

The REDUCE MRSA Trial

Randomized Evaluation of
Decolonization vs. Universal Clearance to
Eliminate MRSA



UCIrvine
University of California, Irvine



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SCHOOL OF MEDICINE

HCA

AHRQ



Trial Rationale

- MRSA important in healthcare associated infections
- Many quality improvement strategies
 - Screen and isolate
 - Screen, isolate, decolonize
 - Universal decolonization
- No head-to-head comparisons
- Debate of high risk pathogen vs high risk populations

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Targeted versus Universal Decolonization to Prevent ICU Infection

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- Hospital Corporation of America
- Harvard Pilgrim Healthcare Institute/Harvard Medical School
- University of California Irvine
- Rush University
- CDC Prevention Epicenters Steering Committee

[Huang SS et al. NEJM Jun 2013;368:2255-2265](#)

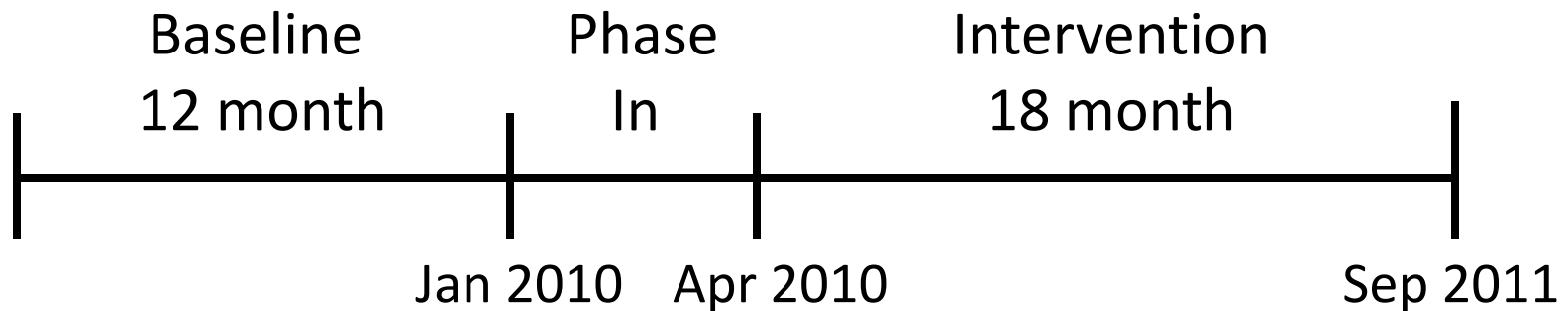
Cluster Randomized Trial

Randomized hospitals and all their adult ICUs to:

- **Arm 1: Routine Care**
 - Screened all patients; isolated known MRSA+
- **Arm 2: Targeted Decolonization**
 - Screened all patients; isolated if known MRSA+
 - Decolonized if MRSA+
- **Arm 3: Universal Decolonization**
 - No screening; isolated if known MRSA+
 - Decolonized all

Decolonization in Community ICUs

- **74 adult ICUs**
- **43 hospitals, 16 states**
 - 1 academic center, 42 community hospitals
 - 3-arm cluster randomized trial of hospitals



Decolonization Regimens

- **Arm 2: Targeted Decolonization**
 - Nasal mupirocin twice daily for 5 days
 - Chlorhexidine baths daily for 5 days
- **Arm 3: Universal Decolonization**
 - Nasal mupirocin twice daily for 5 days
 - Chlorhexidine baths daily for ICU duration

