

Does copper treatment of commonly touched surfaces reduce healthcare-acquired infections? A systematic review and meta-analysis

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1 **Does Copper treating of commonly touched surfaces reduce healthcare**
2 **acquired infections? A Systematic Review and meta-analysis**

3
4 **Running title:** Copper for healthcare acquired infections

5
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41
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45 **Abstract**

46

47 **Background**

48 Healthcare acquired infections (HAIs) cause substantial morbidity and mortality. Copper appears to
49 have strong antimicrobial properties under laboratory conditions.

50 **Aim**

51 We conducted a systematic review to examine the potential effect of copper treating of commonly
52 touched surfaces in healthcare facilities.

53 **Methods**

54 We included controlled trials comparing the effect of copper-treated surfaces (furniture or bed
55 linens) in hospital rooms versus standard rooms on hospital acquired infections (HAIs). Two
56 reviewers independently screened retrieved articles, extracted data, and assessed the risk of bias of
57 included studies. The primary outcome was the occurrence of healthcare acquired infections.

58 **Findings**

59 We screened 638 records; 7 studies comprising 12362 patients were included. From risk of bias
60 assessment, all included studies were judged to be at high risk in ≥ 2 of the 7 domains of bias. All 7
61 included studies reported the effect of various copper-treated surfaces on HAIs. Overall, we found
62 low quality evidence of a potential clinical importance that copper-treated hard surfaces and/or bed
63 linens and clothes reduced healthcare acquired infections by 27% (RR 0.73; 95% CI 0.57 to 0.94; $I^2 =$
64 44%, p-value = 0.01).

65 **Conclusion**

66 Given the clinical and economic costs of healthcare acquired infections, the potentially protective
67 effect of copper-treated surfaces appears important. However, the current evidence is insufficient to
68 make a strong positive recommendation. However, it would appear worthwhile and urgent to
69 conduct larger scale publicly funded clinical trials of the impact of copper coating.

70

71 **Keywords** hospital acquired infections, healthcare acquired infection, healthcare associated
72 infections, copper, copper plating, copper linen, 2wSR

73 INTRODUCTION

74

75 Healthcare acquired infections (HAIs) are infections acquired directly or indirectly by patients while
76 receiving healthcare. HAIs are a major cause of preventable harms, result in substantial morbidity,
77 prolong hospitalisation, increase the cost of healthcare delivery, and contribute to mortality^{1,2}.

78 Despite current efforts aiming to prevent and control HAIs, recent estimates suggest that HAIs are
79 still one of the most prevalent and preventable challenge to patient safety worldwide^{3,4}.

80

81 One strategy to control HAIs is to reduce the fomite pathogen transmission that can occur if
82 common objects such as door handles, stair banisters, table surfaces, utensils or taps are
83 contaminated⁵. Cleaning shared surfaces is one proposed preventive mechanism but would require
84 frequent and extensive cleaning.

85

86 Copper appears to have strong bactericidal and viricidal properties and substantially reduces the
87 duration of pathogen viability on surfaces from days to 30 to 60 minutes under laboratory
88 conditions⁶. The inactivation property of copper has been demonstrated for both Norovirus and for
89 Coronavirus species with inactivation occurring in less than 60 minutes⁶. Inactivation also occurs on
90 copper alloys and the activity appears directly proportional to the percentage of copper present in
91 the alloy. This property has led researchers to examine the potential for copperplating of common
92 surfaces to reduce healthcare acquired infections with multi-resistant bacteria as well as viruses with
93 attempts to copperplate common shared surfaces in hospital wards⁷. These include surfaces such as
94 bedrails, door handles, table surfaces, as well as soft textiles such as bed linen, patient gowns and
95 towels.

96

97 If coating of commonly touched surfaces in hospital rooms could reduce healthcare acquired
98 infections, the impact could be substantial in both health and economic terms⁸. Therefore, we aimed
99 to examine the potential of copper coating of common shared surfaces in hospitals. We aimed to
100 find all controlled trials which had compared copper-treated surfaces in hospital rooms or items with
101 standard rooms or items.

102

103

104 METHODS

105 We aimed to find, appraise, and synthesize eligible studies that have compared the effect of copper-
106 treated hospital room surfaces versus standard room surfaces on healthcare acquired infections.

107 This systematic review is reported following the Preferred Reporting Items for Systematic Reviews
108 and Meta-Analyses (PRISMA) statement and the review protocol was prospectively developed⁹.

109 Eligibility criteria

110 *Participants.* We included studies of patients of any age and with any condition in acute and long-
111 term care settings (including intensive care units, rehabilitation centres, and aged-care facilities).

112 *Interventions.* We included studies that evaluated interventions involving copper (or copper alloy)
113 surfaced rooms or objects in patient care rooms/spaces. We expanded the intervention to include
114 studies evaluated copper-treated soft textiles such as bed linens, clothes, and gowns as sufficient
115 data was available.

