

# **Update on Decolonization for MDROs**

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## Disclosures

- Conducting clinical studies in which participating nursing homes or hospital patients received contributed cleaning or antiseptic products from Medline and Xttrium
- Companies had no role in design, conduct, analysis, or publication

# CDC Surveillance Network: U.S. COVID Impact

	2020 Q1	2020 Q2	2020 Q3	2020 Q4
CLABSI	-11.8%	27.9%	46.4%	47.0%
CAUTI	-21.3%	No Change <sup>1</sup>	12.7%	18.8%
VAE	11.3%	33.7%	29.0%	44.8%
SSI: Colon surgery	-9.1%	No Change <sup>1</sup>	-6.9%	-8.3%
SSI: Abdominal hysterectomy	-16.0%	No Change <sup>1</sup>	No Change <sup>1</sup>	-13.1%
Laboratory-identified MRSA bacteremia	-7.2%	12.2%	22.5%	33.8%
Laboratory-identified CDI	-17.5%	-10.3%	-8.8%	-5.5%

# Worsening Antibiotic Use with COVID-19

- Concern for bacterial co-infection in seriously ill COVID-19 patients
- In 605 U.S. hospitals <sup>1</sup>
  - 76% received antibiotics

**Indiscriminate Use of Antibiotics for COVID-19 Treatment in South Asian Countries is a Threat for Future Pandemics Due to Antibiotic Resistance**

## COVID-19 CREATED A PERFECT STORM

The U.S. lost progress combating antimicrobial resistance in 2020



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pandemic

Abi Manesh · George M Varghese ✉ · on behalf of the CENDRIC Investigators and Collaborators

- 81% received antibiotics
- 80% deemed unnecessary

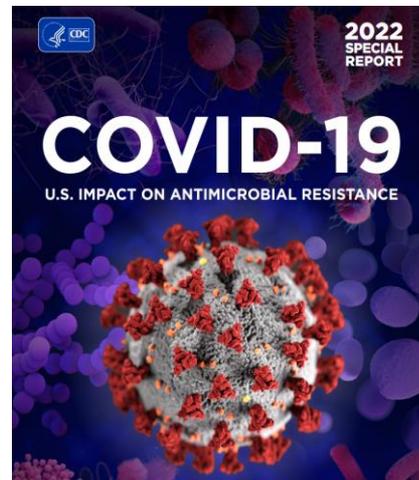
Is there a need to widely prescribe antibiotics in patients hospitalized with COVID-19?

F. Moretto <sup>a</sup>, T. Sixt <sup>a</sup>, H. Devilliers <sup>b, c</sup>, M. Abdallahoui <sup>b</sup>, I. Eberl <sup>a</sup>, T. Rogier <sup>b</sup>, M. Buisson <sup>a</sup>, P. Chavanet <sup>a</sup>, M. Duong <sup>a</sup>, C. Esteve <sup>a</sup>, S. Mahy <sup>a</sup>, A. Salmon-Rousseau <sup>a</sup>, F. Catherine <sup>a</sup>, M. Blot <sup>a, c</sup>, L. Piroth <sup>a, c, d, e</sup>

<sup>1</sup> Baghdadi JD et al. AACT 2021 65e01341-21

# U.S. Antimicrobial Resistance Progress Erased by COVID

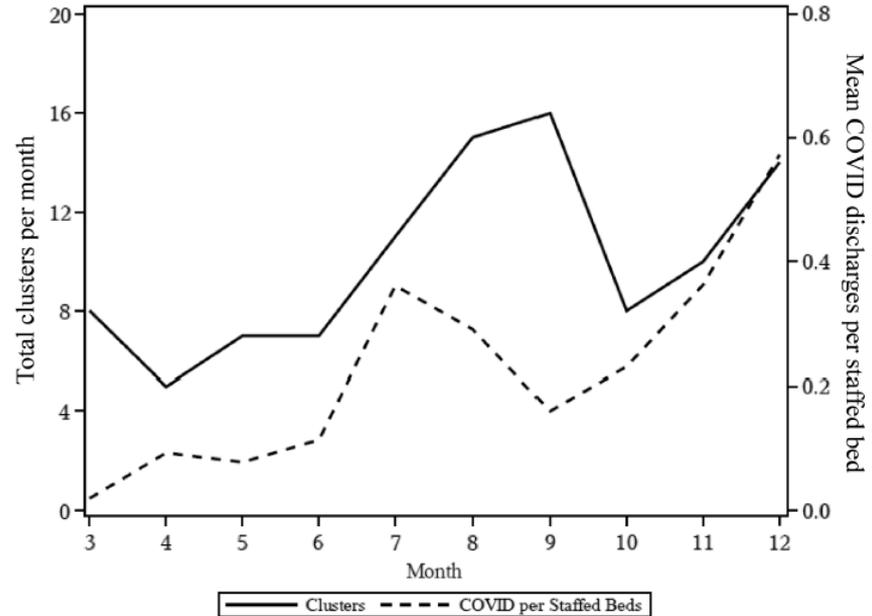
- 80% of COVID patients received antibiotics in 2020
- Hospital-onset MDROs between 2019 to 2020
  - CRAB increased 78%
  - *Candida auris* increased 60%
  - CRE increased 35%
  - ESBL increased 32%
  - MDR-Pseudomonas increased 32%
  - VRE increased 14%
  - MRSA increased 13%



<https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf>

# COVID Impact: Increase in U.S. Hospital Bacterial Outbreaks

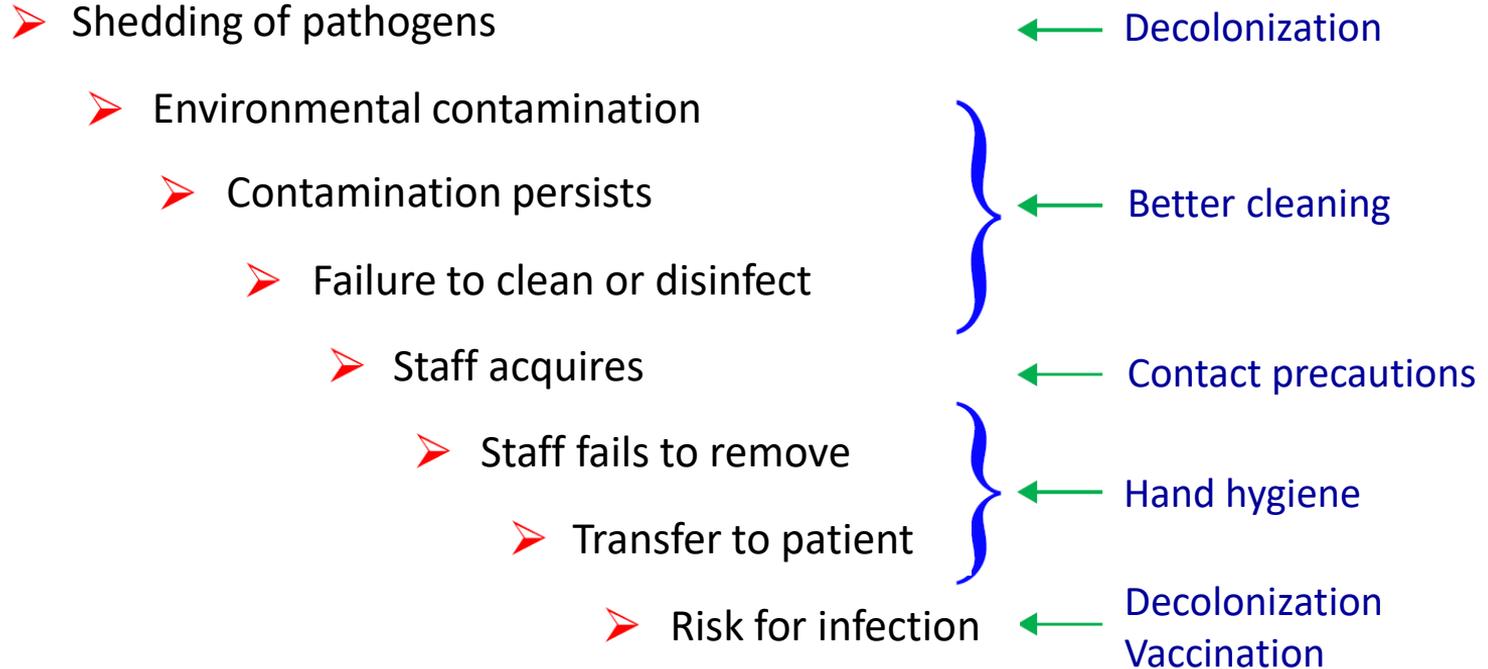
148 U.S. Community Hospitals  
Hospital-onset pathogen clusters  
Statistically-derived



# Human Pathogen Transmission: Cascade of Unfortunate Events

- Shedding of pathogens
  - Environmental contamination
    - Contamination persists
      - Failure to clean or disinfect
        - Staff acquires
          - Staff fails to remove
            - Transfer to patient
              - Risk for infection

# Human Pathogen Transmission: Cascade of Unfortunate Events



# Decolonization Prevents a Cascade of Unfortunate Events

- Shedding of pathogens ← Prevents shedding
- Environmental contamination
- Contamination persists
  - Failure to clean or disinfect
  - Staff acquires
    - Staff fails to remove
      - Transfer to patient

**Broad solution for all MDROs**  
**Benefits carriers too**

- Risk for infection

# What is Topical Decolonization?

- Topical antiseptic or antibiotic agents to remove commensals or pathogens from the skin or nose
- Most studied products:
  - Skin: chlorhexidine, iodophor (povidone-iodine)
  - Nose: mupirocin, iodophor
- Strong safety record
- Targeted and universal uses

# Use of Chlorhexidine

- Antiseptic uses in healthcare
  - Hand antiseptics at 2% and 4%
  - Dental hygiene
  - 1990s: Cleaning of skin prior to line insertion
  - 1990s: Pre-operative bathing
  - 2000s: Surgical prep
  - 2000s: Pre-op *S. aureus* carriers
  - 2010s: Universal ICU bathing
  - 2019: CHG for non-ICU bathing

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  - **2010s: Universal ICU bathing**
  - 2019: CHG for non-ICU bathing

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Effect of Daily Chlorhexidine Bathing on Hospital-Acquired Infection

Michael W. Climo, M.D., Deborah S. Yokoe, M.D., M.P.H., David K. Warren, M.D., Trish M. Perl, M.D., Maureen Bolon, M.D., Loreen A. Herwaldt, M.D., Robert A. Weinstein, M.D., Kent A. Sepkowitz, M.D., John A. Jernigan, M.D., Kakotan Sanogo, M.S., and Edward S. Wong, M.D.

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

JUNE 13, 2013

VOL. 368 NO. 24

## Targeted versus Universal Decolonization to Prevent ICU Infection

Susan S. Huang, M.D., M.P.H., Edward Septimus, M.D., Ken Kleinman, Sc.D., Julia Moody, M.S., Jason Hickok, M.B.A., R.N., Taliser R. Avery, M.S., Julie Lankiewicz, M.P.H., Adrijana Gombose, B.S., Leah Terpstra, B.A., Fallon Hartford, M.S., Mary K. Hayden, M.D., John A. Jernigan, M.D., Robert A. Weinstein, M.D., Victoria J. Fraser, M.D., Katherine Haffner, B.S., Eric Cui, B.S., Rebecca E. Kaganov, B.A., Karen Lolans, B.S., Jonathan B. Perlin, M.D., Ph.D., and Richard Platt, M.D., for the CDC Prevention Epicenters Program and the AHRQ DECIDE Network and Healthcare-Associated Infections Program\*

THE LANCET

## Daily chlorhexidine bathing to reduce bacteraemia in critically ill children: a multicentre, cluster-randomised, crossover trial

Aaron M. Mikstov, Alexis Eward, Xiaoyan Song, Danielle M. Zee, Rachel Orsheim, Kathleen Speck, Daniel Obeng, Nicholas G. Reich, Susan E. Coffin, Trish M. Perl, for the Pediatric SCRUB Trial Study Group

### Summary

**Background** Bacteraemia is an important cause of morbidity and mortality in critically ill children. Our objective was to assess whether daily bathing in chlorhexidine gluconate (CHG) compared with standard bathing practices would reduce bacteraemia in critically ill children.

