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RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL



TITLE: Non-Manual Room Disinfection Techniques for Infection Prevention in Healthcare Facilities: A Review of the Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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CONTEXT AND POLICY ISSUES

Surface contamination in healthcare facilities has been identified as a source of transmission of pathogens and healthcare-associated infections (HAIs). Environmental contamination with pathogens may occur through shedding, and subsequent transmission could be mediated through contact and aerosols from textiles and other sources.^{1,2} Pathogens have the capability of remaining airborne and viable, or settling and re-suspending for extended periods in the indoor environment.³ Since some pathogens have a low infectious dose, the presence of pathogens in the healthcare environment presents a risk of infection transmission even when the concentration is low.

Pathogens usually associated with HAIs include *Clostridium difficile*, vancomycin-resistant enterococci (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.⁴ Subsequent occupancy of a room previously occupied by a patient colonized or infected by any of these organisms increases the risk of acquiring these pathogens by a factor of two or more.² A conventional measure to minimize this risk is terminal cleaning and disinfection following the discharge of patients with these pathogens. However, this approach seems inadequate to reduce contamination sufficiently to prevent all transmission, and increased risk of infection to subsequent occupants persists in these cases.⁵

Healthcare-associated infections are costly, requiring extended hospital stay, increased use of antibiotics, and the need for more rigorous cleaning and disinfection measures which consume additional resource and increase labor cost.^{1,3,6-8} According to an economic burden study based on published literature from the years 2000 to 2011, the cost per case of hospital-acquired infection ranges from \$2,265 to \$22,400.⁸ The estimated annual direct costs of hospital acquired infections in Canada is \$1 billion.⁹ About 8,000 Canadians die from hospital-acquired infections and more than 200,000 others get infected each year.¹⁰ Therefore, measures to improve the effectiveness of cleaning and decontamination methods to prevent HAIs are important.

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The inadequacy of traditional cleaning methods has been linked to operator errors in relation to improper selection, formulation, distribution, and contact time of the disinfectant. Approaches to improve cleaning effectiveness include educational campaigns, feedback of cleaning performance, routine microbiological analysis of surface hygiene, and the use of fluorescent markers or assays to assess the thoroughness of cleaning. While these measures can improve conventional cleaning efficiency, their sustainability has not been studied.^{2,5,11} The use of non-manual room disinfection reduces the chances of operator errors associated with traditional cleaning methods and offers the potential for more effective eradication of pathogens to reduce transmission of infections.^{2,12,13} In this report, non-manual refers to non-touch or automated procedures, or environmentally active agents. A previous Rapid Response report⁴ found low quality evidence for the effectiveness of VHP and an UV room disinfection system to prevent or reduce infection rates in a healthcare setting.

The aim of this review is to review the available evidence for the clinical and cost-effectiveness of non-manual room disinfection techniques for the prevention of infections in healthcare facilities.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?
2. What is the comparative clinical effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?
3. What is the cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?
4. What is the comparative cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?
5. What are the evidence-based guidelines regarding non-manual room disinfection methods for infection prevention in health care facilities?

KEY FINDINGS

There is some evidence that non-manual room disinfection methods based on hydrogen peroxide and UV light are effective at preventing or reducing infection in health care facilities. However, many of the included studies in this report stated that further studies are warranted. Non-manual room disinfection technologies differ significantly even when the base intervention (hydrogen peroxide or UV light) is the same. For this reason, the suitability of one technology over the other has to be determined based on several factors including the intended application, labour cost and availability, and practicality of implementation to fit the nature of operations at health care facilities. Cost-effectiveness models based on the conditions at the local health care facility may be preferable given the various options for acquisition of non-manual room disinfection technologies and the associated cost differentials.

METHODS

Literature Search Methods

A limited literature search was conducted on key resources including Medline, PubMed, The Cochrane Library, ECRI, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic studies and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and April 28, 2015.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Population	Rooms in hospitals or healthcare facilities
Intervention	Non-manual ^a room disinfection techniques, including but not limited to: <ul style="list-style-type: none"> • Steam cleaning • O-zone disinfection • Ultraviolet (UV) light • High-intensity narrow-spectrum (HINS) light • Hydrogen peroxide • Anti-microbial coatings (e.g., triclosan, silver, copper) • Bacteriophage-modified surfaces • Polycationic and light activated antimicrobial surfaces • Sharkskin like surfaces (e.g., Sharklet)
Comparator	Q1, 3, and 5: Standard procedures No intervention No comparator Q2, 4, and 5: Non-manual room disinfection techniques, including but not limited to: <ul style="list-style-type: none"> • Steam cleaning • O-zone disinfection • Ultraviolet (UV) light • High-intensity narrow-spectrum (HINS) light • Hydrogen peroxide • Anti-microbial coatings (e.g., triclosan, silver, copper) • Bacteriophage-modified surfaces

	<ul style="list-style-type: none"> • Polycationic and light activated antimicrobial surfaces • Sharkskin like surfaces (e.g., Sharklet)
Outcomes	<p>Q1 and 2: Clinical effectiveness (e.g., rates of hospital acquired infection, infection control outcomes, infection prevention outcomes, patient colonization rate)</p> <p>Q3 and 4: Cost-effectiveness outcomes</p> <p>Q5: Guidelines and recommendations</p>
Study Designs	Health technology assessments (HTAs), systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), non-RCTs, Economic evaluations, and guidelines
<p>^a Non-manual may also be referred to as non-touch or automated or environmentally active agents.</p>	

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to January 1 2008. Duplicate publications and studies that reported only culture results from room surfaces without patient infection outcomes were excluded. Review articles not based upon a systematic literature search, and guidance documents or consensus statements that did not include a description of the methodology used in their development were also excluded. Studies included in a previous Rapid Response report were also excluded.⁴

Critical Appraisal of Individual Studies

The non-randomized studies were critically appraised using the Downs and Black checklist for measuring study quality.¹⁴ Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described. Appendix 3 provides summary of critical appraisal of the included studies.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 159 citations were identified in the literature search. Following screening of titles and abstracts, 136 citations were excluded and 23 potentially relevant reports from the electronic search were retrieved for full-text review. Five potentially relevant publications were retrieved from the grey literature search. Of these potentially relevant articles, 24 publications were excluded for various reasons, while four publications met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection. Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Characteristics of included studies have been provided in Appendix 2.

