

**Decolonization to Reduce MDROs in Healthcare: Who, What, Where, When, and Why?**  
**Prof. Susan Huang, University of California, Irvine School of Medicine**  
**Broadcast from the 2019 Healthcare Infection Society Conference**

**Live broadcast from**



**The 11th Healthcare Infection Society  
International Conference**  
ACC, Liverpool, UK, 26-28 November 2018



**Healthcare  
Infection  
Society**

**Decolonization to  
Reduce MDROs in Healthcare:  
*Who, What, Where, When, and Why?***

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## **Disclosures**

- Conducting clinical studies in which participating hospitals and nursing homes receive contributed products from Sage Products, Molnlycke, 3M, Xttrium, Clorox, and Medline
- Companies contributing product have no role in design, conduct, analysis, or publication
- Primarily discussing chlorhexidine (CHG)
- Select literature

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## A Lowbury Legacy

### Use of 4% Chlorhexidine Detergent Solution (Hibiscrub) and Other Methods of Skin Disinfection

E. J. L. LOWBURY, H. A. LILLY

*British Medical Journal*, 1973, 1, 510-515

#### Transient skin flora

31  
 m Their removal by cleansing or disinfection in relation to their mode of deposition

*J. Hyg., Camb.* (1979), 82, 89  
 Printed in Great Britain

scrub left a  
 Journal of Clinical Pathology, 1978, 31, 919-922

3  
 n Accident Hospital, Birmingham, UK

### Detergents compared with each other and with antiseptics as skin 'degerming' agents

BY H. A. LILLY, E. J. L. LOWBURY AND M. D. WILKINS  
*MRC Industrial Injuries and Burns Unit, Birmingham Accident Hospital*

E. J. L. LOWBURY, H. A. LILLY, G. A. J. AYLIFFE

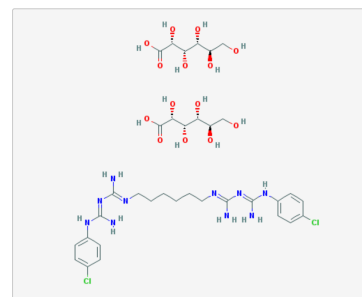
### Surgeons' Hands: Use of Antiseptics and Effects of Gloves on Skin Flora

Lowbury EJL BMJ 1971;1:510-5

## A Tour of Chlorhexidine Decolonization

- Why decolonize?
- Who should be decolonized?
- What concentrations should be used?
- Where on the body and how to apply?
- When and how often?

Chlorhexidine gluconate



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## **A Brief History of Chlorhexidine**

- Cationic antiseptic that disrupts cell membranes
- Discovered early 1950s by UK chemical company
- Antiseptic uses in healthcare
  - Hand antisepsis at 2% and 4%
  - Dental hygiene
  - 1990s: Cleaning of skin prior to central line insertion
  - 1990s: Pre-operative bathing
  - 2000s: Surgical prep
  - 2010s: Universal ICU bathing

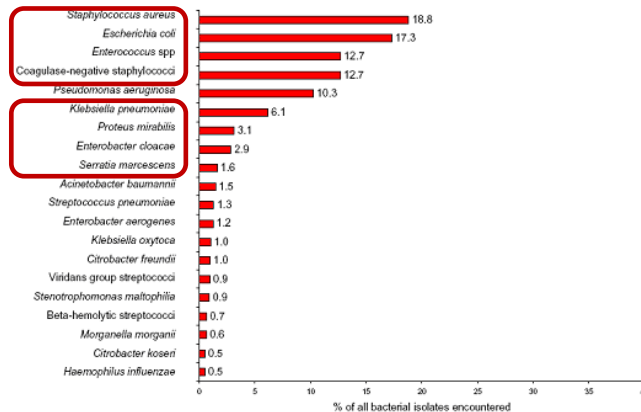
## **A Tour of Chlorhexidine Decolonization**

- **Why decolonize?**
- Who should be decolonized?
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## Frequency of Hospital Pathogens

Relative frequency of bacterial species/groups encountered in clinical specimens from inpatients



<http://www.microresistance.org/bacteriology.cfm>

## The Rise of MultiDrug-Resistant Organisms (MDROs)

- Methicillin Resistant *Staphylococcus aureus* (MRSA)
- Vancomycin Resistant Enterococcus (VRE)
- Multi-Drug Resistant Pseudomonas
- Multi-Drug Resistant Acinetobacter
- Extended Spectrum Beta Lactamase Producers (ESBLs)
- Carbapenem Resistant Enterobacteriaceae (CRE)
- Hypervirulent *Klebsiella pneumoniae* carbapenemase (KPC)
- *Candida auris*

10-15% of hospital patients harbor at least one of the above

64% of nursing home residents harbor at least one of the above

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## What is Decolonization?

- Topical antiseptics prevent bacterial carriage and infection
  - Chlorhexidine (CHG) for skin and wound bathing
  - CHG active against MDROs and other pathogens
  - Mupirocin or iodophor for nasal use
  - Strong safety record
- Universal use for vulnerable times, high risk populations

## 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
              - Risk for infection

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

## A Tour of Chlorhexidine Decolonization

- Why decolonize?
- **Who should be decolonized?**
- What concentrations should be used?
- Where on the body and how to apply?
- When and how often?

## Decolonization Trials

- Targeted Prevention
  - Recurrent *S. aureus* infection<sup>1</sup>
  - Pre-operative *S. aureus* carriers<sup>2-3</sup>
- Universal Prevention
  - ICU<sup>4-7</sup>
  - Non-ICU<sup>8</sup>
  - Post-Discharge<sup>9</sup>
  - Nursing Homes (Care Homes with Nursing)<sup>10</sup>

<sup>1</sup> Liu C CID 2011;52:285-92 (IDSA Guideline)

<sup>2</sup> Bode LGM NEJM 2010;362:9-17

<sup>3</sup> Perl T NEJM 2002;346:1871-7

<sup>4</sup> Climo M NEJM 2013;368:533-42

<sup>5</sup> Milstone A Lancet 2013;381:1099-106

<sup>6</sup> Huang SS NEJM 2013;368:2255-65

<sup>7</sup> Huang SS, clinicaltrials.gov NCT03140423

<sup>8</sup> Huang SS IDWeek 2017, Lancet, in press

<sup>9</sup> Huang SS IDWeek 2016, NCT01209234

<sup>10</sup> Huang SS, clinicaltrials.gov NCT03118232

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## ICU Decolonization Evidence Summary

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

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## The REDUCE MRSA Trial

Hospital Corporation of America (HCA Healthcare)  
Cluster randomized **43 hospitals (74 adult ICUs)** to:

- **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)

