

# No-Touch Modalities for Disinfecting Patient Rooms in Acute Care Settings



## Background and Purpose

### Purpose of Review

To rapidly identify evidence assessing the effect of no-touch modalities for disinfecting acute care hospital rooms on contamination and infection rates.

### Background

As of July 21, 2020, the COVID-19 pandemic has caused over 3.8 million infections and 141,000 deaths in the United States.<sup>1</sup> Many patients with COVID-19 have required prolonged hospitalization for respiratory symptoms, along with cardiac, hematologic, neurologic, and other medical complications.<sup>2-4</sup> Providing quality patient care while protecting healthcare personnel from infection is challenging due, in part, to lack of knowledge regarding the safest and most effective methods for environmental cleaning and disinfection of patient rooms.

Terminal cleaning of patient rooms (i.e., cleaning and disinfection of surfaces and the environment after a patient is discharged or transferred to another room) is typically performed by trained environmental services/housekeeping staff who manually clean and disinfect surfaces using wipes/cloths/sponges moistened with a chemical solution. After manual processes, no-touch disinfection modalities also may be used, including ultraviolet light (UVL) disinfection systems, hydrogen peroxide vapor (also referred to as vaporous hydrogen peroxide [VHP]), steam, ozone, and chlorine dioxide vapor. Environmental surfaces (e.g., tray tables, sink basins) made from solid copper alloy have also been used in healthcare facilities to decrease microbial burden. Several of these modalities have been assessed for mask decontamination.<sup>5-7</sup>

No-touch modalities disinfect through a variety of mechanisms.<sup>8</sup> For instance, UV-C (200 to 280 nm) and UV-B (280 to 320 nm) radiation disrupt DNA/RNA replication and at high intensity can cause cell rupture through overheating. VHP systems coat surfaces with hydrogen peroxide droplets, which generate free radicals that are toxic to microorganisms and spores. Solid copper alloy surfaces generate reactive oxygen species but also may use other mechanisms.



Since data directly assessing no-touch modalities for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are not yet readily available, we conducted a rapid review of no-touch modalities for disinfecting other respiratory viral pathogens in patient rooms in hospital/acute care settings. We also included studies reporting the effect of these modalities on *Clostridioides* (formerly *Clostridium*) *difficile* (CD) environmental contamination or infection (CDI) rates. Since CD spores are easily transmitted to surfaces and difficult to eradicate,<sup>9</sup> the no-touch modalities that are effective against CD spores may be effective against SARS-CoV-2.

## Guiding Question

What data exist for the effectiveness of no-touch modalities for disinfecting patient rooms in hospital or acute care settings for:

- a. Respiratory viral pathogens
- b. Other pathogens with potential relevance to assessing effectiveness vs. SARS-CoV-2 (specifically CD spores)



## Methods

We conducted a rapid review of peer-reviewed literature from the last 10 years to identify research on effectiveness of UVL, VHP, steam, ozone, chlorine dioxide, and solid copper surfaces for decreasing either patient infection rates or surface contamination of patient rooms in acute care settings. For studies assessing impact on severe acute respiratory syndrome coronavirus (SARS-CoV), which emerged in 2002, we searched the last 20 years. To complete the report in only 4 weeks, we took the following steps:

- Defined a narrow scope
- Included both data from relevant systematic reviews (SRs) along with primary studies as evidence
- Limited data extraction and synthesis
- Did not conduct formal risk-of-bias or strength-of-evidence assessment

We refined the scope in consultation with the Agency for Healthcare Research and Quality (AHRQ), discussion with experts, and early literature scoping. The protocol was posted on the AHRQ Effective Health Care Program website (<https://effectivehealthcare.ahrq.gov/products/no-touch-disinfection/protocol>). The final patient/intervention/comparators/outcomes/setting (PICOS) are found in Table 1.

**Table 1. PICOS**

PICOS Element	Description
Population	Not applicable
Intervention/Exposure	No-touch modalities for disinfection: <ul style="list-style-type: none"> <li>• Ultraviolet light disinfection systems</li> <li>• Vaporous or aerosolized hydrogen peroxide, vaporized ozone, vaporized chlorine dioxide</li> <li>• Steam heat</li> <li>• Antimicrobial solid copper surfaces</li> </ul>
Comparator/Control	Any comparator, no comparator (e.g., control)
Outcomes	<ul style="list-style-type: none"> <li>• Surface contamination of patient rooms or</li> <li>• Patient infection rates (incidence) of respiratory viral pathogens, specifically: adenovirus, common human coronaviruses, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), influenza, respiratory syncytial virus, rhinovirus, or <i>Clostridioides difficile</i></li> </ul>
Setting	Patient rooms in hospital/acute care setting

A master's-level librarian searched PubMed, EMBASE, and clinicaltrials.gov for documents relevant to this topic and published between January 1, 2010, and April 22, 2020. Searches for SARS-CoV related literature extended back to 2000. The full search strategy is available in Appendix A.

Two analysts screened studies against prespecified inclusion/exclusion criteria (Table 2). Disagreements were resolved through discussion.

**Table 2. Inclusion/exclusion criteria**

PICOTS	Criteria
Inclusion Criteria	<ul style="list-style-type: none"> <li>• English language</li> <li>• Peer-reviewed, published, full-length studies</li> <li>• All relevant systematic reviews/meta-analyses, randomized controlled trials, quasi-randomized controlled trials, cohort studies, other observational studies, pre/post studies</li> <li>• Studies assessing no-touch intervention(s) of interest for disinfection of patient rooms (including pediatric and obstetric) in hospital/acute care settings</li> <li>• Studies reporting outcomes of surface contamination or patient infection rates for respiratory viruses, specifically: adenovirus, common human coronaviruses, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), influenza, respiratory syncytial virus, rhinovirus, or <i>Clostridioides difficile</i></li> </ul>
Exclusion Criteria	<ul style="list-style-type: none"> <li>• Publication date before 2010 (unless related to SARS)</li> <li>• Preprint studies</li> <li>• Laboratory studies</li> <li>• Studies assessing disinfection of masks or personal protective equipment (PPE)</li> <li>• Studies performed in ambulatory settings</li> <li>• Conference abstracts, editorials, case studies</li> <li>• Studies including &lt;10 patients</li> </ul>



## Evidence Summary

### Evidence of Effectiveness for Hospital Room Disinfection

#### UVL

- Respiratory viruses
  - 1 pre/post study found cleaning with quaternary ammonium agents + UVL was associated with a 44 percent unadjusted reduction on overall incidence of respiratory viral infection; however, the study was small, with potential confounding.
- CDI
  - Meta-analysis of 11 studies of various designs found UVL was associated with lower CDI rates: relative risk (RR): 0.64 (95% confidence interval [CI]: 0.49 to 0.84). Pre/post studies had consistent positive results; however, controlled trials had conflicting results. One additional interrupted time series found no difference in infection rates for UVL + bleach compared with bleach.
  - Two small pre/post studies found UVL + standard cleaning lowered surface contamination, but a third small pre/post study found no difference between UVL + bleach vs. bleach. Another small pre/post study found that compared to standard cleaning (with bleach), UVL + standard cleaning was associated with non-statistically significant lower surface contamination on high-touch surfaces.

#### VHP/Aerosolized Hydrogen Peroxide

- Respiratory viruses
  - No studies identified.
- CDI
  - Pooled analysis of five noncontrolled studies found nonstatistically significant lower CDI rates: RR: 0.52 (95% CI: 0.15 to 1.81). One additional pre/post study also found VHP lowered CDI.
  - One small RCT study compared aerosolized hydrogen peroxide + silver ions to bleach and found no statistically significant difference in surface contamination.

#### Solid Copper Surfaces

- Respiratory viruses
  - No studies identified.
- CDI
  - One pre-post study of copper surfaces found copper surfaces reduced CDI infection rates: 2.4 versus 0.7 per 1,000 patient-days; however, authors noted serious potential confounding in the results. A second pre/post study also found lower CDI rates associated with copper surfaces + copper linens: incidence rate 4.1 (95% CI: 4.05 to 4.14) to 0.69 (95% CI: 0.65 to 0.73). However, serious potential confounders including differences in patient mix and room size were noted.

