

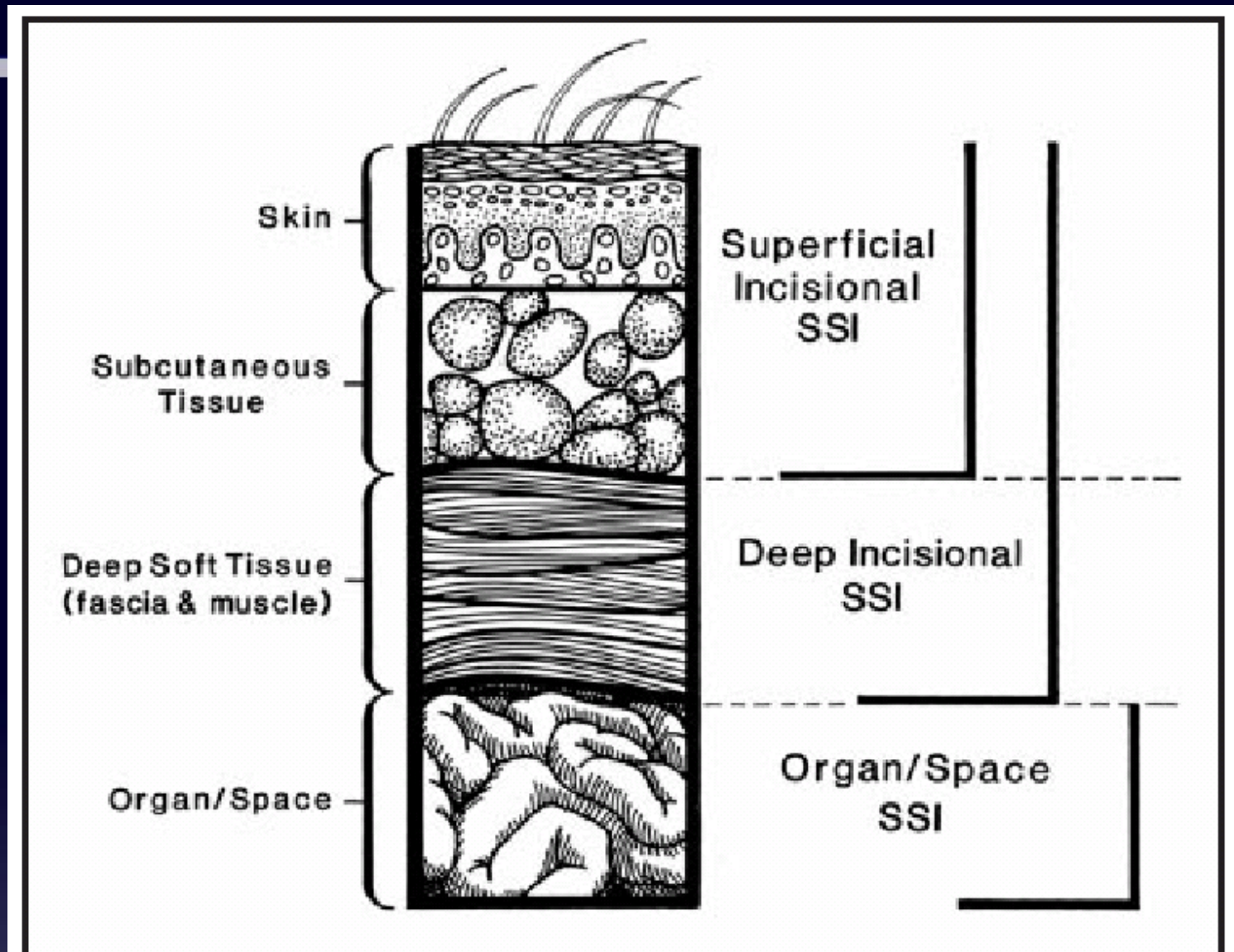
Surgical Site Infection due to MRSA: Facts, Fiction, and Frustrations

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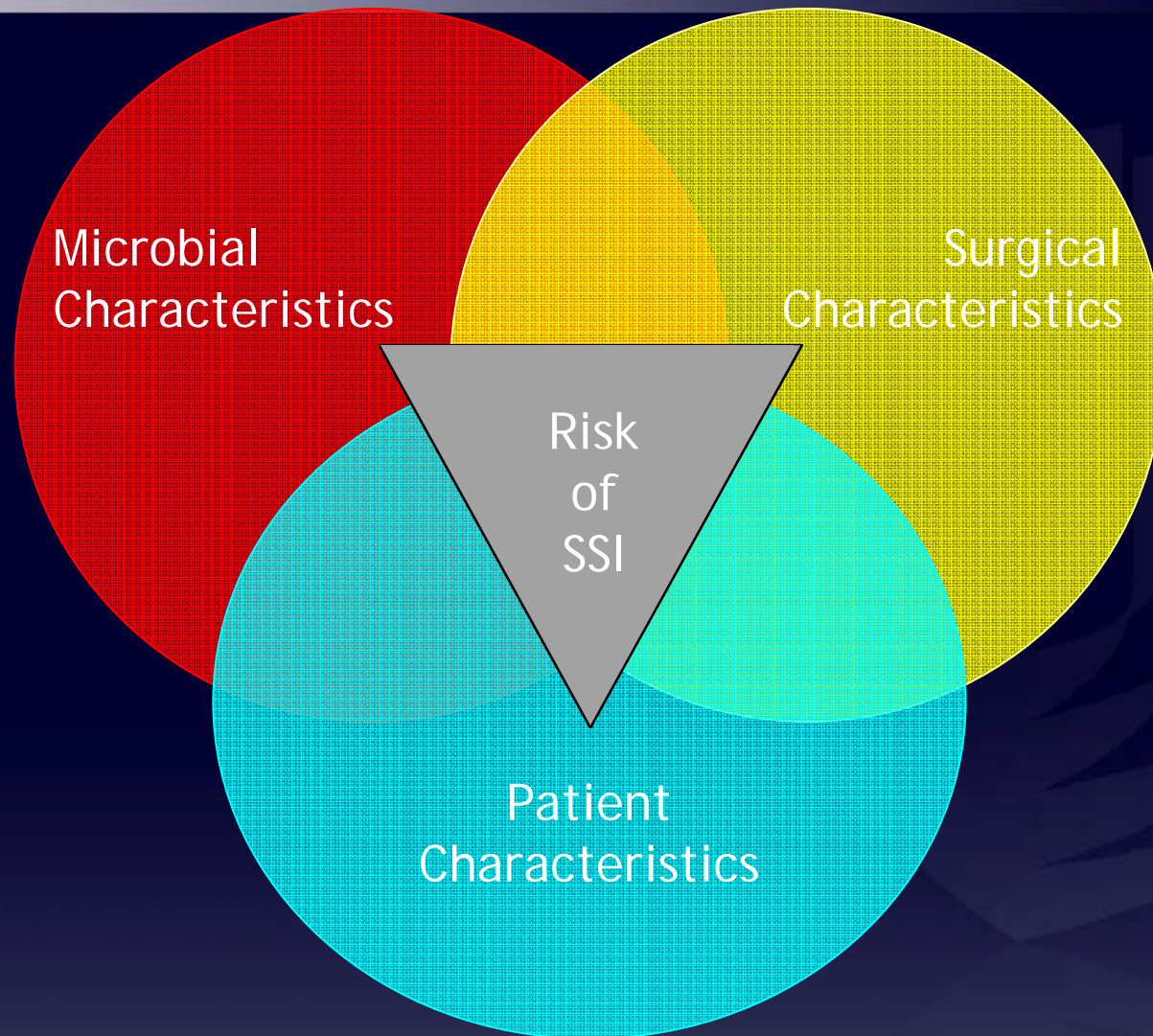
Outline

