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Evaluation of an Ultraviolet C (UVC) Light-Emitting Device for Disinfection of High Touch Surfaces in Hospital Critical Areas

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Abstract: Implementation of environmental cleaning and disinfection has been shown to reduce the incidences of healthcare-associated infections. The effect of an enhanced strategy for terminal room disinfection, applying the pulsed xenon-based ultraviolet light no-touch disinfection systems (PX-UVC) after the current standard operating protocol (SOP) was evaluated. In a teaching hospital, the effectiveness in reducing the total bacterial count (TBC) and in eliminating high-concern microorganisms was assessed on five high-touch surfaces in different critical areas, immediately pre- and post-cleaning and disinfection procedures (345 sampling sites). PX-UVC showed only 18% (15/85) of positive samples after treatment compared to 63% (72/115) after SOP. The effectiveness of PX-UVC was also observed in the absence of manual cleaning and application of a chemical disinfectant. According to the hygienic standards proposed by the Italian Workers Compensation Authority, 9 of 80 (11%) surfaces in operating rooms showed TBC ≥15 CFU/24 cm^2 after the SOP, while all samples were compliant applying the SOP plus PX-UVC disinfection. *Clostridium difficile* (CD) spores and *Klebsiella pneumoniae* (KPC) were isolated only after the SOP. The implementation of the standard cleaning and disinfection procedure with the integration of the PX-UVC treatment had effective results in both the reduction of hygiene failures and in control environmental contamination by high-concern microorganisms.

Keywords: healthcare-associated infections; hospital environmental cleaning and disinfection; ultraviolet C light-emitting device; high-touch surfaces

1. Introduction

The role of healthcare workers (HCW) in the transmission of pathogens from patient-to-patient is well documented; however, increasing evidence reports the contaminated environment as highly significant in pathogen transmission; in particular, high-touch surfaces are recognized as a possible reservoir of infectious agents and their contamination can pose a risk also for the spread of multi-resistant organisms [1–4]. High touch near-patient surfaces have actually higher bioburden and can contribute to secondary transmission by the direct contact with the patient or via the hands of HCW and visitors [5,6].

The relevance of the decontamination of the environment, such as patient-care rooms before admission of subsequent occupants, has therefore grown in recent years and high-touch sites are recommended to be cleaned and disinfected on a more frequent schedule than minimal touch surfaces [7].

Environmental cleaning and disinfection are important components of a comprehensive strategy in order to control healthcare-associated infections [8,9], especially in wards with immuno-compromised patients. However, studies evaluating the effectiveness of improved cleaning interventions have reported that approximately 5–30% of surfaces remain potentially contaminated, due to the inability of existing detergent formulations and disinfectants to disrupt biofilms [10,11]. Dry-surface biofilms on clinical surfaces were recently investigated and the survival of vegetative bacteria for long periods has been demonstrated [12,13].

There has been a lot of interest in the development of effective and more comprehensive environmental disinfection strategies and, in the last year, attention has been focused on improving "no touch" technologies, including the use of the mobile UV-light disinfection system, which has the advantages of not requiring changes in a room's ventilation, not leave residue after treatment, and having a broad spectrum of action and rapid exposure times. The germicidal effects of UVC irradiation results in cellular damage by photohydration, photosplitting, photodimerization, and photocrosslinking, thereby inhibiting cellular replication. UVC can be generated from low-pressure mercury lamps that produce continuous UVC with a peak wavelength of 254 nm, and pulsed xenon lamps that emit pulsed light at high intensity, both in the spectrum of UVC (100–280 nm) and visible (380–700 nm) radiation, with a much broader microbicidal activity spectrum [14]. The UV-light disinfection system must operate in unoccupied rooms, after the patient discharge and in the absence of health personnel. Many devices have motion sensors that shut-off the device if any movement is detected inside the room being disinfected. Damage to materials in the room was not reported during the use of UV-light disinfection systems, although in the Pulsed-UVC device operator manual, high pressure acrylic material may show degradation for prolonged periods of exposure to light UV (e.g., daily or weekly), therefore it is advised to cover them during the treatment.

Implementation of this "no-touch" technology in various hospitals has documented a sustained reduction in surface microbial contamination, reduced cross contamination, and a reduced spread of multi-drug resistant bacterial infections. In the study of Liscynesky et al. [15], in rooms of patients with confirmed *C. difficile* infection (CDI), 32 out of 238 (13%) high-touch surfaces were positive after bleach disinfection and only 1 out of 238 (0.4%) was positive after UVC-treatment (the computer keyboard) at 254 nm emitted by 3 connected devices run for 45 min. Wong et al. reported the persistence environmental contamination by methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococcus (VRE) and *C. difficile*, respectively in 27%, 29,5%, and 22,7% of sites after the standard cleaning and disinfection protocol, whereas only in 3.3%, 4.9%, and 0% after UVC-disinfection ($p < 0.05$). The exposition time varied from 14 min at 46,000 μWs/cm^2 to 57 min at 22,000 μWs/cm^2 for the sporicidal cycle. The ability to disinfect high concentrations of organisms varies in the presence of proteins [16]. The same finding was reported by Ali et al., who observed lower and more variable $\log_{10}$ reductions in MRSA and *K. pneumoniae* after UVC disinfection at 254 nm when heavy soiling was present [17].

An increased reduction of 17% in MRSA, VRE, *Acinetobacter* spp., and carbapenem-resistant Enterobacteriaceae was reported by Hosein after 20 min pulsed xenon-based ultraviolet light disinfection (one device, two cycles) in addition to standard end-of-day manual cleaning [18].

Haddad et al. showed that combining standard between-case manual cleaning of surfaces, followed by a 2-min cycle of disinfection using a portable xenon pulsed ultraviolet light germicidal device, furtherly decreased the bacterial load by at least 70% [19]. The effectiveness of the pulsed xenon-based ultraviolet light systems in reducing aerobic bacteria, also in the absence of manual disinfection, was demonstrated by Jinadatha et al. [20].

Although some studies have reported doses of UVC that yield 3 $\log_{10}$ reductions of specific pathogens using low-pressure mercury lamps UVC devices, data regarding spectrophotometrically determined doses of 200–320 nm light emitted by pulsed xenon lamps are lacking [21].

Hospitals that use UV-light disinfection after cleaning and disinfection standard protocol have actually significantly mitigated infection risks associated with environmentally mediated transmission

routes. In the BETR (Benefits of Enhanced Terminal Room Disinfection) study, the first randomized multicenter trial that compared the effectiveness of different disinfection strategies in rooms previously occupied by colonized/infected patients with the incidence of new colonization and infections in new hospitalized patients, demonstrated that the addition of UVC disinfection treatment to the standard protocol had a direct protective effect on the risk of acquiring *C. difficile* and vancomycin-resistant Enterococci [22,23].

The aim of this study was to evaluate the effectiveness on the field of an ultraviolet C (UVC) light-emitting device in reducing environmental bacterial burden and the presence of pathogens when compared to the current standard operating protocol (SOP).

2. Materials and Methods

A prospective open-labelled cross-over study was conducted in a 1158-bed teaching hospital in Italy with a follow up duration of four months, from September 2017 to December 2017. To evaluate the effectiveness of pulsed xenon-based ultraviolet light no-touch disinfection systems (PX-UVC) in reducing environmental contamination, sampling was performed in different critical areas: 5 patient rooms, 2 Intensive Care Units (ICU) isolation rooms, and 9 operating theatres (OT).

The inclusion criteria for the patient rooms and ICU isolation rooms were: A single occupancy room, occupied for a minimum of 48 h by patient colonized/infected by high concern microorganisms (reported as an alert by the microbiology laboratory). In the hospital, a systematic surveillance for multi-drug resistant organism colonization was performed through weekly rectal swabs and/or bronchial aspirate sampling.

