

Office of Evidence Based Practice – Specific Care Question: Chlorhexidine Bath and Bacteremia DRAFT

Specific Care Question :

Does daily bathing in chlorhexidine (CHG) versus standard bathing reduce bacteremia in critically ill children?

Question Originator:

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Plain Language Summary from The Office of Evidence Based Practice: Summary:

The data to answer the specific care question above comes from two meta-analyses of mainly observational studies and eight single studies. There is data to support using CHG bathing to decrease rates of infection. The evidence is strongest in adults in critical care areas. The meta-analysis by O'Horo, Silva, Munoz-Price, & Safdar (2012) is very low quality because it includes observational studies with inconsistent definitions for infection and colonization. However, it shows a significant reduction in odds to have an infection when CHG bathing protocols are in place, $OR = 0.44$, $p = 0.006$, 95% CI [0.33, 0.59]. Karki & Cheng (2012) is another meta-analysis of observational studies that had major differences in the co-interventions that occurred along with the CHG bathing. However they report a significant reduction in Incidence Risk Ratio (IRR) of when CHG skin cleansing is used to reduce health care associated infections, $IRR = 0.43$, $p = 0.004$, 95% CI [0.26, 0.71].

Single studies published since the two meta-analyses were published Of note, Lee et al. (2011) did a survey of blood levels of CHG from children 3-17 months of age who completed from one to 25 CHG baths. They did not find a trend of increasing concentration of CHG with increasing exposure to CHG. There was not a trend that younger children had higher concentration of CHG, and CHG levels were not higher if take right after a CHG bath or the reverse, levels were higher at times farther from the bath. Rupp et al. (2012) studied 3 cohorts of patients including patients from a pediatric intensive care unit (PICU) who underwent CHG baths (not wipes). They found compliance in the PICU to be low 37% of eligible patients had a CHG bath. They also found a significant decline in infection due to *C. difficile* during the daily bathing intervention, $RR = 0.3$, $p = 0.001$, 95% CI [0.19, 0.49]. And when baths were stopped during the washout period there was an increase in infection due to *C. difficile*, $RR = 2.52$, $p = 0.005$, 95% CI [1.32, 4.80]. Finally, Milstone, et al. (2013) reported a reduction in bacteremia in the group of pediatric patients > 2 months of age in the per protocol analysis of a cross over trial of 4947 children. When intention to treat analysis is used, the difference is not significant. No children < 2 months of age were included in the studies.

The most serious harm reported in the above studies is rash formation where the skin is exposed to CHG. No data was reported on this finding.

Search Strategy:

("Catheterization, Central Venous"[Mesh] OR "Catheters, Indwelling"[Mesh]) AND ("Anti-Infective Agents, Local"[Mesh] OR "Anti-Infective Agents, Local"[Pharmacological Action]) AND (("2009/01/01"[PDAT] : "2012/12/31"[PDAT]) AND (Meta-Analysis[ptyp] OR systematic[sb] OR Practice Guideline[ptyp]))

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Method Used for Appraisal and Synthesis:

Review Manager (RevMan 5)

GradeProfiler (GRADEpro)

Critically Appraised Topic (CAT)

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Table 1. Summary of Findings- O'Horo, et al., (2012)

Question: Chlorhexidine (CHG) bathing versus soap and water of standard for health care associated infection O'Horo, et al. (2012)							No. of Patients		Effect		Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Chlorhexidine (CHG) Bathing Versus Soap and Water of Standard	Control	Relative (95% CI)	Absolute		
Health care associated BSI (assessed with: events per patient days)												
12	observational studies	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias ^{2,3}	291/67775 (0.43%)	557/69617 (0.8%)	OR 0.44 (0.33 to 0.59)	4 fewer per 1000 (from 3 fewer to 5 fewer)	⊕○○○ VERY LOW	CRITICAL
Health care associated BSI - CHG bathing (assessed with: events per patient days)												
5	observational studies	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias ²	222/33359 (0.7%)	386/32218 (1.2%)	OR 0.47 (0.31 to 0.71)	6 fewer per 1000 (from 3 fewer to 8 fewer)	⊕○○○ VERY LOW	CRITICAL
Health care associated BSI - CHG impregnated cloths (assessed with: events per patient days)												
7	observational studies	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias ²	69/34416 (0.2%)	171/37399 (0.46%)	OR 0.41 (0.25 to 0.65)	3 fewer per 1000 (from 2 fewer to 3 fewer)	⊕○○○ VERY LOW	CRITICAL

