

SYNTHESIS

(ARCHIVED) COVID-19 Transmission Through Large Respiratory Droplets and Aerosols... What We Know So Far

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Introduction

Public Health Ontario (PHO) is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents provide a rapid review of the evidence on a specific aspect or emerging issue related to COVID-19. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is transmitted in different ways; however, this document will focus on transmission by respiratory droplets and aerosols.

Key Findings

- The historical dichotomy of droplet versus airborne transmission, while useful in implementing infection prevention and control (IPAC) strategies, does not accurately recognize the complexity of viral respiratory transmission, including for SARS-CoV-2.
- SARS-CoV-2 is transmitted most frequently and easily at short range through exposure to respiratory particles that range in size from large droplets which fall quickly to the ground to smaller droplets, known as aerosols, which can remain suspended in the air.
- There is evidence to suggest long-range transmission can occur under the right set of favourable conditions, implicating aerosols in transmission.

- The relative role of large respiratory droplets versus smaller droplet particles in short-range transmission is challenging to quantify. Their contributions to a specific case-contact interaction vary based on contextual factors including source/receptor characteristics (e.g., forceful expulsions such as singing, coughing, sneezing; viral load) and pathway characteristics (e.g., duration of exposure; environmental conditions such as ventilation, temperature, humidity, ultraviolet light; source control; and use of personal protective equipment).
- Translation of this summary into control measures needs to take into consideration other information, such as evidence around the effectiveness of control measures to date. Several control measures applied together in a layered approach are likely to be effective irrespective of the relative contribution of droplets or aerosols, including achieving high vaccination coverage and avoiding the “3 C’s” (closed spaces, crowded places and close contact).

Background

The diameter of microorganism-containing respiratory particles relevant for respiratory infections ranges from approximately 0.01 micrometres (μm) to greater than 100 μm .¹ Particles larger than about 100 μm play a role in respiratory infection transmission by impacting on mucosal surfaces, such as the nostrils, mouth and eyes. Particles smaller than 100 μm can be inhaled or impact on mucosal surfaces. Some particles are small enough that they can be suspended in the air for various periods of time (known as aerosols).² Environmental factors such as local air currents and humidity affect these particles, e.g., how they move, evaporate, and how long they remain in air.³ Therefore, the mode of transmission is influenced by three key elements: the source, the pathway, and the receptor. Depending on the unique characteristics of each element, certain modes may be more likely than others.

Traditionally, respiratory particles >5 or 10 μm have been termed droplets and were thought to impact directly on mucous membranes, while smaller particles were thought to be inhaled. This dichotomy of transmission routes has been applied to infection prevention controls within health care settings worldwide. However, these transmission routes are not mutually exclusive as droplets well over 5 μm are capable of remaining suspended in air for some time and can be inhaled. At short range within about 2 metres (m), infection can occur from inhaled aerosols as well as droplets landing on mucous membranes (short-range transmission). Herein, we refer to what was traditionally called airborne transmission via inhalation of aerosols that have remained suspended over long distances and periods of time^{4,5} as long-range transmission.

We describe transmission through epidemiological studies, experimental or simulation of transmission studies, and statistical or mathematical modelling. Modelling shows what is possible, experimental studies what is plausible, and epidemiologic studies observe what is actually occurring, and each type of evidence is subject to limitations. However, exact routes of SARS-CoV-2 transmission in real-life scenarios can only be inferred based on the available data.

The purpose of this rapid review is to outline the evidence for droplets and aerosols in SARS-CoV-2 transmission. We have summarized the evidence as either short-range transmission from large respiratory droplets and small droplets or aerosols, or long-range transmission from aerosols.

Methods and Scope

In considering feasibility, scope and timelines, we undertook a rapid review to update our summary of SARS-CoV-2 transmission from large respiratory droplets and aerosols. A rapid review is a knowledge synthesis where certain steps of the systematic review process are omitted in order to be timely (e.g., duplicate screening).⁶

We conducted literature searches in MEDLINE (April 22, 2021) and National Institutes of Health COVID-19 Portfolio (Preprints) (April 27, 2021), search strategies are available upon request. We searched PubMed and Google Scholar on April 28, 2021 for additional articles of interest.

English-language peer-reviewed and non-peer-reviewed records that described large respiratory droplet and aerosol routes of transmission of COVID-19 were included. We restricted the search to articles published after January 1, 2020. This rapid review concentrated on evidence from systematic reviews and meta-analyses, supplemented by primary literature where appropriate. We reviewed citations from included articles to identify additional research.

Prior to publishing, PHO subject-matter experts review all What We Know So Far documents. As the scientific evidence is expanding rapidly, the information provided in this document is only current as of the date of respective literature searches.

Out-of-scope for this document was a review of IPAC practices appropriate for individual transmission scenarios and settings. Application of a hierarchy of control measures for non-health care settings is briefly discussed in the conclusions. For additional information related to IPAC in health care settings, please see PHO's technical briefing *IPAC Recommendations for Use of Personal Protective Equipment for Care of Individuals with Suspect or Confirmed COVID-19* and *Interim Guidance for Infection Prevention and Control of SARS-CoV-2 Variants of Concern for Health Care Settings*.^{7,8} Please note that the *Ministry of Health's Directive 1* is the provincial baseline standard for provision of personal protective equipment for hospitals, long-term care homes and retirement homes and that the *Ministry of Health's Directive 5* provides agency to health care workers to make professional decisions regarding the appropriate personal protective equipment when dealing with suspected, probable or confirmed COVID-19 patients or residents.^{9,10} Evidence for contact/fomite transmission, and virus and host (source/receptor) factors were not reviewed in this document, but are acknowledged as contributors to short- and long-range transmission. Other routes of transmission are reviewed in PHO's synthesis *COVID-19 Routes of Transmission – What We Know So Far*.¹¹

Short-range Transmission

Main Findings

SARS-CoV-2 is transmitted most frequently and easily at short range. Short-range transmission generally occurs within 2 m of an infectious individual (e.g., during a conversation with inadequate distancing, no barriers, no personal protective equipment). Theoretically, short-range transmission may occur due to droplets or aerosols, but the relative contribution of either is specific to each case-contact interaction which varies based on contextual factors including source/receptor and pathway characteristics.

