REALM PROJECT
REopening Archives, Libraries and Museums

Systematic Literature Review of SARS-CoV-2: Spread, Environmental Attenuation, Prevention, and Decontamination

Phase 3 – Gap Analysis – August 15, 2020 to November 30, 2020

Prepared for:

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Executive Summary

As libraries, archives, and museums (LAMs) work to sustain modified operations amid the continuing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, access to the latest scientific research on virus spread and durability is critical. Battelle has conducted three systematic literature reviews of SARS-CoV-2 research published in 2020 to provide LAMs with the informational support needed to make informed decisions about how to develop and implement protocols that can reduce risk of spreading the virus. The Battelle research team gathered, evaluated, and synthesized research literature published on SARS-CoV-2 as it relates to three key topics:

1. Virus spread through indoor settings
2. Virus survival and decay on material surfaces over time
3. Effective prevention and decontamination measures that are readily available in the near term

The first literature review report (Phase 1) was released on June 17, 2020, and presented a synthesis of relevant publications released through mid-May 2020 (view the Phase 1 report here). The second literature review report, released on October 14, 2020, synthesized relevant publications released from mid-May to August 14, 2020 (view the Phase 2 report here). Due to the evolving nature of scientific research on SARS-CoV-2, the third literature review report (Phase 3) was conducted to synthesize research that was published on the three key topics after the Phase 2 report, from August 15 to November 30, 2020. To be responsive to the needs of LAMs, the Phase 3 literature review emphasized recent publications that introduced new information or updated evidence (related to the three key topics) that was not already expressed in the Phase 1 or 2 literature review reports.

Using similar search terms as the Phase 1 and 2 literature reviews, Phase 3 identified relevant documents through a systematic search of four scientific databases: Scopus, Web of Science, SciTech, and MEDLINE, which were selected for their comprehensive coverage of the literature. The search results were closely scrutinized for relevance to the three key topics, resulting in a list of 440 relevant research articles considered for inclusion in the report. Ultimately, 74 relevant articles were prioritized as providing vital new information and then summarized in the report.

After reviewing the relevant, prioritized research articles identified in the Phase 3 systematic literature search, the Battelle team identified several key themes:

- SARS-CoV-2 continues to be understood to spread primarily through virus-containing water droplets expelled from infected persons from sneezes, coughs, speaking, and other respiratory activities. Evidence has also suggested that other pathways for spreading the virus may include breathing air that the virus is suspended in and touching surfaces where the virus has been deposited (sometimes called fomites), then introducing active virus into the body.
- Some factors that seem to increase spread of the virus include higher population density, increased exposure duration in indoor environments where people congregate, and exposure to bathroom environments and shared plumbing used by infected people. Limited air exchange in indoor environments is thought to increase the risk of transmission.

- As with the Phase 2 literature review, very few studies conducted novel empirical research on how long SARS-CoV-2 survives on different surfaces and materials (i.e., Key Topic #2). Instead, the scientific community's focus (in terms of this report's three key topics) seems to have prioritized study of how the virus spreads, how it can be stopped from spreading, and how to inactivate the virus. However, key studies of SARS-CoV-2 surface stability identified for this report indicated that decreased temperatures, decreased humidity, nonporous surfaces, and absence of ultraviolet (UV) light can increase virus stability on surfaces over time. One literature review of surface stability studies concluded that indirect transmission via surfaces is probable due to SARS-CoV-2's ability to persist on dry surfaces over time; however, the scientific consensus overall seems to be that contracting SARS-CoV-2 from contaminated surfaces is not the primary mode of transmission. Additionally, scientists studying the presence of SARS-CoV-2 on water and food packaging reported that neither water nor food packaging were high-risk avenues for human-to-human transmission.
- Prevention and decontamination tactics were the most common topic presented in the literature during this systematic review. As such, several options for reducing the presence of SARS-CoV-2 in environments were demonstrated to be effective, which may help LAMs reduce transmission risk among patrons, staff, and other stakeholders. Tactics found to show efficacy include (See **Table 2** in Section 4.1.3 for a full list of noted tactics):
    - Handwashing with soap for at least 20 seconds.
    - Use of 80% volume/volume (v/v) ethanol or greater than 75% v/v isopropanol-based sanitizer for at least 45 seconds. However, increased hand cleaning over time has been found to contribute to skin sensitivity and eczema.
    - Consistent mask wearing when around other people. Although homemade cloth masks seem to reduce risk, N95s and surgical masks have been demonstrated to be most effective.
    - Ventilation of indoor spaces where people congregate to circulate fresh outdoor air and the use of portable air cleaners with regularly cleaned high-efficiency particulate air (HEPA) filters.
    - Implementation of UV light treatments that avoid UV exposure risk to humans, such as low-dose far-UVC light at lower wavelengths and UV light devices that treat the upper air in indoor spaces (above where humans frequent in rooms). However, LAMs would need to consider UV light-based interventions with caution and follow guidance to avoid exposure risks to humans and collections.
    - Use of surface cleaners, including 70% ethanol (EtOH), 70% isopropanol (IPA), 0.1% hydrogen peroxide (H_2O_2), or 0.1% sodium laureth sulphate (SLS) for at least 60 seconds to decontaminate surfaces that people contact.
    - Several novel interventions needing further study, such as applications of antimicrobial surfaces and coatings for high-touch surfaces, mouthwash, nasal sprays, cleansing stations and tunnels, cold plasma, gaseous ozone, and dry fogging with an aerosolized

mixture of peroxyacetic acid and hydrogen peroxide (aPAA/HP). However, some of these interventions, such as gaseous ozone and dry fogging, may not be viable for use in LAMs due to potential for damage to collections.

In general, additional rigorous experimental research is needed to explore the impacts of diverse variables on the ability of SARS-CoV-2 to spread and persist. This includes closely evaluating the factors that impact spread and transmission in indoor settings where people gather, such as those spaces common in LAMs, to better understand what interventions should be prioritized to mitigate transmission risk. Other opportunities for additional experimentation include variables affecting mask efficacy, natural attenuation of the virus on surfaces and materials (under varying environmental factors), and safe decontamination methods to effectively reduce aerosol transmission risk in indoor settings. Relatedly, this literature review investigated findings about the spread of SARS-CoV-2, but additional research into the mechanisms of *transmission* and *contraction* of the virus, such as the minimum viral count leading to infection (i.e., the infectious dose), may provide key insight into exposure risks and prevention strategies that offer the highest impact. Such research will also help increase certainty about how long the virus remains infectious on surfaces, in the air, and by other potential means of transmission. To date, the infectious dose of this virus for humans remains unknown for all routes of exposure, according to the Department of Homeland Security's Master Question List for COVID-19 (the disease caused by SARS-CoV-2) (January 12, 2021). As these and other factors are further explored by the scientific community, LAMs will be able to refine their protocols and further reduce risk of exposure to SARS-CoV-2 for patrons, staff, and other stakeholders.

1. Introduction

The REopening Archives, Libraries, and Museums (REALM) project is conducting scientific research regarding SARS-CoV-2 and developing information, communications, and materials for LAMs as they plan to resume operations with the public. To help protect patrons, staff, and other stakeholders, LAMs that are resuming operations during the outbreak of SARS-CoV-2 require access to scientific research about how the virus can be spread through their operations. These institutions have unique operations, tactile surfaces, and a high volume of staff and patrons. Through a collaborative relationship, OCLC and Battelle merged their expertise to educate the LAMs community and best support efforts to reduce the transmission of SARS-CoV-2 and the Coronavirus Disease 2019 (COVID-19), the disease caused by SARS-CoV-2.

Battelle conducted three systematic literature reviews of research published in 2020 to provide LAMs with the informational support needed to make informed decisions about how to develop and implement protocols that can reduce risk of spreading the virus when reopening LAM facilities and resuming operations. The Battelle research team gathered, evaluated, and synthesized research literature published on SARS-CoV-2 as it relates to three research questions:

1) How could the virus spread through indoor settings?
2) How long does the virus survive on material surfaces?
3) How effective are various prevention and decontamination measures that are readily available in the near term?

Due to the evolving nature of scientific research on SARS-CoV-2, the three systematic literature reviews were scheduled sequentially, as follows:

- The first literature review report (Phase 1 – view the Phase 1 report here), released on June 17, 2020, presented a synthesis of relevant publications released through mid-May.
- The second literature review report (Phase 2 – view the Phase 2 report here), released on October 14, 2020, synthesized relevant publications released from mid-May to August 14, 2020.
- The third literature review report (Phase 3) covered relevant publications from August 15 to November 30, 2020. To be responsive to the needs of LAMs, the Phase 3 literature review focused specifically on presenting those recent publications that introduced new or updated information that was not already expressed in the Phase 1 or 2 literature review reports.

2. Methods

The literature review consisted of a systematic literature search, the methods of which are outlined in the sections that follow, including a description of the search process, relevancy review and abstraction processes, and quality control (QC) processes. The overall process is visualized in **Figure 1**.

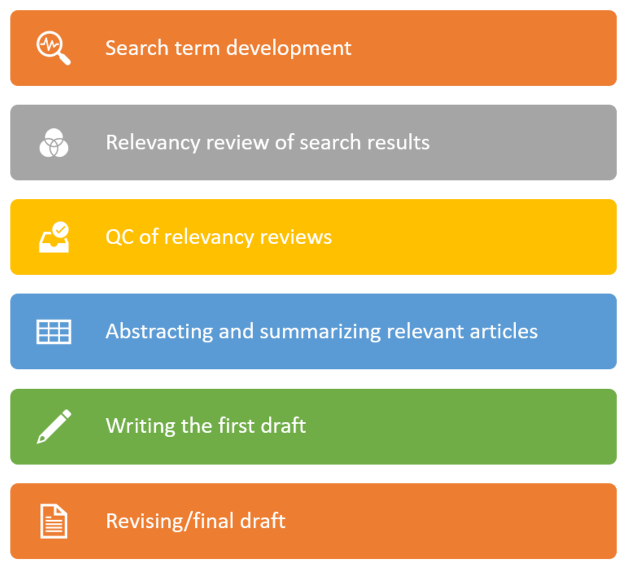

Figure 1. Systematic Literature Review Process

2.1 Systematic Literature Search

The systematic literature search was initiated after confirmation of the project objectives and research questions. It involved search string development, executing the searches, reviewing results for relevancy, abstracting key information from relevant articles, summarizing key findings, and conducting QC reviews.

2.1.1 Search String Development

To expand on the results identified in the Phase 2 literature review, the search strings used for the Phase 3 literature review involved similar syntax but were modified to collect only those articles published after the Phase 2 literature review concluded. As with the Phase 1 and 2 literature reviews, the search strings included variations of the term "SARS-CoV-2" and the research questions (e.g., spread/transmission routes, attenuation, and decontamination/prevention) using Boolean operators. The Boolean operator "AND" was used to separate SARS-CoV-2 and research question terms, while different variations of the virus name and verbs related to the research questions were grouped by category using parentheses and the Boolean operator "OR" (e.g., ["SARS-CoV-2" OR "2019-nCoV" OR "COVID-19"] AND [decontam* OR attenuat*]). Two different search strings were executed:

- One focused on decontamination and surface attenuation of the virus
- Another focused on avenues of indoor spread of the virus

The virus name "SARS-CoV-2" (and its variations, e.g., "2019-nCoV") were included in both searches to focus results on the virus of interest. The search string developed for indoor spread of the virus included an additional parenthetical to focus results on spread relevant to LAMs or other settings (e.g., "indoor" OR "aerosol").

The Phase 3 search strings included a time criterion to capture articles published from August 15, 2020, through the date of search string execution (November 30, 2020). Before officially executing the search strings (**Appendix A**), a Battelle librarian performed ad hoc testing of the search terms to confirm their continued efficacy and optimization. Note: some articles included in this report show a 2021 publication year; however, because research articles are sometimes preprinted and/or pre-released online, some articles with formal publication dates in 2021 occurred in the search results covering August 15 to November 30, 2020.

Searches were conducted on December 1, 2020, using Scopus, SciTech, Web of Science, and MEDLINE databases. These databases were selected due to their ability to provide comprehensive search capacity, being inclusive of many smaller databases. Results from the four databases across the two search strings overlapped frequently, so duplicates were removed from the search results to produce a single results list totaling 1,762 articles that were then reviewed for relevancy.

2.1.2 Relevancy Review and Abstraction Processes

Prior to beginning relevancy reviews and abstraction, Battelle staff were trained and/or re-oriented to the project, the research topics of interest, relevancy considerations, and the abstraction process. Battelle's librarian conducted an initial review of the title and abstract of articles to identify nonrelevant and potentially relevant articles (n=782). The articles identified as potentially relevant were grouped in batches and distributed to research team members, who reviewed the titles and abstracts closely to determine if the articles indicated relevancy to the literature review objectives and, for relevant articles, identified the research question(s) for which the article was most relevant.

Articles identified as relevant after these initial steps (n=440) were consolidated into a list for abstraction. However, a subset of articles (n=80) was set aside at this point as technically relevant but unlikely to be useful to this report because they were articles that provided guidelines for mitigating risk of SARS-CoV-2 infection in specific clinical settings (e.g., guidelines for reducing COVID-19 risk in optometry practices). Although these articles presented prevention and decontamination strategies, they were often too site-specific to be relevant to LAMs, often did not present new scientific search, and/or provided guidance based on literature reviews of articles that were not always restricted to SARS-CoV-2. For the remaining 360 articles, staff found the articles online and reviewed the full text to verify relevancy. For articles that were confirmed to be relevant, the research team reviewed the research question category, indicated if the articles were relevant to either of the other research questions, indicated potential subcategories for the research questions addressed by the articles (e.g., hand hygiene for a decontamination/prevention article focused on hand sanitizer), identified strengths and limitations, and investigated the content for new information not captured in prior literature reviews.