116 *Comparators.* We included studies with any comparator, as long as it did *not* involve the use of
117 copper or copper alloy surfaces.
118 *Outcomes (primary, secondary).* The primary outcome was the incidence of healthcare acquired
119 infection (e.g. bacterial or viral infections – *not* colonisations) in patients. The secondary outcomes
120 were the incidence of deaths and any skin reactions in patients, and any healthcare acquired
121 infection (e.g. bacterial or viral) in hospital staff and visitors. We excluded studies that only reported
122 the rate of colonisations (not infections).
123 *Study design.* We included randomised and pseudo-randomised (e.g. alternate allocation) controlled
124 trials.

125 **Search strategies to identify studies**

126 *Database search strings*

127 We searched PubMed, Cochrane CENTRAL and Embase from inception until 25 March 2020. We
128 designed a search string in PubMed that included the following concepts: Copper AND infections
129 AND healthcare facility AND controlled trial. The PubMed search string was translated using the
130 Polyglot Search Translator¹⁰ and run in the other two databases (**Appendix 1**)

131 *Restriction on publication type*

132 No restrictions by language or publication date were imposed. We included publications that were
133 published in full; publications available as abstract only (e.g. conference abstract) were included if
134 they had a clinical trial registry record, or other public report, with the additional information
135 required for inclusion. We excluded publications available as abstract only (e.g. conference abstract)
136 with no additional information available.

137 *Other searches*

138 On 26 March 2020 we conducted a backwards (cited) and forwards (citing) citation analysis in
139 Scopus on the included studies identified by the database searches. These were screened against the
140 inclusion criteria. Clinical trial registries were searched on 25 March 2020 via Cochrane CENTRAL,
141 which includes the WHO ICTRP and clinicaltrials.gov.

142 **Study selection and screening**

143 Two authors (LA, OB) independently screened the titles and abstracts for inclusion against the
144 inclusion criteria. One author (JC) retrieved full-texts, and two authors (LA, OB) screened the full-
145 texts for inclusion. Any disagreements were resolved by discussion, or reference to a third author
146 (PG). The selection process was recorded in sufficient detail to complete a PRISMA flow diagram (see
147 **Figure 1**) and a list of excluded full-text articles with reasons for exclusions (see **Appendix 2**).

148 **Data extraction**

149 We used a data extraction form for study characteristics and outcome data, which was piloted on
150 two studies in the review. Two authors (LA, OB) extracted the following data from included studies:

- 151 1. Methods: study authors, location, study design, duration of study, duration of follow-up
- 152 2. Participants: N, age (mean or median; range), gender, diagnosis or infection type at admission,
153 ward or room type admitted to (e.g. intensive care, acute care, long-term care)
- 154 3. Interventions and comparators: type of copper coating (e.g. copper percentage in the alloy),
155 type of surfaces covered by copper/copper alloy (e.g. bed controls, tables, etc.), type of
156 comparator, average duration of stay in the room.
- 157 4. Outcomes: primary and secondary outcomes: incidence of healthcare acquired infections (e.g.
158 bacterial or viral infections) in patients (*primary*), or hospital staff or visitors (*secondary*), and the
159 number of deaths (*secondary*) and skin reactions (*secondary*).

160 **Assessment of risk of bias in included studies (assessment of quality of studies)**

161 Two review authors (LA, OB) independently assessed the risk of bias for each included study using
162 the Risk of Bias Tool 1, as outlined on the *Cochrane Handbook*¹¹. All disagreements were resolved by
163 discussion or by referring to a third author (PG). The following domains were assessed:

- 164 1. Random sequence generation
- 165 2. Allocation concealment
- 166 3. Blinding of participants and personnel
- 167 4. Blinding of outcome assessment
- 168 5. Incomplete outcome data
- 169 6. Selective outcome reporting
- 170 7. Other bias (focusing on potential biases due to funding or conflict of interest).

171 Each potential source of bias was graded as low, high or unclear, and each judgement was supported
172 by a quote from the relevant trial.

173 **Measurement of effect and data synthesis**

174 We used risk ratios or rate ratios for dichotomous outcomes – risk ratios for results reporting the
175 number of patients with an event, and rate ratios for the results reporting the number of events
176 only. We undertook meta-analyses only when meaningful (when ≥ 2 studies or comparisons reported
177 the same outcome); anticipating considerable heterogeneity, we used a random effects model. We
178 used *Review Manager 5* to calculate the intervention effect.

179 **Assessment of heterogeneity and reporting biases**

180 We considered both clinical and methodological heterogeneity among included studies (i.e.
181 differences between included studies in terms of population, intervention, comparison, outcomes,
182 and study designs). We supplemented this assessment of clinical and methodological heterogeneity
183 with information regarding statistical heterogeneity, assessed using the Chi² test (we considered a
184 significance level of $P < 0.10$ to indicate statistically significant heterogeneity) in conjunction with the
185 I² statistic (I² $\geq 75\%$ indicates considerable heterogeneity)¹². Because we included fewer than 10
186 trials, we did not create a funnel plot.

187 **Dealing with missing data**

188 We contacted investigators or study sponsors to provide missing data.

189 **Subgroup and sensitivity analyses**

190 We planned to do a subgroup analysis by type of infection/patient and a sensitivity analysis by
191 including versus excluding studies at high risk of bias, however, due to a low number of included
192 studies, these analyses were not done.

