ORIGINAL ARTICLE

Copper Surfaces Reduce the Rate of Healthcare-Acquired Infections in the Intensive Care Unit

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q1   OBJECTIVE.   Healthcare-acquired infections (HAIs) cause substantial patient morbidity and mortality. Items in the environment harbor microorganisms that may contribute to HAIs. Reduction in surface bioburden may be an effective strategy to reduce HAIs. The inherent biocidal properties of copper surfaces offer a theoretical advantage to conventional cleaning, as the effect is continuous rather than episodic. We sought to determine whether placement of copper alloy–surfaced objects in an intensive care unit (ICU) reduced the risk of HAI.

DESIGN.   Intention-to-treat randomized control trial between July 12, 2010, and June 14, 2011.

SETTING.   The ICUs of 3 hospitals.

PATIENTS.   Patients presenting for admission to the ICU.

METHODS.   Patients were randomly placed in available rooms with or without copper alloy surfaces, and the rates of incident HAI and/or colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococcus* (VRE) in each type of room were compared.

RESULTS.   The rate of HAI and/or MRSA or VRE colonization in ICU rooms with copper alloy surfaces was significantly lower than that in standard ICU rooms (0.071 vs 0.123; $P = .020$). For HAI only, the rate was reduced from 0.081 to 0.034 ($P = .013$).

CONCLUSIONS.   Patients cared for in ICU rooms with copper alloy surfaces had a significantly lower rate of incident HAI and/or colonization with MRSA or VRE than did patients treated in standard rooms. Additional studies are needed to determine the clinical effect of copper alloy surfaces in additional patient populations and settings.

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In the United States, 4.5% of hospitalized patients develop hospital-acquired infections (HAIs), resulting in an estimated 100,000 deaths and adding $35.7–$45 billion to healthcare costs.[1,2] Furthermore, patients with HAI have longer length of stay (LOS; 21.6 vs 4.9 days), higher readmission rates within 30 days (29.8% vs 6.2%), and greater mortality (9.4% vs 1.8%).[3]

Intensive care unit (ICU) patients are at further risk for HAI because of severity of illness, invasive procedures, and frequent interaction with healthcare workers (HCWs). Movement of organisms within hospitals is complex and may depend on microbes residing on environmental surfaces, indwelling devices, a patient's own flora, and transiently colonized HCWs' hands, clothing, and equipment.[4-7] Environmental contamination may contribute to acquisition of microbes responsible for HAIs, and microbes can persist for weeks on materials used

to fabricate objects in hospitals.[8] Patients admitted to rooms where previous patients were infected with methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), or *Clostridium difficile* are at increased risk for acquiring these organisms during their stay, suggesting persistence of these organisms in the environment.[9,10]

Numerous strategies have been developed to decrease HAIs. The central venous catheter insertion bundle has perhaps been the most widely adopted, but other measures include enhanced hand hygiene and screening for multidrug-resistant organisms.[11]

