Aerosol Transmission of Infectious Disease and the Efficacy of Personal Protective Equipment (PPE)

A Systematic Review

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Objective: Health care professionals and governmental agencies are in consensus regarding contact and droplet transmission of infectious diseases. However, personal protective equipment (PPE) efficacy is not considered for aerosol or airborne transmission of infectious diseases. This review discusses the inhalation of virus-laden aerosols as a viable mechanism of transmission of various respiratory infectious diseases and PPE efficacy. **Methods:** The Preferred Reporting Items for Systematic reviews, and Meta-Analysis (PRISMA) guidelines was used. **Results:** The transmission of infectious disease is of concern for all respirable diseases discussed (SARS-CoV-1, SARS-CoV-2, MERS, influenza, and tuberculosis), and the effectiveness of facemasks is dependent on the efficiency of the filter, fit, and proper use. **Conclusion:** PPE should be the last resort in preventing the spread of infectious disease and should only be used for protection and not to control the transmission.

Keywords: COVID-19, infectious diseases, influenza, MERS, SARS-CoV-1, SARS-CoV-2, tuberculosis

In general, proximity plays a vital role in transmitting infectious diseases, including influenza, varicella, parvovirus, and SARS-CoV-1.[1] Coronaviruses have long been identified as a significant veterinarian disease and lead to common cold development.[1] However, three outbreaks of severe respiratory disease have resulted from novel coronaviruses within the last 20 years.[1] Severe acute respiratory syndrome (SARS) resulted in a global outbreak in the early 2000s totaling 8096 cases, with 774 proving fatal before strict quarantine measures were implemented to control the outbreak.[1] The SARS outbreak was the first insight into novel coronaviruses' pandemic potential. In 2012, Middle East Respiratory Syndrome (MERS) drew even more attention due to its high fatality rate among reported cases; however, the case amount has remained low given its inefficiency of person-to-person transmission.[1,2] Although SARS and MERS were limited outbreaks, SARS-CoV-2 has developed into a global pandemic due to its efficient person-to-person transmissibility and high fatality rate.

The global outbreak of the Coronavirus disease 2019 (COVID-19) caused by sudden acute respiratory syndrome resulted in a pandemic.[3] According to the World Health Organization (WHO), the United States has far exceeded the total reported cases of other countries with over 33.4 million COVID-19 infections as of June 25, 2021.[4] The disease's severity ranges from asymptomatic to life-threatening, with a fatality rate of approximately 2% globally and in the United States.[5] Center for Disease Control and Prevention (CDC) guidance suggests practicing good hand hygiene, wearing a face covering, adequate ventilation, and socially distancing as an effective means of controlling the spread of infectious diseases, including SARS-CoV-2.[6] However, the importance of understanding the mechanism of aerosolized transmission has often been understated when recommending control measures and remains an open question for various infectious diseases.[7]

Evidence suggest that SARS-CoV-1 can be transmitted via aerosolized droplets within adequately ventilated areas.[8] As a result, international agencies have developed public health and safety guidelines within an indoor environment. Recent articles have indicated that SARS-CoV-2 is present in respirable droplets generated by infected individuals while talking, sneezing, and breathing.[9] This has led to the recommendation that healthcare providers who perform intubation or other aerosol-producing procedures should wear a respirator with an N95 or higher filter.[9,10] Studies have shown that normal breathing and talking produce small aerosol droplets varying in size and amount, even in the absence of cough.[1,8,9,11,12] Contaminated aerosols produced by coughing and breathing of infected individuals have been examined in various settings, suggesting that aerosol transmission of SARS-CoV-2 may occur under certain conditions, such as a sufficient particle count emitted from infected individuals and favorable airflow for transmission.[9]

Select studies have detected SARS-CoV-2 virus in COVID-19 patients exhaled breath[9,13]; one study noted human-generated, virus-laden aerosol remained transmissible for at least 3 hours.[9] Another study collected high-volume air samples in isolated rooms more than 6 ft. from the infected patients to find that 63% of the samples were contaminated with aerosols containing SARS-CoV-2 genetic material.[9,14] Additionally, aerosol samples were taken in two hospitals in Wuhan to determine the particle size distribution of SARS-CoV-2 contaminated droplets. The particle size distribution ranged from less than 0.5 to more than 2.5 μm, with the majority of collected particles being between 0.25 and 1.0 μm and more than 2.5 μm.[9,15] Understanding the role of the droplet and aerosol transmission of infectious diseases is essential in determining the potential of infection from inhalation of various illnesses and providing insight into personal protective equipment (PPE).

PPE has long been used to protect against the spread of disease. Since the early 1900s, medical professionals have used surgical masks to treat disease-infected individuals.[16] Today, masks are offered in various fabrics, filters, and fits to prevent exposure and transmission. In addition, the Occupational Safety and Health Administration (OSHA) and the National Institute of Occupational Safety and Health (NIOSH) regulate the selection of respirators in the workplace and the testing and certification of respiratory equipment, respectively.[16] This shared approach recognizes the importance of filter efficiency and the proper use of respiratory protective equipment.[16] However, masks' adequate protection level for preventing the spread of respiratory infectious disease remains in question.

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Clinical significance: Virus containing aerosols and PPE effectiveness directly impacts health practitioners. This review synthesized the knowledge surrounding infectious disease transmission, including COVID-19 and PPE efficacy.

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This present review aims to discuss the inhalation of virus-laden aerosols as a viable mechanism of transmission of various respiratory infectious diseases and the efficacy of PPE. This review also considered how much SARS-CoV-2 aerosol and other infectious respiratory diseases are generated by breathing, speaking, coughing, and sneezing. Additionally, the implications for transmission and PPE's efficacy in preventing the transmission of infectious diseases, the particle size, and the distribution of infectious respiratory disease aerosols and droplets are discussed.

