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Systematic review of antimicrobial surfaces to reduce infection rates in hospitalised populations

Technical report prepared by Cochrane Australia

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Contents

In June 2016 Cochrane Australia was contracted by the National Health and Medical Research Council (NHMRC) to design and undertake this systematic review. This review is one of several independent contracted evidence evaluations being undertaken to update or inform new sections of the *2010 Australian Guidelines for the Prevention and Control of Infection in Healthcare*. The design and conduct of the review was done in collaboration with the Infection Control Guidelines Advisory Committee (ICGAC) and NHMRC.

Authors and contributors to the protocol

Sue Brennan	Senior Evidence Officer responsible for leading the review. Contributed to the design and conduct of the review (e.g. screening, data extraction, risk of bias assessment). Wrote the protocol and systematic review report with contributions from other authors as described.
Steve McDonald	Developed the search strategy and conducted the search. Wrote the search methods and results. Critical review of the protocol and systematic review report.
Joanne McKenzie	Developed the analysis plan and conducted the analysis. Wrote the analysis methods, method for reporting treatment effects and results from the times series analyses. Critical review of the protocol and systematic review report.
Allen Cheng	Provided expert clinical advice, especially in relation to selection of studies for the review, interpretation of analyses and reporting results. Wrote the implications for clinical practice. Critical review of the protocol and systematic review report.
Sally Green	Critical review of the protocol report.
Kelly Allen	Conducted searches of trial registers. Extracted data for time series analyses.
Jane Reid	Screened citations and full text articles, extracted data, assessed risk of bias assessment of included studies (critical appraisal).

Declarations of interest

All authors declare they have no financial, personal or professional interests that could be construed to have influenced the conduct or results of this systematic review.

Professor Allen Cheng is a member of the Infection Control Guidelines Advisory Committee (ICGAC).

Scope of the technical report

This technical report includes full description of the methods (reported in brief in the main systematic review report), together with appendices for more detailed methods and description of changes to protocol.

Methods

Methods reported were pre-specified in the protocol for this review (Brennan 2016) and are based on the *Cochrane Handbook for Systematic Reviews of Interventions* and the Cochrane Effective Practice and Organisation of Care group (Effective Practice and Organisation of Care (EPOC) 2015). Additional methodological considerations pertinent to public health questions are addressed where appropriate (Armstrong 2011). The review is reported in accordance with the PRISMA statement (Liberati 2009, Moher 2009). Changes to the original protocol and the rationale for each change are reported in Appendix 3. These involved rewording to clarify eligibility criteria and the basis for GRADE judgements; the types of studies eligible for the review and all other methods were unchanged.

3.1 Criteria for considering studies for this review

3.1.1 Types of participants

Any admitted patient in an eligible setting.

3.1.2 Types of settings

Type of healthcare facility: Studies set in hospital wards (primarily acute care), including inpatient facilities and patient rooms, were considered for inclusion in the review.

Studies in ambulatory care (e.g. primary care, hospital outpatient services), residential care facilities (e.g. residential aged care, nursing homes, assisted living), and home and community settings were excluded.

Geographical restrictions: Eligible studies were those set in countries or regions with health systems broadly comparable to those in Australia, especially in terms of the healthcare facilities and resourcing, specifically:

- Australia
- New Zealand
- Europe
- Canada
- United States of America

Eligible studies set in other countries or regions with broadly comparable heath systems were evaluated based on full-text to determine whether the facility was comparable to an Australian setting.

Studies set in low- or middle-income countries were only excluded at abstract review if there was explicit mention that interventions were evaluated in a resource poor setting (or equivalent). Other studies were assessed in full text to determine if the setting might be comparable to hospitals in Australia, and all studies eligible for inclusion based on other criteria were referred to an arbiter (our clinical expert). In practice, most studies excluded on this criterion were clearly ineligible based on other criteria.

3.1.3 Types of interventions

Studies evaluating the effects of environmental surfaces coated or impregnated with antimicrobial (self-disinfecting) materials including:

- Heavy metal alloys (copper, silver) coating or impregnation
- Light activated antimicrobial coatings
- Altered topography designed to inhibit microbial colonisation of surfaces
- Other antimicrobial releasing agents.

These interventions may be used in combination with routine cleaning using detergent solutions (providing the comparator involves an identical method of cleaning) or alone. Studies evaluating the use of these interventions in combination with other interventions (e.g. copper alloy coated surfaces in combination with ultra-microfibre cloths for cleaning) will be excluded unless the additional intervention is also used in the comparator.

Types of surfaces

Eligible studies must have involved interventions for use in patient surroundings, defined in the 2010 Guidelines as "inanimate surfaces that are touched by or in physical contact with the patient and surfaces frequently touched by healthcare workers while caring for the patient" (p262).

Any high-touch (high-risk or frequently touched) surface was eligible including hard non-porous and porous surfaces, such as:

- Bed rails, bedside tables, over-bed tables, chair arms, doorknobs, light switches, ensuite facilities
- Intra-venous stands/poles, medical equipment (e.g. pumps, monitors), knobs, buttons
- Textiles used, for example, in patient linen or gowns, privacy curtains, surgical scrubs

Interventions tested only for minimal touch surfaces (e.g. floors, walls, window curtains or blinds), surfaces in non-patient care areas, invasive medical devices, and disposable items (e.g. dressings) were excluded.

3.1.4 Types of comparators

Studies reporting a standard environment as the comparator were eligible for inclusion.

Studies that directly compared the effects of two or more of the interventions eligible for this review were also excluded.

3.1.5 Types of outcome measures

Primary outcome

Healthcare-associated infection (confirmed or unconfirmed) arising from the following pathogens:

- *Clostridium difficile* (*C. difficile*)
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin resistant enterococcus (VRE)
- *Acinetobacter* spp.
- An Enterobacteriaceae (including *Escherichia coli*, *Klebsiella sp. Enterobacter sp.* and others) where a carbapenemase producing gene is detected (including MBLs and KPC) resulting in a high minimum inhibitory concentration (MIC) to carbapenems in vitro (based on standard lab criteria including EUCAST or CLSI) (Department of Health and Human Services Victoria 2015, Guh 2015)
- Extended spectrum beta lactamase (ESBL) producing organisms (includes extended-spectrum cephalosporin-resistant CPE listed above and *Acinetobacter* sp. (Falagas 2009)

A post hoc decision was made to broaden this criterion to include eligible studies that reported any hospital-acquired infection, irrespective of pathogen. This decision was taken due to the sparsity of evidence that met this a priori inclusion criterion. Only one study, Salgado 2013 met the original inclusion criterion, with only the secondary outcome, not the primary, meeting the criterion. This decision to broaden the criterion led to the inclusion of one additional study, of which we had prior knowledge before changing the criterion. However the decision was taken prior to any data extraction or analysis.

Studies reporting infection as an outcome were included irrespective of the metric reported, for example:

- Risk of infection: calculated as number of patients with an episode of infection as a proportion of the total number of patients

- Rate of infection: calculated as patient episodes of infection per total patient days, or patient episodes of infection per 10,000 patient days (Australian Commission on Safety and Quality in Health Care 2013).

Infection outcomes were eligible if determined through clinical evaluation of symptoms, physical signs of infection, or laboratory test results (Lewis 2016); however, clinical evaluation or signs must have been accompanied by testing to confirm acquisition of an MRO, *C. difficile,* or other pathogen associated with the infection.

Studies that reported outcomes in which infection and colonisation were not distinguished (e.g. acquisition of MRSA), combined outcomes across multiple pathogens (e.g. acquisition of any MRO), or reported unconfirmed infection (e.g. based on clinical isolates alone), were also eligible.

Secondary outcome

Colonisation with multi-resistant organisms (MROs) where colonisation is defined as the "sustained presence of replicating infectious agents on or in the body without the production of an immune response or disease" ((National Health and Medical Research Council 2010), p17). Studies reporting patient colonisation as an outcome were included irrespective of the metric reported (e.g. the proportion of patients positive for colonisation of the pathogen) or the method of detection.

Studies reporting environmental contamination or environmental colonisation as outcomes, without infection or patient colonisation outcomes, were excluded.

Adverse effects

Data on adverse effects (harms, safety) were collected and included in our review when the data were reported in included studies that measured at least one of the primary or secondary outcomes (i.e. infection, colonisation), or in eligible studies that explicitly aimed to examine adverse effects.

3.1.6 Types of studies

The types and definition of study designs eligible for inclusion are based on guidance from the Cochrane Effective Practice and Organisation of Care (EPOC) group (Effective Practice and Organisation of Care 2013).

- Randomised trials (RTs). Given the nature of the interventions, eligible trials were expected to be randomised at cluster level (i.e. at the hospital or ward level) rather than individual level. However, trials were not excluded on the basis of level of randomisation.

- Non-randomised trials (NRTs). Studies in which participants (or clusters) were allocated to groups using a method that is not (truly) random. These studies include controlled trials (CTs).

- Interrupted-time-series (ITS) and repeated measures (RM) studies. To be eligible these studies must have had a clearly defined time point at which the intervention was introduced and at least three

outcome measures before and after intervention. Studies that presented time series data were eligible irrespective of how the study was described or analysed. When analysed appropriately, these studies are designed to detect whether the intervention has an effect greater than the underlying trend over time. These studies may or may not have a control group.

- Controlled before-after (CBA) studies. Studies with both an intervention group and a control group, in which outcomes are measured concurrently in both groups, before and after delivery of the intervention.

Controlled studies must have had at least two intervention and two control clusters to be eligible.

Studies using other designs (uncontrolled before-after studies where no time series data were reported and cross sectional studies) were excluded because it is difficult (if not impossible) to attribute observed changes in outcomes to the intervention (Effective Practice and Organisation of Care 2013). Full-text of all studies with observations pre- and post-introduction of an eligible intervention were retrieved in order to confirm the availability of time series data.

Date and language restrictions. Only studies published from 2006 onwards were eligible for inclusion. Studies published in languages other than English were ineligible, except for randomised trials.

3.2 Search methods for identification of studies

The overall search approach was based on the search methods used for the recent Technical Brief prepared for the Agency for Healthcare Research and Quality (AHRQ) (Leas 2015). In developing the search strategy for this review, we appraised and adapted the AHRQ search strategy. Terms or concepts not relevant to this review were removed and other terms added. The search terms include concepts relevant to a second commissioned review for the 2010 Guidelines (novel disinfectants), for which searching and screening was conducted concurrently because of significant overlap in eligibility criteria of the two reviews.

