The role of active MRSA screening: what's the evidence ?

Stephan Harbarth MD, MS

HUG

Geneva University Hospitals

Agenda

- Recently published studies: Effect of (universal) active screening?

- Cost-effectiveness of rapid screening?

MRSA screening

Universal Screening for Methicillin-Resistant *Staphylococcus aureus* at Hospital Admission and Nosocomial Infection in Surgical Patients

Stephan Harbarth, MD, MS
Carolina Fankhauser, MS
Jacques Schrenzel, MD
Jan Christenson, MD
Pascal Gervaz, MD
Catherine Bandiera-Clerc, RN
Gesuele Renzi, MS
Nathalie Vernaz, PharmD
Hugo Sax, MD
Didier Pittet, MD, MS

Context Experts and policy makers have repeatedly called for universal screening at hospital admission to reduce nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infectio

Objective To
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Impact of rapid screening tests on acquisition of meticillin resistant *Staphylococcus aureus*: cluster randomised crossover trial

Dakshika Jeyaratnam, research fellow,[1,2] Christopher J M Whitty, professor ,[3] Katie Phillips, medical laboratory assistant,[1] Dongmei Liu, medical statistician,[3] Christina Orezzi, information analyst,[1] Uchechukwu Ajoku, research assistant,[1] Gary L French, professor of microbiology[1,2]

Annals of Internal M

Universal Surveillance for Methicillin-Resistant *Staphylococcus aureus* in 3 Affiliated Hospitals

Ari Robicsek, MD; Jennif
Karen L. Kaul, MD, PhD;

Reduction in the rate of methicillin-resistant *Staphylococcus aureus* acquisition in surgical wards by rapid screening for colonization: a prospective, cross-over study

Katherine Hardy[1,2], Charlotte Price[3], Ala Szczepura[3], Savita Gossain[1], Ruth Davies[4], Nigel Stallard[3], Sahida Shabir[5], Claire McMurray[5], Andrew Bradbury[6] and Peter M Hawkey[1,2]

1) *West Midlands Public Health Laboratory, Heart of England NHS Foundation Trust,* 2) *School of Immunity and Infection, University of Birmingham, Birmingham,* 3) *Warwick Medical School, University of Warwick, Coventry,* 4) *Warwick Business School, University of Warwick, Coventry,* 5) *Research & Development, Heart of England NHS Foundation Trust, and* 6) *Department of Vascular Surgery, Heart of England NHS Foundation Trust, Birmingham, UK*

Original article

Impact of ra
Staphylococ

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Universal Screening for Methicillin-Resistant *Staphylococcus aureus* at Hospital Admission and Nosocomial Infection in Surgical Patients

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Context Experts and policy makers have repeatedly called for universal screening at hospital admission to reduce nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infection.

Objective To determine the effect of an early MRSA detection strategy on nosocomial MRSA infection rates in surgical patients.

Design, Setting, and Patients Prospective, interventional cohort study conducted between July 2004 and May 2006 among 21 754 surgical patients at a Swiss teaching hospital using a crossover design to compare 2 MRSA control strategies (rapid screening on admission plus standard infection control measures vs standard infection control alone). Twelve surgical wards including different surgical specialties were enrolled according to a prespecified agenda, assigned to either the control or intervention group for a 9-month period, then switched over to the other group for a further 9 months.

JAMA 2008 Mar 12;299(10):1149-57

Objective

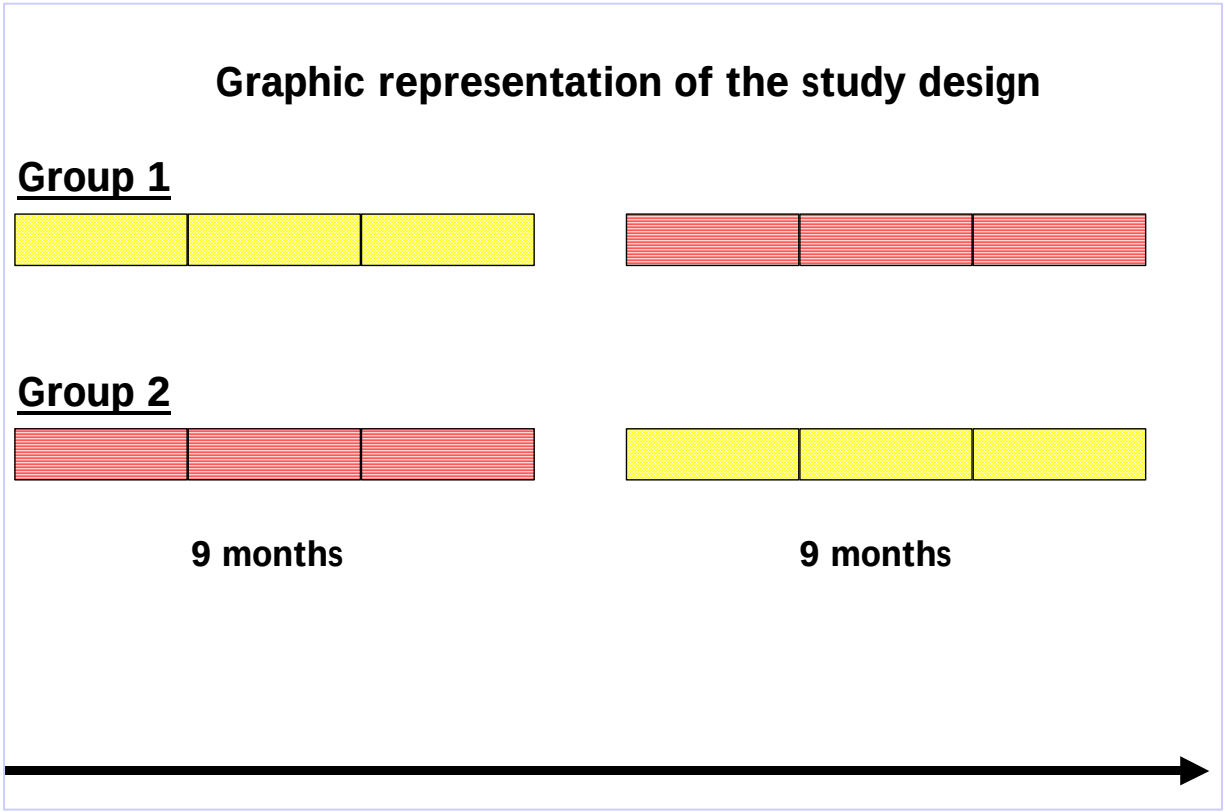
To determine the effect of a universal rapid MRSA detection strategy on nosocomial MRSA infection rates in a large surgical department with endemic MRSA

Methods

Prospective, interventional cohort study with crossover design (July 04 – June 06)

- **Two study groups with 6 surgical wards each and a total of 12,000 annual admissions were enrolled**

  1. **Group I - orthopedics, neurosurgical, plastic, cardiovascular & thoracic surgery**
  2. **Group II – urology, abdominal & transplant surgery**



Group 1:

Orthopedics

Cardiovascular and Thoracic surgery

Neurosurgery & Plastic surgery

Group 2:

Abdominal surgery

Urology

Transplant surgery

Results (I): MRSA infections

	qMRSA period	Control
Orthopedics	27	17
Cardiovascular	6	8
Neurosurgery	2	2
Abdominal	38	32
Urology	12	13
Others	8	4
TOTAL	93	76

Harbarth et al. JAMA 2008;299:1149-57

Results (II): Incidence of MRSA infections

	qMRSA	Control	Adjusted RR
Incidence of MRSA NI (per 1000 pt-days)	1.11	0.91	1.2 (0.9-1.7)
Sites of MRSA infection			
Surgical site	70	60	
Urinary tract	14	10	
Respiratory tract	2	6	
Bacteremia	4	2	
Others	13	10	
Rate of MRSA SSI (per 100 procedures)	1.14	0.99	1.2 (0.8-1.7)

Harbarth et al. JAMA 2008;299:1149-57

Results (III): MRSA infections in the rapid screening arm

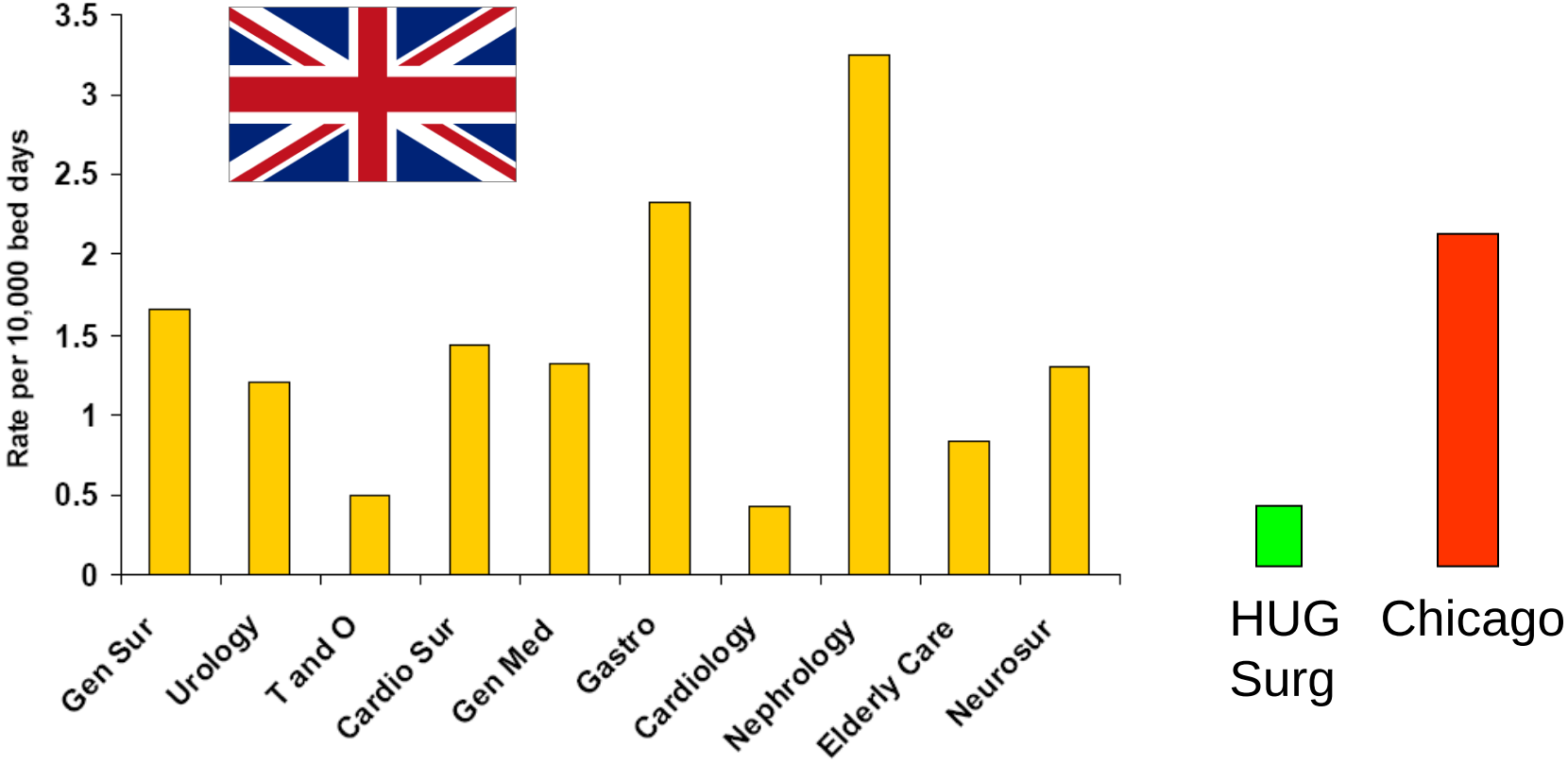
Variable	Total n
Among patients with any type of MRSA-infection:	93
Newly identified MRSA carriers by admission screening	17
Previously known MRSA carriers	23
MRSA-free at admission and identified by clinical isolate during hospitalization	53

Harbarth et al. JAMA 2008;299:1149-57

Limitations

- The majority of MRSA-infections occurred in patients negative on admission
  - Postoperative contamination important
  - Consider weekly screening in the future
- Not all MRSA patients received vancomycin ABP
  - Emergency surgery
  - Reluctance of surgeons
- No preemptive isolation used
- Good hand hygiene compliance
- Relatively low MRSA infection rates

MRSA bacteremia rates



Study 2

Robicsek et al.

Ann Intern Med 2008

Annals of Internal Medicine | ARTICLE

Universal Surveillance for Methicillin-Resistant *Staphylococcus aureus* in 3 Affiliated Hospitals