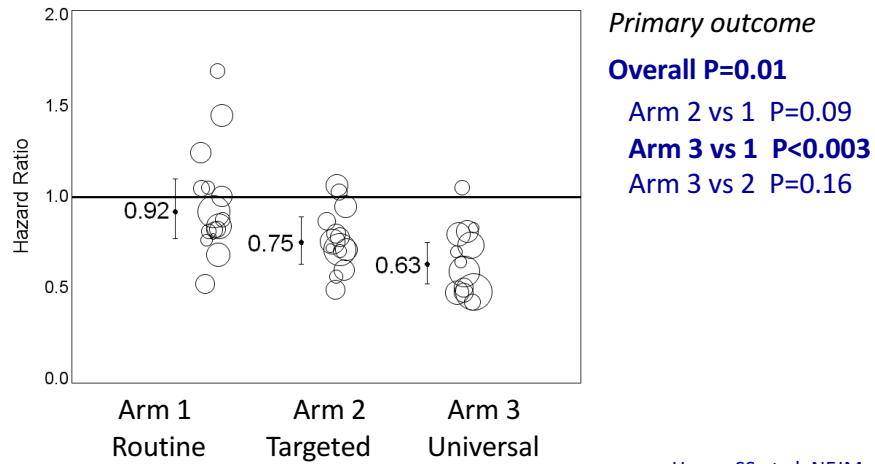
74,256 patients, 282,803 ICU patient days

Funded by AHRQ  
Huang SS NEJM 2013

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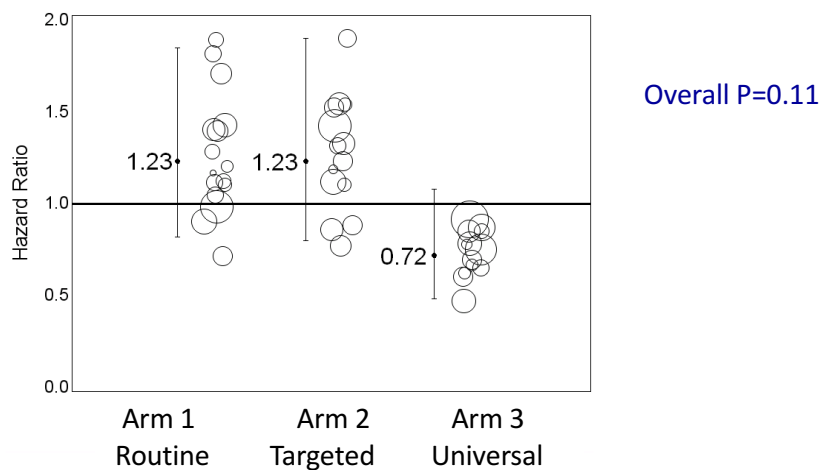
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### MRSA Clinical Cultures



Huang SS et al. NEJM  
2013;368:2255-2265

### MRSA Bloodstream Infection



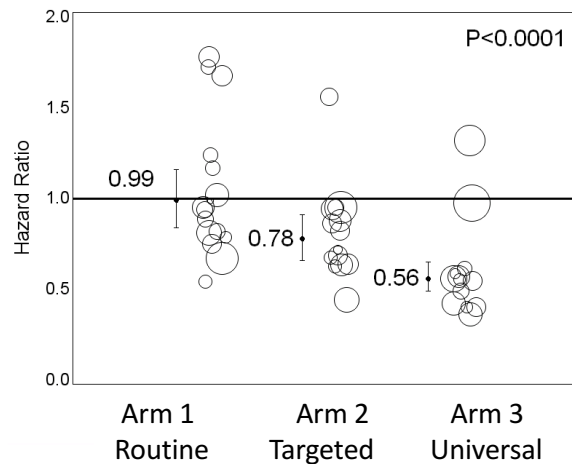
Huang SS et al. NEJM  
2013;368:2255-2265

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### 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  $P = 0.003$**

Huang SS et al. NEJM  
2013;368:2255-2265

### Additional Decolonization Impact

- Universal decolonization
  - 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>
- 80-90% of US hospitals use universal CHG bathing in an ICU <sup>6-7</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> Shuman EK et al. IDWeek 2014

<sup>7</sup> Russell D et al. ICHE 2016; 37(1):36-40

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## **Progression of Decolonization Trials**

- ICU **REDUCE MRSA Trial** and others
- **Non-ICU** **ABATE Infection Trial**



Active Bathing to Eliminate Infection Project

In press, Lancet  
Funded by NIH/NIAID  
Clinicaltrials.gov:NCT02063867

## **ABATE Infection Project** **Active Bathing to Eliminate Infection**

### **Trial Design**

- Cluster randomized trial with HCA Healthcare
- 53 hospitals, 194 adult non critical care units
- Includes: adult medical, surgical, step down, oncology
- Excludes: rehab, psych, peri-partum, BMT

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

- Routine policy for showering/bathing

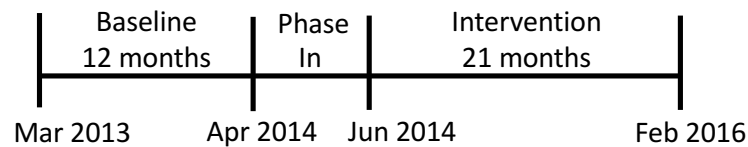
### **Arm 2: Decolonization**

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

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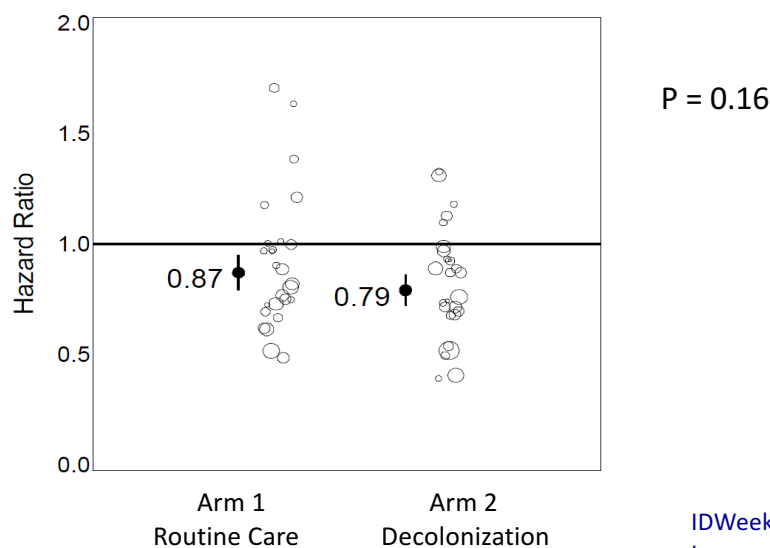
## Outcomes and Study Period

- **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 patients days (intervention)**



