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State of the Science Review

Effectiveness of copper as a preventive tool in health care facilities. A systematic review

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Introduction: Hospital-acquired infections (HAIs) are a significant clinical and economic burden on health systems worldwide. Copper alloys have been certified by the US EPA as solid antimicrobial materials, but their effectiveness in reducing HAIs is not well established

Objectives: This systematic review aimed to assess copper surfaces in situ efficacy in reducing health care's microbial burden compared to control surfaces.

Materials and Methods: A literature search was conducted using three electronic databases: Web of Science, PubMed, and Scopus, with the keywords "copper" and "surfaces" and "antimicrobial" and "antibacterial" and "infections." Studies from 2010 to 2022 were included. The quality of the studies was independently screened and assessed using the Newcastle Ottawa Scale.

Results: A total of 56 articles were screened, with 8 included in the review and 7, added from references. Two third of the studies report a significant reduction in the microbial burden on copper objects compared to control objects. The 2 studies with the highest scores on NOS evaluation indicated that using copper or copper alloys in healthcare settings can effectively decrease the number of bacterial contaminations on touch surfaces.

Conclusions: The results suggest the potential effectiveness of copper as a preventive tool in healthcare facilities, but further studies and longer trials are needed to establish a relationship between copper and reduced nosocomial infections.

INTRODUCTION

Healthcare-associated infections (HAIs) are one of the most frequent adverse events that threaten the lives of hospitalized patients. In 2012, the prevalence of patients with at least one HAI in acute care hospitals in Europe was 6.0%.[24] Updated data estimates that 6, 5% of patients in 28 acute care hospitals had at least one HAI.[1] In Belgium in 2017, the crude prevalence of patients with at least one HAI was 7.3%.[2] According to Eurosuveillance 2018,[25] In ICU, the overall European rate of HAIs is 19.4%,[3] but in some countries, it can rise to 27,6% (Poland)[4] or 35,7% (Serbia)[5] HAIs not only threaten patients' lives but also result in increasing healthcare costs.[26] Studies have shown that HAIs can cause an additional hospital stay of 5-29.5 days for affected patients.[27,28] Hospital-acquired infections (HAIs) are an important problem in Europe. Each year in the European Union and European Economic Area (EU/EEA), there are 2,609,911 new cases of the 6 most critical (pneumonia, urinary tract infection, surgical site infection, Clostridium difficile, neonatal sepsis, and primary bloodstream infection) with a rate of 501 DALYs per 100,000 inhabitants.[6]

In Germany, the estimated annual number of deaths attributable to HAis was 16,245. Although the prevalence of HAIs was lower in

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Germany, the burden of HAIs in Germany was higher than the EU/EEA average. The rate of DALYs was 6.28% higher in Germany than the average of the EU/EEA.[7] According toWeber et al. (2010),[29] 20%-40% of HAIs are due to direct contact with contaminated surfaces or transmission via healthcare workers, while Salgado et al. (2013)[30] reported that the percentage was 58%. Both cases indicate that the hospital environment and contaminated surfaces with pathogens are significant risk factors and contributors to the incidence of HAIs. Pathogens can survive and reproduce on these surfaces for months,[31] with the time varying depending on the type of surface material.[32–34] The current standard for evaluating and monitoring terminal cleaning of hospital surfaces is microbiological: surfaces with >250 colony-forming units (CFU) per 100 cm^2 are allowed and accepted. However, surfaces may be re-contaminated quickly.[8]

Previous reviews have not reached a common conclusion on whether antimicrobial surfaces in patient rooms reduce the incidence of HAIs compared to standard surfaces and have called for further higher-quality studies.[35–37] Given the significance of using materials that may prevent nosocomial diseases, this review aims to update the evidence on the direct connection between lower microbial burden in health care settings and copper by comparing copper and control surfaces."

In 2008, the US Environmental Protection Agency (EPA) certified copper and copper alloys with at least 62% copper as the first solid antimicrobial material,[39] and in 2021, the EPA added residual viral claims to the registration.[40] Solid copper surfaces have been found effective as antimicrobials in vitro, killing 99.9% of microorganisms within two hours of contact.[41] The antimicrobial action of copper is attributed to the release of ions that affect the bacterial wall membrane, resulting in the death of the microorganisms.[42,43] The killing mechanism prevents pathogens from growing and reproducing, avoiding the creation of microorganism resistance. As a result, the number of studies evaluating the use of metal as a strategy to reduce the microbial burden in healthcare environments has increased.[9,30,44,45]

METHODS

The Preferred Reporting Items guided our systematic review for Systematic Reviews and Meta-analyses (PRISMA) statement.[10] The search was conducted using the PubMed, Scopus, and Web of Science databases with keywords "copper, surfaces, antimicrobial, antibacterial, and infections" using the search string ((((copper) AND (surfaces)) AND (antimicrobial)) AND (antibacterial)) AND (infections). Articles in English and Spanish from 2010 (after EPA certification) to 2022 were included. The search was limited to research articles and excluded gray literature.

