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Systematic review of novel disinfection methods to reduce infection rates in high risk hospitalised populations

Protocol 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 the systematic review described in this protocol. This systematic 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 will be 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 of the review. Wrote the protocol with contributions from other authors as described.
Steve McDonald	Developed the search strategy and wrote the search methods. Critical review of the protocol.
Joanne McKenzie	Developed the analysis plan and wrote the analysis plan and method for reporting treatment effects. Critical review of the protocol.
Allen Cheng	Provided expert clinical advice, especially in relation to eligibility criteria. Critical review of the protocol.
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Kelly Allen	Named reviewer with planned contributions to the selection of studies (screening), data extraction, appraisal of studies.
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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).

1. Background

The National Health and Medical Research Council (NHMRC), in collaboration with the Australian Commission on Safety and Quality in Health Care (the Commission), is updating the 2010 *Australian Guidelines for the Prevention and Control of Infection in Healthcare* (2010 Guidelines) to ensure the Guidelines reflect the best available evidence and are current and relevant for the Australian context. This systematic review is one of several contracted evidence evaluations being undertaken to update or inform new sections of the 2010 Guidelines. Cochrane Australia was contracted to undertake this independent systematic review of selected disinfectant modalities (ultra-violet light, hydrogen peroxide vapour, electrolysed water) to provide the NHMRC and the Commission with assurance that this revision of the Guidelines is grounded in the most up-to-date and relevant scientific evidence.

1.1 Description of the condition and setting

The 2010 Guideline identified healthcare-associated infections (HAIs) as the most common complication affecting patients in hospital. Acquired in healthcare facilities or as a result of healthcare interventions, these infections can cause significant morbidity for patients and are costly to the health system. Infections caused by key hospital pathogens, including multiresistant organisms (MROs) and *Clostridium difficile* are of particular concern (National Health and Medical Research Council 2010). Methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant enterococcus (VRE) are clinically significant as they are associated with increased healthcare costs and poorer patient outcomes (McLaws 2009, Slimings 2014). While less prevalent, carbapenemase-producing enterobacteriaceae (CPE) are resistant to antibiotics used to treat the most serious infection (so called "last resort" antibiotics), so preventing their spread is critical to ensuring ongoing availability of effective antibiotics (Falagas 2009, Weber 2013, Public Health England 2014, Department of Health and Human Services Victoria 2015).

1.2 Description of the intervention and how it might work

Healthcare-associated infections are potentially preventable, and hence the aim of the 2010 Guideline was "to promote and facilitate the overall goal of infection prevention and control ... through the implementation of practices that minimise the risk of transmission of infectious agents" ((National Health and Medical Research Council 2010), p7). Based on "the best available evidence and knowledge of the practicalities of clinical procedures" at the time, the guideline made recommendations about implementing a broad range of interventions. These interventions included standard precautions to be applied at all times, and transmission-based precautions to be implemented "in the presence of suspected or known infectious agents that represent an increased risk of transmission" and in "the management of multi-resistant organisms (MROs) or outbreak situations" ((National Health and Medical Research Council 2010), p11).

Environmental controls, including cleaning and disinfection, are used to prevent transmission of infectious agents to patients occurring either through direct contact with surfaces or indirect contact via an intermediary ((National Health and Medical Research Council 2010), p21). The 2010 Guideline recommends routine cleaning of surfaces with detergent solution as a standard precaution (i.e. a first-line approach that should be used with all patients). Disinfection is

recommended in addition to cleaning as a transmission-based precaution. Its use is recommended "where the suspected or confirmed presence of infectious agents represents an increased risk of transmission" and for the management of MROs (e.g. MRSA, MRGN, VRE). Unlike cleaning with detergent, disinfection involves the use of chemical or physical methods to kill microorganisms (including pathogens) (Rutala 2008, Therapeutic Goods Administration 2012). In Australia, claims of disinfectant properties are subject to regulation by the Therapeutic Goods Administration (TGA) and approved disinfectants are registered after demonstrating compliance with essential principles for quality, safety and performance (Therapeutic Goods Administration 2012).

This review focuses on the use of modes of disinfection that have emerged or undergone further development for use in healthcare facilities subsequent to the review of evidence for the 2010 Guideline. Three novel disinfectant technologies are considered in this review: ultra-violet (UV) light, hydrogen peroxide (HP) vapour and electrolysed water. The review will examine the effects (including harms) of using each of these interventions compared to using a detergent solution (standard care), bleach or both. The review will also examine the effects of bleach, a widely used disinfectant, compared to using a detergent solution.

Ultra-violet light

Ultra-violet light in the UV-C wavelength range (200 to 270 nanometers) has microbiocidal properties against multiple pathogens, including *Clostridium difficile* and other healthcare associated pathogens. Technologies have been developed for automated (no-touch) disinfection of hospital rooms using UV light, and these have been suggested as an adjunct to manual application of disinfectants. The technologies only disinfect areas directly in the UV light and can only be used when rooms are vacated, partly because of the potentially harmful effects of UV exposure (Leas 2015).

Hydrogen peroxide vapour/mist

Hydrogen peroxide has microbiocidal properties against multiple pathogens, including *Clostridium difficile.* Automated (no touch) systems for producing hydrogen peroxide vapour and hydrogen peroxide dry mist are designed to disinfect by dispersing vapour or mist evenly across a room. As with UV light, the systems can only be used when rooms are vacated (Leas 2015). Hydrogen peroxide has been suggested to have low toxicity, however previous reviews found little or no evidence about the safety of no-touch hydrogen-peroxide producing systems (Leas 2015).