- SSIs – The Basics
- MRSA – The Facts
 - Epidemiology
 - Risk Factors
 - Outcomes
- Prevention of SSIs
- MRSA – Fiction and Frustrations
- Take Home Points

SSI Classification



Risk Factors



Risk Factors

- Patient Related

- Age
- Diabetes
- Obesity
- Smoking
- Immunosuppression

- Organism

- Colonization
- Virulence
- Drug-Resistance

- Peri-operative

- Hair removal
- Pre-op infections
- Surgical scrub
- Skin prep
- Antimicrobial prophylaxis
 - Agent
 - Timing
- Surgical skill
- Operative time
- OR traffic

Outcomes

- Prolonged duration of hospitalization
 - 7-10 additional days
- Increased costs
 - Depends on type of procedure/SSI
 - Range: \$3,000-\$29,000
 - Up to \$10 billion each year for US healthcare
- Kills patients
 - 2-11-fold higher risk of death than uninfected surgical patients
 - 77% of deaths among surgical patients with SSI

SSI due to MRSA -

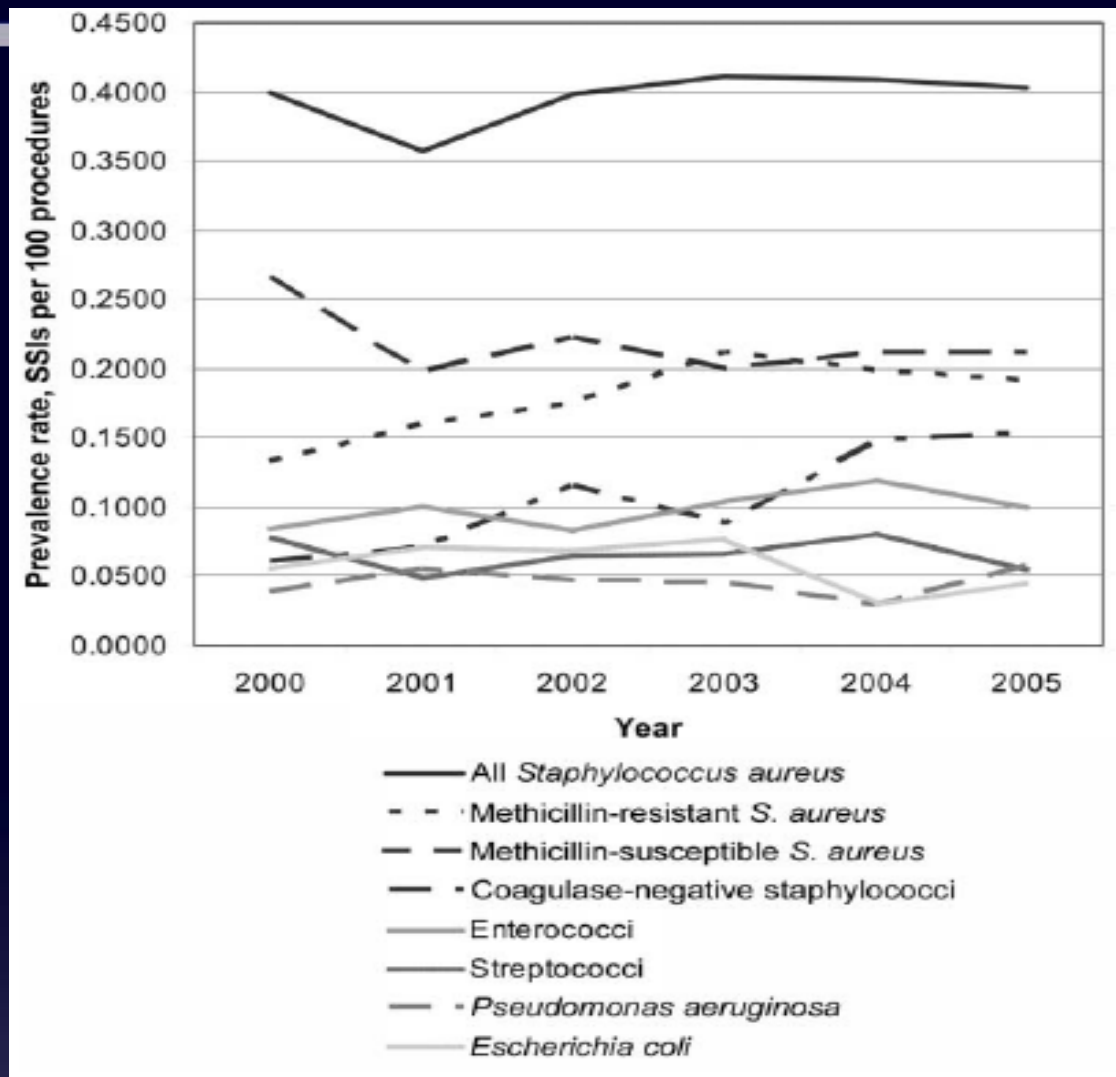
FACTS

SSI due to MRSA is Common...

Pathogen	SSI	
	No. (%) of pathogenic isolates	Rank
CoNS	965 (13.7)	2
<i>Staphylococcus aureus</i>	2,108 (30.0)	1
<i>Enterococcus</i> species		3
<i>E. faecalis</i>	194 (2.8)	
<i>E. faecium</i>	345 (4.9)	
NOS	249 (3.5)	
<i>Candida</i> species		8
<i>C. albicans</i>	115 (1.6)	
Other <i>Candida</i> spp. or NOS	30 (0.4)	
<i>Escherichia coli</i>	671 (9.6)	4
<i>Pseudomonas aeruginosa</i>	390 (5.6)	5
<i>Klebsiella pneumoniae</i>	213 (3.0)	7
<i>Enterobacter</i> species	293 (4.2)	6
<i>Acinetobacter baumannii</i>	42 (0.6)	9
<i>Klebsiella oxytoca</i>	47 (0.7)	9
Other	1,363 (19.4)	
Total	7,025 (100)	

**49.2%
were
MRSA**

...In ALL Locations



Specific Risk Factors - MRSA SSI

- Case-control study (n=77 patients)
 - Post-operative risk factors included discharge to LTCF and post-operative antibiotics > 1 d
- Cohort study (n=35)
 - Multiple operations, cancer, wound drains
- Study of MRSA mediastinitis (n=64)
 - Diabetes, age>70

Manian et al. *Clin Infect Dis* 2003;36:863– 868.

