The CLEAR Trial and Other MRSA Decolonization Studies

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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
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
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
Decolonization Trials

• Targeted Prevention
  ➢ Recurrent *S. aureus* infection ¹
  ➢ Pre-operative *S. aureus* carriers ²-³

• Universal Prevention
  ➢ ICU ⁴-⁷
  ➢ Non-ICU ⁸
  ➢ Post-Discharge ⁹
  ➢ Nursing Homes ¹⁰

¹ Liu C CID 2011;52:285-92 (IDSA Guideline)
² Bode LGM NEJM 2010;362:9-17
³ Perl T NEJM 2002;346:1871-7
⁴ Climo M NEJM 2013;368:533-42
⁵ Milstone A Lancet 2013;381:1099-106
⁶ Huang SS NEJM 2013;368:2255-65
⁷ Huang SS, clinicaltrials.gov NCT03140423
⁸ Huang SS IDWeek 2017, Lancet, in press
⁹ Huang SS IDWeek 2016, NCT01209234
¹⁰ Huang SS, clinicaltrials.gov NCT03118232
Pre-Operative Trials

• Targeted Prevention
  ➢ Screen for *S. aureus* carriage
  ➢ Decolonize with chlorhexidine and mupirocin
  ➢ Cardiac,¹ orthopedic,² all-type surgeries³

• 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

¹ Perl T NEJM 2002;346:1871-7
² Kalmeijer MD 2002 CID 35:353-8
³ Bode LGM NEJM 2010;362:9-17
### ICU Decolonization Evidence Summary

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

Huang SS et al. NEJM 2013:368:2255-2265
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 $P=0.16$

Huang SS et al. NEJM 2013:368:2255-2265
MRSA Bloodstream Infection

Huang SS et al. NEJM 2013:368:2255-2265
All Pathogen Bloodstream Infection

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

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
  – Highly cost-effective and prevents need to screen
  – Reduces blood culture contamination
  – Reduces bacteriuria and candiduria in men
  – No emergence of CHG or mupirocin resistance in trial
  – CLABSI benefit seen with rapid adoption in 95 hospitals

• 80-90% of US hospitals use universal CHG bathing in an ICU

1 Huang SS et al. ICHE 2014; 35 S3:S23-S31
2 Septimus EJ et al. ICHE 2014; 35 S3:S17-S22.
3 Huang SS et al. Lancet ID 2016;16(1):70-9
4 Hayden M et al. JCM 2016; 54(11):2735-42
5 Septimus ES et al. CID 2016;63(2):172-7
6 Shuman EK et al. IDWeek 2014
Decolonization Trials

• Targeted Prevention
  ➢ Recurrent *S. aureus* infection
  ➢ Pre-operative *S. aureus* carriers

• Universal Prevention
  ➢ ICU
  ➢ Non-ICU
  ➢ Post-Discharge
  ➢ Nursing Homes

1 Liu C CID 2011;52:285-92 (IDSA Guideline)
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Progression of Decolonization Trials

- ICU
  REDUCE MRSA Trial and others

- Non-ICU
  ABATE Infection Trial

Huang SS Lancet 2019;393(10177):1205-1215
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
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)**


Huang SS Lancet 2019;393(10177):1205-1215
## Select Population Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Routine Care</th>
<th>Decolonization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean years)</td>
<td>62.3</td>
<td>62.6</td>
</tr>
<tr>
<td>Female</td>
<td>53.9%</td>
<td>54.8%</td>
</tr>
<tr>
<td>Comorbidity Score (Elixhauser)</td>
<td>2.8</td>
<td>2.9</td>
</tr>
<tr>
<td>Surgery</td>
<td>20.9%</td>
<td>22.4%</td>
</tr>
<tr>
<td>Length-of-Stay (median)</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Central Lines</td>
<td>9.1%</td>
<td>10.7%</td>
</tr>
<tr>
<td>MRSA History</td>
<td>1.9%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Huang SS Lancet 2019;393(10177):1205-1215
MRSA & VRE Clinical Cultures