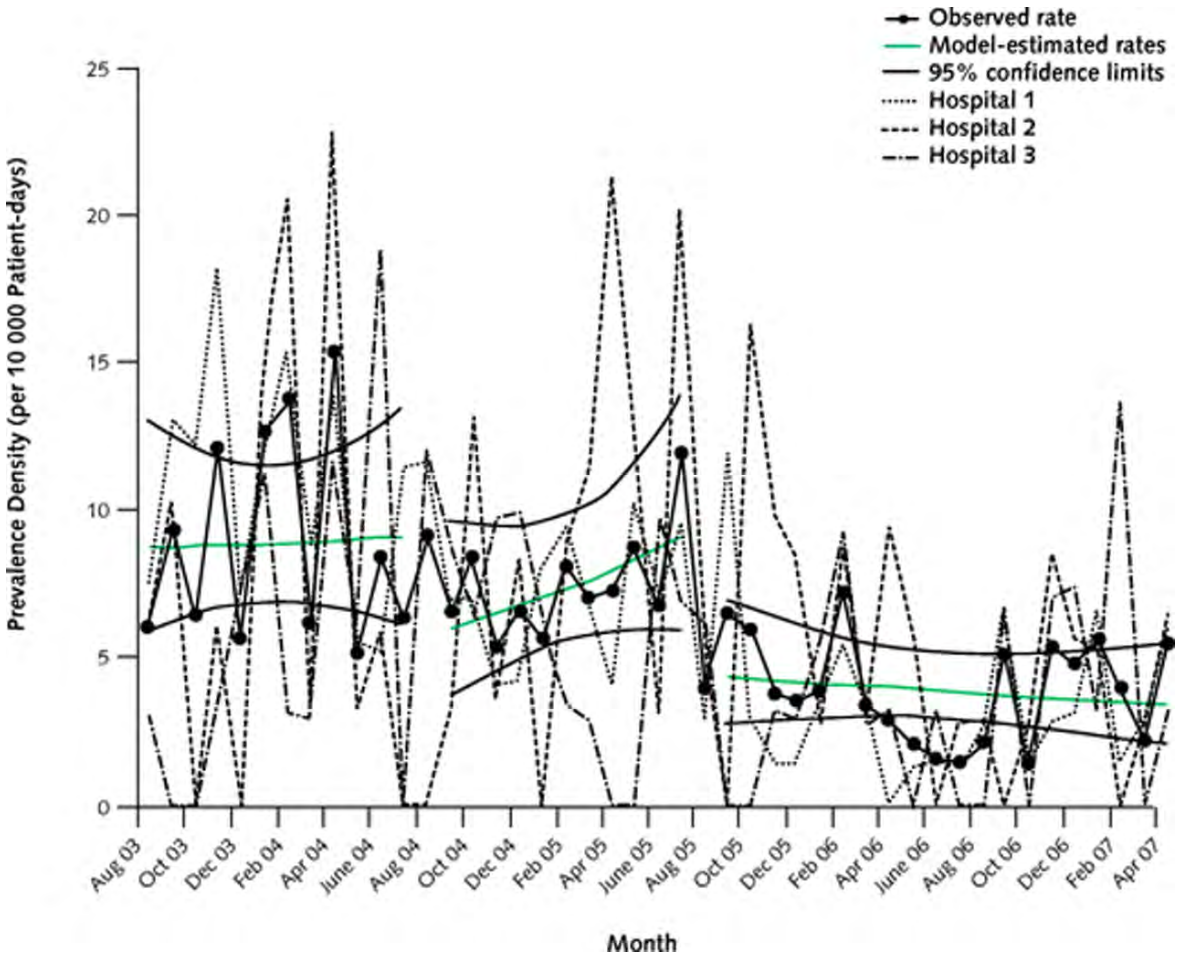
Ari Robicsek, MD; Jennifer L. Beaumont, MS; Suzanne M. Paule, BS; Donna M. Hacek, BS; Richard B. Thomson Jr., PhD; Karen L. Kaul, MD, PhD; Peggy King, RN, MBA; and Lance R. Peterson, MD

Design & intervention

- To examine the effect of 2 expanded surveillance interventions on MRSA disease in 3 hospitals in Chicago
- PCR–based nasal MRSA surveillance followed by topical decolonization therapy and contact isolation of MRSA-positive patients
- Interrupted time-series analysis

Segmented Poisson regression model: Aggregate hospital-associated MRSA prevalence density

Compared to baseline (8.9):
- **MRSA decreased during ICU surveillance (7.4, p=0.15)**
- **MRSA significantly decreased during universal surveillance (3.9, p<.001)**



Robicsek, A. et. al. Ann Intern Med 2008;148:409-418

Potential drawbacks of this study

- Key component of 2nd period: decolonization (mupirocin & chlorhexidine)
- Increase in mupirocin resistance
  - 6-9% of high-level mupirocin-resistant isolates

Robiscek A et al. Infect Control Hosp Epi 2009; in press.

Potential drawbacks of this study

- Key component of 2nd period: decolonization (mupirocin & chlorhexidine)
- Increase in mupirocin resistance
- Dramatic increase in the use of contact isolation ⇨ adverse outcomes?

Diekema D et al. Ann Intern Med 2008; 149: 67-69

Potential drawbacks of this study

- Key component of 2nd period: decolonization (mupirocin & chlorhexidine)
- Increase in mupirocin resistance
- Dramatic increase in the use of contact isolation ⇨ adverse outcomes?
- Unchanged rate of other nosocomial infections

Diekema D et al. Ann Intern Med 2008; 149: 67-69

Limitations of both studies JAMA vs. Ann Intern Med

- No conventional cultures to confirm positive results of the molecular tests
- Lack of active post-discharge surveillance of MRSA surgical site infections
- No random assignment of individual wards to the study arms
- No discharge screening for MRSA

Study 3

Dakshika Jeyaratnam et al.

BMJ 2008

Impact of rapid screening tests on acquisition of meticillin resistant *Staphylococcus aureus*: cluster randomised crossover trial

Dakshika Jeyaratnam, research fellow,[1,2] Christopher J M Whitty, professor ,[3] Katie Phillips, medical laboratory assistant,[1] Dongmei Liu, medical statistician,[3] Christina Orezzi, information analyst,[1] Uchechukwu Ajoku, research assistant,[1] Gary L French, professor of microbiology[1,2]

Methods

- Objective: To compare rapid MRSA screening vs. conventional cultures
- Design: Cluster-randomized clinical trial in 10 wards
- Admission & discharge screening
- Main outcome: acquisition rates

Results

- 6’888 included patients (72%)
- MRSA carriage on admission: 6.7%

	Control	Intervention
Reporting (h)	46	22
Inadequate premptive isolation (d)	399	277
MRSA acquisition	108	99

→ Rates of MRSA transmission, wound infection, and bacteraemia not statistically different

Reduction in the rate of methicillin-resistant *Staphylococcus aureus* acquisition in surgical wards by rapid screening for colonization: a prospective, cross-over study

Katherine Hardy[1,2], Charlotte Price[3], Ala Szczepura[3], Savita Gossain[1], Ruth Davies[4], Nigel Stallard[3], Sahida Shabir[5], Claire McMurray[5], Andrew Bradbury[6] and Peter M Hawkey[1,2]

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Design:

- Cluster-randomized cross-over study
- 8 months intervention phase then crossover
- Endpoint: MRSA transmission & acquisition
- Screening of all patients on discharge
- Industry co-sponsoring

Hardy & Hawkey et al. Clin Micro Infect 2010

MRSA-Screening: Another UK trial

Intervention:

- PCR-based on-admission screening for MRSA vs. conventional screening
- Repeat screening in 4 days intervals
- Decolonisation: Mupirocin & chlorhexidin for 5 days

Study population:

- 10.934 surgical patients in 7 services
- Screening compliance: 90.8%

Hardy & Hawkey et al. Clin Micro Infect 2010

Results: MRSA-Screening

	Standard arm	PCR arm
Patient episodes	7493	6459
MRSA+ on admission	187	266
Time to notification (d)	3.3	0.9
Nosocomial MRSA+	157	111
Decolonisation	142	268

- After adjustment for confounding, MRSA transmission rates were **1.5 times higher** in the standard screening arm (compared to PCR)
- Only 17% of MRSA-patients underwent contact precautions