193

194 **RESULTS**

195 We screened 638 titles and abstracts and assessed 16 full-text articles for inclusion. After excluding 6
196 articles, we included 10 articles pertaining to 7 studies¹³⁻²². We also identified 5 relevant clinical trial
197 registries (2 for studies already identified and included and 3 registries for studies that have not
198 been published). **Figure 1** shows PRISMA flow diagram of studies. Excluded full-text articles are
199 presented in **Appendix 2** with reasons for exclusion.

200 **Characteristics of included studies**

201 We included 7 controlled studies, which enrolled a total of 12,362 participants^{14,15,17,18,20-22}. Included
202 studies were conducted in the last decade in the USA (n=3 studies^{15,18,20}), Chile (n=2 studies^{17,21}),

203 France (n=1 study²²), and Israel (n=1 study¹⁴). Three of the studies were set in adult ICUs^{15,18,20}, one in
204 paediatric ICU²¹, one in aged care facility²², one in acute care ward¹⁷, and one in long-term care for
205 ventilator dependent patients¹⁴. Duration of the studies ranged from 7 to 16 months.

206 Four of the included studies evaluated the effect of copper coating of commonly touched hard
207 surfaces such as bed rails and tables, IV poles, door handles and taps on healthcare acquired
208 infections^{17,18,21,22}. Two studied copper-treated linens (bedding, patient gowns and towels)^{14,15} and
209 one included both hard surfaces and linens²⁰. All included studies reported the effect of copper on
210 healthcare acquired infections in patients (i.e. primary outcome); none reported the effect on
211 hospital staffs or visitors (i.e. secondary outcome).

212 **Risk of bias assessment (quality of studies)**

213 All of the 7 included studies were judged to be at high risk in two or more of the domains of bias. Of
214 the 7 included studies, 5 were judged to be at high or unclear risk for selection bias (either random
215 sequence generation or allocation concealment). All of included studies were judged to be at high or
216 unclear risk in blinding of participants or personnel and conflict of interest (recorded as “other risk of
217 bias”). All of included studies were judged to be at low risk in attrition bias (i.e. incomplete outcome
218 data) and reporting bias (i.e. selective reporting).

219 **Effects of copper-treated surfaces**

220 **Healthcare acquired infections (HAIs)**

221 All 7 included studies reported the effect of copper-treated surfaces on healthcare acquired
222 infections. Overall, we found that copper-treated hard surfaces and/or bed linens and clothes
223 reduced healthcare acquired infections by 27% (RR 0.73; 95% CI 0.57 to 0.94) (**Figure 2**).

224 *Copper-treated hard surfaces (4 studies)*

225 We identified 4 studies (2125 participants) that evaluated the effect of copper-treated hard surfaces
226 on healthcare acquired infections^{17,18,21,22}. There was no statistically significant reduction in HAIs
227 among participants hospitalised in facilities with copper-treated surfaces compared to no copper (RR
228 0.76, 95% CI 0.56 to 1.04; I²=38%).

229 *Copper-treated bed linens and clothes (2 studies)*

230 We identified 2 studies (276 participants) that evaluated the effect of copper-treated bed linens and
231 clothes on HAIs^{14,15}. We observed a statistically significant 25% relative reduction in HAIs among
232 participants hospitalised in facilities with copper-treated bed linens and clothes compared to no
233 copper (RR 0.75, 95% CI 0.58 to 0.98; I²=0%).

234 *Combined copper treated hard surfaces and bed linens and clothes (1 study)*

235 A single study of 9,961 participants evaluated the combined effect of both copper-treated hard
236 surfaces and bed linens and clothes on HAIs²⁰. A statistically significant 86% relative reduction in
237 HAIs was observed among participants hospitalised in facilities with copper-treated surfaces
238 compared to no copper (RR 0.14, 95% CI 0.03 to 0.61).

239 **Mortality**

240 Of the 7 included studies, 3 studies (included a total of 1,569 participants) reported the effect of
241 copper-treated hard surfaces on mortality^{17,18,21}. There was no statistically significant difference in
242 mortality between participants hospitalised in facilities treated with copper compared to no copper
243 (RR 1.06, 95% CI 0.83 to 1.36) (**Figure 3**).

244 **Skin reactions**

245 Of the 7 included studies, 2 studies reported data on skin reactions^{20,21}. von Dessauer et al did not
246 observe any adverse events (i.e. skin or other allergic reactions) among any participants in either

247 group²¹. Sifri et al reported that 10 (of 4707) patients hospitalised in copper-treated rooms
248 developed skin rashes (9 were evaluated by a dermatologist and attributed to alternative aetiology
249 and 1 was discharged before evaluation)²⁰.