#### Steam, Ozone, Chlorine Dioxide

- No studies identified for respiratory viruses or CDI.

## Ongoing Research and Future Research Needs

One sham-controlled randomized controlled trial (RCT)<sup>10</sup> underway (expected completion date May 2022) could provide important information regarding effectiveness of UVL to reduce hospital acquired infections including CDI (see Appendix D). Future controlled trials assessing impact (particularly on respiratory viral infections) are needed. Future trials will benefit from consistent reporting of standard terminal cleaning protocols and contextual factors (e.g., antimicrobial stewardship, hand hygiene) that could affect patient infection rates.



## Evidence Base

Our searches identified 1,378 potential citations, of which 1,037 were excluded at the title level. We performed an abstract/full-text review of the remaining 341 (see Appendix E). Based on the abstract/full-text level review, we included one SR<sup>11</sup> that covered both UVL and VHP (one RCT, one controlled trial [CT], one cohort study, 14 pre/post studies), one RCT,<sup>12</sup> one interrupted time series,<sup>13</sup> seven pre/post studies,<sup>14-20</sup> and one secondary analysis<sup>21</sup> of an RCT already included in the SR.

An overview of evidence and outcomes addressed is presented in Table 3.

**Table 3. Overview of evidence and outcomes**

<b>No-Touch Modalities: Outcomes</b>	<b>Respiratory Viral Pathogens: Infections</b>	<b>Respiratory Viral Pathogens: Surface Contamination</b>	<b><i>Clostridioides difficile</i>: Infections</b>	<b><i>Clostridioides difficile</i>: Surface Contamination</b>
Ultraviolet light	1 pre/post study <sup>14</sup>	No studies	1 SR <sup>11</sup> (1 RCT, 1 CT, 9 pre/post studies), 1 interrupted time series <sup>13</sup> 1 secondary analysis <sup>21</sup>	4 pre/post studies <sup>15-17,19</sup>
Vaporous hydrogen peroxide	No studies	No studies	1 SR <sup>11</sup> (1 cohort study, 5 pre/post studies)	No studies
Aerosolized hydrogen peroxide + silver ions	No studies	No studies	No studies	1 RCT <sup>12</sup>
Solid copper surfaces	No studies	No studies	2 pre/post studies <sup>18,20</sup>	No studies
Steam	No studies	No studies	No studies	No studies
Chlorine dioxide	No studies	No studies	No studies	No studies
Ozone	No studies	No studies	No studies	No studies

CT = controlled trial; RCT = randomized controlled trial; SR = systematic review.

For respiratory viruses, we identified only one pre/post study<sup>14</sup> assessing UVL for inclusion. All other studies evaluated no-touch modalities for reduction in CDI or contamination. Studies identified assessed UVL, VHP, aerosolized hydrogen peroxide + silver ions, and solid copper surfaces; no studies assessed steam, chlorine dioxide, or ozone. Detailed descriptions of included studies are available in Appendix B.

# Ultraviolet Light Disinfection Systems

## Respiratory Viral Infection

One pre/post study (Pavia et al.)<sup>14</sup> assessed UVL for reducing respiratory viral infections in the toddler unit of a children's hospital (selected because it had the highest rate of hospital-acquired infections [HAIs] in the hospital). Toddler rooms/common areas were disinfected with quaternary ammonium agents followed by UVL (Optum Enlight, Clorox Healthcare) 2 to 3 times per week over 12 months. The study did not explicitly report what methods were used for cleaning in the prior 12 months. Compared with the prior 12 months, there was a 44 percent unadjusted reduction on overall incidence of respiratory viral infection (incidence rate ratio [IRR] of 0.56 [95% CI: 0.37 to 0.84]).

## *Clostridioides difficile* Infection

Marra et al. (2018)<sup>11</sup> performed pooled analysis of 11 studies (1 RCT, 1 controlled trial, 9 pre/post). Terminal cleaning with UVL was associated with lower CDI rates: relative risk (RR): 0.64 (95% CI: 0.49 to 0.84,  $I^2=0\%$ ). However, pooled analysis limited to the two controlled studies found no significant reduction on CDI rates: RR: 0.65 (95% CI 0.26 to 1.62). One controlled study (which compared CDI for three units using UVL with three units using standard terminal cleaning over 6 months at a single hospital) reported benefit (11.2 infections/10,000 patient days [UVL] compared to 28.7 [control]). However, the second controlled study, a large, multicenter RCT (Benefits of Enhanced Terminal Room Disinfection [BETR]) did not show a clear benefit.<sup>22</sup> BETR assessed infection rates in patients exposed to seed rooms (a room containing a patient with microbiologically proven current or history of infection or colonization with at least one target organism in the prior 12 months) across nine hospitals. Compared with disinfection with bleach, bleach + UVL was not associated with a difference in CDI in patients exposed to seed rooms: RR: 1.0 (95% CI: 0.57 to 1.75). However, some irregularities occurred with randomization (see Appendix C).

A prespecified secondary analysis of BETR data<sup>21</sup> assessed hospitalwide infection risk with “target” organisms (CDI, vancomycin-resistant *enterococci* [VRE], methicillin-resistant *Staphylococcus aureus* [MRSA], or multidrug-resistant *Acinetobacter*). Compared to standard terminal cleaning (bleach for CD rooms, ammonium-based disinfectant for all others), a reduction occurred in all four “target” infections during the UVL study period: RR: 0.89 (95% CI: 0.79 to 1.0). This lower risk was driven by reductions in CDI and VRE (RR: 0.89 [95% CI: 0.80 to 0.99], RR: 0.56, [95% CI: 0.31 to 0.99], for CDI and VRE, respectively). However, if UVL was responsible for this reduction, it is unclear why CDI was not also lower during the bleach + UVL period (RR: 0.97 [95% CI: 0.84 to 1.12]).

One additional interrupted time series (Brite et al.)<sup>13</sup> evaluated pulsed xenon UVL + bleach versus bleach alone for disinfecting a 25-bed bone marrow transplant unit. Over 20 months (704 admissions), no change in CDI was identified: trend incidence rate ratio (IRR): 1.08 (95% CI: 0.89 to 1.31).

## ***Clostridioides difficile* Surface Contamination**

Four small single-center pre/post studies<sup>15-17,19</sup> assessed UVL for reducing surface contamination of hospital room surfaces with CD. Three studies<sup>16,17,19</sup> found UVL interventions were associated with reductions in CD contamination. Wong et al. (2016)<sup>17</sup> found fewer rooms were contaminated after terminal cleaning with UVL: 31.8 percent (7 of 22) at baseline, 22.7 percent (after standard cleaning with hydrogen peroxide), 0 percent (after UVL),  $p=0.07$ . The proportion of surfaces contaminated was also lower: 7.2 percent at baseline, 4 percent after standard cleaning, and 0 percent after UVL disinfection ( $p=0.07$ ). Another pre/post study<sup>16</sup> evaluated CD contamination at a hospital with high CDI rates after sequential implementation of three tiered interventions: tracking of fluorescent marker removal (after standard cleaning with bleach), UVL, and enhanced standard disinfection with daily disinfection supervision. A combination of fluorescent marker tracking and UVL was associated with a lower contamination rate, from 67 percent to 35 percent (prevalence ratio: 0.52, 95% CI: 0.43 to 0.52). A small pre/post study<sup>19</sup> found that compared to no cleaning, UVL was associated with a lower rate of CD contamination (11.6% to 2.7%,  $p<0.01$ ). When compared to standard cleaning (including bleach), UVL also was associated with lower CD surface contamination of high-touch surfaces (19.4% to 8%), but this result does not appear to have been statistically significant.

Another pre/post study<sup>15</sup> compared UVL + standard cleaning (bleach) to standard cleaning and found no significant difference in surface contamination rates.