¹ Definition for infection and colonization were inconsistent, from "Health Care related BSI" to CLABSI various modifications of the CDC's definition),

² Only one RCT is included. In the remaining quasi experimental studies there is great variability in what was counted, BSI versus CLABSI. Not all papers reported how well the use of CHG was carried out in various units. And finally publication bias is evident, studies that showed lack of benefit of CHG baths has not been published.

³ Did not upgrade for large effect. Although large effect is defined as RR >2 or <0.5 (based on consistent evidence from at least 2 studies, with no plausible confounders)

Figure 1. Forest Plot- O’Horo, et al., (2012)

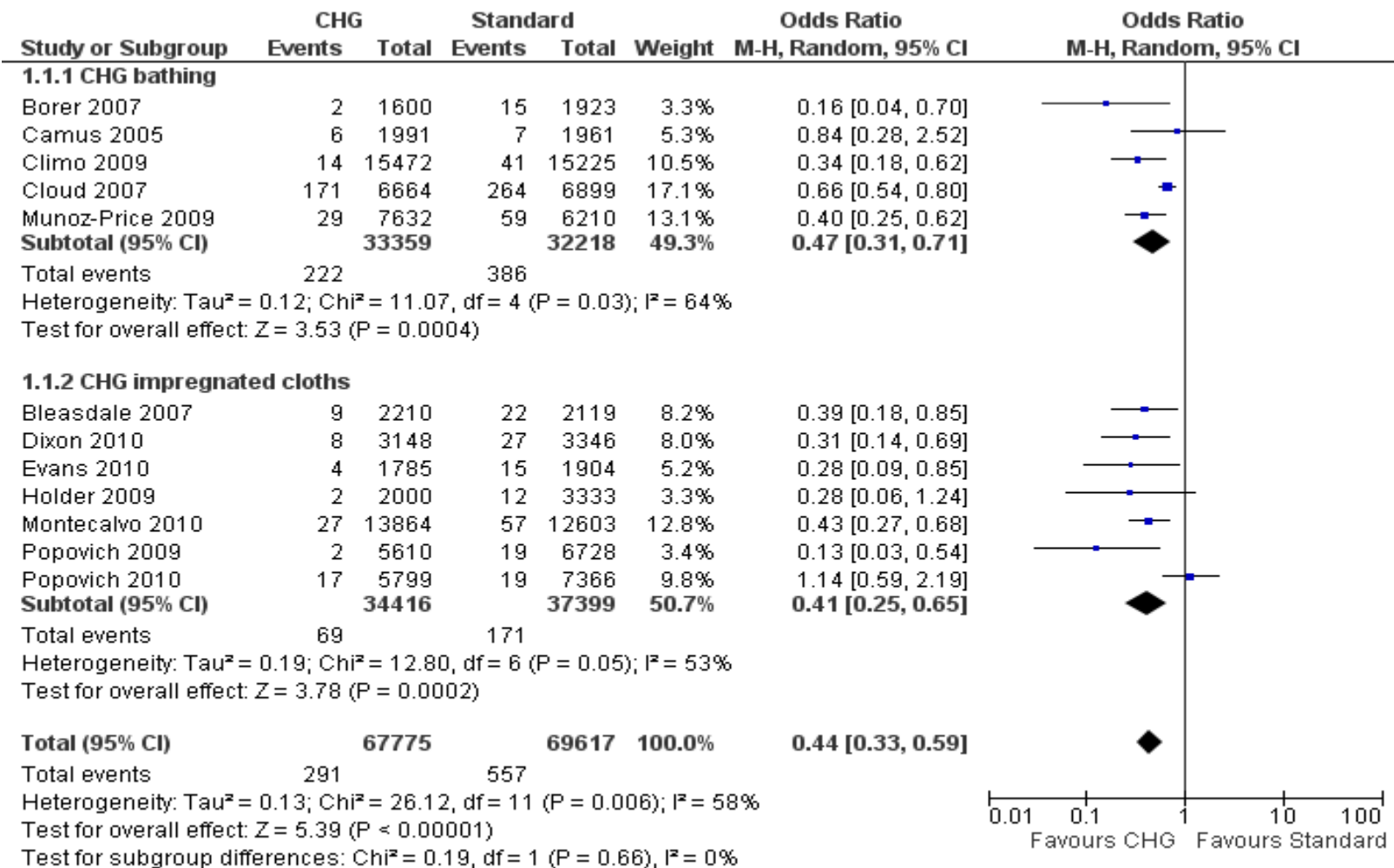


Table 2. Summary of Findings- Karki & Cheng, (2012)

Question: Should non-rinse skin cleansing with CHD be used for prevention of health care associated infections and colonization with multi-resistant organisms?

Quality Assessment Karki & Cheng (2012)							Quality	Importance
No. of Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations		
Central-line-associated bloodstream infections (assessed with: Incident risk ratio)								
8	observational studies ¹	serious ^{2,3}	serious ⁴	no serious indirectness	no serious imprecision		⊕○○○ VERY LOW	CRITICAL

¹ Seven before and after studies and one cross over trial with concurrent controls.

² Attrition bias that is not reporting on those who did not complete the study

³ In four of the seven studies reported the before and after treatment groups scored low on Comparability on the Newcastle Ottawa scale can be used to assess bias in cohort studies. Comparability rates the similarity of the before and after cohorts. The majority of the differences were in the co-interventions that occurred.

⁴ Heterogeneity of studies is high I2 statistic is 67%

Figure 2. Forest Plot Karki and Cheng, (2012)