Ross. *Aust N Z J Surg* 1985;55:13–17.

Dodds Ashley et al. *Clin Infect Dis* 2004;38:1555–1560.

Specific Risk Factors - MRSA SSI

TABLE 3. Independent Predictors of Surgical Site Infection Due to Methicillin-Resistant *Staphylococcus aureus*

Variable	Adjusted OR (95% CI)	P
Need for assistance with ≥ 3 ADLs	3.97 (2.18–7.25)	<.001
Medicaid insurance	3.31 (1.14–9.58)	.03
Wound classification of >2	2.91 (1.07–7.87)	.04
Duration of surgery >75th percentile ^a	1.98 (1.11–3.55)	.02
Obesity	1.86 (1.14–3.02)	.01

150 MRSA SSI, 231 uninfected, 128 MSSA SSI

Anderson et al ICHE 2008; 29: 832-9.

Specific Risk Factors - MRSA SSI

TABLE 4. Independent Predictors of Surgical Site Infection (SSI) Due to Methicillin-Resistant *Staphylococcus aureus*, Compared with SSI Due to Methicillin-Susceptible *S. aureus*

Variable	Adjusted OR (95% CI)	P
Need for assistance with ≥ 3 ADLs	3.88 (1.91–7.87)	<.001
Duration of surgery >75th percentile ^a	2.33 (1.17–4.62)	.02
Congestive heart failure	2.22 (1.17–4.22)	.01
Myocardial infarction	0.52 (0.27–0.99)	.05

150 MRSA SSI, 231 uninfected, 128 MSSA SSI

Anderson et al ICHE 2008; 29: 832-9.

Outcomes due to MRSA SSI

- 3 studies compared MRSA v. MSSA SSI
 - #1 - 15 MRSA v. 26 MSSA mediastinitis
 - Mortality increased 4.6-fold
 - #2 - 73 MRSA v. 145 MSSA mediastinitis
 - Increased LOS and ventilation
 - NOT independent risk factor for mortality
 - #3 - 127 MRSA v. 173 MSSA - all procedures
 - 3-fold higher mortality
 - 3 additional days of hospitalization
 - Additional \$14,000 in charges

Mekontso-Dessap et al. (2001) Clin Infect Dis 32: 877–883.

Combes et al. (2004) Clin Infect Dis 38: 822–829.

Engemann et al. (2003) Clin Infect Dis 36: 592–598.

Outcomes due to MRSA SSI

Independent Predictor	Odds Ratio [95
<i>Readmission within 90 days of surgical procedure^a</i>	
SSI due to MRSA	35.0 [17.3–70.7]
Need assistance with ≥ 3 ADLs	4.28 [1.52–12.0]
<i>Death within 90 days of surgical procedure^b</i>	
SSI due to MRSA	7.27 [2.83–18.7]
Need assistance with ≥ 3 ADLs	6.73 [2.80–16.2]
Age ≥ 65	4.45 [1.41–14.0]
Orthopedic procedure	0.27 [0.10–0.71]

150 patients with MRSA SSI vs. 231 uninfected controls

Outcomes due to MRSA SSI

	Length of Stay Least Squares Mean (IQR)	
	Unadjusted	Adjusted ^b
Cases	23.6 (21.7–25.5)	28.3 (25.7–30.8)
Controls	5.2 (3.7–6.7)	5.2 (3.5–7.0)
Attributable difference	18.4 (16.0–20.8)	23.0 (19.7–26.3)

150 patients with MRSA SSI vs. 231 uninfected controls

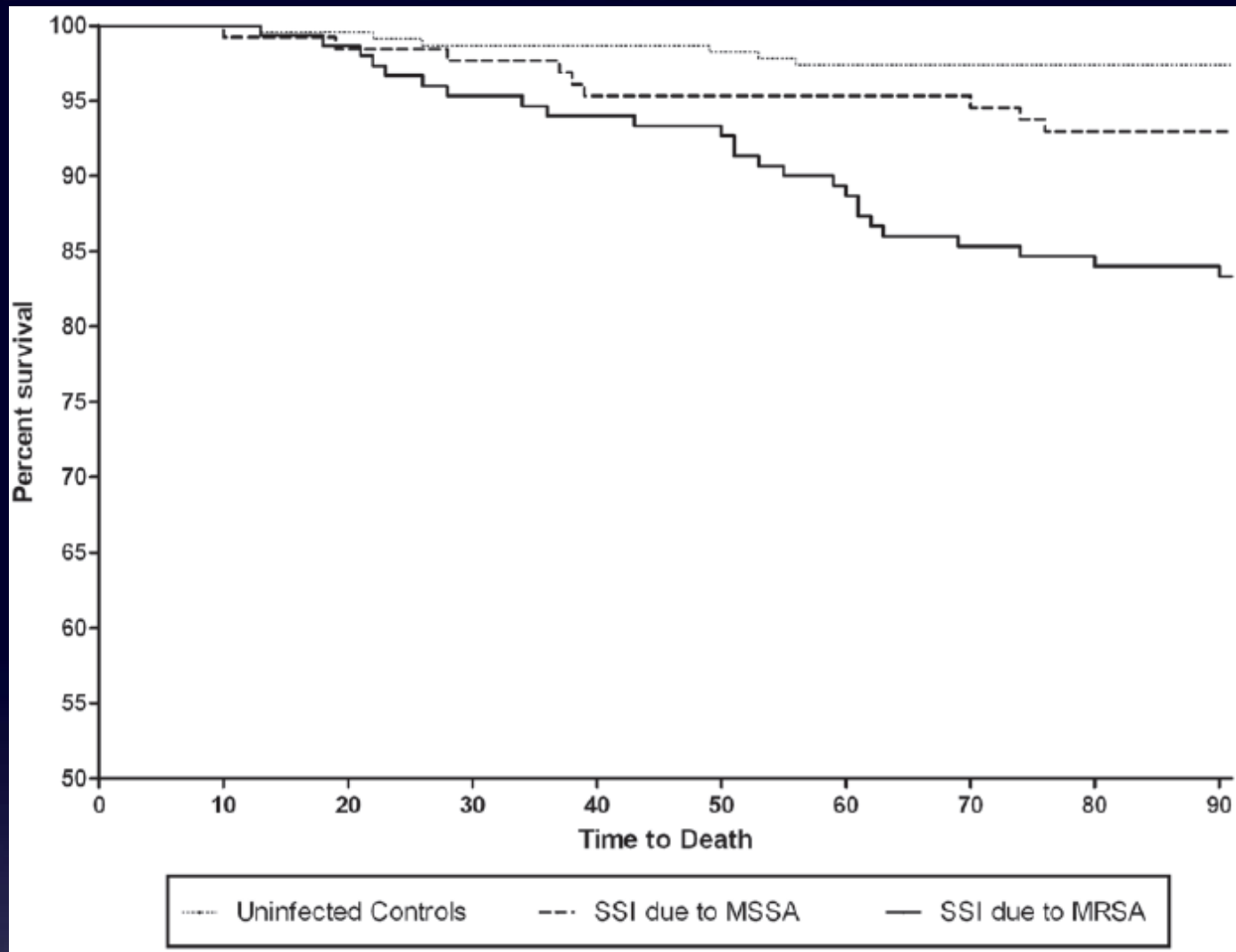
Outcomes due to MRSA SSI

Charges Least Squares Mean (IQR)