## **Vaporous Hydrogen Peroxide**

One SR<sup>11</sup> (with 1 prospective cohort study and 5 pre/post studies) assessed VHP for CDI reduction. Pooled analysis of five studies found nonstatistically significant lower CDI rates: RR: 0.52 (95% CI: 0.15 to 1.81),  $I^2=0\%$ . One additional pre/post study found VHP lowered CDI (no statistical testing performed).

## **Aerosolized Hydrogen Peroxide and Silver Ions**

One small RCT<sup>12</sup> randomized 28 hospital rooms from discharged CDI patients to terminal cleaning with aerosolized solution of hydrogen peroxide <8 percent and silver ions versus manual cleaning with 0.5 percent sodium hypochlorite. Surface contamination rates decreased from 13 percent to 0 percent in the aerosolized hydrogen peroxide + silver ions group, and from 20 percent to 3 percent for rooms cleaned with sodium hypochlorite. However, there was no statistically significant difference in CD surface contamination between groups ( $p=0.3$ ).

## **Solid Copper Surfaces**

One single-center pre/post study<sup>18</sup> assessed impact of antimicrobial solid copper surfaces on CDI rates for three intensive care units (general, neurological care, and burn-trauma) after transition to a new building equipped with EOS Preventive/Biocidal Surface workstations, bedside and vanity tables, bathroom fittings, bedrails, and door handles. After the transition, CDI decreased: CDI: 2.4 versus 0.7 per 1,000 patient-days: IRR: 3.3 (95% CI: 1.4 to 8.7). Authors noted the new building was equipped with modern ventilation systems, which may have been a confounder.

A second pre/post study<sup>20</sup> assessed CDI rates before and after transition to a new hospital wing equipped with antimicrobial solid copper surfaces + copper linens. All acute care rooms in the old and new wings received standard cleaning (quaternary ammonium, with hypochlorite for CDI rooms). Compared with the baseline CDI incidence rate (IR) 4.10 (95% CI: 4.05 to 4.14), the CDI rate in the new wing was lower (IR 0.69, 95% CI 0.65 to 0.73,  $p=0.048$ ). Patients who continued to be hospitalized in the old wing (after the new wing had opened) had similar CDI rates compared to baseline. However, authors noted several potential confounders that may have played a role including a statistically significant difference in case mix between old and new wings. Patients housed in the old wing were more likely to be on medical services, with medical comorbidities, recent hospitalizations, and history of CDI in the past 6 months. Also, compared to the old wing, rooms in the new wing were larger.

## Discussion

Aside from three studies, the evidence base for no-touch modalities for disinfection of hospital rooms consisted of interrupted time series or single-center pre/post studies and primarily evaluated impact on CDI rates or room contamination. Only a single pre/post study<sup>14</sup> assessed UVL disinfection systems for reducing respiratory infections. While a common study design for quality improvement initiatives in health systems, pre/post study designs (also referred to as “before and after” or “quasi-experimental”) lack a true control group, are limited by the Hawthorne effect, and often deploy interventions simultaneously with other quality improvement initiatives. These characteristics place these studies at high risk of bias and pose challenges for accurately assessing cause and effect and applicability.<sup>23</sup>

Of the modalities assessed, UVL systems have the most developed evidence base. UVL was associated with lower rates of respiratory viral infections in a single-center pre/post study<sup>14</sup> and with lower CDI rates and surface contamination; a meta-analysis of 11 studies<sup>11</sup> found statistically significant lower CDI rates. However, five of these studies did not report on compliance with alternative measures (hand hygiene, antimicrobial stewardship) potentially affecting CDI. Furthermore, the only RCT<sup>21</sup> (also the sole multicenter study) did not find UVL was associated with lower CDI in patients exposed to rooms previously occupied by infected patients. Although UVL was associated with lower *hospitalwide* CDI (compared to standard cleaning), no effect was identified for bleach + UVL, raising doubt about whether results should be attributed to UVL. Collectively, these findings highlight the need for further well-designed RCTs. One sham-controlled RCT underway (expected completion date May 2022) could provide important information regarding effectiveness of UVL for room disinfection and reduction of hospital acquired infections including CDI.

For VHP, although meta-analysis of five studies<sup>11</sup> found VHP was associated with lower CDI rates (RR: 0.52, 95% CI 0.15 to 1.81), interpreting these findings is challenging. Although the wide CI could simply indicate lack of power, the evidence base consisted of only single-center pre/post studies and a single prospective cohort study, two of which failed to report compliance to important measures, such as hand hygiene/antimicrobial stewardship. Only a single small RCT<sup>12</sup> assessed aerosolized hydrogen peroxide + silver ions and found no difference in CD surface contamination compared to bleach.

Although two pre/post studies<sup>18,20</sup> found that antimicrobial solid copper surfaces alone, or with copper linens were associated with lower CDI rates, both studies noted clear potential confounders. For both studies, introduction of copper interventions was associated with relocation to or opening of a new hospital care setting. Authors noted that differences in layout, size, and ventilation systems could have played a role. While one study<sup>20</sup> did monitor hand hygiene and fidelity of standard cleaning, CDI rates may have been impacted by clear differences in case mix (patients hospitalized in the new wing had fewer comorbidities and lower rates of prior CDI).

As expected, we found a paucity of studies assessing no-touch modalities for hospital room disinfection assessing impact on respiratory viral infections that could be directly applied to managing COVID-19. However, there are studies assessing no-touch modalities for CDI. As CD spores are generally more difficult to eradicate than viruses, it is reasonable to expect that modalities that effectively reduce CD environmental contamination and CDI rates would also effectively reduce SARS-CoV-2 surface contamination and infection rates when used to disinfect hospital rooms. However, study designs and conflicting results in the evidence base make it challenging to draw firm conclusions.

Finally, as noted, most included studies primarily addressed efficacy of no-touch modalities for CD-related outcomes, with only a single study assessing efficacy for respiratory viruses. However, as CD spores are generally harder to eradicate compared to viruses, it is possible that findings from these studies could potentially underestimate efficacy of no-touch modalities for disinfecting hospital rooms against viruses.



## Limitations

To complete this rapid review in a timely fashion, the scope was narrowly defined and did not include lab studies, studies of decontamination of masks or other items, studies in nonacute settings, or preprint studies. The literature search was confined to PubMed, EMBASE, and clinicaltrials.gov. Data extraction and synthesis were limited and no formal risk-of-bias or strength-of-evidence assessment was performed.



## Conclusions and Future Research

The effectiveness of no-touch disinfection modalities for disinfecting hospital rooms to decrease respiratory viral infections and CDI remains unclear. Although more than a dozen studies of UVL disinfection systems exist, weak study design and conflicting results prevent definite conclusions. The evidence base for VHP and solid copper surfaces is also weak. For VHP, although five noncontrolled studies found an association with lower CDI, studies had important flaws. Only a single small RCT assessed aerosolized hydrogen peroxide vapor + silver, and only two pre/post studies assessed solid copper surfaces.

Higher quality studies, particularly RCTs, are needed to assess the impact of these no-touch modalities for disinfecting hospital rooms. Also, studies directly assessing efficacy for

respiratory viruses are vital. Future studies should include detailed descriptions of what procedures “standard” terminal cleaning involves along with the degree of adherence or efforts to monitor fidelity. Studies should also describe other quality-improvement interventions initiated around or during the study period and other potential confounders (e.g., antimicrobial stewardship, compliance with hand hygiene and isolation precautions) that potentially could affect infection rates.



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## Disclaimers

This report is based on research conducted by ECRI under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00005-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

**None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.**

The information in this report is intended to help health care decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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# Afterword

Recognized for excellence in conducting comprehensive systematic reviews, the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) program is developing a range of rapid evidence products to assist end-users in making specific decisions in a limited timeframe.

To shorten timelines, reviewers make strategic choices about which review processes to abridge. However, the adaptations made for expediency may limit the certainty and generalizability of the findings from the review, particularly in areas with a large literature base. Transparent reporting of the methods used and the resulting limitations of the evidence synthesis are extremely important.

AHRQ expects that these rapid evidence products will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program.