Environmental Factors Affecting Short-range Droplets and Aerosols

In addition to virus and host factors, environmental factors are associated with short-range viral transmission. The distance travelled by large respiratory droplets is generally <2 m, although it can reach up to 8 m in certain circumstances. In a study by Guo et al. (2020), SARS-CoV-2 virus was detected on the floor up to 4 m away from a patient.¹² In a systematic review of studies assessing the horizontal distance travelled by respiratory droplets, Bahl et al. (2020) reported that droplets could travel up to 8 m.¹³ In a mathematical model, Chen et al. (2021) reported that respiratory droplets >100 µm in diameter are only important in transmission at a distance of less than 0.2 m when the infector is talking, or within 0.5 m when the infector is coughing.¹⁴ Modelling by Wang et al. (2021) (preprint) suggested droplets >100 µm would most often not travel past 1.75 m (most droplets >100 µm diameter settle before 1.25 m).¹⁵

In a review of respiratory virus transmission, Leung (2021) reported that environmental factors affecting transmission include temperature, relative humidity, ventilation, airflow and ultraviolet (UV) light.¹⁶ Ventilation, airflow and forceful expulsion (sneezing or coughing) can make respiratory particles travel further than 2 m through momentum.^{14,17} High temperature and low humidity contributes to shrinking of droplets such that they may remain suspended in air for longer periods of time.¹⁸

Even at short-range distances, ventilation may affect transmission. De Oliveira et al. (2021) modelled infection risk in ventilated (10 air changes per hour [ACH]) and unventilated spaces without respiratory protection during a 1-hour exposure at 2-m distance.¹⁹ The impact of decreasing concentration of virus in the air through ventilation was notable. Estimates of infection risk were reduced by at least three times based on the parameters and assumptions of their model. The authors also commented that the direction of airflow can have a significant impact – upward air streams can maintain aerosols at face height significantly increasing infectious risk.

Indoor settings are a predominant risk factor for transmission. In a systematic review of 5 studies, Bulfone et al. (2020) reported that the odds of indoor transmission were 18.7 times (95% confidence interval [CI]: 6.0–57.9) higher than outdoor settings, and less than 10% of infections occurred outdoors.²⁰ Very few superspreading events have been described from exclusively outdoor exposures. The explanation for this observation is likely multifactorial which includes important differences in ventilation, UV light, humidity, as well as possible differences in behaviour.

Epidemiological and Modelling Studies Describing Short-range Transmission

The following section reviews the epidemiologic and modelling evidence supporting short-range transmission of COVID-19. It reviews the reproductive number and summarizes the epidemiological and modelling studies by setting, including transportation, health care and sports.

The reproductive number (R_0) of SARS-CoV-2 is less suggestive of long-range transmission commonly occurring, as viruses where long-range transmission commonly occurs tend to have a higher R_0 .¹⁶ For example, in a systematic review by Guerra et al. (2017), the R_0 for the measles virus in the pre-vaccine era was 6.1–27.0,²¹ compared to the median range of R_0 (2.7–3.3) reported for SARS-CoV-2.²² It is important to note that R_0 is not a direct measure or indication of transmission route, as R_0 can be setting and population-specific, and be impacted by factors such human behaviours. The R_0 for SARS-CoV-2 also displays overdispersion, where the overall R_0 is lower than pathogens that commonly transmit through aerosols at long-range, but a small proportion of cases are associated with reproductive numbers in the

range typical of viruses that commonly transmit through aerosols at long-range (i.e., superspreader events).²³ Such cases illustrate the potential variability in COVID-19 transmission, depending on differences in source/receptor characteristics and environment.

Short-range transmission was favoured in a retrospective cohort study of 18 short-to-medium haul flights (median flight time 115 minutes) to England from the beginning of the pandemic.²⁴ The attack rate was 0.2% (95% confidence interval [CI]: 0.1–0.5) for all aircraft-acquired cases, and was higher at 3.8% (95% CI: 1.3–10.6) if a subgroup analysis was performed only on contacts within a two-seat radius. It was assumed that no masks were worn given that it was early in the pandemic.

Family gatherings for meals are high-risk scenarios for transmission. Lo Menzo et al. (2021) reported transmission of lineage B.1.1.7 variant of concern to 8 of 9 family members during a dinner gathering.²⁵ The only uninfected family member was presumed to have immunity acquired from a previous infection (high antibody titres and polymerase chain reaction (PCR) negative result). Contact and fomite transmission cannot be excluded from this type of event.

In a case-control study of 154 patients 18 years and older in the United States (US), Fisher et al. (2020) reported that close contact with a person with COVID-19 was reported more often among cases (42.2%) than controls (14.5%) ($p < 0.01$).²⁶

Short-range transmission has been documented in school settings. Four student-to-student and one student-to-teacher transmission events were reported in Salt Lake County, Utah.²⁷ For four transmission events, unprotected, short-range exposures were noted. There was a lack of transmission to other students that were a median of 1 m away during class, but adhered to control measures implemented in the school. However, when household transmission associated with the secondary cases was evaluated, transmission was high for 3 of the 5 households of secondary patients. In these three households, 6 of 8 household members were also infected and may be related to challenges with physical distancing, masking, and shared surfaces in the household.

Using whole genome sequencing of SARS-CoV-2 clinical samples ($n=50$) in Dublin, Ireland, Lucey et al. (2020) investigated cases of hospital-acquired COVID-19 and reported that the majority of infections were among patients who required extensive and prolonged care by health care providers.²⁸ The authors concluded that the likely mode of transmission from health care workers to patients was through short-range transmission and close contact, rather than long-range transmission. Notably, the use of masks by health care providers was not universal and patients were not wearing masks either.