The Centers for Disease Control and Prevention recommends routine and terminal cleaning for prevention of HAIs.[12] Evidence for enhanced cleaning or self-sanitizing surfaces is uncertain.[13] Novel methods using ultraviolet light and hydrogen peroxide mist have been shown to reduce envi-
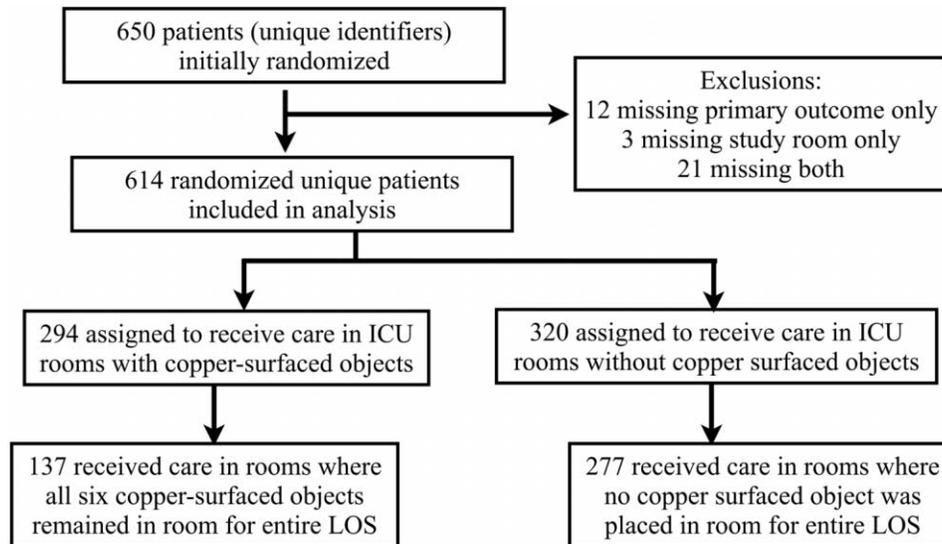
FIGURE 1. Flow diagram of patients included in the trial. ICU, intensive care unit; LOS, length of stay.

ronmental burden, but clinical efficacy for reduction of HAIs is still unresolved.[14,15]

Metallic copper has intrinsic broad-spectrum antimicrobial activity. In vitro, copper surfaces reduce bacterial concentration by at least 7 logs within 2 hours,[16-21] including bacteria commonly encountered in health care.[22,23] Others report that placing copper alloy–surfaced materials in the patient environment significantly reduced burden, but clinical efficacy was not measured.[24-28] We conducted a clinical trial to determine the efficacy of placing 6 copper alloy–surfaced objects in patient ICU rooms.

METHODS

Study Hospitals

The study was conducted at 3 medical centers: (1) the Medical University of South Carolina (MUSC), a 660-bed tertiary care academic hospital with 17 medical ICU beds; (2) the Memorial Sloan-Kettering Cancer Center (MSKCC), a 460-bed academic cancer hospital with 20 medical-surgical ICU beds; and (3) the Ralph H. Johnson Veterans Affairs Medical Center (RHJVA), a 98-bed hospital with 8 medical ICU beds.

Each site screened patients for nasal MRSA colonization. MUSC and MSKCC used Chromagar to identify colonized patients, as described elsewhere,[29] and RHJVA used polymerase chain reaction–based tests for detection of the organism, as described by Jain et al.[30] Perirectal VRE screening was conducted only at MUSC and MSKCC, using routine culture methods described elsewhere.[31]

Each facility followed preexisting comparable cleaning protocols with hospital-grade disinfectants: Virex 256 for routine (at least daily) and terminal cleaning, Dispatch for rooms housing patients with *C. difficile*, and Cavicide for spot cleaning of rooms and equipment. No additional cleaning measures were adopted.

Study Design and Population

To determine the impact of copper alloy surfaces on the incidence rate of HAI and/or MRSA or VRE colonization, copper alloy–surfaced objects were introduced into ICU study rooms in each hospital. At admission, respective bed-control services randomly assigned patients to an available ICU study room. To better control for nursing exposure, room conditions, and potential bias due to the presence of copper surfaces, intervention rooms were placed adjacent to control rooms prior to patient assignment. Bed-control personnel were masked as to which rooms contained copper, but treatment teams were not. A total of 650 admissions to 16 study rooms (8 copper, 8 standard) in the ICUs occurred between July 12, 2010, and June 14, 2011 (Figure 1). This study was approved by each site's institutional review board and the Office of Risk Protection of the US Army.

Patient demographics and clinical characteristics of patients were captured by a data extractor masked to room status. The ICU offered an opportunity to study patients generally confined to their room, reducing potential interactions with nonstudy environments. During the study, no participating hospital introduced new HAI, MRSA, or VRE reduction measures, and no outbreaks of HAIs or epidemiologically important organisms occurred. Each ICU monitored hand hygiene compliance.