Study Design

Four non-randomized studies^{1,3,5,11} were included in this report. Two of the non-randomized studies were published in 2014,^{1,11} while one each was published in 2011,³ and 2008.⁵

Country of Origin

Of the four non-randomized studies, one was a retrospective study from the USA,¹¹ and another was a pre- and post-intervention cohort study from Israel.¹ There were two before-and-after intervention prospective studies from the USA.^{3,5}

Patient Population

One non-randomized study¹¹ included in this report had both adult and pediatric patients, including those receiving specialized services for trauma, burn, neurosurgery, cardiothoracic surgery, transplant, and oncology. Details of patients' characteristics were not provided.

In one study,¹ the similarity in some characteristics and treatments among patient groups hospitalized during and before the period of the intervention were reported. For example, the age of patients admitted before the intervention ranged from 18 to 90 years (mean \pm standard deviation [SD]: 57 ± 19), while those hospitalized during the intervention were between 18 to 83 years old (49.7 ± 22). The patients were mostly immobile and majority received tube feeding during the periods being compared. In the period before the intervention 25.9% of the patients had pressure sores and 30.4% received steroid treatments, compared with 16.7% of patients with pressure sores and 19.4 % who received steroid treatment during the intervention period.

One of the prospective studies³ was conducted among patients in a neonatal intensive care unit (NICU) while the other prospective study⁵ reported infection rates in patients admitted to five wards "with the highest incidence of CDAD" (*Clostridium difficile*-associated disease) as well as among the hospital-wide patients. No other details of patients characteristics were provided in this study.⁵

Interventions and Comparators

One prospective study⁵ included in this report used hydrogen peroxide vapor (HPV) as the decontamination agent and compared infection rates during a 9 months period of intervention (June 2005 through March 2006) to a parallel pre-intervention period of 9 months (June 2004 through March 2005).

One study¹¹ examined infection rates during a period of 22 months when a pulsed xenon UV disinfection (UVD) technique was used in a hospital compared to the preceding 30 month period before the UVD technology was in use. Another study³ used enhanced UV germicidal irradiation (eUVGI) in a NICU and reported before-and-after intervention results for four consecutive 6-month periods (6 months before and 18 months after the introduction). No reason was given for the uneven period lengths. A newsletter concerning the study stated that the eUVGI (also called Pathogen Control System)³ "integrates standard UVGI emitters with MERV15 air filters in such a manner as to predictably destroy harmful viruses, bacteria and fungi at a pre-determined efficiency within a given HVAC's airstream."¹⁵ One study¹ compared the infections rates in a ward during a 6-month hospitalization period when biocidal copper impregnated linens were being used to a parallel 6-month hospitalization period when ordinary linens were used.

In all the included studies, non-manual disinfection interventions were used as adjunct to traditional cleaning and disinfection protocols that already existed in the hospital facilities. Cleaning prior to application removes organic matter that reduces the effectiveness of the non-manual room disinfections intervention systems.

It is noteworthy that within the HP- and UV-based technologies, there are differences in available systems that impact efficacy and suitability, and necessitate trade-off between time and effectiveness. For example, VHP systems (also known as aerosolized hydrogen peroxide systems) usually deliver pressure-generated aerosol containing 5 to 6% HP and <50 part per million (ppm) silver via a unidirectional nozzle, and they have a typical recommended dose of 6 ml/ M³ for hospital rooms.² Following exposure, the aerosol is left to decompose naturally without any active aeration system.² On the other hand, HPV systems achieve a homogeneous distribution throughout an enclosed area by delivering a heat-generated vapor of 30 to 35% w/w aqueous HP through a high velocity air stream. HPV systems have modules to measure the concentration of HP, and the temperature and relative humidity in the enclosure, with some systems having the technology to hold a steady HP concentration throughout the exposure period. Following exposure, HPV systems catalyze the breakdown of HP vapor to oxygen and water vapor using an aeration unit.²

Non-manual technologies based on UV light also vary. Ultraviolet-C (UVC) systems use specifically designated wavelengths (254 nm range) and deliver targeted doses for vegetative bacteria (for example, 12,000 $\mu\text{Ws}/\text{cm}^2$) or for spores (22,000 to 36,000 $\mu\text{Ws}/\text{cm}^2$) on surfaces, while the pulse xenon UV systems emit broad spectrum UV in short pulses and have relatively short cycle time.² Ultraviolet germicidal irradiation (UVGI) is an air purification technology produced by mercury vapour lamp with a predominant wavelength within the UVC bandwidth of the electromagnetic spectrum.^{3,16} The UVGI is a specialized system installed through upper room fixtures and the lamps can be placed inside mechanical ventilation systems.¹⁶ Air currents rapidly carry pathogens into the UVGI energy beam located well above the occupants' heads, which destroys their DNA, interfering with replication, and inactivating them.¹⁶ By locating the UVGI in the upper part of rooms, occupants are protected from direct UV irradiation while the system works safely and effectively to interrupt the transmission of airborne infectious diseases.^{1,16}

The literature search did not find any studies which evaluated steam cleaning, ozone disinfection, high-intensity narrow-spectrum light, or polycationic and light activated surfaces as decontamination technologies that met the specified inclusion criteria for this report (Table 1). Also, no studies meeting the inclusion criteria were found evaluating anti-microbial coating or sharkskin-like surfaces as disinfection techniques. A review¹³ has briefly discussed some of these technologies and may help explain in part why they are not in use currently. Some of limitations of the steam technology are the risk of hazards to switches, computers, and electrical appliances, as well as increased risk of slips and falls due to residual moisture.¹³ Furthermore, while careless handling of steam increases the risk of burns and scalds for nearby persons, including patients, the temperature of steam at delivery may rapidly dissipate depending upon the type and conductivity of exposed surfaces,¹³ with potential for reduced effectiveness at inactivating pathogens. For ozone, its toxicity, limited effectiveness against bacterial spores and fungi, and potentially corrosive effect on materials (metals and rubber) commonly found in hospital equipment were identified as some limitations. Application of surface technologies in general are limited by insufficient information on durability and whether antimicrobial activity is affected by factors such as humidity, temperature, cleaning frequency, and/or the presence of an organic load.¹³ There are also concerns over possible toxicity, resistance, and allergenic

properties, in addition to uncertainty about their relative contribution toward hand contamination and the risk of cross-transmission as a consequence. Moreover, the sites, surfaces, and clinical equipment in patient areas which could be coated with an antimicrobial product are currently unknown.¹³ The HINS light technology also requires further work to investigate any benefits on HAI rates, although, according to the review, one study has evaluated its overall effect for decontaminating the clinical environment.¹³

