



## Major article

# Evaluation and quantitative microbial risk assessment of a unique antimicrobial agent for hospital surface treatment



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## Key Words:

Infectious disease  
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*Staphylococcus aureus*

**Background:** It is generally agreed that contaminated hospital surfaces play a role in the transmission of hospital-acquired infections (HAIs). The ability of an antimicrobial agent, engineered at Emory University, to reduce bacterial bioburden on hospital surfaces was examined. A quantitative microbial risk assessment was also conducted to quantify the potential reduction of human health risks associated with application of this antimicrobial product.

**Methods:** A 1-arm, prospective observational study was conducted. High-frequency contact surfaces within 18 hospital patient rooms were sampled in between patient use. Negative binomial regression with repeated measures was used to examine log CFU/100 cm<sup>2</sup> reductions in total, gram-negative, and *Staphylococcus aureus* microorganisms. Standard risk assessment methods were used.

**Results:** Multivariate regression demonstrated significant reductions in gram-negative ( $P < .0001$ ) and *S. aureus* ( $P = .009$ ) bacteria with increasing patient turnover. No reduction was observed in total bacteria ( $P = .93$ ). Infection risks were reduced by 4 and 3 logs for gram-positive and gram-negative bacteria, respectively. These risk reductions, along with HAI survey studies, suggest that application of this antimicrobial product could prevent as many as 5%–10% of HAIs.

**Conclusions:** This study was the first evaluation of a distinctive antimicrobial agent for hospital surface treatment. The findings provide support for the utility of an antimicrobial product in potentially reducing HAI transmission from contaminated environment surfaces.

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Hospital-acquired infection (HAI) has become a critically important issue due to the tremendous burden HAIs impose on public health and the economic infrastructure. Reported estimates of the annual direct medical costs of HAIs to hospitals in the United States vary from \$28.4–\$33.8 billion (adjusted to 2007 dollars based on the Consumer Price Index for all urban consumers) and from

\$35.7–\$45 billion (adjusted to 2007 dollars based on the Consumer Price Index for inpatient hospital resource use).<sup>1</sup> Estimates, including both direct and indirect costs associated with HAIs in acute-care hospitals, demonstrate a substantially increased public health and financial burden in the United States, with figures ranging from \$96–\$147 billion each year.<sup>2</sup>

Scientific evidence provides strong support indicating that contaminated hospital surfaces play a role in the transmission of pathogens to humans, including methicillin-resistant *Staphylococcus aureus* (MRSA)—a leading cause of HAI—*Acinetobacter baumannii*, and *Clostridium difficile*, among others.<sup>3</sup> Various gram-negative species, mycobacteria, and spore-forming bacteria can survive on dry hospital surfaces for several months.<sup>4</sup> Antibiotic-resistant pathogens like MRSA are also capable of surviving on dry surfaces for extended periods of time in the hospital setting.<sup>5</sup> Complicating our understanding of the role that contaminated hospital surfaces play in patient inoculation and hospital infection

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Exponent was contracted by HealthCure, LLC (HealthCure) to perform statistical analysis of the data provided by HealthCure, and to draft the initial manuscript. The study concept, design, and the collection of data were conducted by HealthCure. KDM was contracted by HealthCure to perform the quantitative microbial risk assessment.

Conflicts of interest: None to report.

