Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Review

The efficacy of ultraviolet light-emitting technology against coronaviruses: a systematic review

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SUMMARY

The ongoing pandemic of COVID-19 has underlined the importance of adopting effective infection prevention and control (IPC) measures in hospital and community settings. Ultraviolet (UV)-based technologies represent promising IPC tools: their effective application for sanitation has been extensively evaluated in the past but scant, heterogeneous and inconclusive evidence is available on their effect on SARS-CoV-2 transmission. With the aim of pooling the available evidence on the efficacy of UV technologies against coronaviruses, we conducted a systematic review following PRISMA guidelines, searching Medline, Embase and the Cochrane Library, and the main clinical trials' registries (WHO ICTRP, ClinicalTrials.gov, Cochrane and EU Clinical Trial Register). Quantitative data on studies' interventions were summarized in tables, pooled by different coronavirus species and strain, UV source, characteristics of UV light exposure and outcomes. Eighteen papers met our inclusion criteria, published between 1972 and 2020. Six focused on SARS-CoV-2, four on SARS-CoV-1, one on MERS-CoV, three on seasonal coronaviruses, and four on animal coronaviruses. All were experimental studies. Overall, despite wide heterogenicity within included studies, complete inactivation of coronaviruses on surfaces or aerosolized, including SARS-CoV-2, was reported to take a maximum exposure time of 15 min and to need a maximum distance from the UV emitter of up to 1 m. Advances in UV-based technologies in the field of sanitation and their proved high virucidal potential against SARS-CoV-2 support their use for IPC in hospital and community settings and their contribution towards ending the COVID-19 pandemic. National and international guidelines are to be updated and parameters and conditions of use need to be identified to ensure both efficacy and safety of UV technology application for effective infection prevention and control in both healthcare and non-healthcare settings.

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Introduction

Since the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic on 11th March 2020, the global burden of COVID-19 has been massive with over 119 million confirmed cases and over 2.6 million deaths across the world in the first year of pandemic (16th March 2021) [1,2]. In such a context, the adoption of effective infection prevention and control (IPC) measures at the community and healthcare levels is of utmost importance. While SARS-CoV-2 infection is considered to be transmitted mainly via the respiratory route [3,4], direct and indirect contact may also be important [5]. Data indicate that the virus can persist in the environment for up to 72 h on different materials [6–10]. Thus, it is crucial to identify effective microbicidal approaches that can inform the design, use and evaluation of technologies supporting infection control, with a particular focus on healthcare-associated outbreaks [11,12].

The germicidal effect of ultraviolet (UV) radiation and its mechanisms on a broad spectrum of micro-organisms, including viruses, is well known [13–18] and UV germicidal irradiation (UVGI)-based technologies for air [19] and surfaces [20] disinfection might offer great potential in the fight against COVID-19 and its transmission in healthcare settings [21,22]. As evidence from both experimental and observational studies is becoming available on the impact of UV-light-emitting technologies on healthcare-associated infection (HAI) control, including healthcare-acquired *Clostridioides difficile*, vancomycin-resistant enterococci (VRE) and other multi-drug-resistant organisms (MDROs) [23,24], research efforts are now focusing on balancing effective disinfection effects, directly related to light intensity and exposure time, with human safety, according to the specific pathogen [25,26].

Despite lively discussion on the role that UV-based technologies can play in reducing SARS-CoV-2 transmission [27–30], available data on its use and impact are still scant, setting-specific and heterogeneous in terms of study design and assessed outcomes. The aim of the current study was to systematically retrieve, pool and critically appraise all available original data on the effect of UV disinfection technologies on coronaviruses.

Methods

We conducted a systematic review of the available published evidence, as well as a systematic search of the registered, completed, active, and ongoing clinical trials (RCTs); the review's methods were defined in advance following the Prepared Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [31].

Published studies were identified by searching the electronic databases Medline, Embase and the Cochrane Library. The search strategy was built using a combination of keywords and MeSH terms for the two main axes of the research question: (1) UV technologies; and (2) coronaviruses. We built our search strategy with terms related to UV light ("UV", "UVC", "ultraviolet", "ultra violet", "ultra-violet", "ultraviolet rays") and terms related to coronaviruses ("coronavirus", "SARS", "MERS", "COVID", "nCoV", "COV"). It was first developed for Medline and then adapted for use in the other two databases (all three search strategies are available in the Supplementary material). Besides, further studies were retrieved from the reference listing of relevant articles and consultation with experts in the field. Registered clinical trials were identified searching the clinical trials' registries and platforms: the WHO International Clinical Trials Registry Platform (ICTRP), the ClinicalTrials.gov registry, the Cochrane Central Register of Controlled Trials and the EU Clinical Trial Register.

We included all studies that quantitatively assessed the effect of UV-based technologies on coronaviruses, alone or compared with other methods of disinfection (i.e. chemical disinfectants, inactivating agents, detergents) [32]. We applied the following inclusion criteria: (1) studies' intervention must include UV-based technologies; (2) interventions' efficacy and effectiveness must be tested on coronaviruses; (3) the coronaviruses contamination must be of the environment, in particular air and surfaces; (4) the primary outcomes of interest were inactivation rate and viral titre reduction, of which all measures were considered. We limited our review to original articles (observational and experimental studies) written in English up to 22nd November 2020. Identified studies were independently reviewed for eligibility by three authors in a two-step-based process; a first screening was performed based on titles and abstracts, while full texts were retrieved for the second screening. At both stages, disagreements between reviewers were resolved by consensus and by consultation with senior authors. Data were extracted by two authors supervised by a third author, using a standardized data-extraction spreadsheet. The data-extraction spreadsheet was piloted on two randomly selected papers and modified accordingly.

Quantitative data on studies' intervention and comparators were summarized in structured tables, pooled by different coronavirus species and strain, the cell line used for viral culture sample preparation, UV source, characteristics of UV light exposure (i.e. irradiance or intensity, distance, exposure time) and outcomes. Studies' findings were pooled by pathogens. RCTs' protocols for data extraction included Trial's title, ClinicalTrials.gov identifier, EudraCT number, sponsor, sponsor protocol number, start date, current status and available preliminary data.

Results

We identified 989 records by searching the selected databases and listing references of relevant articles. After removing duplicates, 744 records were left. These papers were screened, leaving 18 papers meeting our a priori defined inclusion criteria (Figure 1).

A clinical trials registries search retrieved eight potentially relevant records, none of which met the review's inclusion criteria (PRISMA flowchart available in the Supplementary material).