Potentially eligible studies published between 2006 and 2014 were identified from the lists of included and excluded studies from the AHRQ report. The lists were supplemented by additional searches for the same period for terms or concepts not covered by the AHRQ report, and by an update of the AHRQ search for the period January 2015 to August 2016. The review considered both peer reviewed literature, as well as unpublished literature. No language or geographic limitations were applied when searching.

3.2.1 Search terms

The search strategy was developed for Embase via Ovid. Embase was the principal database used for the AHRQ report and includes all MEDLINE records. We appraised the AHRQ search strategy, carefully cross-checking the inclusion criteria of both the AHRQ review and this review. We removed terms and concepts deemed not to be relevant to the two reviews (e.g. cleaning personnel and training; measuring and monitoring cleanliness; and non-bleach disinfectants). We added concepts covered in our inclusion criteria but which were not reflected in the AHRQ criteria (e.g. electrolysed water, acinetobacter, carbapenemase producing Enterobacteriaceae, furnishings and curtains) or which were explicitly excluded (e.g. paediatric studies). We applied the methodological filters for identifying randomised trials and excluding animal studies that Cochrane has developed for Embase. We converted the search syntax from embase.com to the Ovid platform.

3.2.2 Bibliographic and grey literature databases

We searched Embase (via Ovid) using the search strategy in Appendix 1. The search strategy was translated for PubMed (limited to in-process citations and citations not indexed in MEDLINE), the Cochrane Library and CINAHL Plus. We also searched ClinicalTrials.gov. The full search strategies for each source are provided in Appendix 1.

Searches for the AHRQ review were conducted in February 2015. We searched Embase and the other databases for records added since January 2015. For the terms and concepts included in our review but not covered in the AHRQ review we identified unique records going back to 2006 that would not have been included in the original AHRQ search.

We had intended to search OpenGrey and the WHO ICTRP trials register but for pragmatic reasons decided to omit them from the search. This reflected the difficulty of constructing searches of these sources for the review topic and the low likelihood that included studies would have been retrieved through alternative sources.

3.2.3 Other sources

We screened all studies included in the AHRQ report plus all studies that had been excluded from the AHRQ report after full-text screen. The reference lists of eligible studies and any relevant systematic reviews identified were checked for additional studies. We also used Scopus to conduct forward citation searches for all included studies.

3.3 Data collection and analysis

3.3.1 Selection of studies

Citations identified from the literature searches, citation checking, and from the list of included and excluded studies in the AHRQ report were imported to EndNote and duplicates removed. Citations were then imported to Covidence (www.covidence.org), an online tool that streamlines the screening and data extraction stages of a systematic review. Two reviewers (SB, JR) independently screened citations (titles and abstracts) for inclusion in the review using a pre-tested screening guide based on the inclusion criteria. One reviewer screened citations in Covidence, while the second screened in EndNote. Endnote enabled categorisation of citations according to the question to which they pertained, which facilitated concurrent screening for the review of novel disinfectants. Disagreements about eligibility were resolved through discussion, with involvement of a third reviewer if consensus could not be reached.

Full-text of all potentially eligible studies were retrieved and independently screened by two reviewers (SB, JR), with disagreements resolved using the same approach as for citation screening. Advice was sought from our review content expert (AC) to confirm eligibility based on PICO and our biostatistician (JM) to confirm eligibility based on study design. Eligibility of some studies published as conference abstracts could not be confirmed based on information reported in the abstract alone. We searched for published papers for these studies, but did not contact study authors because it was infeasible to include unpublished data in the review. These studies were therefore noted as studies awaiting further assessment. Citations that did not meet the inclusion criteria were excluded and the reasons for exclusion were recorded at full-text screening for all eligibility criteria.

Trial registration numbers (where available), author names, and study titles, locations, sample sizes and dates were used to identify multiple reports arising from the same study.

3.3.2 Data extraction and management

For each included study, two reviewers independently extracted data using a pre-tested data extraction and coding form. Disagreements were resolved by discussion.

Pre-testing of the data extraction and coding form was done by two reviewers (SB, JR), who extracted data from two studies purposefully selected from the included studies to cover the diversity of data types anticipated in the review (e.g. study designs, PICO characteristics). Advice was sought from the review content expert (AC) and biostatistician (JM) to ensure data extracted were as planned. Revisions to the data extraction form were made to maximise the quality and consistency of data collection.

We extracted information relating to the following characteristics of included studies:

- study design, whether the study was registered, and other details required to assess risk of bias

- year conducted
- setting and location (hospital, country, units on which the intervention was delivered)
- participant characteristics (including those needed to characterise risk group)
- intervention and comparator characteristics (e.g. materials, procedures, personnel, surfaces on which antimicrobial materials were used, adherence to cleaning/disinfection protocols)
- outcomes measures (outcome category (infection, colonisation, adverse events), pathogen(s), measurement method/metric, outcome measurement period/follow-up times)
- results for primary and secondary outcomes (where eligible; including number of participants/clusters for each measurement), and adverse events
- ethics approval
- funding sources and funder involvement in study.

Items relating to the characteristics of interventions and comparators are based on the Template for Intervention Description and Replication (TIDieR) (Hoffmann 2014). Appendix 2 summarises how these domains were applied in the review.

3.3.3 Assessment of risk of bias of included studies

Two reviewers (SB, JR) independently assessed the risk of bias for each included study, using the Cochrane risk of bias tool (Higgins 2011) and additional criteria developed by the Cochrane EPOC Group (Effective Practice and Organisation of Care 2015). Disagreements were resolved by discussion, with advice from a third reviewer (JM) if agreement could not be reached.

Both included studies were NRTs, so we assessed the risk of bias associated with the following domains:

1. sequence generation
2. allocation concealment
3. blinding of participants, personnel, and outcome assessors
4. incomplete outcome data
5. selective outcome reporting, and
6. other potential threats to validity (Higgins 2011).

Neither of the included studies were cluster-randomised, so we did not assess domains specific to clustered designs (imbalance of participant characteristics and outcome measures at baseline, and protection against contamination).

For each study, we report our judgment of risk of bias (low, high, unclear) by domain and provide a rationale for the judgment with supporting information. Some domains are assessed separately for different outcome categories (blinding of outcome assessment, incomplete outcome data); where relevant, our judgments are reported by outcome for these domains. Our risk of bias judgments were summarised in tables reporting characteristics of included studies.

For GRADE assessments we first drew conclusions about the overall risk of bias for each outcome (i.e. summarising risk of bias judgments across domains for each outcome within a study), and then summarised risk of bias assessments across studies for each outcome where results were summarised across studies. We followed the Cochrane EPOC guidance to inform judgements for each of these summary assessments (Effective Practice and Organisation of Care 2013). These summary assessments of risk of bias were used in determining the overall quality of the body of evidence using GRADE, and the basis for each is reported as footnotes to the summary of findings tables.

3.3.4 Measures of treatment effect

Non-randomised trials. We calculated incident rate ratios for the infection outcomes. We calculated the ratios, along with 95% confidence intervals and p-values using the epitab command in Stata 14.0 (StataCorp 2015).

3.3.5 Unit of analysis issues

No unit of analysis issues arose.

3.3.6 Dealing with missing data

Attrition rates (where available) are presented for all outcomes. We did not plan to undertake any imputation for missing data, however, we did assess the risk of bias in observed effect estimates resulting from attrition.

3.3.7 Assessment of heterogeneity

We did not assess heterogeneity visually by inspecting the overlap of confidence intervals on the forest plots, or through formal tests for heterogeneity because data were not combined across studies. Instead, the characteristics of studies (setting, population, interventions, comparators, outcomes, study design) were summarised and considered in interpreting results and summarising findings.

3.3.8 Assessment of reporting biases

In addition to undertaking an extensive search of the literature, we searched trial registries (see 'Search methods for identification of studies'). One of the two included studies had been prospectively registered (von Dessauer 2016), enabling assessment of whether any pre-specified outcomes were not reported. The second completed study included in the review was retrospectively registered (Salgado 2013), so we were unable to confirm whether all outcomes for which data were collected and/or analysed were included in the final report. We planned to extract any discrepancies and reasons for discrepancies noted by authors from papers reporting results, however none were reported.

We were unable to investigate the potential for small study-study effects because we did not perform meta-analysis.

3.3.9 Data synthesis

In line without our protocol, we did not combine effect estimates from studies using non-randomised study designs (i.e. both included studies were non-randomised trials). No randomised trials were included in the review, hence no-meta-analyses were conducted.

We present available effect estimates (95% confidence intervals, p-values), along with risk of bias assessments, and other intervention characteristics, in tables structured by comparison, outcome and study design.

3.3.10 Summary of findings tables and assessment of quality of the body of evidence

For each comparison and outcome, we assessed the quality of the evidence using the GRADE approach. In accordance with the detailed GRADE guidance (Schunemann 2013), the following five domains were assessed (as briefly summarised below) and a judgement made about whether there were serious, very serious or no concerns in relation to each domain. Some overall conclusions are drawn across the two studies, and a GRADE assessment is reported for these. We also report GRADE assessments for each of the two included studies. The studies are in different populations (adult and paediatric), so providing a GRADE assessment facilitates interpretation of each study.

1. Risk of bias. Based on the summary assessment across studies for each outcome reported for a comparison (see 'Risk of bias' section). For individual studies, assessment was based on a summary assessment across domains. The risk of bias was considered to be serious when (1) there was no randomisation or allocation concealment (which applies to NRTs) and either there was imbalance between groups (without adjustment in analyses) or participant characteristics at baseline were not reported, or (2) where outcome assessment was judged to be at high risk of bias because assessors had

knowledge of the allocated intervention (subjective outcomes). Where there were concerns about both domains, or the study also had industry ties, the risk of bias was considered very serious.

2. Inconsistency. We assessed (1) whether there was heterogeneity in the observed intervention effects across studies that suggested important differences in the effect of the intervention (based on point estimates from individual studies and overlap in confidence intervals, but not statistical tests of heterogeneity because we did not combine effect estimates), and (2) whether this could potentially be explained (through qualitative assessment of differences across studies, for example arising from differences in PICO, participant characteristics or study design). Where a single study contributed data for a comparison and outcome, inconsistency was rated as serious and the limitations of interpreting single studies was incorporated when formulating conclusions. This was a deviation from our original plan to rate inconsistency as very serious for single studies.