Outcomes

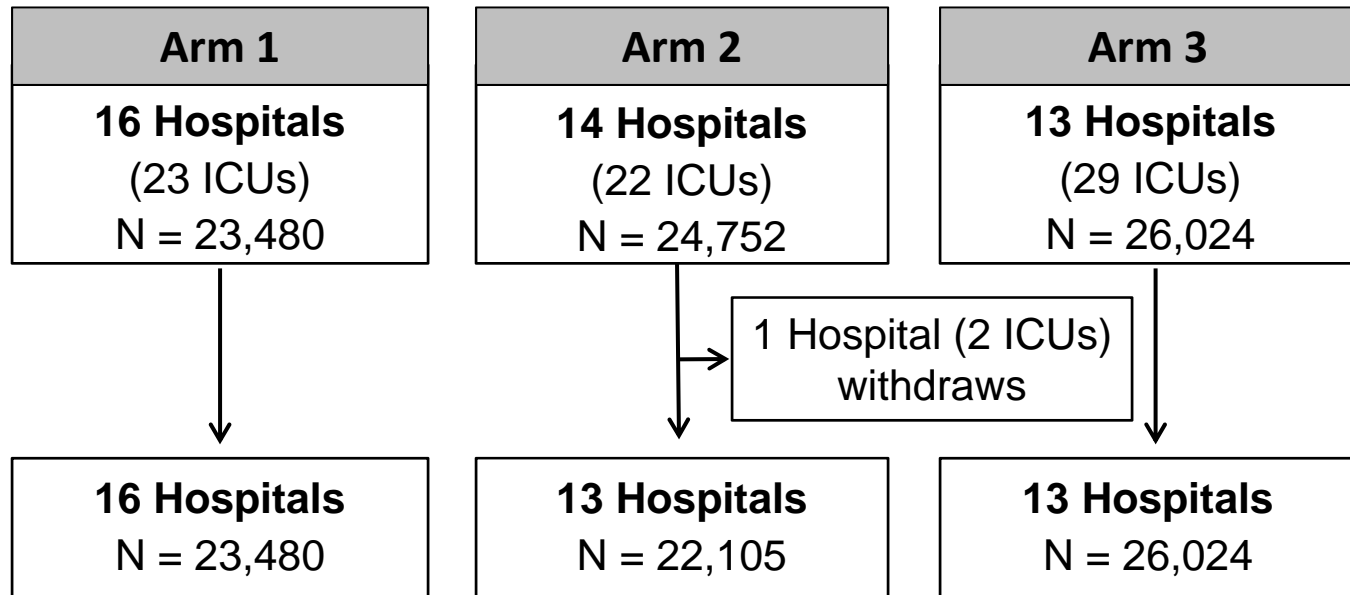
- **Primary**
 - Any MRSA clinical isolate attributed to ICU
- **Secondary**
 - MRSA bloodstream isolate attributed to ICU
 - Any bloodstream isolate attributed to ICU
- **Outcome Definitions**
 - Microbiology results alone
 - > 2d after ICU admit → 2d after ICU discharge

