Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

TITLE: Non-Manual Techniques for Room Disinfection in Healthcare Facilities: A Review of Clinical Effectiveness and Guidelines

DATE: 30 April 2014

CONTEXT AND POLICY ISSUES

Contaminated surfaces in healthcare facilities may contribute to the transmission of pathogens implicated in nosocomial infections, such as *Clostridium difficile*, methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococci* (VRE), gram-negative rods (*Acinetobacter spp*. and *Enterobacteriaceae)* and Norovirus.[1,2] While patient rooms are regularly cleaned and disinfected using manual techniques, evidence suggests that the adequacy of cleaning is often suboptimal, particularly when the focus is only on those surfaces perceived to be high-risk or frequently contacted (high-touch).[1] As well, when cleaning, sufficient wet contact time between the surface and disinfectant is needed to ensure adequate disinfection, but is not always achieved.[1] Wiping of all surfaces where there is hand contact, not just those that are considered to be high risk or high-touch areas, and ensuring adequate wet contact time is required for adequate disinfection of the patient environment.[1]

Inadequate cleaning using manual techniques prompted the development of no-touch systems that can decontaminate objects and surfaces in the patient environment.[1,2] These technologies employ the use of ultraviolet (UV) light or hydrogen peroxide. There are two systems that use vaporized hydrogen peroxide (VHP) in a dry or wet aerosol and one that uses a hydrogen peroxide mist (HPM), which has a larger particle size.[1,2] VHP or HPM is produced using a portable generator that quickly increases the concentration of hydrogen peroxide in the room during a decontamination phase which is repeated several times.[1,2] The process takes approximately two to six hours per room.[2] The UV light systems emit UV light from portable automated units at a wave-length that is germicidal. The unit is placed in a vacant patient room in the centre and can be piloted with a remote to ensure all surfaces are reached as they must be in the line of site to be decontaminated. The units have sensors which stop the irradiation should the door be opened.[2] The process of decontamination takes approximately 45 minutes. One application of these cleaning systems is in terminal or discharge decontamination of vacated patient rooms. They supplement, but do not replace manual cleaning of patient rooms, as surfaces must first be free of dirt and debris prior to their use. Vaporized hydrogen peroxide and UV light systems provide a higher level disinfection or decontamination of all exposed surfaces and equipment in patient rooms, and are not a standalone means of cleaning.[1,2]

Vaporized hydrogen peroxide has also been used for decontamination of rooms and ward spaces in an attempt to terminate outbreaks. This report will review the evidence of clinical effectiveness of non-manual systems that use UV light or vaporized hydrogen peroxide for hospital room disinfection and identify guidelines that address the use of these techniques in healthcare facilities.

RESEARCH QUESTIONS

1. What is the clinical effectiveness and safety of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?

2. What are the evidence-based guidelines for the use of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?

KEY FINDINGS

Low quality evidence from one systematic review and three cohort studies suggests that VHP is effective in reducing the incidence of nosocomial infections due to a number of different pathogens in hospital settings. In three low quality case studies, VHP decontamination successfully terminated *Acinetobacter baumannii* outbreaks. Low quality evidence from one cohort study suggests that UV light reduces the incidence of hospital-associated *C. difficile* infections. Two evidence-based guidelines included VHP and UV light decontamination in their scope and found that there was insufficient evidence to make recommendations about the use of these methods.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 3), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to documents published between January 1, 2009 and March 31, 2014.

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

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications to determine if they were relevant to the review. The same reviewer evaluated the full-text publications for the final article selection into the report based upon the criteria identified in Table 1.

Table 1: Selection Criteria

Population	Hospital or healthcare facility rooms
Intervention	Non-manual techniques that incorporate UV light or hydrogen peroxide (e.g., gaseous hydrogen peroxide; hydrogen peroxide plus ozone; vapourized accelerated hydrogen peroxide)
Comparator	Manual techniques or no comparator
Outcomes	Q1: Transmission of infection to patients; safety Q2: Guidelines
Study Designs	Health technology assessments (HTA), systematic reviews (SR), meta-analyses (MA), randomized controlled trials (RCTs), non-RCTs, and guidelines

HTA - Health technology assessment; MA - Meta-analysis; Q - Question; RCT - Randomized controlled trial; SR - Systematic review

Exclusion Criteria

Articles were excluded if they did not meet the predefined selection criteria as outlined in Table 1 or were outside of the timeframe of the search. As well, review articles that were not based upon a systematic literature search, duplicate publications of the same study, and guidance documents or consensus statements that did not include a description of the methodology used in their development or were not clearly evidence-based were excluded from the report. Studies that reported only laboratory outcomes (e.g., culture results from room surfaces) were also excluded, but are listed in Appendix 5.

Critical Appraisal of Individual Studies

Systematic reviews were critically appraised using the AMSTAR tool.[3] Cohort studies were critically appraised using the SIGN 50 Checklist for Cohort Studies.[4] Guidelines were evaluated using the AGREE II tool.[5] Items from these tools were considered in assessing the quality of the included literature and results of the critical appraisal are discussed narratively. Numeric scores from these tools were not calculated. Case studies were not critically appraised formally using a specific tool or instrument. The quality of these studies will be discussed in the limitations section

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 147 citations. After screening citations from the database and grey literature searches, 16 potentially relevant studies were obtained for full-text review. One systematic review,[6] seven studies of clinical effectiveness[7-13] and two evidence-based guidelines[14,15] met the selection criteria and were included in the review. Of the seven included clinical studies, one was a prospective cohort study,[9] three were cohort studies with historical controls,[7,8,13] and three were case studies.[10-12] The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

1. *What is the clinical effectiveness and safety of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?*

The characteristics of the included systematic review[6] can be found in Appendix 2, Table 3. This systematic review included literature up to 2009 that assessed the effectiveness of VHP as an infection control measure in a hospital environment. There were no reported restrictions on study design or requirement of a comparator. In total 10 studies, were included in the systematic review, four of which evaluated the effectiveness of VHP in reducing the transmission of pathogens or nosocomial infection rates. The remaining six studies reported only on the effectiveness of VHP for disinfection and did not report on patient outcomes, so were not relevant to this Rapid Response report. The research design of the four relevant studies was not specified and it appeared that formal critical appraisal was not performed.