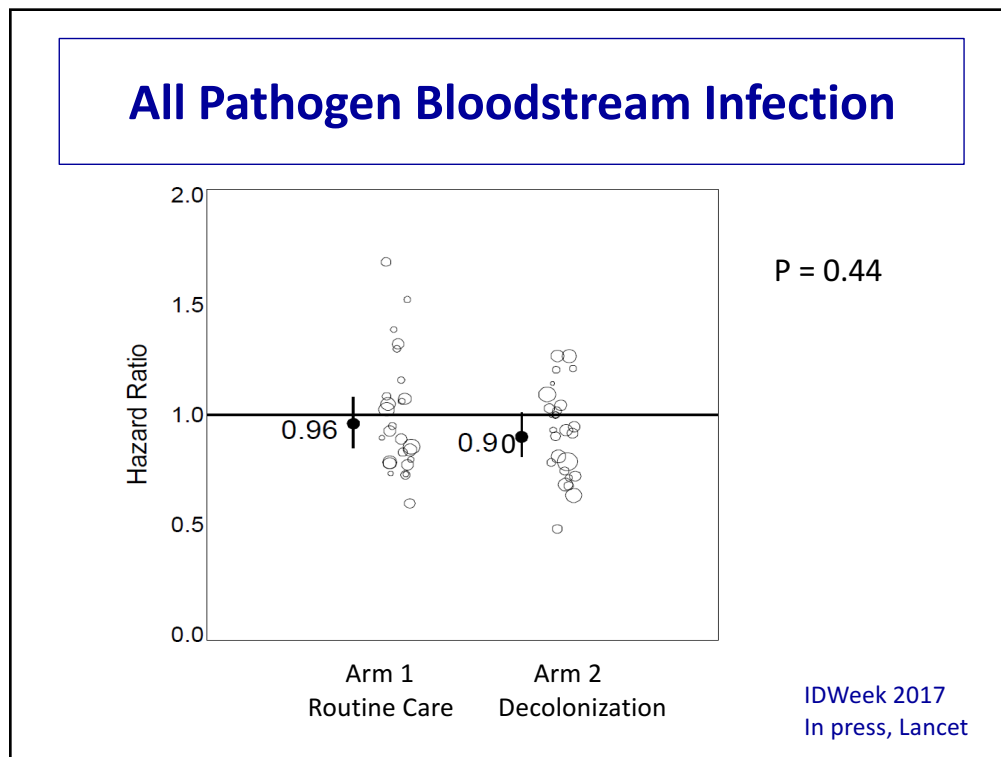
IDWeek 2017  
In press, Lancet

## MRSA & VRE Clinical Cultures



IDWeek 2017  
In press, Lancet

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### Subpopulation Analysis

- Post-hoc evaluation
- Are there subsets that may benefit due to higher risk?
  - High rate hospitals (top quartile)
  - Patients with central lines (CVC) and other devices
  - Oncology patients
  - Surgical patients

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## MRSA and VRE Clinical Cultures

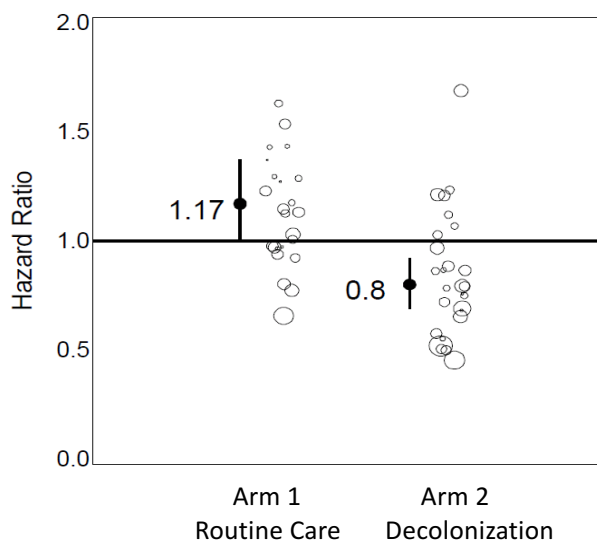
- Event rate per 1,000 patient days

| Population               | Base Event Rate | Arm 2 vs 1 Effect | P-value |
|--------------------------|-----------------|-------------------|---------|
| Full Cohort              | 2.4             | - 8.7%            | 0.16    |
| High Rate Hospitals      | 3.7             | 2.1%              | 0.86    |
| Patients with Devices    | 3.5             | -32.1% ↓          | <0.001  |
| Patients without Devices | 2.1             | 2.9%              | 0.72    |

Patients with Devices: 12% of study population, 35% of all events

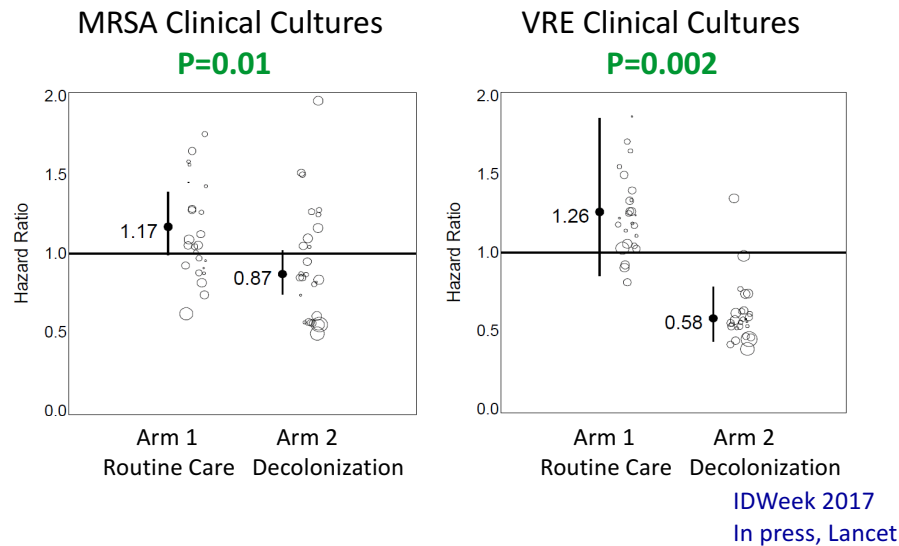
IDWeek 2017  
 In press, Lancet

## MRSA & VRE Clinical Cultures: Patients with Central Lines and Devices



IDWeek 2017  
 In press, Lancet

## MRSA & VRE Cultures Stratified Patients with Central Lines and Devices



## All Pathogen Bloodstream Infection

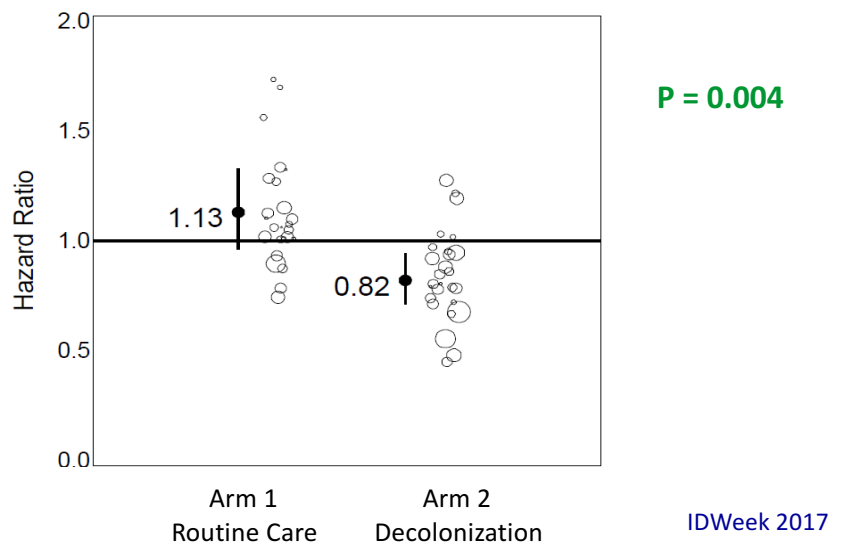
- Event rate per 1,000 patient days

| Population               | Base Event Rate | Arm 2 vs 1 Effect | P-value |
|--------------------------|-----------------|-------------------|---------|
| Full Cohort              | 1.3             | - 6.2%            | 0.44    |
| High Rate Hospitals      | 1.8             | 6.8%              | 0.62    |
| Patients with Devices    | 3.3             | - 27.8% ↓         | 0.004   |
| Patients without Devices | 0.8             | 14.9%             | 0.29    |