Hazard Ratio

Arm 1
Routine Care
Decolonization

Arm 2

P = 0.17

Huang SS Lancet 2019;393(10177):1205-1215
MRSA & VRE Cultures Stratified

MRSA Clinical Cultures
P=0.63

VRE Clinical Cultures
P=0.01

Huang SS Lancet 2019;393(10177):1205-1215
All Pathogen Bloodstream Infection

Hazard Ratio

P = 0.43

Arm 1
Routine Care

Arm 2
Decolonization

Huang SS Lancet 2019;393(10177):1205-1215
Results & Subpopulation Analysis

- Overall non-ICU population – no benefit
- 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
## MRSA and VRE Clinical Cultures

- Event rate per 1,000 patient days

<table>
<thead>
<tr>
<th>Population</th>
<th>Base Event Rate</th>
<th>Arm 2 vs 1 Effect</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Cohort</td>
<td>2.4</td>
<td>-8.7%</td>
<td>0.16</td>
</tr>
<tr>
<td>High Rate Hospitals</td>
<td>3.7</td>
<td>2.1%</td>
<td>0.86</td>
</tr>
<tr>
<td>Patients with Devices</td>
<td>3.5</td>
<td>-32.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patients without Devices</td>
<td>2.1</td>
<td>2.9%</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Patients with Devices: 10% of study population, 37% of all events

Huang SS Lancet 2019; 393(10177):1205-1215
MRSA & VRE Clinical Cultures: Patients with Central Lines and Devices

Arm 1
Routine Care

Arm 2
Decolonization

Hazard Ratio

1.17

0.8

P < 0.001

Huang SS Lancet 2019; 393(10177):1205-1215
MRSA & VRE Cultures Stratified Patients with Central Lines and Devices

MRSA Clinical Cultures

\[ P = 0.01 \]

VRE Clinical Cultures

\[ P = 0.002 \]

Huang SS Lancet 2019; 393(10177):1205-1215
## All Pathogen Bloodstream Infection

- Event rate per 1,000 patient days

<table>
<thead>
<tr>
<th>Population</th>
<th>Base Event Rate</th>
<th>Arm 2 vs 1 Effect</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Cohort</td>
<td>1.3</td>
<td>-6.2%</td>
<td>0.44</td>
</tr>
<tr>
<td>High Rate Hospitals</td>
<td>1.8</td>
<td>6.8%</td>
<td>0.62</td>
</tr>
<tr>
<td>Patients with Devices</td>
<td>3.3</td>
<td>-27.8%</td>
<td>0.004</td>
</tr>
<tr>
<td>Patients without Devices</td>
<td>0.8</td>
<td>14.9%</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Patients with Devices: 10% of study population, 56% of all events

Huang SS Lancet 2019; 393(10177):1205-1215
All Pathogen Bloodstream Infection: Patients with Lines and Devices

![Graph showing hazard ratio comparison between Arm 1 (Routine Care) and Arm 2 (Decolonization). The hazard ratio for Arm 1 is 1.13 and for Arm 2 is 0.82. The p-value is 0.004.]

Huang SS Lancet 2019; 393(10177):1205-1215
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

Huang SS Lancet 2019;393(10177):1205-1215
Progression of Decolonization Trials

• ICU
  REDUCE MRSA Trial and others
  Mupirocin-Iodophor Swapout

• Non-ICU
  ABATE Infection Trial

• Post Discharge
  Project CLEAR Trial
• Individual randomized clinical trial
• MRSA+ patients on hospital discharge
• Education vs decolonization
• Follow up for 1 year for infection

Huang SS NEJM 2019; 380(7):638-650
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, a United States, 2005 and 2011

Project CLEAR Trial

• 2,121 inpatients, ~535,000 days of follow up

• Two Arms
  o Arm 1: Hygienic Education
  o Arm 2: Hygienic Education + Repeated Decolonization

• Inclusion Criteria
  ➢ ≥18 years old
  ➢ Hospitalized within the past 30 days
  ➢ MRSA+ culture within 30 days of hospitalization

Huang SS NEJM 2019; 380(7):638-650
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

Huang SS NEJM 2019; 380(7):638-650
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

Huang SS NEJM 2019; 380(7):638-650
## Types of Infection
### CDC-Defined MRSA Infection