If you have comments on this report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to [epc@ahrq.hhs.gov](mailto:epc@ahrq.hhs.gov).

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# Appendix A. Methods

We searched PubMed and EMBASE from January 1, 2000, through April 22, 2020.

**PubMed. Bethesda (MD): National Library of Medicine [searched January 1, 2000, through April 22, 2020] Available from: <http://www.pubmed.gov>.**

## *Search Strategy:*

- #1 cross infection[mh] OR hospital infection\*[tiab] OR health care acquired infection\*[tiab] OR health care associated infection\*[tiab] OR hospital acquired infection\*[tiab] OR hospital associated infection\*[tiab] OR (infect\*[ti] AND (nosocomial[ti] OR viral[ti] OR virus[ti] OR viruses[ti])) OR (HAI[ti] OR HAIs[ti])
- #2 coronavirus infections[mh] OR covid-19[supplementary concept] OR 2019 ncov[tiab] OR 2019ncov[tiab] OR 2019 novel coronavirus[tiab] OR coronavirinae[tiab] OR coronavirus[tiab] OR coronaviruses[tiab] OR corona virus[tiab] OR corona viruses[tiab] OR covid\*[tiab] OR covid 19[tiab] OR covid19[tiab] OR covid2019[tiab] OR hcov 19[tiab] OR hcov 2019[tiab] OR hcov19[tiab] OR hcov2019[tiab] OR ncov\*[tiab] OR ncov 2019[tiab] OR ncov2019[tiab] OR sars cov 2[tiab] OR sars cov2v[tiab] OR sarscov 2[tiab] OR sarscov2[tiab] OR severe acute respiratory syndrome coronavirus 2[tiab] OR severe acute respiratory syndrome corona virus 2[tiab]
- #3 sars virus[mh] OR "severe acute respiratory syndrome"[tiab] OR sars[tiab]
- #4 adenoviridae[mh] OR adenoviridae infections[mh] OR influenza a virus, h1n1 subtype[mh] OR influenza, human[mh] OR middle east respiratory syndrome coronavirus[mh] OR respiratory syncytial viruses[mh] OR respiratory syncytial virus infections[mh] OR rhinovirus[mh] OR adenovirus\*[tiab] OR flu[tiab] OR h1n1[tiab] OR influenza\*[tiab] OR mers[tiab] OR "mers cov" [tiab] OR merscov[tiab] OR middle east respiratory syndrome[tiab] OR respiratory syncytial virus[tiab] OR rhinovirus[tiab] OR viruses[mh] OR virus diseases[mh] OR virus shedding[mh]
- #5 clostridium difficile[mh] OR clostridioides difficile[tiab] OR clostridium difficile[tiab] OR clostridium difficile[tiab] OR c. difficile[tiab] OR c. diff[tiab] OR c.difficile[tiab] OR c.diff[tiab] OR peptoclostridium difficile[tiab]
- #6 (epidemic\*[ti] OR epidemics[mh] OR pandemic\*[ti] OR pandemics[mh] OR contagion\*[ti] OR crises[ti] OR crisis[ti] OR epidemic\*[ti] OR outbreak\*[ti] OR pandemic\*[ti] OR scourge\*[ti] OR plague\*[ti]) AND (virus OR viruses OR viral)
- #7 emergency service, hospital[mh] OR health facilities[mh] OR hospitals[mh] OR hospitals, isolation[mh] OR intensive care units[mh] OR operating rooms[mh] OR acute care[tiab] OR burn unit\*[tiab] OR emergency room\*[tiab] OR emergency department\*[tiab] OR common area\*[tiab] OR critical care[tiab] OR healthcare facilit\*[tiab] OR health care facilit\*[tiab] OR healthcare setting\*[tiab] OR health care setting\*[tiab] OR hospital\*[tiab] OR hospitalis\*[tiab] OR hospitaliz\*[tiab] OR ICU[tiab] OR institution[tiab] OR institutions[tiab] OR intensive care[tiab] OR isolation room\*[tiab] OR isolation unit\*[tiab] OR medical facilit\*[tiab] OR operating room\*[tiab] OR patient care area\*[tiab] OR patient\* room\*[tiab] OR ward[tiab] OR wards[tiab]
- #8 equipment and supplies, hospital[mh] OR equipment contamination[mh] OR hospital bed\* [tiab] OR (hospital\*[tiab] AND (bar[tiab] OR bars[tiab] OR bathroom\*[tiab] OR bed[tiab] OR beds[tiab] OR bed rail\*[tiab] OR bedrail\*[tiab] OR cart[tiab] OR carts[tiab] OR chair[tiab] OR chairs[tiab] OR commode\*[tiab] OR door[tiab] OR door handle\*[tiab] OR doors[tiab] OR equipment\*[tiab] OR faucet\*[tiab] OR floor[tiab] OR floors[tiab] OR flooring[tiab] OR handle[tiab] OR handles[tiab] OR light switch\*[tiab] OR pole[tiab] OR poles[tiab] OR rail[tiab] OR railing\*[tiab] OR rails[tiab] OR seat[tiab] OR seats[tiab] OR sink[tiab] OR sinks[tiab] OR table\*[tiab] OR toilet\* [tiab] OR wheelchair\*[tiab]))
- #9 fomites[mh] OR counter[tiab] OR counters[tiab] OR countertop\*[tiab] OR counter top\*[tiab] OR surface\*[tiab] OR (surface\*[tiab] AND (contamina\*[tiab] OR environmental[tiab] OR hard[tiab] OR high contact[tiab] OR high touch[tiab] OR hospital\*[tiab] OR hygiene[tiab] OR nonporous[tiab] OR non porous[tiab]))

- #10 disinfection system\*[tiab] OR ((automat\*[tiab] OR "no touch"[tiab] OR "non touch"[tiab] OR robot\*[tiab] OR touchless[tiab]) AND (aerosol\*[tiab] OR air[tiab] OR airborne[tiab] OR clean\*[tiab] OR chlorine[tiab] OR disinfect\*[tiab] OR decontaminat\*[tiab] OR fog\*[tiab] OR fumigat\* [tiab] OR gas[tiab] OR gaseous[tiab] OR gasses[tiab] OR mist\*[tiab] OR purif\*[tiab] OR sanitis\*[tiab] OR sanitiz\*[tiab] OR steam\*[tiab] OR sterilis\*[tiab] OR steriliz\*[tiab] OR vapor\*[tiab] OR vapour\*[tiab]))
- #11 ultraviolet rays[mh] OR "pulsed xenon"[tiab] OR "ultra violet"[tiab] OR ultraviolet[tiab] OR uv[tiab] OR "uv c"[tiab] OR uvc[tiab] OR uvgi[tiab] OR vuv[tiab] OR xenon[tiab]
- #12 lightstrike OR "germ zapping robot\*" OR "optimum uv" OR pathogon OR "rapid disinfectant" OR "rd uvc" OR smartuvc OR "steriliz r d" OR "steriliz rd" OR surfacide OR "tru d" OR "uvc cleaning system"
- #13 hydrogen peroxide[mh] OR hydrogen peroxide[tiab] OR H2O2[tiab] OR "H2 O2"[tiab]
- #14 bioquell\* OR haloc50\* OR halofogger\* OR halohpc\* OR halosil\* OR halomist\* OR 'HC 80TT\*' OR steramist\* OR sterilucent OR tomi
- #15 copper[mh] OR copper[tiab]
- #16 chlorine dioxide[tiab] OR chlorine dioxide[supplementary concept] OR ozone[mh] OR ozone[tiab] OR steam[mh] OR steam\*[tiab] OR water vapor[tiab] OR water vapour[tiab]
- #17 (#1 OR #2 OR #3 OR #4 OR #5 OR #6) AND (#7 OR #8 OR #9) AND (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)

**EMBASE. Amsterdam (The Netherlands): Elsevier B.V. [searched January 1, 2000, through April 22, 2020]. Available from: [www.embase.com](http://www.embase.com). Subscription required.**

