Unintended Microbial Consequences of Routine Chlorhexidine Bathing

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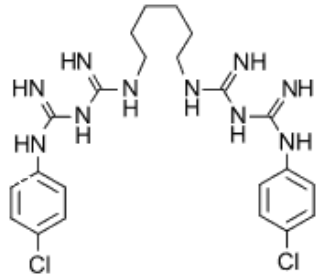
RUSH

Overview

- Rationale for chlorhexidine (CHX) bathing in healthcare settings
- Potential unintended consequences of routine CHX bathing

Chlorhexidine (CHX)

- Biocide
- In use since 1954 for skin antisepsis and other medical indications
- Binds to negatively charged microbial membrane
  - Low concentrations: Alteration of bacterial membrane integrity and cell osmotic equilibrium
  - High concentrations: Precipitation of cell contents and cell death
- Active against most bacteria and yeast
  - Activity varies by genera and species
  - Not active against mycobacteria, spores, viruses



Rationale for Routine CHX Bathing

- Potentially pathogenic microbes commonly contaminate/colonize skin of hospital patients
  - MRSA, *C. difficile*, *C. auris*, MDR-*A. baumannii*, carbapenemase-producing *K. pneumoniae*
- CHX binds to stratum corneum, prolonging effectiveness of antisepsis
- Reducing burden of these microbes on skin by CHX bathing has beneficial effects:
  - Fewer central-line associated bloodstream infections (CLABSIs)
  - Fewer contaminated blood cultures
  - Reduction in cross-transmission of MDROs
- Most studies conducted in ICUs
- Best data for MRSA, VRE

The NEW ENGLAND JOURNAL of MEDICINE

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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*

Clinical Infectious Diseases

MAJOR ARTICLE

Chlorhexidine Bathing to Prevent Central Line–Associated Bloodstream Infections in Hematology Units: A Prospective, Controlled Cohort Study

Kuei-Lien Tien,[1] Wang-Huei Sheng,[2] Shiouh-Chu Shieh,[3] Yen-Ping Hung,[3] Hwei-Fang Tien,[2] Yi-Hsuan Chen,[4] Li-Jung Chien,[5] Jann-Tay Wang,[1,2,a] Chi-Tai Fang,[2,4,a,b], and Yee-Chun Chen[1,2]

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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.

Clinical Microbiology and Infection 25 (2019) 705–710

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Daily bathing with 4% chlorhexidine gluconate in intensive care settings: a randomized controlled trial

C. Pallotto [1,*], M. Fiorio [1], V. De Angelis [2], A. Ripoli [3], E. Franciosini [4], L. Quondam Girolamo [5], F. Volpi [5], P. Iorio [4], D. Francisci [1], C. Tascini [6], F. Baldelli [1]

[1] Infectious Diseases Unit, University Hospital of Perugia, Perugia, Italy
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Chlorhexidine versus routine bathing to prevent multidrug-resistant organisms and all-cause bloodstream infections in general medical and surgical units (ABATE Infection trial): a cluster-randomised trial

Susan S Huang, Edward Septimus, Ken Kleinman, Julia Moody, Jason Hickok, Lauren Heim, Adrijana Gombosev, Taliser R Avery, Katherine Haffenreffer, Lauren Shimelman, Mary K Hayden, Robert A Weinstein, Caren Spencer-Smith, Rebecca E Kaganov, Michael V Murphy, Tyler Forehand, Julie Lankiewicz, Micaela H Coady, Lena Portillo, Jalpa Sarup-Patel, John A Jernigan, Jonathan B Perlin, Richard Platt, for the ABATE Infection trial team

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Chlorhexidine Bathing and Health Care–Associated Infections A Randomized Clinical Trial

Michael J. Noto, MD, PhD; Henry J. Domenico, MS; Daniel W. Byrne, MS; Tom Talbot, MD, MPH; Todd W. Rice, MD, MSc; Gordon R. Bernard, MD; Arthur P. Wheeler, MD

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

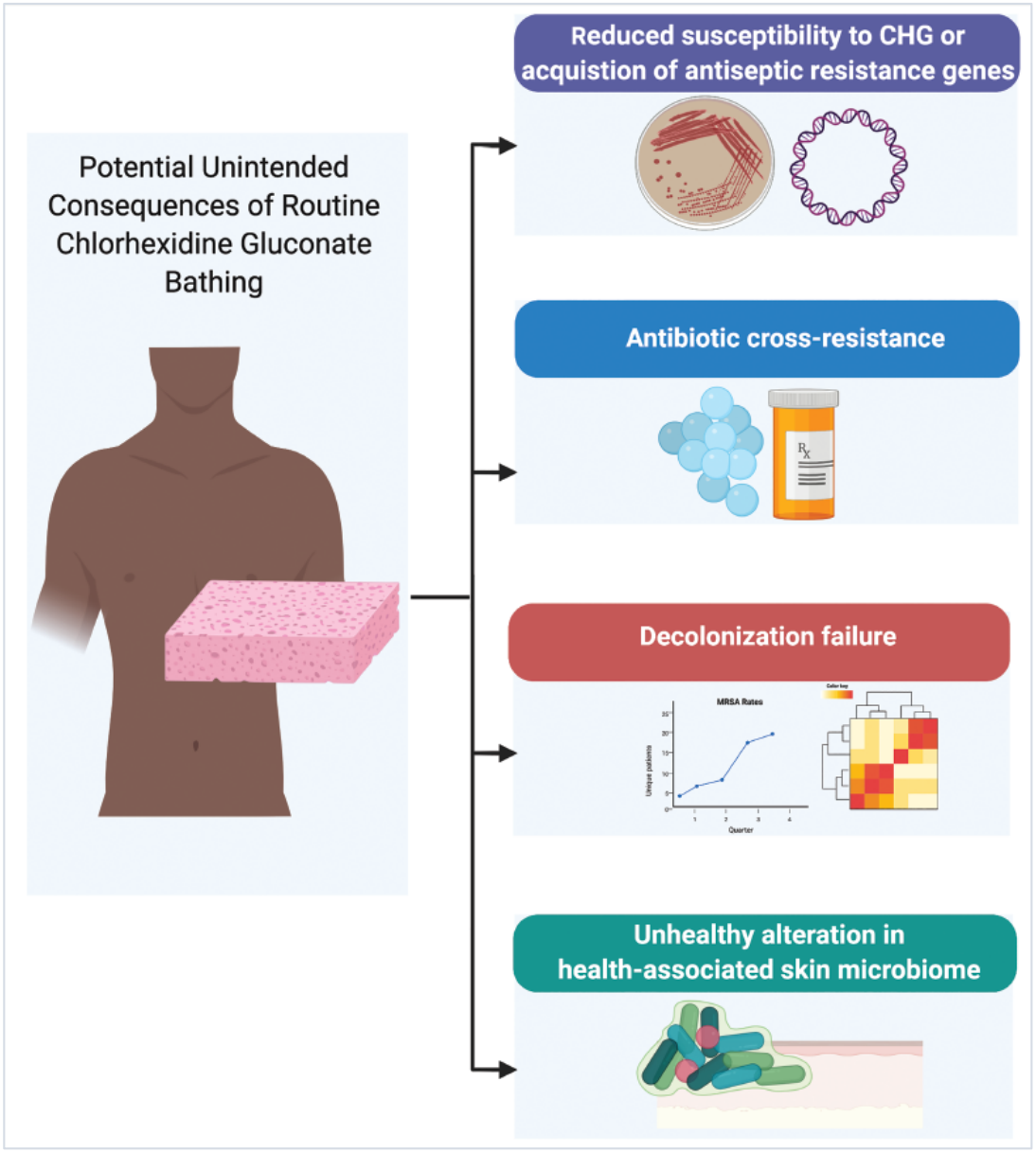
Policies for Controlling Multidrug-Resistant Organisms in US Healthcare Facilities Reporting to the National Healthcare Safety Network, 2014

