PINNACLECARE

Medical Intelligence Report

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Topic: Update on Risks of Transmission of COVID-19

Covered in this Report:

Why is it necessary to continue to slow transmission of SARS-CoV-2?

There have been numerous examples described in peer-reviewed publications that indicate communities can curb transmission of COVID-19 even though there is not a highly effective treatment or vaccine currently available to treat or prevent SARS-CoV-2 infections by using non-pharmacological interventions. The most extreme actions are community-wide lockdowns that are very effective, but lead to substantial economic hardships as well as other negative consequences in regards to care of the elderly and education of the young, among others. After the use of lockdowns, many locales were able to reduce transmission to a level where it was possible to then use less restrictive measures while still maintaining a low infection rate.

Continuation of measures to reduce transmission remains necessary even after more than ten months because the estimates of the infection fatality rate over the course of the pandemic have not changed. With a similar infection fatality rate and 90% or more of most communities still susceptible to the virus, a large number of deaths will continue to occur if there is a high rate of transmission (Rothman et al., 2020). In addition to a high death toll, there is increasing evidence that even people with mild symptoms from a SARS-CoV-2 infection may have debilitating, long-term effects that prevent returning to work and activities of daily life. These types of complications seem to be occurring most often in groups that were classified as having a low risk of severe complications from COVID-19, but now enough time has elapsed in most cases to determine what the overall outcome will be for the most influential health challenge of the 21st century.

Difference between Infection Fatality Rate and Case Fatality Rate

Over the summer there were reports of reductions in the case fatality rate, which differs from the infection fatality rate. The **infection fatality rate** is the percentage of all people infected with COVID-19 who die of the disease. Determining an accurate infection fatality rate requires accurate information on the number of people who have contracted the disease. Due to a lack of enough testing and the high number of individuals who remain asymptomatic, the number of people infected with SARS-CoV-2 is often not known to a degree that allows for accurate calculation of the infection fatality rate. A measurement that is used when the scope of infections is poorly defined is the **case fatality rate**. This rate is the proportion of deaths compared to the total number of people diagnosed with the disease during a particular period.

The infection fatality rate from the United States, calculated by the CDC, in the spring was 0.65%. The infection fatality rate for Arizona as of July 30, calculated by researchers from Yale, was 0.63%, which is **not a statistically significant difference**. Researchers have also calculated an infection fatality rate based on world-wide values through May of 0.68%, which is also similar. Additionally, the ratio of the number of deaths compared to the number of hospitalizations in New York City and Arizona did not show a large difference when determined for all individuals or when stratified by age. This characterization allows for a comparison that does not rely on an accurate number of individuals diagnosed with COVID-19, and any improvements in the effectiveness and/or timeliness of treatment should be apparent as the outbreak in New York City was early in the pandemic and included large numbers of individuals that overwhelmed local healthcare systems.

While the infection fatality rate has been constant, there is a large difference between the case fatality rate measured early in the pandemic in New York City, New York, which went as high as 10%, and the case fatality rate in Arizona over the summer, which at the end of July was 2.1%. The case fatality rate in the United States on October 9 was reported to be 2.8% by the Johns Hopkins University Coronavirus Resource Center (Cha et al., 2020). The differences in the case fatality rate can be attributed to increased levels of diagnosis of the cases that are occurring during the more recent time period. The CDC reported that between March and May the true number of SARS-CoV-2 infections were underestimated by 10-fold. Also there are likely a larger number of younger people who are able to get tested as well as those who are asymptomatic or have only mild, non-life-threatening symptoms.

Therefore, the case fatality rate changes with changes in testing levels, but the infection fatality rate varies in response to interventions that lead to fewer people dying, such as better treatments.

Some examples of the different values for infection fatality rate and case fatality rate with different conditions are listed in Table 1.

Table 1. Examples of indicators under different circumstances.

Number of Actual Cases	Level of Underreporting	Number Diagnosed	Number Predicted to Die	Infection Fatality Rate	Case Fatality Rate
2000	10-fold	200	13	0.65%	6.5%
2000	5-fold	400	13	0.65%	3.25%
2000	none	2000	13	0.65%	0.65%
1000	10-fold	100	6.5	0.65%	6.5%
100	10-fold	10	0.65	0.65%	6.5%
100	none	100	0.65	0.65%	0.65%

Until there are interventions that prevent death from COVID-19, such as highly effective treatments or a vaccine, the infection fatality rate will not decrease, and the only method available to reduce the number of deaths will be to reduce transmission of SARS-CoV-2 infections.

Terms used for Discussion of Transmission

When a virus is transmitted between humans, as opposed to other vectors such as animals or insects, the speed of disease spread depends on a number of factors such as the number of infected individuals and susceptible individuals, human contact patterns, and population demographics (Rotejanaprasert et al., 2020). There are a number of specific terms and measured characteristics that researchers use to quantify the transmission of an infectious disease that are defined below (CDC_Principles of Epidemiology, 2020).

The **index case** is the first infected individual identified in a group of infections. The people that the index case interact with are referred to as **contacts**.

The **incubation period** is the length of time between an exposure to the virus that leads to infection and the onset of symptoms from the infection.

Reproduction number (or the basic reproduction number, R_0) is an indicator of the contagiousness or transmissibility of infectious diseases that is affected by human behavior and the biological characteristics of the pathogen, such as changes in infectivity with temperature (Delamater et al., 2020). It is defined as the number of infections that are caused by one infected individual who interacts with a completely susceptible population. There are other versions of the reproduction number, such as the effective reproduction number, that take into account changes that occur when the entire population is no longer susceptible to infection.

The **dispersion factor** (or k) is a description of the tendency of identified cases to occur in clusters, or when transmission to a group occurs from a small number of people. When the value of k is low, there is a higher likelihood of superspreading events stemming from a few infected individuals.

The **serial interval** of an infectious disease is the time it takes for an infected person to pass the infection to others, or the time between cases in a chain of transmission. The value of this characteristic affects the speed of spread in a population.

The duration of an epidemic is dependent both on the actions of a population, and on the characteristics of the infectious disease. Some of the factors that contribute to the length of an epidemic are the **latent period**, or the length of time from infection to when a person is infectious, and **communicable period**, or **duration of infectiousness**, which is the time interval during which an infected person sheds virus that can infect someone else. The duration of infectiousness on COVID-19 is still under investigation, but based on more than one report appears to be around ten days after the incubation period.

Attack rate is a measure of the risk of disease during the specified period. It is calculated by the number of new cases during a specified time interval per the overall number in the group. It can also be referred to as the incidence proportion, risk, or probability of developing a disease.

The **secondary attack rate** describes how many of one person's contacts catch the disease, and it is calculated as the number of contacts who were infected by an index case per the total number of contacts.

Airborne transmission occurs through small droplets and particles, containing infectious material, that remain suspended in the air and can travel long distances. Airborne particles, which are also referred to as **aerosols**, remain in the air for hours.

The term **aerosol** can be used both to define respiratory droplets of a certain size (e.g., smaller droplets and particles), as well as to describe the collection or cloud of these respiratory droplets in the air.

Droplet transmission occurs through exchange of virus-containing respiratory droplets (i.e., larger and smaller droplets and particles) exhaled by an infectious person. Transmission is most likely to occur when someone is close to the infectious person, generally within about 6 feet.

What are the conditions that lead to spread from person to person?

Discussions about the physical mechanisms that contribute to the spread of the virus can be very technical and the specifics are not particularly relevant to an individual's daily life. However, questions about whether the virus is spread by droplets or aerosols are important to answer because the interventions needed to limit the risk of transmission for each method differ.

When virus particles are expelled in aerosols, they stay suspended longer than droplets, meaning that infectious material may linger in a closed room for hours rather than minutes.

The recommendations for maintaining good hand hygiene and maintaining a distance of six feet from others are based on general studies of droplet transmission of respiratory diseases and not specific trials with SARS-CoV-2. The studies indicate that a **droplet will settle to the ground in 4.6 seconds while an aerosol particle takes 12.4 hours**. The potential for aerosol spread of SARS-CoV-2 suggests that the currently recommended distance will not be sufficient to reduce transmission for indoor conditions where aerosols can remain for hours, accumulate over time, and follow airflows over distances further than six feet. Experts describe the movement of airborne virus particles as similar to the particles observed when a smoker exhales cigarette smoke, and they mention that "the distance from a smoker at which one smells cigarette smoke indicates the distance in those surroundings at which one could inhale infectious aerosols" (Prather et al., 2020).