To help ensure the report provided new information (compared to Phase 1 and 2) and met the needs of LAMs, Battelle identified a list of articles (n=77) likely to present useful new information and presented an abstraction summary to OCLC that outlined the topics represented in these articles. OCLC reviewed and confirmed that Battelle would proceed with development of a report that summarized the articles and topics presented in the abstraction summary.

During the writing process, several articles were removed from inclusion in the report upon closer inspection due to concerns about the articles' relevance or quality. Additionally, an important resource considered in the literature review was the US Department of Homeland Security's Master Question List for COVID-19 (caused by SARS-CoV-2), a literature review updated on a weekly basis to provide up-to-date findings and guidance (note: the latest version available at approximately the same time that report writing commenced was the January 12, 2021 edition). Battelle cross-checked the systematic search results against the "Master Question List" (MQL) and supplemented the relevant results list with any useful new articles found in the MQL. Ultimately, after articles were removed or deleted from the inclusion list, 74 relevant articles were presented in the report, in addition to the MQL (See **Table 1** below for a summary of the number of articles under consideration at different phases of the systematic search process). Battelle synthesized the findings of these documents in the Phase 3 literature review report. In addition, an EndNote database was created to house reference information for all relevant articles captured during this review, which was exported to Excel spreadsheet format. Additionally, a full reference list, including clickable links to the publisher websites, is included at the conclusion of this report.

Table 1. Summary of Article Count

Process Step	Articles Under Consideration After Process Step
Database Searches	1,762
Initial Relevancy Review by Battelle Library	782
Relevancy Reviews	440
Abstraction Summary	77*
Writing and Additional Reference Reviews (e.g., DHS Master Question List)	74*
Final	**75****
*Count excludes 80 articles identified as technically relevant but too focused on specific clinical settings to contribute meaningfully to the literature review results. **Includes DHS Master Question List	

2.1.3 Inclusion/Exclusion Criteria

To be considered relevant for the literature review, articles needed to be written in or translated to English, include information specific to SARS-CoV-2 (or, in some cases, make a strong technical argument for using other analogous methods), and address at least one of the three research questions. Published scholarly peer-reviewed research was prioritized, but other literature meeting the previously stated criteria was also included, such as “preprints,” letters to the editor, reports, and “articles in press.” Additionally, articles had to be published after the search string execution dates for the Phase 2 literature review (i.e., August 14, 2020) and before search string execution for the Phase 3 literature review on December 1, 2020.

Articles published before or after the search period, in languages other than English, not about SARS-CoV-2 (or a strong rationale for analogous methods), or that did not address at least one of the three research questions were excluded from the literature review. Literature reviews and reports were scrutinized closely to ascertain what findings were developed from SARS-CoV-2 research and what arose from research of other coronaviruses (e.g., SARS-CoV-1 and Middle East Respiratory Syndrome [MERS]). As mentioned above, articles that focused on providing guidance to clinical specialties for mitigating SARS-CoV-2 risk were categorized as relevant but were not considered for the report.

2.1.4 Quality Control Process

Quality control (QC) processes designed to verify if articles were appropriately identified as nonrelevant and relevant during relevancy reviews involved Battelle staff performing QC at three levels:

- The first level involved reviewing the initial relevancy review conducted by Battelle’s librarian to ensure articles were not excluded unnecessarily. Articles identified as nonrelevant by the librarian were grouped in batches, and QC staff randomly selected 20% of the articles from each batch to review the titles and abstracts and verify the relevancy determinations. Instances of disagreement were reviewed and reconciled by the project lead.
- The second level occurred after the second relevancy review step conducted by the full research team. QC staff reviewed batches of articles and randomly selected 20% of the articles to review the titles and abstracts and verify the relevancy determinations. If inaccuracies were identified, QC staff conducted a full review of the articles marked nonrelevant in the abstractor’s batch and corrected determinations as needed, ensuring that relevant articles were not excluded unnecessarily.
- The third level occurred during the abstraction and summarizing stage, during which staff reviewed the full text of articles to confirm relevancy. Any articles that proved nonrelevant during this review were excluded.

3. Findings

The Phase 3 literature review explored the findings from 74 research articles. Findings from these articles were synthesized and presented in the following sections according to research topic:

1. Virus spread through indoor settings
2. Virus survival and decay on material surfaces over time
3. Effective prevention and decontamination measures that are readily available in the near term

3.1 Spread of SARS-CoV-2 through Indoor Settings

According to the Department of Homeland Security (DHS) Science and Technology Directorate (2021), SARS-CoV-2 is easily spread between people in close contact to one another and through aerosol transmission. The transmission of SARS-CoV-2 by asymptomatic and presymptomatic individuals has played a significant role in the growing number of COVID-19 cases (DHS Science and Technology Directorate, 2021). SARS-CoV-2 may be spread by vocalizations and exhalations in indoor settings (DHS Science and Technology Directorate, 2021). Studies have found that people who tested positive for SARS-CoV-2 infection were more likely to go to an office or school setting (Fisher, Olson, et al., 2020) or a restaurant (Fisher, Tenforde, et al., 2020) prior to testing positive. Additionally, SARS-CoV-2 clusters have been largely linked to large indoor gatherings (DHS Science and Technology Directorate, 2021). Accordingly, recent research on the spread of SARS-CoV-2 has focused on spread in the built environment, including through plumbing and drainage systems and heating, ventilation, and air-conditioning (HVAC) systems.

Key Findings

- There is an increased risk of transmission of SARS-CoV-2 within indoor environments where infected persons are present.
- Density within the built environment as well as proximity and duration of exposure to infected persons play key roles in SARS-CoV-2 spread.
- SARS-CoV-2 may spread through shared plumbing and draining systems.
- Inadequate or inefficient HVAC systems can contribute to the spread of SARS-CoV-2, particularly when there is limited air exchange.

3.1.1 Built Environment Considerations

The built environment can significantly impact SARS-CoV-2 transmission by influencing other factors such as population density and ability to social distance. Seidlein et al. (2020) conducted a systematic review to study how the built environment leads to crowding and is associated with increased COVID-19 infections. They looked at the US prison system, worker dormitories in Singapore, and informal urban settlements (i.e., slum areas) in places like southern Asia, South America, and sub-Saharan Africa. They reported that there were more COVID-19 infections in these populations than the general population due in part to large numbers of people living in close quarters. These instances of densely packed populations along with inadequate sanitation and disinfection measures help support rapid transmission of SARS-CoV-2.

Huang et al. (2020) examined the relationship between characteristics of the built environment and COVID-19 transmission risk in Hong Kong. The built environment characteristics they studied included nodal accessibility, population density, private residential density, commercial density, green space density, building height, transport facility density, land-use diversity, and sky view (note: sky view is based on the ratio of visible sky with obstructions to that without obstructions). For risk, they looked at case density (the number of confirmed cases per 1,000 people over a specified period), and venue density (the number of venues or buildings visited by confirmed cases). They found that private residential density, transport facilities density, and building height were all significantly positively associated with case density, meaning that as they increase, COVID-19 risk increased as well. Nodal accessibility, private residential density, green space density, and commercial density were all significantly positively associated with venue density, meaning that as they increased the number of establishments visited, the number of confirmed cases increased. Conversely, population density and sky view were significantly negatively associated with venue density. Overall, their findings show that there were more confirmed cases in areas with more densely built environments.

3.1.2 Spread in Indoor Settings

Indoor settings, like retail establishments and office spaces, tend to have reduced airflow and less space available to socially distance in comparison to outdoor settings, which can increase the risk of SARS-CoV-2 transmission. Harrichandra et al. (2020) estimated the risk of airborne SARS-CoV-2 infections in New York City nail salons using five potential exposure scenarios based on estimated outdoor flow rates. In the scenarios, there was either an infected employee or infected customer who was in a salon for varying amounts of time (ranging from 30 minutes to eight hours). The risk for exposure in the different scenarios were created based on estimated total outdoor flow rates—an equation based on V_O = outdoor airflow rate per person (m^3/s), N = CO_2 generation rate per person (0.0000052 m^3/s), C_S = CO_2 average concentration in the space (ppm), and C_O = CO_2 concentration in outdoor air (410 ppm)—in 12 New York City salons of various sizes (85.5 – 427.6m^3). The total outdoor flow rate was calculated by multiplying the outdoor flow rate per person (m^3/s-person) with the number of employees and customers. If employees or customers were wearing face masks, researchers took this into account in their calculations using a value of 60% reduction in viral transmission. They found that the average risk of airborne transmission across all salons and exposure scenarios when not wearing face masks was 24.77%. Wearing a face mask reduced the average infection transmission risk to 7.30%.

Marshall et al. (2020) examined how environmental monitoring could be used as a tool to detect asymptomatic and presymptomatic spreaders of SARS-CoV-2 in workplace settings. Nine workplaces in Europe and the United States conducted two rounds of COVID-19 tests on employees and daily testing of high-frequency touchpoints in the workplace (e.g., floors, door handles, railings, computer accessories) across a two-week period. Findings showed that the presence of SARS-CoV-2 on workplace surfaces was associated with the presence of asymptomatic spreaders of COVID-19. Additionally, locations which found SARS-CoV-2 on environmental surfaces had 10 times greater odds of having employees who tested positive for COVID-19 compared to locations with no positive surfaces.

The authors reported that workplaces that had recurrent positive environmental samples did identify and address deficiencies in decontamination strategies. They concluded that the study supported the utility of environmental monitoring in managing the incidence of COVID-19 in the workplace.

Buonanno et al. (2020) presented a novel, quantitative approach to assessing the infection risk of people exposed to an asymptomatic person infected with SARS-CoV-2 in indoor microenvironments (i.e., a confined indoor space in which an infected person is present such as a hospital room, gym, restaurant, or auditorium). Using a Monte Carlo method, they were able to calculate the probability of infection and individual risk for infection in prospective and retrospective assessments of the airborne transmission of SARS-CoV-2. The researchers applied their approach to four different scenarios that involved variations in room volume, ventilation, and number of exposed people. The results of the prospective assessment revealed that exposure times (i.e., duration of exposure to infected person) that guaranteed acceptable risk were limited in environments with natural ventilation and longer in environments with forced ventilation. In the retrospective assessments focused on two SARS-CoV-2 outbreaks in a restaurant in China and at a choir rehearsal in the United States, the researchers applied their approach using the boundary conditions of the simulation. Findings indicated that there was a high probability that the outbreaks occurred because of (1) reduced ventilation and volume for the restaurant and (2) high emission of the singing infected subject and high exposure times for the choir rehearsal.

Abuhegazy et al. (2020) conducted a numerical investigation of aerosol transport and surface deposition in a realistic classroom setting using computational fluid-particle dynamics (CFPD) simulations. The classroom model was 9m × 9m x 3m, large enough to allow for 2.4m distance between students. Study findings showed that a large fraction of smaller particles exited the room through the air-conditioning system. Larger particles mostly deposited on the ground, desks, and other nearby surfaces. The source location was found to influence the trajectory and deposition of aerosols; thus, mitigation strategies would need to take this into account to be effective. Glass barriers were found to reduce aerosol transmission and a significant proportion of particles exited the system when the windows were open. Though this study did not involve direct measurement of SARS-CoV-2, it provides some insight into minimizing aerosol spread of the virus in indoor settings.

Lelieveld et al. (2020) similarly modeled aerosol transmission and infection risk of COVID-19 in indoor settings. They developed a spreadsheet model that included many environmental factors that might influence transmission in different indoor settings (an office, a classroom, choir practice, and a reception/party). Findings suggested that active room ventilation, wearing of face masks, and high-volume HEPA filtering all significantly reduced the infection risk of SARS-CoV-2.

3.1.2.1 Potential Spread through Plumbing and Drainage Systems

There is growing literature on how plumbing and drainage systems may contribute to the spread of SARS-CoV-2 in multistory buildings. Lin et al. (2020) studied a cluster of nine cases of COVID-19 in an apartment building in Guangzhou, China. Each case was interviewed about their travel history and contact with the first infected patients. Researchers collected respiratory samples from each case to determine if they were from the same strain and studied building properties, including the shared piping, to see if it could have led to the cluster of cases. All nine cases had the same strain of the virus, but researchers found there was no close contact between the first infected patients and those infected later, making transmission through droplets unlikely. Through airflow analyses and a simulation experiment, researchers found that flushing toilets could increase the speed of airflow in the building's pipes and transmit the airflow from the apartment with the first infected patients to other apartments.

Kang et al. (2020) investigated the spread of SARS-CoV-2 among nine individuals in three families who lived in the same building. The researchers obtained throat swabs from participants as well as 247 air and surface samples from a subset of flats in the building, public areas, and building drainage systems. Tracer gas served as a surrogate for virus-laden aerosols in the drainage system. Results showed that the infection likely spread from the master bathroom of one flat to two other flats with which it was vertically aligned. Specifically, SARS-CoV-2-containing fecal aerosols were likely produced during toilet flushing and transmitted to the other flats via vertical stacks and vents.

3.1.2.2 HVAC and Air Exchange

There is continued interest in the role that HVAC systems play in the spread of SARS-CoV-2. In a letter to the editor, de Man et al. (2020) presented data from a COVID-19 outbreak that occurred in a nursing home. The authors found that 81% of residents and 50% of health care workers in a particular ward were diagnosed with COVID-19. Given that measures had been put in place to minimize the risk of COVID-19 transmission, the ventilation system was tested to determine if it might have contributed to the outbreak. They found that the affected ward had recently been renovated and their ventilation and air-conditioning units recirculated indoor air without ventilation compared to the unaffected wards that were ventilated with outdoor air. An examination of the affected ward showed that SARS-CoV-2 was present in the dust on the mesh of the living room air conditioners and in four block filters from three of eight ventilation cabinets. The authors concluded that these findings suggested that the outbreak was a result of the aerosol spread of SARS-CoV-2 within the ward because of inadequate ventilation.

