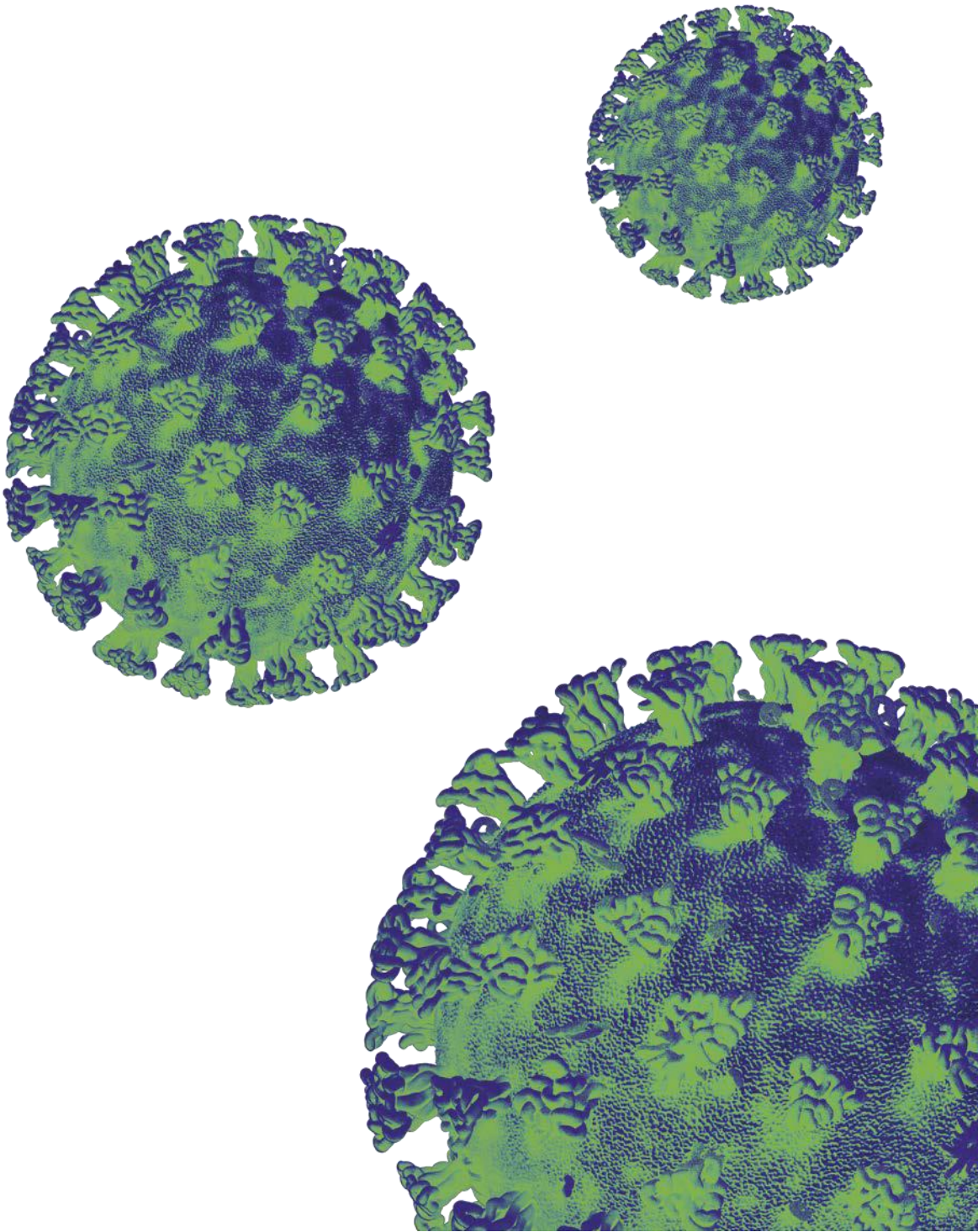
Llywodraeth Cymru
Welsh Government

Technical Advisory Group

TAG-E: Evidence review of ozone generators including appropriateness as mitigation within classrooms.

4th October 2021



A TAG-E review, incorporating the findings of the Wales COVID-19 Evidence Centre's rapid evidence review of "What are the efficacy, effectiveness and safety of SARS CoV-2 disinfection methods (including ozone machines) in educational settings?"

Summary of high confidence conclusions:

- Surface disinfection only mitigates infections acquired from contaminated surfaces. These account for a minor proportion of SARS-CoV-2 infections compared with other routes of infection
- Hand hygiene addresses transmission from hands contaminated by contact with contaminated surfaces or direct contact
- A range of routine cleaning and disinfection options exist to address remaining risks from contaminated surfaces
- Techniques generating airborne disinfection chemicals present potential harms from introducing harmful agents into the indoor atmosphere
- Ozone is a highly harmful indoor pollutant which is associated with harm to human health at low concentrations and damages diverse and integral components of indoor environments
- Children and those with underlying respiratory conditions are particularly sensitive to ozone exposure
- Ozone reacts with a range of compounds present indoors to generate persistent harmful secondary aerosols
- Evidence for effective ozone disinfection is limited in scope and quality
- Deployment of ozone to educational settings will require substantial resources to ensure safety and the protection of sensitive surfaces
- Deployment of ozone to educational settings will be reactive to contamination from transmission events effectively mitigated by other means (e.g. ventilation, routine cleaning, the spontaneous passage of time).

This review considers the potential for ozone disinfection within educational settings. First, the question of whether SARS-CoV-2 transmission from contaminated surfaces represents a problem to be addressed by intensive disinfection, followed by options for intensive disinfection, and the safety, efficacy and effectiveness of ozone disinfection. SAGE 66 (2020) concluded: *Devices based on other technologies (ionisers, plasma, chemical oxidation, photocatalytic oxidation, electrostatic precipitation) have limited evidence base, and can produce undesirable secondary chemical products that could lead to negative health effects (medium confidence).* This followed SAGE-EMG (2020a)'s report on air cleaning devices which recommended against using oxidation-based devices unless their safety and efficacy can be unequivocally and scientifically demonstrated by relevant test data.

This review is informed by a recent Rapid Evidence Summary published by the Wales COVID-19 Evidence Centre, *The efficacy, effectiveness and safety of SARS-CoV-2 disinfection methods (including ozone machines) in educational settings for children and young people.* The summary found that there was no direct evidence for the effectiveness and safety of using ozone machines to deactivate SARS-CoV-2 in real-

world educational settings for children, young people and staff. There was evidence for the risk of potential harm to children and young people from ozone machines due to ozone or secondary pollutants, in particular but not only, if used in uncontrolled ways in educational settings.

The Rapid Evidence Summary is available on the Wales COVID-19 Evidence Centre website here.

1.1 **Placing the surface transmission pathway in the context of SARS-CoV-2 transmission mechanisms**.

Key points:

- SARS-CoV-2 infection can occur by exposure to close range aerosols, long range aerosols, direct contact or contact with contaminated surfaces (fomite)
- For surface transmission to occur, enough infectious virus must reach the susceptible person following transfer to a surface by an infected person, survival on the surface, transfer from the surface to skin, and from the skin to mucous membrane.
- Each stage entails physical loss and spontaneous degradation of infectious virus, attenuating risk
- In high risk, high-touch settings, quantitative microbial risk assessment predicts that 1.6 infections follow hand-to-face contact for every 10,000 people touching a surface
- Effective hand hygiene disrupts both surface transmission and direct contact

SAGE-EMG and NERVTAG (2020) supports the view that SARS-CoV-2 is transmitted by three main mechanisms: exposure to close range aerosols or droplets, longer range respiratory aerosol exposure, and direct contact with contaminated surfaces or items (fomite transmission, Figure 1, Leung, 2021).