Lindsey M. Weiner, MPH;[1] Amy K. Webb, MPH, CHES;[1] Maroya S. Walters, PhD, ScM;[1] Margaret A. Dudeck, MPH, CPH;[1] Alexander J. Kallen, MD, MPH[1]

We examined reported policies for the control of common multidrug-resistant organisms (MDROs) in US healthcare facilities using data from the National Healthcare Safety Network Annual Facility Survey. Policies for the use of Contact Precautions were commonly reported. Chlorhexidine bathing for preventing MDRO transmission was also common among acute care hospitals.

Infect Control Hosp Epidemiol 2016;37:1105–1108

- Survey of 4,000 US hospitals and long-term care facilities participating in NHSN
- 63% of acute care hospitals and 49% of long-term care facilities used routine CHG bathing to reduce transmission of MDROs



Are there unintended microbial consequences of routine chlorhexidine bathing?

Babiker A et al Clinical Infect Dis 2020

Defining CHX Resistance

- Antibiotic resistance: Focus on inhibition of microorganism
- Biocide resistance: Focus on activity of drug
  - Post-exposure colony counts
- CHX resistance: Ability to survive exposure that kills rest of population
  - 1% - 4% CHG =10,000 - 40,000 mg CHX/L

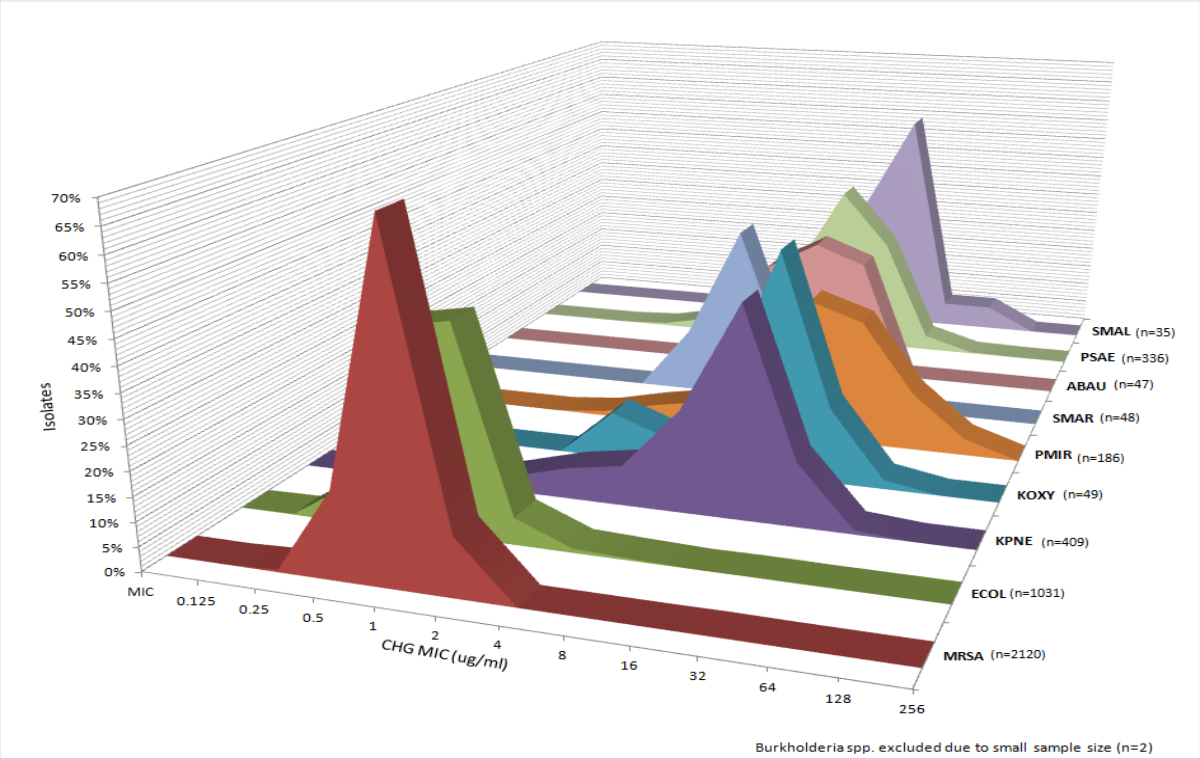
Horner C et al JAC 2012, 67:2547.