Three short-range health care-associated transmission events have been reported where large respiratory droplet transmission was less likely because masks were worn by either the source or the contact and in two of three events, the contact was also wearing eye protection.²⁹ In case 1, an asymptomatic, unmasked patient transmitted infection to two health care workers who wore medical masks and face shields, following multiple hours of exposure in a room with 6 ACH. A second case occurred where a presymptomatic masked health care worker transmitted infection to an unmasked patient in a room with 6 ACH. A third case involved a presymptomatic masked patient transmitting infection to a health care worker who was wearing a mask and goggles during a 45 minute face-to-face discussion at 1 m. Notably in the third case, the patient's mask was removed temporarily for oropharynx inspection. While each case was verified by whole genome sequencing, there was a lack of detail about the specific encounters (e.g., distance, duration, if direct contact occurred, if doffing errors occurred), and no airflow studies were conducted.

An analysis of SARS-CoV-2 infections in an outdoor rugby league, including video evaluation of close contact due to tackling inherent in the game, indicated that no cases among players in the league could be linked to close-contact during the outdoor rugby games.³⁰ Instead, transmissions were linked to other indoor short-range transmission events. While this study demonstrates examples where outdoor close-contact transmission did not occur, there were not enough close-contacts documented to provide evidence that close-contact transmission could not have occurred in the context of outdoor rugby.

In a modelling study, Zhang and Wang (2020) reported that the median infection risk via long-range aerosol transmission (10^{-6} – 10^{-4}) was significantly lower than the risk via close contact (10^{-1}).³¹ The model was based on a 1-hour exposure in a room with an area of 10–400 m², with one infected individual and a ventilation rate of 0.1–2.0 ACH. In a modelling study by Hu et al. (2020), the transmission risk from epidemiological data among train passengers as 0%–10.3% (95% CI: 5.3%–19.0%).³² Travellers directly adjacent to the index patient had a much higher infection risk (relative risk [RR]: 18.0; 95% CI: 13.9–23.4), and the attack rate decreased with increasing distance.

Household and Non-Household Secondary Attack Rates

The consensus among systematic reviews is that household settings, where physical distancing, consistent source control mask-wearing, and disinfection of shared surfaces are potentially not feasible, are associated with a higher risk of infection compared to casual-contact settings (17%–27% compared to 0%–7%). However, the secondary household attack rates are not as high as would be expected if SARS-CoV-2 easily spread through long-range transmission (e.g., >90% in measles).^{16,33}

In a systematic review and meta-analysis of 54 studies and 77,758 patients, Madewell et al. (2020) reported that the household secondary attack rate was 16.6% (95% CI: 14.0–19.3).³⁴ In a systematic review and meta-analysis of 45 studies, Thompson et al. (2021) estimated the household secondary attack rate as 21.1% (95% CI: 17.4–24.8; 29 studies).³⁵ Non-household settings had lower secondary attack rates: 1) social settings with family and friends (5.9%; 95% CI: 0.3–9.8; 7 studies); 2) travel (5.0%; 95% CI: 0.3–9.8; 5 studies); 3) health care facilities (3.6%; 95% CI: 1.0–6.9; 10 studies); workplaces (1.9%; 95% CI: 0.0–3.9; 7 studies); and casual social contacts with strangers (1.2%; 95% CI: 0.3–2.1; 7 studies). Koh et al. (2020), in a meta-analysis of 43 studies, reported that the household secondary attack rate was 18.1% (95% CI: 15.7–20.6; 43 studies), much higher than the secondary attack rate in health care settings (0.7%; 95% CI: 0.4–1.0; 18 studies).³⁶ In a systematic review and meta-analysis of 24 studies, Lei et al. (2020) reported that the secondary attack rate in households was 27% (95% CI: 21–32); the risk of secondary infection was 10 times higher in households compared to non-household settings (odds ratio [OR]: 10.7; 95% CI: 5.7–20.2; $p < 0.001$).³⁷ Tian and Huo (2020), in a meta-analysis of 18 studies, reported that the household secondary attack rate was 20% (95% CI: 15–28; 15 studies; $n = 3,861$ patients), followed by social gatherings at 6% (95% CI: 3–10; 5 studies; $n = 2,154$ patients) and health care settings at 1% (95% CI: 1–2; 4 studies; $n = 1,320$ patients).³⁸

Long-range Transmission

Main Findings

Transmission of SARS-CoV-2 over longer distances (generally >2 m) and time occurs through inhalation of aerosols under favourable circumstances, such as prolonged exposure in an inadequately ventilated space. Current evidence supports long-range transmission of SARS-CoV-2 occurring “opportunistically”, in that long-range transmission can occur under some circumstances, but inconsistently, and is not the

predominant situation in which transmission occurs. Epidemiological and modelling studies support that long-range transmission via aerosols occurs. All of these examples include combinations of favourable source/receptor and pathway conditions such as inadequate ventilation, prolonged exposure time, high viral load, with certain activities (singing, exercising, yelling, etc.), and lack of masking for source control by the index case.

Environmental Factors Affecting Long-range Aerosols

In experimental models, researchers have demonstrated the potential for long-range transmission. In a series of experiments, simulations and modelling, Wang et al. (2021) (preprint) reported that aerosols could remain suspended for a longer period than historically predicted.¹⁵ In general, viral copies/millilitre (ml) or concentration decreased as distance from source increased. The work showed that the evaporation time for large respiratory droplets is longer than predicted, especially at higher relative humidity (90%). In a sneeze plume, the largest respiratory droplets (>100 μm) are centrally located within the plume, with smaller respiratory droplets and aerosols at the periphery. The largest droplets contain more virus copies but are less abundant as they settle quickly to the ground, while smaller droplets carry fewer virus copies but are more abundant and remain in the air. The authors conclude that while aerosol transmission is important past 1 m from the source, aerosol transmission is likely even more important at shorter ranges.