Nissen et al. (2020) examined whether SARS-CoV-2 RNA could be detected in and near air vent openings in isolation rooms and in filters in the central ventilation system on the top floor of a hospital building. They subsequently collected fluid samples to determine the infectivity of any SARS-CoV-2 detected in the systems. In two surface sampling rounds for the COVID-19 ward rooms, both SARS-CoV-2 N and E gene RNA were detected in seven (36.8%) out of 19 vent openings, while 11 days later, four vents (21%) were positive for both genes. In the samples collected from the central ventilation system located outside of the ward rooms, eight out of nine samples were positive for both genes.

3.1.2.3 Air Sampling in Indoor Settings

Dumont-LeBlond, et al. (2020) conducted a study collecting air samples from acute care hospitals with COVID-19 patients to quantify the viral aerosol concentration in an environment that included those infected with SARS-CoV-2. Researchers collected 100 air samples in the acute care hospital rooms hosting 22 patients over the course of two months using three different air sampling protocols. Only 11 samples (from six different patients) were considered positive (SARS-CoV-2 viral RNA was detected). No correlation was found between specific symptoms, length of hospital stays, and time since symptom onset and the detection of airborne viral RNA. The authors noted that their detection rates were lower than airborne viral concentrations found in other studies and suggested the lower detection rates may be due to factors like increased ventilation to 4.85 air changes per hour, which creates negative pressure rooms.

3.2 Survival of SARS-CoV-2 on Material Surfaces Through Environmental Attenuation

Initial studies of the survivability of SARS-CoV-2 on material surfaces before environmental attenuation indicated that SARS-CoV-2 can survive on surfaces for at least several hours to several days, though it is dependent on the presence of UV light, temperature, and humidity (Bedrosian et al, 2020). At present, the scientific community has developed an understanding that environmental contamination (i.e., SARS-CoV-2 deposited on high-touch surfaces that humans contact) is not the primary mode of SARS-CoV-2 transmission in people (DHS Science and Technology Directorate, 2021). Fewer publications on this topic were identified by the systematic search, but the relevant articles that were found are presented in this section.

Key Findings

- Few studies conducted novel empirical research on how long SARS-CoV-2 survives on different surfaces and materials.
- A recent study indicated that decreased temperatures, nonporous surfaces, and absence of ultraviolet (UV) light can increase virus stability on surfaces over time. Recent literature review studies concluded the virus persists on dry surfaces for days and that the virus' survivability on surfaces decreases as temperature and humidity increase.
- Neither water nor food packaging were identified as high-risk avenues for human-to-human transmission.

3.2.1 Survivability on Common Surfaces

In the empirical study by Riddell et al. (2020), the survival rates of SARS-CoV-2 on several surfaces were investigated, including Australian polymer bank notes, demonetized paper bank notes, brushed stainless steel, glass, vinyl, and cotton cloth. The study was conducted in the dark to negate impacts of UV light. Humidity was kept constant at 50% relative humidity (RH), while temperature experiments were completed for 20°C, 30°C, 40°C (68°F, 85°F, 104°F). In the absence of UV light, SARS-CoV-2 was shown to persist on nonporous surfaces (glass, polymer note, stainless steel, vinyl, and paper notes) for at least 28 days at 20°C. Infectious SARS-CoV-2 virus was recoverable on porous surfaces (cotton cloth) up to 14 days. As temperature increased, environmental stability decreased. This length of time is notably longer than other studies previously cited; however, this study used a larger starting viral load and a fluid matrix that are more typical of an infected patient.

A systematic literature review by Bedrosian et al. (2020) conducted a sub-analysis on stainless steel, acrylonitrile butadiene styrene (ABS) plastic, and nitrile gloves using data from seven studies. The half-life of SARS-CoV-2 decreased as temperature and humidity increased across all three surfaces. Notably, this systematic literature review looked at more than these seven studies, but as methodology varied across studies—including organisms tested, deposition media (e.g., water, bovine, saliva), inoculum concentration, surface carrier surface area, relative humidity, temperature, and exposure time—comparing data was difficult.

In a literature review by Bueckert et al. (2020), the researchers considered 26 studies of SARS-CoV-2 surface stability and concluded that the virus remains stable on a variety of dry surfaces for days and its survivability is impacted by temperature and humidity. Indirect transmission is still probable, the authors insisted, though, as noted earlier, transmission via surfaces is not thought to be the primary mode of transmission.

3.2.2 Survivability on Food and Water

This review found no evidence that suggested food, food packaging, or water are significant risks for transmission. In a review article, Anelich et al. (2020) summarized research on SARS-CoV-2 survival in food, food packaging, and possible fecal-oral transmission of the virus. The authors reported that the consensus showed no evidence that SARS-CoV-2 is a food safety risk. The International Commission on Microbiological Specifications for Foods (ICMSF) (2020) came to the same conclusion, as summarized in their opinion piece. ICMSF discussed that there were relatively few reports of the virus being found on food ingredients, food products, or packaging materials.

Although Anelich et al. (2020) reported the consensus that SARS-CoV-2 is not a large food safety risk, Fisher et al. (2020) assessed the survival of SARS-CoV-2 on refrigerated and frozen meat and fish products. In their samples of chicken, salmon, and pork, there was no decline in infectious virus at 4°C (standard refrigeration) and at -20°C (standard freezing) for at least 21 days. The authors stated that their results, along with reports of detection on frozen packaging, should be taken into consideration when discussing food safety. In their review article, Yekta et al. (2021) stated that while recent studies had concluded that there is not a large food safety risk, these suggestions should not be taken for granted and more studies including those on fecal-oral transmission, meat products, produce, and food packaging should be done to understand food transmission risk.

In an empirical study (published online ahead of print), Lee et al. (2020) studied the viability of SARS-CoV-2 in three types of water: fresh, tap, and seawater. When starting with an initial concentration of 104 PFU/mL, SARS-CoV-2 was undetectable after treatment with fresh water and sea water; however, SARS-CoV-2 remained detectable in tap water for two days. Though these results showed a difference between water sources, the authors noted that the experimental conditions were not the same as the natural environmental conditions. While it is possible that there could be human-to-human transmission via water, the authors reported that they expected that it would be very rare.

3.3 Effectiveness of Prevention and Decontamination Measures for SARS-CoV-2

The literature review identified several interventions that have been reported to be effective in preventing or eliminating the presence of SARS-CoV-2 as well as infection risk. The most effective strategies reported were hand hygiene, wearing face masks, and ultraviolet (UV) light treatments. In addition to the evidence reported in Phase 2, effectiveness of air circulation and filtration interventions to remove SARS-CoV-2 from indoor environments were again investigated in the literature. Several surface cleaners and disinfectants were demonstrated to be effective at inactivating SARS-CoV-2. However, usage concerns related to human health and environmental hazards were described. Newly developed strategies, such as cold plasma, show promise in combating transmission of SARS-CoV-2. Lastly, concerns and promise of disinfectant spray tunnels, booths, and rooms are discussed below.

Key Findings

- Prevention and decontamination tactics were the most common topic presented in the literature during this review.
- Hand hygiene, surface disinfectants, and personal protective equipment (PPE), especially face masks, were demonstrated to be effective at reducing the spread of SARS-CoV-2.
- Emerging interventions included antimicrobial surface coatings, cold plasma, mouthwash, and nasal sprays, but these require further study to confirm their ability to reduce viral spread.

One museum-related article found in the systematic search from Wawrzyk et al. (2020) outlined key insights into prevention strategies within a museum setting (Auschwitz-Birkenau State Museum). Risk mitigation measures were implemented to protect employees and limit the spread of SARS-CoV-2 in both public (e.g., entrance room, ticketing, toilets) and employee spaces, including fumigation (6% hydrogen peroxide dry mist), installation of ethanol-based hand disinfectant stations, limitation of visitor/group size limits and spacing (i.e., social distancing), distribution of employee personal protective equipment (PPE) (i.e., face shields, face masks, goggles, and gloves), use of hazardous material disposal bags for trash, and deployment of an optional disinfection gate (i.e., tunnel) for visitors and employees. As a testimony to the effectiveness of these precautions, assessments taken 21 days or more after reopening showed no evidence of infection among employees. However, not all measures can be applied within LAMs (i.e., fumigation) due to potential for damage to collections. These strategies, and additional approaches described below, have shown promise, and can be considered for adoption by LAMs to reduce SARS-CoV-2 transmission risk.

3.3.1 Inactivation Using Ultraviolet Light

Six articles were summarized to show how UV light treatments can be used to prevent the spread of SARS-CoV-2. All articles were published in 2020 and found treatments to be an effective way to inactivate the virus in indoor settings where humans frequently travel. However, UV treatments have the potential to damage sensitive materials.

In a feasibility study, Beggs et al. (2020) addressed the urgent need for disinfection methods in confined spaces with the use of upper air ultraviolet germicidal irradiation (UVGI), or “UV-C light at wavelengths close to 254nm to create an irradiation field above the heads of room occupants that disinfects aerosolized bacteria and viruses suspended in the air” (p. 2). Since the emergence of COVID-19, upper-room UVGI has been discussed as a potential intervention that might prove to be effective against COVID-19 (Morawska et al., 2020; Nardell & Nathavitharana, 2020; Skorzewska, 2020). The UV susceptibility constant (Z) for the virus can be used to assess the behavior of any given virus exposed to UV-C light. The article provided a review of the literature and effective Z values for single-pass UV irradiation performed on other aerosolized viruses in air. To evaluate the effectiveness of this intervention method, a short feasibility study was designed for the SARS-CoV-2 virus. Results showed that SARS-CoV-2 is likely to have a UV susceptibility constant like other coronaviruses and could be inactivated by UV light at 254nm. Results have been proven effective for measles and tuberculosis, but there is no data to prove it is an effective method for SARS-CoV-2. Upper room UVGI could be used in indoor settings where high ventilation rates are hard to achieve.

In another article, Buchan et al. (2020) found that the use of low dose far-UVC at a wavelength of 222 nm is an effective disinfection method for a single occupancy private room. This method proposes the use of low dose far-UVC at a wavelength of 222nm as a safer alternative to typical UVC with a wavelength of 254nm. The room was occupied by a patient laying in a bed. Viral load simulating a single breath was dispersed and flow velocity was assessed at 10, 50, and 100 s with and without far-UVC light. The source of the far-UVC light was a lamp positioned in the top right corner of the room. A far-UVC inactivation value of Z= 4.1 cm^2 mJ-1 for human coronavirus was used based on the most recent estimates and is considered representative of SARS-CoV-2. High ventilation was also used in combination with far-UVC. Reductions in SARS-CoV-2 levels were observed using far-UVC. With ventilation practices of eight air changes per hour (ACH) in place, the far-UVC reduced concentrations by a further 40% and 52% respectively. Although this article presented results about the use of far-UVC that was safer for humans than typical UVC, it should be noted that this reduction was measured in a single occupancy room in a hospital setting.

Liu et al. (2020) presented an efficient sterilization treatment for SARS-CoV-2 using ultra-high power UVC irradiation with the output power as high as 2W at a current of 1.3 A. The UVC light source was found to eliminate the SARS-CoV-2 virus with a concentration of 100 $CCID_{50}$/0.05 mL within one second. There was a complete elimination of the SARS-CoV-2 virus at the cellular level after treatment with the ultra-high power UVC irradiation. Treated specimens had an original virus concentration of 0.1, 1,10, and 100 $CCID_{50}$/0.05 mL and all showed zero positive rates after the sterilization method was used. These results showed the efficiency of a high-power UVC irradiation source as a decontamination method for the SARS-CoV-2 virus.

3.3.2 Thermal Inactivation

Warmer temperatures show a more rapid inactivation of the SARS-CoV-2 virus (compared to cool temperatures). Thermal inactivation has been discussed in terms of outdoor environmental settings as well as laboratory settings. Implementation in indoor settings or collections is not discussed. This type of intervention may not be viable for use in LAMs due to potential for damage to collections. Evidence suggests that the inactivation rate varies depending on the method used for testing, showing the need for further research on this method.

Magurano et al. (2020) observed the influence of environmental temperatures on the endurance of the SARS-CoV-2 virus. The virus was tested on a plastic surface at both room temperature (RT) (20°C-25°C) and the average maximum temperature estimated for the month of June in Italy (JT) (28°C). The virus remained on the plastic surfaces after 84 hours at both RT and JT but was not detected after 96 hours. During the first 24-36 hours, virus vitality on plastic surfaces declined by more than $1\log_{10}$ in $TCID_{50}$ at room temperature. The same decline was observed at JT but at a faster rate. The rapid decline of SARS-CoV-2 observed in the warmer environment suggests that viral infectivity can be influenced by higher temperatures.

Kim et al. (2020) discussed the thermal inactivation of SARS-CoV-2 to prevent transmission of the virus without compromising the viral genome that is necessary for clinical diagnosis. The results showed that viable SARS-CoV-2 is readily inactivated when incubated at 56°C for 30 minutes or 65°C for 10 minutes. This method was effective in inactivating viable viruses without attenuating the Real-Time Quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) diagnostic sensitivity. After inactivation, the virus maintained a similar genomic RNA stability to non-heat inactivated specimens. The temperature sensitivity of SARS-CoV-2 was evaluated with viable viral titers in Vero cells following the treatment of SAR-CoV-2 at the two temperatures. A rapid reduction of the viral infectivity titer below the detection limit was observed at both temperatures after 30 minutes and after just 10 minutes of heat inactivation at 65°C. A rapid decline in infectivity was observed at the higher temperature (65°C), while a more gradual decline was seen at 56°C. The results showed the effectiveness of heat to eliminate viral infectivity, while preserving the genomic structure to allow the virus to be studied in a laboratory setting without the risk of infection from handling the specimen.

