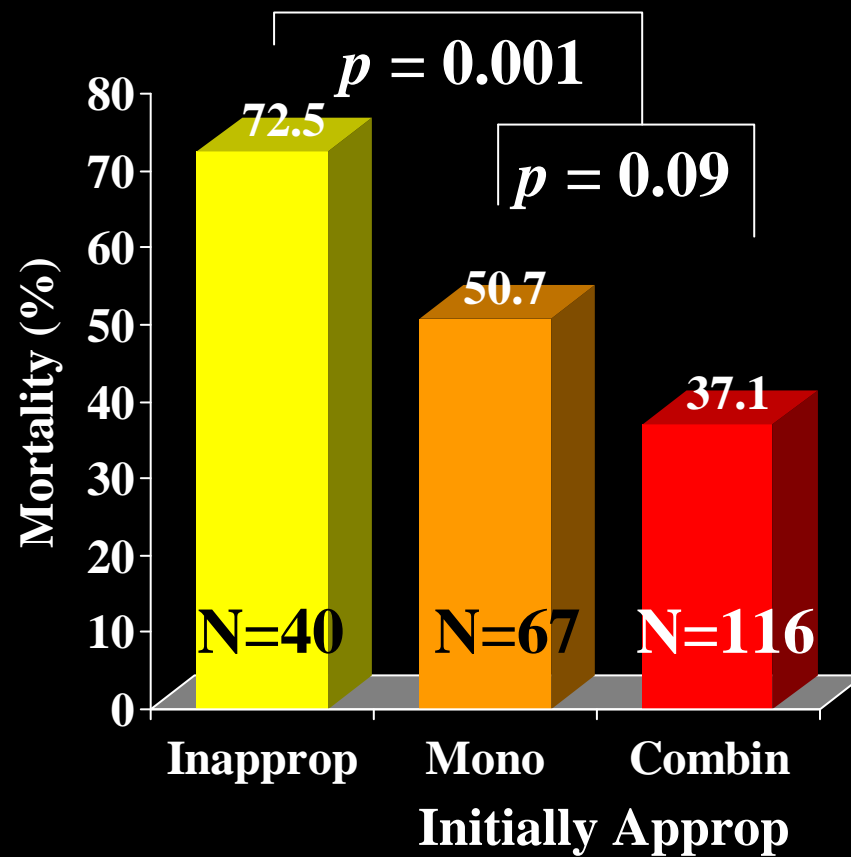


MRSA Treatment with Vancomycin



Combination Therapy of Pseudomonas VAP

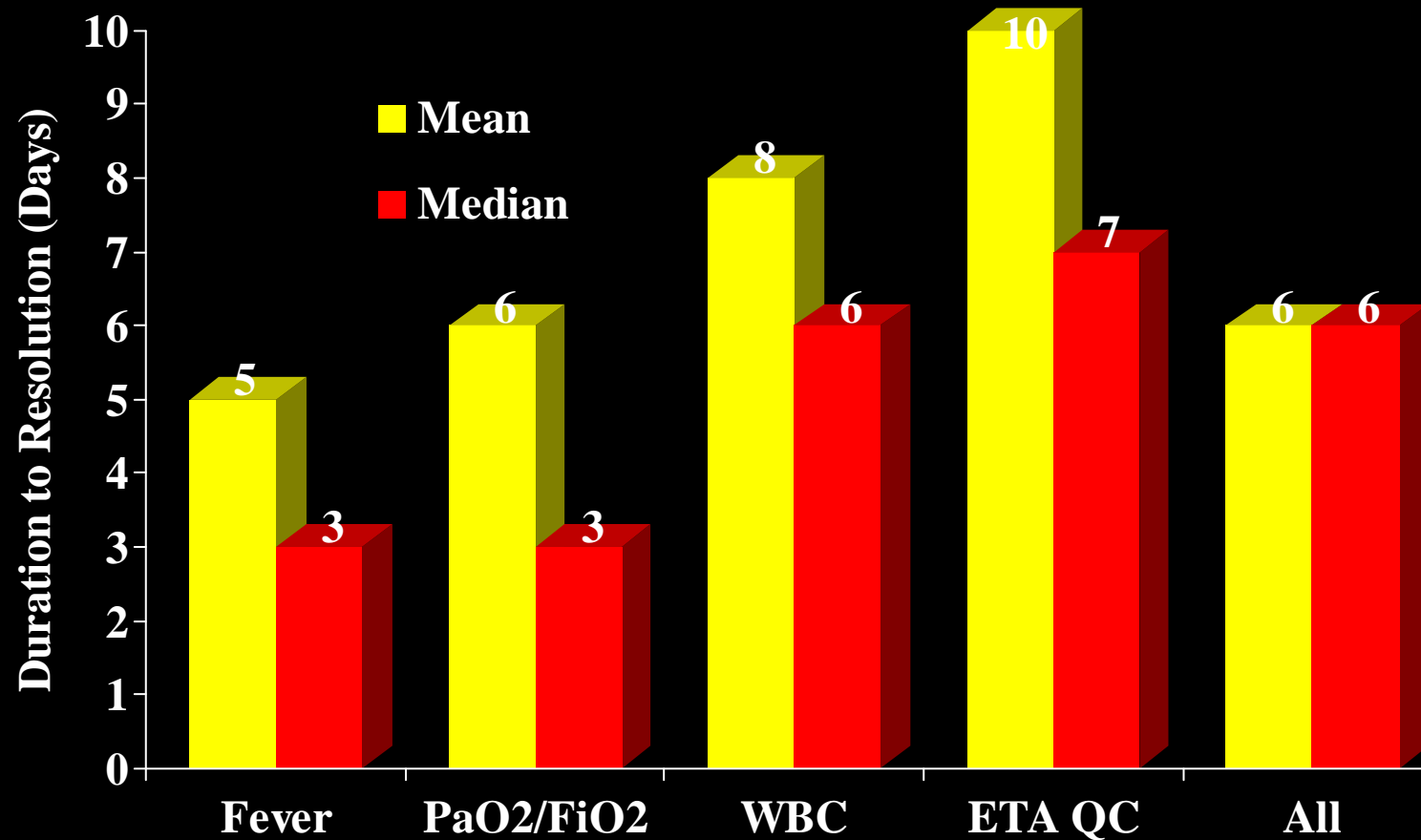
- ❖ Retrospective study of 183 cases of monomicrobial Pseudomonas VAP
- ❖ Initially inappropriate significantly higher with monotherapy ($p = 0.001$)
- ❖ Estimated attributable mortality of monotherapy was 13.6% (95% CI 2.6-29.9)