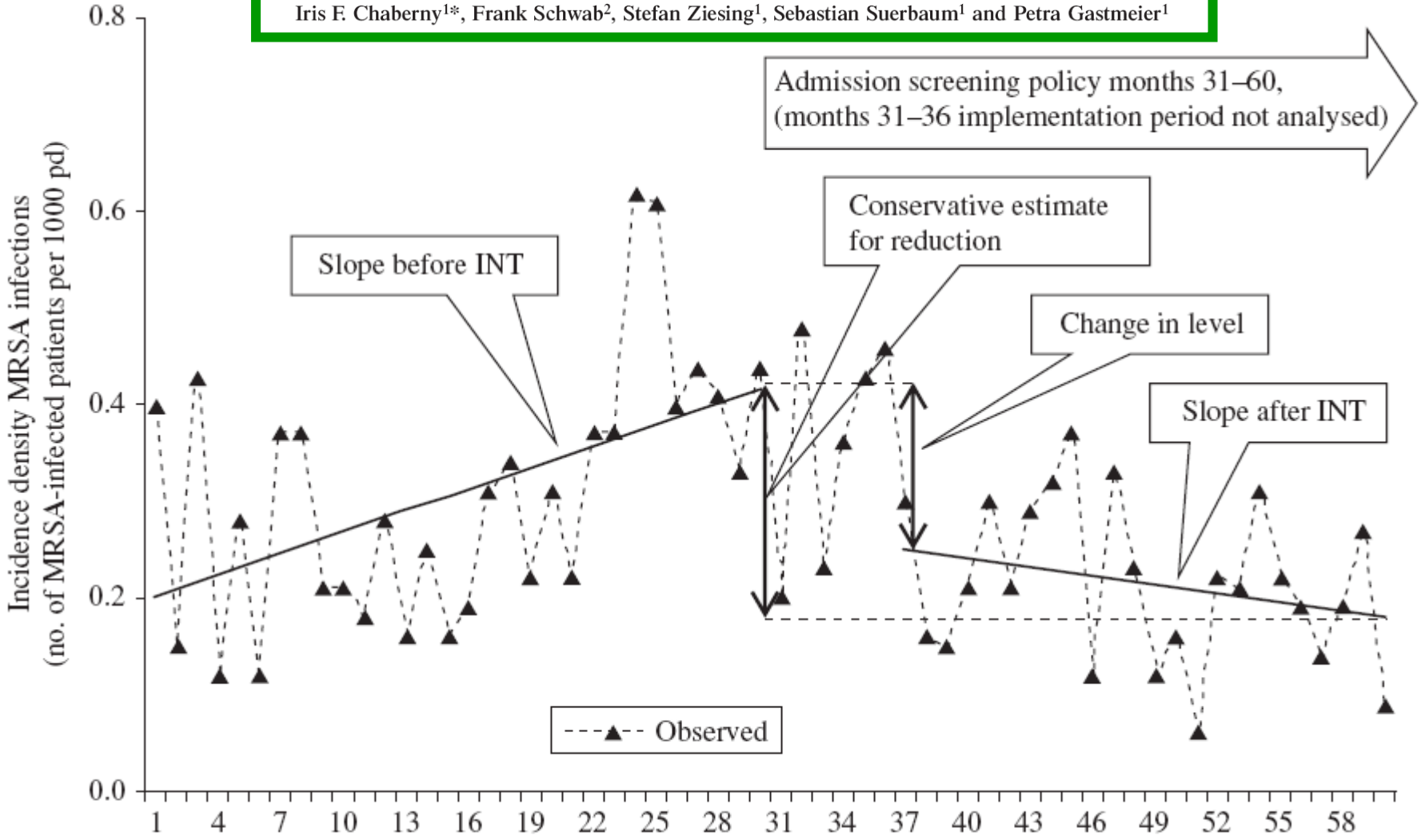
Hardy & Hawkey et al. Clin Micro Infect 2010

Journal of Antimicrobial Chemotherapy (2008) **62**, 1422–1429
doi:10.1093/jac/dkn373
Advance Access publication 1 September 2008

JAC

Impact of routine surgical ward and intensive care unit admission surveillance cultures on hospital-wide nosocomial methicillin-resistant *Staphylococcus aureus* infections in a university hospital: an interrupted time-series analysis

Iris F. Chaberny[1]*, Frank Schwab[2], Stefan Ziesing[1], Sebastian Suerbaum[1] and Petra Gastmeier[1]