While the information on the CDC website has been changed several times, as of October 6, 2020, the CDC states that **COVID-19 can sometimes be spread by airborne transmission under certain circumstances** (CDC_How COVID Spreads, 2020 and CDC_Scientific Brief, 2020).

Circumstances under which airborne transmission of SARS-CoV-2 may occur include:

- Enclosed spaces where an infectious person directly exposes people or where people are exposed shortly after the infectious person has left the space.
- Prolonged exposure to respiratory particles, often generated with expiratory exertion (e.g., shouting, singing, exercising) that increased the concentration of suspended respiratory droplets in the air space.
- Inadequate ventilation or air handling that allowed a build-up of suspended small respiratory droplets and particles.

Other types of transmission, such as fecal to oral transmission and transmission via infectious particles on surfaces (fomites), can potentially occur based the identification of infectious viruses in the material, but they have not proven to have a large contribution to the spread of COVID-19 (CDC_How COVID Spreads, 2020).

Several different animal species have been shown to become infected by contact with humans or other infected animals, including dogs, cats, fruit bats, primates, and ferrets (Schlottau et al., 2020). Mink have found to become infected from humans and to be able to pass the infection back to human contacts. However, at this time, transmission through animals has not been documented to have a large contribution to the pandemic. The possibility of animal reservoirs of SARS-CoV-2 will need to be more thoroughly investigated to ascertain whether new outbreaks can be initiated from animal sources.

Difficulty in Confirming Droplet or Airborne Transmission

There are always difficulties defining how a disease is transmitted in the midst of an ongoing pandemic because of the need to balance investigation with the actions needed to care for those that are ill and implement plans to reduce the harm from the outbreak. It has been no different for researchers attempting to confirm the mode of transmission for SARS-CoV-2 in this on-going pandemic. On the surface, it seems like the advances made in medical and scientific research would make it easier to determine how the virus is spread, but while the general understanding of infectious diseases has improved, the need to make observations during a turbulent time still remains.

When the outbreak of COVID-19 first began in China, researchers began their investigation using the information that had been collected about the transmission of the related coronaviruses responsible for the SARS and MERS pandemics. Both SARS and MERS were known to be transmitted through close person-to-person contact due to dispersion of respiratory droplets from sneezing or coughing. There were also a large number of cases of SARS that were spread within hospital settings from exposure during procedures that lead to an expulsion of aerosols, such as intubation (Peeri et al., 2020).

The global outbreak of SARS was contained in 2003, and no cases have been reported since 2004. The containment was possible, in part, because it was possible to identify and isolate infected individuals based on symptoms that became evident before the individual was able to effectively infect others. This characteristic of SARS-CoV-1 made it possible to interrupt transmission in the population. Cases of MERS have not been fully eradicated as of yet, but it is also possible to identify individuals based on symptoms before they enter the most infectious stage of illness. The epidemiological information collected at the start of the COVID-19 outbreak in Wuhan suggested that transmission occurred similarly to SARS and MERS with an identified link to an animal reservoir at a seafood market in the city that progressed to human-to-human transmission first in hospital staff where primary cases were treated, and later in individuals without a clear connection with the market.

When it became apparent in China that COVID-19 was spreading much more rapidly than either SARS or MERS, broad lockdowns were initiated to get control of the spread as hospitals became overwhelmed. The lockdown helped to reduce contacts between individuals and slowed the transmission, but it may have also masked the propensity of the virus to spread in an airborne-like manner due to the prohibition of large gatherings where this type of transmission often occurs. During this time, researchers determined that SARS-CoV-2 had low reproduction numbers (between 2 and 3) compared to known airborne infections, such as measles, which has a reproduction number between 12 and 18. The lower reproduction number corroborated the researchers' hypothesis that COVID-19 was spread mainly through droplet transmission. Additionally, the review of the outbreak in China revealed that the rate of transmission was highest between people living in the same household while crowd-based spread was rare, and there had been little evidence of transmission between children in schools. This apparent confirmation that the transmission was similar to that with SARS and MERS as well as the immense stress on the health care infrastructure in the areas where outbreaks were occurring made it difficult to fully evaluate other transmission routes that might have been occurring.

As it became possible to perform epidemiological studies and analysis of local transmission dynamics, researchers discovered that the COVID-19 patterns observed did not conform to those that would be expected with droplet-based transmission alone, but getting direct evidence of airborne transmission is always a difficult process even outside of a pandemic situation.

Inconsistent results between different studies is a common occurrence because it is difficult to collect and test air samples with PCR-based methods that contain only a small amount of viral RNA in a given sample.

Detection of infectious, airborne virus is even more difficult. Collection of the virus from the air often damages the virus thereby inactivating it, and the subsequent experimental steps for growing and isolating the virus are difficult and time consuming, meaning that the whole process has a low chance of success even when infectious material is present (Lewis, 2020).

If infectious virus particles are present in airborne samples, there are still questions about both the amount released by an infected individual and how much is required to cause infection in a susceptible person. At this time, the dose of virus required to initiate an infection from SARS-CoV-2 has not been established (Shao, 2020). The combination of difficulty in measurement as well as unknowns about the virus is why scientists have not conclusively proven if airborne transmission through aerosols is occurring.

Evidence of viral RNA in the air of hospitals in both China and the United States was reported after testing in February and March (Lui et al., 2020 and Santarpia et al., 2020). Conversely, testing in late March and April in Korean hospitals resulted in no evidence of viral RNA in the air or transported farther than 2 meters based on sampling in the hospital rooms of patients with COVID-19 (Kim et al., 2020).

Epidemiological data can also be used to assess transmission dynamics without the difficulties inherent in sample collection of infectious virus from the air, but this method only gives indirect evidence based on what is known about other viruses, and the information is only available after an outbreak has occurred. When researchers were able to do full analyses of the spread of SARS-CoV-2 infections that occurred in Northern Italy, they found that there were differences from the spread observed in Wuhan, China (Setti et al., 2020). The outbreak in the Lombardy region spread more quickly than the outbreak reported in Wuhan, and an epidemic model based only on transmission through respiratory droplets and close contact could not fully explain the regional differences in the spread of COVID-19.

One of the measurements used to assess if a virus is spread through airborne processes is the attack rate.

Viruses with airborne transmission typically have high attack rates because transmission through the air allows for the virus to quickly reach and infect many people. The attack rate for SARS-CoV-2 is on the lower end of the spectrum, but there are specific conditions, such as enclosed spaces with low levels of ventilation, where higher attack rates have been observed. There is mounting evidence of aerosol transmission from smaller, airborne particles that remain suspended in poorly ventilated areas for over an hour (Prather et al., 2020).

From the general public's point of view, some of the confusion has arisen from differences in the use of technical versus colloquial definitions in reports on the virus (Van Beusekom, 2020). For example, in a commentary on COVID-19 transmission published by *CIDRAP*, an expert on disease transmission, stated that airborne transmission is typically defined as inhalation of respiratory pathogens that move a distance from the source. In the case of SARS-CoV-2, there is evidence of the generation of small, aerosol-sized particles, which remain near the source for long periods of time. This differs from the technical definition of airborne or aerosol-based transmission, but may be similar enough to merit changes in measures to prevent transmission on a practical level.

While the relative contribution of droplet or aerosol transmission for SARS-CoV-2 is not yet established, it is known that the virus is more infectious than other coronaviruses and the influenza virus, and additional interventions in addition to those normally recommended for strictly droplet-based transmission are required.

How was pre-symptomatic and asymptomatic spread confirmed?

A similar pattern was also observed for the confirmation of whether there was a larger contribution to the pandemic due to transmission of SARS-CoV-2 from individuals without symptoms. The technical definition of asymptomatic transmission differs slightly from the colloquial definition used in everyday communication.