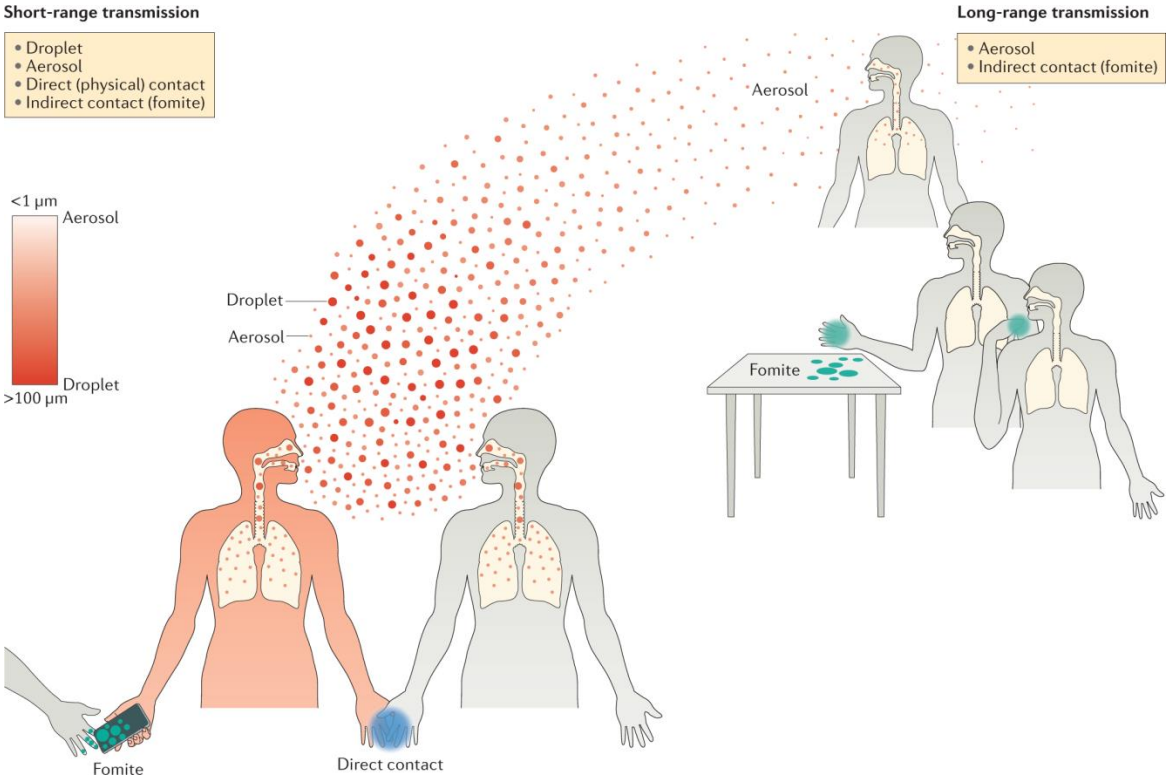


Figure 1: Illustrating the transmission pathways of respiratory viruses such as SARS-CoV-2 by exposure to an infectious person (red). Reproduced from Leung (2021)

From the start of the pandemic, disentangling the relative importance of each transmission pathway to the burden of infection has been challenging (SAGE-EMG

and NERVTAG, 2020) and contentious (e.g. Goldman, 2020; Goldman 2021) however the importance of exposure to SARS-CoV-2 borne within close range aerosols and droplets as well as long range aerosols is increasingly stressed (Leung,2021; Wang 2021) whereas real-world evidence in support of the importance of transmission by contact with contaminated surfaces remains limited (e.g. Goldman, 2020, 2021; Kampf, 2021; Mondelli et al 2021; Pitol & Julian, 2021; Wilson et al 2021).

For infection following contact with a contaminated surface, the following chain of events must occur:

1. A person sheds infectious SARS-CoV-2 virus on to the surface
2. SARS-CoV-2 persists in an infectious form on the surface
3. Infectious SARS-CoV-2 virus particles are transferred to the skin of a susceptible individual
4. SARS-CoV-2 particles remain in infectious form on the person's skin
5. A sufficient dose of infectious SARS-CoV-2 virus particles are transferred from the person's hands to their mucous membranes (e.g. mouth, nose, eyes) to initiate infection

Disruption of any of these five stages prevents fomite transmission. To achieve disruption through targeted intervention, it should be emphasized that interventions targeting the contaminated surface itself play no role in mitigating infection arising from other transmission pathways (high confidence) whereas mitigations against other stages in the transmission pathway can also help mitigate other transmission pathways. For example, reducing the shedding of virus to the surface (e.g. face coverings, isolation of detected cases) reduce exposure to infectious droplets/close range aerosols and long range aerosols, as well as direct contact with infectious individuals, whereas preventing the transfer of infectious virus from the hands to mucous membranes (regular and effective hand washing and sanitization) also mitigates transmission following contamination of hands through direct contact.

Shedding of infectious SARS-CoV-2 particles during acute infection can occur by a variety of routes, for example the deposition of droplets/close range aerosols and long range aerosols or the direct contamination of surfaces by respiratory secretions. There is considerable heterogeneity in the level of shedding from the respiratory tract (e.g. Chen et al 2021). A range of studies have surveyed environmental surfaces for the presence of SARS-CoV-2 as a marker of shedding. These typically use molecular methods detecting SARS-CoV-2 specific gene fragments, which illustrate prior shedding of SARS-CoV-2 but are not synonymous with the presence of infectious virus.

Since early in the pandemic, a number of laboratory studies assessed the persistence of infectious SARS-CoV-2 virus artificially inoculated on to representative surfaces under a range of experimental conditions (e.g. Van Doremalen et al 2020; Riddell et al 2020; Kampf et al 2020; Chin et al 2020). These experiments revealed the survival of infectious SARS-CoV-2 at different timescales, dependent on prevailing environmental conditions and the concentration and form of inoculum. While they are informative of the decay kinetics of SARS-CoV-2 infectious particles, the outcomes of

these experiments should be considered with key caveats in mind. Firstly, the use of culture media supplemented with protein compared to more realistic media significantly enhances stability (as reviewed by Bueckert et al 2021). For example, Van Doremalen et al (2020) determined the half-life of SARS-CoV-2 infectivity on plastic to be 6.8 h when applied in culture medium but reproducing the experiment using virus in dried nasal mucus or saliva reduced the half-life of infectivity to 3.1 h (Matson et al 2020). Secondly, experimental studies commonly use virus stocks obtained freshly from cell cultures at high titre. For SARS-CoV-1 the estimated survival time of viruses in similar experiments proved dependent on the inoculation concentrations. For example, with an inoculum of 1×10^6 $TCID_{50}$ mL^{-1}, infectious virus could be recovered 24 h post inoculation whereas an inoculum 1×10^4 $TCID_{50}$ mL^{-1} did not survive for more than five minutes (Lai et al 2005).

An alternative strategy for addressing the role of surfaces in transmission is to attempt the isolation of SARS-CoV-2 in cell culture from real-world surface samples. At least seven (Onakpoya et al. 2021) studies (Binder et al 2020; Colaneri et al 2020; Döhla et al 2020; Moore et al. 2021; Ong et al. 2020; Santarpia et al. 2020; Zhou et al. 2020) are known to attempt this approach in healthcare or domestic settings, while the presence of SARS-CoV-2 RNA could be demonstrated on a range of samples, six studies were unable to recover infectious virus in cell cultures whereas the remaining study (Santarpia et al. 2020) isolated SARS-CoV-2 from a windowsill of an intensive care unit; in spite of high rates of SARS-CoV-2 RNA detection, 162 other samples were negative upon culture.

Should infectious virus persist upon a surface, to successfully initiate infection, sufficient quantities must be transferred upon contact and persist upon the person's skin. Using an artificial finger, Todt et al (2021) tested the transfer of high (1×10^6 $TCID_{50}$ mL^{-1},) and low (1×10^4 $TCID_{50}$ mL^{-1}) concentrations of virus in culture medium from paper and steel surfaces representing currency while wet or after 1h drying time. Reductions of 0.3 to 3 $\log_{10}$ in infectious virus occurred while transferring the high concentration of virus in wet or dry state to the artificial finger. For the low-dose inoculum, 0.3-0.8 $\log_{10}$ reductions in infectious virus were observed in the wet state. After 1h drying, infectious virus could not be recovered from the surface or transferred to the finger following inoculation on coins and banknotes, and very low doses (2×10^1 $TCID_{50}$ mL^{-1}) recovered or transferred from PVC or steel surfaces. Subsequently, virus survival on human skin has been addressed experimentally using skin patches from cadavers inoculated with 1×10^5 $TCID_{50}$ mL^{-1} (Hirose et al. 2021) with a half-life of 3.1-4.5 h; the virus was completely inactivated by exposure to 80% ethanol for 15 seconds. Taken together, these data indicate that the transfer of infectious SARS-CoV-2 from surfaces to skin is inefficient, however virus residing on skin may remain infectious for some time, but that it is amenable to simple hand hygiene precautions as a means of preventing subsequent transfer to mucous membranes of the mouth/eyes/nose.

