Universal Decolonization

Susan Huang, MD MPH
Associate Professor
University of California Irvine School of Medicine
Medical Director, Epidemiology & Infection Prevention
Division of Infectious Diseases & Health Policy Research Institute

Disclosures

Conducting a clinical trial (ABATE Infection Trial) in which participating hospitals are receiving contributed product from Sage Products and Molnlycke

Universal Decolonization

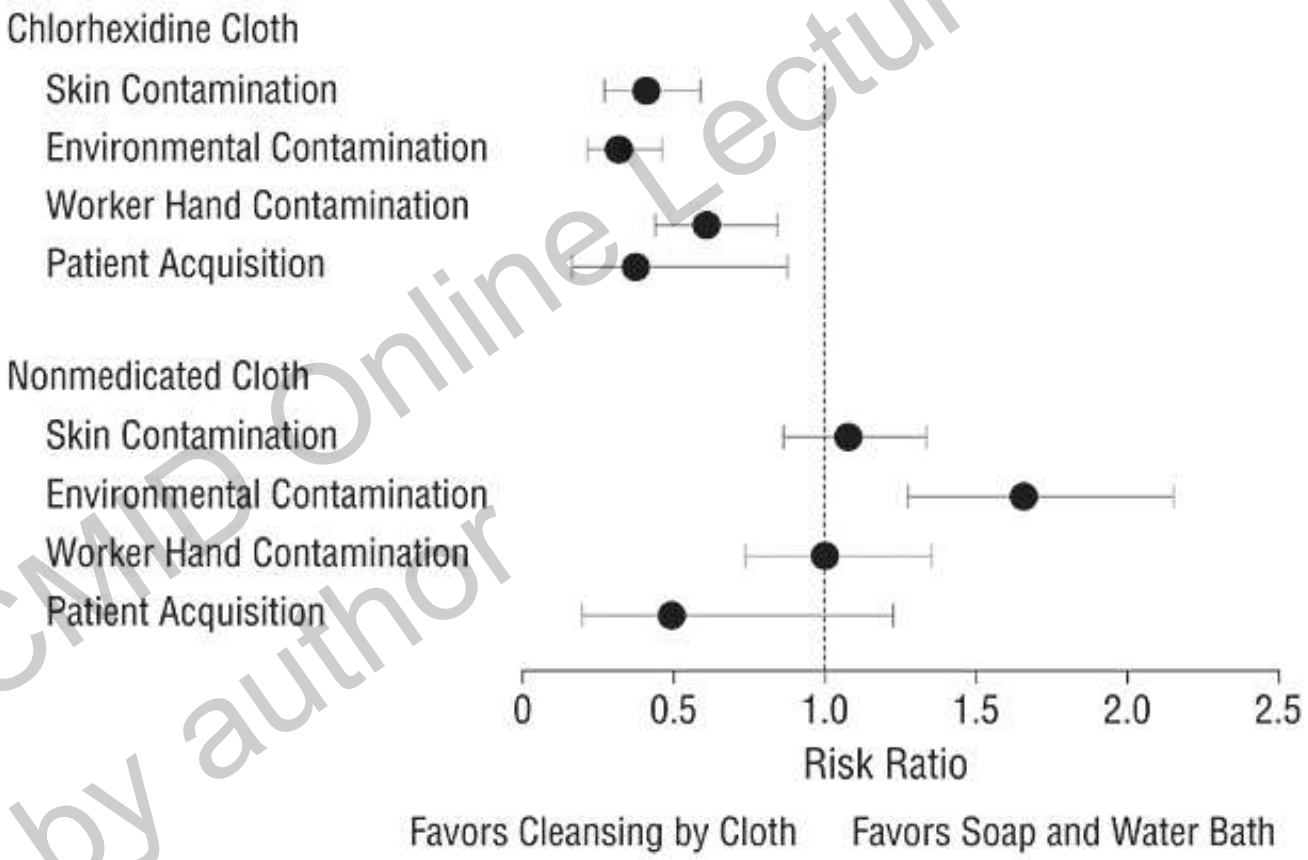
- Body surface decolonization in US studies
- 2% no rinse chlorhexidine (CHG) with and without mupirocin
- Impact in high risk populations: ICUs
- Implementation pearls