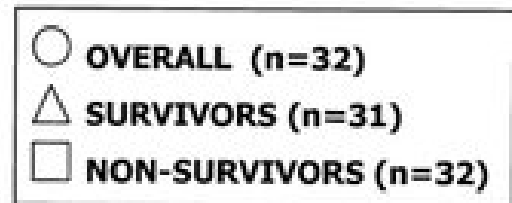
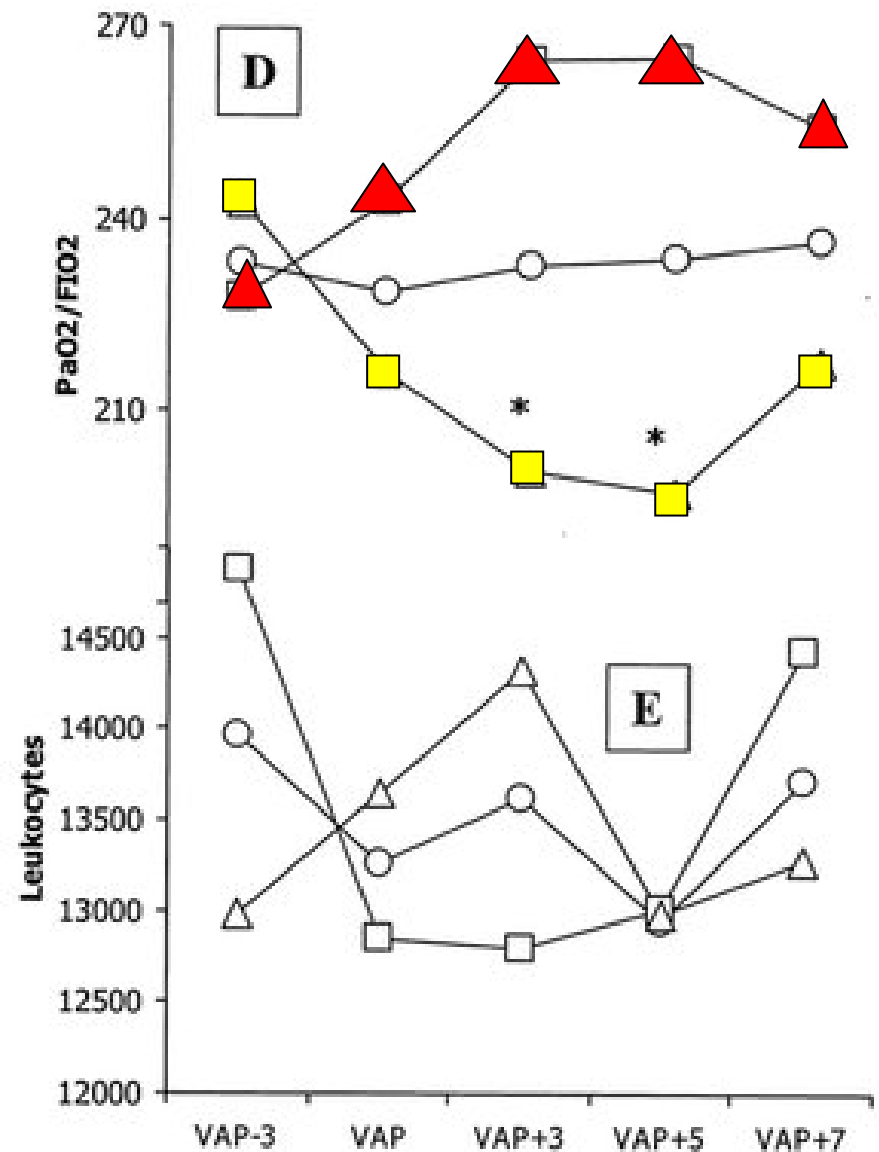
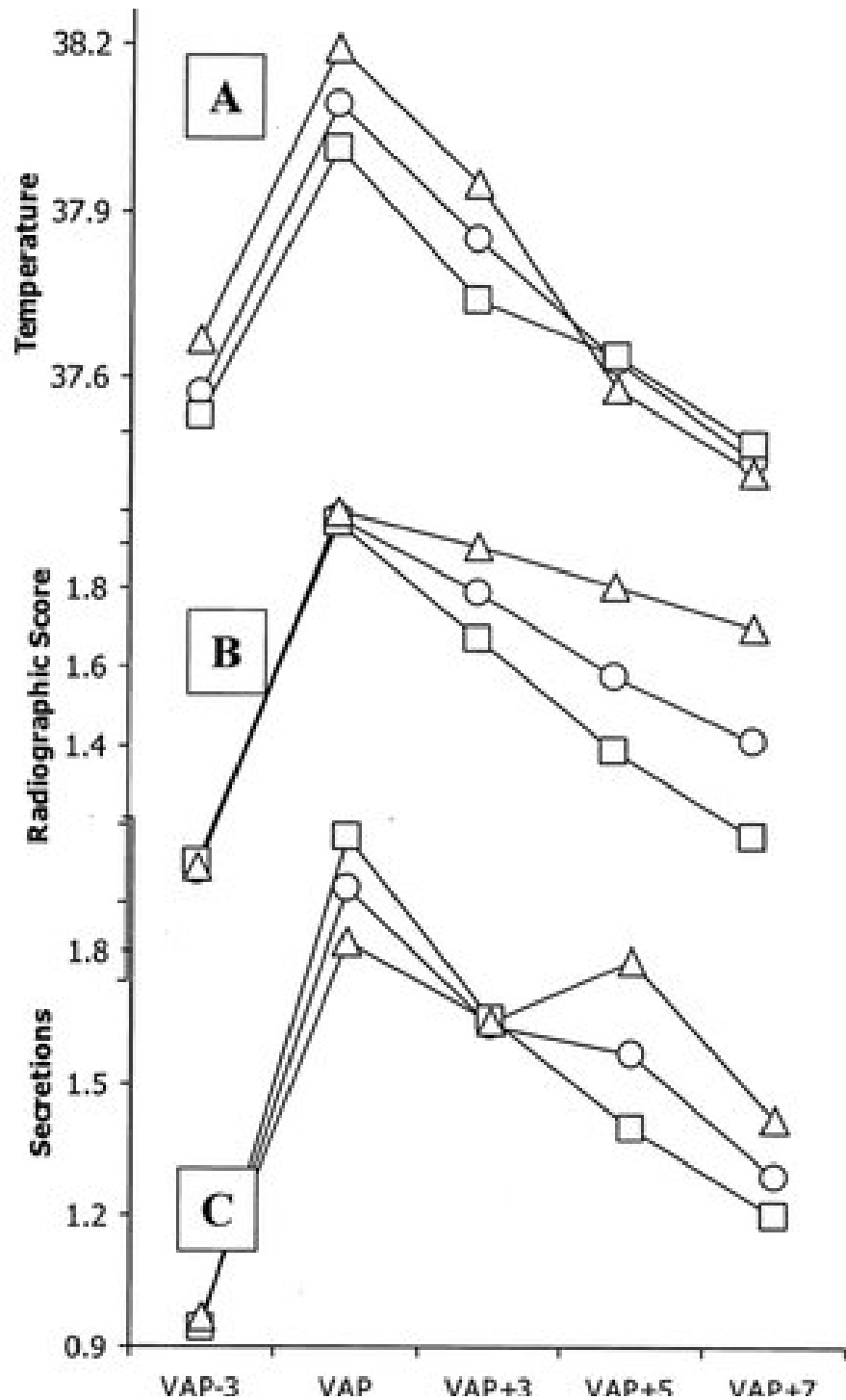
Garnacho-Montero, Crit Care Med, 2007