2.1. PX-UVC Device

The PX-UVC device (Xenex Disinfection Services, San Antonio, TX USA) uses a xenon flash lamp to generate high-energy, broad-spectrum ultraviolet and visible light (UVC 100–280 nm, visible 380–700 nm), in microsecond bursts (pulses) at 67 Hz. No touch UV technology is dependent on the distance between the lamp and the surface being disinfected. The inverse square law states that the doubling of distance between the lamp and the surface being disinfected will quadruple the time required for disinfection. The PX-UVC device uses 5-min disinfection cycles and multiple positions with minimal distances from high-touch surfaces. The manufacturer recommends that high-touch surfaces are within two meters of the lamp in order to achieve optimal efficacy. For patient rooms, the device requires one 5-min disinfection cycle on each side the patient bed and one cycle in the private bathroom (if applicable). For operating theatres, the device requires one 10-min disinfection cycle on each side of the operating bed. Due to the high-intensity broad-spectrum UV light, the device is operated in unoccupied rooms. There are motion sensors that shut-off the device if any movement is detected inside the room being disinfected. The PX-UVC device, like most UVC lamps, causes chemical reactions that increase the concentration of ozone in the air. When the robot is operated in accordance with the procedures, the ozone produced is far below the Occupational Safety and Health Administration OSHA short-term exposure limits (0.1 ppm/8 h), however the manufacturer recommends using the robot in rooms with a system of ventilation, where possible. The robot allows access to the room (a green light turns on) after a delay that allows the ozone to dissipate. In our study, rooms were aerated after using the robot.

2.2. Study Protocol

The OTs were selected based on their different turnover time: two OTs scheduled for 10 surgeries/day (endocrine surgery) and four OTs scheduled for two major surgeries/day (implant of orthopedic prostheses and organ transplants).

In this hospital, the cleaning services were outsourced. According to the contract and the standard operating protocol (SOP), in terminal disinfection the housekeeping staff applied a chlorine-based detergent, Antisapril Detergent 10%, Angelini, followed by a chlorine-based disinfectant, Antisapril

Disinfectant 10%, Angelini (active chlorine 2800 mg/L), on furniture surfaces and electromedical devices. In rooms at discharge of patient with *Clostridium difficile* CD infection, Antisapril Disinfectant was applied at 18%. In operation rooms, the same protocol was performed by in-house auxiliary nurses.

Following the alternative protocol, after SOP, the auxiliary nurses expose the pulsed xenon-based ultraviolet light device, for two 5 min cycles for each bedside in the patient rooms and in the intensive care unit, whereas 10 min cycles were adopted for each surgical table side in operating theaters. Auxiliary nurses were trained on the proper use of the Pulsed-UVC device.

Baseline microbiologic samples were collected after patient discharge or after surgical activity and immediately after sanitization. In each setting, five high-touch surfaces (for the operating room—surgical table, tray table, anaesthetic machine, monitor, infusion pump, scialitic lamp, electrosurgery; for the Intensive Care Units ICU—hydrotherapy tank, tray table, monitor, patient bed, infusion pump; for patient rooms—patient bed, tray table, medication cart, call button, push button) were sampled after healthcare activity (5 samples in dirty condition), after standard operating protocol SOP (5 samples in clean condition), and after Pulsed-UVC disinfection (5 samples in improved clean condition). In the high turnover Operating Theatre OTs, between one procedure and the following one we tested only the efficacy of the Pulsed-UVC disinfection, because internal hospital policy only provides for a terminal cleaning/disinfection. Considering that the Pulsed-UVC treatment in OT was carried out several times a day, as control in the study, one not treated OT was included for each treated one. On this, OT samples were taken before and after the SOP. This has allowed us to eliminate any overestimates of treatment efficiency, due to the cumulative effect of UVC radiation.

According to ISO 14698-1, 55-mm diameter Rodac plates containing plate count agar (PCA) with neutralizers (VWR International PBI, Radnor, Pennsylvania, PA) were used for the total viable count (TVC) enumeration and violet red bile dextrose agar (VRBD), (Oxoid, Basingstoke, UK) for Gram-negative bacteria qualitative evaluation. Contact plates were incubated aerobically at 37 °C for 48 h.

Suspect *Acinetobacter* spp. or *Klebsiella* spp. were subcultured on chromID™ mSuperCARBA (bioMérieux, Marcy l'Etoile, Capronne, France) and identified by the API/ID32 Strep Miniature System (bioMérieux, Marcy l'Etoile, Capronne, France).

In the OT and ICU, the total microbial load and the presence of pathogens were evaluated according to the hygienic standards proposed by the Italian Workers Compensation Authority [24], whereas in patient rooms the evaluation was conducted according to the standard proposed by Dancer et al. [25], (for the ICU: ≤50 CFU/24 cm^2 and absence of pathogens, for the operating theaters: ≤15 CFU/24 cm^2 and absence of pathogens; ≤125 CFU/24 cm^2 for patient rooms).

Microbiologic sampling was performed using Rodac contact plates of 24 cm^2 (Oxoid, Basingstoke, United Kingdom) that were firmly pressed for 5 seconds on each surface. The plates were then incubated at 37 °C for 48 h.

To detect the presence of *C. difficile* spores, the sponge contact method (Sponge-Sticks, 3M St. Paul, MN) was applied. The sponge heads were aseptically placed into sterile stomacher bags (VWR International, Milan Italy) containing 20 mL neutralising solution (0.1% sodium thiosulfate, 3% Tween 80, 0.3% Lecithin), prepared in phosphate-buffered saline solution pre-sterilized (PBS, Sigma-Aldrich). An area of 10 × 10 cm was delimited by a sterile plastic template and then swabbed with the moistened sponge. After sampling, each sponge was returned to the bag in which it was moistened. The total volume of homogenized solution was aliquoted (1.5 mL) into centrifuge sterile tubes, and centrifugated to 8000× *g* for 20 min at 25 °C. The pelleted cells were suspended in 1 mL of PBS, and re-centrifugate at 6000× *g* for 15 min. All pellets were subsequently suspended in 500 µL of PBS and aliquots of 250 µL plated onto Brazier's agar plate (Oxoid, Basingstoke, Hampshire, United Kindom). The plates were incubated at 37 °C under anaerobic condition for 48 h. Presumptive *C. difficile* isolates were determinate by colony morphology (examination of plates for flat, circular colonies yellow/grey in colour with filamentous edges) and confirmed to be *C. difficile* using *C. difficile* selective latex agglutination assays (Oxoid, Basingstoke, United Kingdom).

2.3. Statistical Analysis

To compare the number of hygiene failures and the total number of positive samples obtained after each cleaning and disinfection procedure we applied the Wilcoxon matched-pairs signed rank test to analyse the results obtained in patient rooms and ICUs, while for OTs low turnover and OTs high turnover the analysis was conducted with the Mann–Whitney test. Statistical significance was inferred from $p < 0.05$. Statistical analysis was performed using Prism 8 (GraphPad Software, San Diego, CA, USA).

3. Results

We sampled a total of 345 high-touch surfaces—135 after healthcare activity, 125 after SOP, 85 after application of SOP and Pulsed-UVC treatment. 20 samples were collected after Pulsed-UVC disinfection applied without perform SOP.

A total of 2339 colonies were isolated from environmental surfaces. All but 39 were consistent with skin commensal (106 were *Staphylococcus* spp.) and of these, 6 colonies of mold were grown, 29 Gram negative bacteria (three *Enterobacter cloacae*, one *Vibrio alginoliticus*, 10 *Cryseobacterium menigosepticum*, seven *Edwarsiella hoshinae*, two *Methylobacterium mesofilicum*, four KPC-*K. pneumoniae*, two Extended Spectrum β Lactamase-producing *Klebsiella pneumoniae* (ESBL-*K. pneumoniae)*) and four bacillus identified as *C. difficile*. Before cleaning and disinfection, the average of CFUs was 6 ± 10 standard deviation (SD) CFU/24 cm^2 in OTs with low turnover, 7 ± 12 SD CFU/24 cm^2 in OTs with high turnover, 25 ± 19 SD CFU/24 cm^2 in the ICUs, and 58 ± 54 SD CFU/24 cm^2 in patient rooms at discharge.After SOP, the average of CFUs increased to 11 ± 18 SD CFU/24 cm^2 in OTs with low turnover (+83%), while it decreased to 1 ± 1 SD CFU/24 cm^2 (−7%) in OTs with high turnover, and in ICUs and patient rooms, respectively, to 2 ± 4 SD CFU/24 cm^2 (−92%) and 8 ± 13 SD CFU/24 cm^2 (−86%).

After Pulsed-UVC disinfection, approximately all the average of CFUs were 0 CFU/24 cm^2: 0 ± 1 SD CFU/24 cm^2 in ICUs (−100%), 1 ± 1 SD CFU/24 cm^2 in patient rooms (−98%), 0 ± 1 SD CFU/24 cm^2 in OTs with high turnover (−100%), and 0 ± 0 SD CFU/24 cm^2 in OTs with low turnover (−100%).

