ABATE Infection Project

*Active Bathing to Eliminate Infection Project*

Susan Huang, MD MPH
Ken Kleinman, ScD
Collaboratory Grand Rounds
Agenda

• Project Overview
• Recruitment
• IRB
• Laboratory Strain Collection
• Baseline Data Streams
• Statistical Approach
• Timeline
Project Overview
ABATE Infection Project
Active Bathing to Eliminate Infection

Trial Design

• 2-arm cluster randomized trial to assess the value of chlorhexidine bathing and nasal decolonization in reducing hospital-associated infections in non-critical care units

• 50+ HCA hospitals and their adult non critical care units
Arm 1: Routine Care
- Routine policy for showering/bathing

Arm 2: Decolonization
- Daily CHG shower or CHG cloth bathing routine for all patients
- Mupirocin x 5 days for those MRSA+ by history or screen

Condition*period design
- Baseline period: data collection only
- Intervention period: intervention, in intervention arm; monitoring to ensure no competing intervention in routine care arm
Outcomes obtained from the HCA data warehouse

Primary Outcome
  • Clinical cultures with MRSA and VRE

Secondary Outcomes
  • Clinical cultures with Gram Negative MDROs
  • Bloodstream infections: all pathogens
  • Urinary tract infections: all pathogens
  • Blood culture contamination
  • Infectious readmissions
  • Emergence of resistance (strain collection)
Recruitment
Hospital Recruitment

Response

<table>
<thead>
<tr>
<th># Hospitals</th>
<th>% Total Recruitment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>25%</td>
<td>4 business days</td>
</tr>
<tr>
<td>29</td>
<td>50%</td>
<td>7 business days</td>
</tr>
<tr>
<td>43</td>
<td>75%</td>
<td>9 business days</td>
</tr>
<tr>
<td>55</td>
<td>100%</td>
<td>11 weeks</td>
</tr>
</tbody>
</table>

- 15 states
- 55 CEO participation letters in hand
### 55 Hospitals

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Critical Care Adult Units</td>
<td>197</td>
</tr>
<tr>
<td>Mixed Medical/Surgical</td>
<td>35%</td>
</tr>
<tr>
<td>Cardiac/Telemetry</td>
<td>16%</td>
</tr>
<tr>
<td>Surgical</td>
<td>13%</td>
</tr>
<tr>
<td>Medical</td>
<td>10%</td>
</tr>
<tr>
<td>Step-down</td>
<td>10%</td>
</tr>
<tr>
<td>Oncology</td>
<td>4%</td>
</tr>
<tr>
<td>Other</td>
<td>12%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average annual admissions</td>
<td>11,833</td>
</tr>
<tr>
<td>Mean LOS (median)</td>
<td>4.7 (4.6) days</td>
</tr>
</tbody>
</table>

Confidential: do not cite or distribute 55 Hospitals
Hospital Unit Exclusions

• **Exclusion Criteria**
  – Pediatric, BMT, peri-partum, psychiatry, rehab units
  – Units already performing routine CHG bathing
  – Units with >30% cardiac or hip/knee orthopedic surgeries
  – LOS < 2 days

• **Unit Engagement Survey / Data streams**
  – 9-10% exclusion
Centralized IRB

Central IRB approved Feb 2013 (Harvard Pilgrim)

Reliance Agreements

- 54 of 55 hospitals have agreed to cede to Harvard

<table>
<thead>
<tr>
<th># Hospitals</th>
<th>%</th>
<th>Time to Approval (Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>13%</td>
<td>1</td>
</tr>
<tr>
<td>24</td>
<td>44%</td>
<td>2</td>
</tr>
<tr>
<td>38</td>
<td>69%</td>
<td>3</td>
</tr>
<tr>
<td>46</td>
<td>84%</td>
<td>4</td>
</tr>
<tr>
<td>51</td>
<td>93%</td>
<td>5</td>
</tr>
<tr>
<td>54</td>
<td>98%</td>
<td>6</td>
</tr>
</tbody>
</table>

- 1 hospital providing prisoner oversight
Informed Consent

Will waive informed consent
Will not post informative signs

OHRP waiver conditions met

- Minimal risk criteria
- Evaluation of quality improvement programs
- Population impact due to contagion

FDA

- Confirmed no oversight
## Strain Collection Protocol

### Assess resistance to decolonization agents
- Baseline level of CHG and mupirocin resistance
- Will more resistance emerge in one arm vs the other?