METHODOLOGY

Search Strategy

The Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines were used for this study.[17] A search was conducted from various electronic databases, including PubMed, PubMed Central, Scopus, Medline, and Google Scholar, identifying literature related to aerosol transmission and the effectiveness of PPE in controlling the spread of infectious disease. Search terms utilized were: ''SARS-CoV-2'' or ''COVID-19'' (1), ''MERS'' (2), ''SARS-CoV-1'' (3), ''Influenza'' (4), ''Tuberculosis'' (5), ''Infectious Disease'' or ''Emerging Infectious Disease'' (6), ''Healthcare'' (7), ''Virus'' (8), ''Aerosol'' or ''Bioaerosol'' or ''Aerosol Transmission'' (9), ''Droplet'' or ''Droplet Transmission'' (10), ''Airborne Transmission'' (11), ''Coughing'' or ''Sneezing'' or ''Breathing'' or ''Talking'' (12), and ''Personal Protective Equipment'' or ''Facemask'' or ''Face Covering'' or ''Respirator'' or ''Filtering Facepiece Respirator" (13). The search terms were combined by ([1] or [2] or [3] or [4] or [5] and [9]), ([1] or [2] or [3] or [4] or [5], and [10]), ([1] or [2] or [3] or [4] or [5] and [11], ([1] or [2] or [3] or [4] or [5], and [12]), ([1] or [2] or [3] or [4] or [5] or [6], and [13]), ([6] and [7]). The combined search was intended to capture relevant peer-reviewed journal articles, studies, reviews, and meta-analyses. Finally, a reference list of identified literature was manually searched for relevant articles and case studies.

Definitions

There has been a dispute in the scientific community regarding the definitions of requisite concepts related to routes of disease transmission, including ''aerosol transmission'' and ''droplet transmission,'' as well as disagreement of what is considered an ''aerosol,'' ''small droplet,'' or ''large droplet.'' The following definitions are used throughout this review:

- Aerosol—General term for an assemblage of microscopic particles suspended in air. In the present context, aerosol particles include droplets or residuals of dried droplets in ambient air that may contain infectious pathogens.[18]
- Droplet—General term for a liquid particle varying in particle size. In the context of this review, droplet refers to mucus, saliva, or sputum particles produced from an infected individual.
- Small droplet—Droplets that stay suspended in the air long enough to be inhaled. These droplets can stay airborne for minutes to hours, depending on particle size and ambient conditions. The precise size cutoff is difficult to determine as ambient conditions such as ventilation and airflow affect the suspension in air.[1]
- Large droplet—Droplets that stay airborne for seconds. The suspension of large droplets in the air is mainly affected by gravitational settling rather than ambient airflow. Large droplets typically settle to the ground or surrounding surfaces before drying in ambient air.[1]
- Droplet transmission—Virus laden large droplets produced from talking, sneezing, or speaking that is projected onto the face of an uninfected individual and absorbed by mucous membranes.
- Aerosol transmission—Virus contaminated small droplets produced from talking, sneezing, or speaking that are inhaled by an uninfected individual within 6 ft. from the source.

Inclusion and Exclusion Criteria

Eligible studies included peer-reviewed journal articles, studies, reviews, and meta-analyses investigating aerosol transmission of infectious diseases of interest and the efficacy of respiratory protective equipment. Infectious diseases of interest include SARS-CoV-1, MERS, SARS-CoV-2, influenza, and tuberculosis. The study's respiratory protective equipment was limited to homemade (cloth) masks, surgical masks, and N95 filtering facepiece respirator (FFR). Studies were limited to those published in English. The search included worldwide peer-reviewed studies published between January 2003 and November 2020. The search parameters were chosen to ensure the inclusion of SARS-CoV-1 and MERS coronaviruses. Duplicate studies were removed from the initial compilation of studies. The eligibility criteria were applied to titles and abstracts of studies obtained from the search during the initial screening phase. The remaining studies' full manuscripts were analyzed using the same criteria during the second phase of screening. The studies were then thoroughly examined for similarities or differences in data.

Data Collection

Similar to previous literature reviews, data was collected from included studies using Microsoft Excel.[19] The data extracted included: author(s), year of publication, country, study objective, study design, study group, PPE, and principal findings.[19] Discoveries that pertain to the inclusion and exclusion of aerosol transmission of infectious diseases and the efficacy of PPE were carefully interpreted and included in this review.

RESULTS

Study Selection

The literature search identified 376 potential articles for inclusion from the initial database search. Twelve additional articles were then identified from the manual search. One-hundred twenty (32%) duplicate articles were removed from the 376 total studies. The remaining 256 articles were then evaluated to determine eligibility for inclusion. Of the 256 remaining articles, 70 studies met the inclusion criteria and were used for the systematic review. The process for inclusion is described in Fig. 1. The studies included in the review were published in 12 countries, with most studies published in the United States. The year of publication of the included literature ranged between 2008 and 2020, with most of the studies published in 2020. However, some of the citations for 2020 studies show 2021, especially for SARS-CoV-2 studies, because they were made available online in 2020 but not published until 2021.

Emerging Themes

From the qualitative analysis of each article, we deduced six themes from the literature review to explore the aerosol transmission of infectious diseases and PPE efficacy. These themes are (1) human-generated aerosol transmissions; (2) implications for transmission of generated infectious respiratory disease aerosols; (3) the effectiveness of PPE in preventing transmission of infectious disease; (4) the size distribution and emission rate of aerosol particles produced from breathing, speech, vocalization, and coughing; (5) aerosol particles' fluid dynamics associated with expiratory events; (6) aerosol transmission of infectious disease. Table 1 has the details of all articles reviewed with related themes, and Fig. 2 reports the distribution of articles by theme.