As concerned, the increased reduction obtained after the Pulsed-UVC treatment was 12% in patient rooms, 8% in ICUs, 93% in OTs with low turnover, and 183% in OTs with high turnover.

The median, lower, and higher values of the bacterial load and the interquartile range obtained in each hospital setting are reported in Table 1.

Table 1. Median, lower, and higher values of the bacterial load detected in each hospital setting.

Setting	Timing of Sampling	*n* (Samles)	Median	Lower	Higher	IQR
Patient rooms	Before C&D	25	43	0	180	93
	After SOP	25	2	0	50	7
	After SOP + Pulsed-UVC	25	0	0	3	1
ICU	Before C&D	10	23	1	50	45
	After SOP	10	1	0	14	2
	After SOP + Pulsed-UVC	10	0	0	1	0
OT low turnover	Before C&D	60	1	0	100	4
	After SOP	80	1	0	100	6
	After SOP + Pulsed-UVC	30	0	0	1	0
OT high turnover	Before C&D	40	7	0	38	25
	After SOP	10	0	0	3	1
	After Pulsed-UVC	20	0	0	4	0

Note: ICU—Intensive Care Unit; OT—Operative Theatre; C&D—Cleaning and Disinfection; SOP—Standard Operative Procedure; IQR—Interquartile Range.

After the application of SOP, 11% (9/80) surfaces in OTs with low turnover showed TBC ≥ 15 CFU/24 cm^2 (hygiene failures) (4 infusion pumps, 2 scialitic lamps, 2 anaesthetic machines, 1 surgical table). The CFU average did not undergo significant variation after the application of SOP,

rather we underlined an increase on the CFU amount. Probably, when the housekeeping combined detergent/hypochlorite treatment failed to eliminate the microbial contamination from the surface and the cleaning cloth was then used to wipe another surface, the bacterial was transferred to other surfaces and to the hands of the auxiliary nurses handling the cloth.

One hundred percent (10/10) of surfaces in OTs with high turnover were compliant after SOP and after Pulsed-UVC treatment without application of SOP (20/20) ($p < 0.18$; $n = 20$).

In the ICUs, 100% (10/10) of samples were found to be compliant already after application of SOP as well as after the Pulsed-UVC treatment ($p < 0.16$; $n = 20$) as for surfaces in patient rooms, 100% (50/50) compliant for TBC level (less than 125 CFU/24 cm^2) after SOP ($p < 0.0001$; $n = 50$).

Before the surgical activity on OTs with high turnover, between one surgery and another, the SOP was not applied and 7 surfaces were non-compliant with the standard (1 tray table, 1 anaesthetic machine, 2 scialitic lamps, 2 electrosurgeries). The total number of non-compliant samples after application of the SOP were 9/115 (8%) against 0/85 (0%) after Pulsed-UVC treatment ($p < 0.05$).

The total number of positive samples, after the SOP, were found to be 72/115 (63%), whereas 15/85 (18%) after treatment with Pulsed-UVC (Figure 1) ($p < 0.05$).

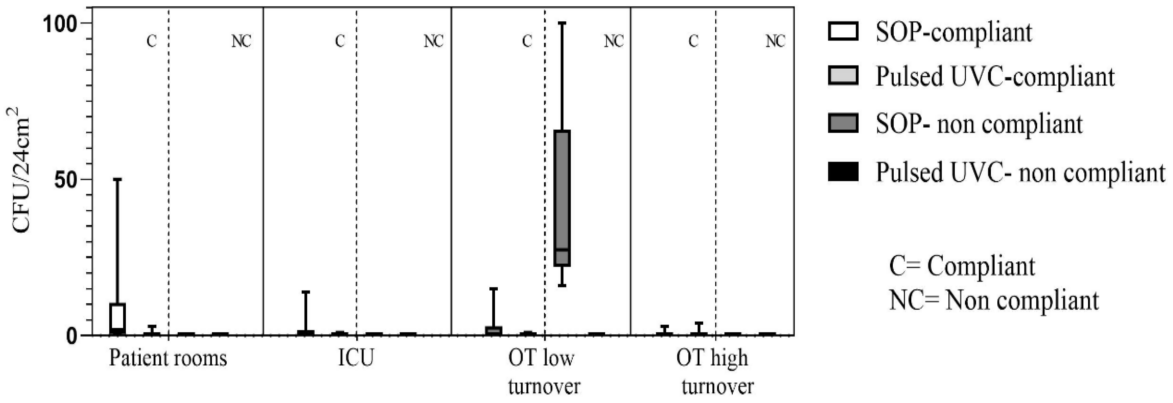

Figure 1. Median, lower, and higher values of the bacterial load detected in each hospital setting, distinguishing compliant on non-compliant values. Note: ICU—Intensive Care Unit; OT—Operative Theatre; C&D—Cleaning and Disinfection; SOP—Standard Operative Procedure; IQR—Interquartile Range.

High Concern Microorganisms

During the studied period, in a room previously occupied by a patient in contact precautions due to gastrointestinal colonization by KPC-producing *K. pneumoniae*, we detected three surface sample positives for KPC-*K. pneumoniae* on the tray table, the bedside table and the nurse call bell respectively, after discharge of patient; the bedside table remained positive after application of SOP.

In a room where a patient with ESBL-*K. pneumoniae* gastrointestinal colonization was hospitalized for a week, after patient discharge, we detected ESBL-*K. pneumoniae* on a tray table, but not after SOP.

After discharge, *C. difficile* spores were detected on 4 surfaces out of 5 in a room where the patient was admitted for 3 days: Bed patient, tray table, call button and push button. After the application of SOP, the bed patient surface remained positive for *C. difficile* spores, that was no longer found after the application of the Pulsed-UVC treatment.

In conclusion, in the post-application of SOP, 96% (24/25) of surface samples were compliant with the absence of high concern microorganisms and 100% (25/25) after Pulsed-UVC treatment.

4. Discussion

The manual terminal cleaning of clinical areas is aimed to reduce the burden of microbial contamination, but often is not able to completely eliminate it [26,27] and furthermore there is growing evidence that the contaminated environment is highly significant in pathogen transmission

leading to healthcare-associated infections (HCIs) [28,29]. Decontamination of the environment such as patient-care rooms before admission of subsequent occupants has therefore become of more importance in recent years and the assurance of sufficient decontamination more vital [30]; its importance was noted as pivotal in blocking norovirus and *C. difficile* transmission [31].

The role of housekeepers in a hospital is fundamental because they influence on the effectiveness of cleaning disinfection practice. Their high turnover, incorrect disinfectant contact times, and over-dilution of disinfectant solutions are negative factors for successful cleaning [32].

Numerous studies have demonstrated that current strategies for terminal room disinfection are inadequate and 50% or more hospital surfaces may go untouched and uncleaned following terminal room disinfection [3].

Cleaning is a complex, multifaceted process, plagued with random variation and the potential for introducing pathogens if cleaning cloths and solutions become contaminated and not correctly used.

Extensive outsourcing of hospital cleaning services to private sector contractors that employ staff with precarious working conditions and hence low motivation, achieving lower levels of cleanliness than the in-house staff, is frequent in Italy as well as in other countries. In-house staff have more perception on the importance of the cleaning in reducing the environmental microbial contamination. Toffolutti et al. found that outsourcing cleaning services was associated with greater incidence of MRSA and worse patient perceptions of cleanliness [33].

Pre-impregnated disinfectant cloths are used in an attempt to increase the efficacy of cleaning, because the sanitization process is faster and easier with a consequent increase in cleaning staff compliance. The effectiveness depends on the active ingredients they contain and its quantity, as well as the method of use [34,35]. The microfibre cloths remove more bacteria than cotton and synthetic fibre cloths [36]. Improper use of wipes could spread potential pathogens across surfaces if a "1 wipe, 1 application" per surface policy is not adopted [37].

In the last few years, no-touch systems for environmental decontamination are increasingly being considered, such as the UVC no-touch technology that can be done routinely and rapidly in different hospital settings after patient discharge or transfer.

