

New Strategies to Reduce MRSA in ICUs

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Disclosures: None

MRSA in Hospitals

- In US
 - 55% of hospital *S. aureus* infections are MRSA ¹
 - 5-8% of general inpatients harbor MRSA ^{2 3}
 - 8-20% of ICU patients harbor MRSA ⁴⁻⁶
- Up to 33% of newly-identified chronically ill hospitalized carriers experience invasive disease in 1y ⁴
- Increased cost, hospital stay, risk of death

¹ Sievert et al. ICHE 2013;34(1):1-14

² Jarvis et al. AJIC 2007;35:631-7

³ Moody et al. J Healthcare Q 2013 In press

⁴ Honda et al. ICHE 2010;31(6):584-591

⁵ Huang et al. JID 2007;195(3):330-8

⁶ Huang et al. ICHE 2006;27(10):1032-1040

⁷ Huang et al. PLoS ONE 2011;6(9):e24340

MRSA as a Key Hospital Pathogen

- 2009-10 CDC Data, National Healthcare Safety Network
- *S aureus*
 - #1 Healthcare-association pathogen
 - #1 Ventilator-associated pneumonia
 - #1 Surgical site infection
 - #2 Central line associated bloodstream infections
- Majority MRSA

Options to Reduce MRSA

- Vaccinate
- Contact precautions
- Enhanced cleaning
- Active screening
- Screen and Decolonize
- Universal Decolonization

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Decolonization

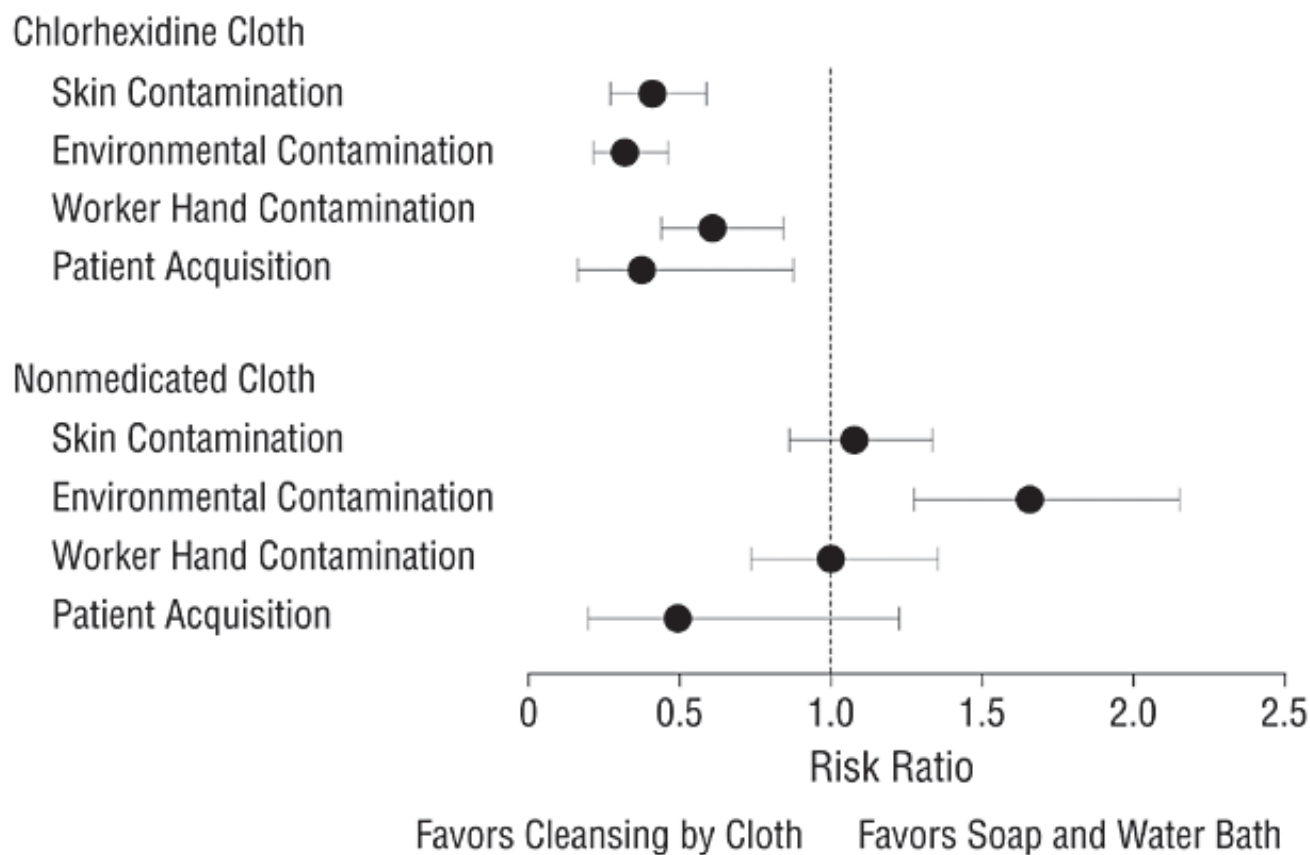
Chlorhexidine Uses

- Dental – gingivitis, periodontal disease
- Central line skin prep
- Surgical skin prep
- Surgical pre-operative bathing
- Wound cleanser
- Bathing to reduce microbial burden and infection