From these articles, 14 investigated human-generated aerosol transmissions, and 37 examined the implications for the transmission of generated infectious respiratory disease aerosols. Additionally, 22 studies discussed the effectiveness of PPE in preventing the transmission of infectious diseases. The majority of the article

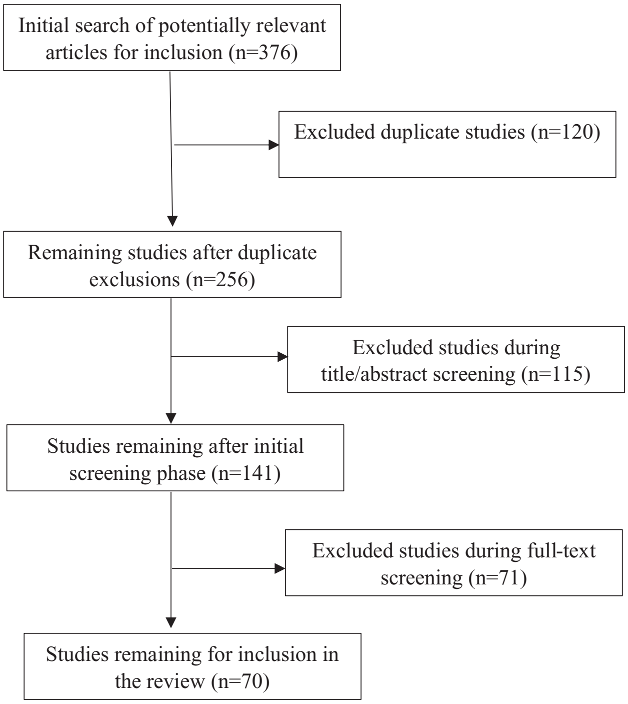

FIGURE 1. Process of selecting studies for inclusion in the review.

revealed that aerosol transmission is of great concern for various infectious diseases, including SARS-CoV-1, SARS-CoV-2, MERS, influenza, and tuberculosis, with the effectiveness of PPE being dependent on the efficiency of the filter, fit, and proper use of masks and respirators.

Details of Human-Generated Aerosols

From the 14 articles investigating human-generated aerosols, two studies in this group determined that coughing generates a greater concentration of aerosol particles than speaking.[20,21] However, increasing the loudness of voice increases particles' emission rate.[10] Another study examining size distribution and emission rate observed that sub-micron particles make up the most significant fraction of exhaled particles from tidal breathing.[22] He et al[23] extracted viable viruses from samples collected from Wuhan hospitals to corroborate this. One study examined the aerosol concentration generated from 10 woodwind and brass instruments. The study determined that several variables affect aerosol generation, including changing individuals' dynamics and respiratory behavior.[23] The remaining studies discussed aerosol particles' fluid dynamics associated with expiratory events, with five of them suggesting that large droplet particles tend to fall within several meters. However, small respirable droplets covering a large size range (aerodynamic d less than 10 μm, after evaporation), stay suspended in the air extending the range of potential exposure.[1,20,24–27] In another study, the cough jet of expired particles is deflected downward when the momentum of two jets is equal, or the downward jet has greater velocity.[28] The final study results determined that droplets are generated more frequently in high-temperature and low-humidity; however, droplets can travel distances up to three times further in low-temperature and high-humidity.[27]

Infectious Diseases Investigated

Figure 3 shows the aerosol transmission of infectious diseases; 31 examined SARS-CoV-2, nine influenza, nine SARS-CoV-1, six MERS, and three tuberculosis. In most of these studies, four main factors determine potential aerosol transmission: (1) aerosol generation; (2) infectious dose; (3) viability in the environment; (4) access to the target tissue.[29,30] Twenty-five studies discussed aerosol generation and exposure, six estimated the infectious dose, nine investigated the viability of disease-laden particles in the environment, five studies examined the target tissue for infection, and the remaining observed in-direct transmission in mice.

SARS-CoV-1 and MERS

For both SARS-CoV-1 and MERS, the potential risk of transmission was dependent on the amount of viable virus within the aerosol particle and the amount of time exposed.[30,31] Additionally, environmental factors such as temperature and humidity can affect the viability of SARS and MERS.[32,33] Some of the studies suggest that aerosols can stay suspended in the air for extended periods and, when in high concentrations, can present a viable risk of exposure via aerosol transmission.[29,33–36]

SARS-CoV-2

Some studies reported that asymptomatic individuals produce high emission rates during light activity and that transmission is a function of concentration and exposure time.[1,29,37,38] At the same time, others reported virus-laden aerosols' viability in the environment.[32,33,36,39–44] Two of these studies found viable SARS-CoV-2 RNA in the saliva, oropharynx, nasopharynx, and sputum of infected individuals.[42,43] Another study estimated viable viral concentrations ranging from 6 to 74 tissue culture infective dose (TCID50) units/L of air.[40] Additionally, it was determined that SARS-CoV-2 could remain viable in aerosol for hours and on surfaces for days with higher temperatures and humidity, having a modest effect on the virus's viability in the environment.[32,36] There were discussions on the potential for exposure to target tissue.[45–48] These studies concluded that the primary mechanism of exposure was through the angiotensin-converting enzyme 2 (ACE-2) receptor in various tissues, including oral mucosa, respiratory tract, lungs, and gastrointestinal tract. Most studies concluded aerosol transmission as a potential route of transmission given the viability in the environment and the primary exposure mechanism. The remaining study identified droplet transmission in mice; however, aerosol transmission rarely occurred.[49]

