REVIEW

Systematic review on use, cost and clinical efficacy of automated decontamination devices

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Abstract

Background: More evidence is emerging on the role of surface decontamination for reducing hospital-acquired infection (HAI). Timely and adequate removal of environmental pathogens leads to measurable clinical benefit in both routine and outbreak situations.

Objectives: This systematic review aimed to evaluate published studies describing the effect of automated technologies delivering hydrogen peroxide (H_2O_2) or ultra-violet (UV) light on HAI rates.

Methods: A systematic review was performed using relevant search terms. Databases were scanned from January 2005 to March 2020 for studies reporting clinical outcome after use of automated devices on healthcare surfaces. Information collected included device type, overall findings; hospital and ward data; study location, length and size; antimicrobial consumption; domestic monitoring; and infection control interventions. Study sponsorship and duplicate publications were also noted.

Results: While there are clear benefits from non-touch devices in vitro, we found insufficient objective assessment of patient outcome due to the before-and-after nature of 36 of 43 (84%) studies. Of 43 studies, 20 (47%) used hydrogen peroxide (14 for outbreaks) and 23 (53%) used UV technology (none for outbreaks). The most popular pathogen targeted, either alone or in combination with others, was *Clostridium difficile* (27 of 43 studies: 63%), followed by methicillin-resistant *Staphylococcus aureus* (MRSA) (16 of 43: 37%). Many owed funding and/or personnel to industry sponsorship (28 of 43: 65%) and most were confounded by concurrent infection control, antimicrobial stewardship and/or cleaning audit initiatives. Few contained data on device costs and rarely on comparable costs (1 of 43: 2%). There were expected relationships between the country hosting the study and location of device companies. None mentioned the potential for environmental damage, including effects on microbial survivors.

Conclusion: There were mixed results for patient benefit from this review of automated devices using H_2O_2 or UV for surface decontamination. Most non-outbreak studies lacked an appropriate control group and were potentially compromised by industry sponsorship. Concern over HAI encourages delivery of powerful disinfectants for eliminating pathogens without appreciating toxicity or cost benefit. Routine use of these devices requires justification from standardized and controlled studies to understand how best to manage contaminated healthcare environments.

Keywords: Decontamination, Environment, Hospital-acquired infection, Ultraviolet light, Hydrogen peroxide, Toxicity, Cost

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Introduction

Hospital-based cleaning and disinfection of environmental surfaces is now recognised as a crucial component of infection prevention and control [1]. This has generated interest in a range of automated decontamination technologies over the past decade. So-called 'no-touch'

devices disperse chosen microbiocidal products into the healthcare environment in order to disinfect surfaces and reduce the risk of hospital-acquired infection (HAI) [2]. Given that the agents utilised by these devices are toxic to humans, the mobile equipment designed to deliver them are necessarily controlled through remote access. Chemical products include chlorine dioxide, hydrogen peroxide and ozone in gaseous form; and peracetic acid, quaternary ammonium compounds and hydrogen peroxide as aerosols [1–3]. Another compound, peroxone, combines hydrogen peroxide and ozone to create a dual system with enhanced oxidation [4]. Alternative decontamination technology makes use of ultra-violet (UV) light, which is produced using either mercury or xenon bulbs [1–3]. There are multiple reports describing the in vitro effect of these systems, but studies investigating the clinical impact on hospital patients tend to favour devices dispelling either hydrogen peroxide or UV light. It was decided to review these specific technologies in order to further examine their effects on clinical benefit and cost.

Most UV devices use low-pressure mercury gas bulbs to generate UV-C light with a targeted wavelength of 254 nm; pulsed xenon devices produce a broader spectrum of UV light in short pulses with a target wavelength of 200–315 nm [3]. UV light breaks DNA bonds resulting in death of microorganisms, including spores [5]. Aerosolized hydrogen peroxide systems utilize 3–7% hydrogen peroxide, sometimes with silver ions, with particle sizes ranging from 2 to 12 μm [6]. These particles are released into a room, followed by passive aeration. The vapour system is based on micro-condensation, which allows the vaporization of concentrated (30–35%) hydrogen peroxide under controlled humidity [6].

While there is no doubt over the in vitro capacity of these technologies to eliminate surface pathogens, there are concerns over practicalities of use, toxicity and cost-benefits in vivo [7, 8]. Not all studies report complete removal of specific pathogen reservoirs or, indeed, significant reductions in HAI rates. It is clear that prior removal of dirt is essential before deployment of these devices [9–11]. There is additional concern over the data provided since selective reporting from quasi-experimental studies does not necessarily offer a balanced view of the technology evaluated [12]. Some studies are conflicted by ongoing or newly introduced infection prevention or cleaning interventions during the study period; others report, or fail to report, concurrent or newly introduced antimicrobial stewardship initiatives [13, 14]. Many studies omit mention of environmental monitoring, cleaning efficacy or even baseline cleaning protocols [7, 14]. Furthermore, studies using these devices do not necessarily disclose sources of funding or declare potential conflicts from industry sponsorship, including the provision of training, equipment, report writing and/or personnel [1, 15].
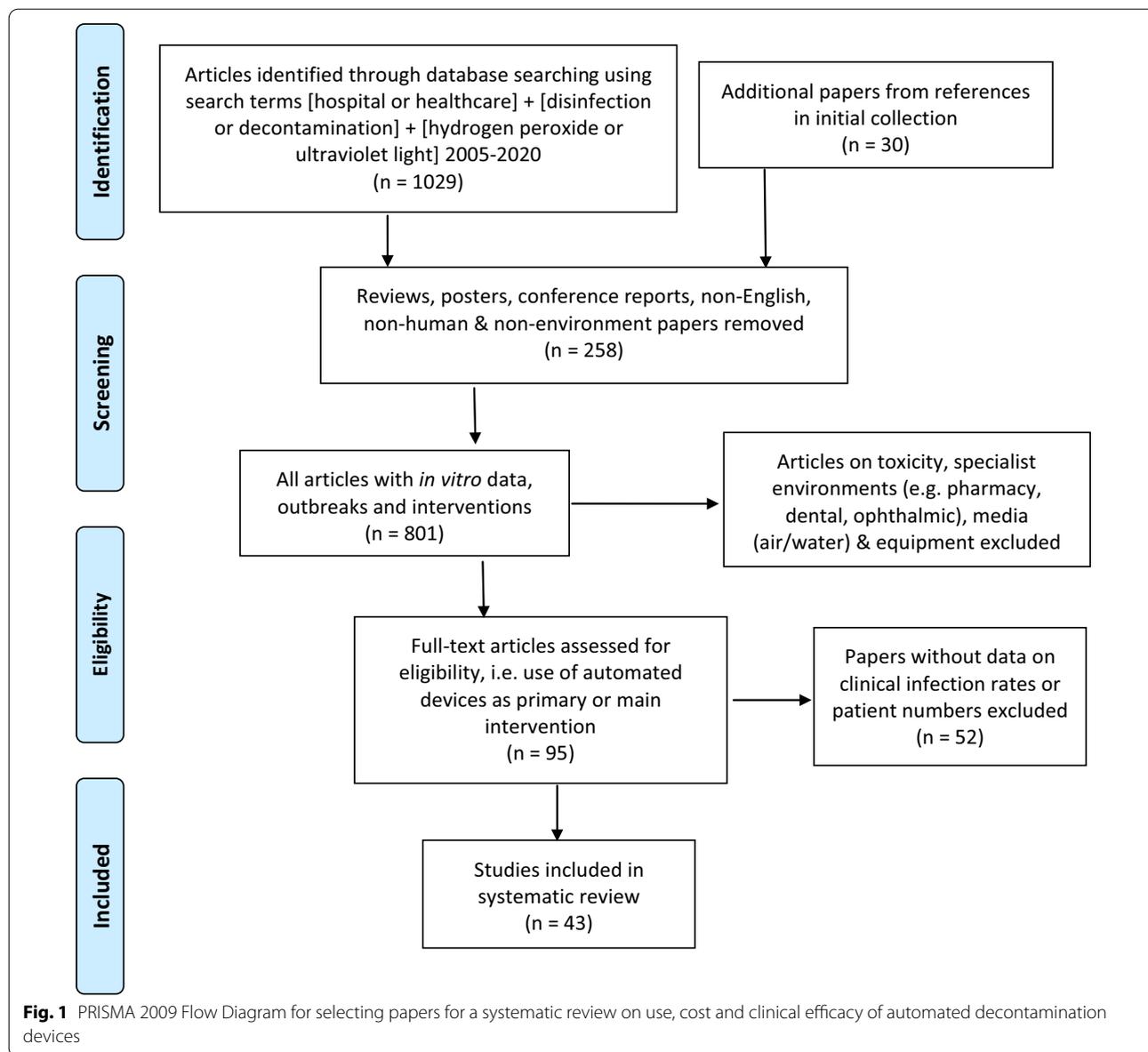
The aim of this systematic review is to critically assess study design, confounders, costs and overall clinical outcome for decontamination devices using hydrogen peroxide or UV light for surfaces in the healthcare environment. Given the recent increase in use of these devices, it is timely to offer objective comments on real life impact for patients and healthcare budgets [7].