Patients with Devices: 12% of study population, 59% of all events

IDWeek 2017  
 In press, Lancet

## All Pathogen Bloodstream Infection: Patients with Lines and Devices



## Decolonization in General Wards

- Did not see overall impact, unlike ICU trials
  - Lower risk and smaller effect size
  - 8.7% for MDROs, 6.2% bloodstream infection (P=NS)
- Benefit seen in **higher risk patients with lines and devices**
  - 32% reduction in MRSA and VRE clinical cultures
  - 28% reduction in all pathogen bloodstream infection
  - ~10% of population, but a third of MRSA+VRE cultures
  - ~10% of population, but 60% of bloodstream infections

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## **Progression of Decolonization Trials**

- ICU                                      REDUCE MRSA Trial and others  
   Mupirocin-Iodophor Swapout
- Non-ICU                                ABATE Infection Trial
- **Post Discharge**                    **Project CLEAR Trial**



CHANGING LIVES BY ERADICATING ANTIBIOTIC RESISTANCE

- Individual randomized clinical trial
- MRSA+ patients on hospital discharge
- Education vs decolonization
- Follow up for 1 year for infection

IDWeek 2016  
Funded by AHRQ  
clinicaltrials.gov: NCT01209234

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## Post-Discharge MRSA Infection Risks

Figure 1. Distribution of Weeks Between Previous Hospitalization and Current Admission Date, Stratified by Long-term Care Facility Residence

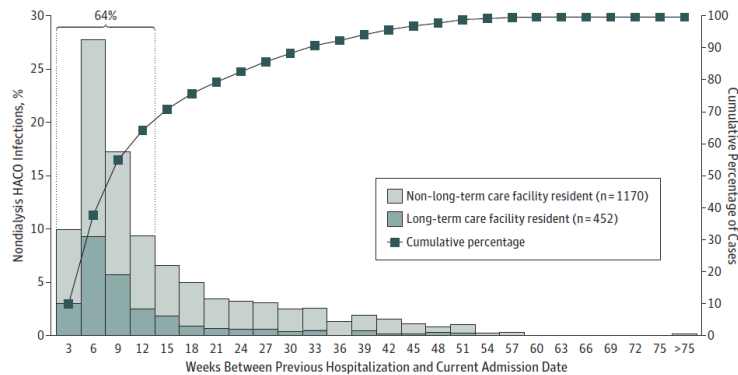


Table 3. National Estimated Incidence and Mortality of Invasive MRSA Infections,<sup>a</sup> United States, 2005 and 2011

Dantes et al. JAMA Int Med 2013;173(21):1970-8

## Project CLEAR Trial

- **2,121 inpatients, ~535,000 days of follow up**
- **Two Arms**
  - Arm 1: Hygienic Education
  - Arm 2: Hygienic Education + Repeated Decolonization
- **Inclusion Criteria**
  - $\geq 18$  years old
  - Hospitalized within the past 30 days
  - MRSA+ culture within 30 days of hospitalization

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## Serial Decolonization

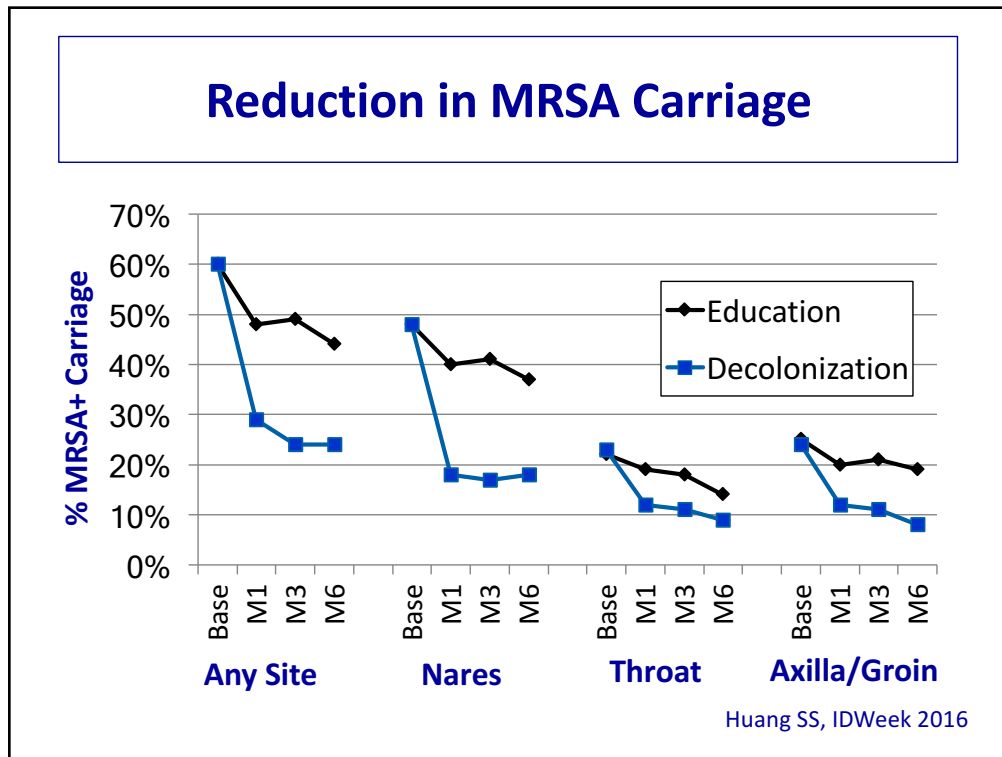
- 5-day regimen twice monthly for 6 months
  - Twice daily 2% nasal mupirocin
  - Twice daily 0.12% chlorhexidine oral rinse
  - Daily 4% rinse-off chlorhexidine bath/shower
- 1 Year follow up
  - Body swabs and surveys
  - Months 1, 3, 6, 9 post-recruitment
  - Phone exit survey at month 12



## Project CLEAR Outcomes

- **Primary Outcome**
  - Time until MRSA infection (US CDC NHSN criteria)
- **Secondary Outcomes**
  - Time to any infection (US CDC NHSN criteria)
  - Time to MRSA infection (ID clinical judgment)
  - Time to any infection (ID clinical judgment)
  - Readmissions due to MRSA
  - Resistance to mupirocin, chlorhexidine
- Blinded assessment of 8,000+ redacted records
- Each chart reviewed by two ID physicians