250 **Heterogeneity in included studies**

251 We noted both clinical and methodological heterogeneity between included studies. For example,
252 we found differences on how included studies defined and measured the primary outcome (i.e.
253 HAIs). For instance, although 6 of the 7 included studies directly measured HAIs (i.e. infections not
254 just colonisations), the RCT of 112 ventilator-dependent patients in a long-term care did not
255 measure HAIs, instead, measured antibiotic initiation events as an indicator for HAIs¹⁴. Further, 4 of
256 the 7 included studies determined HAIs following comparable definitions: 3 used the National
257 Healthcare Safety Network (NHSN) definitions^{15,18,20} and 1 used National Surveillance System of the
258 Ministry of Health of Chile (i.e. infections on and after third admission day)²¹; but the remaining 3
259 studies did not clearly report how they define HAIs. Despite these differences, the quantified Q and
260 I² statistics did not identify substantial statistically heterogeneity - I² statistics of all metaanalyses of
261 all outcomes ranges between 0% to 44%, with all not significant P > 0.10).

262

263

264 **DISCUSSION**

265 We found seven controlled trials, which when combined suggest that copper surfacing or use in bed
266 linen may have some effect on reducing healthcare acquired infections. The combined studies
267 suggest a modest but potentially important effect.

268

269 There are several limitations to our findings. First, many of the studies were poorly reported,
270 preventing a clear appraisal of the methods. Second, even when reporting was clear, the research
271 methods often involved flaws in study design which might introduce bias. Third, studies reported
272 HAIs caused by different organisms, most of them bacterial (e.g. *Pseudomonas* spp., meticillin-
273 resistant *Staphylococcus aureus*, vancomycin-resistant enterococci) but also viral (e.g. norovirus and
274 adenovirus), and different body system affected (e.g. respiratory, bloodstream, urinary). Fourth,
275 although we did not identify substantial statistical heterogeneity (i.e. evaluated using Q test and I²
276 statistics), observed clinical and methodological heterogeneity between studies limit our certainty in
277 the effect estimates and poses interpretive challenges. Finally, the small total numbers of infections
278 meant that the confidence intervals around effects were wide, indicating considerable uncertainty in
279 the size of any effect. The poor quality of reporting and methods, and small sizes of the studies
280 would both downgrade the overall quality of the evidence, rating it - in GRADE terms - as low-quality
281 evidence but of a potentially clinically important effect. In addition to these problems, many of the
282 investigator teams had a conflict of interest with companies involved in copper use.

283

284 We report one difference between the protocol and the review: we had initially intended to include
285 only studies of copper-plating of hard surfaces such as furniture. However, as several studies
286 assessed the impact of copper-treating of textiles (clothing and/or bed linens) we broadened our
287 inclusion criteria. This resulted in an inclusion of two clothing/linen-only studies^{14,15} and one study
288 that assessed the impact of both furniture coating and Copper-impregnated textiles²⁰.

289

290 The only previous systematic review we could identify was a 2017 report prepared by Cochrane

291 Australia for Australia's National Health and Medical Research Council (NHMRC) which found 2 of
292 these studies^{18,21}, and concluded that "With only two non-randomised trials, both with uncertain
293 results, it is not possible to draw conclusions from this evidence." The three trials since then, plus
294 two not identified in the 2017 review, have strengthened the body of evidence, but not sufficiently
295 to be able to make strong recommendations.

296

297 Finding effective and sustainable ways of reducing pathogen transmission is important for all
298 epidemics but particularly urgent in the current SARS coronavirus 2 (SARS-CoV-2) pandemic²³.
299 Though the exact relative importance of different modes of transmission is currently unknown there
300 appears to be three main avenues, namely direct aerosol, contact with fomites, and the most
301 controversial, airborne transmission²⁴. Reducing the incidence of infections will require addressing
302 all modes of transmission. While social distancing is widely promoted it may not completely prevent
303 fomite transmission if common objects such as door handles, stair banisters, table surfaces, utensils
304 or taps are contaminated⁵. Therefore, our findings might be also relevant to the current COVID-19
305 pandemic.

306

307 Given the clinical and economic costs of healthcare acquired infections, the potential effect of
308 copper coating appears important. We feel the current evidence is insufficient to make a positive
309 recommendation. However, it would appear worthwhile and urgent to conduct larger scale publicly
310 funded clinical trials with clearly defined outcomes into the impact of copper coating. If such studies
311 were to be funded, it would also be important to collect additional data such as the separation of
312 bacterial and viral infections and measuring outcomes for healthcare workers as well particularly for
313 viral infections.

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318

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320 **Contributions** LA, OB, JC, AMS, and PG designed the study. LA and OB screened articles, assessed
321 study eligibility and quality, and extracted data. JC with the help of all study authors designed the
322 search strategy. LA, PG, AMS wrote the first draft of the manuscript. All authors contributed to the
323 interpretation and subsequent edits of the manuscript. LA is the guarantor.

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327 interpretation of the data, or decision to submit results.

328 **Data sharing** Extracted data are available on request to the corresponding author.