# Use of Chlorhexidine

- Antiseptic uses in healthcare
  - Hand antisepsis at 2% and 4%
  - Dental hygiene
  - 1990s: Cleaning of skin prior to line insertion
  - 1990s: Pre-operative bathing
  - 2000s: Surgical prep
  - 2000s: Pre-op *S. aureus* carriers
  - 2010s: Universal ICU bathing
  - **2019: CHG for non-ICU bathing**

## THE LANCET

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Chlorhexidine versus routine bathing to prevent multidrug-resistant organisms and all-cause bloodstream infections in general medical and surgical units (ABATE Infection trial): a cluster-randomised trial

Susan S Huang, Edward Septimus, Ken Kleinman, Julia Moody, Jason Hickok, Lauren Heim, Adrijana Gombosov, Taliser R Avery, Katherine Haffnerreffer, Lauren Shimelman, Mary K Hayden, Robert A Weinstein, Caren Spencer-Smith, Rebecca E Kaganov, Michael V Murphy, Tyler Forehand, Julie Lankiewicz, Micaela H Coady, Lena Portillo, Jalpa Sarup-Patel, John A Jernigan, Jonathan B Perlin, Richard Platt, for the ABATE Infection trial team

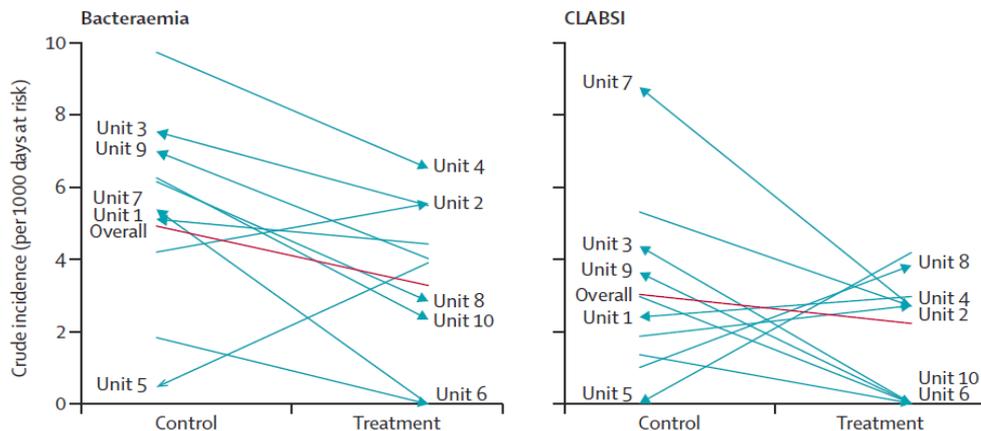
# Universal CHG Decolonization in Academic ICUs

- 12 Adult ICU cluster randomized cross-over trial
- 1 hospital dropped out → 9 ICUs, 7,727 patients in 6 hospitals
  - ICUs: daily CHG baths & routine soap for 6 months each
  - As-treated analysis
    - ✓ **Reduced MRSA and VRE acquisition by 23%**
    - ✓ **Reduced bacteremia by 28%**
    - ✓ **Reduced CLABSI by 53%**
- No evidence of CHG resistance

# Pediatric SCRUB Trial

## Universal CHG in 10 Academic PICUs

- Randomized cross-over trial of universal CHG bathing, N=1,547
- Two-thirds of parents consented
- As-treated analysis, 36% reduction in bloodstream infections



# Reducing MRSA and Bloodstream Infections in Community ICUs

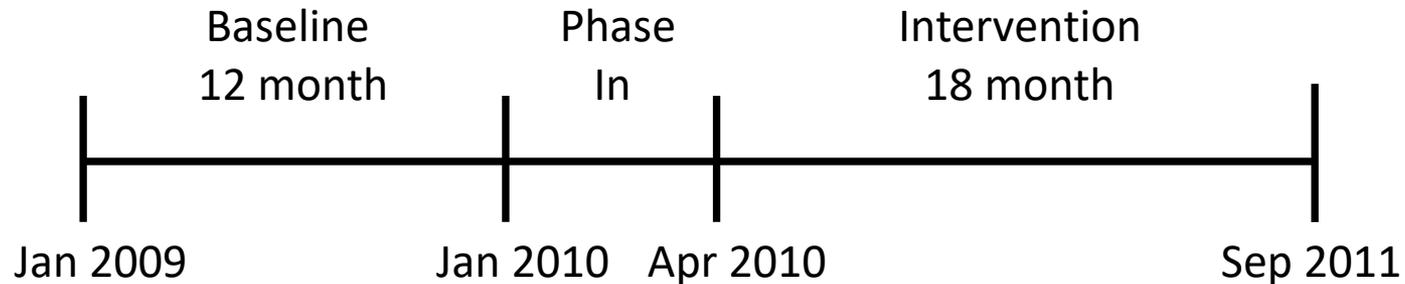
## REDUCE MRSA Cluster Randomized Trial of Hospitals

Randomized Evaluation of Decolonization vs. Universal Clearance to Eliminate MRSA

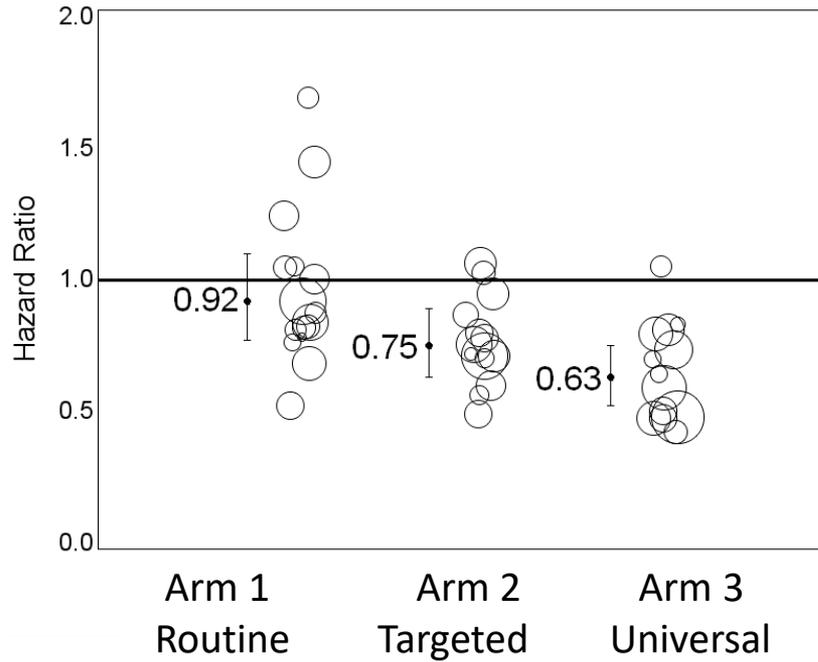
- **Arm 1: Routine Care**
  - Screened all patients; isolated known MRSA+
- **Arm 2: Targeted Decolonization**
  - Screened all patients; isolated known MRSA+
  - Decolonized if MRSA+ (5 days mupirocin, 5 days CHG)
- **Arm 3: Universal Decolonization**
  - No screening; isolated known MRSA+
  - Decolonized all (5 days mupirocin, daily CHG)

## Baseline and Intervention Periods

43 HCA Healthcare hospitals (formerly Hospital Corporation of America)  
74 adult ICUs and 282,803 ICU patient days  
74,256 patients



# MRSA Clinical Cultures



*Primary outcome*

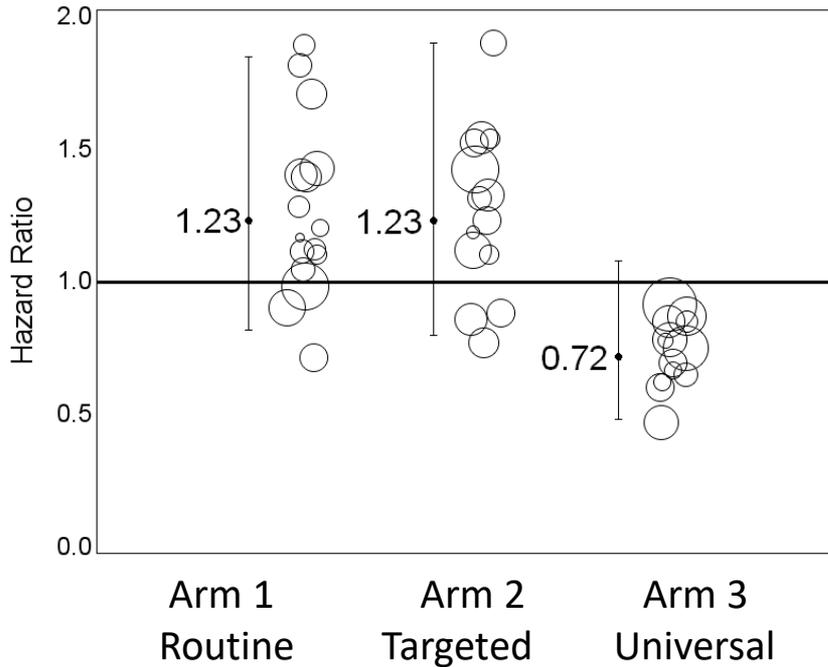
**Overall P=0.01**

Arm 2 vs 1 P=0.09

**Arm 3 vs 1 P<0.003**

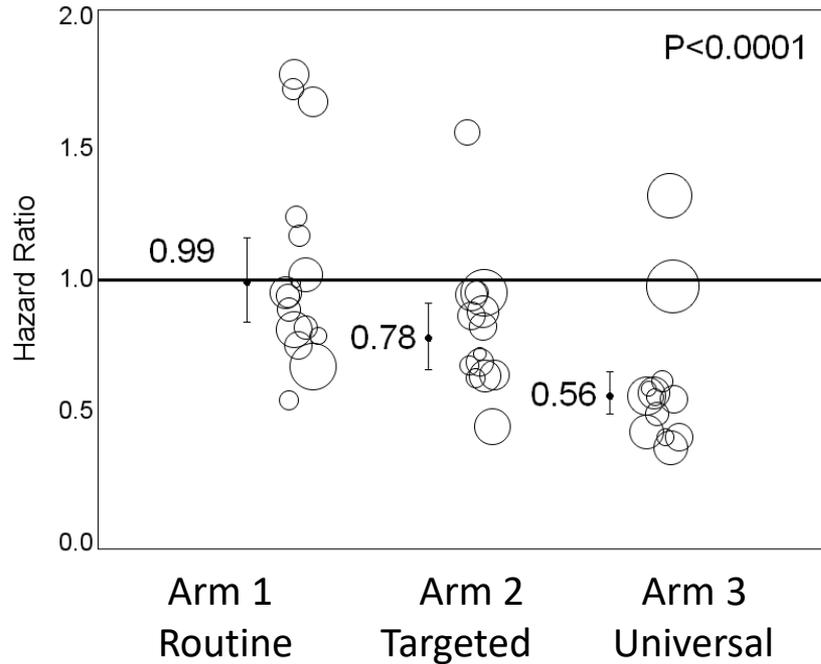
Arm 3 vs 2 P=0.16

# 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  $P = 0.003$**

# Additional Decolonization Impact

- Universal decolonization with mupirocin and CHG
  - Highly cost-effective and prevents need to screen <sup>1</sup>
  - Reduces blood culture contamination <sup>2</sup>
  - Reduces bacteriuria and candiduria in men <sup>3</sup>
  - No emergence of CHG or mupirocin resistance in trial <sup>4</sup>
  - CLABSI benefit seen with rapid adoption in 95 hospitals <sup>5</sup>
- 63% of all US hospitals use universal ICU decolonization<sup>6</sup>

<sup>1</sup> Huang SS et al. ICHE 2014; 35 S3:S23-S31

<sup>2</sup> Septimus EJ et al. ICHE 2014; 35 S3:S17-S22.