Modelling studies have also highlighted the potential for aerosol transmission at varying distances. Xu et al. (2021) analysed the data of 197 symptomatic COVID-19 cases in the Diamond Princess cruise ship outbreak and concluded that long-range transmission did not occur between cabins based on the random distribution of symptomatic cases on all decks and the lack of spatial clusters of close contact (within cabin) infection.³⁹ The authors inferred that most transmission had occurred in public areas before the quarantine, possibly due to crowding and insufficient ventilation in those spaces. The authors also inferred that there was no transmission between passenger rooms during the quarantine period, and suggested that the ship's central heating, ventilation, and air conditioning (HVAC) system did not play a role in SARS-CoV-2 transmission. However, the authors noted that the lack of data on 109 of the 306 symptomatic individuals and on the 328 asymptomatic individuals may alter their estimation. In addition, their estimation did not take into consideration possible transmission between crew and passengers. Another model of the same outbreak estimated that the contribution of short-range transmission (from large droplets or aerosols) accounted for a median of 36% (mean: 35%) of transmission events, fomite (median: 21%; mean: 30%) and long-range (median: 41%; mean: 35%) contributing to the remainder.⁴⁰

A study of aerosol particles (<5 μm diameter) by Dobramysl et al. (2021) (preprint) reported that time to infection increases approximately linearly as distance from source increases, the most important parameter for time to infection.⁴¹ Exposure to a person breathing normally (simulating an asymptomatic individual) at a distance of 1 m led to infection after 90 minutes; however, coughing every 5 minutes led to infection in 15 minutes. Mask use and even minimal ventilation increased time to infection at a given distance. The importance of ventilation is also described in a modelling study by Jones (2020) which suggested that exposure to inhalable particles mostly (80%) occurs within close proximity to the patient.⁴² In still air, aerosols will rise above head-level; however, turbulent air can change the trajectory of virus-laden aerosols, bringing aerosols closer to the head.⁴³⁻⁴⁵ A modelling study by Sen (2021) found that when the ceiling-mounted elevator fan was off, about 11% of the droplets expelled by coughing fell to the ground while 89% evaporated and became smaller.⁴⁶ After travelling downward in cough-induced turbulence for approximately 6 seconds, droplets about 50 μm tended to move up and spread in the upper part of the elevator. If the cough happened at 30° to another rider, up to 40% of the droplets may

fall on the face of another elevator rider. However, when the fan is operating, up to 50% of the droplets were dragged down to the floor in less than 3 seconds.

The basement of a large wholesale market was investigated as the source of a major outbreak in Beijing, China.⁴⁷ Many factors contributed to spread across multiple possible modes of transmission including long-range transmission. A field study of the area using fluorescent powders and microspheres as tracers allowed authors to conclude that while air was circulated, the air was unfiltered and there was very little fresh air, there was high humidity, low temperature, inadequate hand sanitization supplies in washrooms, and significant contamination of surfaces possibly due in part to resuspension of droplets from wet floors.

Given that persistence of aerosols over time is a factor in long-range transmission, the viability of SARS-CoV-2 in aerosols is important to consider. The half-life of SARS-CoV-2 in aerosols is approximately 1 hour.^{48,49} Humidity seems to have less of an effect on SARS-CoV-2 viability in aerosols compared to the effect of sunlight or temperature.^{50,51} Increasing temperature is associated with a reduction in the half-life of SARS-CoV-2 in aerosols.⁵²⁻⁵⁴ Using a rotating drum experiment similar to other studies for viability of SARS-CoV-2, simulated sunlight (UVA/UVB) was applied to aerosolized virus through a window on the drum.⁵¹ Results indicated 90% inactivation of virus within 20 minutes.

Inadequate ventilation can contribute to spread of aerosols, where the buildup of infectious aerosols is inversely proportional to the number of air exchanges.⁵⁵⁻⁵⁷ In a modelling study, Schijven et al. (2021) assessed the risk of aerosol transmission of SARS-CoV-2 at a distance beyond 1.5 m from continuous breathing, speaking, or singing, or from one cough or one sneeze, in an indoor environment of 100 m³.⁵⁸ Where there was no ventilation, the mean risk of transmission (derived from dose-response data for human coronavirus 229E) after 20 minutes of exposure to a person with 10⁷ RNA copies/ml of mucous was estimated at 0.1%, except for sneezing with high aerosol volume (40,000 picolitres/sneeze). The mean risk of transmission increased to above 30% for sneezing with high aerosol volume and above 10% for singing after an exposure of 2 hours to a person with mucous RNA concentration above 10⁸ copies/ml. Ventilation at 1 ACH reduced the risk by approximately half and at 6 ACH, the risk of transmission was reduced by a factor of 8–13 for sneezing and coughing, and by a factor of 4–9 for singing, speaking and breathing.

Estimates for minimum infectious dose, amount of viable virus in aerosols and quantified exposure rates are lacking. One preprint study assessed superspreading events related to long-range transmission in order to determine a minimum infectious dose for transmission.⁵⁹ The model used rate of aerosolized virion shedding based on data from other coronaviruses and a destabilization rate measured for SARS-CoV-2. They reported a critical exposure threshold for aerosol transmission of 50 virions. A computational characterization of inhaled droplets by Basu (2021) reported an estimated inhaled infectious dose around 300 virions, which was similar to estimates of 500 virions for ferrets.⁶⁰ The author acknowledged that this estimate could vary widely depending on environmental and individual biological factors.

Epidemiological and Modelling Studies Describing Long-range Transmission

Epidemiological case studies have reported long-range transmission of SARS-CoV-2, exclusively in indoor settings (e.g., bus, church, restaurant, concert halls, apartment building, office building).⁶¹⁻⁶⁷ In most of these case studies, long-range transmission was inferred as the dominant route of transmission, given

that infectees were usually further than 2 m away from index cases. In addition, in these case studies, susceptible people were exposed to index cases for prolonged periods (>50 minutes) in indoor environments with inadequate ventilation and, in some instances, with increased respirations (e.g., singing, yelling, or exercising) and/or no face mask use (by case and/or contact). As with most epidemiological studies on transmission events, it was difficult to exclude other contributing routes of transmission. We summarize a few of these case studies, highlighting settings and contributing contextual factors to long-range transmission.