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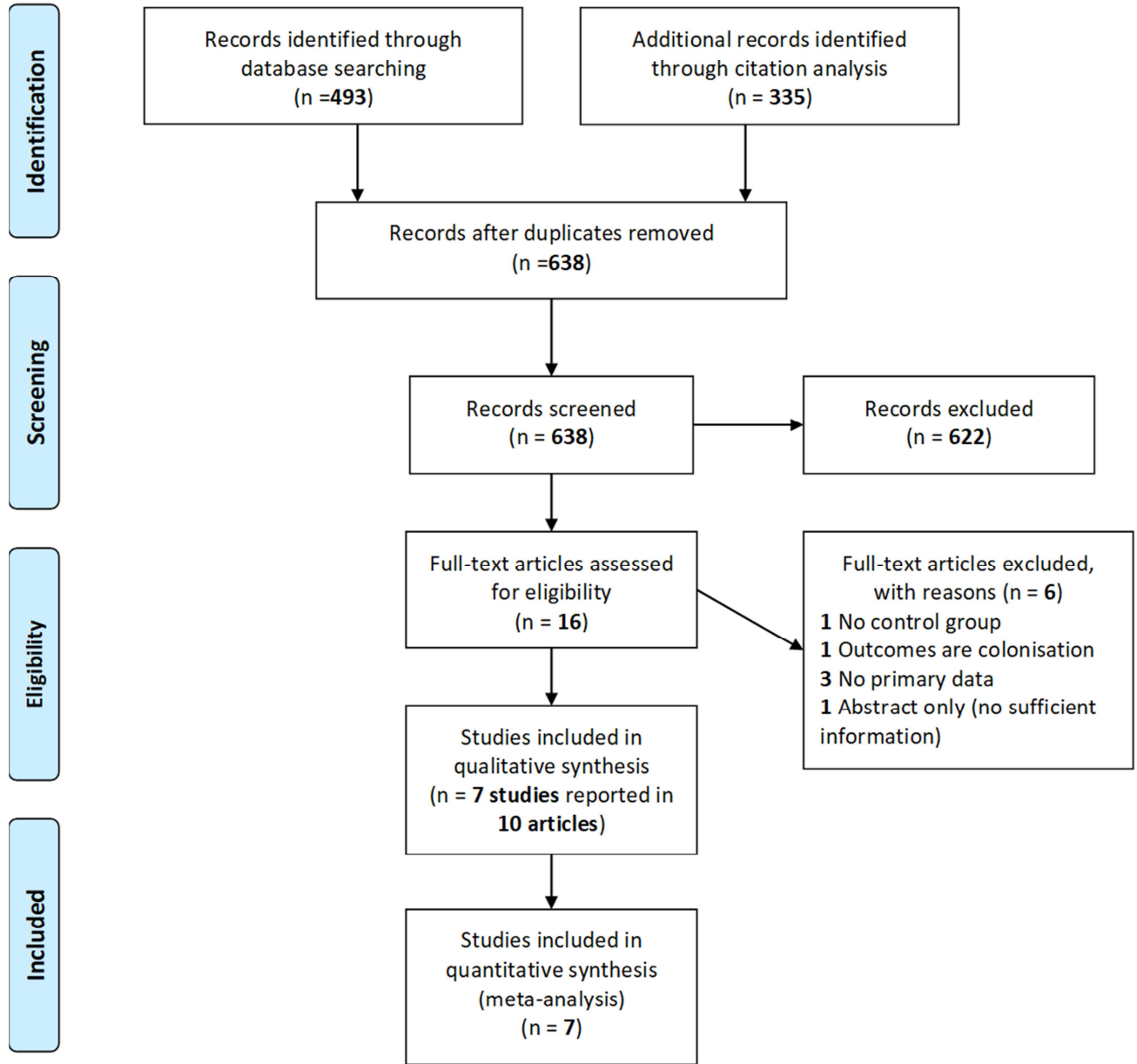
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404 **Tables and Figures**

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407 **Figure 1.** PRISMA flow diagram of included articles