Electrolysed water

Electrolysed water systems pass an electric current through tap water with added salt to produce neutral electrolysed water. Electrolysed water has antimicrobial properties that have led to use in other industries (e.g. food production), where advantages are suggested to include not needing hazardous chemicals, ease of handling and low operating costs (Stewart 2014, Leas 2015).

Bleach

Sodium hypochlorite (bleach) is a commonly used chlorine-based disinfectant with broad spectrum antimicrobial properties. Bleach may cause irritation to skin, eyes and other mucous membranes. It can also corrode metals and discolour or stain fabrics (Leas 2015).

2. Objectives

To examine the effect of ultra-violet (UV) light, hydrogen peroxide (HP) vapour and/or electrolysed water on infection rates in high risk population groups compared with standard care (cleaning with detergent, disinfection with bleach, or both).

To examine the effect of disinfection with bleach on infection rates in high risk population groups compared with cleaning with detergent.

3. Methods

Methods reported in this protocol are based on the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), and address additional methodological considerations pertinent to public health questions where appropriate (Armstrong 2011). The protocol is reported in accordance with the PRISMA-P statement (Moher 2015, Shamseer 2015). Covidence, a web-based platform for the producing systematic reviews, will be used to store data that are compatible with the Covidence data collection tools. RevMan files will be provided for the main analyses and summary of findings tables.

3.1 Criteria for considering studies for this review

3.1.1 Types of participants

High risk population groups, defined in the 2010 Guideline as "patients with an increased probability of infection due to their underlying medical condition." ((National Health and Medical Research Council 2010), p261)

Examples of high risk population groups are:

- patients in intensive care units (ICU)
- oncology, haematology, burns and renal patients
- patients who have received a solid organ transplantation (especially liver)
- neonates
- patients in any ward where there is a known outbreak of an eligible pathogen.

A high risk ward will be defined as one that has a predominant population of high risk patients.

3.1.2 Types of settings

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

Inclusion of studies involving sub-acute and non-acute care will be limited to the following:

- Rehabilitation care (e.g. rehabilitation provided on an acute care ward or in a dedicated facility)
- Transitional aged care and sub-acute geriatric care (delivered in an acute care ward).

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 will be excluded.

Geographical restrictions: Studies must be set in countries with health systems broadly comparable to those in Australia, especially in terms of the healthcare facilities and resourcing. These countries include:

- Australia
- New Zealand
- Europe
- Canada
- United States of America, and
- Other countries with broadly comparable heath systems.

Studies set in low or middle income countries will generally be excluded, unless there is information demonstrating that the setting is comparable to hospitals in Australia.

3.1.3 Types of interventions

Studies evaluating the effects of the following agents or modalities for disinfection will be eligible for inclusion.

- Bleach (sodium hypochlorite): preparations of sodium hypochlorite, at any concentration, applied using any method and at any frequency.
- Automated ('no touch') systems or modalities of room decontamination involving ultra-violet light (UV light devices) or hydrogen peroxide vapour (HP vapour, HP mist and other systems).
- Electrolysed water. applied using any method and at any frequency.

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

Types of surfaces
Eligible studies must involve interventions for use in patient surroundings, defined in the 2010 Guideline 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).

Eligible surfaces must be high-touch (high-risk or frequently touched) surfaces. Hard nonporous surfaces and porous surfaces are eligible, such as:

- Bed rails, bedside tables, over-bed tables, chairs, mattresses, bed curtains (but not window curtains or blinds), bedside commodes, doorknobs, light switches, ensuite facilities
- Intra-venous stands/poles, medical equipment (e.g. pumps, monitors), knobs, buttons.

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

3.1.4 Types of comparators

For studies testing the effects of UV light, HP vapour or electrolysed water, eligible comparators are those considered as the standard of care.

- *Detergents:* Cleaning with a detergent solution is generally the standard of care for routine infection control and prevention. Agents explicitly described as detergents (or detergent solutions) will be considered for inclusion. Any type or preparation of detergent, applied using any method and at any frequency, will be eligible. Information reported in the study will be used to confirm that the agent is a detergent (for cleaning not disinfection; no antimicrobial claims on the label (Rutala 2008, Therapeutic Goods Administration 2012). Where this information is not reported, agents described as detergents will be assumed to meet this definition.
- *Bleach (sodium hypochlorite)*: Bleach disinfection is generally the standard of care for patients known to have significant organisms (an MRO or *C. difficile*) or in outbreaks. Preparations of sodium hypochlorite, at any concentration, applied using any method and at any frequency will be eligible comparators (for UV light, HP vapour, electrolysed water only).

- A combination of both (i.e. detergent-based cleaning, then bleach disinfection).

Where the intervention arm includes any of the above, the preparation, frequency and methods of cleaning should be the same in both arms.

Studies that directly compare the effects of two or more of the interventions eligible for this review will also be excluded.

3.1.5 Types of outcome measures

Primary outcome

Healthcare associated infection arising from the following pathogens:

- *Clostridium difficile* (*C. difficile*)
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin resistant enterococcus (VRE)
- *Acinetobacter sp*.
- 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).

Studies reporting infection as an outcome will be 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 may be determined through clinical evaluation of symptoms, physical signs of infection, or laboratory test results (Lewis 2016).