Stagnant indoor conditions can contribute to aerosol transmission. One example is a series of transmissions linked to an individual who developed symptoms around the time they were playing squash in an unventilated squash court.⁶⁸ Players who arrived hours after the index case and played in the same squash court were later identified as positive cases, though the role of other potential routes (e.g. unidentified staff contacts, shared surfaces) may have contributed as well and the source of transmission could not be confirmed. In contrast, a post-operative analysis of susceptible patients (no previous SARS-CoV-2 infection or vaccination) in a surgical suite within 48 hours following the use of the suite by SARS-CoV-2 positive patients indicated that there were no transmission events. The event rate was lower than the number of events in a control group (0% vs. 1.9%).⁶⁹ Ventilation was likely a significant factor that prevented transmission in the surgical suite.

In a study of six indoor singing events (five with transmission) in the Netherlands, Shah et al. (2021) (preprint) reported that long-range transmission was the likely route of transmission (short-range transmission possibly contributing to transmission at three of these events and indirect contact transmission possibly contributing to transmission at one of the events).⁶² The authors assigned transmission likelihood as either less likely or possible; however, the authors do not state how these were defined. Attack rates at these events ranged from 25%–74% (9–21 people aged 20–79 years attended the events) and authors hypothesize that singing led to transmission. The authors note that they cannot quantify the contribution of each route of transmission. Genomic sequencing was not performed to help rule out other sources of SARS-CoV-2.

In a choir group (Washington, US), 53 of 60 individuals (excluding the index patient) were confirmed or strongly suspected to have been infected during a 2.5 hour rehearsal in a main hall.⁶⁴ Individuals who moved to another area of the building from the index case to practice for 45 minutes were less likely to become infected than those who remained in the main hall for the full duration of the rehearsal.

Twelve secondary cases of SARS-CoV-2 were linked to an index case, an 18-year-old chorister with high viral load who sang at four 1-hour services.⁷⁰ The index case was seated at a piano raised approximately 3 m from the ground floor and facing away from the secondary cases. Secondary cases sat between 1–15 m (horizontal distance) from the index case. Use of masks was not in place and there was minimal ventilation during the service (ventilation system was off, fans were off and doors and windows were largely closed). Interestingly, no new cases were linked to exposure that occurred the day of respiratory symptom-onset, and no explanation could be provided for why only a certain section near the chorister was affected and other sections (including those directly in front of the index case) were not.

In a case study by Shen et al. (2020), passengers who were not wearing masks were exposed to a presymptomatic index patient for 100 minutes while on a bus in eastern China.⁶¹ Twenty-four of 67 passengers became infected, including several passengers seated beyond 2 m distance. The bus containing the index patient was heated and air was recirculated without filtration. Infections occurred in individuals at either end of the bus and the index case was located roughly in the middle. Risk of infection was only moderately higher for individuals sitting closer to the index patient. In contrast, seven

of 172 other people attending the same religious event were positive for SARS-CoV-2. Some of the cases became positive after 14 days from exposure; thus, transmission likely did not occur on the bus for these cases. The authors of this study postulate that the poor ventilation in the bus supports aerosol transmission in this cluster; however, other routes of transmission such as close contact from movement within the bus or fomites could not be excluded.

Vehicles are also potential environments for short-range and long-range transmission. A patient transport van was implicated in long-range aerosol transmission despite physical distancing observed by the infected drivers in two distinct transmission events.⁷¹ One driver did not wear a mask, but all passengers wore a single-layer mask. The passengers were exposed for 2 hours during both events. Transmission was confirmed by whole genome sequencing. Fans were on medium speed and windows were closed. Airflow experiments were conducted with different size aerosols demonstrating plausibility of spread from the driver.

An epidemiological investigation of a chain of transmissions was reported beginning with a flight from India to New Zealand, a bus ride to a quarantine facility, a stay at a quarantine facility, a bus ride to the airport, and subsequent household transmissions.⁷² Based on positivity test dates, genome sequencing, flight positions and hotel room placement the transmission events were ascribed to both short-range and long-range transmission on flights, within the quarantine facility, and within households. Masks were required on flights and bus rides. One of the transmission events occurred between two adjacent hotel rooms in the quarantine facility. The authors used recorded video and observed >20 hours between any shared items and no direct contact. The authors concluded that fomite transmission was unlikely and attributed transmission to aerosols in the corridor outside of the hotel rooms wherein the space was enclosed and unventilated. Notably, the hotel rooms themselves, based on a review of the ventilation system, exerted positive pressure relative to the corridor.

An investigation by Lin et al. (2021) into an outbreak of nine COVID-19 cases from three families living in vertically-aligned units of an apartment building in Wuhan, China supported the possibility of long-range transmission.⁶⁶ Phylogenetic analysis of respiratory samples showed that all cases were infected by the same strain of SARS-CoV-2. Epidemiological investigation revealed that 4/5 cases of the index family in apartment 15-b had a travelling history to Wuhan, while the other four cases in apartments 25-b and 27-b had neither a travelling history to Wuhan nor close contact with any COVID-19 cases prior to their infection. Transmission through close contact in the elevators was considered unlikely as video records in the elevator did not show any close contact between the index family and the cases from units 25-b and 27-b. However, there was an incident where one unmasked occupant of unit 27-b took the elevator 8 minutes after two unmasked occupants from the index family had left the elevator. Epidemiologically, the infection rate for residents in units b was significantly higher ($p < 0.05$) than that in units a and c. Testing of wind speed at the bathtub drain and floor drain found that the airflow produced by toilet flushing on one storey can influence the entire building as the drain pipes for toilets and the sewage pipes connected with floor drains were connected with the exhaust pipe. An experiment with a tracer gas indicated that gas could spread from one storey to another via the drainage and vent systems, especially as the seals in U-shaped traps in the floor drains were dried out in some units and the use of exhaust fans could create a negative pressure in the pipeline system. A similar situation was reported involving air ducts in a naturally ventilated apartment complex in Seoul, South Korea.⁶⁷ There were no valves blocking air from entering the bathrooms from the shared natural ventilation shafts (not for building or apartment unit ventilation). Limitations of this outbreak investigation included no genome sequencing or air sampling. Direct applicability to Canadian contexts may be limited by different building construction standards and practices.