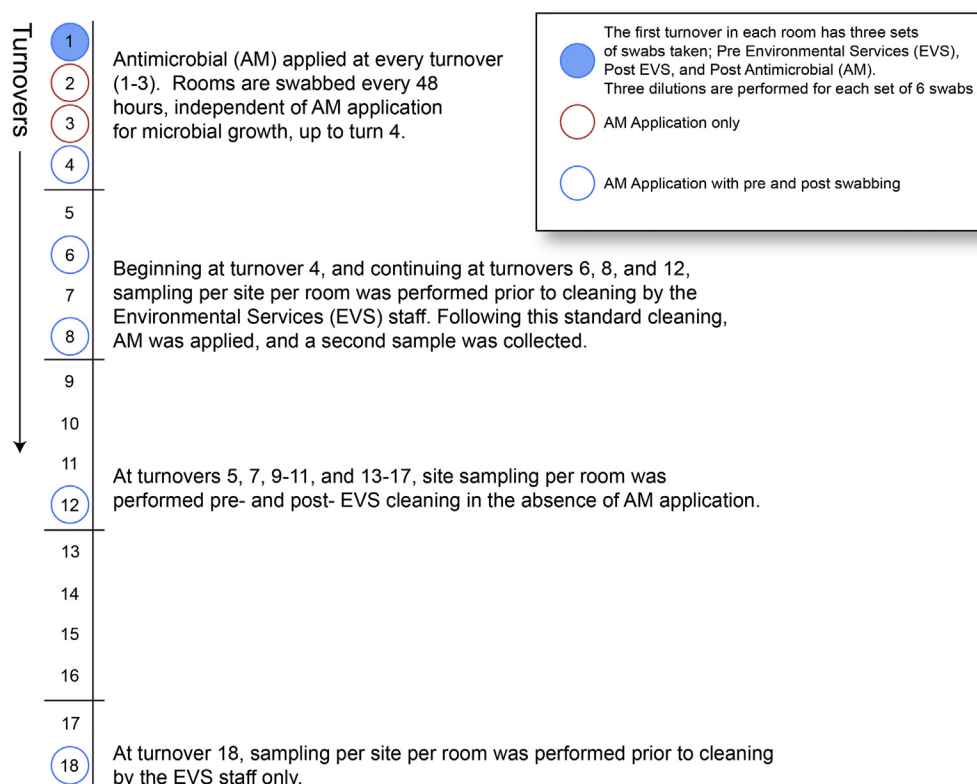


Fig 1. Oakwood Hospital and Medical Center antimicrobial study design.

rates is the fact that transmission pathways are complex. For example, Hardy et al<sup>6</sup> reported that 35% of MRSA isolates cultured from the immediate patient environment were genetically matched to patients with an HAI.

Pathogens from contaminated surfaces may be transmitted to patients either directly or indirectly via health care workers' (HCWs) frequent contact with these surfaces.<sup>7</sup> Residual contamination from previous occupants adds to the complex nature of HAIs, with 1 study demonstrating that 7% of volunteers acquired *S aureus* on their hands after touching bed rails and overbed tables in vacant rooms that had been terminally cleaned.<sup>7,8</sup> Research also shows that contamination from potentially life-threatening HAIs persists on visibly clean surfaces following the application of detergent sanitizer, bleach and steam cleaning, and phenolic disinfection in the hospital setting.<sup>5</sup>

A growing body of literature demonstrates that surface cleaning or disinfection may reduce the transmission of HAIs, and in some cases may be critical in the termination of an infectious disease outbreak.<sup>5,7</sup> Dancer<sup>9</sup> makes a compelling case for rigorous environment cleaning and disinfection coupled with key interventions in addition to hand hygiene compliance for infection prevention. Given that routine cleaning of contaminated surfaces may not fully eradicate microorganisms, the implementation of improved infection control technology is needed to enhance hospital cleanliness and patient safety. Particularly desirable may be the application of an antimicrobial agent with prolonged residual protection. Previous research has reported a rebound of aerobic bacteria within 6 hours to between 30% and 40% of precleaning/disinfection status<sup>10</sup> and other assessments have also been unable to show residual antimicrobial activity.<sup>11</sup>

Our study was undertaken to examine the influence of an antimicrobial agent against bacterial bioburden, including gram-negative bacteria and *S aureus* microorganisms, on

high-frequency contact surfaces in the hospital setting. A quantitative microbial risk assessment (QMRA) using these data was also conducted to quantify the potential reduction of human health risks associated with application of this antimicrobial agent.

## MATERIALS AND METHODS

### Study population, setting, and design

A 1-arm, prospective study was conducted at the Oakwood Hospital and Medical Center, a full-service, not-for-profit, 650-bed teaching and research hospital affiliated with Wayne State University School of Medicine in Dearborn, Michigan. Eighteen patient rooms and 6 high-frequency contact surfaces within each room, selected a priori, served as the study population. The 6 high-frequency contact sampling sites per room consisted of the bathroom doorhandle/rail, the bed rail, the bedside table drawer, the patient call pad, the privacy curtain, and the sink basin. All samples collected and product applications made as a part of the study were performed by microbiology staff contracted from a staffing agency by HealthCure, LLC. This was performed in addition to all normal hospital room cleaning that was performed by the hospital Environmental Services Department (EVS) staff. The study was approved by the Institutional Review Board at Wayne State University.