Details of the included individual clinical effectiveness studies can be found in Appendix 2, Table 4. The effectiveness of VHP decontamination in reducing the rates of nosocomial infection when added to standard cleaning was evaluated in three studies, relative to standard cleaning alone.[7-9] One cohort study evaluated the clinical effectiveness of a portable pulsed xenon UV device when added to standard cleaning, relative to standard cleaning alone.[13] Three of the cohort studies were carried out in the United States[8,9,13] and one in France.[7] One included cohort study assessed the clinical effectiveness of VHP using a concurrent design, with three units undergoing decontamination with VHP in addition to standard cleaning (exposed cohort) and the three units undergoing standard cleaning alone (unexposed cohort).[9] The remaining three cohort studies[7,8,13] compared a cohort of patients who were hospitalized during a time period when VHP was used as an additional method of room decontamination at a specific site to a historical cohort of unexposed patients (e.g., those admitted to the same units over a time period prior to decontamination). Three studies included patients hospital-wide[8,9,13] and one study included only patients on burn units.[7] Two studies assessed the impact of decontamination with VHP[8] or UV light[13] on rates of nosocomial *C. difficile* infection. The remaining two cohort studies evaluated the efficacy of VHP on reducing rates of nosocomial infections with a number of different organisms.[7,9]

Details of the three included case studies[10-12] are also found in Appendix 2, Table 4. One case study was from Poland[10], one from the United Kingdom,[11] and one from the United States.[12] In all case studies VHP was used after initial attempts at outbreak control without VHP decontamination were unsuccessful. *A. baumannii* was the pathogen implicated in two outbreaks[10,12] and in one, *Enterobacter cloacae* was also implicated in addition to *A. baumannii*.[11] One case study was specific to an intensive care unit[11] and two were hospital-wide.[10,12] In two case studies, decontamination with VHP was performed a single time[11,12] and in one case study, it was not clear if decontamination was implemented one-time or was ongoing.[10]

2. *What are the evidence-based guidelines for the use of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?*

Two evidence-based guidelines included statements about use of VHP or UV light decontamination (Appendix 2, Table 5).[14,15] One guideline was from the United Kingdom's National Health Service (NHS)[15] and one was from the Centers for Disease Control and Prevention (CDC) in the United States.[14] The NHS guideline addressed standard infection

control measures in hospital, not specific to a particular pathogen, while the CDC guideline was specific to Norovirus. Both guidelines identified the relevant literature through systematic search methods, used standard systematic review techniques for screening, literature selection, and data extraction, and used working groups to formulate recommendations based upon graded literature. For both guidelines, the recommendations were subsequently reviewed by experts and stakeholders prior to finalization.

Summary of Critical Appraisal

1. *What is the clinical effectiveness and safety of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?*

Details of the critical appraisal of the included clinical effectiveness studies are summarized in Appendix 3, Table 6. The systematic review of the clinical effectiveness of VHP was a carried out using an a priori design (as stated by the authors, but additional details were not provided), described the characteristics of included studies, and provided a statement of conflict of interest.[6] Limited selection criteria were described and was unclear if study selection and data extraction occurred in duplicate. The literature search did not appear to be comprehensive as Pubmed was the only database searched and the grey literature was not searched. As well, the authors did not provide a list of excluded studies, critically appraise the included studies, or assess the likelihood of publication bias.

The included cohort studies had a number of limitations (Appendix 3, Table 6). It was unclear if the exposed and unexposed patients were similar as patient characteristics were not reported in three of the four studies.[7,8,13] In three studies, the exposed and unexposed cohorts were from different time periods, which may increase the potential for differences in characteristics between groups and in cleaning methods used.[7,8,13] In the concurrent cohort study,[9] the source populations came from different unit types and differences between the two populations were observed. The outcome was clearly defined in two studies,[7,9] but the definition of what was considered to a nosocomial infection was unclear in the other two. In one study, 44% of rooms did not undergo decontamination with UV light. Thus, there was potential for misclassification on exposure.[13] While it was unclear if the outcome assessment was blind the four cohort studies, the outcome itself was generally objective (i.e., a positive culture or immunoassay). Two studies ensured that patients did not have the outcome (an infection with the pathogen of interest) at the time of exposure (i.e, admission to the facility or unit),[7,9] while two studies (both reporting on *C. difficile* infection rates) did not appear to do so.[8,13] In three studies, it was unclear if all patients admitted to the hospital or units of interest were included in the analysis or had complete follow-up data.[7,8,13] One of the four cohort studies controlled for potential confounders in the statistical analysis and included confidence intervals for its estimates of risk.[9] One study reported on rates of co-intervention (such as hand hygiene, glove and gown precaution) and identified these as potential confounders, but did not attempt to adjust for these in the analysis.[8]

A formal quality assessment of case reports was not conducted since they provide limited information. The quality of these studies will be discussed in the limitations section.

2. *What are the evidence-based guidelines for the use of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?*

Details of the critical appraisal of the included guidelines are summarized in Appendix 3, Table 7. Both guidelines were developed by national organizations with established, standardized, rigorous methods for guideline development for the systematic literature review component and development of recommendations. As such, the criteria from the Agree II tool that relate to these and most other domains were met by both guidelines.[14,15] However, neither guideline described barriers or facilitators to implementation or application. Advice on implementation and auditing criteria was limited.[14,15]

Summary of Findings

Main findings of included studies are summarized in detail in Appendix 4, Table 8.

1. *What is the clinical effectiveness and safety of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?*

The included systematic review reported the results of two case studies, one with successful termination of an outbreak of MRSA and one with successful termination of an outbreak of *Serratia* spp.[6] A reduction in *C. difficile* nosocomial infections with VHP decontamination was also reported, however, further detail was not reported in the publication with respect to the study design or data for this outcome.