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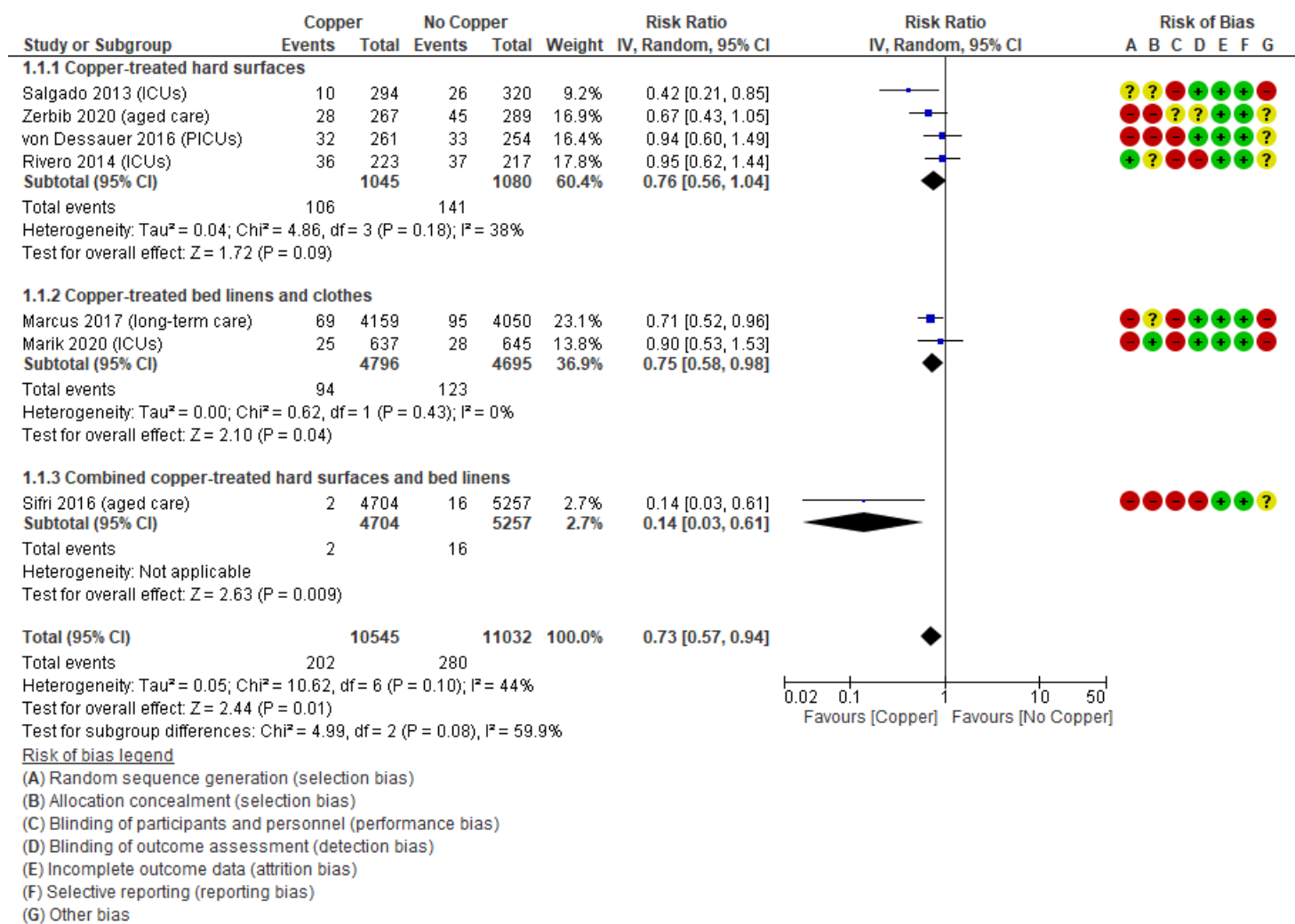


Figure 2: Forest plot of healthcare acquired infections in copper treated surfaces versus no copper.

Abbreviation: ICUs, Intensive Care Units; PICUs, Paediatric ICUs.

Marcus 2017 data refers to the antibiotic treatment initiation events, rather than HAIs, and reported as the number of events per hospitalisation days.