Influenza

Nine studies examined the risk of aerosol transmission for novel influenza viruses. Most of the studies discuss the dependence of viral concentration in the aerosol particle as contributing to the viability of transmission.[30,50–53] The studies suggest that high concentrated doses and length of exposure are essential to aerosol transmission. For example, a study described respirable droplet generation as the driving factor for medium to long-term epidemics; however, inspirable droplets—defined as larger droplets with an aerodynamic diameter in the range of 10 to 100 μm—are characteristic of short-term epidemics with high attack rates.[26] Another study models the risk of infection among swine workers.[54]

Tuberculosis (TB)

Three studies detailed the risk of exposure for aerosol transmission of TB.[30,31,34] Two studies suggest that aerosol transmission is correlated with the severity of the illness and that aerosol particles can remain viable in the environment for an extended period.[30,31] The other study was inconclusive in determining aerosol generation from medical intervention procedures.[34]

PPE Effectiveness

From the studies that examined the efficacy of PPE in preventing the spread of infectious disease, the majority of the studies examined the effectiveness of surgical masks ($n = 18$), N95 FFR ($n = 12$), and homemade masks ($n = 7$). All of the studies

TABLE 1. List of all Articles Selected for this Review and Themes Discussed

S/N	Author(s), Year	Paper Title	Themes Discussed
1.	Ahrenhoz et al, 2018	Assessment of environmental and surgical mask contamination at a student health center—2012–2013 influenza season	VI
2.	Asadi et al, 2019	Aerosol emission and superemission during human speech increase with voice loudness	I, IV
3.	Asadi et al, 2020	The coronavirus pandemic and aerosols: does COVID-19 transmit via expiratory particles?	VI
4.	Asadi et al, 2020b	Efficacy of masks and face coverings in controlling outward aerosol particle emission from expiratory activities	III, VI
5.	Bao et al, 2020	Transmission of severe acute respiratory syndrome coronavirus 2 via close contact and respiratory droplets among human angiotensin-converting enzyme 2 mice	II, VI
6.	Bouroubia et al, 2014	Violent expiratory events: on coughing and sneezing	I, V, VI
7.	Buonanno et al, 2020	Estimation of airborne viral emission: quanta emission rate of SARS-CoV-2 for infection risk assessment	II, VI
8.	Cao et al, 2017	Dynamic interaction of a downward plane jet and a cough jet with respect to particle transmission: an analytical and experimental study	I, V, VI
9.	Chaabna et al, 2020	Facemask use in community settings to prevent respiratory infection transmission: a rapid review and meta-analysis	VI
10.	Chamseddine et al, 2021	Detection of influenza virus in air samples of patient rooms	II, VI
11.	Chen et al, 2020	Short-range airborne route dominates exposure of respiratory infection during close contact	I, III, IV, V, VI
12.	Comber et al, 2021	Airborne transmission of SARS-CoV-2 via aerosols	II
13.	Couper et al, 2020	COVID-19 in cardiac arrest and infection risk to rescuers: a systematic review	II, VI
14.	Davies et al, 2013	Testing the efficacy of homemade masks: would they protect in an influenza pandemic?	III, VI
15.	Dhama et al, 2020	Coronavirus disease 2019-COVID-19	III, VI
16.	Dhand and Li, 2020	Coughs and sneezes: their role in transmission of respiratory viral infections, including SARS-CoV-2	I, II, IV, VI
17.	Doremalen et al, 2020	Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1	II, VI
18.	Douglas et al, 2020	COVID-19: smoke testing of surgical mask and respirators	III, VI
19.	Evans, 2020	Avoiding COVID-19: aerosol guidelines	II, VI
20.	Fears et al, 2020	Persistence of severe acute respiratory syndrome coronavirus 2 in aerosol suspensions	II, VI
21.	Guha et al, 2017	Quantification of leakage of sub-micron aerosols through surgical masks and facemasks for pediatric use	III, VI
22.	Harnish et al, 2016	Capture of 0.1-μm aerosol particles containing viable H1N1 influenza virus by N95 filtering facepiece respirators	III, VI
23.	Harrison et al, 2020	Mechanisms of SARS-CoV-2 transmission and pathogenesis	II, VI
24.	He et al, 2021	Aerosol generation from different wind instruments	I, V, VI
25.	Hill et al, 2020	Testing of commercial masks and respirators and cotton mask insert materials using SARS-CoV-2 virion-sized particulates: comparison of ideal aerosol filtration efficiency versus fitted filtration efficiency	III, VI
26.	Hu et al, 2020	Distribution of airborne SARS-CoV-2 and possible aerosol transmission in Wuhan hospitals, China	I, VI
27.	Johnson et al, 2011	Modality of human expired aerosol size distributions	I, IV
28.	Jones and Brousseau, 2015	Aerosol transmission of infectious disease	II, VI
29.	Kampf et al, 2020	Potential sources, modes of transmission and effectiveness of prevention measures against SARS-CoV-2	II, III, VI
30.	Kennedy et al, 2021	Modeling aerosol transmission of SARS-CoV-2 in multi-room facility	II, VI
31.	Kohanski et al, 2020	Review of indoor aerosol generation, transport, and control in the context of COVID-19	II, VI
32.	Lednicky et al, 2020	Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients	II, VI
33.	Lee, 2020	Minimum sizes of respiratory particles carrying SARS-CoV-2 and the possibility of aerosol generation	II, VI
34.	Leung et al, 2020	ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19	II, VI
35.	Li et al, 2021	Placing a mask on COVID-19 patients during high-flow nasal cannula therapy reduces aerosol particle dispersion	II, III, VI
36.	Lin et al, 2021	Community evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission through air	II, VI
37.	Lindsley et al, 2012	Quantity and size distribution of cough-generated aerosol particles produced by influenza patients during and after illness	I, VI
38.	Lindsley et al, 2015	Viable influenza A virus in airborne particles from human coughs	VI
39.	Meyerowitz et al, 2020	Transmission of SARS-CoV-2: a review of viral, host, and environmental factors	II
40.	Milton et al, 2013	Influenza virus aerosols in human exhaled breath: particle size, culturability, and effect of surgical masks	II, III, VI