### 2 phases of strain collection
- Baseline Collection
- Intervention Collection
As received

1) clear plastic Biohazard Bag,
2) white Secondary Biohazard envelope
3) Saf-T-Pak shipping box
4) bubble wrap for slants
5) absorbent sheet
6) Pre-paid & pre-addressed FedEx slip

Assembled

Please make sure ‘BIOLOGICAL SUBSTANCE, CATEGORY B’ is checked
### Overall Collection Goals

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>1200</td>
<td>1200</td>
</tr>
<tr>
<td>GNR</td>
<td>1400</td>
<td>1400</td>
</tr>
<tr>
<td>Total</td>
<td>2600</td>
<td>2600</td>
</tr>
</tbody>
</table>

### Monthly Lab Collection Goals

<table>
<thead>
<tr>
<th></th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>up to 10 MRSA+ isolates</td>
</tr>
<tr>
<td>GNR</td>
<td>up to 10 select GNR isolates</td>
</tr>
<tr>
<td>Total</td>
<td>max of 20 total isolates/month</td>
</tr>
</tbody>
</table>
## MRSA Collection Estimates

<table>
<thead>
<tr>
<th>MRSA Collection Totals &amp; Rates</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td># Facilities Eligible to Ship</td>
<td>54</td>
</tr>
<tr>
<td># Facilities that Have Shipped</td>
<td>48</td>
</tr>
<tr>
<td>Total Number of Isolates Shipped</td>
<td>1035</td>
</tr>
<tr>
<td>Total Number of Isolates Confirmed</td>
<td>899</td>
</tr>
<tr>
<td>Monthly Shipping Average per Lab</td>
<td>3.9/lab</td>
</tr>
</tbody>
</table>
MRSA Collection Estimates

Baseline Completion – MRSA Collection

- 1200 isolates = overall goal
- 1035 isolates = total shipped to date
- 351 isolates = total >2 day* isolates shipped to date

*Day 1 = day of hospital admission

Ongoing collection
## GNR Collection Estimates

<table>
<thead>
<tr>
<th>GNR Collection Totals &amp; Rates</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td># Facilities Eligible to Ship</td>
<td>54</td>
</tr>
<tr>
<td># Facilities that Have Shipped</td>
<td>48</td>
</tr>
<tr>
<td>Total Number of Isolates Shipped</td>
<td>1652</td>
</tr>
<tr>
<td>Total Number of Isolates Confirmed</td>
<td>1474</td>
</tr>
<tr>
<td>Monthly Shipping Average per Lab</td>
<td>6.3/lab</td>
</tr>
</tbody>
</table>
GNR Collection Estimates

Select GNRs

- E. Coli
- K. pneumoniae
- P. aeruginosa
- P. mirabilis
- K. oxytoca
- S. marcescens
- A. baumannii
- S. maltophilia
- Burkholderia sp

GNR Breakdown by Organism

- # E. coli: 707
- # KPN: 295
- # PAER: 218
- # PMIR: 133
- # KOXY: 36
- # SMAR: 36
- # ABAU: 24
- # SMALTO: 24
- # BURK: 1
Goal reached!

GNR collection complete as of Aug 31

Baseline Completion – GNR Collection

1400 isolates = overall goal

1652 isolates = total shipped to date

754 isolates = total >2 day* isolates shipped to date

*Day 1 = day of hospital admission
Strain Collection Timeline

Feb 2013: Lab Coaching Call
Mar 2013: 9-month BASELINE COLLECTION
Nov 2013 - Oct 2014: 12-month Collection "Break"
Oct 2014: Refresher Coaching Call
Nov 2014: 9-month INTERVENTION COLLECTION
Educational & Training Materials
Arm-Specific Toolkit Binders

Universal Decolorization – Arm 2

**DO**

- Use either 2% chlorhexidine (CHG) cloth for daily bed bathing or 4% liquid CHG for daily showers. Use CHG for all shower/bathing needs.
- Apply to all patients, every day, for entire unit stay.
- Massage CHG onto skin for best effect.
- Use CHG on lines, tubes, drains, and over non-gauze dressings. Use on superficial wounds and rashes to remove germs.
- For MRSA+ patients, use nasal mupirocin twice a day for 5 days of unit stay.
- Restate for patients who are readmitted or transferred from another ward.
- Report mupirocin/CHG related events to treating physician and unit nursing director.