Considering the multiple rate limiting steps in the chain of events required for successful fomite transmission, assessing its probability on the basis of those steps in isolation is challenging as their impact upon the probability of transmission is cumulative. Pitol & Julian (2021) applied a quantitative microbial risk assessment (QMRA) approach to evaluate the risk of fomite transmission within community

settings at different prevalence of SARS-CoV-2 infection. For communities with very high prevalence (5%) the risk of infection following contact with a high touch surface was estimated at 1.6×10^{-4}, equivalent to 1.6 infections following hand-to-face contact for every 10,000 people touching a surface. While the outcome of QMRA is sensitive to the parameters selected, and uncertainties may exist for some parameters, these results are consistent with other QMRA studies (Wilson et al 2021). For comparison a risk of 1×10^{-4} is the threshold for the risk of interplanetary contamination per spacecraft lander mission accepted by NASA (McCoy et al 2021) whereas systematic review of COVID-19 transmission presents an infection risk of 12.8% from contact within 1m and 2.8% at 2m (Chu et al 2020). Figure 2 reproduced from Pitol & Julian (2021) compares the predicted risk of such infection in the baseline scenarios, and its mitigation by hand hygiene or surface cleaning.

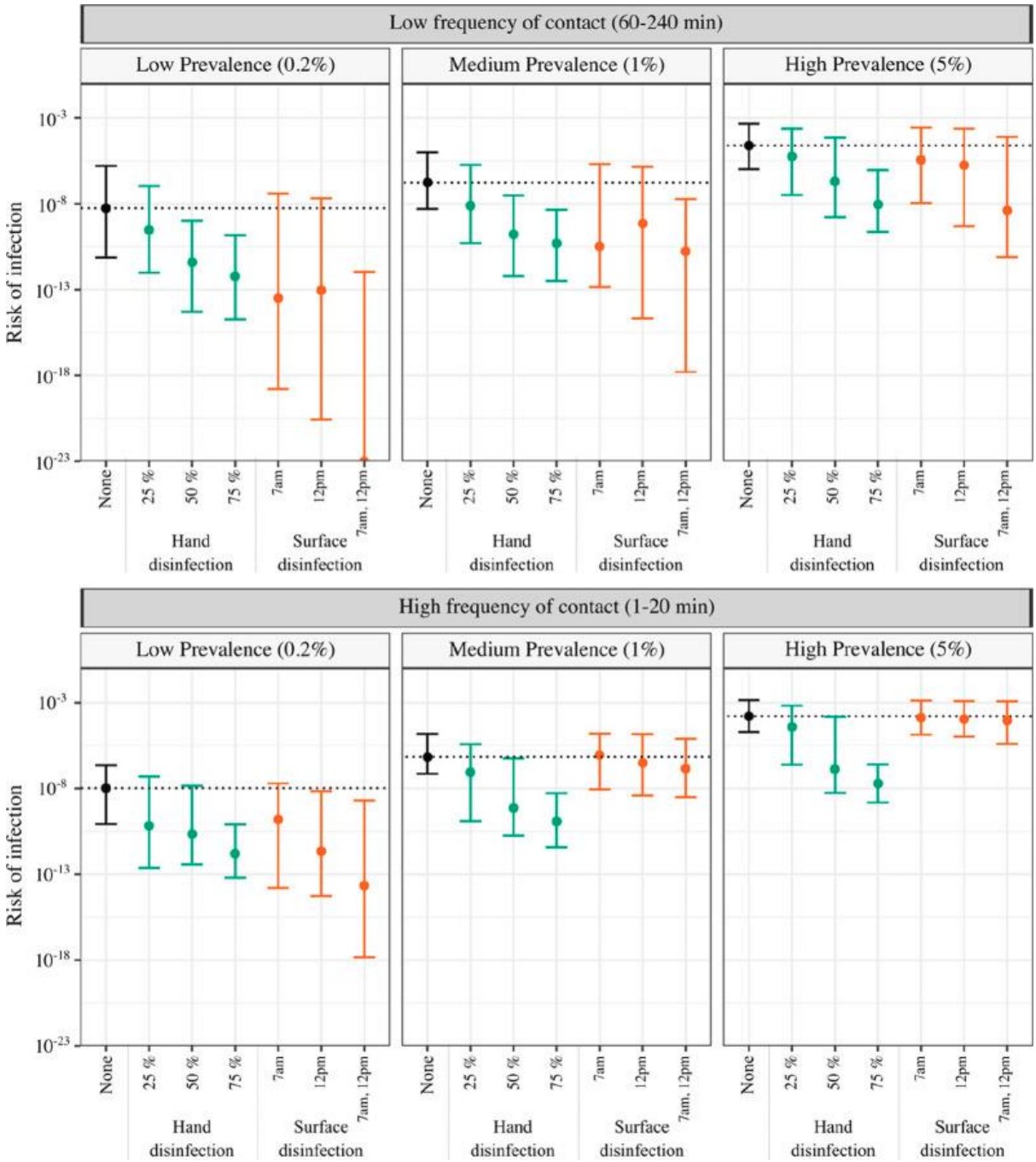


Figure 2: Predicted median (± interquartile range) community-based risk of SARS-CoV-2 infection due to hand-to-surface contact followed by hand-to-face contact. The baseline median risk of infection is shown by the horizontal dotted line and the impact of hand hygiene (green) or surface disinfection (orange). The risk of infection of 1×10^{-6} is equivalent to one infection as a result of hand-to-mouth contact for every million people touching the surface. Compliance for hand disinfection was set to 25%, 50%, and 75% of the population. Surface disinfection regimes were every day at 7 am, 12 pm, or 7 am and 12 pm. Reproduced from Pitol & Julian (2021).

In summary, fomite transmission appears to account for a minor component of the burden of SARS-CoV-2 infection, and hand hygiene offers a critical opportunity for controlling infections from both contact with contaminated surfaces or from hand contamination arising from direct contact with infectious persons whereas surface cleaning only mitigates the surface transmission pathway. Consideration should be given to the effectiveness of hand hygiene as a control measure in isolation for some educational settings where learners' compliance may be lower (e.g. reception classes).

1.2 Options for cleaning and disinfection of surfaces

Various options can be considered for cleaning and disinfection:

1.2.1: Surface disinfection with microbicides

A range of common disinfectant agents have been evaluated for their ability to inactivate SARS-CoV-2. In the UK, clear recommendations (https://www.gov.uk/government/publications/covid-19-decontamination-in-non-healthcare-settings/covid-19-decontamination-in-non-healthcare-settings) , are made for the use of either a combined detergent disinfection solution offering 1000 parts per million (ppm) available chlorine or detergent followed by disinfectant solution offering 1000 ppm available chlorine, or an alternative proven to be effective against enveloped viruses. EN14476 is a quantitative test for virucidal activity, typically using vaccinia virus as a surrogate enveloped virus. The test is carried out in suspension, but the results allow claims to be made about surface disinfection. A pass result is given when a product reduces infectious titres by 4 $\log_{10}$ (99.99%) in the presence of a soil (i.e. contaminating protein) load. The US Environmental Protection Agency developed List N (https://www.epa.gov/coronavirus/about-list-n-disinfectants-coronavirus-covid-19-0) comprising of over 400 different agents with >30 different types of active ingredients. Tyan et al (2020) list key questions and considerations for the selection of appropriate agents on List N:

Efficacy against SARS-CoV-2:

- Does this product have an emerging viral pathogen claim?
- What is the wet-contact time required to kill SARS-CoV-2?

Safety profile

- What is the pH of the product?

- Does the product have potential for toxicity or irritation?

Practicality (ease of use, surface compatibility)

- What is the method of delivery (pre-moistened wipe, spray, concentrate requiring dilution, etc.)?
- Can this product be delivered through multiple modalities to allow for flexibility (spray bottle with dry wipe packs vs saturating wipe rolls in a bucket, etc.)?
- What surface types/equipment is the disinfectant compatible with?

Availability and cost

- Is this product currently commercially available, and will it remain available for repurchase?
- Is this product economical for the (health care) institution?

As noted above, typical agents of concern in educational settings include non-enveloped viruses such as norovirus which are more recalcitrant to disinfection (e.g. Barker et al. 2004; Barclay et al. 2014), and therefore the selection of agent should consider its effectiveness against a range of agents including SARS-CoV-2 rather than just SARS-CoV-2 in isolation.