In our study, we found Pulsed-UVC disinfection effective in reducing microbial contamination, showing only 18% (15/85) of positive samples after treatment compared to 63% (72/115) after SOP, and 12% increased reduction of positive samples in patient rooms, 8% in ICUs, 93% in OTs with low turnover, and 183% in OTs with high turnover. The treatment effectiveness was observed also in absence of any manual cleaning and application of a chemical disinfectant. In OT with high turnover, between one surgical operation and another, the standard protocol was not applied, and although the average bacterial load detected before the cleaning and disinfection procedures was low (7 ± 12 SD CFU/24 cm^2), 13 sampling sites out of 20 showed bacterial load, three sites over 15 CFU/24 cm^2. Pulsed-UV disinfection reduced aerobic bacteria in the absence of manual cleaning and disinfection. The same results were obtained in a study conducted by Jinadatha et al. where Pulsed-UV disinfection effectively reduced MRSA colony counts in the absence of manual disinfection and the authors suggested the use of Pulsed-UV disinfection as an adjunct to existing terminal cleaning protocols since it offers a safety net when the primary approaches fail [20].

Our study is one of the few in which the effectiveness of Pulsed-UVC on surfaces of hospital settings where manual cleaning was not performed was evaluated. Several studies [16,17] have demonstrated that the effectiveness of continuous UVC produced by low-pressure mercury lamps systems is diminished with increasing concentrations of organic or protein matter. The effectiveness of high-energy, broad-spectrum light produced by the Pulsed-UV system has not been shown to be affected by the lack of manual surface cleaning. Our results confirmed that this no-touch technology does not replace the traditional manual terminal cleaning and disinfection protocol, but it can improve it when a surface was missed by the housekeeping staff. Pulsed-UVC disinfection can be an excellent adjunct to the standard cleaning protocol, but it is important that infection preventionists maximize its usage to

achieve the most efficiency, taking into account the facility's patient flow and operational needs, to obtain a return on the investment cost.

Our study had several limitations. This is an experimental study and the hospital where it was conducted, despite being available for experimentation, had to reconcile the delays caused by the application of the protocol to the healthcare activity. In particular, the number of surfaces sampled after Pulsed-UV exposure was not high due to the difficulty of applying the treatment in operating theaters, where the scheduling of surgical activity cannot be delayed. Moreover, only isolation single rooms in ICU were included in the study, since the treatment was not applicable in multi-bed rooms.

In this regard, our proposal is to use this approach of implementing environmental disinfection in hospital rooms or in ICUs at patient discharge. In operating theaters, the possibility of exposure times reduced to few minutes should be considered, as already demonstrated by Haddad et al. [19].

5. Conclusions

No-touch surface decontamination technologies that use ultraviolet light may be effective in enhancing the results of the effort spent to reduce the microbial burden and potentially achieving lower Healthcare-associated Infections HAIs rates, as aimed for in infection control strategies.

Hence, these data are important for hospitals that plan to adopt this technology as adjunct to routine manual disinfection; providing the goal is to eliminate surface bioburden and as a consequence, HAIs, hospitals will need to continue to improve in both hand hygiene and environmental disinfection.

In conclusion, Pulsed-UV technology was effective at reducing overall bacterial counts and significantly more successful than manual disinfection alone on hospital surfaces. Further evaluation focusing on clinically meaningful reduction in HAIs is of paramount importance in justifying the cost and effort in implementing this promising technology in the battle against pernicious hospital infections. Our results underline important critical issues in standard terminal cleaning (combined manual cleaning and chemical disinfection) on high touch surfaces, to adequately remove microbial contamination from the environment.

We have demonstrated that the Pulsed-UVC device, associated with SOP, significantly reduced microorganisms from common high-touch surfaces.

Author Contributions: B.C., G.P.P. and M.L.C. conceived and designed the experiments. B.C., G.P.P., M.L.C, B.T., M.T., A.B. and A.M.S. performed the experiments and wrote the paper and analyzed the data.

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Conflicts of Interest: The authors declare no conflict of interest.

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Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and *Clostridium difficile* (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study

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Summary

Background—Patients admitted to hospital can acquire multidrug-resistant organisms and *Clostridium difficile* from inadequately disinfected environmental surfaces. We determined the effect of three enhanced strategies for terminal room disinfection (disinfection of a room between occupying patients) on acquisition and infection due to meticillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, *C difficile*, and multidrug-resistant *Acinetobacter*.

Methods—We did a pragmatic, cluster-randomised, crossover trial at nine hospitals in the southeastern USA. Rooms from which a patient with infection or colonisation with a target organism was discharged were terminally disinfected with one of four strategies: reference

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See **Online** for appendix

Contributors

DJA did the literature search, prepared the figures, designed the study, collected, analysed, and interpreted data, wrote the Article, and approved the final version. LFC, DJW, RWM, SSL, WAR, and DJS designed the study, collected and interpreted data, revised the Article, and approved the final version. PFT, MB, PB, JCS, LPK, HK, and MGT collected data, revised the Article, and approved the final version. YL analysed and interpreted data, revised the Article, and approved the final version.

Declaration of interests

WAR and DJW have received consulting fees from Clorox. The other authors declare no competing interests.

(quaternary ammonium disinfectant except for *C difficile*, for which bleach was used); UV (quaternary ammonium disinfectant and disinfecting ultraviolet [UV-C] light except for *C difficile*, for which bleach and UV-C were used); bleach; and bleach and UV-C. The next patient admitted to the targeted room was considered exposed. Every strategy was used at each hospital in four consecutive 7-month periods. We randomly assigned the sequence of strategies for each hospital (1:1:1:1). The primary outcomes were the incidence of infection or colonisation with all target organisms among exposed patients and the incidence of *C difficile* infection among exposed patients in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, NCT01579370.

Findings—31 226 patients were exposed; 21 395 (69%) met all inclusion criteria, including 4916 in the reference group, 5178 in the UV group, 5438 in the bleach group, and 5863 in the bleach and UV group. 115 patients had the primary outcome during 22 426 exposure days in the reference group (51·3 per 10 000 exposure days). The incidence of target organisms among exposed patients was significantly lower after adding UV to standard cleaning strategies (n=76; 33·9 cases per 10 000 exposure days; relative risk [RR] 0·70, 95% CI 0·50–0·98; p=0·036). The primary outcome was not statistically lower with bleach (n=101; 41·6 cases per 10 000 exposure days; RR 0·85, 95% CI 0·69–1·04; p=0·116), or bleach and UV (n=131; 45·6 cases per 10 000 exposure days; RR 0·91, 95% CI 0·76–1·09; p=0·303) among exposed patients. Similarly, the incidence of *C difficile* infection among exposed patients was not changed after adding UV to cleaning with bleach (n=38 *vs* 36; 30·4 cases *vs* 31·6 cases per 10 000 exposure days; RR 1·0, 95% CI 0·57–1·75; p=0·997).

Interpretation—A contaminated health-care environment is an important source for acquisition of pathogens; enhanced terminal room disinfection decreases this risk.

Funding—US Centers for Disease Control and Prevention.

Introduction

Multidrug-resistant organisms and *Clostridium difficile* are common causes of health-care-associated infections that lead to adverse patient outcomes.[1] The hospital environment may be an important source for transmission of these organisms. First, hospitals are contaminated with clinically important multidrug-resistant organisms and *C difficile*.[2] Meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and *Acinetobacter* spp can survive on inanimate surfaces for days, and *C difficile* can survive for months.[3] Second, only 50% of surfaces in hospital rooms are sufficiently cleaned between patient stays.[4] As a result, patients admitted to rooms previously occupied by patients with multidrug-resistant organisms and *C difficile* are at an increased risk of subsequent infection or colonisation with these organisms.[5] Finally, the contaminated environment is an important source of health-care personnel hand contamination.[6–8]

Terminal room disinfection (disinfection of a room between occupying patients) can be enhanced by using a chemical disinfectant with sporicidal activity or by use of supplemental disinfection technologies. However, to our knowledge, no multicentre randomised assessment of enhanced terminal room disinfection strategies has been done.[9] We designed the Benefits of Enhanced Terminal Room Disinfection study to assess the effects of four

different strategies for terminal room disinfection on acquisition of multidrug-resistant organisms and *C difficile*.

Methods

Study design and participants

We did this pragmatic, multicentre, cluster-randomised, crossover trial in nine hospitals in the USA from April, 2012, to July, 2014 (appendix). We tested one of four strategies for terminal room disinfection. Three strategies included enhanced terminal disinfection, and one included the standard terminal disinfection.