- **Pre-symptomatic transmission**-spread of a disease before the onset of symptoms
- **Asymptomatic transmission**- transmission of a disease from someone who never develops symptoms

Many people, including media sources, refer to a lack of symptoms as asymptomatic without making reference to the presence of symptoms at other times, which can lead to confusion when combined with technical discussions.

The first signs that asymptomatic and pre-symptomatic transmission was possible were observed during contact tracing in China and Korea. However, based on the researchers' interpretation of the spread in the community, it was presumed that pre-symptomatic transmission could occur in some instances, but asymptomatic transmission was thought to be rare (Park, 2020).

Researchers began to notice that the spread of COVID-19 was not effectively controlled by isolating a patient after the illness onset, suggesting transmission may be occurring before symptoms were evident.

A study in England investigated the information on individuals diagnosed with COVID-19 complied in a database maintained by the Office for National Statistics Coronavirus Infection Survey (Peterson et al., 2020). This study used information about 36,061 individuals who took a PCR-based test for COVID-19 between April 26 and June 27. There were 115 positive tests during this time period, corresponding to 0.32% of the group. On the day of the testing, 625 people, or 1.7%, reported that they were having symptoms consistent with COVID-19. Out of the 115 people who tested positive, 23.5% were symptomatic on the day they were tested and 76.5% were not.

Based on the results, the researchers concluded that symptoms are a poor marker for COVID-19 and silent transmissions may be a widespread occurrence.

Multiple clinical studies in hospitals, nursing homes or long-term care facilities, and prisons have since indicated that pre-symptomatic and asymptomatic transmission is not a rare occurrence. The characteristics of these types of facilities make it possible, and necessary, to do numerous tests of staff or residents regardless of whether they have symptoms.

In two long-term care facilities in Minneapolis, Minnesota staff were tested daily after the middle of March due to difficulties in controlling outbreaks in residents (Taylor et al., 2020).

Of the staff at the facilities that tested positive, only 51% were experiencing symptoms on the day of testing.

Multiple rounds of testing at a correctional facility in Louisiana were performed to assess the level of infection in staff and inmates after identification of an outbreak (Njuguna et al., 2020). The outbreak was first identified when a staff member developed symptoms and was tested, and 36 symptomatic inmates tested positive for COVID-19 and were subsequently isolated. The other individuals in the dormitories where the sick inmates had lived were placed under quarantine.

The prevalence of SARS-CoV-2 infection in the quarantined group was evaluated based on the presence of symptoms and serial testing. Testing revealed that 72% of the individuals in quarantine had COVID-19, and 45% had no symptoms at the time of testing. Importantly, 25% of the newly identified cases had previously tested negative, reiterating that a previous negative test does not mean that infection had not occurred, but that levels of viral RNA may be too low to detect or infection occurred after the initial test.

The authors concluded that screening based on symptoms alone would have missed a large number of the infected individuals.

Asymptomatic transmission was also observed during the outbreak that occurred on the Diamond Princess cruise ship (Plucinski et al., 2020). Testing of the passengers revealed 21% of those infected on the ship remained asymptomatic, and transmission from people without symptoms at the time of testing occurred. The attack rate for passengers in single-person cabins or whose cabin-mate was not infected was 18%. This is compared to a 63% attack rate for those sharing a cabin with an infected individual without symptoms, and 81% for those in a cabin with a symptomatic person.

Based on available evidence, it is now accepted that both asymptomatic and pre-symptomatic transmission of SARS-CoV-2 occur, and these forms of transmission have a sizeable contribution to community transmission of the virus.

When are people infectious?

A study conducted in Korea has shown that there is not a difference between the amount of virus located in the upper respiratory tract of individuals who tested positive for COVID-19 with symptoms and those without symptoms (Ra et al., 2020). Participants for the study were located at an isolation facility in March. There were 213 participants, and 19% remained asymptomatic throughout the entire study period, and the remaining participants had mild symptoms that did not require hospitalization. The amount of virus detected in respiratory samples was the same for both individuals with symptoms and those without, suggesting that similar amounts of infectious particles would be emitted while breathing, talking, and other day-to-day activities. A difference may occur if an individual's symptoms include coughing or sneezing, but the breakdown of symptoms reported by the participants was not included in the report.

Researchers have determined that production of virus peaks in the **one to two days** before the onset of symptoms (He et al., 2020).

> **This means that ALL people infected with SARS-CoV-2 are able to infect others approximately 2 days before symptom onset, and infectiousness peaks at around one day before symptom onset.**

Researchers have estimated that 50% of transmission of SARS-CoV-2 occurs while individuals do not have symptoms, but only 20% of individuals remain asymptomatic throughout the course of the infection (Miller et al., 2020).

Evaluation of Transmission Events

The CDC defines a **disease cluster** as an unusual aggregation of health events that are grouped together in time and space. A **superspreader** is an individual who transmits an infection to an unusually large number of other people. The superspreading individual is presumed to emit a large viral load compared to those who do not cause a large number of infections. **Superspreading events** lead to infection of a large number of people, but do not necessarily require a superspreader. Rather, the conditions at the event are ideal for spread within the group. Cases that do not have traceable contact with another case or cluster are referred to as **sporadic cases**.

What amount of Transmission Occurs from Random Encounters?

Information collected in Hong Kong about the transmission of COVID-19 is very complete due to extensive contract tracing and a widespread adoption of suppression measures (Adam et al., 2020).

> **A study reporting sporadic local cases in the area indicates that the proportion of transmission that occurs from anonymous interactions, fomites, or aerosols that are encountered during the activities of daily life is around 14%**.

This is the proportion of people infected in Hong Kong where detailed contact tracing was not able to identify a source of the infection, suggesting infection occurred due to a random encounter. This value is highly dependent on the local level of community infection, and this specific value would only apply to similar regions with similar suppression measures in place.

How do clusters and superspreading events contribute to SARS-CoV-2 spread?

The dispersion factor is a measure of the propensity of infections in a community to cluster together. The lower the value of the dispersion factor, the more likely cases of a virus will be found clustered together. Influenza is an example of a virus that does not spread through clustering, and cases of influenza spread evenly through the population, leading to a dispersion factor of around one. For both SARS and MERS, researchers observed a large amount of clustering, and the dispersion factor values were estimated to be around 0.16 to 0.25, respectively (Kupferschmidt, 2020 and Endo et al., 2020).

> **SARS-CoV-2 infections are often found in clusters as well, and current estimates suggest the dispersion factor for COVID-19 is similar to SARS and MERS with about 10% to 20% of COVID-19 cases leading to 80% of the transmission.**

While viruses with low dispersion factors involve a small number of people causing a large proportion of the transmission, it also means that most chains of transmission die out, and the majority of individuals with COVID-19 do not infect anyone else.

This suggests that there are specific conditions that lead to the easy spread of SARS-CoV-2 where a single person can infect 80% of the people in a room, and other conditions where an individual is much less contagious (Tufekci, 2020). Some of the factors that can lead to this pattern of transmission include a short time-period where individuals are highly infectious before the onset of symptoms and exposure of an infectious person to a large group that is in close contact with poor ventilation, leading to airborne-like infectious particles that linger in an area.

COVID-19 Clusters in Hong Kong

Researchers in Hong Kong investigated the potential for superspreader events of SARS-CoV-2 between January 23 and April 28 and found that 19% of SARS-CoV-2 infections were responsible for 80% of transmissions (Adam et al., 2020). During this time frame, 69% of the identified cases did not transmit the virus to anyone else. There were around four to seven superspreader events that included 51 different clusters and 309 total cases.

Social gatherings at locations such as bars, restaurants, weddings, and religious sites were found to have an increased risk of being a superspreading event. While the most frequent form of transmission observed was between members of households (54.4%), transmission at social gatherings was the second most common site (33.1%) with work related transmission at the lowest level. However, while there was a higher rate of initial transmission in households, there was a higher rate of secondary cases at social gatherings when compared to the rate in households or in the workplace.

Based on the results of the study, the authors propose that there is an increased risk of large outbreaks at social gatherings due to the greater number of contacts possible in these settings, which is an effect that has been observed in other areas of the world as well.