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

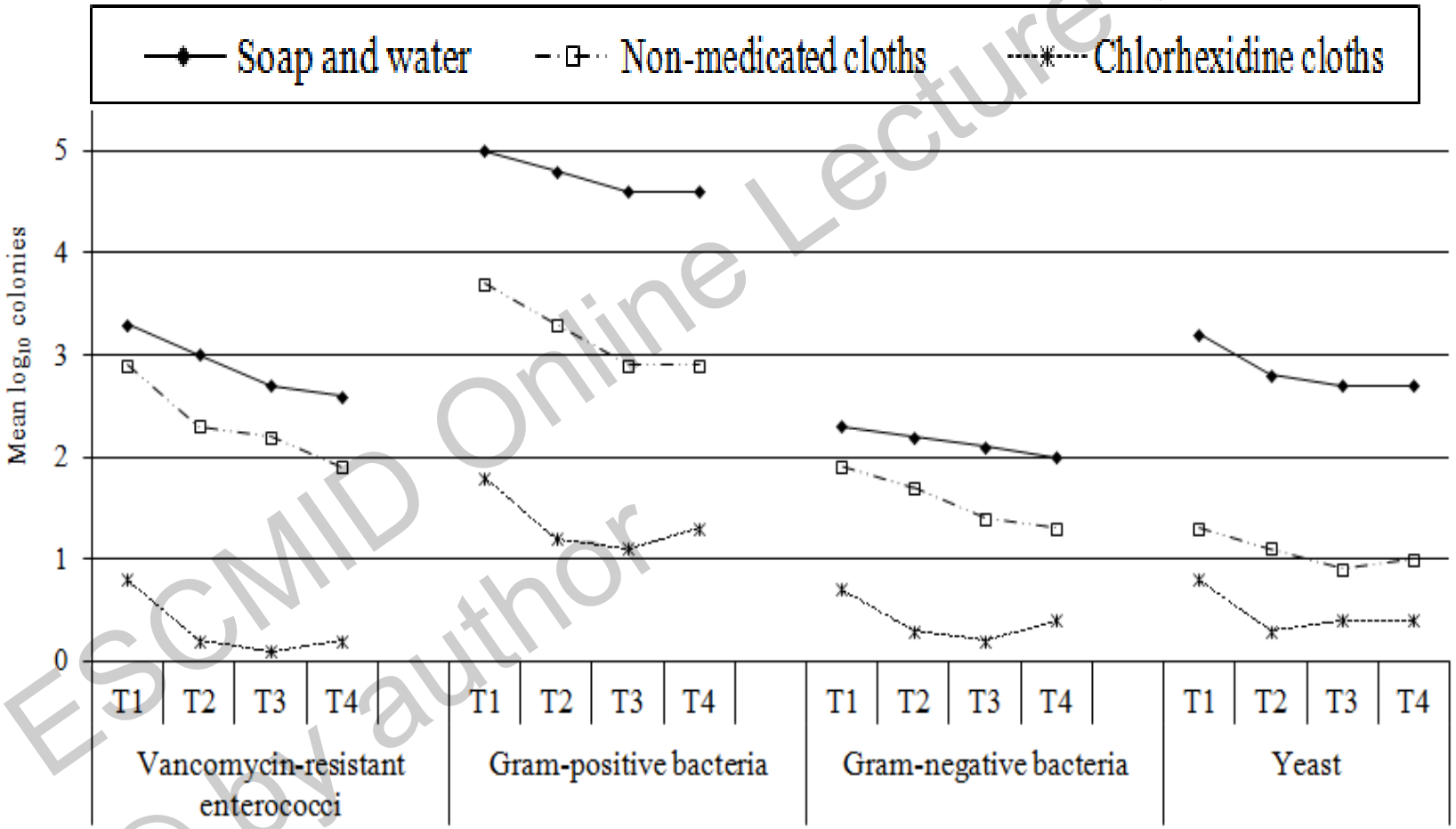
Vernon et al, *Arch Intern Med* 2006; 166:306-12.

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



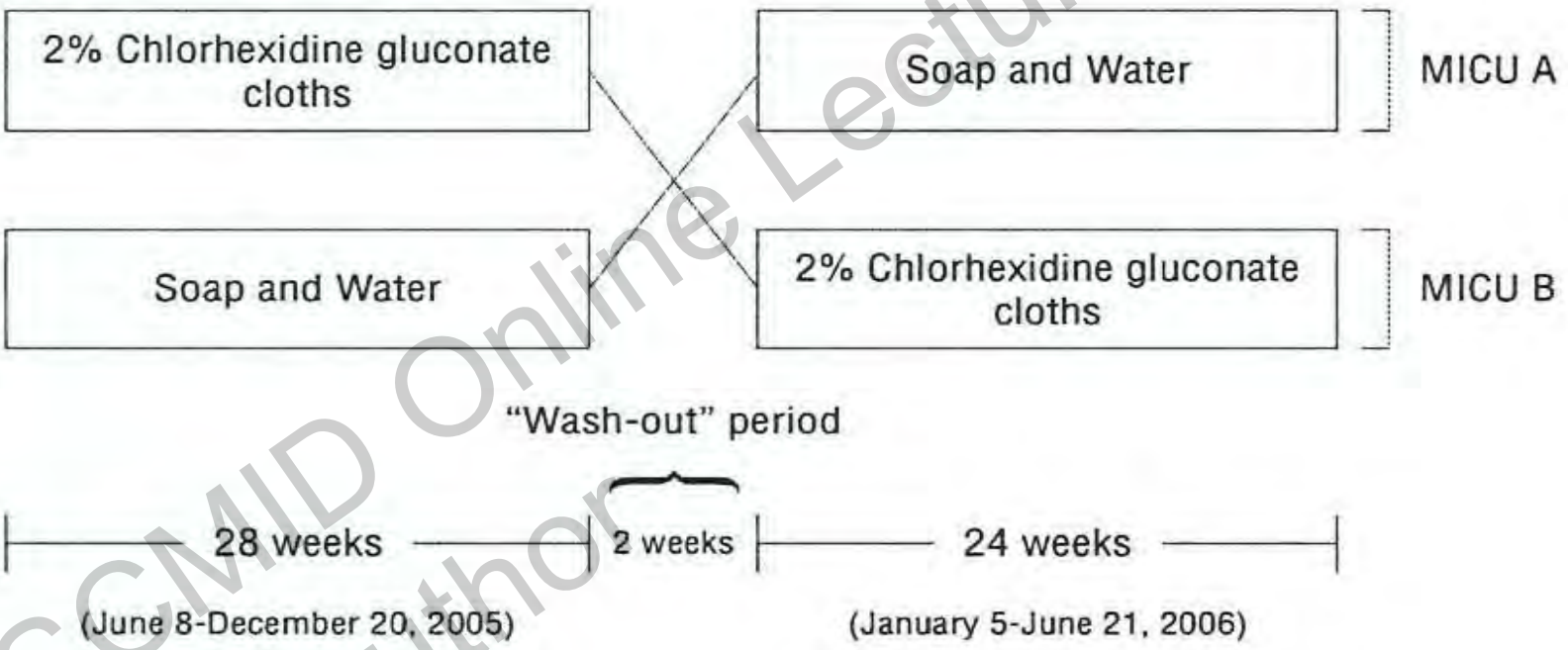
Vernon et al, *Arch Intern Med* 2006; 166:306-12.

