

# Using Meta-Analyses to Inform Interventions and Quality Improvement

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# Outline

- Introduction to Systematic Literature Reviews and Meta-analyses
  
- Meta-analyses to inform interventions implemented in our VA CREATE grants
  - ▣ Interventions to reduce *S. aureus* surgical site infections
  - ▣ Interventions to improve hand hygiene compliance
  
- Meta-analyses to be used in decision-analytical model for my VA HSRD CDA grant

# Poll Question

□ How familiar are you with meta-analyses?

(Pick one answer)

- I performed  $>1$  meta-analyses
- I performed 1 meta-analysis
- I took a course on meta-analysis
- I have read about meta-analyses
- Not at all familiar

# Introduction to Systematic Literature Reviews and Meta-analyses

# Systematic Literature Reviews

- **SYSTEMATIC** method of finding articles
  - ▣ Not just pulling out convenient/popular articles
  - ▣ Research librarian
- **SYSTEMATIC** method of collecting data from articles
  - ▣ Data collection form
  - ▣ 2 reviewers
- **SYSTEMATIC** method of reporting findings

# Systematic Search



# Systematic Method of Reporting



Journal of Clinical Epidemiology 62 (2009) 1006–1012

**Journal of  
Clinical  
Epidemiology**

## METHODS OF SYSTEMATIC REVIEWS AND META-ANALYSIS

### Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

David Moher<sup>1,2,\*</sup>, Alessandro Liberati<sup>3,4</sup>, Jennifer Tetzlaff<sup>1</sup>, Douglas G. Altman<sup>5</sup>,  
The PRISMA Group<sup>¶</sup>

#### CONSENSUS STATEMENT

## Meta-analysis of Observational Studies in Epidemiology A Proposal for Reporting

Donna F. Stroup, PhD, MSc

Jesse A. Berlin, ScD

Sally C. Morton, PhD

Ingram Olkin, PhD

G. David Williamson, PhD

Drummond Rennie, MD

**Objective** Because of the pressure for timely, informed decisions in public health and clinical practice and the explosion of information in the scientific literature, research results must be synthesized. Meta-analyses are increasingly used to address this problem, and they often evaluate observational studies. A workshop was held in Atlanta, Ga, in April 1997, to examine the reporting of meta-analyses of observational studies and to make recommendations to aid authors, reviewers, editors, and readers.

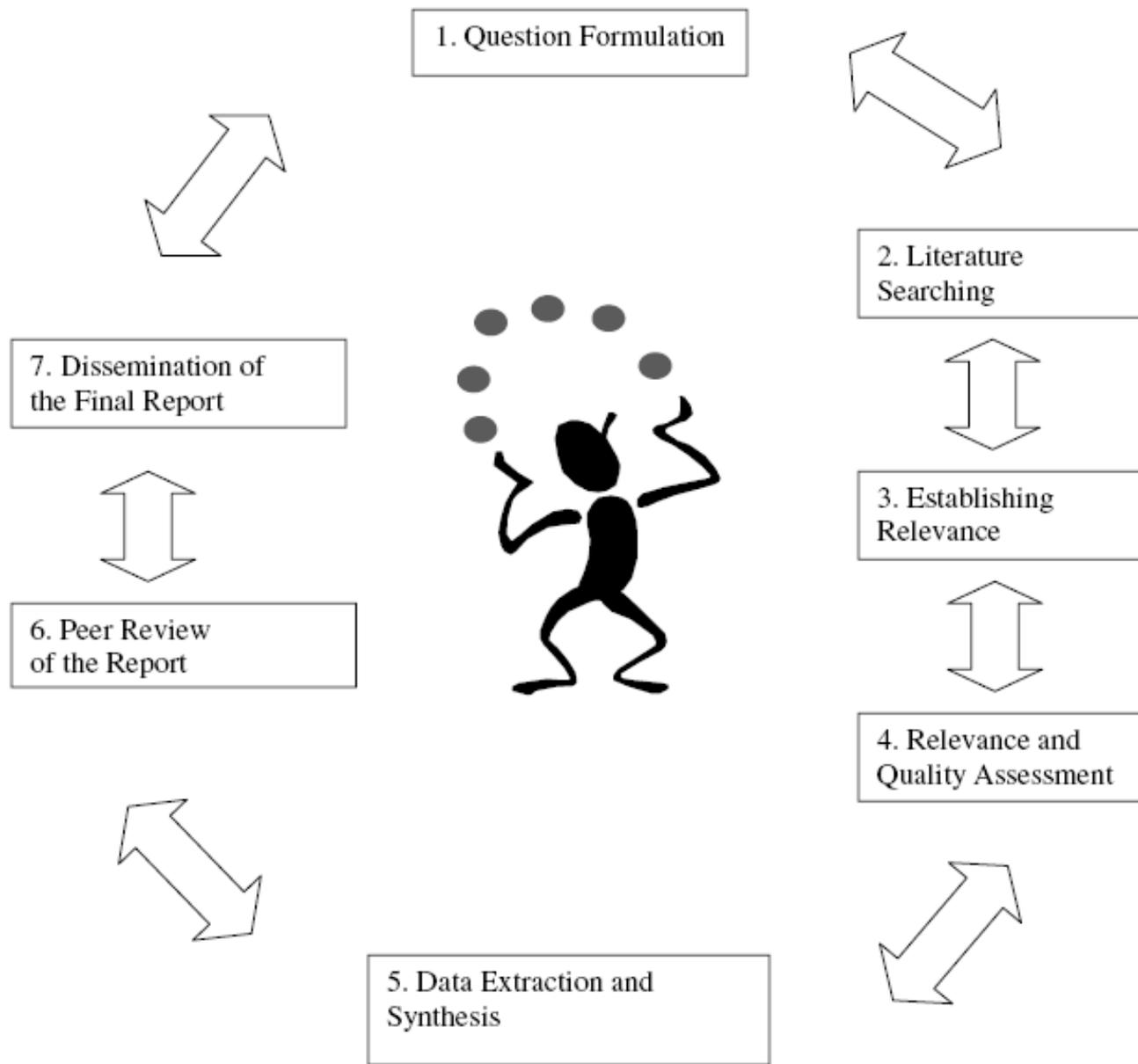
**Participants** Twenty-seven participants were selected by a steering committee, based on expertise in clinical practice, trials, statistics, epidemiology, social sciences, and biomedicine.

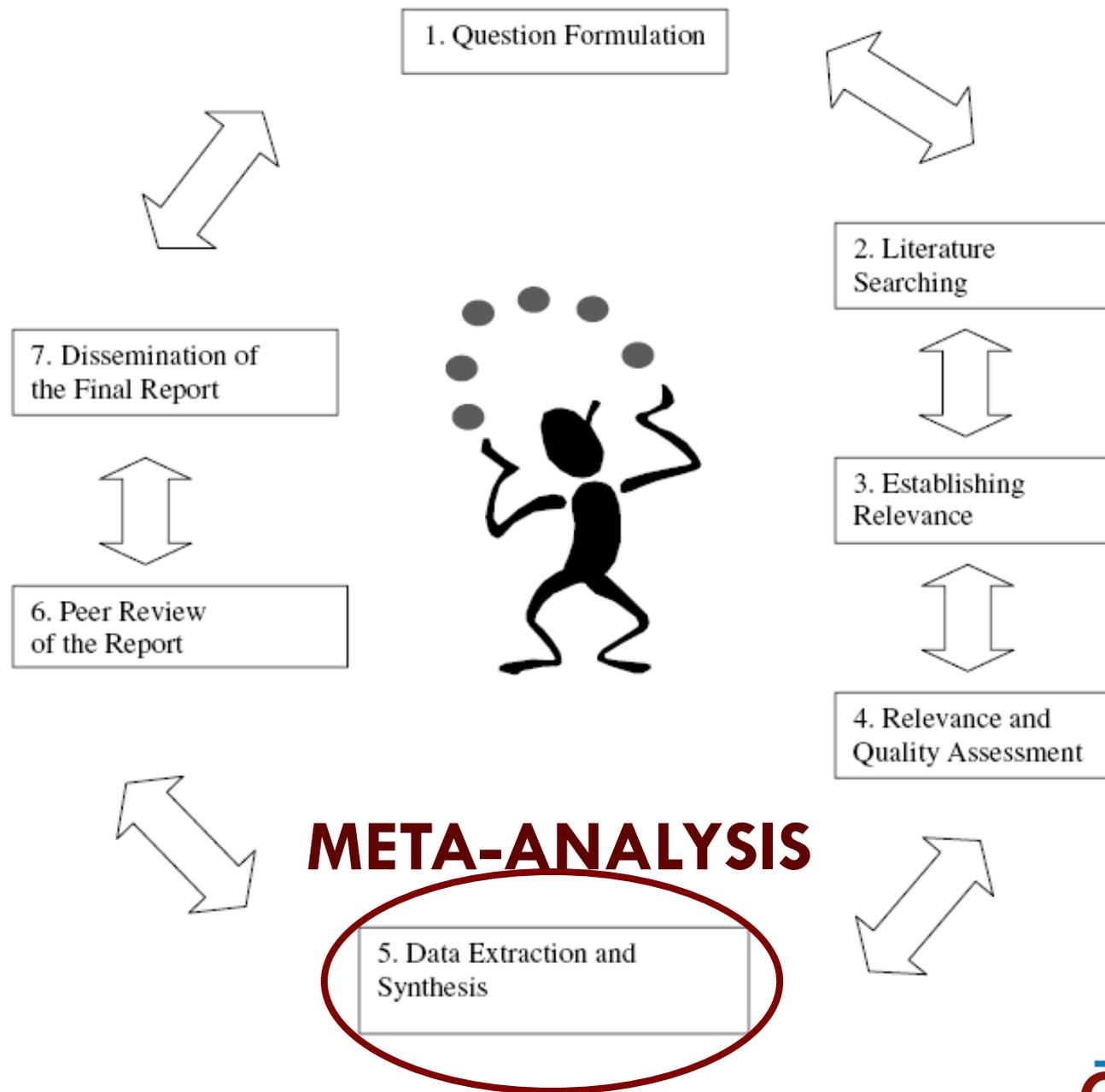


# PRISMA 2009 Checklist



| Section/topic                      | #  | Checklist item  | Reported on page # |
|------------------------------------|----|---|--------------------|
| <b>TITLE</b>                       |    |   |                    |
| Title                              | 1  | Identify the report as a systematic review, meta-analysis, or both.   | 1                  |
| <b>ABSTRACT</b>                    |    |   |                    |
| Structured summary                 | 2  | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 3                  |
| <b>INTRODUCTION</b>                |    |   |                    |
| Rationale                          | 3  | Describe the rationale for the review in the context of what is already known.  | 5,6                |
| Objectives                         | 4  | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).  | 6                  |
| <b>METHODS</b>                     |    |   |                    |
| Protocol and registration          | 5  | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.   | N/A                |
| Eligibility criteria               | 6  | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.  | 7                  |
| Information sources                | 7  | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.  | 6,7                |
| Search                             | 8  | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.   | 6                  |
| Study selection                    | 9  | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).   | 7,8                |
| Data collection process            | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.  | 7,8                |
| Data items                         | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.   | 8                  |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.  | 8,9                |
| Summary measures                   | 13 | State the principal summary measures (e.g., risk ratio, difference in means).   | 9                  |
| Synthesis of results               | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.   | 9                  |



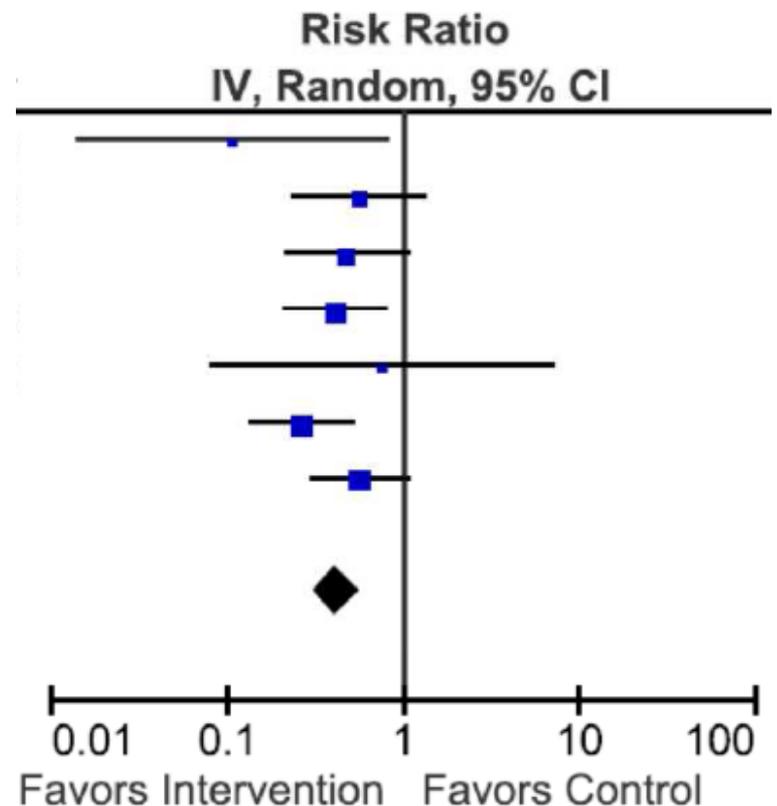


# Definitions

- Systematic Literature Review: research summary that addresses focused clinical question in a structured, reproducible manner
- Meta-Analysis: statistical pooling or aggregation of results from different studies providing a single estimate of effect

“There is a well-known expression that says ‘A picture is worth a thousand words.’ We would like to add that, in meta-analysis, a picture may be worth more than a million numbers.”