Gamble et al. (2020) discussed how heat-treated virus inactivation can differ depending on the treatment procedure. They proved that the inactivation rate of SARS-CoV-2 in a cell culture medium at 70°C showed a half-life of 0.86 minutes in a closed vial, where uncovered plates in a dried oven had a half-life of 37.0 minutes. The speed of inactivation from heat treatments was significantly reduced for samples in open or uncovered containers. Viable virus titer estimates by end-point titration were reported on a logarithmic scale showing how inactivation of the virus differed in a closed vial, a covered plate oven, and an uncovered plate oven. The results showed that the choice of procedure has an impact on the inactivation of the virus using dry heat. Open containers showed a significantly higher half-life compared to a closed vial. Evaporation was suggested to play a critical role in the inactivation of the virus using dry heat. A better understanding of the impacts of temperature and humidity on viral stability is necessary when designing decontamination protocols in various environmental conditions. Limitations of this study include that results were reported on virus inactivation in liquid substances and only discuss heat. Other factors such as, pH, salinity, and protein concentration were also thought to play a role in virus inactivation in a liquid specimen.

3.3.3 Personal Protective Equipment

As COVID-19 continues to spread, researchers have investigated how masks can best be used to mitigate transmission. It is well documented that wearing a mask mitigates the spread of COVID-19 (Chua et al., 2020; Fischer et al., 2020; Ueki et al., 2020). N95s and surgical masks remain the most effective at containing respiratory droplets, while other mask types (layered cloth, disposable masks, neck gaiters, etc.) offer varying levels of protection against droplets. Researchers around the world are innovating to increase the effectiveness of masks.

3.3.3.1 Efficacy of Mask Materials

Masks provide dual protection against respiratory pathogens. They protect the wearer from breathing in infectious droplets or aerosols while mitigating spread of infectious material from the wearer themselves. In a peer-reviewed manuscript, Doung-ngren et al. (2020) investigated the efficacy of masks for protecting wearers from SARS-CoV-2 using a case-control study. They contacted individuals who had been in the same location as someone who was positive for SARS-CoV-2. They asked questions about mask wearing and other protective behaviors during the period of exposure. The research team found that mask wearing was associated with lower SARS-CoV-2 infection risk. However, the authors noted that only wearing a mask sometimes was not protective against SARS-CoV-2. Those who reported always wearing a mask were also more likely to practice social distancing, handwashing, and other protective behaviors. Notably, the type of mask worn was not associated with risk of infection. Limitations of the study included recall bias and potential exposure to multiple index cases.

Ueki et al. (2020) sought to understand in more detail how masks, and different types of masks, can protect people from SARS-CoV-2. In their observation, Ueki and colleagues created an airborne transmission simulator to mimic spread via breathing and coughing using live SARS-CoV-2. Two mannequins were used as a virus spreader and a virus receiver. For the receiver, the research team found that cotton masks, surgical masks, and N95 masks were all protective against SARS-CoV-2, although the N95 mask provided the most protection (80% to 90% reduction in virus uptake when compared to no mask; cotton masks provided 20% to 40% reduction in uptake). When affixed to the virus-spreading mannequin, cotton and surgical masks blocked over 50% of virus uptake and N95 masks blocked significantly more. Lastly, the authors taped the N95 mask to the test mannequin to completely seal the breathing space. Virus particles were still able to penetrate, although the authors were unsure if the number of particles that penetrated would result in infection. The authors used relatively high viral loads to generate droplets and it is likely that mask efficacy increases with lower viral loads.

Fischer et al. (2020) measured the number of droplets that passed through a given mask material while a human subject spoke. Fourteen different mask materials were tested. A fitted N95 or surgical mask were the most effective at mitigating the release of droplets into the air. Bandanas and neck gaiters were least effective. In fact, neck gaiters were found to turn large droplets into smaller droplets and resulted in a higher number of particles than those in the control condition (no mask). It should be noted that this article was a proof-of-concept study on an inexpensive method to measure respiratory droplets using lasers and a cell phone camera. The goal of the study was not to evaluate different mask materials, so results should be interpreted as such. SARS-CoV-2 was not used in this research.

Asadi et al. (2020) reported conclusions about the high effectiveness of N95 masks, measuring outward emissions of micron-scale breath particles from healthy individuals that did not have SARS-CoV-2. Research subjects wore different types of masks including surgical, unvented N95, paper towel, single-layer t-shirt, double-layer t-shirt, and vented N95. Surgical masks and unvented N95 respirators were the most effective at reducing outward particle transmission during speaking and coughing (90% and 74%, respectively). Notably, particle emission from paper and cloth masks were no different from the no mask condition or were markedly increased. The results for paper and cloth masks were confounded by a test in which the mask was rubbed against itself for 10 seconds. The authors found that rubbing paper and cloth masks released fiber particulates that could potentially carry the virus. It is unknown whether these virus-laden fibers could transmit SARS-CoV-2. The authors also noted that the research subjects tended to speak louder when wearing masks, but louder speech alone did not account for the increased particle output for some masked conditions. The authors also utilized a coughing “super emitter” to test the effects of different masks on this individual’s particle emissions (as opposed to speech super emitters and breathing super emitters). When worn by the coughing super emitter, particles emitted increased across all mask types. One limitation of this study was that the authors did not measure redirected expiratory airflow (air that escapes through the sides and nose portion of the mask) or factor this into analysis. In their conclusions, the authors called for more testing on used masks and the impact of fiber shedding on mask efficacy. They asserted that homemade masks should be washed regularly and that materials like polyester might mitigate shedding of fibers.

3.3.3.2 Mask Innovations

Scientists around the world have been working on improving mask construction. It is important to note that none of the articles referenced in this subsection used SARS-CoV-2 to test their novel approaches. Future mask innovations should be tested with SARS-CoV-2 to ensure that the technology functions as expected against the coronavirus (as opposed to testing with a surrogate pathogen or testing without a pathogen).

Mask innovations have been reported in literature reviews to include masks with a plasma layer and thermosensitive masks that change color if a person has a fever. In their peer-reviewed literature synthesis, O’Dowd et al. (2020) noted that “advanced manufacturing and information technologies” will only continue to increase in the coming years. The emergence of 3D printing, wearable technology, smartphone integration, state-of-the-art fabrics, and antibacterial coatings will lead to masks that are more effective at keeping out pathogens. Chua et al. (2020) echo these sentiments in their literature review on face masks.

Masna et al. (2020) have introduced a mask that incorporates more advanced technologies. The group’s active mask has sensors that detect rapid changes in droplet amounts and neutralizes them using a water mist. The mask contains a commercial particulate matter sensor and when needed, activates the mist. The mist adheres to respiratory droplets, so they become heavier and sink to the ground more quickly. The active mask is connected via smartphone application, which lets the user know when the mask needs to be recharged. The mask was shown to reduce the number of droplets in the air by 40%.

Another innovative form for PPE is the Pressure Optimized Powered Respirator (PROPER). Nazarious et al. (2020) describe this hood-based system in their peer-reviewed article. The hood functions as a wearable clean room. The fabric on the hood and suit are designed for single use, but the air filter components can be cleaned and reused. Several components of PROPER can be 3D printed. The air inside the hood (with a human subject) was measured to be 175 times cleaner than the air outside the hood. This low-cost technology could be beneficial for front-line workers.

3.3.4 Hand Hygiene

This section describes the importance of hand hygiene in the prevention of SARS-CoV-2 transmission. As a supplement to handwashing, hand-sanitizing rubs have become more popular due to their convenience. However, not all formulations are effective against SARS-CoV-2, and different regulating bodies may have divergent guidance regarding what formulation is best.

Alzyood et al. (2020) discussed CDC guidance to wash hands for a minimum of 20 seconds with soap as an efficacious approach to thwarting microorganism transmission. Several informational campaigns released between 2009 and 2018 are discussed (e.g., My five moments for hand hygiene, Clean Your Hands, It's OK to Ask). Further, authors described handwashing as a simple method that should be promoted during and after the pandemic in the health sector (i.e., nurses) and more broadly in the public. They note that enthusiasm and commitment to clear messaging regarding handwashing/sanitization practices will be required to protect against future infectious threats.

Suchomel et al. (2020) wrote a review to provide a summary of published efficacy data on original World Health Organization (WHO) recommended hand-rub formulations and their modifications. WHO alcohol-based formulations have not been tested with Food and Drug Administration (FDA) American Society for Testing Materials efficacy standards. The original WHO-recommended alcohol-based formulations did not meet European efficacy standards and the bactericidal efficacy was found to be partly insufficient. The first modification increased alcohol concentration resulting in improved efficacy. The original and second modified formulations were tested and demonstrated sufficient activity against SARS-CoV-2 and other enveloped viruses in 30 seconds.

Singh et al. (2020) summarized findings about the efficacy of alcohol-based hand sanitizers and their disinfectant potential against SARS-CoV-2 and other infectious viruses. The most important factors for hand sanitizer efficacy are the "type and concentration of alcohol, formulation and nature of product, presence of excipients, applied volume, contact time and viral contamination load" (p. 1). Isopropanol is more effective against SARS-CoV-2 than ethanol due to its lipophilic properties. To maximize the largest reduction in viral load of SARS-CoV-2, a hand sanitizer should ideally contain more than 80% volume/volume (v/v) ethanol or more than 75% v/v isopropanol. At least three milliliters of product should be used with a total contact time of around 45–50 seconds. Unclean hands and the presence of excipients can impact the efficacy of alcohol-based products. It is recommended that for isopropanol-based hand sanitizers, glycerol should be replaced with other emollients.

3.3.4.1 Eczema, Dermatitis, and Other Concerns

The following articles discuss the relationship between increased handwashing behaviors and use of hand sanitizers with skin irritation and eczema among various sectors of the population. The evidence suggests that more frequent handwashing can result in skin irritation. Additionally, some researchers have raised concerns about antimicrobial resistance and the environmental impact of soaps that are not biodegradable and potentially toxic.

Borch et al. (2020) summarized findings from an observational study conducted in Denmark during the reopening of schools and daycare facilities. A questionnaire consisting of 20 questions about frequency of handwashing, use of hand sanitizer, symptoms of irritant contact dermatitis (ICD; dry, red, and itchy skin), atopic dermatitis, allergy, and predispositions was administered to parents. In children without any dermatitis history, 42.4% experienced ICD due to increased handwashing. Use of alcohol-based hand sanitizer was not a risk factor for ICD but frequency of handwashing was. “Hand washing 7-10 times/day and >10 times/day increased the relative risk by 1.83 and 2.23 times, respectively” (p. 6). While proper hand hygiene is critical to prevent and reduce the spread of novel coronavirus, prophylactic measures need to be considered to reduce possible long-term consequences.

Guertler et al. (2020) reported survey results that described the onset of hand eczema among health care workers with direct and indirect contact with COVID-19 patients in a hospital setting as infrequent. The study found handwashing, disinfection, and hand cream use increased significantly among all participants. There was no significant association between direct care of COVID-19 patients and handwashing frequency. While acute hand dermatitis symptoms were reported by 90.4% of all health care workers, hand eczema was only reported by 14.9%. Protective skincare behaviors should be implemented to prevent serious or chronic hand eczema among health care workers.

Daverey and Dutta (2020) highlighted the health and environmental concerns associated with the frequent use of soaps, detergents, and alcohol-based hand sanitizers and discussed the potential of eco-friendly natural detergents and sanitizing agents for hand hygiene. The main raw component of soaps is petrochemical based surfactant and for alcohol-based hand sanitizers it is ethanol or isopropanol. These formulations are nonbiodegradable, can contribute to antimicrobial resistance, can be hazardous, and are toxic to both humans and the environment. Microbial biosurfactants are suitable candidates for the key components of hand hygiene formulations due to their antiviral, antimicrobial, low-toxicity, skin biocompatibility, wettability, and detergent properties. With greater market demand, eco-friendly agents have immense potential to supplement or eliminate conventional soaps and hand sanitizers.

3.3.5 Ventilation and Air Filtration

The SARS-CoV-2 pandemic has illustrated the need for more information and understanding about how indoor ventilation systems in public buildings may contribute to the spread of infectious diseases. The following articles discuss potential solutions to mitigate infectious disease transmission and protect the health of individuals in shared indoor spaces.

Bhagat and Linden (2020) discussed the benefits of either natural or mechanical displacement ventilation and provide guidelines for displacement ventilation to reduce the transmission of airborne infectious diseases. Ceiling fans or air-conditioning units should not be used. When used, air-conditioning should be combined with underfloor air distribution. In warmer climates, cold air should be distributed near the floor and hot air should be vented near the ceiling. If utilized properly, displacement ventilation in public buildings can provide additional mitigation safeguards for asymptomatic transmission.

Cees van et al. (2020) researched aerosol droplets in elevators by replicating a single cough using a spray nozzle to spread glycerol/ethanol droplets detected by a laser sheet placed in the back of the elevator. The authors noted it took “12-18 minutes before the number of aerosol particles decreased 100-fold during normal operation of both medium- and large-sized elevator cabins” (p. 1065). When elevator doors remained completely open, it took only two to four minutes. Efforts to reduce SARS-CoV-2 transmission may include leaving elevator doors permanently open when not in use, increasing the mechanical ventilation capacity, changing the direction of the ventilation so there is a unidirectional flow of filtered air from the ceiling to the floor, and wearing proper PPE. While SARS-CoV-2 was not specifically used in this study, the authors made a strong case for keeping elevator doors open when not in use, increasing air filtration, and ventilation capacity to reduce aerosols and potential disease transmission.

Marcone (2020) summarized guidelines to reduce SARS-CoV-2 infection risk related to the air-conditioning systems in occupational settings. The author recommended “dilution, filtration, pressurization, and disinfection" (p. S478) of indoor air to reduce infection risk. Steps to reduce transmission should be to stop the use of internal air recirculation, turn off autonomous recirculation systems, open windows to promote good air exchange, ventilate rooms at night and when people are present, and if possible, use external air systems only.

Guo et al. (2021) reviewed heating, cooling, and ventilation guidelines from the United States, Europe, Japan, and China. The most effective strategy to reduce SARS-CoV-2 transmission risk is to ventilate an area using ample outdoor air and effective airflow patterns. Among the guidelines reviewed, the main recommendations are listed as follows: provide as much outdoor air as possible. If possible, the outdoor air damper should be as high as 100%. The running time of HVAC systems should be increased. The Federation of European of Heating, Ventilation, and Air-Conditioning Associations and the American Society of Heating, Refrigeration, and Air-Conditioning Engineers both recommend opening HVAC related devices, such as the exhaust fan and outside air damper, two hours before and after occupancies. Portable room air cleaners are recommended with the condition that filters are cleaned regularly. The recirculation sector on air handling units should be disabled if possible. Water seals on toilets should be checked regularly and negative pressure should be kept in toilets.