**DON’T**

- Do NOT get CHG into eyes or ears.
- Do NOT wipe off after applying CHG cloths. Let air dry.
- Do NOT flush CHG cloths.
- Do NOT continue protocol after unit discharge.
- Do NOT include patients who are:
  - <12 years old.
  - Allergic to mupirocin and/or CHG.

Refer to nursing protocol for step-by-step instructions.

**Phone Matrix**

<table>
<thead>
<tr>
<th>Topic</th>
<th>What to do</th>
<th>Who to contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>General questions</td>
<td>Call or email</td>
<td>ABATE Infection Project Staff</td>
</tr>
<tr>
<td>Chlorhexidine bathing or mupirocin application</td>
<td>Call or email</td>
<td>Lauren Hahn</td>
</tr>
<tr>
<td>Study related event questions</td>
<td>Call or email</td>
<td>Rebecca Kagan</td>
</tr>
<tr>
<td>Study related event reporting</td>
<td>Fax Study Related Event Form</td>
<td>ATTN Rebecca Kagan</td>
</tr>
<tr>
<td>Lab strain collection</td>
<td>Call or email</td>
<td>Katie Hoffert</td>
</tr>
<tr>
<td>IRB questions</td>
<td>Call or email</td>
<td>Rebecca Kagan</td>
</tr>
<tr>
<td>Lead Investigator questions</td>
<td>Call or email</td>
<td>Susan Huang, MD</td>
</tr>
</tbody>
</table>

For questions related to HCA hospital policy, please contact:

<table>
<thead>
<tr>
<th>Name</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ed. September MD</td>
<td>(281) 714-5689</td>
</tr>
<tr>
<td>Medical Director, Infection Prevention and Epidemiology</td>
<td>Edna</td>
</tr>
<tr>
<td>Julia Moody, MS (ASCP) Director, Infection Prevention</td>
<td>(615) 344-1692, Juli</td>
</tr>
</tbody>
</table>

General Questions
(855) 332-2282
ABATEstudy@gmail.com

Study Related Events
(617) 509-4141, phone
(617) 509-4260, fax
Arm-Specific CBT Training

Nursing Protocol Training
Universal Decolonization
ARM 2

Bathing Clean Up

Dispose of each washcloth in the trash

Do NOT flush washcloths in the toilet
Patient and Staff Flyers

Prevent infections during the hospital stay
Bathe daily with Chlorhexidine (CHG) soap

**STAFF**

While in the hospital, bathe patients every day with a special antiseptic soap (CHG) to help remove germs and prevent infection.

6 cloths should be applied as below:

1.  
2.  
3.  
4.  
5.  
6.  

**PATIENT**

Prevent infections during your hospital stay
Bathe daily with Chlorhexidine (CHG) soap

While in the hospital, bathe every day with a special antiseptic soap (CHG) shown to remove germs and prevent infection better than soap and water.

6 cloths should be applied as below:

1.  
2.  
3.  
4.  
5.  
6.  