Studies were eligible if they met the criteria established by the authors: involved hard, nonporous copper or copper alloy surfaces or copper nanoparticle technology used on hard surfaces. Exclusions included textiles or removable objects. All studies had to be conducted in hospital settings and involve copper or control objects as permanent furniture.

Authors (PA and FG) screened selected articles, extracted data, and assessed quality and risk of bias, with a consensus reached on inclusion. The third author (BP) reviewed the initially extracted data, expanded the data extraction for the data tables, and revised and corrected the manuscript. PA wrote the main body, and FG provided feedback on the draft. All 3 authors approved the final manuscript.

The quality of the studies was assessed using the Newcastle Ottawa Scale (NOS).[38] The authors used the cohort studies NOS scale and scored studies using the NOS Star system, with a maximum of 9 stars possible. The complete quality assessments are displayed in Table 1, with study characteristics described in Table 2 and results summarized in Table 3. Data from the 15 included articles were gathered and analyzed. Results marked with an asterisk (*) in Table 3 were from implicit data extraction and may differ from the original information. Implicit data depended on the factual analysis by the current paper's authors. In one study,[11] data was collected from a graph, and the numbers obtained were approximate.

RESULTS

The electronic search of databases resulted in 514 potentially eligible results, with 458 records removed before the screening: 31 were duplicates, and 427 were removed after reading the title or abstract. Of the 56 articles screened, 11 were assessed full-text for eligibility, and 8 met the inclusion criteria, with 7 references included, as shown on the PRISMA flow diagram (Fig 1).

Description of included studies

All included studies after screening[11–18] were conducted in hospitals with regular cleaning and disinfection protocols. The study design was either crossover, parallel, or multicentric parallel, and copper/control objects were part of the permanent furniture. A total

Table 1
NOS Newcastle–Ottawa quality assessment scale cohort studies

Study	Selection				Comparability	Exposure			Final Score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that the current outcome of interest was not present at the start of the study	Comparability of cohorts based on the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
Schmidt et al.[12]	*	*	*		**	*	*	*	8
Palza et al.[13]	*	*	*		**	*	*	*	8
Karpanen et al.[11]	*		*			*	*	*	5
Choi et al.[14]	*	*	*	*	**	*	*	*	9
Colin et al.[15]	*	*	*		**	*	*	*	8
Colin et al.[16]	*	*	*		**	*	*	*	8
Inkinen et al.[17]	*	*	*		**	*	*	*	8
Krause & Dolák[18]	*	*	*		**	*	*	*	8
Casey et al.[19]	*	*	*		**	*	*	*	8
Mikolay et al.[20]	*	*	*	*	**	*	*	*	9
Marais et al.[21]	*	*	*		**	*	*	*	8
Rai et al.[22]	*	*	*		**	*	*	*	8
Schmidt et al.[9]	*	*	*		**	*	*	*	8
Schmidt et al.[8]	*	*	*		**	*	*	*	8
Schmidt et al.[23]	*	*	*		**	*	*	*	8

Table 2
Characteristics of the study.

Study (Author and region)	Study design	Type of health facilities	Name of Facility	Facility Description	Setting(s)	Duration	Sampling schedule	Sampling methods	incubation methods	Types of copper objects	Composition of copper Item
Schmidt et al.[12] (USA)	Crossover design	Acute care Hospital	Highpoint Health Hospital (HPH)	62-licensed-bed acute care hospital	Medical intensive care unit (ICU)	23 months	Daily	Swab	37°C for 48 h.	Bed control panels	Injection molded polypropylene encapsulated with antimicrobial copper (US-EPA reg num 89266-2)
				Eight single-patient rooms ICU						Bed surfaces	US-EPA antimicrobial copper foil (reg number 82012-2)
Palza et al.[13] (Chile)	Parallel design	Closed Attention - High Complexity	La Florida Hospital		Waiting for public areas	10 weeks	weekly	Swab	37°C for 48 h.	Plastic waiting room chairs	Embedded metal copper nanoparticles sizes around 500 nm and lamellar morphologies were used as fillers of commercial-grade isotactic polypropylene thermoplastic
					Operating rooms					Metal IV pools	Nanostructured synthetic zeolite/copper nanocrystals particles filler in a polyester surface coating paint
Karpanen *et al.*[11] (UK)	Crossover design	University Hospital		19 beds Acute care medical ward	Acute care medical ward	12 weeks 4-month washout. And 12 weeks more	Weekly (some of the items only in alternating weeks)	Swab	37°C for 48 h.	Door push plate	CuZn37 (63); CuZn30 (70); CuOF (99.95)
										Door pull handle	CuZn39Pb3 (58); CuSn8 (92)
										Door lever handle	CuSn8 (92)
										Grab rail	CuZn30 (70)
										Toilet seat	CuOF composite/sprayed coating (~70)
										Toilet cistern lever	Thick copper plate over ZA3 zinc alloy (99.95)
										Commode (seat and arm pads)	CuOF composite/sprayed coating (~70)
										Tap handles	CuZn39Pb1Al (60)
										Sink waste trap	CuDHP (99.9)
										Light switch rocker	CuOF (99.95)
										Light pull-toggle	CuDHP (99.9)
										Socket rocker	CuOF (99.95)
										Dressing trolley	CuZn30 (70)
										Patient overbed table (top surface)	CuDHP (99.9); CuOF composite/sprayed coating (~70)
Choi *et al.*[14] (Korea)	Parallel design		Asan Medical Center	18 medical ICU beds	medical intensive care unit (ICU)	3 months	weekly	Swab	_	Infusion pole Bed-side rail door Drawer Drug cart	copper-containing surfaces
Colin *et al.*[16] (France)	Multicentric Paralell design		A B C D E	53/99 54/117 12/25 30/57 158/347	Five extended term-care facilities were outfitted with copper alloy 18 months before the study	18 months	weekly (sequences)	Swab	37°C for 24/48/72 h.	Handrails Door handles	70% Cu alloy 90% Cu alloy

