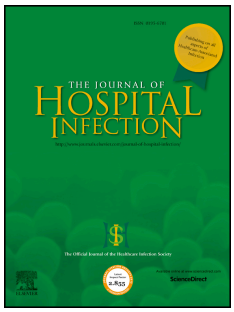
Accepted Manuscript



Antimicrobial surfaces to prevent healthcare-associated infections: a systematic review: a different view

Michael G. Schmidt, Ph.D, MD, MS Cassandra D. Salgado, DrPH Katherine D. Freeman, Joseph F. John, Jr., MD, MD Robert J. Cantey, MBA Peter A. Sharpe, Ph.D. PE Harold T. Michels

PII: S0195-6701(18)30099-9

DOI: 10.1016/j.jhin.2018.02.007

Reference: YJHIN 5344

To appear in: *Journal of Hospital Infection*

Received Date: 29 January 2018

Accepted Date: 6 February 2018

Please cite this article as: Schmidt MG, Salgado CD, Freeman KD, John Jr. JF, Cantey RJ, Sharpe PA, Michels HT, Antimicrobial surfaces to prevent healthcare-associated infections: a systematic review: a different view, *Journal of Hospital Infection* (2018), doi: 10.1016/j.jhin.2018.02.007.

ANTIMICROBIAL SURFACES TO PREVENT HEALTHCARE- ASSOCIATED INFECTIONS: A SYSTEMATIC REVIEW: A DIFFERENT VIEW

[1*]Michael G. Schmidt, Ph.D., [2]Cassandra D. Salgado, MD, MS, [3]Katherine D. Freeman, DrPH, [4]Joseph F. John, Jr. MD, [2]Robert J. Cantey, MD, [5]Peter A. Sharpe, MBA and [6]Harold T. Michels, Ph.D. PE.

[1]Department of Microbiology and Immunology, Medical University of South Carolina, 173 Ashley Ave, Charleston, SC 29425, USA, schmidtm@musc.edu; +011-843-792-9532

[2]Department of Medicine, Division of Infectious Disease, Medical University of South Carolina, Charleston, South Carolina, USA. salgado@musc.edu, canteyjr@musc.edu

[3]Extrapolate LLC, Delray Beach, Florida, USA kfreeman@extrapolatestatistics.com

[4]Department of Medicine, Ralph H. Johnson VA Medical Center, Charleston, South Carolina, USA. Joseph.John2@med.va.gov

[5]Sharpe and Associates, Westfield, New Jersey, USA. pas@sharpeassociates.com

[6]Copper Development Association, New York, New York, USA. harold.michels@copperalliance.us

*Corresponding author.

Keywords: Healthcare Associated Infections (HCAI), Antimicrobial Copper, Infection Control, GRADE

Commentary/Letter to Editor

Muller and colleagues' review of antimicrobial surfaces,[1] mistakenly interpreted the study by Salgado and colleagues when reporting an overall GRADE of very low.[2] Based on work by Atkins and Kavanagh,[3, 4] we suggest that GRADE is not an appropriate criteria from which to evaluate the study and respectfully request the conclusions reached by Muller be withdrawn.

GRADE requires a clear specification of the relevant setting, population, intervention, comparator, and outcomes.[5] The Salgado study was a first-of-its-kind clinical trial evaluating the effectiveness of a continuously active antimicrobial surface on reducing HCAI. Thus, before GRADE could be effectively used to assess the validity of the data, clinical practice guidelines establishing criteria of how these studies might be performed should have been established by an appropriate expert panel in concert with a GRADE group. While it is true that GRADE has been adopted as a gold standard from which clinical trials are judged, absence of a standards-setting body defining how bias and data quality should be defined suggests that review of the data using GRADE was premature.

Additionally, the statement that "the study suffered from inappropriate randomization that impacted the validity of their data" is misguided. The randomization process was explained in detail and data collected without bias.[2, 6] Specifically, patient assignment to intervention, and control rooms was made using the hospitals' usual process of bed assignment (i.e. any available ICU room) by individuals unaware of the research room status. Although this is a 'random' process, it was not the process used for 'randomization.' Rather at the outset of the study, rooms were randomized by side of hallway/location using a formal randomization process to assign whether or not to have copper equipment. It appears that Muller and colleagues were confusing

patients entering the study 'randomly' with a 'randomization process'.