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 will be included irrespective of the metric reported (e.g. the proportion of patients positive for colonisation of the pathogen).

Studies that report a composite of infection and colonisation, and those reporting unconfirmed infection, will also be considered for inclusion but will be analysed separately.

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

Adverse effects
Data on adverse effects (harms) will be collected and included in our synthesis when the data are reported in studies that measure at least one of the primary or secondary outcomes (i.e. infection, colonisation), or in eligible studies that explicitly aim to examine adverse effects.

3.1.6 Types of studies

Eligible studies are those designed to examine treatment effects. 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 are expected to be randomised at cluster level (i.e. at the hospital or ward level) rather than individual level. However, trials will not be 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 a clearly defined time point at which the intervention was introduced and at least three outcome measures before and after intervention. 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 at least two intervention and two control clusters to be eligible.

Studies using other designs (uncontrolled before-after and cross sectional studies) will be excluded because it is difficult (if not impossible) to attribute observed changes in outcomes to the intervention (Effective Practice and Organisation of Care 2013). Uncontrolled before-after studies are studies without a control group, in which outcomes are measured before and after intervention.

Date and language restrictions. Studies published from 2006 onwards will be eligible for inclusion. Studies published in languages other than English will be exclude unless they are randomised trials.

3.2 Search methods for identification of studies

The overall search approach is based on the search methods used for a 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.

Potentially eligible studies published between 2006 and 2014 will be identified from the lists of included and excluded studies from the AHRQ report. The lists will be 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 current. The review will consider both peer reviewed literature, as well as unpublished and grey literature. No language or geographic limitations will be 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 since it now includes all MEDLINE records, there are efficiencies to be gained by searching Embase alone.

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 this review (e.g. cleaning personnel and training; measuring and monitoring cleanliness; and non-bleach disinfectants). We added concepts covered in these 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) (Appendix 1). 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 will search Embase (via Ovid) using the search strategy in Appendix 1. The search strategy has been translated for PubMed (limited to in-process citations and citations not indexed in MEDLINE), the Cochrane Library and CINAHL Plus. We will also search the grey literature database, OpenGrey, and the trial registers, ClinicalTrials.gov and WHO ICTRP.

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

3.2.3 Other sources

The reference lists of eligible studies and any relevant systematic reviews identified will be searched for additional studies. We will use Scopus to do forward citations searches on all eligible studies and systematic reviews.

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 will be imported to EndNote and duplicates removed. Citations will then be 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 or KA) will independently screen citations (titles and abstracts) for inclusion in the review using a pre-tested coding form based on the inclusion criteria (Appendix 2a). Disagreements about eligibility will be resolved through discussion, with involvement of a third reviewer if consensus cannot be reached.

Full-text of all potentially eligible studies will be retrieved and independently screened by two reviewers (SB, JR or KA), with disagreements resolved using the same approach as for citation screening (see Appendix 2b for coding form). Advice may be sought from the review content expert (AC) to confirm eligibility based on PICO or biostatistician (JM) to confirm eligibility based on study design. If a study does not contain sufficient information for a decision to be made about its eligibility, further information may be sought from the study's authors. Citations that do not meet the inclusion criteria will be excluded and the reason for exclusion will be recorded at full-text screening.

Trial registration numbers, author names, and study titles, locations and dates will be used to identify multiple reports arising from the same study.

3.3.2 Data extraction and management

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

Pre-testing of the data extraction and coding form will be done by three reviewers (SB, KA, JR), who will extract 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 will be sought from the review content expert (AC) and biostatistician (JM) to ensure data are extracted as planned. Revisions to the data extraction form will be made as required to maximise the quality and consistency of data collection.

We will extract information relating to the following characteristics of included studies:

- study design
- year conducted
- setting and location
- participant characteristics (including those needed to characterise risk group)
- intervention and comparator characteristics (e.g. materials, procedures, duration of process/contact time, frequency of use, surfaces cleaned)
- outcomes measures (outcome category (infection, colonisation, adverse events), pathogen(s), measurement method/metric, follow-up times)
- results for primary and secondary outcomes (including number of participants/clusters for each measurement), and adverse events
- 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)

3.3.3 Assessment of risk of bias of included studies

Two reviewers (SB, JR or KA) will independently assess 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 will be resolved by discussion, with advice from a third reviewer (SB or JM) if agreement cannot be reached.

For RTs and CTs we will assess 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).

For cluster RTs we will assess additional design-specific domains:

7. imbalance of outcome measures at baseline, and
8. protection against contamination.

We will assess risk of bias in CBA studies using the same domains and criteria applied to RTs (Effective Practice and Organisation of Care 2015). For ITS studies, we will assess risk of bias associated with the following seven domains: intervention independent of other changes; shape of intervention effect pre-specified; intervention unlikely to affect data collection; blinding of outcome assessors to intervention allocation; incomplete outcome data; selective outcome reporting; and other sources of bias (Effective Practice and Organisation of Care 2015).

For each study, we will 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); judgments will be reported by outcome for these domains. Our risk of bias judgments will be described in the characteristics of included studies table.

For GRADE assessments it will be necessary to first draw 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 summarise risk of bias assessments across studies for each outcome. We will follow 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 will be used in determining the overall quality of the body of evidence using GRADE, and the basis for each will be reported as footnotes to the summary of findings tables.