(*continued on next page*)

Table 2 (*Continued*)

Study (Author and region)	Study design	Type of health facilities	Name of Facility	Facility Description	Setting(s)	Duration	Sampling schedule	Sampling methods	incubation methods	Types of copper objects	Composition of copper Item
Inkinen *et al.*[17] (Finland)	Multicentric Paralell design		Hospital in the Satakunta area, on the west coast of Finland	Child patients 0-17 years in randomly occupied rooms. The average length of stay/patient is 2.6 days (copper) and 3.4 (reference) rooms	Patient room toilets (4 reference and four copper* rooms)	not reported	weekly	Swab	22°C for 5 days	Toilet flush button toilet support rail	99.90% Cu
Krause, M; Dolák, F.[18] (Czech Republic)	Parallel design	Regional			Clinical workplace (standard surgical departments) of a regional hospital	12 weeks	weekly	Swab	7 days at 36°C.	Boxes intended for storing medical supplies Trays Emesis basins	nanolayer composed of a hybrid organic, inorganic sol based on 3-(trimethoxysilyl) propyl methacrylate with silver, copper, and zinc cations under the designation AD30 according to patent CZ303861
Casey et al.[19] (UK)	Crossover design				Acute care medical ward	2.5 months	weekly	Swab	37° C for 24/ 48 h	Toilet seat Set the tap handle Door push plate	Coated with a pure copper /resin composite ~70% Cu 60% Cu 70% Cu
Mikolay et al.[20] (Germany)	Parallel design		Asklepios Hospital Wandsbek		Oncological/pneumatological ward, geriatric ward	8 months	weekly (1 or 2 samples)	Petrifilm™	30°C for 36 h	Push plates Doorknobs Light switches	CuZn21Si3 CuZn23Al3Co
Marais et al.[21] (South Africa	Parallel design	Primary healthcare clinic (PHC)		busy walk-in PHC Rural	consulting rooms	6 months	weekly/ every 6 weeks, 3 samplings per day	Swab	room temperature 16 h	Desk, trolleys Top of cupboard Windowsill	copper sheets (BS 2870, Alloy C101: 99.9% pure copper)
Rai et al.[22] (USA)	Parallel design			outpatient infectious disease clinic	Outpatient infectious disease clinic	4 months	weekly (2 samples)	Wipes	_	Phlebotomy chairs (Arm tops and trays)	Solid copper alloy metal (90% copper, 10% nickel)
Schmidt et al.[9] (USA)	Multicentric parallel design		1.- Medical University of South Carolina	a 660-bed academic facility / 17 medical ICU beds	3 intensive care units (ICU)	43 months	weekly	Wipes	_	IV stand Pole(s)	C710 and C706 (80% Cu and 90% Cu)
			2.- Memorial Sloan Kettering Cancer Center	432-bed cancer hospital / 20 medical-surgical ICU beds						IV hanger loops	C693 (75% Cu)
			3.- Ralph H. Johnson Veterans Administration Medical Center	a 98-bed hospital / with 8 medical ICU beds.						IV Base IV Handle IV Brackets Bed-side rails Over-bed table top Over-bed table bottom Over-bed table Release lever Visitor chair (arms) Nurse call button Nurse call button Clamshell (hospitals 1 and 3)	C87610 (90% Cu) C706 (90% Cu) C706 (90% Cu) C110 (99.99% Cu) C706 (90% Cu) C110 (99.99% Cu) C464 (60% Cu) C706 (90% Cu) C638 (80% Cu) C260 (80% Cu) C260 (70% Cu)

(*continued on next page*)

Table 2 (*Continued*)