Intervention Period

Intervention: 74,256 patients

282,803 ICU patient days

**As
Randomized**

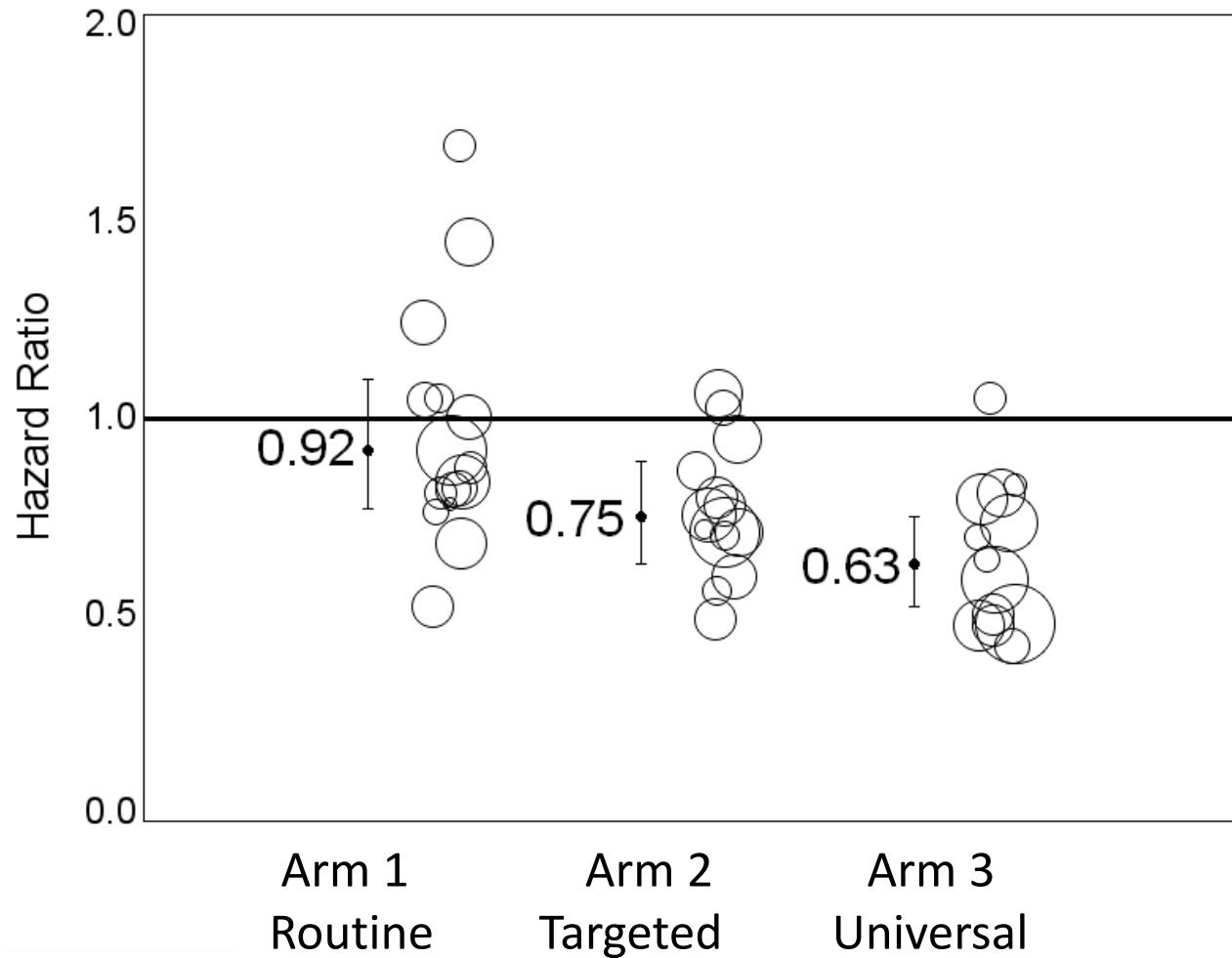


Select Population Characteristics

Variable	Arm 1 Routine	Arm 2 Targeted	Arm 3 Universal
ICU Stay in Days (median)	3	3	3
Age (median)	65	66	65
Comorbidities (%)			
Diabetes	31.3	33.0	30.7
Renal Failure	20.0	20.4	19.0
Cancer	10.4	10.8	14.1
Liver Failure	3.4	4.4	3.9
History of MRSA (%)	10.2	11.5	10.6
Surgery During Admission (%)	40.5	38.6	47.5