Methods
A systematic review was performed using relevant search terms: [hospital or healthcare] + [disinfection or decontamination] + [hydrogen peroxide or ultraviolet light] (Fig. 1). The databases employed were PubMed, CINAHL, CDSR, DARE and EMBASE from Jan 2005 to March 2020 for studies evaluating automated device technology using ultraviolet microbiocidal light (UV) or hydrogen peroxide (H202) in healthcare facilities for contamination on surfaces ± air using indicator pathogens ± aerobic colony counts; cost of technology; and HAI rates for *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), coliforms (*Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Serratia* spp.), *Pseudomonas* spp., *Acinetobacter* spp., and generic multidrug-resistant organisms (MDROs) including extended-spectrum-beta-lactamase producing coliforms (ESBLs). Studies describing in vitro; in situ; experimental and/or surface effects of non-touch technologies without concurrent data on patient impact were scanned before exclusion, along with non-English papers, posters and conference reports (Fig. 1). Hospital location, types, study ward/unit, study length and size, antimicrobial consumption (total; specific classes); domestic monitoring, infection control interventions and other variables that might impact on the results were noted. Specialist healthcare environments such as outpatients, pharmacies and clean rooms were excluded, as were articles describing microbiological impact of automated devices on specific items of equipment. Published data was checked for duplicate or linked publications, funding, sponsors and industry involvement if acknowledged.

Statistical analysis
Statistical review and analysis was applied to common data presented in selected device papers. Risk of bias was assessed for each study by evaluating study design, methodological consistency, infection control confounders, population and study unit heterogeneity, sampling bias, outcome evaluation, involvement of sponsor and selective reporting. Power calculations and overall numbers were examined against reported significance values.

Fig. 1 PRISMA 2009 Flow Diagram for selecting papers for a systematic review on use, cost and clinical efficacy of automated decontamination devices

Results

Study demographics

There were a total of 43 studies presenting the effects on HAI rates from automated devices delivering either hydrogen peroxide or UV light (Table 1; Figs. 1, 2) [16–58]. These were published between 2005 and 2020 and include brief reports and letters describing either intervention or outbreak control studies involving different hospitals from eight countries in the developed world. Of these, 20 (47%) used some form of hydrogen peroxide delivery (14 for outbreaks) and 23 (53%) used UV technology (none for outbreaks). Over half the papers (28; 65%) originated from the USA, with six describing the effects of hydrogen peroxide devices [37, 38, 47, 49, 55, 57] and 22 utilising UV technology (Fig. 3) [16, 18, 21–31, 34–36, 39–41, 43, 48, 50]. Five (12%) studies were based in the UK, all using hydrogen peroxide, [32, 44, 53, 56, 58] and three (7%) others using hydrogen peroxide were performed in France (Fig. 4) [45, 46, 51]. Two (5%) studies each using hydrogen peroxide originated from Spain [19, 33] and The Netherlands, [20, 54] and there was one (2%) study each from Japan (UV) [17], Poland (hydrogen peroxide) [52] and Tasmania (hydrogen peroxide) [42]. There were no studies reporting use of UV in Europe.

Most (36: 84%) were before-and-after studies, including 14 (33%) outbreak interventions [19, 20, 33, 44–46,

Table 1 Data from 43 original or outbreak studies reporting patient benefit from use of UV or H202 automated devices

Reference; Study length; Location	Trial design	Industry sponsored	Hospital type and unit	Concurrent or additional infection control actions	Monitoring Cleaning	Environment sampling	Study pathogens and HAI rates	Data mining	Statistical concerns	Costs included
16. Murphy P et al AmJIC 2020 2 yrs Richmond, Virginia, USA	BA UV No details given on type of device; Possibly Tru D or Clorox?	None reported	BMT unit (21 beds) and oncology unit (28 beds) in 865-bed urban academic hospital	Sporicidal agent introduced during study; meropenem restriction in both units; nurse-focused CLABSI prevention education and improved HH in BMT unit	None reported	No	CD and CLABSI rates decreased significantly in BMT but not in the oncology unit; no effect on rate of respiratory viral infections	Study performed alongside previous study by Fleming et al, AJIC 2018 (ref. 28)	Results confounded by other variables; needed a prospective randomised control design	Not reported
17. Morikane K et al BMC Infect Dis 2020 2 yrs and 6 mths Yamagata University Hospital, Yamagata, Japan	BA UV Pulsed xenon (Xenex) Tokyo, Japan	Statistical analysis and Rodac plates provided by Xenex; Terumo corporation (Xenex outlet in Japan) provided honarium for lead author and technical support	ICU in 629 bed university hospital	Prior bleach cleaning, HH, contact precautions and restricted admission to ICU during UV intervention (?); patient screening for MRSA and MDRAB No mention of antimicrobial consumption	None reported	Rodac plates used to monitor 10 high touch sites after patient discharge; before bleach cleaning; and after UV. Only measured total ACC not MRSA or MDRAB	MRSA & MDRAB MRSA rates decreased by 29% (from 4-2 pts) and MDRAB by 63% (from 14 to 4pts) but small numbers	No	Very small numbers of patients	Not reported
18. Attia F et al AmJIC 2020 18 mths Hershey Medical Centre, Hershey, Pennsylvania, USA	BA UV Pulsed xenon *Presume San Antonio, TX, USA*	None declared	CD patient rooms in six high risk units in 500-bed academic hospital	Prior cleaning with sporicidal disinfectant; A/B and HH mentioned but no data	Fluorescent tagging with immediate feedback	No	CD rate increased from 1.57-1.61/1000 pt days	No	No	Not reported
19. García-Arenzana N et al Microb Drug Resist 2019 5 mths La Paz University hospital, Madrid, Spain	BA aH202 O/B Particle size <10 microns Jose´ Collado S.A., Barcelona Spain	None declared	One medical ward in a 1,300 bed University hospital	HH education and monitoring; compliance improved from 36-85%; Ongoing CRE control plan with screening and pt bathing with chlorhex A/B mentioned but no data	Education for cleaners after O/B confirmed; No monitoring mentioned	CRE	Outbreak of CRE finished	Possibly related to outbreak reported by Robustillo–Rodela et al, AmJIC 2017 (ref. 33)	No	Not reported
20. Frakking F et al JHI 2018 22 mths Utrecht, The Netherlands	BA vH202 O/B Alpheios, Heerlen, The Netherlands	None declared	Three wards including haemato-oncology ward in 800 bed teaching hospital	Stewardship intervention; also isolation and quarantine HH & uniform policy; Patient screening	No	VRE	Outbreak of VRE finished	No	No	Outbreak cost 2 million euros
21. Rutala W et al ICHE 2018 2 yrs and 3 mths 3 study hospitals in central North Carolina, USA	Cluster randomised prospective trial Prior UV *in vitro* study, also in ICHE 2018 Tru D, Memphis, Tennessee	Funding for lead author from Kenall Ltd for prior *in vitro* study; not stated here other than CDC grant. Parent study received contribution from TruD SmartUVC, Ecolab, and Clorox	Randomly selected 92 pt rooms in 3 hospitals, 1 academic and 2 community; data taken from the BETR study	Confounders mentioned; HH compliance recorded in original study	Not stated in this paper but domestic monitoring was done in original Anderson study	CD, VRE, MRSA, MDRAB Used RODAC plates for aerobic and anaerobic pathogens	MRSA, MDRAB, CD and VRE 35% decrease in subsequent patient colonization and/or infection. Quat +UV superior to bleach and bleach +UV	Assumed data from Anderson study (refs. 24 & 30); No mention of strategy for selecting hospital; Rooms were 'randomly' selected	Selective statistical analysis: lack of statistical description with no use of post-hoc test so assume paired tests which are over liberal	Not reported
22. Raggi R et al AmJIC 2018 1 year Providence Holy Cross MC, Mission Hills, California, USA	BA UV Clean Sweep Group, Los Angeles, California, USA	Clean Sweep company supplied two authors, with one for stats analyses; Paper states that the hospital funded the study	377 bed single centre community hospital	No additional HH interventions; No screening so some MDRO patients may have been community acquired; No microbiology data; CD excluded from analyses due to change in lab testing method	None reported	No	Whole hospital incidence of MDRO (MRSA, pyo, VRE, AB, KP) infection and/or colonisation	One author also on Napolitano AmJIC 2015 (ref 39), but two different studies; this author funded by Clean Sweep co. to do stats	Aggregated HAI rates; No control arm; there would have been benefit from split regression modelling	Yes... saved $1.2 million but UV costs not stated or subtracted

51–58]; three (7%) originated from the same cluster randomised prospective study (Benefits of Enhanced Terminal Room Disinfection: BETR study) [21, 24, 30] and the remaining four (9%) were controlled studies, [25, 27, 47] with one interrupted time series that included a control arm [31].