Study Environment and Objects Surfaced with Copper Alloy

MUSC and MSKCC had 3 rooms with copper-surfaced objects and 3 control rooms with standard-surfaced objects, and

TABLE 1. Demographic and Clinical Characteristics by Treatment Assignment

Characteristic	Copper	Noncopper	Total	P
Age				.17
<40 years	23 (7.82)	38 (11.91)	61 (9.95)	
40–64 years	147 (50.00)	162 (50.78)	309 (50.41)	
≥65 years	124 (42.18)	119 (37.30)	243 (39.64)	
Male sex	185 (62.93)	199 (62.19)	384 (62.54)	.85
Race/ethnicity				.25
Asian	5 (1.74)	8 (2.61)	13 (2.19)	
African American	78 (27.18)	100 (32.57)	178 (29.97)	
White	198 (68.99)	197 (64.17)	395 (66.50)	
Hispanic	4 (1.39)	2 (0.65)	6 (1.01)	
Other	2 (0.70)	0 (0)	2 (0.34)	
Infection at admission	140 (47.62)	169 (52.81)	309 (50.33)	.20
APACHE II score				.51
<20	119 (40.48)	111 (34.69)	230 (37.46)	
20–30	120 (40.82)	145 (45.31)	265 (43.16)	
31–40	49 (16.67)	58 (18.13)	107 (17.43)	
>40	6 (2.04)	6 (1.88)	12 (1.95)	
Site[a]				.43
MSKCC (6 rooms)	108 (36.73)	113 (35.31)	221 (35.99)	
MUSC (6 rooms)	97 (32.99)	121 (37.81)	218 (35.50)	
RHJVA (4 rooms)	89 (30.27)	86 (26.88)	175 (28.50)	

NOTE. Data are no. (%). APACHE, Acute Physiology and Chronic Health Evaluation; MSKCC, Memorial Sloan-Kettering Cancer Center; MUSC, Medical University of South Carolina; RHJVA, Ralph H. Johnson Veterans Affairs Medical Center.
[a] Total number of rooms designated as either copper or noncopper.

RHJVA had 2 of each. On the basis of previous work to determine the burden of ICU objects, 6—those with a consistently high burden as well as those frequently touched—were chosen to be fabricated from copper alloys. Four items were identical at all hospitals: bed rails, overbed tables, intravenous poles, and arms of the visitor's chair. The other 2 items varied slightly: the nurses' call button (MUSC and RHJVA) and computer mouse (MSKCC), and the bezel of the touchscreen monitor (MUSC and MSKCC) and the palm rest of a laptop computer (RHJVA).[25]

Objects were fabricated by the same manufacturers for each site from a variety of solid copper alloys selected on the basis of ease of fabrication for each component, durability, ability to withstand cleaning, and aesthetics.[25,32] Each alloy was registered with the US Environmental Protection Agency (EPA) for its antimicrobial ability.[16]

Environmental Sampling

Weekly sampling of the 6 objects was performed in study rooms across the sites. A sterile template was laid over the surface with the exposed area wiped 5 times horizontally and 5 times vertically with uniform, vigorous pressure. Samples were transported to MUSC for processing. Microbiologic methods have been described elsewhere.[25,33] The temperature of samples was maintained at 4°C using a frozen refrigerant pack in accordance with the manufacturer's specifications, and this was continuously monitored using a Dickson SP425

data logger. Samples exceeding 20°C for more than 3 hours during shipping were discarded. The shipping protocol used to establish the concentration of microbes on surfaces at MSKCC and RHJVA was validated by placing defined concentrations of MRSA, VRE, *Pseudomonas aeruginosa*, *Acinetobacter baumanni*, and *Escherichia coli* onto premoistened swabs, which were assessed before and after shipping. No appreciable differences in concentrations of the microbes were observed. To control for bias toward cleaning objects differently in copper versus standard rooms, a noncopper object (bed footboard) was sampled in each room unbeknownst to participating study clinicians, environmental services, or healthcare teams.