Independent of ventilation, movement of air from an infected individual to others nearby can be an important factor in long-range transmission. Direct airflow was deemed responsible for a long-range transmission event in a restaurant in Korea.⁷³ The suspected index case sat 4.8 m and 6.5 m away and directly upwind of the airflow from two secondary cases at different tables. Nine other visitors in the restaurant did not test positive for SARS-CoV-2 even though at least two were closer to the index case for longer but not in the direct path of airflow originating from the index case. Notably the transmission in one case was suspected to have occurred from an exposure as short as five minutes, and three patrons sitting with the secondary cases but facing away from the index cases were not infected.

An investigation by Lu et al. (2020) into a COVID-19 outbreak in a restaurant in Guangzhou, China involving three families sitting at three tables in close proximity for about 1 hour concluded that the air conditioning (AC) system likely contributed to transmission.⁶³ In this scenario, a presymptomatic index case and secondary cases were present in the same area for 53–73 minutes. The location of a consistently running AC unit was in the airflow path of the secondary cases and was in an enclosed environment. No secondary cases occurred in staff or at adjacent tables that were outside of the likely “air column”. The furthest distance between index and secondary cases was approximately 3 m. Additional investigation indicated that the exhaust fans had been closed due to cold outside temperatures.⁷⁴ The airflow assessment indicated that air was recirculating in a defined area, which exposed the three families.

A report involving group exercise at three facilities in Hawaii, US calculated attack rates of 25%–100%.⁷⁵ There was no fresh air ventilation and exposure occurred over a duration of 1 hour. Extended close contact and lack of masks in some cases were concluded as contributing to the transmission.

An outbreak in a multi-bed hospital room occurred wherein three patients and six health care workers became infected despite the use of masks and presence of ventilation of 3–4 ACH.⁷⁶ The presymptomatic index case was a parent located in a chair beside their child’s bed who constantly wore a surgical mask, near the entrance to the room. Notably the air conditioning unit appeared to be located on the ceiling and no details were given about how it operated (e.g., constant versus timed/triggered) and what amount of fresh air circulation it provided. There were no exhaust vents indicated on the room diagram. Exposures for health care workers were in the range of 10–15 minutes, most at distances further than 2 m from the index patient. The report noted that masks were worn as personal protective equipment by health care workers. Transmission was based on the epidemiology of the outbreak without corroboration by genomic analysis of infections.

Detection of SARS-CoV-2 in Air Samples

Air sampling for virus refers to the process of collecting volumes of air by a device to determine if aerosols may contain virus. Collection can vary by aerodynamic size captured, duration of collection, volume per second collected, and media on which samples deposit. Air samples can then be tested by molecular methods such as reverse transcription PCR (RT-PCR) to amplify viral nucleic acids and/or viral culture. RT-PCR cannot determine whether the microorganisms detected are viable. Viral culture is used to determine whether a sample containing the virus is capable of replication. While there are several factors that contribute to the probability of infection, replication is a surrogate measure for inducing infection. To detect viability, researchers apply a sample to a susceptible cell culture and incubate up to a few weeks to detect morphological changes.

Detection of SARS-CoV-2 RNA in air samples has been inconsistent.⁷⁷ Multiple air sampling studies performed in proximity to confirmed COVID-19 cases were unable to detect any virus by RT-PCR.⁷⁸⁻⁸⁶

Kenarkoohi et al. detected SARS-CoV-2 RNA by RT-PCR in 1/5 samples from a ward containing intubated, severely ill patients, but did not find any positive air samples in other areas of the hospital such as wards with suspected, confirmed and mild patients (culturing of virus was not attempted in this study).⁸⁷ Chia et al. (2020), in an extended study of Ong et al. (2020), detected SARS-CoV-2 RNA by RT-PCR in air samples collected within 1 m of patients in two of three airborne infection isolation rooms (AIIRs) (no culture of virus attempted).⁸⁸ Lei et al. (2020) reported limited detection of SARS-CoV-2 RNA virus by air sampling in open wards, private isolation rooms and bathrooms.⁸⁵ One PCR-positive air sample was obtained during an endotracheal intubation within 10 cm of the patient's head in a naturally ventilated room (window open with fan attached), eleven other air samples near patients and 17 samples outside patient rooms and at nursing stations were PCR-negative.⁸⁹ The stage of infection and level of infectiousness of the patient populations sampled were not reported.

In a study of SARS-CoV-2 RNA in air samples collected from a variety of settings, Liu et al. (2020) reported that the highest concentration of viral RNA was reported from patient and staff areas of hospitals, compared to public areas.⁹⁰ Gharehchahi et al. (2021) (preprint) found SARS-CoV-2 RNA in 7/17 (41.2%) of air samples in a hospital for COVID-19 patients, including a mechanically-ventilated temporary waste storage area, two naturally-ventilated offices (one in the admission and discharge area, the other in an administrative department), and within 2 m of patients' beds in two intensive care units (ICUs), a negative pressure room, and an accident and emergency ward that are mechanically-ventilated with or without natural ventilation.⁹¹ SARS-CoV-2 RNA was not detected from the four samples at nursing stations 2–5 m from patients' beds. The authors speculated that the detection of RNA in non-clinical areas could be due to inadequate ventilation and the occasional presence of infected health care workers.