3.3.4 Measures of treatment effect

Randomised trials, non-randomised trials, controlled before-after studies. For binary outcomes (e.g. whether a patient acquired an infection) and count outcomes (e.g. number of episodes of infection) we will report risk ratios and rate ratios (along with 95% confidence intervals), respectively.

Interrupted time series studies. For interrupted time series designs, we will report the following estimates (along with 95% confidence intervals) from regression analyses that adjust for autocorrelation: (i) change in level of the outcome at the first point after the introduction of the intervention (immediate effect of the intervention), (ii) the post-intervention slope minus the pre-intervention slope (long term effect of the intervention).

3.3.5 Unit of analysis issues

In this review, the unit of analysis issues are likely to arise from (i) cluster trials/controlled before-after studies (e.g. allocation of hospital wards to different interventions), (ii) studies with multiple intervention arms, and (iii) interrupted time series designs analysed as before after studies. We will attempt to adjust standard errors from cluster trials that have not appropriately adjusted for potential clustering of participants within clusters in their analysis. The variance of the intervention effects will be inflated by a design effect (DEFF) (Higgins 2011). Calculation of a DEFF involves estimation of an intra-cluster correlation (ICC). Estimates of ICCs will be imputed using estimates from other included trials that report ICCs, or using external estimates (e.g. www.abdn.ac.uk/hsru/research/research-tools/study-design/). Where we make an adjustment to the variance, we will report details of this adjustment.

If more than one comparison from the same trial is eligible for inclusion in the same meta-analysis, we will appropriately reduce the sample size so that participants do not contribute multiply.

For interrupted time series studies that have been inappropriately analysed as before-after studies, but where data are available in graphs or tables in the publication, we will fit time series regression analysis accounting for first order autocorrelation to estimate a change in level of the outcome at the first point after the introduction of the intervention, and the post intervention slope minus the pre-intervention slope, along with 95% confidence intervals for these estimates (Gebski 2012).

3.3.6 Dealing with missing data

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

3.3.7 Assessment of heterogeneity

We will assess heterogeneity visually by inspecting the overlap of confidence intervals on the forest plots, formally test for heterogeneity using the Chi^2 test (using a significance level of $\alpha=0.1$), and quantify heterogeneity using the I^2 statistic (Higgins 2002).

3.3.8 Assessment of reporting biases

In addition to undertaking an extensive search of the literature, we plan to search trial registries (see 'Search methods for identification of studies'). We will compare the outcomes noted in trial registry entries to those in reports to identify discrepancies and any reasons for discrepancies.

We will investigate the potential for small study-study effects (if there are at least 10 trials) using funnel plots, contour-enhanced funnel plots, and formal statistical tests for funnel plot asymmetry. Contour-enhanced funnel plots aid in determining if funnel plot asymmetry is due to publication bias or other factors (Peters 2008). We will use the statistical test proposed by Harbord et al to test for small-study effects (Harbord 2006), and assess the potential impact of small-study effects using cumulative meta-analysis.

3.3.9 Data synthesis

For randomised trials, within each comparison, we will combine effect estimates across studies for each outcome using a random effects model with inverse-variance weighting. We will use the restricted maximum likelihood between-trial variance estimator (Raudenbush 2009) with the Knapp and Hartung adjustment (Knapp 2003). We will not combine effect estimates across outcome categories (i.e. infection, colonisation, and composite outcomes will be analysed separately) or from other study designs.

We will 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. For studies where the results are incompletely reported (e.g. no effect estimate is reported, but the direction of effect is reported along with a p-value), we will report the available information.

Forest plots will be used to visually depict effect estimates, even when these effects are not meta-analysed. If there are a substantial number of incompletely reported results, we will consider other graphical methods such as harvest plots (Ogilvie 2008).

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

For each comparison and outcome, we will assess the quality of the evidence using the GRADE approach. In accordance with the detailed GRADE guidance (Schunemann 2013), the following five domains will be assessed (as briefly summarised below) and a judgement made about whether there are serious, very serious or no concerns in relation to each domain.

1. Risk of bias. Based on the summary assessment across studies for each outcome reported for a comparison (see 'Risk of bias' section).
2. Inconsistency. We will assess (1) whether there is heterogeneity in the observed intervention effects across studies that suggests important differences in the effect of the intervention (based on point estimates, overlap in confidence intervals, and statistical tests of heterogeneity), and (2) whether this can be explained (e.g. by variance in effects across sub groups). Where a single study contributes data for a comparison and outcome, inconsistency will be rated as very serious.
3. Imprecision. We will assess (1) whether interpretation of the upper and lower confidence limits leads to conflicting interpretations about whether the intervention has a clinically important effect, and (2) whether the optimal information size is met (whether the total number of participants included in a meta-analysis is equal to or greater than the number required for an adequately powered trial).
4. Indirectness. We will assess whether there are important differences between the review questions and the characteristics of included studies that may lead to important differences in the intervention effects (i.e. the applicability of the evidence). For example, for the

question focusing on patients at high risk of poor outcome from infection, if included studies only reported combined results for patients irrespective of risk, we would rate indirectness as serious.

5. Publication bias. Our judgement of suspected publication bias will be based on the extent to which the evidence is limited to a small number of small trials, with many showing benefits of the intervention. Publication bias would be suspected in these circumstance.

GRADEpro GDT software (www.gradepro.org) will be used to record decisions and derive an overall GRADE (high, moderate, low or very low) for the quality of evidence for each outcome, using the 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. For non-randomised studies, additional criteria will be considered for upgrading the quality of evidence in accordance with GRADE guidelines.