Characteristics of included studies

Characteristics of the included studies are reported in Table I. Most of the studies ($N = 8$) were conducted in the USA [33–40], one of which also conducted in Korea [40], four in Japan [41–44], two in Italy [45,46], and one each in China [47], Israel [48], Germany [49] and Brazil [50]. They were published between 1972 and 2020, with three published before 2000

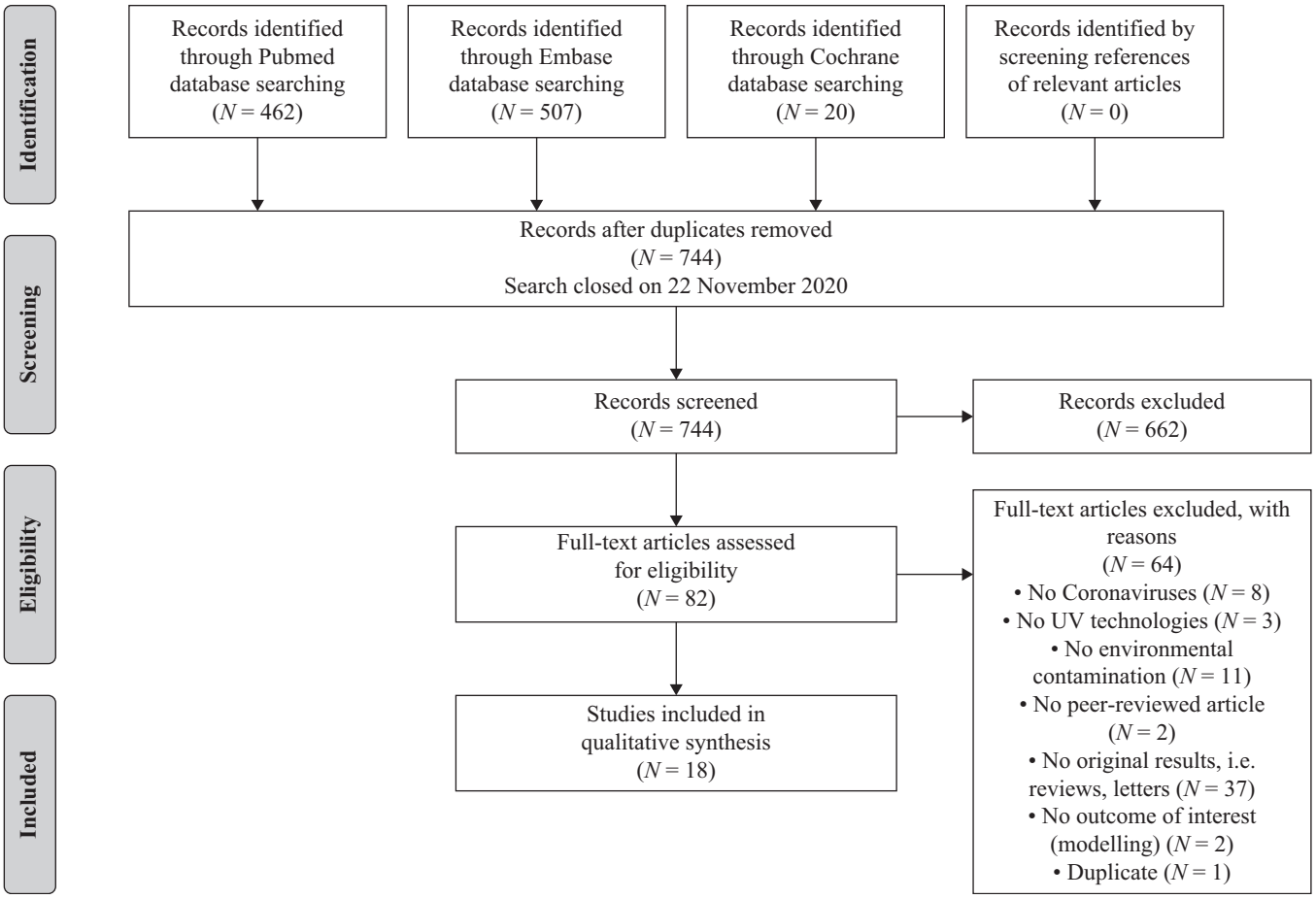

Figure 1. PRISMA flow diagram of published studies.

[34,37,44] and eight published in 2020 [35,38,39,41,43,48–50]. All were experimental studies, conducted in laboratory settings: four focused on SARS-CoV-1 [36,42,45,47], one study on MERS-CoV [33], three on seasonal human coronaviruses [34,35,48] and six on SARS-CoV-2 [38,39,41,43,49,50]. Four studies focused on animal coronaviruses: three were on murine hepatitis virus (MHV) [33,40,44], two on canine coronavirus (CCV) [44,46] and one on transmissible swine gastroenteritis virus (TGEV) [37].

Most of the included studies ($N = 14$) tested the efficacy of UV light on a liquid viral stock [34,36–38,41–50], two on aerosolized virus [35,40], one on dried MHV and MERS-CoV in droplets [33], and one on dried SARS-CoV-2 [39]. Details on viral sample preparation are available in the Supplementary material.

Seven of the included studies compared UV-based technologies with other disinfection methods [34,36,42,44–47]. In detail, among chemical disinfectants, UV radiation was compared with sodium hypochlorite [44,45], sodium chlorite [44], ethanol [44,45], methanol [42], benzalkonium chloride [44,45], chlorhexidine [45], 2-benzyl-chlorophenol [45], peracetic acid [45], formaldehyde [36,42,44,46], paraformaldehyde [42], glutaraldehyde [36,42,46], iodopovidone [42], acetone [42], isopropanol [44], iodophors [44], cresol soap [44], pH variations [36,46]; among physical inactivating agents UV radiation was compared with heat inactivation [34,36,42,44,46,47] and gamma ray inactivation [36].

In four studies, UV-based technology's effect on coronaviruses was compared with that observed on other viruses, including influenza virus [34], Kilham rat virus [44], canine parvovirus [44], bacteriophage MS2 [40] and adenovirus serotype 2 [40].