Stern et al. (2021) sampled air in locations outside of patient care areas in an acute care hospital and found 8/90 (9%) of the samples positive for SARS-CoV-2 RNA, with concentrations ranging from 5–51 copies/m³.⁹² The size of the RNA-positive samples ranged from ≤ 2.5 to ≥ 10 μm . Locations adjacent to negative-pressured wards designated for COVID-19 patients did not appear to increase the likelihood of detecting viral RNA, having higher viral concentration, or finding particles of specific sizes in air samples. However, a significant positive association was observed between the average number of COVID-19 patients staying in the hospital during each sampling period, and the likelihood of an air sample testing positive for SARS-CoV-2 RNA. Furthermore, areas where staff congregated during times of high community rates of COVID-19 were associated with positive air samples. Of note, one RNA-positive air sample was taken when the unit was closed for cleaning and not under negative pressure, and the unit doors were left open for cleaning staff who had to pass by the air sampler to access the area for cleaning.

When air samples were RT-PCR-positive, culturing attempts were infrequently successful. In a systematic review and meta-analysis of 24 studies, Birgand et al. (2020) reported that 17.4% (82/471) of air samples from patient environments were RNA-positive (there was no difference in positivity at ≤ 1 m [2.5%] or 1–5 m [5.5%]; $p=0.22$), while culturing produced viable virus in 8.6% (7/81; 2 out of 5 studies) of samples.⁹³ A study by Guo et al. (2020) detected SARS-CoV-2 by RT-PCR in 35% (14/40) of air samples in an ICU and 12.5% (2/16) of air samples in the general ward that managed patients with COVID-19. Fifteen of 16 RT-PCR-positive air samples were from within 2 m of patients, with 1/8 samples positive at 4 m away.¹² Ben-Shmuel et al. (2020) conducted limited sampling (generally one air sample per area) in rooms with ventilated and non-ventilated patients, at a nursing station, and in private and public areas of a quarantine hotel.⁹⁴ RT-PCR-positive air samples were detected in a room with a ventilated patient (distance from patient was not reported) ($n=1/1$), at a nursing station ($n=1/1$), and in a quarantine hotel

room (n=1/1). However, there were no positive air samples in rooms of non-ventilated patients (n=0/3), a doffing area (n=0/1), and a public area of a quarantine hotel (n=0/1). The authors attempted viral culturing; however, no samples were positive.

At this time, only three studies, two from the same research group and one preprint from July 2020, have successfully cultured viable virus from the air. The preprint and one published study were already referred to above in the summary of Birgand et al. (2020). Sampling techniques and equipment may have caused the lack of culture viability despite RT-PCR detection in other studies. Future studies should aim to replicate the use of equipment and culture methods as these studies.

Lednicky et al. (2021) used a prototype and commercial version of an air sampler and custom RT-PCR probes for detection of SARS-CoV-2 in a patient room with two patients. One patient was discharged soon after sampling periods began and after receiving a negative RT-PCR test.⁹⁵ The remaining patient began experiencing respiratory illness two days prior to admission to the room. The study detected RT-PCR-positive air samples following 3 hours of sampling as well as positive viral cultures. Researchers positioned samplers 2–4.8 m from the recently symptomatic patient's head. The ventilation unit provided 6 ACH, filtering air and treating air with UV irradiation before recycling the air. Estimates of virus per volume of air ranged from 6–74 tissue culture infective dose (TCID)₅₀ units/L of air. Recently, a second study by Lednicky et al. was performed to detect viable SARS-CoV-2 virus from the front passenger seat area of a car driven by a SARS-CoV-2-positive patient without cough symptoms.⁹⁶ This study involved a sampler affixed to the sun visor in the passenger seat collecting particles sizes in ranges of <0.25 µm, 0.25–0.50 µm, 0.50–1.0 µm, 1.0–2.5 µm and >2.5 µm. The patient drove for 15 minutes with the windows up and air conditioner on. The sampler was turned off 2 hour after the patient completed the 15 minute drive. Viable virus was cultured only from the 0.25–0.5 µm fraction, which also had the highest quantity of detectable copies of viral RNA.

Further research is needed to reconcile differences in viral RNA detection and virus viability in air samples, despite RT-PCR-positive samples found on the surfaces of ventilation units.⁹⁷ Differences may be due to several factors, including: 1) air sampling devices are potentially not capable of maintaining viability of captured virus; 2) timing of air sampling varies by time since onset of symptoms, severity of disease or viral load; and 3) the conditions of ventilation (engineering controls) reducing concentrations of viral aerosols to undetectable levels. Even in rooms with high air exchanges, Tang et al.'s review of SARS-CoV-2 aerosols indicates that viral RNA copies can still be detected in air samples from patient rooms (1.8–3.4 viral RNA copies/m³), toilet rooms (19 copies/m³), and personal protective equipment doffing rooms (18–42 copies/m³).⁹⁸ In a series of distinct room types (two AIIR with 15+ ACH, an isolation room without negative pressure and a shared cohort room) for patients admitted within 7 days of symptom-onset, Kim et al. reported that 32 air samples were negative and 20 air samples from anterooms were also negative.⁸⁶ Culturing viruses is technically challenging; therefore, the lack of positive cultures does not necessarily indicate an absence of infectious virus. On the other hand, the detection of SARS-CoV-2 viral RNA on surfaces that are rarely touched suggests that the virus may be transported through the air to those no-touch surfaces.⁹⁹

Conclusions

Respiratory virus transmission occurs on a spectrum, from larger droplets that spread at short range, to aerosols that are present at short ranges but may also contribute to long-range transmission. As a result, categorizing SARS-CoV-2 transmission as either droplet or airborne does not accurately reflect this spectrum. Other respiratory viruses, like influenza, have similarly been described to demonstrate a spectrum of droplet sizes contributing to transmission.^{100,101}