Table 1 (continued)

23. Brite J et al ICHE 2018 20 mths Cancer unit in New York, USA	BA UV Pulsed xenon (Xenex) San Antonio, TX, USA	Funded by author institutions	25 bed BMT unit in 474 bedded tertiary care cancer centre	Patient VRE screening; swabs stored for detection of toxigenic CD; Retrospective therefore some data missing; HH compliance and A/B consumption monitored throughout with no change	ATP measurements after cleaning and before UV	No	CD and VRE rates reported, but UV did **not** reduce rates in this patient cohort	No	Small numbers only	Not reported
24. Anderson D et al Lancet ID 2018 2 yrs and 3 mths Nine hospitals in SE USA: Durham, Chapel Hill, Highpoint, Burlington, Charlotte and Raleigh (all NC), and Chesapeake (VA)	Cluster randomised prospective trial UV UV brand not stated in the paper presume Tru D, Memphis, Tennessee	Consumable and devices supplied (TruD Smart UV, Ecolab, and Clorox); 2 authors received fees from Clorox	Targeted rooms in 9 hospitals in the USA (prespecified secondary analysis of Lancet study, examining whole hospital acquisition of target pathogens)	A/B consumption not measured; pts not screened; HH compliance monitored in original study	Not mentioned in this paper but room cleaning compliance recorded in original study	Not reported in this study	MRSA, VRE, CD, AB acquisition for overall hospital; AB not analysed due to small numbers. No reduction in CD with either bleach or UV but reduction in VRE with combination cleaning but not UV alone	Data from this trial first published in Lancet 2017 (ref 30); plus several other papers (please see text)	None	Not reported
25. Sampathkumar P et al AmJIC 2018 >4 yrs Mayo clinic, Rochester, Minnesota, USA	CT UV Xenex, San Antonio, TX, USA	Xenex donated 2 PX-UV devices	Two haematology & BMT units & medical/ surgical unit in 2059 bed tertiary care hospital; 3 control units	Ongoing bleach cleaning; HH compliance, isolation compliance and A/B consumption; NB. Different patient population mix between study and control units	None reported	No	CD rates reduced by 47%; also noted incidental decrease in VRE rates	No	Standard deviations must be very large compared with the mean to use negative binomial regression; this could swamp results	Mentioned; no data
26. Ethington T et al AmJIC 2018 2 years Kindred Hospital, Louisville, Kentucky, USA	BA Continuous shielded UV units American Green Tech., South Bend, Indiana	24 UV units and one author funded by company VidaShield (American Green Technology)	SCU rooms x16, hallway and biohazard room in long term acute care hospital 123 beds	A/B not mentioned; no infection prevention strategies including HH; Terminal cleaning with vH2O2 as per routine!	No monitoring	ACC collected from air before and after UV installation; Total cfu/m³ decreased by 42%; counts increased in 2 rooms; No isolates identified	Reduced overall HAI rate, CD, MRSA and VRE rates, along with CAUTI & CLABSI; Overall HAI 8.8 per mth vs 3.5 (P< 0.001)	Text similarities with Kane DW et al (ref. 27).	Corrected pre- and post- mean cfu/metre³ values from each area compared; exogenous type HAI added to endogenous HAI; small numbers	Quoted different HAI costs in Introduction but no study specific costs
27. Kane DW et al Can J Infect Control 2018 6 mths Cookeville, Tennessee, USA	CT Continuous UV (Vidashield treats and recirculates air) American Green Tech., Indiana	UV units provided by Vidashield (American Green Technology)	18 pt rooms, 5 shared pt bathrooms, hall, resp therapy room in long term ventilator unit (nursing facility); 17 patient rooms in control arm	HAI assumed as soon as ventilated patient was started on A/B; Hygiene strategies mentioned including HH but no data	None reported	No	Reduced HAI rate by 28%; also assessed HAI caused by MDRAB, MRSA, VRE and CD but not significantly reduced in Vidashield cohort	Identical text in Methods & Discussion in ref 36, Ethington et al; presume writing support from sponsor	Study underpowered	HAI costs quoted but no study specific costs
28. Fleming M et al, AmJIC 2018 25 mths VCU Health System, Richmond, Virginia, USA	BA UV No details given on type of device Possibly Tru D or Clorox.	None reported	CD patient rooms in 865 bed urban academic centre	Terminal bleach clean before UV	No monitoring Feedback on capture rate of UV for CD pt rooms because no impact on pt CD rates	No	CD rates showed no significant decrease over 25 month period (linked paper Bearman et al ICHE 2018 showed increased rates for MRSA and VRE).[1] Paper focussed on improving rate of use with education, audit & feedback	Possible duplication of data used for Murphy P et al, AmJIC 2020 (ref. 16)	None	None reported

There were many different types of hospitals involved in assessing decontamination devices, mostly university and tertiary hospitals with 400–2000 beds; and some district general or community hospitals (100–400 beds) or long term care hospitals (50–170 beds). There were two studies performed exclusively in burns unit [34, 51]; these, along with others, did not indicate the type of host hospital. Other specialist units included intensive care [17, 26, 32, 33, 35, 39, 40, 45, 46, 52, 54]; neonatal [58]; biohazard [26] and treatment rooms [51]; bone marrow transplant [16, 23, 25]; haematology and/or oncology [16, 20, 25, 31]; respiratory therapy room [27]; operating theatres [36, 43, 48]; dialysis unit [43]; stroke rehabilitation [44]; accident and emergency [48]; and three studies

Table 1 (continued)

29. Kovach CR BMC Infect Dis 2017 4 years Milwaukee, Wisconsin, USA	BA Pulsed UV (Xenex) San Antonio, TX, USA	Study funded by the Jewish Home Foundation	160 bed long term care facility	New state empirical A/B stewardship guidance mentioned as confounder; No HH intervention; bleach cleaning before UV	ATP monitoring	Selected hand touch sites screened for ACC and ATP; isolates not identified (Gram stain only)	Overall HAI rates decreased when compared against acute hospital rates (resp, skin/soft tissue & UTI's)	No	All HAI types used for stats; small numbers; Use of parametric statistics	None reported
30. Anderson D et al Lancet 2017 2 yrs and 3 mths Nine hospitals in SE USA: Durham, Chapel Hill, Highpoint, Burlington, Charlotte, Raleigh (all NC) and, Chesapeake (VA)	Cluster randomised prospective trial UV Origin of UV not stated but presumed to be Tru D, Memphis, Tennessee	Consumables and devices supplied (TruD Smart UV, Ecolab, and Clorox); 2 authors received consulting fees from Chlorox	Targeted 'seed' rooms in 9 hospitals in the USA (terminal cleaning only); the BETR study	No pt screening; HH compliance and colonisation pressure recorded; also protocol compliance and turnover time; No A/B consumption data	Room cleaning compliance recorded	CD, VRE, MRSA, MDRAB in 92 randomly selected 'seed' rooms in 2 of 9 hospitals. Data shared with ref. 21: Rutala et al, ICHE 2018?	CD, VRE,MRSA, & MDRAB acquisition among pts in targeted rooms; no difference between bleach and bleach/UV combination for infection or colonisation for target organisms; CD infection rate was unchanged after adding UV to bleach cleaning	Several other papers used data from this study TransFER study done at the same time (ref. 63: Chen et al ICHE 2019); please see text.	Multiple statistical analyses; data for individual pathogens amalgamated to achieve overall significance	None reported
31. Pegues et al ICHE 2017 2 years Philadelphia, Pennsylvania, USA	CT UV Interrupted time-series with comparison on arm; quasi-experimental study with existing multi component CD control program. Clorox Healthcare, California, USA	2 UV devices on loan from Clorox; presume training was given to Estates staff	CD patient rooms prioritised for UV (& VRE +MRSA after) rooms in 3 adult haematology-oncology units in 789 bed tertiary hospital 12 month study	A/B stewardship, pt bathing with chlorhex, isolation, antimicrobial soap, daily and terminal bleach cleaning; Terminal bleach cleaning before UV and curtains replaced Mean monthly broad-spectrum A/B use monitored on study and non-study units; Monitored HH compliance	Used standardised ATP monitoring of 6 high touch sites and visual assessment with check list; Cleaning monitoring with ATP and visual inspection before study	No	CD rate declined 25% on study units and increased 16% on non-study units during intervention compared with baseline period; No effect on rates of other HAI pathogens including MRSA; no data on VRE	No	No data on VRE; MRSA & CLABSI rates unchanged; terminal room cleaning higher during intervention; no differences for environ monitoring or A/B consumption; choice of outcome is selective	Annual costs for first year estimated as $294,342, (personnel & devices) and $194,250 for year 2; total= $488,592; 53 fewer CD cases means cost averted of $348,528 to $1,537,000
32. Yui S et al ICHE 2017 1 year UCLH, London, UK	BA aH2O2 Deprox system Kings Lynn, UK	Funding from institution but device operating staff provided by Hygiene Solutions	Single rooms & ICU in a teaching hospital hosting patients with CD, VRE, norovirus and MDROs	Prior cleaning with peracetic acid based disinfectant; higher concentration used for patients with diarrhoea	Sampling feedback to cleaners every 2 weeks	CD sampled from 16 high touch or difficult to clean sites in 190 room/bays over 1 year; CD isolation rate declined	CD rate **increased** from 37-40% during the study	Previous similar papers;[2, 3] data in this paper from 2013-4	None	None reported
33. Robustillo-Rodela A et al AmJIC 2017 17 mths Madrid, Spain	BA vH2O2 O/B Steris, Mentor, Ohio, USA (Spanish branch in Madrid)	None declared	ICU in 1200 bed university hospital	Chlorine disinfectant before H2O2; increased patient screening; A/B consumption mentioned but no data	None reported	MDR KP and MDRAB	Outbreak of MDRGN (KP oxa-48 and AB); residual patient cases of oxa-48 and environmental contamination found after vH2O2 deployed	O/B of oxa-48 KP at the same time, same hospital & reported in Garcia-Arenzana et al (ref. 19)	Possibly coincidental	High cost mentioned
34. Green C et al Burns 2017 17 mths JBSA-Fort Sam, Houston, Texas, USA	BA Pulsed xenon UV San Antonio, TX, USA	Equipment loaned from Xenex, who also provided training, lab support and sampling, etc.	Burn unit with 16 ICU beds; monitored 9 rooms and 2 operating rooms	Routine prescribing of vancomycin and amikacin, with some use of topical agents; disinfectant-based cleaning including use of bleach	No	MRDO on 5 high touch sites in pt rooms & from passive air sampling decreased after UV	MDRO, device-associated infections and MDRGN monitored but no significant impact; Trend downwards for CD but very small numbers	None	Air and surface data should not be amalgamated; multiple statistical analyses on clinical data	None reported
35. Vianna P et al AmJIC 2016 22 mths Orlando, Florida, USA	BA pulsed xenon UV San Antonio, TX, USA	Three authors employed by Xenex	ICU & CD pt rooms in 126 bed community hospital with 80 bed acute psychiatry unit	Major reduction in quinolones 11 months before UV introduced Main confounders mentioned included HH intervention	None reported	No	Significant CD reduction, non-significant VRE reduction and MRSA **increase** outside ICU; significant decrease of VRE in ICU	Many papers with Xenex funded author	Added HAI rates from ICU to rates from non ICU to gain 'facility-wide' significance	Estimated facility savings on fewer VRE and CD cases was >$730,000 but no study costs