Passerretti et al.[9] and Barbut et al.[7] reported on the clinical effectiveness of VHP in reducing the nosocomial infection rates of several different pathogens. Passeretti et al.[9] found a 75% reduction in the rate of nosocomial infections attributed to VRE [incidence rate ratio (IRR) 0.25 (95% CI: 0.10 to 0.60, P < 0.01)] with VHP decontamination and reduction of 64% [IRR: 0.36 (95% CI: 0.19 to 0.70, P < 0.01) when the results for all of the pathogens of interest were combined. The individual rate ratios (RRs) for MRSA, multi-drug resistant gram-negative rods, and *C. difficile* were not statistically significant. Barbut et al.[7] found a statistically significant reduction in the MRSA (89.3%, P < 0.0001), *A. baumannii* (88.8%, P = 0.002) and combined multi-drug resistant infection or colonization rate (84.9%, P < 0.0001) following decontamination with VHP. The reduction in nosocomial infection or colonization rate with extended spectrum beta lactamase-producing *Enterobacteriaceae* was not statistically significant.[7] Manian et al.[8] also found a statistically significant reduction (37%, P < 0.0001) in the rate of nosocomial infection with *C. difficile* in the time period following VHP decontamination [RR: 0.63 (95% CI: 0.50 to 0.79)]. The use of UV light for decontamination was also associated with a reduction (53%, P < 0.01, RR not reported) in the rate of nosocomial *C. difficile* infection.[13] Deaths and colectomies related to *C. difficile* infection were also reduced; however, no statistical analyses of these endpoints were performed.

Three case studies reported successful termination of *A. baumannii* outbreaks following VHP decontamination.[10-12] In one case study a second outbreak of *A. baumannii* occurred and decontamination was repeated.[10] No new cases were reported approximately one year following the second decontamination. In another case study, new cases of *A. baumannii* reappeared four to six months following decontamination.[11] Cases of *E. cloacae* also appeared following decontamination in this case study.[11]

2. *What are the evidence-based guidelines for the use of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities?*

Two guidelines included decontamination with VHP and UV light in their scope and their recommendations are summarized in Table 2.[14,15] Both guidelines suggested that evidence was insufficient at the time of guideline writing to make a recommendation about the use of VHP or UV light for decontamination in healthcare settings.

Table 2: Evidence-based guidelines for the use of non-manual techniques utilizing UV light or hydrogen peroxide for room disinfection in healthcare facilities

Guideline, Publication Year	Recommendations
National Health Service, 2014[15]	"*New technologies for cleaning and decontaminating the healthcare environment have become available over the past 10 years, including hydrogen peroxide, and others are in the early stages of development.* *The effectiveness, cost-effectiveness and practicality of this and other new technologies in terms of reducing HCAI and routine use in the variety of facilities in UK hospitals has yet to be demonstrated." p. S15* No grade of recommendation provided.
Centers for Disease Control and Prevention, 2011[14]	*"More research is required to clarify the effectiveness and reliability of fogging, UV irradiation, and ozone mists to reduce norovirus environmental contamination." p.16* No recommendation/unresolved issue.

HCAI: healthcare associated infection; UV: ultraviolet

Limitations

There were a number of limitations to the included systematic review and individual studies of clinical effectiveness of VHP and UV light as decontamination methods to reduce the incidence of nosocomial infections. The systematic review did not clearly describe its methodology for study selection or data extraction, the literature search did not appear to be comprehensive and the quality of the included studies was not assessed.[6] As well, the literature search was prior to 2010. Since then, a number of studies of VHP have been published, so the body of included evidence cannot be considered current. As well, while no quality assessment was presented, it is likely that the four included studies would have been lower quality since they do not report outcomes consistent with a randomized, controlled design.

There were no individual randomized controlled trials (RCTs) of the clinical effectiveness of VHP identified by the literature search. While three cohort studies were identified that assessed the clinical effectiveness of VHP in reducing the rate of nosocomial infections, these studies had a number of methodological limitations.[7-9] All studies were carried out at single institutions, which may limit their generalizability to other institutions and countries. Confounding was a concern in the included studies. Often other interventions or initiatives were active during the evaluation period which limits the ability to solely attribute the reduction in nosocomial infection rates to the decontamination specifically. Given that historical controls were used in two studies, it would not be possible to determine adherence to cleaning standards during that time. Patient characteristics were not reported in two of the cohort studies, so it was not possible to assess if potential confounders were evenly distributed between groups.[7,8] While the concurrent cohort

study attempted to control for confounders and differences between the exposed and unexposed groups, it is not possible to control for unknown confounders.[9] Moreover, the rates of nosocomial infections with some pathogens were small, which reduced the power to detect a statistically significant difference in the exposed and unexposed groups.[9] Due to difficulties with logistics, not all rooms underwent decontamination following terminal cleaning, which creates the potential for misclassification on exposure. Finally, the longest follow-up period was approximately 18 months.[9] It is unclear if the reduction in rates of nosocomial infections would be maintained over longer periods of time.

Three case studies provide additional evidence on the clinical effectiveness of VHP in the termination of outbreaks, but the lack of a control or comparison groups precludes the ability to attribute termination of the outbreak solely to decontamination with VHP. As well, these case studies were limited to gram negative rods (*A. baumannii* and *E. cloacae)*.

One cohort study with poor quality of reporting assessed the clinical effectiveness of UV light in reducing the incidence of nosocomial infections and this study was specific to *C. difficile*.[13] None of the SIGN 50 checklist items were satisfied for this study, which compromises that ability to attribute the reduction in nosocomial infection with *C. difficile* to decontamination with UV light. No literature on the effectiveness of UV light decontamination in reducing the risk of nosocomial infections for other pathogens was found, nor were any RCTs.

No literature was identified that assessed the safety or risk of adverse effects of decontamination with UV light or VHP for either patients or healthcare workers.

While two methodologically rigorous guidelines were identified that included UV light or VHP in their scope, evidence was considered insufficient to formulate recommendations about their use.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

No high quality systematic reviews or RCTs were identified that assessed the clinical effectiveness and safety of VHP or UV light for decontamination in healthcare settings. Low quality evidence suggests that VHP is effective in reducing the incidence of nosocomial infections due to a number of different pathogens in hospital settings. However, given the limitations of the literature included in this Rapid Response report, higher quality evidence is likely required prior to a decision to adopt the use of VHP devices on a routine basis following terminal cleaning. Further, given that healthcare workers and patients cannot be in the room during decontamination and the time required for the decontamination cycles (up to four hours), there is a potential for a delay in bed turnover when using VHP as a means of decontamination following terminal cleaning. Thus, logistics related to its integration are an additional consideration with its application. Low quality case study evidence suggests VHP may be potentially useful for decontamination to terminate outbreaks of gram negative rods, failing termination with other measures. In the included case reports, decontamination was performed on a one-time basis, and not as a routine measure.