<sup>3</sup> Huang SS et al. Lancet ID 2016;16(1):70-9

<sup>4</sup> Hayden M et al. JCM 2016; 54(11):2735-42

<sup>5</sup> Septimus ES et al. CID 2016;63(2):172-7

<sup>6</sup> NHSN survey, 2021

# **Decolonization Outside of ICUs**

# ABATE Infection Trial

## Active Bathing to Eliminate Infection

Cluster-randomized trial of 53 U.S. hospitals

194 adult non-ICU medical, surgical, step down, oncology units

### **Arm 1: Routine Care**

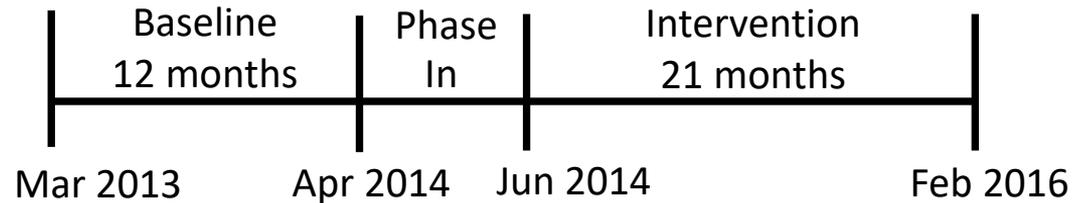
- Routine policy for showering/bathing

### **Arm 2: Decolonization**

- Daily 4% rinse-off CHG shower or 2% leave-on CHG bed bath
- Mupirocin x 5 days if MRSA+ by history, culture, or screen

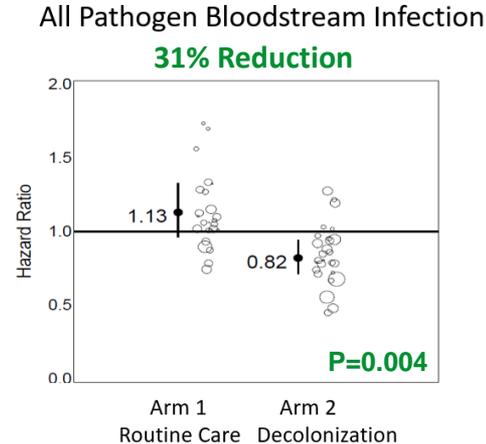
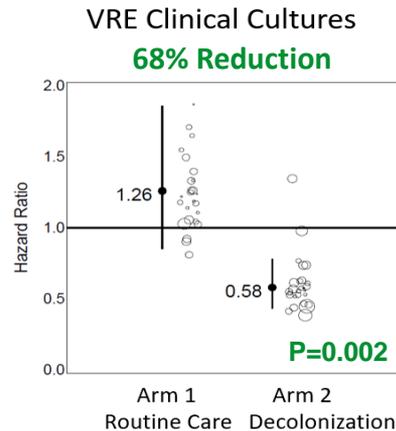
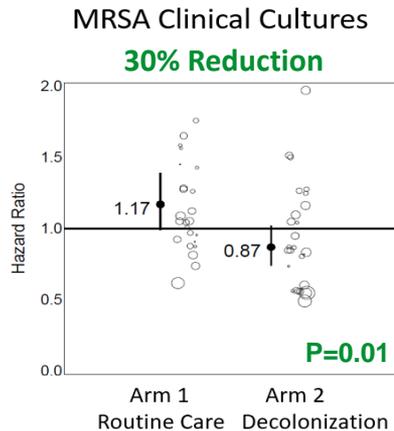
# Outcomes and Study Period

- **Primary Outcome**
  - Any MRSA or VRE isolate attributed to unit
- **Key Secondary Outcome**
  - Any bloodstream isolate attributed to unit  
(2 positives for skin commensals)
- **339,904 patients, 1,294,153 patient days (intervention)**



# Results: Decolonization Outside of ICUs

- No overall population benefit, unlike ICU trials
  - Lower risk and small effect size
- Benefit seen in **higher risk patients with lines and devices**



# Medical Devices: Attributable Impact

- Benefit seen in **higher risk patients with lines and devices**
  - 37% reduction in MRSA and VRE clinical cultures
  - 32% reduction in all pathogen bloodstream infection
  - 10% of population, but a third of MRSA+VRE cultures
  - 10% of population, but 60% of bloodstream infections

# CLEAR Trial

## Changing Lives by Eradicating Antibiotic Resistance

RCT of 2,121 MRSA+ recently hospitalized patients

Randomized on discharge, followed for 1 year

### **Arm 1: Routine Care**

### **Arm 2: Post-Discharge Decolonization**

- 5-day regimen, twice monthly for 6 months
  - Twice daily 2% nasal mupirocin
  - Twice daily 0.12% chlorhexidine oral rinse
  - Daily 4% rinse-off chlorhexidine bath/shower

# Time to Infection Outcomes

	Hazard Ratio (95% CI) Decolonization vs Education	P-value
<b>CDC NHSN Criteria</b>		
MRSA Infection	0.70 (0.52-0.96)	0.026
Any Infection	0.84 (0.70-1.01)	0.061
<b>Clinical Criteria</b>		
MRSA Infection	0.71 (0.52-0.97)	0.031
Any Infection	0.83 (0.70-0.99)	0.035

- As randomized analysis
- Blinded assessment by two ID physicians, redacted records
- Infection types (control): skin/soft tissue (35%), pneumonia (18%), primary bloodstream/vascular (13%), bone/joint (13%), SSI (11%), UTI (3%), Other (6%)

# Primary Outcome, by Adherence

## Time to CDC-Defined Infection

- Adherence measured at each visit, time-varying covariate
- Cox proportional hazards model

<i>Adherence Relative to Education</i>	<i>MRSA Infection</i>		<i>All-Cause Infection</i>	
	<i>Est. HR (95% CI)</i>	<i>P-value</i>	<i>Est. HR (95% CI)</i>	<i>P-value</i>
- Education	1.0		1.0	
- None	1.31 (0.72,2.38)	0.383	1.68 (1.19,2.36)	0.003
- Partial	0.64 (0.40,1.00)	0.050	0.86 (0.67,1.11)	0.241
- Full	0.56 (0.36,0.86)	0.009	0.60 (0.46,0.78)	<.001

- Non-adherent subjects fared worse than the average control
- Fully adherent subjects had 44% reduction in MRSA infection and 40% reduction in all-cause infections

## Number Needed to Treat

	Overall	Full Adherence
<b>MRSA Infection</b>	30	26
<b>MRSA Hospitalization</b>	34	27
<b>Any Infection</b>	26	11
<b>Hospitalization due to Infection</b>	28	12

# Decolonization Trials Across the Continuum of Care

- **MRSA Outcomes**
  - ICU
  - Non-ICU
  - Post-Discharge
  - Nursing Homes

# Protect Trial

## **Trial Design**

- 28 nursing home cluster randomized trial
- 18-month baseline, 18-month intervention period

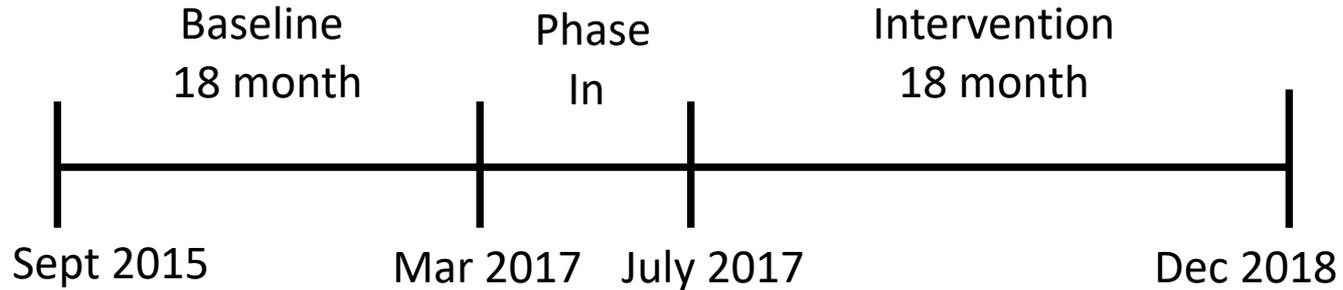
## **Arm 1: Routine Care**

- Usual practice for showering/bathing

## **Arm 2: Decolonization**

- CHG bathing for all residents (on admit, then per routine)
- Nasal iodophor twice daily x 5 days, facility-wide every other week

# Protect Trial



15,004 residents in baseline period

13,952 residents in intervention period

# Trial Outcomes

## **Primary Outcome**

- Hospital transfers due to infection  
(% of discharges to a hospital due to infection)

## **Secondary Outcome**

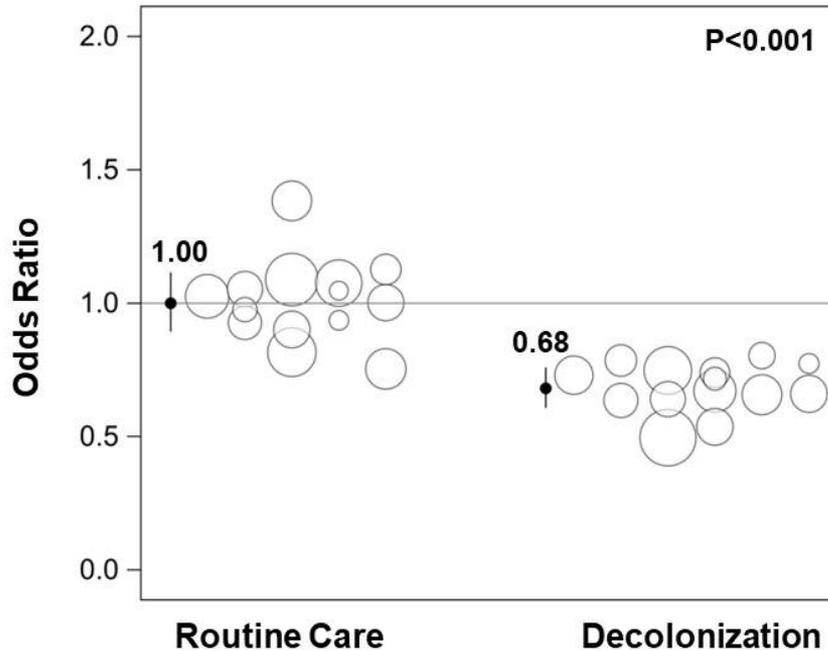
- All hospital transfers  
(% of discharges to a hospital)

# Protect Trial

## MDRO Prevalence Reductions (Nares/Skin Only)

	Trial Group	Baseline Prevalence	Intervention Prevalence	Adjusted OR	P-value
Any MDRO	Routine Care	48%	47%	<b>0.50 (0.39-0.65)</b>	<0.001
	Decolonization	49%	31%		
MRSA	Routine Care	38%	36%	<b>0.59 (0.46-0.77)</b>	0.01
	Decolonization	37%	24%		
VRE	Routine Care	6%	5%	<b>0.24 (0.13-0.45)</b>	0.003
	Decolonization	8%	2%		
ESBL	Routine Care	16%	18%	<b>0.49 (0.34-0.70)</b>	<0.001
	Decolonization	17%	9%		

# % Hospital Transfers Due to Infection



## Intervention vs Baseline

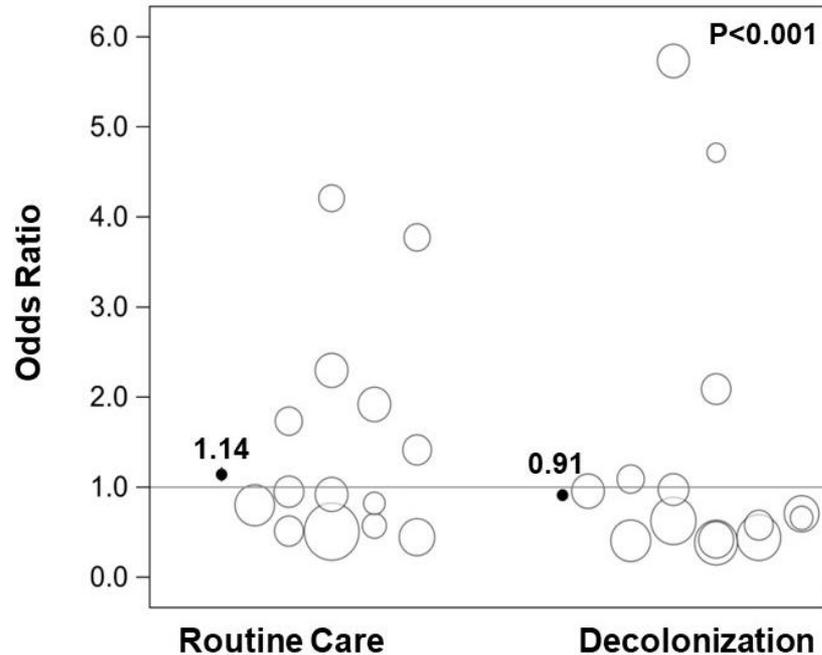
Decolonization = 0.68

Routine = 1.00

Difference in Differences: **32%**

**$P < 0.001$**

# % Discharges to Hospitals



## Intervention vs Baseline

Decolonization = 0.91

Routine = 1.14

Difference in Differences: **23%**

**$P < 0.001$**

# Number Needed to Treat

## Hospitalization due to infection

- Treat 10 residents to prevent one hospitalization
- 1.9 hospitalizations prevented per month for a 100-bed NH

# **Training Guides & Ready-to-Use Tools**

# Decolonization Success Depends on Application

- Lack of training shown to yield no benefit
- Training pearls for CHG
  - Massage firmly
  - Avoid cotton cloths
  - Clean wounds, devices, breaks in skin
  - Check lotion, skin product compatibility
  - 4% rinse-off CHG, 2% leave-on (air dry)

Chlorhexidine Only Works If Applied Correctly: Use of a Simple Colorimetric Assay to Provide Monitoring and Feedback on Effectiveness of Chlorhexidine Application

Laura Supple, BS;<sup>1</sup> Monika Kumaraswami, MD;<sup>1</sup> Sirisha Kundrapu, MD, MS;<sup>2</sup> Venkata Sunkesula, MD, MS;<sup>2</sup> Jennifer L. Cadnum, BS;<sup>2</sup> Michelle M. Nerandzic, BS;<sup>1</sup> Myreen Tomas, MD;<sup>3</sup> Curtis J. Donskey, MD<sup>2,3</sup>

We used a colorimetric assay to determine the presence of chlorhexidine on skin, and we identified deficiencies in preoperative bathing and daily bathing in the intensive care unit. Both types of bathing improved with an intervention that included feedback to nursing staff. The assay provides a simple and rapid method of monitoring the performance of chlorhexidine bathing.