3. Imprecision. We did not combine effect estimates, therefore imprecision was primarily assessed for individual studies. We examined whether interpretation of the upper and lower confidence limits leads to conflicting interpretations about whether the intervention has a clinically important effect (such studies were considered imprecise). A clinically important difference was judged to be a 30-50% reduction in rates of infection or colonisation. Where conclusions were drawn across studies our assessment was qualitative, based on whether there was sufficient studies with precise effect estimates and consistent direction of effect to be confident about the intervention effects. Such decisions are inherently subjective, especially in the absence of multiple large studies showing large intervention effects.

4. Indirectness. We assessed whether there were important differences between the review questions (PICO) and the characteristics of included studies that may lead to important differences in the intervention effects (i.e. the applicability of the evidence). These assessment took account, for example, of whether outcome data were reported for high risk populations only or hospital wide. In the latter case, we would rate indirectness as serious.

5. Publication bias. Due to the small number of studies included in the review, it was not possible to use graphical or statistical methods (e.g. visual inspection of funnel plots or tests for funnel plot asymmetry) to assess publication bias. Instead, decisions to downgrade because of 'suspected publication bias' were based on whether the evidence was largely comprised of small studies that showed effects favouring intervention.

We planned to use GRADEpro GDT software (www.gradepro.org) to record decisions and derive an overall GRADE (high, moderate, low or very low) for the quality of evidence for each outcome, however because of the small number of studies and no meta-analysis, this proved impractical. We used GRADE rules in which randomised trials begin as 'high' quality evidence (score=4) and can be downgraded by -1 for each domain with serious concerns or -2 for very serious concerns. Non-randomised studies are considered at high risk of bias (and downgraded accordingly). We considered additional criteria for upgrading the quality of evidence in accordance with GRADE guidelines.

Evidence profiles (summary of findings and evidence statements) were prepared with minor a modifications to the template from the GRADEpro GDT software. For each comparison and outcome, the evidence profile includes estimates of treatment effects and the overall GRADE (rating of quality). The evidence profiles also includes (1) the study design(s), number of studies and participants contributing data (i.e. the type and size of the evidence base), (2) our assessment of each of the five GRADE domains (risk of bias, inconsistency, indirectness, imprecision, other considerations including publication bias), and (3) a plain language statement interpreting the evidence (an evidence statement describing clinical impact) for each comparison and outcome. Explanation of the judgements made when downgrading the rating of the quality of the evidence are reported in footnotes.

The plain language evidence statements were formulated using standard phrasing recommended by the Cochrane EPOC group and based on guidance for Cochrane Plain Language Summaries (Table 1).

Table 1 Standard phrasing used in plain language evidence statements (source (Effective Practice and Organisation of Care 2013))

	Important difference	**Small difference (May not be important)**	**Little or no difference**
High certainty evidence	Improves/decreases/ prevents/ leads to [outcome]	Improves slightly/decreases slightly/leads to slightly fewer (more) [outcome]	Results in little or no difference in [outcome]
Moderate certainty evidence	Probably improves/ decreases/ prevents/ leads to [outcome]	Probably improves slightly/decreases slightly/leads to slightly fewer (more) [outcome]	Probably leads to little or no difference in [outcome]
Low certainty evidence	May improve/ decrease/prevent/lead to [outcome]	May slightly improve/slightly decrease/ lead to slightly fewer (more) [outcome]	May lead to little or no difference in [outcome]
Very low certainty evidence	It is uncertain whether [intervention] improves, decreases, prevents, leads to [outcome] because the certainty of the evidence is very low		
No data or no studies	[Outcome] was not measured or not reported, or no studies were found that evaluated the impact of [intervention] on [outcome]		

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Appendices

Appendix 1. Database search strategies

Embase

The search below is for Ovid Embase <1974 to 2016 August 23>and includes records that are unique to MEDLINE.

#	Concept	Query	Results
1	Infections (healthcare-associated)	healthcare associated infection/	2107
2		hospital infection/	37463
3		1 or 2	39251
4		(("health care acquired" adj1 (infection$ or pathogen$)) or ("healthcare acquired" adj1 (infection$ or pathogen$)) or ("hospital acquired" adj1 (infection$ or pathogen$)) or ("health care associated" adj1 (infection$ or pathogen$)) or ("healthcare associated" adj1 (infection$ or pathogen$)) or ("hospital associated" adj1 (infection$ or pathogen$))).ti,ab.	8375
5		(HAI or HAIs).ti.	449
6	Infections (specific terms bacterial	peptoclostridium difficile/	2065
7		clostridium difficile infection/	8503
8		methicillin resistant Staphylococcus aureus/	34931
9		methicillin resistant Staphylococcus aureus infection/	7533
10		enterococcus/	15071
11		vancomycin resistant Enterococcus/	3894
12		enterococcal infection/	1663
13		carbapenemase producing enterobacteriaceae/	384
14		actinobacteria/	8876
15		acinetobacter infection/	1797
16		extended spectrum beta lactamase/	6178
17		6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	78898
18		(((antibiotic or "multi-drug" or multidrug or methicillin or vancomycin) adj1 resistan$) or difficile or ("methicillin resistant" adj2 aureus) or ("vancomycin resistant" adj1 enterococc$)).ti,ab.	123311
19		("carbapenemase producing enterobacteriaceae" or acinetobacter or "extended spectrum beta lactase" or ESBL).ti,ab.	22764
20		(CDI or MRSA or VRE).ti.	6363
21	Limit to patients	exp patient/	1897096
22		(inpatient$ or patient$).ti,ab.	7344555
23		21 or 22	7470985
24		(17 or 18 or 19 or 20) and 23	65695
25	Combine infection sets	3 or 4 or 5 or 24	101084
26	Setting (facilities)	health care facility/	60225
27		hospital discharge/	81865
28		exp hospital/	889884
29		26 or 27 or 28	994208
30		("acute care" or "burn$1 unit" or "common area$1" or "critical care" or "healthcare facility" or "healthcare facilities" or "healthcare setting$1" or "health care setting$1" or hospital$1 or hospitalis$ or hospitaliz$ or ICU or institution$1 or "intensive care" or "patient care area$1" or "medical facility" or "medical facilities" or "patient room$1" or ward$1).ti,ab.	1754394
31	Setting (surfaces)	fomite/	329
32		hospital bed/	3530
33		exp hospital equipment/	81117
34		exp furniture/	24055

35		31 or 32 or 33 or 34	87494
36		(fomes or fomite$ or "environmental reservoir$1" or "surface contamination" or "surface microbes").ti,ab.	2313
37		(bathroom$ or "bed rail$1" or bedrail$ or cart$1 or chair$1 or "clinical surfaces" or commode$ or "environmental surfaces" or "high contact" or "high-touch" or "hospital bed$1" or "hospital surfaces" or "mobile equipment" or "portable medical equipment" or railing or toilet$ or "shared medical equipment" or wheelchair$).ti,ab.	47250
38		(furniture$ or furnishing$ or curtain$).ti,ab.	5189
39	Combine setting sets	29 or 30 or 35 or 36 or 37 or 38	2231743
40	Combine sets infection or setting	25 or 39	2276835
41	General cleaning	cleaning/	7586
42		disinfection/	21319
43		environmental sanitation/	6395
44		*infection control/	27219
45		41 or 42 or 43 or 44	59672
46		("cleaning method$1" or "cleaning practice$1" or "cleaning protocol$1" or "cleaning regimen$1" or "cleaning routines" or "cleaning technique$1" or "discharge cleaning" or "discharge room cleaning" or "enhanced cleaning" or "environmental cleaning" or "environmental decontamination" or "environmental disinfection" or "environmental sanitation" or "hospital cleaning" or "pre cleaning" or precleaning or "room cleaning" or "room decontamination" or "routine cleaning" or "surface cleaning" or "surface disinfection" or "surface decontamination" or "terminal cleaning" or "terminal disinfection" or "terminal room").ti,ab.	3675
47		(cleaning or decontamination or disinfect$ or "infection control").ti.	26037
48	Disinfectants	exp disinfectant agent/	203033
49		bleaching agent/	1380
50		48 or 49	204096
51		(biocidal or biocide$ or "chemical agent$1" or "chemical disinfection" or "cleaning agent$1" or disinfectant$ or "disinfecting agent$1" or "disinfection agent$1" or germicidal or germicide$ or sporicidal or sporicide$).ti,ab.	21008
52		("accelerated hydrogen peroxide" or bleach or bleaching or "calcium hypochlorite" or hypochlorite$ or "sodium hypochlorite").ti,ab.	15974
53		50 or 51 or 52	227456
54	Limit to disinfectant studies to cleaning	(clean$ or decontaminat$ or disinfect$ or housekeep$).ti,ab.	132167
55		53 and 54	19737
56	Automated devices	disinfection system/	115
57		ultraviolet irradiation/	11532
58		ultraviolet radiation/	83874
59		hydrogen peroxide/	74235
60		vapor/	7733
61		water vapor/	6987
62		56 or 57 or 58 or (59 and (60 or 61))	94957
63		((automated adj2 (cleaning or device$ or decontamination or disinfection)) or (("no-touch" or "non touch") adj1 disinfect$) or ("room sterili?ation" or "self disinfecting")).ti,ab.	1728
64		(("pulsed xenon" or ((ultraviolet or UV) adj1 (disinfection or light or irradiation or radiation))) and (clean$ or decontaminat$ or disinfect$ or room$1)).ti,ab.	2360
65		(("superoxidi?ed water" or "electroly?ed water" or ("hydrogen peroxide" or H2O2)) and (aerosol$ or fogging or mist or steam or system$1 or vapor$ or vapour$)).ti,ab.	17829
66	Enhanced coatings and surfaces	copper/	95566
67		material coating/	12219