One low quality cohort study assessed the effectiveness of UV light for decontamination in healthcare settings and found that it reduced the incidence of hospital associated *C. difficile* infection. However, given the limitations of this study, no clear conclusions can be made with respect to its clinical effectiveness.

No conclusions can be made with respect to the safety and adverse effects of UV light or VHP for either patients or healthcare workers given the lack of evidence identified. Further, while two high quality evidence-based guidelines were identified that included UV light or VHP in their scope, recommendations about the use of these decontamination methods were not made, due to the limited evidence available.

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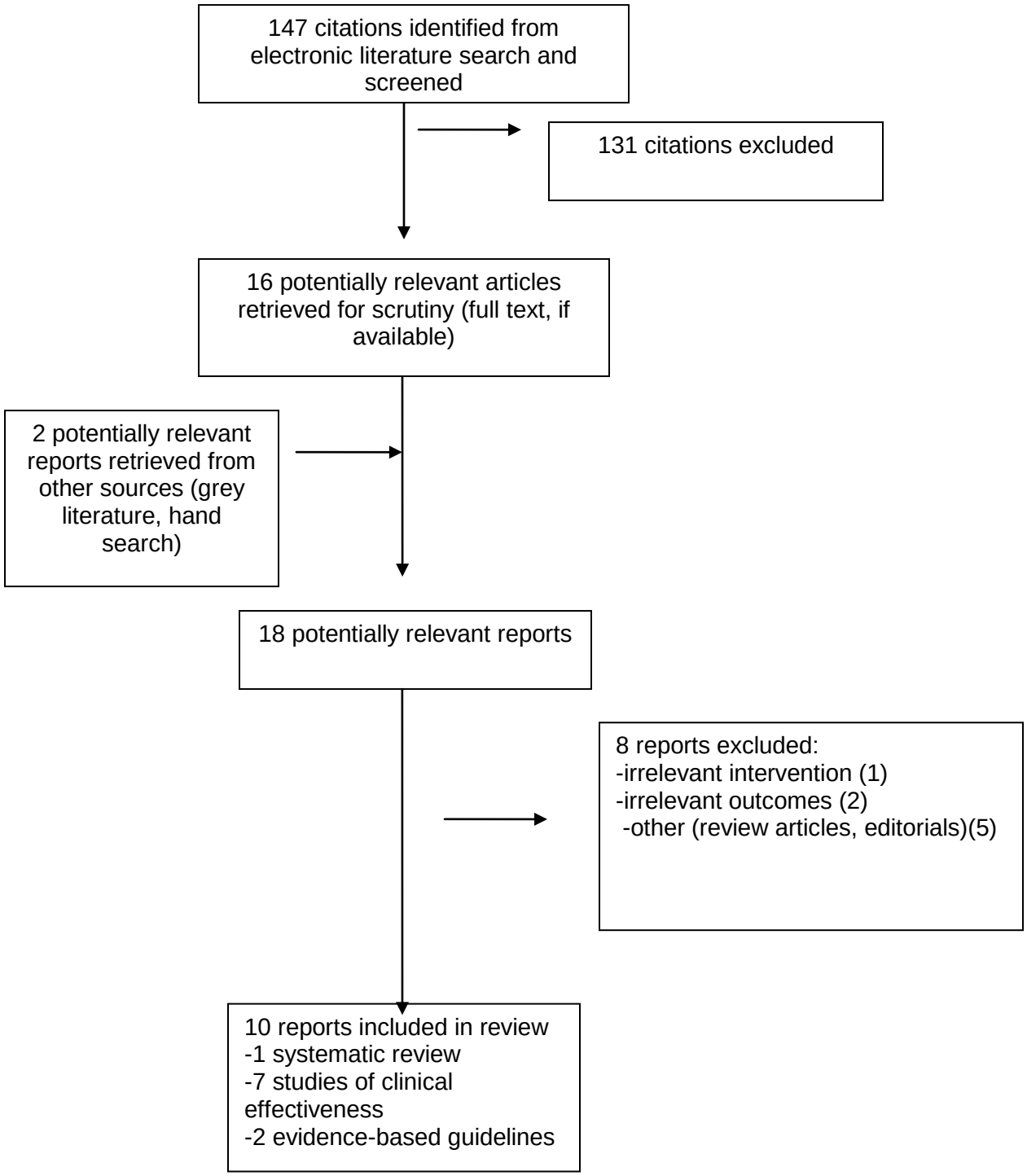
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Summary of Individual Study Characteristics

Table 3: Table of Characteristics of Included Systematic Reviews

First Author, Publication Year, Country	Literature Search Strategy	Inclusion Criteria	Exclusion Criteria	Number of Included Relevant Studies	Critical Appraisal of Included Studies
Flagas et al., 2011[6] Greece	Pubmed search up to December 2009 Reviewed bibliographies of relevant studies	Published studies Population: hospital environment Intervention: airborne hydrogen peroxide (VHP) as an infection control measure Comparator: not stated Outcome: not stated	Pathogens must be naturally dispersed, not artificially inoculated.	Four studies of VHP as an infection control measure in a clinical setting	Not reported

VHP – Vaporized hydrogen peroxide

Table 4: Table of Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design	Setting	Intervention	Comparator	Clinical Outcomes
Hydrogen Peroxide					
Barbut et al, 2013[7] France	Cohort study with historical controls Pre-intervention period December 2006 to August 2008 Intervention period September 2008 to December 2009	Burn units a single hospital	Infection control bundle that consisted of: • Regular VHP disinfection of the rooms following discharge of patients colonized or infected by MDROs • Pre-emptive isolation of newly admitted patients before proven	Infection control bundle that consisted of (pre-intervention period): • Screening patients for MDROs • Contact precautions for colonized patients with MDROs • Promotion of alcohol based hand hygiene products	Nosocomial infection rates • MRSA • *baumannii* • ESBL- producing Enterobacteriaceae • Combined