Study (Author and region)	Study design	Type of health facilities	Name of Facility	Facility Description	Setting(s)	Duration	Sampling schedule	Sampling methods	incubation methods	Types of copper objects	Composition of copper Item
										Computer mouse (hospital 2 only)	
										Data input device base of monitor bezel (hospitals 1 and 2)	C524 (90% Cu)
										Laptop palm rest (hospital 3 only)	C710 (80% Cu)
Schmidt et al.[8] (USA)	Parallel design	Academic Hospital		660-bed academic hospital / 17-bed medical intensive care unit (MICU)	ICU	3 months	5 sampling sessions/ 5 sampling per session over 3 months	Wipes	_	Side rails of patients' bed	UNS# CI 10 99.9% metallic copper
Schmidt et al.[23] (USA/Chile)	Parallel design	Tertiary care	Hospital de Niños Roberto del Río	249-bed pediatric hospital	Pediatric ICU (PICU), Pediatric intermediate care unit (PIMCU)	12 months	Twice monthly	Wipes	_	Bed rails	C27200 and C23000
										Cradles	Copper alloy registered with the U.S. EPA
										Faucet and faucet handles	C69300
										IV stand Pole(s)	Copper alloy registered with the U.S. EPA
										Work surface	C27200 and C23000

Table 3
Number of evaluated samples and results.

Study	Total number of evaluated samples	Control surfaces result CFU/100 cm^2	Copper surfaces result CFU/100 cm^2	Copper compared to control: Difference (-) / Reduction (%) CFU/100 cm^2
Schmidt et al.[12] (USA)	565	1541 Means of MB TBR 3,029 ACC/100m^2 (Object with the highest count)	96 Means of MB TBR 50 ACC/100 m^2	94% Accumulative Mean
Palza et al.[13] (Chile)	Not reported	Chairs: 2,490 / IV Pools: 130 Means of MB	Chairs: 680	Chairs 73% Means of MB / IV Pools 53% from week 5-7
Karpanen et al.[11] (UK)	* 672 < N < 1,344	* Door push plates 200 Median	* Door push plates 0	Door push plates Median difference −140 / *100%
		* Door pull handles 300 Median	Door pull handles 0	Door pull handles Median difference −230/*100%
		* Door lever handles 400 Median	* Door lever handles 200 Median	* 50%
		Grab rails 0 Median	Grab rails 0 Median	Not reported
		* Tap handles 1500 Median	* Tap handles 200 Median	*86,7%
		* Toilet seats 1800 Median	* Toilet seats 900 Median	Tap handles Median difference -960/*50%
		* Toilet flush lever handles 10800 Median	* Toilet flush lever handles 1400 Median	toilet flush lever handles Median difference −8,030/*87%
		* Commodes 300 Median	* Commodes 200 Median	*33,3%
		* Patient's over-bed tables (Cu sprayed) 900 Median	* Patient's over-bed tables (Cu sprayed)500 Median	Cu- sprayed overbed tables Median difference −380/ *44,4%
		* Patient's over-bed tables (Cu plated) 900 Median	* Patient's over-bed tables (Cu plated) 300 Median	Cu-plated overbed tables Median difference −420/*66,6%
		* Dressing trolleys 100 Median	Dressing trolleys 0	Dressing trolleys Median difference- 40/*100%
		* Electrical sockets (switches) 800 Median	Electrical sockets (switches) 0	socket switches Median difference −640/*100%
		* Light switches 200 Median	Light switches 0	*100%
		* Light pull cords (toggles) 3000 Median	*Light pull cords (toggles) 600 Median	light pull cord toggles Median difference −4,100/*80%
Choi et al.[14] (Korea)	* 160	MRSA by SS (9:30/11:30): Infusion pole (18,8/10,4) Bed-side rail (50/47,2) Door (8,8/29,6)	MRSA by SS (9:30/11:30): Infusion pole (1,2 /1,2) Bed-side rail (14,8/ 53,2) Door (2,8/1,6)	* MRSA % (9:30/11:30): Infusion pole (93,6 /88,5) Bed-side rail (70,4/12,7 increase) Door (68,2/94,6)

(*continued on next page*)

Table 3 (*Continued*)