No established, standardized method of testing for CHX resistance

- Phenotypic methods
  - Agar or broth macro/microdilution MICs/MBCs
  - Time kill assays
  - Post-exposure colony counts
  - Efflux over-expression
  - Epidemiologic cutoff

- Genotypic methods
  - Detection of efflux pump genes by PCR
    - *qac*A/B, *smr*, *norA/B*, *cepA*, *qacE*

CHX susceptibility of clinical bacterial isolates and concentrations of CHX detected on patients' skin after routine CHX bathing



- CHX concentrations applied to skin in clinical use = 2- 4%
  = 20,000- 40,000 µg /mL
- Concentration of CHX detected on patients' skin after routine bathing dependent on time since bathing and anatomic site
  - Median after bath, 312.5 µg/mL*
  - Range, 0 – 1250 µg/mL

Huang SS et al Lancet 2019

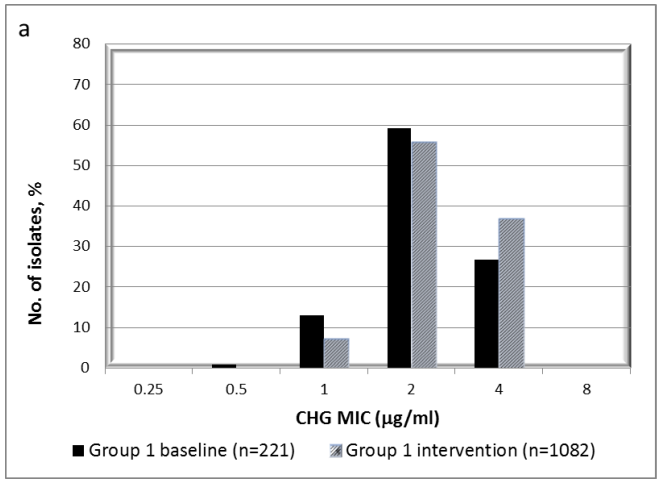
*Lin MY et al ICHE 2014
Rhee Y et al ICHE 2018
Proctor DM et al Nature Med 2021
Nadimalli G et al ICHE 2019

Secondary analyses of clinical trials data to evaluate the microbial effects of routine CHX bathing

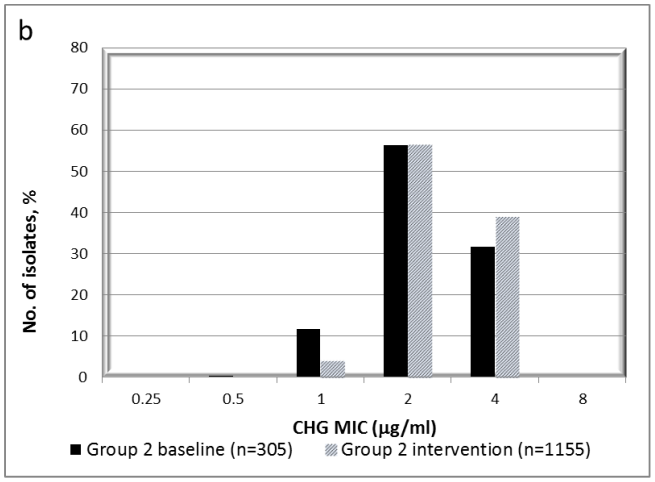
Study Design	Population	Period of CHG exposure	Microbes Studied	Change in CHG Susceptibility?	Reference
Multicenter, cluster-randomized, nonblinded crossover study of CHX-impregnated washcloths vs soap & water bathing	7,727 patients in 9 ICUs and BMTUs in 6 US hospitals	6 months	713 MRSA 393 VRE	**No change in CHX MIC_{90} for MRSA or VRE**	Climo 2013
Multicenter, cluster-randomized trial comparing universal vs targeted vs screening & isolation	74,256 patients in 74 ICUs in 43 hospitals	18 months	3,123 MRSA	**No change in CHX MIC_{50}/MIC_{90} or in *qac*A/B carriage**	Hayden 2016
Community-based, cluster-randomized trial of every-other-day CHX cloth bathing vs soap & water bathing	10,030 soldiers	20 months	615 MRSA	**No difference in *qacA/B* carriage**	Schlett 2014

Distribution of CHX MICs among MRSA isolates from the REDUCE MRSA Trial (N=3173)