Bas American Journal of Epidemiology 2008



# Why Perform Systematic Literature Reviews and Meta-analyses?

- Determine evidence base for an intervention or association of interest
  - ▣ Assesses and resolves uncertainty when reports disagree
  - ▣ Increased precision of risk estimates
- Find where the literature is lacking
- Increases statistical power of primary end points and for subgroups

# Meta-Analyses to Inform our VA CREATE Grants

# VA MRSA CREATE Grant

- 4 VA HSRD IIRs to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) infections
- Prevention efforts include:
  - Nasal mupirocin ointment to prevent spread of MRSA from patient's nose to other sites (surgical sites, dialysis entry sites)
  - Promotion of healthcare worker hand hygiene to prevent spread of MRSA from healthcare worker hands to patients

# Meta-analysis to Find Optimal Bundled Intervention to Prevent Surgical Site Infections

## RESEARCH

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# Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease Gram positive surgical site infections after cardiac or orthopedic surgery: systematic review and meta-analysis

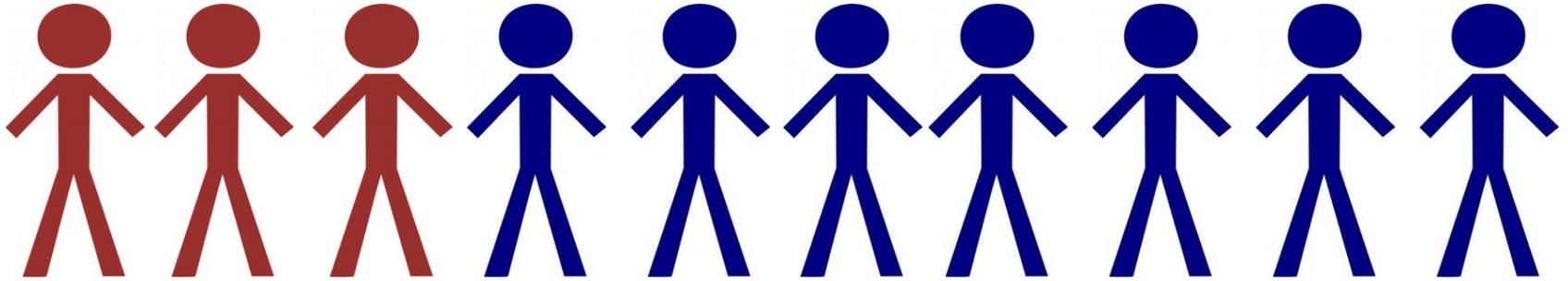
 OPEN ACCESS

Marin Schweizer assistant professor<sup>1,2,3</sup>, Eli Perencevich professor<sup>1,2,3,4</sup>, Jennifer McDanel student research assistant<sup>2</sup>, Jennifer Carson research assistant<sup>1</sup>, Michelle Formanek student research assistant<sup>2,3</sup>, Joanne Hafner associate project director<sup>5</sup>, Barbara Braun project director<sup>5</sup>, Loreen Herwaldt professor<sup>1,2,4</sup>

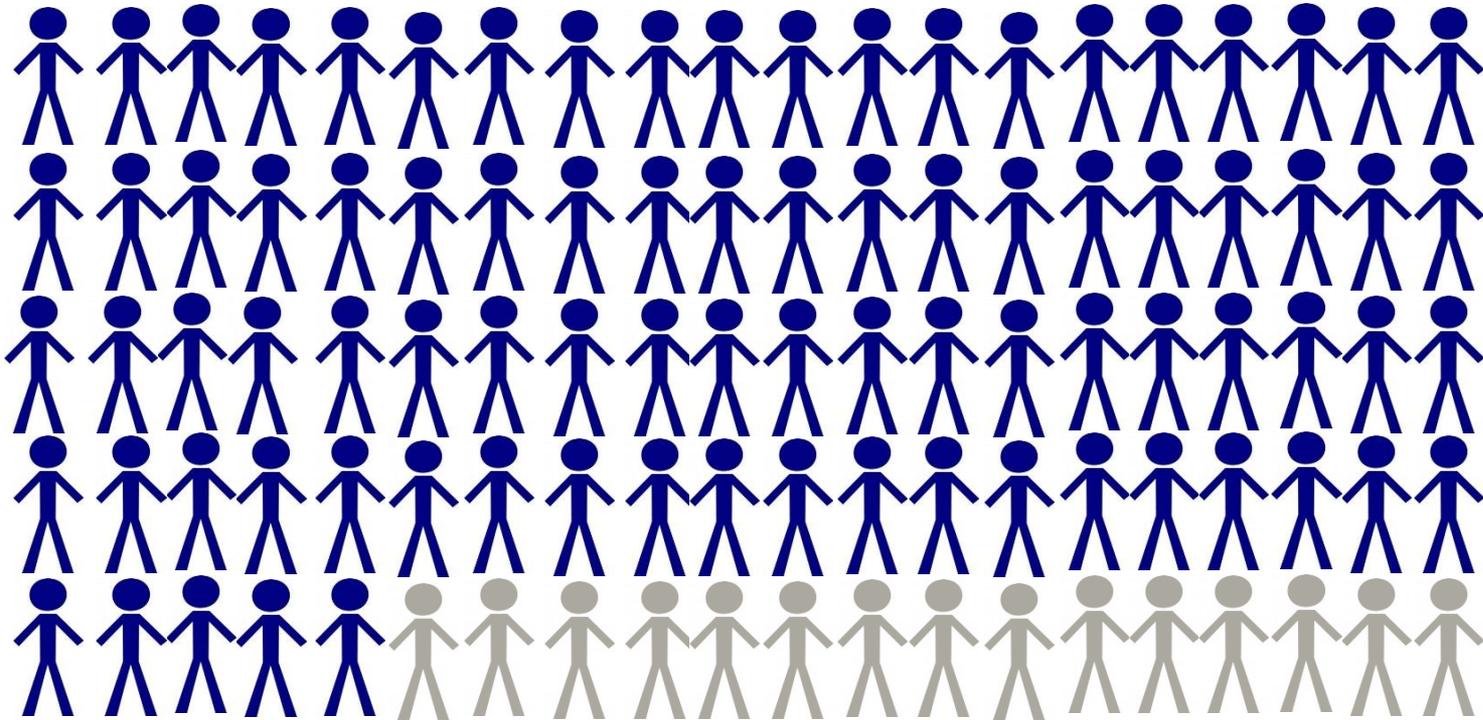
# Background

- Surgical site infections (SSI) associated with longer hospital length of stay and higher readmission rates
- *S. aureus* (a gram-positive bacteria) most common cause of SSI among cardiac and orthopedic surgical patients
- 2 categories of *S. aureus*:
  - ▣ Methicillin-resistant *S. aureus* (MRSA)
  - ▣ Methicillin-susceptible *S. aureus* (MSSA)

- 3 in 10 people carry *S. aureus* in their noses



- 85% of surgical site infections involving *S. aureus* come from the patient's own bacteria



# Objective

To analyze the literature to determine the best evidence-based intervention to decrease *S. aureus* (and other gram-positive) SSIs after cardiac surgery, hip arthroplasty or knee arthroplasty

Focused on: decolonization and/or glycopeptide prophylaxis

# Potential Bundled Intervention



Nasal  
Decolonization

Methicillin-  
resistant *S.*  
*aureus* (MRSA)  
directed  
antibiotic  
prophylaxis



*Glycopeptides  
instead of beta-  
lactams*

Bundle Combining Both

# Systematic Literature Review

## 5 databases :

1. National Institutes of Health PubMed
2. National Institutes of Health ClinicalTrials.gov
3. The Cumulative Index to Nursing and Allied Health Literature (CINAHL)
4. The Cochrane Library
5. EMBASE

# Inclusion Criteria

- ❑ Published or presented January 1995-January 2012
- ❑ Adults ( $\geq 18$ )
- ❑ Cardiac procedure
- ❑ Orthopedic procedure
  - Knee
  - Hip
- ❑ Gram-positive organisms (*S. aureus*) outcome

Articles or abstracts on surgical procedures (n=1432)

Excluded (n=1358):

- Did not evaluate SSI as an outcome (n=694)
- Did not evaluate Gram positive SSIs (n=110)
- Did not include an intervention (n=132)
- Evaluated other procedure types (n=91)
- Studied pediatric cohorts (n=79)
- Were reviews or commentaries (n=74)
- Evaluated other surgical interventions (n=68)
- Studied risk factors (n=42)
- Studied treatment for current SSI (n=19)
- Did not include a comparison group (n=18)
- Studied animals or were done in a laboratory (n=17)
- Written in a language other than English (n=10)
- Studied a previous cohort (n=3)
- Did mathematical modeling (n=1)

Articles identified for full review (n=74)

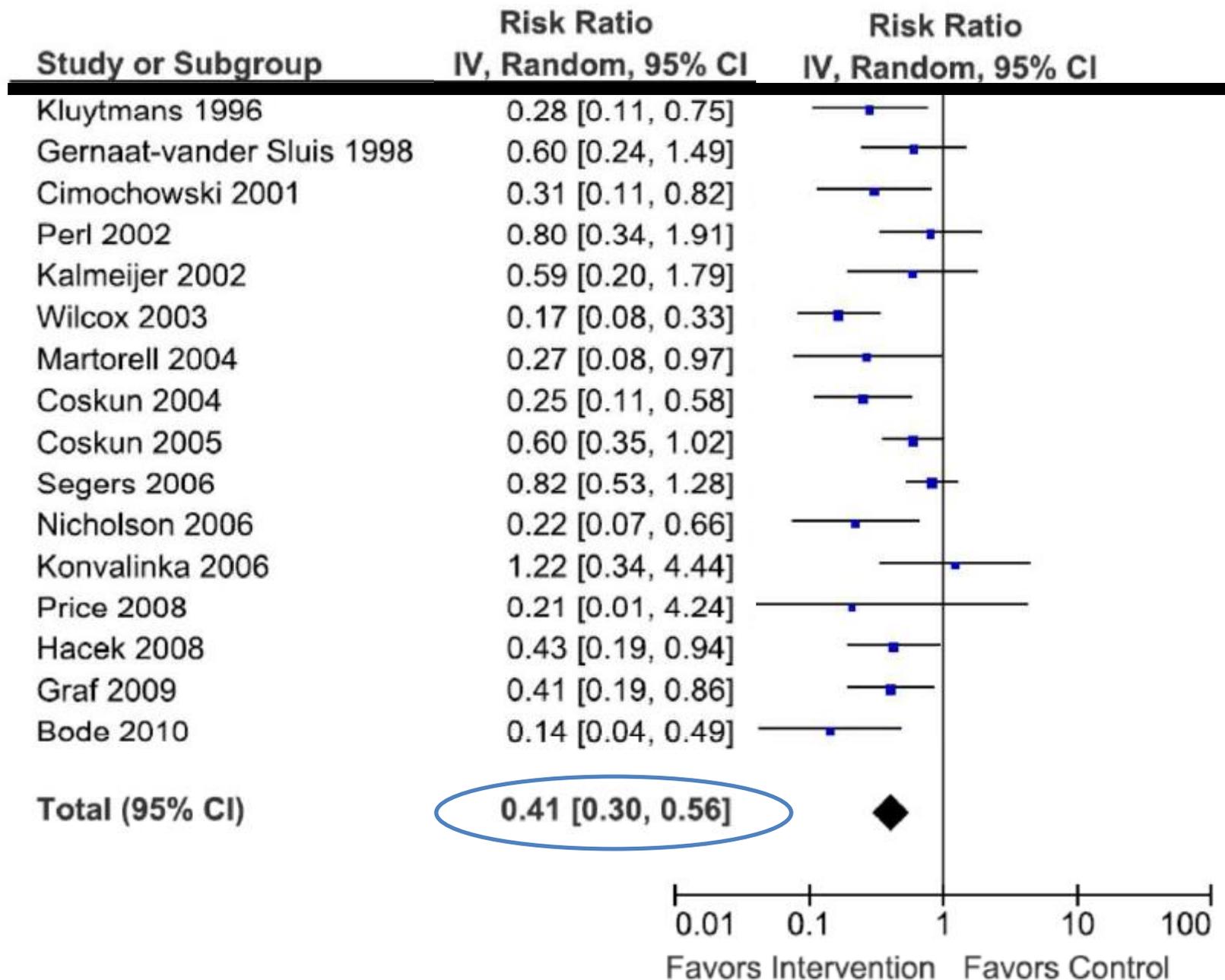
Excluded (n=35):