These four strategies were used in targeted rooms, defined as single-patient rooms from which a patient on contact precautions was discharged or transferred. In the reference group, targeted rooms were disinfected with quaternary ammonium-containing disinfectant for all rooms except those with patients with *C difficile*, in which a hypochlorite-containing disinfectant (bleach) was used. In the UV group, targeted rooms were disinfected with quaternary ammonium-containing disinfectant and a UV-C device except rooms of patients with *C difficile*, in which a bleach-containing disinfectant and UV-C device were used. In the bleach group, a bleach-containing disinfectant was used in all targeted rooms. In the bleach and UV group, a bleach-containing disinfectant and a UV-C device were used for all targeted rooms.

Each strategy was used at every study hospital for four consecutive 7-month study periods. Each study period consisted of a 1-month wash-in period followed by a 6-month period of data collection. The sequence of disinfection strategies was randomly selected for each hospital.

We selected study hospitals to include multiple types of hospitals (tertiary, community, Veterans Affairs) as a convenience sample. All microbiological cultures were considered for inclusion in our outcomes. Cultures may have been representative of infection or colonisation and included surveillance cultures, if obtained by policy at the study hospital. No screening cultures were obtained specifically for the study.

The Duke University Health System Institutional Review Board served as the central institutional review board. We received a waiver of informed consent for this study.

Randomisation and masking

We did resource-dependent randomisation of hospitals, taking into account the number of UV devices available (nine). First, we used a random number generator to determine the order in which hospitals would be randomly assigned a disinfection strategy. Then, we used a random number generator to determine the order in which disinfection strategies were used in each hospital. We continued this process for each hospital but counted the number of machines already assigned for other hospitals in each study period. If all nine UV-C devices were already assigned for a period, subsequent hospitals could not be assigned to one of the UV strategies for that period. Ultimately, all hospitals used all four strategies in a 1:1:1:1 ratio (appendix p 9). Allocation was not masked.

Procedures

All hospitals used gown and glove precautions (ie, contact precautions) for patients known or suspected to harbour multidrug-resistant organisms or *C difficile*. Environmental services personnel were trained on the appropriate use of the disinfectants, cleaning protocols, and UV-C device. The appendix provides information on standardisation of disinfection practices, implementation, and measures of protocol fidelity (appendix pp 1–2).

We did a microbiological analysis of 92 randomly selected seed rooms at two study hospitals to determine the total and average number of colony-forming units of the four target organisms that remained in the hospital room after terminal room disinfection (appendix p 4). Microbiological analyses and identification were done with standard protocols.[10] All hospitals used PCR-based nucleic acid amplification tests to identify *C difficile* throughout the study.

We designed this study to detect infection or colonisation with one of four target organisms: MRSA, VRE, *C difficile*, or multidrug-resistant *Acinetobacter*.[11] A seed room was defined as a room containing a patient with microbiologically proven current or history of infection or colonisation with one or more target organisms. History of infection or colonisation was defined as any positive culture within the 12 months before admission. The next patient admitted to the seed room was an exposed patient. Community-onset was defined as the isolation of a target organism within the first 48 h of hospital admission. Hospital-acquired was defined as the isolation of a target organism after 48 h of hospital admission.

Outcomes

We had two primary outcomes: first, the incidence of all target organisms among patients exposed to seed rooms, and second, the incidence of *C difficile* infection among patients exposed to seed rooms, in the intention-to-treat population. Secondary outcomes were incidence among exposed patients of MRSA, of VRE, and of multidrug-resistant *Acinetobacter*; incidence in the whole hospital of all target organisms, of MRSA, of VRE, of *C difficile*, and of multidrug-resistant *Acinetobacter*; and adverse events (rate of UV-C device failure, time on diversion, emergency room wait time, health-care worker perception of cleaning methods, and room turnover time [time between patient discharge and completion of terminal room disinfection]; appendix pp 4–5). Incidence was calculated as the number of qualifying incident cases per 10 000 exposure days. Exposure days were calculated as the number of days the exposed patient spent in the seed room. Patients excluded from the numerator were also excluded from the denominator. Adverse outcomes were assessed at the hospital-level (ie, all patients or rooms were included in the analyses unless otherwise stated).

Three additional predetermined variables were measured at each study hospital: hand hygiene compliance, room cleaning compliance, and colonisation pressure (appendix pp 10–11).[12] We obtained demographic data and comorbid conditions for all exposed patients through administrative databases to calculate Charlson scores.[13]

We did two post-hoc analyses: (1) of the incidence of target organisms among exposed patients after removing the criteria requiring a minimum of 24 h in the seed room; and (2) of

the incidence of target organisms due to vegetative bacteria (MRSA, VRE, and multidrug-resistant *Acinetobacter*; appendix p 4).

Exposed patients qualified as an incident case of acquisition[14] if they met the following criteria: in a seed room for 24 h or more AND a positive clinical culture or test with one of the target organisms AND the organism identified in the clinical culture or test was the same target organism isolated from the preceding patient in the seed room AND the positive culture or test was obtained during the index admission either during exposure to the seed room OR the positive culture or test was obtained after exposure to the seed room during the index admission or readmission within 90 days of discharge from the room for MRSA, VRE, and multidrug-resistant *Acinetobacter*[15] or within 28 days of discharge from the room for *C difficile*.[16] We excluded incident cases if they were community-onset infections or the exposed patient had a microbiologically proven history of infection or colonisation with the same target organism during the 12 months before admission.

Statistical analysis

We did power calculations based on a review of 4 years of surveillance data from study hospitals and published literature. All power calculations were done with two-sided significance level of 0·05. We projected that 1·96 million patient-days of care would be provided at the nine study hospitals (after excluding the wash-in periods). For each 6-month intervention period, we projected that approximately 491 200 patient-days of care would occur (distributed across nine participating hospitals). Based on data from our pre-existing surveillance databases, we projected that 959 outcomes due to the four target organisms would occur during the baseline (or reference) 6-month period (ie, with standard terminal room disinfection and no use of UV-C), for a baseline incidence of 1·95 per 1000 patient-days. Under these assumptions, the study would have 60% power to detect a 10% decrease in incidence rate, 92% power to detect a 15% decrease, and more than 99% power to detect a 20% decrease. The power analysis was done using simulation and was based on a Poisson regression model with hospital-level incidence rate as the outcome and disinfection strategy and hospital as the covariates.

All qualifying incident cases were included in the intention-to-treat population. The per-protocol population was identical to the intention-to-treat population for the reference strategy and bleach strategy. For the two strategies involving the UV device, the per-protocol population included qualifying incident cases who entered a seed room with documented use of the UV device. For the purposes of this study, the UV device only had to be turned on, the cycle did not have to be completed. The appendix contains a more detailed discussion of the differences between the analysis populations (pp 2–3).

We summarised patient characteristics using percentages for categorical variables and medians for continuous variables. We analysed outcomes using intention-to-treat and per-protocol principles for outcomes among exposed patients. We analysed incidence rates using overdispersed Poisson models with disinfection group (reference, UV, bleach, and bleach and UV), order of the strategies within the study (whether a particular strategy was used in the first, second, third, or fourth study period), and hospital as fixed-effect categorical covariates. We used generalised estimating equations to account for correlation between

different study strategies within the same hospital. Each of the study groups was compared to the reference group except for the analysis of *C difficile* among exposed patients. Because this comparison involved the comparison of bleach *vs* bleach and UV-C, results from the UV group and the bleach and UV group were compared to results from the reference group and the bleach group. We used the same model construction strategy for all outcome analyses. We calculated relative risk (RR), 95% CIs, and risk reductions for each model. Statistical tests were done at a two-sided significance level of 0·05. In light of the pragmatic nature of the trial, we made no adjustments for multiple comparisons. We did all statistical analyses using SAS (version 9.4).

The study is registered on ClinicalTrials.gov (NCT01579370).

Role of the funding source

The funder served an advisory role in the development of the study protocol. All authors had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

All nine hospitals participated in the study from April, 2012, to July, 2014. The appendix shows the randomised assignment for each hospital (p 13). The average cluster size was 7807 (SD 644) patients. 31 226 patients were exposed to a seed room; 24 585 (79%) stayed in the seed room for 24 h or more, and 21 395 (69%) met all inclusion criteria (figure). Baseline characteristics of qualifying exposed patients were similar for all four cleaning strategies (table 1).