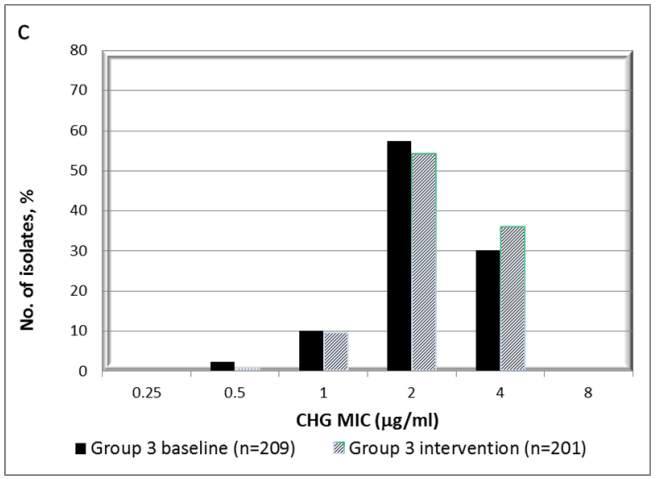
Screening & Isolation



Targeted Decolonization



Universal Decolonization



- Narrow distribution of CHX MICs
- No differences between arms or across time

Hayden MK et al JCM 2016

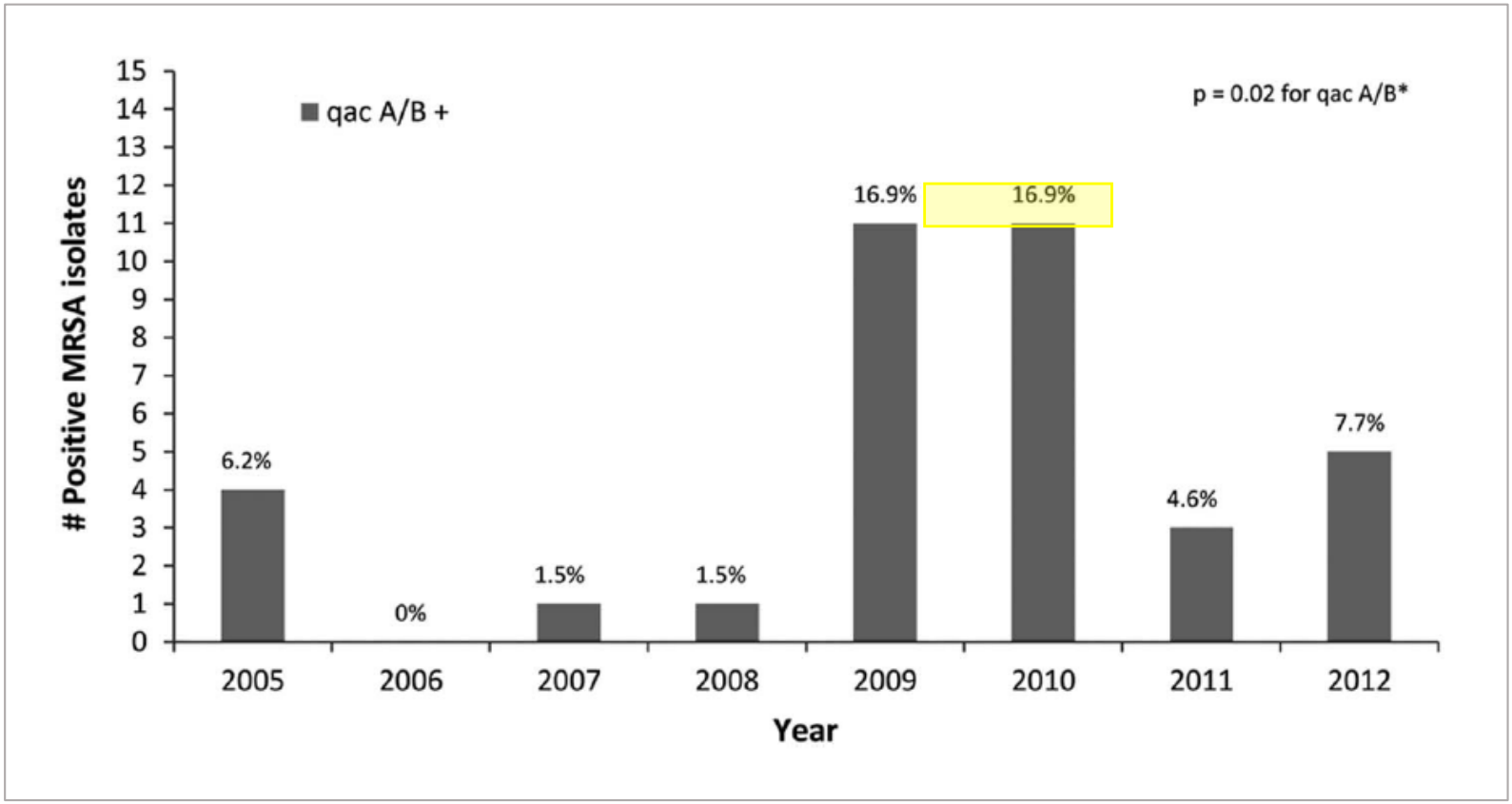
Characteristics of MRSA isolates that carried *qac*A or *qac*B genes

Hospital location	Intervention group	Study period	Culture type	*qac* identity	MLST	CHX MIC (mg/L)	CHX MBC (mg/L)	Mupirocin susceptibility profile
Florida	1	baseline	screen	*qac*A	ST8	4	4	S
Florida	1	intervention	screen	*qac*B	ST8	4	8	S
Florida	1	intervention	screen	*qac*A	ST2484	8	8	S
Texas	1	intervention	clinical	*qac*A	ST8	8	8	LL
Florida	3	intervention	clinical	*qac*A	ST450	4	16	HL

- 814 MRSA isolates tested for *qac*A/B by PCR
- 5 (0.6%) positive isolates

Hayden MK et al JCM 2016

Non-linear increase in *qac*A/B in MRSA isolates from anterior nares screening after introduction of routine CHX bathing



- Retrospective, single surgical ICU cohort
- 2005-2012
- Daily CHX bathing
- Non-linear increase in *qacA/B* detection in colonizing MRSA isolates over time

Warren D et al Infect Control and Hosp Epidemiol 2016

Reduction in CHG susceptibility after introduction of a bundled intervention to control XDR *A. baumannii* that included daily CHX bathing

TABLE 1. Comparison of the Epidemiology of Chlorhexidine Minimum Inhibitory Concentrations (MICs) among Extensively Drug-Resistant (XDR) *Acinetobacter baumannii* Clinical Isolates before and after Implementation of Advanced Source Control

		Prechlorhexidine (n = 50)			Postchlorhexidine (n = 50)		
Hospital unit	n	Chlorhexidine consumption (L/unit/month)	Chlorhexidine MIC 50/90	Incidence of XDR *A. baumannii* per 1,000 patient-days	Chlorhexidine consumption (L/unit/month)	Chlorhexidine MIC 50/90	Incidence of XDR *A. baumannii* per 1,000 patient-days
Intensive care	70	2.4	32/32	12.5	15.5	64/128	2.9
General medicine	15	0.9	32/32	11.4	9.8	64/128	6.3
General surgical	10	0.5	16/32	9.6	4.5	64/128	4.6
Other[a]	5	0.1	16/32	1.2	2.5	64/128	0.6

- Bundled intervention that included daily CHG bathing
- ICUs, general medical & surgical wards
- 12-month exposure

Apisarnthanarak A et al Infect Control Hosp Epidemiol 2014

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- Bundled intervention that included daily CHG bathing
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Apisarnthanarak A et al Infect Control Hosp Epidemiol 2014

Is CHX resistance associated with antibiotic resistance?