<table>
<thead>
<tr>
<th>Types of Infection</th>
<th>Education N (%)</th>
<th>Decolonization N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (first per person)</td>
<td>98 (100%)</td>
<td>67 (100%)</td>
</tr>
<tr>
<td>Skin and Soft Tissue</td>
<td>34 (35%)</td>
<td>32 (48%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>18 (18%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Primary Blood/Vascular</td>
<td>13 (13%)</td>
<td>10 (15%)</td>
</tr>
<tr>
<td>Bone and Joint Infection</td>
<td>13 (13%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Surgical Site Infection</td>
<td>13 (13%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (7%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>Involving Bacteremia</td>
<td>28 (29%)</td>
<td>19 (28%)</td>
</tr>
<tr>
<td>Requiring Hospitalization</td>
<td>83 (85%)</td>
<td>57 (85%)</td>
</tr>
<tr>
<td>Time to Infection, Mean (SD)</td>
<td>110.6 (91.1)</td>
<td>117.3 (93.4)</td>
</tr>
</tbody>
</table>

Huang SS NEJM 2019; 380(7):638-650
## Types of Infection

### CDC-Defined All-Cause Infection

<table>
<thead>
<tr>
<th>Types of Infection</th>
<th>Education N (%)</th>
<th>Decolonization N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (first per person)</td>
<td>252</td>
<td>207</td>
</tr>
<tr>
<td>Skin and Soft Tissue</td>
<td>80 (32%)</td>
<td>59 (29%)</td>
</tr>
<tr>
<td>UTI</td>
<td>38 (15%)</td>
<td>46 (22%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>39 (15%)</td>
<td>25 (12%)</td>
</tr>
<tr>
<td>Primary Blood/Vascular</td>
<td>20 (8%)</td>
<td>14 (7%)</td>
</tr>
<tr>
<td>Bone and Joint Infection</td>
<td>20 (8%)</td>
<td>14 (7%)</td>
</tr>
<tr>
<td>Surgical Site Infection</td>
<td>20 (8%)</td>
<td>8 (4%)</td>
</tr>
<tr>
<td>GI Infection</td>
<td>20 (8%)</td>
<td>21 (10%)</td>
</tr>
<tr>
<td><strong>Involving Bacteremia</strong></td>
<td>46 (18%)</td>
<td>37 (18%)</td>
</tr>
<tr>
<td><strong>Requiring Hospitalization</strong></td>
<td>225 (89%)</td>
<td>169 (82%)</td>
</tr>
<tr>
<td><strong>Time to Infection (Mean)</strong></td>
<td>103.3 (87.3)</td>
<td>109.6 (90.5)</td>
</tr>
</tbody>
</table>
## Time to Infection Outcomes, Unadjusted

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

* Primary Outcome, main unadjusted analysis
Proportional hazards model assumption met
** Blinded assessment by 2 ID physicians, redacted records

Huang SS NEJM 2019; 380(7):638-650
Adherence with Decolonization

Person-time distribution

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

Huang SS NEJM 2019; 380(7):638-650
Primary Outcome, by Adherence
Time to CDC-Defined Infection

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

<table>
<thead>
<tr>
<th>Adherence Relative to Education</th>
<th>MRSA Infection</th>
<th>All-Cause Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Est. HR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Education</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.31 (0.72,2.38)</td>
<td>0.383</td>
</tr>
<tr>
<td>Partial</td>
<td>0.64 (0.40,1.00)</td>
<td>0.050</td>
</tr>
<tr>
<td>Full</td>
<td>0.56 (0.36,0.86)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

- 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 NEJM 2019; 380(7):638-650
Primary Outcome, by Adherence
Time to Clinically-Defined Infection

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

<table>
<thead>
<tr>
<th>Adherence Relative to Education</th>
<th>MRSA Infection</th>
<th>All-Cause Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Est. HR (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Education</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.09(0.57,2.10)</td>
<td>0.792</td>
</tr>
<tr>
<td>Partial</td>
<td>0.72(0.47,1.11)</td>
<td>0.140</td>
</tr>
<tr>
<td>Full</td>
<td>0.53(0.34,0.83)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

- 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
## Number Needed to Treat

<table>
<thead>
<tr>
<th>Condition</th>
<th>Overall</th>
<th>Full Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA Infection</td>
<td>30</td>
<td>26</td>
</tr>
<tr>
<td>MRSA Hospitalization</td>
<td>34</td>
<td>27</td>
</tr>
<tr>
<td>Any Infection</td>
<td>26</td>
<td>11</td>
</tr>
<tr>
<td>Hospitalization due to Infection</td>
<td>28</td>
<td>12</td>
</tr>
</tbody>
</table>