*Search Strategy.*

- #1 'hospital infection'/de OR nosocomial\*:ti OR (('health care acquired' OR 'health care associated' OR 'hospital acquired' OR 'hospital associated') NEXT/1 (infect\* OR nosocomial OR pathogen\* OR viral OR virus\*)):ab,ti,kw OR (HAI OR HAIs):ti
- #2 'coronavirinae'/exp OR '2019 ncov':ab,ti,kw OR 2019ncov:ab,ti,kw OR '2019 novel coronavirus':ab,ti,kw OR 'corona virus':ab,ti,kw OR 'corona viruses':ab,ti,kw OR coronavirus:ab,ti,kw OR coronaviruses:ab,ti,kw OR covid\*:ab,ti,kw OR 'covid 19':ab,ti,kw OR covid19:ab,ti,kw OR covid2019:ab,ti,kw OR 'hcov 19':ab,ti,kw OR 'hcov 2019':ab,ti,kw OR hcov19:ab,ti,kw OR hcov2019:ab,ti,kw OR ncov\*:ab,ti,kw OR 'ncov 2019':ab,ti,kw OR ncov2019:ab,ti,kw OR 'sars cov 2':ab,ti,kw OR 'sars cov2':ab,ti,kw OR 'sarscov 2':ab,ti,kw OR sarscov2:ab,ti,kw OR 'severe acute respiratory syndrome coronavirus 2':ab,ti,kw OR 'severe acute respiratory syndrome corona virus 2':ab,ti,kw OR (((asia\* OR china OR chinese OR epidemic OR new OR novel OR pandemic OR wuhan) NEAR/5 (coronavirus OR coronaviruses OR 'corona virus' OR 'corona viruses' OR covid\* OR hcov)):ab,ti,kw)
- #3 'severe acute respiratory syndrome'/de OR sars:ab,ti,kw OR 'severe acute respiratory syndrome':ab,ti,kw
- #4 'adenoviridae'/de OR 'influenza a virus (h1n1)'/de OR 'influenza virus'/de OR 'middle east respiratory syndrome coronavirus'/de OR 'human respiratory syncytial virus'/de OR 'rhinovirus'/de OR 'rhinovirus infection'/de OR 'viral respiratory tract infection'/de OR (adenovirus\* OR flu OR h1n1 OR influenza\* OR mers OR 'mers cov' OR merscov OR 'middle east respiratory syndrome' OR 'respiratory syncytial virus' OR rhinovirus):ab,ti,kw
- #5 'clostridioides difficile'/de OR 'clostridium difficile infection'/de OR ('clostridioides difficile' OR 'clostridium difficile' OR 'clostridium difficilis' OR 'c. difficile' OR 'c. diff' OR 'c.difficile' OR 'c.diff' OR 'peptoclostridium difficile'):ab,ti,kw
- #6 ('epidemic'/de OR 'pandemic'/de OR 'pandemic influenza'/de OR contagion\*:ti OR crises:ti OR crisis:ti OR epidemic\*:ti OR outbreak\*:ti OR pandemic\*:ti OR scourge\*:ti OR plague\*:ti) AND ('viral contamination'/de OR 'virus'/exp OR 'virus infection'/exp OR 'virus shedding'/de OR 'virus transmission'/de OR virus/de OR 'viral contamination'/de OR viral:ti OR viruses:ti OR viral:ti)
- #7 'emergency care'/de OR 'health care facility'/de OR hospital/de OR 'isolation facility'/de OR ('acute care' OR 'burn unit\*' OR 'emergency room\*' OR 'emergency department\*' OR 'common area\*' OR 'critical care' OR 'healthcare facilit\*' OR 'health care facilit\*' OR 'healthcare setting\*' OR 'health care setting\*' OR hospital\* OR hospitalis\* OR hospitaliz\* OR ICU OR institution OR institutions OR 'intensive care' OR

- 'isolation room\*' OR 'isolation unit\*' OR 'medical facilit\*' OR 'patient care area\*' OR 'patient\* room\*' OR ward OR wards):ab,ti,kw
- #8 'hospital equipment'/de OR 'hospital bed\*':ab,ti,kw OR (hospital\* AND (bar OR bars OR bathroom\* OR bed OR beds OR 'bed rail\*' OR bedrail\* OR cart OR carts OR chair OR chairs OR commode\* OR door OR 'door handle\*' OR doors OR equipment\* OR faucet\* OR floor OR floors OR flooring OR handle OR handles OR 'light switch\*' OR pole OR poles OR rail OR railing\* OR rails OR seat OR seats OR sink OR sinks OR table\* OR toilet\* OR vent:ti,ab OR ventilation:ti,ab OR vents:ti,ab OR wheelchair\*)):ab,ti,kw
  - #9 fomite\*:ab,ti,kw OR fomite/de OR 'surface area'/de OR (counter OR counters OR countertop\* OR 'counter top\*' OR surface\*):ti OR (surface\* NEAR/2 (clinical OR contamina\* OR environmental OR hard OR 'high contact' OR 'high touch' OR hospital\* OR hygiene OR nonporous OR 'non porous')):ab,ti,kw
  - #10 'disinfection system'/exp OR 'disinfection system\*':ab,ti OR ((automat\* OR 'no touch' OR 'non touch' OR robot\* OR touchless) NEAR/2 (aerosol\* OR air OR airborne OR chlorine OR clean\* OR disinfect\* OR decontaminat\* OR fog\* OR fumigat\* OR gas OR gaseous OR gasses OR mist\* OR ozone OR purif\* OR sanitis\* OR sanitiz\* OR steam\* OR sterilis\* OR steriliz\* OR vapor\* OR vapour\*)):ab,ti
  - #11 'ultraviolet irradiation'/de OR 'ultraviolet radiation'/de OR ('pulsed xenon' OR 'ultra violet' OR ultraviolet OR uv OR 'uv c' OR uvc OR uvgi OR vuv OR xenon):ab,ti,kw
  - #12 (lightstrike OR 'germ zapping robot\*' OR 'optimum uv' OR pathogon OR 'rapid disinfectant' OR 'rd uvc' OR smartuvc OR 'steriliz r d' OR 'steriliz rd' OR surfacide OR 'tru d' OR 'uvc cleaning system\*'):ab,ti,kw,df
  - #13 'hydrogen peroxide'/de OR ('hydrogen peroxide' OR H2O2 OR 'H2 O2'):ab,ti,kw
  - #14 (bioquell\* OR halo OR haloc50\* OR halofogger\* OR halohpc\* OR halosil\* OR halomist\* OR 'HC 80TT\*' OR steramist\* OR sterilucent OR tomi):ab,ti,kw,df
  - #15 copper/de OR copper\*:ti OR (copper NEAR/2 (antimicrobial\* OR coated OR coating\* OR impregnated OR surface\*)):ab,ti,kw
  - #16 'chlorine dioxide'/de OR ozone/de OR 'water vapor'/de OR ('chlorine dioxide' OR ozone OR steam\* OR 'water vapor' OR 'water vapour'):ab,ti,kw
  - #17 (#1 OR #2 OR #3 OR #4 OR #5 OR #6) AND (#7 OR #8 OR #9) AND (#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)

## Appendix B. Evidence Tables

Note: References located in references section of main report.