*Infect Control Hosp Epidemiol* 2015;00(0):1-3

Popovich KJ *Int Care Med* 2010;36(5):854-8  
Supple L *ICHE* 2015;36(9):1095-7



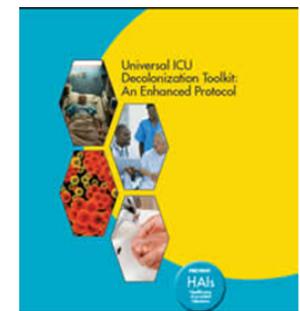
- Clinicians & Providers
- Education & Training
- Hospitals & Health Systems**
  - Hospital Resources
    - Emergency Department Tools and Resources
    - Emergency Severity Index
    - Guides for Patients and Families

## Universal ICU Decolonization: An Enhanced Protocol

### Introduction and Welcome

This enhanced protocol is based on materials successfully used in the REDUCE MRSA Trial (**R**andomized **E**valuation of **D**ecolonization vs. **U**niversal **C**learance to **E**liminate Methicillin-Resistant *Staphylococcus aureus*), which found that universal decolonization was the most effective intervention. Universal decolonization led to a 37 percent reduction in MRSA clinical cultures and a 44 percent reduction in all-cause bloodstream infections.

Publication # 13-0052-EF



<https://www.ahrq.gov/hai/universal-icu-decolonization/index.html>



## Healthcare-Associated Infections Program

Combating Antibiotic-Resistant Bacteria

Comprehensive Unit-based Safety Program (CUSP)

National Scorecard Reports

Reducing Hospital-Acquired Conditions

Tools

Ambulatory Surgery Centers Toolkit

C difficile Toolkit

Central Line Insertion Checklist

CLABSI and CAUTI Prevention in ...

# Toolkit for Decolonization of Non-ICU Patients With Devices

This toolkit can help hospital infection prevention programs implement a decolonization protocol that was found to reduce bloodstream infections by more than 30 percent in adult inpatients who were not in intensive care units (ICUs) and who had specific medical devices. It includes implementation instructions, demonstration videos, and customizable tools.

## Toolkit Contents

The toolkit contains protocols for implementing decolonization with chlorhexidine gluconate antiseptic soap and mupirocin along with instructional handouts for staff and patients, written and video training materials to educate staff, staff skills assessments, “huddle” documents with key reminders, and frequently asked questions for staff and patients. It is suggested that you start with Introduction—Toolkit Overview and Recommended Prelaunch Activities, but use the other materials in any order or combination that meets your facility’s needs.

The contents of this toolkit are below:

[Introduction—Toolkit Overview, Decision Making, and Recommended Prelaunch Activities](#)

[Nursing Protocols](#)

[Instructional Handouts for Staff and Patients](#)

[Staff Training Documents and Videos](#)

[Staff Training Videos](#)

[Adherence and Skills Assessment](#)

<https://www.ahrq.gov/hai/tools/abate/index.html>

# SHIELD MDRO Acute & Long-Term Care Toolkits

## Is SHIELD Right for You?

The SHIELD intervention is right for you if:

- Your facility is experiencing cultures or infections due to MDROs
- Your facility is worried about MDROs in general
- Your facility is willing to do a campaign to reduce MDROs
- Your facility is interested in the benefits of “decolonization” but needs “how to” help

The SHIELD program is effective against the following organisms:

- CRE: carbapenem-resistant Enterobacteriaceae
- MRSA: methicillin resistant *Staphylococcus aureus*
- VRE: vancomycin-resistant Enterococcus
- ESBL: extended spectrum beta-lactamase producers



**S**hared  
**H**ealthcare  
**I**ntervention to  
**E**liminate  
**L**ife-threatening  
**D**issemination of MDROs

Hospital Toolkit

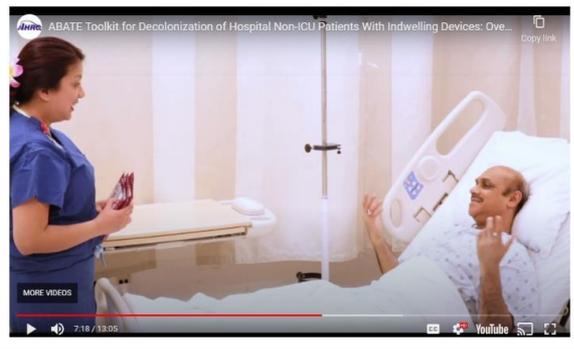
Nursing Home Toolkit

LTACH Toolkit

[www.ucihealth.org/shield](http://www.ucihealth.org/shield)

# Training Video for CHG Bathing

- CHG bathing and showering instructions
- Scenarios for how to encourage patients to accept bath
- Commonly missed and important protocol details (i.e., cleaning lines, tubes, drains, superficial wounds)
- Instructions for patients wishing to self-bathe



<https://www.ahrq.gov/hai/tools/abate/index.html>

# **Importance of Nasal Decolonization**

## *S. aureus* and MRSA Infections in ICUs

- Adult ICU infections assessed in single-day multi-center chart review
- 1150 centers in 88 countries

Causal Agent	Africa	America (North)	America (Central/South)	Asia/ Middle East	Australasia	Europe (Eastern)	Europe (Western)
<i>S. aureus</i>	8%	23%	17%	10%	17%	16%	15%
MRSA	5%	10%	7%	5%	4%	6%	2%

## ***S. aureus* Prevention in ICUs**

- *S. aureus* main reservoir is the nose
- Nasal decolonization key to preventing *S. aureus* disease <sup>1</sup>
- Adoption of nasal mupirocin for universal ICU decolonization is variable despite burden of *S. aureus* ICU infections

<sup>1</sup> van Rijen M et al. Cochrane Rev 2008;4:CD006216

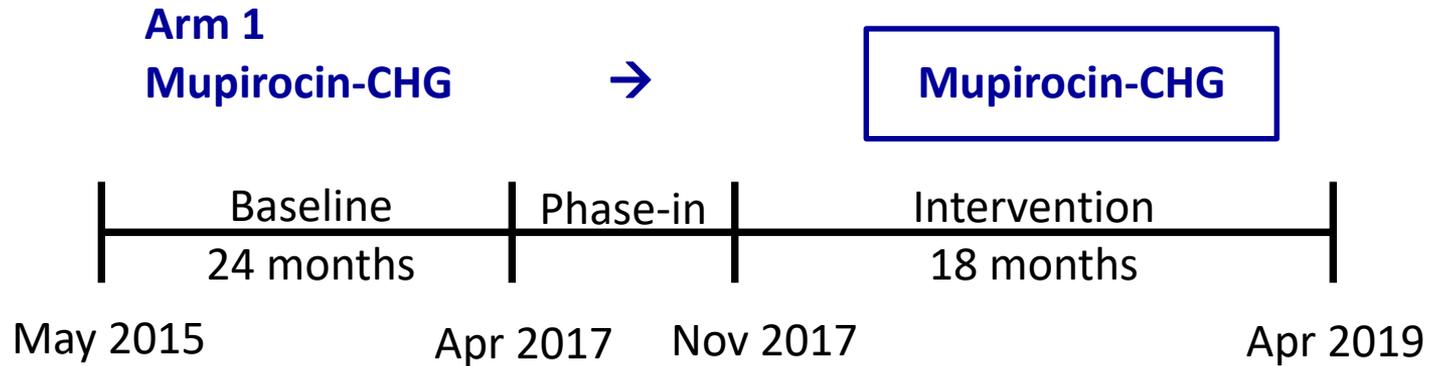
# Rationale for Mupirocin-Iodophor Swap Out Trial

- Some are concerned universal ICU mupirocin will elicit resistance
- Iodophor and other antiseptics are less likely to lead to resistance
- Swap Out Trial: **non-inferiority cluster randomized trial** to assess if iodophor is as effective as mupirocin in preventing *S aureus* cultures when combined with CHG baths for ICU universal decolonization

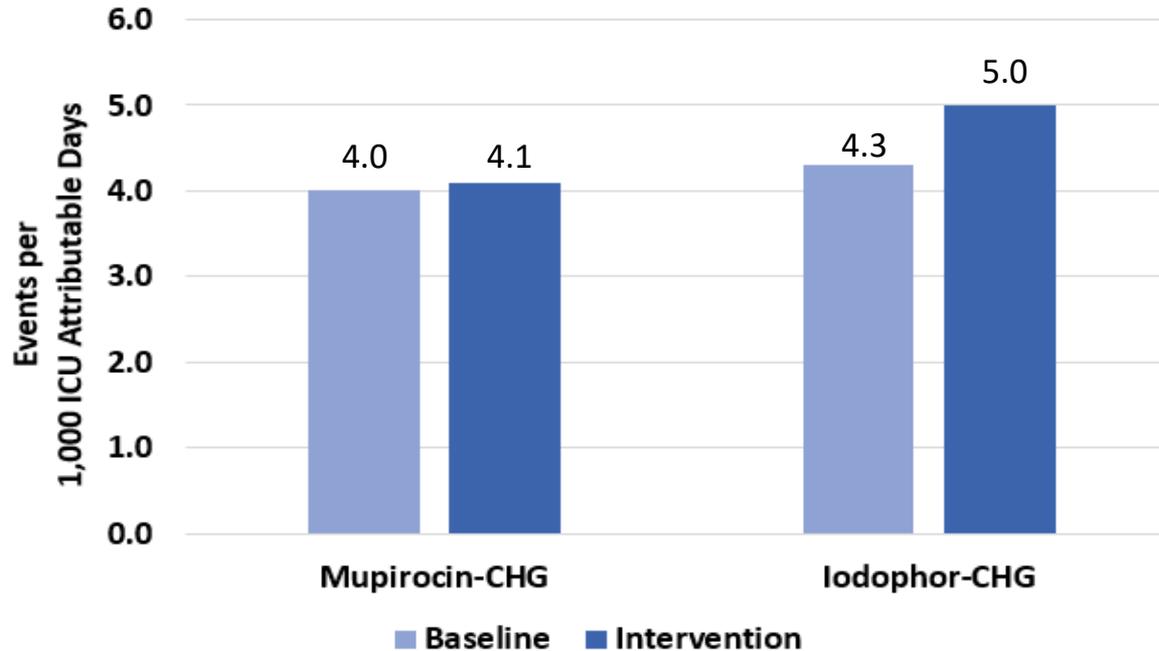
# Mupirocin-Iodophor Swap Out Trial

- 18 Month cluster-randomized ICU non-inferiority study
- 137 HCA hospitals, 233 adult ICUs
  - **Mupirocin Arm:** Daily CHG & 5 days twice daily 2% mupirocin
  - **Iodophor Arm:** Daily CHG & 5 days twice daily 10% iodophor
- Outcomes
  - *S. aureus* (MRSA & MSSA) ICU clinical cultures (**primary**)
  - MRSA clinical cultures
  - All-cause bacteremia
  - Emergence of resistance to mupirocin, iodophor