The study period was March 12–November 7, 2012, and spanned 18 patient turnovers for each of the 18 hospital rooms included in the study (Fig 1). Sampling by patient room was performed in an independent fashion by members of the microbiology staff. At the first turnover in each room, sampling was performed before cleaning by the hospital's EVS staff. Following the standard cleaning by EVS staff, which included use of 2 different antimicrobial products, Virex 256 (JohnsonDiversity, Inc, Sturtevant, Wisc) and

Clorox Healthcare Bleach Germicidal Wipes (The Clorox Company, Oakland, Calif), a second sample was taken. Goldshield 75 (AP Goldshield, LLC, Locust Valley, NY) was applied next by members of the microbiology staff, followed by the collection of a third sample. Sampling at the first turnover per room was therefore performed 3 times (ie, pre- and post-EVS clean, followed by Goldshield 75 application and a third sample post-Goldshield application). Up to the fourth turnover, Goldshield was applied at each turnover and after standard cleaning by EVS staff. Sampling was performed every 48 hours within this time period, independent of EVS cleaning and Goldshield application, as part of a product safety evaluation.

Beginning at turnover 4, and continuing at turnovers 6, 8, and 12, sampling per site per room was performed before cleaning by EVS staff. Following the standard cleaning by EVS staff, Goldshield was applied, and a second sample was collected. Sampling at these turnovers therefore occurred twice (pre- and post-EVS cleaning plus Goldshield application). At turnovers 5, 7, 9–11, and 13–17, site sampling per room was performed pre- and post-EVS cleaning in the absence of Goldshield application. At turnover 18, sampling per site per room was performed before cleaning by EVS staff only.

#### Study intervention: Goldshield antimicrobial agent

Goldshield 5 (5% active ingredient) is a distinctive, water-stable antimicrobial agent that provides residual antimicrobial activity to surfaces that have already been cleaned per EVS standard cleaning protocols. Goldshield 5 is an organosilane formulation in a nano assembly of molecules consisting of a siloxane covalent bonding agent (an attraction to repulsion stability that forms between the atoms contained in the formulation and the electrons of the substrate), a nitrogen molecule that positively charges the substrates to which it has bonded, a long carbon chain that releases an ionic charge, and quaternary ammonium salts. Thus the antimicrobial functionality is an electrochemical action that is expected to provide durable, residual protection. This infection control technology was developed by scientists at Emory University (Atlanta, GA), and is exclusively licensed to AP Goldshield LLC, and is currently registered with the United States Environmental Protection Agency (85,556–1). The US patent numbers associated with this product are 5,959,014; 6,221,944; and 6,632,805.<sup>12</sup> For use in this study, Goldshield 5 was diluted in tap water at a ratio of 1 part Goldshield:5 parts water resulting in a product for application at a concentration of 0.83% active ingredient (Goldshield 75).

#### Microbiologic methods

Prepared agar plates of plate count agar, tryptic soy agar with 5% sheep blood, and MacConkey's agar (all from BD Diagnostic Systems, Sparks, MD) were used to culture total bacterial count, *Staphylococcus aureus* (golden yellow colonies showing beta hemolysis were counted as putative *S aureus*), and gram-negative bacteria, respectively. Tubes containing the swab samples in Dey/Engley neutralizing broth were vortexed for 20 seconds, followed by serial dilutions. Each set of diluted samples was cultured on the 3 different agar plates in duplicate using the spread plate method. Plates were incubated at 35 °C and read at 24 hours and 48 hours. Plates with >250 colonies were recorded as too numerous to count.

#### Analytic methods

##### Power calculations

Because a fixed number of patient rooms was decided upon a priori, a power calculation was conducted to determine if a sample size of 18 would allow for a statistically significant decrease in antimicrobial activity to be detected. Assuming a

2-tailed paired *t* test analytic approach, an alpha level of 0.05, and further assuming a moderate to large effect size ( $\geq 0.7$ ) based on Cohen's criteria<sup>13</sup> it was determined that the study would have at least 80% power to detect a statistically significant effect on the log CFU/100 cm<sup>2</sup> reduction of microbial counts.<sup>14</sup> A secondary power calculation based on a multivariate repeated measures analysis, within-factors model, was performed and provided further support that the study would be sufficiently powered to detect a statistically significant decrease in antimicrobial activity over time.

#### Statistical analysis

All nondetect values were substituted with a value of 0.1 before analysis. The number of countable colonies (CFU/100 cm<sup>2</sup>) per dilution was determined and subsequently used to calculate the geometric mean across dilutions.<sup>15</sup> Empirical growth plots for each outcome stratified by sampling location (ie, bathroom doorhandle/rail, bed rail, bedside table drawer, patient call pad, privacy curtain, and sink basin) were constructed to visually examine trends in the log CFU/100 cm<sup>2</sup> bacteria count across the study period.