Unadjusted	Adjusted ^c
105,214 (91,458–118,971)	112,144 (85,850–138,438)
47,099 (35,485–58,714)	50,463 (34,551–66,375)
58,115 (40,111–76,119)	61,681 (23,352–100,011)

150 patients with MRSA SSI vs. 231 uninfected controls

Outcomes due to MRSA SSI



Outcomes due to MRSA SSI

Independent Predictor	Odds Ratio [95
<i>Readmission within 90 days of surgical procedure</i> ^a	
Methicillin-resistance	0.43 [0.21–0.89]
Underwent coronary artery bypass grafting	4.35 [1.31–14.5]
Procedure performed at tertiary care facility	2.19 [1.03–4.63]
Admission to ICU prior to infection	0.20 [0.05–0.72]
<i>Death within 90 days of surgical procedure</i> ^b	
Methicillin-resistance	1.72 [0.70–4.20]
Need assistance with ≥ 3 ADLs	3.79 [1.33–10.8]
Antimicrobial prophylaxis administered appropriately	0.35 [0.14–0.88]

150 patients with MRSA SSI vs. 128 MSSA

Outcomes due to MRSA SSI

	Length of Stay Least Squares Mean (IQR)	
	Unadjusted	Adjusted ^b
SSI due to MRSA	24.3 (21.7–26.8)	23.7 (21.3–26.0)
SSI due to MSSA	17.4 (14.6–20.2)	18.1 (15.5–20.7)
Attributable difference	6.86 (3.07–10.4)	5.5 (1.97–9.11)

150 patients with MRSA SSI vs. 128 MSSA

Outcomes due to MRSA SSI

Charges Least Squares Mean (IQR)	
Unadjusted	Adjusted ^c
105,214 (89,558–120,871)	99,466 (86,352–112,580)
68,835 (52,164–85,506)	75,353 (61,351–89,355)
36,379 (13,509–59,250)	24,113 (4,521–43,704)

150 patients with MRSA SSI vs. 128 MSSA

Prevention of MRSA SSI – The Basics

Spoiler Alert: There are
NO specific recommendations
for prevention of MRSA SSI
in published guidelines!!

SUPPLEMENT ARTICLE: SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent Surgical Site Infections in Acute Care Hospitals

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Robert A. Weinstein, MD; Robert Wise, MD; Deborah S. Yokoe, MD, MPH

The Basics

- Perform surveillance for SSIs (A-II)
 - Feedback
 - Enhance with automated data collection
- Peri-operative antimicrobial prophylaxis (A-I)
 - Agent
 - Timing
 - Discontinue within 24 hours
- Do not shave hair (A-II)

The Basics

- Control blood glucose during immediate post-operative period (A-I)
 - Cardiac procedures
- Feedback data on process measures (A-III)
- Implement policies to reduce risk of SSI that are aligned with evidence-based standards (A-II)

Examples: Evidence-Based Standards

Risk factor	Recommendation	Grade ^a
Intrinsic, patient related (preoperative)		
Unmodifiable		
Age	No formal recommendation: relationship to increased risk of SSI may be secondary to comorbidities or immune senescence [28-30]	...
Modifiable		
Glucose control, diabetes	Control serum blood glucose levels [5]; reduce glycosylated hemoglobin A1c levels to <7% before surgery, if possible [31]	A-II
Obesity	Increase dosing of prophylactic antimicrobial agent for morbidly obese patients [32]	A-II
Smoking cessation	Encourage smoking cessation within 30 days before procedure [5]	A-II
Immunosuppressive medications	No formal recommendation; in general, avoid immunosuppressive medications in perioperative period, if possible	C-II

Extrinsic, procedure related (perioperative)

Preparation of patient

Hair removal Do not remove unless hair will interfere with the operation [5]; if hair removal is necessary, remove by clipping and do not use razors A-I

Preoperative infections Identify and treat infections (eg, urinary tract infection) remote to the surgical site before elective surgery [5] A-II

Operative characteristics

Surgical scrub (surgical team members' hands and forearms) Use appropriate antiseptic agent to perform 2-5-minute preoperative surgical scrub [5] or use an alcohol-based surgical hand antisepsis product A-II

Skin preparation Wash and clean skin around incision site; use an appropriate antiseptic agent [5] A-II

Antimicrobial prophylaxis Administer only when indicated [5] A-I

Timing Administer within 1 hour before incision to maximize tissue concentration^b [5, 33] A-I

Choice Select appropriate agents on the basis of surgical procedure, most common pathogens causing SSI for a specific procedure, and published recommendations [5, 33] A-I

Duration of therapy Stop prophylaxis within 24 hours after the procedure for all procedures except cardiac surgery; for cardiac surgery, antimicrobial prophylaxis should be stopped within 48 hours [5, 33] A-I

Surgeon skill/technique Handle tissue carefully and eradicate dead space [5] A-III

Asepsis Adhere to standard principles of operating room asepsis [5] A-III

Operative time No formal recommendation in most recent guidelines; minimize as much as possible [34] A-III


Operating room characteristics

Ventilation	Follow American Institute of Architects' recommendations [5]	C-I
Traffic	Minimize operating room traffic [5]	B-II
Environmental surfaces	Use a US Environmental Protection Agency–approved hospital disinfectant to clean surfaces and equipment [5]	B-III
Sterilization of surgical equipment	Sterilize all surgical equipment according to published guidelines; minimize the use of flash sterilization [5]	B-I

SSI due to MRSA

Fiction and Frustrations

Strategies for Prevention of MRSA SSI

- Decolonization
 - Issues include
 - Method of surveillance
 - Which patients?
 - Change prophylaxis
 - Issues include
 - Problems with alternative agents
 - Which patients?
- 

Colonization with MRSA - Who Cares?

- Operative patients who are colonized with *S. aureus*/MRSA are 2-9 times more likely to develop SSI
- Infecting organism usually the same as organism colonizing patient in pre-operative period

Methods for MRSA Screening

- Time required to detect MRSA in nasal swabs varies considerably based on methods used

Method	Time (hr)
Blood agar + Suscep testing	48-96
Mannitol salt/oxa plate	24-48
Chromogenic media	28-24
PCR	≤ 2

- PCR vs. standard culture: faster, but more expensive

Screening Does Nothing (without additional processes)

- Who performs tests?
- Who follows-up on results?
- What is done with results?
- Are test results available in time to act upon?
- What are consequences of process failure?
 - ? Delay surgery
 - ? Change prophylaxis
 - ? Litigation

Different Approaches

- Can empirically decolonize, treat
 - Decolonization for all preoperative patients
- Can “search and destroy” (for *S. aureus* or MRSA)
 - Screen for *S. aureus*/MRSA and decolonize/treat patients who are screen or culture-positive

Decolonization

- Mupirocin temporarily decolonizes many patients of *S. aureus*
 - Colonization often returns, depending on level/number of additional co-morbidities
- “Standard” method: mupirocin applied to nares for 3-5 days prior to surgery
- ? Chlorhexidine gluconate (CHG) on skin
 - Soap
 - Wipes

Can Routine Decolonization Prevent SSI?