Outcome Measures

The primary outcome was incident rate of HAI and/or MRSA or VRE colonization. Patients were prospectively monitored from ICU admission to hospital discharge. Incident HAI or colonization with MRSA or VRE was determined using National Healthcare Safety Network definitions by a study clinician at each hospital masked to room status.[34] Colonization could have been identified by surveillance or clinical cultures. HAI or colonization was attributed to the ICU if it occurred more than 48 hours after ICU admission or within 48 hours after ICU discharge.

Demographics, clinical characteristics, and outcomes were recorded on a web-based form automatically transferred into

TABLE 2. Distribution of Patients by Treatment Assignment for Primary and Secondary Outcomes

	Copper (n = 294)	Noncopper (n = 320)	Total	P
Primary outcome: new HAI or colonization				.020
No HAI or colonization	273 (92.86)	279 (87.19)	552 (89.90)	
HAI and/or colonization	21 (7.14)	41 (12.81)	62 (10.10)	
Secondary outcomes				
HAI only	10 (3.40)	26 (8.12)	36 (5.86)	.013
Colonization only	4 (1.36)	12 (3.75)	16 (2.61)	.063
ICU length of stay				.96
0–2 days	72 (24.49)	73 (22.81)	145 (23.62)	
3–4 days	95 (32.31)	108 (33.75)	203 (33.06)	
5–7 days	63 (21.43)	69 (21.56)	132 (21.50)	
>7 days	64 (21.77)	70 (21.88)	134 (21.82)	
Died in ICU	42 (14.29)	50 (15.63)	92 (14.98)	.64

NOTE. Data are no. (%). ICU, intensive care unit.

an electronic database for analysis. Independent clinicians at each hospital, masked to study group, validated all patients with HAI and a random sample of twice this number of patients without HAI.

Statistical Analysis

Distributions of continuous characteristics were assessed for normality using normal probability curves with the Shapiro-Wilk test and were presented as means with standard deviations (SDs) or medians with interquartile ranges (IQRs). Differences between intervention and control groups were analyzed using t tests or Wilcoxon rank sum tests if assumptions of normality were not met. Categorical data were presented as relative frequencies, and differences were analyzed using the χ^2 or exact tests; the primary analysis of the difference between groups with regard to incidence rate of HAI and/or colonization was tested similarly. Secondary analyses exploring potential confounding and effect modification were performed as follows: in preparation for determining independent factors to be included in logistic regression models to assess the effect of demographics and clinical characteristics on dichotomous outcomes, bivariate associations between each of these factors and the primary outcome were tested using the methods described above. Additionally, logistic regression models were used to identify whether individual factors (ie, age, sex) may be effect modifiers of the association between room assignment and the dichotomous outcome of new infection and/or colonization. Initial multivariate models to control for confounding and effect modification included variables with bivariate associations yielding P less than .20. Final models retained only independent variables and/or interactions significant at P less than .05. With regard to agreement between original HAI determinations and those for the validated subsample, a κ statistic and corresponding 95% confidence interval (CI) were derived. SAS, version 9.2 (SAS Institute), was utilized.

Analysis revealed that to obtain at least 90% power (for a 2-sided test with $\alpha = .05$) to detect a 50% difference in HAI and/or acquisition of MRSA or VRE colonization rates between intervention and control groups, a total of 620 patients (310 per group) was required. We assumed that the rate for control patients was 20% and accounted for 10% dropout.