Study	Total number of evaluated samples	Control surfaces result CFU/100 cm^2	Copper surfaces result CFU/100 cm^2	Copper compared to control: Difference (-) / Reduction (%) CFU/100 cm^2
		Drawer (22,4 / 8)	Drawer (4,8 / 1,2)	Drawer (78,6 / 85)
		Drug cart (48,4/44)	Drug cart (19,2/22,8)	Drug cart (60,3/48,2)
		VRE by SS (9:30/11:30):	VRE by SS (9:30/11:30):	* VRE % (9:30/11:30):
		Infusion pole (17,2/16,8)	Infusion pole (2,8/1,6)	Infusion pole (83,7/90,5)
		Bed-side rail (32,8/35,2)	Bed-side rail (8,4/19,6)	Bed-side rail (74,4/44,3)
		Door (14,4 / 6,8)	Door (9,6 / 2)	Door (33,3 / 70,6)
		Drawer (3.2/24,8)	Drawer (4,4/26)	Drawer (37,5 increase/4,8 increase)
		Drug cart (14,4/18,8)	Drug cart (10/8,4)	Drug cart (10/8,4)
Colin et al.[15] (France)	>1,300	Door handles 63,700	Door handles 45,200	* Door handles 29%
		Handrails 74500	Handrails 57300	* Handrails 23%
Colin et al.[16] (France)	1,400	Low contamination <100 CFU/100 cm^2: Door Handles 11%	Low contamination <100 CFU/100 cm^2: Door Handles 21%	Copper door handle Median difference −100 / 59%
		High contaminations >20 × 10^3 CFU/100 cm^2: Door handles 9%	High contaminations >20 × 10^3 CFU/100 cm^2: Door handles 2%	copper handrails Median difference −200 / 33%
		extreme contaminations ≥10 × 10^4 CFU/100 cm^2: 14 control door handles (4%) / 6 handrails (2%)	extreme contaminations ≥10 × 10^4 CFU/100 cm^2: 3 copper door handles (1%) (4%) / 3 copper handrails (1%)	
Inkinen et al.[17] (Finland)	42	Toilet Flush Button: 7,300	Toilet Flush Button: 500	* Toilet Flush Button 93,2%
		Toilet Support rail: 200	Toilet Support rail: 10	* Toilet Support rail 95%
Krause, M; Dolák, F.[18] (Czech Republic)*	1780	Emesis basins: 33.3% with BC.	Emesis basins: 28.8% with BC.	Emesis basins: 28.8% with BC
		Trays: 37.5% with BC	Trays: 38.9% with BC	
		Boxes: 50% with BC	Boxes: 50% with BC	
Casey et al.[19] (UK)	* 100	Medians by SS (07:00/17:00):	Medians by SS (07:00/17:00):	* % (07:00/17:00):
		Upper side of the toilet seat (305,4/258)	Upper side of the toilet seat (8,4/4,8)	Upper side of the toilet seat (97,2/98,1)
		The underside of the toilet seat (43,2/6)	The underside of the toilet seat (0/0)	Underside of toilet seat(100/100)
		Push plate (7,2/2,4)	Push plate (0 / 0)	Push plate (100 / 100)
		Hot tal handle (26,4/12)	Hot tal handle (0/0)	Hot tal handle (100 / 100)
		Cold tap handle (30 / 18)	Cold tap handle (0 / 0)	Cold tap handle (100/100)
Mikolay et al.[20] (Germany)	* 540	Doorknobs: 269,99	Doorknobs: 195,21	* Doorknobs: 27,7%
		Push plates: 36,87	Push plates: 36,41	* Push plates: 1,2%
		Light switches: 45,63	Light switches: 43,05	*Light switches: 5,7%
Marais et al.[21] (South Africa	* 88	0,2 overall mean	5,9 overall mean	71% means of MB
Rai et al.[22] (USA)	150	Arm top: 1,305 median	Arm top: 135 median	88% (trays) to 90% (arm tops) reduction of the total median burden
		Arm side: 1,095 median	Arm side: 330 median	70% reported a “halo effect” on the copperized arm
		Tray: 1,290 median	Tray: 150 median	
Schmidt et al.[9] (USA)	5545	2674 mean in one object	465 mean in one object	83% mean reduction of MB
		14.813 overall mean	2.531 overall mean	
Schmidt et al.[8] (USA)	* 150	mean (± SE):	mean(± SE):	
		Precleaning 6,102 ± 2572	Precleaning 698 ± 368	* Precleaning 88,6%
		Hour 0.5 1112 ± 802	Hour 0.5 362 ± 282	* Hour 0.5 67,4%
		Hour 2.5 1560 ± 936	Hour 2.5 530 ± 530	* Hour 2.5 66%
		Hour 4.5 2396 ± 1502	Hour 4.5 224 ± 94	* Hour 4.5 90,7%
		Hour 6.5 5198 ± 2,386	Hour 6.5 434 ± 236	* Hour 6.5 91,7%
Schmidt et al.[23] (USA/Chile)	1320	mean 1,381	mean 172	88% Sum of (MB)
		median 574	median 0	

Note: ACC, aerobic colony count; CFU, colony forming unit; MB, microbial burden; BC, bacterial contamination; ± SE, standard error; SS: sampling schedule; SD, standard deviation; BC, bacterial contamination; MRSA, methicillin-resistant Staphylococcus aureus; VRE, vancomycin-resistant enterococcus.
*Calculated by authors with paper data