**Table B-1. Systematic reviews assessing any modality**

Modality	Citation	Objective	Search Strategy	Key Inclusion/ Exclusion Criteria	Evidence Base	Interventions	Relevant Findings	Authors' Conclusions
<b>Ultraviolet Light and Vaporous Hydrogen Peroxide</b>	Marra et al. 2018 <sup>11</sup>	To review evidence for impact of ultraviolet light (UVL) and hydrogen peroxide mist or vapor (VHP) on multidrug-resistant organisms [MDRO], including <i>Clostridium (now Clostridioides) difficile</i> infection (CDI).	PubMed, CINAHL, Cochrane Library, CENTRAL, Database of Abstracts of Reviews of Effects (DARE), and Scopus (which includes EMBASE), inception to April 30, 2017.	<p><b>Inclusion Criteria:</b> Peer-reviewed published studies, conducted in acute care settings, implemented UVL or VHP for reduction of multi drug resistant organism hospital-acquired infections (HAIs), controlled trial (CT), or quasi-experimental design.</p> <p><b>Exclusion Criteria:</b> Editorials, commentaries, outbreak studies; studies assessing reduced contamination of hospital surfaces.</p>	<p>20 articles were included, of which 17 addressed UVL or VHP for outcomes of interest.</p> <p><b>UVL:</b> 11 studies total: 1 randomized controlled trial (RCT)*, 1 controlled trial (CT)**, and 9 pre/post studies</p> <p><b>VHP:</b> 6 studies total: 1 prospective cohort study and 5 pre/post studies</p> <p>* A prespecified secondary analysis of this RCT is also included as a separate study (Anderson 2018).<sup>21</sup></p> <p>** Data from this CT were taken from a conference abstract; the full paper was published as Sampathkumar 2019.<sup>24</sup></p>	<p>UVL:</p> <ul style="list-style-type: none"> <li>• Pulsed Xenon (6 studies)</li> <li>• UV-C radiation (4 studies)</li> <li>• Type not reported (1 study)</li> </ul> <p>VHP: No further details provided.</p>	<p><b>UVL:</b> Pooled analysis of 11 studies found terminal cleaning with UVL no-touch technology was associated with statistically significant lower CDI infection rates: pooled relative risk (RR): 0.64 (95% confidence interval [CI]: 0.49 to 0.84, p=0.001, I<sup>2</sup>=0%).</p> <p>Stratified analysis found a statistically significant lowering of CDI rates in studies with high baseline CDI rates (RR: 0.60, 95% CI: 0.43 to 0.86), but not low rates (RR: 0.70, 95% CI: 0.17 to 2.9). However, pooled analysis of 2 controlled studies alone found no significant lowering of CDI rates: RR: 0.65, 95% CI: 0.26 to 1.62.</p> <p><b>VHP:</b> Pooled analysis of 5 studies found a nonsignificant lowering in CDI rates: RR: 0.52 (95% CI: 0.15 to 1.81, p=0.30). 1 additional pre/post study found decreased CDI rates (but did not perform statistical testing).</p>	<p>"...using UVL no-touch technology to enhance environmental hygiene can decrease HAIs for specific pathogens, specifically CDI and VRE [vancomycin-resistant <i>enterococci</i>] infections."</p> <p>"We believe that no-touch methods (UVL and VHP systems) augment traditional cleaning but cannot replace it...More randomized trials should be performed to evaluate these no-touch systems, as well as cost-effectiveness analyses to determine the role that no-touch systems can have in hospital infection control."</p>

Modality	Citation	Objective	Search Strategy	Key Inclusion/ Exclusion Criteria	Evidence Base	Interventions	Relevant Findings	Authors' Conclusions
Copper Surfaces, Chlorine Dioxide, Ozone	No systematic reviews identified	N/A	N/A	N/A	N/A	N/A	N/A	N/A

**Table B-2. Characteristics of primary studies assessing ultraviolet light**

Pathogen	Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
<b>Respiratory Viral Pathogens</b>	Pavia et al. 2018 <sup>14</sup> United States	Single-center, pre/post study  Study authors performed an interrupted time series analysis for hospital-acquired infections (HAIs), but did not clearly state that HAIs were respiratory viral infections.	Toddler unit and common areas of a 97-bed children's hospital	February 2015 to January 2017, 24 months	Standard cleaning* vs. quaternary ammonium + ultraviolet (UV) light (Enlight)  Toddler rooms and common areas were treated 2 to 3 times per week.  *Standard cleaning protocol not explicitly described.	Compared to 12 months before UV-C deployment, a 44% unadjusted reduction in overall respiratory viral infection incidence was found (p=0.003, based on 2-sample Poisson rate test), corresponding to an incidence rate ratio of 0.56 (95% confidence interval [CI]: 0.37 to 0.84).  Segmented regression of the 2 parts of the interrupted time series demonstrated a 44% reduction in slope with use of UV-C:  <ul style="list-style-type: none"> <li>• Before UV-C: 82.0 HAIs/ 10,000 patient days, 95% CI: 72.5 to 91.5</li> <li>• After UV-C: 50.3 HAIs/ 10,000 patient days, 95% CI: 41.0 to 59.6</li> </ul> Of note, authors specify the toddler unit had a high infection rate before use of UV intervention.	Authors note toddler rooms were chosen for intervention because they were known to have the highest HAI rates in the hospital.  Viral respiratory infections were identified using reverse transcription PCR (BioFire® FilmArray®) on samples from patients placed on contact/droplet precautions. Viruses identified included influenza, rhinovirus, enterovirus, and human metapneumovirus.  Clorox Healthcare provided the UVL device.

Pathogen	Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
<b>Clostridioides difficile Infection (CDI)</b>	Anderson et al. 2018 <sup>21</sup> United States This article is a secondary analysis of Anderson 2017 <sup>22</sup> , which is included in the meta-analysis reported in Marra et al. <sup>11</sup>	Multicenter pragmatic cluster randomized controlled trial (RCT)  9 hospitals randomly assigned each intervention's order (1-month washout + 6 months of intervention).	Acute care hospital rooms	April 2012 to July 2014  (28 months)	Standard cleaning (ammonium-based disinfectant, except for rooms with CDI, which were cleaned with bleach [10% hypochlorite containing disinfectant, Clorox Germicidal Wipes]) vs. Standard cleaning + UV vs. bleach vs. bleach + UV  Chemical disinfectants were standardized across hospitals.	No significant difference in hospital-wide risk of target organism acquisition (CDI, vancomycin resistant <i>enterococci</i> [VRE], methicillin-resistant <i>Staphylococcus aureus</i> [MRSA], or multidrug-resistant <i>Acinetobacter</i> ) between standard disinfection and the 3 enhanced terminal disinfection strategies for all target multidrug-resistant organisms:  <ul style="list-style-type: none"> <li>• UV study period relative risk [RR]: 0.89, 95% CI: 0.79 to 1.00; p=0.052</li> <li>• Bleach study period 0.92, 0.79 to 1.08; p=0.32</li> <li>• Bleach and UV study period 0.99, 0.89 to 1.11; p=0.89</li> </ul> Decreased risk in the UV study period was driven by reductions in risk of acquisition of CDI (RR: 0.89, 95% CI: 0.80 to 0.99; p=0.031) and VRE (0.56, 0.31 to 0.996; p=0.048).  However, risk of CDI was not significantly lower in the bleach period (RR: 0.91, 95% CI: 0.75 to 1.1) or bleach and UV period (RR: 0.97, 95% CI: 0.84 to 1.12).	Note: Intervention was used for contact precaution rooms only.

Pathogen	Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
	Brite et al. 2018 <sup>13</sup> United States	Single-center interrupted time series	Disinfection of a 25-bed bone marrow transplant (BMT) unit for preventing hospital-associated VRE and CDI.	April 2015 to November 2016, 20 months	<p>Standard cleaning* + Pulsed Xenon (PX)-UV vs. Standard cleaning</p> <p>*Rooms of patients with a CDI diagnosis were cleaned with hypochlorite solution (bleach) according to the recommended institutional protocol. A hospital-grade disinfectant (quaternary ammonium compound) was used for other hospital rooms.</p> <p>During the intervention period, additional unit-wide daily PX-UV disinfection of patient bathrooms was performed. For daily bathroom cleanings, the device was operated in one 5-minute cycle, whereas for discharge cleanings, three 5-minute cycles at different positions within the patient room (including the bathroom) were completed. The study did not report whether these daily bathroom cleanings also included standard cleaning.</p>	<p>During the 20-month study period, 579 patients had 704 admissions to the BMT unit, and 2,160 surveillance tests were performed.</p> <p>No change in level or trend in the incidence of VRE or CDI was observed:</p> <ul style="list-style-type: none"> <li>• VRE: trend incidence rate ratio [IRR]: 0.96, 95% confidence interval [CI]: 0.81 to 1.14; level IRR: 1.34, 95% CI: 0.37 to 1.18</li> <li>• CDI: trend IRR: 1.08, 95% CI: 0.89 to 1.31; level IRR: 0.51, 95% CI: 0.13 to 2.11</li> </ul>	<p>ATP (adenosine triphosphate) measurements of high-touch surfaces (HTSs) were taken at the end of manual cleaning, before UV disinfection. Bioluminescent ATP product used to monitor quality of manual cleaning. Any areas that met preset thresholds for an emitted bioluminescent signal from premarked areas required repeat manual cleaning.</p>