Table II shows the UV technology, manufacturer, technical details (i.e. UV wavelength or spectrum, power, irradiance, intensity or dose) and other characteristics described in included studies. Bedell *et al.* [33] provided an accurate description of the UV technology employed in the study, which is an automated triple UVC emitter, for whole-room disinfection. This technology was able to calculate the time needed for a cycle of disinfection while rotating 360°, utilizing a laser to identify the size of the area to be disinfected and the presence of objects in the near field. Simmons *et al.* [39] tested the efficacy of a pulsed-xenon UV-robot. Walker *et al.* [40] described the design of an experimental chamber containing six 36-W UV emitters. Ratnesar-Shumate *et al.* [38] tested UVB and UVA efficacy using a solar simulator with a xenon arc lamp and optical filtres. Buonanno *et al.* [35] also provides an accurate description of the irradiation chamber used to test efficacy of far-UVC light at 222 nm on aerosolized virus. Far-UVC light at 222 nm was used also by Kitagawa *et al.* [43] with a krypton-chloride excimer lamp module. Darnell *et al.* [36] and Heilingloh *et al.* [49] employed both UVA and UVC sources to compare their efficacy. Three studies [34,46,47] specified that they employed a UVC or germicidal lamp and, in

Table I
Characteristics of included studies

First author	Year	Country	Study design	Target coronavirus	Medium	Study setting	Comparison
Ansaldi *et al.* [45]	2004	Italy	Experimental	SARS-CoV-1	Liquid suspension	Laboratory	UV, sodium hypochlorite, ethanol, benzalkonium-chloride, chlorhexidine digluconate, 2-benzil-chlorophenol, peracetic acid, on SARS-CoV-1, influenza A and RSV
Bedell *et al.* [33]	2016	USA	Experimental	MHV-A59 and MERS-CoV	Dried MHV-A59 MERS-COV in droplets	Laboratory	UV exposed vs not exposed MHV-A59; vs UV exposed MERS-CoV
Bucknall *et al.* [34]	1972	USA	Experimental	HCoV-229E and HCoV-OC43	Liquid suspension	Laboratory	UV irradiation and thermal inactivation of OC43 coronavirus, 229E coronavirus and influenza virus
Buonanno *et al.* [35]	2020	USA	Experimental	HCoV-229E and HCoV-OC43	Aerosolized	Laboratory	No comparison
Darnell *et al.* [36]	2004	USA	Experimental	SARS-CoV-1 (Urbani strain)	Liquid suspension	Laboratory	UVA and UVC irradiation vs gamma irradiation, heat treatment, formaldehyde, glutaraldehyde, pH treatment
Duan *et al.* [47]	2003	China	Experimental	SARS-CoV-1 (CoV-P9 strain)	Liquid suspension	Laboratory	Resistance to UV irradiation and heating, persistence in the environment on different materials
Gerchman *et al.* [48]	2020	Israel	Experimental	HCoV-OC43	Liquid suspension	Laboratory	No comparison
Heilingloh *et al.* [49]	2020	Germany	Experimental	SARS-CoV-2	Liquid suspension	Laboratory	No comparison
Inagaki *et al.* [41]	2020	Japan	Experimental	SARS-CoV-2	Liquid suspension	Laboratory	No comparison
Kariwa *et al.* [42]	2006	Japan	Experimental	SARS-CoV-1 (Hanoi strain)	Liquid suspension	Laboratory	UV irradiation vs povidone-iodine products, chemical reagents (acetone, methanol, paraformaldehyde, glutaraldehyde), heat inactivation
Kitagawa *et al.* [43]	2020	Japan	Experimental	SARS-CoV-2	Liquid suspension	Laboratory	No comparison
Morilla *et al.* [37]	1977	USA	Experimental	TGE virus (Illinois strain and M-HP strain or cell-culture adapted strain)	Liquid suspension	Laboratory	UV irradiated Illinois field virus and M-HP tissue culture virus
Pratelli *et al.* [46]	2008	Italy	Experimental	CCV (strain S378)	Liquid suspension	Laboratory	UV irradiation vs heat, pH, formaldehyde and glutaraldehyde of CCV, vs not irradiated CCV
Ratnesar-Shumate *et al.* [38]	2020	USA	Experimental	SARS-CoV-2 (USA-WA1/2020)	Liquid suspension	Laboratory	No comparison
Sabino *et al.* [50]	2020	Brazil	Experimental	SARS-CoV-2	Liquid suspension	Laboratory	No comparison

Saknimit *et al.* [44]	1988	Japan	Experimental	MHV (MHV-2 and MHV-N) and CCV	Liquid suspension	Laboratory	UV irradiation vs ethanol, isopropanol, benzalkonium chloride, iodophor, sodium hypochlorite, sodium chlorite, cresol soap and formaldehyde and by heating at 60°C for 15 min, on MHV, CCV, KRV, CPV
Simmons *et al.* [39]	2020	USA	Experimental	SARS-CoV-2	Dried	Laboratory	No comparison
Walker *et al.* [40]	2007	USA and Korea	Experimental	MHV	Aerosol	Laboratory	UV irradiation of MHV, Bacteriophages MS2 and Adenovirus serotype 2

CCV, canine coronavirus; CPV, canine parvovirus; HCoV, human coronavirus; KRV, Kilham rat virus; MERS-CoV, Middle East respiratory syndrome-related coronavirus; MHV, murine hepatitis virus; RSV, respiratory syncytial virus; SARS-CoV-1, severe acute respiratory syndrome coronavirus 1; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TGE, transmissible gastroenteritis of swine coronavirus; UV, ultraviolet.

particular, Bucknall [34] tested a 60-W germicidal lamp and Pratelli a 27.1-μW/cm^2 UVC lamp [46]. Inagaki *et al.* [41] used a deep-UV light-emitting diode (LED). Gerchman *et al.* [48] employed a UV-LED system emitting four UV spectra at 267, 279, 286 and 297 nm, respectively. Morilla *et al.* [37] and Saknimit *et al.* [44] only provided the power of the source utilized (8 W and 15 W, respectively), as Sabino *et al.* [50] specified the use of a mercury UVC lamp at 254 nm with a 2.2-mW/cm^2 irradiance. Two studies [42,45] did not provide any technical details on the UV source employed.

Tables III–V also include the outcomes on which viral inactivation was assessed. The effect on the different viruses was studied using different outcome measures, including modification of the observed cytopathic effect (CPE) ($N = 6$) [34–36,41,45,47], 50% tissue culture infectious dose ($TCID_{50}$) determination ($N = 8$) [34–36,38,42,43,46,49], plaque assay ($N = 4$) [33,37,39,40,44], lethal dose ($N = 1$) [50], molecular assays ($N = 3$) [43,45,48].

Results of included studies

SARS-CoV-2

Efficacy of UV-based technologies. Results from included studies assessing the efficacy of UV-based technologies against SARS-CoV-2 are reported in Table III.

Five of six studies tested the UV efficacy on viral stock prepared in liquid suspension, at a distance between the UV emitters and the viral samples of less than 30 cm; one study tested the UV efficacy on dried virus and at 1-m distance.