Summary of findings tables (evidence profiles or evidence statements) will be prepared using the GRADEpro GDT software. For each comparison and outcome, the evidence profile will include estimates of treatment effects reported as absolute and relative risks, and the overall GRADE (rating of quality). The evidence profiles will also include (1) the study design(s), number of studies and number of participants contributing data (the type and size of the evidence base), (2) our assessment of each of the five domains (risk of bias, inconsistency, indirectness, imprecision, other considerations including publication bias), and (3) a plain language statement interpreting the evidence (clinical impact) for each comparison and outcome. Footnotes will be used to explain judgements made about downgrading or upgrading the rating of the quality of the evidence.

4. References

Armstrong, R., E. Waters and J. Doyle (2011). Reviews in health promotion and public health. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). J. Higgins and S. Green, The Cochrane Collaboration.

Australian Commission on Safety and Quality in Health Care (2013). Implementation guide for surveillance of *Clostridium difficile* infection. Canberra, Commonwealth of Australia

Department of Health and Human Services Victoria (2015). Victorian guideline on carbapenemase-producing Enterobacteriaceae. Melbourne https://www2.health.vic.gov.au/Api/downloadmedia/%7B8ED077BE-4006-4854-83DA-5A0606ADD242%7D

Effective Practice and Organisation of Care (2013). Summary assessments of the risk of bias. EPOC Resources for review authors. Oslo, Norwegian Knowledge Centre for the Health Services Available at: http://epoc.cochrane.org/epoc-specific-resources-review-author

Effective Practice and Organisation of Care (2013). What study designs should be included in an EPOC review? EPOC Resources for review authors. Oslo, Norwegian Knowledge Centre for the Health Services Available at: http://epoc.cochrane.org/epoc-specific-resources-review-author

Effective Practice and Organisation of Care (2015). Suggested risk of bias criteria for EPOC reviews. EPOC Resources for review authors. Oslo, Norwegian Knowledge Centre for the Health Services Available at: http://epoc.cochrane.org/epoc-specific-resources-review-author

Falagas, M. E. and D. E. Karageorgopoulos (2009). "Extended-spectrum β-lactamase-producing organisms." Journal of Hospital Infection **73**(4): 345-354.

Gebski, V., K. Ellingson, J. Edwards, J. Jernigan and D. Kleinbaum (2012). "Modelling interrupted time series to evaluate prevention and control of infection in healthcare." Epidemiol Infect **140**(12): 2131-2141.

Guh, A. Y., S. N. Bulens, Y. Mu, J. T. Jacob, J. Reno, J. Scott, L. E. Wilson, E. Vaeth, R. Lynfield, K. M. Shaw, P. M. Vagnone, W. M. Bamberg, S. J. Janelle, G. Dumyati, C. Concannon, Z. Beldavs, M. Cunningham, P. M. Cassidy, E. C. Phipps, N. Kenslow, T. Travis, D. Lonsway, J. K. Rasheed, B. M. Limbago and A. J. Kallen (2015). "Epidemiology of Carbapenem-Resistant Enterobacteriaceae in 7 US Communities, 2012-2013." JAMA **314**(14): 1479-1487.

Harbord, R. M., M. Egger and J. A. Sterne (2006). "A modified test for small-study effects in meta-analyses of controlled trials with binary endpoints." Stat Med **25**(20): 3443-3457.

Higgins, J., J. Deeks and D. Altman (2011). Special topics in statistics. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). J. Higgins and S. Green, The Cochrane Collaboration.

Higgins, J. and S. Green, Eds. (2011). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration.

Higgins, J. P. and S. G. Thompson (2002). "Quantifying heterogeneity in a meta-analysis." Stat Med **21**(11): 1539-1558.

Hoffmann, T., P. Glasziou, V. Barbour and H. Macdonald (2014). "Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide." BMJ **1687**: 1 - 13.

Knapp, G. and J. Hartung (2003). "Improved tests for a random effects meta-regression with a single covariate." Stat Med **22**(17): 2693-2710.

Leas, B., N. Sullivan, J. Han, D. Pegues, J. Kaczmarek and C. Umscheid (2015). Environmental Cleaning for the Prevention of Healthcare-Associated Infections (HAI) Technical Brief No 22 (Prepared by the ECRI Institute – Penn Medicine Evidence-based Practice Center under Contract No 290-2012-00011-I) AHRQ Publication No 15-EHC020-EF. Rockville, MD, Agency for Healthcare Research and Quality**:** 121 http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=2103&pageaction=displayproduct