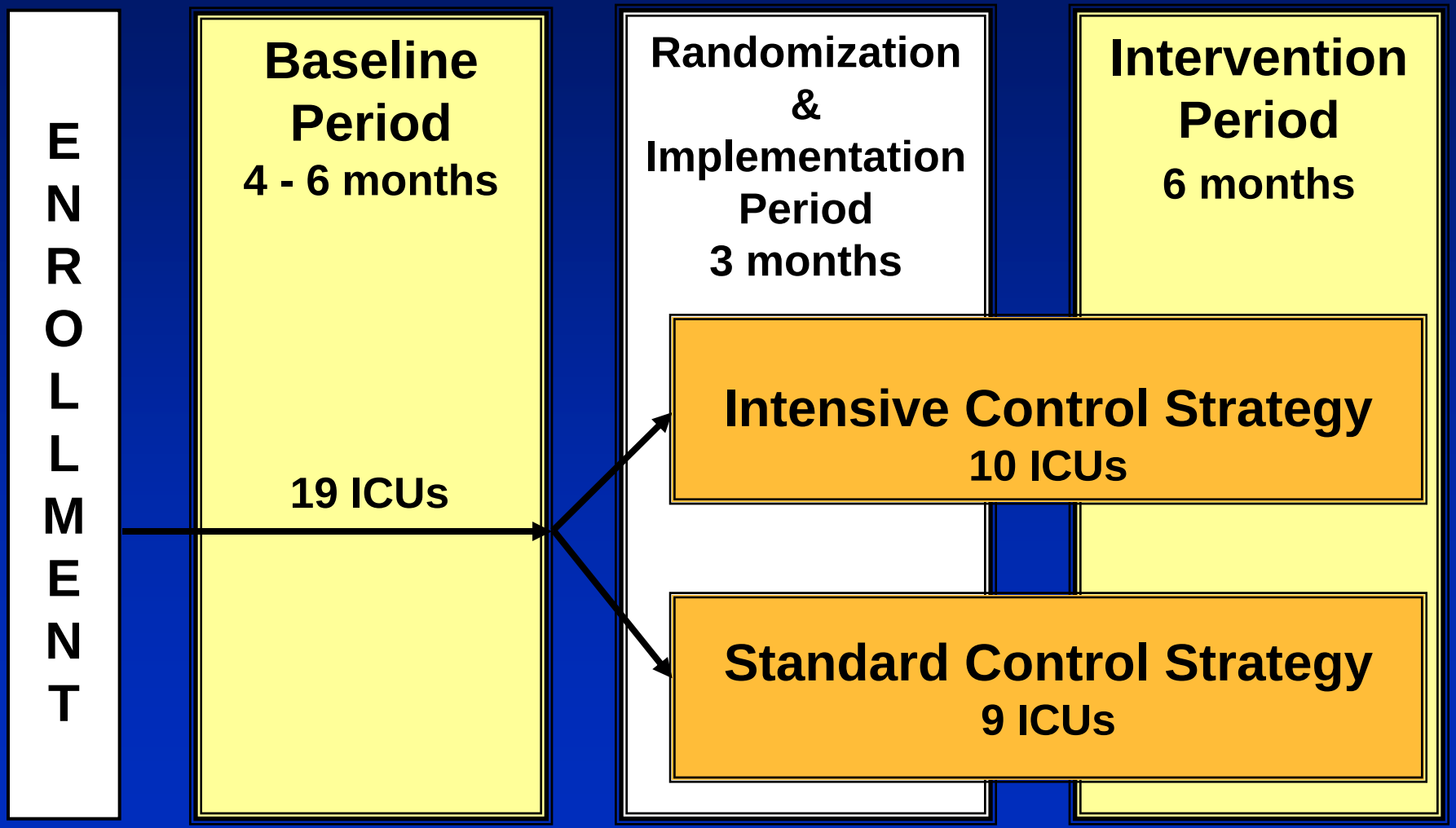
Results of the STAR*ICU Trial

Strategies to Reduce **T**ransmission of **A**ntimicrobial **R**esistant Bacteria in Adult **I**ntensive **C**are **U**nits

W. Charles Huskins, MD, MSc
Mayo Clinic College of Medicine, Rochester, MN

conducted by the
Bacteriology and Mycology Study Group (BAMSG)
19 US academic medical centers

Study Design

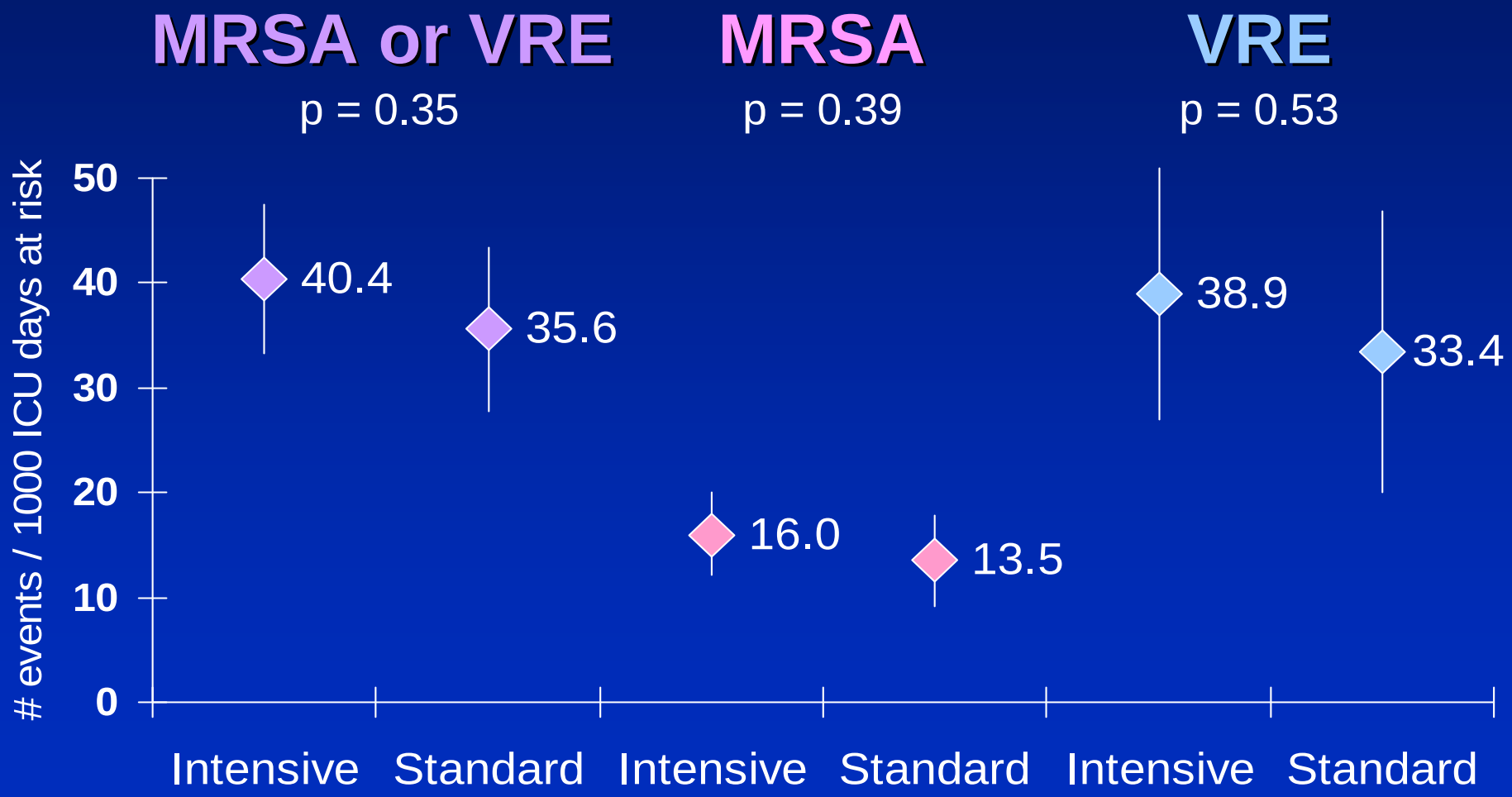


Infection Control Strategies

	Intensive	Standard
Hand hygiene / SP promotion program	Yes	Yes
Surveillance cultures for MRSA & VRE		
ICU admission (day 0 - 2)	Yes	Yes
Weekly while in ICU	Yes	Yes
Discharge (+ / - 2 days)	Yes	Yes
Report surveillance culture results	Yes	No
Barrier precautions for MRSA / VRE		
ICU admission (cultures pending)	UG	SP
MRSA & VRE negative	SP	SP
MRSA or VRE positive	CP	existing precautions