Lipinski et al. (2020) performed a review where the authors assessed current building ventilation strategies and considered additional steps to reduce the risk of infectious disease transmission. The authors recommend against recirculating ventilation strategies since they facilitate the distribution of stale and/or contaminated air and can prevent the dilution of harmful particles. The preferred ventilation method is displacement ventilation with a large sized natural inlet due to its ability to “move stale, contaminated air directly to the exhaust of the room in a laminar fashion whilst the concentration of small droplets and airborne particles in the indoor air is significantly reduced" (p. 21). Displacement ventilation inhibits horizontal movement of airborne particles, allowing the smaller droplets to move up and the larger droplets to fall out of breathable level air. This lowers disease transmission risk indoors. Supplying a large volume of fresh air inside reduces contaminant concentration levels and can increase the indoor air quality to optimal levels.

Siddiqui et al. (2020) highlighted that centralized air-conditioning systems are ideal environments for virus viability due to low temperatures with extremes in humidity. The authors proposed the fabrication of surfaces, filtration, and ultraviolet disinfection as strategies to remove infectious agents from air-conditioning systems to prevent disease transmission. Air-conditioning systems could be modified by coating surfaces with microbicides or antimicrobial enzymes or air-conditioning unit filters could be coated with a novel and effective coating based on ionic liquids and surface-active agents. Additional work is necessary to develop "surfaces with sharp structures that penetrate the pathogen cell membranes resulting in inactivation and facilitation of pathogen killing or pathogen repellency" (p. 3178). The development and implementation of 0.1 µm pore-size filters (i.e., the approximate size of SARS-CoV-2) could be an effective eradication strategy for viral particles. While promising, the efficiency of UV irradiation on SARS-CoV-2 is unclear and needs to be explored before it is recommended as a widespread disinfection tool for the virus.

Ntounis et al. (2020) presented a methodology to establish maximum occupancy levels for different retail environments based on social distancing guidelines in relation to movement of people (and in turn, air) in those environments. The retail environments included high street stores (under 500 square meters); large retailers or commercial spaces (individual retailers over 500 square meters or group of stores in the same space); and outdoor commercial spaces. They also looked at static spaces (i.e., where people are seated or waiting in line) and dynamic spaces (i.e., stores where people are shopping or moving around). For a retail space under 500 square meters, the lower bound (i.e., the minimum number of square meters needed) or the amount of space a single individual needs to be allocated to social distance in both fixed (i.e., people in queues) and dynamic spaces (i.e., inside a shop where people need to move around freely). For social distancing guidelines of two square meters, they proposed the following: a minimum of four-square meters per person in static spaces; in a retail space under 500 square meters a minimum of 10 square meters per person; and in a large retailer, a minimum of 11 square meters per person.

3.3.6 Surface Cleaners and Disinfectants

With the ongoing use of chemical disinfectants and hand hygiene products, human health hazards associated with sustained use, overuse, and misuse have emerged. Researchers have noted these hazards and provided recommendations to mitigate health impacts from use of these products. Researchers have also explored the use of less toxic alternatives and have identified novel uses of existing disinfection technologies for use against SARS-CoV-2.

There are many disinfectants on the market that destroy coronavirus particles within seconds or minutes. To effectively combat transmission of SARS-CoV-2 from fomites, surfaces need to be sanitized using the appropriate protocol for a given product. High-touch surfaces should be cleaned as often as possible, including those often overlooked (e.g., toilet handles, elevator buttons, sinks).

Tyan et al. (2020) presented an approach for the rapid evaluation and selection of surface disinfectants on US EPA List N: Disinfectants for Coronavirus (COVID-19) that includes key questions for consideration related to efficacy (i.e., required wet-contact time and whether a product has an emerging viral pathogen claim), safety (i.e., pH, toxicity profile, and irritation potential), ease of use (i.e., delivery method), surface compatibility (i.e., the types of surfaces a disinfectant is compatible with), availability (i.e., commercial availability and ability to repurchase), and cost (i.e., whether a disinfectant is economical). The authors provided supplementary information not readily available on ingredient concentrations, pH, formulation type, delivery method (e.g., wipes), and surface compatibility (e.g., hard nonporous) for List N disinfectants compiled from Material Safety Data Sheets (MSDS) and US EPA registration data.

Al-Gheethi et al. (2020), in a bibliometric analysis, collected and analyzed 2,000 articles with a focus on reviewing literature related to the efficiency of various disinfection technologies. Although most of the review focused on a broad discussion of viral response to disinfectants (not specific to SARS-CoV-2), the authors noted “SARS-CoV-2 has the ability to survive for longer periods (possibly up to 24 hours) compared to chemical disinfectants that disperse on contaminated surfaces” in outdoor environments (p. 8). However, a limitation with this finding was that the authors did not specify the chemical disinfectant(s) to which they referred. They noted that the most common disinfectants were ethanol, hydrogen peroxide, and sodium hypochlorite, which “have the ability to inactivate the virus within 1 minute” (p. 8). The authors also note that zinc oxide nanoparticles smaller than 100 nanometers “may have the potential to inactivate SARS-CoV-2 (with a size of 400 nm) and physically destroy the viral genome” (p. 8). The authors concluded that effective disinfection is crucial to inactivate SARS-CoV-2 on surfaces.

Shimabukuro et al. (2020) reviewed studies that evaluated disinfectants used to inactivate SARS-CoV-2 on surfaces and in sewage. A total of seven studies were included in the qualitative synthesis. These studies included two conducted in a hospital setting and five laboratory tests. Products analyzed included sodium hypochlorite (dilutions of 0.1-0.5%); peroxygen compounds; hydrogen peroxide; household detergents; a product containing 70% alcohol, glutaraldehyde, iodine detergent, and household bleach; ultraviolet C germicide; and plasma for air purification. The authors concluded that cleaning and disinfection should occur “in places and surfaces that are touched very frequently” to prevent the spread of SARS-CoV-2 (p. 511). The authors also noted that inactivation of SARS-CoV-2 occurred when inanimate objects were cleaned with “chlorine-based disinfectants, alcohol, detergents, glutaraldehyde, iodine-containing detergents, hydrogen peroxide compounds and household bleaches” and alcohol “showed efficient immediate activity” (p. 513). However, a limitation of this article was lack of specific regarding time required for the disinfectant to sanitize.

Ge et al. (2020) assessed the efficacy of air and surface disinfection of isolation wards in a hospital. In a peer-reviewed empirical study, routine disinfection was performed three times a day in general wards and six times a day in ICU. For air disinfection, plasma air disinfection machines (model PM-B1000Z2, manufactured by Peijieer Medical Technology) were continuously run, while “ultraviolet lights were used for air disinfection three times a day when no one was present if there were no plasma air equipment" (p. 2). Surfaces and fomites were "wiped with 1,000 mg/L chlorine containing disinfectant twice and waited for 30 minutes, then wiped with clean water" (p. 2). A total of 105 surface samples were collected and assessed for viral RNA detection. The study found that only "two surface samples were positive for viral detection [toilet flush button and wash basin]," which they concluded suggested "that more attention should be paid when disinfecting places easy to be ignored" (p. 1). However, one limitation of the study was the authors did not collect air samples due to lack of sampling equipment, and another limitation was the use of single time point surface sampling.

Gerlach et al. (2020) presented the results of their study assessing the efficacy of individual ingredients of common surface disinfectants in inactivating SARS-CoV-2 on a variety of surfaces including stainless steel, plastic (PET), glass, polyvinyl chloride (PVC), cardboard, and cotton fabric. For this study, surfaces contaminated with viable dehydrated SARS-CoV-2 were treated with 70% ethanol (EtOH), 70% isopropanol (IPA), 0.1% hydrogen peroxide (H_2O_2), or 0.1% sodium laureth sulphate (SLS) for 30 seconds and 60 seconds. The concentrations tested were based on WHO formulations I and II for disinfectants and/or pervasive presence in household cleaning and hygiene products. The authors found that "SARS-CoV-2 was highly susceptible" to all test substances and "for EtOH and IPA, complete viral inactivation to the limit of detection was observed within 30 s of treatment," while "viable SARS-CoV-2 could be detected after 30 s of treatment with H_2O_2 and SLS" (p. 633). However, after 60 seconds of treatment "effective SARS-CoV-2 inactivation with logarithmic reduction of viral infectivity by more than 4.0 log10 was documented for all tested chemicals" (p. 633). The authors concluded that ingredients of common household cleaning and hygiene products are capable of rapidly inactivating SARS-CoV-2.

Martins et al. (2020) evaluated the use of ozonated water at the faucet-level to inactivate SARS-CoV-2 in water supplies. The authors used a special faucet (DOCOL®) that produced normal and ozonated water. Ozone concentration in the water was 0.6 ppm. SARS-CoV-2 virus stock was diluted in each of the following: Dulbecco minimal essential medium (DMEM) with no fetal bovine serum, a one percent antibiotic/antimycotic solution; Milli-Q water (water purified by a system manufactured by Millipore Corp.); ozonated water; or 70% alcohol in Milli-Q water. Genome quantification was performed immediately after treatment. "Titration of infectious SARS-CoV-2 showed a significant reduction in virus infectivity upon 1 min exposure to ozonated water and alcohol, with, respectively, 2 and 2.8 log10 reductions as compared to the virus in DMEM" (p. 2), and "the quantification of the virus genome upon exposure to ozonated water for one min indicated no reduction in genome quantification as compared to milli-Q water" (p. 3). However, there was a "significant reduction in genome copies ($p < 0.05$) of progeny SARS-CoV-2 per copy of housekeeping gene RNase-P as compared to milli-Q water" (p. 3). Collectively, these results indicated that ozonated water at a concentration of 0.6 ppm at one-minute exposure "inactivates SARS-CoV-2 by a mechanism targeting its structure, and not the virus genome" (p. 3). The authors conclude that further testing at higher ozone concentrations is needed to clarify the mechanisms involved.

3.3.7 Hazards of Using Cleaners, Disinfectants, and Hand Sanitizers

Despite widespread benefits of surface cleaners, disinfectants, and hand sanitizers, scientists have pointed to risks associated with improper use of these products. While many disinfectants are efficacious against SARS-CoV-2, researchers encourage use of disinfectants that contain more natural ingredients. PPE should be worn when using a disinfectant or surface cleaner to reduce exposure to potentially harmful chemicals. Hand sanitizers can be an effective method of mitigating spread of SARS-CoV-2, but consumers should investigate the formulations of these products before purchasing, especially if intending to use with small children.

Samara et al. (2020) present previously published data on the known health effects of prolonged use of common disinfectants approved by US EPA for use against SARS-CoV-2, including household bleach, alcohol, quaternary ammonium-based hand sanitizer, and ethanol-based hand sanitizer. Based on a review of risks associated with these products, the authors comment that “disinfection should be carried out with appropriate precautions to reduce exposure to harmful byproducts” (p. 497), and noted that less toxic alternatives are available, such as thymol, which the US EPA recently added to their list of approved SARS-CoV-2 disinfectants. The authors suggested that there are less harmful alternatives to disinfectants containing quaternary ammonium compounds (e.g., benzalkonium chloride) by stating “alternative measures can include the use of less toxic chemical disinfectants such as naturally occurring substances, which include thymol, ethanol, and hydrogen peroxide” (p. 497). The authors also noted that appropriate PPE should be worn when disinfecting and hand sanitizer use should be limited as “no safe chemicals exist” (p. 498). Ultimately, the authors concluded that there is a need for safer, less toxic alternatives, and consumer awareness about potential health impacts associated with disinfectant use.

Atolani et al. (2020) discussed risks associated with alcohol-based hand sanitizers (ABHS) and non-alcohol-based hand sanitizers (NABHS), as well as safer alternatives for use in preventing transmission of SARS-CoV-2. The authors described the typical chemical compositions of ABHS and NABHS based on previous research and WHO guidelines and concluded that ABHS were fire hazards due to low flash points, may cause poisoning if ingested, and may cause organ toxicity through skin absorption or skin irritation. The authors also noted that NABHS may cause eye irritation or other health effects if accidentally ingested, and that some ingredients in hand sanitizers (e.g., antimicrobial agent triclosan), are toxic to the environment). Authors deduced that “some hand rubs, soaps and sanitizers contain some chemical compounds which may only be most appropriate for use on non-skin surfaces” (p. 792), and that “ordinary soap solution is effective at killing and eliminating the virus and other germs in the hand” (p. 793). Finally, the authors provided recommendations for the use of ABHS and some liquid soaps that suggested frequency and hand area of use should be limited, among others. They concluded that consumers should be cautious when using hand sanitizers.