RESULTS

The trial included 614 patients. Mean age was 60.4 years (SD, 14.9 years); 69% were white, and 62.9% were male. Median Acute Physiology and Chronic Health Evaluation (APACHE) II score was 23 (IQR, 18–28), and 47.6% presented with infection on ICU admission. Demographic and clinical characteristics between patients admitted to rooms with copper-surfaced objects and those admitted to noncopper rooms were comparable (Table 1). Because of movement of furniture necessitated by patient care, 46.6% of patients in copper rooms had all 6 of the copper-surfaced objects remain in the room throughout their ICU stay. In contrast, 86.6% of those assigned to noncopper rooms were never exposed to a copper object during their stay.

Rates of HAI and/or Acquisition of MRSA or VRE Colonization

Forty-six patients (7.5%) developed HAI (36 with HAI only, 10 with HAI and colonization), and 26 (4.2%) became colonized with MRSA or VRE (16 with colonization only). Compared with that among patients admitted to noncopper rooms, the proportion who developed HAI and/or colonization with MRSA or VRE was significantly lower among patients admitted to copper rooms (0.071 vs 0.128; $P = .020$; Table 2). Additionally, the proportion developing HAI alone was significantly lower among those assigned to copper rooms (0.034 vs 0.081; $P = .013$). MRSA or VRE colonization was also decreased by 2.7-fold among patients admitted to copper rooms, but this failed to reach significance ($P = .063$). Forty-two organisms were identified among the 46 pa-

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TABLE 3.   Hospital-Acquired Infections and Pathogens among Patients Admitted to Copper and Noncopper (Control) Rooms

Type of infection	Copper room	Noncopper room
BSI[a]	$n = 3$	$n = 11$
	Gram positive: 2 (1 *Enterococcus*, 1 CNS)	Gram positive: 7 (3 CNS, 2 VRE, 1 *Enterococcus*, 1 MSSA)
	Candida: 2	Gram negative: 3 (1 *Pseudomonas*, 1 *Escherichia coli*, 1 *Serratia*)
		Candida: 1
Pneumonia[b]	$n = 10$	$n = 8$
	Gram positive: 5 (2 MRSA, 2 MSSA, 1 *Streptococcus*)	Gram positive: 4 (2 MRSA, 2 MSSA)
	Gram negative: 1 (*Pseudomonas*)	Gram negative: 4 (2 *Pseudomonas*, 2 *Enterobacter*)
UTI[c]	$n = 4$	$n = 5$
	Gram negative: 2 (*E. coli*)	Gram positive: 3 (2 MRSA, 1 MSSA, 1 *Enterococcus*)
	Candida: 2	Gram negative: 2 (1 *Pseudomonas*, 1 *E. coli*)
		Candida: 1
Other[d]	$n = 0$	$n = 5$
		Gram positive: 2 (*Clostridium difficile*)
		Gram negative: 1 (*E. coli*)

NOTE.   CNS, coagulase-negative *Staphylococcus*; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococcus*.
[a] One bloodstream infection (BSI), in a patient cared for in a copper room, was polymicrobial.
[b] Six pneumonia episodes, 4 in patients cared for in copper rooms and 2 in noncopper rooms, did not have associated microbiologic data.
[c] One urinary tract infection (UTI), in a patient cared for in a noncopper room, was polymicrobial.
[d] Two other infections, both in patients cared for in noncopper rooms, did not have associated microbiologic data.

tients who developed HAI (Table 3). There were no differences between the distribution of types of HAIs or associated microbiology between patients treated in copper and noncopper rooms.

ICU LOS was not different between groups (median for both, 4 days; $P = 0.74$). Mortality also was not different (14.3% in copper rooms, 15.0% in control rooms; $P = .64$), nor was average ICU LOS prior to development of HAI (12.3 days in copper rooms, 8.8 days in control rooms; $P = .20$). The HAI rate did not vary significantly over the study period in copper rooms or standard rooms ($P = .30$ for both), and hand hygiene compliance, which ranged from 61% to 95%, was not significantly associated with HAI rates ($P = .53$).