Bioburden on Inguinal Skin by Cleansing Method



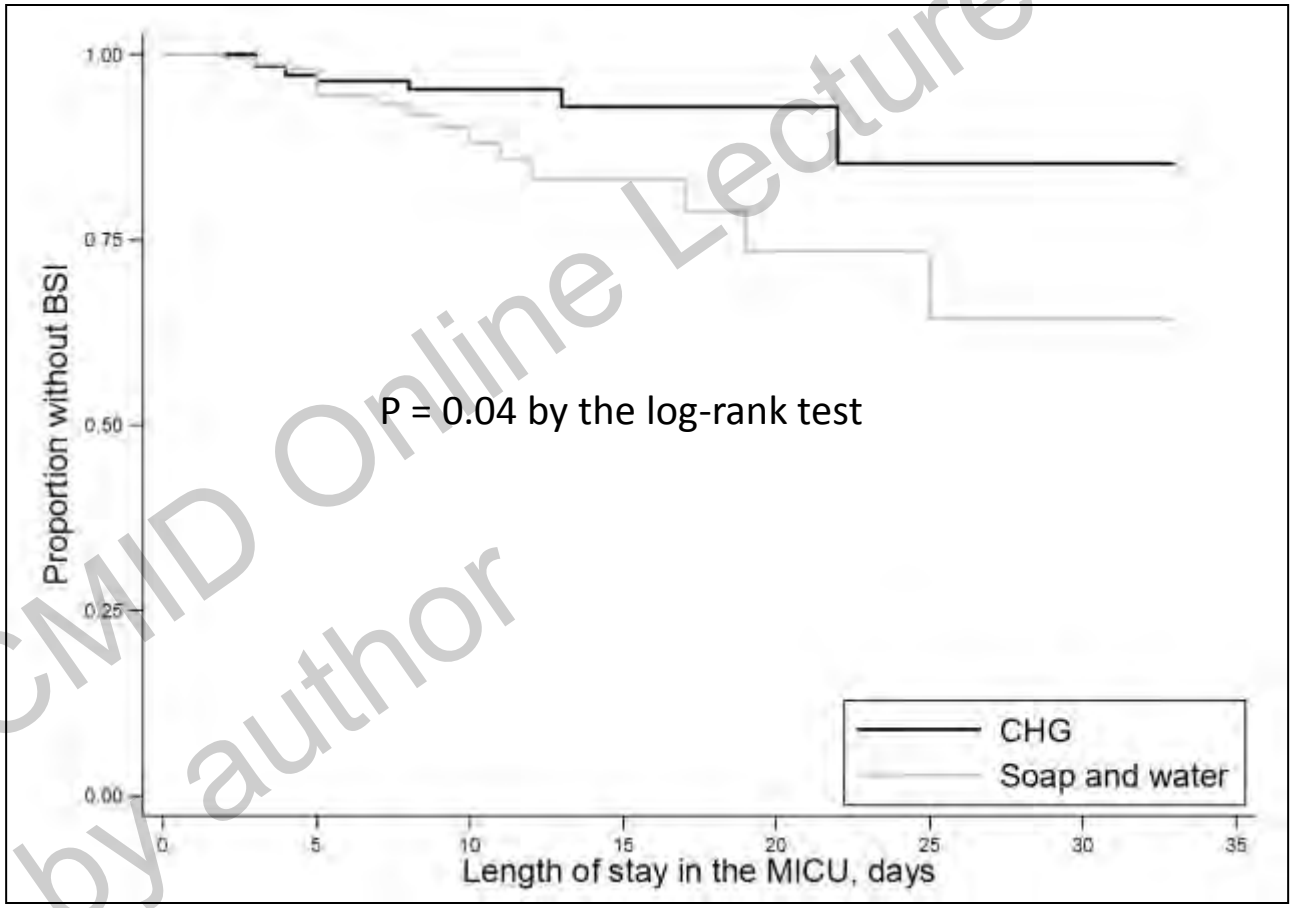
Popovich KJ et al. ICHE 2012;33(9):889-896