To account for overdispersion in the data and continuous sampling of patient rooms, negative binomial regression models using the Proc Genmod procedure in SAS (version 9.4, SAS Institute Inc, Cary, NC) were used to examine log CFU/100 cm<sup>2</sup> reductions in the pre-EVS levels of total microbial, gram-negative, and *S aureus* bacteria count (separate models for each dependent variable). Statistically significant trends in bacteria count (dependent variable) were examined in regression models specifying patient turnover as the only independent variable. Trends in pre-EVS levels of total microbial, gram-negative, and *S aureus* bacteria count were further examined in multivariate negative binomial regression models. Independent variables included patient turnover, Goldshield application (yes/no), and sampling location. All models accounted for repeated sampling of patient rooms and included only patient turnovers 1 and 4–18 due to differences in the study design at patient turnovers 2 and 3. *P* < .05 was considered statistically significant in all analyses.

#### QMRA

A QMRA approach was undertaken to estimate the reduction of infection risks associated with the effectiveness of Goldshield to minimize exposure to pathogenic bacteria within a hospital setting.<sup>16</sup> The 4-step paradigm includes hazard identification, exposure assessment, dose–response assessment, and risk characterization. Infection risks were estimated assuming exposure to higher and lower concentrations of bacteria (CFU/100 cm<sup>2</sup>) that were recorded in our study from various hospital surfaces. Specifically, *S aureus* and *Pseudomonas aeruginosa* were selected to represent gram-positive and gram-negative bacteria, respectively, with the latter chosen due to its association with HAIs.<sup>17</sup> The exponential model was applied in the dose–response assessment to best represent the microorganism–host interaction for both bacteria:

$$P_{(\text{infection})} = 1 - \exp(-k \times d) \quad \text{Eq. 1}$$

In equation 1,  $P_{(\text{infection})}$  is the probability of infection, *k* represents the fraction of microorganisms that survive and initiate infection ( $7.64 \times 10^{-8}$  for *S aureus* and  $1.05 \times 10^{-4}$  for *P aeruginosa*), and *d* represents the dose in the exposure.<sup>16,18,19</sup> A range of infection risks was estimated for *S aureus* and *P aeruginosa* assuming all microorganisms in an exposure were pathogenic.

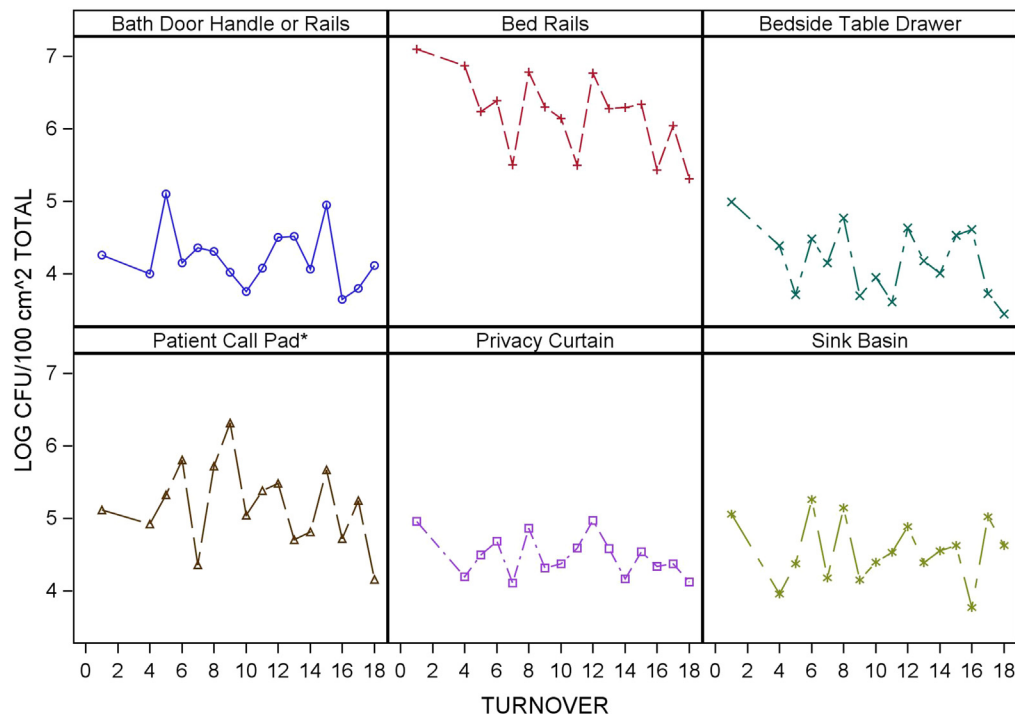


Fig 2. Trends over time in log CFU/100 cm<sup>2</sup> total microbial count by sampling location \*Statistically significant at  $P < .05$ .