**Can't you just follow clinical signs
and labs to determine if they are
responding appropriately?**

Resolution of VAP



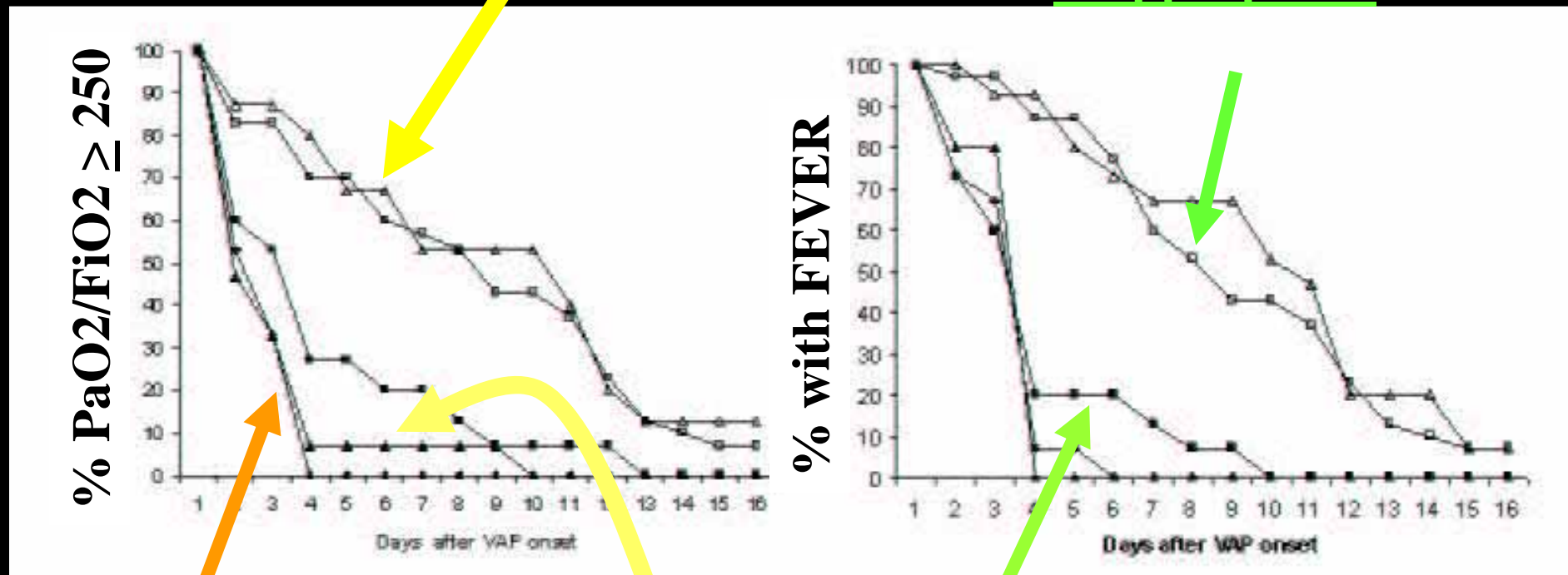
Dennesen, AJRCCM, 2001



Effect of Microorganism and Initially Appropriate Antibiotics on VAP Resolution

Vidaur, Chest, 2008

Pseudomonas with initially Inappropriate Tx



H. influenzae

MRSA

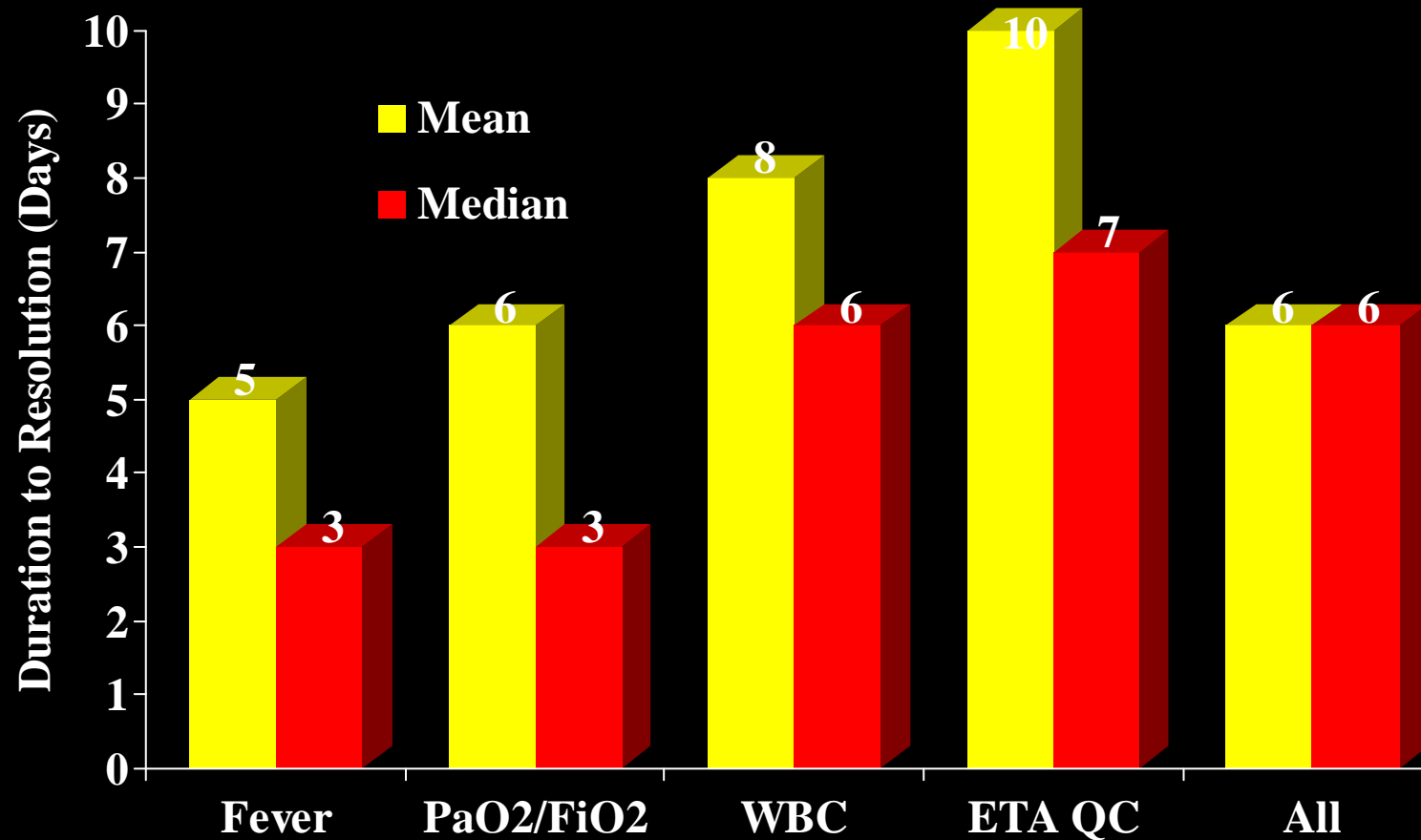
MSSA

Pseudomonas with Appropriate initial Tx

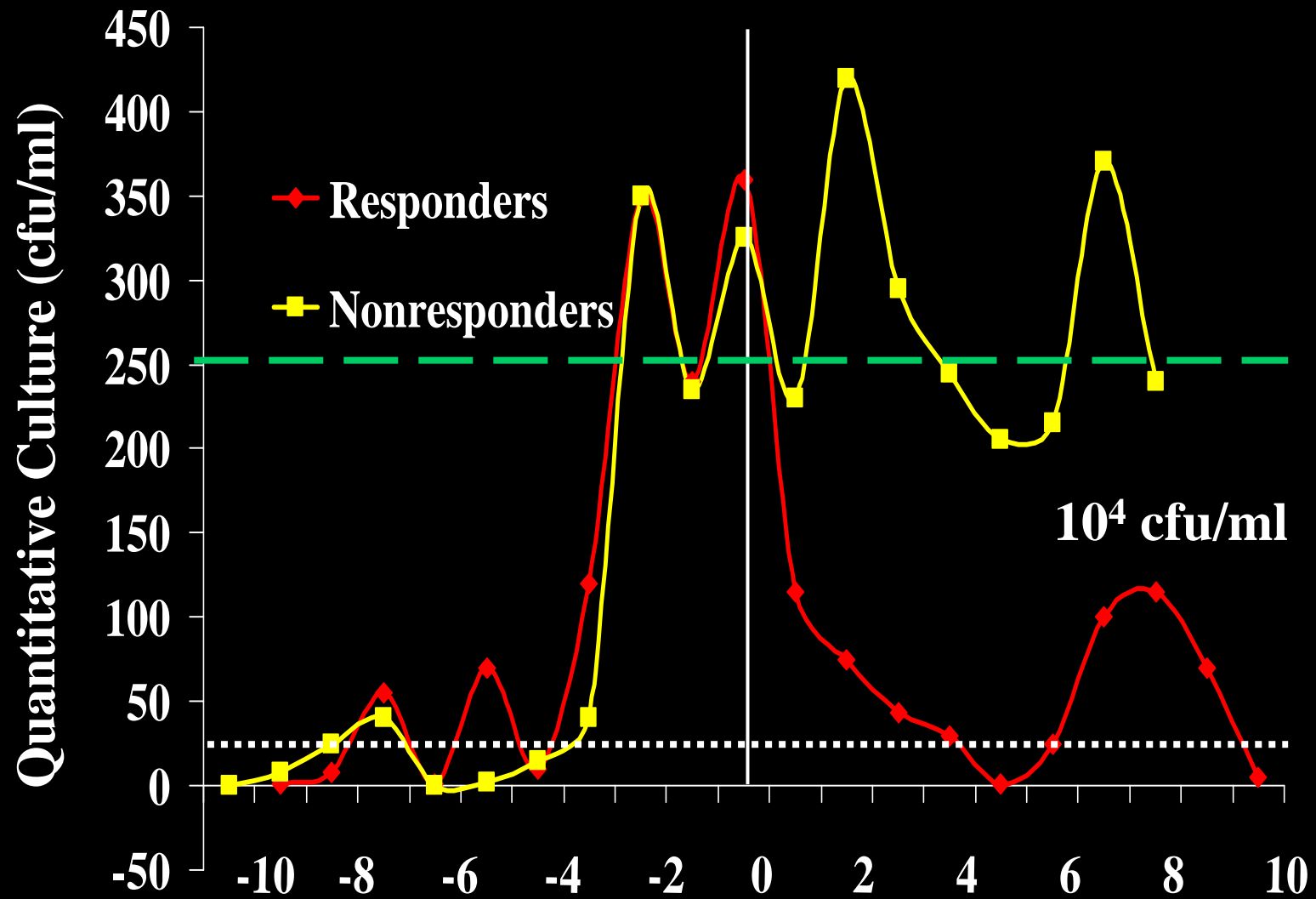
Why not follow microbiologic response?