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### Persons Experiencing $\geq 1$ Infection

|                          | Education<br>N=1063 | Decolonization<br>N=1058 | % Raw Reduction |
|--------------------------|---------------------|--------------------------|-----------------|
| <b>CDC NHSN Criteria</b> |                     |                          |                 |
| MRSA Infection           | 98 (9.2%)           | 67 (6.3%)                | 32%             |
| Any Infection            | 253 (23.8%)         | 207 (19.6%)              | 18%             |
| <b>Clinical Criteria</b> |                     |                          |                 |
| MRSA Infection           | 98 (9.2%)           | 68 (6.4%)                | 30%             |
| Any Infection            | 298 (28.0%)         | 246 (23.3%)              | 17%             |

Among those with MRSA infections, 20% in the education arm and 16% in the decolonization arm had 2 or more distinct infections during follow up

Huang SS, IDWeek 2016

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**Types of Infection**  
**CDC-Defined MRSA Infection**

|                                     | Education<br>N (%) | Decolonization<br>N (%) |
|-------------------------------------|--------------------|-------------------------|
| <b>N (first per person)</b>         | 98                 | 67                      |
| <b>Skin and Soft Tissue</b>         | 34 (35%)           | 32 (48%)                |
| <b>Pneumonia</b>                    | 18 (18%)           | 9 (13%)                 |
| <b>Primary Blood/Vascular</b>       | 13 (13%)           | 10 (15%)                |
| <b>Bone and Joint Infection</b>     | 13 (13%)           | 9 (13%)                 |
| <b>Surgical Site Infection</b>      | 13 (13%)           | 2 (3%)                  |
| <b>Other</b>                        | 7 (7%)             | 5 (7%)                  |
| <b>Involving Bacteremia</b>         | 26 (27%)           | 19 (28%)                |
| <b>Requiring Hospitalization</b>    | 86 (88%)           | 58 (87%)                |
| <b>Time to Infection, Mean (SD)</b> | 110.6 (91.1)       | 117.3 (93.4)            |

Huang SS, IDWeek 2016

**Types of Infection**  
**CDC-Defined All-Cause Infection**

|                                  | Education<br>N (%) | Decolonization<br>N (%) |
|----------------------------------|--------------------|-------------------------|
| <b>N (first per person)</b>      | 253                | 207                     |
| <b>Skin and Soft Tissue</b>      | 81 (32%)           | 59 (29%)                |
| <b>UTI</b>                       | 38 (15%)           | 46 (22%)                |
| <b>Pneumonia</b>                 | 39 (15%)           | 25 (12%)                |
| <b>Primary Blood/Vascular</b>    | 24 (10%)           | 15 (8%)                 |
| <b>Bone and Joint Infection</b>  | 20 (8%)            | 14 (7%)                 |
| <b>Surgical Site Infection</b>   | 20 (8%)            | 8 (4%)                  |
| <b>GI Infection</b>              | 20 (8%)            | 5 (7%)                  |
| <b>Involving Bacteremia</b>      | 46 (18%)           | 36 (17%)                |
| <b>Requiring Hospitalization</b> | 234 (92%)          | 179 (86%)               |
| <b>Time to Infection (Mean)</b>  | 103.3 (87.3)       | 109.6 (90.5)            |

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## Time to Infection Outcomes, Unadjusted

|                            | Hazard Ratio (95% CI)<br>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   |

\* Primary Outcome, main unadjusted analysis  
 Proportional hazards model assumption met

\*\* Blinded assessment by 2 ID physicians, redacted records

Huang SS, IDWeek 2016

## Adherence with Decolonization

Person-time distribution

- Non-adherent 15%
- Partially adherent 20%
- Fully adherent 65%

Huang SS, IDWeek 2016

## Primary Outcome, by Adherence Time to CDC-Defined Infection

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

| <i>Adherence<br/>Relative to<br/>Education</i> | <i>MRSA Infection</i>       |                | <i>All-Cause Infection</i>  |                |
|--|-----------------------------|----------------|-----------------------------|----------------|
|  | <i>Est. HR<br/>(95% CI)</i> | <i>P-value</i> | <i>Est. HR<br/>(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

Huang SS, IDWeek 2016

## Primary Outcome, by Adherence Time to Clinically-Defined Infection

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

| <i>Adherence<br/>Relative to<br/>Education</i> | <i>MRSA Infection</i>       |                | <i>All-Cause Infection</i>  |                |
|--|-----------------------------|----------------|-----------------------------|----------------|
|  | <i>Est. HR<br/>(95% CI)</i> | <i>P-value</i> | <i>Est. HR<br/>(95% CI)</i> | <i>P-value</i> |
| - Education                                    | 1.0                         |                | 1.0                         |                |
| - None   | 1.09(0.57,2.10)             | 0.792          | 1.53(1.11,2.13)             | 0.01           |
| - Partial                                      | 0.72(0.47,1.11)             | 0.140          | 0.92(0.74,1.16)             | 0.483          |
| - Full   | 0.53(0.34,0.83)             | 0.006          | 0.58(0.45,0.74)             | <.001          |

- Non-adherent subjects fared worse than the average control
- Fully adherent subject had 47% reduction in MRSA infection and 42% reduction in all-cause infections

Huang SS, IDWeek 2016

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## 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             |

Huang SS, IDWeek 2016

## Progression of Decolonization Trials

- ICU                                      REDUCE MRSA Trial and others  
   Mupirocin-Iodophor Swapout
- Non-ICU                                      ABATE Infection Trial
- Post Discharge                                      Project CLEAR Trial
- **Nursing Homes**                                      **Protect Trial**

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## MDRO Carriage in Long Term Care

|  | N  | Residents Swabbed | Any MDRO | MRSA | VRE | ESBL | CRE |
|--|----|-------------------|----------|------|-----|------|-----|
| <b>Nursing Homes</b>                           |    |                   |          |      |     |      |     |
| Nares, axilla, groin                           | 28 | 1,400             | 49%      | 37%  | 7%  | 16%  | 1%  |
| Add peri-rectal                                | 18 | 900               | 64%      | 42%  | 16% | 34%  | 2%  |
| <b>Long Term Acute Care Hospitals (LTACHs)</b> |    |                   |          |      |     |      |     |
| Nares, axilla, groin, peri-rectal              | 3  | 150               | 80%      | 33%  | 55% | 39%  | 9%  |

Only 12% of MDROs known to nursing homes

Only 29% of MDROs known to LTACHs

IDWeek, 2017

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## The Protect Trial to Prevent Infections and Readmissions

### Trial Design

- 28 nursing home cluster randomized trial
- 18-month intervention, ends Dec 2018

### Arm 1: Routine Care

- Routine policy for showering/bathing

### Arm 2: Decolonization

- CHG bathing routine for all patients (admit, per routine)
- Nasal iodophor x 5d bid, facility-wide every other week

Funded by AHRQ  
[clinicaltrials.gov: NCT03118232](http://clinicaltrials.gov/NCT03118232)

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## The PROTECT Trial Outcomes

### Primary Outcomes

- Infectious admissions  
(% of discharges to a hospital due to infection)

### Additional Outcomes

- All-cause admissions (% of discharges to a hospital)
- Antibiotic usage
- MDRO prevalence (MRSA, VRE, ESBL, CRE)
- Emergence of resistance (strain collection)

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## Summary: Who Should Decolonize?