Li et al. (2020) present results from an indoor fate and chemical exposure model that aimed to estimate human exposure and health risks associated with 22 active ingredients used in chemical disinfectants against SARS-CoV-2 for three age groups (3, 14, and 25 years of age). The 22 ingredients “include 14 quaternary ammonium salts, four phenolic compounds (chloroxylenol, thymol, O-phenylphenol, triclosan), a urea (triclocarban), two diols (Triethylene glycol, and bronopol), and a bisbiguanide (chlorhexidine gluconate)" (p. 3). Two application scenarios were simulated: surface disinfection (indoor fate and transport) and handwashing (dermal uptake). Using the PROTEX model to estimate indoor fate and human exposure of the 22 active ingredients, the authors predicted "chemical-specific dermal loadings ranging from 0.14 to 0.70 mg/cm2" for the surface application scenario and "dermal absorption of 2.2x10-4 and 2.1x10-4 mg/kg/d (medians) of triclosan by 14- and 25-year-old females, respectively" for a scenario of 20 second handwashing once per day using a disinfectant (p. 5). In the surface application scenario, "the modeled individuals are exposed to quaternary ammonium salts (notably C12 to C18BAC) the highest, regardless of age group, because these chemicals are most strongly retained on the treated hard surface" (p. 7). In the handwashing scenario, modeled individuals were "exposed to phenolic compounds the highest, regardless of age group. In both scenarios, exposure to chlorhexidine gluconate is the lowest among all disinfecting chemicals" (p. 7). Across scenarios, the modeled 3-year-old had higher uptake than the 14-year-old and the 25-year-olds. In the surface exposure scenario, "exposure to quaternary ammonium salts mostly come from mouthing-mediated ingestion," particularly in small children where there is more frequent surface contact and hand-to-mouth contact (p. 7). Thus, establishments with environments frequented by children require special care to ensure safety. Authors concluded that, "regardless of the age group and effect thresholds, the 'hand hygiene' scenario is found to pose no risks to human health," and for the surface application scenario, all groups were "at risk for cetrimonium bromide after a single application, while they are not at risk for chloroxylenol, thymol, triethylene glycol, and chlorhexidine gluconate despite variations in exposures and maximum acceptable doses" (p. 9). The authors concluded that while "no health risks are identified with the hand hygiene scenario for any investigated disinfecting chemicals, some may pose risks with the surface application, especially for young children," and that it is hazardous to not wipe disinfecting chemicals off of high touch hard surfaces.

Steinemann et al. (2020), in a peer-reviewed study, investigated the emission of volatile organic compounds (VOCs) from a total of 26 fragranced products (13 regular and 13 "green"), including hand sanitizers, air disinfectants, multipurpose cleaners, and hand soap commonly used by consumers to prevent the spread of SARS-CoV-2. Limonene was most prevalent in both regular and green products. Of the VOCs emitted, about 30% were classified as "potentially hazardous" and "all products emitted between 1 and 4 VOCs classified as potentially hazardous" (p. 49). "The most prevalent potentially hazardous VOCs (in at least 25% of all cleaning products) were limonene, ethanol, acetaldehyde, 3-carene, and methanol" (p. 49). The study found "no significant difference" in the VOCs between green products and regular products (p. 49). The study also found that "only 4% of all VOCs, and 11% of the potentially hazardous VOCs, were disclosed to the public on product labels or safety data sheets" (p. 49); however, fragrance is exempt from ingredient disclosure, which may account for this finding. VOCs were deemed potentially hazardous according to classifications by US EPA, the Hazardous Chemical Information System, Safe Work Australia, and the Association of Occupational and Environmental Clinics. The authors noted that the study did not assess the interaction of multiple products and no testing was done to assess secondary reactions caused by the interaction of chemicals with ambient air.

Dindarloo et al. (2020), in a peer-reviewed descriptive-analytical study, administered an electronic checklist to gather data on use patterns and related health effects from using disinfectants to prevent COVID-19 infection (N = 1,090). Participants reported experiencing health problems due to the use of disinfectants (e.g., 41.4% had health problems in at least one organ). The most common issues were skin dryness (76.3%) followed by obsession, skin itching, coughing, eye irritation, burning throat, hand redness, lung shortness of breath, headache, tiredness, and others. The authors noted significant participant familiarity with disinfectant preparation and use, which may lead to avoidable accidents and health impacts. Authors recommended consumer training on appropriate disinfectant use. A limitation was lack of specificity related to the chemical composition of disinfectants used by participants.

MacGibeny et al. (2020), in a peer-reviewed report, reviewed information on adverse skin reactions from hand hygiene and cleaning products used to prevent spread of SARS-CoV-2 and strategies to mitigate skin irritation. The authors noted that these products can result in skin “dryness, roughness, itching, burning, erythema, edema, blistering, scaling, and fissuring” and that “milder irritants like hot water, detergents, or alcohols” can cause skin damage over multiple exposures, whereas caustic chemicals can cause a reaction immediately upon contact (p. 2). The authors asserted moisturizing one's skin and avoiding allergens are important strategies to minimize skin irritation and suggested that consumers should wear gloves and wash their hands when they finish using cleaning products. They also recommended consumers avoid sanitizers that contain fragrance.

3.3.8 Gas-based Interventions

Three investigations reported on the decontamination efficacy of gas-based interventions in laboratory settings. However, gaseous ozone and dry fogging may not be viable for use in LAMs due to potential for damage to collections.

In a preprint article, Schinköthe et al. (2020) evaluated the ability of dry fogging with an aerosolized mixture of peroxyacetic acid and hydrogen peroxide (aPAA/HP) to inactivate airborne SARS-CoV-2. The authors used quantitative carrier testing to assess the sensitivity of different test viruses, including SARS-CoV-2, and “to determine relevant process parameters to develop and validate effective disinfection protocols (≥ 4 log10 reduction) in various large and complex facilities” (p. 2). Airborne disinfection tests were conducted using a dry fog system (Mini Dry Fog) to generate aerosol droplets smaller than 6.5 μm in diameter at a feed air pressure of at least 350 kPa. The authors later noted that their method reduced infectivity in 1 to 4 hours” (p. 10). The results showed that “dry fogging a mixture of aPAA/HP is highly microbicidal, efficient, fast, robust, environmentally neutral, and a suitable airborne disinfection method” for SARS-CoV-2 and may be a suitable disinfection method for public spaces (p. 2). However, the authors also noted that room surface temperatures, particularly in rooms with complex layouts, can be “highly variable and can range from 20°C to 50°C” resulting microenvironments that can inhibit effective and uniform distribution of an aerosolized disinfectant (p. 14).

Yano et. al (2020) discussed the inactivation of SARS-CoV-2 with gaseous ozone treatment. Ozone gas was an effective method for inactivation of bacteria, fungus, parasites, and viruses at low concentrations. This article presented the use of ozone at a higher concentration to inactivate the novel SARS-CoV-2 virus. To test this method, plates with virus culture broths were placed in an ozone-proof airtight acrylic box 15cm away from ozone generating device (TM-04OZ; Tamura TECO ltd, Japan). The virus was exposed to a concentration of 1.0 ppm of ozone for 60 minutes and 6.0 ppm of ozone for

55 minutes, at a temperature of 25°C and relative humidity of 60-80%. Plates placed for 55-60 minutes without ozone exposure were used as controls. Before the exposure of ozone, the plaque assay was 1.7x 107pfu/mL. This decreased significantly following ozone exposure of 1.0 ppm for 60 minutes where the titer was 1.7x104 pfu/mL compared to 5.8 x10 pfu/mL in the control. The titer was less than or equal to 1.0 x10 3 pfu/mL after an exposure to 6.0 ppm of ozone for 55 minutes compared with 2.0x10 6 pfu/mL for the control. These results suggested that the exposure of SARS-CoV-2 to ozone at higher concentrations causes inactivation of the virus.

Pezzotti et al. (2020), in a letter to the editor of a peer-reviewed journal, proposed the use of silicon nitride, an FDA-cleared bioceramic, as a nontoxic alternative to toxic chemicals for the disinfection of surfaces contaminated with SARS-CoV-2. The authors presented results from an empirical study in which they assessed the ability of silicon nitride bioceramic, aluminum nitride, and copper (positive control) powder suspensions to inactivate SARS-CoV-2 virions in water at 15 wt% at one-minute inactivation time. The experiment showed that the "three powders produced equally effective inactivation of SARS-CoV2 virions (>99%)" (p. 1). Furthermore, during an experiment in which cells were inoculated with the SARS-CoV-2 virion and treated with the three substances, imaging showed that "cells inoculated with [silicon nitrate] supernatants showed only 2% infection and with [aluminum nitrate] supernatants showed 8% infection" (p. 2). Cells treated with copper-treated virion supernatant died from copper toxicity. The authors concluded that while all three powder suspensions are effective at inactivating SARS-CoV-2, only silicon nitrate is nontoxic to humans. They suggest that micron-sized silicon nitrate particles suspended in a spray liquid could be a safe alternative to toxic chemical disinfectants.

3.3.9 Antimicrobial Materials and Coatings

Antimicrobial materials and coatings have been found to inactive SARS-CoV-2 surfaces, which may lead to reduced transmission. Relevant reviews, letters to editors, and laboratory investigations are discussed in turn.

Imani et al. (2020), in a peer-reviewed literature review, presented an overview of the state of research on antiviral surface coatings and materials that may have potential for reducing transmission of SARS-CoV-2 via contaminated surfaces. The review focused on research related to the antimicrobial properties of copper, silver, zinc, and titanium dioxide materials and nanomaterials that have antiviral properties, with a brief overview of gold nanoparticles, transition metals (e.g., iron, magnesium, and manganese), silica nanoparticles, and perovskites. The authors also reviewed research related to polyelectrolyte-coated surfaces and photosensitizer compounds that are capable of inactivating viruses. Emerging technologies were also discussed, as was environmental and toxicity concerns related to using metals and inorganic materials. The authors noted that most copper research has focused on antibacterial properties and virucidal action has been largely hypothetical. They also noted that "solid-state silver compounds do not appear to have strong antiviral capabilities" (p. 12350). Based on their literature review, the authors concluded that accurate systematic research and development of antiviral surfaces is vital as "surfaces capable of immediately repelling and/or inactivating pathogens are urgently needed" (p. 12365).

Hutasoit et al. (2020) presented a cold-spray technique to rapidly apply a copper coating to stainless steel with the aim of inactivating SARS-CoV-2 on high-touch surfaces. The authors also assessed the virucidal capability of the copper coating as applied via the cold-spray technique. Cold-spray technology was a proven technique in which a “high-pressure carrier gas (air, nitrogen or helium) propels metal particles at supersonic velocity onto a substrate,” then “mechanically interlock with each other, thereby producing a thin dense deposit” of the coating onto the substrate (p. 94). For this study, stainless steel touch plates often used on doors were substrates. The authors applied a copper coating to the touch plates using the cold-spray technique, resulting in “a thickness of around 0.7 mm, produced within 7 min of spraying time,” which was then polished, “reducing the effective coating thickness to about 0.45 mm” (p. 94). After exposing the test surfaces to SARS-CoV-2, the authors found that after a two-hour incubation period, “96% of the virus was inactivated when exposed to the as-deposited (N) copper coating, whereas 92% virus inactivation was achieved on the annealed (A) copper coating. When the virus had a prolonged exposure of up to 5-hrs to these surfaces, an inactivation efficiency of 99.2% and 97.9% for the as-deposited (N) and annealed (A) copper coatings, respectively” (p. 94). Furthermore, the as-deposited copper coating was “found to have substantially higher SARS-CoV-2 (COVID-19) inactivation characteristic compared to stainless steel” (p. 96). The authors concluded that copper applied using a cold-spray technique could be useful for inactivating SARS-CoV-2 on high touch metal surfaces without the need for replacing the surface with copper. A particular strength of this article was that the authors use common commercial metals, as compared to metal scraps used in other studies.

Campos et al. (2020) presented results from tests to assess the ability of fabric bonded with Duritex™, a natural biopolymer and disinfectant, to inactivate SARS-CoV-2. For the experiment, the authors used 80/20 polycotton fabric thermally bonded with Duritex™, which was contaminated with SARS-CoV-2 in a laboratory setting. After the virus was added to the Duritex™-treated fabric, the authors observed “reductions in the titers compared with the untreated fabric of 1 log10 after 15 min of contact, 1.8 log10 after 30 min of contact and 2.5 log10 after 45 min of contact,” and “after 1 h of exposure, the decrease was approximately 3.5 log10, and after 2 h of exposure, the virus was decreased to titers below the detection limit of 30 PFU/sample” (p. 836). The authors conclude that “these results demonstrate that treatment of fabric with Duritex™ via thermal bonding can be used to render it self-disinfecting against SARS-CoV-2” (p. 836).

Hasan et al. (2020) discussed how nanostructured aluminum AL 6063 can inactivate SARS-CoV-2. Randomly oriented nanostructured surfaces were fabricated using a wet-etching technique with 2 M NaOH for three hours. Unetched AL 6063 was used as the control. The viability of the virus was reduced significantly on the etched surface within six hours compared to exposure to both the smooth AL 6063 control and polystyrene tissue culture plate (TCP) surfaces. After six hours of exposure, there was practically no viable live virus recovered. The authors asserted that the installation of nanostructured surfaces as an efficacious strategy to reduce transmission of SARS-CoV-2 in health care settings. Additional applications with such surfaces could show promise in additional settings; however, surface fabrication and installation has yet to be thoroughly tested in other contexts.

3.3.10 Cold Plasma

An emerging strategy to decontaminate surfaces from SARS-CoV-2 is cold plasma. Generally, this approach has been shown to inactivate aerosolized microorganisms on a variety of sources within short time frames (≤60 seconds).

Chen et al. (2020) employed an efficient cold atmospheric plasma (CAP) with argon feed gas to inactivate SARS-CoV-2 on plastic, metal, cardboard, basketball composite leather, football leather, and baseball leather surfaces. The CAP was administered by atmospheric pressure plasma jet. The SARS-CoV-2 sample was obtained via swab from a patient who developed COVID-19 in January 2020 in Washington, US. Surfaces were treated with SARS-CoV-2 at 2 × 105 PFU in 25 µL volume. Surfaces contaminated with the virus were exposed to helium or argon plasma for predetermined durations (e.g., 30 seconds, 60 seconds). Contaminated surfaces not exposed to plasma were included as the control. Results show CAP treatment inactivated all SARS-CoV-2 on the six surfaces in under 180s. Furthermore, at 30s of exposure, metal surfaces were decontaminated. Most measurements of the plastic and leather football surfaces showed virus inactivation during 30s and 60s treatment durations. Cardboard and basketball surfaces were decontaminated after 60s treatment (few measurements showed decontamination at the shorter 30s duration). Similar virus inactivation was observed for cotton cloth material (from face masks). Results demonstrate CAP as a safe and effective means to prevent virus transmission and infections for a wide range of surfaces with which people often come into contact.