In particular, Heilingloh *et al.* [49] exposed the viral stock to both UVC and UVA sources and UVA only. At a distance of 3 cm and UV irradiance of 1,940 μW/cm^2 (UVC) and 540 μW/cm^2 (UVA), the SARS-CoV-2 sample was inactivated entirely after 9 min. In contrast, after the same time exposure, UVA irradiation only did not determine complete viral inactivation.

Inagaki *et al.* [41] used a deep UV LED instrument to irradiate the viral stock at 2 cm distance with an intensity of 3.75 mW/cm^2, achieving an infection titre reduction ratio >99.9% after 10 s.

Moreover, Ratnesar-Shumate *et al.* [38] simulated UV solar spectrum (UVA and UVB) in order to evaluate solar light efficacy in inactivating SARS-CoV-2 suspended both in simulated saliva and growth medium. With 1.6 W/m^2 UVB intensity, a 90% viral inactivation was obtained at 6.8 min in simulated saliva, while in the growth medium, the same results were performed in 14.3 min. Distance was not reported.

Sabino *et al.* [50] obtained a 99.999% inactivation of SARS-CoV-2 in liquid suspension with a mercury UVC lamp (254 nm) with 2.2 mW/cm^2 at 30 cm of distance with 49.42 s of exposure.

Kitagawa *et al.* [43] investigated the titre of SARS-CoV-2 after UV irradiation (0.1 mW/cm^2) at 222 nm by krypton-chloride excimer lamp. Thirty seconds of irradiation resulted in 99.7% reduction of viable SARS-CoV-2. Conversely, under the same conditions after 300 s the viral RNA was still detectable by real-time quantitative polymerase chain reaction (RTq-PCR).

Lastly, Simmons *et al.* [39] employed a pulsed-xenon UVC robot to test the UV efficacy on dried viral stocks and at a distance of 1 m; under these specific conditions, the viral titres were reduced by >99.99% to an undetectable level, after both 2 and 5 min.

Table II
Ultraviolet technologies applied in included studies

Reference	UV technology	Manufacturer	UV spectrum, wavelength (nm)	Power (W)	Intensity (Irradiance) (μW/cm^2)	Other UV technology characteristics
Ansaldi *et al.* [45]	Not reported	Not reported	Not reported	Not reported	40,000 (measured at the distance between the virus samples and the UV source)	Not reported
Bedell *et al.* [33]	Automated triple emitter whole-room UVC disinfection system	Surfacide, Naperville, IL, USA	UVC	Not reported	Not reported	n. UV emitters = 3 Emitters diameter = 59 cm Emitters height = 195 cm Rotating system (360°) Integrated disinfection time cycle calculator (LASER)
Bucknall *et al.* [34]	Germicidal UV lamp tube	Not reported	Not reported	60	Not reported	n. UV emitter = 1
Buonanno *et al.* [35]	Far UVC source	USHIO America, Cypress, CA, USA	UVC, 222	12	90–100	222-nm KrCl excimer lamp module
Darnell *et al.* [36]	UVA and UVC sources	Spectronics Corporation, Westbury, NY, USA	UVC, 254 UVA, 365	Not reported	UVC 4,016 UVA 2,133 (measured at 3 cm, which is the distance between the virus samples and the UV source)	Not reported
Duan *et al.* [47]	UVC source	Not reported	UVC, 260	Not reported	>90 (measured at the distance between the virus samples and the UV source)	Not reported
Gerchman *et al.* [48]	UV LED system emitting four UV spectra	AquiSense Technologies, Charlotte, NC, USA	UV, 267, 279, 286, 297	Not reported	267 nm: 12; 279 and 286 nm: 25; 297 nm: 32	A circular UV LEDs system emitting at 267 and 297 nm and a custom-made rectangular UV LEDs system emitting 279 and 286 nm
Heilingloh *et al.* [49]	UVA and UVC sources (UV-4 S/L)	Herolab, Wiesloch, Germany	UVA, UVC	Not reported	UVC 1,940 UVA 540	Not reported
Inagaki *et al.* [41]	Deep UV LED device	Nikkiso Co., Tokyo, Japan	UVC, 280	Not reported	3,750 (at 20 cm)	narrow-range wavelength (280 nm ±5)
Kariwa *et al.* [42]	Not reported	Not reported	Not reported	Not reported	134 (measured at the distance between the virus samples and the UV source)	Not reported
Kitagawa *et al.* [43]	Krypton-chloride excimer lamp module (Care222)	Ushio Inc., Tokyo, Japan	222-nm UV light	Not reported	0.1 mW/cm^2	Not reported
Morilla *et al.* [37]	UV lamp	Not reported	Not reported	8	Not reported	Not reported
Pratelli *et al.* [46]	UVC lamp	Bio air instrument	UVC	Not reported	27.1 (measured at 1 m, which is not the distance between the virus samples and the UV source)	Not reported

Ratnesar-Shumate *et al.* [38]	Solar simulator with a xenon arc lamp and optical filters	Sciencetech	UVB and UVA (range 280—400 nm)	Not reported	1.6 W/m^2 UVB, 0.7 W/m^2 UVB and 0.3 W/m^2 UVB	Not reported
Sabino *et al.* [50]	Mercury UVC lamp	UVsurface, Biolambda, Brazil	UVC, 254	Not reported	2.2 ± 0.2 mW/cm^2	Not reported
Saknimit *et al.* [44]	UV lamp (GL-15)	Toshiba	Not reported	15	Not reported	Not reported
Simmons *et al.* [39]	Pulsed-xenon UV robot	Xenen Disinfection Services, San Antonio, TX, USA	UVC	Not reported	Not reported	PX-UV robot model PXUV4D
Walker *et al.* [40]	UVC lamps (experimental chambers)	Lumalier, Memphis, TN, USA	UVC, 254	36	Not reported	n UV emitter = 6 Fused quartz UV exposure window (260 mmx260 mm)

LASER, light amplification by stimulated emission of radiation; LED, light-emitting diode; UV, ultraviolet.

SARS-CoV-1

Efficacy of UV-based technologies. Results from included studies assessing the efficacy of UV-based technologies on SARS-CoV-1 are reported in Table IV.

Ansaldi *et al*. [45] tested the effect of UV irradiation at 40 mW/cm^2 on SARS-CoV-1 in liquid suspension. In less than 2 min, nested RT-PCR showed damage in the genome integrity. At the same time, complete inhibition of viral replication was demonstrated by inoculation in cell culture.

A study conducted by Darnell *et al*. [36] compared the germicidal efficacy of 254 nm UVC light to 365 nm UVA light on the Urbani strain of SARS-CoV-1 in liquid suspension. After 15 min and from a distance of 3 cm, UVC irradiation at 4,016 μW/cm^2 resulted in complete viral inactivation, demonstrated by median $TCID_{50}$ assay determination ($\leq$1.0 $TCID_{50}$ (log10)/mL). Under the same conditions, irradiating the sample with UVA light at 2133 μW/cm^2 did not show any effect on viral inactivation.