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

- 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	MRSA Prevalence	VRE Prevalence	Baseline Rate of Primary Bloodstream Infections†
			days	*percent of admissions*		*no./1000 patient-days*
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

	Intervention	Control	
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

- 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 **E**valuation of **D**ecolonization vs. **U**niversal **C**learance to **E**liminate MRSA

Targeted versus Universal Decolonization to Prevent ICU Infection

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

- Hospital Corporation of America
- Harvard Pilgrim Healthcare Institute/Harvard Medical School
- University of California Irvine
- Rush University
- CDC Prevention Epicenters Steering Committee

N Engl J Med 2013:368:2255-2265

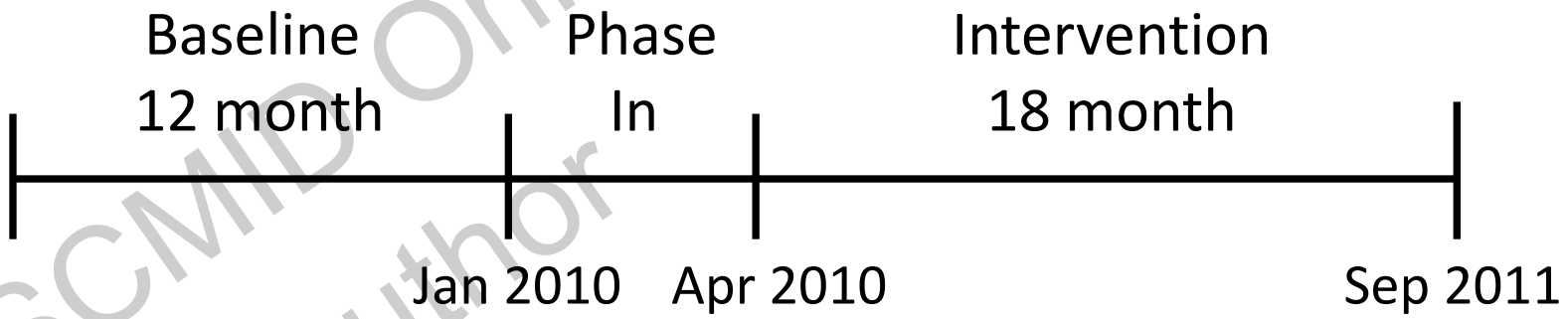
Cluster Randomized Trial

Randomized hospitals and all their adult ICUs to:

- **Arm 1: Routine Care**
  - Screened all patients; isolated known MRSA+
- **Arm 2: Targeted Decolonization**
  - Screened all patients; isolated if known MRSA+
  - Decolonized if MRSA+
- **Arm 3: Universal Decolonization**
  - No screening; isolated if known MRSA+
  - Decolonized all