The authors propose that these types of interactions constitute the core behavioral risk factor for increased transmission SARS-CoV-2 or superspreader events, and they suggest that suppression measures should focus on eliminating the risk of superspreading by reducing the numbers of contacts at the events.

COVID-19 Clusters in New Zealand

Because New Zealand is an island country separated from other populated areas, it was possible to impose very effective lockdowns that all but eradicated COVID-19 from the island (Geoghegan et al., 2020). At the start of the outbreak, the reproduction number in one area was estimated to be around 7, and after lockdown, the reproduction number had been reduced to 0.2. Between February 26 and July 1, there were 1,178 laboratory-confirmed cases with 350 probable cases in the country. Researchers were able to genetically sequence 649 of the viruses, which represents 56% of the confirmed cases. The genetic sequences along with traditional contact tracing allowed the researchers to better track transmission in the country.

The evaluation identified 277 separate introductions of the virus to New Zealand that led to the 649 cases. The researchers reported that 24% of the introduced cases led to transmission to only one other person while 19% caused a transmission chain that resulted in more than one other case. The remaining 57% did not lead to a transmission event.

The clusters identified in New Zealand were mainly associated with social gatherings. The largest cluster was introduced from the United States with local transmission accelerated from superspreading that occurred at a wedding.

COVID-19 Clusters in South Korea

The transmission documented in South Korea at the start of the pandemic is a classic example of a virus with a low dispersion factor causing a superspreading event that led to a larger cluster of cases (Reuters, 2020). The cluster began with the 31st person to be diagnosed in South Korea, who has been referred to as Patient 31. Officials were not able to determine where Patient 31 was infected because she had traveled in numerous crowded areas. However, due to attendance at two church services that lasted two hours each with 9,300 people present, she is connected to 1,160 symptomatic cases of COVID-19 within the church members. A possible second cluster occurring at a funeral may also be connected as members of the church were present at the ceremony.

Overall, it was estimated that, as of March 18, 60% of the cases in South Korea were linked to people exposed at the church by Patient 31.

What are the indoor environmental factors that contribute to transmission risk?

The general factors that have been associated with episodes of high rates of transmission include crowded indoor venues with poor ventilation. The following description of a simulation of SARS-CoV-2 transmission allows for identification of the specifics of the contributing factors.

Contribution of Exposure Time and Ventilation on Transmission

Researchers have performed a detailed analysis of the exposure time, type of ventilation, and activities of people at both hypothetical and real-life events to assess the individual infection risk in indoor settings (Buonanno et al., 2020).

Terms used in the study:

- **Air exchange rate**- the amount of air in an area that is exchanged in a time period.
- **Natural ventilation**- the process of supplying air to and removing air from an indoor space without using mechanical systems. It refers to the flow of external air to an indoor space as a result of pressure differences arising from natural forces. The typical air exchange rate for natural ventilation is 0.5 per hour.
- **Mechanical ventilation**- a method of forced ventilation using mechanical air handling systems, commonly called HVAC systems. Blowers, fans, filters, and ducts are used for transporting and removing air from a space. With mechanical ventilation, the air exchange rate can be increased to around 3 per hour or up to 10 per hour.

The conditions of the hypothetical scenarios are listed below. Other factors included in the analysis are the viral load emitted by infected individuals, the infectivity of the virus, the survival of viruses in droplets, transport of droplets through the air, airflow patterns, inhalation rate of individuals in the room, type of respiratory activity, and the activity level of those present.

The hypothetical scenarios evaluated were

1. A hospital room (100 m^3) housing an infected patient at rest with an exposed healthcare worker performing their normal duties.
2. A hospital room (100 m^3) with two patients, where one is infected and one is an exposed patient.
3. A gym (300 m^3) with an infected person and an exposed person during heavy exercising.
4. An office (300 m^3) with an infected and exposed person both doing light activity while speaking
5. An auditorium (800 m^3) with an infected individual singing or talking loudly with exposed individuals listening.

The researchers found that there are tradeoffs in environmental conditions that can reduce the risk from an increased time at an event, but there is a threshold after which alteration of physical conditions no longer reduces the risk.

In one example, increasing the airflow in an auditorium from natural ventilation without mechanical assistance to low levels of mechanical ventilation (an air exchange rate from 0.5 per hour to 3 per hour) would lead to a 2-fold decrease in the risk of an audience member listening to an infected singer or speaker. Increasing the air exchange rate to 10 per hour would lead a further 2.7-fold decrease in the risk.

The amount of virus produced by an infected person also influences the risk of a particular situation. When the amount of virus emitted was varied during the simulation, it was found that **the probability of infection increases approximately 10 times between medium and high levels of emitted virus.** For example, in the hypothetical scenario of a person singing or talking loudly in an auditorium, a medium rate of virus emission over two hours would result in a median probability of infection of 2.1%. If the singer/speaker had a high rate of viral emission with the same conditions, the median probability of infection increases to 27%.

The researchers also calculated the maximum exposure time in minutes for the different exposure scenarios using an acceptable individual risk of 1 in 100 (Table 2). This level of risk corresponds to a situation where the reproduction number is less than one in crowds up to 1000 people, which is considered a lower risk by the authors.

The results of the analysis suggest that hospital staff have a low risk of infection if they are in a patient's room for short times while performing their duties. However, having two patients in the same room would lead to a high risk if they were exposed for an entire length of a hospital stay.

Table 2. Maximum exposure time in minutes.

Hypothetical scenarios	Air exchange rate per hour	Exposure time for a 1 in 100 individual infection risk
Scenario 1: Hospital patient and staff	0.5	30 minutes
	3.0	39 minutes
	10.0	72 minutes
Scenario 2: Hospital patient and patient	0.5	54 minutes
	3.0	84 minutes
	10.0	192 minutes
Scenario 3: Gym workout	0.5	12 minutes
	3.0	13 minutes
	10.0	17 minutes
Scenario 4: Office	0.5	14 minutes
	3.0	15 minutes
	10.0	20 minutes
Scenario 5: Auditorium with singer/speaker	0.5	14 minutes
	3.0	16 minutes
	10.0	21 minutes

In the scenario of a gym workout, increased air exchange rates did little to change the length of the acceptable exposure time. If the number of people in the gym is kept lower, at a maximum of 100 people rather than 1000 in 300 m^3, than the time can be increased to 132 minutes with mechanical ventilation air exchange rate at 10 per hour.

The maximum time of exposure in a conference room or auditorium is also shorter than the length of most programs. Based on the simulations, exposure for two hours in a room 800 m^3 without mechanical ventilation that has 100 people (e.g. conference room) or 267 people (e.g. auditorium) would lead to reproduction numbers of 3.8 for the conference room and 10.2 for the auditorium.

> **As the reproduction numbers are well over one, this scenario would lead to an increase in infection in the people in the room.**

In order to guarantee that the reproduction number is below one, the maximum number of people that could attend this type of gathering is 26 without mechanical ventilation and 135 with mechanical ventilation air exchange rates at 10 per hour in a room 800 m^3.

> **The authors stress that these results show that controlling the pandemic requires reducing the number of people and their exposure time to each other, and that ventilation conditions strongly influence risk.**

As mentioned above, the researchers also used their simulations to evaluate two real-world scenarios, a cluster in a restaurant in China and a second cluster that occurred after choir practice in Washington state.

In the restaurant, the index case ate lunch with ten members of his family at a single table in a restaurant in Guangzhou, China on January 24. The index case began having symptoms later on January 24, and nine other individuals were eventually diagnosed with COVID-19 from the contact. Four of the individuals were at the table with the index case, and five other individuals were seated at two nearby tables. The restaurant was 145 m^3 in size and on the third floor of a five-floor building with no windows. There were 15 tables about a meter apart, and a total of 91 individuals in the restaurant at the time. Exposure time was 53 minutes and 73 minutes for the neighboring tables. The room used natural ventilation without access to an outdoor air supply.

At the choir practice, 61 members of a 121 member choir in Skagit County, Washington met in an 810 m^3 hall for rehearsal on March 10. Due to known transmission in the area, the members used hand sanitizer at the door, refrained from contact (handshakes, etc.), and brought their own sheet music. None had symptoms at the time of rehearsal, and the practice lasted for approximately 2.5 hours. The ventilation system was not well described, but was reported to be a newer forced-air furnace. No external doors or windows were open during the rehearsal. A total of 33 members were officially diagnosed with COVID-19, and another 20 cases were suspected but not confirmed.