Duan *et al*. [47] employed a 260-nm UVC light to irradiate SARS-CoV-1 (COV-P9 strain) in liquid suspension. With an intensity higher than 90 μW/cm^2 and from a distance of 80 cm, after 60 min, the inoculated cells did not show any sign of cytopathic effect.

Conversely, in a study conducted by Kariwa *et al*. [42], after 60 min exposure to 134 μW/cm^2 of UV light, the Hanoi strain of SARS-CoV-1 was still detectable (18.8 $TCID_{50}$/mL).

Efficacy of chemical and physical agents. Among the effective chemical and physical agents tested against SARS-CoV-1 were: sodium hypochlorite 0.05% and sodium hypochlorite 0,1% (1 min of contact) [45], 2-benzil-chlorophenol 2% [45], peracetic acid 0.035% [45] and ethanol 70% [42,45] (<2 min of contact), povidone-iodine products (2 min of contact) [42], benzalkonium-chloride 1% and chlorhexidine digluconate 1% (5 min of contact) [45], acetone 100%, paraformaldehyde 3.5% and glutaraldehyde 2.5% (5 min of contact) [42], methanol 100% (30 min of contact) [42], glutaraldehyde 1:1,000 (by day 1 at 37°C) [36], glutaraldehyde 1:4,000 (by day 2 at 25°C) [36], 56°C (30min [42] and 90 min [47] of exposure), 67°C (60 min of exposure) [47], 75°C (30 min [47] to 45 min [45] of exposure), pH <3 or >12 (60 min of exposure) [36] (results of comparators are available in the Supplementary material).

MERS-CoV

Efficacy of UV-based technologies. Only one study was included on MERS-CoV (Bedell *et al*.; Table IV) [33]. A triple UVC emitter irradiated the sample from a distance of 122 cm, and after 5 min, by plaque counts, the viral titre was reduced to an undetectable level (5.91 log10 reductions).

Seasonal human coronaviruses

Efficacy of UV-based technologies. Bucknall *et al*. [34] employed UV irradiation to investigate the physical and biological properties of HCoV-229E and HCoV-OC43, human coronaviruses responsible of seasonal respiratory infections (Table IV). When the samples suspended in 2% fetal calf serum were exposed to a 60-W UV emitter from a distance of 45 cm, the viral titre reduction curves were convex, suggesting a 'multi-hit' process of inactivation (229E <2 $TCID_{50}$ (log10)/0.2 mL after 7 min, OC43 around 1 $TCID_{50}$ (log10)/0.2 mL after 11 min). Based on this data, the authors hypothesized that the original samples might contain clumps of the virus, possibly due

Table III
Results of ultraviolet (UV) light interventions on SARS-CoV-2 in included studies

Reference	Virus	UV source	Intensity (irradiance)	Distance	Exposure time	Outcome	Results
Heilingloh *et al.* [49]	SARS-CoV-2 in liquid suspension	UV-4 S/L light source (UVC 254 nm and UVA 365 nm)	1,940 μW/cm^2 (UVC) and 540 μW/cm^2 (UVA)	3 cm	1.4 min	Infectivity	50% inactivation
					9 min	Viral titre reduction, by $TCID_{50}$	Complete inactivation
			Radiant exposure: UVA dose 292 mJ/cm^2	3 cm	9 min	Viral titre reduction, by $TCID_{50}$	Partial inactivation
Inagaki *et al.* [41]	SARS-CoV-2 (SARS-CoV-2/Hu/DP/Kng/19–027) in liquid suspension	Deep ultraviolet light-emitting diode (DUV-LED)	3.75 mW/cm^2	2 cm	1 s	Infectivity, by CPE	4.7*10^3 pfu/mL, 87.4% reduction
					10 s	Infectivity, by CPE	2.7*10^1 pfu/mL, 99.9% reduction
					20 s	Infectivity, by CPE	6.7 pfu/mL, >99.9% reduction
					30 s	Infectivity, by CPE	<20 pfu/mL, >99.9% reduction
Kitagawa *et al.* [43]	SARS-CoV-2 in liquid suspension	222-nm Kr–Cl excimer lamp module	0.1 mW/cm^2	24 cm	10 s	Viral titre by $TCID_{50}$	$2.34 \pm 0.86 \times 10^3$, $TCID_{50}$/mL, 0.94 log reduction
					30 s	Viral titre by $TCID_{50}$	$6.32 \pm 0.0 \times 10^1$, $TCID_{50}$/mL, 2.51 log reduction (undetectable levels)
					10 s	RNA copy number by RTq-PCR	$5.75 \pm 0.82 \times 10^7$ copies/test
					30 s	RNA copy number by RTq-PCR	$3.41 \pm 1.08 \times 10^7$ copies/test
					60 s	RNA copy number by RTq-PCR	$2.95 \pm 0.41 \times 10^7$ copies/test
					300 s	RNA copy number by RTq-PCR	$3.03 \pm 1.73 \times 10^7$ copies/test
Ratnesar-Shumate *et al.* [38]	SARS-Cov-2 (USA-WA1/2020) in simulated saliva	Solar simulator with a xenon arc lamp	1.6 W/m^2 UVB	Not reported	6.8 min	Inactivation rate, by $TCID_{50}$	90% inactivation
			0.7 W/m^2 UVB	Not reported	8 min	Inactivation rate, by $TCID_{50}$	90% inactivation
			0.3 W/m^2 UVB	Not reported	12.8 min	Inactivation rate, by $TCID_{50}$	90% inactivation
	SARS-Cov-2 (USA-WA1/2020) in growth medium (gMEM)	Solar simulator with a xenon arc lamp	1.6 W/m^2 UVB	Not reported	14.3 min	Inactivation rate, by $TCID_{50}$	90% inactivation
			0.7 W/m^2 UVB	Not reported	17.6 min	Inactivation rate, by $TCID_{50}$	90% inactivation
Sabino *et al.* [50]	SARS-CoV-2 in liquid suspension	Mercury UVC lamp (254 nm)	0.016 mJ/cm^2 (2.2 mW/cm^2)	30 cm	0.01 s	Inactivation, by lethal dose	LD90 (viral inactivation 90%)
			108.714 mJ/cm^2 (2.2 mW/cm^2)	30 cm	49.42 s	Inactivation, by lethal dose	LD99 (viral inactivation 99.999%)

Simmons *et al.* [39]	SARS-CoV-2 prepared in liquid suspension and dried on the test surface	PX-UV robot model PXUV4D	Not reported	1 m	1 min	Decrease of infectivity titre, by plaque assay	2.67 pfu/mL (log10), 99.97% reduction
					2 min	Decrease of infectivity titre, by plaque assay	<1.66 pfu/mL (log10), >99.997% reduction
					5 min	Decrease of infectivity titre, by plaque assay	<2.08 pfu/mL (log10), >99.992% reduction

CPE, cytopathic effect; LD, lethal dose; pfu, plaque-forming unit; RTqPCR, real-time quantitative polymerase chain reaction; $TCID_{50}$, 50% tissue culture infectious dose; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

to the composition of the medium. Subsequently, they applied the same experimental conditions to viral samples suspended in 0.2% bovine plasma albumin and found that the viral titre was reduced to 2 $TCID_{50}$ (log10)/0.2 mL after only 30 s (229E) and 40 s (OC43) of irradiation.