68		66 and 67	180
69		(("self disinfecting" or (antimicrobial or copper or silver)) adj2 (coated or coating or impregnated or surface$)).ti,ab.	4133
70	Combine sets (cleaning concepts)	45 or 46 or 47 or 55 or 62 or 63 or 64 or 65 or 68 or 69	197512
71	Combine infection and cleaning concepts	40 and 70	22314
72	Trials filter	Randomized controlled trial/	416927
73		Controlled clinical study/	395470
74		random$.ti,ab.	1117107
75		randomization/	71561
76		intermethod comparison/	211445
77		placebo.ti,ab.	241668
78		(compare or compared or comparison).ti.	425289
79		((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.	1439897
80		(open adj label).ti,ab.	51936
81		((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.	187645
82		double blind procedure/	133477
83		parallel group$1.ti,ab.	18709
84		(crossover or cross over).ti,ab.	82484
85		((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab.	240883
86		(assigned or allocated).ti,ab.	285205
87		(controlled adj7 (study or design or trial)).ti,ab.	249336
88		(volunteer or volunteers).ti,ab.	202985
89		human experiment/	357321
90		trial.ti.	211566
91		or/72-90	3699732
92	Animal studies filter	exp experimental organism/	551028
93		animal tissue/	1037101
94		animal cell/	1211677
95		exp animal disease/	285121
96		exp carnivore disease/	46998
97		exp bird/	221571
98		exp experimental animal welfare/	2921
99		exp animal husbandry/	41172
100		animal behavior/	79051
101		exp animal cell culture/	10628
102		exp mammalian disease/	170834
103		exp mammal/	21046787
104		exp marine species/	4925
105		nonhuman/	4820652
106		animal.hw.	4989598
107		or/92-106	23477323
108		107 not human/	6091716
109	Non-randomised study design filter	exp comparative study/	1137587
110		exp controlled study/	5270883
111		exp experimental study/	19170
112		exp observational study/	95264
113		exp field study/	2198
114		exp pilot study/	100224
115		exp prevention study/	2958
116		exp quasi experimental study/	3096
117		time series analysis/	17371
118		("interrupted time series" or "ITS analys?s" or cohort or "before and after").ti,ab.	813100
119		or/109-118	6734251
120	Combine study design sets	91 or 119	8397668

121	Combine infection control and study design	71 and 120	6426
122	Exclude animal-only records	121 not 108	5658
123	Limit to records added to Embase since 01 Jan 2015	(2015$ or 2016$).ew.	3437428
124		122 and 123	**1204**
125	Identify paediatric records excluded from original AHRQ search (from 2006 onwards)	(adolescen$ or babies or child$ or fetal or infant or infants or neonat$ or newborn$ or NICU or paediatric$ or pediatric$ or school or schools or teen$ or youth$).ti.	1531605
126		limit 125 to yr="2006 -Current"	659844
127		122 and 126	303
128		127 not 124	**215**
129	Identify additional records for bacteria and fittings terms not included in original AHRQ search (from 2006 onwards)	13 or 15 or 16 or (19 and 23) or 34 or 38	42610
130		122 and 129	544
131		limit 130 to yr="2006 -Current"	412
132		131 not 124	**289**
133	Combine sets	124 or 128 or 132	**1679**

Ovid syntax

$	truncation character (unlimited truncation)
$*n*	truncation limited to specified number (*n*) of characters (e.g. time$1 identifies time, timed, timer, times but not timetable)
?	substitutes any letter (e.g. oxidi?ed identifies oxidised and oxidized)
adj*n*	search terms within a specified number (*n*) of words from each other in any order
exp	explodes controlled vocabulary term (i.e. includes all narrower terms in the hierarchy)
/	denotes controlled vocabulary terms (EMTREE)
*	denotes a term that has been searched as a major subject heading
.ti.	limit to title field
.ti,ab.	limit to title and abstract fields
.ew.	entry week to Embase

PubMed

The PubMed search is restricted to records that are not indexed for MEDLINE (i.e. in-process citations and citations from journals (or parts of journals) that are not currently MEDLINE-indexed) and to records added to PubMed since January 2006. The search comprises free-text terms only and replicates the free-text sets in the Embase search (converted from the Ovid syntax).

Date of search: 24/08/16

#	Query	Results[1]
1	((((("health care acquired"[TIAB] AND (infection*[TIAB] OR pathogen*[TIAB])) OR ("healthcare acquired"[TIAB] AND (infection*[TIAB] OR pathogen*[TIAB])) OR ("hospital acquired"[TIAB] AND (infection*[TIAB] OR pathogen*[TIAB])) OR ("health care associated"[TIAB] AND (infection*[TIAB] OR pathogen*[TIAB])) OR ("healthcare associated"[TIAB] AND (infection*[TIAB] OR pathogen*[TIAB])) OR ("hospital associated"[TIAB] AND (infection*[TIAB] OR pathogen*[TIAB]))))))	
2	((HAI[TI] OR HAIs[TI]))	
3	(((((antibiotic[TIAB] OR "multi-drug"[TIAB] OR multidrug[TIAB] OR methicillin[TIAB] OR vancomycin[TIAB]) AND resistan*[TIAB]) OR difficile[TIAB] OR ("methicillin resistant"[TIAB] AND aureus[TIAB]) OR ("vancomycin resistant"[TIAB] AND enterococc*[TIAB]))))	
4	((("carbapenemase producing enterobacteriaceae"[TIAB] OR acinetobacter[TIAB] OR "extended spectrum beta lactase"[TIAB] OR ESBL[TIAB])))	
5	((CDI[TI] OR MRSA[TI] OR VRE[TI]))	
6	((inpatient*[TIAB] OR patient*[TIAB]))	
7	((#3 OR #4 OR #5) AND #6)	
8	(#1 OR #2 OR #7)	

9	(("acute care"[TIAB] OR "burn* unit"[TIAB] OR "common area*"[TIAB] OR "critical care"[TIAB] OR "healthcare facility"[TIAB] OR "healthcare facilities"[TIAB] OR "healthcare setting*"[TIAB] OR "health care setting*"[TIAB] OR hospital*[TIAB] OR hospitalis*[TIAB] OR hospitaliz*[TIAB] OR ICU[TIAB] OR institution*[TIAB] OR "intensive care"[TIAB] OR "patient care area*"☐[TIAB] OR "medical facility"[TIAB] OR "medical facilities"[TIAB] OR "patient room*"[TIAB] OR ward*[TIAB]))	
10	((fomes[TIAB] OR fomite*[TIAB] OR "environmental reservoir*"[TIAB] OR "surface contamination"[TIAB] OR "surface microbes"[TIAB]))	
11	((bathroom*[TIAB] OR "bed rail*"[TIAB] OR bedrail*[TIAB] OR cart*[TIAB] OR chair*[TIAB] OR "clinical surfaces"[TIAB] OR commode*[TIAB] OR "environmental surfaces"[TIAB] OR "high contact"[TIAB] OR "high-touch"[TIAB] OR "hospital bed*"[TIAB] OR "hospital surfaces"[TIAB] OR "mobile equipment"[TIAB] OR "portable medical equipment"[TIAB] OR railing[TIAB] OR toilet*[TIAB] OR "shared medical equipment"[TIAB] OR wheelchair*[TIAB]))	
12	(furniture*[TIAB] OR furnishing*[TIAB] OR curtain*[TIAB])	
13	(#9 OR #10 OR #11 OR #12)	
14	(#8 OR #13)	
15	(("cleaning method*"[TIAB] OR "cleaning practice*"[TIAB] OR "cleaning protocol*"[TIAB] OR "cleaning regimen*"[TIAB] OR "cleaning routines"[TIAB] OR "cleaning technique*"[TIAB] OR "discharge cleaning"[TIAB] OR "discharge room cleaning"[TIAB] OR "enhanced cleaning"[TIAB] OR "environmental cleaning"[TIAB] OR "environmental decontamination"[TIAB] OR "environmental disinfection"[TIAB] OR "environmental sanitation"[TIAB] OR "hospital cleaning"[TIAB] OR "pre cleaning"[TIAB] OR precleaning[TIAB] OR "room cleaning"[TIAB] OR "room decontamination"[TIAB] OR "routine cleaning"[TIAB] OR "surface cleaning"[TIAB] OR "surface disinfection"[TIAB] OR "surface decontamination"[TIAB] OR "terminal cleaning"[TIAB] OR "terminal disinfection"[TIAB] OR "terminal room"[TIAB]))	
16	(cleaning[TI] OR decontamination[TI] OR disinfect*[TI] OR "infection control"[TI])	
17	((biocidal[TIAB] OR biocide*[TIAB] OR "chemical agent*"[TIAB] OR "chemical disinfection"[TIAB] OR "cleaning agent*"[TIAB] OR disinfectant*[TIAB] OR "disinfecting agent*"[TIAB] OR "disinfection agent*"[TIAB] OR germicidal[TIAB] OR germicide*[TIAB] OR sporicidal[TIAB] OR sporicide*[TIAB]))	
18	(("accelerated hydrogen peroxide"[TIAB] OR bleach[TIAB] OR bleaching[TIAB] OR "calcium hypochlorite"[TIAB] OR hypochlorite*[TIAB] OR "sodium hypochlorite"[TIAB]))	
19	(#17 OR #18)	
20	((clean*[TIAB] OR decontaminat*[TIAB] OR disinfect*[TIAB] OR housekeep*[TIAB]))	
21	(#19 AND #20)	
22	(((automated[TIAB] AND (cleaning[TIAB] OR device*[TIAB] OR decontamination[TIAB] OR disinfection[TIAB])) OR (("no-touch"[TIAB] OR "non touch"[TIAB]) AND disinfect*[TIAB]) OR ("room sterilization"[TIAB] OR "room sterilisation"[TIAB] OR "self disinfecting"[TIAB])))	
23	((("pulsed xenon"[TIAB] OR ((ultraviolet[TIAB] OR UV[TIAB]) AND (disinfection[TIAB] OR light[TIAB] OR irradiation[TIAB] OR radiation[TIAB]))) and (clean*[TIAB] OR decontaminat*[TIAB] OR disinfect*[TIAB] OR room*[TIAB])))	
24	((("superoxidized water"[TIAB] OR "superoxidised water"[TIAB] OR "electrolyzed water"[TIAB] OR "electrolysed water"[TIAB] OR ("hydrogen peroxide"[TIAB] OR H2O2[TIAB])) and (aerosol*[TIAB] OR fogging[TIAB] OR mist[TIAB] OR steam[TIAB] OR system*[TIAB] OR vapor*[TIAB] OR vapour*[TIAB])))	
25	((("self disinfecting"[TIAB] OR (antimicrobial[TIAB] OR copper[TIAB] OR silver[TIAB])) AND (coated[TIAB] OR coating[TIAB] OR impregnated[TIAB] OR surface*[TIAB])))	
26	(#15 OR #16 OR #21 OR #22 OR #23 OR #24 OR #25)	
27	(#14 AND #26)	
28	(2006/01:2016/08[EDAT] AND pubmednotmedline[SB])	
29	(#27 AND #28)	**274**

[1] Saved searches in PubMed are rendered as a single search string, not individual search lines.

PubMed syntax

*	truncation character (unlimited truncation)
[TI]	limit to title field
[TIAB]	limit to title and abstract fields
[EDAT]	date citation added to PubMed
[SB]	PubMed subset

Cochrane Central Register of Controlled Trials

The search is restricted to free-text terms since MEDLINE-indexed records will been have been identified through the Embase search. The search also excludes records indexed with randomized controlled trial as a publication type to remove records from MEDLINE and Embase, as these too will have been identified through the Embase search.