The attack rates of the two scenarios were 45% in the restaurant and at least 53% at the choir practice.

The researchers found that the high attack rates observed in both cases could only be explained if aerosol-based infection occurred.

Additionally, based on the limits of the situations, it would not be able to lower the risk through optimization of the room ventilation as it was calculated that an air exchange rate of more than 1000 per hour would be required. Reduction of risk on infection was only possible by limiting the time of exposure, or if it were possible to develop an advanced ventilation system that could remove exhaled air before it mixes with the room air, which is unlikely.

The main conclusion the authors made is that in order to guarantee an acceptable risk for people exposed to SARS-CoV-2 in naturally ventilated indoor environments without mechanical ventilation, the exposure time would need to be brief, and with mechanical ventilation the exposure times would still remain under an hour for most situations.

Rate of Particle Emission by the Choir in Washington State

Several of the same researchers, in coordination with other experts, further characterized the outbreak that occurred at the choral practice in Skagit County, Washington (Miller et al., 2020). Again, it was found that the high rate of transmission of COVID-19 that was observed could only have occurred through inhalation of aerosols created while singing. The members of the choir were separated by approximately 0.75 meters on each side and around 1.4 meters in the front. No one was located within 3.0 meters in front of the index case, and individuals infected with the virus were located behind and to the side of the index case. The ventilation rate in the room was found to be too low to blow droplets behind the infected individual, which would have been necessary without aerosol-based transmission. There was only approximately 15 minutes of socialization time during the practice, and it would not have been possible for the index case to converse with all the members who became ill for the duration and in the proximity needed for droplet-based transmission. The rate of particle emission from the mouths of the singers was very high, leading to large amounts of aerosolized virus.

The researchers conclude that the best measure to improve indoor environmental conditions is to minimize indoor emission by limiting the number of people at gatherings, shortening the duration of gatherings, and having attendees wear masks because it is not always possible to increase ventilation to levels that reduce the risk of infection.

Effect of Ventilation on Particle Movement

Researchers have combined measurements of the particle emission that occurs during normal breathing with simulations of air movement in three common daily scenarios, including an elevator ride, attending a lecture in a classroom, and shopping at a small supermarket (Shao et al., 2020). Measurements of people breathing normally were used to simulate asymptomatic, infected individuals who would not create particles from coughing or sneezing.

The researchers found there is a large variability in the amount of particles emitted while breathing between different people. One participant in the trial, out of the eight total, that had a much larger amount of emitted particles, suggesting that some people can be "super-emitters" even while simply breathing normally. Other researchers have also reported super-emitters that produce a much larger than normal amount of particles when coughing or speaking. The researchers hypothesize that the presence of a super-emitter at an event may also contribute to the possibility of having a cluster of infections, but to date, all of the investigations that have identified such individuals have not been large enough to determine the proportion of super-emitters that occur in a population.

The simulations of air-flow in an elevator, classroom, and supermarket combined with the measured particle emission indicates that while ventilation enables the removal of virus-containing particles, it can also spread particles beyond the proximity of an infectious individual.

The particle emission used in the simulations was an average of the values measured from the participants, and not the elevated value from the super-emitter.

The placement of ventilation within a space can lead to air currents that produce hot spots where the risk of encountering virus particles are orders of magnitude higher than other areas in the space, and the location of the hot spots depends on the relative positioning of infected individual, ventilation ducts, and characteristics of the room. The authors mentioned that the outcome observed in these simulations confirmed the interpretation made by Buonanno and colleagues about the cluster of infections that occurred at the restaurant in Guangzhou, China, which is described in more detail above.

The simulations in this study also illustrated that ventilation currents can enhance the amount of emitted particles that are deposited on surfaces within the room. Based on the specific placement of the ventilation ducts, a patchy network of regions with high surface contamination will develop. This situation was observed in previous studies examining the spread of SARS-CoV-2 in hospital rooms in both the United States and China (also described briefly above), leading to an increased level of virus around air vents and on the floor.

A concerning revelation was that when ventilation was placed at only a single location in an area, it was very inefficient at removing particles from the air even at high flow rates. When there was only one ventilation site, the authors observed circulation zones and other areas where particles were deposited in concentrated spots rather than removal of particles through the air system.

This suggests that simply adding filters to most currently available ventilation systems would not lead to filtration of the air and may not enhance particle removal.

The practical steps suggested to reduce the risk of airborne transmission include

- Addition of more sites of ventilation, even if the total air flow capacity isn't increased, would lead to a more efficient particle removal
- Placement of occupants, such as cashiers or students, outside of hot spots
- Increased frequency of cleaning of areas where particles are likely to be deposited
- Wearing masks to reduce particle generation in the space

Do outdoor environmental factors influence transmission?

A review and analysis of the published reports investigating the influence outdoor environmental factors have on SAR-CoV-2 transmission indicates that there is little evidence to date of a large enough effect to lead to a change in recommendations for reducing the risk of COVID-19 (Mecenas et al., 2020). The review of published reports located 17 investigations of weather factors on the transmission of SARS-CoV-2. The available studies were assessed, and the certainty of the evidence in each was found to be low. There was a consistent general conclusion between the studies that lower temperatures and low humidity increase the risk of transmission. There were numerous other factors, however, that had a higher contribution to the risk of transmission than the environmental conditions. Some of the other factors found to have a greater impact were population density, purchasing power, public health interventions, containment measures, general health policies, transportation, and cultural aspects.

Based on the results, the authors conclude that the contribution of weather to transmission is not been proven to be large enough to lead to a change in public health policies.

A report that was published after the review also found that changes in temperature and humidity in China did not have a large contribution to the differences in reproduction number between different locales (Poirier et al, 2020).

From their evaluation, they proposed that increases of temperature and humidity with the beginning of spring and summer the Northern Hemisphere would not lead to declines in case counts without the implementation of drastic public health interventions.

Does transmission of SARS-CoV-2 differ in children and young adults?

The investigation of transmission in younger age groups was less of a priority in the early part of the pandemic due to a lower risk of this age group experiencing severe symptoms. As of September 25, it is estimated that only 1% to 3% of the confirmed cases of COVID-19 world-wide were children (Viner et al., 2020).

However, fewer children have been tested for COVID-19 compared to adults, and as children are less likely to have symptoms, the number of cases is expected to be an underestimate. To identify the majority of cases in a community, the percentage of people who test positive should be around 5% (Leeb et al., 2020). At the end of May, the CDC reported that the percentage of positive tests for children between 5 and 11 was near 10% and was around 11% for children between 12 and 17. The values were similar between both age groups, but the high value suggests that testing of children has been inadequate. The positivity rate increased to a peak around the end of June. At this point a difference had developed between the two age groups in the study, and the positivity rate for 12 to 17-year-olds was between 14% and 15% while the younger group had a peak positivity rate of around 12%. Since the peak at the end of June, the positivity rate has been decreasing while the number of tests collected has remained steady. In the first weeks of September, the positivity rate was under 6% for 5 to 11-year-olds, and around 7% for 12 to 17-year-olds.

Additionally, individuals under the age of 18 have not been included in most of the seroprevalence studies conducted to estimate the number of people in a community who were exposed to SARS-CoV-2. The overall lack of information makes it difficult to predict how or if children contribute to community spread of COVID-19. However, even with a better idea of the prevalence of infections occurring in a specific group, it would not be possible to determine the susceptibility of or transmission from a group because these characteristics depend on a number of other factors, including exposure, the proportions of children in the population, mixing rates among children and between adults and children, and timing of social distancing interventions that disrupt mixing.

Researchers have complied the information from 32 relevant publications that are currently available to determine what is known about the susceptibility to and transmission of SARS-CoV-2 among children and adolescents compared with adults (Viner, 2020). Six of the studies were from mainland China, and two were from the United States with single studies from other countries around the world. The results of the individual studies have varied widely. For example, some observed no difference in secondary attack rates between children and adults while others reported lower attack rates for young children, and some found that older children had similar attack rates to adults. The authors of the review were able to perform a statistical analysis called a meta-analysis that allows for the combination of information from different studies to identify trends and estimate values. It is not possible to directly compare different studies due to differences in the design of the studies, but a meta-analysis can allow for a broad view of the available research.