Bivariate analysis to determine whether demographic or clinical characteristics were effect modifiers of room assignment or whether they independently increased the risk of HAI or colonization revealed that higher APACHE II scores were significantly associated with incident HAI or colonization ($P = .011$). Infection on admission was a significant effect modifier of room assignment ($P = .047$); among those in noncopper rooms with infection on admission, the rate of further HAI or colonization was 16.6%, compared with 5.7% among patients in copper rooms. However, in multivariate analyses controlling for APACHE II score, infection on admission was neither a significant effect modifier of room assignment nor independently associated with the incidence of HAI or colonization. The final model indicated that both APACHE II score ($P = .011$) and room assignment ($P = .027$) were significantly associated with incident HAI or colonization. Validation analysis revealed a κ statistic of 0.52 (95% CI, 0.34–0.70). In the vast majority of instances when

there was disagreement on validation, it was due to a case of pneumonia. Difficulty in consistently defining pneumonia has been previously documented.[35]

Fifty percent of 614 patients had environmental sampling of their room while receiving care in the ICU. Thirty-seven HAIs occurred among this subpopulation. Burden was stratified into quartiles regardless of the presence or absence of copper. There was a significant association between burden and HAI risk (Figure 2). Cumulative burden was lower for rooms with copper-surfaced objects. Of the 4,450,545 bacteria recovered during the trial, only 17%, rather than an expected 50%, were isolated from rooms with copper objects (0.76 log reduction; $P < .0001$).[25] Of note, the mean burden of the standard-surfaced footboard was not significantly different between copper and control rooms (2,786 vs 2,388 colony-forming units [CFUs]/100 cm²).

DISCUSSION

Our study demonstrated that placing a copper alloy surface onto 6 common, highly touched objects in ICU rooms reduced the risk of HAI by more than half at all study sites.

We believe that HAI reduction was due to the continuous antimicrobial effect of copper on environmental pathogens. We previously reported that copper surfaces reduced burden by 83%, compared with standard surfaces in patient rooms.[25] Patients in rooms with high burden were significantly more likely to develop HAI than were those in rooms with low burden, regardless of the presence or absence of copper. This may relate to the possibility that persons with active infection are more likely to shed bacteria captured by environmental
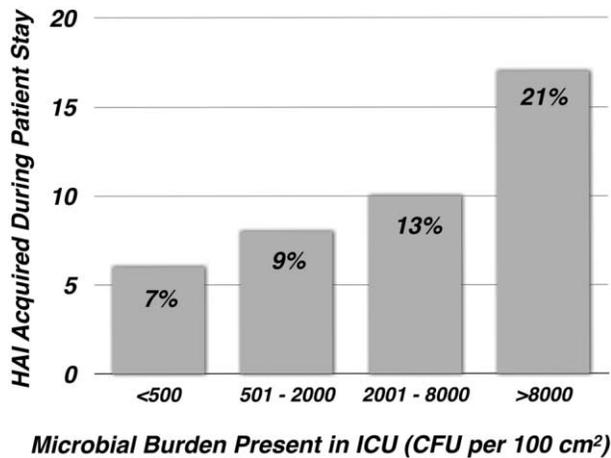
FIGURE 2.   Quartile distribution of healthcare-acquired infections (HAIs) stratified by microbial burden measured in the intensive care unit (ICU) room during the patient's stay. There was a significant association between burden and HAI risk ($P = .038$), with 89% of HAIs occurring among patients cared for in a room with a burden of more than 500 colony-forming units (CFUs)/100 cm^2.

sampling, but this does not fully explain the difference; the environment of patients with infections or colonizations showed an array of bacteria.[25] Additionally, mean ICU stay prior to HAI did not differ between patients cared for in the 2 room types.