- Targeted Prevention of *S. aureus* Carriers
  - Recurrent infection <sup>1</sup>
  - Pre-operative <sup>2-3</sup>
  - Post-discharge <sup>4</sup>
- Universal Prevention
  - Pre-operative bathing?
  - ICU <sup>5-8</sup>
  - Non-ICU patients with medical devices <sup>9</sup>
  - Nursing Homes? <sup>10</sup>

<sup>1</sup> Liu C CID 2011;52:285-92 (IDSA Guideline)

<sup>2</sup> Bode LGM NEJM 2010;362:9-17

<sup>3</sup> Perl T NEJM 2002;346:1871-7

<sup>4</sup> Huang SS IDWeek 2016, NCT01209234

<sup>5</sup> Climo M NEJM 2013;368:533-42

<sup>6</sup> Milstone A Lancet 2013;381:1099-106

<sup>7</sup> Huang SS NEJM 2013;368:2255-65

<sup>8</sup> Huang SS, clinicaltrials.gov NCT03140423

<sup>9</sup> Huang SS IDWeek 2017, Lancet, in press

<sup>10</sup> Huang SS, clinicaltrials.gov NCT03118232

## **A Tour of Chlorhexidine Decolonization**

- Why decolonize?
- Who should be decolonized?
- **What concentrations should be used?**
- Where on the body and how to apply?
- When and how often?

## **Chlorhexidine Concentration**

Three reasons concentration is important

- Effectiveness
- Side effects
- Reduce opportunities to engender resistance

## Effective CHG Concentrations

- Effective bathing concentrations in clinical trials
  - 2% no-rinse cloth for bed bathing
  - 4% rinse-off liquid for showering
  - Lower concentrations → unknown
- Residual antimicrobial levels persist for 24 hours <sup>1</sup>
- 2% no-rinse
  - Higher skin concentrations (2x) <sup>2</sup>
  - May be especially important for Gram-negative bacteria <sup>3</sup>

<sup>1</sup> Popovich K et al. ICHE 2012;33:889-96

<sup>2</sup> Rhee Y et al. ICHE 2018;39:405-11

<sup>3</sup> Lin MY et al. ICHE 2014;35:440-2

## CHG Side Effects by Concentration

- 2% no-rinse cloth well tolerated
  - 1+ million baths across trials
  - Side effects similar to placebo <sup>1 2</sup>
  - Mild rash, irritation <<1%
  - Safe on dermatitis, erythema, papules, blisters, ulceration, denuded skin, loss of epidermis <sup>3</sup>
- 4% rinse-off well tolerated
  - Mild rash, irritation 2.3%, one-third opt to continue <sup>4</sup>
- 4% no-rinse: higher risk for dryness <sup>2 5</sup>

<sup>1</sup> Climo M NEJM 2013;368:533-42

<sup>2</sup> Grove GL AJIC 2001;29:361-9

<sup>3</sup> Bleasdale SC Arch Int Med 2007;167:2073-9

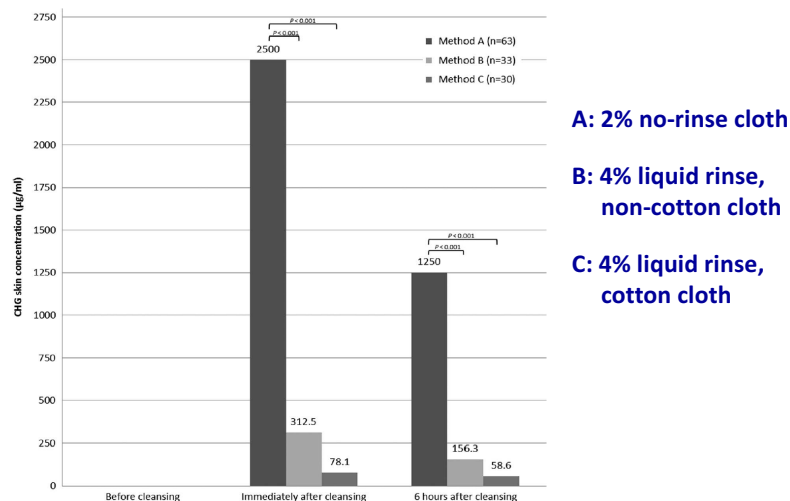
<sup>4</sup> Project CLEAR Trial, IDWeek 2016, NCT01209234

<sup>5</sup> Liu C CID 2011;52:285-92 (IDSA Guideline)

## CHG Concentration and Resistance

- CHG minimum inhibitory concentration
  - *S. aureus* “resistance” defined as 8 µg/ml
  - GNR “resistance” defined as 100-300 µg/ml
- Bathing concentrations
  - 2% no-rinse cloths: 20,000 µg/ml
  - 4% rinse off: 40,000 µg/ml
- Proper bathing immediately critical upon drying
  - Residual persists, dissipates with time
  - Levels after 24 hours highly variable 10-1000+

## Residual CHG Concentration



Rhee Y et al. ICHE 2018;39:405-11

## No Evidence of Resistance in Trials

- Climo et al. ICU Trial: No associated CHG resistance <sup>1</sup>
- REDUCE MRSA Trial: No associated CHG or mupirocin resistance <sup>2</sup>
- Project CLEAR Trial: No associated CHG or mupirocin resistance <sup>3</sup>

Regardless, ongoing surveillance for resistance needed

- Efflux mechanisms
- Need higher fidelity resistance genes than qac

<sup>1</sup> Climo M et al. NEJM 2013;368:533-42

<sup>2</sup> Hayden M et al. JCM 2016;54(11):2735-2742

<sup>3</sup> Huang SS et al. IDWeek 2016

## Adding Nasal Products?

Critical if *S. aureus* infection is a target for reduction

- Mupirocin most commonly used in trials
- Iodophor may be relevant as mupirocin-resistance rises

### Methods of Preventing Emergence of Resistant Bacteria

Three procedures may help to prevent, or at least delay, the emergence of resistant bacteria : (1) economy in the use of chemotherapeutic agents ; this implies not only restricting their use for cases in which they are specially indicated, but also giving them in sufficient amount to achieve a complete effect in the shortest possible time—an approach to the *therapia sterilisans magna* of Ehrlich ; (2) avoidance of agents which readily induce resistance—especially streptomycin—when other agents will do as well ; and (3) the use of two or more agents together. This third method has been vindicated in the treatment of tuberculosis by com

1. Economy of use
2. Shortest possible course
3. Avoid agents prone to resistance
4. Use two or more

Lowbury EJJ Br Med J 1955:985-990

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## Pre-Operative Trials

- Targeted Prevention
  - Screen for *S. aureus* carriage
  - Decolonize with chlorhexidine and mupirocin
  - Cardiac,<sup>1</sup> orthopedic,<sup>2</sup> all-type surgeries<sup>3</sup>
- Reduction in *S. aureus* Infection
  - Cardiac: ↓51% hospital *S. aureus* infection (not SSI)
  - Orthopedic: ↓81% hospital *S. aureus* infection (not SSI)
  - Inpatient surgery: ↓59% *S. aureus* SSI

<sup>1</sup> Perl T NEJM 2002;346:1871-7

<sup>2</sup> Kalmeijer MD 2002 CID 35:353-8

<sup>3</sup> Bode LGM NEJM 2010;362:9-17



*Is nasal iodophor equivalent to mupirocin to prevent *S. aureus*?*  
*Will nasal iodophor reduce the chance of resistance?*

Funded by CDC  
[clinicaltrials.gov/ct2/show/NCT03140423](https://clinicaltrials.gov/ct2/show/NCT03140423)

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## Mupirocin-Iodophor Swap Out Trial

- Cluster-randomized ICU non-inferiority study
- 138 HCA hospitals, 204 adult ICUs
  - **Mupirocin Arm:** Daily CHG & 5d mupirocin
  - **Iodophor Arm:** Daily CHG & 5d iodophor
- 18 month trial, ends April 2019
- Outcomes
  - *S. aureus* (MRSA & MSSA) ICU clinical cultures (**primary**)
  - All-cause bacteremia
  - Emergence of resistance to mupirocin, iodophor

## A Tour of Chlorhexidine Decolonization

- Why decolonize?
- Who should be decolonized?
- What concentrations and nasal products should be used?
- **Where on the body and how to apply?**
- When and how often?