Huang SS NEJM 2019; 380(7):638-650
SHIELD OC Regional Collaborative

- CDC, California state, and OC county public health collaborative
- Coordinated by UC Irvine, Harbor UCLA
- 35-facility decolonization intervention
- **Invited based on network analysis for hospitals and nursing homes with highest shared patients**
- Outcomes
  - Point prevalence MDROs (swabs)
  - Countywide MDRO clinical cultures
  - Stratified by participants and non-participants

*Shared Healthcare Intervention to Eliminate Life-threatening Dissemination of MDROs in Orange County*
SHIELD OC Decolonization Intervention

• **Hospitals** – decolonize patients in contact precautions
  ✓ Daily chlorhexidine (CHG) bathing/showering
  ✓ Nasal iodophor decolonization for 5 days
  ✓ Support ongoing ICU CHG daily bathing

• **Nursing homes and LTACHs** – decolonize all patients/residents
  ✓ Replaced regular soap with CHG antiseptic soap
  ✓ CHG on admit and for all routine bathing/showering
  ✓ Nasal iodophor on admit and every other week

https://www.cdc.gov/hai/research/cdc-mdro-project.html
35 Participating Healthcare Facilities

**Nursing Homes (16)**
- Alamitos West Health Care Center
- Anaheim Healthcare Center
- Beachside Nursing Center
- Crystal Cove Care Center
- French Park Care Center
- Garden Park Care Center
- Healthcare Center of Orange County
- Laguna Hills Health and Rehab Center
- Lake Forest Nursing Center
- Mesa Verde Post Acute Care Center
- New Orange Hills
- Orange Healthcare & Wellness Centre
- Regents Point – Windcrest
- Seal Beach Health and Rehab Center
- Town and Country Manor
- Victoria Healthcare and Rehab Center

**Long-Term Acute Care Hospitals (3)**
- Kindred Hospital Brea
- Kindred Hospital Santa Ana
- Kindred Hospital Westminster

**Hospitals (16)**
- AHMC Anaheim Regional Medical Center
- Chapman Global Medical Center
- Fountain Valley Regional Hospital
- Garden Grove Hospital and Medical Center
- Hoag Memorial Hospital Presbyterian (with Hoag Irvine, Hoag Orthopedics Hospitals)
- Huntington Beach Hospital
- Kaiser Foundation Hospital – Anaheim
- Mission Hospital Regional Medical Center
- Orange Coast Memorial Medical Center
- Placentia Linda Hospital
- Saddleback Memorial Medical Center
- South Coast Global Medical Center
- St. Joseph Hospital – Orange
- St. Jude Medical Center
- UC Irvine Medical Center
### SHIELD OC Timeline

**Timeline**

- **Baseline prevalence**: Sept 2016-Jan 2017
- **Training**: March 2017
- **Phase In (3 month)**: April-June 2017
- **Intervention (25 months)**: July 1, 2017 – July 31, 2019

**OC Public Health Laboratory Reporting Mandate**

- July 2016, all laboratories serving inpatients (hospitals, nursing homes) → report MRSA, ESBL, CRE

https://www.cdc.gov/hai/research/cdc-mdro-project.html
Pre & Post Swabbing Assessment

- Point prevalence assessment for quality improvement
- Body swabs: nasal, skin, peri-rectal
  - Hospitals: 50 patients in contact precautions
  - LTACHs: 50 representative patients
  - Nursing homes
    - Pre: 50 representative residents
    - Post: All residents
- Logistical support by SHIELD OC team
  - Provided materials, de-identified labels
  - Transport and process swabs at central laboratory (UCI)
- Summary results used by facility leadership
### Characteristics of SHIELD OC Facilities