A total of 423 outcomes were recorded: 228 (54%) cultures represented infection and 195 (46%) represented colonisation. 115 patients had a primary outcome during 22 426 exposure days during the reference period (51·3 per 10 000 exposure days); the median incidence of target organisms in the baseline period per hospital was 37·1 per 10 000 exposure days (range 17·5–101·6). The addition of a UV-C device to the standard disinfection strategy significantly decreased the incidence of target organisms to 33·9 per 10 000 exposure-days (n=76; RR 0·70, 95% CI 0·50–0·98; p=0·036; table 2; appendix p 14). The incidence of target organisms was lower in eight of the nine study hospitals in the UV group (appendix p 15).

There was no significant difference in the incidence of target organisms from rooms treated with bleach compared with reference (table 2). Similarly, there was no significant difference between use of bleach and UV compared with reference (table 2). The appendix shows outcomes from individual study hospitals by intention to treat for each disinfection strategy (p 7).

The incidence of *C difficile* was not significantly different with or without UV-C devices (table 2). The incidence of MRSA was not significantly lower in the UV group and essentially unchanged in the bleach and bleach and UV groups (table 2). The incidence of VRE was not significantly lower in the UV group but was significantly lower in both groups

that used a bleach-containing disinfectant (table 2). The use of bleach decreased the incidence of VRE by 57% compared to reference; the use of bleach and a UV-C device decreased incidence of VRE by 64% (table 2). Only one patient acquired multidrug-resistant *Acinetobacter* after exposure in a seed room. Thus, no comparisons or models were constructed for this organism.

2848 (55%) of 5178 eligible rooms in the UV group and 3701 (63%) of 5863 eligible of rooms in the bleach and UV group were included in the per-protocol analyses. Effect estimates were generally similar in per-protocol analyses to the intention-to-treat analyses (table 3). The incidence of MRSA, however, was significantly lower in the UV group compared with the reference group (table 3).

Our microbiological assessment of 92 seed rooms after terminal disinfection showed that all enhanced strategies decreased the bioburden of target organisms, but the largest decrease occurred in the UV group (table 4). Protocol compliance, hand hygiene compliance, cleaning compliance, and colonisation pressure were similar across study groups (table 5; appendix p 4).

The median room cleaning time was approximately 4 min longer in the UV and UV and bleach groups (table 5). The total wait time in the emergency department and days on diversion were unchanged across disinfection strategies. Time from admit decision to departure from the emergency department was approximately 10–20 min longer in each of the enhanced disinfection groups compared with the reference group. One hospital reported a single UV-C exposure event during the study (appendix p 5). Additional secondary analyses, including incidence in the whole hospital of all target organisms, of MRSA, of VRE, of *C difficile*, and of multidrug-resistant *Acinetobacter*, and health-care worker perception of cleaning methods, will be presented elsewhere.

We did two post-hoc analyses (appendix p 9). First, removing the 24-h exposure requirement for exposed patients did not change the effect measures. Second, after excluding patients admitted to *C difficile* seed rooms, the decrease in incidence of target vegetative multidrug-resistant organisms was strengthened in the UV group and significantly lower in the bleach and UV group.

Discussion

Our large, prospective, multicentre, cluster-randomised trial is the first, to our knowledge, to demonstrate a decrease in acquisition and infection with epidemiologically important pathogens following the use of enhanced room disinfection strategies. Patients admitted to rooms previously occupied by patients harbouring a multidrug-resistant organism or *C difficile* were 10–30% less likely to acquire the same organism if the room was terminally disinfected using an enhanced strategy. The largest risk reduction occurred when a UV-C device was added to the standard disinfectant strategy. By contrast, we showed no statistically significant decrease in outcomes when we used enhanced terminal disinfection with bleach or bleach and UV. Similarly, the incidence of *C difficile* infection was not different among exposed patients after adding UV to bleach disinfection.

Our results need to be interpreted in the appropriate context. First, decreases in acquisition of target organisms associated with the use of enhanced disinfection strategies were recorded even though our reference group was also an enhanced strategy of sorts. Overall compliance with thoroughness of cleaning in the reference group was roughly 90%. By contrast, most previous studies conclude that approximately half of all hospital room surfaces are not cleaned during terminal cleaning.[4] Improved cleaning compliance decreases environmental bioburden[17] and risk of acquisition, particularly of MRSA and VRE.[18,19] Second, in the reference group, the quaternary ammonium-containing disinfectant was delivered with microfibre cloths, which remove more bacteria than cotton and synthetic fibre cloths.[20] Third, the enhanced nature of the reference group and lack of multidrug-resistant *Acinetobacter* outcomes probably led to a decrease in power. Thus, the absence of a decrease in the incidence of target organisms among exposed patients in the bleach and bleach and UV groups might have been related to type II error.

No randomised controlled trials have previously been done using a UV device or enhanced chemical disinfectant. To our knowledge, only one other randomised controlled trial has investigated an enhanced terminal room disinfection strategy. A hydrogen peroxide vapour system was evaluated over 30 months in six high-risk units in a single tertiary care centre.[21] Patients in intervention units had a 64% decrease in acquisition of multidrug-resistant organisms and *C difficile* and a 75% decrease in acquisition of VRE compared to patients in control units.

UV devices reduce the environmental bioburden of MRSA, VRE, *C difficile*, and *Acinetobacter* spp.[10,22] Of four published studies on the clinical effectiveness of UV devices, one showed a 20% decrease in hospital-acquired multidrug-resistant organisms[23] and three showed 22–53% decreases in *C difficile* infection.[24–26] In light of these results, we were surprised by the lack of change in rates of *C difficile* among exposed patients. This lack of change might have been caused by the following factors. First, the reference group for our *C difficile*-specific outcome involved the use of bleach. As we had high (around 90%) compliance with the use of bleach, there may have been relatively few residual spores for the UV device to eliminate.[17] Second, UV is less effective against *C difficile* than against vegetative bacteria, especially in areas of shadow.[10,22] Third, we used a single-stage cycle with the UV-C device placed adjacent to but outside of the bathroom.[27] Thus, we may not have effectively eliminated *C difficile* from bathrooms. Finally, the environment might not play as large a role in *C difficile* transmission as previously suspected.[28] Eyre and colleagues[29] assessed 1250 cases of symptomatic *C difficile* in Oxfordshire, UK, over a 4-year period using whole genome sequencing and reported that 45% of *C difficile* cases were genetically distinct from previous cases. Although this analysis did not consider asymptomatic colonisation, only 2% of patients with related *C difficile* isolates were linked by possible environmental contamination. Our post-hoc analysis excluding patients exposed to *C difficile* showed that the effect in the UV group was strengthened and the effect in the bleach and UV group became statistically significant.

To our knowledge, no other randomised controlled trials have assessed the effect of using a sporicidal disinfectant on the incidence of our target organisms. Grabsch and colleagues[30] recorded a 67% decrease in acquisition of VRE and an 83% decrease in VRE bacteraemia

with use of bleach. Results from the intention-to-treat analysis in our trial did not show a significant decrease in the incidence of target organisms following the routine use of bleach for terminal disinfection of contact precaution rooms. Results from a prespecified secondary analysis, however, validate the decrease in VRE reported by Grabsch and colleagues. Our clinical results were largely corroborated by our microbiological assessment of seed rooms after terminal disinfection; greater reductions in colony-forming units occurred in the UV group than in the bleach and UV and bleach groups.

Our study has limitations. First, we relied on clinical cultures obtained during the course of standard care, which might have introduced ascertainment bias. Clinicians might have changed their culturing practices during the course of the study. Additionally, because we did not screen seed patients with a history of infection or colonisation or all exposed patients on exit from the seed rooms, we did not capture all acquisitions, might have failed to exclude a patient with community-onset colonisation, and our denominators might have included extra exposure days. We doubt, however, that any of these scenarios affected our results given randomisation. Second, we did not do molecular analyses to confirm that the organisms included in our outcomes were related to organisms in the environment, as this task was impossible given the scope of our study. Third, we did not account for multiplicity in our statistical testing given the pragmatic nature of our study; thus, the p values generated from our analyses should be interpreted with caution. Fourth, as noted above, our study had an enhanced reference group and thus decreased power. As a result, we suspect the effect measures in our study represent minimum effects of these strategies. Finally, our intervention was directed towards three multidrug-resistant organisms and *C difficile*. We suspect that enhanced terminal room disinfection strategies decrease risk of acquisition of non-multidrug-resistant organisms, such as meticillin-susceptible *S aureus* and vancomycin-susceptible enterococci.