Lewis, S. R., A. R. Butler, D. J. W. Evans, P. Alderson and A. F. Smith (2016). "Chlorhexidine bathing of the critically ill for the prevention of hospital-acquired infection." Cochrane Database of Systematic Reviews(6).
McLaws, M. L., A. C. Pantle, K. R. Fitzpatrick and C. F. Hughes (2009). "More than hand hygiene is needed to affect methicillin-resistant Staphylococcus aureus clinical indicator rates: clean hands save lives, part IV." Med J Aust **191**(8 Suppl): S26-31.
Moher, D., L. Shamseer, M. Clarke, D. Ghersi, A. Liberati, M. Petticrew, P. Shekelle, L. A. Stewart and P.-P. Group (2015). "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement." Syst Rev **4**(1): 1.
National Health and Medical Research Council (2010). Australian guidelines for the prevention and control of infection in healthcare. Canberra, Commonwealth of Australia
Ogilvie, D., D. Fayter, M. Petticrew, A. Sowden, S. Thomas, M. Whitehead and G. Worthy (2008). "The harvest plot: a method for synthesising evidence about the differential effects of interventions." BMC Med Res Methodol **8**: 8.
Peters, J. L., A. J. Sutton, D. R. Jones, K. R. Abrams and L. Rushton (2008). "Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry." J Clin Epidemiol **61**(10): 991-996.
Public Health England. (2014). "Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae." Retrieved 13 July, 2016, from https://www.gov.uk/government/publications/carbapenemase-producing-enterobacteriaceae-non-acute-and-community-toolkit.
Raudenbush, S., H. Cooper, L. Hedges and J. Valentine (2009). Analyzing effect sizes: random-effects models. The Handbook of Research Synthesis and Meta-Analysis. New York, Rusell Sage Foundation.
Rutala, W. A., D. J. Weber and the Healthcare Infection Control Practices Advisory Committe (HICPAC) (2008). Guideline for disinfection and sterilization in healthcare facilities. Atlanta, CDC, Department of Health and Human Services
Schunemann, H. J., J. Brozek, G. Guyatt and A. D. Oxman, Eds. (2013). Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. Accessed 5 July 2016. Hamilton, Canada, McMaster University.
Shamseer, L., D. Moher, M. Clarke, D. Ghersi, A. Liberati, M. Petticrew, P. Shekelle, L. A. Stewart and P.-P. Group (2015). "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation." BMJ **349**: g7647.
Slimings, C., P. Armstrong, W. D. Beckingham, A. L. Bull, L. Hall, K. J. Kennedy, J. Marquess, R. McCann, A. Menzies, B. G. Mitchell, M. J. Richards, P. C. Smollen, L. Tracey, I. J. Wilkinson, F. L. Wilson, L. J. Worth and T. V. Riley (2014). "Increasing incidence of Clostridium difficile infection, Australia, 2011-2012." Med J Aust **200**(5): 272-276.
Stewart, M., A. Bogusz, J. Hunter, I. Devanny, B. Yip, D. Reid, C. Robertson and S. J. Dancer (2014). "Evaluating use of neutral electrolyzed water for cleaning near-patient surfaces." Infect Control Hosp Epidemiol **35**(12): 1505-1510.
Therapeutic Goods Administration. (2012). "The regulation of disinfectants and sterilants." Retrieved 11 July, 2016, from https://www.tga.gov.au/disinfectants-sterilants.
Weber, D. J., D. Anderson and W. A. Rutala (2013). "The role of the surface environment in healthcare-associated infections." Curr Opin Infect Dis **26**(4): 338-344.

Appendices

Appendix 1 – Database search strategies

Embase

The search below is for Embase via Ovid and includes records that are unique to MEDLINE.

#	Concept	Search Statement
1	Infections (healthcare-associated)	healthcare associated infection/
2		hospital infection/
3		1 or 2
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$))).ti,ab.
5		(HAI or HAIs).ti.
6	Infections (specific terms bacterial	peptoclostridium difficile/
7		clostridium difficile infection/
8		methicillin resistant Staphylococcus aureus/
9		methicillin resistant Staphylococcus aureus infection/
10		enterococcus/
11		vancomycin resistant Enterococcus/
12		enterococcal infection/
13		carbapenemase producing enterobacteriaceae/
14		actinobacteria/
15		acinetobacter infection/
16		extended spectrum beta lactamase/
17		6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18		(((antibiotic or "multi-drug" or multidrug or methicillin or vancomycin) adj1 resistan$) or difficile or ("methicillin resistant" adj2 aureus) or ("vancomycin resistant" adj1 enterococc$)).ti,ab.
19		("carbapenemase producing enterobacteriaceae" or acinetobacter or "extended spectrum beta lactase" or ESBL).ti,ab.
20		(CDI or MRSA or VRE).ti.
21	Limit to patients	exp patient/
22		(inpatient$ or patient$).ti,ab.
23		21 or 22
24		(17 or 18 or 19 or 20) and 23
25	Combine infection sets	3 or 4 or 5 or 24
26	Setting (facilities)	health care facility/
27		hospital discharge/
28		exp hospital/
29		26 or 27 or 28
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.
31	Setting (surfaces)	fomite/
32		hospital bed/
33		exp hospital equipment/
34		exp furniture/
35		31 or 32 or 33 or 34