– if the bug is gone, the patient is cured.

Resolution of VAP



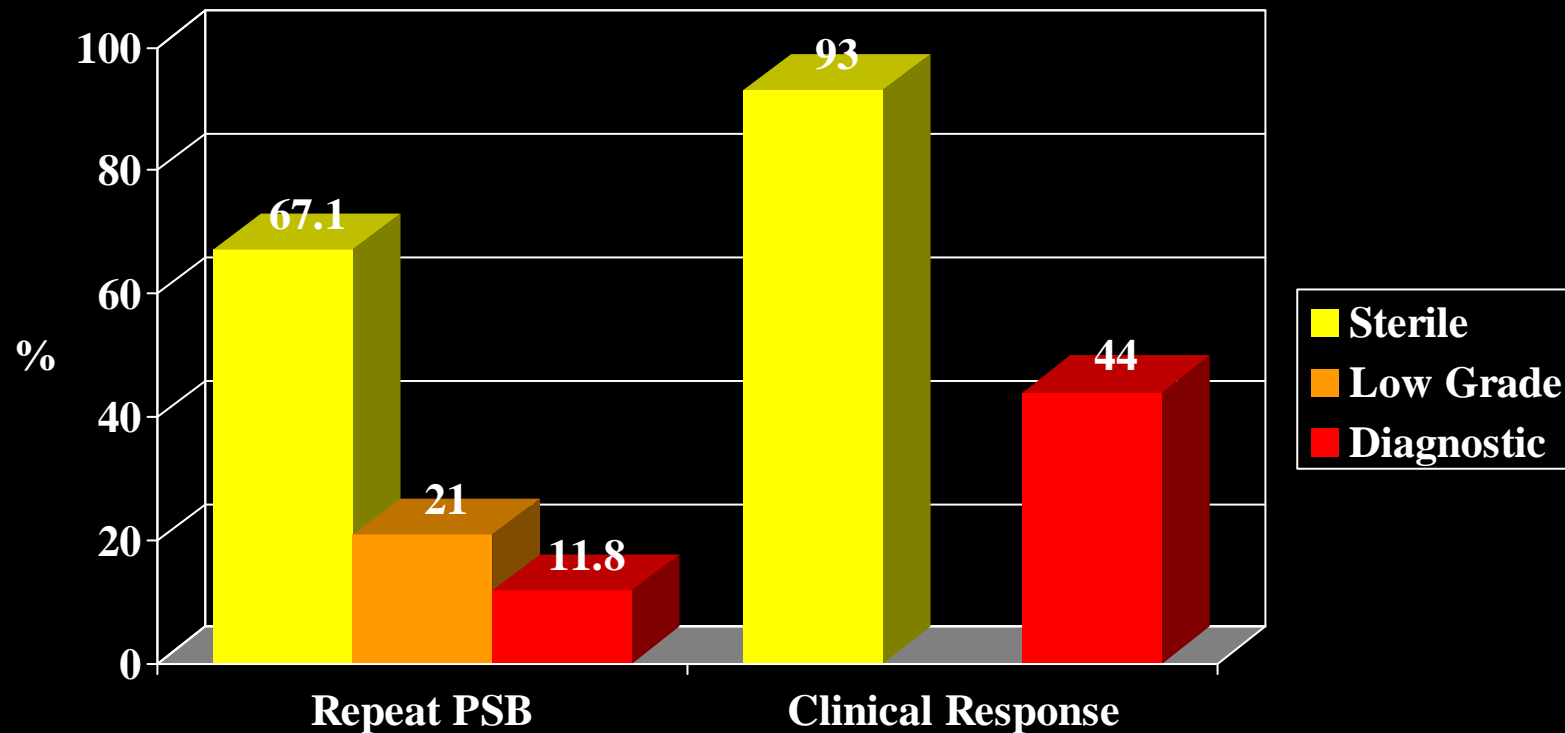
Dennesen, AJRCCM, 2001



A'Court et al, Q J Med, 1993

Followup Protected Specimen Brush in VAP

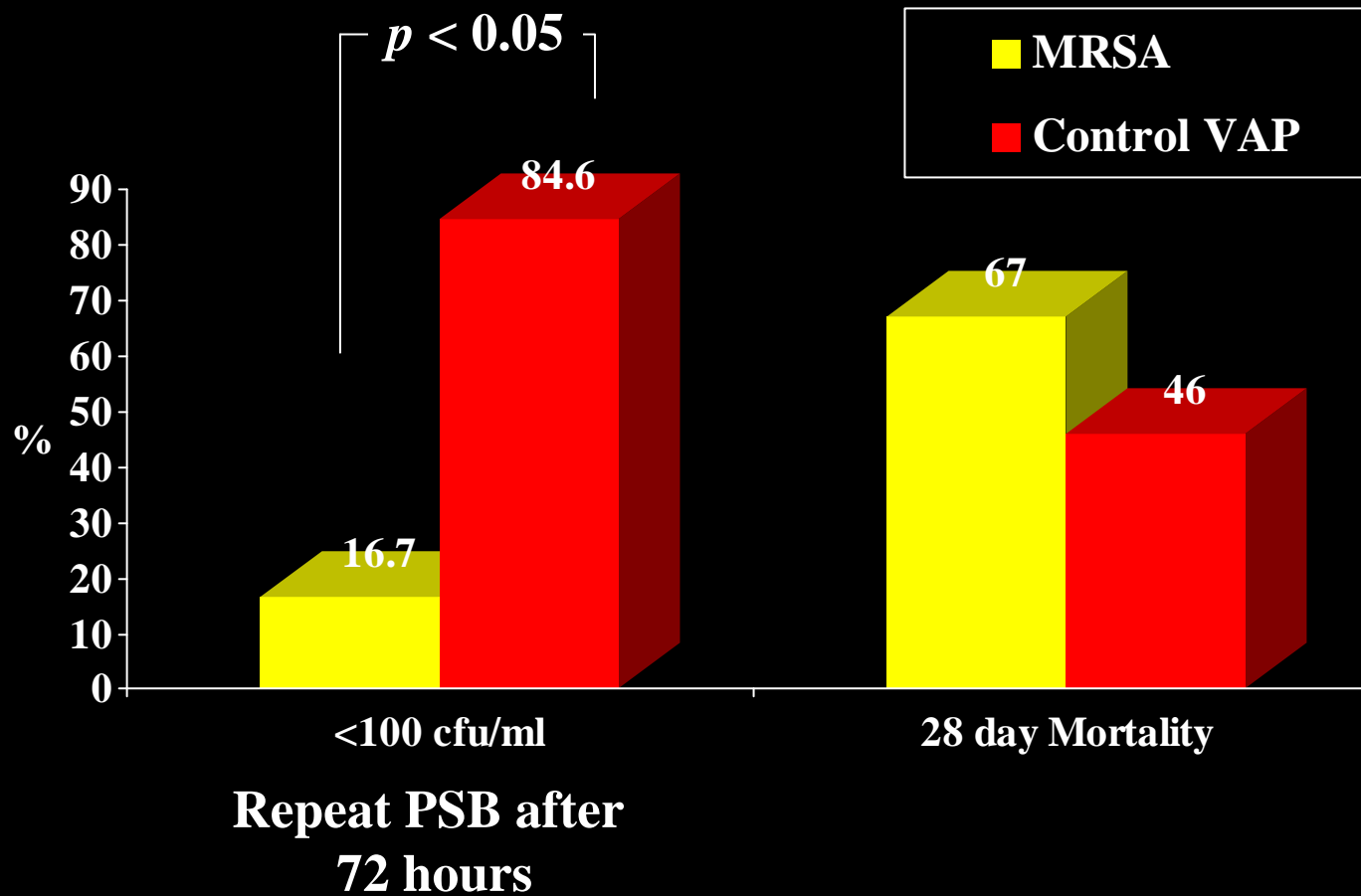
Montravers, ARRD, 1993



Repeat PSB also demonstrated 32 new pathogens, 9 at diagnostic levels (81% resistant to antibiotic used)

MRSA VAP:

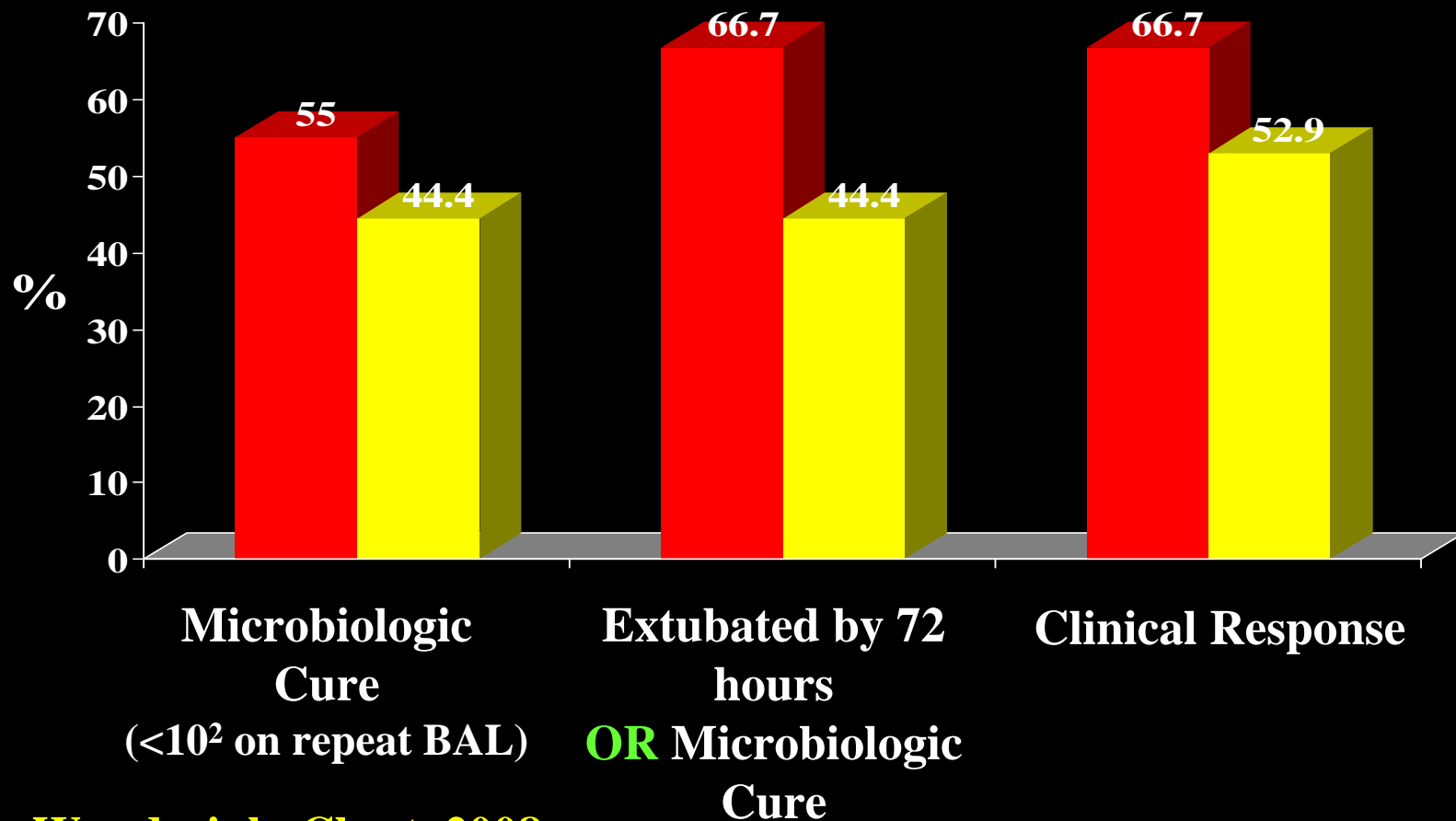
Microbiologic Response to Vancomycin



Baughman, J Intensive Care Med, 2003

Microbiologic Response in Confirmed MRSA VAP

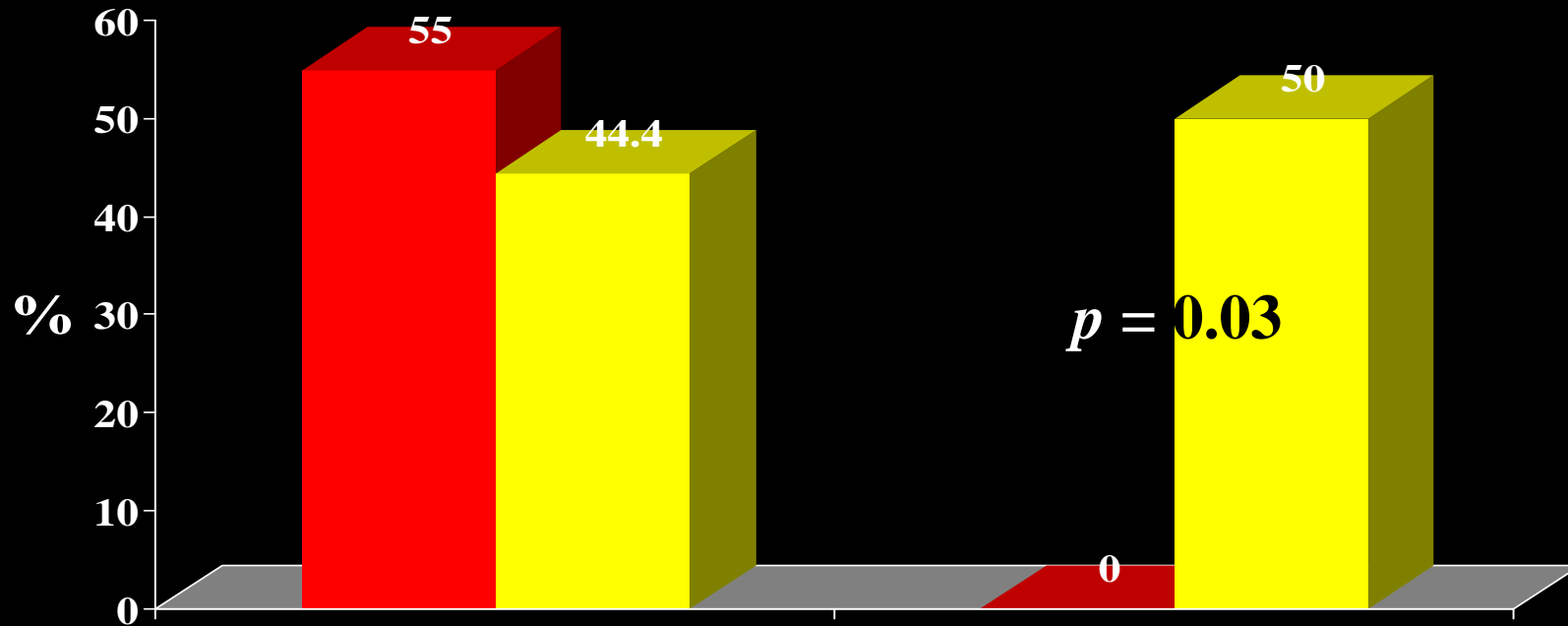
■ Linezolid ■ Vancomycin



Wunderink, Chest, 2008

Microbiologic Response in Confirmed MRSA VAP

■ Linezolid ■ Vancomycin



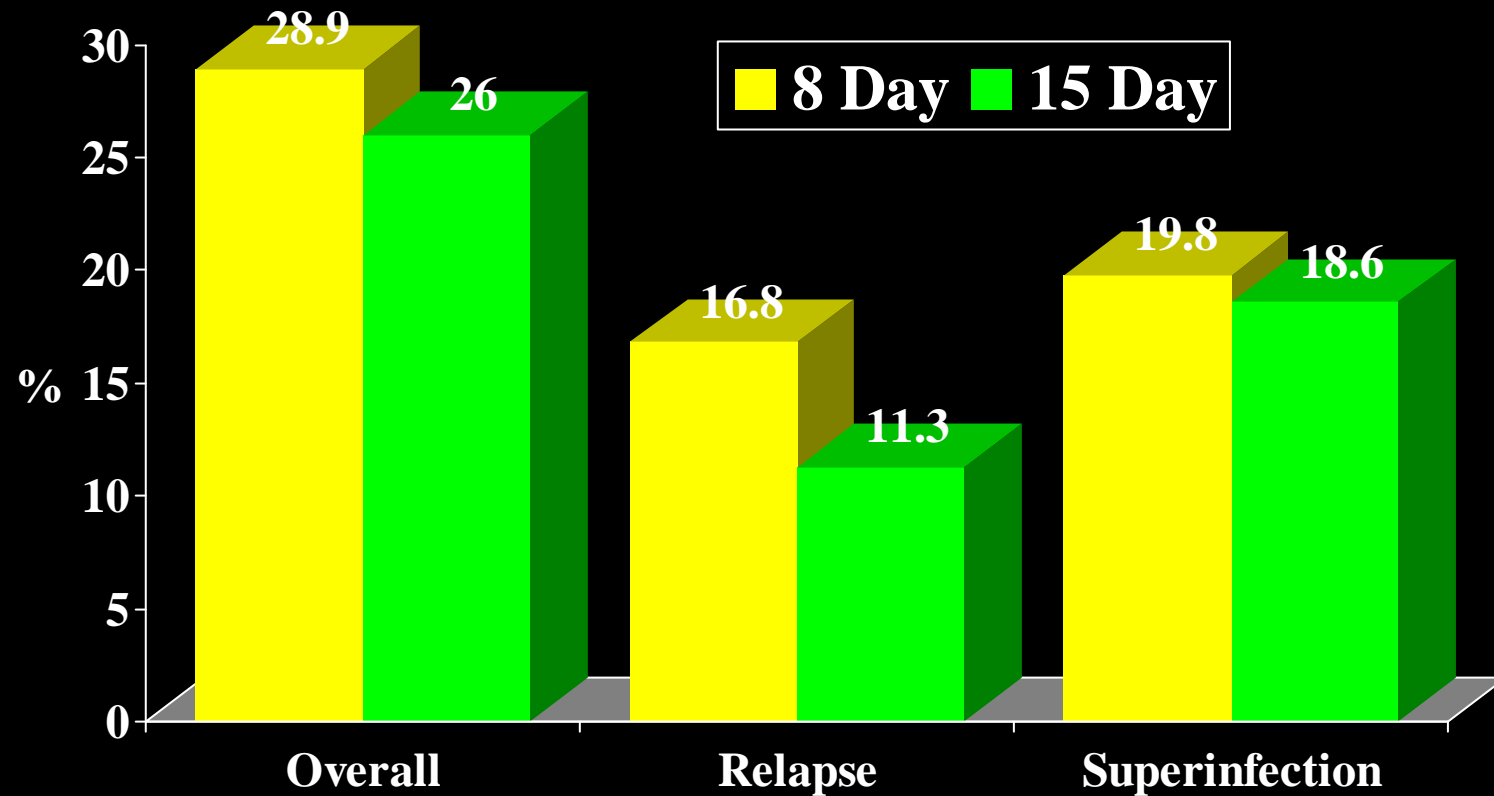
Microbiologic Cure
($<10^2$ on repeat BAL)

Mortality in
Microbiologic Failures

Wunderink, Chest, 2008

(N = 10 patients each)

VAP Relapse/Recurrence Rates



Chastre, JAMA, 2003

Followup Quantitative Cultures