No important differences between Baseline, Intervention Periods

MRSA Clinical Cultures



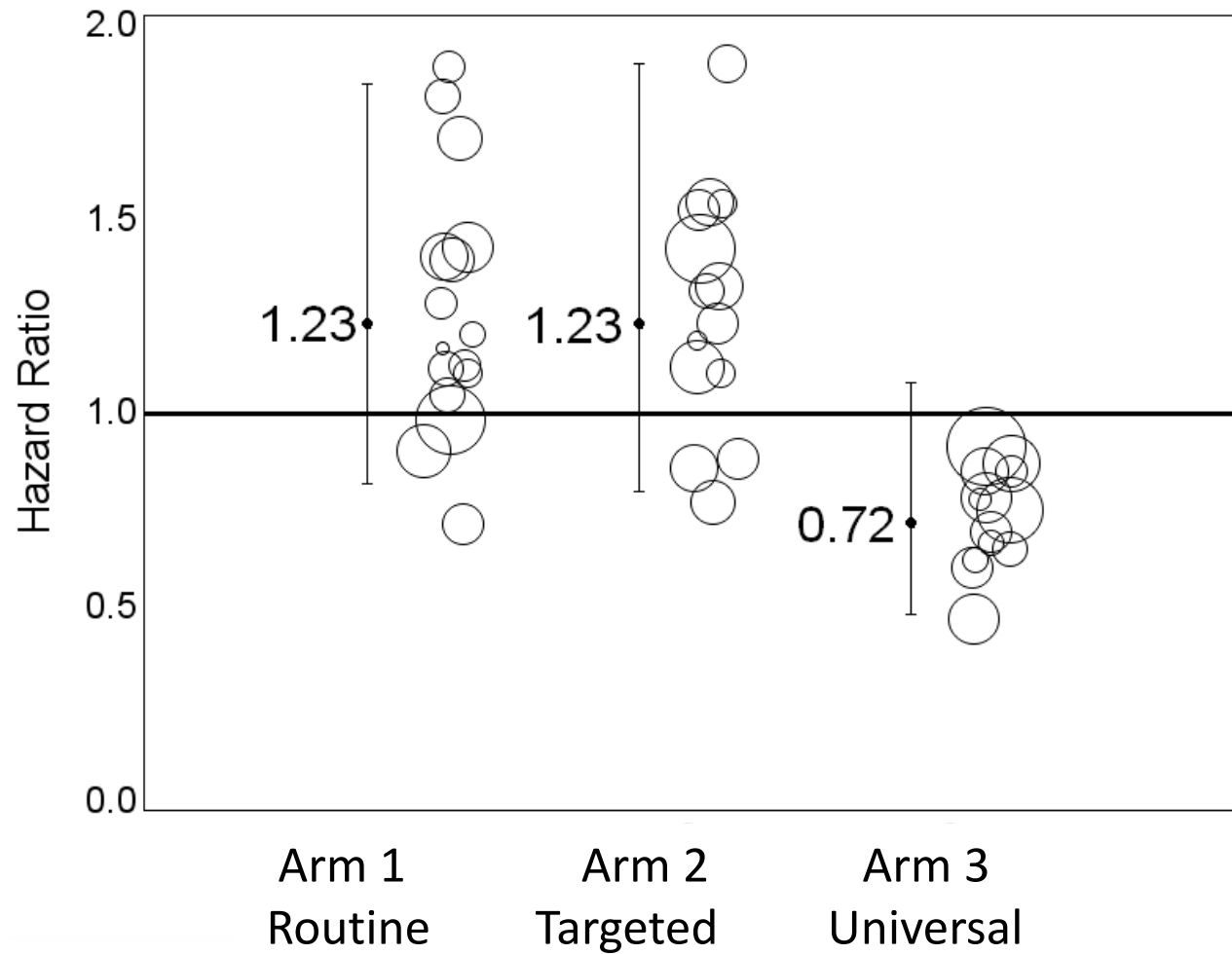
Overall P=0.01

Arm 2 vs 1 P=0.09

Arm 3 vs 1 P<0.003

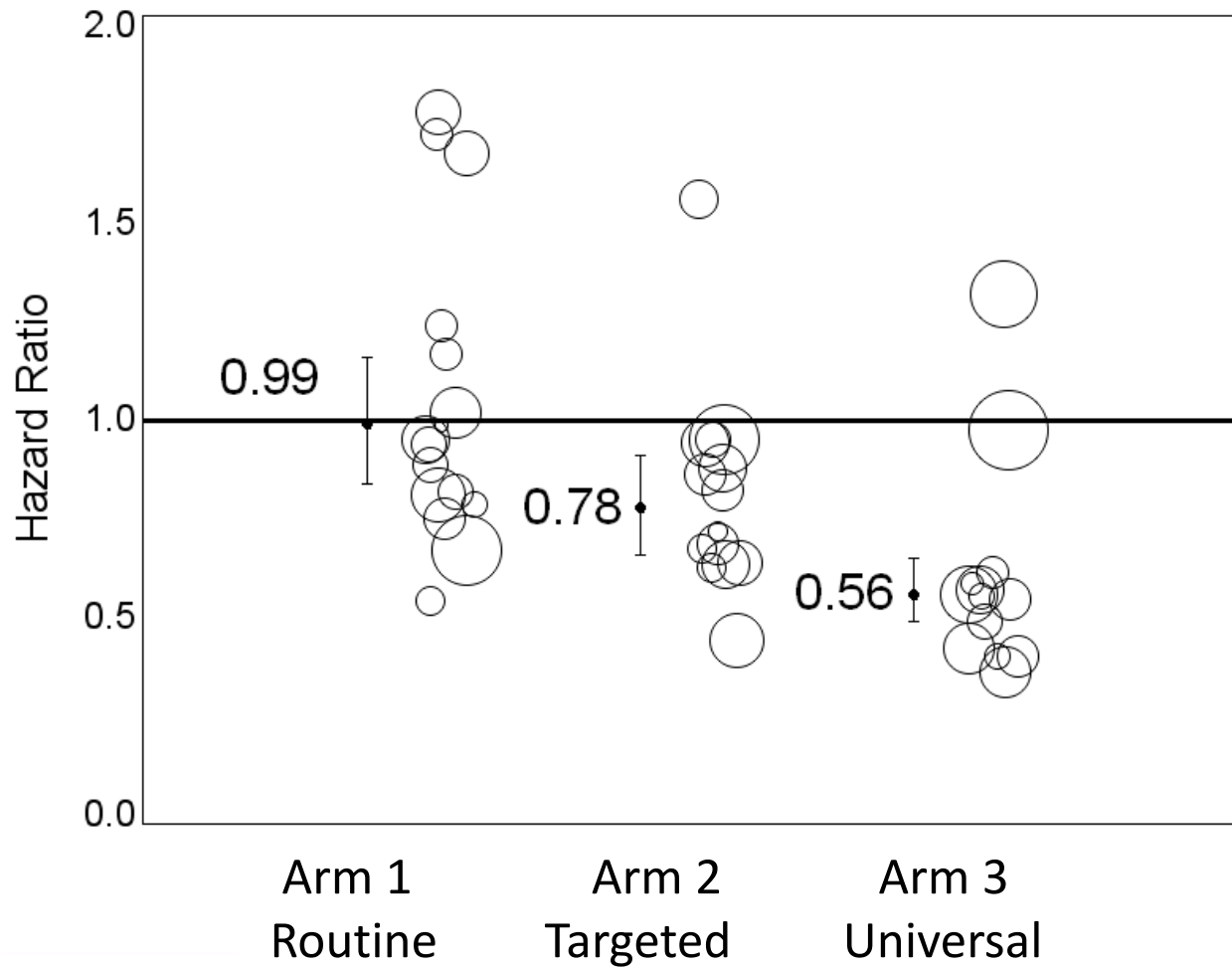
Arm 3 vs 2 P=0.16

MRSA Bloodstream Infection



Overall P=0.11

All Pathogen Bloodstream Infection