TABLE 1. (*Continued*)

S/N	Author(s), Year	Paper Title	Themes Discussed
41.	Niazi et al, 2020	The role of respiratory droplet physicochemistry in limiting and promoting the airborne transmission of human coronaviruses: a critical review	II, VI
42.	Nikitin et al, 2014	Influenza virus aerosols in the air and their infectiousness	II, III, VI
43.	Oberg et al, 2008	Surgical mask filter and fit performance	III, VI
44.	Paccha et al, 2016	Modeling risk of occupational zoonotic influenza infection in swine workers	II, III, VI
45.	Parienta et al, 2011	Theoretical analysis of the motion and evaporation of exhaled respiratory droplets of mixed composition	I, V, VI
46.	Patel et al, 2016	Respiratory source control using a surgical mask: an in vitro study	III, VI
47.	Perrotta et al, 2020	Severe respiratory SARS-CoV2 infection: does ACE2 receptor matter?	II, VI
48.	Rahman et al, 2020	The transmission modes and sources of COVID-19: a systematic review	II, VI
49.	Ramaraj et al, 2020	Riaging of respiratory protective equipment on the assumed risk of SARS-CoV-2 aerosol exposure in patient-facing healthcare workers delivering secondary care: a rapid review	III, VI
50.	Rengasamy et al, 2010	Simple respiratory protection–evaluation of the filtration performance of cloth masks and common fabric materials against 20–1000 nm size particles	III, VI
51.	Silva et al, 2021	Airborne spread of infectious SARS-CoV-2: moving forward using lessons from SARS-CoV and MERS-CoV	II, VI
52.	Smith et al, 2021	Aerosol persistence in relation to possible transmission of SARS-CoV-2	II, VI
53.	Sommerstein et al, 2020	Risk of SARS-CoV-2 transmission by aerosols, the rational use of masks, and protection of healthcare workers from COVID-19	III, VI
54.	Stilianakis and Drossinos, 2010	Dynamics of infectious disease transmission by inhalable respiratory droplets	II, VI
55.	Strauch et al, 2016	Assessing the efficacy of tabs on filtering facepiece respirator straps to increase proper doffing techniques while reducing contact transmission of pathogens	III, VI
56.	Tang et al, 2020	Aerosol transmission of SARS-CoV-2? Evidence, prevention and control	II, VI
57.	Tellier et al, 2019	Recognition of aerosol transmission of infectious agents: a commentary	II, VI
58.	To et al, 2020	Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study	II, VI
59.	Vuorinen et al, 2020	Modelling aerosol transport and virus exposure with numerical simulations in relation to SARS-CoV-2 transmission by inhalation indoors	I, V, VI
60.	Walawalkar et al, 2020	Particle removal from air by face masks made from sterilization wraps: effectiveness and reusability	III, VI
61.	Wibisono et al, 2020	Facile approaches of polymeric face masks reuse and reinforcements for micro-aerosol droplets and viruses filtration: a review	III, VI
62.	Wolfel et al, 2020	Virological assessment of hospitalized patients with COVID-2019	II, VI
63.	Wurie et al, 2013	Characteristics of exhaled particle production in healthy volunteers: possible implications for infectious disease transmission	I, IV
64.	Xu et al, 2020	High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa	II, VI
65.	Yip et al, 2019	Influenza virus RNA recovered from droplets and droplet nuclei emitted by adults in an acute care setting	I, V, VI
66.	Zhang and Duchaine, 2020	SARS-CoV-2 and health care worker protection in low-risk settings: a review of modes of transmission and a novel airborne model involving inhalable particles	III, VI
67.	Zhang and Wang, 2020	Dose-response relation deduced for coronaviruses from coronavirus disease 2019, severe acute respiratory syndrome, and middle east respiratory syndrome: meta-analysis results and its application for infection risk assessment of aerosol transmission.	II, VI
68.	Zhao et al, 2020	Effects of environmental conditions on the propagation of respiratory droplets	I, V, VI
69.	Zhou et al., 2020	Breath-, air- and surface-borne SARS-CoV-2 in hospitals	II, VI
70.	Zou et al., 2020	Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection	II, VI

Note: themes include, (I) human-generated aerosol transmissions; (II) implications for transmission of generated infectious respiratory disease aerosols; (III) the effectiveness of PPE in preventing transmission of infectious disease; (IV) the size distribution and emission rate of aerosol particles produced from breathing, speech, vocalization, and coughing; (V) aerosol particles' fluid dynamics associated with expiratory events; (VI) aerosol transmission of infectious disease.

examined the three critical factors in determining the effectiveness of respiratory protection equipment: (1) efficiency of the filter, (2) fit, (3) proper use.