Buonanno *et al.* [35] explored 222-nm far-UVC light efficacy against HCoV-229E and HCoV-OC43 in an aerosol model. UV doses of 1.7 and 1.2 mJ/cm^2 inactivated 99.9% of aerosolized coronavirus.

Gerchman *et al.* [48] investigated the effect of four UV light emission spectra on HCoV-OC43. In detail, they exposed the viral samples to four different UV wavelengths, each one at a time. The UV sources were two UV LED systems; a circular one, emitting 279-nm or 297-nm UV light, and a custom-made rectangular one, emitting 267-nm or 286-nm UV light. The stocks were exposed at same distance and time, although not explicitly reported. The effective inactivation of the virus was defined as the 3-log reduction after the exposure, also the reported limit of quantification. All the UV wavelengths were proven to be effective in achieving this reduction and, as the wavelength increased, the UV dose needed was 5.7, 7.0, 12.9 and 32.0 mJ/cm^2, respectively. In particular, the 267-nm UVC light determined the 3-log inactivation at the lower UV dose.

Efficacy of chemical and physical agents. Coronavirus strains 229E and OC43 growth were inhibited at 37°C at pH 7.4 [34] (results of comparators are available in the Supplementary material).

Animal coronaviruses

Efficacy of UV-based technologies. Results from included studies' assessing the efficacy of UV-based technologies on animal coronaviruses are reported in Table V.

Bedell *et al.* [33] employed a triple UVC emitter to irradiate a dried MHV-A59 sample from a distance of 122 cm. After 10 min, the viral titre was reduced to an undetectable level (6.11 log10 reduction), as shown by plaque counts.

MHV was also the object of a study conducted by Saknimit *et al.* [44], in which the viral samples were exposed to a 15-W UV emitter for 15 min from a distance of 1 m. They performed plaque assays and found a decrease of infectivity titre to complete inactivation, which was >4.67 log plaque-forming units (pfu)/0.1 mL for MHV-2, and >3.34 log pfu/0.1 mL for MHV-N.

As the only study to test aerosolized virus, Walker *et al.* [40] engineered an experimental chamber equipped with six 36-W emitters of 254 nm UVC. In the chamber, the MHV viral samples were nebulized and exposed to a UV dose of 599 μWs/cm^2 after 16.2 s. They recorded a 12% viral survival, expressed as the ratio between the number of plaques in the presence of UV exposure and the number of plaques in the absence of UV exposure.

Two studies focused on CCV in liquid suspension. As noted earlier, Saknimit *et al.* [44] exposed the virus to a 15-W UV source for 15 min, from 1 m, and found a decrease of infectivity titre to complete inactivation (>3.84 log pfu/0.1 mL). Pratelli *et al.* [46] irradiated CCV (S378 strain) from a distance of 4 cm, with an irradiance of 27.1 μW/cm^2 calculated at 1 m. Under these conditions, after 72 h, the viral titre was reduced to 2 $TCID_{50}$ (log10)/50 mL.

Morilla *et al.* [37] performed a comparison of intestinal (Illinois strain) and cell culture-adapted (M-HP strain) of TGE

Table IV
Results of ultraviolet (UV) light interventions on SARS-CoV-1, MERS-CoV and human coronaviruses in included studies

Reference	Virus	UV source	Intensity (irradiance)	Distance	Exposure time	Outcome	Results
Ansaldi *et al.* [45]	SARS-CoV-1 in liquid suspension	Not reported	40 mW/cm^2	Not reported	<2 min	Infectivity, by inoculation in cell culture	Complete inhibition of viral replication
			40 mW/cm^2	Not reported	<2 min	Genome integrity by nested RT-PCR	Damaged
Darnell *et al.* [36]	SARS-CoV-1 (Urbani strain) in liquid suspension	UVC (254 nm)	4,016 μW/cm^2	3 cm	15 min	Inactivation by $TCID_{50}$ assay and by CPE	Complete ≤1.0 $TCID_{50}$ (log10)/mL (limit of detection of the assay)
		UVA (365 nm)	2,133 μW/cm^2	3 cm	15 min	Inactivation by $TCID_{50}$ assay and by CPE	No effect
Duan *et al.* [47]	SARS-CoV-1 (CoV-P9 strain) in liquid suspension	UVC (260 nm)	>90 μW/cm^2 (UV dose >162 mW*s/cm^2 after 30 min)	80 cm	60 min	Infectivity, by CPE	Cells with no signs of CPE
Kariwa *et al.* [42]	SARS-CoV-1 (Hanoi strain) in liquid suspension	Not reported	134 μW/cm^2	Not reported	60 min	Viral titre reduction, by $TCID_{50}$	Still detectable 18.8 $TCID_{50}$/mL
Bedell *et al.* [33]	MERS-CoV droplets	Triple UVC emitter	Not reported	122 cm	5 min	Viral titre reduction by plaque counts	Reduction of 5.91 log10 undetectable levels (mean of triplicate samples)
Bucknall *et al.* [34]	Coronavirus strain 229E in liquid suspension (2% fetal calf serum)	1 emitter 60 W	Not reported	45 cm	7 min	Viral titre reduction by CPE, measured by $TCID_{50}$	<2 log10 $TCID_{50}$/0.2 mL
						Inactivation rate	0.005 log/min
	Coronavirus strain 229E in liquid suspension (0.2% bovine plasma albumin)	1 emitter 60 W	Not reported	45 cm	30 s	Viral titre reduction by CPE, measured by $TCID_{50}$	2 log10 $TCID_{50}$/0.2 mL
						Inactivation rate	0.08 log/min
	Coronavirus strain OC43 in liquid suspension (2% fetal calf serum)	1 emitter 60 W	Not reported	45 cm	11 min	Viral titre reduction by hemadsorption	around 1 log10 $TCID_{50}$/0.2 mL
						Inactivation rate	0.005 log/min
	Coronavirus strain OC43 in liquid suspension (0.2% bovine plasma albumin)	1 emitter 60 W	Not reported	45 cm	40 s	Viral titre reduction by hemadsorption	2 log10 $TCID_{50}$/0.2 mL
						Inactivation rate	0.11 log/min