Date of search: 24/08/16

#	Query	Results[2]
#1	(("health care acquired" near/1 (infection or pathogen)) or ("healthcare acquired" near/1 (infection or pathogen)) or ("hospital acquired" near/1 (infection or pathogen)) or ("health care associated" near/1 (infection or pathogen)) or ("healthcare associated" near/1 (infection or pathogen)) or ("hospital associated" near/1 (infection or pathogen))):ti,ab,kw (Word variations have been searched)	192
#2	(HAI or HAIs):ti,ab,kw (Word variations have been searched)	335
#3	(((antibiotic or "multi-drug" or multidrug or methicillin or vancomycin) near/1 resistan*) or difficile or ("methicillin resistant" near/2 aureus) or ("vancomycin resistant" near/1 enterococc*)):ti,ab,kw (Word variations have been searched)	3032
#4	("carbapenemase producing enterobacteriaceae" or acinetobacter or "extended spectrum beta lactase" or ESBL):ti,ab,kw (Word variations have been searched)	264
#5	(CDI or MRSA or VRE):ti,ab,kw (Word variations have been searched)	692
#6	(inpatient or patient):ti,ab,kw (Word variations have been searched)	527250
#7	(#3 or #4 or #5) and #6	2371
#8	#1 or #2 or #7	2838
#9	("acute care" or "burn unit" or "burns unit" or "common area" or "common areas" or "critical care" or "healthcare facility" or "healthcare facilities" or "healthcare setting" or "healthcare settings" or "health care setting" or hospital or hospitalis* or hospitaliz* or ICU or institution or "intensive care" or "patient care area" or "patient care areas" or "medical facility" or "medical facilities" or "patient room" or "patient rooms" or ward):ti,ab,kw (Word variations have been searched)	97208
#10	(fomes or fomite or "environmental reservoir" or "environmental reservoirs" or "surface contamination" or "surface microbes"):ti,ab,kw (Word variations have been searched)	14
#11	(bathroom or "bed rail" or "bed rails" or bedrail or cart or chair or "clinical surfaces" or commode or "environmental surfaces" or "high contact" or "high-touch" or "hospital bed" or "hospital beds" or "hospital surfaces" or "mobile equipment" or "portable medical equipment" or railing or toilet or "shared medical equipment" or wheelchair):ti,ab,kw (Word variations have been searched)	2385
#12	(furniture or furnishing or curtain):ti,ab,kw (Word variations have been searched)	283
#13	#9 or #10 or #11 or #12	99163
#14	#8 or #13	101021
#15	("cleaning method" or "cleaning methods" or "cleaning practice" or "cleaning practices" or "cleaning protocol" or "cleaning protocols" or "cleaning regimen" or "cleaning regimens" or "cleaning routines" or "cleaning technique" or "cleaning techniques" or "discharge cleaning" or "discharge room cleaning" or "enhanced cleaning" or "environmental cleaning" or "environmental decontamination" or "environmental disinfection" or "environmental sanitation" or "hospital cleaning" or "pre cleaning" or precleaning or "room cleaning" or "room decontamination" or "routine cleaning" or "surface cleaning" or "surface disinfection" or "surface decontamination" or "terminal cleaning" or "terminal disinfection" or "terminal room"):ti,ab,kw (Word variations have been searched)	155
#16	(cleaning or decontamination or disinfect* or "infection control"):ti,ab,kw (Word variations have been searched)	5289
#17	(biocidal or biocide or "chemical agent" or "chemical agents" or "chemical disinfection" or "cleaning agent" or "cleaning agents" or disinfectant or "disinfecting agent" or "disinfecting agents" or "disinfection agent" or "disinfection agents" or germicidal or germicide or sporicidal or sporicide):ti,ab,kw (Word variations have been searched)	591
#18	("accelerated hydrogen peroxide" or bleach or bleaching or "calcium hypochlorite" or hypochlorite or "sodium hypochlorite"):ti,ab,kw (Word variations have been searched)	1093
#19	(clean* or decontaminat* or disinfect* or housekeep*):ti,ab,kw (Word variations have been searched)	5341

#20	(#17 or #18) and #19	621
#21	((automated near/2 (cleaning or device or decontamination or disinfection)) or (("no-touch" or "non touch") near/1 disinfect*) or ("room sterilisation" or "room sterilization" or "self disinfecting")):ti,ab,kw (Word variations have been searched)	126
#22	(("pulsed xenon" or ((ultraviolet or UV) near/1 (disinfection or light or irradiation or radiation))) and (clean* or decontaminat* or disinfect* or room)):ti,ab,kw (Word variations have been searched)	28
#23	(("superoxidised water" or "superoxidized water" or "electrolyzed water" or "electrolysed water" or ("hydrogen peroxide" or H2O2)) and (aerosol or fogging or mist or steam or system or vapor or vapour)):ti,ab,kw (Word variations have been searched)	170
#24	(("self disinfecting" or (antimicrobial or copper or silver)) near/2 (coated or coating or impregnated or surface)):ti,ab,kw (Word variations have been searched)	233
#25	#15 or #16 or #19 or #21 or #22 or #23 or #24	6864
#26	#14 and #25	1518
#27	randomized controlled trial:pt (Word variations have been searched)	396856
#28	#26 not #27 Publication Year from 2006 to 2016	**504 (367)**

[2] These searches reflect results across all databases in the Cochrane Library. Of the 504 records in the final set, 367 were retrieved from the Trials database

CINAHL Plus (via EBSCO)

Search excludes records that are also indexed in MEDLINE. For 2015-2016, searches were not limited to study design terms. For 2006-2014, the additional terms excluded from the original AHRQ report were included and a study design limit applied (S59 to S71).

Date of search: 24/08/16

#	Query	Results
S71	S69 AND S70 Limiters - Exclude MEDLINE records	**79**
S70	(MH "Study Design+")	46,267
S69	S62 OR S68	1,268
S68	S67 NOT S58	342
S67	S54 AND S65	360
S66	S54 AND S65	480
S65	S63 OR S64	5,487
S64	S24 OR S29	4,363
S63	S11 AND S15	1,126
S62	S61 NOT S58	940
S61	S54 AND S60	1,014
S60	TI adolescen* or babies or child* or fetal or infant or infants or neonat* or newborn* or NICU or paediatric* or pediatric* or school or schools or teen* or youth*	285,600
S59	EM 2006* OR EM 2007* OR EM 2008* OR EM 2009* or EM 2010* OR EM 2011* OR EM 2012* OR EM 2013* OR EM 2014*	1,192,123
S58	S54 AND S57 Limiters - Exclude MEDLINE records	**989**
S57	S55 OR S56	206,350
S56	EM 2016*	82,863
S55	EM 2015*	123,487
S54	S31 AND S53	23,746
S53	S36 OR S37 OR S38 OR S39 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52	66,661
S52	(("self disinfecting" or (antimicrobial or copper or silver)) N2 (coated or coating or impregnated or surface))	373
S51	(MH "Copper")	1,403
S50	(("superoxidised water" or "superoxidized water" or "electrolyzed water" or "electrolysed water" or ("hydrogen peroxide" or H2O2)) and (aerosol or fogging or mist or steam or system or vapor or vapour))	352
S49	(("pulsed xenon" or ((ultraviolet or UV) N1 (disinfection or light or irradiation or radiation))) and (clean* or decontaminat* or disinfect* or room))	183
S48	((automated N2 (cleaning or device or decontamination or disinfection)) or (("no-touch" or	353

	"non touch") N1 disinfect*) or ("room sterilisation" or "room sterilization" or "self disinfecting"))	
S47	(MH "Hydrogen Peroxide")	1,424
S46	S44 AND S45	3,004
S45	(clean* or decontaminat* or disinfect* or housekeep*)	21,208
S44	S41 OR S42 OR S43	4,824
S43	("accelerated hydrogen peroxide" or bleach or bleaching or "calcium hypochlorite" or hypochlorite or "sodium hypochlorite")	2,013
S42	(biocidal or biocide or "chemical agent" or "chemical agents" or "chemical disinfection" or "cleaning agent" or "cleaning agents" or disinfectant or "disinfecting agent" or "disinfecting agents" or "disinfection agent" or "disinfection agents" or germicidal or germicide or sporicidal or sporicide)	3,047
S41	S40	614
S40	(MH "Sodium Hypochlorite")	614
S39	(MH "Disinfectants")	2,099
S38	TI (cleaning or decontamination or disinfect* or "infection control")	8,102
S37	("cleaning method" or "cleaning methods" or "cleaning practice" or "cleaning practices" or "cleaning protocol" or "cleaning protocols" or "cleaning regimen" or "cleaning regimens" or "cleaning routines" or "cleaning technique" or "cleaning techniques" or "discharge cleaning" or "discharge room cleaning" or "enhanced cleaning" or "environmental cleaning" or "environmental decontamination" or "environmental disinfection" or "environmental sanitation" or "hospital cleaning" or "pre cleaning" or precleaning or "room cleaning" or "room decontamination" or "routine cleaning" or "surface cleaning" or "surface disinfection" or "surface decontamination" or "terminal cleaning" or "terminal disinfection" or "terminal room")	833
S36	S32 OR S33 OR S34 OR S35	62,043
S35	(MH "Infection Control+")	52,491
S34	(MH "Sanitation+")	10,019
S33	(MH "Sterilization and Disinfection+")	8,215
S32	(MH "Cleaning Compounds")	812
S31	S18 OR S30	609,064
S30	S21 OR S22 OR S26 OR S27 OR S28 OR S29	594,563
S29	(furniture or furnishing or curtain)	4,325
S28	(bathroom or "bed rail" or "bed rails" or bedrail or cart or chair or "clinical surfaces" or commode or "environmental surfaces" or "high contact" or "high-touch" or "hospital bed" or "hospital beds" or "hospital surfaces" or "mobile equipment" or "portable medical equipment" or railing or toilet or "shared medical equipment" or wheelchair)	15,111
S27	(fomes or fomite or "environmental reservoir" or "environmental reservoirs" or "surface contamination" or "surface microbes")	281
S26	S23 OR S24 OR S25	7,427
S25	(MH "Floors and Floorcoverings")	290
S24	(MH "Interior Design and Furnishings+")	3,722
S23	(MH "Beds and Mattresses+")	3,499
S22	("acute care" or "burn unit" or "burns unit" or "common area" or "common areas" or "critical care" or "healthcare facility" or "healthcare facilities" or "healthcare setting" or "healthcare settings" or "health care setting" or hospital or hospitalis* or hospitaliz* or ICU or institution or "intensive care" or "patient care area" or "patient care areas" or "medical facility" or "medical facilities" or "patient room" or "patient rooms" or ward)	416,501
S21	S19 OR S20	325,527
S20	(MH "Hospitals+")	84,785
S19	(MH "Health Facilities+")	325,527
S18	S1 OR S2 OR S3 OR S17	33,643
S17	S15 AND S16	9,562
S16	S9 OR S10 OR S11 OR S12	24,771
S15	S13 OR S14	1,221,750
S14	(inpatient* or patient*)	1,205,754
S13	(MH "Patients+")	195,306
S12	TI (CDI or MRSA or VRE)	2,325
S11	("carbapenemase producing enterobacteriaceae" or actinobacteria or acinetobacter or "extended spectrum beta lactase" or ESBL)	2,133
S10	(((antibiotic or "multi-drug" or multidrug or methicillin or vancomycin) N1 resistan*) or difficile or ("methicillin resistant" N2 aureus) or ("vancomycin resistant" N1 enterococc*))	19,016
S9	S4 OR S5 OR S6 OR S7 OR S8	10,818
S8	(MH "Actinobacteria+")	55