mentioned bathrooms [27] and/or communal areas [26, 27, 41].

Figure 2 shows the year of publication for each study. From 2005 to 2014, most of the studies employed hydrogen peroxide devices (14 of 17: 82%) whereas from 2015 to 2020, the studies predominantly focussed on UV devices (20 of 26: 77%). The total length of the studies, i.e. period of time over which data was

Table 1 (continued)

Study	Technology	Funding	Hospital	Confounders/limitations	Monitoring	Hand touch/cleaning	HAI outcome	Author bias	Notes	Cost
36. Catalanotti A et al AmJIC 2016 2 years Lowell, Massachusetts, USA	BA UV San Antonio, TX, USA	Funded by Xenex; Two authors employed by Xenex	200 bed community hospital with 13 operating theatres	None reported	No	No	SSI reduced only for 'clean' surgery but not for 'clean contaminated', which increased by 23%.	Many papers with Xenex funded author	No	Potential savings of $478,055 and 1 life but no study costs reported
37. McCord J et al JHI 2016 4 years Tupelo, Mississippi, USA	BA vH202 Bioquell, Pennsylvania, USA	Author employed part time by Bioquell	CD pt rooms; no indication as to type or size of hospital	A/B use not monitored but mentioned as a limitation; Bleach used for daily but not terminal cleaning before H2O2; No infection prevention activities detailed during the study	No	No	CD rate reduced from 1.0-0.4 cases per 1000 pat-days from 24 months before vH202 compared with the first 24 months of vH202	No	Used breakpoint time series analysis model that highlighted a seasonal effect; rates from nearby hospitals over the same time period would have been useful	vH202 cost per annum (amount not given) was less than the minimum estimate of HA CDI costs, from 2014 JHI review (68 CDI cases averted over 24 months: $201,960)[4]
38. Horn K & Otter J AmJIC 2015 3 years Flagstaff, N. Arizona, USA	BA vH202 Bioquell, Andover, Hampshire, UK	Author employed by Bioquell	Isolation rooms in whole hospital; ?type of hospital	HH compliance increased with possible major confounding effect; no data on HAI definition	No	No	Overall 47% reduction in MRSA, CD, VRE, ESBL rates; MRSA reduction not significant	No	Small numbers	None reported
39. Napolitano N et al AmJIC 2015 27 mths Culver City, California, USA	BA UV Clean Sweep Group, Los Angeles, California, USA	Clean Sweep Group Inc. Equipment, UV technicians and one author paid for stats analyses	420 bed community hospital; every ICU room and every non-ICU room with pt on contact precautions BUT 125 rooms chosen for HAI analyses	Infection control confounders mentioned, including lack of patient screening; no details on routine cleaning	ATP used for monitoring	Hand touch sites sampled (not the same in different rooms); no detail on counts or specific organisms, just comment that cultures were lower after UV	CD, AB, MRSA, VRE and KP 29-32% lower after UV; Not significant for MRSA and VRE	One author on several similar papers	HAI data aggregated to obtain overall significance Included 'new' colonisations; no wash out period; potential mathematical coupling in the co-variates might confound the results	None reported
40. Nagaraja A et al AmJIC 2015 USA 2 years New York, USA	BA pulsed xenon UV Presume Xenex system, San Antonio, TX, USA	None reported	Academic tertiary hospital with 180 ICU beds CD pt rooms	No A/B data; More sensitive diagnostic tests for CD introduced	Routine monitoring but no details	No	CD rates reduced 22% but borderline significance	Study time and place overlaps with Haas et al, AmJIC 2014: ref 43	Authors acknowledge confounders	None reported
41. Miller R et al AmJIC 2015 39 mths Marietta, Georgia, USA	BA pulsed xenon UV San Antonio, TX, USA	Four authors employed by Xenex	Urban LTC CD rooms and communal areas	Multidisciplinary team on CD control including HH; A/B not mentioned	Check list for terminal cleaning	No	CD patient rates decreased 57% with team and UV	Many papers with Xenex funded author	No	Potential savings of $300,000 (for 29 cases saved) but no specific study costs
42. Mitchell B et al BMJ Open 2014 7 years Launceston, Tasmania, Australia	BA vH202 Nocospray system North Ryde, New South Wales, Australia	Manufacturer gave preliminary training and ongoing supervision	MRSA patient rooms in 300 bed hospital	H2O2 applied as liquid in shared rooms; vH202 monitored with indicator strips; HH compliance and A/B consumption monitored; Additional MRSA screening and MRSA chromogenic agar introduced during the study	Cleaners received documented training and feedback and were supervised; Also external quality control process by manufacturer	MRSA environmental contamination reduced in HP arm compared with rooms cleaned with detergent	MRSA reduction in new patient acquisitions	No	No	Mentioned but no data

gathered, ranged from 18 weeks to 3 years for outbreaks (n = 14), with a median time of 17–18 months and an average duration of 16 months. For intervention studies (n = 29), the total length of time ranged from 6 months to 7 years; the median time was 27 months and the average was 30 months (Table 1).

Effect on HAI rates

All 43 studies presented an assessment of chosen technology on HAI rates, which described the effect on one specific pathogen or a combination; from *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), multi-drug resistant Gram-negative coliforms

Table 1 (continued)

Study	Device	Conflict	Setting	Cleaning/measures	Monitoring	Organisms	Outcomes	O/B	Other	Cost
43. Haas J et al AmJIC 2014; 4 years 4 mths; New York, USA	BA UV Pulsed xenon Xenex system San Antonio, TX, USA	None declared	Patients on contact precautions rooms in 643 bed academic tertiary hospital; also operating theatres, dialysis unit and burn patient rooms	Daily and terminal cleaning with bleach; paediatric rooms were cleaned with quat; introduced ATP and DAZO during study; possible A/B use as confounder	Monitoring cleaning & cleanliness using both DAZO and ATP; used a check list; introduced new environmental services contractor	No	CD, MRSA, VRE, MDRGN showed overall 20% reduction in HAI rates during 22 month study; none achieved individual significance	No	Amalgamated rates of different pathogens to obtain overall significance	None reported
44. Best EL et al J Hosp Infect 2014; 20 mths; Leeds, UK	BA aH202 O/B Deprox system Kings Lynn, UK	Devices supplied by Hygiene Solutions	30 bed Stroke rehab unit in 2000 bed tertiary hospital	A/B review, patient cohorts, HH education and staff training before and during study; Detergent & chlorine deep clean before H202	No monitoring; staff training before the study	CD recovered using Polywipe sponges from high, medium and low placed sites; genotyping using MVLA and STRD	CD patients decreased from 20 to 7 from 10 months before H202 to 10 months after; concluded that H202 might be useful for high incidence of CD	No	Confounding exposures	Briefly mentioned: H2O2 cost £7000 per ward. Is cost benefit sufficient to employ H2O2?
45. Alfandari S et al Med Mal Infect 2014; 27 weeks; Tourcoing, France	BA aH202 O/B No details on type of H202	None declared	16 bed ICU in 400 bed in University hospital	Ongoing screening enhanced; BP cuffs implicated even after H202 exposure; Staff cohorting, HH education, patient isolation and limited carb consumption; External audit of IC actions; Double disinfection of patient rooms	No	MDRAB	Two prolonged O/Bs 4 weeks apart despite H202 & additional infection control activities	No	No	High cost of outbreak mentioned but no data
46. Landelle C et al ICHE 2013; 18 mths; Paris, France	BA v/a H202 O/B Sterinis-Sterusil, Gloster Sante Europe, Toulouse, France for dry-mist H202; Bioquell for vH202, presume Andover, Hampshire, UK, or Marne, France	None declared	860 beds in university hospital with 5 ICUs	ICU patients screened for MDRGN including AB; Unit closure; Cohorting in isolation unit with dedicated staff; HH and contact precautions; chlorhex baths for patients; Twice daily cleaning with disinfectant and terminal clean with H202; Bleach cleaning of sinks; No AB data	None reported	Environmental screening before and after H202 incl. sinks faucets and water splashes; also air sampling for MDRAB	18 month outbreak of MDRAB	O/B recurred several times	No wash out period	None reported
47. Passaretti C et al Clin Infect Dis 2013; 30 mths; John Hopkins, Baltimore, Maryland, USA	Prospective cohort randomised control study vH202 Bioquell system, Horsham, Pennsylvania, USA	Bioquell provided devices and trained personnel; one author employed by Bioquell	Patient rooms in 6 high risk units in 994 bed tertiary care hospital H202 use at beginning of study and then for terminal cleaning for pts with MDROs Mon-Fri	Patients in two of 3 control units were also involved in a trial of chlorhexidine bathing and were excluded from this study; All pts screened for VRE and MRSA; Cleaning with quat; and liquid H202 used for rooms of CD pts	Sampling data fed back to cleaning staff	CD, VRE, MRSA, MDRGN with results fed back to staff Frequency of room contamination decreased from 0.6% to 0% Sampling methods not quantified.	CD, VRE, MRSA, MDRGN Risk of acquiring CD was reduced but not significant (incidence rate of CD down from 2.1 to 0.7/1000 pat days) (P =0.19) Risk not significantly reduced for either MRSA or MDRGN; Reduction in risk of acquiring MDRO attributed to VRE data, which was endemic in this institution	No	Overall statistical significance came from decrease in VRE not MRSA, CD or MDRGN	No costs reported; 28 MDRO transmissions were prevented in 3 high risk units in this hospital over 18 months
48. Levin J et al AmJIC 2013; 4 years; Northampton, Massachusetts, USA	BA pulsed xenon UV Xenex system San Antonio, TX, USA	None reported	140-bed acute care community hospital, CD patient rooms; also operating theatres, A&E, etc	Quinolone consumption reduced before and during intervention; Rooms cleaned with chlorine products	No monitoring during the study; Cleaners received an educational initiative for 2 years before the intervention	No	53% decrease of hospital-acquired CD incidence (from 9.46 to 4.45/10,000 pat-days) (P =0.01)	No	No	Overall costs not supplied; rent for 2 units cost $5000 per month