- ❖ **May be valuable to discriminate microbiologic failure (persistence) from superinfection**
- ❖ **Quantitation may be able to discriminate colonization from persistence but threshold not well determined**
- ❖ **Timing after initiation of antibiotics is unclear**
 - **Early may be more relevant for cell-wall active agents whereas slower response with protein synthesis inhibitors/bacteriostatic agents**

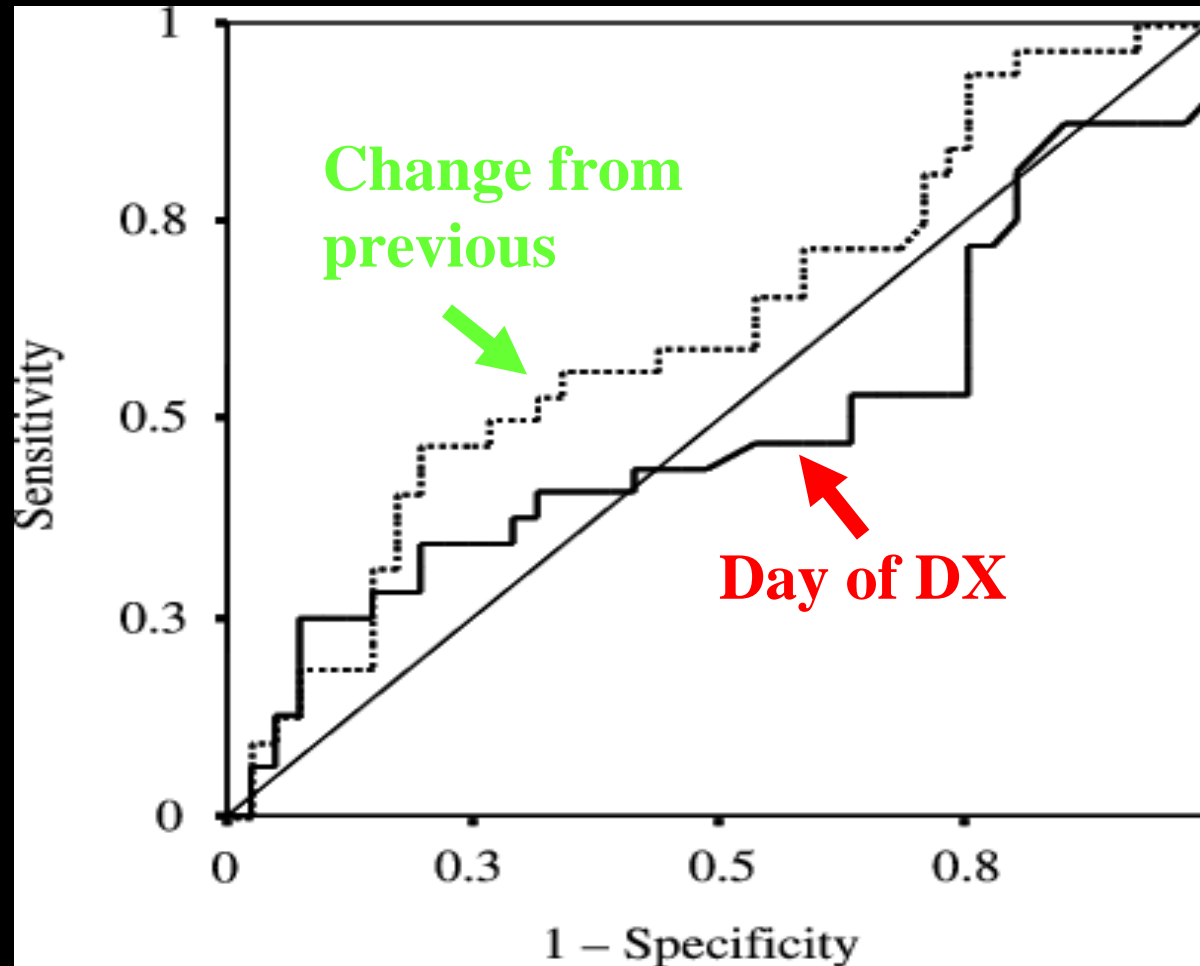
Surrogate Endpoints

Def (NIH): Biomarker intended to substitute for clinical endpoint

- used when number of clinical events is small
- must track with endpoint both from an epidemiologic and therapeutic perspective