Decolonization in Community ICUs

- **74 adult ICUs, 43 hospitals**
  - 1 academic center, 42 community hospitals



NEJM Jun 2013:368:2255-2265

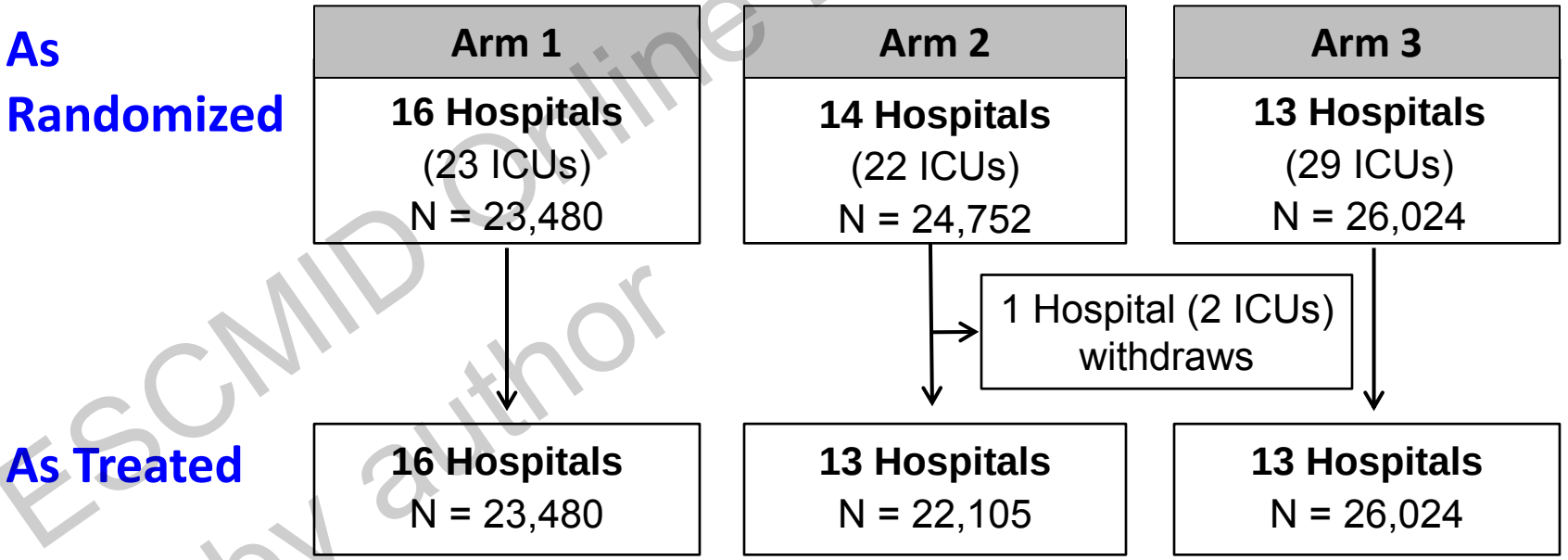
Outcomes

- **Primary**
  - Any MRSA clinical isolate attributed to ICU
- **Secondary**
  - MRSA bloodstream isolate attributed to ICU
  - Any bloodstream isolate attributed to ICU