First Author, Publication Year, Country	Study Design	Setting	Intervention	Comparator	Clinical Outcomes
			culture negative • Cohorting of colonized patients • Installation air disinfection systems in the corridors • Improved material storage • Increased emphasis on hand hygiene		
Manian et al., 2013[8] United States	Cohort study with historical controls Pre-intervention period January 2007 to November 2008 Intervention period January 2009 to December 2009	Community teaching hospital with 900 beds	• VHP decontamination • Contact precautions • Compliance with hand hygiene • Routine terminal cleaning with 1 round of bleach	• Contact precautions • Compliance with hand hygiene • Routine terminal cleaning with 4 rounds of bleach for patients with CDAD and 1 round for other patients	Rates of nosocomial CDAD
Passarettti et al, 2013[9] United States	Prospective cohort study Pre-intervention period January 2007 to December 2007 Intervention period January 2008 to June 2009	Tertiary referral hospital with 994 beds 3 units had intervention (n=437 patients) and 3 units served as the control (standard cleaning only; n=927 patients)	VHP decontamination plus standard cleaning: • Daily cleaning of floors and surfaces with a quaternary ammonium compound • Liquid hydrogen peroxide used for cleaning of rooms of patients with *C. difficile* Other infection control measures: • Swabs for VRE and MRSA on admission and weekly thereafter	Standard cleaning • Daily cleaning of floors and surfaces with a quaternary ammonium compound • Liquid hydrogen peroxide used for cleaning of rooms of patients with *C. difficile* Other infection control measures: • Swabs for VRE and MRSA on admission and weekly thereafter	Acquisition rates of MDROs per 1000 patient days* • VRE • MRSA • MDR-GNR • *C. difficile* • Combined Incidence rate ratios adjusted for age, mortality risk score, unit, HIV status, ESRD, calendar time and

First Author, Publication Year, Country	Study Design	Setting	Intervention	Comparator	Clinical Outcomes
			• *C. difficile* cultures where clinically indicated.	• *C. difficile* cultures where clinically indicated.	compliance with MDRO surveillance procedures.
Chmielarczyk et al., 2012[10] Poland	Case study Two outbreaks of multi-drug resistant *A. baumannii* in 2009 and 2010	526-bed teaching hospital	VHP combined with routine decontamination and additional measures: • Closure of affected units for VHP decontamination • Daily cleaning of all equipment with a hypochlorite-based agent • Standardized CDC infection prevention measures • Staff education	Initial attempt at outbreak control: • "Preparations containing hydrogen peroxide, chlorides and quaternary ammonium compounds for large surfaces. • Preparations containing chlorides and cyanuric acid or sodium bisulphate and sodium tetraborate for sinks, toilets and fluid spills. • An alcohol-based preparation for rapid disinfection of small surfaces" p. 240	Control of outbreak
Otter et al., 2010[11] United Kingdom	Case study Outbreak of *Acinetobacter* spp. and *Enterobacter cloacae* between June 2005 and March 2006	12 bed ICU	One time VHP decontamination of the entire ICU	Initial attempt at outbreak control: • Standard infection control measures, education of staff, routine use of sodium hypochlorite; 70% alcohol for cleaning of equipment.	Control of outbreak
Ray et al., 2010[12] United States	Case study Outbreak of *A. baumannii* in January	54 bed long-term acute care hospital	One time VHP decontamination of all rooms after terminal cleaning.	Initial attempt at outbreak control: • "Tightening of basic infection control	Control of outbreak

First Author, Publication Year, Country	Study Design	Setting	Intervention	Comparator	Clinical Outcomes
	2008			strategies, such as hand hygiene, environmental cleaning, and adherence to use of personal protective equipment."p.2	
UV Light					
Levin et al., 2013[13] United States	Cohort study with historical controls Pre-intervention: 2010 Intervention: 2011	140 bed acute care community hospital	Portable pulsed xenon UV device after terminal cleaning of *C. difficile* rooms with a chlorine based product. Device also used in other rooms according to priority: ICU, medical/surgical, labor and delivery, operating, and emergency department rooms, and on shared medical equipment. Soap and water for hand hygiene. Contact precautions	Terminal cleaning with a chlorine based product of *C. difficile* rooms. Soap and water for hand hygiene. Contact precautions. Staff education. Beeper system to alert when chlorine-based cleaning was required.	Control of hospital-associated *C. difficile* infection. Deaths Colectomies

CDC – Centers for Disease Control; CDAD – *C. difficile* associated diarrhea; ERSD – End stage renal disease ESBL – Extended spectrum beta lactamase; HIV – Human immunodeficiency virus; ICU – Intensive care unit; MDROs - multi-drug resistant organisms; MRAB – multi-drug resistant *Acinetobacter baumannii*; MDR-GNR – multi drug resistant gram negative rod; UV – Ultra violet; VHP – Vaporized hydrogen peroxide; VRE – Vancomycin Resistant *Enterococci*
*Included those patients admitted to a room previously occupied by a patient with MDROs.

Table 5: Characteristics of Included Evidence-Based Guidelines

Target	Scope, Purpose, Country of Origin	Evidence Collection, Selection and Synthesis	Strength of Recommendation	Formulation of Recommendations
National Health Service, 2014[15]				
National Health Service hospitals and other acute care settings in England For healthcare providers	**Purpose:** "These guidelines describe clinically effective measures that are used by healthcare workers for preventing infections in hospital and other acute healthcare settings." p. S11 **Scope:** "standard infection control principles: including best practice recommendations for hospital environmental hygiene, effective hand hygiene, the appropriate use of PPE, the safe use and disposal of sharps, and the principles of asepsis" p.S11	Systematic literature search of multiple electronic databases for systematic reviews, guidelines, additional evidence. Titles and abstracts screened by a two reviewers; full-text citations screened by two reviewers and selected for inclusion based upon predetermined criteria. Data extracted by one experienced reviewer.	According to the SIGN classification scheme: **A -** At least one meta-analysis, systematic review or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results **B -** A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+ **C -** A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++ **D -** Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+ **Good Practice Point -** Recommended best practice based on the clinical experience of the Guideline Development Advisory Points Group and patient preference and experience	Guideline Development Advisory Group reviewed evidence tables and drafted guidelines after extensive discussion. External consultation with stakeholders and experts and comments sent to the Guideline Development Advisory Group for consideration.