S7	(MH "Vancomycin Resistant Enterococci")	84
S6	(MH "Enterococcus+")	1,355
S5	(MH "Methicillin-Resistant Staphylococcus Aureus")	3,497
S4	(MH "Clostridium Infections+") OR (MH "Clostridium Difficile")	6,521
S3	HAI or HAIs	882
S2	(("health care acquired" N1 (infection or pathogen)) or ("healthcare acquired" N1 (infection or pathogen)) or ("hospital acquired" N1 (infection or pathogen)) or ("health care associated" N1 (infection or pathogen)) or ("healthcare associated" N1 (infection or pathogen)) or ("hospital associated" N1 (infection or pathogen)))	2,887
S1	(MH "Cross Infection+")	26,028

ClinicalTrials.gov

Date of search: 02/11/16

#	Query	Results
	("hospital acquired infection" OR "hospital-associated infection" OR "healthcare acquired infection" OR "healthcare associated infection" OR "HAI" OR "Multidrug Resistant" OR "MDRO" OR "Clostridium difficile")	1292
	The above search was combined with the terms below	
	"Antimicrobial"	433
	"Silver"	7
	"Copper"	5
	"Bleach"	1
	"Hydrogen peroxide"	3
	"UV" or "ultraviolet" or "ultra violet"	5
	"electrolysed" or "electrolyse" or "electrolyzed" or "electrolyze"	1
	Total unique records screened	**445**

Appendix 2. Intervention data collection mapped to TIDieR reporting items

TIDieR item	Infection control review item and subheadings	Notes (not all in DE form, additional guidance)
1. **Name**	Name or label used for the intervention	
2. **Why** – rationale, goal	What mechanism of action or rationale was provided for the intervention? [verbatim extract or precis]	Use for background, not in table reporting characteristics of included studies.
What 3. Materials	Materials • Equipment or physical materials • Dilution/preparation/composition	
4. Procedures	Procedures - Process	See additional elements under who provided, when & how much.
5. **Who provided** – including expertise, specialist training	Procedures – Personnel - note if a specialist or training required	
6. **How** – modes of delivery	Procedures - Process	
7. **Where** – types of location where intervention occurred	Facilities disinfected (or using antimicrobial materials) – units or wards or rooms Location (country, hospital location and description) Surfaces disinfected (or using antimicrobial materials)	[e.g. ward, patient room, isolation room; indicate if terminal clean]
8. **When & how much** – schedule, duration, intensity, dose	Procedures - Frequency of process Procedures - Duration of process/contact time	
9. **Tailoring** – if planned, what, why, when, how	Not collected other than if described under procedures.	Any changes to procedures etc for different pathogens, risk groups, other?
10. **Modifications** – if occurred, describe (what, why, when, how)	Did the investigators modify the intervention in any way during the intervention period? [verbatim extract or precis]	
How well 11. **Planned** – if adherence to protocol assessed, how, by whom, any attempt to increase adherence	Was there any assessment of *adherence to planned protocols* for disinfection or use of materials? [verbatim extract]	Including assessment of bacterial contamination of surfaces (measure of treatment fidelity)
12. **Actual** - if adherence to protocol assessed, describe extent to which intervention delivered a planned?	If 'yes' to previous, what were the findings (i.e. to what extent was there *adherence to/deviation from protocol*)? [verbatim extract]	Note availability of quantitative data on contamination of surfaces, but don't report data or analyses (typically covers all sites sampled, multiple time points).

Appendix 3. Changes to protocol

Types of surfaces

We added textiles to the list of eligible surfaces to clarify that this fell within our definition of porous high-touch surfaces, as follows: "Textiles used, for example, in patient linen or gowns, surgical scrubs

Types of outcomes

Because of the sparsity of evidence on this topic, we broadened our inclusion criteria to include studies that measured any hospital-acquired infection, not just those arising from the list of pre-specified pathogens. The implications of this decision were that we were able to include (1) the a second study in the review (von Dessaur 2016), and (2) ensure we included the primary outcome from Salgado 2013 (any HAI or colonisation). This decision was taken after we had screened studies (so we were aware that the change would lead to inclusion of von Dessaur) but before extracting or analysing any results data. We re-checked all inclusion decisions to ensure no other eligible studies had been excluded on this basis.

Search methods

As described in the methods, we decided not to search OpenGrey and the WHO ICTRP trials register because of the difficulty of constructing searches of these sources for the review topic and the low likelihood that included studies would have been retrieved through alternative sources.

GRADE assessment

We were unable to meta-analyse studies (as no RTs were included in the review), which had implications for the way in which GRADE was applied. We therefore revised the description of the GRADE process to clarify how GRADE was applied to single studies (especially regarding assessment of imprecision and reporting of effects from time series studies), and how conclusions were drawn across time series studies.

Appendix 4. Characteristics of included studies

Study ID Salgado 2013

Study design(s)	Non-randomised trial
Setting / Population	Units: rooms in intensive care units (8 intervention rooms; 8 control rooms) in three hospitals. Within each hospital, intervention rooms were adjacent to control rooms. Number of patients: n=614 contributed data for analysis (n= 294 in rooms with copper-surfaced objects; n=320 in rooms without copper-surfaced objects) Location: USA. Participating hospitals: tertiary care academic hospital (660 beds; 17 medical ICU beds, 3 intervention and 3 control rooms); academic cancer hospital (460 beds; 20 medical-surgical ICU beds, 3 intervention and 3 control rooms); Veterans' Affairs hospital (98 beds; 8 medical ICU beds, 2 intervention and 2 control rooms).
Intervention(s)	Rooms fitted with copper alloy-surfaced objects (e.g. bedrails, intravenous poles)
	July 12, 2010, and June 14, 2011 (12 months)
	Materials: copper alloy-surfaced objects, fabricated by the same manufacturers for each site. The alloys used were registered with the US Environmental Protection Agency (EPA) as antimicrobial materials. The copper-surfaced objects were installed 9 months prior to the commencement of the trial. Composition: "..solid copper alloys [were] selected on the basis of ease of fabrication for each component, durability, ability to withstand cleaning, and aesthetics." (p481)
	Concurrent cleaning/disinfection process: Pre-existing cleaning protocols were followed, without additional measures. Hospital-grade disinfectants were used for routine (daily or more frequently) and discharge cleaning. Agents: Virex 256 (Johnson-Diversey) (routine cleaning); Dispatch (Caltech Industries) (rooms occupied by patients with C. difficile); Cavicide (Metrex) (spot cleaning). Frequency of process: daily and discharge cleaning Personnel: Not reported
	Surfaces disinfected: Hard non-porous: frequently touched surfaces that had been shown in an earlier study to have a consistently high bacterial burden. The surfaces were: bed rails, overbed tables, intravenous poles, and arms of visitor chairs (all 3 hospitals); call buttons and bezel of the touchscreen monitor (2 hospitals); computer mouse, and palm rest of a laptop computer (single hospital).
Comparator(s)	Standard-surfaced objects
	Concurrent with intervention: July 2010 - June 2011 (12 months)
	Standard surface objects, with cleaning/disinfection process as per intervention arm.
Adherence	Daily inventories were kept of copper-surfaced objects. Among patients assigned to intervention rooms, 53.4% had at least one copper-surfaced object removed during their ICU stay (most commonly, substitution of copper-surfaced beds). In control rooms, 13.4% had some exposure to copper (most commonly, introduction of copper-surfaced visitor chairs).
Outcomes	Outcome category: Colonisation and/or infection (composite; primary outcome) Outcome (metric): Incident rate of hospital-acquired infection (infection of any type, any pathogen), colonisation (MRSA or VRE), or both (number of patients with outcome per group/total number of patients per group) Level of meaurement: patients randomised to intervention or control rooms Data collection periods: intervention period July 2010 - June 2011 (number of cases reported for 12 month period)

	Data collection methods: Patients were 'prospectively monitored' from ICU admission to discharge, but it is unclear what this monitoring involved or who was responsible. Data were entered into an electronic database (via a web-based form). Routine nasal screening for MRSA occurred at all 3 hospitals; and perirectal screening for VRE at 2 hospitals. HAIs or colonizations were determined by a study clinician at each site, and diagnoses were "validated" by an independent clinician at each site (all patients with an HAI diagnosis; random selection of 2 times as many patients without). Outcome definition (ICU acquired infection or colonisation): infection or colonisation > 48 hours after ICU admission or within 48 hours after ICU discharge. Definitions were based on National Healthcare Safety Network definitions (USA).
	Outcome category: Colonisation (secondary outcome) Outcome (metric): Incident rate of hospital-acquired MRSA or VRE (combined) (number of patients with outcome per group/total number of patients per group) Level of measurement, timing of data collection, data collection methods and outcome definition: As per composite colonisation/infection outcome
Other outcomes	(1) Adverse effects, safety: outcome not reported (2) Hospital-acquired infection only (any type of infection, any pathogen; secondary outcome) (3) ICU length of stay (number of days categorised as 0-2, 3-4, 5-7, >7) (4) Death in the ICU (number) (5) Bacterial contamination of surfaces was measured (weekly samples, all objects including a non-copper object to control for differences in cleaning, all sites).
Pathogen(s)	Any (infection); MRSA or VRE (colonisation)