- Compared two  $\beta$  lactam antimicrobial agents (n=8)
- Assessed antimicrobial timing (n=6)
- Did not evaluate Gram positive SSIs (n=5)
- Evaluated other surgical interventions (n=5)
- Provided insufficient data (n=4)
- Did not include a comparison group (n=3)
- Studied risk factors (n=2)
- Did not include an intervention (n=1)
- Did mathematical modeling (n=1)

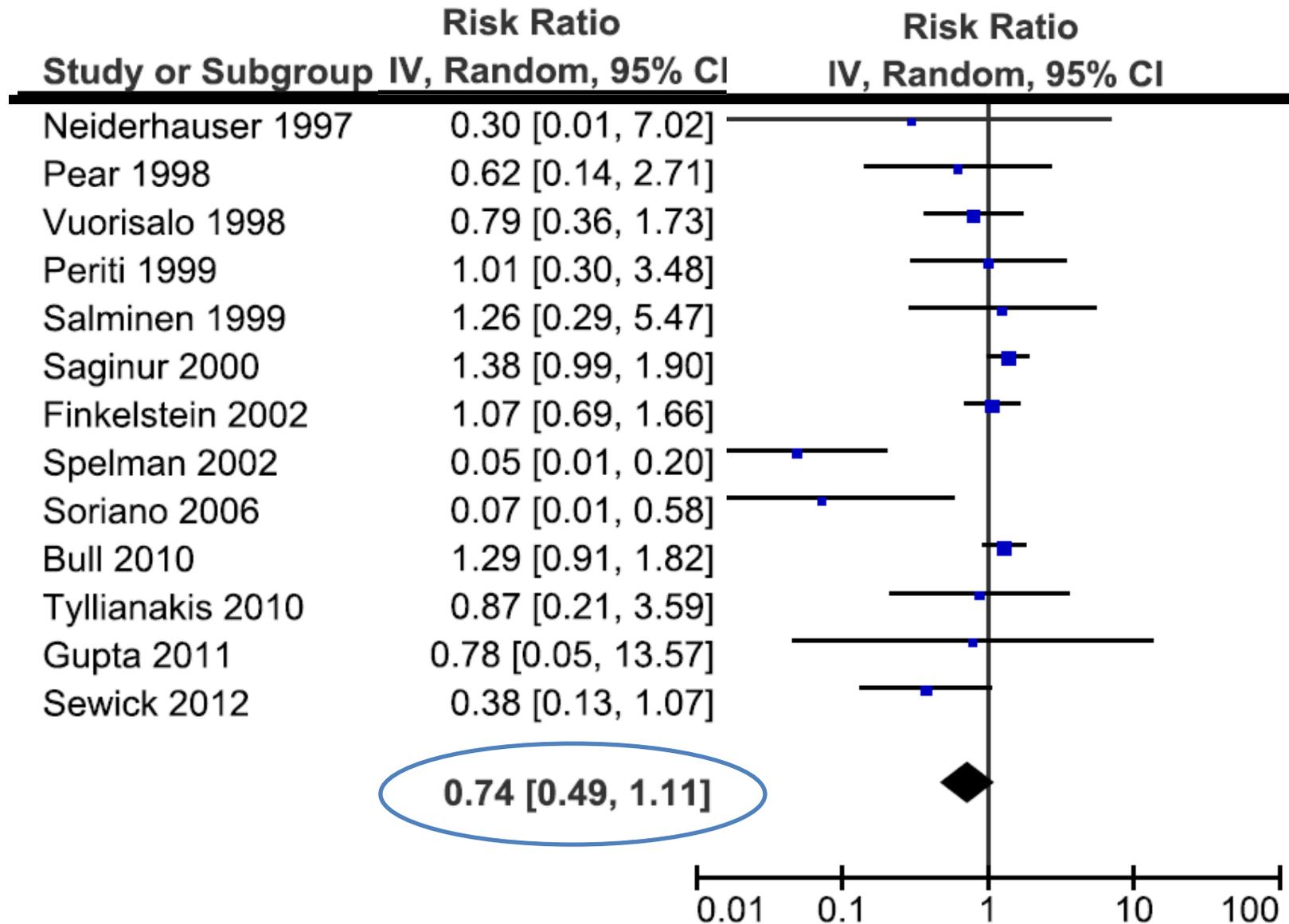
Articles included in meta-analyses (n=39):

- Studied nasal decolonization (n=17)
- Studied glycopeptide prophylaxis (n=15)
- Studied decolonization and glycopeptide prophylaxis in a bundle (n=7)

# Nasal Decolonization



# Glycopeptides relative to Beta-lactams

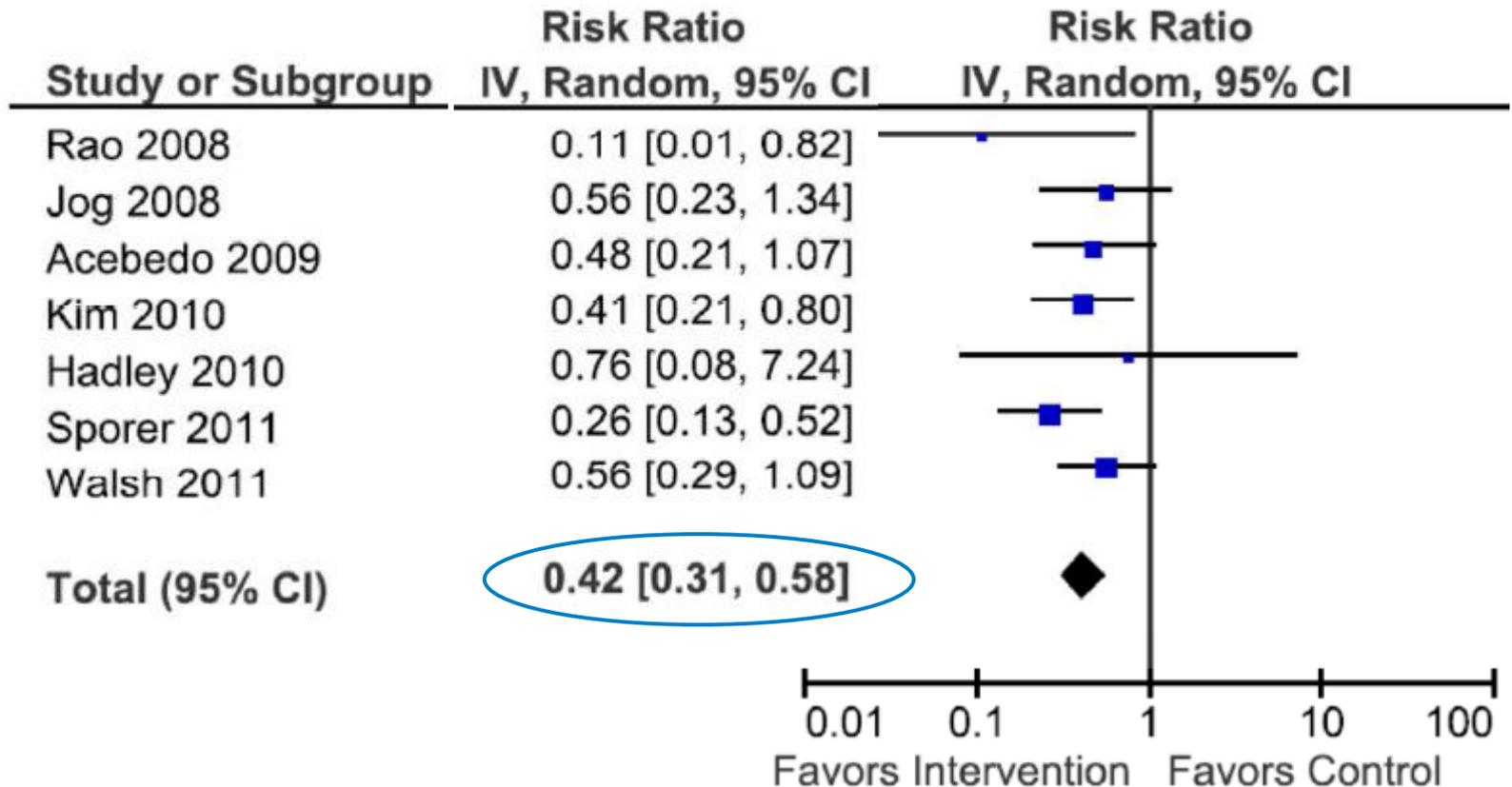


# Stratified Analysis: Glycopeptide surgical prophylaxis to prevent *S. aureus* Surgical Site Infection

|                      | Pooled relative risk (95% CI) |
|----------------------|-------------------------------|
| <i>S aureus</i> SSIs | 0.53 (0.24 to 1.16)†          |
| MRSA SSIs            | 0.40 (0.20 to 0.80)           |
| MSSA SSIs            | 1.47 (0.91 to 2.38)           |

†Studies are heterogeneous ( $P < 0.1$ ) and results should be interpreted with caution.

# Decolonization + Glycopeptide for MRSA Carriers



# Bundled Intervention



Nasal  
Decolonization

Methicillin-  
resistant *S.*  
*aureus* (MRSA)  
directed  
antibiotic  
prophylaxis



*Glycopeptides*  
*instead of beta-*  
*lactams*

Bundle Combining Both

## Original Investigation

# Association of a Bundled Intervention With Surgical Site Infections Among Patients Undergoing Cardiac, Hip, or Knee Surgery

Marin L. Schweizer, PhD; Hsiu-Yin Chiang, MS, PhD; Edward Septimus, MD; Julia Moody, MS; Barbara Braun, PhD; Joanne Hafner, RN, MS; Melissa A. Ward, MS; Jason Hickok, MBA, RN; Eli N. Perencevich, MD, MS; Daniel J. Diekema, MD; Cheryl L. Richards, MJ, LPN, LMT; Joseph E. Cavanaugh, PhD; Jonathan B. Perlin, MD, PhD; Loreen A. Herwaldt, MD

**IMPORTANCE** Previous studies suggested that a bundled intervention was associated with lower rates of *Staphylococcus aureus* surgical site infections (SSIs) among patients having cardiac or orthopedic operations.