## RESULTS

The study protocol is shown in Figure 1 and demonstrates the difference in study design at patient turnovers 2 and 3, where antimicrobial monitoring was conducted, compared with all other patient turnovers, where monitoring of the antimicrobial was not conducted.

Trends over time in log CFU/100 cm<sup>2</sup> pre-EVS levels of total microbial, gram-negative, and *S aureus* bacteria count by sampling location are presented in Figures 2–4, respectively. Negative binomial regression results showed statistically significant decreasing trends in total microbial load on the patient call pad ( $P = .048$ ); in gram-negative load on the bathroom doorhandle/rail, bed rail, bedside table drawer, patient call pad, privacy curtain, and sink basin (all  $P < .05$ ); and in *S aureus* bacteria on the bed rail, bedside table drawer, privacy curtain, and sink basin (all  $P < .05$ ).

Regression analyses were performed using 2 different models. Model 1 (bivariate regression analysis) that adjusted for patient turnover and the sampling correlation within a patient room, showed statistically significant decreases with increasing patient turnover in overall counts of gram-negative ( $P = .0001$ ) and *S aureus* ( $P = .04$ ) bacteria, but not total microbial load ( $P = .62$ ) during the study (Table 1). Further adjustment of the model for application of the antimicrobial product and sampling location (model 2: Multivariate regression analysis) also demonstrated statistically significant decreases with increasing patient turnover in overall counts of gram-negative ( $P < .0001$ ) and *S aureus* ( $P = .009$ ) bacteria, but not total microbial load ( $P = .93$ ) during the study (Table 1).

Infection risks associated with exposure to bacteria-laden hospital surfaces (in centimeters<sup>2</sup>) ranged from  $8 \times 10^{-9}$  (for *S aureus*) to  $3 \times 10^{-2}$  (for *P aeruginosa*). The worst-case, single exposure scenario for *S aureus* resulted in an infection risk of  $2 \times 10^{-5}$ . Bacterial infection risks were potentially reduced by 4 logs for *S aureus* and 3 logs for *P aeruginosa* when evaluating the influence of the application of the antimicrobial agent. Risk estimates assume

100% transfer rate of pathogens from surface to fingertip, and from fingertip to face.

## DISCUSSION

Our study examined the ability of a unique antimicrobial agent to reduce bacterial bioburden on high-frequency contact surfaces in patient rooms within a single hospital setting. A QMRA was performed secondarily to quantify the potential reduction of human health risks associated with antimicrobial application. The main findings demonstrated statistically significant reductions in gram-negative and *S aureus* microorganisms during the study period. No statistically significant reduction in total microbial count was observed, indicating that further investigation into specific pathogens and the potential for resistance of selected infectious agents following repeated exposure is warranted. Findings from the QMRA revealed that antimicrobial application reduced bacterial infection risks by as much as 4 logs, providing support for the usefulness of an intervention with antimicrobial agents in potentially reducing the transmission of HAIs from contaminated environment surfaces to humans.

No evidence of a decreasing trend was observed for total microbial count in our study. This finding contrasts with the statistically significant and comparable reductions observed for gram-negative and *S aureus* microorganisms. Antimicrobial product application in our study was performed in addition to the standard cleaning by hospital EVS staff with the intention of providing continued protection. It is, however, possible that the presence of certain pathogens with an ability to survive on dry surfaces for months at a time and that are difficult to eradicate may have influenced the results for total microbial count.<sup>3,4,20</sup> Hand hygiene among hospital staff may have also influenced the results for total microbial count. Frequent surface contamination via the hands of HCWs is always possible.<sup>3</sup> Hand hygiene compliance was not evaluated as part of our study and therefore the extent to which this factor may have influenced the results is not known. On the other