# Baseline and Intervention Periods

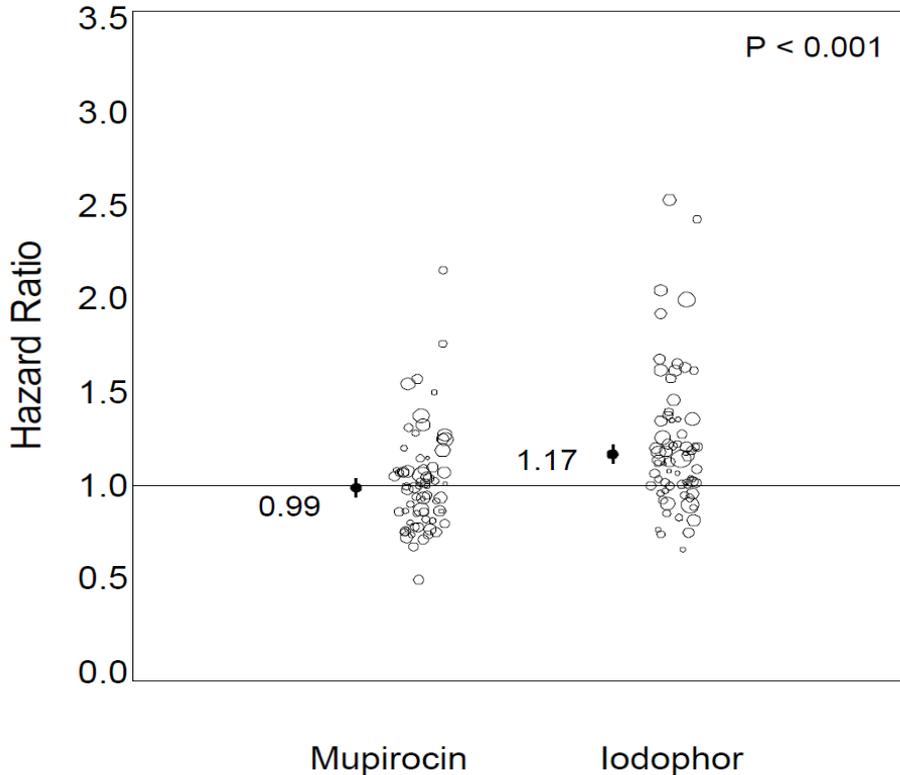


# ICU-Attributable *S. aureus* Clinical Cultures As Randomized: Crude Event Rates



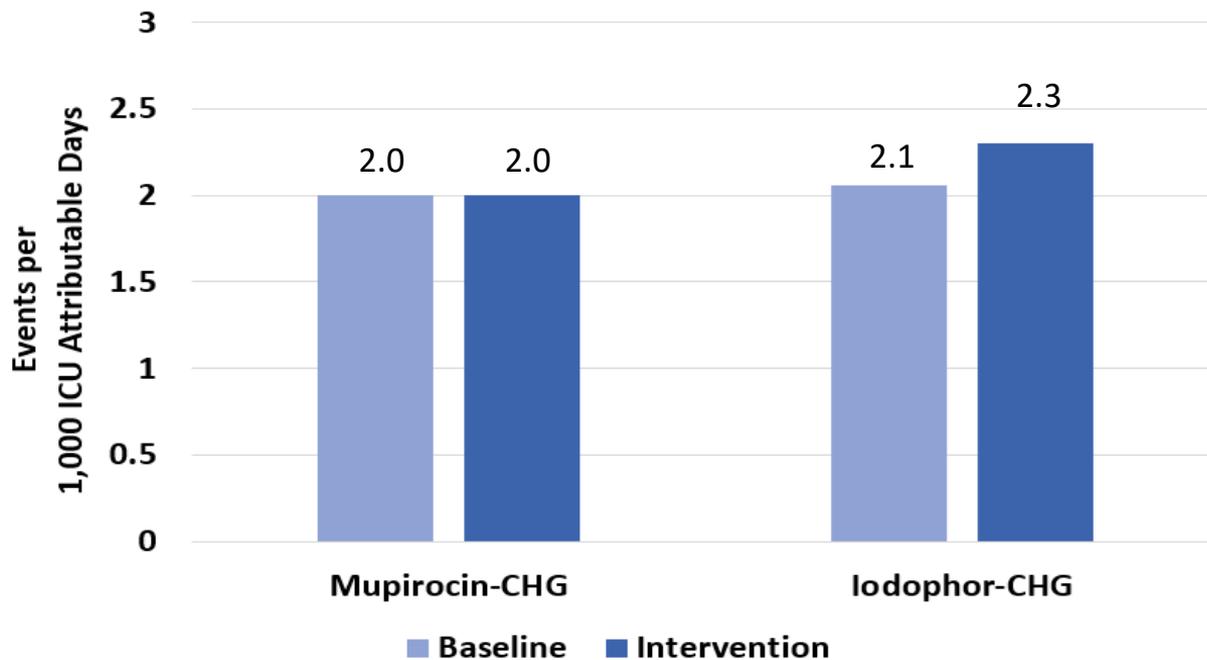
Provided rates are crude rates summed across all participating hospitals. Patient-days after each event were excluded

# ICU-Attributable *S. aureus* Clinical Cultures As Randomized Clustered Analysis



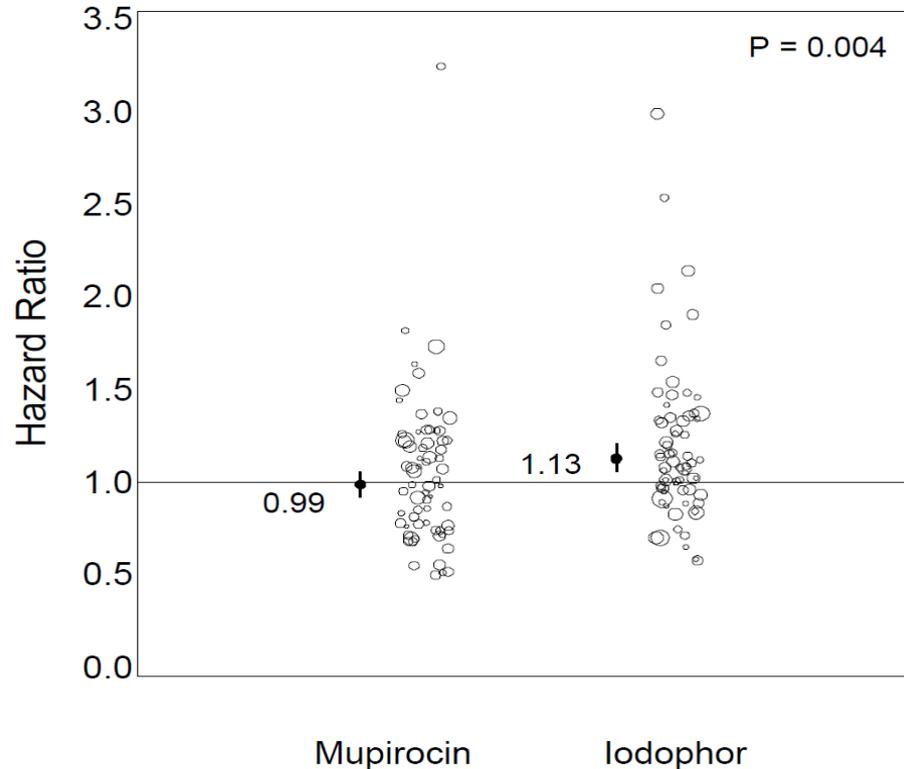
**As Randomized Conclusion:  
Mupirocin superior to iodophor  
18% fewer *S. aureus* cultures  
 $P < 0.001$**

# ICU-Attributable MRSA Clinical Cultures As Randomized Crude Event Rates



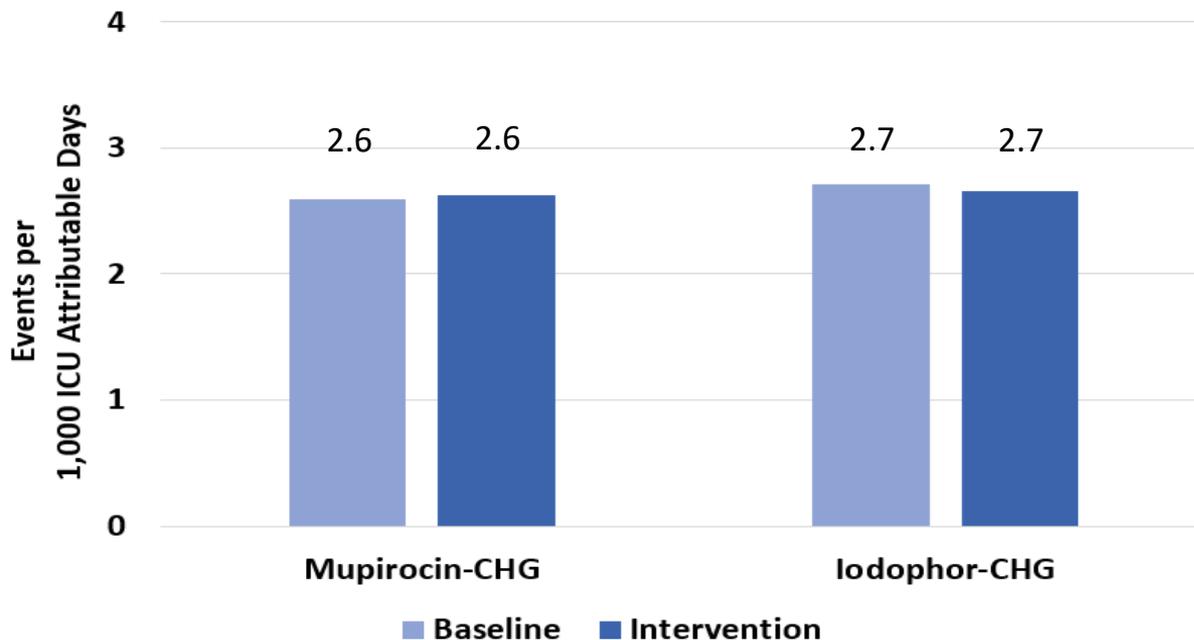
Provided rates are crude rates summed across all participating hospitals. Patient-days after each event were excluded

# ICU-Attributable MRSA Clinical Cultures As Randomized Clustered Analysis



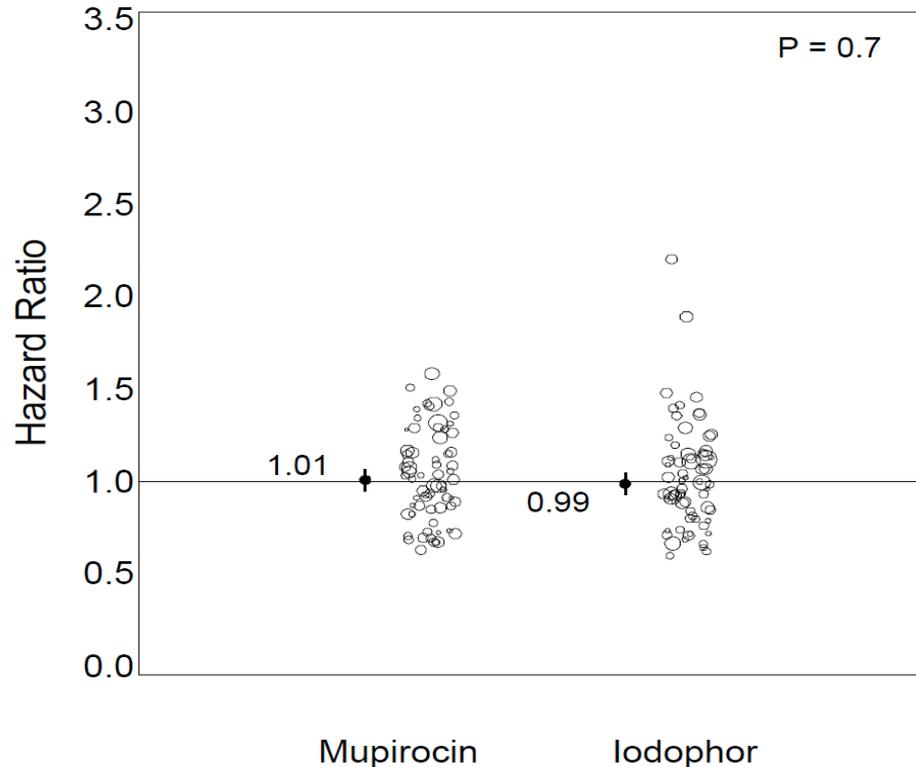
**As Randomized Conclusion:**  
**Mupirocin superior to iodophor**  
**14% fewer MRSA cultures**  
**P<0.004**