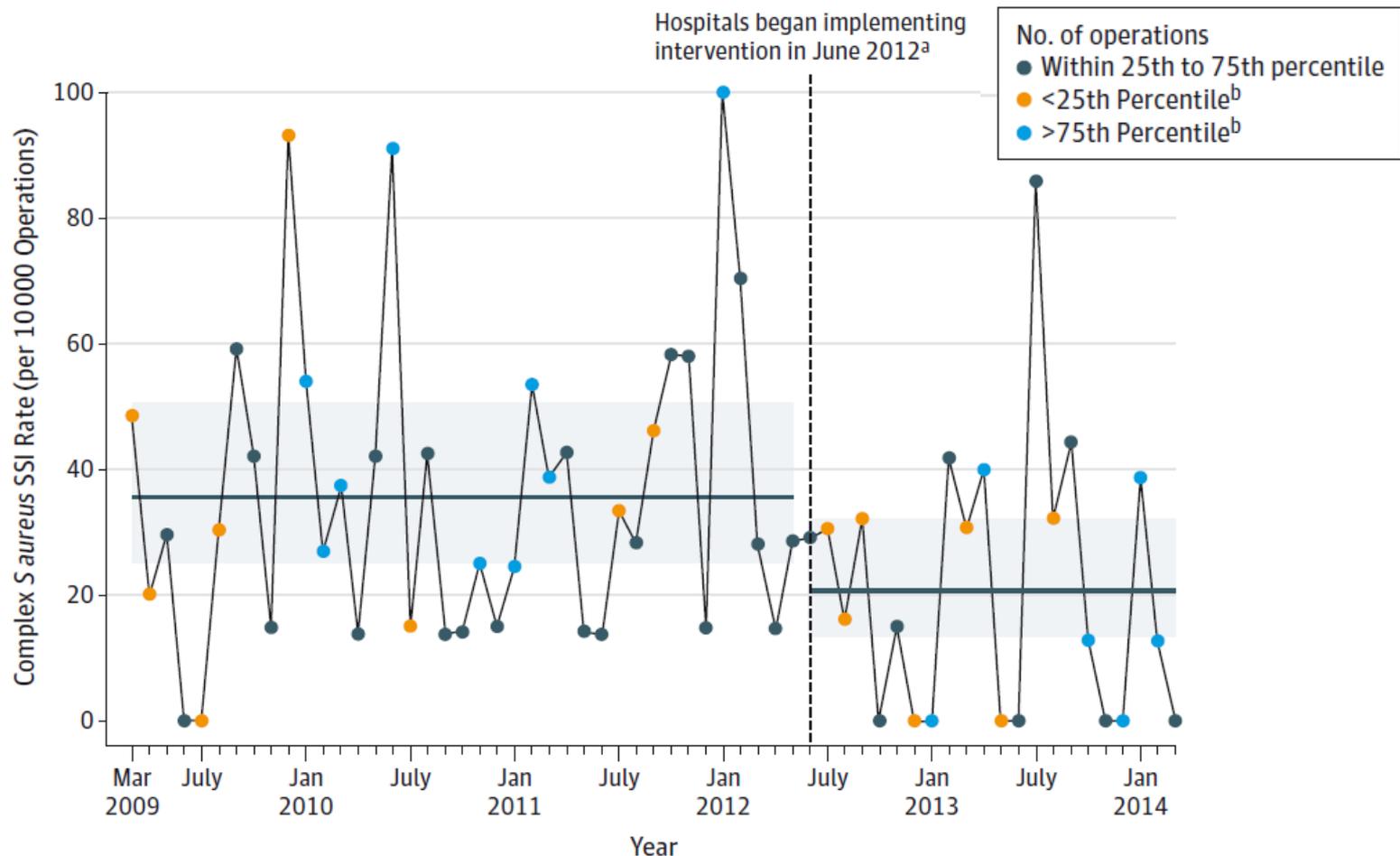
**OBJECTIVE** To evaluate whether the implementation of an evidence-based bundle is associated with a lower risk of *S aureus* SSIs in patients undergoing cardiac operations or hip or knee arthroplasties.

**DESIGN, SETTING, AND PARTICIPANTS** Twenty hospitals in 9 US states participated in this pragmatic study; rates of SSIs were collected for a median of 39 months (range, 39-43) during the preintervention period (March 1, 2009, to intervention) and a median of 21 months (range, 14-22) during the intervention period (from intervention start through March 31,

 Editorial page 2131

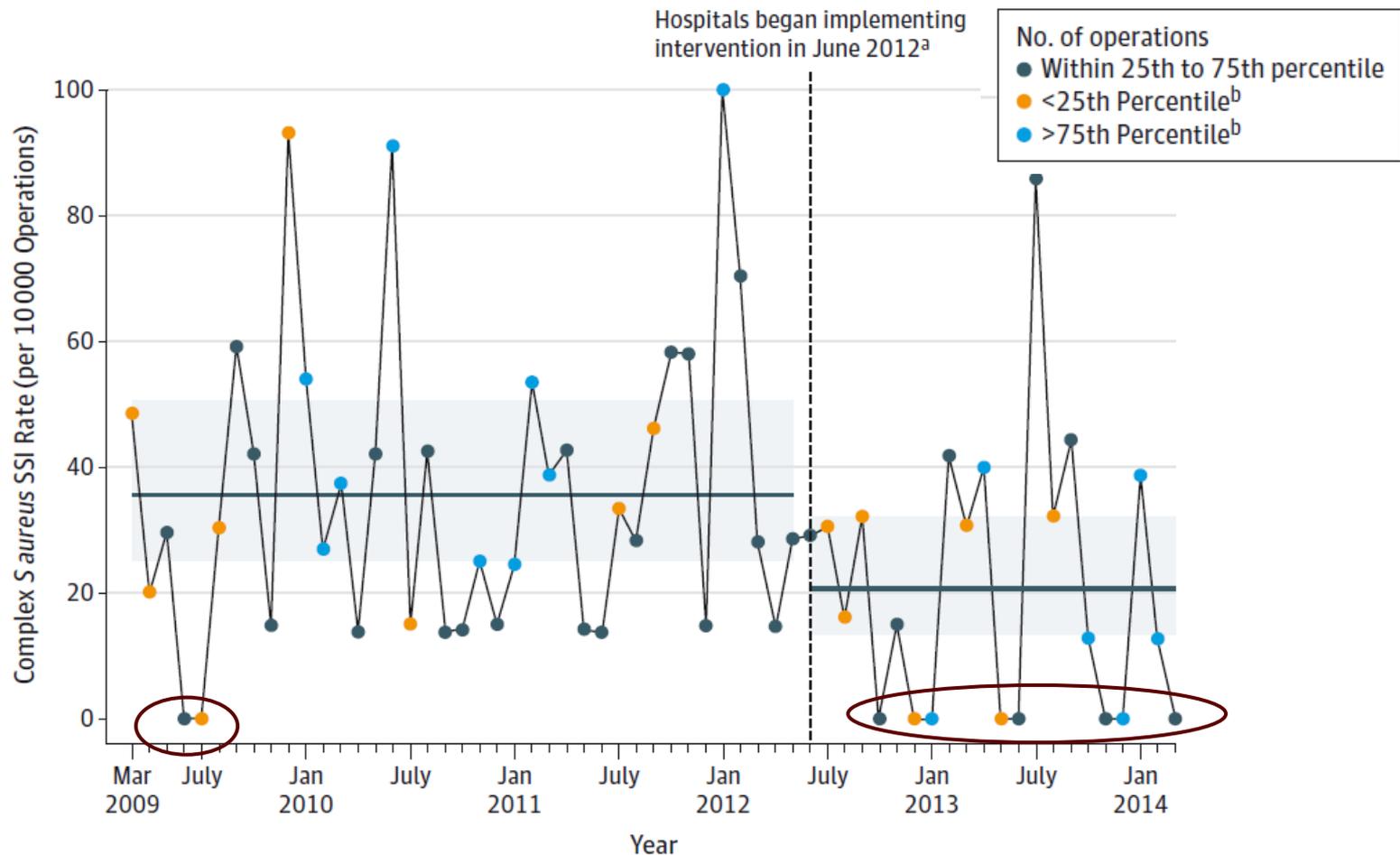
 Supplemental content at [jama.com](http://jama.com)

## Pooled Rate of Complex *Staphylococcus aureus* Surgical Site Infections (SSIs) by Admission Month



Hospital-level time-series analysis, Poisson regression model found that the monthly rates of complex *S. aureus* SSIs decreased significantly (rate ratio = 0.58; 95% CI, 0.37 to 0.92)

## Pooled Rate of Complex *Staphylococcus aureus* Surgical Site Infections (SSIs) by Admission Month



The number of months without any complex *S aureus* SSIs increased from 2 of 39 months (5.1%) to 8 of 22 months (36.4%;  $P < 0.01$ )

# VA CREATE SSI Aims

- **Specific Aims 1 and 2:** Implement and evaluate the effectiveness and cost effectiveness of a SSI Bundle to reduce rates of MRSA SSIs:
  - ▣ Aim 1. Among patients undergoing total joint arthroplasty
  - ▣ Aim 2. Among patients undergoing cardiac surgery
  
- **Specific Aim 3:** To identify and compare barriers and facilitators of implementing the SSI bundle across a diverse set of VA hospitals

# MRSA CREATE SSI Project



# Meta-analysis to Find Optimal Bundled Intervention to Improve Hand Hygiene Compliance Among Health Care Workers

# Searching for an Optimal Hand Hygiene Bundle: A Meta-analysis

**Marin L. Schweizer,<sup>1,2,3</sup> Heather Schacht Reisinger,<sup>1,2</sup> Michael Ohl,<sup>1,2</sup> Michelle B. Formanek,<sup>1,3</sup> Amy Blevins,<sup>4</sup> Melissa A. Ward,<sup>2</sup> and Eli N. Perencevich<sup>1,2</sup>**

<sup>1</sup>The Center for Comprehensive Access and Delivery Research and Evaluation, Iowa City Veterans Affairs Health Care System; <sup>2</sup>Department of Internal Medicine, Carver College of Medicine; <sup>3</sup>Department of Epidemiology, College of Public Health, and <sup>4</sup>Hardin Library for the Health Sciences, University of Iowa, Iowa City

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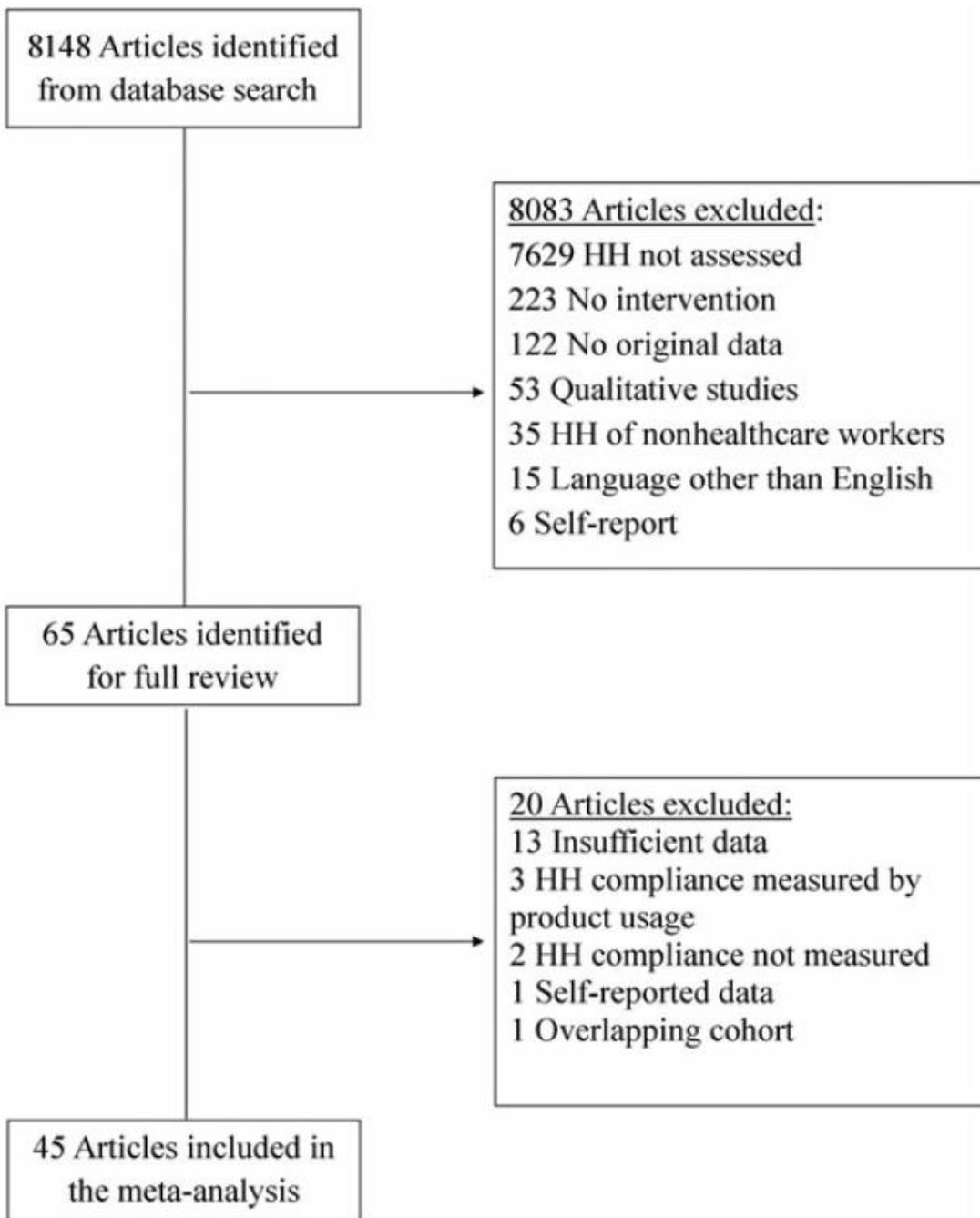
**Many studies have evaluated bundled interventions to improve hand hygiene compliance. However, there are few evidence-based recommendations on optimal interventions for implementation. We aimed to systematically review all studies on interventions to improve hand hygiene compliance to evaluate existing bundles and**

# Handwashing & Hand Hygiene

Hand hygiene (HH) is one of the most important ways to protect against transmission of infectious agents such as *S. aureus*