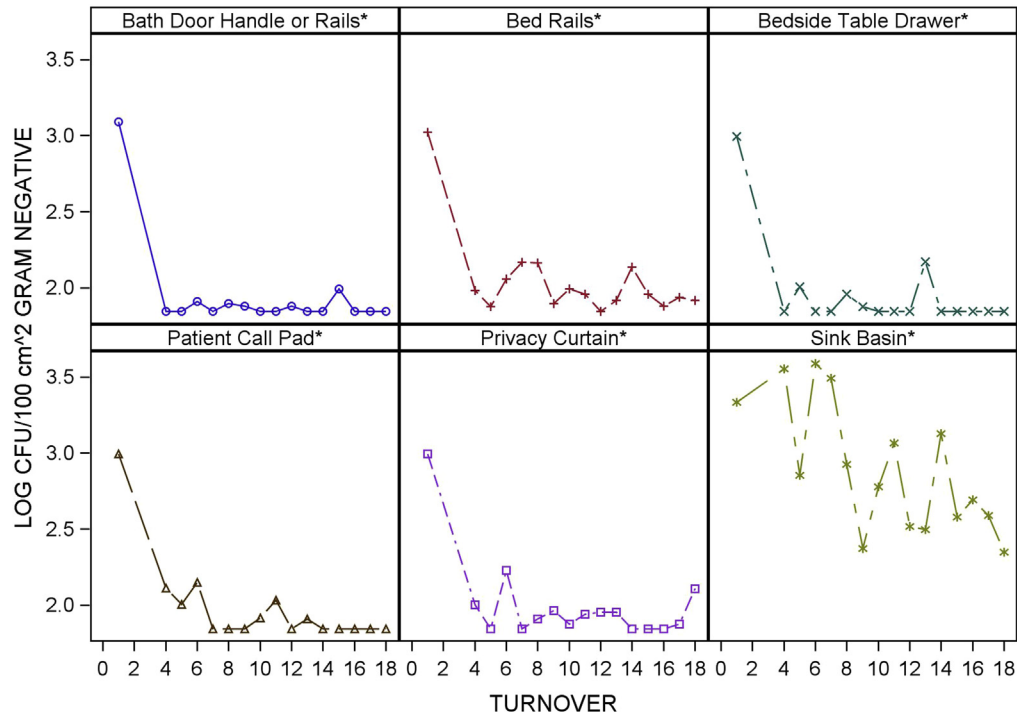


Fig 3. Trends over time in log CFU/100 cm<sup>2</sup> gram-negative by sampling location. \*Statistically significant at  $P < .05$ .

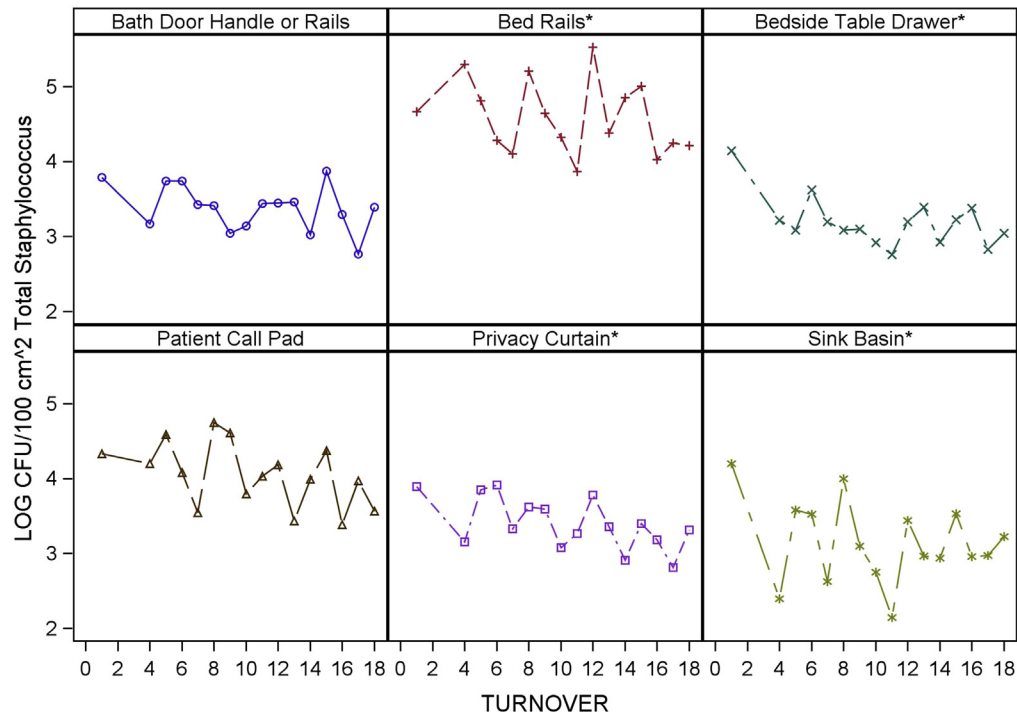


Fig 4. Trends over time in log CFU/100 cm<sup>2</sup> *Staphylococcus aureus* by sampling location. \*Statistically significant at  $P < .05$ .