SP = Standard Precautions; UG = Universal Gloving; CP = Contact Precautions

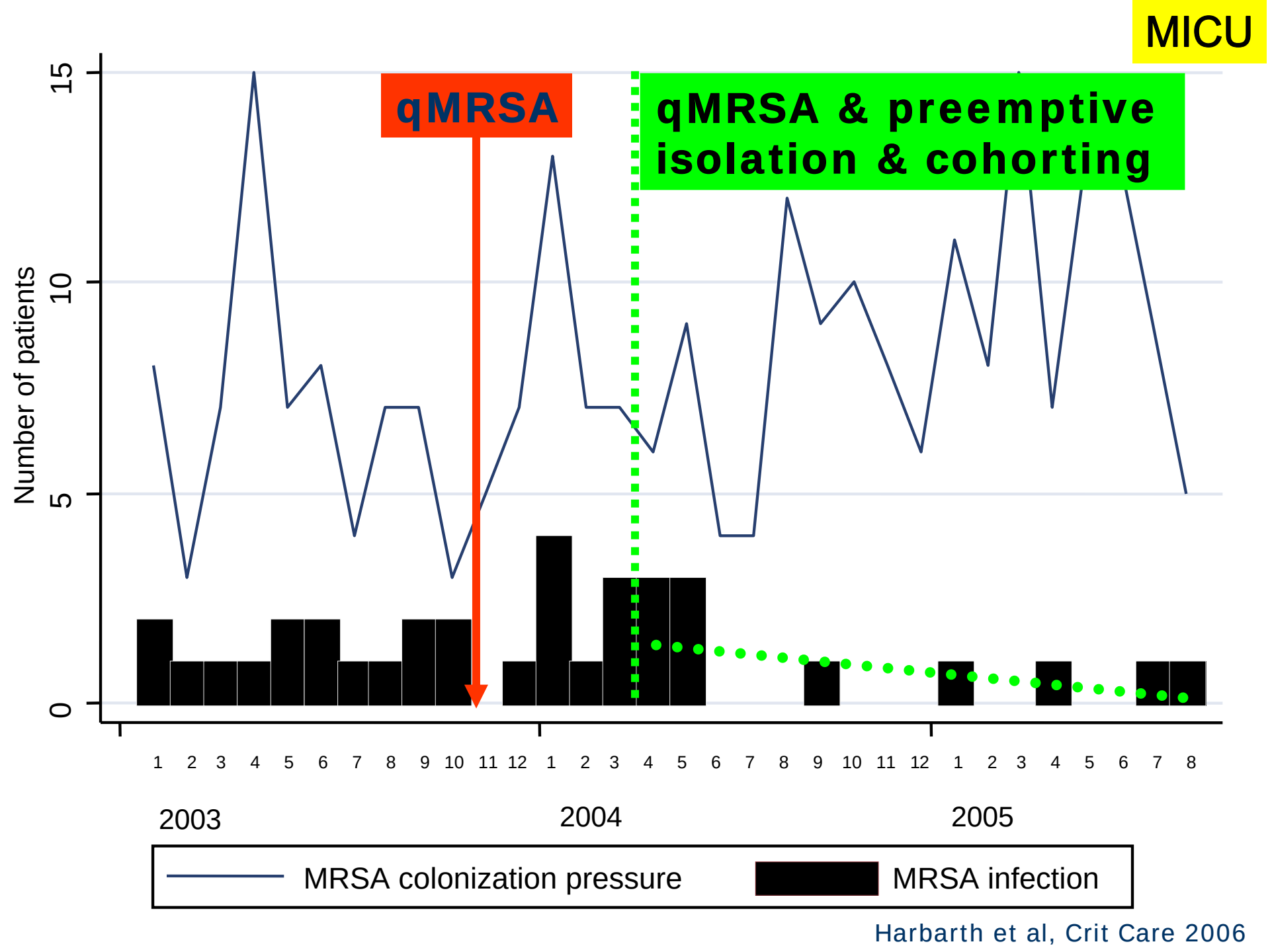
Incidence Density of New Colonization / Infection Events in Intensive vs. Standard Control Strategy ICUs



Point estimates, 95% CI & p-values from ANCOVA adjusted for baseline ID

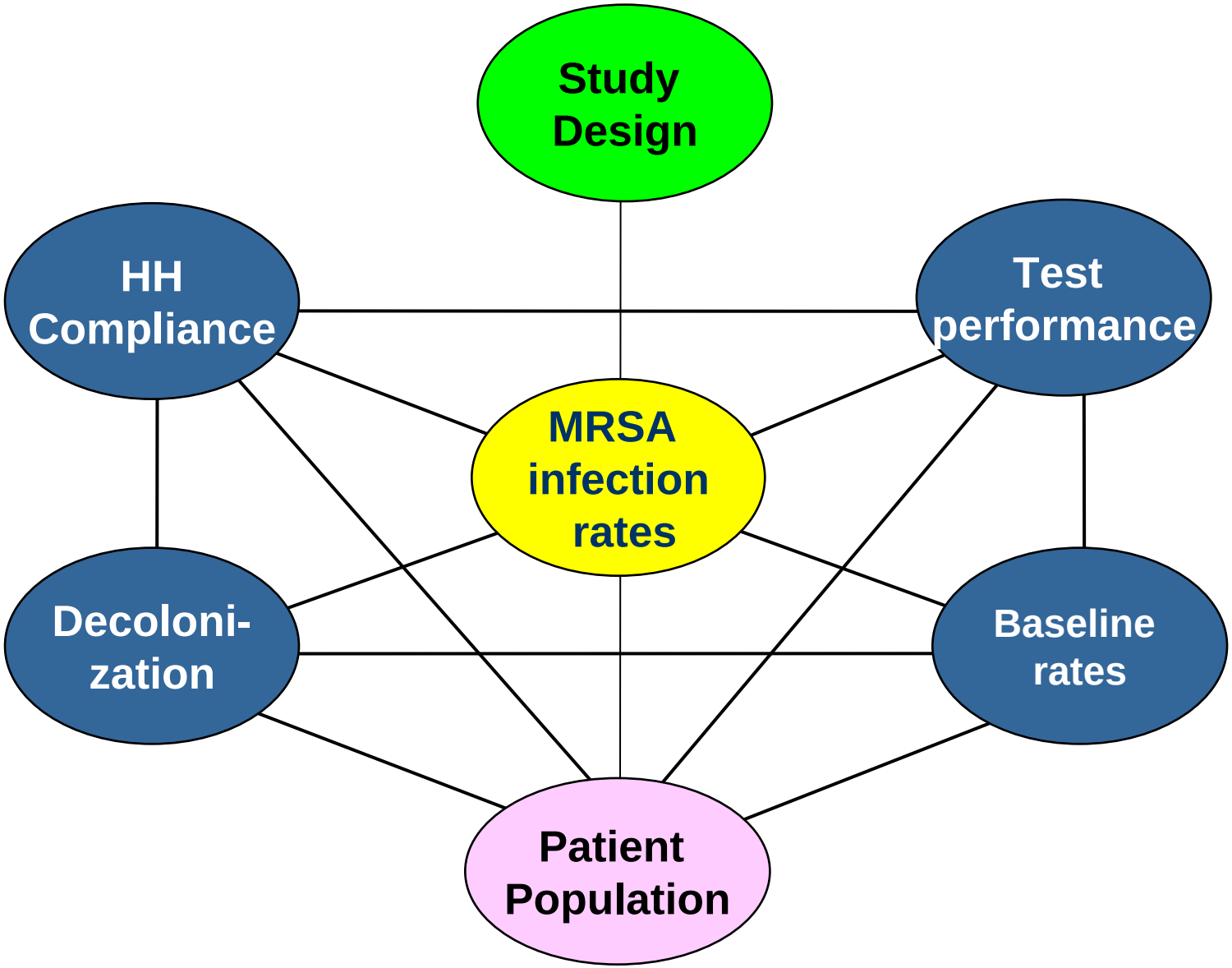
Possible reasons for failure

- High rates of acquisition in both arms
- No intensive search & destroy
  - No uniform decontamination approach
  - No environmental control
  - No HCW screening
- Central laboratory facility
  - No rapid testing available



Harbarth et al, Crit Care 2006

Possible explanations



Active MRSA screening:

Cost-effectiveness of rapid PCR tests?