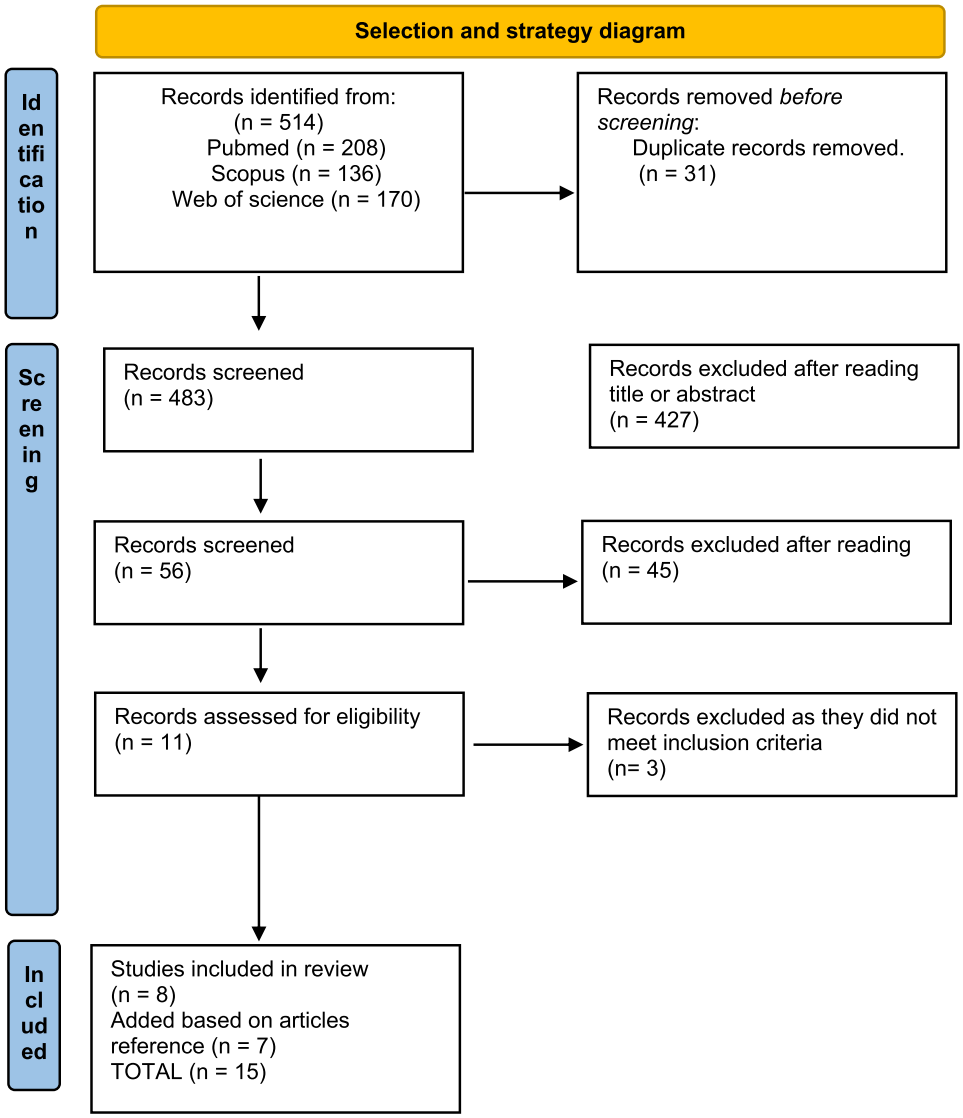

Fig 1. PRISMA flow diagram.

of 15 in situ trials were included, published between January 2010 and March 8, 2022. Twenty percent were crossover,[11,12,19] 53.3% were parallel,[8,13,14,18,20,21-23] and 26.6% were multicentric parallel designs.[9,15-17] The study duration varied from 2.5 months to 23 months, with bacterial count as the outcome reported in all studies. Table 2 describes the study design characteristics, settings, duration, sampling schedule, incubation, Type of copper objects, and Type of copper.

The Finnish study[17] took place in real-life settings, including hospitals, kindergartens, retirement homes, and office buildings, while all other studies took place in healthcare settings, including ICUs, acute care medical wards, surgical/operation rooms, long-term care facilities, outpatient/primary healthcare clinics, and an oncological/pneumology/geriatric ward. The frequency of sampling was very heterogeneous among the various studies. Sampling was weekly in 11 studies,[9,11,13-22] once or twice monthly in 2 studies,[8,23] and one daily sample was taken on the study conducted by Schmidt.[12] The sampling methodology was also very diverse. There was sampling with swabs,[11,12,13-19,21] with wipes,[8,9,22,23] or with Petrifilm.[20]

Regarding the quality assessment of the selected studies, 80% scored eight stars on the NOS evaluation, 13.3%[14,20] scored 9 stars, and 6.7%[11] scored 5 stars. Most of the studies were funded either fully or partially by institutions related to copper or by a university or national research grants.

Financial support for the selected studies

Most studies have been funded totally or partially by institutions related to copper (Copper Development Association, Copper Institute, National Copper Corporation). The funding resources declared in five studies are the local Copper Development Association.[11,14,19,21,22] Financial Support from the German Copper Institute was received for the study in Hamburg, Germany,[20] and the study conducted by Schmidt in 2016[23] received funding from the Chilean National Copper Corporation (CODELCO by the acronym in Spanish). The studies conducted by Schmidt[8,9] were supported by the U.S. Army Material Command. In both studies, assistance, and technical support from Copper Development Association members are acknowledged, and in the 2013 study, the potential conflict of interest is declared. A research grant from a bed supplier financed a 2020 study conducted by Schmidt. Colin[15,16] declared that his studies were partially conducted with support from the copper industry. Three studies were financed by a university or national research grants.[13,17,18]