**Take a CHG shower or bed bath**

**Reminders**

- CHG is proven to work better than soap and water in removing germs
- Once massaged onto skin, it works to kill germs for 24 hours
- Use CHG every day. Starting on admission is best, before IVs, lines, urinary catheters, and procedures/surgery
- Be thorough. Ask for help to cover all skin
- CHG is safe on rashes, burns, and wounds that are not large or deep to remove germs and prevent infection
- Clean lines, drains, tubes attached to body
- Allow to air dry for best effect

**Clean all skin areas with special attention to:**

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

**Protect yourself every day**

**SHOWERING with CHG soap**

1. Rinse body with warm water.
2. Wash hair with CHG or regular shampoo
3. Turn off the water and lather washcloth with plenty of CHG soap
4. Lather and massage soap in all six areas
5. Leave soap for 2 minutes before rinsing

**BATHING with CHG cloths**

1. These cloths are your protective bath
2. Use all 6 cloths. More, if needed
3. Firmly massage to clean skin. CHG will kill germs for 24 hours if applied well
4. Clean over non-absorbable dressings
5. Clean 6 inches of lines, tubes and drains nearest the body
6. Dispose of CHG cloths in a regular trash bin. Do not flush

Caution: Avoid eyes and ear canals
Arm-Specific Protocols

How to use
Nasal Mupirocin Ointment

For MRSA+ patients:

- Place patient’s bed at 30 degrees, if tolerated
- Apply 1 inch of ointment from tube directly into each nostril
- Press nostrils together and massage gently for 60 seconds
- Do this twice a day for 5 days
- Avoid contact with eyes and other intranasal products
  (contact study team if any questions)
Compatibility Guidance

Commonly Used HCA Approved Compatible Products

Lotions, Creams, & Ointments

- Compatible
  - ConvaTec Aloe Vesta 2 – Moisturizing Skin Conditioner*
  - Baby Magic Baby Lotion
- NOT Compatible
  - Medline Hand & Body Lotion
  - Johnson’s Baby Lotion
  - Keesler Cream

Barrier Products

- Compatible
  - ConvaTec Aloe Vesta 3 – Protective Ointment*
  - ConvaTec Aloe Vesta 3 – Protective Barrier Spray*
Adverse Event Reporting

STUDY-RELATED EVENT SUBMISSION FORM

Please use this form to report all study-related events to your Unit Nursing Director. For clinical decisions related to possible study-related events, please contact the treating physician. Unit Director to fax completed study-related event forms to ABATE study staff on bi-weekly basis.

Fax completed form to (617) 509-4260, ATTN: Rebecca Kaganov
For questions, please contact ABATE Infection Study staff at ABATEinjc@gmail.com or (617) 509-4141

Name of individual filing report: ___________________________ 34 ID Number: ____________________
Title/Position of individual filing report: ___________________________
Facility Name: ___________________________ Facility COID: ____________________

Please provide all forms of contact information below:
E-mail address: ___________________________ Unit General Phone: (___) ___ - ______
Unit Manager Name: ___________________________ Unit Manager Phone: (___) ___ - ______

Section I: General Information
Today’s Date: ___/___/_______ Date of First Symptom Onset: ___/___/_______
Please fill out one form per adverse event.

Patient Name: ___________________________ Medical Record Number (MRN): ___________________________
Unit Name: ___________________________ Patient Age: _______ Patient Gender: M F

Please choose the option that best describes the event:

☐ Skin/mucosa related, continue to Section II: Skin Related Events

☐ Non-skin related, please provide a brief description of the event. We will contact you for more information.
Baseline Data Streams
Data Streams

Data Sources
  • HCA Data Warehouse
  • Meditech

Baseline Data Streams
  • Nursing Queries
  • Admission Discharge Transfer (census by unit)
  • Administrative
  • Pharmacy
  • Central supply
  • Financial
  • Microbiology
### Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>4 month Baseline Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admissions with non-ICU stay (N)</td>
<td>73,648</td>
</tr>
<tr>
<td>Non-ICU Patient Days</td>
<td>394,011</td>
</tr>
<tr>
<td>Hospital Stay in Days (Mean (SD))</td>
<td>6.6 (5.1)</td>
</tr>
<tr>
<td>Non-ICU stay in Days (Mean (SD))</td>
<td>5.3 (3.8)</td>
</tr>
<tr>
<td>Age in Years (Mean (SD))</td>
<td>63.8 (17.9)</td>
</tr>
<tr>
<td>Female</td>
<td>55%</td>
</tr>
<tr>
<td>Race (%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>68%</td>
</tr>
<tr>
<td>Black</td>
<td>12%</td>
</tr>
<tr>
<td>Other</td>
<td>20%</td>
</tr>
<tr>
<td>Comorbidities (%)</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>27%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>32%</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>17%</td>
</tr>
<tr>
<td>Renal failure</td>
<td>19%</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>7%</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>8%</td>
</tr>
<tr>
<td>Cancer</td>
<td>9%</td>
</tr>
<tr>
<td>Surgery During Admission (%)</td>
<td>29%</td>
</tr>
</tbody>
</table>
### Baseline Outcomes