Initial Studies of Chlorhexidine Bathing for MDRO Control

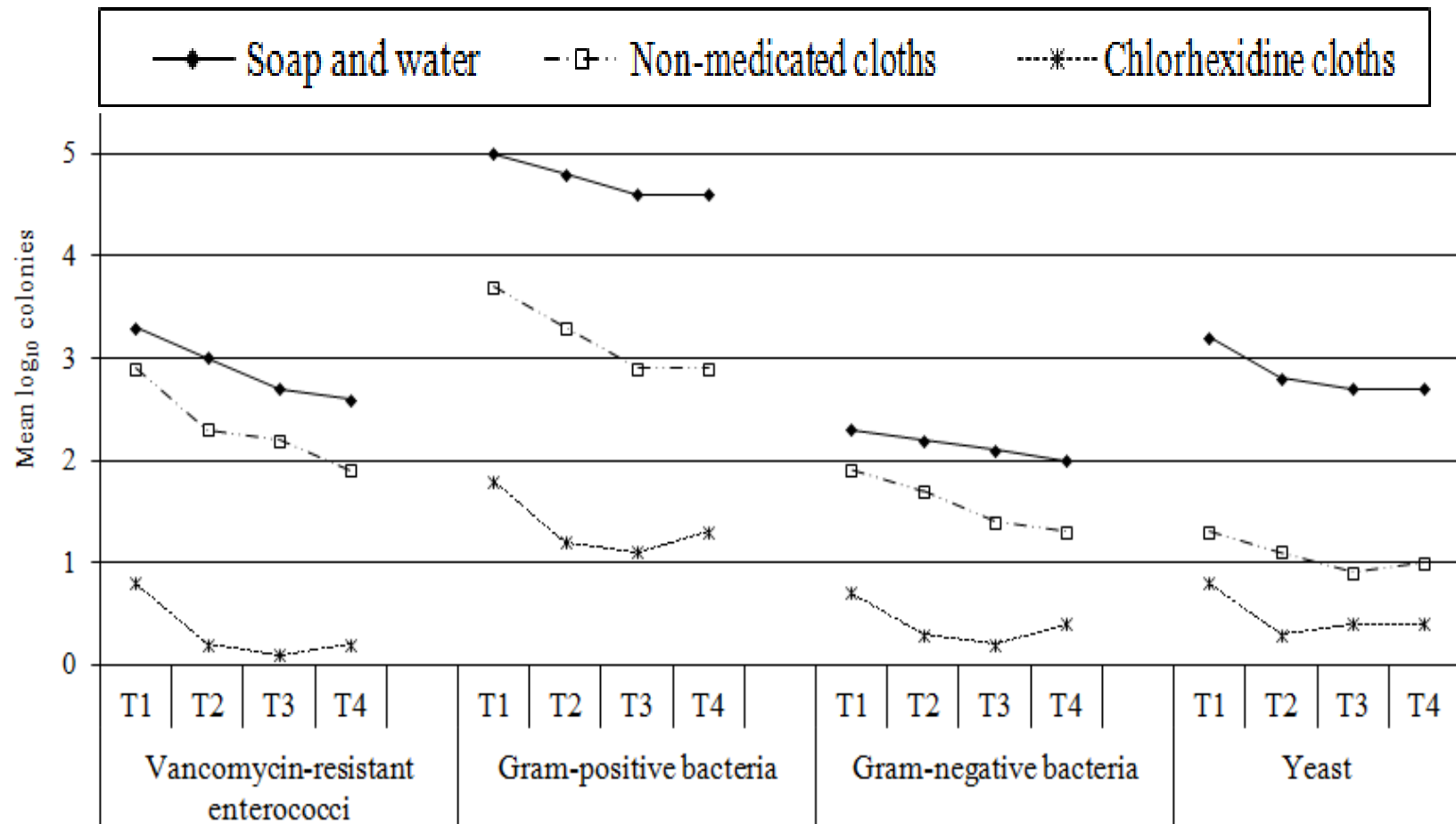
- Single center study in MICU
- 2002-2003
- 5 months soap and water → 5 months 2% CHG cloths → 5 months non-medicated cloths
- Serial rectal, skin, and environmental sampling
- Outcome: acquisition of VRE

CHG Impact on Skin, Environment, Staff Contamination and VRE Acquisition



Vernon et al, *Arch Intern Med* 2006; 166:306-12.