DISCUSSION

Several biological and physical processes direct aerosol transmission of respirable infectious diseases such as SARS, MERS, influenza, and tuberculosis. More recently, SARS-CoV-2 has emerged as a global pandemic infecting over 177 million, resulting in more than 3.82 million fatalities.[3] Approximately 17% of the world's fatalities have occurred in the United States.[4] Before vaccination started, the CDC guidance on the transmission of SARS-CoV-2 indicates the virus is primarily spread from person to person within 6 ft via droplet transmission. However, recent evidence suggests respiratory droplets are being produced from talking, coughing, and sneezing.[55] Additionally, these droplets are thought to be small enough for inhalation into the lungs to occur, indicating aerosol transmission of SARS-CoV-2.[55] Given the sudden emergence of SARS-CoV-2, there is relatively limited research on transmission via aerosol exposure. Nonetheless, aerosol

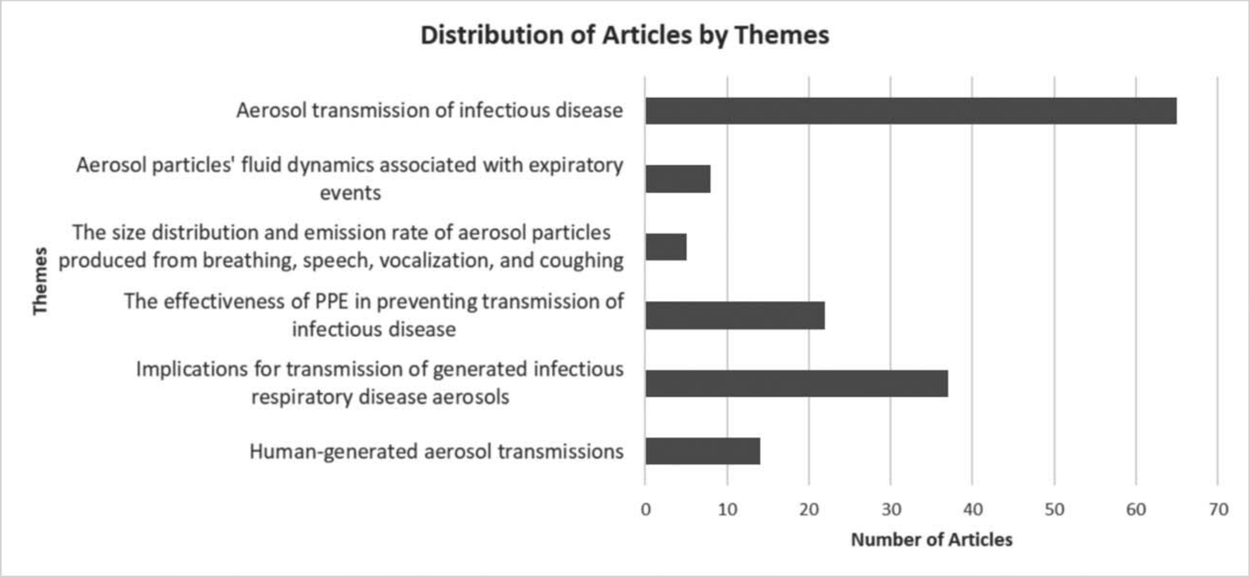

FIGURE 2. Themes deduced from the review.

transmission of infectious disease is of great concern and the effectiveness of PPE (ie, face masks) depends on the filter's efficiency, fit, and proper use.

Aerosol Transmission of Infectious Diseases

The aerosol transmission of infectious disease is affected by several factors, including size, particle diameter, and aerosolized particle shape. Multiple studies have been conducted on human-generated aerosols when speaking, coughing, and sneezing. These studies' are consistent, reporting that particles vary significantly in size and distribution when coughing, breathing, speaking, and sneezing. Speaking and coughing have been found to generate particle sizes ranging from less than 1 μm to more than 500 μm, with coughing producing higher concentrations than speaking.[21] Furthermore, the number of aerosol particles generated is dependent on the individual, with more particles produced during illness.[51] In general, smaller particles are generated when speaking and can take longer to settle in still air.[10] Aerosolized particles tend to stay suspended longer based on air movement.[24]

The inhalation of infectious particles is a common characteristic of aerosol transmission. Several studies characterized the