- 4 RCTS compared mupirocin to placebo
- All showed essentially the same thing:
 - Rate of *S. aureus* nasal carriage decreased, but not real impact on SSI
- Largest included 4,000 surgical patients
 - No effect on incidence of *S. aureus* SSI (~2.3% in each group)
 - For patients with pre-operative colonization with *S. aureus*, decrease in risk for *S. aureus* SSI (3.7% vs. 5.9%, NS)

Perl et al. *NEJM* 2002; 346:1871–7.

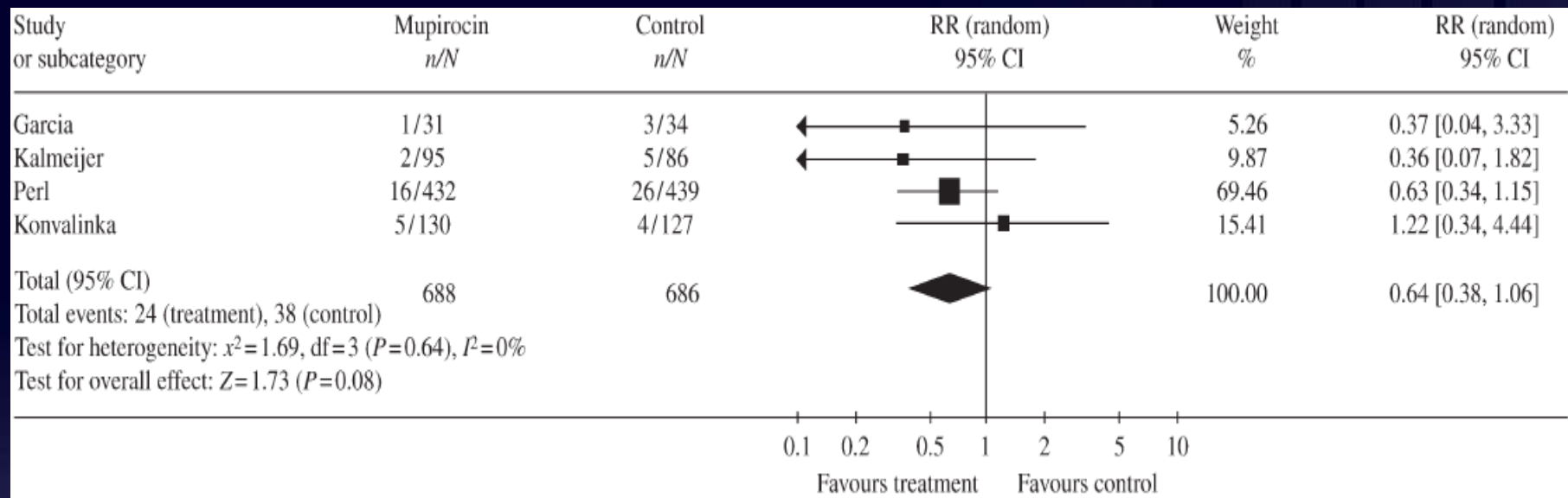
Kalmeijer et al. *CID* 2002; 35:353–8.

Garcia et al. *Biomedica* 2003; 23:173–9.

Konvalinka et al. *J Hosp Infect* 2006; 64:162–8.

Can Decolonization of Patients with *S. aureus* Prevent SSI?

- Systematic review of 4 RCTs
 - Analyzed patients with *S. aureus* colonization only



Can Routine Decolonization Prevent SSI?

- Systematic review and meta-analysis
 - 3 RCTs
 - 4 “before-after” studies
- Correlation depended on type of surgery and type of study
 - No effect in RCTs
 - In observational studies, appeared to be some benefit when used in non-general surgical procedures
 - 5,946 patients in 3 studies: RR=0.40 (0.29-0.56)

Can Decolonization of Patients with *S. aureus* Prevent SSI?

- Some more recent studies have demonstrated that screening for MRSA led to lower rates of MRSA SSI
 - Most before-after, single-center experiences
- Cardiac surgery (n=1,462)
 - Decolonization and change prophylaxis
 - MRSA SSI rate fell from 3.30% to 2.22% (RR=0.7, 95% CI 0.06-0.95)
- SCIP procedures (n=5,094)
 - Institution of broad screening program for MRSA
 - Screen positive operative patients treated with mupirocin + CHG X 5 days
 - Changes in pre-operative prophylaxis left up to the surgeon