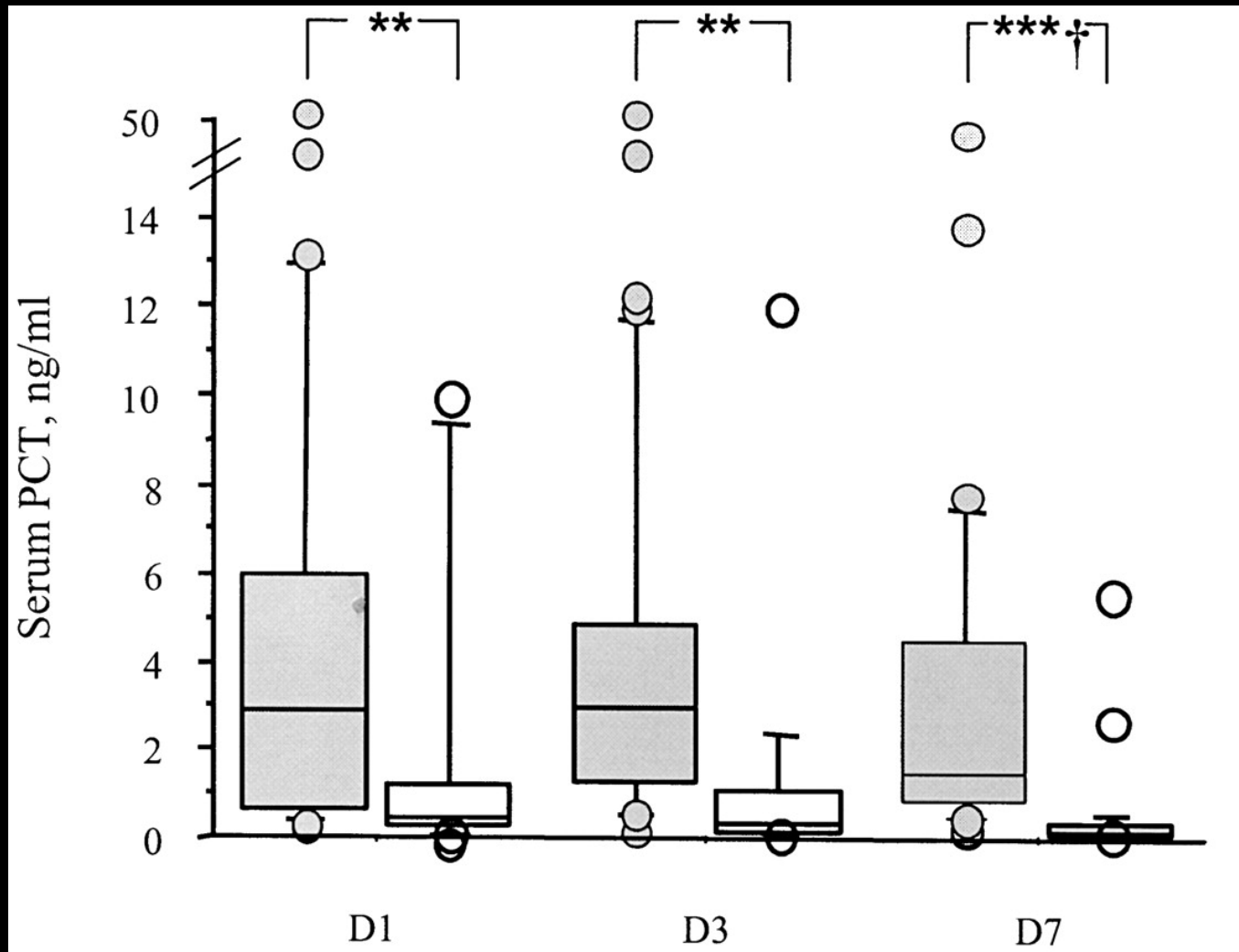
Procalcitonin to Diagnose VAP

Luyt, Intens Care Med, 2008

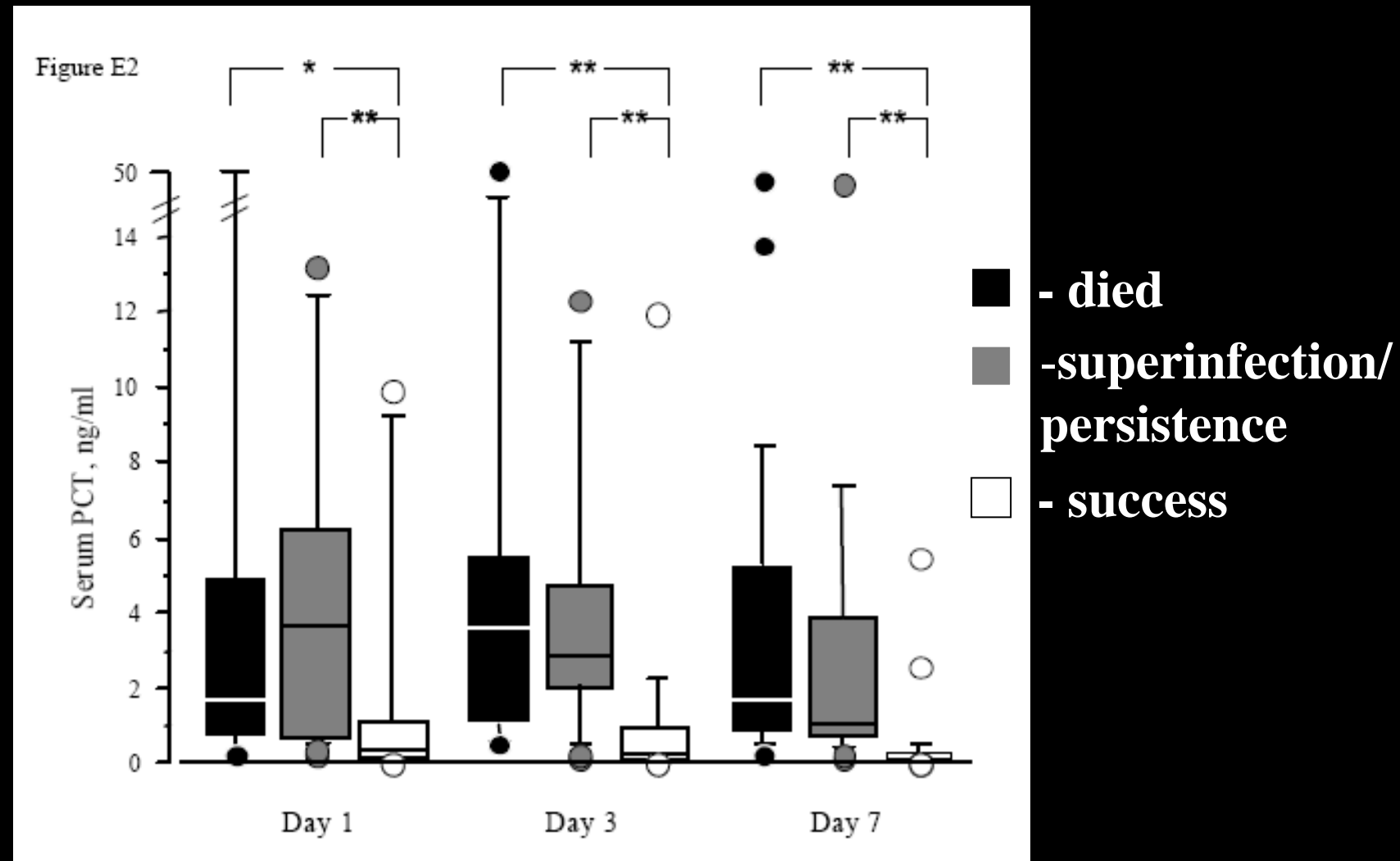


Serum PCT in Patient with VAP

Luyt, AJRCCM, 2005

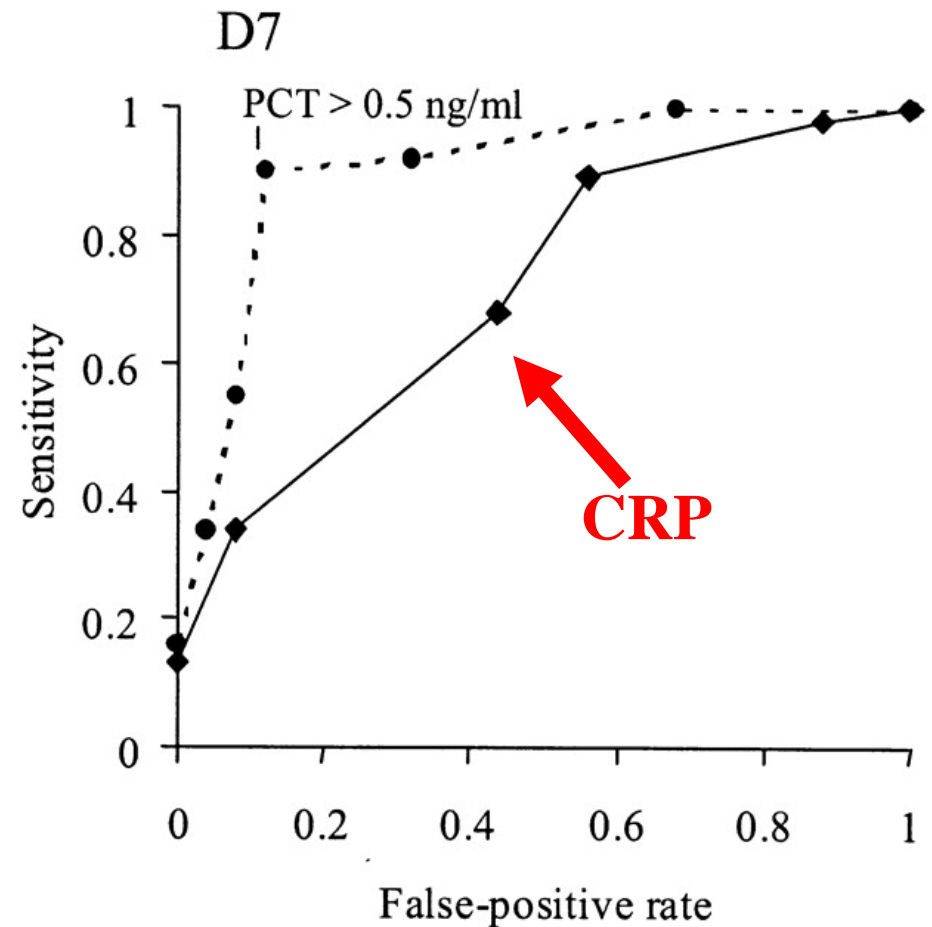
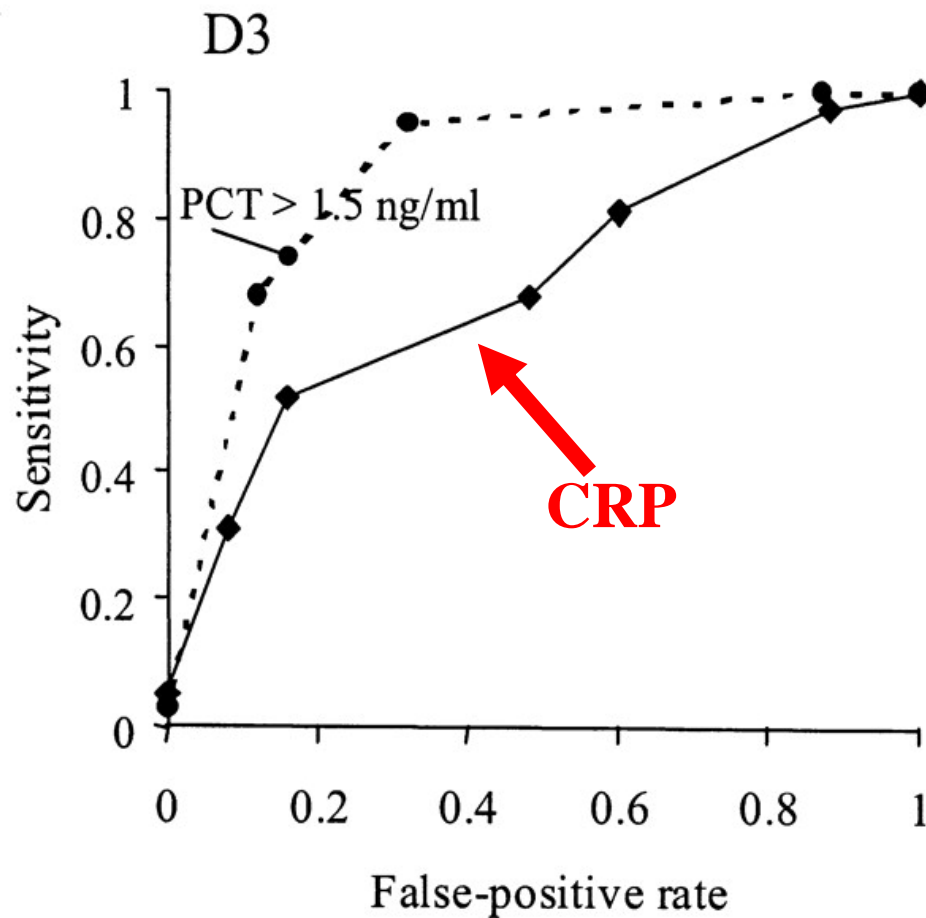


PCT Response to Therapy in VAP



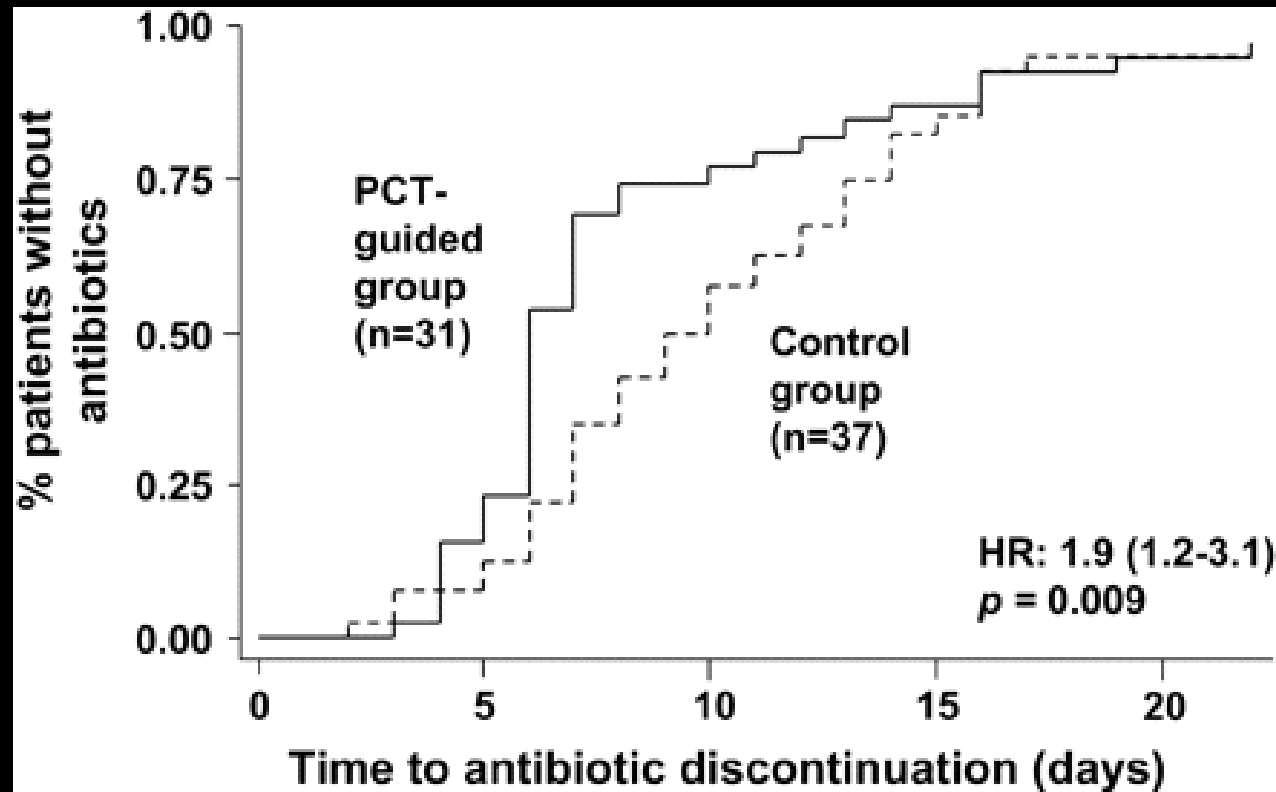
Procalcitonin Response in VAP

Luyt, AJRCCM, 2005



Procalcitonin to Guide Duration of Antibiotic Therapy in Sepsis

Nobre, AJRCCM, 2008



Majority were pulmonary infections, both CAP and HAP
Pseudomonas, Acinetobacter, Legionella were *a priori* excluded
because of perceived need for prolonged antibiotics

Surrogate Markers in HAP/VAP

- ❖ Of potentially available non-traditional markers, serial procalcitonin has best support
- ❖ Negative predictive value is best i.e. low PCT correlates with clinical cure
- ❖ Persistent high PCT would need further investigation
 - May be high risk of death, superinfection pneumonia, or extrapulmonary infection rather than failure of initial therapy
 - May be valuable to trigger further microbiologic evaluation
- ❖ Best value may be in defining patients whose treatment duration can be shortened
 - ? < 7-8 day

Conclusions

- ❖ Improving outcome of VAP will require greater vigilance for treatment failure
- ❖ Clinical criteria are neither sensitive nor specific
- ❖ Repeat quantitative cultures are best method to discriminate varied causes
- ❖ PCT (or CRP) may be preliminary step to decrease need for repeat sampling