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## Decolonization Success Requires Training

- Bathing not intuitive
- Many incorrect assumptions
- Training imperative for success
  - ✓ High turnover of staff
  - ✓ Multiple competing knowledge priorities

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

<sup>1</sup> Popovich et al. *Intensive Care Med* 2010; 36(5):854-8

<sup>2</sup> Supple et al. *ICHE* 2015;36(9):1095-7

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### Universal ICU Decolonization

#### DO

- Ensure CHG compatibility of lotions, skin products
- Apply with firm massage
- Safe on face and perineum
- Special protection for disrupted skin
  - ✓ Apply to abraded skin, rashes
  - ✓ Apply to wounds, burns, superficial ulcers
  - ✓ Apply to lines, tubes, drains, devices within 6 inches of body, over dressings
- Dry without wiping off or rinsing
- If must shower
  - ✓ Apply for 2 minutes prior to rinsing
  - ✓ Apply with mesh sponge




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# Decolonization to Reduce MDROs in Healthcare: Who, What, Where, When, and Why?

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## Universal ICU Decolonization

DON'T

- Don't use other soaps first, CHG is not a "top coat"
- Avoid contact with shampoos (inactivates CHG)
- Avoid eyes and ears
- Avoid cotton cloths (binds CHG)
- If possible, avoid rinsing or wiping off
- Do not flush cloths

## Invest in Simple Staff Handouts

Prevent infections during each nursing home stay  
**BATHE or SHOWER** with Chlorhexidine (CHG) soap
STAFF

**Bathe with CHG to remove germs and prevent infection**

**CHG works better than soap and water**

**CHG is a protective bath**

**CHG cloths are less drying than soap**

Apply as shown below



Avoid eyes, mouth, & ear canals

REMINDERS

- **Your enthusiasm** helps residents understand why CHG is important
- Bathing on admission removes germs to protect the resident and nursing home
- CHG works for 24 hours to kill germs
- **Firmly massage** CHG onto skin
- Clean **6 inches** of lines, drains, tubes
- Safe on surface wounds, rashes, burns
- Use only CHG-compatible lotions
- If barrier protection needed, apply CHG then apply barrier protection

Clean all skin areas with attention to:



- Neck
- All skin folds
- Skin around all devices (line/tube/drain)
- Wounds unless deep or large
- Armpit, groin, between fingers/toes

SHOWERING with CHG soap

1. Rinse body with warm water
2. Wash hair and face with CHG
3. Avoid getting into eyes and ears
4. Turn off water and lather non-cotton cloth or sponge with plenty of CHG
5. Massage CHG onto all skin areas
6. Leave CHG on for **2 minutes** then rinse

BATHING with CHG cloths

1. Tell residents these cloths are their protective bath
2. Use all 6 cloths. More, if needed.
3. **Firmly massage** skin with cloth
4. Clean over semi-permeable dressings
5. Clean 6 inches of lines, tubes, and drains
6. Air dry. Do not wipe off.
7. Put used cloths in trash. Do **not** flush.

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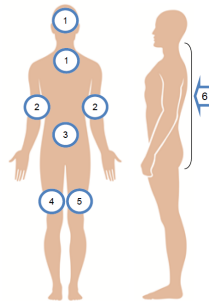
## Invest in Simple Patient Handouts

Prevent infections during your hospital stay  
**BATHE** daily with Chlorhexidine (CHG) cloths

**PATIENT**

During your stay, we will bathe you every day with a special antiseptic (CHG) which removes germs and prevents infection better than soap and water.

Each packet has 6 cloths to be used on all skin areas as shown below:



Avoid eyes and ear canals

### Take a CHG Bed Bath

#### BATHING with CHG cloths

1. Use CHG every day. Starting on the admission day works best to remove germs before IVs, lines, urinary catheters, and procedures/surgery.
2. These no-rinse cloths are your protective bath. The CHG continues to get rid of germs for 24 hours.
3. Use all 6 cloths. More, if needed.
4. **Firmly massage** on all skin areas to ensure deep cleaning of skin
5. Clean over non-gauze dressings
6. **Your nurse will clean parts of lines, tubes and drains nearest the body**
7. Throw away in trash. **Do not flush.**



### Protect yourself every day

#### Important Points and Reminders

- CHG is proven to work better than soap and water to get rid of germs
- CHG cloths have aloe and are good for your skin. CHG is less drying than soap.
- **Do not rinse.** Once massaged onto skin, CHG works to kill germs for 24 hours.
- **Be thorough. Ask for help for hard to reach areas, backside, around devices.**
- CHG is safe on rashes and wounds that are not very large or deep
- **Clean lines, drains, tubes 6 inches from the body.** Ask for help, if needed.

#### Clean all skin areas with attention to:

- Neck
- All skin folds
- Skin around all devices (tubes/drains)
- Wounds and open skin
- Armpits, groin, between fingers/toes

Keeping germs away

**Have you had  
 your bath today?**

Every patient, every day

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## Just in Time Training

### Decolonization Protocol

#### 1. Iodophor Nasal Treatment

- Use nasal iodophor twice daily for five days or until discharge, whichever comes first

#### 2. Chlorhexidine Treatment

- Applies to patients on contact precautions (intended to capture carriers or those with a recent history of MDROs including MRSA, VRE, CRE, ESBL, and *C. difficile*)
- Use 2% no-rinse chlorhexidine (CHG) cloths or 4% liquid rinse-off CHG for showers on admission, and for all subsequent routine bathing needs
- Devices, rashes and wounds need the most protection. CHG is safe for rashes and wounds that are not packed or deep. Apply CHG cloth to lines, tubes, drains, and non-gauze dressings.
- Decolonization stops when discharged or transferred
- If readmitted, protocol begins anew

#### 3. How to Bathe with CHG Cloths

- Pair with a "buddy" who can teach you
- Review attached 1-page staff education
- To save time, give 1-page bath/shower patient instructions handout prior to bath
- Apply CHG to skin with **firm massage**
- Avoid eyes and ears
- **Let air dry. Do not wipe off.**
- Do NOT flush cloths
- Do NOT use soap (can inactivate CHG)
- For incontinence, clean with incontinence wipes (water if needed), cleanse with CHG cloth, then use CHG-compatible barrier product

Please return completed form to the Nursing Director

Signature \_\_\_\_\_

Print Last Name \_\_\_\_\_

Print First Name \_\_\_\_\_

Date \_\_\_\_\_

### STAFF Skills Assessment: CHG Cloth Observation Checklist

#### Individual Giving CHG Bath

Please indicate who performed the CHG bath.