Acquisition and infection with multidrug-resistant organisms and *C difficile* in health care is a complex and multifaceted process. Our study suggests that (1) the health-care environment is an important source for acquisition of multidrug-resistant organisms and *C difficile,* and (2) the risk of acquisition of these pathogens from the environment can be modified. More than a century after Semmelweis and Lister's landmark studies, our results suggest that methods to improve disinfection can still lead to better patient outcomes.

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Research in context

Evidence before this study

The hospital environment is contaminated with multidrug-resistant organisms and *Clostridium difficile* and is often disinfected inadequately. As a result, patients who enter contaminated hospital rooms are at increased risk for acquisition and infection from these organisms. Enhanced disinfection strategies may decrease the risk for transmission of such bacteria through the hospital environment, but supportive evidence is limited to single centre or quasi-experimental studies. According to a systematic review by Han and colleagues, no randomised multicentre trials have been done to determine the efficacy of enhanced strategies.

Added value of this study

Our study is, to our knowledge, the first multicentre randomised controlled trial to evaluate the effect of enhanced disinfection strategies on acquisition and infection due to four target organisms (meticillin-resistant *Staphylococcus aureus*, vancomycin-resistant staphylococci, multidrug-resistant *Acinetobacter*, and *C difficile*). Adding a UV-C device to quaternary ammonium disinfection decreased the risk of subsequent acquisition and infection by target organisms. Our study shows the efficacy of enhanced disinfection and confirms that the contaminated hospital environment is a modifiable risk factor.

Implications of all the available evidence

Multidrug-resistant organisms and *C difficile* lead to adverse patient outcomes. Novel and improved prevention strategies are needed. Prevention of the spread of these organisms will probably require a multifaceted approach, including enhanced disinfection, improved hand hygiene, and antimicrobial stewardship.

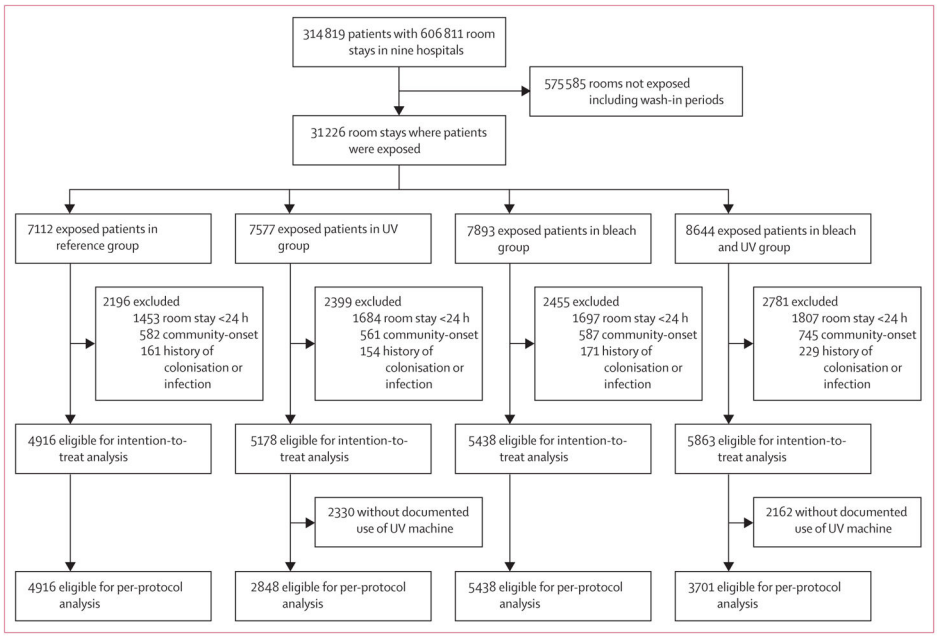

Figure.
Trial profile

Table 1

Baseline characteristics

	Reference (n=4916)	UV group (n=5178)	Bleach group (n=5438)	Bleach and UV group (n=5863)
Demographics *				
Mean age (SD)	57·9 (20·9)	58·5 (21·3)	58·6 (20·7)	57·7 (21·8)
Race				
White	3042 (63%)	3228 (65%)	3416 (64%)	3747 (64%)
African American	1418 (30%)	1411 (28%)	1591 (30%)	1655 (28%)
Other	243 (5%)	233 (5%)	249 (5%)	329 (6%)
Unknown	102 (2%)	97 (2%)	95 (2%)	111 (2%)
Male sex	2475 (51%)	2518 (51%)	2768 (52%)	3017 (52%)
Comorbidities *				
Median Charlson index (IQR)	2 (1–4)	2 (0–4)	2 (1–4)	2 (0–4)
Myocardial infarction	499 (11%)	457 (10%)	475 (9%)	583 (10%)
Congestive heart failure	937 (20%)	950 (20%)	1014 (20%)	1151 (21%)
Cerebrovascular disease	571 (12%)	540 (11%)	582 (11%)	610 (11%)
Hemiplegia or paraplegia	97 (2%)	118 (2%)	139 (3%)	166 (3%)
Peripheral vascular disease	450 (10%)	498 (10%)	524 (10%)	543 (10%)
Dementia	75 (2%)	101 (2%)	138 (3%)	111 (2%)
COPD	1248 (27%)	1325 (28%)	1339 (26%)	1516 (27%)
Rheumatic disease	161 (3%)	181 (4%)	183 (4%)	224 (4%)
Peptic ulcer disease	143 (3%)	97 (2%)	126 (2%)	178 (3%)
Liver disease				
Mild	475 (10%)	452 (9%)	484 (9%)	557 (10%)
Moderate or severe	120 (3%)	142 (3%)	135 (3%)	177 (3%)
Diabetes mellitus	1302 (28%)	1248 (26%)	1371 (27%)	1505 (27%)
Complicated	303 (7%)	273 (6%)	350 (7%)	350 (6%)
Renal disease	980 (21%)	986 (21%)	1083 (21%)	1171 (21%)
Malignancy	842 (18%)	807 (17%)	864 (17%)	961 (17%)
Metastatic solid tumour	305 (7%)	340 (7%)	330 (6%)	367 (7%)
AIDS/HIV	49 (1%)	48 (1%)	52 (1%)	55 (1%)
Arrhythmia	1542 (33%)	1425 (30%)	1513 (30%)	1824 (33%)
Valvular heart disease	420 (9%)	415 (9%)	412 (8%)	566 (10%)
Pulmonary circulation disease	386 (8%)	452 (9%)	439 (9%)	495 (9%)
Hypertension	2264 (49%)	2237 (47%)	2336 (46%)	2709 (48%)
Complicated	826 (18%)	839 (18%)	959 (19%)	1007 (18%)
Other neurological disease	682 (15%)	665 (14%)	671 (13%)	792 (14%)
Hypothyroid disease	523 (11%)	545 (11%)	599 (12%)	637 (11%)

Data are n (%) unless stated otherwise.

*The majority of patient-specific data were not available from one study hospital because of changes in electronic health record systems as follows: age (406 had data missing), race (428 missing), sex (407 missing), comorbidity data (1267 missing).

COPD=chronic obstructive pulmonary disease.