> **When the information from the studies was analyzed, the researchers found that children and adolescents younger than 20 years had 44% lower odds of infection after contact with an index patient compared with adults over 20 years of age.**

The lowest odds of infection were observed for those aged ten to 14 years. The comparisons between different aged children were more difficult to evaluate because different studies used different cutoffs in age for the participant groups. There were ten seroprevalence studies with children included that were also evaluated, but a formal analysis was not possible because of the large variations in the designs of the studies. The researchers identified that the results from the population seroprevalence studies support a lower number of infections compared to adults, but the statistical significance of the difference could not be determined.

> **The available data from the studies was not sufficient to determine if there is a difference in the transmission from children to others.**

A report published by the CDC observed that children 12 to 17 years of age had an incidence of COVID-19 (37.4%) that was 2-times that of children between the ages of five to 11 (19%) (Leeb et al., 2020). There was a rapid rise in the number of cases at the beginning of June, which coincided with the relaxation of community mitigation measures at the end of May. A peak in the number of infections for children under 18 over the summer occurred in the middle of July. There was a 3-fold increase in the number of confirmed COVID-19 cases during this time in people under the age of 19. The number of new cases plateaued during August and has slowly been decreasing through September. However, the number of cases has not yet returned to the levels observed in May.

Transmission within Households

The risk for younger individuals developing severe symptoms is smaller, but the increased number of contacts within a community by this age group may make them more likely to cause clusters of infection. These clusters then increase the risk for groups in that community who are more likely to have poorer outcomes.

A study from South Korea reported the results of contact tracing of 59,073 contacts of 5,706 individuals in South Korea who were the first person in their family to test positive for COVID-19. The researchers defined two types of contacts with the index patient, a **household contact** was a person who lived in the household of a COVID-19 patient and a **non-household contact** was a person who did not reside in the same household as the individual with COVID-19.

Of the 10,592 household contacts investigated, 11.8% tested positive for SARS-CoV-2, while only 1.9% of contacts outside a household were identified as having COVID-19. The index patients were then categorized by age to evaluate if there was a group most likely to infect their household (Table 3).

> **While those between the age of 20 and 19 had the highest number of household contacts, children between 10 and 19 had the highest rate of transmission of SARS-CoV-2 to their household.**

Table 3. Household contacts and rate of positive COVID-19 tests by index patient age.

Index Patient Age in Years	Proportion (and Number) of the Total Household Contacts	Rate of Household Contacts Positive for COVID-19	Rate of Non-Household Contacts Positive for COVID-19
0–9	0.5% (57)	5.3%	1.1%
10–19	2.1% (231)	**18.6%**	0.9%
20–29	**32.3% (3,417)**	7.0%	1.1%
30–39	11.6% (1,229)	11.6%	0.9%
40–49	16.5% (1,749)	11.8%	2.0%
50–59	19.3% (2,045)	14.7%	1.8%
60–69	9.8% (1,039)	17.0%	2.9%
70-79	4.5% (477)	**18.0%**	**4.8%**
Over 80	3.2% (348)	14.4%	**4.6%**

The study was completed while interventions were in place to limit interactions in the community, which suggests that the levels observed for all groups would most likely increase as more interactions in the community occurred, including the opening of schools.

A real-world example of household transmission from an adolescent was described in a published report from the CDC (Schwartz et al., 2020). The incident occurred during a three-week holiday gathering that included five households over the summer. The index patient, who was 13 years old, had been exposed while away from home in June. Upon return, she had a rapid antigen test four days after exposure. She had no symptoms at the time and the test was negative. Two days later she reported nasal congestion, and no other symptoms occurred. On the day of onset of the nasal congestion, the index patient and her immediate family, her parents and two brothers, traveled to a family gathering with 15 other relatives from five households in four states with an age range from 9 to 72 years. The members of the group stayed in a five-bedroom house for between eight and 25 days. Six other relatives visited on two days but did not stay in the same residence, and stayed physically distanced outdoors without masks during the visit. Twelve of the 14 people staying at the vacation house reported symptoms of COVID-19, with six confirmed with PCR-based testing, four were classified as probable based on antigen testing and clinical symptoms, and two had positive antibody tests, which included the index patient. One person with COVID-19 was hospitalized and another sought emergency department care for respiratory symptoms, and both recovered. None of the relatives who visited had symptoms, and four had negative PCR-based tests. It was proposed that the original negative antigen test received by the index patient occurred because it was administered before the onset of symptoms, and the Emergency Use Authorization stipulated use within the first five days after the onset of symptoms to ensure sufficient levels of antigens are present for detection.

> **The authors conclude that children and adolescents can serve as the source for COVID-19 outbreaks within families, even when their symptoms are mild, and adherence to physical distancing outdoors, as practiced by the visiting relatives, can reduce the risk of transmission.**

Another important factor is that people who have had a high-risk exposure to known cases of COVID-19 should quarantine themselves even after receiving a negative test result because of the possibility of false-negative results.

Transmission from Young People to Older People

There is growing evidence that younger adults likely contribute to community transmission of COVID-19 based on studies that have identified increases in transmission in the younger groups that precede increases for older groups.

In the first article from the CDC, it was reported that the highest incidence of COVID-19 between June and August was in people between the ages of 20 and 29, who made up 20% of the cases in the United States during that period (Boehmer et al., 2020). It was found that between May and July, there was a surge in the number of cases in the United States, and the number of people diagnosed increased for all age groups except those over the age of 80. The largest increase was observed in people less than 30 years of age. The shift was large enough to lower the median age of confirmed COVID-19 cases in the United Stated from 46 in May to 37 in July and 38 in August. The decrease in the age of new COVID-19 cases was observed in all regions of the country.

Assessment of regional outbreaks in the southern part of the United States indicated that increases in the percentage of positive SARS-CoV-2 test results among adults aged 20 to 39 years preceded increases among adults older than 60 years by an average of 8.7 days with a range between four and 15 days. This time period corresponds to approximately one to three incubation periods of SARS-CoV-2.

> **The authors state that this report provides preliminary evidence that younger adults contributed to community transmission of COVID-19 to older adults.**

Another study from the CDC on the transmission from the young to the old reported monitoring of COVID-19 hotspots by the CDC between June 1 and July 31 (Oster et al., 2020). The report states that increases in the percent positivity among individuals under 24 years were followed by several weeks of increasing percent positivity in individuals aged over 25 years. A hotspot was defined at an area with greater than 100 cases in the last seven days that is experiencing an increase in cases over the last three to ten days. There were 767 hotspot counties identified during this time period, which accounts for 24% of the counties in the United States.

Table 4. Changes in percent positivity in hotspot counties.

Age Group	Time between Increase in Positivity for Those Under 25 and Other Age Groups	Percent Positivity at Time of Hotspot Identification
0 to 17	Not Applicable	11%
18 to 24	Not Applicable	14%
25 to 44	28 days	10%
45 to 64	23 days	8%
65 and over	20 days	6%

The highest level of positivity was 15% for individuals 18 to 24 years of age, and the peak in positivity for those between 18 and 24 occurred shortly after an area was designated as a hotspot. In the other age groups, the number of people testing positive continued to increase for 21 to 33 days after the designation as a hotspot. The height of the peak was similar for all age groups, and ranged between 10% and 14%, but along with an initial delay, there was also a slower decline in the proportion of people testing positive in age groups other than 10 to 24 after the hotspot was identified.

When the data was evaluated by United States Census Regions of the country, differences were identified for different regions. In the South and West, the trends in the changes of the positivity rate followed the national trends with a peak in positivity in individuals under 25 followed by peaks in other age groups. In the Midwest, there was a peak in the positivity rate of those under 25 before the designation of the county as a hotspot with only a minimal increase in positivity in other age groups, and in the Northeast, there was a small increase in positivity of people under 25 followed by only a minimal or no increase for the other age groups.