hand, total microbial count may have been affected by other factors, including the culture-dependent method used, the sampling protocol, and the degree of environment contamination.<sup>20</sup>

In a previously published study,<sup>12</sup> this unique antimicrobial agent at 5% solution (compared with the 0.75% solution used in our study) was used to treat patient gowns inoculated with patient isolates of MRSA, *Escherichia coli*, and *P aeruginosa*. Sampling was

performed every 7 days for a period of 2 weeks. Baxa et al<sup>12</sup> reported that application of the antimicrobial agent inhibited the viability of these bacteria for 2 weeks compared with untreated material, and that *E coli* and *P aeruginosa*, 2 types of gram-negative bacteria, exhibited a considerably slower decay in the number of recovered microorganisms compared with MRSA, a gram-positive strain. Furthermore, Baxa et al<sup>12</sup> applied the antimicrobial agent



**Table 1**

Trends in the expected log CFU/100 cm<sup>2</sup> change of total, gram-negative, and *Staphylococcus aureus* microorganisms

Outcome	Model 1 <sup>a</sup>	P value	Model 2 <sup>b</sup>	P value
Log CFU/100 cm <sup>2</sup> total	0.004 (−0.01 to 0.02)	.62	0.001 (−0.02 to 0.02)	.93
Log CFU/100 cm <sup>2</sup> gram negative	−0.06 (−0.09 to −0.03)	.0001 <sup>‡</sup>	−0.03 (−0.05 to −0.02)	<.0001 <sup>‡</sup>
Log CFU/100 cm <sup>2</sup> <i>Staphylococcus aureus</i>	−0.03 (−0.07 to −0.002)	.04 <sup>‡</sup>	−0.04 (−0.07 to −0.01)	.009 <sup>‡</sup>

NOTE. Results derived from regression models specifying the negative binomial distribution to properly account for overdispersed data, and are expressed as the regression coefficient ( $\beta$ ) and 95% confidence interval. Interpretation: if  $\beta$  is negative, then the expected log CFU/100 cm<sup>2</sup> decreases by  $\beta$  with each patient turnover (turnovers 1, 4–18, and inclusive).

<sup>a</sup>Model 1 adjusts for patient turnover and the sampling correlation within a patient room.

<sup>b</sup>Model 2 further adjusts Model 1 for antimicrobial product application and sampling location.

<sup>‡</sup>P values are statistically significant at <.05.

at a 1% dilution with a 10% nonionic detergent as an antimicrobial agent on environment surfaces and reported the greatest log reductions after the initial inoculation and at rechallenge among MRSA isolates ( $\geq 2$  log<sub>10</sub> reduction) compared with both types of gram-negative bacteria (<1 log<sub>10</sub> reduction). Although the study designs and methodologies that were implemented differed considerably between our study and that of Baxa et al,<sup>12</sup> the antimicrobial product used in the 2 protocols was identical. As in the Baxa et al study,<sup>12</sup> our Oakwood Study results demonstrate a slightly greater log CFU/100 cm<sup>2</sup> reduction in *S aureus* compared with gram-negative microorganisms, providing support for the usefulness of an intervention with an antimicrobial agent in reducing the level of environment contamination in a hospital setting.

Given the almost universally accepted axiom that hospital environment surfaces, especially high-touch surfaces, play a major role in the transmission of pathogenic organisms, the challenge for infection control professionals (ICPs) is to reduce the presence of these organisms in patient environments. In addition to EVS basic terminal and daily cleaning, a nontoxic antimicrobial agent with prolonged efficacy (days or weeks) would be a welcome addition to an ICP's resources.

The patented quaternary ammonium salt antimicrobial agent employed in our study has been demonstrated to have prolonged residual protection in a previously published study.<sup>12</sup> This study provides highly suggestive if not convincing evidence of initial and prolonged surface protection from both gram-positive and gram-negative organisms.