Outcomes

One non-randomized study¹¹ had incidence rates of hospital acquired multidrug resistant organisms (MDROs) and *C. difficile* as outcomes, and another study¹ reported general hospital acquired infection (HAI) rates in a long-term care ward. One study³ measured changes in tracheal colonization and prevalence of ventilator-associated pneumonia (VAP) among intubated NICU patients. Tracheal colonization was defined by the investigators using an airway microbial load index (MLI) which quantified each pathogen per patient sample on a scale of 1 to 4 for rare, few, moderate, or heavy growth. Patients whose tracheal aspirates showed no growth were assigned a zero.³ Cultures from the environment and intubated NICU patients' tracheas were obtained before eUVGI installation and over the next 12 months. Episodes of VAP, number of antibiotic courses, and antibiotic days, among other outcomes, were compared between the pre- and post-eUVGI time periods. Another study⁵ measured new *C. difficile*-associated disease (CDAD) cases, both hospital-wide and in five rooms designated as high-incidence CDAD wards.

Although the included studies also measured colony forming units (CFU), these are not discussed because the focus of this report is on clinical outcomes such as infection prevention/reduction following disinfection by the non-manual room disinfection interventions of interest.

Summary of Critical Appraisal

Reporting

The objectives and the main study outcomes of each of the four non-randomized studies were clearly defined, and the non-manual disinfection techniques being evaluated were specified.^{1,3,5,11} All the studies reported percentage reductions in the specific incidence of hospital-acquired infections they had pre-specified as outcome of interest. Although they also indicated degree of statistical significance with *P*-values, because the confidence intervals (CI) were not reported the level of certainty of the reported outcomes in these studies is unknown. However, one of the studies¹¹ also reported rate ratios with corresponding 95% CI. Only two studies^{1,3} provided any information on patient characteristics, making it difficult to evaluate the potential for confounding. One study¹ reported some demographic and medical conditions of the hospitalized patients before and during the intervention, and another study³ reported the demographic profile of NICU and high-risk cohort. One study³ reported procedure and outcome determination in sufficient detail to facilitate replicability. Another study⁵ reported trends in rates of antimicrobial and proton pump inhibitor (PPI) use, which are known to be risk factors for infections, in both the pre-intervention and the intervention phases of the study. Overall there was similarity between hospitalized patients groups in the two study periods, with respect to the use these medications.

External validity

Each of the non-randomized studies was conducted in a single hospital, or hospital department. This may limit the extent to which the findings of the study can be generalizable. The hospitals where each of the studies took place provided specialized services or had logistics and staff that may not be commonly found in other health care facilities.

The study that evaluated the pulsed xenon UVD¹¹ took place in a tertiary care hospital that offers full services to adult and pediatric patients including specialized services for trauma, burn, neurosurgery, cardiothoracic surgery, transplant, and oncology. The broad scope of patients and services suggests commonality with many healthcare facilities. However, all pediatric rooms were single occupancy, while most adult patient rooms outside of the intensive care units were double occupancy. Patients with MDROs or *C. difficile* received care in a private room or semiprivate room with the other bed blocked from occupancy, or they may have been cohorted with another patient who harbored the same organism.¹¹ It is reasonable to expect that such measures could contribute to minimizing dissemination of pathogens and spread of infection in the hospital. Thus, it is uncertain whether the same extent of success with UVD could be replicated in hospitals without sufficient room to allow this sort of occupancy arrangement.

One study¹ was conducted in a severe head injury long-term care ward and it is unclear whether its findings would be generalizable to other health care settings. One study³ was conducted in the NICU of a university-affiliated regional perinatal center, and the study benefited from environmental sample collection services provided by a research-based company. Another study⁵ was conducted in a university-affiliated hospital and focused on a particular strain of *C. difficile* which has enhanced virulence properties – the North American pulsed-field (NAPI) strain. Therefore, the generalizability of findings of these studies is unknown.

Internal validity

The adequacy of sample sizes to detect differences in effect of the interventions was not discussed in any of the studies. However, the non-manual room disinfection methods were used over at least 6 months and/or repeatedly for many cycles to allow sufficient data to be collected for analysis. The pre- and post-intervention comparisons used by all the non-randomized studies^{1,3,5,11} are subject to possible clinical care and/or environmental changes over time, and there is no way of evaluating the extent to which such variations, if they occurred, influenced the reported outcomes of the studies. In all the studies,^{1,3,5,11} it was not reported whether or not cleaning staff were aware of the use of the non-manual room disinfection procedures. It is reasonable to expect that knowledge of the investigation could influence behavioral change among housekeeping staff to increased or decreased intensity of cleaning which could impact the outcomes of the studies.

In one study,¹¹ the UVD system was used a high number of times (11,389 times) following discharge cleaning of contact precautions rooms and other high-risk area during the study period. This reduced the probability that the results were due to chance, although the study was conducted in a single institution. However, in this study,¹¹ the UVD was used exclusively at a setting recommended to inactivate *C. difficile* spores which is higher than the setting required for vegetative forms of *C. difficile*. Thus, we are unable to tell how effective the UVD would be against vegetative form of *C. difficile* using the appropriate recommended setting. However, this may not be problematic since disinfection against the transmission of *C. difficile* associated

disease usually targets both the spores and vegetative forms. Although there were several initiatives to optimize environmental disinfection during both the UVD and pre-intervention periods of the study,¹¹ they were not adjusted for in the analysis despite being potential confounding factors. On the other hand, although investigators indicated the use of a more sensitive diagnostic test (a change from *C. difficile* cytotoxin A + B enzyme immunoassay to polymerase chain reaction) increased overall test positivity from 10% to 13% during the study,¹¹ *C. difficile* infection rates decreased during UVD which supports the effectiveness of the intervention for this purpose.