Table 1 (continued)

49. Manian F et al AmJIC 2013 3 years Mercy Hospital, St Louis, Missouri, USA	BA vH202 Bioquell, Andover, UK	Bioquell employee reviewed manuscript; Bioquell managed devices and technical support (latter not available at weekends)	Selected CD and MDRO rooms in 900 bed community teaching hospital	Tazocin and levofloxacin use increased; carbs clind & cephs decreased; Bleach cleaning as adjunct and done X4 for rooms not receiving H202; Covert monitoring of HH compliance and gown & glove use openly monitored; Contact precautions for CD patients	Induction and weekly educative programme for cleaners including updates on problem areas	None reported	VRE, MRSA, MDRGN, MDRAB pt rooms were afforded H202 treatment but no infection rates either before the intervention or after were reported CD rates reduced from 0.88-0.55 cases/1000 pt days (37%)	Possible data mining from Manian F et al, ICHE 2011,[5] which focussed on MRSA and MDRAB in the same hospital during the same time period	Analysis did not control for bleach cleaning	Stated reasons for not performing a cost benefit analysis
50. Sitzlar et al ICHE 2013 21 mths Cleveland, Ohio, USA	BA Three-tiered decon trial with UV (air & surface equipment?) during 2nd phase TruD, Lumalier, Memphis, Tennessee, USA	UV devices from Lumalier & Tru-D but may have been paid for by scientific grants stated	CD patient rooms in 215 bed hospital and 165 bed LTC facility; 2 UV devices used as cleaning adjunct in 2 medical wards and CD patient rooms	Daily disinfection of high touch sites in CD pt rooms during 3rd phase of the study performed with Chlorox wipes; no detail on antibiotic prescribing.	Used DAZO gel and ATP, supported by educational programme & feedback; checklists for monitored sites; CD patient rooms targeted during first study phase; created dedicated team of cleaners for CD patient rooms; direct observation of cleaning CD pt rooms during third study phase; supervisory sign off by lead housekeeper	CD cultured from high touch sites after terminal cleaning of CD pt rooms, and after UVC Relative to baseline period, the addition of UV device resulted in a statistically significant 48% decrease in the prevalence of CD rooms with positive cultures	Incidence of healthcare-associated CD remained stable at approx. 10 cases per 10,000 pt days during the study until 3rd phase, when the incidence decreased to 6 cases per 10,000 pt days.	Several papers from same authors on CD in 2012-13, eg. Kundrapu et al ICHE 2012;[6] Deshpande et al ICHE 2013[7]	No	None reported
51. Barbut F et al Burns 2013 3 years Paris, France	BA vH202 O/B Bioquell, France	Two authors sponsored by Bioquell	Burns unit 10 beds, operating room and treatment room	Cohorting of infected and non-infected pts and two air disinfection systems; HH initiative and measurement of alcohol gel use	No	MDRAB & MRSA ACC (including fungi) and pathogens reduced on surfaces	MDRAB, ESBL and MRSA infection and colonisation rates reduced by about 89% due to the infection control bundle; no significant decrease in ESBL	No	H202 part of a bundle	None reported
52. Chmielarczyk et al JHI 2012 26 mths Krakow, Poland	BA Dry gas vH202 O/B Steris, Basingstoke, UK	None reported; Assume Steris equipment resourced by institution	2 ICUs (85 beds) in 526 bed teaching hospital	Isolation; staff education; HH programme; all equipment cleaned with hypochlorite; patient screening, etc	No	MDRAB	MDRAB O/B terminated but 2nd O/B eight months later	No	No	None reported
53. Cooper et al JHI 2011 28 mths Southampton, UK	BA H202 O/B Bioquell, Andover, Hampshire, UK	Two authors employed by Bioquell	CD patient rooms in university hospital	Letter states the presence of confounders but no details	No	No	Little change for CD rates on first introduction of H202, but rates increased after H202 removed, then fell again on restarting	No	No	Mentioned but no data
54. Otter et al, AmJIC 2010 6 mths Ede, The Netherlands	BA vH202 O/B Bioquell, Andover, Hampshire, UK	Two authors employed by Bioquell	12 bed ICU In Dutch district general hospital	Extensive cleaning with 2000 ppm bleach and 70% alcohol wipes before deployment of H202; Patient screening for MDRGN after H202.	None reported	Used one sample to swab multiple hand touch sites in each bedspace for MDRAB and EC after cleaning but before H202 (5 of 12 bed spaces still positive); no positive cultures found after H202	15 cases of MDR AB and EC before H202; Patients (n=6) positive for both outbreak organisms from 3-4 months after H202, and reported as indistinguishable using PFGE genotyping	No	No	None reported

(MDRGN), multi-drug resistant Acinetobacter (MDRA), *Pseudomonas aeruginosa*, vancomycin-resistant enterococci (VRE), combined multiply drug resistant organisms (MDROs); or overall HAI rates; or surgical site, catheter and device infection rates (Table 1). The most popular pathogen to control with automated devices, either alone,

Table 1 (continued)

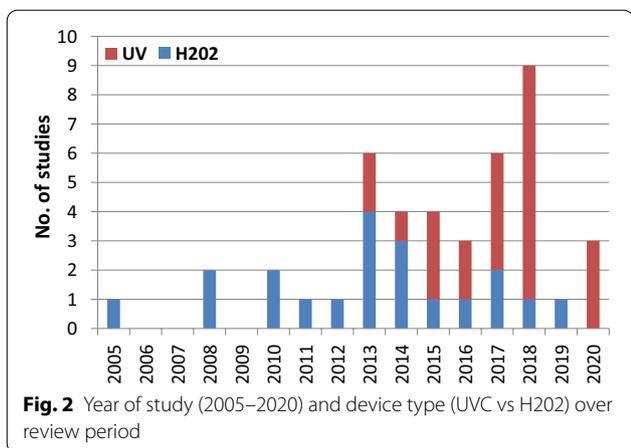|										
55. Ray A et al ICHE 2010 8 mths Cleveland, Ohio, USA	BA Dry gas vH2O2 O/B Vaprosure (Steris) Mentor, Ohio, USA	Two authors funded by Steris; one author on the Steris board	54 beds in 2 wards in a long term acute care hospital	O/B committee implemented IC plan before H2O2, including HH, cleaning & barrier nursing; Patient screening for a prevalence survey; routine screening after treated ward reopened; Ward was closed during H2O2 treatment so reducing opportunities for transmission & confounding effect of H2O2	No formal monitoring Sampling after terminal clean and at different times after H2O2	MDRAB positive in 8 of 93 samples before H2O2; no positive samples found at 1 day and 1 week after H2O2, but isolates were found 2 &3 weeks after H2O2; PCR based genotyping linked clinical and environmental isolates	13 MDRAB cases before H2O2; none after H2O2.	No	No	None reported
56. Dryden M et al, JHI 2008 160 days Winchester, UK	BA vH2O2 O/B Bioquell, Andover, Hampshire, UK	Sponsored by Bioquell at discounted rates; one author employed by Bioquell	28 bed surgical ward in large DGH	Patient admission and discharge screening, staff screening (6 of 52 staff were +ve), patient cohorting and HH programme; Environmental sampling before and after H2O2; MRSA +ve patients & staff decolonised	No	MRSA 28% sites positive for MRSA before H2O2; 1 of 29 swabs positive for MRSA after H2O2	MRSA outbreak terminated following combined H2O2 and infection control interventions	No	No	None reported
57. Boyce et al ICHE 2008 28 mths New Haven, Connecticut, USA	BA vH2O2 O/B Bioquell, Andover, Hampshire, UK	Sponsored by Bioquell One author employed by Bioquell	Five high incidence wards and CD patient rooms in 500 bed university hospital	Reduction in total A/B consumption, including quinolones, cephs and clind; outbreak ended before H2O2 use (see ref 44 Best et al, JHI 2014); Cleaning before H2O2; also HH monitoring and contact precautions	None reported	H2O2 reduced CD surface contamination from 11 of 43 (25.6%) to 0% Isolates typed using PFGE	43% hospital-acquired CD decrease (from 2.3 to 1.3 CD cases/1000 pat days) in five high-incidence wards (P=0.047); less reduction in CD for the whole hospital	No	Possible missing of interaction terms in regression model	Mentioned but no data
58. Bates CJ & Pearse, JHI 2005 18 weeks Sheffield, UK	BA vH2O2 O/B Bioquell, Andover, Hampshire, UK	Bioquell managed decontamination; exact nature of sponsorship not clarified	Neonatal ICU in a Teaching hospital	Neonatal unit and equipment cleaned with detergent sanitizer before H2O2	Not mentioned	*Serratia marcescens* found x2 along with other environment flora including MSSA	Four babies with *Serratia marcescens*; outbreak terminated after cleaning and H2O2	No	No	None reported