The highest risk of SARS-CoV-2 transmission likely occurs via close (<2 m), unprotected exposure (lacking multiple prevention measures) to an infectious individual. While there is a lower risk of transmission at longer distances with unprotected exposure, this kind of transmission has only been documented to occur under certain conditions, usually involving inadequate ventilation or with recirculation of unfiltered or untreated air in combination with activities involving increased exhalation/expulsion (e.g., shouting, singing, exercising), and often with a lack of source control masking.¹⁰² Defining measures or cutoffs for inadequate ventilation was not possible based on the available descriptions of the contexts in which inadequate ventilation was reported to contribute to transmission. However, they included situations where air is circulated without filtration or exchange with fresh air, where there is no ventilation (e.g., windowless rooms without a ventilation system), and where the size of the room and ventilation rate relative to the quantity of infectious aerosols generated exceeds an unknown threshold of risk for infection. VOCs may be more effectively transmitted across all modes of transmission; however, there is no evidence that any VOCs transmit by fundamentally different routes.¹⁰³⁻¹⁰⁵

The delineation of relative contributions of short-range large respiratory droplets and aerosols and long-range aerosols to overall transmission patterns is complicated by the variable confluence of dynamic source/receptor factors and pathway factors. For example, each infector/infectee interaction is affected by source activities and amount of source viral load (e.g., forceful expulsion of droplets during coughing or singing, and timing in the course of illness), source/receptor adherence to preventative measures in place (e.g., hand hygiene, physical distancing, surface disinfection, mask-wearing and ventilation), and pathway factors that include airflow, UV, temperature, and humidity in indoor or outdoor environments.¹⁶ It is likely that the relative contribution of respiratory particle size to transmission will depend on these combination of factors.

A large body of evidence is emerging related to SARS-CoV-2. Studies related to identification of a specific mode of transmission are generally low quality. Moreover, data from different fields (e.g., epidemiology versus modelling) can be at odds with respect to conclusions drawn about the role of different sized droplets in short-range transmission and relative importance of long-range transmission events. Ongoing study is needed for further evidence regarding the quantity of viral particles required to cause infection. Additional assessment of SARS-CoV-2 viability in aerosols is needed. Lastly, elucidation of setting-specific risk factors for transmission (e.g., differences between source/receptor and pathway factors in health care settings, residential buildings, schools, warehouses, transportation) may provide further insight into mechanisms for transmission.

The COVID-19 pandemic has identified the importance of interdisciplinary collaboration towards understanding and having a common lexicon for describing virus transmission. When the analysis and interpretation of data is challenged by variable terminology used between and within public health, clinicians, aerosol scientists and the public, this can limit progress towards identification and application of appropriate mitigation measures.¹⁰⁶

Implications for Practice

This document summarizes the evolving evidence on transmission through respiratory particles and acknowledges the role for both larger droplets and aerosols in transmission. While our understanding of how transmission occurs has evolved and the relative contribution of droplets and aerosols continues to be studied, this may not necessitate a change in infection control measures, but highlights the importance of incorporating multiple infection control layers to mitigate transmission. Translation of this information into recommendations for control measures also needs to take into consideration evidence not reviewed in this document on the overall effectiveness of control measures to date: 1) effectiveness

of measures in isolation and in combination as layered mitigation; 2) effectiveness in the community vs. health care settings; and 3) effectiveness and the impact of implementation fidelity.

A detailed assessment of the evidence for infection prevention and control measures was out of scope for this document and thus limits discussion of recommendations for specific measures in different contexts. Of note, vaccination against SARS-CoV-2 is a relatively recent measure that is very effective at reducing transmission regardless of the mode of transmission and should be the priority control measure both in health care and community settings.¹⁰⁷

In health care settings, recommendations for IPAC measures are described in *IPAC Recommendations for Use of Personal Protective Equipment for Care of Individuals with Suspect or Confirmed COVID-19* and *Interim Guidance for Infection Prevention and Control of SARS-CoV-2 Variants of Concern for Health Care Settings*.^{7,8} These documents integrate the existing evidence around droplet, aerosol and contact transmission with jurisdictional experience with control measures and outbreak management to date, and recommends the use of the hierarchy of hazard controls to reduce the risk of transmission.

The bulk of disease transmission occurs in the community and in workplaces, not in health care settings. As SARS-CoV-2 transmits early in the course of infection, most commonly in the asymptomatic or presymptomatic period¹⁰⁸⁻¹¹¹ and within the first two days of symptom-onset, cases may not seek health care during their most transmissible phase. In all settings it is necessary to utilize multiple control measures to mitigate the dynamic transmission factors and address potential routes of transmission. Infection prevention controls should also be context-dependent and take into account vaccination status/coverage, the ability to physically distance and avoid crowding, the feasibility of proper wearing of appropriate personal protective and source control equipment, training and education on the appropriate use of personal protective equipment, hand hygiene, surface disinfection, indoor ventilation, and early identification and isolation of infectious persons. Finally, application of measures should also be in the context of overall rates of community transmission and risk of exposure.

Several resources exist for community guidance (e.g., non-health care workplaces, public and private spaces) on how to reduce the risk of SARS-CoV-2 transmission through a layered approach of multiple public health measures designed to mitigate short-range and long-range transmission.¹¹²⁻¹¹⁴ In general these involve avoiding the “3 C’s”: losed spaces, crowded places, and close contact. The degree to which various mitigation layers are necessary or possible will depend on the setting and risk context. Transmission can be mitigated through:

- Getting vaccinated^{115,116} (higher vaccine coverage in the population can reduce risk for individuals unable to receive a vaccine)
- Staying home when sick^{117,118} (e.g., active and passive screening prior to entry into public settings)
- Limiting the number and duration of contacts with individuals outside your household
- Physical distancing¹¹⁴ and avoiding crowded spaces
- Consistently and appropriately using a well-fitted, well-constructed (2-3-layer) mask for source control and personal protective equipment.¹¹⁹⁻¹²²
- Ensuring that ventilation systems¹²³ are well-maintained and optimized with the support of professionals according to relevant recommendations (e.g., from American Society of Heating,

Refrigerating and Air-Conditioning Engineers) and/or using outdoor environments whenever possible.

- Performing hand hygiene, respiratory etiquette, and environmental cleaning¹²⁴

The above measures are effective means of reducing risk of transmission irrespective of the relative contribution of larger droplets or aerosols to transmission. Some controls will be more effective than others and it is the combination and consistent application of these controls that is most effective for reducing disease spread.

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