# VA Directive 2011-007

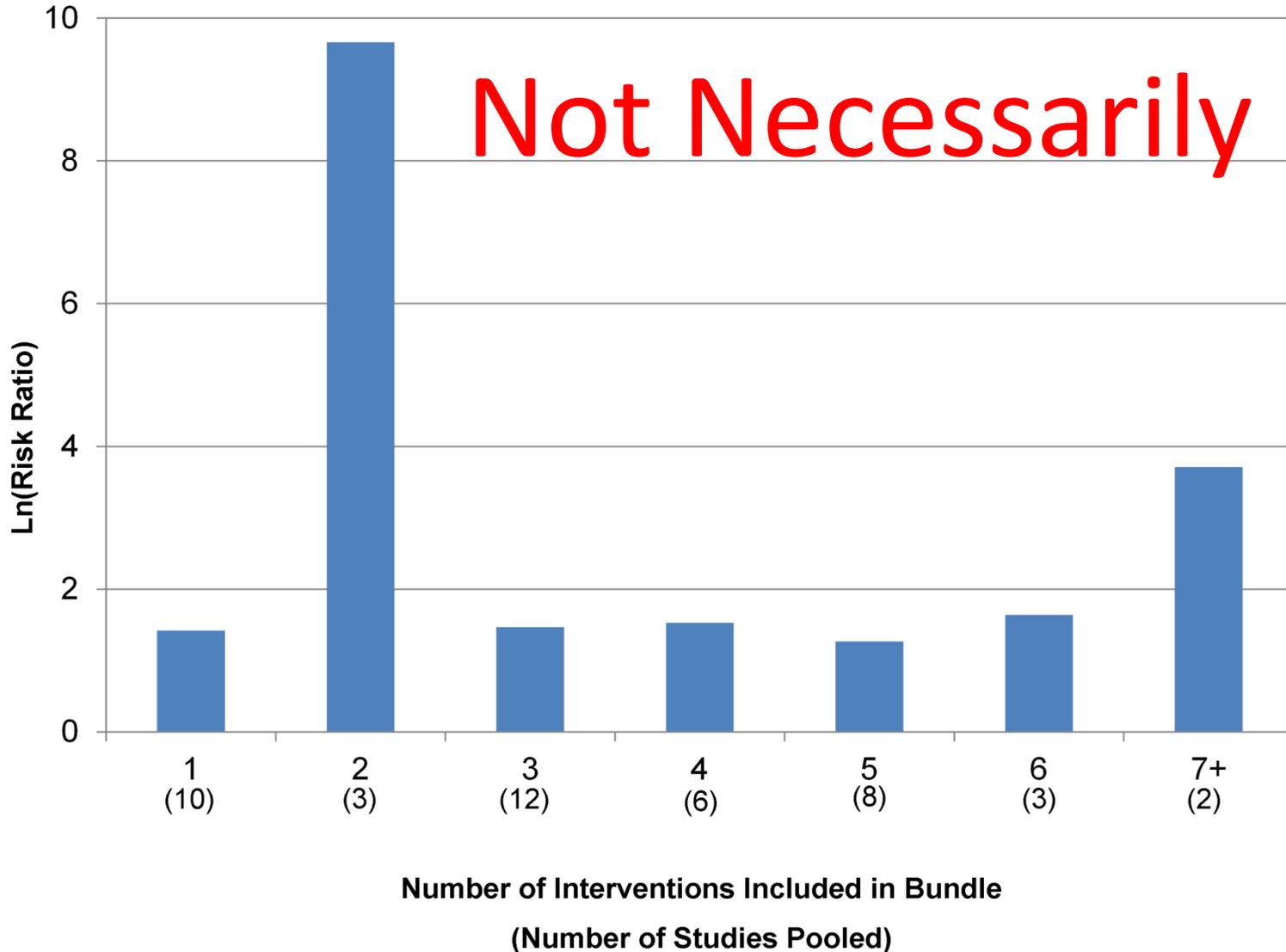
- Recommends:
  - ▣ Education
  - ▣ Access to dispensers/pocket size hand rub
  - ▣ Administrative support
  - ▣ Feedback
- Infection: Don't Pass it On Hand Hygiene Toolkit also includes signs
- Is there a bundle with a stronger evidence base in the literature?



# Study Location



# Does a bigger bundle lead to better results?



# Results

- 6 randomized controlled trials (RCTs), 39 quasi-experimental studies
  - ▣ *Discovery 1: Not enough RCTs in the field*
  
- 4 Studies evaluated bundle used by VA (called the WHO Bundle)
  - ▣ Associated with improved hand hygiene compliance (pooled RR=1.88; 95% CI: 1.69, 2.09)
  - ▣ *Discovery 2: VA bundle is effective*

# Results

- 5 other studies evaluated smaller bundle (education, signs, feedback)
  - Similar association between bundle and hand hygiene compliance (pooled OR=2.68; 95% CI: 1.24, 5.81)
  
- Other bundles varied too widely to pool but had interesting strategies
  - *Discovery 3: Much more research needs to be done on bundles to improve hand hygiene compliance*

# Summary

- VA is currently doing the most evidence based bundled intervention
- However, hand hygiene rates still not optimal
  - ▣ Prior VA study found hand hygiene compliance <70%  
others found only 38%
- Needed to think outside the box



# Hand Hygiene CREATE Project

- PI: Dr. Heather Reisinger
- Cluster Randomized Trial
- 3 Novel Interventions
  - Frequency of changing point-of-use reminder signs
  - Individual hand sanitizer dispensers
  - Healthcare worker hand cultures



# PHASE OF PROJECT #2 BUILDING AN OPTIMAL HH BUNDLE

## QUALITATIVE PROCESS EVALUATION (BASELINE)

### INTERVENTIONAL PHASES

#### PHASE 1

BASELINE

#### PHASE 2

FREQUENCY OF CHANGING HH SIGNS

#### PHASE 3

WASH-OUT

#### PHASE 4

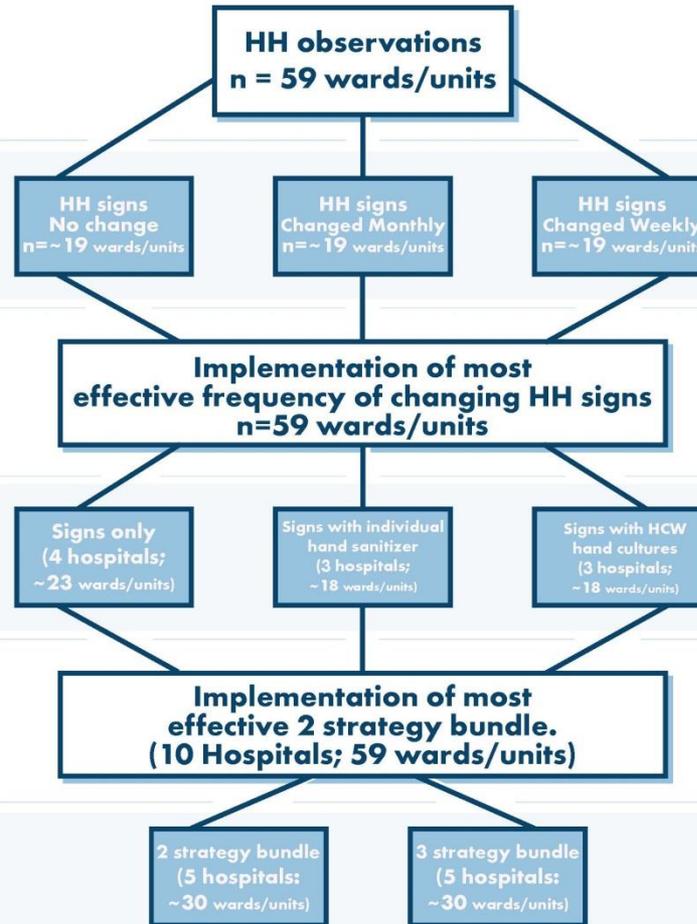
SIGNS AND 1 HH STRATEGY

#### PHASE 5

WASH-OUT

#### PHASE 6

2 STRATEGY VS 3 STRATEGY HH BUNDLE



## QUALITATIVE PROCESS EVALUATION (POST-INTERVENTION)

# Meta-analyses to Inform Parameters for Decision Analytical Model (my CDA)

# My CDA: Strategies to Prevent and Treat *S. aureus* Infections

- **Aim 1:** Complete meta-analyses of the effectiveness and costs of different organization-level *S. aureus* infection prevention strategies
- **Aim 2:** Analysis of large database
- **Aim 3:** Using data collected in Aims 1 and 2, create a decision model to compare the effectiveness, costs, and cost-effectiveness of interventions to prevent and treat *S. aureus* infections
  - Compare interventions head-to-head in model

HEALTHCARE EPIDEMIOLOGY: Robert A. Weinstein, Section Editor

# Clinical Effectiveness of Mupirocin for Preventing *Staphylococcus aureus* Infections in Nonsurgical Settings: A Meta-analysis

Rajeshwari Nair,<sup>1,2,3</sup> Eli N. Perencevich,<sup>1,2,3</sup> Amy E. Blevins,<sup>4</sup> Michihiko Goto,<sup>2,3</sup> Richard E. Nelson,<sup>5</sup> and Marin L. Schweizer<sup>1,2,3</sup>

<sup>1</sup>Department of Epidemiology, University of Iowa College of Public Health, <sup>2</sup>Center for Comprehensive Access and Delivery Research and Evaluation, Iowa City Veterans Affairs Health Care System, <sup>3</sup>Department of Internal Medicine, University of Iowa Carver College of Medicine, and <sup>4</sup>Hardin Library for Health Sciences, University of Iowa, Iowa City; and <sup>5</sup>IDEAS Center, Veterans Affairs Salt Lake City Health Care System, Utah

A systematic literature review and meta-analysis was performed to identify effectiveness of mupirocin decolonization in prevention of *Staphylococcus aureus* infections, among nonsurgical settings. Of the 15 662 unique studies identified up to August 2015, 13 randomized controlled trials, 22 quasi-experimental studies, and 1 retrospective cohort study met the inclusion criteria. Studies were excluded if mupirocin was not used for decolonization, there was no control group, or the study was conducted in an outbreak setting. The crude risk ratios were pooled (cpRR) using a random-effects model. We observed substantial heterogeneity among included studies ( $I^2 = 80\%$ ). Mupirocin was observed to reduce the risk for *S. aureus* infections by 59% (cpRR, 0.41; 95% confidence interval

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A systematic literature review and meta-analysis was performed to identify effectiveness of mupirocin decolonization in prevention of *Staphylococcus aureus* infections, among nonsurgical settings. Of the 15 662 unique studies identified up to August 2015, 13 randomized controlled trials, 10 quasi-experimental studies, and 1 retrospective cohort study met the inclusion criteria. Studies were excluded if mupirocin was not used for decolonization, there was no control group, or the study was conducted in an outbreak setting. The meta-analysis was pooled (cpRR) using a random-effects model. We observed substantial heterogeneity among included studies. Mupirocin decolonization was observed to reduce the risk for *S. aureus* infections by 59% (cpRR, 0.41; 95% confidence interval