Risk of bias assessment

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	unclear risk of bias	The authors describe the group allocation as randomised, but do not describe the methods used to generate their allocation sequence: "At admission, respective bed-control services randomly assigned patients to an available ICU study room" (p480). In the trial registry entry, reference to sequential placement of patients into intervention or control rooms suggests that alternate allocation (an inadequate method of sequence generation) may have been used: "patients are sequentially placed into rooms with or without copper-alloy surfaced objects" (NCT01565798).
Allocation concealment (selection bias)	high risk of bias	Bed-control services were responsible for randomly assigning "patients to an available ICU study room" and "were masked as to which rooms contained copper" (p480). However, the mention in the trial registry entry (NCT01565798) of sequential placement of patients into intervention or control rooms, suggests that it may have been possible for bed-control services to guess the group allocation.
Incomplete outcome data (attrition bias) All outcomes	low risk of bias	All missing data were accounted for (Figure 1, p480). Although data were not reported per group, the number of participants for which data were missing was small (36/650).
Knowledge of the allocated interventions adequately prevented during the study (performance and detection	low risk of bias	Detection bias (outcome assessment). The trial registry entry reports the study is 'single blind (Outcomes Assessor)', meaning that outcome assessors were unaware of the intervention (NCT01565798). Outcomes were assessed from data in an electronic database by clinicians masked to intervention group, and independently validated. Although it is possible that treatment teams may have altered their clinical behaviour in response to the intervention (e.g. test ordering to identify colonisation),

Bias	Authors' judgement	Support for judgement
bias)		the intervention was in place 9 months prior to data collection and teams were unaware of the timing of trial data collection. Performance bias. It was not possible to prevent participants and clinical personnel knowing which rooms were allocated to copper-surfaced objects because the objects had a distinct appearance and odour. While movement of copper-surfaced objects into control rooms did occur, it is unlikely that the intervention could be manipulated to enhance intervention effects (any changes would likely diminish effects, by reducing exposure to copper in the intervention group or increasing control group exposure). In both intervention and control rooms, samples were also taken from a non-copper-surfaced objects (bed rail) to identify differences in bacterial contamination that might arise from differences in room cleaning; no differences were identified.
Selective outcome reporting (reporting bias)	low risk of bias	The study was retrospectively registered on clinicaltrials.gov (registration date March 26, 2012; data collection was completed June 14, 2011), and no published protocol for the study was identified. As such it is not possible to confirm whether any outcome data are missing or whether outcomes may have changed (primary and secondary outcomes swapped), however the outcomes appear completely reported, so the study was judged at low risk of bias for this domain.
Other risks of bias	high risk of bias	Several authors declared competing interests that may put the study at risk of bias: (1) three authors were in receipt of a grant or travel support from the Copper Development Association (CDA, an industry body that promotes the use of copper), (2) one author is a staff member of the CDA, (3) two authors consulted for the copper industry. There is no mention of steps taken to safegaurd against potential biases, such as pre-registration of the trial (the trial was retrospectively registered) or publication of a study protocol. Hence the study is considered to be at risk of bias.

Study ID von Dessauer 2016

Study design(s)	Non-randomised trial
Setting / Population	Units: All rooms in a pediatric intensive care unit (PICU; n=4 intervention rooms, n=4 control rooms) and an intermediate pediatric care unit (PIMCU; n=4 intervention rooms, n=4 control rooms). Every alternate rooms was an intervention room. Number of patients: 1012 (N=261 intervention; N=254 control) Location: Chile; 249-bed tertiary hospital.
Intervention(s)	Rooms fitted with copper alloy-surfaced objects (e.g. bedrails, intravenous poles)
	12 November 2012 - 15 November 2013 (~ 12 months)
	Materials: Copper-alloy surfaced items. The alloys used were registered with the US Environmental Protection Agency (EPA) as antimicrobial materials. Composition: brass and ecobrass fittings manufacturers in Chile and the USA.
	Concurrent cleaning/disinfection process: Cleaning and hand hygiene practices followed standard protocols (details not reported), and were the same throughout the study period in both intervention and control rooms. Hand hygiene compliance was monitored, but data were not reported separately for groups.
	Surfaces disinfected: Hard non-porous: bed rails, bed rail levers, intravenous poles, sink handles, nurses' workstation
Comparator(s)	Standard-surfaced objects

	Concurrent with intervention: Nov 2012 - Nov 2013 (12 months)
	Rooms furnished with standard-surfaced items. Cleaning and hand hygiene practices followed standard protocols, as per intervention group.
Adherence	Inventories were kept of copper-surfaced objects (data not reported). Excess occupancy rates in the PICU over a 2 month period (July - August 2013) resulted in non-copper-surfaced items and additional beds in intervention rooms.
Outcomes	Outcome category: Infection Outcome (metric): Incident rate of hospital-acquired infection (any type, any pathogen) (cases per 1,000 patient days) Level of measurement: patients allocated to intervention or control rooms Data collection periods: intervention period 12 November 2012 - 15 November 2013 (data collected throughout 12 month period) Data collection methods: Data collected at entry to unit, then daily until discharge from the unit (including HAI suspicion status). On study completion, a subset of patient records (122/515; 24%) were independently reviewed by an assessor masked to whether the patient was assigned to intervention or control, and unaware of the status of HAI acquisition. Outcome definition: Infection occuring > 72 hours after admission to an intervention or control room. Type of infection was based on standard definitions used by the National Surveillance System of the Ministry of Health of Chile.
Other outcomes	(1) Adverse effects, safety. Monitored skin or other allergic reactions (patients, hospital staff). None were identified. Patient mortality during the course of care. There was no indication of an increase in mortality (n=8 intervention group; n=9 control group). (2) Bacterial contamination of surfaces (bacterial burden; twice monthly from 3 surfaces in all rooms). Outcome reported in Schmidt 2016.
Pathogen(s)	Any (including non-MDROs)

Risk of bias assessment

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	high risk of bias	The study was not randomised (NCT01678612). "On admission, to each unit, patients were sequentially assigned to either an intervened or control room" (p e134) suggests patients were assigned to groups by alternation, although it is not clear whether this method was adhered to. While this method may result in groups with similar characteristics, it is an inadequate method of sequence generation because it is possible for those assigning patients to groups to guess the group to which the patient has been assigned.
Allocation concealment (selection bias)	high risk of bias	The use of alternation (sequential assignment of patient to intervention or control rooms), means it is highly likely that those allocating patients to rooms could influence which patients were placed in intervention rooms.
Incomplete outcome data (attrition bias) All outcomes	high risk of bias	Patients in one control room were excluded from analysis because they were long-term or chronic patients because their inclusion "in the analysis ... would skew the overall study occupancy rate and patient demographics" (p e135). However, these exclusion criteria (upper limit on LoS, or chronic patient) were not pre-specified (NCT01678612). Instead the eligibiility criteria specified that all patients admitted to either ward were eligible for the study, and those with a stay >72 hours would be included in the analysis.

Bias	Authors' judgement	Support for judgement
Knowledge of the allocated interventions adequately prevented during the study (performance and detection bias)	low risk of bias	In the trial registry entry, the study is described as 'open label', meaning that participants, providers and outcome assessors were not masked to the intervention (NCT01678612). It was not possible to blind participants or providers to the allocated intervention. Nor was it possible to mask treatment teams, responsible for assessments of HAIs, to the allocated intervention. The authors state that "the nonblinded characteristic of the study design was a major concern" (p e137), but they took steps to ensure more objective outcome assessment through independent review of patient records (122/515; 24%) by an individual who was masked to whether the patient was assigned to intervention or control, and unaware of the status of HAI acquisition.
Selective outcome reporting (reporting bias)	low risk of bias	The study was prospectively registered (NCT01678612), and outcomes were pre-specified in the registry. One outcome was listed in the registry entry but is not reported here or in the paper by Schmidt 2016: "Other Outcome Measures: Incidence of new events of colonization with selected pathogens per 1000 patient days at risk" (NCT01678612). Given the recency of publication of the two papers arising from this study, it is possible a third paper reporting this outcome is yet to be published.
Other risks of bias	high risk of bias	The authors declared that they had no conflicts of interest to report, although in a previous study (Salgado 2013), one of the authors (M. Schmidt) reported receiving grant funding from the Copper Development Association (CDA) - a not-for-profit industry body - and acting as a consultant to the copper industry. The study was funded by Corporación Nacional del Cobre de Chile (CODELCO), a Chilean state owned copper mining company. There is nothing in the paper to indicate the funders had any involvement in the study; however, study details registered on clinicaltrials.gov were provided by the sponsor, Coldelco (not the Principle investigator) and Coldelco is listed as the party responsible for the study. The study was prospectively registered, but the registry entry is brief and no published protocol was identified. Hence, the study was considered to be at risk of bias because it is not clear that there were safegaurds to protect against potential biases arising from the funders involvement.

Appendix 5. Characteristics of ongoing studies

Study ID Lautenbach 2015

Trial registry number	NCT02627092
Are data available?	No - estimated completion date of study is May 2017 (primary outcome data May 2017)
Study design(s)	Randomised trial
Setting / Population	High risk patients: adults in intensive care unit (No. wards not reported; 424 patients, 18 years and above) One university affiliated hospital Country: USA
Intervention(s)	Copper: copper oxide impregnated textiles (bed linen, patient gowns)
	Surfaces: High touch, porous: bed linen (top and bottom sheet, pillowcase, patient gowns)
Comparator(s)	Standard linen on the bed and as patient gowns
Outcomes	Infection, colonisation or both (primary outcome): incidence rate of MDROs or hospital-acquired infection
Pathogen(s)	Unspecified MDROs

Study ID Shankaran 2015

Trial registry number	NCT02351895
Are data available?	No - estimated completion date of study was August 2015 (primary outcome data Aug 2015)
Study design(s)	Non-randomised trial: cross-over design (3 week washout period)
Setting / Population	High risk patients: adults in intensive care unit (2 wards; 1302 patients, 18 - 90 years) One university affiliated hospital Country: USA
Intervention(s)	Copper: copper impregnated linen on the bed and patient gowns (23 weeks)
	Surfaces: High touch, porous: bed linen, patient gowns
Comparator(s)	Standard linen on the bed and patient gowns (23 weeks)
Outcomes	Infection (secondary outcome): (1) clinical infection (diagnosed by physician, followed by initiation of antibiotic use), (2) infections that meet National Healthcare Safety Network (NHSN) criteria. Primary outcome: antibiotic use.
Pathogen(s)	Unclear (pathogens not reported; may report type of infection, any pathogen)

Appendix 6. Characteristics of excluded studies (near miss exclusions)