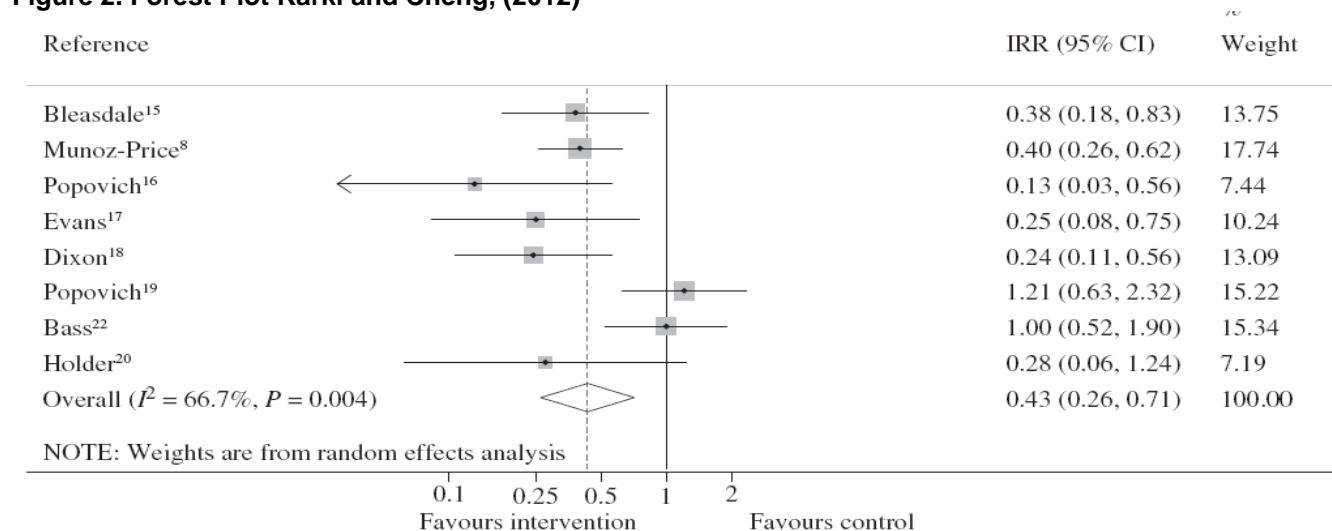


Table 3. Critically Appraised Topic- CHG Bath and Bacteremia

Author, Date, Country, and Industry of Funding	Patient Group	Level of Evidence (Oxford)	Research Design	Significant Results	Limitations
Bass 2012 Australia	Adults N= 439 subjects on an hematology- oncology unit 229 = in the baseline group 210 in the intervention group	2 b	Individual cohort study Before and after cohorts	1. No difference in the risk of acquiring VRE between groups. See forest plot, Figure 2	The projected VRE colonization rate used to calculate the number of subjects was higher than the rate actually seen. Power was not met. Could not add subjects to the observational study, because they had a set amount of CDG washcloths and all were used. Bathing was not monitored for compliance
Batra 2010 Thailand	4570 adult subjects in two ICUs Pre CHG bathing = 2480 Post CHG bathing = 2090	2 b	Interrupted time series	1. For the MRSA-TW strain there was no difference in the number of isolations of the organism before and after antiseptic protocol	They looked at the effect of CHG bathing in two groups of MRSA strains. TW strain- an outbreak strain that was shown to be resistant to CHG Non-TW strain- all other MRSA strains
Huang 2013 USA	74,256 adult subjects, in 43 ICUs	1b Individual RCT	Cluster randomized trial. Hospitals were randomized Three treatments: 1. MRSA screening and isolation	2. Universal decolonization resulted in greater reduction in the hazard of MRSA positive clinical cultures than did MRSA screening and isolation n group 3 –HR=0.63, 95% CI [0.52, 0.75] group 1- HR= 0.92, [0.77, 1.10] p= 0.003. 3. The three groups were not significantly different from each other for the outcome: MRSA bloodstream infection	Although they state intention to treat analysis, they randomized 45 sites. Two sites are not included in the analysis. They were excluded after randomization, but before the study began. Reported adverse effects: mild pruritus after CHG bathing in 7 subjects, two in the targeted decolonization group and 5 in the universal decolonization group.