In another study,¹ data from parallel periods before and after the intervention were analyzed using rigorous statistical methods to compare the differences between the two populations in terms of patient medical characteristics, treatments, and nosocomial infections.¹ The period before the non-manual room disinfection was introduced had more patients with pressure sores or who were using steroidal treatments. Pressure sores may suggest very ill patients on admission for a prolonged period, who may be more susceptible to infection by reason of longer exposure and/or reduced immunity. Steroid use has also been linked to reduced immunity and infections. However, the effect of possible potential cofounders, such as patient age, gender, mobility, presence of sores, steroid administration, tracheostomy, urinary catheter, and inhalation treatments, on the differences found in fever days, use of antibiotics, and rates of hospital-acquired infections, was analyzed and accounted for using multivariate analysis of covariance (ANCOVA). According to the authors, the study was designed to use parallel periods to minimize seasonal variations between the study periods. However, no mechanisms were described to show how variations would be detected if they occurred. Thus, it is unknown if seasonal changes affected the reported outcomes and to what extent. Furthermore, although the study used data from two 6-month parallel periods, the number of patients who were hospitalized before and during the intervention was relatively low (57 and 51, respectively). It is therefore, uncertain whether the sample size was enough to detect clinically relevant differences between the two periods.

In one of the studies,³ the periods before and after intervention were neither parallel or equal in length. Data was collected for the 6-month period before the installation of the non-manual room disinfection intervention, and for four 6-month periods after the intervention was installed. Therefore, although the data from the duration of the intervention show reduced VAP gains compared to the 6 months before the intervention, the influence of seasonal variations and changes in clinical care over time on the reported findings cannot be ruled out.

In another study,⁵ the incidence of nosocomial CDAD was investigated hospital-wide and in five high-incidence wards before and after HPV decontamination. Patient groups hospitalized during the two study periods had similar levels of treatment with antibiotics and PPIs (both of which are known to be risk factors for *C. difficile* transmission) without statistically significant differences which could influence the reported HAIs. Although an analysis to examine the effects of antimicrobial medication and PPI use on outcomes was done, details about patient characteristics, medical history and other potential confounding factors were not provided. To distinguish between patients with hospital-acquired CDAD and patients who were infected before hospital admission, nosocomial CDAD case diagnosis was limited to patients with a positive *C. difficile* toxin test result for a test obtained more than 72 hours after admission.

Funding Support

One of the non-randomized studies¹¹ reported no conflict of interest. One study¹ was funded in part by the company that developed the copper oxide in linen technology that was being studied. In addition one of the investigators was the Chief Medical Scientist of the company. In one study,³ the investigators received an eUVGI system, which was the non-manual disinfection technology being investigated, along with installation as an in-kind contribution from the manufacturer who also provided environmental sample collection services for the study. Another study⁵ received price discounts for HPV decontamination services from the manufacturer of the HPV technology under study, and two out of 10 investigators received salary, at least in part, from the same manufacturer.

Summary of Findings

What is the clinical effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?

One retrospective study¹¹ reported a reduction in the incidence of hospital-acquired MDROs and *C. difficile* from 2.67 cases per 1,000 patient-days in the 30-month period before UVD to 2.14 cases per 1,000 patient-days during the 22 months when UVD was used. This represented a decrease of 20% with a rate ratio of 0.80 (95% confidence interval [CI]: 0.73 to 0.88; $P < 0.001$).

A cohort study¹ found the use of biocidal copper-impregnated linens reduced hospital-acquired infection (HAI) rate per 1,000 hospitalization-days by 24% ($P < 0.05$) compared with the use of ordinary linens. The use of biocidal copper impregnated linens also reduced the number of days patients had fever (body temperature >38.5 °C) per 1000 hospitalization-days by 47% ($P < 0.01$), and total number of days of antibiotic administration per 1000 hospitalization-days by 32.8% ($P < 0.0001$) compared to the use of ordinary linens. Expectedly, there was a reported cost saving (approximately 27%, data not provided) as a result of reductions in antibiotics use, HAI-related treatments, X-rays, disposables, labor, and laundry expenses during the period when biocidal copper impregnated linens were used.

In one prospective study,³ fewer NICU patients were found to be colonized following eUVGI, and tracheal microbial loads decreased by 45% ($P = 0.004$). The percentage of patients who had little or no tracheal colonization ($MLI \leq 1$) was 44% post-eUVGI compared with 14% pre-eUVGI. In addition, VAP rates among high risk cohorts, defined as infants with less than 30 weeks gestation who were ventilated for 14 weeks or more, declined significantly ($P = 0.04$) from 74% at baseline ($n = 31$) to 44% ($n = 18$) at 18 months. The overall antibiotic usage fell by 62% ($P = 0.013$) while episodes of VAP per patient also decreased significantly ($P = 0.04$) from 1.2 to 0.4 for the period before and during the 12 months of eUVGI, respectively.

Another prospective study⁵ reported that the incidence of nosocomial CDAD in the five high-incidence wards reduced from 2.28 cases per 1,000 patient-days in the pre-intervention period to 1.28 cases per 1,000 patient-days during a similar time period for the intervention ($P = 0.047$). For the hospital-wide incidence of CDAD, although HPV intervention resulted in lower incidence, the difference between the pre-intervention and the intervention periods reached the level of significance only when the analysis was limited to months when an epidemic strain was known to be present. During that time, 0.88 versus 1.89 cases per 1,000 patient-days ($P = 0.047$) was reported for the intervention and pre-intervention periods, respectively.

What is the comparative clinical effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?

The literature search did not find any study with a direct or indirect comparison of non-manual room disinfection methods for the prevention of infection in health care facilities. .

What is the cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?

The literature search did not produce any studies on the cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities.

What is the comparative cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities?

The literature search for this report did not identify any studies on the comparative cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities.

What are the evidence-based guidelines regarding non-manual room disinfection methods for infection prevention in health care facilities?

The literature search for this report did not identify evidence-based guidelines regarding non-manual room disinfection methods for infection prevention in health care facilities.