# ICU-Attributable Bloodstream Infections As Randomized Crude Event Rates



Provided rates are crude rates summed across all participating hospitals. Patient-days after each event were excluded

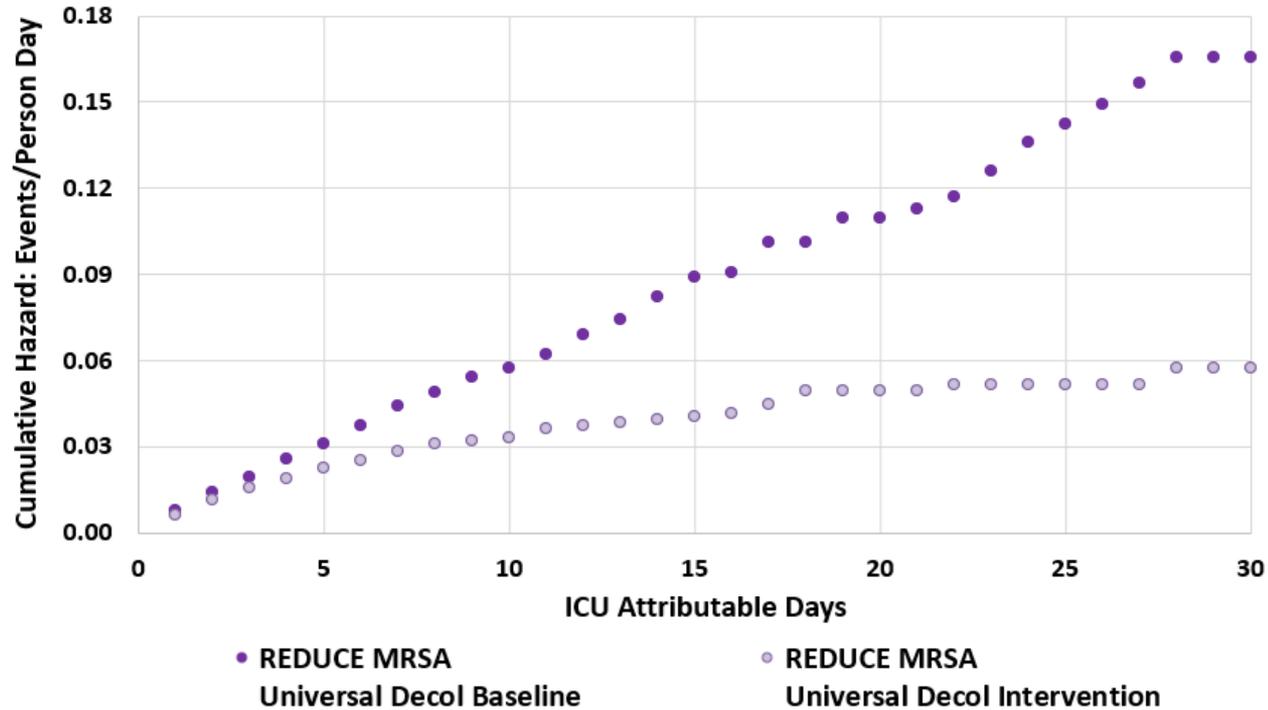
# ICU-Attributable Bloodstream Infections As Randomized Clustered Analysis



**As Randomized Conclusion:  
Iodophor non-inferior to  
mupirocin  
P=0.7**

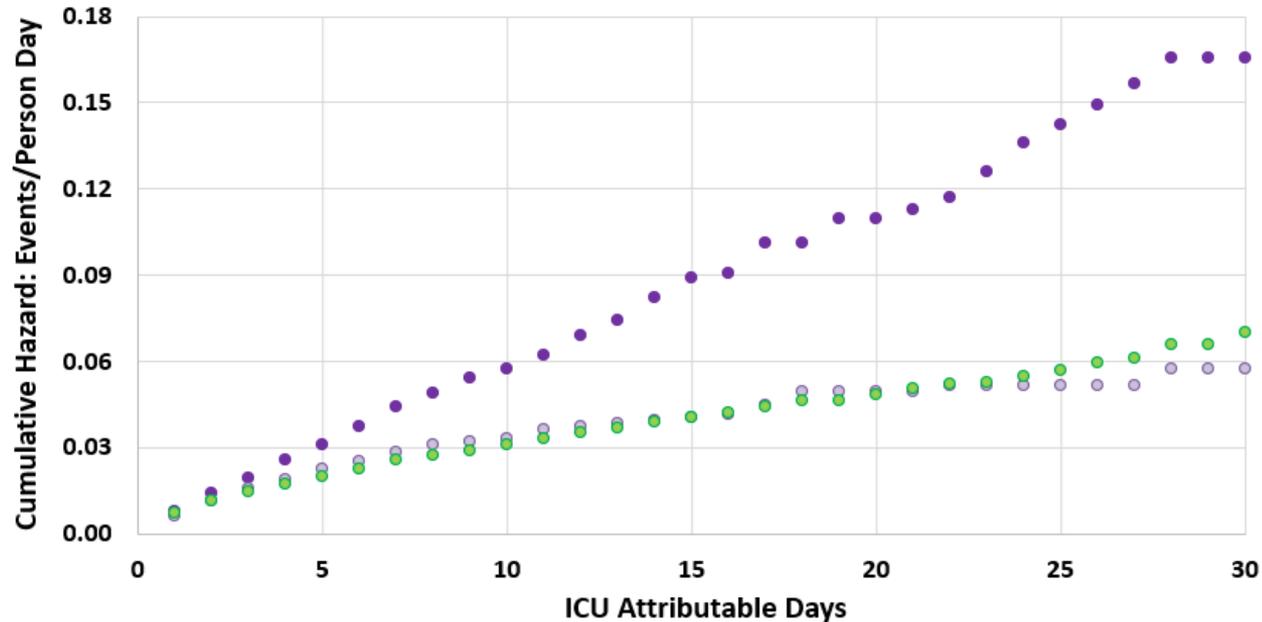
# REDUCE MRSA & Swap Out Trials

## Cumulative Hazard of *S. aureus* Clinical Cultures



# REDUCE MRSA & Swap Out Trials

## Cumulative Hazard of *S. aureus* Clinical Cultures



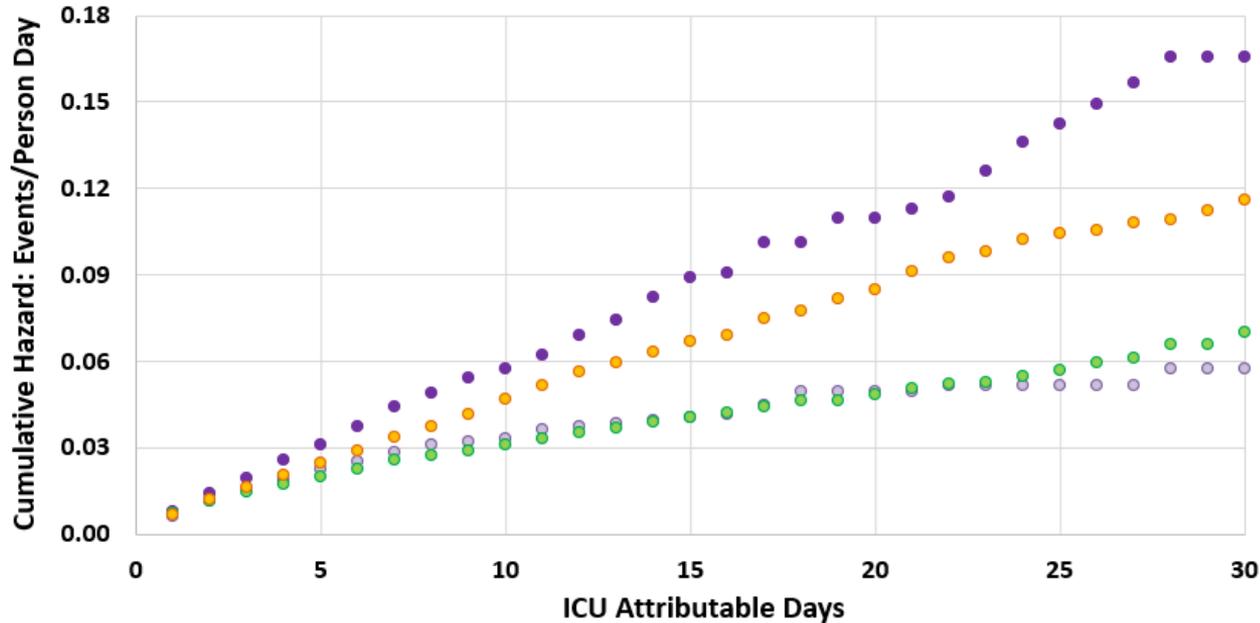
● REDUCE MRSA  
Universal Decol Baseline

● Swap Out  
Mupirocin Intervention

● REDUCE MRSA  
Universal Decol Intervention

# REDUCE MRSA & Swap Out Trials

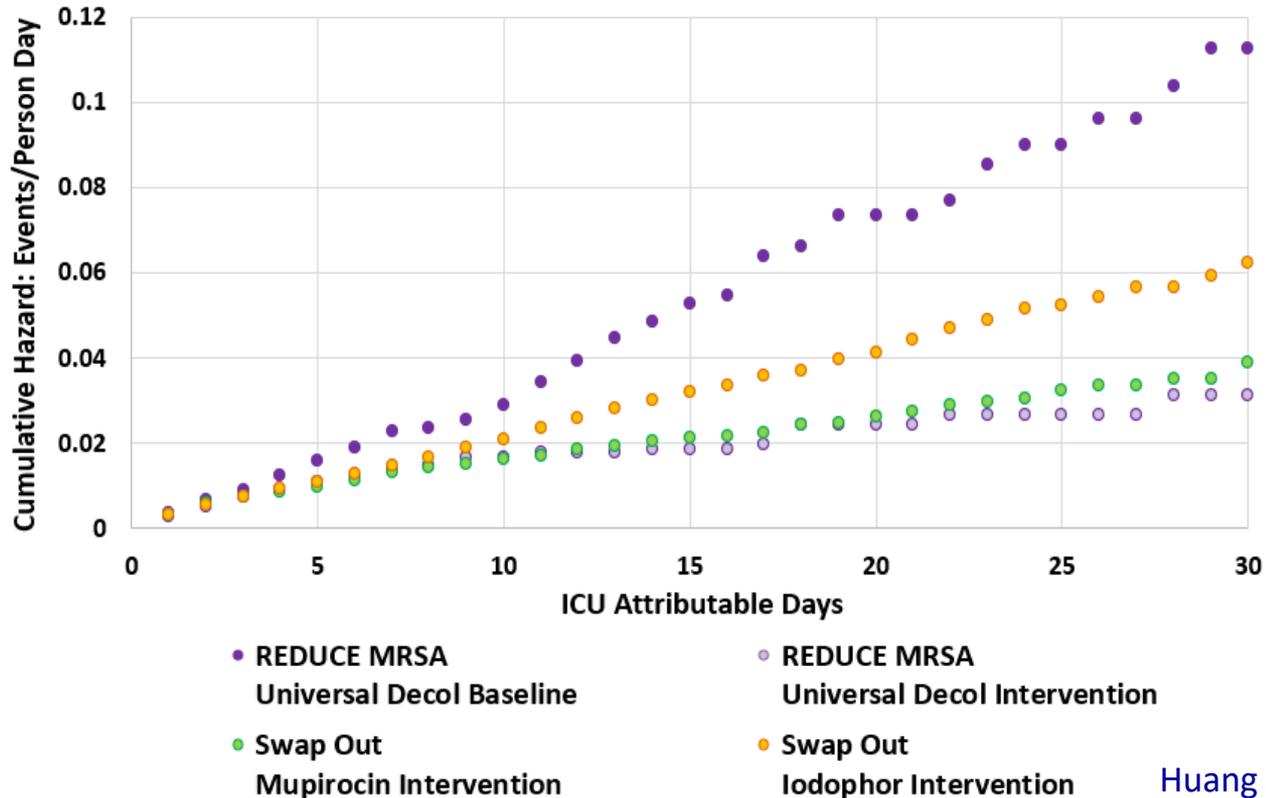
## Cumulative Hazard of *S. aureus* Clinical Cultures