Bioburden on Inguinal Skin by Cleansing Method



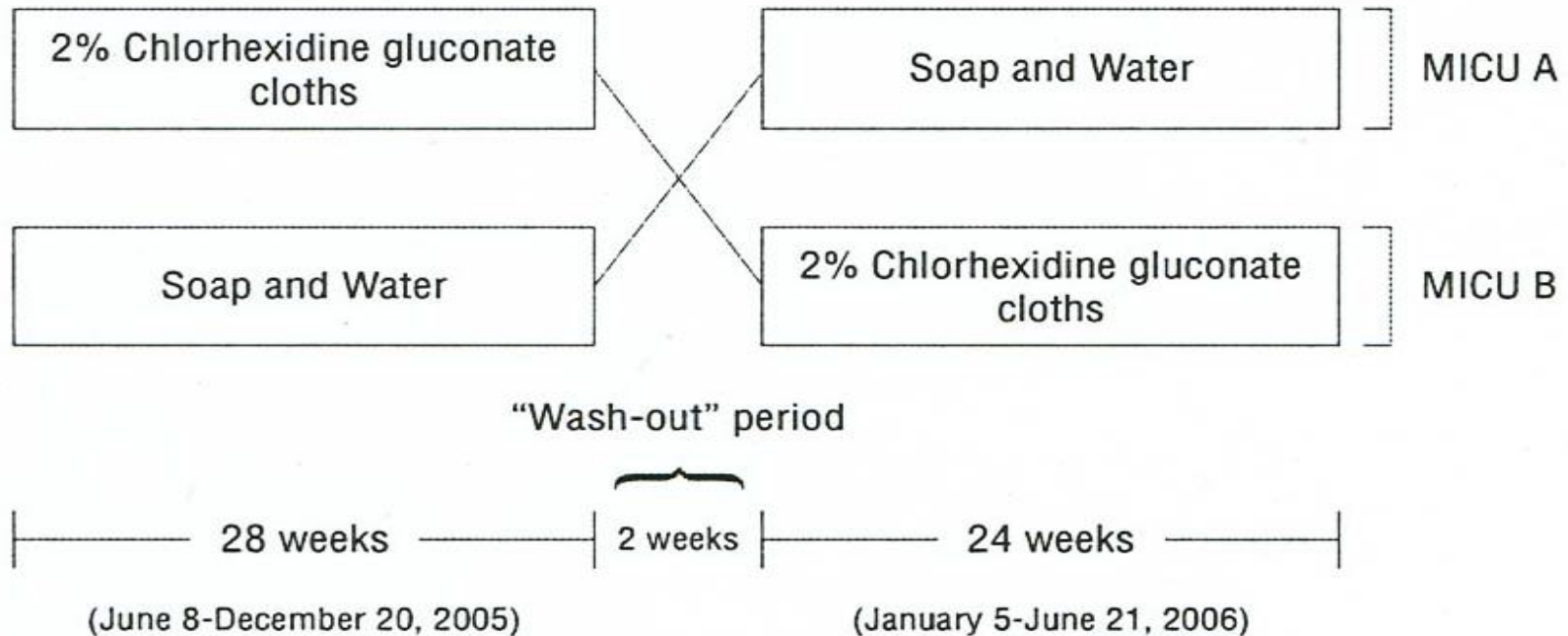
Reduction in MRSA and VRE Acquisition with Chlorhexidine Bathing

- 4 Center pre-post evaluation of adult ICUs
- 6 months of routine soap → 6 months of 2% CHG cloths

	Baseline Period	Intervention Period
Admissions	2670	2650
Total bed days of care	15,472	15,225
Total central venous catheter days ^a	10,062	9,633
Mean length of stay (days)	5.99	5.82
MRSA acquisition		
Number of cases	67	45
Number of eligible patient days	13,300	13,096
Incidence rate ^b	5.04	3.44 ($p = 0.046$) ^c
MRSA prevalence rate ^b	22.80	21.80
VRE acquisition		
Number of cases	61	30
Number of eligible patient days	13,412	13,610
Incidence rate ^b	4.35	2.19 ($p = 0.008$) ^c
VRE prevalence rate ^a	17.97	16.75