Buonanno *et al.* [35]	HCoV-229E (VR-740) aerosolized	12-W 222-nm KrCl excimer lamp module	100 μW/cm^2 (1,7 mJ/cm^2)	22 cm	20 s	Viral titre reduction, by $TCID_{50}$ and CPE	99.9% inactivation rate (constant k = 4.1 cm^2/mJ)
	HCoV-OC43 (VR-1558) aerosolized	12-W 222-nm KrCl excimer lamp module	100 μW/cm^2 (1.2 mJ/cm^2)	22 cm	20 s	Viral titre reduction, by $TCID_{50}$ and CPE	99.9% inactivation rate (constant k = 5.9 cm^2/mJ)
Gerchman *et al.* [48]	HCoV-OC43	267-nm rectangular LED system	5.7 mJ/cm^2	Not reported	Not reported	Viral titre reduction by ICC-RTqPCR	3 log10 pfu/mL (defined as limit of quantification)
		279-nm circular LED system	7.0 mJ/cm^2	Not reported	Not reported	Viral titre reduction by ICC-RTqPCR	3 log10 pfu/mL (defined as limit of quantification)
		286-nm rectangular LED system	12.9 mJ/cm^2	Not reported	Not reported	Viral titre reduction by ICC-RTqPCR	3 log10 pfu/mL (defined as limit of quantification)
		297-nm circular LED system	32.0 mJ/cm^2	Not reported	Not reported	Viral titre reduction by ICC-RTqPCR	3 log10 pfu/mL (defined as limit of quantification)

CPE, cytopathic effect; HCoV, human coronavirus; ICC-RTqPCR, integrated cell culture real-time quantitative polymerase chain reaction; LED, light-emitting diode; MERS-CoV, Middle East respiratory syndrome–related coronavirus; pfu, plaque-forming unit; RT-PCR, real-time polymerase chain reaction; $TCID_{50}$, 50% tissue culture infectious dose; SARS-CoV-1, severe acute respiratory syndrome coronavirus 1.

virus in liquid suspension. Results showed that after exposure to an 8-W UV emitter, the samples were utterly inactivated, in 90 and 120 s, respectively.

Efficacy of chemical and physical agents. Saknimit *et al.* [44] proved the following agents to effectively decrease MHV infectivity titre: ethanol 70%, isopropanol 50%, benzalkonium chloride 0.05%, iodophor 50 ppm, sodium hypochlorite 100 ppm, sodium chlorite 0.23%, cresol soap 1.0%, formaldehyde 0.7%, 60°C for 1 min of exposure.

Against CCV, Saknimit *et al.* [44] proved the following agents to be effective: ethanol 70%, isopropanol 50%, benzalkonium chloride 0.05%, iodophor 50 ppm, sodium chlorite 0.23%, cresol soap 1.0%, formaldehyde 0.7%, 60°C for 5 min of exposure and 80°C for 1 min.

Besides, Pratelli *et al.* [46] found CCV to be inactivated at 65°C for 40 min, 75°C for 30 min, pH >9.98 at 37°C (60 min of exposure), pH >11.09 at 25°C (60 min of exposure), pH 2.26–4.38 at 37°C (60 min of exposure). Glutaraldehyde 0.002% completely inactivated the virus at 25°C and 37°C by day 1 and glutaraldehyde 0.001% by day 2 at 37°C [46] (results of comparators are available in the Supplementary material).

Discussion

We systematically retrieved and pooled all the available evidence on UV virucidal properties against coronaviruses. We report that, although virus persistence was tested under different experimental conditions with regard to UV exposure and sample preparation (dried sample, liquid suspension and aerosolized), evidence suggests that UV light has a definite action on coronaviruses titre reduction and inactivation.

The two main parameters that affect UV light efficacy and safety for environmental disinfection are wavelength and dose. The dose is defined as UV energy received by a surface per unit area (J/m^2) or, in other words, irradiance (W/m^2) multiplied by time. Irradiance, also commonly called 'light intensity', indicates the radiant flux (power) received by a surface per unit area, and depends on the power of the UV source and the distance between the source and the target surface: it increases proportionally to the emitted power, and decreases proportionally to the square of the distance. At a specific wavelength, three additional parameters can affect UV light efficacy, safety and applicability: (1) exposure time, (2) UV power, and (3) distance between the UV emitter and the target surfaces; ideally, to maintain UV effectiveness, the first two should be as small as possible, and the latter the highest allowed.

Under the experimental conditions reported in the included studies, complete inactivation of coronaviruses on surfaces took a maximum exposure time of 15 min, while the maximum distance between the UV emitter and surfaces to be disinfected was explored up to 1 m. The balancing of these parameters might affect UV light use in everyday scenarios, although it is important to remember that the same dose can be obtained by increasing either power or exposure time.

Because of a lack of standardized methods to compare different UV technologies, the general consensus is to follow manufacturers' technical manuals of use [51]. Moreover, some of the studies included in our review did not even report UV source detailed parameters, e.g. UV spectrum [34,37,42,44,45] or irradiance [33,34,37,39,40,44].

Table V
Results of ultraviolet (UV) light interventions on animal coronaviruses in included studies

Reference	Virus	UV source	Intensity (irradiance)	Distance	Exposure time	Outcome	Results
Bedell *et al.* [33]	Dried MHV-A59	Not reported	Not reported	122 cm	10 min	Viral titre reduction by plaque counts	Reduction of 6.11 log10 undetectable (mean of triplicate samples)
Saknimit *et al.* [44]	MHV-2 in liquid suspension	1 emitter 15 W	Not reported	1 m	15 min	Decrease of infectivity titre, by plaque assay	>4.67 log pfu/0.1 mL (complete)
	MHV-N in liquid suspension	1 emitter 15 W	Not reported	1 m	15 min	Decrease of infectivity titre, by plaque assay	>3.34 log pfu/0.1 mL (complete)
Walker *et al.* [40]	Aerosolized MHV	6 emitters 36 W (254 nm UVC)	Radiant exposure (UV dose) = 599 $\mu W^*S/cm^2$ (after 16.2 s)	Not reported	16.2 s	Percent survival (100 × (number of plaques in the presence of UV exposure)/(number of plaques in the absence of UV exposure))	12% survival
Pratelli *et al.* [46]	CCV (S378 Strain) in liquid suspension	UVC	27.1 $\mu W/cm^2$ at 1-m distance	4 cm	72 h	Viral titre reduction, by $TCID_{50}$	2 $TCID_{50}$ (log10)/50 μL
Saknimit *et al.* [44]	CCV in liquid suspension	Not reported	Not reported	1 m	15 min	Decrease of infectivity titre, by plaque assay	>3.84 log pfu/0.1 mL (complete)
Morilla *et al.* [37]	TGE (Illinois strain) in liquid suspension	1 emitter 8 W	Not reported	Not reported	90 s	Inactivation, by log10 virus titre	Complete Log10 virus titre = 0
	TGE (M-HP strain) in liquid suspension	1 emitter 8 W	Not reported	Not reported	120 s	Inactivation, by log10 virus titre	Complete Log10 virus titre = 0