Future research examining the relative long-term effectiveness of application of this antimicrobial agent in hospital settings is warranted to further elucidate the clinical significance of hospital decontamination with antimicrobial product use. This can be achieved by extending our study design to incorporate intervention and control groups consisting of the same number of patient rooms and sampling sites, and consequently evaluating between-group trends in bacterial bioburden over time. An examination of the potential clinical significance of using an antimicrobial agent in reducing the bioburden of antibiotic-resistant pathogens, including MRSA, is warranted.

The findings from the QMRA indicate that if a bacterial infection would be expected for every 100 exposures to a hospital surface containing pathogenic bacteria, as suggested by the analysis of gram-negative bacteria counts, then the infection probability per patient could be reduced to as low as 1 in 1,000,000 with the use of

the antimicrobial agent, and assuming typical transfer rates for gram-negative bacteria from surfaces to fingertips and faces.<sup>21</sup> A risk of 1 in 1,000,000 has been considered an infection risk goal for this type of exposure scenario, because it has been deemed comparable to US Environmental Protection Agency infection risk recommendation for drinking water.<sup>21</sup>

A recent survey of HAIs related to acute care hospitals throughout the United States found that 1 in 25 hospitalized patients may be expected to acquire some type of infection from a daily exposure and estimated a total of 722,000 HAIs in 2011.<sup>22</sup> The survey concluded that *S aureus* was one of the most common pathogens associated with HAIs (second only to *C difficile*), and was responsible for approximately 10% of the HAIs reported in the survey (n = 504 HAIs). The survey also concluded that fewer than half of all reported HAIs were due to surgery-related complications or contaminated medical devices, suggesting the importance of other exposure sources in hospital settings. Another study suggests that 20%–40% of HAIs are from patient exposure to hands of HCWs that are contaminated either from other patients, or from inanimate surfaces within the hospital.<sup>3</sup> Assuming even 5% of the 722,000 HAIs estimated for 2011 were due to exposure to hospital surfaces contaminated with bacteria such as *S aureus*, the application of the antimicrobial agent could possibly have prevented as many as 36,000 HAIs given the log reductions demonstrated in our study. Further research quantifying the occurrence of various types of pathogens in the hospital setting and improved exposure assessment parameters would help delineate the role of antimicrobial product use in reducing human health risks.

Caution should be taken when interpreting the results from any QMRA. Assumptions are an inherent part of the process, and subsequently can lead to over- and underestimation of human health risk. Infection risk may be overestimated in this study because the QMRA assumed bacteria exposure through hospital surfaces by susceptible individuals was imminent, and that any bacteria in an exposure were capable of initiating infection. In addition, our assessment incorporated a worst-case scenario by assuming exposure to the highest recorded numbers of bacteria. Estimated infection risks may be underestimated, because not all potential microbial exposures in the health care environment were translated to human health risks. Overall, the findings from our study provide evidence that antimicrobial application may be associated with clinically significant reductions in hospital pathogens, including gram-negative and *S aureus* microorganisms.

Our study is limited due to the absence of a control group where no antimicrobial agent was applied, making it difficult to determine the extent to which the antimicrobial application played a role in reducing the levels of gram-negative and *S aureus* microorganisms over time. Of importance is that the only difference in the method of hospital cleaning between the start and end of the study period was the application of this antimicrobial product in patient environments. Therefore, these data, based on a large number of samples per site, do provide convincing evidence of this antimicrobial product's sustained ability to persistently reduce environment contamination on hospital surfaces. Additional comparative analyses of antimicrobial product application in hospital settings will enhance the generalizability of the results.

## CONCLUSIONS

Although contaminated hospital surfaces are known to play a role in the transmission of HAIs, the degree to which they contribute to the HAI-related burden placed on public health and the economic infrastructure in the United States remains under investigation. Identifying the optimal strategies for hospital surface cleaning and disinfection, and the potential implications stemming from the

eradication of pathogens known to cause severe HAI morbidity and mortality, should remain among the top research priorities. In our antimicrobial application study, statistically significant reductions in gram-negative and *S aureus* microorganisms—but not total bacteria count—were observed on hospital surfaces across a 9-month study period. The QMRA demonstrated a 4-log infection risk reduction in some cases. Future comparative analyses involving this antimicrobial product application and an examination of the rates of patient infection attributed to selected pathogens would be justified to better understand the clinical significance associated with the use of this antimicrobial product.

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