The authors of the report conclude that there is evidence that young adults, and specifically those between 18 and 24, were recently the first group to show an increase in positivity in counties designated hotspots.

They also stress the importance of continuing to reduce the transmission from younger individuals to those groups with a higher risk of severe illness. This can be achieved by following the CDC recommendations even if you do not have a high risk of severe illness yourself.

Transmission in Schools and Care Facilities

There has been a heated debate recently about the return of children to school and daycare facilities. With the lower rates of transmission observed for young children, a return to education and care facilities seems like a reasonable goal.

However, the same dynamics of clustering and superspreading of SARS-CoV-2 occur in these facilities, and modifications are required to reduce the transmission.

There have been several examples of successful return to care facilities and schools, and several examples of unsuccessful return as well.

In the successful examples, cases of COVID-19 sporadically occur, but there are processes in place that prevent transmission within the school. For example, Rhode Island was able to reopen child care facilities at 74% of the normal capacity over the summer with only a few instances of transmission occurring within the facilities. There were 18,945 children being served in 666 programs, and cases were identified in only 29 programs, involving 101 individuals. Of the potential cases, 49% had symptoms but received negative tests, 33% had laboratory confirmed cases, and the remaining were not confirmed but were presumed positive based on exposure and/or symptoms.

Importantly, 69% of the programs with a confirmed case only had a single sick individual and there was no evidence of secondary transmission.

Secondary transmission was controlled through high levels of compliance with requirements assessed by unannounced inspections. Requirements included reduced enrollment with set groups (or cohorts) that remained in physically separated spaces, universal use of masks for adults, daily symptom screening of adults and children, and enhanced cleaning and disinfection according to CDC guidelines.

Programs that were found to have secondary spread of infections did not follow the requirements for establishing set groups that did not interact during the day.

While transmission within the childcare facility can be controlled with infection control measures, there are now documented cases where young children have transmitted SARS-CoV-2 that they caught at school to people in their households (Lopez et al., 2020). The CDC evaluated three outbreaks that occurred at childcare facilities in Utah between April and July, and it was found that in all three cases the index patient was an adult. Secondary transmission to children at the facility occurred, and the children in turn transmitted COVID-19 to both household and non-household contacts. There were 12 children, out of a total 83 between the three facilities, who caught COVID-19 at their facility. The children who became sick from direct exposure at the facility were either asymptomatic or had mild symptoms. In one case, a child who was 8 months old infected both her parents.

Table 5. Attack rates at the facilities and with all contacts

Facility	Attack Rate for People at the Facility	Overall Attack Rate Including Outside Contacts
A	17%	7%
B	100%	36%
C	18%	19%

The infected children spread the infection to 26% of their contacts outside of the facility, and one parent was hospitalized.

There have also been a number of school systems around the world that have been able to maintain a low level of secondary transmission. In Germany, assessments taken about a month after school was restarted showed that there were cases occurring that necessitated quarantines and some closures, but secondary transmission at school was rare, and schools were not found to be driving an increase in community transmission (Morris and Weber-Steinhaus, 2020). Officials mentioned that starting the process with a low level of community transmission was important. Due to staffing constraints, most schools are operating a normal capacity, but within the schools, groups are kept separate. Ventilation is increased by keeping windows open, and students have been warned that classrooms will be cold during winter. Masks are required in the halls, but not in classrooms. Teachers report that many use masks voluntarily.

A published assessment of the transmission of SARS-CoV-2 in individuals aged zero to 19 in school or childcare facilities in Baden-Württemberg, Germany also reported a lack of transmission in the schools (Ehrhardt et al., 2020). The facilities in the area were closed until June, except for parents who were employed in essential roles or could not do their jobs from home. The schools reopened in a stepwise manner in June with first the graduating classes of secondary schools returning, followed by the graduating classes of primary schools, and finally all remaining classes. The measures enacted in the different schools are listed in Table 6.

During the study period, 17.9% of the confirmed cases in Baden-Württemberg were people between the ages of zero and 19 years. The researchers found that 30% of the positive cases in this age range attended school or childcare settings for at least one day during the time that they were infectious while the remaining were at home during their entire infectious period. In the school setting, six of the 137 confirmed cases infected eleven other pupils, and no other secondary cases could be identified with thorough contact tracing. Two teachers were found to have infected four pupils. All the other cases were found to have been caused by contacts outside of the school.

Table 6. Measures enacted in the different types of schools in Baden-Württemberg.

Infection control measure	Childcare Facility	Primary School	Secondary School
Group sizes reduced by 50%	Yes	Yes	Yes
Cleaning of contact surfaces	Yes	Yes	Yes
Regular and interim ventilation of rooms	Yes	Yes	Yes
Exclusion of sick children	Yes	Yes	Yes
Individual hygiene (hand hygiene, cough etiquette)	Yes	Yes	Yes
Face mask in classroom	No	No	No
Face mask outside classroom	No	Some	Some
Physical distancing between children	No	No	Yes
Cancelling singing and use of wind instruments during music lesson	Some	Yes	Yes
Cancelling physical education	Not Applicable	Yes	Yes

Israel has had the opposite experience with a large increase in community spread that was linked to the reopening of schools in May (Stein-Zamir et al., 2020). The process of reopening began on May 3 with small groups of children in kindergarten, grades 1 to 3 and 11 to 12. All classes opened on May 17, and reopening included requirements for daily health reports, hygiene, facemasks, social distancing, and minimal interaction between classes. After opening, an outbreak began on May 26 when the first person at a school with grades seven to twelve tested positive for COVID-19. A second case was identified the next day. Eventual testing of the entire school revealed 153 students and 25 staff members were infected. This corresponds to an attack rate of 16.6% for students and 13.2% for staff. With contact tracing, it was found that there were a total of 260 people associated with the cluster.

Characteristics of the outbreak in Israel

- The proportion of positive cases with symptoms was 43%
- The school had crowded conditions where distancing between students and teachers was not possible
- Air conditioning units were run continuously due to a heat wave, and units were separate for each class
- Masks were not required due to the extreme heat

The conditions that occurred in the school are those that have been identified in studies discussed above that are more likely to lead to a cluster of infections, mainly a large number of asymptomatic individuals who may unknowingly spread the infection, crowded conditions, a lack of ventilation with fresh air, and reduced used of masks.

The authors also investigated whether there was a change in the age distribution in the area a week after the reopening of all schools, on May 24. Before May 24, the proportion of 10 to 19 year-olds with confirmed COVID-19 was 19.8%, which increased to 40.9% in the three weeks after May 24.

Virus Transmission at Colleges

Researchers from the CDC have reported that there has been an increase in the number of people between the ages of 18 and 22 years infected with SARS-CoV-2 between August 2 and September 5 (Salvatore et al., 2020). On a national level, the number of cases in this age group increased by 55%. By region, the increase was the largest in the Northeast (144%) and the Midwest (123%). The weekly incidence in the Northeast increased from 53 per 100,000 to 130 per 100,000 for persons aged 18 to 22 years during August to September while the weekly incidence in all other age groups in the region has remained steady at 53 per 100,000 since July 4. As might be expected from the age range, the reopening of universities and colleges are attributed to the increase in infection. It was estimated that 45% of the adults aged 18 to 22 years are enrolled in college or university in 2019.

In a departure from previous time periods, the period from August to September included an increase in the proportion of white individuals (designated as non-Hispanic white) in this age group infected from 33.8% to 77.3%. This correlates to an increase of 149.7% in the weekly incidence among white persons aged 18 to 22 years during the time period, while incidence among persons of other racial and ethnic minority groups remained stable or declined.

Number of At-Risk Adults who are Exposed to Children at Home or Work

A transmission cluster within a school would most likely not lead to a large number of severe illness within the children, but as mentioned above, the rate of transmission within a household setting is very high with attack rates ranging from around 70% to 80%.