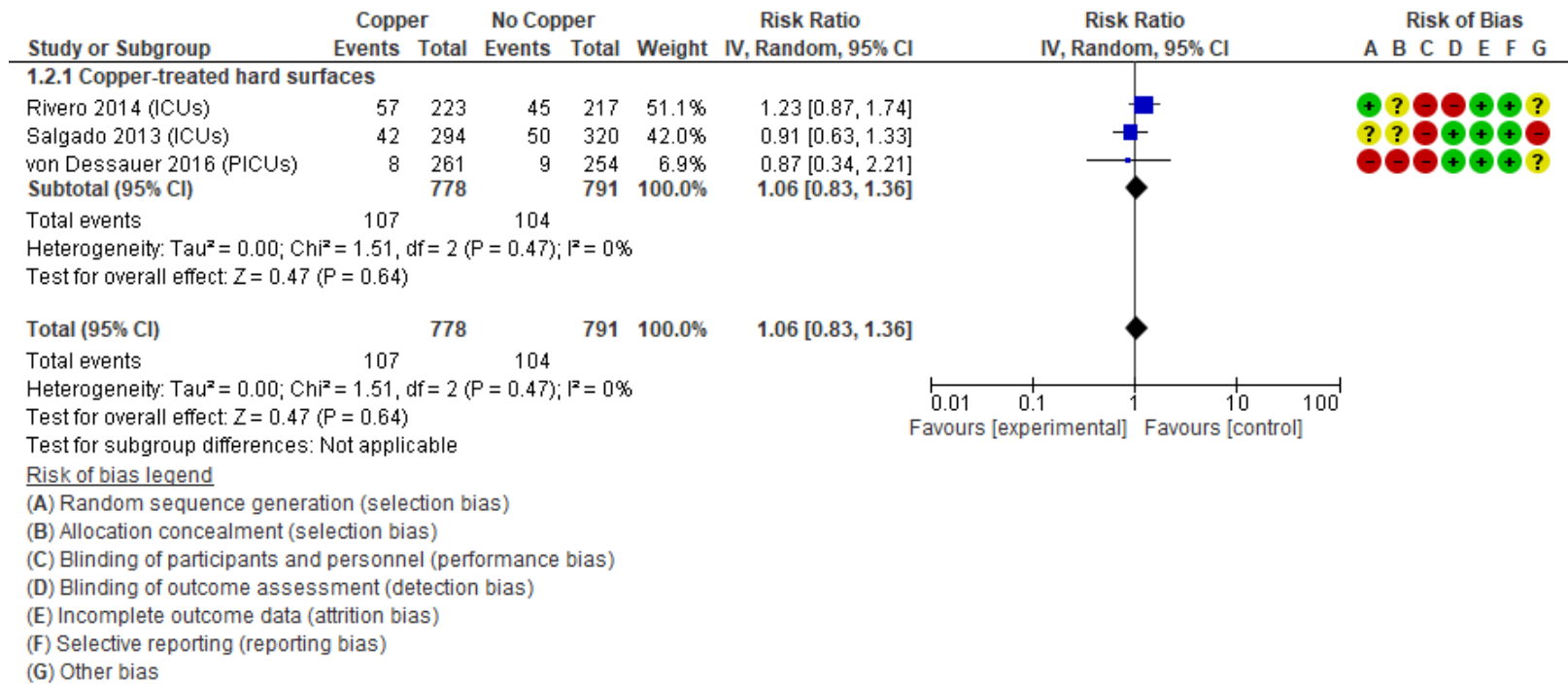


Figure 3: Forest plot of mortality in copper treated surfaces versus no copper.

Abbreviation: ICUs, Intensive Care Units; PICUs, Paediatric ICUs.

Table 1. Characteristics of included studies (n=7)

Study ID, year and location	Study type and duration	Participants, Setting	Intervention	Control	Primary outcomes* (as reported in original studies)
Salgado 2013 (USA) ¹⁸	Double-blind RCT, 11 months	614 adult ICU patients (60.4 yrs)	<i>Copper-treated surfaces</i> Copper covering of bed rails, overbed tables, intravenous poles, and arms of the visitor's chair the nurses' call button, computer mouse, bezel of touchscreen monitor, palm rest of laptop were different depending on the hospitals)	Regular ICU	Incident Rate of HAI and/or MRSA or VRE colonization. HAIs were determined using NHSN definitions (i.e. infections on and after third admission day)
Rivero 2014 (Chile) ¹⁷	Controlled trial, 13 months	440 adult ICU patients (51 yrs)	<i>Copper-treated surfaces</i> C11000 copper alloy (99% copper) equivalent to approximately 80% of the areas most touched by patients (four bed rails, patient table and two IV poles)	Regular ICU	HAIs, associated mortality, cost of antimicrobials.
von Dessauer 2016 (Chile) ²¹	Non-randomized, unmasked, controlled clinical trial, 12 months	65 paediatric ICU (1 yr)	<i>Copper-treated surfaces</i> Copper covering of bed rails, bed rail levers, intravenous poles, sink handles, and the nurses' workstation	Regular PICU	Diagnosis of a HAI event associated with patient stay within the PICU or PIMCU. HAIs were determined by standard definitions used by the National Surveillance System of the Ministry of Health of Chile (i.e. infections on and after third admission day)
Zerbib 2020 (France) ²²	Controlled trial, 16 months	556 nursing home residents (85.4 yrs)	<i>Copper-treated surfaces</i> 438 door handles, 322 m of handrails, and 10 grab-bars in copper alloy (containing 90% copper)	Regular nursing home setting	Rates of infection during outbreak (5 cases in 4 days)

Marcus 2017 (Israel) ¹⁴	Double-blind, controlled cross-over, 7 months (2 x 3 months, separated by a 1-month washout period)	112 ventilator-dependent patients in a long-term care hospital (69.8 vs 71.3 yrs)	<i>Copper-treated textiles</i> Copper oxide-impregnated linen and hospital patients' clothes and towels.	Regular ICU	Antibiotic treatment initiation events (ATIEs), fever days, days of antibiotic treatment, and antibiotic defined daily dose (DDD) per 1,000 hospitalization days (HDs). We used ATIEs as an indirect indication for HAIs.
Marik 2020 (USA) ¹⁵	Prospective, cluster, cross-over, randomized control trial, 11 months (2 x 5 months separated by 2 weeks of wash-out)	1282 adult ICU patients (60 yrs)	<i>Copper-treated textiles</i> Copper-oxide-treated linens (top sheets, fitted sheets, pillowcases, under pads, wash cloths, towels, and patient gowns)	Regular ICU	HCAIs were determined using NHSN definitions (i.e. infections on and after third admission day)
Sifri 2016 (USA) ²⁰	Quasi-experimental study with a control group, 10 months	9961 adult acute care patients (58.5 vs 60.5 yrs)	<i>Combined Copper treated textiles and surfaces</i> 16% copper oxide-impregnated composite countertops (sinks, vanities, desks, computer stations, soiled utility rooms, nurse workstations) and moulded surfaces (overbed tray tables, bedrails) and copper-impregnated woven linens (patient gowns, bedding, washcloths, towels, bath blankets, thermal blankets)	Regular ICU	Incidence Rate of hospital-onset infections (C difficile or MDRO). HAIs were determined using NHSN definitions (i.e. infections on and after third admission day)

ICU – Intensive Care Unit/s; HAI -healthcare acquired infection/s; MRSA – methicillin-resistant Staphylococcus aureus; VRE - vancomycin-resistant Enterococcus; PICU – Paediatric Intensive Care Unit/s; PIMCU - intermediate paediatric care unit; HCAI - healthcare-associated infections; MDRO - multidrug resistant organisms; NHSN - National Healthcare Safety Network

* This is as reported by the authors of included studies, however, we extracted only the outcomes that we proposed in the methods (e.g. if authors reported both colonization and HAIs, we only extracted and reported HAIs – per our proposed methods).