Can Decolonization of Patients

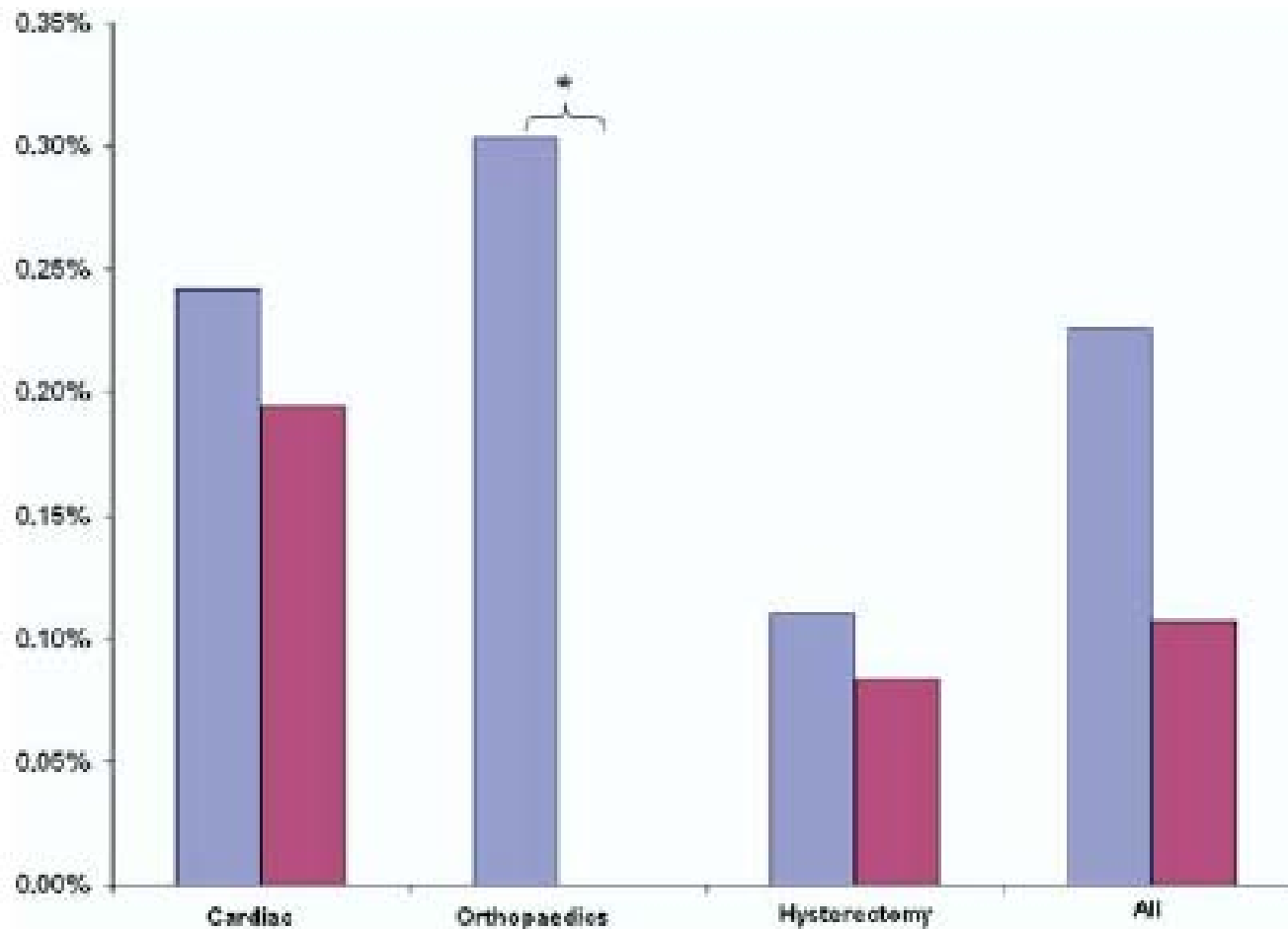
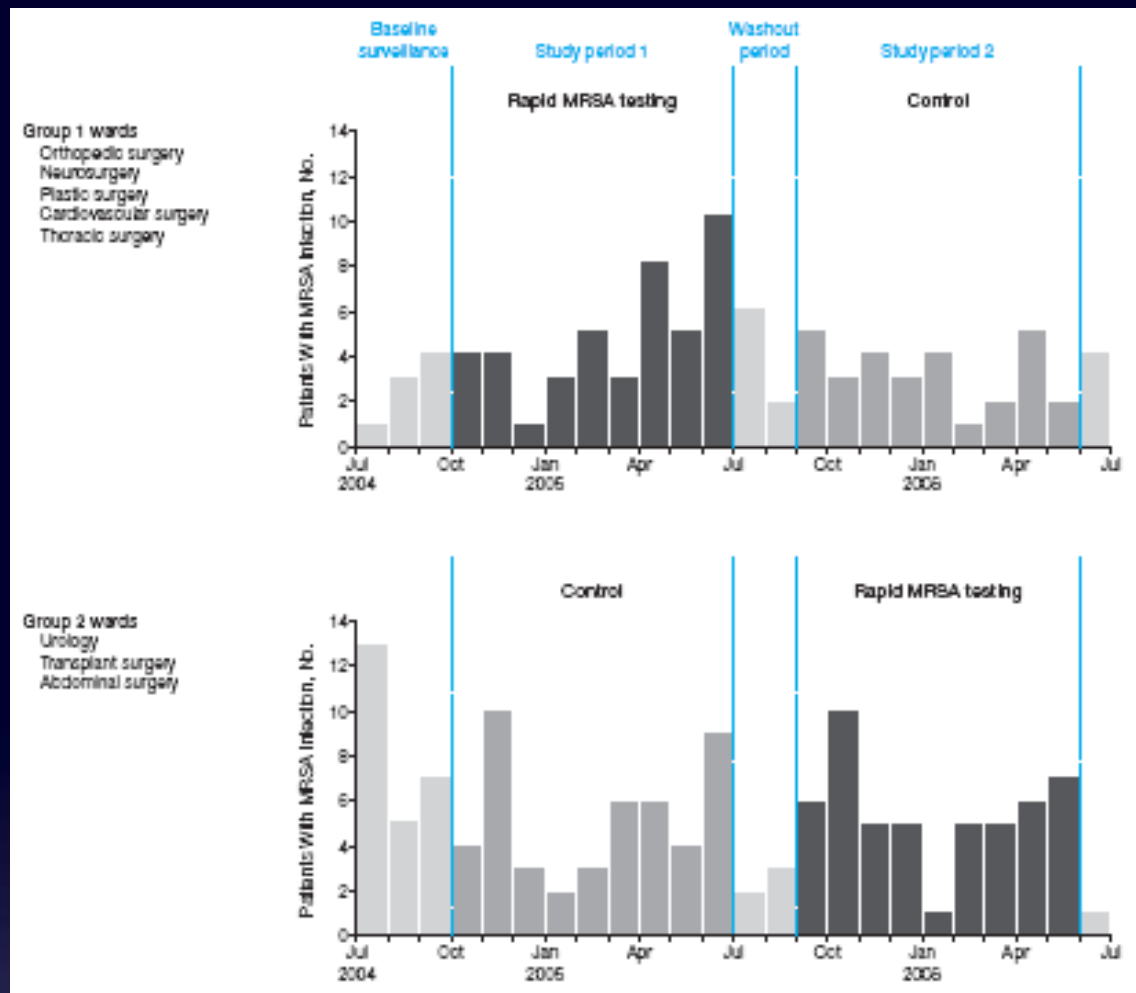


Figure 1. Rate of MRSA surgical-site infections before (blue bar) and after (red bar) universal screening. * $p = 0.04$ before versus after.

Can Decolonization of Patients with *S. aureus* Prevent SSI?

- Prospective, interventional cohort study of 20,000 surgical patients with crossover design comparing standard IC plus rapid screening for MRSA with standard IC methods alone.
- Bottom line: Rates of MRSA infection did not change

Can Decolonization of Patients with *S. aureus* Prevent SSI?