Target	Scope, Purpose, Country of Origin	Evidence Collection, Selection and Synthesis	Strength of Recommendation	Formulation of Recommendations
			IP - Recommendation from NICE Interventional Procedures guidance	
Centers for Disease Control and Prevention, 2011[14]				
All patient populations and healthcare settings Specific to Norovirus	"…intended for use by infection prevention staff, physicians, healthcare epidemiologists, healthcare administrators, nurses, other healthcare providers, and persons responsible for developing, implementing, and evaluating infection prevention and control programs for healthcare settings across the continuum of care" p.10 United States	Systematic literature search of multiple electronic databases. Titles and abstracts screened by a single reviewer; full-text citations screened by two reviewers and selected for inclusion based upon predetermined criteria. Data extracted into standardized forms and verified by a second reviewer. Meta-analysis only performed when considered critical to making a recommendation.	**Category IA** – A strong recommendation supported by high to moderate quality evidence suggesting net clinical benefits or harms. **Category IB** – A strong recommendation supported by low-quality evidence suggesting net clinical benefits or harms, or an accepted practice (e.g., aseptic technique) supported by low to very low-quality evidence. **Category IC** – A strong recommendation required by state or federal regulation. **Category II -** A weak recommendation supported by any quality evidence suggesting a tradeoff between clinical benefits and harms. **Recommendation for further research** - An unresolved issue for which there is low to very low-quality evidence with uncertain tradeoffs between benefits and harms.	Narrative evidence summaries drafted by a working group using the evidence and GRADE tables and used as the basis of making recommendations. Content of the draft is reviewed in depth by experts and revisions made. Entire draft guideline is then presented to HICPAC for review.

GRADE - Grading of Recommendations Assessment, Development and Evaluation; HICPAC - Healthcare Infection Control Practices Advisory Committee; RCT – randomized controlled trial; NICE – National Institute of Health and Care Excellence; PPE – personal protective equipment; SIGN – Scottish Intercollegiate Guidelines Network;

APPENDIX 3: Summary of Critical Appraisal

Table 6: Critical Appraisal of Included Studies of Clinical Effectiveness*

First Author, Publication Year	Strengths	Limitations
Systematic Reviews (AMSTAR)[3]		
Flagas et al., 2011[6]	• *a priori* design provided • Characteristics of included studies provided • Conflict of interest stated (none declared)	• Unclear if duplication study selection and data extraction • Literature search only included PubMed • Did not appear to have searched the grey literature • No list of excluded studies • Did not formally assess study quality and did not discuss quality when formulating conclusions • Did not assess likelihood of publication bias.
Cohort Studies (SIGN-50 Checklist for Cohort Studies)[4]		
Vaporized Hydrogen Peroxide		
Passarettti et al, 2013[9]	• Appropriate and clearly focused research question • Reported percentage who participated in each group • Likelihood that some eligible participants might have the outcome was assessed. Those participants were removed from the analysis. • Follow-up was complete • Assessment of exposure was reliable • Outcome was clearly defined • Potential confounders accounted for in the analysis • Confidence intervals reported with the statistical analysis	• Unclear if source populations were comparable as the VHP and control patients were from different types of units • Unclear of outcome assessment was blind, but objective outcome measure (positive culture)
Barbut et al, 2013[7]	• Unlikely that participants could have the outcome at time of enrolment (swabbed for MDROs at time of admission) • Outcome clearly defined • Assessment of exposure was reliable	• Objective was not clearly stated • No patient characteristics reported. Exposed and unexposed cohorts from a different period of time. • The percentage of patients from each period included in the analysis was unclear • Unclear if data were available for all participants. • Unclear if blind to outcome assessment, but objective outcome measure (positive culture) • No confidence intervals provided • Confounders not controlled for
Manian et al., 2013[8]	• Reported on potential confounding related to hand hygiene, glove and gown precautions and volume of antimicrobial use during the two study periods.	• Objective was not clearly stated • Unclear how they defined *C. difficile* -associated diarrhea. • No patient characteristics reported. Exposed and

First Author, Publication Year	Strengths	Limitations
		unexposed cohorts from a different period of time. • The percentage of patients from each period included in the analysis was unclear. • Did not report if they assessed patients at time of enrolment to determine if they had *C. difficile* • Unclear if follow-up data were available for all participants • Unclear if blind to outcome assessment • No confidence intervals provided • Confounders related to patient characteristics not controlled for.
UV Light		
Levin et al., 2013[13]	• No major strengths identified	• Objective was not clearly stated • No patient characteristics reported so unclear is comparable. Exposed and unexposed cohorts from a different period of time. • Unclear how they defined *C. difficile* -associated diarrhea. • No all patient-rooms (56%) received the intervention. • The percentage of patients from each period included in the analysis was unclear. • Did not report if they assessed patients at time of enrolment to determine if they had *C. difficile* • Unclear if follow-up data were available for all participants • Unclear if blind to outcome assessment, but objective outcome measure (immunoassay or PCR test) • Method of outcome assessment changed during the two time periods from immunoassay to PCR test • No confidence intervals provided • Did not control for confounders.

* Items that were 'not applicable' based upon study design or other characteristics are not reported
MDRO – Multi-drug resistant organisms; PCR – Polymerase chain reaction

Table 7: Critical Appraisal of Included Evidence-Based Guidelines

First Author, Publication Year	Strengths	Limitations
Evidence-Based Guidelines (Agree II)[5]		
National Health Service, 2014[15]	• Overall objective clearly described • Health questions covered by guideline specifically described • Population to whom the guideline is meant to apply is specifically described • Relevant professional groups included in guideline development o Infectious disease, epidemiology, nursing, urology, anesthesiology, methodologists included. • Target users of the guideline clearly defined • Views and preferences of the target population were sought • Systematic methods used for literature search • Selection criteria for the evidence described clearly • Strengths and limitations of the body of evidence clearly described • Method for formulating recommendations clearly described. • Health benefits, side effects, risks considered in formulating recommendations • Explicit link between recommendations and supporting literature • External review of guideline by experts • Procedure for updating guidelines described • Specific and unambiguous recommendations • Options for management clearly described • Recommendations easily identifiable • Competing interests of develop group members stated (none) • Consideration given to resource implications of applying recommendations	• Did not describe facilitators and barriers to application of guideline • Did not provide tools and advice for implementation • While the importance of monitoring and auditing was mentioned, specific criteria were not described. • Unclear if views of the funding body would influence the content of guideline