36		(fomes or fomite$ or "environmental reservoir$1" or "surface contamination" or "surface microbes").ti,ab.
37		(bathroom$ 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$).ti,ab.
38		(furniture$ or furnishing$ or curtain$).ti,ab.
39	Combine setting sets	29 or 30 or 35 or 36 or 37 or 38
40	Combine sets infection or setting	25 or 39
41	General cleaning	cleaning/
42		disinfection/
43		environmental sanitation/
44		*infection control/
45		41 or 42 or 43 or 44
46		("cleaning method$1" or "cleaning practice$1" or "cleaning protocol$1" or "cleaning regimen$1" or "cleaning routines" or "cleaning technique$1" or "discharge cleaning" or "discharge room cleaning" or "enhanced cleaning" or "environmental cleaning" or "environmental decontamination" or "environmental disinfection" or "environmental sanitation" or "hospital cleaning" or "pre cleaning" or precleaning or "room cleaning" or "room decontamination" or "routine cleaning" or "surface cleaning" or "surface disinfection" or "surface decontamination" or "terminal cleaning" or "terminal disinfection" or "terminal room").ti,ab.
47		(cleaning or decontamination or disinfect$ or "infection control").ti.
48	Disinfectants	exp disinfectant agent/
49		bleaching agent/
50		48 or 49
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$).ti,ab.
52		("accelerated hydrogen peroxide" or bleach or bleaching or "calcium hypochlorite" or hypochlorite$ or "sodium hypochlorite").ti,ab.
53		50 or 51 or 52
54	Limit to disinfectant studies to cleaning	(clean$ or decontaminat$ or disinfect$ or housekeep$).ti,ab.
55		53 and 54
56	Automated devices	disinfection system/
57		ultraviolet irradiation/
58		ultraviolet radiation/
59		hydrogen peroxide/
60		vapor/
61		water vapor/
62		56 or 57 or 58 or (59 and (60 or 61))
63		((automated adj2 (cleaning or device$ or decontamination or disinfection)) or (("no-touch" or "non touch") adj1 disinfect$) or ("room sterili?ation" or "self disinfecting")).ti,ab.
64		(("pulsed xenon" or ((ultraviolet or UV) adj1 (disinfection or light or irradiation or radiation))) and (clean$ or decontaminat$ or disinfect$ or room$1)).ti,ab.
65		(("superoxidi?ed water" or "electroly?ed water" or ("hydrogen peroxide" or H2O2)) and (aerosol$ or fogging or mist or steam or system$1 or vapor$ or vapour$)).ti,ab.
66	Enhanced coatings and surfaces	copper/
67		material coating/
68		66 and 67
69		(("self disinfecting" or (antimicrobial or copper or silver)) adj2

		(coated or coating or impregnated or surface$)).ti,ab.
70	Combine sets (cleaning concepts)	45 or 46 or 47 or 55 or 62 or 63 or 64 or 65 or 68 or 69
71	Combine infection and cleaning concepts	40 and 70
72	Trials filter	Randomized controlled trial/
73		Controlled clinical study/
74		random$.ti,ab.
75		randomization/
76		intermethod comparison/
77		placebo.ti,ab.
78		(compare or compared or comparison).ti.
79		((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.
80		(open adj label).ti,ab.
81		((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.
82		double blind procedure/
83		parallel group$1.ti,ab.
84		(crossover or cross over).ti,ab.
85		((assign$ 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.
86		(assigned or allocated).ti,ab.
87		(controlled adj7 (study or design or trial)).ti,ab.
88		(volunteer or volunteers).ti,ab.
89		human experiment/
90		trial.ti.
91		or/72-90
92	Animal studies filter	exp experimental organism/
93		animal tissue/
94		animal cell/
95		exp animal disease/
96		exp carnivore disease/
97		exp bird/
98		exp experimental animal welfare/
99		exp animal husbandry/
100		animal behavior/
101		exp animal cell culture/
102		exp mammalian disease/
103		exp mammal/
104		exp marine species/
105		nonhuman/
106		animal.hw.
107		or/92-106
108		107 not human/
109	Non-randomised study design filter	exp comparative study/
110		exp controlled study/
111		exp experimental study/
112		exp observational study/
113		exp field study/
114		exp pilot study/
115		exp prevention study/
116		exp quasi experimental study/
117		time series analysis/
118		("interrupted time series" or "ITS analys?s" or cohort or "before and after").ti,ab.
119		or/109-118
120	Combine study design sets	91 or 119

121	Combine infection control and study design	71 and 120
122	Exclude animal-only records	121 not 108
123	Limit to records added to Embase since 01 Jan 2015	(2015$ or 2016$).ew.
124		122 and 123
125	Identify paediatric records excluded from original AHRQ search	(adolescen$ 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.
126		limit 125 to yr="2006 -Current"
127		122 and 126
128		127 not 124
129	Identify additional records for bacteria and fittings terms not included in original AHRQ search	13 or 15 or 16 or (19 and 23) or 34 or 38
130		122 and 129
131		limit 130 to yr="2006 -Current"
132		131 not 124

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 1 January 2015. The search comprises free-text terms only, and replicates the free-text sets in the Embase search (converted from the Ovid syntax). For terms and concepts not covered by the AHRQ report, the search was extended to records added since 1 January 2006 (syntax not reported here).

Search	Query
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*â€ [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	(2015/01:2016/07[EDAT] AND pubmednotmedline[SB])
29	(#27 AND #28)

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.