1.2.2: Ultraviolet-C irradiation

Ultraviolet-C (200-280 nm) radiation is a well-known means of inactivating pathogens through the degradation of pathogen genetic material. SAGE-EMG (2020b) has reviewed considerations pertaining to UV-C in detail, and the reader is directed to this report for more detailed consideration of its potential benefits and harms, with the caveat that since publication, the base of peer-reviewed evidence on the effectiveness of UV-C against SARS-CoV-2 has developed (e.g. 2.5 $\log_{10}$ reduction in 30 seconds of 222 nm UV-C; Kitagawa et al. 2021; 3 $\log_{10}$ reduction upon 3.7 mJ cm^{-2} and complete inactivation at 16.9 mJ cm^{-2}; Biasin et al 2021). A crucial limitation of UV-C irradiation is the impact of “shadowing”, where disinfection of complex environments is limited by concealment of surfaces from UV-C within areas of shadow. UV-C systems deployable to classrooms require the closure of the classroom to prevent exposure of staff or students to UV-C, which can damage skin and eyes. Germicidal UV-C radiation is typically generated using mercury vapour lamps, with the potential for exposure to the mercury in the event of breakage; moreover, some UV-C sources can produce ozone, a harmful indoor pollutant (Claus, 2021).

A distinctive application is the use of upper-room UV-C germicidal irradiation (UVGI), a means of inactivating aerosolized virus particles by irradiating air handling ducts or the upper zone of an occupied room (SAGE-EMG, 2020).

Public Health England have assessed a number of UV-C products markets for home use disinfection and concluded that many commercial devices were not effective, and some were potentially hazardous to users (Khazova et al 2021). They also cautioned against the inappropriate use of UV-C as direct exposure of eyes and skin has been associated with health effects. If UV-C disinfection devices are used as a mitigation

measure for preventing viral spread in indoor environments, it is recommended that their efficacy and safety be demonstrated with relevant data. Effectiveness of disinfection depends on multiple parameters including the underlying technology, design of the device, surface area covered, whether surfaces are in direct line-of-sight, exposure time and distance between the UV-C device and the treated surface.

1.2.3: Airborne disinfection chemicals

A range of different fumigation, fogging or spraying techniques for decontaminating indoor spaces have emerged. These include the use of hydrogen peroxide, ozone, or chlorine dioxide (Otter et al 2013). Ozone generation will be considered separately (Section 1.3), but SAGE-EMG (2020 a, b) have considered the application of airborne disinfection chemicals in detail leading to HSE guidance (https://www.hse.gov.uk/coronavirus/disinfecting-premises-during-coronavirus-outbreak.htm) In summary, while there is evidence that these agents may inactivate harmful pathogens, careful consideration needs to be given to:

- The ability to exclude all persons from the disinfection area to prevent exposure to toxic fumigants
- The requirement for full operator protection and training
- Sealing the area to prevent escape of toxic fumigants to occupied areas, and to retain effective concentrations of the fumigant during the disinfecting process
- Potential for damage to fixtures and fittings, including electrical equipment
- The persistent retention of residual fumigant for extended periods of time after cessation of fumigation, even in well-ventilated spaces such as containment laboratories (Beswick et al. 2011)

Evidence for efficacy against SARS-CoV-2 is limited for hydrogen peroxide or chlorine dioxide, but Beswick et al. 2011 found both agents were highly effective against another enveloped virus (vaccinia). Hydrogen peroxide is toxic by inhalation, ingestion and by skin or eye contact and it has a low Workplace Exposure Limit (WEL) of 1 ppm (long term exposure limit, LTEL 8h) or 2 ppm (short term exposure limit, STEL 15 minute). Chlorine dioxide is toxic by inhalation, ingestion and skin/eye irritation, with a low WEL of 0.1 ppm (LTEL 8h) and 0.3 ppm (STEL 15 minute). Moreover, it should be noted that WEL are established for workplace scenarios i.e. typically settings with an adult workforce rather than children. The systems reviewed by SAGE-EMG (2020) typically generate 100-800 ppm hydrogen peroxide or use 2% chlorine dioxide (Beswick et al 2021), highlighting the critical challenge of ensuring highly effective control and removal of fumigant residues. Indeed, Siegel (2016) observes that any device which introduces compounds into indoor air cannot be considered an air cleaning device, for the burden of harms could outweigh their potential benefits.

1.3 Ozone disinfection

This section considers the available evidence on the safety, efficacy, and feasibility of ozone (O_3) disinfection with reference to educational settings. TAG-E identifies concern with respect to all three aspects of ozone disinfection. Moreover the evidence

base pertaining to use of ozone disinfection within educational settings is itself limited and therefore insights from other comparable indoor environments are considered where appropriate. This report considers ozone disinfection through the generation of ozone *in situ* by devices intended to disinfect an indoor space and potentially its catalytic destruction at the end of a disinfection cycle.

1.3.1 Safety of ozone

Key points

- Ozone is a highly reactive gas which is harmful to human health at low concentrations
- Impacts on human health from indoor ozone can be aggravated by underlying health conditions (e.g. asthma, respiratory infections)
- Ozone is highly reactive, damaging substrates integral or common in educational settings
- Ozone reactions with common or integral substrates in educational settings can create an array of harmful pollutants

Ozone (O_3) is a colourless, highly reactive oxygen gas which is 1.6 × denser than air (https://www.hse.gov.uk/pubns/eh38.pdf). Ozone is formed through natural processes, as a pollutant, and for specific applications, including disinfection. A general principle regarding ozone is stated by the US EPA: *good up high, bad nearby* (https://www.epa.gov/sites/default/files/documents/gooduphigh.pdf) recognizing that stratospheric ozone is important for the Earth system while low-level ozone is harmful. The indoor penetration of outdoor low-level ozone is an established concern for some school settings, with some establishments exceeding WHO recommended limits (Salonen et al 2018).

Ozone is an irritant gas. The effects of exposure are predominantly respiratory, but adverse effects on the cardiovascular system have also been reported (https://www.gov.uk/government/publications/health-matters-air-pollution/health-matters-air-pollution). There is a wide variation in individuals' sensitivity to the effects of ozone; children, older people and people with respiratory conditions are at a greater risk of symptoms. Potential harms for child health following ozone exposure have been established for decades (e.g. Zwick et al. 1991; Berry et al 1991; Kinney et al 1996; Gent et al. 2003). People with asthma may find they need to use their reliever inhaler more often (Pepper et al 2020).

The Committee on the Medical Effects of Air Pollutants (COMEAP) examined population based epidemiological studies and concluded that there is sufficient evidence of adverse effects of short-term exposure to ambient outdoor concentrations of ozone for all-cause mortality and for respiratory hospital admissions (COMEAP 2015). While the evidence for cardiovascular hospital admissions was not as strong, they still felt it sufficient to be included in their quantification of the short-term effects of ozone.

It is important to appreciate that this review considered studies relating to the general population rather than susceptible groups or individuals. In panel studies, ozone has been associated with asthma exacerbation with increased symptoms of cough, wheeze and chest pain, as well as measured decreases in lung function (Li et al. 2012, Schachter et al 2016, Samoli et al 2017). Human clinical studies where individuals are exposed in a controlled setting have also shown increased respiratory symptoms and decreased lung function (Adams 2002, Adams 2003, Rohr 2018). While responses among individuals vary considerably, effects from short-term exposure have been noted at ozone levels as low as 80 ppb (approx. 170 µg/m^3) (Adams 2002)

The current UK Air Quality Objective for ozone is 100 µg/m^3 measured as an 8 hour mean, not to be exceeded more than 10 times a year. This is the same as the recommended WHO air quality guideline. In addition, the UK also issues air pollution alerts and for ozone the public should be informed when hourly levels are above an 'information threshold' of 180 µg/m^3 for 1 hour or an 'alert threshold' of 240 µg/m3 for 1 hour. There is currently no convincing evidence of a threshold for short-term exposure to ozone (COMEAP 2015). This means that there is no safe level of exposure and some individuals may experience adverse effects at concentrations below current UK and WHO guidelines.

There is surprisingly little information on ozone concentrations indoors. A review of published literature reported that ozone concentrations in schools and office settings were typically well below the WHO air quality guideline value of 100 µg/m^3 but that there was a large range of reported concentrations including cases where indoor levels exceeded this value (Salonen et al 2018). The main source of ozone was from outdoor air, but significant indoor sources include ozone from printers, photocopiers and cleaning products.