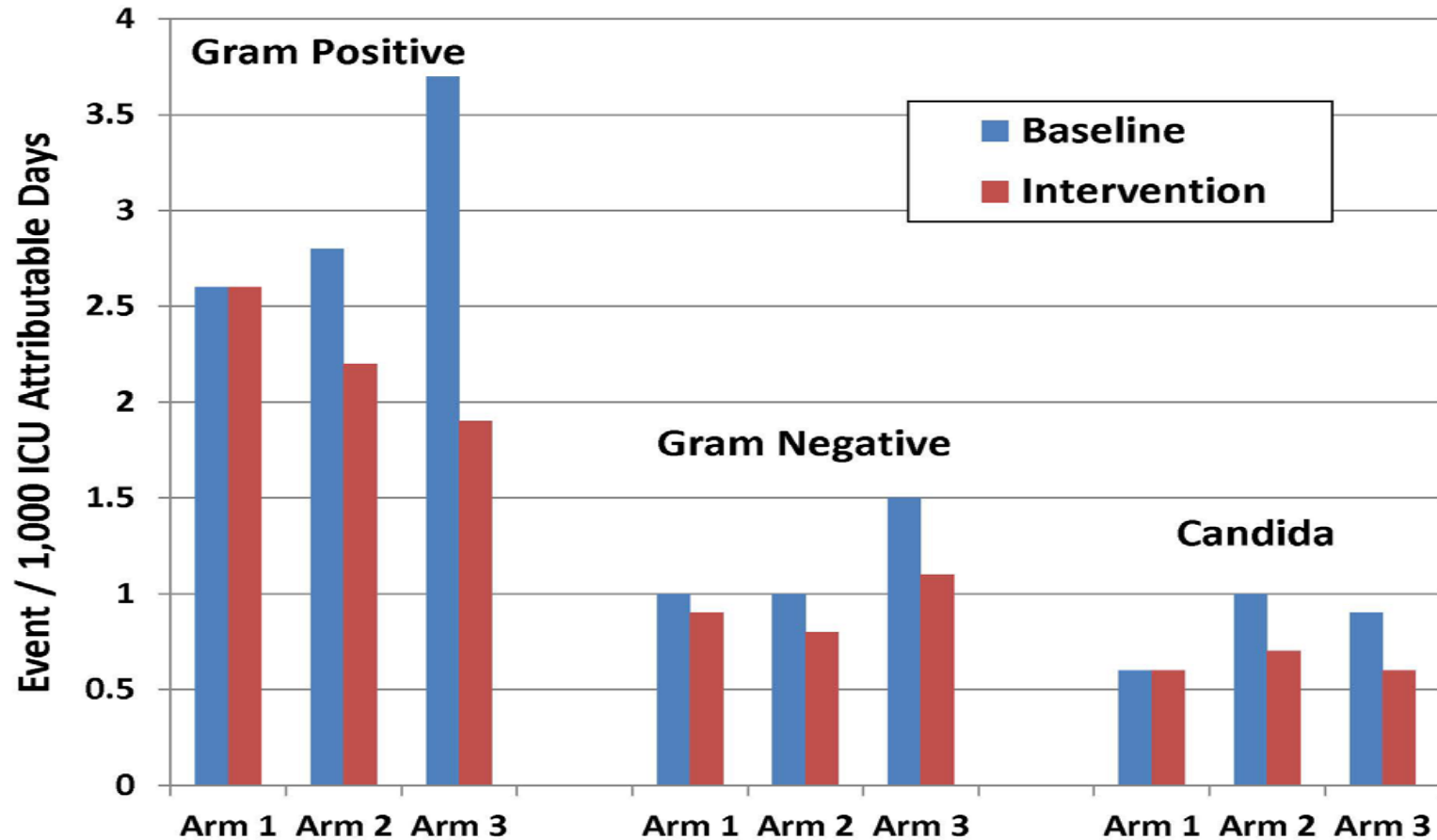
Overall $P < 0.0001$

Arm 2 vs 1 $P = 0.04$

Arm 3 vs 1 $P < 0.0001$

Arm 3 vs 2 $P = 0.003$

BSI Reduction by Pathogen Type



Elevated baseline bloodstream rate in Arm 3 maybe related to higher acuity. Arm 3 had 2 of 3 BMT units in the trial, and 3 of 4 solid organ transplant units.