CCV, canine coronavirus; MHV, murine hepatitis virus; pfu, plaque-forming unit; $TCID_{50}$, 50% tissue culture infectious dose; TGE, transmissible gastroenteritis of swine coronavirus.

The existing literature on hospital environmental cleaning and disinfection reports on the efficacy of light-based [52—54] and UV-based technologies for air and surfaces disinfection [13—20]. Among the three types of UV radiation (UVA 320—400 nm, UVB 290—320 nm, UVC 200—290 nm), UVC light has a potent germicidal effect capable of inactivating a broad spectrum of micro-organisms, such as viruses [13,55], bacteria, protozoa, fungi and algae [14], through the formation of pyrimidine dimers, the photoproducts of genetic materials [15,56]. Antimicrobial activities have been mostly observed in the UVC range at 254 nm [57,58].

While the germicidal effect of UV light-emitting technologies is well known, their application for environmental disinfection in healthcare settings is less well studied [22,55,67,68,59—66]. Recently, Hadi *et al.* [69] and Horton *et al.* [70] summarized the literature on all light-based (UV, UVC, UVB, UVA, blue and red lights, visible light, and infrared radiation) sanitization methods for the inactivation of single-stranded-RNA viruses [69] or viral surrogates [70], highlighting the efficacy of germicidal UV. Although UV efficacy is directly related to light intensity and exposure time, the time required to be effective is considerably shorter than other non-touch technologies [16—18,71—74]. Moreover, it is noteworthy that pathogen concentration does not significantly affect the efficacy of UV and similar surfaces generally have similar reduction rates [75].

The possible role of UV irradiation as environmental sterilization adjunct for standard protocols against a wide range of pathogens (viruses and bacteria) or air disinfection methods for viruses only was systematically assessed by, respectively, Ramos *et al.* [76] and Beggs *et al.* [77]; Sharafi *et al.* [78] and Shimabukuro *et al.* [79] focused specifically on SARS-CoV-2.

With reference to safety, exposure to UV lamps is associated with health risks as conventional UV light sources are recognized as a health hazard for humans, being both carcinogenic and cataractogenic, involved in damage to eyes and skin [25,26,80,81]. Recent evidence suggested that UVC at 222 nm has germicidal activity [82,83] but does not cause damage in mice [84—86]. Considering the potential health hazards associated with UV light-emitting technologies, strict rules must be followed when they are put into use. The WHO and the Emergency Care Research Institute (ECRI) guidances state that UV-based technologies can only be employed following standard cleaning practices, and cannot replace them as a stand-alone procedure [51,87]. In addition, both CDC and ECRI guidelines advise on the fact that UV light disinfection action is limited to directly exposed surfaces, warning of the need to overcome the risk of shadowing [51,88]. Finally, the WHO, the ECRI and the International Commission Non-Ionizing Radiation Protection (ICNIRP) jointly state that human exposure to artificial UV light should be avoided, thus most devices cannot be operated in the presence of people, but used only in empty rooms and with motion sensors [51,87,89]. ICNIRP reports the calculated human occupational daily UV dose exposure limits by wavelength: human UV exposure should not exceed 30 J/m^2 for 270 nm, 60 J/m^2 for 254 nm and 240 J/m^2 for 222 nm. As reported in two of the included studies [35,43], far-UVC light (222 nm) guarantees an effective viral inactivation with a better safety profile. However, wavelengths shorter than 240 nm need an additional risk assessment due to a greater associated ozone production [90].

Our work has both strengths and limitations. To our knowledge, our review is the first to systematically analyse the efficacy of UV emitting technologies as an environmental disinfection method against coronaviruses. The use of PRISMA guidelines [31] ensured a thorough reporting framework. Another strength of this review is the inclusion without date limitations of all the available studies on coronaviruses, in order to have a broader perspective on the susceptibility of subfamily *Orthocoronavirinae* to UV light. Furthermore, we used a comprehensive range of databases and search terms to maximize the number of studies retrieved and minimize the chance of publication bias. Therefore, we included studies from a wide range of academic fields.

Our study does have some limitations. First, the original available studies were all conducted under experimental laboratory conditions; no quantitative data on UV impact against coronavirus in real-world scenarios were available. Operational research is needed to estimate measures such as infections prevented, or contamination averted with the use of UV-based technologies and to assess virucidal efficacy of UV radiation in the field. We could not perform a standardized quality appraisal of the included studies, due to a lack of shared reporting standards for *in vitro* studies [91,92]. Finally, quantitative data synthesis was not possible due to the heterogenicity of the included studies.

In the 2020 emergency context, the use of UV light has been assessed for sterilization of personal protective equipment to be reused [93], for example, to reduce contamination on respirators [94—97]. New protocols for infection control and operating room management in the hospital environment were proposed [98], as well as the use of UV light devices for the inactivation of SARS-CoV-2 on everyday objects [99]. Outside the healthcare sector, further evidence and updated recommendations are needed before employing UV-based technologies on larger scales, including household environments and public transports, monitoring and controlling improper installation and use by untrained and unexperienced subjects [100,101].

In conclusion, SARS-CoV-2 and coronaviruses are relatively easily inactivated by UV light, even when aerosolized, and UV irradiation can be used as an adjunct to terminal cleaning protocols in healthcare settings. UV light could be used on highly touched surfaces in crowded spaces, where rapid and efficient disinfection of indoor environments is crucial to control the spread of highly infective agents such as SARS-CoV-2 [102]. UVGI fixture designs for sanitization technologies with high virucidal and energy efficiencies are quickly evolving, becoming more effective while remaining safe. However, more evidence is needed to assess these technologies, including applying Health Technology Assessment (HTA) evaluations, at the healthcare and community levels, to balance efficacy, safety and costs.

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Appendix A. Supplementary data

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