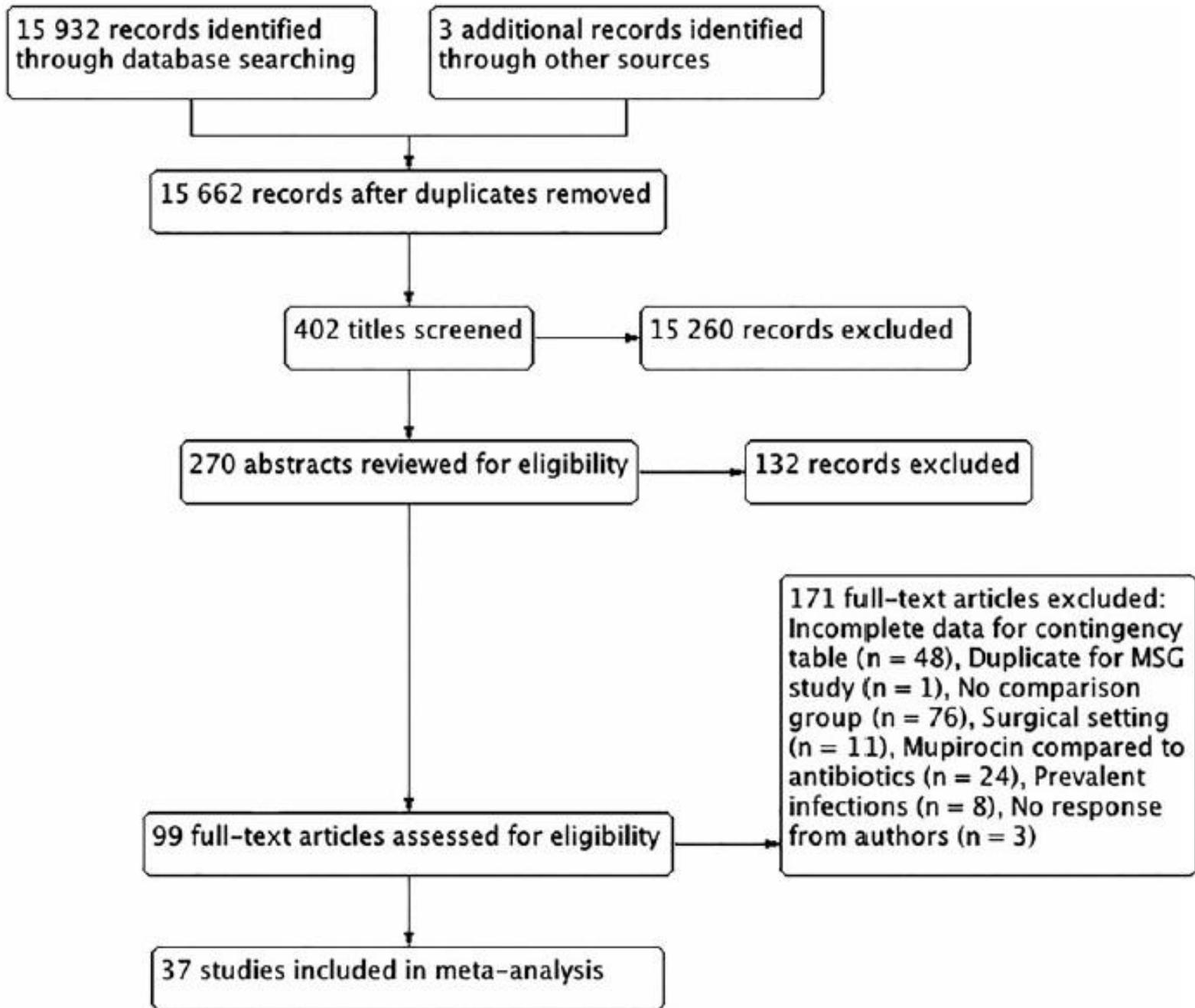


# Objectives

- Summarize evidence for mupirocin decolonization for prevention of *S. aureus* infections in non-surgical healthcare settings
- To identify the optimal setting and patient population to implement mupirocin decolonization for prevention of *S. aureus* infections using meta-analytic methods

# Inclusion Criteria

- All languages
  - ▣ French translator
  - ▣ Spanish and Japanese speaking colleagues
  - ▣ Google translate (Italian)
  
- No date filters
  - ▣ ~1960-2015
  
- Mupirocin use among non-surgical populations



# Non-surgical Decolonization Results

- 13 clinical trials, 22 quasi-experimental studies and 1 cohort study
- Studies so different from each other (heterogeneous) need to perform subgroup analysis

# Subgroup Analyses

| Group   | Subgroup                    | Intervention             | No. of Studies | pRR (95% CI)    | P Value         | I <sup>2</sup>  |
|---|-----------------------------|--------------------------|----------------|-----------------|-----------------|-----------------|
| Study design                                    | Clinical trials             | Mupirocin-only           | 5              | 0.54 (.46-.63)  | .56             | 0%              |
|   |                             | Mupirocin in combination | 6              | 0.47 (.28-.79)  | <.01            | 85%             |
|   | Nonequivalent control group | Mupirocin-only           | 12             | 0.46 (.38-.56)  | <.01            | 80%             |
|   |                             | Mupirocin in combination | 2              | 0.43 (.22-.84)  | .003            | 83%             |
|   | Pre-post                    | Mupirocin-only           | 5              | 0.44 (.29-.67)  | <.01            | 89%             |
|   |                             | Mupirocin in combination | 3              | 0.59 (.49-.71)  | .89             | 0%              |
| Healthcare setting <sup>a</sup>                 | Nondialysis                 | Mupirocin-only           | 6              | 0.64 (.37-1.10) | <.01            | 87%             |
|   |                             | Mupirocin in combination | 8              | 0.58 (.40-.77)  | .001            | 73%             |
|   | Dialysis                    | Mupirocin-only           | 15             | 0.42 (.35-.50)  | <.01            | 78%             |
|   |                             | Mupirocin in combination | 5              | 0.39 (.28-.55)  | .07             | 57%             |
| Type of decolonization                          | Targeted                    | Mupirocin-only           | 11             | 0.51 (.41-.64)  | <.01            | 81%             |
|   |                             | Mupirocin in combination | 13             | 0.57 (.46-.71)  | .001            | 65%             |
|   | Universal                   | Mupirocin-only           | 7              | 0.35 (.27-.44)  | .003            | 70%             |
|   |                             | Mupirocin in combination | 4              | 0.38 (.22-.67)  | .05             | 68%             |
| Type of <i>S. aureus</i> infection <sup>b</sup> | Bacteremia                  | Mupirocin-only           | 5              | 0.44 (.34-.58)  | .04             | 60%             |
|   |                             | Mupirocin in combination | 4              | 0.59 (.39-.87)  | .001            | 81%             |
|   | ESI                         | Mupirocin-only           | 10             | 0.43 (.34-.55)  | <.00001         | 84%             |
|   |                             | Mupirocin in combination | 2              | 0.27 (.18-.41)  | NA <sup>c</sup> | NA <sup>c</sup> |
|   | Other                       | Mupirocin-only           | 1              | 0.76 (.22-2.62) | NA <sup>d</sup> | NA <sup>d</sup> |
|   |                             | Mupirocin in combination | 2              | 0.47 (.23-.98)  | .10             | 62%             |

# Subgroup Analyses- Clinical Trials Saw Significant Preventive Effect of Decolonization

| Group   | Subgroup                    | Intervention             | No. of Studies | pRR (95% CI)    | P Value         | I <sup>2</sup>  |
|---|-----------------------------|--------------------------|----------------|-----------------|-----------------|-----------------|
| Study design                                    | Clinical trials             | Mupirocin-only           | 5              | 0.54 (.46-.63)  | .56             | 0%              |
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|   | Pre-post                    | Mupirocin-only           | 5              | 0.44 (.29-.67)  | <.01            | 89%             |
|   |                             | Mupirocin in combination | 3              | 0.59 (.49-.71)  | .89             | 0%              |
| Healthcare setting <sup>a</sup>                 | Nondialysis                 | Mupirocin-only           | 6              | 0.64 (.37-1.10) | <.01            | 87%             |
|   |                             | Mupirocin in combination | 8              | 0.58 (.40-.77)  | .001            | 73%             |
|   | Dialysis                    | Mupirocin-only           | 15             | 0.42 (.35-.50)  | <.01            | 78%             |
|   |                             | Mupirocin in combination | 5              | 0.39 (.28-.55)  | .07             | 57%             |
| Type of decolonization                          | Targeted                    | Mupirocin-only           | 11             | 0.51 (.41-.64)  | <.01            | 81%             |
|   |                             | Mupirocin in combination | 13             | 0.57 (.46-.71)  | .001            | 65%             |
|   | Universal                   | Mupirocin-only           | 7              | 0.35 (.27-.44)  | .003            | 70%             |
|   |                             | Mupirocin in combination | 4              | 0.38 (.22-.67)  | .05             | 68%             |
| Type of <i>S. aureus</i> infection <sup>b</sup> | Bacteremia                  | Mupirocin-only           | 5              | 0.44 (.34-.58)  | .04             | 60%             |
|   |                             | Mupirocin in combination | 4              | 0.59 (.39-.87)  | .001            | 81%             |
|   | ESI                         | Mupirocin-only           | 10             | 0.43 (.34-.55)  | <.00001         | 84%             |
|   |                             | Mupirocin in combination | 2              | 0.27 (.18-.41)  | NA <sup>c</sup> | NA <sup>c</sup> |
|   | Other                       | Mupirocin-only           | 1              | 0.76 (.22-2.62) | NA <sup>d</sup> | NA <sup>d</sup> |
|   |                             | Mupirocin in combination | 2              | 0.47 (.23-.98)  | .10             | 62%             |

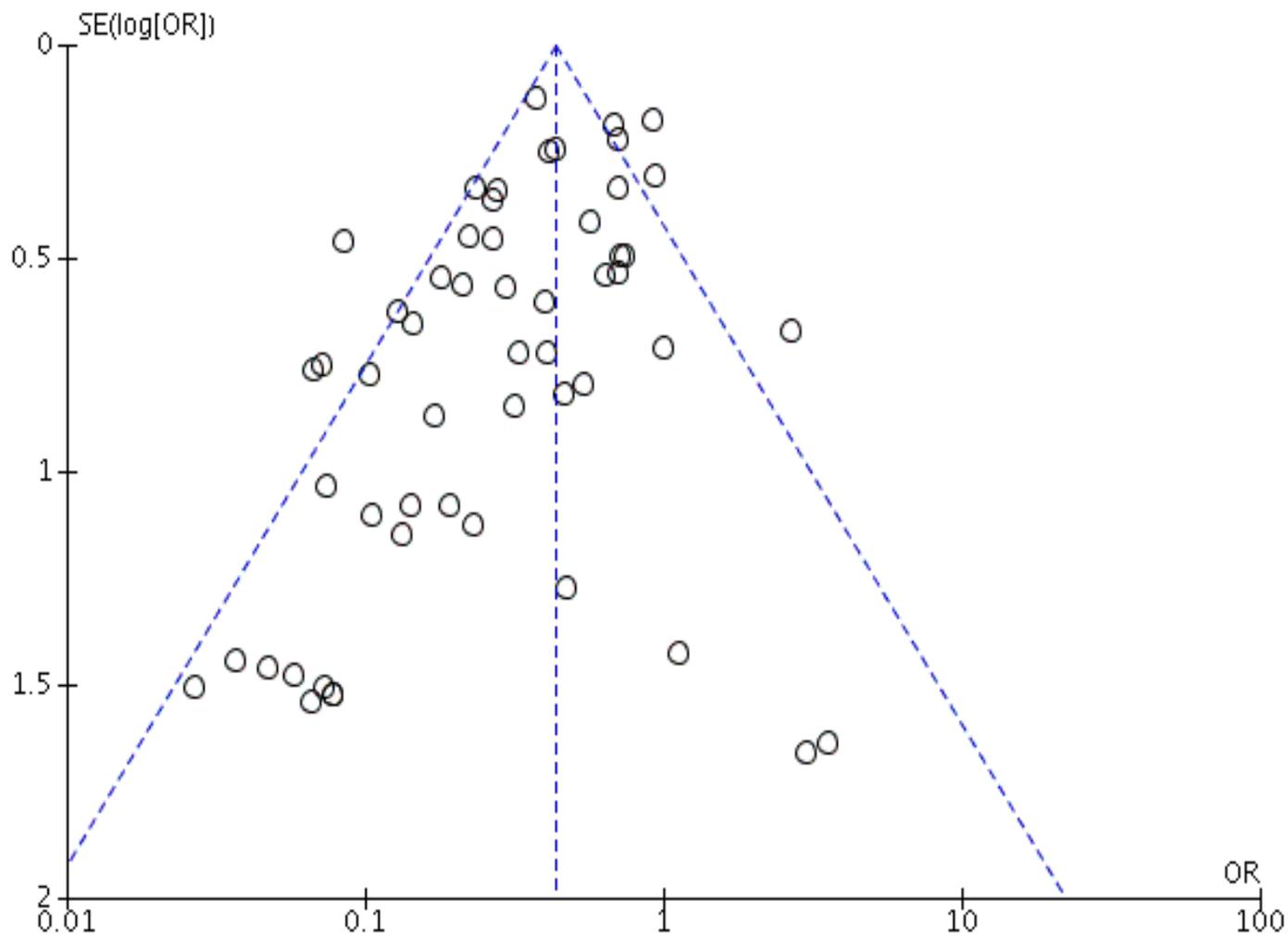
# Subgroup Analyses- protective effect among dialysis patients

| Group   | Subgroup                    | Intervention             | No. of Studies | pRR (95% CI)    | P Value         | I <sup>2</sup>  |
|---|-----------------------------|--------------------------|----------------|-----------------|-----------------|-----------------|
| Study design                                    | Clinical trials             | Mupirocin-only           | 5              | 0.54 (.46-.63)  | .56             | 0%              |
|   |                             | Mupirocin in combination | 6              | 0.47 (.28-.79)  | <.01            | 85%             |
|   | Nonequivalent control group | Mupirocin-only           | 12             | 0.46 (.38-.56)  | <.01            | 80%             |
|   |                             | Mupirocin in combination | 2              | 0.43 (.22-.84)  | .003            | 83%             |
|   | Pre-post                    | Mupirocin-only           | 5              | 0.44 (.29-.67)  | <.01            | 89%             |
|   |                             | Mupirocin in combination | 3              | 0.59 (.49-.71)  | .89             | 0%              |
| Healthcare setting <sup>a</sup>                 | Nondialysis                 | Mupirocin-only           | 6              | 0.64 (.37-1.10) | <.01            | 87%             |
|   |                             | Mupirocin in combination | 8              | 0.58 (.40-.77)  | .001            | 73%             |
|   | Dialysis                    | Mupirocin-only           | 15             | 0.42 (.35-.50)  | <.01            | 78%             |
|   |                             | Mupirocin in combination | 5              | 0.39 (.28-.55)  | .07             | 57%             |
| Type of decolonization                          | Targeted                    | Mupirocin-only           | 11             | 0.51 (.41-.64)  | <.01            | 81%             |
|   |                             | Mupirocin in combination | 13             | 0.57 (.46-.71)  | .001            | 65%             |
|   | Universal                   | Mupirocin-only           | 7              | 0.35 (.27-.44)  | .003            | 70%             |
|   |                             | Mupirocin in combination | 4              | 0.38 (.22-.67)  | .05             | 68%             |
| Type of <i>S. aureus</i> infection <sup>b</sup> | Bacteremia                  | Mupirocin-only           | 5              | 0.44 (.34-.58)  | .04             | 60%             |
|   |                             | Mupirocin in combination | 4              | 0.59 (.39-.87)  | .001            | 81%             |
|   | ESI                         | Mupirocin-only           | 10             | 0.43 (.34-.55)  | <.00001         | 84%             |
|   |                             | Mupirocin in combination | 2              | 0.27 (.18-.41)  | NA <sup>c</sup> | NA <sup>c</sup> |
|   | Other                       | Mupirocin-only           | 1              | 0.76 (.22-2.62) | NA <sup>d</sup> | NA <sup>d</sup> |
|   |                             | Mupirocin in combination | 2              | 0.47 (.23-.98)  | .10             | 62%             |