Table 4
Statistical results and outcome

Study	Statistical differences ($P < .05$)	Statistical test results $P =$	Confidence intervals	outcome
Schmidt et al.[12] (USA)	Significant	Control to interventional groups comparison: all significant at $P < 0.0001$		ACC/100 cm^2
Palza et al.[13] (Chile)	Significant in chairs			CFU/cm^2 Staphylococcus and molds concentrations
Karpanen et al.[11] (UK)	Significant in 8/14 surfaces	Door push plates $P < 0.0001$ Door pull handles $P < 0.0001$ Door lever handles $P = 0.276$ Grab rails $P = 0.603$ Tap handles $P < 0.0001$ Toilet seats P = 0.334 Toilet flush lever handles $P = 0.012$ Commodes $P = 0.691$ Patient's over-bed tables (Cu sprayed) $P = 0.019$ Patient's over-bed tables (Cu plated) $P = 0.001$ Dressing trolleys $P = 0.003$ Electrical sockets (switches) $P < .0001$ Light switches $P = 0.064$ Light pull cords (toggles) $P = 0.019$	95% CI −2.0 to −0.8 95% CI −4.2 to −1.5 95% CI −19.6 to −3.8 95% CI −147.7 to −3.9 95% CI −9.4 to −0.4 95% CI −9.0 to −1.4 95% CI −0.6 to −0.1 95% CI −9.6 to −3.2 95% CI −104.0 to −6.0	CFU/cm^2 Presence of MSSA, MRSA, VRE, C.difficile, and coliform bacteria
Choi et al.[14] (Korea)	9:30 am MRSA significant in 4 out of 5 objects 11:30 am MRSA significant in 1 out of 5 objects 9:30 am VRE significant in 1 out of 5 objects 11:30 am VRE significant in 3 out of 5 objects	MRSA (P at 9:30 am / P at 11:30 am): Infusion pole (0.001 / 0.04) Bed-side rail (0.001 / 0.15) Door (0.001 / 0.001) Drawer (0.01 / 0.14) Drug cart (0.11 / 0.02) VRE (P at 9:30 am / P at 11:30 am): Infusion pole (0.001 / 0.001) Bed-side rail (0.10 / 0.07) Door (0.06 / <0.001) Drawer (0.84 / 0.12) Drug cart (0.04 / 0.003)		MRSA VRE
Colin et al.[15] (France)	Significant in 3 bacteria			bacterial diversity
Colin et al.[16] (France)	significant differences between the five long-term care facilities	A P = (0.0022 door handles /0.1446 handrails) B P = (0.0034 door handles /0.0006 handrails) C P = (0.0042 door handles /0.0918 handrails) D P = (0.0010 door handles /0.3518 handrails) E P = (.0003 door handles /0.0063 handrails)		CFU/cm^2
Inkinen *et al.*[17] (Finland)	Not reported for healthcare separately			CFU/cm^2
Krause, M; Dolák, F.[18] (Czech Republic)	Not significant			
Casey et al.[19] (UK)	Significant	(P at 07:00 am / P at 17:00 pm): The upper side of the toilet seat (<0.0001/ <0.0001) Under side of toilet seat(0.007/0.019) Push plate (0.0002/0.009) Hot tal handle (0.023/0.019) Cold tap handle (0.005/0.005)		CFU/cm^2 Presence of MSSA, MRSA, VRE, C.difficile, and coliform bacteria
Mikolay et al.[20] (Germany)	Not significant			CFU/mm^2 Presence of ciprofloxacin-resistant Staphylococcus
Marais et al.[21] (South Africa	Significant	<0.001 for all copper surfaces		CFU/100 cm^2
Rai et al.[22] (USA)	Significant	<0.0001 on trays and arm tops		CFU/100 cm^2 Presence of MRSA, VRE

(*continued on next page*)

Table 4 (*Continued*)

Study	Statistical differences ($P < .05$)	Statistical test results $P =$	Confidence intervals	outcome
Schmidt et al.[9] (USA)	Significant in some surfaces	<0.0001		CFU/100 cm^2 Presence of Staphylococci, MRSA, Gram-negative bacteria, VRE
Schmidt et al.[8] (USA)	Significant in some surfaces	$P = 0.0001$ difference observed between the copper-surfaced and plastic-surfaced rails		CFU/100 cm^2
Schmidt et al.[23] (USA/Chile)	Significant	$P < 0.00011$		CFU/100 cm^2

Note: ACC, aerobic colony count; CFU, colony forming unit; MB, microbial burden; BC, bacterial contamination; ± SE, standard error; SS, sampling schedule; SD, standard deviation; BC, bacterial contamination; MRSA, Methicillin-resistant Staphylococcus aureus; VRE, vancomycin-resistant enterococcus.