◻ Studies using UV

◻ Studies using H2O2

◻ Studies reporting outbreaks

Key: BA, before-and-after; UV, ultraviolet light; H2O2, hydrogen peroxide (v=vapourised; a=aerosolized); pt, patient; BMT, bone marrow transplant; CD, *Clostridium difficile*; CLABSI, central line-associated blood stream infection; ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; MDRAB, multidrug resistant *Acinetobacter baumannii*; ACC, aerobic colony counts; O/B, outbreak; HH, hand hygiene; VRE, vancomycin-resistant enterococci; CRE, carbapenem-resistant enterobacteriaceae; chlorhex, chlorhexidine; A/B, antibiotics; Quat, quaternary ammonium compound; MDR(O), multidrug resistant (organisms); pyo, pseudomonas; AB, *Acinetobacter baumannii*; KP, *Klebsiella pneumoniae*; CT, controlled trial; SCU, special care unit; cfu, colony forming units; HAI, hospital-acquired infection; resp, respiratory; ATP, adenosine triphosphate; UTI, urinary tract infection; MDRGN, multidrug resistant Gram-negative organisms; SSI, surgical site infections; ESBL, extended spectrum beta-lactamase producing coliforms; LTC, long term care; DAZO™, fluorescent gel; A/E, accident and emergency; carbs, carbapenems; clin, clindamycin; cephs, cephalosporins; EC, *Enterobacter cloacae*; PFGE, pulsed field electrophoresis; PCR, polymerase chain reaction; IC, infection control
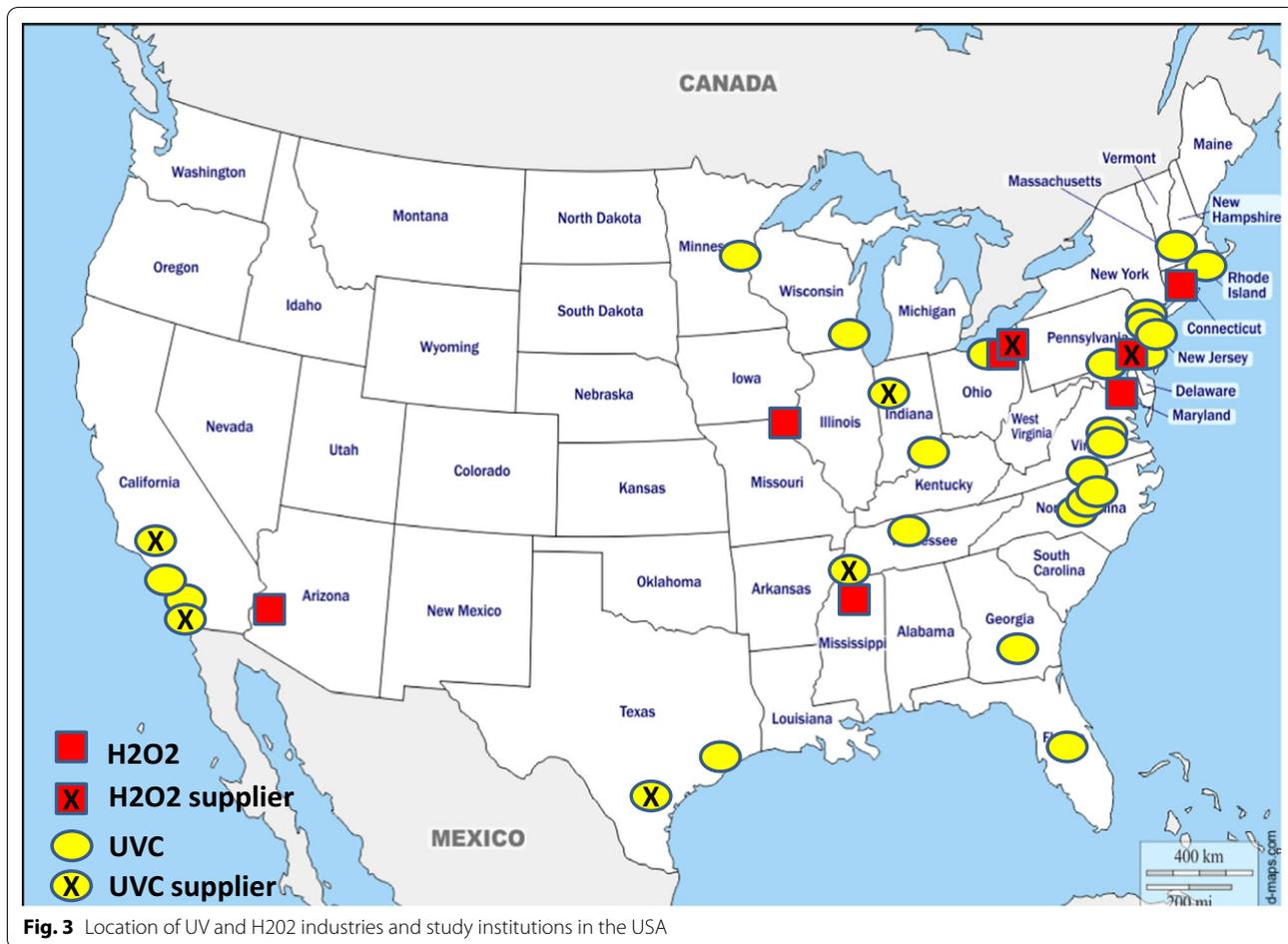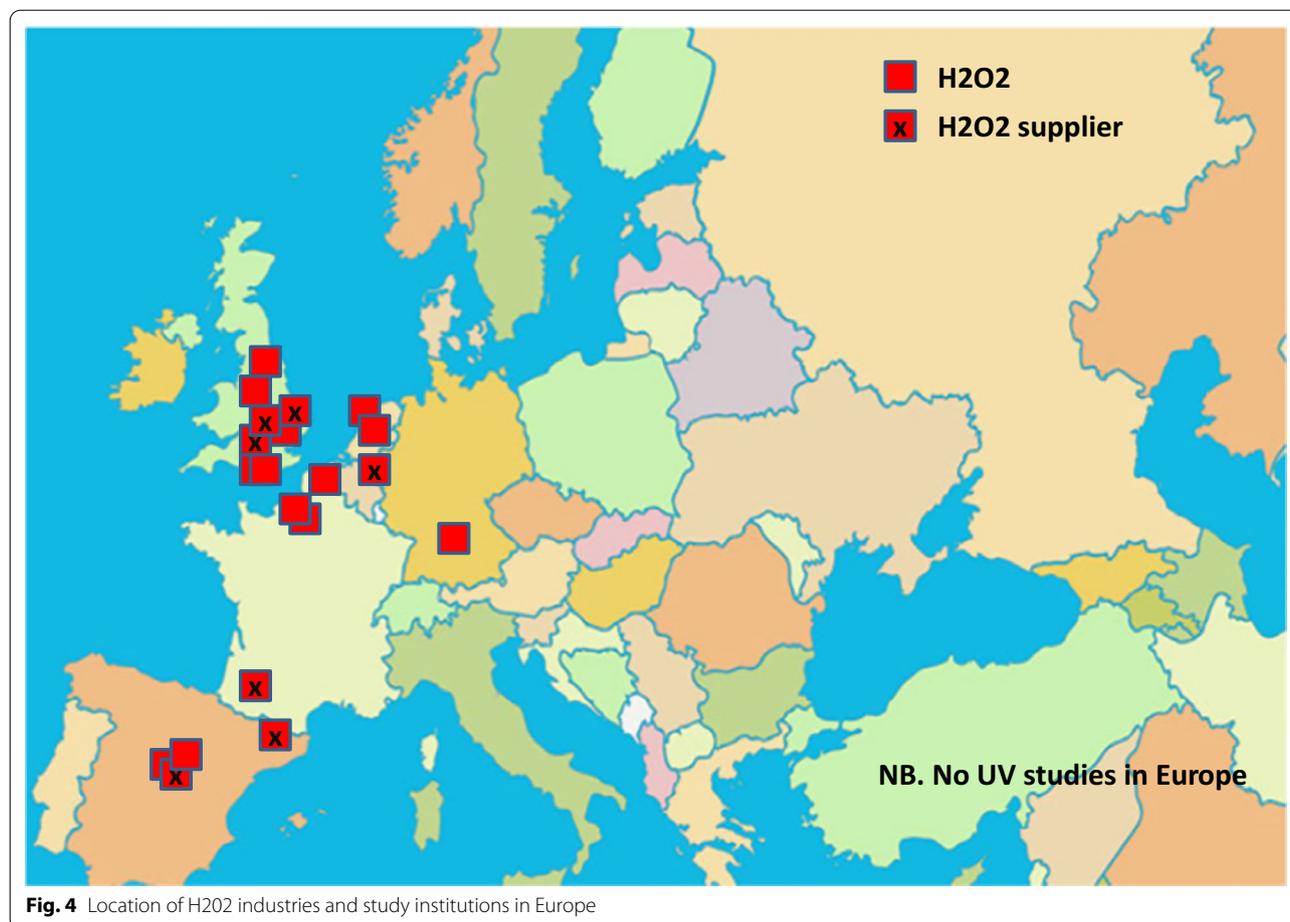
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Fig. 2 Year of study (2005–2020) and device type (UVC vs H2O2) over review period