Search	Query
#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)
#2	(HAI or HAIs):ti,ab,kw (Word variations have been searched)
#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)
#4	("carbapenemase producing enterobacteriaceae" or acinetobacter or "extended spectrum beta lactase" or ESBL):ti,ab,kw (Word variations have been searched)
#5	(CDI or MRSA or VRE):ti,ab,kw (Word variations have been searched)
#6	(inpatient or patient):ti,ab,kw (Word variations have been searched)
#7	(#3 or #4 or #5) and #6
#8	#1 or #2 or #7
#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)
#10	(fomes or fomite or "environmental reservoir" or "environmental reservoirs" or "surface contamination" or "surface microbes"):ti,ab,kw (Word variations have been searched)
#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)
#12	(furniture or furnishing or curtain):ti,ab,kw (Word variations have been searched)
#13	#9 or #10 or #11 or #12
#14	#8 or #13
#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)
#16	(cleaning or decontamination or disinfect* or "infection control"):ti,ab,kw (Word variations have been searched)
#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)
#18	("accelerated hydrogen peroxide" or bleach or bleaching or "calcium hypochlorite" or hypochlorite or "sodium hypochlorite"):ti,ab,kw (Word variations have been searched)
#19	(clean* or decontaminat* or disinfect* or housekeep*):ti,ab,kw (Word variations have been searched)
#20	(#17 or #18) and #19

#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)
#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)
#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)
#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)
#25	#15 or #16 or #19 or #21 or #22 or #23 or #24
#26	#14 and #25
#27	randomized controlled trial:pt (Word variations have been searched)
#28	#26 not #27 Publication Year from 2006 to 2016

CINAHL Plus (via EBSCO)

Search excludes records that are also indexed in MEDLINE. For terms and concepts not covered by the AHRQ report, the search was extended to records added since 1 January 2006 and a methodological filter was used (subject headings for study design (exploded) and randomised trials) (syntax not reported here).

Search	Query
S58	S54 AND S57 Limiters - Exclude MEDLINE records
S57	S55 OR S56
S56	EM 2016*
S55	EM 2015*
S54	S31 AND S53
S53	S36 OR S37 OR S38 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52
S52	(("self disinfecting" or (antimicrobial or copper or silver)) N2 (coated or coating or impregnated or surface))
S51	(MH "Copper")
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))
S49	(("pulsed xenon" or ((ultraviolet or UV) N1 (disinfection or light or irradiation or radiation))) and (clean* or decontaminat* or disinfect* or room))
S48	((automated N2 (cleaning or device or decontamination or disinfection)) or (("no-touch" or "non touch") N1 disinfect*) or ("room sterilisation" or "room sterilization" or "self disinfecting"))
S47	(MH "Hydrogen Peroxide")
S46	S44 AND S45
S45	(clean* or decontaminat* or disinfect* or housekeep*)
S44	S41 OR S42 OR S43
S43	("accelerated hydrogen peroxide" or bleach or bleaching or "calcium hypochlorite" or hypochlorite or "sodium hypochlorite")
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)
S41	S40
S40	(MH "Sodium Hypochlorite")
S39	(MH "Disinfectants")
S38	TI (cleaning or decontamination or disinfect* or "infection control")
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")
S36	S32 OR S33 OR S34 OR S35
S35	(MH "Infection Control+")
S34	(MH "Sanitation+")
S33	(MH "Sterilization and Disinfection+")
S32	(MH "Cleaning Compounds")
S31	S18 OR S30
S30	S21 OR S22 OR S26 OR S27 OR S28 OR S29
S29	(furniture or furnishing or curtain)
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)
S27	(fomes or fomite or "environmental reservoir" or "environmental reservoirs" or "surface contamination" or "surface microbes")
S26	S23 OR S24 OR S25
S25	(MH "Floors and Floorcoverings")
S24	(MH "Interior Design and Furnishings+")
S23	(MH "Beds and Mattresses+")
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)
S21	S19 OR S20
S20	(MH "Hospitals+")
S19	(MH "Health Facilities+")
S18	S1 OR S2 OR S3 OR S17
S17	S15 AND S16
S16	S9 OR S10 OR S11 OR S12
S15	S13 OR S14
S14	(inpatient* or patient*)
S13	(MH "Patients+")
S12	TI (CDI or MRSA or VRE)
S11	("carbapenemase producing enterobacteriaceae" or actinobacteria or acinetobacter or "extended spectrum beta lactase" or ESBL)
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*))
S9	S4 OR S5 OR S6 OR S7 OR S8
S8	(MH "Actinobacteria+")
S7	(MH "Vancomycin Resistant Enterococci")
S6	(MH "Enterococcus+")
S5	(MH "Methicillin-Resistant Staphylococcus Aureus")
S4	(MH "Clostridium Infections+") OR (MH "Clostridium Difficile")
S3	HAI or HAIs
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)))
S1	(MH "Cross Infection+")

Appendix 2a – Coding for citation (title and abstract) screening

- Exclude – Clearly irrelevant
- Exclude – Not an eligible intervention [not UV light, HP system, electrolysed water, bleach/hypochlorite]
- Exclude – Not an eligible intervention [not copper, silver, antimicrobial material, altered topography]
- Exclude – Not an eligible country [not high income or potentially equivalent facility]
- Exclude – Not an eligible setting [not hospital-based care; confirm inpatient/admitted based on FT]
- Exclude – Not an eligible study design [only if can CLEARLY rule out an eligible design]
- Include for full text screen – appears to meet all criteria
- Include for full text screen – unclear eligibility for one or more criteria
- Include as secondary – review or useful background paper

Appendix 2b – Additional coding for full text screening

These additional codes are for criteria for which there is not likely to be sufficient information in the abstract to assess

- Exclude – Not an eligible population [not high risk]
- Exclude – Not an eligible comparator [not detergent, bleach or both; not standard environment]
- Exclude – Does not meet minimum design for ITS, CBA [ITS – clearly defined intervention point, 3 outcome measures pre and post; CBA - 2 intervention and 2 control clusters]
- Exclude – Not an eligible surface [not patient environment, high touch; Is an invasive device, disposable]
- Exclude – Published prior to 2006