The intervention rooms represented only 35.5% of total rooms available for assignment and study units routinely had occupancy rates exceeding 90%. We believe that the stochastic nature associated with patient discharge and the fact that bed control assignments came from three distinct hospitals—each unaware both to which rooms were associated with the study and to when study rooms were available for patient placement—also contributed to the unbiased assignment of subjects into control and interventional rooms.

The study members responsible for determining acquisition of HCAI were also blinded as to whether or not cases under review were from an interventional or control room. Multivariate analyses controlling for APACHE II score, found infection on admission was neither a significant effect modifier of room assignment nor independently associated with the incidence of HCAI or colonization; however, both APACHE II score (P = 0.011) and room assignment (P= 0.027) were significantly associated with incident HCAI or colonization.

We find it curious that Muller elected not to comment on the fundamental observation that infection and microbial burden (MB) were significantly associated. Eighty-nine percent of HCAI resulted in patients in rooms where the cumulative MB for the monitored objects exceeded 500 cfu/100 cm^2.[2] The intent of the study was to assess whether or not the intrinsic environmental MB would impact HCAI rate. It did. The study was not powered to evaluate the transmission of antibiotic-resistant organisms per se, but rather whether or not the limited placement of copper within the environment would impact subsequent colonization of patients by MRSA or VRE. On a per sample basis, copper surfaces were approximately six-times less likely to harbor MRSA or VRE and based on the summative MB of the surfaces sampled, the

combined MRSA and VRE burden was 96.8% lower on copper surfaces compared to non-copper surfaces.[6] This reduction to the MRSA and VRE levels within the study environment was likely responsible for the lowered risk of transmission.

The utility of the intrinsic antimicrobial activity of cooper surfaces for controlling environmental MB burden within clinical environments has since been confirmed by two independent trials subsequent to the Salgado study.[7, 8] Again, the use of innuendo to suggest that the reduction in HCAI appeared implausible is unfortunate.

The issue of blinding was a given as copper surfaces do indeed look different than plastic or wood; however, this fact, in no way accounts for the consistency with which these antimicrobial surfaces have been shown to control the concentration of bacteria in the environment.[6-8]

The global HCAI crisis continues despite the best efforts of infection control communities and environmental services teams. In 2008, using limited funds from a peer evaluated government contract, an interdisciplinary team from three institutions set out to evaluate whether surfaces in close proximity to patient care could impact HCAIs. The work of Salgado and colleagues was not perfect but was pioneering. It offered, for the first time, evidence that when the MB associated with objects frequently encountered by patients, healthcare workers and visitors was controlled, HCAI were lower.[2, 6]

REFERENCES

[1] Muller MP, MacDougall C, Lim M, Ontario Agency for Health P, Promotion Public Health O, Provincial Infectious Diseases Advisory Committee on Infection P *et al.* Antimicrobial surfaces to prevent healthcare-associated infections: a systematic review. *J Hosp Infect* 2016; **92**: 7-13.

[2] Salgado CD, Sepkowitz KA, John JF, Cantey JR, Attaway HH, Freeman KD *et al.* Copper surfaces reduce the rate of healthcare-acquired infections in the intensive care unit. *Infect Control Hosp Epidemiol* 2013; **34**: 479-86.

[3] Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S *et al.* Grading quality of evidence and strength of recommendations. *Bmj* 2004; **328**: 1490.

[4] Kavanagh BP The GRADE system for rating clinical guidelines. *PLoS Med* 2009; **6**: e1000094.

[5] Guyatt GH, Oxman AD, Kunz R, Atkins D, Brozek J, Vist G *et al.* GRADE guidelines: 2. Framing the question and deciding on important outcomes. *J Clin Epidemiol* 2011; **64**: 395-400.

[6] Schmidt MG, Attaway HH, Sharpe PA, John J, Jr., Sepkowitz KA, Morgan A *et al.* Sustained Reduction of Microbial Burden on Common Hospital Surfaces through Introduction of Copper. *J Clin Microbiol* 2012; **50**: 2217-23.

[7] Hinsa-Leasure SM, Nartey Q, Vaverka J, Schmidt MG Copper alloy surfaces sustain terminal cleaning levels in a rural hospital. *Am J Infect Control* 2016; **44**: e195-e203.

[8] Schmidt MG, von Dessauer B, Benavente C, Benadof D, Cifuentes P, Elgueta A *et al.* Copper surfaces are associated with significantly lower concentrations of bacteria on selected surfaces within a pediatric intensive care unit. *Am J Infect Control* 2016; **44**: 203-9.