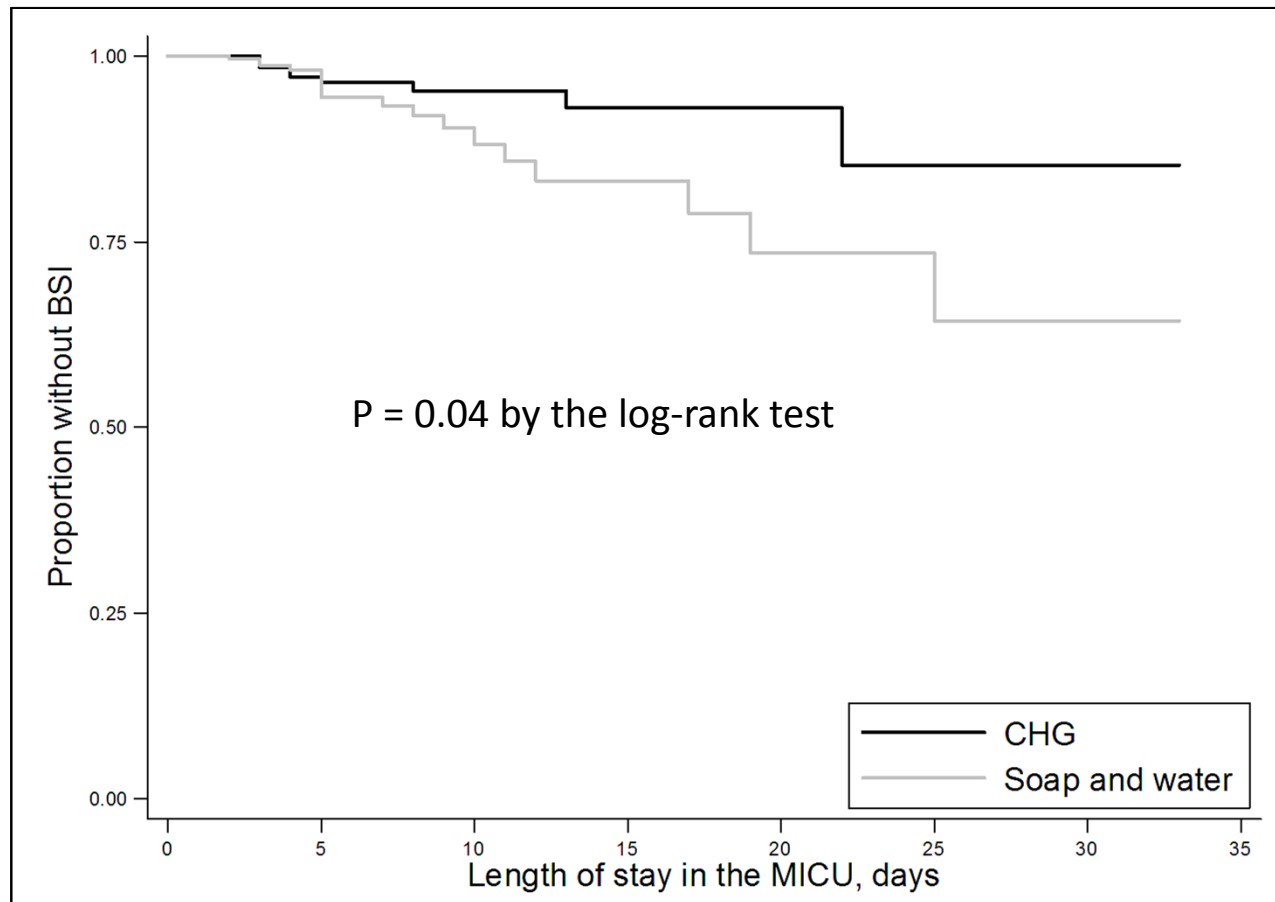
Climo et al, *Crit Care Med* 2009; 37(6):1858-65.

Chlorhexidine Prevention of Bloodstream Infections



Bleasdale et al, *Arch Intern Med* 2007; 167:2073-9.

Chlorhexidine Impact on Central Line Bloodstream Infections



Bleasdale et al, *Arch Intern Med* 2007; 167:2073-9.

3 Decolonization Trials - 2013

- **Adult ICUs**
 - Academic teaching centers (Climo et al)
 - Community hospitals (Huang et al)
- **Pediatric ICUs**
 - Academic teaching centers (Milstone et al)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Daily Chlorhexidine Bathing on Hospital-Acquired Infection

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

[Climo et al. N Engl J Med 2013;368:533-42](#)

Decolonization in Academic Adult ICUs

- **12 adult ICUs, 7 academic medical centers**
 - Randomized cross-over design (6 months each)
 - All units performing admission MRSA/VRE screens
- **Outcomes**
 - Composite: MRSA and VRE acquisition
 - All-cause ICU-attributable BSI
 - Primary BSI
 - CLABSI

Climo et al. N Engl J Med 2013;368:533-42

Decolonization in Academic Adult ICUs

- **Study Conduct**

- 3 ICUs, 1 hospital dropped, low compliance
- 9 ICUs, 6 hospitals, 7,727 patients remained
- As-treated analysis

Climo et al. N Engl J Med 2013;368:533-42

Participating ICUs

Hospital	Unit	Mean No. of Monthly Admissions	Mean Length of Stay <i>days</i>	MRSA Prevalence <i>percent of admissions</i>	VRE Prevalence	Baseline Rate of Primary Bloodstream Infections† <i>no./1000 patient-days</i>
Group 1						
A	MICU	123.8 (114–142)	5.6	11.0	21.0	8.1
C	SICU	46.3 (31–59)	6.2	11.4	4.3	9.6
D	SICU 2	51.6 (32–71)	5.5	4.4	2.8	0
E	CSICU	85.3 (80–100)	5.0	6.6	8.3	0.4
F	BMT	41.8 (32–58)	18.8	2.4	21.6	5.5
Group 2						
B	MICU	111.6 (98–126)	5.4	21.8	21.0	3.1
C	MICU–CCU	55.8 (43–73)	5.4	16.1	9.7	8.5
D	SICU 1	62.3 (47–76)	5.1	10.8	8.2	2.2
E	MICU	72.7 (56–88)	6.4	23.3	27.9	8.7

Climo et al. N Engl J Med 2013;368:533-42

Decolonization Success

MDRO acquisition				
No. of infections	127	165		0.03
Incidence rate (no./1000 patient-days)	5.10	6.60		
VRE acquisition				
No. of infections	80	107		0.05
Incidence rate (no./1000 patient-days)	3.21	4.28		
MRSA acquisition				
No. of infections	47	58		0.29
Incidence rate (no./1000 patient-days)	1.89	2.32		
Hospital-acquired bloodstream infection				
No. of infections	119	165		0.007
Incidence rate (no./1000 patient-days)	4.78	6.60		
Primary bloodstream infection				
No. of infections	90	131		0.006
Incidence rate (no./1000 patient-days)	3.61	5.24		
Central-catheter-associated bloodstream infection				
No. of infections	21	43		0.004
Incidence rate (no./1000 catheter-days)	1.55	3.30		