In order for any ozone cleaning device to be considered safe for use indoors, it is important that residual ozone concentrations are below current health-based ambient air guidelines. Application of workplace guidelines, such as the HSE short term workplace exposure limit (WEL) of 0.2ppm (200 ppb or 428 µg/m^3) averaged over a 15-minute period is not recommended for children and teachers. Workplace exposure limits are designed for people exposed to ozone in the course of their work and are not necessarily protective of children and susceptible individuals.

Currently neither the UK nor WHO have published an indoor air quality guideline for ozone. Health Canada recommends a residential maximum exposure limit of 40 µg/m3 (approx. 20 ppb) based on an 8-hour averaging time (https://www.canada.ca/en/health-canada/services/publications/healthy-living/residential-indoor-air-quality-guideline-ozone.html). This is half the No Observed Adverse Exposure Level (NOAEL) derived from a chamber study which reported no statistically significant effects at 40 ppb (Adams 2002).

Two principal categories of hazard are identified for ozone, firstly the impacts of ozone itself on humans and the indoor environment, and the creation of harmful secondary pollutants.

For ozone itself, within the UK, ozone has a 15 minute workplace exposure limit of 0.2 ppm (https://www.hse.gov.uk/pubns/eh38.pdf) requiring a substantial package of control measures and mitigations for safe use. It is emphasized ozone disinfection systems typically generate ozone at considerable excess of these levels (Morrison et al. 2021). Again, the WEL should be interpreted conservatively as educational settings will have different demographics of risk compared to industrial workplaces. The HSE (https://www.hse.gov.uk/pubns/eh38.pdf) summarizes "*the adverse health effects of ozone exposure as occurring at the sites of initial contact: the respiratory tract (nose, throat and airways), the lungs, and at higher concentrations, the eyes. The principal health effects are produced by irritation of and damage to the small airways of the lung. However, people have considerable variation in sensitivity. Uncontrolled exposure to relatively high levels of ozone could lead to more severe health effects, including lung damage. At the levels of exposure likely to be normally found in the workplace the main concern is irritation of the (upper) airways, characterised by coughing and a feeling of tightness in the chest."*

Furthermore, the US EPA does not recommend the use of ozone devices for air cleaning (https://www.epa.gov/indoor-air-quality-iaq/ozone-generators-are-sold-air-cleaners) citing health impacts following ozone exposure (decreases in lung function, aggravation of asthma, throat irritation and cough, chest pain and shortness of breath, inflammation of lung tissue and higher susceptibility to respiratory infection). US EPA identifies these health impacts can be aggravated in certain situations (increased ozone concentration or duration of exposure, activities raising breathing rate, certain pre-existing lung diseases such as asthma). Considering the increased potential for harms on individuals with underlying respiratory conditions, educational establishments will need to consider the greater risk for these individuals. These would include the operators of devices, for example through occupational health monitoring, and those at risk of inadvertent exposure.

The US EPA (2020) has produced an integrated science assessment for ozone and its impacts on human health and the environment which is exhaustive in scope and detail.

A strategy to reduce potential exposure to ozone generated during disinfection processes would be to exclude all occupants and remove sensitive items from the disinfection zone during the generation of ozone, however this depends on (i) ensuring the complete security of the space to prevent intrusion and protecting operators tasked with managing the ozone disinfection process (ii) ensuring ozone does not escape through natural or mechanical ventilation to neighbouring indoor environments and (iii) assured removal of ozone before the space is reoccupied. The consequence of failure to assure all three mitigations would be exposure to significant quantities of ozone during or after the disinfection process. Since ozone is a gas, deployed at high concentrations for disinfection, the potential for diffusion to other indoor spaces through gaps in doors etc. to contaminate other indoor spaces beyond the disinfection zone is highlighted. Furthermore, within educational settings, the type of rooms to be disinfected will vary considerably in size, geometry, and ventilation rate. Assurance that virucidal concentrations of ozone are generated as well as removed catalytically must take the form of accurate measurements of ozone concentration, rather than

time-based assumptions. Ozone sensors for this purpose require sensitivity across a broad dynamic range and regular recalibration (high confidence).

Furthermore, the reactions of ozone with a diverse range of compounds within the indoor environment results in the formation of secondary pollutants. Critically, any process intended to remove ozone itself will not target the products of its reactions created while ozone is present at high concentrations during the disinfection process (e.g. Poppendieck et al 2007). The sources of the reactants summarized in a review by Wechsler (2006 and references therein) are extensive within educational settings. These include occupants and their secreted skin oils or personal hygiene products, soft wood surfaces, carpets and carpet backing, linoleum and linseed- or latex- based paints, cleaning products, natural rubber, photocopier toner and printed papers, styrene polymers, soiled clothing or fabrics, ventilation ducts and liners, “urban grime”, perfumes and oils, and other emissions from the indoor environment. Collectively, their reactants include styrenes, polycyclic aromatic hydrocarbons, isoprene, terpenes, unsaturated fatty acids, limonene, nitric oxide, squalene and alpha-pinene. Secondary organic aerosols of particular concern produced from these reactions include formaldehyde, oxidized polyalicyclic hydrocarbons, hexanal, methacrolein, methyl vinyl ketone. Ultrafine particle formation as a result of ozone reacting with terpenes (which are found in consumer products such as air fresheners, surface cleaners, and perfumes) has been reported in the scientific literature (Waring and Siegal, 2011). These harmful products are stable and may be persistent within the indoor environment, but a range of relative short lived products which can persist for long enough to be respired (Wechsler, 2006 and references therein). For example formaldehyde can cause irritation of the mucous membranes and respiratory tract. Sore throat, rhinitis, nasal irritation, bronchospasm and breathlessness are common features following exposure by inhalation (PHE https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/582279/Formaldehyde__toxicological_overview.pdf) but, as with ozone, there is a wide range of individual variation to exposure. Some individuals report subjective sensory irritation (such as headache and nausea) at levels below those thought to cause health effects. There are reports of airway sensitisation following formaldehyde exposure although there is still some uncertainty around whether formaldehyde can trigger an allergic response.

Within the classroom environment, Fischer et al (2013) identified sebum deposited from the skin of children and staff as a major sink for ozone. They conclude: “*It is unavoidable that humans in the presence of ozone give rise to reaction products that may influence health in the form of pulmonary and dermatological allergic reactions. The only way of avoiding this exposure indoors is by reducing the O_3 concentration.”* Liu et al (2021) affirm the importance of off-body skin lipids on indoor ozone reactions.

Meanwhile, the potential for interactions with the additional use of cleaning products should be noted; for example Nørgaard et al (2014) found terpene emissions from floor cleaning products reacted with indoor ozone to create formaldehyde, 4-acetyl-1-methylcyclohexene, 3-isopropenyl-6-oxo-heptanal, 6-methyl-5-heptene-2-one, 4-oxopentanal, and dihydrocarvone. Substitution of the cleaning products ameliorated the creation of these secondary organic aerosols, indicating that the choice of routine

cleaning agent may need reconsideration if the same space is subject to ozone disinfection. Studies in aircraft have reported ozone reacting with cleaning and scenting agents to form formaldehyde and other aldehydes. These reactions have been reported at ozone concentrations as low as 60-70 ppb (Wisthaler et al 2005, Weschler et al 2007). Hubbard et al (2005) found similar interactions between cleaning products and ozone generated within residential spaces, concluding that exposure to secondary organic aerosols can be reduced by avoiding the deliberate production of ozone indoors, especially if terpene-based cleaning products are used within those locations. Reactant dynamics within "hidden" or interstitial spaces (e.g. false ceilings) is less well studied (Young et al 2019), with the potential for reactions to occur between ozone and substrates beyond the reach of cleaning operatives.
Therefore, it may be possible to remove some sources of ozone reactants from a space to be disinfected, but the list of sources is extensive, posing resource implications for their disinfection as required, and some significant sources will be integral (e.g. interior partitions, medium density fibreboard; Poppendieck et al 2007; sealants and liners for ventilation ducts; Morrison et al 2021) to the classroom environment.