TABLE 3 Genotypic chlorhexidine resistance by antimicrobial resistance

Antibiotic and phenotype	No. (%)			
	Clinical isolates (n = 341)		Colonizing isolates (n = 274)	
	qacA/B negative (n = 336)	*qacA/B* positive (n = 5)	*qacA/B* negative (n = 269)	*qacA/B* positive (n = 5)
Ciprofloxacin[a]				
Susceptible	216 (100.0)	0 (0)	179 (100.0)	0 (0)
Resistant	120 (96.0)	5 (4.0)	90 (94.7)	5 (5.3)
Clindamycin[b]				
Susceptible	302 (98.4)	5 (1.6)	225 (97.9)	5 (2.1)
Resistant	34 (100.0)	0 (0)	44 (100.0)	0 (0)
Daptomycin				
Susceptible	335 (98.5)	5 (1.5)	269 (98.2)	5 (1.8)
Resistant	0 (0)	0 (0)	0 (0)	0 (0)
Erythromycin				
Susceptible	35 (100.0)	0 (0)	32 (100.0)	0 (0)
Resistant	301 (98.4)	5 (1.6)	237 (97.9)	5 (2.0)
Gentamicin				
Susceptible	334 (98.5)	5 (1.5)	268 (98.2)	5 (1.8)
Resistant	1 (100.0)	0 (0)	1 (100.0)	0 (0)

Schlett C et al AAC 2014

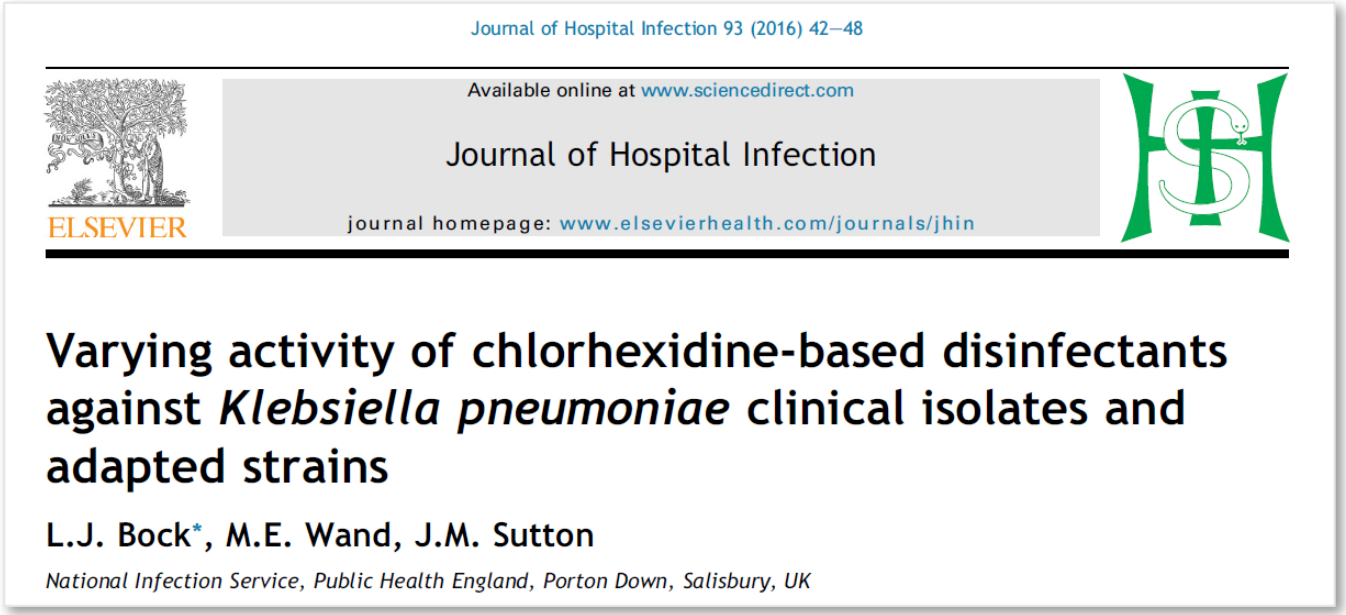
Is reduced CHX susceptibility associated with decolonization failure?

- Report of CHX decolonization failure associated with *qacA*+ epidemic MRSA strain ST239
  - Mean CHG MBC of epidemic strain 3X that of non-epidemic strains
    - Mean MBC epidemic MRSA strain: 78 mg/L
    - Mean MBC non-epidemic MRSA strains: 26 mg/L

- Case-control study found combination of *qacA/B* and LL-mupirocin resistance independent risk factor for MRSA decolonization failure.
  - OR 3.4 [95% CI, 1.5-7.8]

Batra R et al CID 2010 50:210
Lee AS CID 2011, 52:1422

Is CHX resistance associated with antibiotic resistance?



Journal of Hospital Infection 93 (2016) 42–48

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Journal of Hospital Infection

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Varying activity of chlorhexidine-based disinfectants against *Klebsiella pneumoniae* clinical isolates and adapted strains

L.J. Bock*, M.E. Wand, J.M. Sutton

National Infection Service, Public Health England, Porton Down, Salisbury, UK

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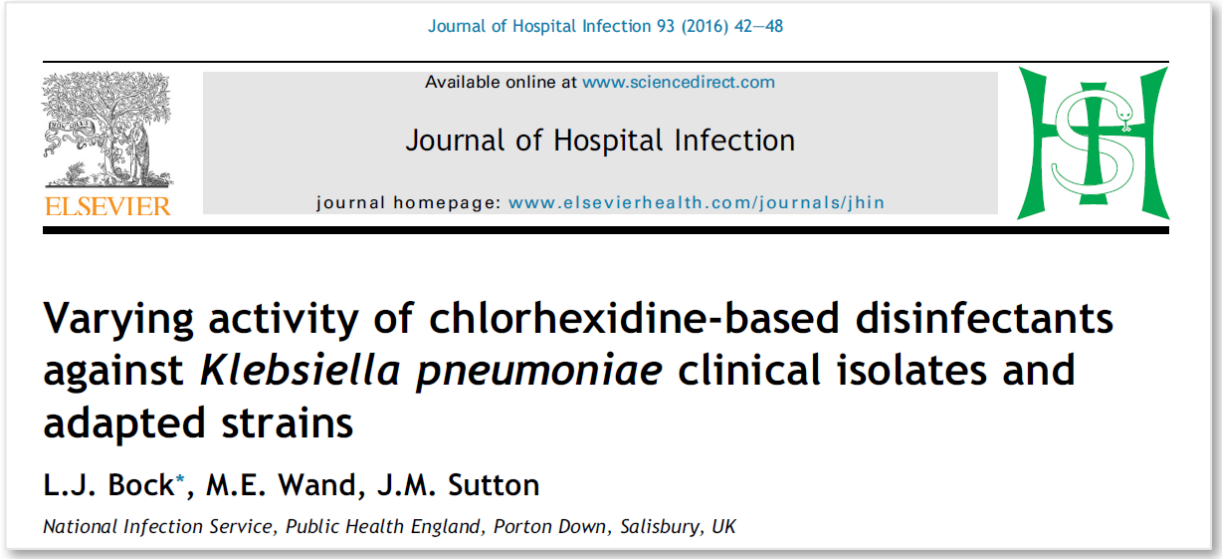