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			<p>2. Targeted decolonization</p> <p>3. Universal decolonization</p>	<p>4. Universal decolonization resulted in greater reduction than either screening and isolation HR = 0.99, 95% CI [0.84, 1.16] p=0.001 or targeted decolonization. HR = 0.78, 95% CI [0.66, 0.91] p= 0.04</p> <p>5. Targeted decolonization resulted in significantly lower rates of blood stream infection from any pathogen</p>	<p>By chance, the universal group contained 3 of the four hospitals that did bone marrow and solid organ transplantation.</p>
Lee 2005 USA	12 pediatric subject (age 3-17months)	5 Survey of blood CHG levels	Samples from children who had 1-25 CHG baths	<p>CHG could not be detected at levels < 4.5 ng/mL</p> <p>Four different subjects a CHG level > 4.5 ng/mL</p> <p>There was not a trend of increasing concentration of CHG with increasing exposures</p> <p>There was not a trend of younger subjects having higher concentration of CHG.</p> <p>There was not a trend of higher concentration of CHG closer to the time of the bath, nor the reverse, higher levels farther from the time of the bath.</p>	<p>Children > 2 months of age only</p> <p>Not randomized</p> <p>Blood samples collected with other blood draws, not at similar times after CHG baths.</p>
Lopez 2011 USA	24-bed medical surgical ICU in regional medical center	26 month QI project	CLABSI rate/month	<p>Pre: No CHG baths</p> <p>Post :CHG baths(≥ 1 per day)</p> <p>Pre-intervention CLABSI rate: 5.7(1000 device days; 28/4875) to a post-intervention CLABSI rate of 0.2(1000 device days; 1/4171) (P< 0.001)</p>	<p>State it is an 18 mo pre/post intervention comparison, but only report on 13 mo pre/post intervention</p> <p>Policy states “all patients receive a CHG bath once in a 24 hour period” but go on to say “each ICU nurse is responsible for completing 1 CHG bath during his/her shift.</p>
Milstone 2013 USA	4947 children ≥ 2 months of age and in the PICU ≥ 2 days	2b low quality RCT	Randomized by ICU, unmasked, two period cross-over trial	<p>Per protocol analysis showed significant reduction of bacteremia in the CHG group – adjusted incidence rate ratio = 0.64, 95% CI [0.42-0.98]</p> <p>Intention to treat analysis showed non-significant change in bacteremia between the two groups = 0.71, 95% CI 0.[42-1.20]</p> <p>Although the adjusted incident rate is similar in the two groups in the ITT group, the CI crosses the line of no effect.</p>	<p>Randomized by unit, not by subject. Unable to obtain consent for CHG bath in 36% of subjects after randomization.</p> <p>Per protocol analysis is used to state significant reduction.</p> <p>There is no description of timing of blood cultures (per protocol or when a child had symptoms)</p> <p>The source of blood cultures is not described.</p> <p>The study was funded by Sage Products who manufacture the CHG</p>

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					wipes. It is stated the commercial sponsor had no role in the study design, data collection data analysis or writing the manuscript. Sage Products was permitted to review the manuscript prior to publication.
Ritz, 2012 USA	All patients admitted to a medical oncology unit for a 6 month study period Control (3 months) group= 454 subjects Treatment group (3 months) 405 subjects	5	Observational before and after design	<ol style="list-style-type: none"> 1. VRE and MRSA transmission rates were not significantly different between the two groups. 2. Nursing time decreased. In the basin bath group a bath took 4.065 minutes, in the CHG wipe bath group a bath took 3.314 minutes.(P=0.008) 3. 94% of nurses preferred the wipes to basin baths 4. 75% of nurses indicated wipes were more comfortable for the patient 5. CHG solution for basis baths cost \$5.22/d while CHG wipe baths cost \$7.85/d 	Nursing satisfaction survey was not reliable nor validated
Rupp 2012 USA	3 cohorts of patients determined by hospital geography Included a pediatric unit.	5	Observational dose ranging staged introduction in 3 cohorts of patients 1- 6 months CHG bathing 3 days per week 2- 6 months CHG bathing every day 3- 4 month washout period CHG bathing was discontinued	<p>CHG baths NOT wipes.</p> <p>Adherence</p> <ul style="list-style-type: none"> Adult critical care units (90%). Adult hematology/oncology unit 45.6% Pediatric intensive care (37%) <p>Significant decline in infections due to <i>C. difficile</i> during the daily bathing intervention in all cohorts (RR, 0.30 [95% CI, 0.19–0.49]; <i>P</i> (0.001).</p> <p>During washout , there was a increase in infections due to <i>C. difficile</i> compared to daily CHG bathing (RR, 2.52 [95% CI, 1.32–4.80] <i>P</i>= 0.0050</p> <p>Newly detected VRE decreased significantly during the intervention but did not rebound during the washout period</p> <p>In non-critical care areas there was not consistent pattern.</p>	<p>There was a low number of infections, which makes including enough subjects to detect a statistical difference difficult.</p> <p>The laboratory procedures for determining <i>C. difficile</i> were changed in the middle of the study, but did not appear to have an effect on the outcome.</p>