Supporting Information

APPENDIX 1

DATABASE SEARCH STRINGS

PubMed

("Copper"[Mesh] OR Copper[tiab])

AND

("Infections"[Mesh] OR "Equipment Contamination"[Mesh] OR "Infection Control"[Mesh] OR "Cross Infection"[Mesh] OR Infection[tiab] OR Infections[tiab] OR Colonization[tiab])

AND

("Health Facilities"[Mesh] OR Hospital[tiab] OR Hospitals[tiab] OR "Healthcare facility"[tiab] OR "Healthcare facilities"[tiab] OR "Intensive care"[tiab] OR "Intensive-care"[tiab] OR ICU[tiab] OR PICU[tiab] OR Ward[tiab] OR Wards[tiab])

AND

(Randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR placebo[tiab] OR "drug therapy"[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Control[tiab] OR Controlled[tiab] OR Comparing[tiab] OR Compared[tiab])

NOT

(Animals[Mesh] not (Animals[Mesh] and Humans[Mesh]))

NOT

("Case Reports"[pt] OR Editorial[pt] OR Letter[pt] OR "Comment"[pt] OR Meta-Analysis[pt] OR "Observational Study"[pt] OR "Systematic Review"[pt] OR "Case Report"[ti] OR "Case series"[ti] OR Meta-Analysis[ti] OR "Meta Analysis"[ti] OR "Systematic Review"[ti])

Cochrane CENTRAL

([mh Copper] OR Copper:ti,ab)

AND

([mh Infections] OR [mh "Equipment Contamination"] OR [mh "Infection Control"] OR [mh "Cross Infection"] OR Infection:ti,ab OR Infections:ti,ab OR Colonization:ti,ab)

AND

([mh "Health Facilities"] OR Hospital:ti,ab OR Hospitals:ti,ab OR "Healthcare facility":ti,ab OR "Healthcare facilities":ti,ab OR "Intensive care":ti,ab OR ICU:ti,ab OR PICU:ti,ab OR Ward:ti,ab OR Wards:ti,ab)

Embase (via Elsevier)

('Copper'/exp OR Copper:ti,ab)
AND
(('Infection'/exp OR 'medical device contamination'/exp OR 'Infection Control'/exp OR 'Cross Infection'/exp OR Infection:ti,ab OR Infections:ti,ab OR Colonization:ti,ab)
AND
(('health care facility'/exp OR Hospital:ti,ab OR Hospitals:ti,ab OR "Healthcare facility":ti,ab OR "Healthcare facilities":ti,ab OR "Intensive care":ti,ab OR Intensive-care:ti,ab OR ICU:ti,ab OR PICU:ti,ab OR Ward:ti,ab OR Wards:ti,ab)
AND
(random* OR factorial OR crossover OR placebo OR blind OR blinded OR assign OR assigned OR allocate OR allocated OR 'crossover procedure'/exp OR 'double-blind procedure'/exp OR 'randomized controlled trial'/exp OR 'single-blind procedure'/exp OR Control:ti,ab OR Controlled:ti,ab OR Comparing:ti,ab OR Compared:ti,ab)
NOT
(('animal'/exp NOT ('animal'/exp AND 'human'/exp))

APPENDIX 2

Excluded studies: Details of the 6 full-text articles screened in full text but excluded from the review with reason for their ineligibility

Author, Year	Title	Journal	Reason for exclusion
Butler 2016	Effect of copper-impregnated composite bed linens and patient gowns on healthcare-associated infection rates in six hospitals	J Hosp Infect	Study design (No control group)
Lautenbach 2018	A randomized controlled trial of the effect of accelerated copper textiles on healthcare-associated infections and multidrug-resistant organisms: The “investigating microbial pathogen activity of copper textiles” (impact) study	Open Forum Infectious Diseases	Abstract without enough information
Anderson 2017	The antimicrobial scrub contamination and transmission (ASCOT) trial: A three-arm, blinded, randomized controlled trial with crossover design to determine the efficacy of antimicrobial-impregnated scrubs in preventing healthcare provider contamination	Infection Control and Hospital Epidemiology	Outcome – colonisation (not HAIs)
Cavicchioli 2017	Superfici al rame e infezioni ospedaliere	Assistenza Infermieristica e Ricerca	No primary data
Abbas 2019	Infection prevention: is copper the new gold?	Journal of Hospital Infection	No primary data
Butler 2019	Reply to Abbas et al. “Infection prevention: Is copper the new gold?”	Journal of Hospital Infection	No primary data