Limitations

All the included non-randomized studies^{1,3,5,11} followed a pre-intervention-and-intervention design which is susceptible to changes in clinical care and/or environment, as well as changes in patient health status. Only two of the studies reported analyses that considered some potential confounding factors such as patients demographic characteristics and antibiotic use history.^{1,5} None of the studies adjusted for the potential confounding effect of pre-cleaning and simultaneous infection prevention protocols that were in use at the various settings of the studies.^{1,3,5,11} Therefore, the possibility that some observed reductions in nosocomial CDAD incidence may not be attributable to a specific intervention cannot be ruled out. For the retrospective study,¹¹ there is increased likelihood that not all important factors that could impact the results were captured or adequately recorded. Therefore the probability of bias cannot be ruled out. Studies^{1,3} which tried to minimize effects of seasonal changes on outcomes using parallel periods had no mechanism to determine if significant changes occurred despite the precaution, and no sensitivity analysis was done to test the findings. Therefore, the impact of seasonal variations on the outcome could not be assessed.

The generalizability of the findings of the studies may be limited because each was conducted in a single hospital or a department within a hospital, and the intervention in each study differed from the others.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

A previous Rapid Response report⁴ (published in April 2014) included studies with transmission of infection among patients in long-term care, community teaching hospitals, and tertiary referral

hospitals, as well as from specific hospital departments such as intensive care unit (ICU) and the burns unit. It included seven studies with vaporized hydrogen peroxide (VHP) as the intervention, and one prospective study with UV as the intervention. The review⁴ found low quality evidence from seven studies, including a systematic review, suggesting that VHP is effective in reducing the incidence of nosocomial infections caused by a number of different pathogens in hospital settings. It also found one low quality cohort study which reported reduced incidence of hospital associated *C. difficile* infection rate following terminal decontamination of rooms previously occupied by *C. difficile*-colonized patients with a portable pulse xenon UV light device used as an adjunct to standard cleaning and disinfection protocols.

In the current review, one prospective study⁵ found HPV to be effective at reducing nosocomial *C. difficile* infections in a hospital and in high-incidence wards. One retrospective study¹¹ reported that a pulsed xenon UV system was effective at reducing the incidence rates of hospital acquired MDROs and *C. difficile* infections, while one prospective study³ found that a eUVGI decontamination system significantly reduced VAP and tracheal colonization rates at a NICU. A cohort study¹ reported that the use of copper impregnated linens resulted in significant reductions in HAI compared with the use of ordinary linens, and the use of copper impregnated linens was associated with cost savings due to reduced expenses on antibiotic use, HAI-related treatments, X-rays, disposables, labor, and laundry. However, given the limitations of the included studies discussed elsewhere in this report, and the fact that no randomized studies were found through the literature search for this review, more rigorous studies with sensitivity analyses for changes in clinical care and patients' health status over time, as well as traditional cleaning methods and infection prevention protocols may be warranted to test the findings of this review.

Although the literature search did not find any study with a direct or indirect comparison of non-manual room disinfection methods for the prevention of infection in health care facilities, it is known from *in vitro* studies that some non-manual disinfection systems are better able to inactivate vegetative pathogens and spores than others.² For example, HPV systems are capable of $>6\text{-log}_{10}$ reduction of a range of pathogens *in vitro*. They consistently achieve inactivation of 6-log_{10} biological indicators (BIs), and are associated with the elimination of pathogens from surfaces. Biological indicators contain known concentrations of a microbe, usually a bacterial endospore, used in place of microbiological sampling to assess effects of a disinfectant system. On the contrary, VPV and UVC systems reduce pathogens *in vitro* by $<6\text{-log}_{10}$.^{17,18} They cannot reliably inactivate BIs to either the 6-log_{10} or 4-log_{10} level, and they have not demonstrated consistency at eliminating surface pathogen.² However, given that the usual pathogen contamination concentration associated with hospital surfaces is reported to be in the 2-log_{10} range, *in vitro* standards such as 6-log_{10} BIs may be too stringent. Furthermore, since the level of reduction in various pathogen concentrations required to interrupt transmission has not been determined,² it is difficult to predict infection prevention outcomes of non-manual room disinfection methods using *in vitro* disinfection only.

Although the literature search did not produce any studies on the cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities, a review has suggested that a hospital may own and operate a non-manual disinfection system, be a customer of an outsourced service, or use a leasing option that can avoid high capital costs, based on the intended application, the evidence base for effectiveness, practicalities of implementation, and cost constraints.² Thus cost-effectiveness studies based on local hospital conditions and needs may be more suitable than a generic cost-effectiveness approach to

select the most appropriate system. Labour cost and labour availability have been recommended to be an integral part of any assessment in this regard. One of the included studies in this review reported that for 30% of the total available time, their UVD machines were not in use largely because of labor constraints. As a result, 24% of opportunities to use the UVD method in contact precaution discharge were missed.¹¹ Two other reviews were found through literature which have information that may help guide cost estimation of non-manual disinfection systems for infection prevention in a health care facility.^{12,13}

No studies on the comparative cost-effectiveness of non-manual room disinfection methods for infection prevention in health care facilities were identified by the literature search for this report. However, a review has projected that the relative purchase cost of non-manual room disinfection equipment may be in the order of UVC > Pulse Xenon-UV > VHP systems > HPV.² However, other costs like consumables, cost of operation, and the opportunity cost can change this order.

Specific clinical guidelines regarding non-manual room disinfection methods were not identified through the literature. The previous Rapid Response report⁴ cited a 2014 National Health Service (NHS) guideline for preventing HAI in hospitals in England, and a 2011 Centers for Disease Control and Prevention (CDC) guideline for the prevention and control of norovirus gastroenteritis outbreak in healthcare settings, both of which had statements about decontamination using VHP or UV-light. Each of guidelines suggested that at the time of writing the available evidence was not sufficient to make a recommendation about the use of VHP or UV light for decontamination in healthcare settings.