# Subgroup Analyses- most subsets were heterogeneous (too different to pool?)

| Group   | Subgroup                    | Intervention             | No. of Studies | pRR (95% CI)    | P Value         | I <sup>2</sup>  |
|---|-----------------------------|--------------------------|----------------|-----------------|-----------------|-----------------|
| Study design                                    | Clinical trials             | Mupirocin-only           | 5              | 0.54 (.46-.63)  | .56             | 0%              |
|   |                             | Mupirocin in combination | 6              | 0.47 (.28-.79)  | <.01            | 85%             |
|   | Nonequivalent control group | Mupirocin-only           | 12             | 0.46 (.38-.56)  | <.01            | 80%             |
|   |                             | Mupirocin in combination | 2              | 0.43 (.22-.84)  | .003            | 83%             |
|   | Pre-post                    | Mupirocin-only           | 5              | 0.44 (.29-.67)  | <.01            | 89%             |
|   |                             | Mupirocin in combination | 3              | 0.59 (.49-.71)  | .89             | 0%              |
| Healthcare setting <sup>a</sup>                 | Nondialysis                 | Mupirocin-only           | 6              | 0.64 (.37-1.10) | <.01            | 87%             |
|   |                             | Mupirocin in combination | 8              | 0.58 (.40-.77)  | .001            | 73%             |
|   | Dialysis                    | Mupirocin-only           | 15             | 0.42 (.35-.50)  | <.01            | 78%             |
|   |                             | Mupirocin in combination | 5              | 0.39 (.28-.55)  | .07             | 57%             |
| Type of decolonization                          | Targeted                    | Mupirocin-only           | 11             | 0.51 (.41-.64)  | <.01            | 81%             |
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|   |                             | Mupirocin in combination | 4              | 0.38 (.22-.67)  | .05             | 68%             |
| Type of <i>S. aureus</i> infection <sup>b</sup> | Bacteremia                  | Mupirocin-only           | 5              | 0.44 (.34-.58)  | .04             | 60%             |
|   |                             | Mupirocin in combination | 4              | 0.59 (.39-.87)  | .001            | 81%             |
|   | ESI                         | Mupirocin-only           | 10             | 0.43 (.34-.55)  | <.00001         | 84%             |
|   |                             | Mupirocin in combination | 2              | 0.27 (.18-.41)  | NA <sup>c</sup> | NA <sup>c</sup> |
|   | Other                       | Mupirocin-only           | 1              | 0.76 (.22-2.62) | NA <sup>d</sup> | NA <sup>d</sup> |
|   |                             | Mupirocin in combination | 2              | 0.47 (.23-.98)  | .10             | 62%             |

# No Evidence of Publication Bias



# Summary

- Mupirocin decolonization protective against *S. aureus* infections
- Can be recommended for dialysis patients
- More high quality studies should be performed

# Universal Glove Use

- Intervention, Universal Glove Use, defined as use of gloves for every patient interaction regardless of infection or colonization status
  - ▣ Treat all patients as if infectious
- Intervention can also include universal gown use



# Universal Gloving Compared with Standard Practice

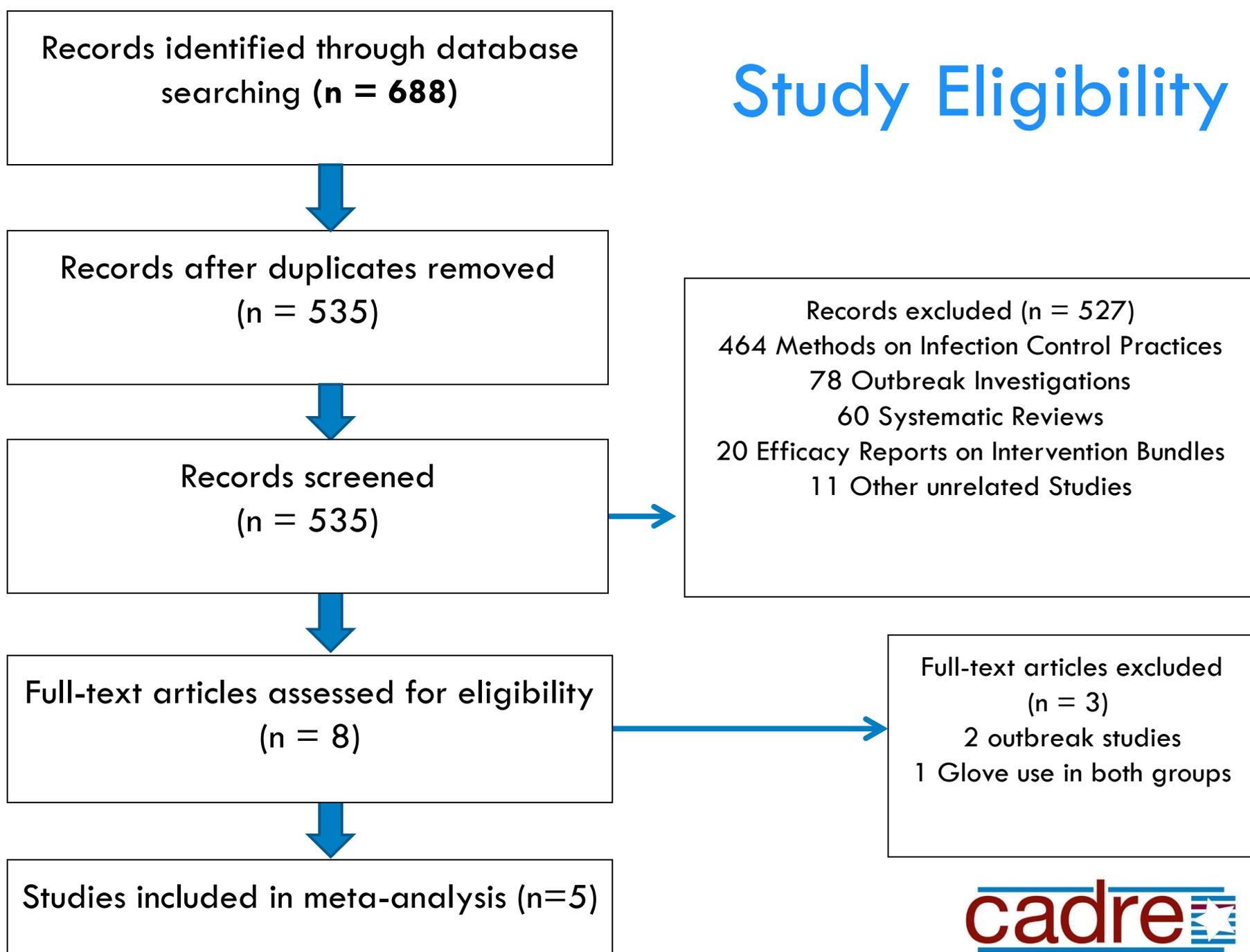
- Universal gloving (or universal gloving and gowning) can prevent the spread of multiple healthcare-associated infections including multidrug resistant organisms (MDRO) such as MRSA
- May be less expensive/time consuming to implement than current practice

# Systematic Literature Review

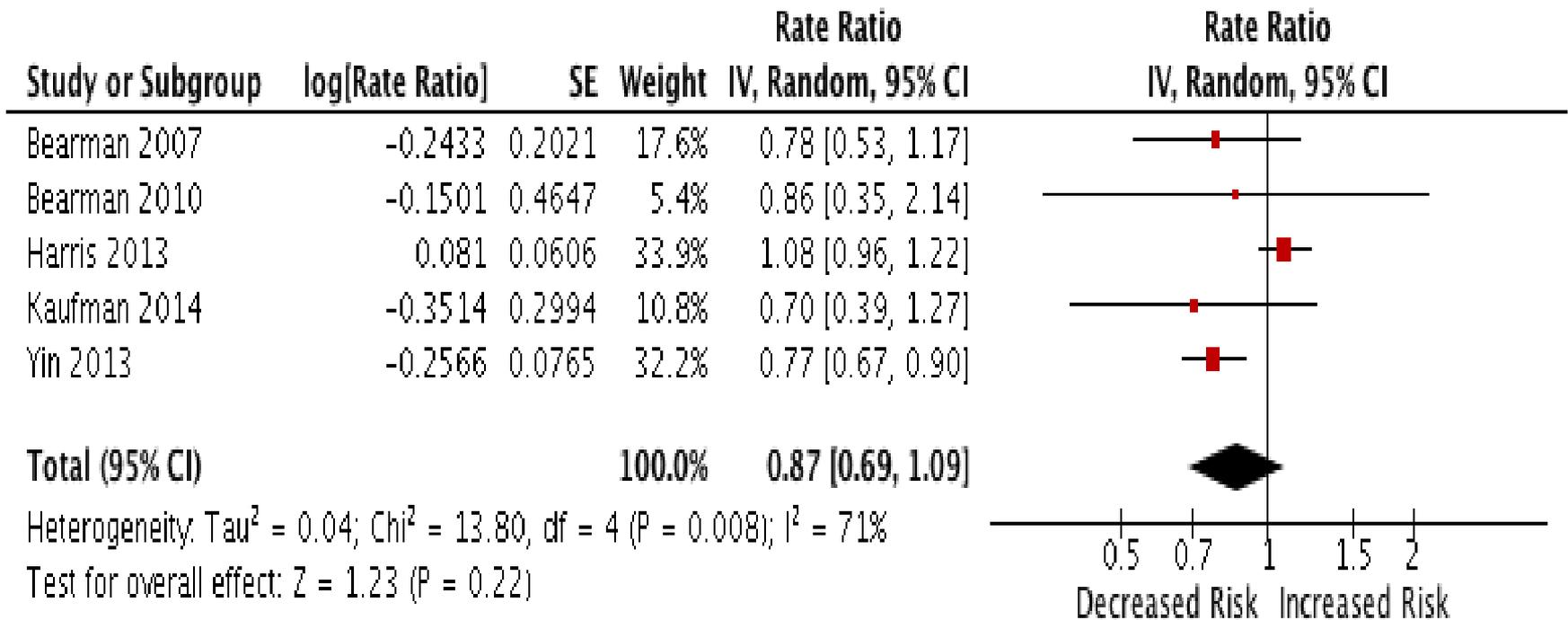


- No language filters
  
- Systematic Literature Review
  - ▣ MEDLINE/PubMed
  - ▣ Cochrane Library
  - ▣ CINAHL (the Cumulative Index of Nursing and Allied Health Literature)
  - ▣ EMBASE
  - ▣ PsychInfo
  - ▣ ClinicalTrials.gov
  