- Nursing Assistant (CNA)    Nurse    LVN    Other: \_\_\_\_\_

#### Observed CHG Bathing Practices

Please check the appropriate response for each observation.

- Y    N   Patient received CHG cloth bathing handout
- Y    N   Patient told that bath is a no rinse cloth that provides protection from germs
- Y    N   Provided rationale to the patient for not using soap at any time while in unit
- Y    N   Massaged skin **firmly** with CHG cloth to ensure adequate cleansing
- Y    N   Cleaned face and neck well
- Y    N   Cleaned between fingers and toes
- Y    N   Cleaned between all folds
- Y    N    N/A   Cleaned occlusive and semi-permeable dressings with CHG cloth
- Y    N    N/A   Cleaned 6 inches of all tubes, central lines, and drains closest to body
- Y    N    N/A   Used CHG on superficial wounds, rash, and stage 1 & 2 decubitus ulcers
- Y    N    N/A   Used CHG on surgical wounds (unless primary dressing or packed)
- Y    N   Allowed CHG to air-dry / does not wipe off CHG
- Y    N   Disposed of used cloths in trash / does not flush

#### Query to Bathing Assistant/Nurse

1. How many cloths were used for the bath? (1 cloth set = 3 cloth packs with 2 cloths each, 1 single cloth pack = 2 cloths)  
\_\_\_\_\_
2. If more than 1 cloth set (6 cloths) was used, provide reason.  
\_\_\_\_\_
3. Do you reapply CHG after an episode of incontinence has been cleaned up?  
\_\_\_\_\_
4. Are you comfortable applying CHG to superficial wounds, including surgical wounds?  
\_\_\_\_\_
5. Are you comfortable applying CHG to lines, tubes, drains and non-gauze dressings?  
\_\_\_\_\_
6. Do you ever wipe off the CHG after bathing?  
\_\_\_\_\_

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## AHRQ Website: Toolkit

Agency for Healthcare Research and Quality  
Advancing Excellence in Health Care

Health Care Information | For Patients & Consumers | For Professionals | For Policymakers | Research Tools & Data | Funding & Grants | Centers, Portfolios & Initiatives | News & Events

Home > For Professionals > Hospitals & Health Systems > Hospital Resources > Universal ICU Decolonization Protocol

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Clinicians & Providers  
Education & Training  
Hospitals & Health Systems  
Hospital Resources  
Emergency Department Tools and Resources  
Emergency Severity Index

### Universal ICU Decolonization: An Enhanced Protocol

Publication # 13-0052-EF

#### Introduction and Welcome

This enhanced protocol is based on materials successfully used in the REDUCE MRSA Trial (Randomized Evaluation of Decolonization vs. Universal Clearance to Eliminate 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.

[http://www.ahrq.gov/professionals/systems/hospital/universal\\_icu\\_decolonization.html](http://www.ahrq.gov/professionals/systems/hospital/universal_icu_decolonization.html)

## ABATE Infection Trial Downloadable Video

For Liquid CHG:

- Apply CHG soap to all body areas out of the water
- Keep on for at least 2 minutes before rinsing
- Use the provided mesh cloth or sponge to lather.

<https://vimeo.com/164608558>

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## A Tour of Chlorhexidine Decolonization

- Why decolonize?
- Who should be decolonized?
- What concentrations and nasal products should be used?
- Where on the body and how to apply?
- **When and how often?**

## Frequency of Chlorhexidine Application

- Admission bathing critical
- Concept of continuous protection
- During vulnerable times
- Daily application can ensure sufficient levels
- Proper application
  - ✓ Maintain high residual levels after 24 hours
  - ✓ Exceed GP and GN MICs
- Some benefit reported with every other day bathing

<sup>1</sup>Swan JT Crit Care Med 2016;44:1822-32

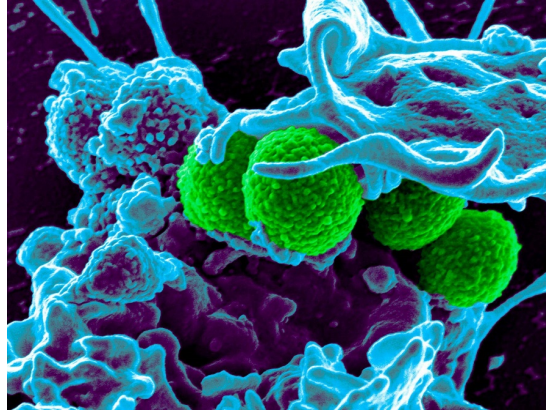
## **A Tour of Chlorhexidine Decolonization**

- **Why** decolonize?
- **Who** should be decolonized?
- **What** concentrations and nasal products should be used?
- **Where** on the body and how to apply?
- **When** and how often?

## **Summary of Chlorhexidine Bathing**

- Nearly 70 years of discovery and protection
- Simple bathing
  - Effective decolonization across spectrum of care
  - ICUs, devices, post-discharge MRSA carriers
  - Reduces MDROs, infection, antibiotics, hospitalizations
- Adoptable process
- Safe and effective
- No evidence of engendered resistance, ongoing surveillance

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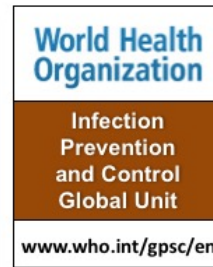
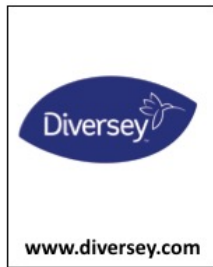
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| December 6, 2018  | <p><a href="#"><u>INFECTIOUS DISEASE HIGHLIGHTS AND LOWLIGHTS IN 2018, AND WHAT TO EXPECT IN 2019</u></a><br/>Speaker: <b>Dr. Larry Madoff</b>, ProMED Editor, Director, Division of Epidemiology and Immunization, Massachusetts Dept. of Public Health</p> <p><i>(South Pacific Teleclass)</i></p> |
| December 12, 2018 | <p><a href="#"><u>CONTROL OF CARBAPENEMASE-PRODUCING ENTEROBACTERIACEA IN AN ENDEMIC SETTING: DO CLASSICAL IPC METHODS WORK FOR NEW AGE BUGS?</u></a><br/>Speaker: <b>Dr. Kalisvar Marimuthu</b>, Tan Tock Seng Hospital, Singapore</p> <p><i>(FREE Teleclass)</i></p>                               |
| December 13, 2018 | <p><a href="#"><u>THE BEST WAYS TO GET YOUR HOSPITAL TO TALK ABOUT INFECTION CONTROL</u></a><br/>Speaker: <b>Prof. Andreas Voss</b>, Radboud University, The Netherlands</p> <p>Sponsored by Lonza (<a href="http://www.lonza.com">www.lonza.com</a>) ***</p>  |

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