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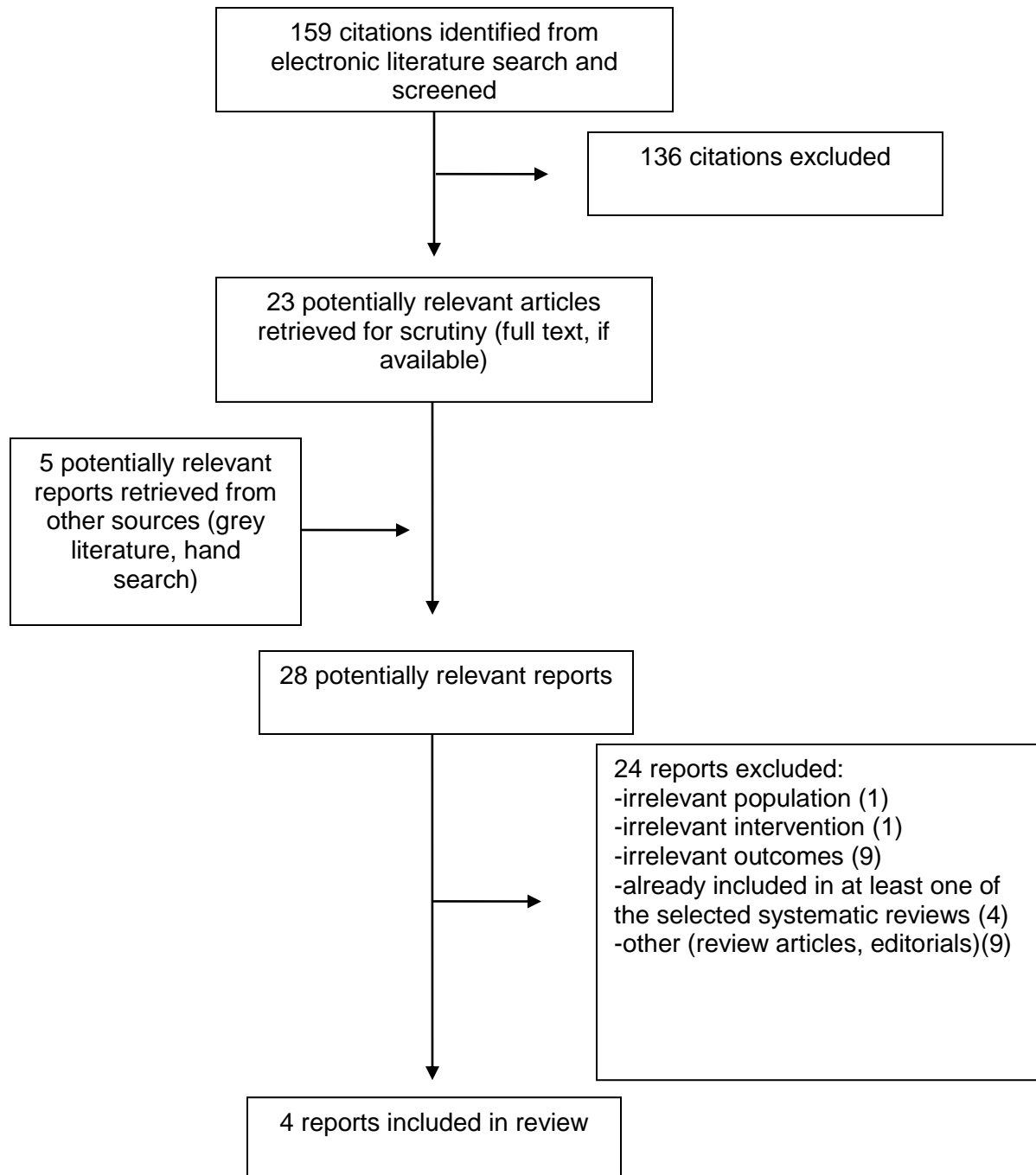
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APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Publications

Table A1: Characteristics of Included Clinical Studies

First Author, Publication Year, Country, Study Name	Study Design	Patient Characteristics	Intervention(s)	Comparator(s)	Clinical Outcomes
Haas, ¹ 2014 The USA	A retrospective study	Adult and pediatric patients including those receiving specialized services for trauma, burn, neurosurgery, cardiothoracic surgery, transplant, and oncology.	Pulsed xenon UVD following discharge cleaning of contact precautions rooms and other high-risk areas	Standard cleaning/disinfection before UVC	Incidence rates of hospital acquired MDROs plus <i>C. difficile</i> before and during the UVD
Lazary, ¹ 2014 Israel	A Cohort study over two parallel periods; one before (period A) and the other after (period B)	Two analogous patient cohorts with severe head injuries and in long-term care for head injury.	Biocidal copper oxide impregnated linens	Non-biocidal linens	HAI rates in a long-term care ward
Ryan, ³ 2011, The USA	Prospective pre- and post-intervention design	NICU patients who had an endotracheal tube in place	eUVGI applied to central coil components of HVAC	Standard cleaning/disinfection before eUVGI	Decreased pathogens in the NICU air and surfaces, decreased tracheal colonization and VAP prevalence in intubated NICU patients
Boyce, ⁵ 2008 The USA	A prospective before-after intervention study	Patients on admission at a university-affiliated hospital.	HPV decontamination	Standard cleaning with detergent, and disinfection with sodium hypochlorite solution (1,000 ppm) where applicable	Reduced environmental contamination and nosocomial transmission of <i>C. difficile</i> measured by changes in CDAD

CDAD = *Clostridium difficile*-associated disease; eUVGI = enhanced ultraviolet germicidal irradiation; HAI = healthcare-associated infections; HPV = hydrogen peroxide vapour; HVAC = heating ventilation and air conditioning; MDRO = Multiple-drug-resistant organisms; NICU = neonatal intensive care unit; USA = United States of America; UV = ultraviolet; UVD = UV disinfection; VAP = ventilator-associated pneumonia; VHP = vaporized hydrogen peroxide; VRE = vancomycin-resistant Enterococcus;

APPENDIX 3: Critical Appraisal of Included Publications

Table A2: Strengths and Limitations of Non-Randomized Studies using the Down and Black Checklist for Measuring Study Quality.¹⁴