- Searched from database inception to July 2015

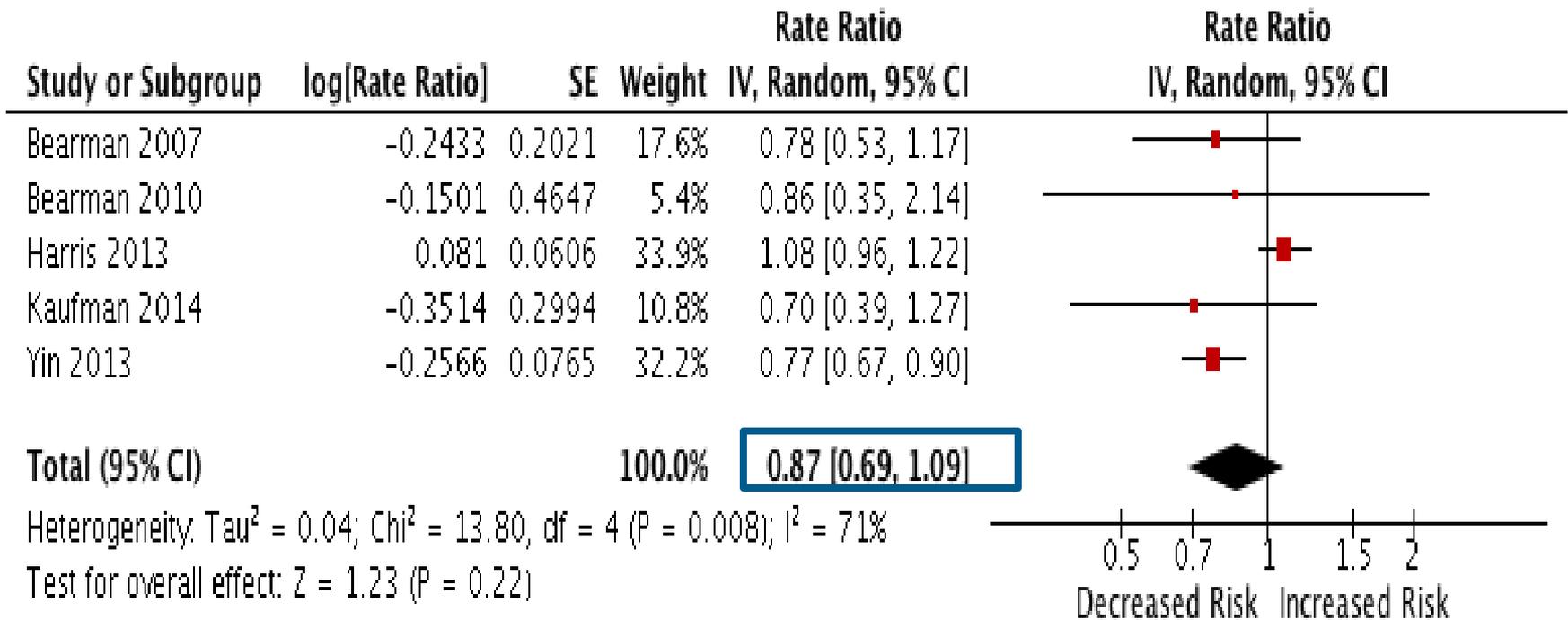
# Study Eligibility



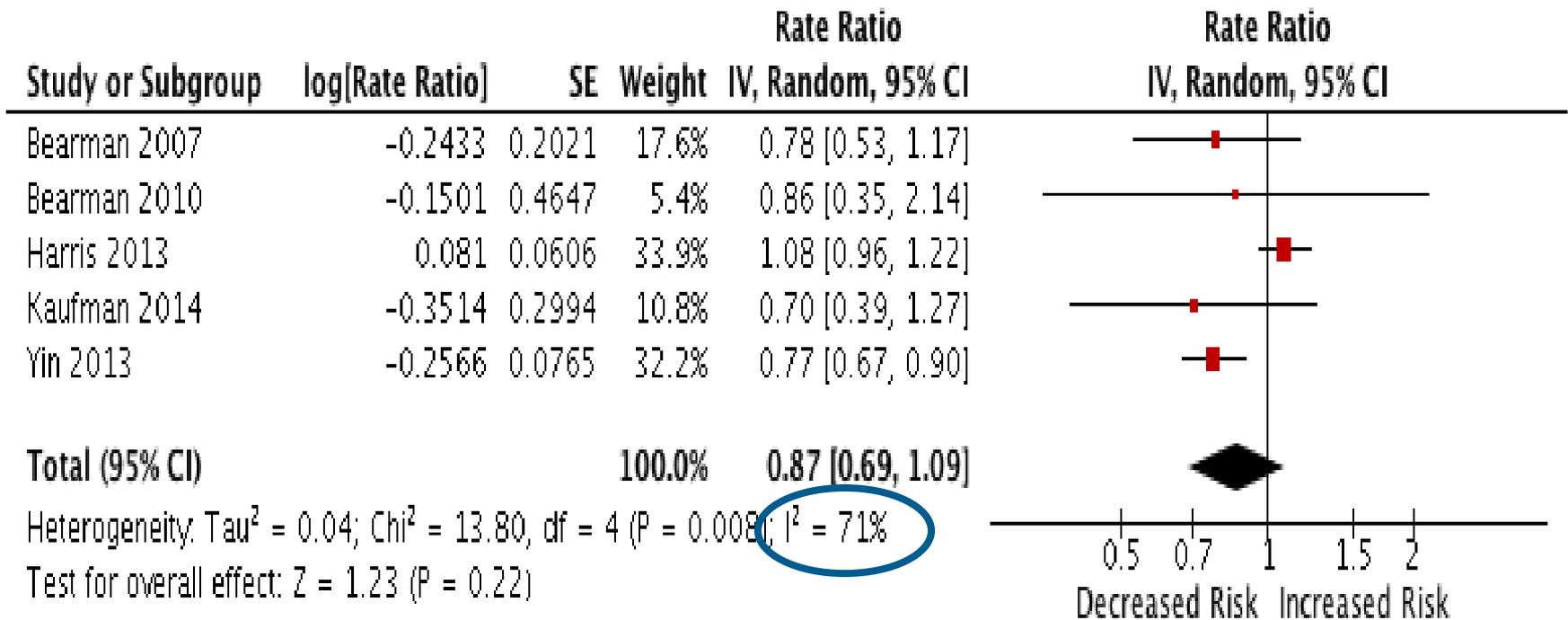
# Pooled Association between Universal Gloving (+/- Gowning) and Healthcare Associated Infections



# Pooled Association between Universal Gloving (+/- Gowning) and Healthcare Associated Infections



# Pooled Association between Universal Gloving (+/- Gowning) and Healthcare Associated Infections



# Stratified Analysis by Organism

| Outcome   | Number of Studies | IRR (95% CI)         | Heterogeneity Estimate ( $I^2$ ) |
|---|-------------------|----------------------|----------------------------------|
| <b>MRSA Acquisition</b>                             | 4                 | 0.95<br>(0.79, 1.14) | 12%                              |
| <b>Vancomycin-resistant Enterococci Acquisition</b> | 3                 | 1.10<br>(0.69, 1.75) | 60%                              |

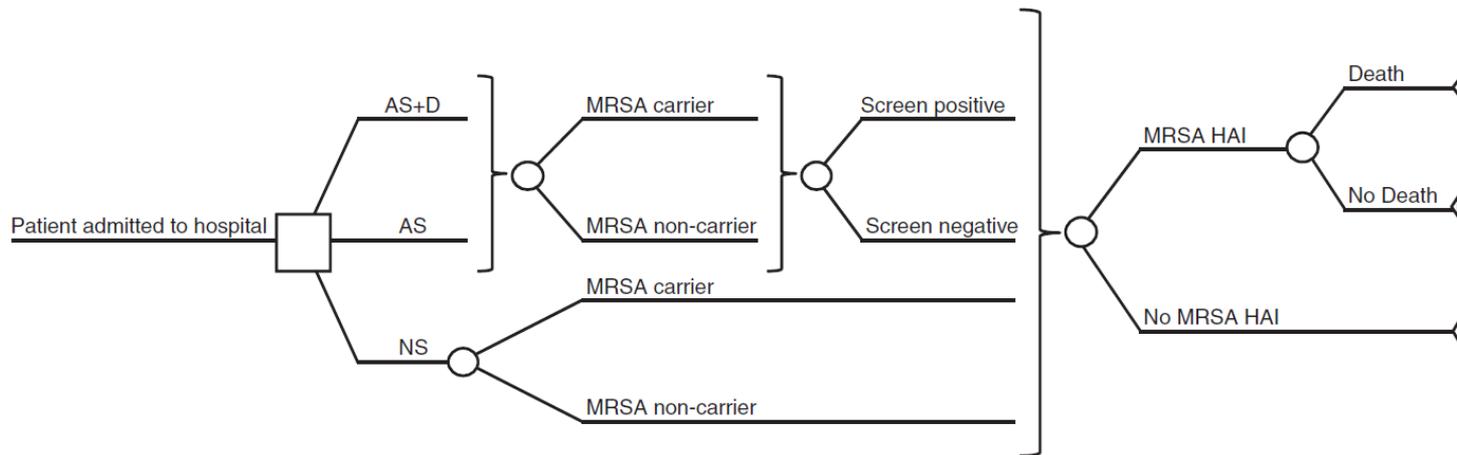
Unpublished Data

# Universal Gloving Summary

- Implementation of universal glove use was not associated with a statistically significant decrease in transmission or infection with multidrug resistant organisms
- Studies should be done to evaluate healthcare worker preference, other outcomes and cost-effectiveness comparing universal gloving with standard care

# Creation of a Decision-Analytical Model

- Virtual method of comparing effectiveness and costs of interventions head-to-head
- Need to populate each model parameter
  - ▣ Event probabilities- base-case and plausible range



Nelson et al., Clin Micro Infect 2010

For More Information: Dr. Rich Nelson CDA cyberseminar June 2016

<http://www.hsr.d.research.va.gov/cdp/cda-061416.cfm>

# Can Meta-analyses be Trusted?

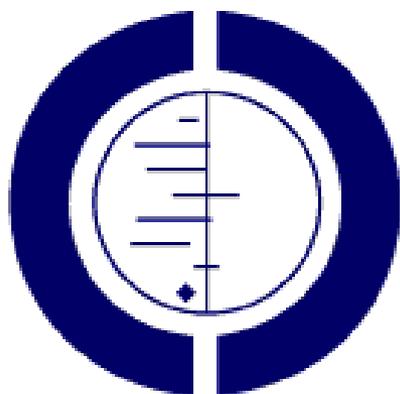
- Meta-analysis is a useful tool for summarizing existing research as long as limitations are recognized
- Meta-analyses are only as valid as the studies that contribute to the pooled risk ratio



# Usefulness of Meta-analyses

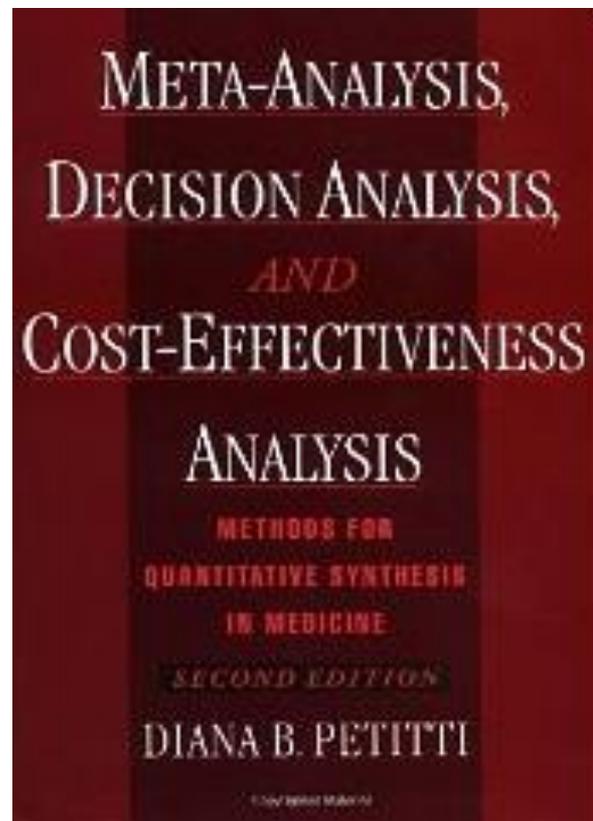
- Estimate the effectiveness of an intervention based on current knowledge
- Identify gaps in the literature
- Examine subgroups that original studies do not have power to examine
- Parameters for mathematical models
- Guide direction of future research

# Resources

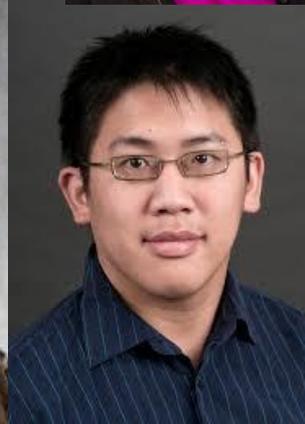


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# Our Meta-Analysis Team



# MRSA CREATE Team



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# CADRE COIN



# Questions/Comments?

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