Bisag et al. (2020) presented a peer-reviewed study that asserted cold atmospheric pressure plasmas can represent a promising solution due to production of a blend of reactive species, which can inactivate airborne aerosolized microorganisms. Authors employed a dielectric barrier discharge plasma source to inactivate bioaerosols containing purified SARS-CoV-2 RNA or Staphylococcus epidermidis flowing through it. Results indicated that cold atmospheric plasma was successful at degrading viral RNA in a short residence time (<0.2 s).

3.3.11 Decontamination Booths, Stations, Rooms

WHO guidance, letters, and investigations provide mixed support related to the use of technologies such as booths, stations, and rooms. These strategies are designed for application in public settings. Concerns related to safety as well as claims of efficacy are summarized below.

Rabby et al. (2020) describe considerations such as physical and psychological consequences of deploying "smart" handwashing stations. The WHO, CDC, Health ministry, and others have noted concern for transmission and negative health effects due to deployment of handwashing stations and disinfection booths. Specifically, widespread installation of disinfection booths in government (and nongovernment) buildings, malls, hospitals, police stations, and open city streets of Bangladesh are noted. Authors alert the reader to the glaring lack of evidence showing any reduction in spread after deployment of such booths.

Gray and Van Niekerk (2020) expressed concern about spray approaches via tunnels, condemning all uses due to potential dangers for individuals, especially those with existing allergic conditions.

Composition of spray chemicals were described as unknown and inappropriate for application to the human body both with short-term (e.g., eye and skin irritation) and long-term (e.g., cancer) health effects. Authors asserted that "disinfection tunnels are expensive, driven by false, profit-driven advertising" (p. 751). Relatedly, spray technology used in tunnels and booths do not affect respiratory tracts and hands (the primary transmission points). Further, the authors noted surface disinfection approaches that do not involve the five-to-ten-minute required contact with a surface are not effective. However, concerns related to efficacy, harmful chemical effects, and environmental consequences lacked robust supporting citations.

According to a journal article published by Herbert et al. (2020), handwashing stations in school settings may be an effective way to combat spread of SARS-CoV-2. Authors note that after a 10-day deployment in an Australian school, the electrical components of a prototype "smart" station were operational during field testing and were subjected to thorough cleaning protocols each day. In terms of use, the handwashing station was used 1,138 times during the testing period. Importantly, there was no COVID-19 transmission observed at the school during testing. The authors concluded that this study demonstrated a successful use of technology to improve hand hygiene among school-aged children.

3.3.12 Mouthwash and Nasal Sprays

A review by Burton et al. (2020) assessed benefits and harms of mouthwash and nasal spray products, specifically those administered to health care workers and/or patients undertaking aerosol generating procedures (AGPs). Generally, mouthwashes and sprays benefits were shown to help avoid cold/flu and upper respiratory tract infections caused by viruses. Mechanically, they did so by eradicating particles and preventing transmission. However, harmful outcomes such as irritation, allergic reactions, and damage resulting in loss of sense of smell (intranasal use) from changes microbiota were noted.

4. Discussion, Gaps, and Recommendations for Future Research

4.1 Discussion

Scientific research about SARS-CoV-2 has continued to evolve since the Phase 1 and 2 literature reviews conducted by REALM. Although the literature remains a work in progress, the results of the Phase 3 literature review indicate that researchers seem to prioritize the study of prevention and decontamination methods as well as how the virus spreads. Syntheses of these results, which emphasize new findings informing the three research questions, are described in this section.

4.1.1 Spread of SARS-CoV-2 through Indoor Settings

The Phase 3 literature review highlights a continued interest in the environmental factors that influence the spread of SARS-CoV-2 within the built environment. The literature suggests that several characteristics of the built environment contribute to the spread of the virus, including population density, private residential and commercial density, green space density, and land-use diversity (Huang et al., 2020). As more indoor spaces (e.g., workplaces and schools) reopen, there is an increased interest in the aerosol spread of SARS-CoV-2 in these settings. Research has examined how exposure to presymptomatic and asymptomatic persons might impact indoor environments. Exposure duration and distance between individuals appear to be key factors in the spread of the virus indoors.

Airborne spread of SARS-CoV-2 continues to be a topic of interest in the literature as studies show what a critical role it may play in transmission. Research has linked poor ventilation to COVID-19 outbreaks. Thus, researchers have focused on how ventilation and HVAC systems promote air exchange in indoor environments. Additionally, there is growing research on the role plumbing and drainage systems play in the spread of SARS-CoV-2. Evidence suggests that flushing toilets may increase airflow in bathroom settings and transmit fecal aerosols through plumbing and vents from one part of a building to another. More research is needed to better understand the mechanisms by which spread occurs via plumbing and drainage and to provide solutions for minimizing transmission.

Overall, there is a high risk of spreading SARS-CoV-2 throughout the built environment, especially within indoor settings where people can congregate in proximity and the virus can readily travel by air from person to person and onto high-touch surfaces. Additional research is needed to understand the unique factors that contribute to the spread of the virus in nonmedical settings and what specific guidelines are needed on how these settings might adapt their air exchange and HVAC operations to mitigate most effectively the spread of SARS-CoV-2.

4.1.2 Survival of SARS-CoV-2 on Material Surfaces through Environmental Attenuation

During the publication period considered in this report, very few articles presented novel data pertaining to natural attenuation of SARS-CoV-2 on surfaces and materials. One key article did find that in the absence of UV light, SARS-CoV-2 persisted on nonporous surfaces for at least 28 days and porous surfaces for up to 14 days at 20°C (Riddell et al., 2020). The report's findings suggested SARS-CoV-2 surface stability can increase in relation to decreased temperatures, nonporous surfaces, and absence of ultraviolet (UV) light. Another systematic review article by Bedrosian et al. (2020) was able to conduct a sub-analysis of viral survivability on three surfaces from seven studies and found that the half-life of the virus decreased as temperature and humidity increased. Additionally, although there were recent studies of virus attenuation on food packaging and water, the consensus is that neither are a primary route of transmission. Accordingly, these findings contribute to an understanding that SARS-CoV-2 persists on surfaces for varying amounts of time depending on environmental factors (e.g., temperature, surface dryness, and UV light exposure), and although indirect transmission via surfaces may not be a primary route of transmission, it has been identified as a potential route of transmission due to viral stability on some surfaces.

4.1.3 Effectiveness of Prevention and Decontamination Measures for SARS-CoV-2

The literature review identified several measures that have been reported to be effective in eliminating the presence of SARS-CoV-2, including UV light, PPE, hand hygiene, ventilation and open space, surface cleaners and disinfectants, antimicrobial materials and coatings, cold plasma, disinfection tunnels, and mouthwashes and nasal sprays (see **Table 2** below). However, some of these interventions, such as gaseous ozone, dry fogging, and UV treatments, may not be viable for use in LAMs due to potential for damage to collections.

Table 2 lists the decontamination and prevention strategies that were presented as effective against SARS-CoV-2 in the Phase 3 literature review.

Table 2. Decontamination/Prevention Strategies

Strategy	Details
Hand Hygiene	• Total contact hand sanitizing time of 45-50 seconds is necessary for disinfection (Singh et al., 2020). • Increased handwashing and use of sanitizers have contributed to an increase in skin sensitivity and eczema among different cohorts (Borch et al., 2020; Guertler et al., 2020).
PPE	• N95 and surgical masks have been found to be the most effective at keeping respiratory droplets from entering the air (Doung-ngren et al., 2020). • Bandanas and neck gaiters are the least effective at keeping respiratory droplets from entering the air. In fact, gaiters may lead to an increased number of droplets in the air when compared to no mask (Fischer et al., 2020; Ueki et al., 2020; Asadi et al., 2020). • Cloth masks shed fibers that could potentially carry coronavirus, although it is not clear whether viral transmission is possible via cloth fibers (Asadi et al., 2020). • Nazarious et al. (2020) describe the Pressure Optimized Powered Respirator (PROPER) hood-based system as a wearable clean room.
Ventilation and Open Space	• Building operations need to replace current recirculating ventilation strategies to natural or displacement ventilation systems to reduce SARS-CoV-2 transmission in high-density buildings (Lipinski et al., 2020). • Effective interventions include incorporating as much fresh outside air as possible indoors (Bhagat & Linden, 2020), opening the ventilation system's outdoor air damper as high as 100% (Guo et al., 2021), and to utilizing portable air cleaners (e.g., HEPA filters) (Marcone, 2020). • Thermal inactivation of SARS-CoV-2 was observed at a temperature of 55°C for 30 minutes and 65°C for 10 minutes (Kim et al., 2020).
UV Light	• Low dose far-UVC at a wavelength of 222nm could be an effective decontamination method that is safer for humans than the standard 254nm UVC (Buchan et al., 2020). • Upper air ultraviolet germicidal irradiation (UVGI) used above the heads of occupants in a room offers another solution for decontamination that can be applied to indoor environments where humans frequently travel without increasing radiation exposure risk (Beggs et al., 2020).
Surface Cleaners and Disinfectants	• Ethanol, hydrogen peroxide, and sodium hypochlorite can inactivate the virus within 60 seconds (Al-Gheethi et al., 2020). • Zinc oxide nanoparticles smaller than 100 nanometers can inactivate SARS-CoV-2 (with a size of 400 nm) (Al-Gheethi et al., 2020). • Inactivation is most efficacious when inanimate objects were cleaned with "chlorine-based disinfectants, alcohol, detergents, glutaraldehyde, iodine-containing detergents, hydrogen peroxide compounds and household bleaches,"

	and alcohol "showed efficient immediate activity" (Shimabukuro et al., 2020, p. 513). • Inactivation of SARS-CoV-2 on stainless steel, plastic (PET), glass, polyvinyl chloride (PVC), cardboard, and cotton fabric via treatment of 70% ethanol (EtOH), 70% isopropanol (IPA), 0.1% hydrogen peroxide (H_2O_2), or 0.1% sodium laureth sulphate (SLS) occurs at 30 seconds and 60 seconds (Gerlach et al., 2020). Thus, ingredients of common household cleaning and hygiene products are capable of rapidly inactivating SARS-CoV-2. • Dry fogging with an aerosolized mixture of peroxyacetic acid and hydrogen peroxide (aPAA/HP) is fast-acting, microbicidal, efficient, robust, and environmentally neutral method (Schinköthe et al., 2020). • Gaseous ozone exposure at a concentration of 1.0 ppm and 6.0 ppm showed inactivation of SARS-CoV-2 after 55-60 minutes (Yano et al., 2020).
Antimicrobial Materials and Coatings	• Antiviral surface coatings and materials have potential for reducing transmission of SARS-CoV-2 via contaminated surfaces (e.g., antimicrobial properties of copper, silver, zinc, and titanium dioxide materials and nanomaterials) (Imani et al., 2020). • Copper cold spray has potential for reducing transmission of SARS-CoV-2 via contaminated surfaces (Hutasoit et al., 2020). • Two hours of exposure to fabric bonded with Duritex™ (a natural biopolymer and disinfectant) has potential for reducing transmission of SARS-CoV-2 via contaminated surfaces (Campos et al., 2020).
Other	• Smart handwashing stations were shown to be an effective way to combat spread of SARS-COV-2 in a school setting, as a particular station was used 1,138 times during a testing period with no evidence of COVID-19 transmission observed at the school during testing (Herbert et al., 2020). However, Rabby et al. (2020) describe WHO, CDC, Health ministry considerations such as physical and psychological consequences of deploying such "smart" handwashing stations, specifically, concern for transmission and negative health effects. • Concerns related to decontamination booths and tunnels were reported (Gray & Van Niekerk, 2020) due to potential dangers for individuals with existing allergic conditions, unknown composition of spray chemicals being applied to the human body, and inability to affect respiratory tracts and hands (i.e., primary transmission points). • Cold plasma has been shown to inactivate aerosolized microorganisms on a variety of sources within short time frames (≤60 seconds) (Chen et al., 2020; Bisag et al., 2020). • Mouthwash and nasal spray products show efficacy in reducing spread of viruses (Burton et al., 2020).

To prevent the spread of SARS-CoV-2, handwashing for 20 seconds with soap and water was recommended (Alzyood, 2020). Hand sanitizers are also effective when individuals use at least 3 mL of 80% v/v ethanol or more than 75% v/v isopropanol-based sanitizer (Singh et al., 2020). Singh et al. (2020) recommend a total contact time of 45-50 seconds as necessary for disinfection. However, exploration of the health impacts of sustained use of hand hygiene has indicated that increased handwashing and use of sanitizers contribute to an increase in skin sensitivity and eczema among children and nurses (Borch et al., 2020; Guertler et al., 2020).

Further exploration of the importance of air circulation and filtration interventions were present in recently published literature. Recent articles emphasize the need to update recirculating ventilation strategies to natural or displacement ventilation systems to reduce SARS-CoV-2 transmission in high-density buildings (Lipinski et al., 2020). Additional recommendations are to incorporate as much fresh outside air as possible (Bhagat & Linden, 2020), to open the outdoor air damper as high as 100% (Guo et al., 2021), and to utilize portable air cleaners (e.g., HEPA filters) (Marcone, 2020). These interventions are demonstrated to reduce the presence of SARS-CoV-2 in indoor environments.

Some studies note the potential for UV light treatments to deactivate SARS-CoV-2. The existing literature suggested that the use of low dose far-UVC at a wavelength of 222nm compared to the standard 254nm UVC could be an effective decontamination method that is safer for humans (Buchan et al., 2020). Upper air ultraviolet germicidal irradiation (UVGI) used above the heads of occupants in a room offers another solution for decontamination that can be applied to indoor environments where humans frequently travel while reducing radiation exposure risk (Beggs et al., 2020).