- REDUCE MRSA Universal Decol Baseline
- REDUCE MRSA Universal Decol Intervention
- Swap Out Mupirocin Intervention
- Swap Out Iodophor Intervention

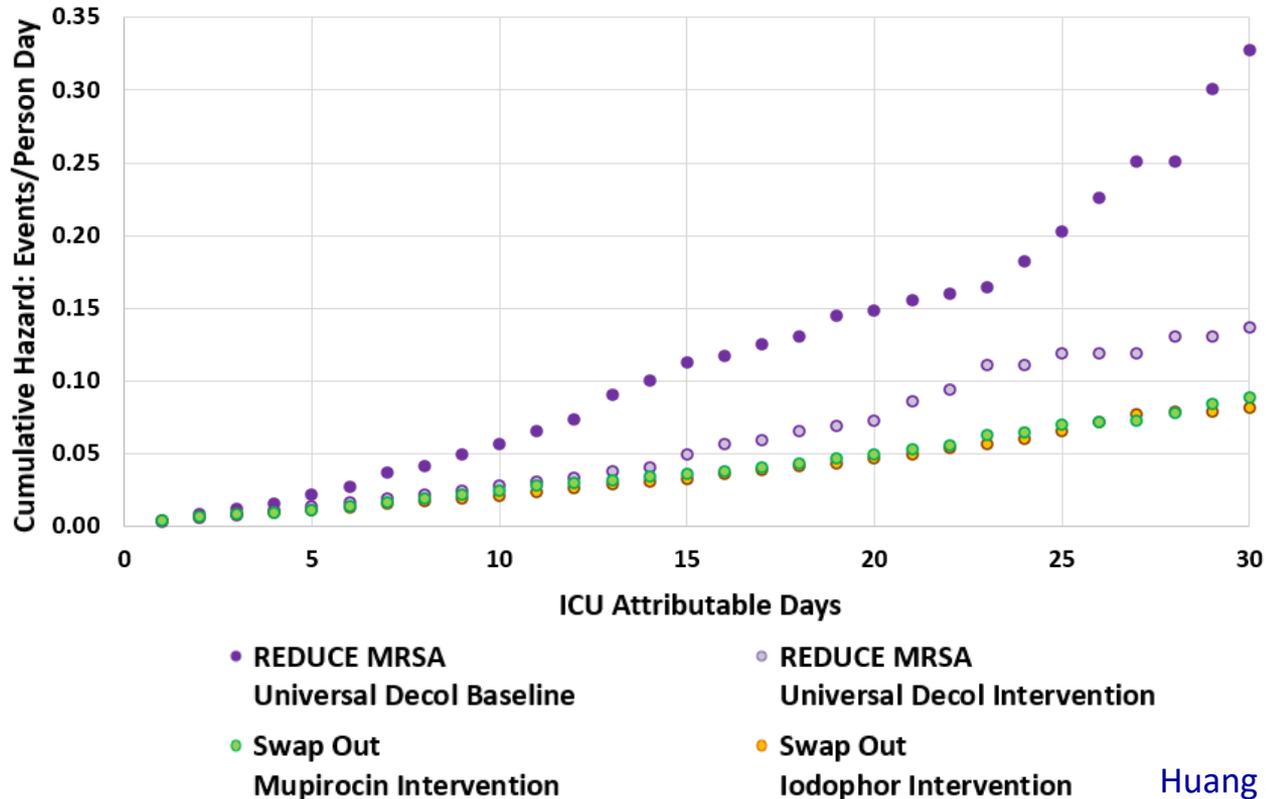
# REDUCE MRSA & Swap Out Trials

## Cumulative Hazard of MRSA Clinical Cultures



# REDUCE MRSA & Swap Out Trials

## Cumulative Hazard of Bloodstream Infection

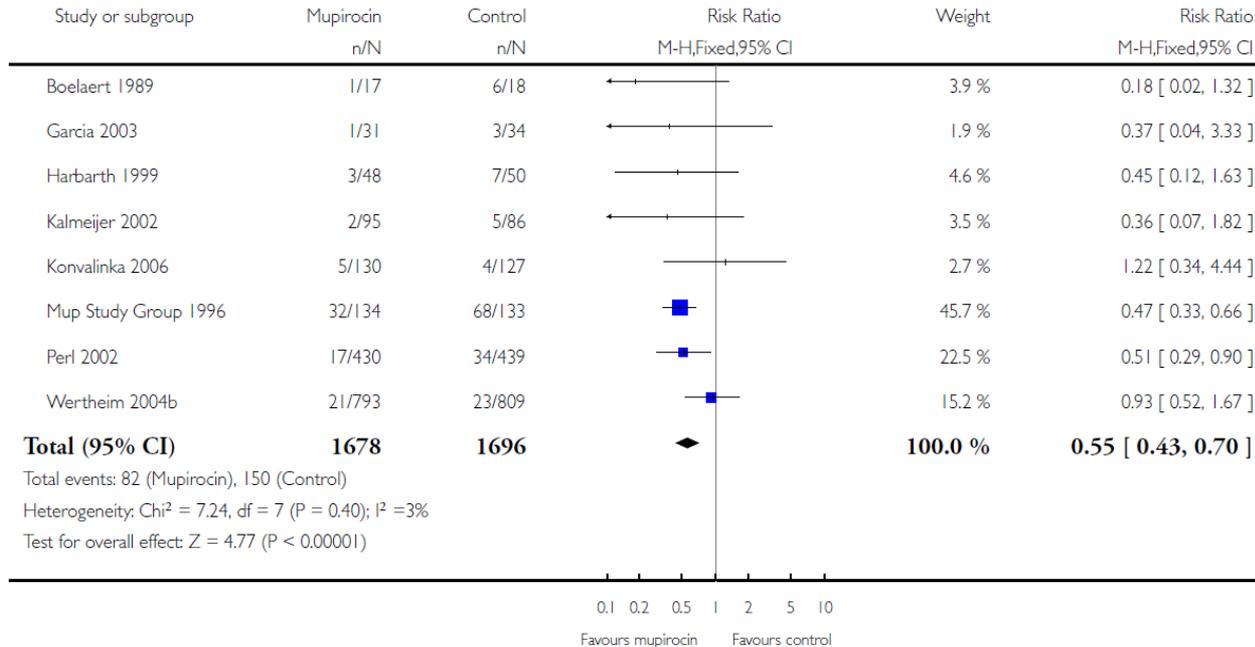


# Importance of ICU Nasal Decolonization for MRSA

- *S. aureus* remains a formidable pathogen in ICUs
- Superiority of mupirocin over iodophor supports value of nasal decolonization
- Iodophor is superior to no nasal decolonization. May be preferred if mupirocin resistance is high or prescription logistics are problematic
- Mupirocin-CHG effect in reducing *S. aureus*, MRSA, and bloodstream infections persisted over 10 years, suggesting minimal emergence of resistance

# Mupirocin Alone Works

**45%** ↓ nosocomial MRSA infection among treated carriers



# Role of CHG for MRSA and Disease Prevention

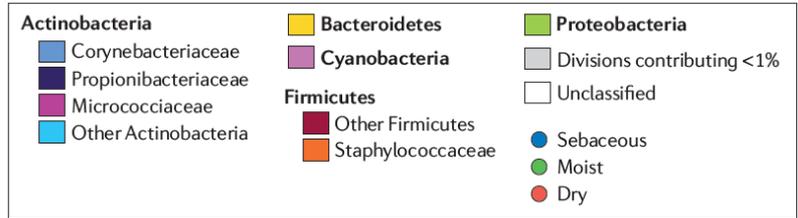
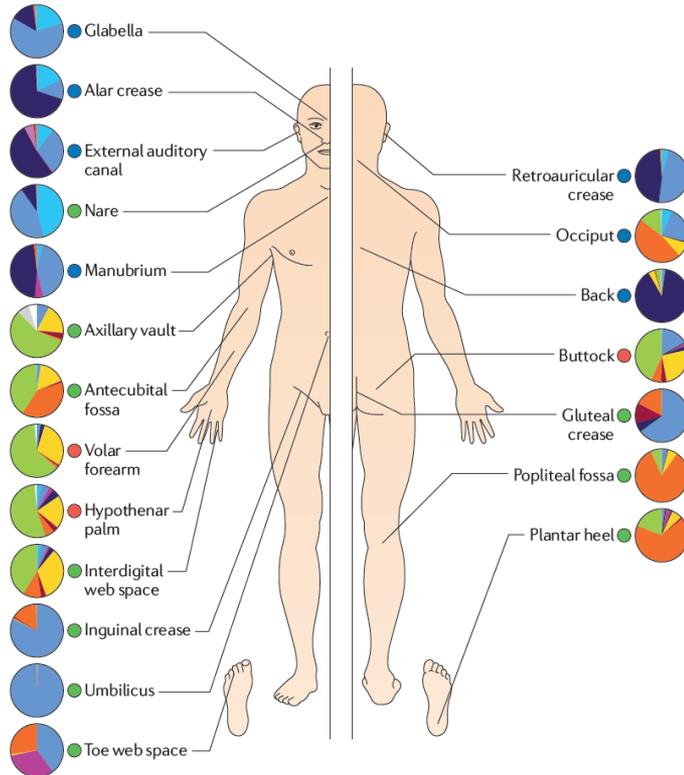
- As solo agent, CHG
  - Does not sufficiently clear MRSA for individual carriers<sup>1-2</sup>
  - Does reduce skin burden and transmission to others
  - Is active against other MDROs and pathogens

<sup>1</sup> Harbarth et al. AACT 1999;43(6):1412-16

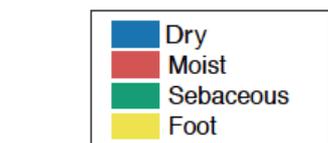
<sup>2</sup> Fritz et al. ICHE 2011;32(9):872-80

# **Microbiome Effects by Decolonization**

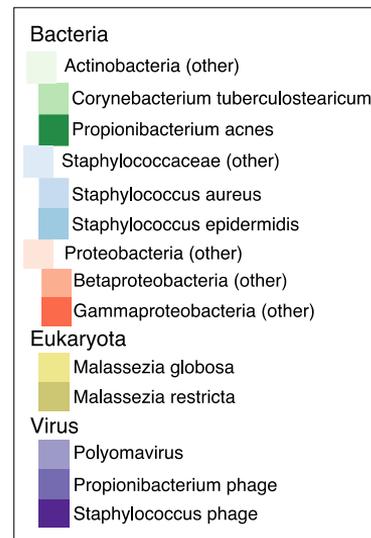
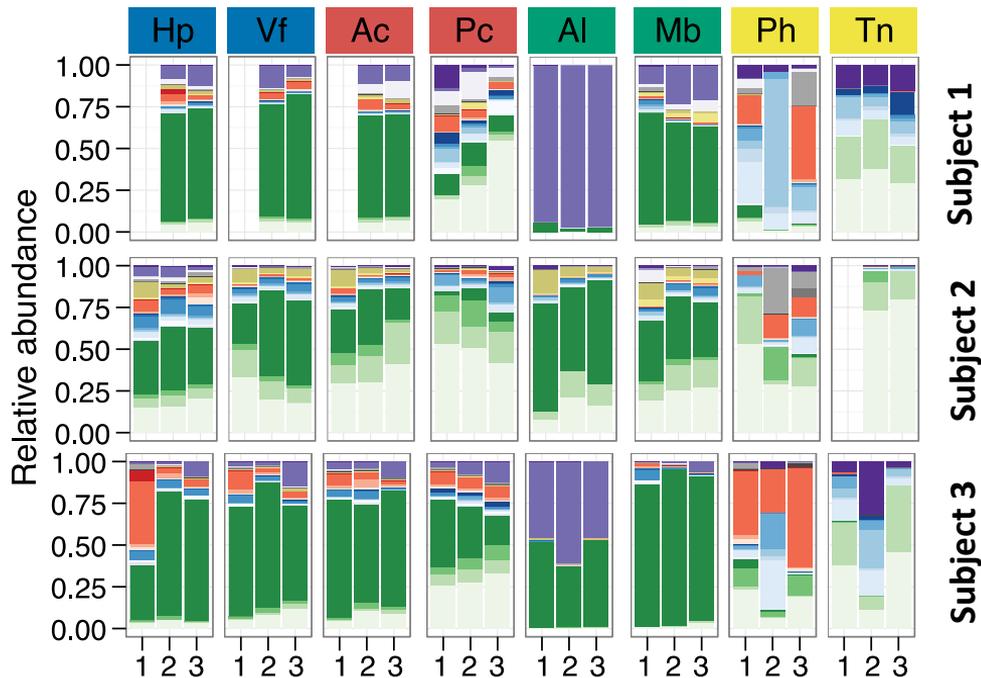
# Biogeography of Human Skin Microbiota