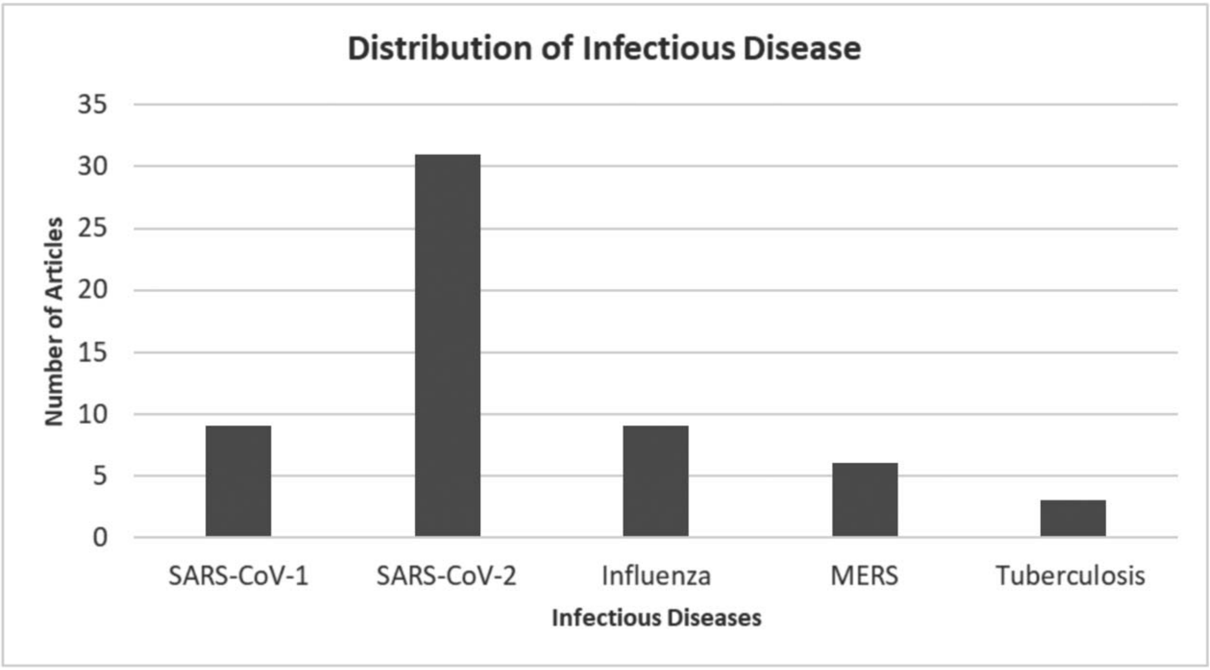

FIGURE 3. Infectious diseases from articles reviewed.

inhalation and deposition of respirable particles. Aerosol inhalation was determined to be the dominate transmission mode at most distances during speech and coughing; additionally, large droplet transmission poses an exposure risk primarily within 0.5 m or 1.5 m away from the source while speaking or coughing, respectively.[20] Additionally, particles less than 50 μm tend to fall from the breathing zone when greater than 0.3 m apart and contribute to less than 10% of exposures.[20] However, droplets more than 100 μm can travel distances up to 4 m from cough expulsion and less than 2 m from speech expulsion.[25] Droplets less than 20 μm can travel distances greater than 8 m from both cough and speech expulsion.[25]

Most of the studies examined provided evidence for the aerosol transmission of infectious diseases; aerosol generation, the viability in the environment, and access to a target tissue are the three main factors when considering infectious dose and potential aerosol transmission.[29,30,37] From a physiological perspective, the probability of infection is dependent on the inhalation of an infectious dose.[29] The infectious dose is considered the number of virus-laden particles needed to make infection probable.[29] Additionally, the infectious dose is a function of the deposition of aerosol particles in the lungs. Recent studies suggest that aerosol deposition in the respiratory tract depends on the particle's aerodynamic diameter.[56] Smaller particles can reach the lungs' pulmonary region, whereas larger particles deposit in the nasopharyngeal and tracheobronchial areas of the respiratory tract. Another study details the risk of infection based on an aerosol emission's viral load.[37] The emission rate of contaminated aerosol particles depends on the viral load in bodily fluids and individual dependent variables such as the volume of exhaled air per breath, breathing rate, number of particles emitted per breath, and the particle size distribution.[37]

Viable SARS-CoV-2 virus has been found in saliva, sputum, nasopharynx, and oropharynx of infected individuals.[42,43] Evidence suggests viral shedding peaks early with active replication in the throat, and the virus is detectable for up to 25 days suggesting possible transmission after symptoms cease.[42,43] Furthermore, evidence has shown that SARS-CoV-2 contaminated aerosol particles can remain viable in the air for a period ranging between 0.64 to 2.64 hours, with a median half-life of 1.1 to 1.2 hours.[36] Several studies have demonstrated the mechanism of action of how the disease infects an individual. SARS-CoV-2 binds to the ACE-2 receptor, which can be found in different tissue types, including mucous membranes, trachea epithelium, lung tissue, heart cells, arteriole smooth muscle cells, and intestine.[46,48]

Additionally, cigarette smoking has been shown to increase ACE-2 enzymes production in the lower respiratory tract, suggesting that individuals who smoke may be more susceptible to aerosol transmission of SARS-CoV-2.[45] The main exposure routes to target tissues were aerosol inhalation and droplet generating events such as coughing or sneezing and contact transmission with oral and mucous membranes.[46–48] Another study using experimental and theoretical modeling estimates the minimum size of a respirable droplet containing a viable virus is calculated to be 4.7 μm.[57] Experimental animal testing has indicated that the indirect transmission of SARS-CoV-2 can provide further aerosol transmission evidence.[49,58] These studies provide evidence of the potential aerosol transmission of SARS-CoV-2. However, further studies are needed to confirm the particle size containing the viable virus to determine the infectious dose of SARS-CoV-2. Additionally, further tests are required to identify the individual factors (speech patterns, mouth and nose physiology, coughing and sneezing behaviors, etc) determining how much SARS-CoV-2 containing aerosol is emitted from people.

Consistent across SARS-CoV-2, SARS-CoV-1, and MERS infections, aerosol transmission depends on the exposure time and the viral load of the aerosolized particles.[30,31] Similar to SARS-CoV-2, SARS-CoV-1 aerosolized median half-life was estimated at approximately 1.1 to 1.2 hours, with a 95% confidence interval of 0.78 to 2.43 hours.[36] Moreover, SARS-Cov-1 binds to the ACE-2 enzyme suggesting a similar target tissue as COVID-19.[46,48] One study found insufficient evidence indicating aerosol transmission of novel coronaviruses from lifesaving medical intervention procedures.[34] This is inconsistent with other studies that reported medical intervention procedures such as intubation to produce copious amounts of aerosol particles and have the potential for short-term viral exposure at a high concentration or cumulative exposure over an extended time frame.[38]

Viable influenza has been detected in aerosolized respirable particles ranging from 0.3 to 8.0 μm from 41% of the subjects in which samples were collected.[59] Another study demonstrated that respirable particles less than 5 μm contained an 8.8-fold more viable viral load than particles more than 5 μm.[52] Additionally, epidemiological studies modeling three influenza epidemic scenarios suggested that aerosol transmission would constitute the dominant transmission mode for long-term epidemics. In contrast, droplet transmission would characterize short-term epidemics, albeit with high attack rates.[26] It has been reported that aerosolized influenza-contaminated particles have a much lower infectious dose than droplet transmission of the virus.[31] The evidence of low influenza infectious dose and viable virus-contaminated aerosol particles within a respirable fraction (less than 5 μm) indicates that aerosol transmission has a significant role in transmitting novel influenza viruses.