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>Rate (Event/1,000 patient days)</th>
<th>Event/Attributable Patient Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA and VRE Clinical Cultures</td>
<td>2.2</td>
<td>547/253,329</td>
</tr>
<tr>
<td><strong>Select Secondary Outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GNR Multi-Drug Resistant Org.</td>
<td>0.6</td>
<td>163/255,436</td>
</tr>
<tr>
<td>All-Cause Bloodstream Infection</td>
<td>1.1</td>
<td>272/254,318</td>
</tr>
</tbody>
</table>

Based Upon March-June, 2013 Data

* a Events occurring >2 days into unit admission through 2 days following unit discharge

* b Denominators differ due to censoring of patient days following an identified event

* c Select key outcomes provided
STATISTICAL DESIGN
Lack of balance on key covariates can open the door to confounding: a threat to cluster-randomized trials

Our approach: stratified randomization

Key covariates
- Volume
- Baseline outcome rates
- Case mix
- Product use
- Type of unit (medical/surgical)
How to balance all of these at once?
We can’t, but we can try different stratification/pairing schemes assess their impact on the balance.

Schemes:
1. Choose pairs that minimize the total Mahalanobis distance between pairs. (1a: weight variables)
2. Rank by volume, then within classes of similar volume, rank by baseline rates, etc.
3. ...
Plans for Randomization

There can be no one “correct” stratification scheme. If we had no preliminary or baseline data, we’d have to just take a shot in the dark. But we have a lot of baseline data.

Approach:
1) Implement each stratification scheme many times;
2) Assess the resulting balance
3) Choose the scheme with the results we like best
Mock-up of assessment

Blue scheme matches poorly on volume and outcome but well on baseline chlorhexidine use and bathing. Black scheme is reversed, while green and red are approximately balanced.
Planned data analysis

The primary outcome: clinical culture with MRSA or VRE.
Length of stay differs between individuals, probability of positive culture may vary over time of stay:

➡ Survival analysis via proportional hazards, a.k.a Cox, regression

Randomization by hospital, not by patient:

➡ Frailty model, random effects for proportional hazards
ABATE Study Timeline

- **Oct 29, 2013**: Coaching Call: Instructions for Randomization
- **Nov-Dec, 2013**: Randomize, Schedule Committee Review
- **Jan-Feb, 2014**: Committee Approvals
- **Feb-Mar, 2014**: CBT Training Site Visits
- **Apr-May, 2014**: Product Phase In
- **Jun 2014**: Intervention Phase Launch
**ABATE Infection Trial**  
**Active Bathing to Eliminate Infection**

**Principal Investigator:** Susan Huang, MD MPH  
**Content Expertise**  
**Infectious Diseases & Hospital Epidemiology:** Susan Huang MD MPH, Ed Septimus MD, Julia Moody RN MS, John Jernigan MD MS, Mary Hayden MD, Robert Weinstein MD  
**Health System**  
Hospital Corporation of America  
Ed Septimus, MD *HCA site lead*  
Jason Hickok, MBA RN *HCA administrative lead*  
Julia Moody, MS SM  
Jonathan Perlin, MD PhD  
**Statistics**  
Ken Kleinman ScD, Dan Gillen PhD  
**Microbiology**  
Mary Hayden, MD, Chris Bushe, MHSA  
**Project Coordination**  
Adrijana Gombosev BS, Lauren Heim BS, Julie Lankiewicz MPH CCRC, Katie Haffenreffer BS  
**IRB**  
David Vulcano, MBA, VP Clinical Research  
Sheila Fireman JD, Rebecca Kagenov, BS
ABATE Infection Project

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