# Skin Microbiome: Individual Signatures



Hp = palm  
 Vf = forearm  
 Ac = antecube  
 Pc = popliteal crease  
 Al = alar crease  
 Mb = manubrium  
 Ph = phalanx  
 Tn = toenail

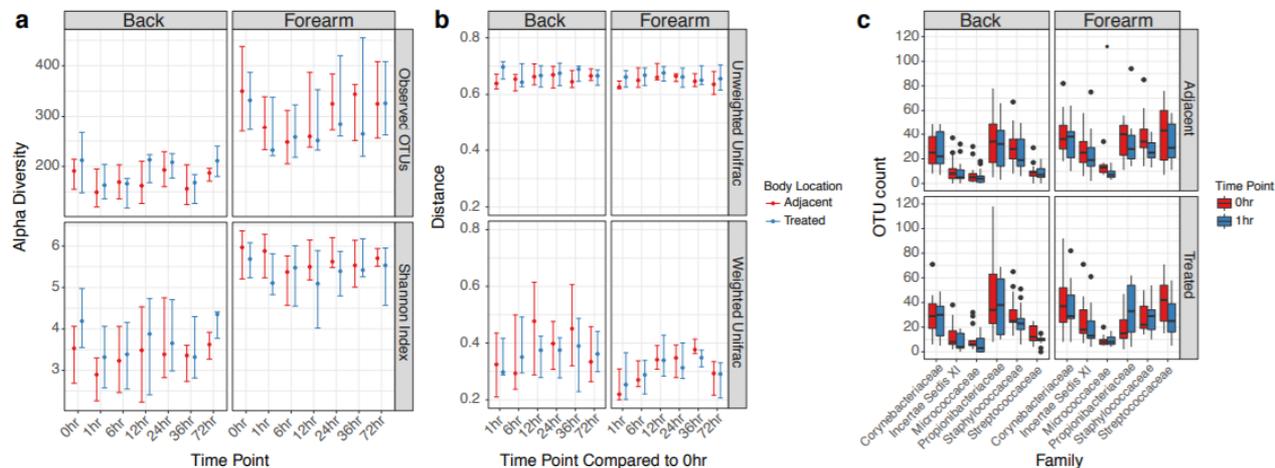


Timepoint 1-3 represent >1 year

**Does CHG Reduce or Change  
Skin Biodiversity?**

# CHG and Healthy Subjects: No Change in Diversity or Richness

13 healthy subjects 23-30y tested several antiseptics on forearm and upper back. Sampled 1, 6, 12, 24, 36, 72h

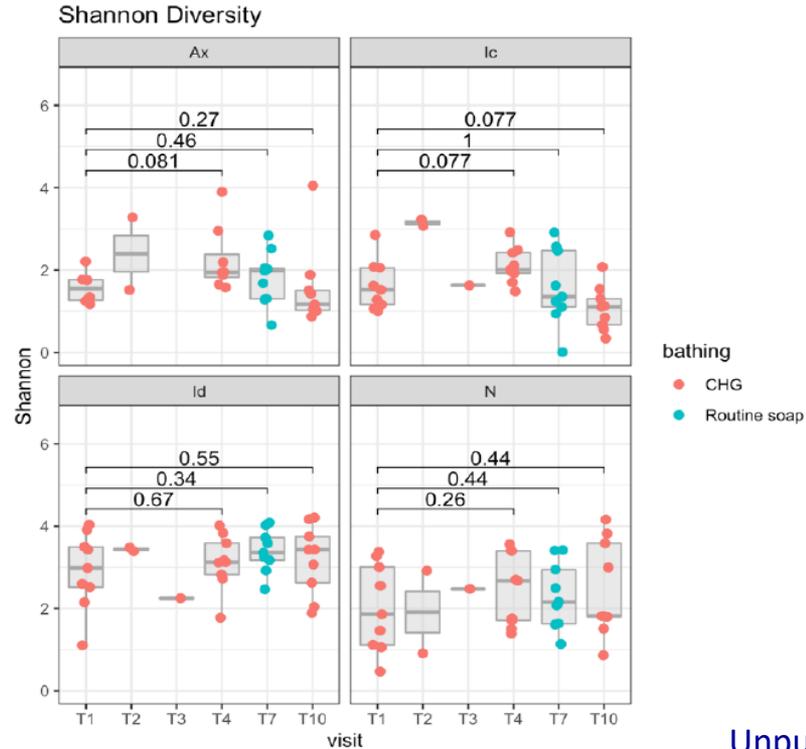


**Fig. S7.** Chlorhexidine treatment does not elicit bacterial shifts. (A) Longitudinal measurements of observed species and Shannon diversity for adjacent and chlorhexidine treated body sites at the back and forearm. Data is presented by median points and interquartile regions. (B) Weighted and Unweighted UniFrac distances of subjects' longitudinal time points compared to their individual baseline communities at chlorhexidine treated and adjacent body sites. Points represent the median of participants. Error bars designate interquartile regions. (C) Box and whisker plots of OTU richness for major taxa at adjacent and chlorhexidine treated body sites between baseline and 1hr time points. \*  $P < 0.05$  by Wilcoxon rank sum test (Mann-Whitney U test).

# CHG and Hospitalized Patients: Skin Microbiome Diversity Preserved

10 hospitalized adults  
receiving the following  
weekly bathing regimens:

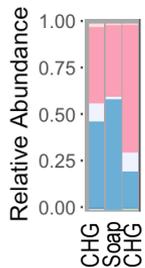
- 1) CHG in the hospital
- 2) Routine soap at home
- 3) CHG at home



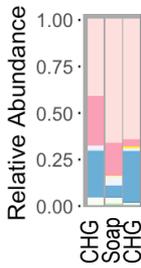
Unpublished data

# CHG and Hospitalized Patients: Axillary Skin Microbiome Taxa

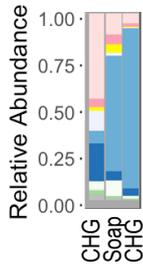
**Patient 1**



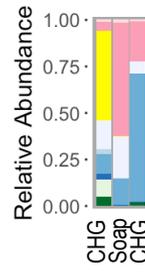
**Patient 2**



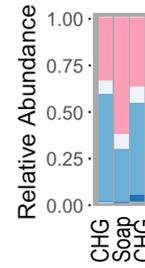
**Patient 3**



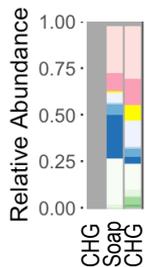
**Patient 4**



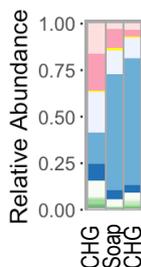
**Patient 5**



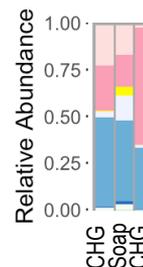
**Patient 6**



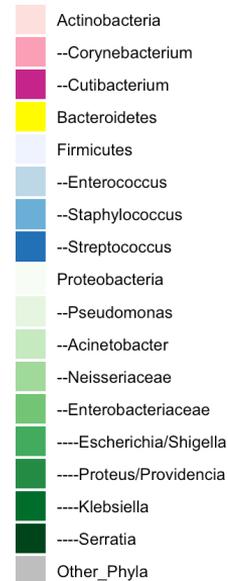
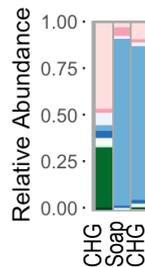
**Patient 7**



**Patient 8**

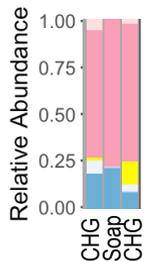


**Patient 9**

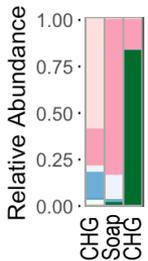


# CHG and Hospitalized Patients: Inguinal Skin Microbiome Taxa

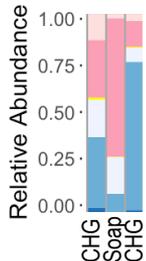
**Patient 1**



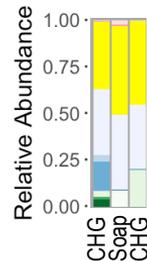
**Patient 2**



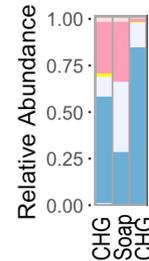
**Patient 3**



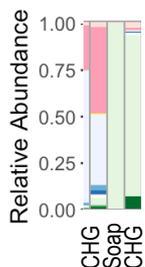
**Patient 4**



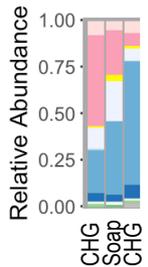
**Patient 5**



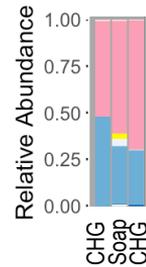
**Patient 6**



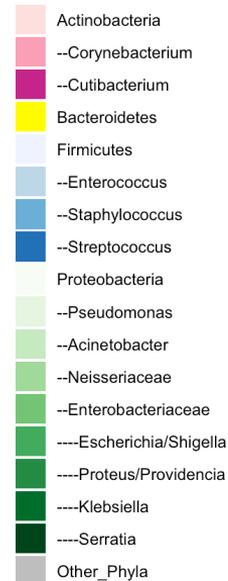
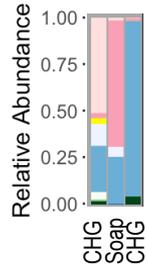
**Patient 7**



**Patient 8**



**Patient 9**

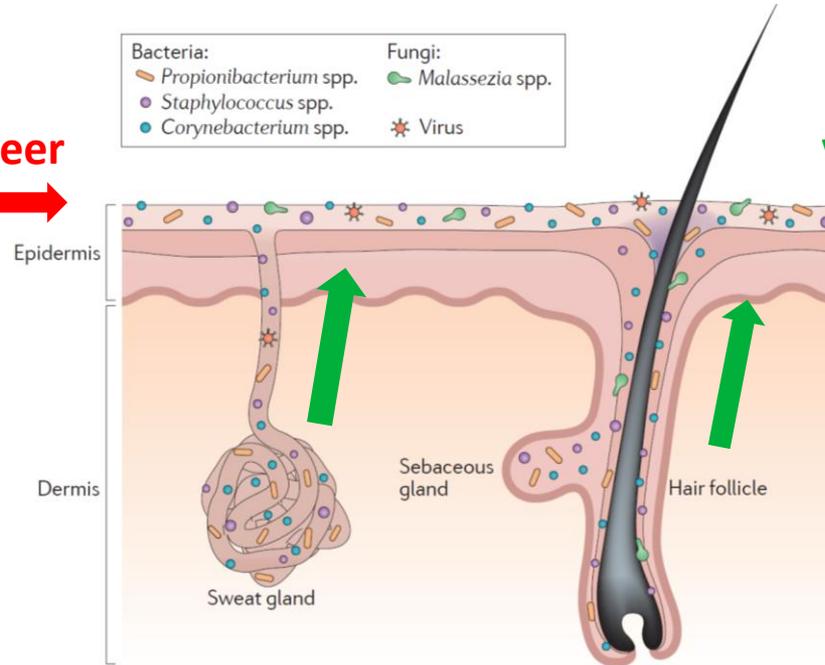


# Microbial Layers of the Skin

Unwanted MDRO veneer



Resident vs  
Transient Bacteria



Veneer cleared by CHG

# Summary: Decolonization for High-Risk Patients

- **Impact**

- Protects ICU patients & those with devices from infection
- Reduces MDRO prevalence, spread, and infection
- Prevents hospitalization and infection in nursing homes
- Reduces bloodstream infections
- Stable benefit over nearly a decade
- Microbiome preserved



- **Future Work**

- Assess and expand study of high-risk patients
- Quantify risk of resistance vs averted infections
- Disentangle patient factors, antibiotics
- Expand arsenal to additional effective products