Protocol Compliance

- Compliance monitoring
 - Once a week point prevalence checks
 - Quarterly direct observation of bathing with checklist

	Arm 1	Arm 2 (among MRSA+)	Arm 3
Screening	98%	99%	1%
CHG bathing	< 1%	89%	81%
Mupirocin	< 1%	91%	86%

- Reasons for non-compliance
 - < 1 day stay, discharge before scheduled activity, decline, moribund


Implementation – Key Features

- Usual quality improvement personnel
- No on-site investigators
- Rapid response email/phone
- Bi-weekly coaching calls
- Educational material provided
 - Protocols
 - Binders
 - Computer based training modules
 - FAQs
 - Bathing video, podcast
- Site visits for bathing training and as requested
- CDC Prevention Epicenters Steering Committee

Electronic Solutions

- Electronic nursing queries for compliance
- Coaching calls
 - Attendance tracked
 - Presentations recorded and posted
- Educational materials
 - Computer based training module and tracking
 - Bathing video
 - Podcast
- Analytic datasets
 - Descriptive variables and adjustors
 - Outcomes

Education Materials

5 Day Protocol HCA  CDC

DECOLONIZATION FOR SELECT CONTACT PRECAUTION PATIENTS

Day 1	Day 2	Day 3	Day 4	Day 5
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- Select patients receive Bactroban NASAL & CHG baths for 5 days while in the ICU.
- Chlorhexidine (CHG) replaces routine bathing.
- CHG bathing begins once patient's status is identified.
- DO NOT use soap below the jawline. Certain soaps & lotions can inactivate CHG.
- Only use CHG compatible lotions and/or barrier products.

BATHE WITH CHG USING FIRM MASSAGE TO REMOVE BACTERIA

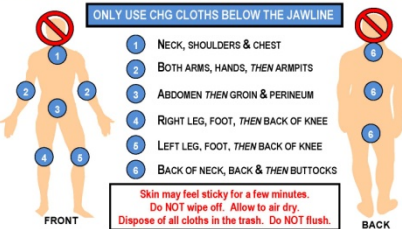
INCONTINENCE:

- Clean with chux & water, NOT soap
- Then bathe with CHG cloths, air dry
- Use as many CHG cloths as needed
- Apply CHG compatible barrier
- OK to repeat throughout the day

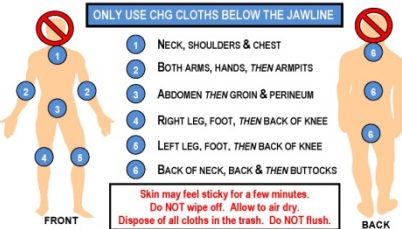
LINES AND TUBES:

- CHG is safe on lines, tubes & devices
- Bathe with CHG right up to dressing
- OK to bathe over occlusive dressings
- After bathing skin, clean 6 in. of tubes/Foley nearest patient

ONLY USE CHG CLOTHS BELOW THE JAWLINE



FRONT



BACK


Skin may feel sticky for a few minutes.
Do NOT wipe off. Allow to air dry.
Dispose of all cloths in the trash. Do NOT flush.