Decolonization: Other Considerations

- Can't be done in emergency settings
- Patients can be colonized in multiple, diverse anatomic sites (eg peri-rectal, IV sites, axilla)
- Mupirocin resistance is a concern
 - With prolonged use, usually see emergence of mupirocin-resistant strains
- MRSA may be acquired AFTER surgery

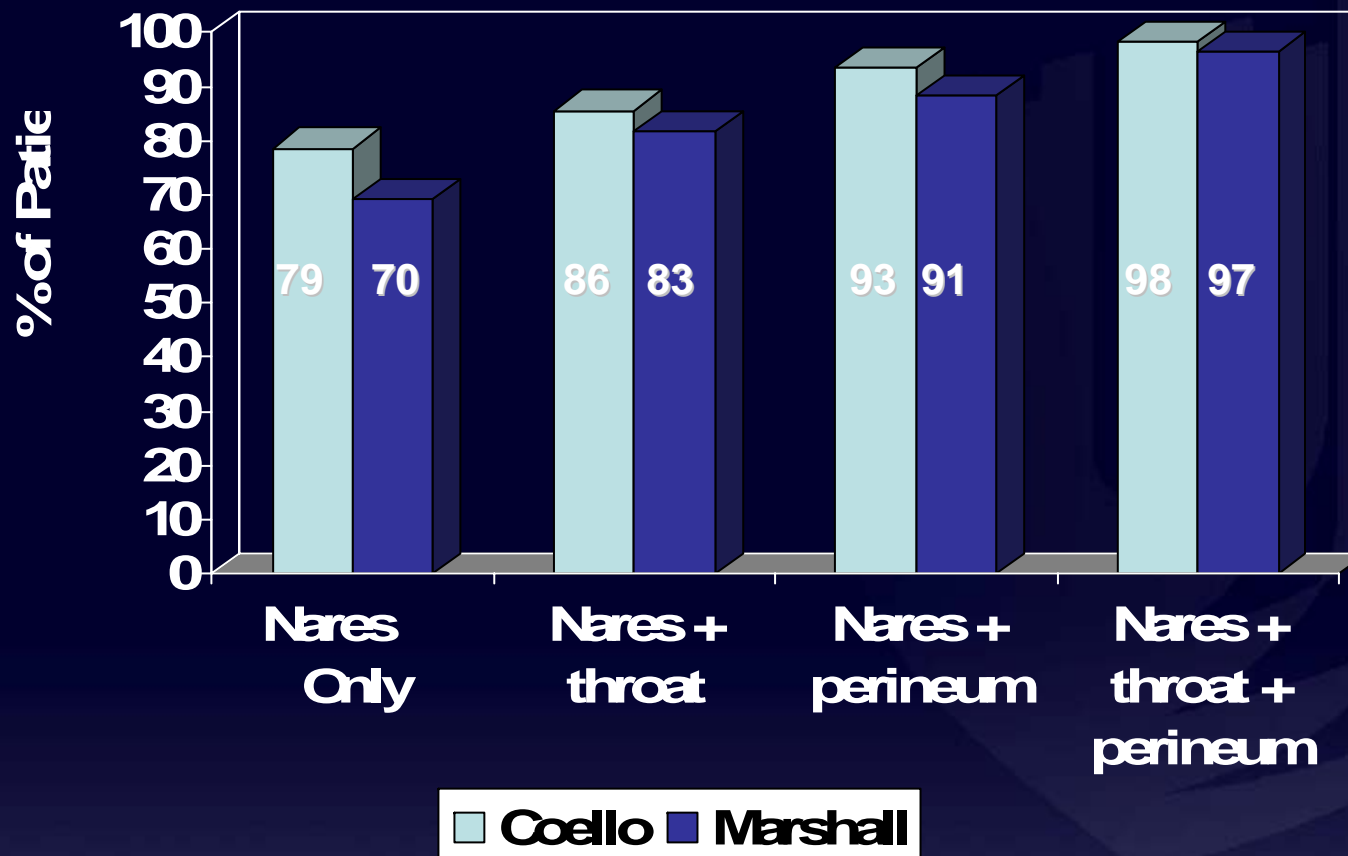
MRSA Screening Cultures

- Best method (where to culture?) is unclear
- Presence of skin lesions or chronic wounds is an important risk factor for MRSA colonization at the time of hospital admission
- Community-associated MRSA infections often present as skin and soft tissue infections
 - Rarely isolated from nares cultures

Papia G ICHE 1999;20:473.

Lucet JC Arch Intern Med 2003;163:181. Moran GJ et al. N Engl J Med 2006;355:666.

Percent of Patients Positive for MRSA by Body Site



Coello R et al. Eur J Clin Microbiol Infect Dis 1994;13:74
Marshall C et al. J Clin Microbiol 2007

Change Prophylaxis?

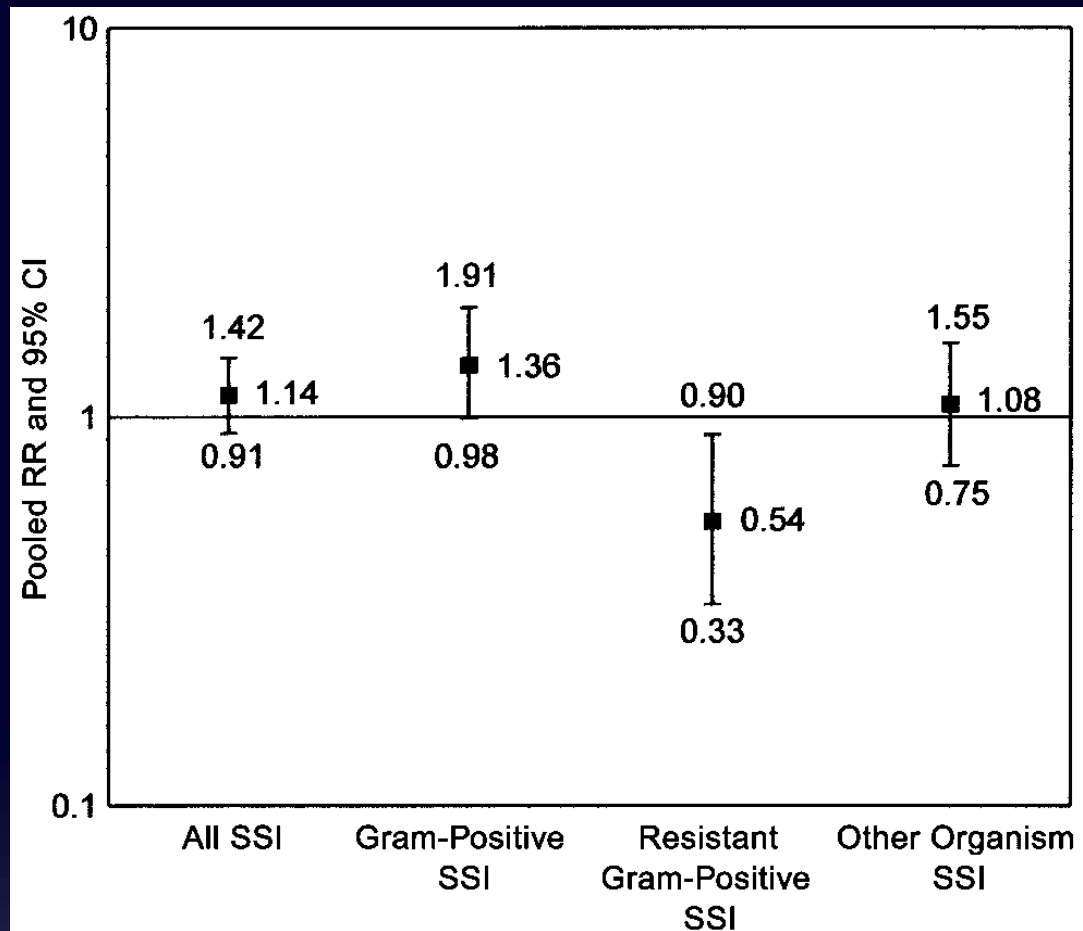
- No current guidelines recommend routine use of vancomycin (or other anti-MRSA agent) for peri-operative prophylaxis
- Specific scenarios where appropriate
 - Proven outbreak of SSI due to MRSA
 - Institutions with “high endemic rates” of SSI due to MRSA
 - Targeted high-risk patients who are at increased risk for SSI due to MRSA
- Disadvantages
 - Vancomycin takes >1 hour to infuse
 - Beta-lactams more active against susceptible gram-positive organisms
 - Vancomycin has no activity against gram-negative organisms
 - Wide spread use may lead to increased vancomycin resistance

Bratzler CID 2004.
Bolon. CID 2004;38:1357-63.
Dodds CID 2004;38:1555-60.