Pathogen	Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
<b>Clostridioides difficile</b> <b>Surface Contamination</b>	Wong et al. 2016 <sup>17</sup> Canada	Single-center pre/post study  Cultured 6 surfaces (overbed table, bed adjustment control, sink, toilet rim, washroom handrail, and floor) in isolation rooms of recently discharged CDI, MRSA, and VRE patients before and after cleaning.	728-bed tertiary care academic hospital	February 2013 to November 2013	Standard cleaning* vs. Standard cleaning + UV-C (low-pressure mercury lights, Tru-D SmartUVC, Lumalier Corp., Memphis, TN)  Sporicidal setting (22,000 uWs/cm <sup>2</sup> ) used for CD.  *Standard cleaning consisted of accelerated hydrogen peroxide for surfaces and neutral detergent for floors.	% of rooms contaminated with CD:  <ul style="list-style-type: none"> <li>• Before standard cleaning: 31.8% (7/22)</li> <li>• After standard cleaning: 22.7% (5/22), p=0.6</li> <li>• After UV-C disinfection: 0% (0/22), p=0.07</li> </ul> % of surfaces contaminated with CD:  <ul style="list-style-type: none"> <li>• Before standard cleaning: 7.2% (9/125)</li> <li>• After manual cleaning: 4% (5/125), p=0.3</li> <li>• After UV-C disinfection: 0% (0/125), p=0.07</li> </ul>	
	Ghantoji et al. 2015 <sup>15</sup> United States	Single-center pre/post study  5 surfaces (bathroom handrail, horizontal/vertical surface facing into room, bed control panel, bedrail, top of bedside table, IV pump control panel or other equipment control panel) in 30 CDI isolation rooms were sampled immediately after patients with a CDI were discharged.	Comprehensive cancer center	2012 to 2013	Standard cleaning* (including bleach) vs. Standard cleaning (no bleach) + PX-UV (Xenex Disinfection Services)  *Consisted of activated hydrogen peroxide disinfectant and bleach at 10% of sodium hypochlorite.  Device was placed in the bathroom and on both sides of the bed and run for 5 minutes in each position.	298 samples were collected using a moistened wipe specifically designed for spore removal.  Bleach (control):  <ul style="list-style-type: none"> <li>• Before: 35% positive (26 of 74)</li> <li>• After: 24% positive (18 of 74), p=0.13</li> </ul> PX-UV  <ul style="list-style-type: none"> <li>• Before: 41% positive (29 of 70)</li> <li>• After: 23% positive (16 of 70), p=0.007</li> </ul> The difference in final contamination levels between the 2 cleaning protocols was not significantly different (p=0.98).	

Pathogen	Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
	Nerandzic et al. 2015 <sup>19</sup> United States	Single-center pre/post study  Cultured high-touch surfaces (call lights, bedside tables, phones, chairs, intravenous poles, keyboards, bedrails), 10x10 cm area per sample, in rooms of discharged patients. Only Phase 2 included rooms housing patients with CDI.	Acute care tertiary care facility	NR	PX-UV (Xenex; Xenex Disinfection Services)  Phase I: (16 rooms) No cleaning vs. PX-UV run for 5 minutes on each side of the bed.  (No rooms with CDI patients.)  Phase II: (24 rooms)  Standard terminal cleaning* vs. Standard terminal cleaning + PX-UV run for 5 minutes on each side of the bed  (42% of rooms housed patients with CDI.)  *Included bleach on high touch surfaces (no additional details provided)	450 samples were collected on swabs and gauze pads and cultured to determine % of surfaces positive for CDI.  Phase 1: PX-UV <ul style="list-style-type: none"> <li>• Before: 11.6% positive (13/112)</li> <li>• After: 2.7% positive (3/112), p&lt;0.01</li> </ul> Phase II: Standard cleaning (including bleach) + PX-UV <ul style="list-style-type: none"> <li>• Before: 19.5% positive (22/113)</li> <li>• After: 8.0% positive (9/113)</li> </ul> Does not appear to have been statistically significant.	

Pathogen	Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
	Sitzlar et al. 2013 <sup>16</sup> United States	Single-center pre/post study	215-bed hospital and 165-bed long-term care facility	21 months January 2011 through September 2012	<p>Standard cleaning (Clorox Clean-Up Cleaner with Bleach)</p> <p>Tiered set of 3 added interventions:</p> <ul style="list-style-type: none"> <li>• Fluorescent marker removal (14 months)</li> <li>• UVL (Tru-D, Lumalier) (4 months)</li> <li>• Enhanced standard disinfection of high-touch surfaces (Clorox Germicidal Wipes, daily disinfection team and supervision) (3 months)</li> </ul> <p>These interventions were added to one another (e.g., Standard cleaning + Fluorescent Marker + UVL were used together when UVL was added).</p>	<p>Compared to baseline, interventions resulted in the following decrease in prevalence of CD contamination:</p> <ul style="list-style-type: none"> <li>• Baseline (Standard cleaning alone): 67% (14 of 21 positive)</li> <li>• Fluorescent marker intervention: 57% (16 of 28), p=0.024</li> <li>• UVL: 35% (8 of 23), significant decrease compared to baseline, prevalence ratio 0.52 (95 % CI: 0.43 to 0.62) p &lt;0.001</li> </ul> <p>Authors note that the positive samples of CD after UV light disinfection were found only in shaded areas of the room.</p>	Authors note the hospital had a high baseline CDI incidence (15 cases per 10,000 patient days).

**Table B-3. Studies evaluating vaporous hydrogen peroxide or aerosolized hydrogen peroxide**

Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
Mosci et al. 2017 <sup>12</sup> Italy	Randomized controlled trial Rooms from discharged <i>Clostridioides difficile</i> infection (CDI) patients were randomized; in each arm, surfaces were swabbed before and after disinfection.  Specifically, 100 cm <sup>2</sup> plain surface of bedside table, washbasin, handle or inlet of nightstand drawer, light/nursing-call devices, drip stand, foot bed tubular, inner door-handle of the room, inner bathroom door handle	4 hospitals (mix of public and private)  Included single patient rooms used by medicine, orthopedics, long-term care, recover and functional rehabilitation	December 2014 to September 2015	“Cleaning phase”* + Atomized Hydrogen peroxide <8% + Silver ion vs. “Cleaning phase” + Manual cleaning (0.5% sodium hypochlorite solution)  *Cleaning phase only described as involving furniture, walls, floor and bathroom  For atomized hydrogen peroxide + silver: 99S solution was atomized into microparticles of submicron size, by setting the modulator 99M at a speed of 1.5 mL/m <sup>3</sup> , to uniformly distribute solution; Discharge period was 20 minutes, followed by 35 minutes for decrease of hydrogen peroxide	28 hospital rooms housing patients with CDI for at least 48 hours, and available for decontamination at time of discharge were randomized.  Surfaces contaminated with CD: Atomized hydrogen peroxide + Silver Ion: 13% (before), 0% (after), p<0.001  Sodium hypochlorite (0.5%): 20% (before), 3% (after), p<0.001  No significant between group differences p=0.267)	Authors note that personnel for cleaning differed for public vs. private hospitals. Public facilities outsourced cleaning to service company, while cleaning at private hospitals was performed by in-house services. “All staff employed were aware of the study being conducted.”