1.3.2 Efficacy of SARS-CoV-2 inactivation by ozone

The ability of ozone to control microbial contamination has long been established (e.g. Postgate, 1999) and this property of ozone has been used in a variety of settings, for example water disinfection (e.g. Gray, 2014). Ozone disinfection has been considered in different contexts during the pandemic (e.g. disinfection of personal protective equipment; Dennis et al 2020) and a number of articles highlight the potential application of ozone against SARS-CoV-2 (e.g. Morrison, et al 2021; Tiazoui, 2020; Bayarri et al 2021). To our knowledge, assessments of ozone efficacy are proof of principle studies at small scale (e.g. in Plexiglas boxes, Percivalle et al 2021 Clavo et al 2021; or use safe surrogates of SARS-CoV-2 deposited on substrates exposed to ozone from generators). While these represent necessary compromises in the interests of safety, it is notable that most studies do not demonstrate the 4 $\log_{10}$ reduction in virus titres that would result in a 'pass' of EN14476. Furthermore, most do not include an assessment of disinfection efficacy in the presence of a soil load.

For practical reasons, the evidence base relating to the effective use of ozone against SARS-CoV-2 at the room scale is limited. Franke et al (2021) tested the ability of an automated ozone disinfection system to inactivate bovine coronavirus and Phi6 bacteriophage suspensions on ceramic tiles, stainless steel and furniture boards within a 6 m^3 test room. Effective disinfection was reported (> 4 $\log_{10}$) within a 60 minute treatment of ca. 80-90 ppm ozone. Since ozone is a gas, and inactivation of other viruses in aerosols is demonstrated (summarized in Bayarri et al 2021) it is reasonable to anticipate ozone may inactivate SARS-CoV-2 in aerosols, but no evidence for the effective inactivation of aerosolized SARS-CoV-2 has been found.

Within the European Union, products making claim for ozone as a disinfectant must meet the requirements of the biocidal products regulation (BPR 528/2012), a requirement which has been copied into GB law (https://www.hse.gov.uk/biocides/).

Ozone generated from oxygen is listed as an active substance in GB and NI under the BPR, but in the most recent (30th of July 2021) listing, no products using ozone were authorised under the BPR in GB and NI (https://www.hse.gov.uk/biocides/uk-authorised-biocidal-products.htm, accessed 16th September 2021).

1.4 Assessing the effectiveness of SARS CoV-2 disinfection methods (including ozone machines) in educational settings?

It is important to distinguish between two potential modes of employment of cleaning and disinfection agents, including ozone disinfection:

Scenario A: Routine cleaning for infection prevention
Scenario B: Additional cleaning in response to an outbreak.

Routine cleaning and disinfection helps address any remaining risks of SARS-CoV-2 infection arising from contact with contaminated surfaces, as well as risks of infection by other agents potentially present on surfaces in educational settings (e.g. influenza, rhinoviruses, noroviruses). The effect of cycles of routine cleaning and disinfection was considered in the QMRA presented above (Figure 2, Pitol & Julian, 2021). The risk-reducing effect of cleaning once or twice a day (0700h, 1200h) was greatest under conditions of low community prevalence, with limited impact upon high touch surfaces at high prevalence, whereas hand hygiene had the greatest predicted impact under all conditions. For routine disinfection, ozone generators are unlikely to be feasible for three reasons. Firstly, the disinfection time per room is significant (>1h to 16h, Poppendieck et al 2007) meaning a high ratio of devices per establishment would be required for deployment overnight, accumulating the number of units required, each at significant cost per unit. Secondly, while the ozone generators may disinfect a space, they would not replace the need to physically clean the space for other reasons, and the requirement to remove and independently disinfect incompatible surfaces would incur considerable staff resource. Thirdly, with increased frequency and range of use of ozone generators, the potential for adverse events and deterioration of sensitive surfaces following regular exposures to ozone is enhanced.

Initiation of specific measures for “deep” cleaning or disinfection in the wake of a suspected outbreak is reactive to an ascertained risk of transmission. However, the evidence base for deep cleaning as an effective mitigation for SARS-CoV-2 transmission in educational or communities is highly limited, leading to questions of its utility (e.g. Lewis et al 2021) and recognition of its costs to educational providers (Burki et al 2020). To TAG-E’s knowledge there are no published systematic evaluations of deep cleaning as a mitigation (high confidence).

Furthermore, the time required for the development of symptoms (median incubation period: 5.1 days, McAloon et al 2020) or test positivity on asymptomatic testing plus targeting of the intervention means that (i) aerosolized virus will be spontaneously inactivated through decay (e.g. 1.1h half-life in experimental aerosols; Van Doremalen, et al 2020), deposited onto surfaces and/or diluted to the external atmosphere (ii) virus deposited on surfaces will have decayed considerably over time, as detailed above. The potential benefits of “deep” cleaning are therefore highly limited to mitigating

sustained contamination within the same environment (high confidence). As assessed above, surface-mediated transmission of SARS-CoV-2 appears a minor component of transmission. This is in contrast to the paramount importance of transmission pathways requiring in-person or proximal exposure (direct contact, droplet/close range aerosol, long range aerosol).

In either scenario, the introduction of ozone disinfection devices to educational establishments would require detailed risk control plans, with specific measures to monitor and mitigate the potential harms arising from exposure to ozone or secondary pollutants, and to contain and manage adverse events. The performance of devices would also require validation. Educational settings are not ozone-free zones thanks to the penetration of ozone from outside and release from other processes (Salonen et al 2018) but the use of ozone disinfection devices introduces a new category of hazard, with the potential of additive impacts on harms arising from ozone and secondary pollutant exposures already present in the classroom (Salonen et al 2018; Fischer et al 2013). Consideration to the behavioural aspects of safety culture and human factors should be given since the novelty of the solution means it presents a new range of potential harms and benefits to a sector without prior experience of the technology.

References

Adams, W.C., 2002. Comparison of chamber and face-mask 6.6-hour exposures to ozone on pulmonary function and symptoms responses. Inhalation Toxicology, 14(7), pp.745-764.

Adams, W.C., 2003. Relation of pulmonary responses induced by 6.6-h exposures to 0.08 ppm ozone and 2-h exposures to 0.30 ppm ozone via chamber and face-mask inhalation. Inhalation toxicology, 15(8), pp.745-759.

Barclay, L., Park, G.W., Vega, E., Hall, A., Parashar, U., Vinjé, J. and Lopman, B., 2014. Infection control for norovirus. Clinical microbiology and infection, 20(8), pp.731-740.

Barker, J., Vipond, I.B. and Bloomfield, S.F., 2004. Effects of cleaning and disinfection in reducing the spread of Norovirus contamination via environmental surfaces. Journal of hospital infection, 58(1), pp.42-49.

Bayarri, B., Cruz-Alcalde, A., Lopez-Vinent, N., Micó, M.M. and Sans, C., 2021. Can ozone inactivate SARS-CoV-2? A review of mechanisms and performance on viruses. Journal of hazardous materials, p.125658.

Berry, M., Lioy, P.J., Gelperin, K., Buckler, G. and Klotz, J., 1991. Accumulated exposure to ozone and measurement of health effects in children and counselors at two summer camps. Environmental research, 54(2), pp.135-150.

Beswick, A.J., Farrant, J., Makison, C., Gawn, J., Frost, G., Crook, B. and Pride, J., 2011. Comparison of multiple systems for laboratory whole room fumigation. Applied Biosafety, 16(3), pp.139-157.

Biasin, M., Bianco, A., Pareschi, G., Cavalleri, A., Cavatorta, C., Fenizia, C., Galli, P., Lessio, L., Lualdi, M., Tombetti, E. and Ambrosi, A., 2021. UV-C irradiation is highly effective in inactivating SARS-CoV-2 replication. Scientific Reports, 11(1), pp.1-7.

Binder RA, Alarja NA, Robie ER, Kochek KE, Xiu L, Rocha-Melogno L, et al. Environmental and aerosolized severe acute respiratory syndrome coronavirus 2 among hospitalized coronavirus disease 2019 patients. J Infect Dis. 2020;222(11):1798-806. Available from: https://doi.org/10.1093/infdis/jiaa575.

Bueckert, M., Gupta, R., Gupta, A., Garg, M. and Mazumder, A., 2020. Infectivity of SARS-CoV-2 and other coronaviruses on dry surfaces: potential for indirect transmission. Materials, 13(22), p.5211.

Burki, T.K., 2020. COVID-19: consequences for higher education. The Lancet Oncology, 21(6), p.758.

Chen, P.Z., Bobrovitz, N., Premji, Z., Koopmans, M., Fisman, D.N. and Gu, F.X., 2021. Heterogeneity in transmissibility and shedding SARS-CoV-2 via droplets and aerosols. Elife, 10, p.e65774.

Chin, A.W., Chu, J.T., Perera, M.R., Hui, K.P., Yen, H.L., Chan, M.C., Peiris, M. and Poon, L.L., 2020. Stability of SARS-CoV-2 in different environmental conditions. The Lancet Microbe, 1(1), p.e10.