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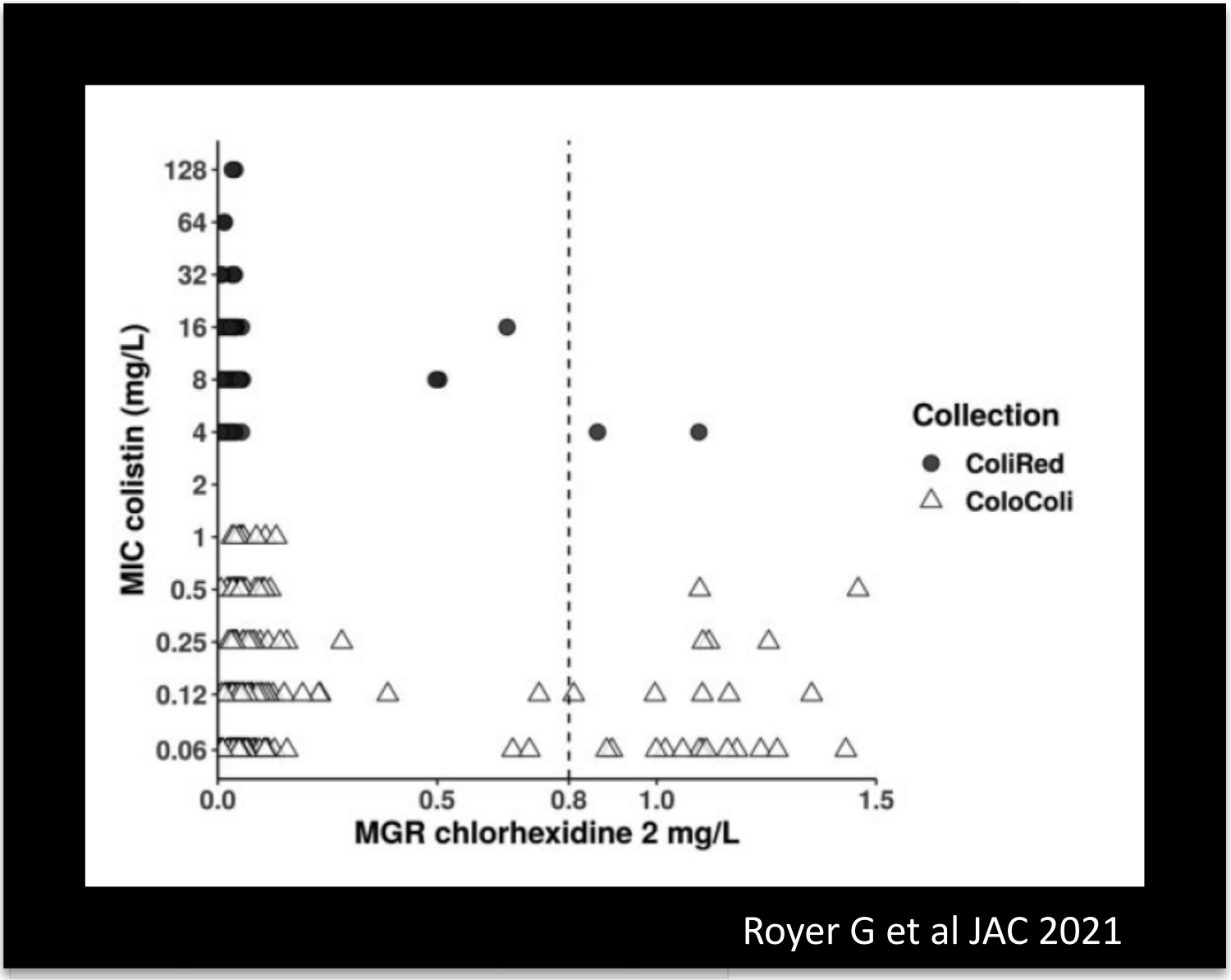
Mechanisms of Increased Resistance to Chlorhexidine and Cross-Resistance to Colistin following Exposure of *Klebsiella pneumoniae* Clinical Isolates to Chlorhexidine