<table>
<thead>
<tr>
<th></th>
<th>NH</th>
<th>LTACH</th>
<th>Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age</strong></td>
<td>76</td>
<td>72</td>
<td>47</td>
</tr>
<tr>
<td><strong>% Male</strong></td>
<td>40%</td>
<td>53%</td>
<td>42%</td>
</tr>
<tr>
<td><strong>Mean Licensed Beds</strong></td>
<td>133</td>
<td>83</td>
<td>247</td>
</tr>
<tr>
<td><strong>Average Daily Census</strong></td>
<td>115</td>
<td>63</td>
<td>141</td>
</tr>
<tr>
<td><strong>Mean LOS</strong></td>
<td>69.3</td>
<td>30.6</td>
<td>4.1</td>
</tr>
<tr>
<td><strong>Elixhauser Comorbidity Score</strong></td>
<td>3.8</td>
<td>2.9</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>% Diabetes</strong></td>
<td>36%</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td><strong>% Chronic Lung Disease</strong></td>
<td>22%</td>
<td>21%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>% Chronic Kidney Disease</strong></td>
<td>21%</td>
<td>23%</td>
<td>8%</td>
</tr>
</tbody>
</table>
SHIELD Impact: *Nursing Homes*
25% Reduction in All MDROs

![Graph showing 25% reduction in MDROs in nursing homes during intervention compared to baseline. The graph uses different colors to represent different types of MDROs: Any MRSA, Any ESBL, Any VRE, Any CRE.]
SHIELD Impact: *LTACHs*

34% Reduction in All MDROs
SHIELD OC Summary

• Regional decolonization intervention in 35 facilities
  ✓ Hospitals, nursing homes, LTACHs
  ✓ 25% overall MDRO reduction
  ✓ Reduction in Orange County CRE
• Reductions in endemic and epidemic healthcare MDROs
• If simulation models correct, more benefit to come if we continue to work together with this decolonization intervention
Chlorhexidine: Pragmatic Pearls
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
- 2% no-rinse
  - Higher skin concentrations (2x)
  - May be especially important for Gram-negative bacteria

1 Popovich K et al. ICHE 2012;33:889-96
2 Rhee Y et al. ICHE 2018;39:405-11
3 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
  - Mild rash, irritation <<1%
  - Safe on dermatitis, erythema, papules, blisters, ulceration, denuded skin, loss of epidermis

- 4% rinse-off well tolerated
  - Mild rash, irritation 2.3%, one-third opt to continue

- 4% no-rinse: higher risk for dryness

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1 Climo M NEJM 2013;368:533-42
2 Grove GL AJIC 2001;29:361-9
3 Bleasdale SC Arch Int Med 2007;167:2073-9
4 Project CLEAR Trial, IDWeek 2016, NCT01209234
5 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 32-128 μg/ml
- Bathing concentrations
  - 2% no-rinse cloths: 20,000 μg/ml
  - 4% rinse off: 40,000 μg/ml
- Proper bathing immediately cidal upon drying
  - Residual persists, dissipates with time
  - Levels after 24 hours highly variable 10-1000+
Residual CHG Concentration

- **A:** 2% no-rinse cloth
- **B:** 4% liquid rinse, non-cotton cloth
- **C:** 4% liquid rinse, cotton cloth

Rhee Y et al. ICHE 2018;39:405-11
No Evidence of Resistance in Trials

- Climo et al. ICU Trial: No associated CHG resistance
- REDUCE MRSA Trial: No associated CHG or mupirocin resistance
- Project CLEAR Trial: No associated CHG or mupirocin resistance

Regardless, ongoing surveillance for resistance needed

- Efflux mechanisms
- Need higher fidelity resistance genes than qac

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1 Climo M et al. NEJM 2013;368:533-42
2 Hayden M et al. JCM 2016;54(11):2735-2742
3 Huang SS et al. IDWeek 2016
Critical if *S. aureus* infection is a target for reduction

- Mupirocin most commonly used in trials
- Iodophor may be relevant as mupirocin-resistance rises
  - Mupirocin resistance varies <5-18% across country
  - Iodophor shown to suppress MRSA for surgery
  - Being used twice daily x 5 days in clinical trials
  - One swab thrice around equivalent to two swabs 30s each
  - Low risk, no adverse events
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
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; Monika Kumaraswami, MD; Sirisha Kundrapu, MD, MS; Venkata Sunkesula, MD, MS; Jennifer L. Cadnum, BS; Michelle M. Nerandzic, BS; Myrean Tomas, MD; Curtis J. Donskey, MD

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

2 Supple et al. ICHE 2015;36(9):1095-7
• 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
• 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

**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.
Invest in Simple Patient Handouts

Prevent infections during your hospital stay

**BATHE** daily with Chlorhexidine (CHG) cloths

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:

1. **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
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?
Universal ICU Decolonization: An Enhanced Protocol

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.
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