Chu, D.K., Akl, E.A., Duda, S., Solo, K., Yaacoub, S., Schünemann, H.J., El-harakeh, A., Bognanni, A., Lotfi, T., Loeb, M. and Hajizadeh, A., 2020. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. The lancet, 395(10242), pp.1973-1987.

Claus, H., 2021. Ozone generation by ultraviolet lamps. Photochemistry and Photobiology.

Clavo, B., Córdoba-Lanús, E., Rodríguez-Esparragón, F., Cazorla-Rivero, S.E., García-Pérez, O., Piñero, J.E., Villar, J., Blanco, A., Torres-Ascensión, C., Martín-Barrasa, J.L. and González-Martin, J.M., 2020. Effects of ozone treatment on personal protective equipment contaminated with SARS-CoV-2. Antioxidants, 9(12), p.1222

Colaneri M, Seminari E, Novati S, Asperges E, Biscarini S, Piralla A, et al. 2020 Severe acute respiratory syndrome coronavirus 2 RNA contamination of inanimate surfaces and virus viability in a health care emergency unit. Clin Microbiol Infect.;26(8):1094.e1-.e5.

COMEAP, 2015 COMEAP: quantification of mortality and hospital admissions associated with ground-level ozone. A report by the Committee on the Medical Effects of Air Pollutants (COMEAP). https://www.gov.uk/government/publications/comeap-quantification-of-mortality-and-hospital-admissions-associated-with-ground-level-ozone

Dennis, R., Pourdeyhimi, B., Cashion, A., Emanuel, S. and Hubbard, D., 2020. Durability of disposable N95 mask material when exposed to improvised ozone gas disinfection. The Journal of Science and Medicine, 2(SAND-2020-4308J).

Döhla M, Wilbring G, Schulte B, Kümmerer BM, Diegmann C, Sib E, et al. SARS-CoV-2 in environmental samples of quarantined households. medRxiv. 2020. Available from: https://www.medrxiv.org/content/medrxiv/early/2020/06/02/2020.05.28.20114041.full.pdf. PREPRINT

Fischer, A., Ljungström, E. and Langer, S., 2013. Ozone removal by occupants in a classroom. Atmospheric environment, 81, pp.11-17.

Franke, G., Knobling, B., Brill, F.H., Becker, B., Klupp, E.M., Campos, C.B., Pfefferle, S., Lütgehetmann, M. and Knobloch, J.K., 2021. An automated room disinfection system using ozone is highly active against surrogates for SARS-CoV-2. Journal of Hospital Infection, 112, pp.108-113.

Gent, J.F., Triche, E.W., Holford, T.R., Belanger, K., Bracken, M.B., Beckett, W.S. and Leaderer, B.P., 2003. Association of low-level ozone and fine particles with respiratory symptoms in children with asthma. Jama, 290(14), pp.1859-1867.

Goldman, E., 2020. Exaggerated risk of transmission of COVID-19 by fomites. The Lancet Infectious Diseases, 20(8), pp.892-893.

Goldman, E., 2021. SARS Wars: the fomites strike back. Applied and Environmental Microbiology, pp.AEM-00653.

Gray, N.F., 2014. Ozone disinfection. In Microbiology of Waterborne Diseases (pp. 599-615). Academic press.

Hirose, R., Ikegaya, H., Naito, Y., Watanabe, N., Yoshida, T., Bandou, R., Daidoji, T., Itoh, Y. and Nakaya, T., 2020. Survival of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza virus on human skin: importance of hand hygiene in coronavirus disease 2019 (COVID-19). Clinical infectious diseases: an official publication of the Infectious Diseases Society of America.

Hubbard, H.F., Coleman, B.K., Sarwar, G. and Corsi, R.L., 2005. Effects of an ozone-generating air purifier on indoor secondary particles in three residential dwellings. Indoor air, 15(6), pp.432-444.

Kampf, G., Todt, D., Pfaender, S. and Steinmann, E., 2020. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. Journal of hospital infection, 104(3), pp.246-251.

Kampf, G., Pfaender, S., Goldman, E. and Steinmann, E., 2021. SARS-CoV-2 Detection Rates from Surface Samples Do Not Implicate Public Surfaces as Relevant Sources for Transmission. Hygiene, 1(1), pp.24-40.

Khazova, M., Johnstone, L., Naldzhiev, D. and O'Hagan, J.B., 2021. Survey of Home-Use UV Disinfection Products. Photochemistry and Photobiology.

Kinney, P.L., Thurston, G.D. and Raizenne, M., 1996. The effects of ambient ozone on lung function in children: a reanalysis of six summer camp studies. Environmental health perspectives, 104(2), pp.170-174.

Kitagawa, H., Nomura, T., Nazmul, T., Omori, K., Shigemoto, N., Sakaguchi, T. and Ohge, H., 2021. Effectiveness of 222-nm ultraviolet light on disinfecting SARS-CoV-2 surface contamination. American journal of infection control, 49(3), pp.299-301.

Lai, M.Y., Cheng, P.K. and Lim, W.W., 2005. Survival of severe acute respiratory syndrome coronavirus. Clinical infectious diseases, 41(7), pp.e67-e71.

Leung, N.H.L. Transmissibility and transmission of respiratory viruses. Nat Rev Microbiol (2021). https://doi.org/10.1038/s41579-021-00535-6

Lewis, D., 2021. COVID-19 rarely spreads through surfaces. So why are we still deep cleaning. Nature, 590(7844), pp.26-28.

Li, S., Williams, G., Jalaludin, B. and Baker, P., 2012. Panel studies of air pollution on children’s lung function and respiratory symptoms: a literature review. Journal of Asthma, 49(9), pp.895-910.

Liu, Y., Misztal, P.K., Arata, C., Weschler, C.J., Nazaroff, W.W. and Goldstein, A.H., 2021. Observing ozone chemistry in an occupied residence. Proceedings of the National Academy of Sciences, 118(6).

Matson, M.J., Yinda, C.K., Seifert, S.N., Bushmaker, T., Fischer, R.J., van Doremalen, N., Lloyd-Smith, J.O. and Munster, V.J., 2020. Effect of environmental conditions on SARS-CoV-2 stability in human nasal mucus and sputum. Emerging infectious diseases, 26(9), p.2276.

McAloon, C.G., Collins, Á., Hunt, K., Barber, A., Byrne, A. and Butler, F., Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research. BMJ Open. 2020; 10 (8): e039652.

McCoy, K.J., DiNicola, M., Everline, C., Burgoyne, H., Reinholtz, K. and Clement, B., 2021. Europa Clipper planetary protection probabilistic risk assessment summary. Planetary and Space Science, 196, p.105139.

Mondelli MU, Colaneri M, Seminari EM, Baldanti F, Bruno R. 2021. Low risk of SARS-CoV-2 transmission by fomites in real-life conditions. Lancet Infect Dis 21:E112.

Moore G, Rickard H, Stevenson D, Aranega-Bou P, Pitman J, Crook A, et al. Detection of SARS-CoV-2 within the healthcare environment: a multi-centre study conducted during the first wave of the COVID-19 outbreak in England. J Hosp Infect. 2021 Feb;108:189-96.

Morrison, G.C., Nazaroff, W.W., Cano-Ruiz, J.A., Hodgson, A.T. and Modera, M.P., 1998. Indoor air quality impacts of ventilation ducts: ozone removal and emissions of volatile organic compounds. Journal of the Air & Waste Management Association, 48(10), pp.941-952.

Morrison, C., Atkinson, A., Zamyadi, A., Kibuye, F., McKie, M., Hogard, S., Mollica, P., Jasim, S. and Wert, E.C., 2021. Critical review and research needs of ozone applications related to virus inactivation: potential implications for SARS-CoV-2. Ozone: Science & Engineering, 43(1), pp.2-20.

Nørgaard, A.W., Kofoed-Sørensen, V., Mandin, C., Ventura, G., Mabilia, R., Perreca, E., Cattaneo, A., Spinazzè, A., Mihucz, V.G., Szigeti, T. and Kluizenaar, Y.D., 2014. Ozone-initiated terpene reaction products in five European offices: replacement of a floor cleaning agent. Environmental science & technology, 48(22), pp.13331-13339.