Matthew E. Wand, Lucy J. Bock, Laura C. Bonney, J. Mark Sutton

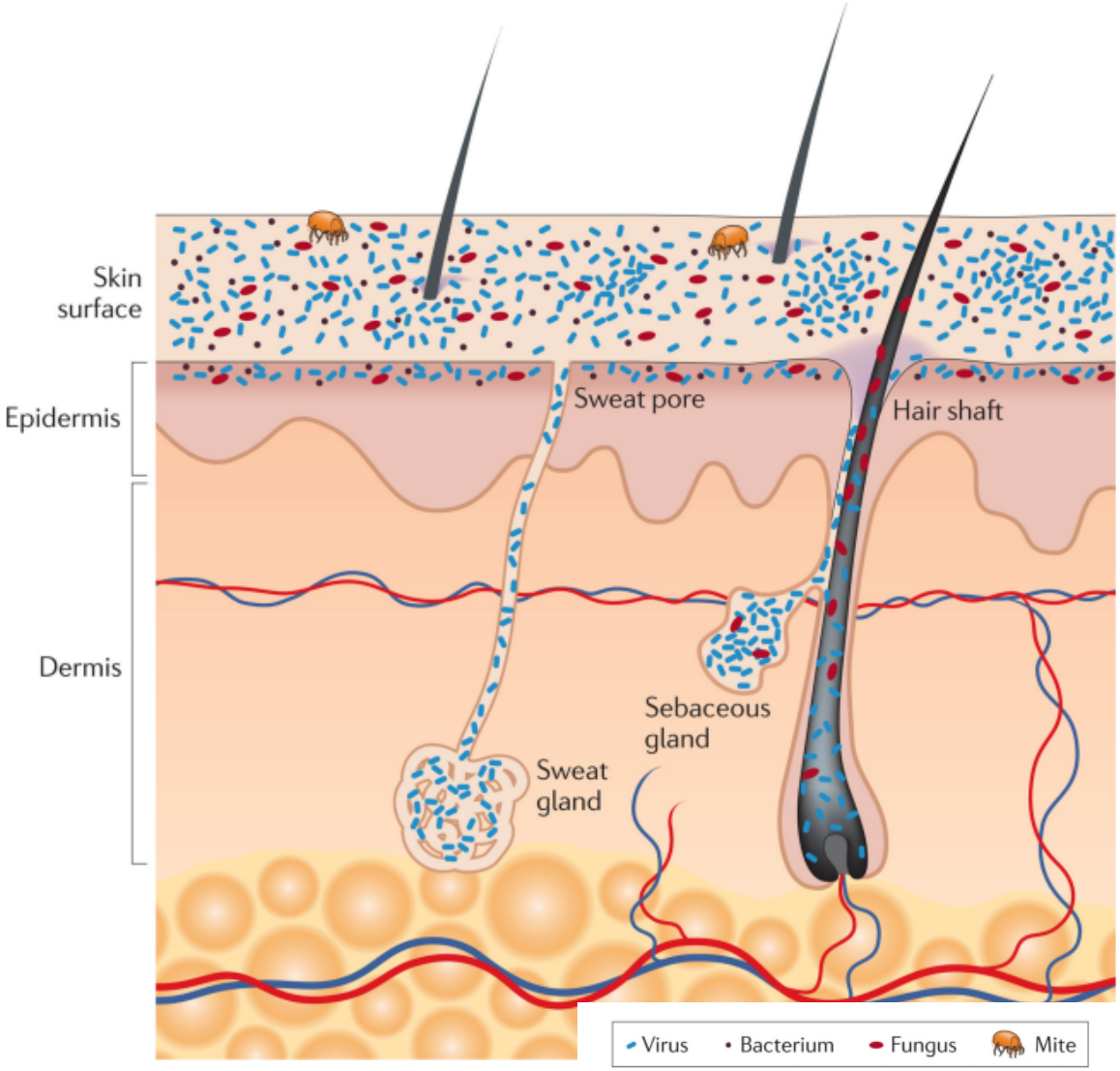
Public Health England, National Infection Service, Porton Down, Salisbury, Wiltshire, United Kingdom

Is CHX resistance associated with antibiotic resistance?



Royer G et al JAC 2021

Does CHX bathing harm the indigenous, health-associated skin microbiota?



Grice EA & Segre JA Nature Rev Microbiol 2011

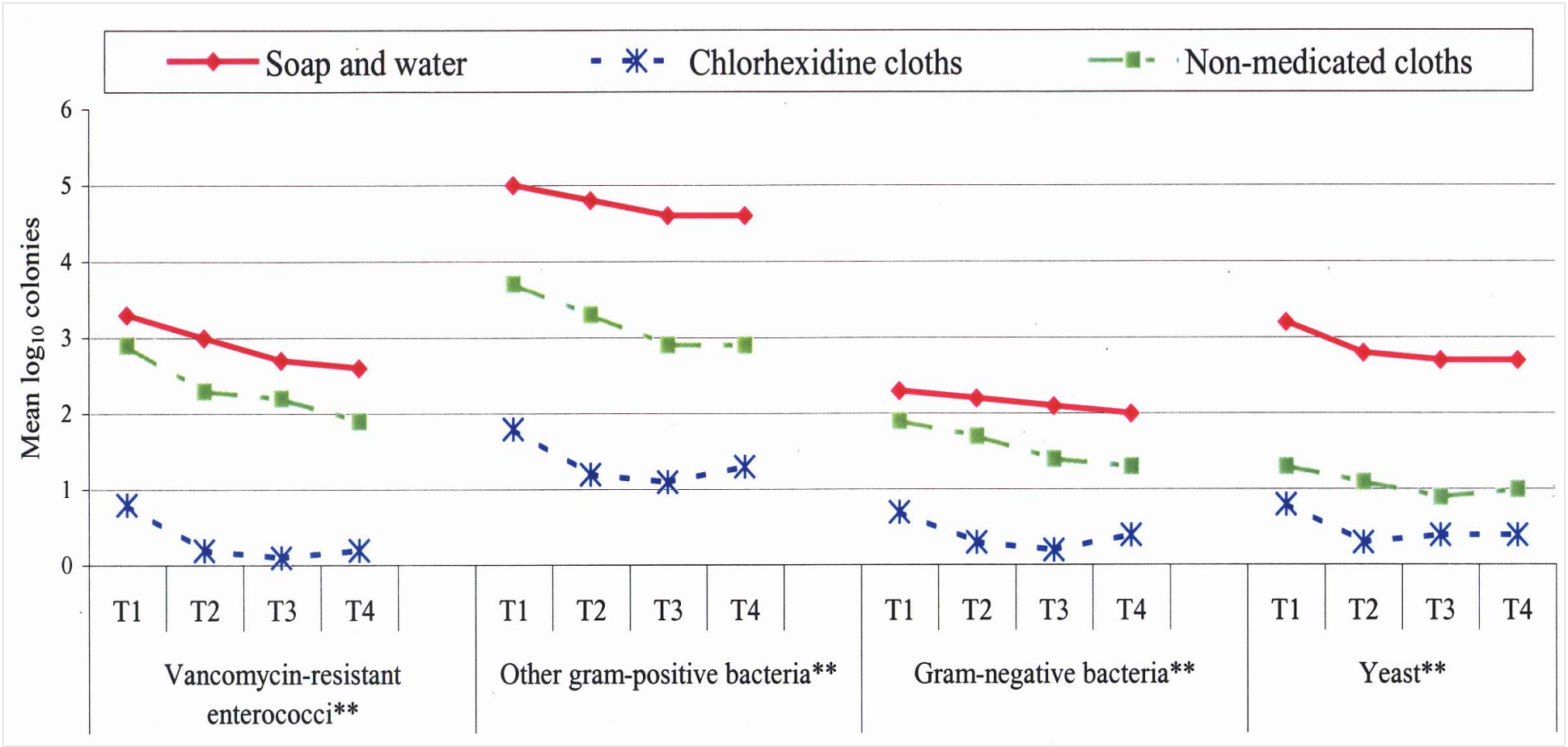
Change in skin condition from admission to discharge after daily CHX bathing (N=1,088 MICU patients)

	No change n (%)	Worsening n (%)	Improvement n (%)
Soap & Water Bathing	250 (88)	18 (6.4)	17 (6)
CHG Cloth Bathing	340 (86)	10 (2.3)	43 (10.8)