It has been established that TB can be transmitted through many routes, including via aerosol.[31] TB has experimental evidence showing aerosol transmission through guinea pigs, which is consistent with other studies.[31,59] Epidemiological studies have further confirmed the aerosol transmission of tuberculosis.[31]

PPE Effectiveness

All of the studies examined agreed that the factors determining PPE's effectiveness were efficiency of the filter, fit of the facemask or respirator, and proper use of the equipment. The studies examined a range of respiratory PPE, including cloth masks, surgical masks, and N95 FFR. It was reported that cloth masks and surgical masks provided marginal protection against particles meeting aerosols' definition.[16,20,60–62] N95 FFR was determined to provide better protection than cloth and surgical masks based on filter alone; however, the effectiveness was still dependent on the fit and proper use of the FFR.[62–65] Given the evidence, PPE is not sufficient in preventing the spread of infectious disease and should only be considered a measure of protection rather than a complete control method for mitigating transmission.

It was noteworthy to see that cloth masks are sometimes referred to as homemade masks, but there is a distinction. Materials used in making cloth masks range from varying thickness of cotton or silk,[63,66] while homemade masks include all of these materials plus paper towel.[63] Cloth masks were determined to provide marginal protection against viable-virus-containing particles with only a 10% collection efficiency of particles in the most penetrating particle size—0.3 μm.[66] Furthermore, cloth masks provided a median fit factor of two and surgical masks, a median fit factor of five.[67] Conversely, cloth masks were determined to be inefficient in preventing transmission; however, they were better than no protection.[53,63,68] Multiple surgical mask styles representing those used in hospitals and dental care facilities were found to have high variability in collection efficiency ranging from 2% to 98%; however, the majority ranged between 30% and 50%.[16] To corroborate this finding, another study examined the efficacy of surgical masks as source controls for influenza and found that earloop surgical masks only prevented the emission of droplets more than 5 μm.[52] Most of the studies reviewed suggested surgical masks are insufficient in preventing disease transmission. However, there are reports that surgical masks are effective in lowering the exposure concentration.[61,63,69–72] For N95 FFR, it was established that the effectiveness of preventing transmission were based on the efficiency of the filter, fit, and proper use of the mask and provided better protection than surgical and cloth masks.[54,62–66,73–76]

This study has reported evidence of potential aerosol transmission of novel coronaviruses, novel influenza viruses, and TB. Furthermore, PPE effectively prevents contact and droplet transmission; however, in the context of aerosol and airborne transmission, PPE is not as efficient.[20,65,66,71] The strength of this systematic review is the primary focus on human-generated aerosol particle size and distribution, evidence of aerosol transmission of infectious disease, and PPE's efficacy. Although the present literature review has performed its due diligence in synthesizing information on the aerosol transmission of infectious disease and PPE efficacy, a few limitations should be noted. First, solely studies written in English and submitted to peer-reviewed journals were considered for inclusion; as such, articles written in other languages containing pertinent information were excluded. Second, the studies included were published between January 2003 and November 2020. Studies published before January 2003 and after November 2020 containing valuable evidence regarding the effectiveness of PPE and aerosol transmission of infectious diseases, including SARS-CoV-2, are missing from this work. Third, there are limited epidemiological studies providing evidence of aerosol transmission of SARS-CoV-2, given its sudden emergence as a global pandemic. Further studies examining the transmission and pathology are needed to characterize the disease fully. Fourth, only one study examined the half-life of the SARS-CoV-2 suspended in air and on various surfaces. However, the study did not determine the half-life of SARS-CoV-2 on cloth surfaces. More studies are needed to determine the stability of SARS-CoV-2 and other novel coronaviruses in the environment, particularly cloth surfaces, to determine the potential fomite exposure of face masks.

CONCLUSION

This study reviewed available articles to understand and establish two goals; the first is to analyze sufficient evidence establishing aerosol transfer of various respiratory infectious diseases. The second is determining the effectiveness of masks and respirators in protecting against transmission. Reported evidence was discovered across different articles meeting the first goal, suggesting that the inhalation of virus-laden aerosol is a viable means of infectious disease transmission. For the second goal, the effectiveness of PPE such as cloth masks, surgical masks, and N95 FFR was examined. The findings concluded that these face masks' efficacy varies and depends on the material, filter efficiency, fit, and proper use of the PPE. Moreover, based on the hierarchy of hazard control, PPE should be the last resort in preventing the spread of infectious disease and should only be used for protection and not to control the transmission.

Although studies reviewed have addressed the research questions for this study, particularly in the area of particle size and distribution of human-generated aerosols to determine aerosol transmission potential, further studies are needed to examine the mechanisms of transmission and pathology to characterize SARS-CoV-2 fully. Furthermore, individual characteristics that affect the size and distribution of emitted aerosol particles should be considered for future studies. Studies detailing the infectious dose of SARS-CoV-2 and the size of virus-laden aerosol particles are needed. There are limited epidemiological studies regarding SARS-CoV-2, given its sudden emergence. Therefore, epidemiological studies such as cohort and cross-sectional studies should be conducted as the disease progresses with time.

Understanding the modes of transmission is critical in determining appropriate control measures. Future research should be conducted regarding the infectious dose of diseases, particle size and distribution of virus-contaminated aerosols, and the stability of infectious diseases on cloth surfaces to determine applicable exposure limits and effective control measures.

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