or in combination with others, was *C. difficile* (27 of 43 studies: 63%), followed by MRSA (16 of 43: 37%); MDRA (15 of 43: 35%); VRE (14 of 43: 33%) and MDRGN (12 of 43: 28%). There were 29 of 43 studies (67%) that also performed before and after sampling of the environment for the same pathogens as monitored for patient infections.

Most studies reported either reductions in HAI rates for the study pathogen(s) or resolution of an outbreak. Some studies reported effects on one or more pathogen rates along with no change or even increases in other pathogen rates. Two studies reported an increase in *C.difficile* rates using UV and H2O2 [18, 32] and another reported static rates for *C. difficile* and VRE following UV use in a bone marrow transplant unit [23]. One analysis of the BETR study (using UV) saw a reduction only in VRE and not in rates of infection due to *C. difficile*, MRSA or Acinetobacter, although the latter numbers were so small, the effect could not be analysed [24]. Other *C. difficile* studies using UV showed no statistically significant decrease over a 25 month period, [28] while at the same time rates decreased for the bone marrow transplant unit in the same hospital; [16] another UV study reported a decline in *C. difficile* but not for other pathogens including MRSA [31]. Mixed results for UV were also found by Vianna et al., with reductions in *C. difficile* and VRE in the study ICU but increasing MRSA and static VRE rates outside the ICU [35]. One study using UV on a burn

Fig. 3 Location of UV and H2O2 industries and study institutions in the USA

Fig. 4 Location of H202 industries and study institutions in Europe

unit found no significant impact on total MDRO, device-associated infections or MDRGNs [34]. One study targeted operating theatres and measured the impact of UV on surgical site infection rates; these decreased for 'clean' but not for 'clean contaminated' surgery, which actually increased by 23% [36]. Several studies saw non-significant effects on MRSA using both H2O2 [38, 47] and UV [39], and another UV study achieved a reduction in *C. difficile* rates only after introducing a supervised cleaning team targeting hand-touch sites with bleach wipes [50]. One protracted outbreak of MDRA reoccurred despite hydrogen peroxide and additional infection control interventions [45] and another recovered the outbreak MDRA from the environment 2–3 weeks after hydrogen peroxide treatment [55].

Common confounders
Infection prevention and control
Controlling an environmental decontamination study is fraught with confounders, often due to concurrent or new initiatives in infection prevention and control introduced before, or during, the study. Some authors recognised the

importance of these confounders and collected additional data in order to regulate possible conflicting effects, e.g. antimicrobial consumption; hand hygiene; and patient screening. These studies usually discussed the potential impact on overall findings. Others mentioned infection control activities implemented before or during the study without providing any detail or discussion on potential impact; this may have been mandated by a bundled approach during an outbreak or lack of space in a brief publication. Some demonstrated obvious conflicts, such as lack of admission screening, antimicrobial prescribing changes, staff education programmes or use of powerful disinfectants before, or during, device deployment. These studies would have been seriously compromised by such initiatives, when such activities are already known to have a major impact of HAI rates. The studies by Raggi et al. [22] and Haas et al. [43], Ethington et al. [26], Kane et al. [27], McCord et al. [37] and Horn and Otter [38] illustrate a range of pitfalls in a decontamination assessment [59]. Conversely, the articles by Pegues et al. [31] and Brite et al. [23] are good examples of studies that attempted to control confounders.

Monitoring cleaning and cleanliness

Cleaning staff are very susceptible to Hawthorne effects when a research study involves sampling general surfaces in the clinical environment [60, 61]. One mechanism for controlling changes in compliance by domestic staff is to introduce some type of monitoring; either by measuring cleaning compliance using fluorescent tagging, or by evaluating cleanliness using ATP detection to assess surface levels of organic soil [7]. Other methods involve direct observation of cleaners; supervisory sign-off; check lists; feed-back; and visual monitoring [2]. The microbiological sampling performed in many studies would have had an effect on cleaning staff because this would have been difficult to blind and would have sent out strong messages regarding cleaning efficiency. If cleaning staff detect interest in the work they do, then they usually 'up the game' in order to alleviate any threat toward their jobs [61]. This would have impacted on overall outcome, environmental sampling data and even HAI rates.

There is little, if any, mention of this predictable psychological reaction in any of the studies in this review. Formal monitoring is, however, mentioned in 16 of 43 (37%) studies, with use of ATP and feedback to cleaning staff as the two most common methods employed (Table 1). One study introduced both ATP and fluorescent gel tagging along with a cleaning check list and new environmental services contractor [43]. Sitzlar et al. used several methods of monitoring in their study; this proved helpful, given that a newly formed cleaning team for CD patient rooms with supervisory sign off achieved the outcome sought after UV failed to eradicate hospital-acquired *C.difficile* [50].

Business and industry involvement

Inevitably, sponsorship issues arise in this review of automated decontamination devices. Environmental cleaning studies are often funded by manufacturers of cleaning agents or disinfection technologies and this encourages potential conflicts of interest and the introduction of real or perceived biases into the evidence base [62]. There are many forms of sponsorship available from business and industry, ranging from full or part study funding; donation or lending of equipment; device discounts; implementation and engineering technicians; scientific support including article writing and statistical analyses; industry personnel with in the research team; study supervision; free education and training; and device maintenance, among others. A total of 28 of 43 (65%) studies reported some form or other of industry support, with at least 20 of 43 (46%) studies including industry personnel in the authorship (Table 1). Among reported declarations, there were three main companies providing support and

authors for 20 of 43 (46%) studies; these were Bioquell [37, 38, 47, 49, 51, 53, 54, 56–58], Xenex [17, 25, 34–36, 41], and Clorox [21, 24, 30, 31].

There is an additional sideways strategy for industry involvement in promoting device evaluation. This comes in the form of sharing authors with specific expertise for independent studies using the same brand of device. These authors are not necessarily employees of the company but may be contracted or asked to provide support such as statistical analysis, writing or laboratory testing. This was evident in studies using UV devices, in particular [22, 26, 27, 35, 36, 39, 41]. Another strategy is so-called 'salami slicing', whereby multiple publications are linked with one original study; this is seen with the BETR study, which generated several papers examining whole or partial datasets using different objectives and/or perspectives for analyses [21, 24, 30, 63–65]. While none of these approaches necessarily challenge long held editorial standards on plagiarism, they could inflict bias from subtle advertising. Multiple papers from one set of data skew any future metanalyses on efficacy and hence generate uncertainty for scientists, clinical staff and policy makers [66]. Furthermore, Figs. 3 and 4 highlight the geographical relationships between the country of publication and home location of industry supplying the technology; this may well be obvious, but could add bias by encouraging similar studies from one or two countries dominating the literature.

Data on costs

Very few of the studies in this review offered tangible data on costs. There was no mention of any resources required or cost savings for 24 of 43 (56%) studies, with 8 (19%) giving brief mention of the importance of cost benefit without specific data [25–27, 33, 42, 45, 53, 57]. Ten (23%) studies offered incomplete costings, mostly based on potential savings from cases averted but lacking a balance against costs of the technology used [20, 22, 35–37, 41, 44, 47–49]. There was just one study (2%) that provided a complete breakdown of costs incurred alongside costs saved from cases of *C.difficile* [31]. It is not possible to compare the costs of an outbreak or HAI against overall costs of devices, maintenance, technical needs and implementation without robust data on expenses; healthcare managers need to know the full range of cost benefits when considering all options for infection prevention.