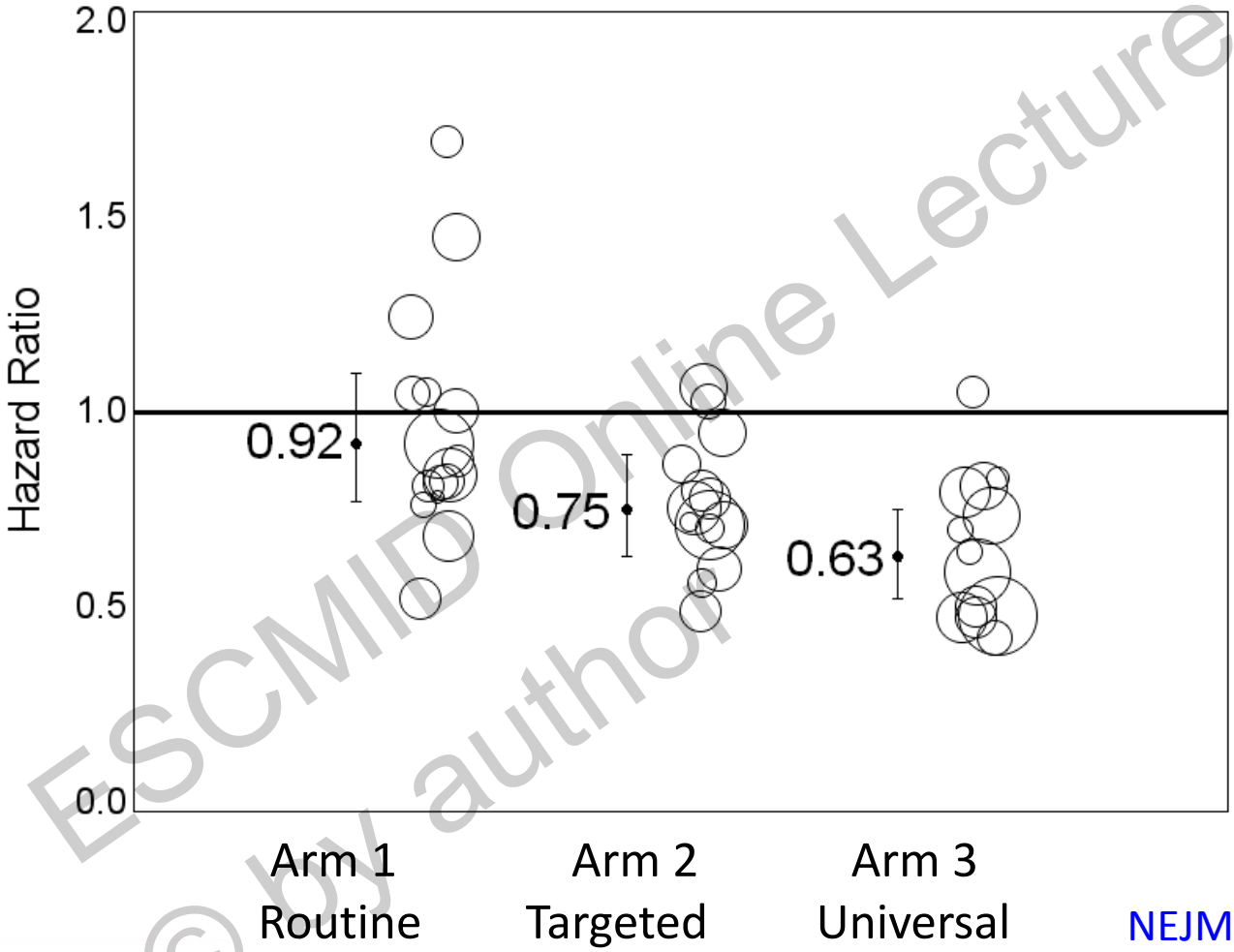
Intervention Period

Intervention: 74,256 patients

282,803 ICU patient days



MRSA Clinical Cultures



Overall P=0.01

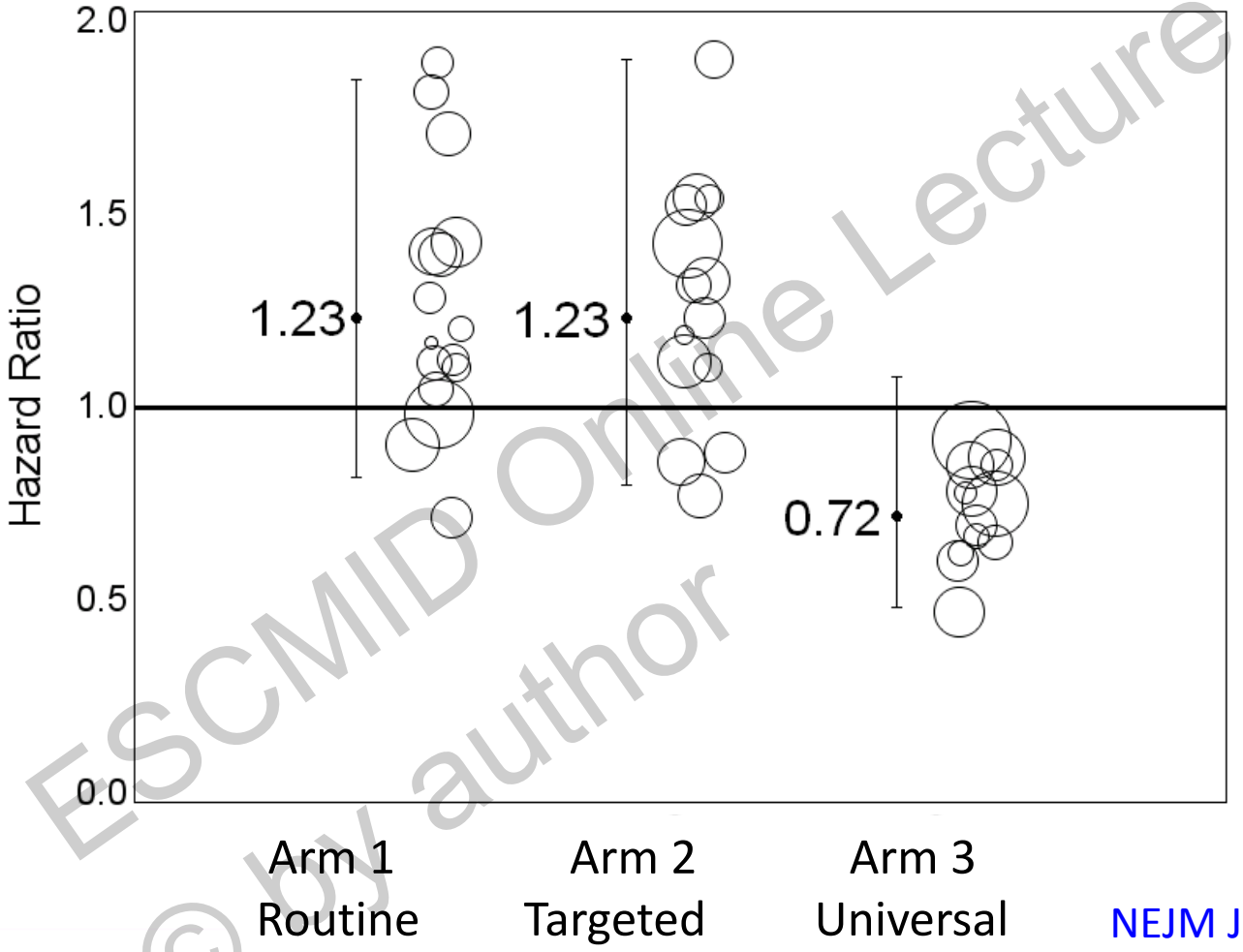
Arm 2 vs 1 P=0.09

Arm 3 vs 1 P<0.003

Arm 3 vs 2 P=0.16

NEJM Jun 2013:368:2255-2265

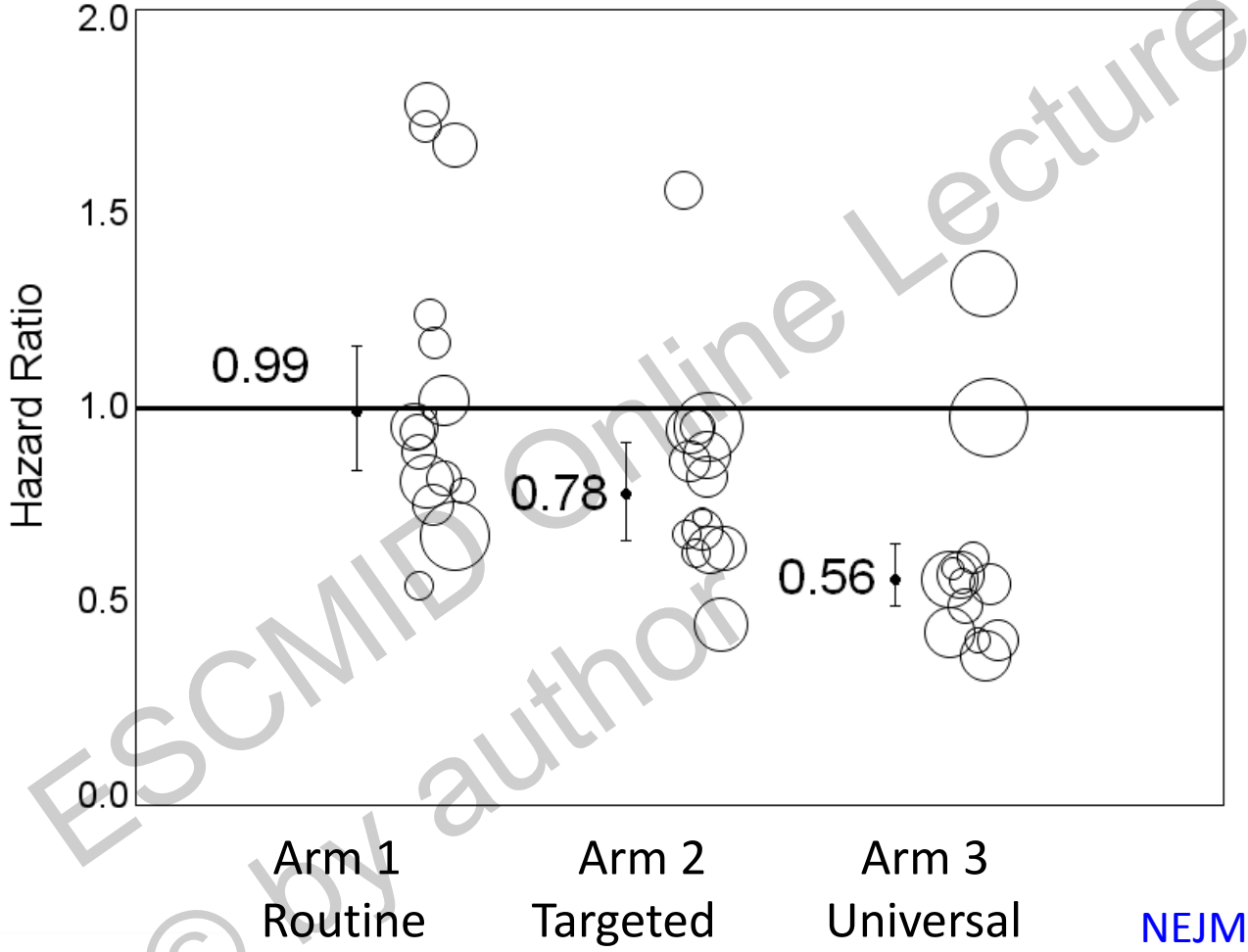
MRSA Bloodstream Infection



Overall P=0.11

NEJM Jun 2013:368:2255-2265

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

NEJM Jun 2013:368:2255-2265

Pragmatic Design

- **No Onsite Investigators**
  - Roll out by local infection prevention/QI teams
  - Protocol, education, coaching calls provided

Decolonization in Community ICUs

- **Universal Decolonization: CHG and mupirocin**
  - Reduces MRSA and all BSI
  - Saves effort and cost of screening
  - May reduce need for contact precautions
- **Horizontal vs Vertical Approaches**
  - Universal better than targeted

Limitations and Considerations

- No information re: impact of CHG separate from mupirocin
- Concern about engendering mupirocin resistance

REASON to AVOID	REASON to USE
• CHG effective alone	• CHG alone less effective for *S. aureus* • High impact to #1 HAI pathogen for devices, wounds, SSI
• Potential for rise in Mup-R	• Local assessment helpful • Inconsistent evidence for causing R • Would not lose treatment agent
• Consider targeted use	• 30% humans are *S. aureus* carriers • MRSA only partially captured by screening, especially nares alone • Used in less ill populations. Do not withhold for critically ill
• Limited alternatives	• Alternatives available

Pediatric SCRUB Trial

Scrubbing with CHG Reduces Unwanted Bacteria

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).

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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 ≤ 2 days
  - Feb 2008 – Sept 2010
- **Outcome**
  - Bacteremia (single positive blood culture)

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

Recruitment by Consent

	Period 1		Period 2	
	Control Arm	Intervention Arm	Control Arm	Intervention Arm
Eligible	1202	1327	1326	1106
Refused PHI consent	-3	-8	0	-3
Refused treatment	0	-68	0	-286
Unable to consent	0	-371	0	-150
Per protocol	1999	880	1326	667