REDUCE MRSA Trial
Arm 3: Implementation Questions and Answers

MRSA Screening Questions

- Are participating ICUs supposed to stop all MRSA screening in the ICU?**
Yes, all routine MRSA screening for ICU admissions should stop. This includes stopping screening for all high risk groups admitted to the ICU setting (e.g. dialysis patients, nursing home residents...). Nurses must be educated so that screening stops during the entire study period. If there is a hospital-wide policy to screen select high risk patients (for example, patients newly starting dialysis), or all patients with a prior MRSA history, then refer to CD to develop a facility specific plan to initiate screening or transfer out of a participating ICU to a non-participating location (e.g. non-ICU).
- Why is stopping screening a component of Arm 3?**
It is not known whether screening and isolating MRSA+ patients is the only effective strategy to reduce MRSA burden and infection. Screening is costly and results do not return immediately. Some people have raised the important issue that screening for all antibiotic-resistant pathogens is not feasible and that a different strategy should be entertained. Still others are concerned that placing more and more people on contact precautions raises unintended consequences such as issues about patients feeling isolated and having less visits by clinical staff. Arm 3 tests the important hypothesis that universal decolonization may be just as effective or more effective in reducing MRSA than either screening and isolating alone (Arm 1) or screening and targeting MRSA+ patients for decolonization (Arm 2). If universal decolonization is shown to be most effective, it will allow screening to stop and the cost of screening to cease.
- If screening stops, how will you measure the effectiveness of Arm 3 in the trial?**
MRSA prevalence based on screening is not an outcome of this trial. Instead, we will be evaluating the persistence of ICU MRSA+ diluted cultures occurring more than 2 days into the ICU stay. In addition, we will be evaluating MRSA (and all pathogen) sterile site cultures as a measure of infection. We hypothesize that universal decolonization may have a significant effect in reducing all these measures. All outcome measures will be collected from centralized databases. Importantly, the structuring of the trial in this way allows us to answer whether or not universal decolonization can replace screening (which is expensive and time consuming) as a reasonable and possibly superior method for preventing MRSA disease.
- Isn't decolonization more costly than screening with nasal swabs?**
We believe it may be cost-saving. The cost burden of decolonization is a shift from lab costs (MRSA swab, nurse time, technician time, Chromagar, incubator etc.) and isolation supplies (gowns, gloves, masks) to pharmacy (Bactroban NASAL) and bathing supplies (CHG cloths). In addition, by removing bacteria, decolonization may prevent infections and their associated costs. In fact, universal decolonization can potentially prevent a broad spectrum of infection due to multidrug resistant organisms (VRE, VISA, acinetobacter, etc.) rather than just infection due to MRSA.

Version 2.3.10


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REDUCE MRSA Trial

Randomized Evaluation of
Decolonization vs. Universal Clearance to
Eliminate MRSA

**Targeted Decolonization
ICU Toolkit Binder**

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 **REDUCE MRSA Trial**
Targeted Decolonization – Arm 2

For MRSA-Positive Patients Only

DO

- Use CHG baths in place of daily routine bathing
- Give CHG baths every day for 5 days while in ICU
- Use Bactroban NASAL[®] twice daily for 5 days while in ICU
- Only use approved HCA lotions
- Restart entire protocol for readmitted ICU patients
- Refer to Decolonization Protocol for special circumstances
- Report suspected mupirocin/CHG related events to study staff

DON'T


- Do NOT use above jawline
- Do NOT wipe off CHG. Let air dry.
- Do NOT flush CHG cloths
- Do NOT continue protocol after ICU discharge
- Do NOT include patients who are:
 - < 13 years old
 - Allergic to mupirocin and/or CHG

REFER TO DECOLONIZATION PROTOCOL FOR STEP-BY-STEP INSTRUCTIONS

General Questions
(877) 294-9865
(617) 509-4141
Reduce.MRSA@gmail.com
Decolonization Protocol
(877) 294-9865
Study Related Events
(617) 509-4141 phone
(617) 509-4260 fax

REDUCE – MRSA TRIAL
Randomized Evaluation of Decolonization vs.
Universal Clearance to Eliminate MRSA
Project FAQs: Targeted MRSA Decolonization – Arm 2

- What is the REDUCE-MRSA Trial?**
A cluster randomized trial of adult ICUs comparing 3 top strategies to reduce MRSA. Approximately 60 HCA hospitals are participating. Your hospital's adult ICUs have been randomized to Targeted MRSA Decolonization.
- What is Targeted MRSA Decolonization?**
Your ICU will be screening and then decolonizing MRSA+ patients by applying nasal mupirocin twice daily for 5 days and bathing once daily with chlorhexidine baths for 5 days. MRSA+ status is determined by admission nares screen or prior history.
- How should mupirocin and chlorhexidine be applied?**
Please refer to the Decolonization Protocol in your ICU Toolkit Binder. A detailed flyer is provided for each room in your ICU Toolkit Binder. For any questions, contact the Protocol Helpline at (877) 294-9865.
- What about MRSA-negative patients?**
MRSA-negative patients should not receive mupirocin or chlorhexidine. Prior ICU policies for pre-operative patients should remain as before, but new interventions related to these agents should NOT be pursued.
- How do I report a study related event?**
Complete the Study Related Event Submission Form in the REDUCE MRSA ICU Toolkit Binder. Fax the completed form to Julie Dunn at (617) 509-4260. REDUCE MRSA study staff will make daily weekday calls to the patient's nurse for follow up.
- Who do I contact with questions?**
General questions:
Reduce.MRSA@gmail.com, (877) 294-9865 or (617) 509-4141
Decolonization Protocol questions:
Leah Terpsira or Adrijana Gombosov (877) 294-9865
Study Related Event questions:
Fallon Onufrak or Katie Haffeneffer (617) 509-4141