Masks continue to be recommended as PPE. It is well documented that masks mitigate virus transmission, especially if worn consistently (Chua et al., 2020; Doung-ngren et al., 2020; Fischer et al., 2020; Ueki et al., 2020). However, researchers have explored the complexities of how this intervention mitigates risk of SARS-CoV-2 transmission. N95 and surgical masks have been found to be the most effective at keeping the wearer’s respiratory droplets from entering the air, and bandanas and neck gaiters are the least effective. In fact, gaiters may lead to an increased number of droplets in the air when compared to no mask (Fischer et al., 2020; Ueki et al., 2020; Asadi et al., 2020). Cloth masks have become increasingly popular because they can be made from home, are inexpensive, reusable, and able to be personalized. However, Asadi and colleagues (2020) noted in their research that shedding fibers from cloth masks may impact their effectiveness at mitigating spread.

The most salient limitation of the mask literature at this time is that the SARS-CoV-2 virus itself has not been widely used to test mask efficacy or innovations. This is likely due to safety concerns for researchers and human subjects. SARS-CoV-2 is transported via droplets, and many of the studies included here used simulated droplets or droplets from healthy individuals to test efficacy. Since the properties of a given fabric or fabric treatment are physical and should be consistent across studies (as with the N95), it is reasonable to assume that droplets carrying the coronavirus would behave in the same way as droplets not carrying the virus. At present, the research does not indicate otherwise. Despite this assertion, mask innovations should be tested with SARS-CoV-2 to ensure their novel technology effectively combats the pathogen it was designed to mitigate. However, one of the biggest unknowns is how virus titer and number of droplets released (via a super emitter, for example) affect mask efficacy, so these variables warrant further exploration.

This literature review identifies several surface cleaners and disinfectants that were found to be effective at inactivating SARS-CoV-2, and overall, surface decontamination is recommended to reduce risk of transmission. For example, Al-Gheethi et al.'s (2020) bibliometric analysis noted that the most common disinfectants were ethanol, hydrogen peroxide, and sodium hypochlorite, which could inactivate SARS-CoV-2 within one minute. The authors also noted that zinc oxide nanoparticles smaller than 100 nanometers “could inactivate SARS-CoV-2.” Further, Shimabukuro et al. (2020) concluded that inactivation of SARS-CoV-2 occurred when inanimate objects were cleaned with a variety of compositions (e.g., chlorine-based disinfectants, glutaraldehyde, iodine-containing detergents, hydrogen peroxide, bleaches) and alcohol shows efficient immediate disinfection activity. Gerlach et al.'s (2020) results indicated inactivation of SARS-CoV-2 on stainless steel, PET, glass, PVC, cardboard, and cotton fabric was possible with ingredients of common household cleaning and hygiene products. Schinköthe et al. (2020) evaluated dry fogging with an aerosolized mixture of peroxyacetic acid and hydrogen peroxide (aPAA/HP) to inactivate airborne SARS-CoV-2. The results show the dry fogging approach to be "highly microbicidal, efficient, fast, robust, environmentally neutral, and a suitable airborne disinfection method" for SARS-CoV-2 and may be a suitable disinfection method for public spaces (p. 2). Overall, these findings indicate that a wide range of available surface cleaners can be used to effectively reduce the presence of SARS-CoV-2 in buildings and on materials.

Lastly, this literature review identifies several recently developed approaches to decontamination and prevention: mouthwashes and nasal spray products (Burton et al., 2020), smart handwashing stations (Herbert et al., 2020; Rabby et al., 2020), tunnels (Gray & Van Niekerk, 2020), and cold plasma (Chen et al., 2020; Bisag et al., 2020). These interventions warrant additional study.

4.2 Gaps and Recommendations

4.2.1 Gaps in the SARS-CoV-2 Literature

Given the emerging and evolving nature of SARS-CoV-2 and its impact on humans, researchers are actively working to produce new data and develop a comprehensive understanding of the virus, especially how it spreads, its transmissibility, how long it persists on surfaces, effective means to mitigate transmission and spread, and effective means to destroy the virus in the environment. As such, the gaps identified in the literature by this review include areas previously identified in the Phase 1 or 2 literature reviews that have not yet been clarified as well as new gaps arising from recent scientific study. At the time of this report, the scientific community's understanding of the virus has continued to evolve as peer-reviewed publications related to the research questions continue to be released. In general, additional rigorous experimental research is needed that focuses specifically on SARS-CoV-2 to (1) replicate and verify (or challenge) the findings of the experiments released to date, (2) resolve discrepancies in the current literature, and (3) explore the diverse variables that could affect the virus' ability to spread in LAMs and other similar environments. Some of the gaps in the literature that may prove useful to understanding the research questions of this literature review include:

- Comprehensive studies employing experimental research methods to investigate the relative risks for transmission of the virus through the known routes of transmission: droplets, aerosols, fomites/surfaces, and biological substances unrelated to respiration (e.g., urine, feces, vomit, etc.). Such research will help LAMs accurately prioritize prevention and decontamination efforts. Furthermore, additional experimental research can clarify the risks for airborne spread of the virus, including testing the dispersion of SARS-CoV-2 specifically through talking, breathing, coughing, sneezing, and other respiratory activities.
- Many research articles about the spread of the virus report on findings from medical environments, especially hospital areas devoted to patients with COVID-19 infection, so further

research about SARS-CoV-2 spread in nonmedical settings (e.g., LAMs, offices, and other workplaces) may illuminate unique features and factors of spread in those environments.

- Current studies of mask efficacy tend to be theoretical in nature by substituting surrogate viruses or using other substances altogether, which perhaps mistakenly assumes similarity to how SARS-CoV-2 interacts with masks. Additionally, further study of effects of mask wearing on transmission, including differences when infector or infected wears a mask, may elucidate further understanding of mask efficacy. Accordingly, further study of the efficacy of different mask types using SARS-CoV-2 specifically, as well as different threats (e.g., direct droplet-to-droplet v. aerosol transmission) may more closely approximate actual transmission risks.
- Empirical study of SARS-CoV-2 surface attenuation patterns continues to be reported in markedly fewer publications than other types of studies relevant to this report. As such, additional laboratory testing across surface types, especially those most relevant to LAMs, and under varying environmental variables (e.g., temperature, humidity, and surface pH) is needed to expand understanding of risk via fomite transmission. These studies should use tests able to detect viable SARS-CoV-2 instead of simply detecting for RNA, the latter providing less certainty around transmission risks. Ideally, such studies would seek to standardize methodologies to allow for robust meta-analyses to consolidate the field’s findings in the future.
- Investigations of the virus’ infectious dose for humans (i.e., the minimum viral load that results in infection in humans), including variations introduced by individual differences (e.g., immunological capabilities) and different exposure routes (e.g., aerosol v. fomite), are still needed to clarify what end point(s) for prevention, attenuation, and decontamination are necessary to prevent spread of the virus and/or transmission to other people. Further, it seems some people have been able to transmit the virus more readily than others (i.e., “super-spreaders”), so further understanding of this population may help identify viable interventions to reduce virus spread and transmission. Note: direct investigation of the clinical research on this topic is beyond the scope of this literature review, but knowledge about this topic could be used to promote clear guidelines for prevention and spread of the virus by providing a metric for maximum tolerance of the virus in environments where humans gather.
- This literature review identified few studies of the survival of SARS-CoV-2 on fomites sampled in public settings, and research on the survival of SARS-CoV-2 on surfaces (e.g., metal, plastic) is not always reflective of fomite materials in the natural environment, including those found in LAMs. More information is needed on the survival of the virus on common fomites such as floors, shoes, ventilation grates, and cell phones to better understand transmission risk in LAMs.
- Further exploration of decontamination methods for airborne SARS-CoV-2 is needed to reduce risk of transmission in indoor environments.
- Although numerous decontamination and prevention interventions have been found effective, this literature review did not encounter studies of transmission risk reduction achieved by exercising these interventions in combination.

4.2.2 Recommendations for Specific Research to Inform Building Operations

Recommendations for additional research include those items listed in the gaps above, and novel research on these topics should be conducted with SARS-CoV-2, in particular (where safe and feasible). Additional testing is recommended to gather data on the impacts of ambient environmental conditions (temperature and humidity) on SARS-CoV-2 located on surfaces and materials representative of those found in LAMs, as this area remains less studied. Further, rigorous scientific experiments that expand the scientific community's understanding of how SARS-CoV-2 is spread indoors through air and fomites are needed, as are studies of how people can contract the virus through these avenues. These findings could help inform how building operations can be modified and how interventions (for decontamination and prevention) should be prioritized to protect staff, patrons, and visitors by reducing the risks of viral transmission. Lastly, the body of peer-reviewed scientific publications about SARS-CoV-2 only continues to grow, so ongoing monitoring and periodic reviews of updates to the literature are recommended to ensure operations are informed by the latest, highest-quality, and most significant research findings.

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Appendix A. Search Strings

Focus Area	Database	Search String	Search Date	Results Yielded*
Decontamination and Attenuation	Scopus	(TITLE-ABS (coronavir* OR "SARS-CoV-2" OR "2019-nCoV" OR "COVID-19") AND TITLE-ABS (sanitiz* OR decontam* OR steriliz* OR disinfect* OR inactivat* OR "half life" OR attenuat* OR persist* OR stabil*) AND NOT TITLE-ABS (peptide OR cytokine OR pregnancy OR aperture OR iron OR cancer OR vaccine OR glycoprotein OR protease OR antibod* OR intravascular OR clinical OR opioid OR pollution OR mental OR therap* OR recept* OR protein OR immun*)) AND ((PUBDATETXT ("August 2020" OR "September 2020" OR "October 2020" OR "November 2020" OR "December 2020") OR PUBYEAR > 2020)	1-Dec -2020	1,286
	SciTech	"(noft(coronavir* OR ""SARS-CoV-2"" OR ""2019-nCoV"" OR ""COVID-19"") AND noft(sanitiz* OR decontam* OR steriliz* OR disinfect* OR inactivat* OR ""half life"" OR attenuat* OR persist* OR stabil*)) NOT noft(peptide OR cytokine OR pregnancy OR aperture OR iron OR cancer OR vaccine OR glycoprotein OR protease OR antibod* OR intravascular OR clinical OR opioid OR pollution OR mental OR therap* OR recept* OR protein OR immun*) Additional limits - Date: After August 01 2020 Scholarly Journals OR Working Papers OR Other Sources OR Reports OR Conference Papers & Proceedings		
	Web of Science	(TS=(coronavir* OR "SARS-CoV-2" OR "2019-nCoV" OR "COVID-19") AND TS=(sanitiz* OR decontam* OR steriliz* OR disinfect* OR inactivat* OR "half life" OR attenuat* OR persist* OR stabil*)) NOT TS=(peptide OR cytokine OR pregnancy OR aperture OR iron OR cancer OR vaccine OR glycoprotein OR protease OR antibod* OR intravascular OR clinical OR opioid OR pollution OR mental OR therap* OR recept* OR protein OR immun*) Refined by: [excluding] DOCUMENT TYPES: (NEWS OR DATA SET OR REFERENCE MATERIAL OR PATENT OR CLINICAL TRIAL) AND LANGUAGES: (ENGLISH)Timespan: 2020		
	MED-LINE	(AB (coronavir* OR "SARS-CoV-2" OR "2019-nCoV" OR "COVID-19") AND AB (sanitiz* OR decontam* OR steriliz* OR disinfect* OR inactivat* OR "half life" OR attenuat* OR persist* OR stabil*) NOT AB (peptide OR cytokine OR pregnancy OR aperture OR iron OR cancer OR vaccine OR glycoprotein OR protease OR antibod* OR intravascular OR clinical OR opioid OR pollution OR mental OR therap* OR recept* OR protein OR immun*)) OR (TI(coronavir* OR "SARS-CoV-2" OR "2019-nCoV" OR "COVID-19") AND TI(sanitiz* OR decontam* OR steriliz* OR disinfect* OR inactivat* OR "half life" OR attenuat* OR persist* OR stabil*) NOT TI(peptide OR cytokine OR pregnancy OR aperture OR iron OR cancer OR vaccine OR glycoprotein OR protease OR antibod* OR intravascular OR clinical OR opioid OR pollution OR		

		mental OR therap* OR recept* OR protein OR immun*) Limiters - Date of Publication: 20200801-		

***Articles duplicated across the 4 databases were removed from these counts**

Focus Area	Database	Search String	Search Date	Results Yielded*
Transmission	Scopus	((TITLE-ABS ((coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV")) AND TITLE-ABS (spread* OR transfer* OR transmi* OR persist* OR surviv*) AND TITLE (indoor OR office OR "climate controlled" OR ambient OR environment* OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat*)) AND (PUBDATETXT ("August 2020" OR "September 2020" OR "October 2020" OR "November 2020" OR "December 2020") OR PUBYEAR > 2020))	1-Dec-2020	648
	SciTech	"ti,ab(coronavir* OR covid OR ""COVID-19"" OR ""SARS-CoV-2"" OR ""2019-nCoV"") AND ti,ab(spread* OR transfer* OR transmi* OR persist* OR surviv*) AND ti(indoor OR office OR ""climate controlled"" OR ambient OR environment* OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat*)Additional limits - Date: After August 01 2020 NOT (Trade Journals AND Wire Feeds AND Blogs, Podcasts, & Websites AND Magazines)”		
	Web of Science	TS=(coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND TS=(spread* OR transfer* OR transmi* OR persist* OR surviv*) AND TI=(indoor OR office OR "climate controlled" OR ambient OR environment* OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat*) Refined by: [excluding] DOCUMENT TYPES: (DATA SET OR NEWS OR PATENT OR CLINICAL TRIAL) Timespan: 2020		
	MED-LINE	AB ((coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND AB (spread* OR transfer* OR transmi* OR persist* OR surviv*) AND TI (indoor OR office OR "climate controlled" OR ambient OR environment* OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat*) OR TI ((coronavir* OR covid OR "COVID-19" OR "SARS-CoV-2" OR "2019-nCoV") AND TI (spread* OR transfer* OR transmi* OR persist* OR surviv*) AND TI (indoor OR office OR "climate controlled" OR ambient OR environment* OR air OR airborne OR aerosol* OR hvac OR merv OR filter* OR filtrat* OR ventilat*) Pub Date: August 2020- current		