Decolonization in Academic Adult ICUs

- **Sub-analyses**
 - BSI reductions in medical and BMT units
 - Primarily reductions in GP and fungal infections
- **Adverse events**
 - 2.0% CHG skin reactions vs 3.4% regular soap
 - No CHG resistance

Decolonization in Academic Adult ICUs

- **Advantages**
 - Randomized, multicenter
 - Findings highly supportive of prior observational studies
- **Disadvantages**
 - As treated analysis
 - Academic centers only

Climo et al. N Engl J Med 2013;368:533-42

The REDUCE MRSA Trial

Randomized Evaluation of
Decolonization vs. Universal Clearance to
Eliminate MRSA



UCIrvine
University of California, Irvine



Washington
University in St. Louis
SCHOOL OF MEDICINE



Pediatric SCRUB Trial

Articles

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



Aaron M Milstone, Alexis Elward, Xiaoyan Song, Danielle M Zerr, Rachel Orscheln, Kathleen Speck, Daniel Obeng, Nicholas G Reich, Susan E Coffin, Trish M Perl, for the Pediatric SCRUB Trial Study Group

Summary

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

Methods In an unmasked, cluster-randomised, two-period crossover trial, ten paediatric intensive-care units at five hospitals in the USA were randomly assigned a daily bathing routine for admitted patients older than 2 months, either standard bathing practices or using a cloth impregnated with 2% CHG, for a 6-month period. Units switched to the alternative bathing method for a second 6-month period. 6482 admissions were screened for eligibility. The primary outcome was an episode of bacteraemia. We did intention-to-treat (ITT) and per-protocol (PP) analyses. This study is registered with ClinicalTrials.gov (identifier NCT00549393).

Published Online
January 28, 2013
[http://dx.doi.org/10.1016/S0140-6736\(12\)61687-0](http://dx.doi.org/10.1016/S0140-6736(12)61687-0)

See Online/Comment
[http://dx.doi.org/10.1016/S0140-6736\(12\)61996-5](http://dx.doi.org/10.1016/S0140-6736(12)61996-5)

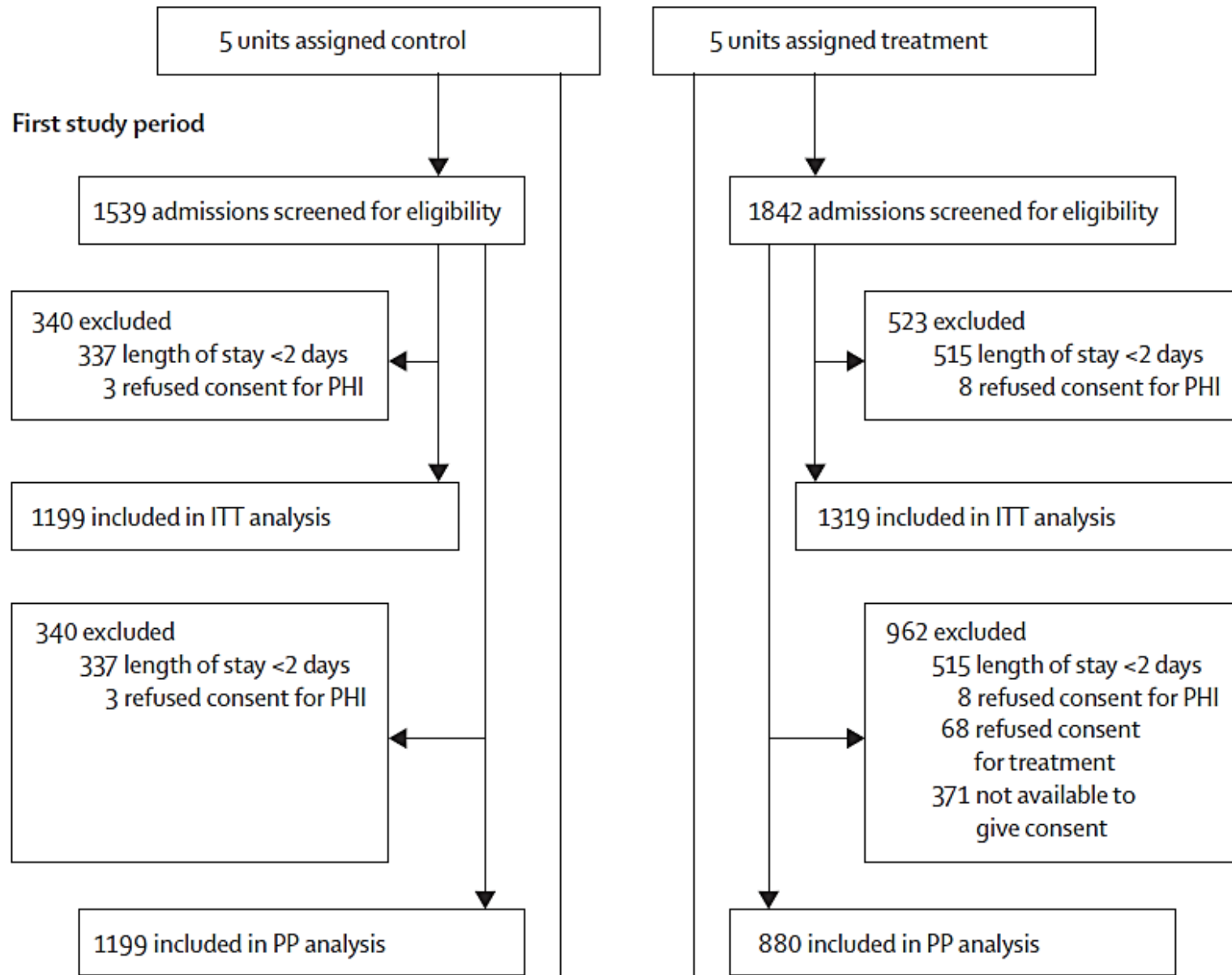
Department of Pediatrics,
Division of Pediatric Infectious
Diseases (A M Milstone MD),
and Department of Medicine,
Division of Infectious Diseases