P=0.02

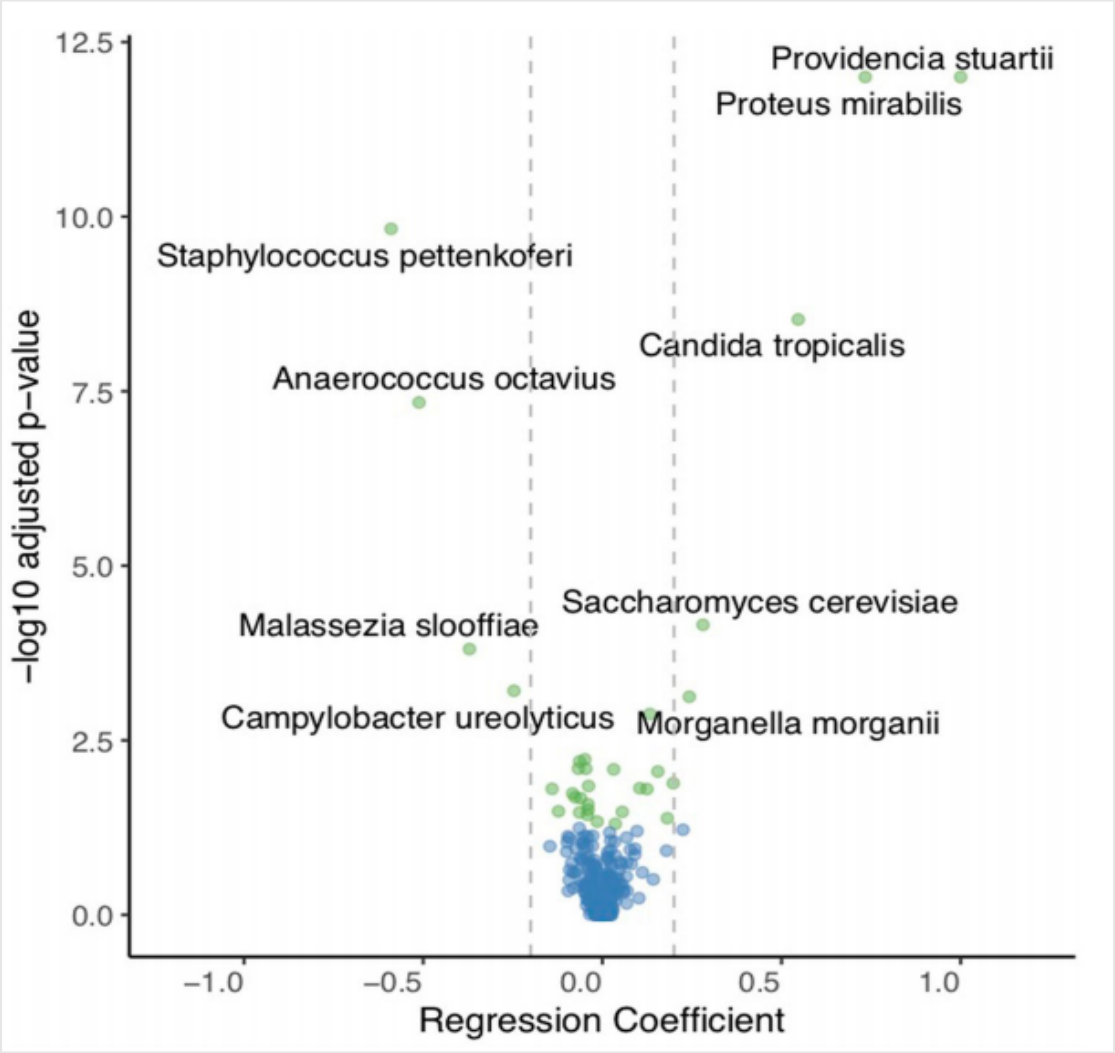
Vernon, M. O. et al. Arch Intern Med 2006;166:306-312.

Microbial Colonization on Inguinal Skin of MICU Patients



Vernon, M. O. et al. Arch Intern Med 2006;166:306.

Differential association of bacterial and fungal taxa with CHX concentrations on of skilled nursing facility patients



- No association between CHX concentration and detection of *C. auris*

Proctor DM et al Nature Med 2021

Conclusions

- Routine patient bathing with CHX has many demonstrated benefits
- The likelihood of clinically relevant reductions in microbial susceptibility to CHX resulting from routine CHX bathing is low
- Concerns for unintended microbial consequences of CHX bathing should not be a barrier to its use on patients for whom there is strong evidence for benefits of routine CHX bathing
- Gaps in knowledge remain, including how best to measure and monitor the effect of CHX on skin microbiota


Thank you!

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March 10, 2022	**HAND HYGIENE: NOT JUST FOR HEALTH CARE WORKERS ANYMORE!!** Speaker: **Dr. Jocelyn Srigley**, University of British Columbia
March 17, 2022	**INFECTION CONTROL IN CORRECTIONAL FACILITIES** Speaker: **Nyreith Adeyemi**, California Correctional Health Care Services
April 7, 2022	**MANAGEMENT PRACTICES FOR LEADERS TO PROMOTE INFECTION PREVENTION** Speaker: **Dr. Ann Scheck McAlearney**, Ohio State University College of Medicine
April 14, 2022	**LIFECYCLE OF MOLECULAR MICROBIOLOGY DIAGNOSTIC TECHNOLOGY: COST VERSUS CLINICAL BENEFIT BEFORE BECOMING OBSOLETE** Speaker: **Professor Colum Dunne**, School of Medicine, University of Limerick, Ireland
April 28, 2022	*(FREE Teleclass)* **HOW DO WE IMAGINE OUR FUTURE? THE INFECTION PREVENTION "CRYSTAL BALL INITIATIVE"** Speaker: **Dr. Hugo Sax**, HumanLabZ, Switzerland
May 5, 2022	*(FREE Teleclass)* **SPECIAL LECTURE FOR WHO CLEAN HANDS DAY** Speaker: **Prof. Didier Pittet**, University of Geneva Hospitals, Switzerland
May 12, 2022	**PREVENTION AND MANAGEMENT OF POST-OPERATIVE SEPSIS**

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