Table 2

Results of intention-to-treat analysis

	Reference	UV group	Bleach group	Bleach and UV group
All target organisms				
Exposed patients	4916	5178	5438	5863
Incident cases (%)	115 (2·3%)	76 (1·5%)	101 (1·9%)	131 (2·2%)
Exposure days	22 426	22 389	24 261	28 757
Rate (per 10 000 exposure-days)	51·3	33·9	41·6	45·6
Risk reduction (95% CI)	Reference	17·4 (5·8 to 28·9)	9·7 (–2·7 to 22·0)	5·7 (–6·2 to 17·7)
RR (95% CI); p value	Reference	0·70 (0·50 to 0·98); 0·036	0·85 (0·69 to 1·04); 0·116	0·91 (0·76 to 1·09); 0·303
Clostridium difficile [*]				
Exposed patients	··	··	2499	2678
Incident cases (%)	··	··	36 (1·4%)	38 (1·4%)
Exposure days	··	··	11 385	12 509
Rate (per 10 000 exposure-days)	··	··	31·6	30·4
Risk reduction (95% CI)	··	··	Reference	1·2 (–12·7 to 15·2)
RR (95% CI); p value	··	··	Reference	1·0 (0·57 to 1·75); 0·997
Meticillin-resistant *Staphylococcus aureus*				
Exposed patients	3300	3451	3631	3848
Incident cases (%)	73 (2·2%)	54 (1·6)	74 (2·0)	89 (2·3)
Exposure days	14 524	14 780	15 343	18 960
Rate (per 10 000 exposure-days)	50·3	36·5	48·2	46·9
Risk reduction (95% CI)	Reference	13·8 (0·1 to 27·3)	2·1 (–13·8 to 17·8)	3·4 (–8·9 to 15·5)
RR (95% CI); p value	Reference	0·78 (0·58 to 1·05); 0·104	1·00 (0·82 to 1·21); 0·967	0·97 (0·78 to 1·22); 0·819
Vancomycin-resistant enterococci				
Exposed patients	1055	1206	1468	1753
Incident cases (%)	37 (3·5%)	17 (1·4%)	24 (1·6%)	37 (2·1%)
Exposure days	5838	5780	7522	9488
Rate (per 10 000 exposure-days)	63·4	29·4	31·9	39·0
Risk reduction (95% CI)	Reference	34·0 (9·3 to 58·6)	31·5 (12·7 to 50·2)	24·4 (0·5 to 48·2)
RR (95% CI); p-value	Reference	0·41 (0·15 to 1·13); 0·084	0·43 (0·19 to 1·00); 0·049	0·36 (0·18 to 0·70); 0·003
Multidrug-resistant *Acinetobacter* [†]				
Exposed patients	31	47	28	62
Incident cases (%)	0	0	1 (3·6)	0
Exposure days	156	199	98	244
Rate (per 10 000 exposure-days)	0	0	102·4	0

RR=relative risk.

[*] Rooms with patients known or suspected of having *C difficile* infection were terminally cleaned with bleach-containing solutions in all study disinfection strategies.

[†] We created no models for multidrug-resistant *Acinetobacter* because only one outcome occurred in the nine study hospitals across all four study groups.

Table 3

Results of per-protocol analysis

	Reference group	UV group	Bleach group	Bleach and UV group
All target organisms				
Exposed patients	4916	2848	5438	3701
Incident cases (%)	115 (2·3%)	46 (1·6%)	101 (1·9%)	93 (2·5%)
Exposure days	22 426	12 299	24 261	17 354
Rate (per 10 000 exposure-days)	51·3	37·4	41·6	53·6
Risk reduction (95% CI)	Reference	13·9 (–0·1 to 27·9)	9·7 (–2·7 to 22·0)	–2·3 (–15·7 to 11·1)
RR (95% CI); p value	Reference	0·69 (0·50 to 0·95); 0·025	0·74 (0·61 to 0·91); 0·004	1·0 (0·81 to 1·23); 1·00
Clostridium difficile *				
Exposed patients	··	··	2499	1712
Incident cases (%)	··	··	36 (1·4%)	30 (1·8%)
Exposure days	··	··	11 385	8015
Rate (per 10 000 exposure-days)	··	··	31·6	37·4
Risk reduction (95% CI)	··	··	Reference	–5·8 (–17·1 to 5·5)
RR (95% CI); p value	··	··	Reference	1·22 (0·68 to 2·17); 0·511
Meticillin-resistant *Staphylococcus aureus*				
Exposed patients	3300	1872	3631	2425
Incident cases (%)	73 (2·2%)	28 (1·5%)	74 (2·0%)	63 (2·6%)
Exposure days	14 525	7934	15 343	10 681
Rate (per 10 000 exposure-days)	50·3	35·3	48·2	59·0
Risk reduction (95% CI)	Reference	15·0 (–0·6 to 30·6)	2·1 (–13·8 to 17·8)	–8·7 (–18·0 to 0·5)
RR (95% CI); p value	Reference	0·67 (0·48 to 0·94); 0·019	0·89 (0·72 to 1·09); 0·260	1·09 (0·85 to 1·39); 0·503
Vancomycin-resistant enterococci				
Exposed patients	1055	659	1468	1134
Incident cases (%)	37 (3·5%)	13 (2·0%)	24 (1·6%)	24 (2·1%)
Exposure days	5838	3265	7522	6237
Rate (per 10 000 exposure-days)	63·4	39·8	31·9	38·5
Risk reduction (95% CI)	Reference	23·6 (–6·1 to 53·2)	31·5 (12·7 to 50·2)	24·9 (–0·6 to 50·4)
RR (95% CI); p value	Reference	0·56 (0·21 to 1·50); 0·248	0·35 (0·16 to 0·78); 0·010	0·41 (0·22 to 0·77); 0·006

Data are unchanged for multidrug-resistant *Acinetobacter baumaunii* (table 2).

* Rooms with patients known or suspected of having *C difficile* infection were terminally cleaned with hypochlorite-containing solutions.

Table 4

Microbiological assessment

	Reference (n=21)		UV group (n=28)		Bleach group (n=23)		Bleach and UV group (n=20)	
	Total CFU	**Mean CFU per room (SD)**	**Total CFU**	**Mean CFU per room (SD)**	**Total CFU**	**Mean CFU per room (SD)**	**Total CFU**	**Mean CFU per room (SD)**
Clostridium difficile	79	3·8 (14·2)	80	2·9 (12·6)	103	4·5 (14·5)	65	3·3 (10·4)
MRSA	179	8·5 (27·1)	3	0·1 (0·6)	101	4·4 (15·0)	17	0·9 (2·5)
VRE	831	39·6 (127·5)	6	0·2 (0·8)	56	2·4 (5·6)	38	1·9 (6·1)
MDR *Acinetobacter* spp	188	9·0 (36·4)	5	0·2 (0·9)	9	0·4 (1·9)	5	0·3 (0·9)
Total target organisms	1277	60·8 (161·3)	94	3·4 (13·4)	269	11·7 (21·4)	125	6·3 (16·1)

MRSA=meticillin-resistant *Staphylococcus aureus*. VRE=vancomycin-resistant enterococci. MDR=multidrug-resistant. CFU=colony-forming units.

Table 5

Hospital outcomes

	Reference	UV group	Bleach group	Bleach and UV group
Hospital-level variables				
Hand hygiene compliance				
Observations	59 519	64 810	64 950	57 650
Median per hospital (IQR)	89·7 (86·3–94·7)	88·1 (84·6–95·7)	91·4 (86·2–96·1)	90·8 (82·8–94·1)
Room cleaning				
Room observations	5717	4312	4538	5869
Mean number of locations monitored per room	12·4	11·6	12·5	12·0
Locations monitored	70 704	50 081	56 753	70 312
Median compliance (IQR)	100% (91–100)	95% (86–100)	100% (87–100)	100% (84–100)
Median colonisation pressure (IQR)	4·6% (3·1–9·7)	4·3% (3·6–6·6)	4·5% (3·7–5·8)	4·8% (3·4–6·7)
Protocol compliance				
pH pen use (%)	4836/5024 (96%)	2970/3262 (91%)	1161/1206 (96%)	5899/6002 (98%)
Median (IQR)	100 (91–100)	93 (89–97)	96 (95–98)	99 (97–99)
UV-C devices used in contact precaution rooms (%)	··	6214/7137 (87%)	··	10 006/11 274 (89%)
Median (IQR)	··	92 (85–93)	··	91 (87–91)
Adverse events				
Room turnover times				
Median total turnover time (IQR)	79·4 (74·4–117·3)	88·9 (80·0–93·4)	82·6 (73·1–123·3)	87·5 (76·2–127·0)
Rooms	78 413	127 028	114 101	102 227
Median room cleaning time (IQR)	35·9 (32·5–38·5)	40·7 (38·4–42·1)	35·6 (32·3–38·9)	40·1 (39·1–44·2)
Rooms	133 744	144 183	132 753	137 814
Emergency department waiting times (min)				
Median total time in emergency department (range; n=7)	392 (290–537)	390 (286–534)	392 (290–533)	399 (294–544)
Observations	34 532	31 961	30 613	32 320
Median time from admit decision to departure from emergency department (range; n=4)	92 (64–135)	110 (72–180)	116 (75–194)	108 (70–184)
Observations	18 443	24 025	21 566	23 732
Time on diversion (days)				
Total	63·8	53·8	34·2	38·2
Median per hospital (IQR)	2·7 (0·3–11·7)	2·5 (1·7–7)	2·9 (0·6–7·5)	1·3 (0·6–6·6)