Milstone et al. Lancet. 2013; 381(9872):1099-1106

Decolonization in Academic PICUs

- **10 Pediatric ICUs, 5 academic medical centers**
 - Randomized cross-over design (6 months each)
 - Excluded those with
 - Anticipated LOS \leq 2 days
 - Lumbar drains
 - Severe skin issues
- **Outcome**
 - Bacteremia (single positive blood culture)

Milstone et al. Lancet. 2013; 381(9872):1099-1106



Milstone et al. Lancet. 2013; 381(9872):1099-1106

As Treated Analysis: 36% Less BSI

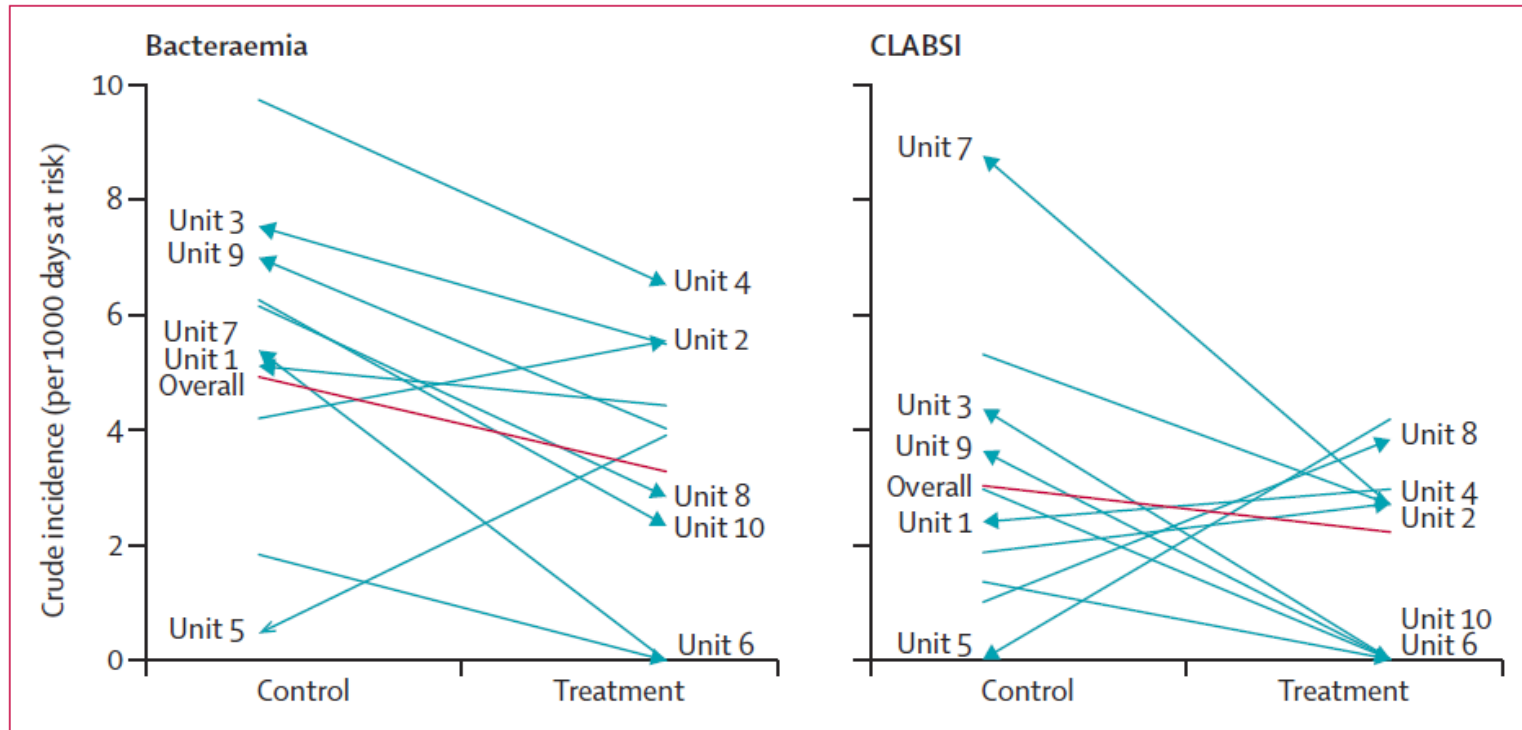


Figure 2: Change in crude incidence of bacteraemia and CLABSI, per-protocol population

Every line represents one unit (appendix p 7); the slope shows the change in incidence of bacteraemia or CLABSI between control and treatment study periods, and the arrow indicates the assignment change from period one to two (eg, an arrow pointing to the treatment side shows the unit assignment started as control and moved to treatment). The red line represents the overall crude incidence between control and treatment units.