Strengths	Limitations
Haas ¹¹	
<ul style="list-style-type: none"> Findings were derived from analysis of a large number (n=11,389) of UVD cycles performed over 22 months, so that they are unlikely to be due to chance. Patient population in the hospital where the technology was applied cut across adult and pediatric patients presenting with a wide variety of clinical conditions, which suggests that the UVD may be applicability over a wide diversity of patient groups. Steps were taken to segregate patients with hospital-acquired MDROs or <i>C. difficile</i> from those without, which reduced the chance of contamination that could increase confounding of the reported outcomes. The implementation approach was reported in sufficient detail in the article to promote understanding and facilitate possible reproducibility by others. Rigorous statistical analyses were done which accounted for important details including missed UVD upon discharge, rate ratios with corresponding 95% CI, and the difference between the incident rates. 	<ul style="list-style-type: none"> This was retrospective study using a before and after implementation of UVD design. There is increased likelihood that not all important factors that could impact the results were captured or adequately recorded. Therefore the probability of bias cannot be ruled out. This study was conducted at a single tertiary care hospital which is likely to have state-of-the art facilities and staff with specialty not commonly found in other hospitals. The extent to which such cutting edge logistics and staff influenced the successful implementation of the UVD disinfection technology and how its absence may impact implementation is unknown. The investigators did not adjust for confounding factors such as antibiotic utilization and simultaneous interventions to reduced acquisition of MDROs and <i>C. difficile</i>.
Lazary ¹	
<ul style="list-style-type: none"> The data from the study were gathered during two 6-month parallel periods to minimize seasonal variations between the examined periods which are potential confounders. Environmental and textile cleaning, and treatment modality remained the same. The consistency in procedures reduced sources of confounding that could impact reported out comes. All the data on parameters monitored and studied were collected from the patients' medical files and from pharmacy and laboratory reports, without the knowledge or involvement of the ward medical staff. Such concealment further reduced sources of bias. 	<ul style="list-style-type: none"> Although data for the study were gathered during parallel periods to minimize seasonal variations, no mechanisms were reported to ensure whether there were actual changes or not. The clinical care and medical conditions of the individual patients could change over time, which could influence the outcomes in period B. Therefore, seasonal influence and outcomes not related to a specific intervention cannot be ruled out. The study was funded by the manufacturer of the technology that was investigated. In addition, one of the investigators is the Chief Medical Scientist of the sponsor. Thus an independent objective perspective and appraisal of study results cannot be

Table A2: Strengths and Limitations of Non-Randomized Studies using the Down and Black Checklist for Measuring Study Quality.¹⁴

Strengths	Limitations
<ul style="list-style-type: none"> ANCOVA analyses negated the influence of potential confounders, such as patient age, gender, mobility, presence of sores, steroid administration, tracheostomy, urinary catheter, and inhalation treatments, on the differences found in fever days, use of antibiotics, and rates of HAI. 	<p>assured with this study.</p>
<p>Ryan³</p>	
<ul style="list-style-type: none"> Detailed reporting to facilitate understanding and reproducibility. Diagnosis and treatment decision for VAP were made by qualified neonatologist, who was unaware that VAP was being ascertained. 	<ul style="list-style-type: none"> Pre- and post-comparisons are subject to possible clinical care and medical conditions changes over time. We cannot rule out that VAP may have decreased over time because of unidentified clinical or environmental interventions
<p>Boyce⁵</p>	
<ul style="list-style-type: none"> Trends in antimicrobial and proton pump inhibitor use were reported. These are known risk factors for infection acquisition, therefore reporting on them helps to put the hospital acquire CDAD in some perspective. Statistical analyses were employed to determine whether CDAD incidence was correlated with antibiotic use, and time variation for better understanding of study findings. 	<ul style="list-style-type: none"> No adjustments were made for potential confounding factors such as traditional cleaning and disinfection procedures. Therefore, the possibility that some observed reductions in nosocomial CDAD incidence may not be attributable to a specific intervention cannot be ruled out. The generalizability of the study findings may be limited because it was conducted in a single university affiliated hospital affected by a particular epidemic strain of <i>C. difficile</i>.

CDAD = *Clostridium difficile*-associated disease; HAI = healthcare-associated infections; MDRO = Multiple-drug-resistant organisms; UVD = UV environmental disinfection; VAP = ventilator-associated pneumonia

APPENDIX 4: Main Study Findings and Author’s Conclusions

Table A3: Summary of Findings of Included Studies	
Main Study Findings	Author’s Conclusions
Haas, 2014 ¹¹	
<ul style="list-style-type: none"> The overall rates of hospital-acquired MDROs plus CD were significantly lower during the 22 months of UVD use compared with the 30-month period before UVD (2.14 cases per 1,000 patient-days vs 2.67 cases per 1,000 patient-days, respectively; rate ratio, 0.80; 95% CI: 0.73 to 0.88, $P < 0.001$). Beside the overall significantly decreased infection rate during UVD, a piecewise regression model and sub-analysis of the incidence rates showed significant reductions in each of VRE (0.82 [95% CI 0.70 to 0.95] $P = 0.002$), MRSA (0.73 [95% CI 0.58 to 0.92] $P = 0.007$) <i>C. difficile</i> (0.83 [95% CI 0.70 to 0.97] $P = 0.02$), and multiple-drug resistant gram-negative bacteria (0.81 [95% CI 0.66 to 0.98] $P = 0.04$). 	<ul style="list-style-type: none"> During the period of UVD, there was a 20% decrease in overall hospital-acquired MDRO plus CD. This statistically significant decrease in MDROs plus CD occurred in spite of missing 24% of opportunities for UVD of contact precautions rooms at discharge.”¹¹ page 588 “Use of UVD as an adjunct to routine discharge cleaning of contact precautions rooms was feasible and temporally associated with a significant decrease in hospital acquired MDRO plus CD in our institution.”¹¹ page 590 “Further study is needed to optimize the use of UVD and to further assess the effect of UVD use on acquisition rates of MDROs and CD. In addition, a cost-benefit analysis of UVD use that includes labor costs is also needed.”¹¹ page 590
Lazary, 2014 ¹	
<ul style="list-style-type: none"> There was a 24% reduction in HAI events in period B when copper oxide impregnated textiles were used compared with period A when ordinary linen was used ($P = 0.046$). The number of days that patients had fever was significantly decrease in period B compared with period A (47%; $P = 0.0085$). The number of events in which patients received antibiotics during period B reduced by 23% compared to period A ($P = 0.052$), and the total days of antibiotic administration during period B was 32.8% lower than in period A ($P < 0.0001$) 	<ul style="list-style-type: none"> “This study demonstrated that the use of copper oxide containing linens reduced HAI in a long-term care ward. There is no reason to believe that reducing the bioburden in a regular ward by using biocidal linens would not affect the HAI rates. The use of biocidal textiles should be a complementary approach to fight nosocomial infections in all medical institutions, as well as care homes for the elderly, where the risks of acquiring an infection are high.”¹ page 28
Ryan, 2011 ³	
<ul style="list-style-type: none"> Percentage of high-risk sub-population who had VAP decreased from approximately 74% before eUVGI was installed to 55% 6 months after eUVGI and to 44% at 18 months ($P = 0.04$). There was a significant decrease in the 	<ul style="list-style-type: none"> “In conclusion, eUVGI eradicated microbes in HVACs, and was associated with a decrease in NICU environmental pathogens and tracheal colonization. Significant reductions in VAP and antibiotic use in NICU high-risk patients were