Centers for Disease Control and Prevention, 2011[14]	• Overall objective clearly described
	• Health questions covered by guideline specifically described
	• Population to whom the guideline is meant to apply is specifically described
	• Relevant professional groups included in guideline development
	  o Infectious disease, epidemiology, pediatrics, medical officers, patient safety, critical care and surgery all represented
	  o Other groups consulted such as nursing, patient groups
	• Views and preferences of the target population were sought
	• Target users of the guideline clearly defined
		• There was limited description of facilitators and barriers to application of guideline
		• Limited advice for implementation provided, but suggested prioritizing the recommended and highlighted those that would be given the highest priority.
		• Resource implications of applying recommendations not considered
		• Unclear if views of the funding body would influence the content of guideline

First Author, Publication Year	Strengths	Limitations
	• Systematic methods used for literature search • Selection criteria for the evidence described clearly • Strengths and limitations of the body of evidence clearly described • Method for formulating recommendations clearly described. • Health benefits, side effects, risks considered in formulating recommendations • Explicit link between recommendations and supporting literature • External review of guideline by experts • Procedure for updating provided • Specific and unambiguous recommendations • Options for management clearly described • Recommendations easily identifiable • Monitoring and auditing criteria provided • Competing interests of develop group members stated	

APPENDIX 4: Summary of Study Findings

Table 8: Table of Main Study Findings and Authors' Conclusions

First Author, Publication Year	Main Study Findings	Authors' Conclusions
Vaporized Hydrogen Peroxide		
Systematic Review		
Falagas et al, 2011[6]	Four included studies assessed VHP for infection control. **Termination of outbreaks** • Successful termination of a Serratia spp. outbreak in a neonatal ICU (1 study) • Successful termination of a polyclonal MRSA outbreak at a 28-bed surgical ward (1 study) **Eradication of contamination** • Successful eradication of persistent MRSA environmental contamination in a 20-bed surgical ward. (1 study) **Incidence of nosocomial infections** • Significant reduction of the incidence of *C. difficile* in a 500-bed hospital (1 study)	*"Few studies have evaluated the use of airborne hydrogen peroxide disinfection as an adjunctive infection control measure in actual hospital practice. These limited relevant data are favourable, but further studies are needed to assess the effectiveness, safety, costs, and applicability of this novel method against other available cleaning methods." p.176*
Cohort Studies		
Passarettti et al, 2013[9]	IRR* (95% CI) VHP versus Standard Cleaning **VRE** 0.25 (95 % CI: 0.10 to 0.60); P <0.01 **MRSA** 0.53 (95 % CI: 0.16 to 1.79); P =0.30 **MDR-GNR** 0.55 (95 % CI: 0.20 to 1.57); P=0.26 ***C. difficile*** 0.49 (95 % CI: 0.16 to1.47); P=0.19 **Combined** 0.36 (95 % CI: 0.19 to 0.70); P <0.01	*"In summary, HPV decontamination used as an adjunct to standard cleaning and disinfection reduced the risk of MDRO acquisition among high-risk patients when patients are admitted to a room previously occupied by a patient infected or colonized with an MDRO. These findings suggest that HPV should be considered for decontamination of MDRO patient rooms." p.34*
Barbut et al, 2013[7]	**Nosocomial MRSA infection or colonization rate** (cases per 1000 days): Control period – 7.22 Post-exposure period – 0.77	"*The infection control bundled stopped the MRSA outbreak, resulted in a significant reduction in the incidence of nosocomial MRSA and A. baumannii and prevented further outbreaks of these organisms in our burns unit." p.401*

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	89.3% reduction; p < 0.0001 **Nosocomial *A. baumannii* infection or colonization rate** (cases per 1000 days): Control – 6.92 Post-exposure – 0.77 88.8% reduction; p = 0.002 **Nosocomial ESBL- producing *Enterobacteriaceae* infection or colonization rate** (cases per 1000 days): Control period – 1.20 Post-exposure period – 0.77 36% reduction; P =0.7 **Combined nosocomial MDRO infection or colonization rate** (cases per 1000 days): Control period – 15.34 Post-exposure period – 2.31 84.9% reduction; P < 0.0001	
Manian et al., 2013[8]	**Nosocomial *C. difficile* infection rate** (cases per 1000 days): Control period I – 0.83 Post-exposure period – 0.55 Rate ratio – 0.63 (95% CI: 0.50 to 0.79); p < 0.0001	*"In conclusion, implementation of an enhanced hospital-wide terminal cleaning program revolving around HPV decontamination of targeted hospital rooms was practical, safe, and associated with a significant reduction in the endemic rate of CDAD at our hospital. Further studies are needed to delineate better the role of HPV decontamination in reducing the endemic rate of transmission of other pathogens with significant environmental presence in hospitals*." p. 540
Chmielarczyk et al., 2012[10]	• No further MRAB infections on the units between January and August 2010, but a second outbreak occurred in September 2010. • Decontamination procedures repeated and no new cases as of October 2011.	*"The results of this study demonstrate that rigorous infection prevention and control measures including strict isolation, environmental cleaning, staff education and proper hand hygiene, along with VHP decontamination were successful in controlling MRAB in an intensive therapy unit setting."p.244*
Otter et al., 2010[11]	• No new cases of *Acinetobacter* were identified for three months following the use of VHP.	"*In conclusion, HPV decontamination was more efficacious than conventional terminal cleaning for the eradication of MDR-GNR*

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	• Three cases of *E. cloacae* three to four months following decontamination. • Three new cases of *Acinetobacter* were identified for four to six months following the use of VHP.	*contamination in our ICU, and the removal of the environmental reservoirs of MDR-GNR may have interrupted the cycle of transmission of these organisms." p.756*
Ray et al., 2010[12]	Nosocomial acquisition of MDR *A. baumannii* stopped after the use of VHP.	"*Environmental decontamination using VHP combined with comprehensive infection control measures interrupted nosocomial transmission of MDR A. baumannii in an LTACH. The application of this novel approach to halt the transmission of MDR A. baumannii warrants further investigation." p.1*
Ultra Violet Light		
Levin et al., 2013[13]	**HA-CDI rate per 10,000 patient-days** Control period– 9.46 Post-exposure period– 4.45 53% reduction; P <0.01 **Deaths in Patients with HA-CDI** Control period– 6 Post-exposure period– 1 No statistical analysis **Colectomies in Patients with HA-CDI** Control period– 3 Post-exposure period– 0 No statistical analysis	"*The dramatic reduction in infection, death, and colectomy due to HA-CDI after PPX-UV was added to standard infection prevention interventions makes this technique well worth investigating further in a large center with well-controlled variables." p. 748*