Economic evaluation: Challenges

⇨ ***It is not clear from the current literature if, when, for whom rapid MRSA screening is cost-effective***

Common limitations of existing studies:

- No explicit goal or decision choice
- No clear perspective (Hospital? Society?)
- Poor costing methods
- Limited clinical & economic data available

Complications with Economic Analyses of MRSA Screening

- **Limited availability of cost data**
  - *"What does an MRSA infection cost?"*
    - Attributing costs to MRSA is not easy
    - Controlling for confounders difficult to achieve
    - Endogeneity bias*
      (correlation between infection risk and LoS)
  - Overestimation of direct MRSA costs
  - Underestimation of indirect MRSA costs

* Graves, N, et al. ICHE, 2007.

What about cost-effectiveness? *UK HTA of MRSA screening*

- Economic model of MRSA screening
- Compared rapid PCR vs. culture vs. chromogenic agar
- Compared universal vs. targeted screening

Effectiveness?

- Universal screening with pre-emptive isolation most effective at reducing MRSA prevalence
- Ignoring pre-emptive isolation only marginally less effective
- Targeted screening (high-risk wards) was least effective

Which test?

- Chromogenic agar was most effective given high sensitivity and specificity and low turn-around time
- ChromAgar the most cost-effective – Dominates PCR

Ritchie K et al. HTA report 9. NHS Quality Improvement Scotland, 2007 (**www.nhshealthquality.org**)

HTA of MRSA screening

Key drivers of cost-effectiveness

- **Economic analysis sensitive to:**
  - Baseline prevalence of MRSA (7.1% estimate)
  - MRSA transmission rate
  - Hospital factors: availability of isolation rooms, LoS
- **Significant uncertainty & limited generalizability**
  - Variable sensitivity and specificity of MRSA tests
  - Impact of other MRSA containment policies
- **Major limitation:** Performed prior to publication of recent high-quality studies of MRSA screening

Ritchie K et al. HTA report 9. NHS Quality Improvement Scotland, 2007 (**www.nhshealthquality.org**)

Rapid PCR
Economic assessments

- Significant reduction of TaT time by PCR
- Yet at a higher cost (false positives)
- Cost per patient higher with PCR

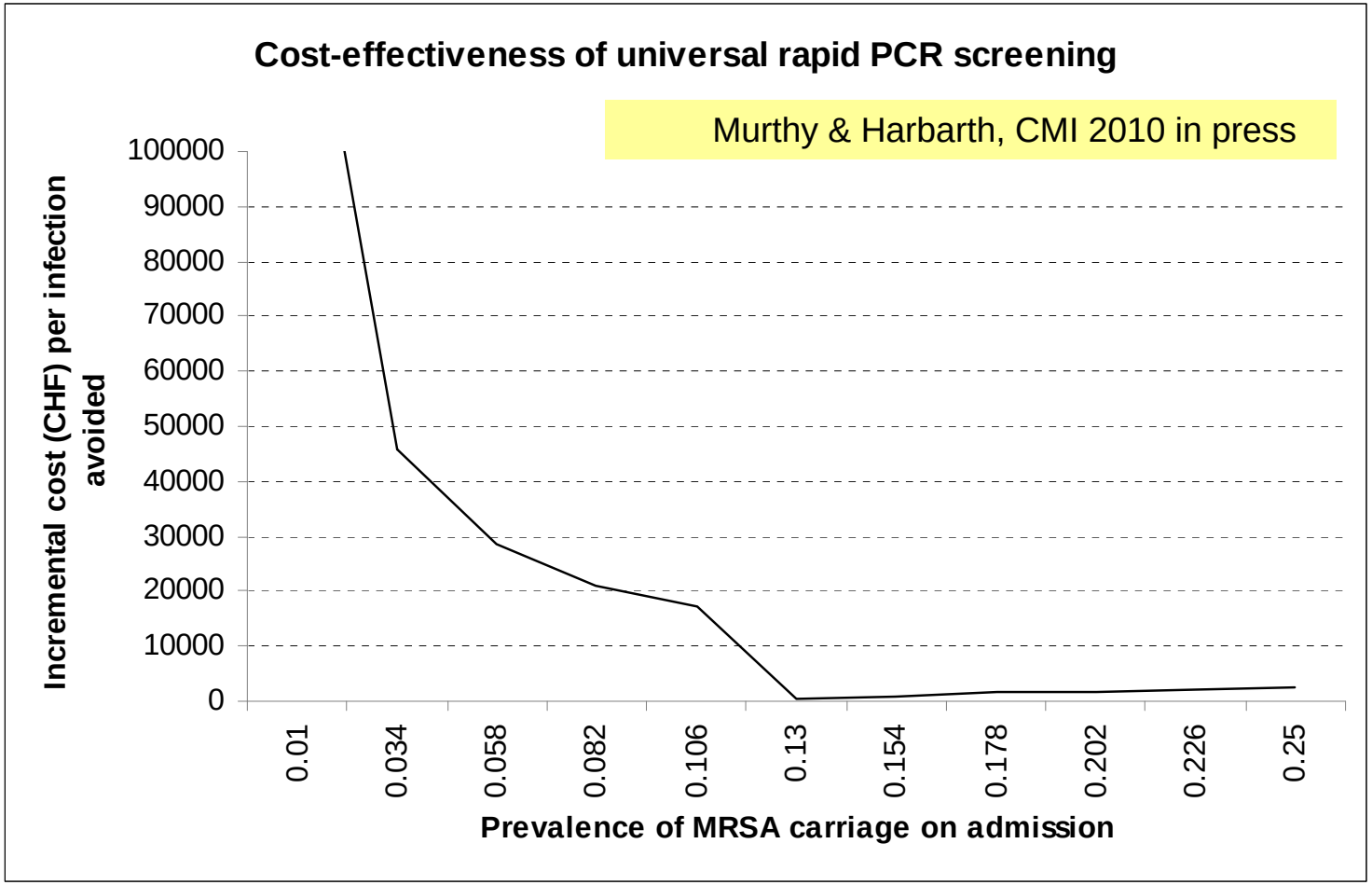
Conterno LO et al. ICHE 2007; 28: 1134-41

- PCR valuable for rapid MRSA detection but high costs suggest prudent use
- In settings with low MRSA endemicity, the broad use of PCR is *not cost-effective*.