HCA  CDC

Challenges and Lessons Learned

- State legislation
 - 5 hospitals randomized separately to only Arms 1 or 2
 - Sensitivity analysis
- Coaching call structure and accountability
 - Roll call
 - Required questions each call
- Compatibility issues
- Tracking competing interventions
 - 69 interventions proposed
 - 36 not pursued due to trial conflict

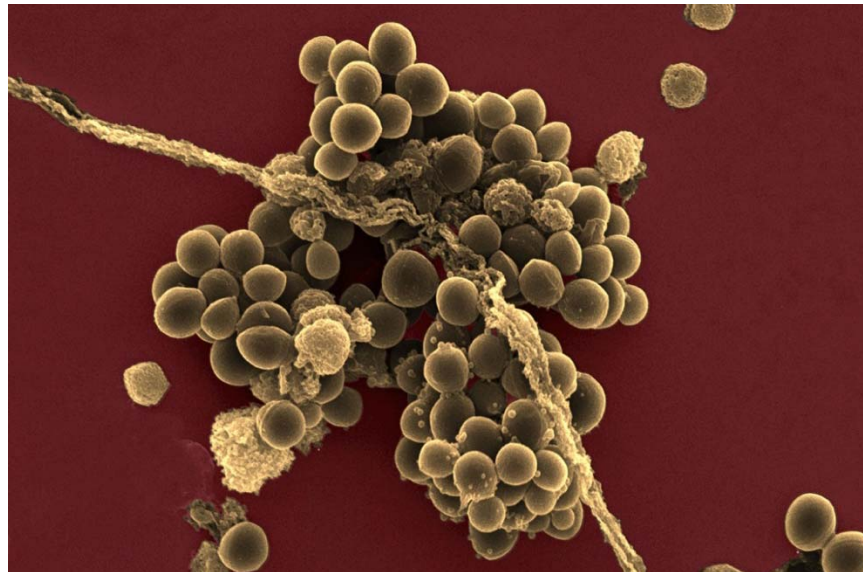
REDUCE MRSA Trial Summary

- **Effective pragmatic trial**
 - Trial cost: \$40/patient
- **Universal decolonization: CHG and mupirocin**
 - Reduces MRSA and all BSI
 - Saves effort and cost of screening
 - May reduce need for contact precautions
 - Minimal adverse events
- **Horizontal vs Vertical Approaches**
 - Universal better than targeted

Evidence Summary

Author	Study Year	Study Type	Hospital	ICU	N	Findings	Publication	Funding
Vernon	10/02-12/03	Observational	1	1	1,787	65% less VRE acquisition 40-70% less VRE on skin, HCW hands, environment	Arch Intern Med 2006; 166:306-312	CDC, Sage
Climo	12/04-1/06	Observational	4	6	5,293	66% less VRE BSI 32% less MRSA acquisition 50% less VRE acquisition	Crit Care Med 2009; 37:1858-1865	CDC
Bleasdale	12/05-6/06	Observational	1	2	836	61% less primary BSI	Arch Intern Med 2007; 167(19):2073-2079	CDC, Sage
Popovich	9/04-10/06	Observational	1	1	3,816	87% less CLABSI 41% less blood contaminants	ICHE 2009; 30(10):959-63	CDC
Climo	8/07-2/09	Cluster RCT	6	9	7,727	23% less MRSA/VRE acquisition	N Engl J Med 2013; 368:533-42	CDC (Sage: product)
Milestone	2/08-9/10	Cluster RCT	5	10	4,947	36% less total BSI (as treated)	Lancet. 2013; 381(9872):1099-106	Sage, NIH
Huang	1/09-9/11	Cluster RCT	43	74	122,646	37% less MRSA clinical cultures 44% less all-cause BSI	N Engl J Med 2013 368:2255-2265	AHRQ, CDC, HCA

Questions?



Decision for Universal Mupirocin

- Pro
 - S. aureus #1 HAI ¹
 - Screening not comprehensive ²
 - Decolonization: CHG alone less effective than combination ²
 - Highly effective in REDUCE MRSA trial vs proactive control
 - Will not lose systemic agent
 - Alternatives in pipeline
- Con
 - Potential for resistance
 - Requires risk:benefit

¹ Sievert et al. ICHE 2013;34(1):1-14

² Harbarth et al. AACT 1999;43(6):1412-6