ESBL – Extended spectrum beta lactamase; HA- CDI – Hospital acquired C.difficile infection; HPV – hydrogen peroxide vapor; IRR – Incidence rate ratio; LATCH - long-term acute care hospital; MDR – Multi-drug resistant; MDR-GNR – multi drug resistant gram negative rod; MDRO – Multi-drug resistant organism; MRSA - methicillin-resistant *Staphylococcus aureus*; PPX-UV – Portable pulsated xenon ultra-violet; UV Ultra-violet; VRE - vancomycin-resistant *Enterococci*; VHP – vaporized hydrogen peroxide;
* Adjusted for unit, age, mortality risk score, HIV status, end stage renal disease status, surveillance compliance of the unit

APPENDIX 5: Additional studies of vaporized hydrogen peroxide and ultra violet light that did not report patient outcomes

Vaporized Hydrogen Peroxide

1. Otter JA, Nowakowski E, Salkeld JA, Duclos M, Passaretti CL, Yezli S, et al. Saving costs through the decontamination of the packaging of unused medical supplies using hydrogen peroxide vapor. Infect Control Hosp Epidemiol. 2013 May;34(5):472-8.
PubMed: PM23571363

2. Doan L, Forrest H, Fakis A, Craig J, Claxton L, Khare M. Clinical and cost effectiveness of eight disinfection methods for terminal disinfection of hospital isolation rooms contaminated with Clostridium difficile 027. J Hosp Infect. 2012 Oct;82(2):114-21.
PubMed: PM22902081

3. 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.
PubMed: PM22476278

4. Bentley K, Dove BK, Parks SR, Walker JT, Bennett AM. Hydrogen peroxide vapour decontamination of surfaces artificially contaminated with norovirus surrogate feline calicivirus. J Hosp Infect. 2012 Feb;80(2):116-21.
PubMed: PM22169115

5. Holmdahl T, Lanbeck P, Wullt M, Walder MH. A head-to-head comparison of hydrogen peroxide vapor and aerosol room decontamination systems. Infect Control Hosp Epidemiol. 2011 Sep;32(9):831-6.
PubMed: PM21828962

6. Chan HT, White P, Sheorey H, Cocks J, Waters MJ. Evaluation of the biological efficacy of hydrogen peroxide vapour decontamination in wards of an Australian hospital. J Hosp Infect. 2011 Oct;79(2):125-8.
PubMed: PM21824681

7. Manian FA, Griesenauer S, Senkel D, Setzer JM, Doll SA, Perry AM, et al. Isolation of Acinetobacter baumannii complex and methicillin-resistant Staphylococcus aureus from hospital rooms following terminal cleaning and disinfection: can we do better? Infect Control Hosp Epidemiol. 2011 Jul;32(7):667-72.
PubMed: PM21666397

8. Alfa MJ, Lo E, Wald A, Dueck C, DeGagne P, Harding GK. Improved eradication of Clostridium difficile spores from toilets of hospitalized patients using an accelerated hydrogen peroxide as the cleaning agent. BMC Infect Dis [Internet]. 2010 [cited 2014 Apr 29];10:268. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2949757
PubMed: PM20843348

9. Barbut F, Menuet D, Verachten M, Girou E. Comparison of the efficacy of a hydrogen peroxide dry-mist disinfection system and sodium hypochlorite solution for eradication of Clostridium difficile spores. Infect Control Hosp Epidemiol. 2009 Jun;30(6):507-14.

PubMed: PM19379098

10. Fu TY, Gent P, Kumar V. Efficacy, efficiency and safety aspects of hydrogen peroxide vapour and aerosolized hydrogen peroxide room disinfection systems. J Hosp Infect. 2012 Mar;80(3):199-205.
PubMed: PM22306442

Ultraviolet Light

1. Mahida N, Vaughan N, Boswell T. First UK evaluation of an automated ultraviolet-C room decontamination device (Tru-D). J Hosp Infect. 2013 Aug;84(4):332-5.
PubMed: PM23846236

2. Rutala WA, Gergen MF, Tande BM, Weber DJ. Rapid hospital room decontamination using ultraviolet (UV) light with a nanostructured UV-reflective wall coating. Infect Control Hosp Epidemiol. 2013 May;34(5):527-9.
PubMed: PM23571373

3. Anderson DJ, Gergen MF, Smathers E, Sexton DJ, Chen LF, Weber DJ, et al. Decontamination of targeted pathogens from patient rooms using an automated ultraviolet-C-emitting device. Infect Control Hosp Epidemiol [Internet]. 2013 May [cited 2014 Apr 29];34(5):466-71. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3703853
PubMed: PM23571362

4. 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.
PubMed: PM23571361

5. Nerandzic MM, Cadnum JL, Eckart KE, Donskey CJ. Evaluation of a hand-held far-ultraviolet radiation device for decontamination of Clostridium difficile and other healthcare-associated pathogens. BMC Infect Dis [Internet]. 2012 [cited 2014 Apr 29];12:120. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3419611
PubMed: PM22591268

6. Umezawa K, Asai S, Inokuchi S, Miyachi H. A comparative study of the bactericidal activity and daily disinfection housekeeping surfaces by a new portable pulsed UV radiation device. Curr Microbiol. 2012 Jun;64(6):581-7.
PubMed: PM22447288

7. 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.
PubMed: PM21768755

8. Stibich M, Stachowiak J, Tanner B, Berkheiser M, Moore L, Raad I, et al. Evaluation of a pulsed-xenon ultraviolet room disinfection device for impact on hospital operations and microbial reduction. Infect Control Hosp Epidemiol. 2011 Mar;32(3):286-8.
PubMed: PM21460515

9. Rutala WA, Gergen MF, Weber DJ. Room decontamination with UV radiation. Infect Control Hosp Epidemiol. 2010 Oct;31(10):1025-9.
PubMed: PM20804377

10. Nerandzic MM, Cadnum JL, Pultz MJ, Donskey CJ. Evaluation of an automated ultraviolet radiation device for decontamination of Clostridium difficile and other healthcare-associated pathogens in hospital rooms. BMC Infect Dis [Internet]. 2010 [cited 2014 Apr 29];10:197. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2910020
PubMed: PM20615229