Efficacy of copper in the health care setting

Measures of sampling, microbial culture, and comparison of copper and control surfaces were part of the presentation of the results. The results of the selected studies show heterogeneity. 57,14%[8,9,15-17,20,22,23] of trials using solid pure copper or copper alloys,14,29%[11,19] using a mix solution between solid copper alloys and others (resin composite, sprayed coatings coated with pure copper). No solid solution was used in 28, 57%[12-14,18] of the studies (polypropylene encapsulated with copper, copper foil, embedded metal copper nanoparticles, and copper nanocrystals particles filler in a polyester surface coating paint). The results of the studies showed heterogeneity.

The results obtained from copper or control surfaces were not reported by two studies.[11,17] Furthermore, one reported the results by objects.[14]

Results were reported by means in 6 studies,[8,9,12,13,21,23] And the study authored by Casey reported the results by medians.[19] The rest of the studies communicates the results by percentage.

Eight studies did not report a reduction in the microbial burden on copper compared to the control. Of the rest, 2 studies reported a reduction by objects[13]: reported a 73% means reduction retrieved from chairs surfaces and 53% in IV pools from week 5-7 and Colin study[16] copper door handle showed an average of 59% reduction (median difference) and copper handrails showed an average of 33% reduction (median difference). The reduction reported in the rest of the studies was greater than 70%[12]: stated a 94% cumulative reduction retrieved from surfaces (means).[23]

Table 3 describes the results of control/copper objects and microbial burden between copper surfaces and control retrieved at different time points and also informs the number of evaluated samples of each study when reported.

Table 4 summarizes statistical differences with $P < .05$, confidence intervals, and outcomes. Results of 5 studies[12,16,21-23] were reported as significant overall. In 7 other studies, the significance of statistical differences was partially observed for surfaces, objects, or organisms. Palza et al.[13] found significance in chairs, while Karpanen et al.[11] reported significance in 57% of objects. Choi et al.[14] reported significance in 80% of objects contaminated with Methicillin-resistant Staphylococcus aureus (MRSA). Colin et al.[15] observed significance in streptococcus, roseomonas, and Staphylococcus spp. Schmidt et al.[9] reported significant results on 83% of surfaces. In the 2013 study by Schmidt et al.,[8] 4 out of 5 points had significant mean results and significance in the percentage pooled results.

DISCUSSION AND PERSPECTIVES

This systematic review analyzed the results from 15 in situ studies on the antimicrobial properties of copper in frequently touched objects in health care settings. The results showed that while a third of the studies did not report a significant reduction in microbial burden, the majority of studies demonstrated a decrease in microbial contamination on copper objects compared to control objects.[12,16,21-23]

The 2 studies with the highest scores on NOS evaluation[14,20] indicated that using copper or copper alloys in health care settings can effectively decrease the number of bacterial contaminations on touch surfaces. In the case of these studies, the quality of the studies was very heterogeneous.

Furthermore, the NOS assessment tool may allow a sub-analysis of groups based on study quality, which could be a source of heterogeneity. In the future, it would be interesting to do a meta-analysis according to the object type and surface to reduce heterogeneity. These additional studies are beyond the scope of this study.

There are numerous possible sources of heterogeneity, such as the type of health facilities, settings, sampling schedule and methods (swipes, wipes), and Types and composition of copper objects. In this

study, the measurement units (CFU/100 cm^2, CFU/25 cm^2, CFU/m^2) were a source of heterogeneity that we reduced by converting the results to the same unit of measure.

Several factors contribute to the spread of healthcare-associated infections (HAIs), and material selection plays a crucial role in reducing the spread of these infections. During hospitalization, patients are exposed to more microorganisms, which can be transmitted through fomites or contact with environmental sources of infection.

Despite the evidence of a decrease in microbial burden due to copper use, there is a lack of data on the connection between reducing environmental pollution by copper and reducing HAIs. Currently, only 2 randomized trials[30,45] exist on the role of copper in reducing HAIs in healthcare facilities. Therefore, further research is needed to strengthen the evidence and reach a definitive conclusion.

The COVID-19 pandemic has brought attention to reducing the microbial load on surfaces in healthcare settings. The evidence shows that copper is more effective in reducing microbial load in less time than other materials used in health care infrastructure.[34]

Future research should focus on measuring the effectiveness of interventions in reducing HAIs, including passive measures such as using copper in contact surfaces and active measures such as hand washing, proper execution of procedures, and isolation. Hospital infection rates must be reported and taken into consideration when conducting studies. Additionally, studies should be conducted in centers with high hospital infection rates to detect significant differences, and larger sample sizes may be necessary. Economic evaluation studies would also provide valuable information on the costs and benefits of installing and maintaining copper surfaces in hospitals.

Finally, conducting economic evaluation studies would be beneficial, as installing and maintaining copper surfaces represents a significant investment for hospitals.

AUTHORS' CONTRIBUTION

A-GP: Dra. Arquitecta; Postdoctoral Researcher; **P-LB:** Prof. Titular; Dr. Ing. Naval y Lda. en Derecho; **G-GF:** Catedrático de Medicina Preventiva y Salud Pública Universidad Pública de Navarra; Director de Medicina Preventiva Clínica Universidad de Navarra

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