Reason for exclusion	Reference	Excluded on 2 or more criteria
INTERVENTION		
Excluded intervention: copper biocide used in an ultra-microfibre cloth or mop	Hamilton, D., A. Foster, L. Ballantyne, P. Kingsmore, D. Bedwell, T. J. Hall, S. S. Hickok, A. Jeanes, P. G. Coen and V. A. Gant (2010). "Performance of ultramicrofibre cleaning technology with or without addition of a novel copper-based biocide." J Hosp Infect 74(1): 62-71.	yes
Excluded intervention: copper biocide	Wilson, A. P., D. Smyth, G. Moore, J. Singleton, R. Jackson, V. Gant, A. Jeanes, S. Shaw, E. James, B. Cooper, G. Kafatos, B. Cookson, M. Singer and G. Bellingan (2011). "The impact of enhanced cleaning within the intensive care unit on contamination of the near-patient environment with hospital pathogens: a randomized crossover study in critical care units in two hospitals." Crit Care Med 39(4): 651-658.	no
Excluded setting: dental surgeries	Ismail, S., S. Perni, J. Pratten, I. Parkin and M. Wilson (2011). "Efficacy of a novel light-activated antimicrobial coating for disinfecting hospital surfaces." Infect Control Hosp Epidemiol 32(11): 1130-1132.	yes
COUNTRY		
Excluded country: Taiwan	Lee WS, Hsieh TC, Shiau JC, Ou TY, Chen FL, Liu YH, Yen MY, Hsueh PR: Bio-Kil, a nano-based disinfectant, reduces environmental bacterial burden and multidrug-resistant organisms in intensive care units. Journal of Microbiology, Immunology and Infection 2016.	no
Excluded country: Taiwan Excluded intervention: long acting surface disinfectant	Yen, M. Y., W. S. Lee, T. C. Hsieh and P. R. Hsueh (2015). "Recent development of nanotechnology for environmental control of colonization due to multidrug-resistant bacteria in healthcare facilities." Journal of Microbiology, Immunology and Infection 48(2 SUPPL. 1): S23-S24.	no
OUTCOME		
Excluded outcome: Bacterial count on healthcare workers' hands (neither infection nor colonisation)	Bearman, G. M. L., A. Rosato, K. Elam, K. Sanogo, M. P. Stevens, C. N. Sessler and R. P. Wenzel (2012) "A crossover trial of antimicrobial scrubs to reduce methicillin-resistant Staphylococcus aureus burden on healthcare worker apparel." Infection control and hospital epidemiology 33, 268-275 DOI: 10.1086/664045.	no
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	Boyce, J. M., N. L. Havill, K. A. Guercia, S. J. Schweon and B. A. Moore (2014). "Evaluation of two organosilane products for sustained antimicrobial activity on high-touch surfaces in patient rooms." Am J Infect Control 42(3): 326-328.	no
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	Casey, A. L., D. Adams, T. J. Karpanen, P. A. Lambert, B. D. Cookson, P. Nightingale, L. Miruszenko, R. Shillam, P. Christian and T. S. Elliott (2010). "Role of copper in reducing hospital environment contamination." J Hosp Infect 74(1): 72-77.	no
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	Chow, W. L., W. W. Lim, F. Y. J. Lim, A. S. Tin, A. Kurup, M. L. Ling, A. L. Tan and B. C. Ong (2010). "Is Titanium dioxide coating an effective adjunct to conventional terminal cleaning in preventing MRSA environmental reconta mination?" Proceedings of Singapore Healthcare 19: S302.	no
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	de Jong. Effect of MVX (Titanium Dioxide) on the Microbial Colonization of Surfaces in an Intensive Care Unit (TITANIC). 2015. NCT02348346	yes
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	Hedin, G., J. Rynback and B. Lore (2010). "Reduction of bacterial surface contamination in the hospital environment by application of a new product with persistent effect." J Hosp Infect 75(2): 112-115.	no
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	Karpanen, T. J., A. L. Casey, P. A. Lambert, B. D. Cookson, P. Nightingale, L. Miruszenko and T. S. Elliott (2012). "The antimicrobial efficacy of copper alloy furnishing in the clinical environment: a crossover study." Infect Control Hosp Epidemiol 33(1): 3-9.	no
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	Karpanen, T. J., A. L. Casey, P. A. Lambert, B. D. Cookson, P. Nightingale, L. Miruszenko and T. S. J. Elliott (2010). "An evaluation of the antimicrobial properties of healthcare fomites (furnishings and equipment) made of copper alloys." Journal of Hospital Infection 76: S34.	no
Excluded outcome: Bacterial	Schmidt, M. G., H. H. Attaway Iii, S. E. Fairey, L. L. Steed, H. T. Michels and C.	no

Reason for exclusion	Reference	Excluded on 2 or more criteria
count on surface (neither infection nor colonisation)	D. Salgado (2013). "Copper continuously limits the concentration of bacteria resident on bed rails within the intensive care unit." Infect Control Hosp Epidemiol 34(5): 530-533.	
Excluded outcome: Bacterial count on surface (neither infection nor colonisation)	Schmidt, M. G., H. H. Attaway, P. A. Sharpe, J. John, Jr., K. A. Sepkowitz, A. Morgan, S. E. Fairey, S. Singh, L. L. Steed, J. R. Cantey, K. D. Freeman, H. T. Michels and C. D. Salgado (2012). "Sustained reduction of microbial burden on common hospital surfaces through introduction of copper." J Clin Microbiol 50(7): 2217-2223.	no

Appendix 7. List of all studies excluded following full text review

1. (2015). "Benefits of Ultraviolet Light as a Room Disinfectant." AACN Bold Voices 7(11): 8-8.
2. (2015). "Prevention Update...Healthcare-Associated Infections." Healthcare Purchasing News 39(5): 20-20.
3. (2015). "Rapid onset of asthma in healthcare workers." Hospital Employee Health 34(9): 100-100.
4. (2016). "Cleaning Agent Leads to Asthma-Like Symptoms." Hospital Infection Control & Prevention 43(8): 95-95.
5. (2016). "New paper supports hydrogen peroxide vapour (HPV) efficacy." Operating Theatre Journal (304): 3-3.
6. Alfa, M. J., E. Lo, A. Wald, C. Dueck, P. DeGagne and G. K. Harding (2010). "Improved eradication of Clostridium difficile spores from toilets of hospitalized patients using an accelerated hydrogen peroxide as the cleaning agent." BMC Infect Dis 10: 268.
7. Alfa, M. J., E. Lo, N. Olson, M. MacRae and L. Buelow-Smith (2015). "Use of a daily disinfectant cleaner instead of a daily cleaner reduced hospital-acquired infection rates." Am J Infect Control 43(2): 141-146.
8. Allen, V., L. Barnes, M. Scott and B. Yoder (2015). "Environmental Disinfection, Monitoring and Training: The Impact of Combined Environmental Hygiene Interventions on Environmental Hygiene and Infection Control Outcomes...42nd Annual Conference Abstracts, APIC 2015, Nashville, TN June 2015." American Journal of Infection Control 43: S42-S43.
9. Andersen, B. M., H. Banrud, E. Boe, O. Bjordal and F. Drangsholt (2006). "Comparison of UV C light and chemicals for disinfection of surfaces in hospital isolation units." Infection Control and Hospital Epidemiology 27(7): 729-734.
10. Anderson, D. J., et al. "Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and Clostridium difficile (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study." The Lancet.
11. Anderson, D. J., M. F. Gergen, E. Smathers, D. J. Sexton, L. F. Chen, D. J. Weber and W. A. Rutala (2013). "Decontamination of targeted pathogens from patient rooms using an automated ultraviolet-C-emitting device." Infect Control Hosp Epidemiol 34(5): 466-471.
12. Anonymous (2015). "Abstracts from the 3rd International Conference on Prevention and Infection Control, ICPIC 2015." Antimicrobial Resistance and Infection Control 4: no pagination.
13. Bache, S. E., M. MacLean, J. G. Anderson, G. Gettinby, J. E. Coia, S. J. MacGregor and I. Taggart (2011). "Laboratory inactivation of healthcare-associated isolates by a visible HINS-light source and its clinical application in the burns unit." Burns 37: S6.
14. Bailey, C., R. Kay, P. Starling, B. Saltford, T. Jones, K. Walsh, V. Samuel, M. Maynard and K. Murray (2015). "A Health System Approach to Improving High Level Disinfection Practices...42nd Annual Conference Abstracts, APIC 2015, Nashville, TN June 2015." American Journal of Infection Control 43: S14-S14.
15. Barbut, F., D. Menuet, M. Verachten and E. Girou (2009). "Comparison of the efficacy of a hydrogen peroxide dry-mist disinfection system and sodium hypochlorite solution for eradication of clostridium difficile spores." Infection Control and Hospital Epidemiology 30(6): 507-514.
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Appendix 8. Abbreviations used in this report

AHRQ	Agency for Healthcare Research and Quality
C. difficile	*Clostridium difficile*
CDAD	*C. difficile* associated diarrhoea (or disease)
CBA	Controlled before-after studies
CLSI	Clinical and Laboratory Standards Institute
CPE	Carbapenemase-producing Enterobacteriaceae
CPE	Cephalosporin-resistant
EPOC	Cochrane Effective Practice and Organisation of Care
ESBL	Extended spectrum beta lactamase
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GRADE	Grading of recommendations assessment, development and evaluation
HAIs	Healthcare-associated infections
HP	Hydrogen peroxide
HPV	Hydrogen peroxide (vapour)
ICGAC	Infection Control Guidelines Advisory Committee
ICU	Intensive care unit
ITS	Interrupted-time-series studies
KPC	Klebsiella pneumoniae carbapenemases (carbapenemase producing gene)
MBLs	metallo-β-lactamases (carbapenemase producing gene)
MIC	Minimum inhibitory concentration
MICU	Medical intensive care unit
MRGN	Multi-resistant Gram-negative
MROs	Multiresistant organisms
MRSA	*Methicillin-resistant Staphylococcus aureus*
NHMRC	National Health and Medical Research Council
NICU	Neonatal intensive care unit
NRT	Non-randomised trials
PCR	Polymerase chain reaction
PICO	Participants/Population, Intervention, Comparator, Outcomes
PICU	Paediatric intensive care unit
RM	Repeated measures
RoB	Risk of bias
RT	Randomised trials
SICU	Surgical intensive care unit
TGA	Therapeutic Goods Administration
the Commission	Australian Commission on Safety and Quality in Health Care
TIDieR	Template for Intervention Description and Replication
UV	Ultra-violet
UVD	Ultra-violet disinfection
VRE	vancomycin resistant enterococcus
WHO ICTRP	World Health Organisation International Clinical Trials Registry Platform