As Treated Analysis: 36% Less BSI

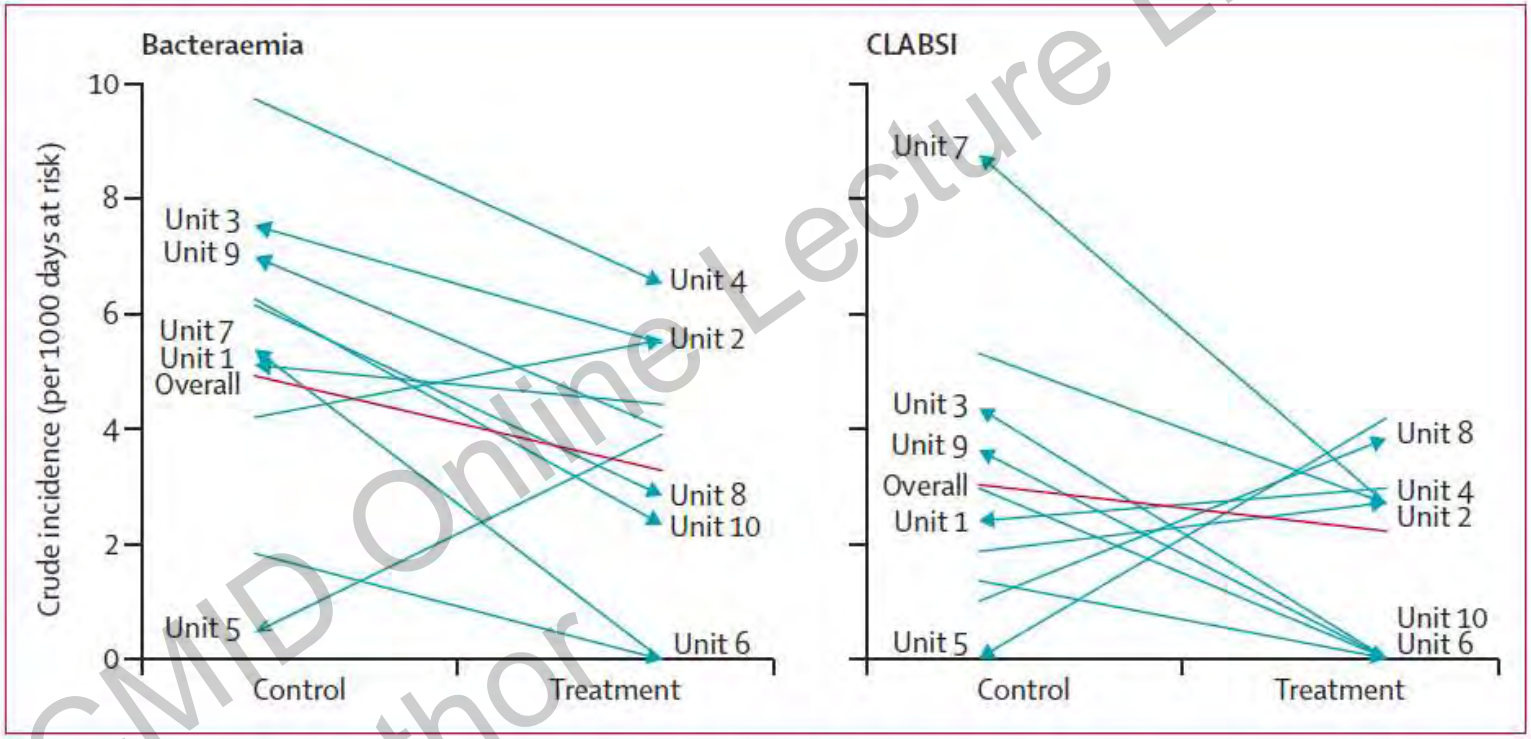

Figure 2: **Change in crude incidence of bacteraemia and CLABSI, per-protocol population**
Every line represents one unit (appendix p 7); the slope shows the change in incidence of bacteraemia or CLABSI between control and treatment study periods, and the arrow indicates the assignment change from period 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

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)
Milstone	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

Things That Matter

- Method
- Concentration
- Consistency
- Safety

Decolonization Method

- Technique
  - Massage into skin for sustained 24 hour activity
  - No rinse
- Protocol
  - Attention to high risk skin areas
  - Clean over non-gauze dressings
  - Proximal 6 inches of lines, catheters, devices
  - Perineum and wounds
  - Interactions – many soaps and shampoos inactivate

Chlorhexidine Concentration

- Concentration
  - 2% no-rinse cloth most commonly studied
  - 4% no rinse solution → higher skin adverse events
  - 4% rinse solution in shower or bath
    - Lower but adequate concentrations
    - 2 minute contact time → rinse
    - Mesh sponge works well for liquid application

Consistency

- Consistency
  - 24 hour effect → daily application
  - Staff training [1]
    - Include night and temporary staff
    - Reinforce method: no rinse and high risk areas
    - Compliance checks

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

Safety: Minimal Adverse Events

- <1% Attributable Mild Skin Reactions
- Climo et al.
  - 2.0% CHG skin reactions vs 3.4% regular soap
- REDUCE MRSA
  - 7 mild events (<0.1%)
- Pediatric SCRUB Trial
  - 3% (n=43) CHG vs 1% (n=26) of controls
  - Mild skin reactions, only 12 believed to be related
- Anaphylaxis rare

Questions?