CLABSI=central line-associated bloodstream infection.

As Randomized vs As Treated

	Events		Crude control incidence per 1000 at-risk days (95% CI)	Crude treatment incidence per 1000 at-risk days (95% CI)	Adjusted incidence rate ratio (95% CI)*	p
	Control	Treatment				
Per-protocol population						
Primary outcome (bacteraemia)	79	34	4.93 (3.91 to 6.15)	3.28 (2.27 to 4.58)	0.64 (0.42 to 0.98)	0.044
Bacteraemia in patients with central venous catheters	70	31	6.31 (4.92 to 7.97)	4.37 (2.97 to 6.21)	0.66 (0.47 to 0.94)	0.021
Secondary outcome (CLABSI)	28	13	3.00 (2.00 to 4.33)	2.20 (1.17 to 3.76)	0.68 (0.35 to 1.31)	0.249
Intention-to-treat population						
Primary outcome (bacteraemia)	79	53	4.93 (3.91 to 6.15)	3.52 (2.64 to 4.61)	0.71 (0.42 to 1.20)	0.199
Bacteraemia in patients with central venous catheters	70	43	6.31 (4.92 to 7.97)	4.36 (3.16 to 5.88)	0.65 (0.44 to 0.97)	0.034
Secondary outcome (CLABSI)	28	13	3.00 (2.00 to 4.33)	1.63 (0.87 to 2.79)	0.52 (0.25 to 1.08)	0.081

Milstone et al. Lancet. 2013; 381(9872):1099-1106

Decolonization in Academic PICUs

- Primarily gram positive reduction
- Adverse events
 - 3% (n=43) CHG vs 1% (n=26) of controls
 - Mild skin reactions, only 12 believed to be related

Milstone et al. Lancet. 2013; 381(9872):1099-1106

Evidence Summary

Author	Study Year	Study Type	Hospital	ICU	N	Findings	Publication	Funding
Vernon	10/02-12/03	Observational	1	1	1,787	65% less VRE acquisition 40-70% less VRE on skin, HCW hands, environment	Arch Intern Med 2006; 166:306-312	CDC, Sage
Climo	12/04-1/06	Observational	4	6	5,293	66% less VRE BSI 32% less MRSA acquisition 50% less VRE acquisition	Crit Care Med 2009; 37:1858-1865	CDC
Bleasdale	12/05-6/06	Observational	1	2	836	61% less primary BSI	Arch Intern Med 2007; 167(19):2073-2079	CDC, Sage
Popovich	9/04-10/06	Observational	1	1	3,816	87% less CLABSI 41% less blood contaminants	ICHE 2009; 30(10):959-63	CDC
Climo	8/07-2/09	Cluster RCT	6	9	7,727	23% less MRSA/VRE acquisition	N Engl J Med 2013; 368:533-42	CDC (Sage: product)
Milestone	2/08-9/10	Cluster RCT	5	10	4,947	36% less total BSI (as treated)	Lancet. 2013; 381(9872):1099-106	Sage, NIH
Huang	1/09-9/11	Cluster RCT	43	74	122,646	37% less MRSA clinical cultures 44% less all-cause BSI	IDWeek 2012; 2013 In press	AHRQ, CDC, HCA



Implementation Pearls for Chlorhexidine Bathing

Top Implementation Facts

- Training, oversight, compliance required ¹
- Massage onto skin to allow binding and 24h protection
- Soaps and shampoos can inactivate CHG
- Clean neck, web spaces well
- Wipe proximal 6 inches of devices (lines, foleys, drains)
- Safe on wounds, rashes, decubs, burns if not large or deep
- Minimal concern for facial washing – avoid eye, ear
- Warmth is for comfort, works warm or cold
- Cloths have lubricants; better for skin than soap and water

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

Implementation Aids Forthcoming

5 Day Protocol HCA  

DECOLONIZATION FOR SELECT CONTACT PRECAUTION PATIENTS


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

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

BATHE WITH CHG USING FIRM MASSAGE TO REMOVE BACTERIA

INCONTINENCE:

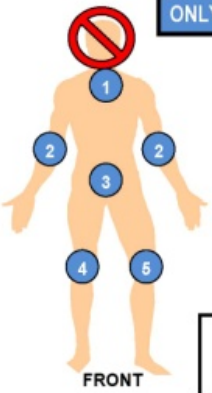
- Clean with chux & water, NOT soap
- Then bathe with CHG cloths, air dry
- Use as many CHG cloths as needed
- Apply CHG compatible barrier
- OK to repeat throughout the day




LINES AND TUBES:

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

ONLY USE CHG CLOTHS BELOW THE JAWLINE




FRONT



BACK

- 1 NECK, SHOULDERS & CHEST
- 2 BOTH ARMS, HANDS, THEN ARMPITS
- 3 ABDOMEN THEN GROIN & PERINEUM
- 4 RIGHT LEG, FOOT, THEN BACK OF KNEE
- 5 LEFT LEG, FOOT, THEN BACK OF KNEE
- 6 BACK OF NECK, BACK & THEN BUTTOCKS

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



REDUCE MRSA Trial
Targeted Decolonization – Arm 2

For MRSA-Positive Patients Only

DO

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

DON'T

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

REFER TO DECOLONIZATION PROTOCOL FOR STEP-BY-STEP INSTRUCTIONS

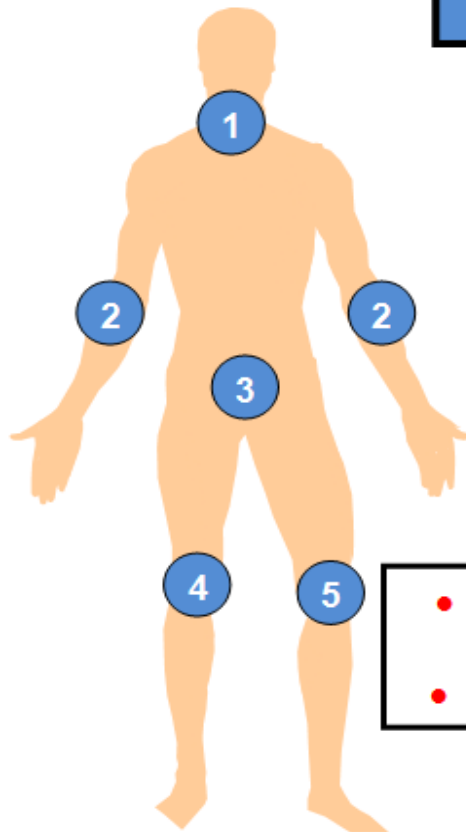
General Questions
(877) 294-9865
(617) 509-4141
Reduce.MRSA@gmail.com

Decolonization Protocol
(877) 294-9865

Study Related Events
(617) 509-4141 phone
(617) 509-4260 fax

Apply Chlorhexidine **WITH FIRM MASSAGE** to remove bacteria

USE ALL 6 CHG CLOTHS
Avoid EYES & EAR CANAL



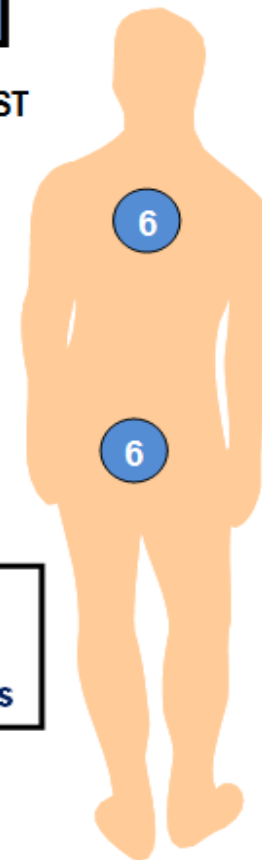
FRONT

- 1 FACE, NECK SHOULDERS & CHEST
- 2 BOTH ARMS & HANDS
- 3 ABDOMEN, GROIN & PERINEUM
- 4 RIGHT LEG & FOOT
- 5 LEFT LEG & FOOT
- 6 BACK, THEN BUTTOCKS

- Clean 6 inches of all tubes, lines, and drains closest to patient with CHG
- Safe on superficial wounds, rash, burns

Skin may feel sticky for a few minutes after CHG application.

Do NOT wipe off. Allow to air dry.



BACK

THIS IS a PROTECTIVE BATH
Do not use soap which can inactivate CHG

Chlorhexidine Adverse Events

Adverse events	Frequency
Dermatitis	Rare 1/5,000 days
Hypersensitivity reaction & anaphylaxis	Case reports ¹
Ototoxicity	Case reports ²
Corneal injury	Case report

¹ Anaphylaxis after topical application and impregnated catheter insertion.

² Bicknell, *J Laryngol Otol* 1971; 85:957-61.

Milstone et al, *Clin Infect Dis* 2008; 46:274–81.

G.W. Denton, Chlorhexidine *In: Sterilization and Disinfection* 5th Edition, Block SS, Ed. Lippincott Williams & Williams, Philadelphia PA, 2001; p321-36.

Change in Skin Assessment Score from Admission to Discharge

Study Period	Change in Score: Number (%)			Total # Patients
	Worse ^b	No Change	Better	
Soap & water bath	18 (6.3)	250 (88)	17 (6)	285
CHG bath	10 (2.5)	340 (86)	43 (10.9)	393
Non-medicated bath	5 (1.2)	377 (92)	28 (6.8)	410
Total	33	967	88	1088

- CHG cloths have emollients and moisturizers, including dimethicone
- Compares patient skin score on admission and discharge from the MICU.
- **Worse skin more likely in soap & water arm than CHG (p=.02) or non-medicated cloth (p=.001) arms.**

Questions?