**Table B-4. Studies evaluating copper surfaces**

Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
Marik et al. 2020 <sup>18</sup>  United States	Single-center pre/post study  Before and after relocation of 3 intensive care units (ICUs) into new ICU tower.	ICU beds of academic hospital (563 hospital)  3 ICUs were general, neuro-intensive, and burn-trauma units.	25 months (July 2017 to August 2019)	Standard care before (9,890 patient-days) vs. after (11,169 patient-days) ward relocation to a new facility equipped with EOS <sup>CU</sup> Preventive/Biocidal Surface on workstations, bedside and vanity tables, bathroom fittings, bedrails, and door handles.	Compared to before moving to a new ICU tower, both health-care-associated infections and <i>Clostridium difficile</i> infections (CDIs) decreased.  Healthcare-associated infections (HAIs):  • Significant reduction: (3.9 vs. 1.3 per 1000 patient-days, incidence rate ratio: 2.9, 95% confidence interval [CI]: 1.5 to 5.7, p=0.0002  CDI:  • Significant reduction: 2.4 vs 0.7 per 1000 patient-days, incidence rate ratio: 3.3, 95% CI: 1.4 to 8.7, p=0.002  The infection rate due to central-line-associated bloodstream infections and catheter-associated urinary tract infections did not differ between these 2 time periods.	Authors note the new ICU tower had a different layout and was equipped with modern ventilation systems, which may been a confounder.

Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
Sifri et al. 2016 <sup>20</sup>  United States	Single center pre/post study  Before and after construction of a new hospital wing equipped with copper surfaces and linens.  Baseline period (1 year) followed by assessment period with CDI rates from new wing and old wing compared.	Acute care non-ICU hospital beds at a community hospital	25.5 months, including 3.5 months washout period  (November 2012 to December 2014)	Standard cleaning* vs. Standard cleaning + Solid Copper Surfaces + Copper Linens  *Standard cleaning involved quaternary ammonium disinfectants, except for CDI patient rooms for which a hypochlorite product was used. Fidelity of cleaning was monitored with Dazo fluorescent marking gel.  <u>Copper surfaces:</u> 16% copper oxide impregnated composite countertops and molded surfaces (Cupron Enhanced EOS Solid Surfaces; Cupron, Inc, Richmond, VA, and EOS Surfaces LLC, Norfolk, VA), targeting high touch surfaces. Countertops included sinks, vanities, patient room desks, computer stations, soiled utility rooms, and nurse workstations. Form-fitting copper impregnated composite molded surfaces included over-the-bed tray tables and bed rails.  <u>Copper linens:</u> Patient gowns, pillowcases, fitted and flat sheets, washcloths, bath towels bath blankets, and thermal blankets. Sequentially deployed to 1 new unit every few weeks during assessment period. Deployed by environmental services personnel to new wing with audits by unit management staff and infection prevention staff to ensure correct placement.	The baseline period (old wing) included 46,391 patient-days and had an incidence rate (IR) of CDI of 4.10 (95% CI 4.05 to 4.14).  Compared to baseline rate, during the assessment period the CDI was lower in the new hospital wing (14,479 patient-days) with copper linens + solid copper surfaces: IR 0.69 (95% CI 0.65 to 0.73), p=0.048.  In contrast, the rate of CDI in the old hospital wing (19,177 patient days, without copper) was incidence rate (IR) 4.69 (95% CI 4.62 to 4.76), with no statistically significant difference compared to baseline (p=0.736).  Authors note that types of admissions to new vs. old wings significantly differed: a majority of new wing patients were surgical (with fewer medical comorbidities), whereas old wing patients were nearly exclusively medicine patients (with more medical comorbidities with higher rates of hospital admission, and CDI infection in prior 6 months).  Specifically, for patients in the new wing only 16 cases/1000 admissions had prior CDI, compared to 29/1000 admissions in the old wing during the assessment period (p=0.002).  63% of new wing patients were surgical (and 37% medical), while only 6.9% of new wing patients were surgical (93.1% medical), p <0.001.  Also, rooms in new wing were 112% larger than existing rooms in the old wing.	Study was conducted during the replacement of a 1970s-era clinical wing with a new hospital wing in November 2013  Laundering protocols were the same for both sets of linens and followed established protocols.  Unit-level hand hygiene compliance rates were assessed through an ongoing, anonymous auditing program and unit-based staff; no major changes in the hand hygiene program occurred during the study period.

**Table B-5. Studies evaluating steam, chlorine dioxide, or ozone**

Study	Study Type, Design	Setting	Study Duration	Intervention	Results	Comment
No studies identified	N/A	N/A	N/A	N/A	N/A	N/A

## Appendix C. Risk of Bias Assessments

**Table C-1. Study characteristics relevant to risk of bias (formal assessments not performed)**

Study	Study Design	Characteristics	Comments
Marra et al. 2018 <sup>11</sup>	Systematic review (SR) and meta-analysis	Comprehensive search with dates and strategy provided, inclusion/exclusion criteria, standard appraisal of included studies, assessed for publication bias, performed sensitivity analyses.	No significant flaws in SR methods. Of note, many studies did not report compliance with “alternative measures” (hand hygiene, antimicrobial stewardship), which may have affected infection rates.
Anderson et al. 2018 <sup>21</sup> A secondary analysis of Anderson 2017 <sup>22</sup> , which is included in meta-analysis reported in Marra et al. <sup>11</sup>	Pragmatic cluster randomized controlled trial (RCT)	Randomization was “resource dependent” and accounted for the number of ultraviolet (UV) devices available. After randomization of hospital and order of interventions, the number of available devices dictated the final order. Allocation was not masked. No sham was used.	The largest of included studies and only primary study to involve more than a single site.
Mosci et al. 2017 <sup>12</sup>	RCT	Computerized randomization, criteria for inclusion of room included that the room would “be available for decontamination at the time of discharge” –unclear if this impacted what rooms were eligible. No significant difference in baseline rates of <i>Clostridioides difficile</i> (CD) contamination between groups; however, the study enrolled a very small number of rooms (n=28), potential differences in cleaning procedures across 4 hospitals noted; standard cleaning procedures not described, no monitoring of fidelity of standard cleaning or either intervention arm.	
Brite et al. 2018 <sup>13</sup> United States.	Interrupted time series	Single center; standard cleaning procedures described and adequacy verified with bioluminescent product.	
Pavia et al. 2018 <sup>14</sup> United States	Pre/post study	Single center; standard cleaning procedures not described.	
Wong et al. 2016 <sup>17</sup> Canada	Pre/post study	Single center; standard cleaning procedures described; baseline infection rates reported.	
Ghantoji et al. 2015 <sup>15</sup> United States	Pre/post study	Single center; full description of standard cleaning procedures not provided; some study samples noted to be outliers. Very small n (only 30 rooms).	
Nerandzic et al. 2015 <sup>19</sup> United States	Pre/post study	Single center, standard cleaning procedures only described as including bleach for high touch surfaces; fidelity of standard cleaning procedures not monitored;	
Sitzlar et al. 2013 <sup>16</sup> United States	Pre/post study	Single center; standard cleaning procedures described; intervention part of a tiered multicomponent intervention; hospital noted to have high baseline <i>Clostridioides difficile</i> infection (CDI) rate.	

Study	Study Design	Characteristics	Comments
Marik et al. 2020 <sup>18</sup> United States	Pre/post study	Single center; confounders (new ventilation system, new layout and many other environmental changes) noted by study authors.	
Sifri et al. 2016 <sup>20</sup> United States	Pre/post study	Single center, standard cleaning described, fidelity of standard cleaning and hand hygiene compliance monitored and statement that no new interventions were introduced during this time. However, many potential confounders including statistically significant differences in case mix between old and new wings (medical vs. surgical patients, history of CDI infection, history of recent hospitalization). In addition, new wing had significantly larger rooms (112%) compared to the old wing.	

# Appendix D. Ongoing Studies

**Table D-1. Ongoing trials in Clinicaltrials.gov**

Title, Registration Number	Registration Number	Trial Design	Planned Enrollment	Estimated Date of Completion
Pulsed UV Xenon Disinfection to Prevent Resistant Healthcare Associated Infection	<a href="#">NCT03349268</a>	Randomized sham controlled crossover trial	500	May 2022

## Appendix E. Flow Diagram