Prophylaxis with Vancomycin

- Most studies done in cardiac surgery
- Meta-analysis of 7 studies comparing vancomycin to cephalosporin
 - No difference in overall rate of SSI
 - Issue: studies were published before MRSA became such a big problem

Prophylaxis with Vancomycin



Prophylaxis with Vancomycin

- More recent studies continue to provide conflicting results

Pathogen ^a	CABG surgery	
	Feb 2001 to Sept 2002, cefuroxime	Oct 2002 to Aug 2005, vancomycin
Coagulase-negative <i>Staphylococcus</i>	4.8 ± 2.4	3.8 ± 3.0
MRSA	0.79 ± 0.93	0.52 ± 0.87
Other gram-positive organisms	1.8 ± 1.4	1.9 ± 2.0
Gram-negative organisms	3.2 ± 2.3	3.2 ± 2.6

- None have showed increase in gram-negative infections
 - Our own data shows that there may be a trend

Garey et al. AAC 2008;52:446

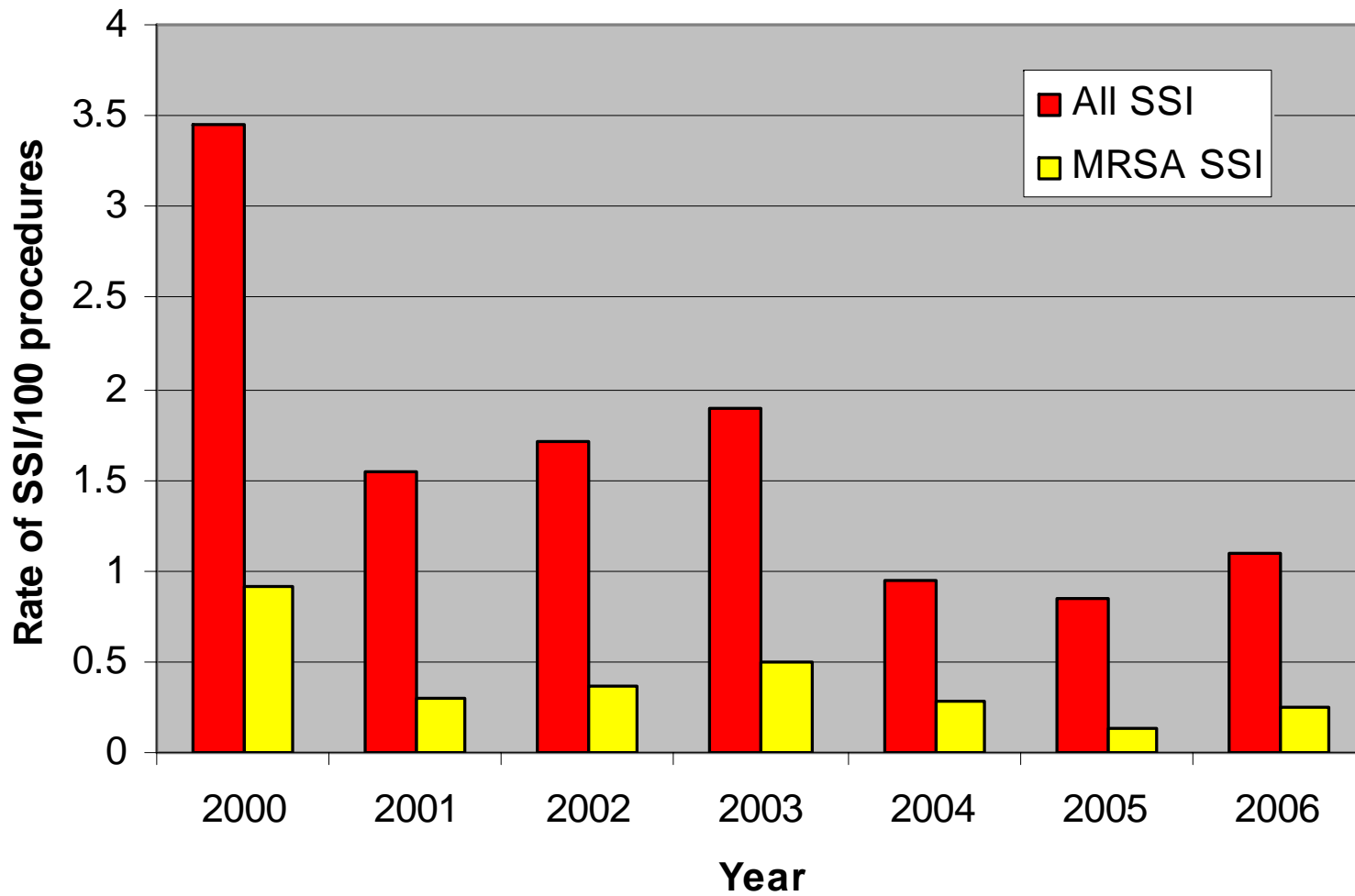
Finkelstein et al. J Thorac Cardiovasc Surg 2002;123:326.

Trinh et al. ICHE 2009; 30:440.

Vancomycin + Beta-lactam?

- At Duke, program to decrease rates of mediastinitis due to MRSA
 - Aggressive glucose control
 - Increased compliance with pre-operative antiseptic CHG shower
 - Addition of vancomycin and rifampin to cefuroxime for antibiotic prophylaxis in "high risk patients"
- Before-after design
- Sustained decrease

Rate of SSI and MRSA SSI following CARD or CABG



Take Home Points

- MRSA is the leading cause of SSI
 - Leads to adverse outcomes
 - Patients with decreased function appear to be at highest risk
- No well-proven interventions to specifically prevent MRSA exist
 - “UNRESOLVED ISSUES”
- Make sure evidence-based measures are in place for SSI prevention before you target MRSA specifically

Take Home Points

- Targeted efforts to screen, decolonize and/or broaden antibiotic prophylaxis are options
 - But ALL remain controversial
 - NO data to support general application of these methods
 - Have process in place to manage results from screening tests BEFORE you start screening
- Make decisions based on local epidemiology:
 - Know your rates and bugs
 - Is MRSA a problem pathogen for SSI?
 - If not, specific interventions might not be worth it