Onakpoya, I.J., Heneghan, C.J., Spencer, E.A., Brassey, J., Plüddemann, A., Evans, D.H., Conly, J.M. and Jefferson, T., 2021. SARS-CoV-2 and the role of fomite transmission: a systematic review. F1000Research, 10.

Ong SWX, Lee PH, Tan YK, Ling LM, Ho BCH, Ng CG, et al. Environmental contamination in a coronavirus disease 2019 (COVID-19) intensive care unit—What is the risk? Infect Control Hosp Epidemiol. 2020:1-9.

Otter, J.A., Yezli, S., Perl, T.M., Barbut, F. and French, G.L., 2013. The role of 'no-touch' automated room disinfection systems in infection prevention and control. Journal of Hospital Infection, 83(1), pp.1-13.

Pepper, J.R., Barrett, M.A., Su, J.G., Merchant, R., Henderson, K., Van Sickle, D. and Balmes, J.R., 2020. Geospatial-temporal analysis of the impact of ozone on asthma rescue inhaler use. Environment international, 136, p.105331.

Percivalle, E., Clerici, M., Cassaniti, I., Nepita, E.V., Marchese, P., Olivati, D., Catelli, C., Berri, A., Baldanti, F., Marone, P. and Bruno, R., 2021. SARS-CoV-2 viability on different surfaces after gaseous ozone treatment: a preliminary evaluation. Journal of Hospital Infection, 110, pp.33-36.

Pitol, A.K. and Julian, T.R., 2021. Community transmission of SARS-CoV-2 by surfaces: risks and risk reduction strategies. Environmental Science & Technology Letters, 8(3), pp.263-269.

Poppendieck, D., Hubbard, H., Ward, M., Weschler, C. and Corsi, R.L., 2007. Ozone reactions with indoor materials during building disinfection. Atmospheric Environment, 41(15), pp.3166-3176.

Postgate, J., 2000. Microbes and man. Cambridge university press.

Riddell, S., Goldie, S., Hill, A., Eagles, D. and Drew, T.W., 2020. The effect of temperature on persistence of SARS-CoV-2 on common surfaces. Virology journal, 17(1), pp.1-7.

Rohr, A.C., 2018. Ozone exposure and pulmonary effects in panel and human clinical studies: Considerations for design and interpretation. Journal of the Air & Waste Management Association, 68(4), pp.288-307.

SAGE 66 (2020): https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/938974/S0868_Sixty-sixth_SAGE_meeting_on_Covid-19.pdf

SAGE-EMG (2020 a) Potential application of Air Cleaning devices and personal decontamination to manage transmission of COVID-19 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/939173/S0867_EMG_Potential_application_of_air_cleaning_devices_and_personal_decontamination_to_manage_transmission_of_COVID-19.pdf

SAGE-EMG (2020 b) Application of UV disinfection, visible light, local air filtration and fumigation technologies to microbial control https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/904656/S0440_EMG_-_Application_of_UV_disinfection__visible_light__local_air_filtration_and_fumigation.pdf

SAGE-EMG & NERVTAG (2020) SARS-COV-2 TRANSMISSION ROUTES AND ENVIRONMENTS SAGE – 22 OCTOBER https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/933225/S0824_SARS-CoV-2_Transmission_routes_and_environments.pdf

Salonen, H., Salthammer, T. and Morawska, L., 2018. Human exposure to ozone in school and office indoor environments. Environment international, 119, pp.503-514.

Samoli, E., Dimakopoulou, K., Evangelopoulos, D., Rodopoulou, S., Karakatsani, A., Veneti, L., Sionidou, M., Tsolakoglou, I., Krasanaki, I., Grivas, G. and Papakosta, D., 2017. Is daily exposure to ozone associated with respiratory morbidity and lung function in a representative sample of schoolchildren? Results from a panel study in Greece. Journal of exposure science & environmental epidemiology, 27(3), pp.346-351.

Santarpia, J.L., Rivera, D.N., Herrera, V.L., Morwitzer, M.J., Creager, H.M., Santarpia, G.W., Crown, K.K., Brett-Major, D.M., Schnaubelt, E.R., Broadhurst, M.J. and Lawler, J.V., 2020. Aerosol and surface contamination of SARS-CoV-2 observed in quarantine and isolation care. Scientific reports, 10(1), pp.1-8.

Schachter, E.N., Moshier, E., Habre, R., Rohr, A., Godbold, J., Nath, A., Grunin, A., Coull, B., Koutrakis, P. and Kattan, M., 2016. Outdoor air pollution and health effects in urban children with moderate to severe asthma. Air Quality, Atmosphere & Health, 9(3), pp.251-263.

Siegel, J.A., 2016. Primary and secondary consequences of indoor air cleaners. Indoor air, 26(1), pp.88-96.

Todt, D., Meister, T.L., Tamele, B., Howes, J., Paulmann, D., Becker, B., Brill, F.H., Wind, M., Schijven, J., Heinen, N. and Kinast, V., 2021. A realistic transfer method reveals low risk of SARS-CoV-2 transmission via contaminated euro coins and banknotes. Iscience, 24(8), p.102908.

Tyan, K., Levin, A., Avalos-Pacheco, A., Plana, D., Rand, E.A., Yang, H., Maliszewski, L.E., Chylek, L.A., Atta, L., Tye, M.A. and Carmack, M.M., 2020, September. Considerations for the selection and use of disinfectants against SARS-CoV-2 in a health care setting. In Open Forum Infectious Diseases (Vol. 7, No. 9, p. ofaa396). US: Oxford University Press.

US EPA (2020) Integrated Science Assessment for Ozone and Related Photochemical Oxidants EPA/600/R-20/012 www.epa.gov/isa

Van Doremalen, N.; Bushmaker, T.; Morris, D.; Holbrook, M.G.; Gamble, A.; Williamson, B.N.; Tamin, A.; Harcourt, J.L.; Thornburg, N.J.; Gerber, S.I.; et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N. Engl. J. Med. 2020, 382, 1564–1567

Waring, M.S. and Siegel, J.A., 2011. The effect of an ion generator on indoor air quality in a residential room. Indoor Air, 21(4), pp.267-276.

Weschler, C.J., Brauer, M. and Koutrakis, P., 1992. Indoor ozone and nitrogen dioxide: A potential pathway to the generation of nitrate radicals, dinitrogen pentoxide, and nitric acid indoors. Environmental science & technology, 26(1), pp.179-184.

Weschler, C.J., 2000. Ozone in indoor environments: concentration and chemistry. Indoor air, 10(4), pp.269-288.

Weschler, C.J., 2006. Ozone's impact on public health: contributions from indoor exposures to ozone and products of ozone-initiated chemistry. Environmental health perspectives, 114(10), pp.1489-1496.

Weschler, C.J., Wisthaler, A., Cowlin, S., Tamás, G., Strøm-Tejsen, P., Hodgson, A.T., Destaillats, H., Herrington, J., Zhang, J. and Nazaroff, W.W., 2007. Ozone-initiated chemistry in an occupied simulated aircraft cabin. Environmental Science & Technology, 41(17), pp.6177-6184.

Wilson, A.M., Weir, M.H., Bloomfield, S.F., Scott, E.A. and Reynolds, K.A., 2021. Modeling COVID-19 infection risks for a single hand-to-fomite scenario and potential risk reductions offered by surface disinfection. American journal of infection control, 49(6), pp.846-848.

Wisthaler, A., Tamás, G., Wyon, D.P., Strøm-Tejsen, P., Space, D., Beauchamp, J., Hansel, A., Märk, T.D. and Weschler, C.J., 2005. Products of ozone-initiated chemistry in a simulated aircraft environment. Environmental Science & Technology, 39(13), pp.4823-4832.

Young, C.J., Zhou, S., Siegel, J.A. and Kahan, T.F., 2019. Illuminating the dark side of indoor oxidants. Environmental Science: Processes & Impacts, 21(8), pp.1229-1239.

Zhou J, Otter JA, Price JR, Cimpeanu C, Garcia DM, Kinross J, et al. Investigating SARS-CoV-2 surface and air contamination in an acute healthcare setting during the peak of the COVID-19 pandemic in London. Clin Infect Dis. 2020 Jun 2.

Zwick, H., Popp, W., Wagner, C., Reiser, K., Schmöger, J., Bock, A.N.D.R.E.A.S., Herkner, K. and Radunsky, K., 1991. Effects of ozone on the respiratory health, allergic sensitization, and cellular immune system in children. American Journal of Respiratory and Critical Care Medicine, 144(5), pp.1075-1079.