Bühlmann M et al. J Clin Micro 2008; 46: 2151-54
Wassenberg M et al. ECCMID 2009

Cost-effectiveness

1 Baseline prevalence is an important predictor of cost-effectiveness: PCR may be more appropriate in settings with high MRSA prevalence



MRSA screening

- Universal screening not a mandatory prerequisite to reduce MRSA infections
- Use of targeted screening is probably cost-effective if linked to rapid action
- Conflicting recent evidence about value of rapid screening
- Risk profiling needs to be adapted to local epidemiology (C-MRSA)
- Competing infection control strategies need to be evaluated

SHEA/IDSA Practice Recommendations Oct 2008

S62 INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY OCTOBER 2008, VOL. 29, SUPPLEMENT 1

SUPPLEMENT ARTICLE: SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent Transmission of Methicillin-Resistant *Staphylococcus aureus* in Acute Care Hospitals

David P. Calfee, MD, MS; Cassandra D. Salgado, MD, MS; David Classen, MD, MS; Kathleen M. Arias, MS, CIC; Kelly Podgorny, RN, MS, CPHQ; Deverick J. Anderson, MD, MPH; Helen Burstin, MD; Susan E. Coffin, MD, MPH; Erik R. Dubberke, MD; Victoria Fraser, MD; Dale N. Gerding, MD; Frances A. Griffin, RRT, MPA; Peter Gross, MD; Keith S. Kaye, MD; Michael Klompas, MD; Evelyn Lo, MD; Jonas Marschall, MD; Leonard A. Mermel, DO, ScM; Lindsay Nicolle, MD; David A. Pegues, MD; Trish M. Perl, MD; Sanjay Saint, MD; Robert A. Weinstein, MD; Robert Wise, MD; Deborah S. Yokoe, MD, MPH

SHEA/IDSA Practice Recommendations

- Specific recommendation regarding universal screening for MRSA cannot be made
  - Conflicting results from recent studies
  - Differences among hospitals and patient populations

SHEA/IDSA Practice Recommendations

- Active surveillance as a single intervention in the absence of a multifaceted approach to MRSA control unlikely to be effective

- Active surveillance potentially useful in facilities with optimized adherence to basic MRSA control but still high MRSA rates

RESERVE

Rapid screening tests for meticillin-resistant *Staphylococcus aureus* at hospital admission: systematic review and meta-analysis

Evelina Tacconelli, Giulia De Angelis, Chiara de Waure, Maria A Cataldo, Giuseppe La Torre, Roberto Cauda

- Compared with culture screening, use of rapid screening tests was <u>not</u> associated with a significant decrease in MRSA acquisition rate (RR 0·87, 95% CI 0·61–1·24).

Tacconelli E et al. Lancet Infect Dis 2009; 9: 546-54

Rapid testing & MRSA SSI-rate

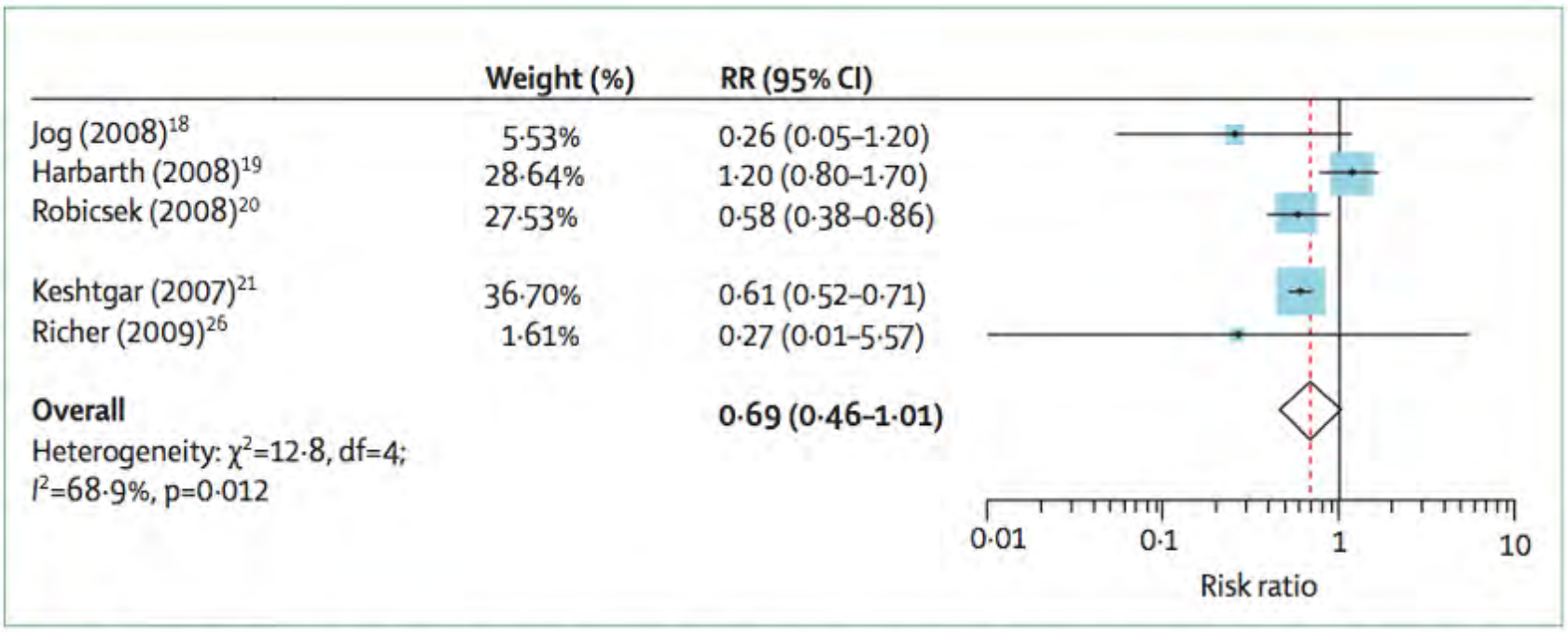


Figure 4: **Effect of rapid molecular tests for meticillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission on the incidence of MRSA surgical-site infections per 100 surgical procedures**

Comparison is between units in which screening was done by molecular tests and units in which screening was not

Almost significant decrease in MRSA SSI infections !

meta-analysis.

Tacconelli E et al. Lancet Infect Dis 2009; 9: 546-54

Author, Journal, Year	Harbarth, JAMA 2008	Robicsek, Annals 2008	Jeyaratnam, BMJ 2008	Hardy, Clin Micro Infect 09
Aim	Evaluate the efficacy of universal rapid MRSA screening	Examine the effect of screening & decolonization on MRSA rates	Compare rapid MRSA screening vs. conventional cultures	Compare rapid MRSA screening vs. conventional cultures
Country	Switzerland	USA	UK	UK
Setting	Surgery	Hospital-wide	Geriatrics, oncology, surgery	Surgery
Design	Cross-over	Before-after	Cross-over	Cross-over
Control group	Yes	No	Yes	Yes
Rapid test	Yes (homemade)	Yes (commercial)	Yes (commercial)	Yes (commercial)
Decolonization	Yes	Partial	Yes	Yes
Total study period	24 months	45 months	14 months	16 months
Admission MRSA prevalence	5.1%	6.3%	6.7%	3.6%
Baseline MRSA infection rates	Medium	High	High	Unknown
Hand hygiene compliance	Excellent	Unknown	Good	Unknown
Conclusion	Rapid MRSA screening did not reduce nosocomial MRSA infections	Universal admission screening reduced MRSA disease	Universal rapid MRSA screening is not recommended	Universal rapid MRSA screening is recommended