Table A3: Summary of Findings of Included Studies

Main Study Findings	Author's Conclusions
<p>number of VAP episodes (1.7 pre-eUVGI to 1.1 after 18 months of eUVGI, $P = 0.01$) and in the number of antibiotics per high-risk patient (means [SD]: 2.6 [2.7] pre-eUVGI to 1.0 [1.5] after 18 months of eUVGI, $P = 0.01$).</p> <ul style="list-style-type: none"> The use of eUVGI results in decreased bioload of tracheal secretions, with the percent of patients who had little or no tracheal colonization ($MLI \leq 1$) increasing from 14% pre-eUVGI to 44%. 	<p>associated with eUVGI in this limited study. Large multicenter randomized trials are needed to further characterize the effects of eUVGI on the full spectrum of adult, pediatric and neonatal hospital populations.”³ page 613</p>
<p>Boyce, 2008⁵</p>	
<ul style="list-style-type: none"> The incidence of CDAD on five high-incidence wards reduced significantly from 2.28 cases per 1,00 patient-days in the pre-HPV period to 1.28 per 1,000 patient days during the intervention period ($p = 0.047$). The overall hospital-wide incidence of nosocomial CDAD reduced from 1.36 to 0.84 cases per 1,000 patient-days ($p = 0.26$) from the pre-intervention to intervention periods, respectively. Hospital-wide incidence of CDAD reduced from 1.89 to 0.88 cases per 1,000 patient-days ($p = 0.047$), from pre-intervention to intervention periods, respectively, when analysis were confined to the months when epidemic strain was known to be present in both of the two periods. 	<ul style="list-style-type: none"> “Our study found that the HPV decontamination process we used (Bioquell) was efficacious in eradicating <i>C. difficile</i> from contaminated surfaces in a hospital setting. Furthermore, HPV decontamination may have reduced transmission of <i>C. difficile</i> with the facility, although further studies are warranted to confirm this finding.”⁵ page 728

CD = *Clostridium difficile*; CDAD = *Clostridium difficile*-associated disease; CI = confidence interval; eUVGI = enhanced ultraviolet germicidal irradiation; HAI = healthcare-associated infections; HPV = hydrogen peroxide vapor HVAC = heating ventilation and air conditioning; IRR = incidence rate ratio; MDRO = Multiple-drug-resistant organisms; MLI = microbial load index; MRSA = methicillin-resistant *Staphylococcus aureus*; NICU = neonatal intensive care unit; SD = standard deviation SR = systematic review; UV = ultraviolet; UVD = UV environmental disinfection; VAP = ventilator-associated pneumonia; VHP = vaporized hydrogen peroxide; VRE = vancomycin-resistant enterococcus;

APPENDIX 5: Additional References of Potential Interest*Included in Previous Rapid Response Report*

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Passaretti CL, Otter JA, Reich NG, Myers J, Shepard J, Ross T, et al. An evaluation of environmental decontamination with hydrogen peroxide vapor for reducing the risk of patient acquisition of multidrug-resistant organisms. *Clin Infect Dis*. 2013 Jan;56(1):27-35.

Inappropriate (Mixed) Intervention

Mitchell BG, Digney W, Locket P, Dancer SJ. Controlling methicillin-resistant *Staphylococcus aureus* (MRSA) in a hospital and the role of hydrogen peroxide decontamination: an interrupted time series analysis. *BMJ Open* [Internet]. 2014 [2015 May 27];4(4):e004522, 2014. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3996814>

Non-clinical Outcomes

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Boyce JM, Havill NL, Moore BA. Terminal decontamination of patient rooms using an automated mobile UV light unit. *Infect Control Hosp Epidemiol*. 2011 Aug;32(8):737-42.

Havill NL, Moore BA, Boyce JM. Comparison of the microbiological efficacy of hydrogen peroxide vapor and ultraviolet light processes for room decontamination. *Infect Control Hosp Epidemiol*. 2012 May;33(5):507-12.

Sitzlar B, Deshpande A, Fertelli D, Kundrapu S, Sethi AK, Donskey CJ. An environmental disinfection odyssey: evaluation of sequential interventions to improve disinfection of *Clostridium difficile* isolation rooms. *Infect Control Hosp Epidemiol*. 2013 May;34(5):459-65.

Irrelevant Outcomes

Nardell EA, Bucher SJ, Brickner PW, Wang C, Vincent RL, Becan-McBride K, et al. Safety of upper-room ultraviolet germicidal air disinfection for room occupants: results from the Tuberculosis Ultraviolet Shelter Study. *Public Health Rep* [Internet]. 2008 Jan [cited 2015 May 27];123(1):52-60. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2099326>

Non-systematic Reviews

Chemaly RF, Simmons S, Dale C, Jr., Ghantaji SS, Rodriguez M, Gubb J, et al. The role of the healthcare environment in the spread of multidrug-resistant organisms: update on current best practices for containment. *Ther adv infect dis* [Internet]. 2014 Jun [cited 2015 May 27]; 2(3-4):79-90. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4250270>