We feel our approach is novel and the implications far-reaching. Previous attempts to reduce HAIs have required HCW engagement with such approaches as prevention bundles, hand hygiene, and patient screening. Additionally, systems designed to decrease burden, such as hydrogen peroxide mist, ultraviolet light, and increased cleaning, may be limited because of regrowth of organisms after the intervention.[26]

In contrast, copper alloy surfaces offer a passive way to reduce burden. Staff need not take additional steps, follow complex algorithms, or obtain buy-in from other providers. Additionally, because the antimicrobial effect is a continuous property of copper, rapid regrowth of microbes is mitigated. Importantly, in this study copper surfaces were shown to work in tandem with standard infection prevention practices to significantly reduce burden and HAIs.

There were study limitations. Because of the kinetic nature of care, all 6 copper objects were not always present in copper rooms. Daily inventory found that 53.4% of patients assigned to copper rooms had at least 1 of the copper objects removed during their stay. The most common reason was substitution of a nonstudy bed into a copper room to accommodate patient needs. Similarly, 13.4% of patients assigned to noncopper rooms had some exposure to copper objects, most often through introduction of a chair with copper arms by visitors. However, these events likely led to an underestimation of the effect of copper on HAIs and colonization.

It was not possible to definitively ascribe lower HAI rates

in rooms with copper objects solely to a reduction in burden. Other explanations are possible; most notably, since rooms appeared different, the effect may have been mediated by a change in HCW behavior. Because this study was a first-of-its-kind proof of concept, we did not conduct it under double-blind conditions. Effective blinding is dubious because copper alloys have a distinct look and may emit a distinctive odor. Arguing against the possibility that the observed reduction was mediated by HCW behavior change is the fact that copper objects were placed in rooms 9 months prior to the beginning of the trial, and ICU staff were not made aware of when the clinical phase of the study commenced. Furthermore, as previously stated the burden was significantly lower in copper rooms ($P < .0001$) at each of the sites.[25] Additionally, the burden from a standard-surfaced object, sampled unbeknownst to personnel and staff, was not different in copper versus control rooms. Finally, the HAI rate did not vary significantly over the study period in copper or standard rooms. That this rate was not lower in the beginning months of the study suggests that HCW behavior as a cause of the observed reduction in HAIs in copper rooms was minimized.

Moreover, our study design does not make it entirely possible to respond to other potential limitations of copper proposed by other researchers, such as the effect of soiling and tarnishing.[22,36] However, the US EPA requires that registered antimicrobial copper materials exert a 99.9% antimicrobial activity after 8 successive applications of 1×10^6 CFUs of viable pathogens without cleaning.[16] Each hospital required that frequently touched surfaces in the patient setting be cleaned at least daily. Furthermore, over the 2 years of environmental monitoring tarnishing was minimal and the antimicrobial activity of the copper surfaces did not diminish with time. Consequently, while soiling and or tarnishing are possible, given the scope of burden encountered on copper surfaces (average, 465 CFUs/100 cm^2) and the requirement for daily cleaning, it is not likely that they had a significant impact on the effectiveness of copper.

We have shown a reduction in incident HAIs and MRSA/VRE colonization in patients treated in ICU rooms with copper alloy–surfaced objects. This represents the first time an intervention designed to reduce burden has had a clinical impact among ICU patients. Because this was a pilot study, it may raise more questions than it resolves. Development of HAIs is complex and influenced by multiple host (underlying disease, immunosuppression) and external (indwelling devices, receipt of antibiotics) factors. Environmental contamination may contribute to HAIs by contaminating hands, clothing, and equipment of HCWs, who subsequently may transmit microbes during routine patient and device (central venous catheter, endotracheal tube, bladder catheter) care. Our findings suggest that reduction in environmental contamination could lead to fewer HAIs, presumably by decreasing the likelihood of introducing microbes into the patient. However, our study was not powered to assess which HAIs

are more likely to be influenced by burden reduction. Additional studies are necessary to address this important issue, to determine whether reduction in burden is a central element to the control of HAIs, and to confirm the observed efficacy of copper alloy surfaces. If confirmed for other patient care environments, these findings could have a substantial impact on preventing HAIs.

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