Statistical aberrations

Comments on statistical findings are shown in Table 1. The most important finding for non-outbreak studies was use of aggregated data that leads to the conclusion that the author wishes to report. This is called Simpson's paradox, where a trend appears to be positive when the

data is aggregated but negative when it is disaggregated (when examining individual groups or data collections). Several studies amalgamated selected outcomes together in order to achieve statistical significance [21, 22, 26, 29, 30, 34, 35, 39, 43, 47]. This clearly skews reporting and future conclusions from metanalyses.

There was also selective reporting, in that some pathogen rates were monitored but no outcome data was offered. Pegues et al. did not provide any VRE data despite using UV devices for VRE patients; Morikane et al. only measured total ACCs and not MRSA or MDRAB from environmental sampling, despite measuring MRSA and MDRAB HAI rates [17, 31].

Several papers presented statistical analysis which were either underpowered [27] or were performed on small numbers of patients [17, 23, 26, 29, 38]; two papers openly acknowledged statistical limitations [24, 40].

Discussion
Design anomalies
Most of the studies in this review relied upon historical controls or comparison between clinical units with different patient population mixes. A before-and-after or one-size-fits-all design are not sufficiently reliable to present robust evidence for interventions aimed at controlling HAI [1, 12]. There were also many confounding practices, some of which were mentioned, or actively controlled and even discussed, but there were probably many more that were ignored and indeed, impossible to predict. The BETR study, in particular, attempted to control several potential confounders but failed to deliver incontrovertible results, which might have encouraged a plethora of linked publications [21, 24, 30, 63–65]. These were, perhaps, an attempt to justify implementation of a complex and no doubt costly sponsored study but despite controls and randomisation, adding UV to routine disinfection had little clinical impact, except possibly for VRE acquisition. An accompanying editorial emphasised the need for multimodal strategies for preventing HAI, particularly antimicrobial stewardship, since enhanced disinfection is only one piece of the puzzle [13]. Universal success in controlling healthcare pathogens with automated decontamination equipment is not necessarily guaranteed.

Another study questioned the lower-than-anticipated effectiveness of UV devices in eradicating *C. difficile* [50]. Since there was only < 50% removal of DAZO fluorescent gel during the mid-part of this study, it was thought that the cleaners had assumed superlative killing from the devices and relaxed their cleaning vigilance. Certainly, these devices are less effective at killing *C. difficile* spores in shaded areas. There was, however, an immediate and dramatic reduction of culture positive rooms during

phase 3 of the study. Declining *C. difficile* from sampled surfaces was attributed not to the UV devices, but to the creation of a 3-person cleaning team, with daily disinfection of high risk sites using bleach, observed monitoring and supervisory sign off by the lead housekeeper [50].

Comparisons between traditional cleaning and use of automated devices
There have been comparisons between traditional cleaning, with or without disinfectants, and decontamination using automated devices. Manual cleaning with bleach has been compared against several different disinfection methods, including H202, for terminal cleaning of hospital rooms contaminated with *C. difficile* spores [67]. Products were ranked according to log10 reductions in colony count from contamination to disinfection. While the most effective products were hydrogen peroxide, bleach (1000 ppm chlorine-releasing agent) and peracetic acid wipes, it was concluded that cheaper traditional methods using bleach were just as effective as modern systems. Comparative studies directly comparing disinfection modalities and cost benefits are limited [3, 67].

At least five studies compared routine terminal disinfection with UV devices [68–72]. Penno et al. described the effectiveness of a UV-C emitter in 22 hospital discharge rooms in a tertiary care academic hospital and compared it against terminal disinfection [72]. Using a cleanliness standard of < 5 cfu/cm^2 for selected hand-touch sites, there were no differences between observed routine disinfection and use of UV-C. Previous studies have shown that non-covert observation of cleaners usually improves housekeeper disinfection [60, 61]. It is likely that carefully constructed standard operating procedures for cleaning staff, along with sufficient time, supervision and monitoring, represents the most cost effective strategy for protecting patients from HAI. Supervisors should tailor job requirements against staffing resources and cleaners should be supported, trained and adequately renumerated [2].

While patient and staff perceptions toward decontamination devices tend to be quite positive, the paucity of evidence for cost–benefit in this review challenges healthcare economists to recommend such technology for routine use [73]. This is not just because the devices are expensive. The equipment can generally only be used after the patient's discharge because patients and staff must vacate the room. However, near-patient sites constitute the highest risk as pathogen reservoirs and these need cleaning every day. [2] For 'long stay' patients, manual cleaning is the only option unless the patients are moved out of their rooms on a daily basis. This means that automated technology for room disinfection can only supplement, not replace, daily cleaning, which

essentially means retention, rather than replacement, of the domestic workforce [74]. Thus, there is little opportunity for managers to off-set labour savings following device purchase, particularly when non-manual devices are unable to dispose of rubbish or deal with visible soil [11].

Collateral damage

There are additional issues to consider for these devices. Despite initial eradication of surface flora in exposed areas, we know that surfaces are rapidly recolonised by environmental organisms within hours, including pathogens [75]. Secondly, the resources required to install, run and maintain these devices are considerable, even for hospitals in developed countries [14]. Low income countries might struggle to afford their use on a regular basis. Thirdly, the decontamination effect is not uniform, given that H202 cannot penetrate linen and soft furnishings and UV misses shaded areas. Neither product delivers expected outcome without first removing surface soil [11, 76].

There are further concerns over the long term impact of these devices, particularly if used on general wards rather than specialist units or when there is less risk of healthcare pathogen transmission. In common with all powerful disinfectants, they damage the environment in ways that we cannot always see. Both H202 and UV are toxic to people, pets and plants. [11] Adverse effects include the formation of high concentrations of hydroxyl and chlorine radicals, which encourage harmful reaction products when exposed to other chemicals found in indoor air [77]. Microbes themselves may survive noxious emissions from UV and H202 devices, which may be linked with emerging tolerance, resistance and cross-resistance among environmental pathogens [78–82]. For example, insufficient H202 would, as with bleach, activate microbial 'SOS' mechanisms, which encourage formation of new, or re-emergence of dormant, survival mechanisms. These facilitate DNA transfer to neighbouring organisms in a veritable shower of plasmid (and other genetic) exchanges coding for resistance to environmental assault [83].

UV light can cause bacterial mutations from a distance [81]. Laboratory trials of UV-A and UV-B exposure highlight the ability of microbial communities to enhance their radiation resistance over time if they are insufficiently exposed [84]. This suggests that resistance to UV-C is highly likely without contained use and surveillance. Microbial communities adapt, reassemble, and persist, and recent theory in microbial ecology suggests that more gentle manipulation of the healthcare surface microbiome may be more sustainable than perpetual attempts at total removal [11, 82].

There is additional suspicion that introducing enhanced use of powerful disinfectants can release viable pathogens enmeshed in hard surface biofilm [85]. These organisms have been previously captured in microscopic crevices and their release reflects or even stimulates re-emergence of a previous outbreak [86, 87]. The biofilm lifestyles of microorganisms present a high risk for horizontal gene transfer, with transmission of antibiotic resistance and future recurrence [88]. Given these findings, routine use of microbiocidal products, including H202 and UV light, should be challenged [89].

Universal standards and regulation

It has already been mentioned that there is no regulation of automated decontamination devices [79]. Chemical disinfectants used in the UK and Europe undergo stringent regulation by the European Chemicals Agency (ECHA) and by the Environmental Protection Agency (EPA) in the USA. Registration of a disinfectant against a given pathogen requires proof of efficacy using standardized test methods. Decontamination devices have not yet been regulated and consequently companies have engineered several different methods to demonstrate efficacy. This is less of a problem for hydrogen peroxide, because it has already been tested as a liquid disinfectant, albeit in different formulations to device-generated aerosol or vapour. UV technologies have not been standardized and this has created concern over in-use variations that have a substantial impact on measuring pathogen reduction, let alone any other effects. Factors such as shadowing; distance from UV source; targeted surface area; carrier orientation; and presence and type of organic material all affect the overall efficacy of UV devices [79, 90]. If these devices become commonplace for universal healthcare, they should undergo standardized testing to receive registration against different pathogens. This would provide consumers with a modicum of assurance that products are effective as well as encourage urgently needed cost–benefit evaluation. This is clearly in the interests of business and industry as well as healthcare.

Conclusion

It was felt timely to independently review all available studies reporting an effect on HAI rates attributed to automated devices dispelling UV or H202. This systematic review is not just an assimilation of the clinical effects from these devices but a critical expose of the methods and pitfalls uncovered in the majority of studies reporting use. Device technologies offer a solution to just one aspect of infection prevention; this is because antimicrobial stewardship, isolation, hand hygiene and screening have already earned their place as useful strategies to control infection and all have been shown to

reduce HAI rates [13, 91]. Doubtless there are yet more activities that can be added. It may be tempting to engage with modern technology when confronting HAI risks from environmental contamination, especially during an outbreak, but the findings in this review cannot support automated devices as a reliable alternative to manual and basic housekeeping practices. Current cleaning advice for occupied bed spaces, 'One wipe; one site; and one direction', with detergent and water, is easy, cheap and effective; and will not upset the surface ecology or create a futuristic 'superbug' [82, 92]. We should continue to support traditional infection control practices, including cleaning, without undue reliance on novel technology at the present time. [18].

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