To estimate the number of people at high risk who might be exposed from transmission of COVID-19 in school settings, researchers accessed the data from the 2018 National Health Interview Survey that is conducted by the CDC (Gaffney et al., 2020). They evaluated the prevalence of conditions that are considered either “a definite or possible risk factor for severe COVID-19 in adults who are employed in a profession other than teacher, adults employed as teachers, and adults living with school-aged children (those aged 5 to 17 years)”. Based on the assessment, 39.8% of teachers had definite risk factors and 50% had either definite or possible risk factors. There were a similar proportion of adults who live with school aged children with a definite risk (41%) and a definite or possible risk (54%). There was not a difference in the proportions of adults at risk for severe COVID-19 based on the age of the children in the household. There was a higher prevalence of people with high risk for COVID-19 in low-income households and in households with children of African descent.

Interventions to Reduce Transmission

As with the discussions of transmission above, there are interventions that apply to both personal and population-based levels of transmission. For example, it is possible to reduce the transmission of a virus in a population through frequent testing and isolation of sick individuals. This was observed in the study mentioned above involving an outbreak in a prison facility in

Louisiana (Njuguna et al., 2020). The attack rate between the dormitories differed (ranging from 57% to 82%), and the dormitory with the lowest attack rate had their first case after the new testing regimen was already in place. By performing multiple tests and separating those who were sick from those who were susceptible, each sick individual infected fewer other people, reducing the attack rate.

However, on a personal level, testing will not reduce the risk of infection. Testing only informs you after the event. In one analogy, it would be like trying to prevent a pregnancy by taking a pregnancy test. Instead, changes to personal behaviors are required to prevent COVID-19 on an individual level.

> **There is an increasing amount of evidence that most individuals with COVID-19 do not contribute to the expansion of the epidemic, which means that containment efforts that can prevent superspreading events have a disproportionately large effect on the reduction of transmission.**

CDC Recommendation for Reducing the Risk of Transmission

The measures being recommended have changed somewhat over the course of the pandemic, but as of October 22, the CDC recommends the following measures.

Recommendation from the CDC to protect yourself and others from COVID-19

- Wash your hands often with soap and water for at least 20 seconds, or use a hand sanitizer that contains at least 60% alcohol, especially after you have been in a public place, or after blowing your nose, coughing, or sneezing.
- Avoid touching your eyes, nose, and mouth with unwashed hands.
- Put 6 feet of distance between yourself and people who don't live in your household.
- Everyone (except for the individuals listed below) should wear a mask in public settings and when around people who don't live in your household, especially when other social distancing measures are difficult to maintain. Masks should not be placed on young children under age 2, anyone who has trouble breathing, or is unconscious, incapacitated, or otherwise unable to remove the mask without assistance.
- Keep about 6 feet between yourself and people not in your household even when wearing a mask as a mask is not a substitute for social distancing.
- Always cover your mouth and nose with a tissue when you cough or sneeze or use the inside of your elbow and do not spit.
- Throw used tissues in the trash then immediately wash your hands with soap and water for at least 20 seconds. If soap and water are not readily available, clean your hands with a hand sanitizer that contains at least 60% alcohol.
- Clean and disinfect frequently touched surfaces daily.
- Monitor your health daily, and be alert for potential symptoms, such as fever, cough, shortness of breath, or other symptoms of COVID-19.

How can reverse contact tracing help reduce transmission?

The traditional method of contact tracing is to identify infected individuals and the people they have come into close contact with. However, when a virus spreads through clustering and superspreading events as with SARS-CoV-2, reverse, or backwards, contact tracing may be more effective at curtailing the size of clusters (Tufekci, 2020). Due to the fact that 80% of transmission is from 10% to 20% of cases of COVID-19, most people will have been infected by someone who also infected other people. Finding the index patient of a cluster and then tracing their contacts will identify more people with COVID-19 than tracing all the people with a positive diagnosis because most of the people with a positive test will not infect more than one other person.

Put another way, it is more effective to backtrack to the superspreading event, and then track and trace based on an individual's presence at the venue rather than forward tracing from positive cases, which identifies potential exposures that are less likely to lead to additional infections.

The use of reverse contact tracing allows for a more efficient use of resources when resources are scarce, but both forms of tracing help to reduce transmission by identifying infections and potential infections for isolation and quarantine if there are adequate resources to perform both.

What is the evidence that masks reduce the risk of transmission?

While the consensus on mask use has changed over the course of the pandemic, it has now been well established that use of a mask both protects the wearer from infectious particles in the environment as well as prevents the individual wearing the mask from producing particulates that can contain infectious particles. Medical grade masks, such as N95 and surgical masks, are very effective at both stopping the emission of particles and preventing particles in the air from coming into contact with the nose and mouth. However, people who do not have close contact with people with a known diagnosis of COVID-19 every day do not require medical grade masks. Reusable cloth masks of varying design are sufficient for the general public, and have been found to filter between 70% and 90% of air particles, and while they do not effectively filter out small, aerosol-sized particles, they can reduce the risk of transmission (Salter, 2020). There have been both real-world reports of mask efficacy and laboratory experiments that are available.

An analysis of one real-world event, researchers from the CDC show that use of face masks was able to prevent transmission of SARS-CoV-2 from two stylists who were experiencing symptoms at a hair salon in Missouri (Hendrix et al., 2020). The incident occurred in May at a hair salon where two of the stylists tested positive for COVID-19 after having served 139 customers over the course of eight days.

In accordance with local recommendations, both the stylists and their clients wore masks, and based on testing and symptom tracking, none of the exposed customers were infected.

Additionally, none of the other stylists at the salon became ill. Based on the timing of the symptoms of the two infected stylists, it was determined that one most likely infected the other as they had several encounters when they had removed their masks to talk. The first stylist had attributed her symptoms to allergies that she normally experienced at that time of year (Wu, 2020). Close contacts to the stylists from outside of the salon were also followed for contact tracing, and all of the people who were in contact with the first stylist outside of the salon developed symptoms and tested positive for COVID-19, and none of those in contact with the other stylist showed symptoms.

The customers ranged in age from 21 to 93 years, and the length of appointments ranged from 15 minutes to 45 minutes. When clients were asked what type of mask they wore, it was determined that 47.1% wore cloth face coverings, 46.1% wore surgical masks, 4.8% wore N95 respirators, and 1.9% did not know what kind of face covering they wore. One of the infected stylists wore a double-layered cotton face covering, and the other wore either a double-layered cotton face covering or a surgical mask.

> **Based on the outcome of the situation, the authors from the CDC concluded that adherence to the community's and company's face-covering policy mitigated spread of SARS-CoV-2 and broader implementation of face covering policies could mitigate the spread of infection in the general population.**

In a small study that approximated real-world circumstances, researchers investigated the amount of virus spread that occurred from two patients with COVID-19 in a hospital room with and without masks (Landi et al., 2020). There were four total participants who had a confirmed COVID-19 diagnosis and were hospitalized within a week of the onset of symptoms. All four participants were experiencing fever and cough at the time of the study and had evidence of pneumonia based on CT scans. While the participants were hospitalized, they did not require supplemental oxygen and were able to take care of their own hygiene needs.

The participants were staying two to a room, and on the third day after admission, the two rooms were sanitized after the noon meal. After the rooms were sanitized, one of the pair of participants wore masks for the rest of the day (five hours), and the two participants in the other room did not. At the time, the participants were not informed that the mask use was part of a study. The surfaces in the room were swabbed before and after the five hour study period to determine the extent virus spread. During the day, the participants reported spending the majority of their time in the bed except for trips to the restroom. The presence of virus was detected using PCR-based testing. In the room where the participants did not wear masks, virus was found on the headboard and sides of the bed, but not in other parts of the room, including the bedside table, dining table, and bathroom handles. In the room where the participants wore masks, none of the swabs of the same surfaces were positive for SARS-CoV-2.

A new report in the CDC publication, *Emerging Infectious Diseases*, presents evidence that use of a mask also protects wearers from infection through close contact with individuals who are infected with COVID-19. The study was performed in Thailand, and involved contact tracing of 1049 people who had a known exposure to someone with COVID-19 (Doung-ngern et al., 2020). The exposures occurred within three clusters, a group of nightclubs, boxing stadiums, and a state office building. The participants in the study were asymptomatic when tested, but

84% of the people involved were considered to have had a high-risk exposure to COVID-19. Subsequent testing revealed that 211 had COVID-19, and 839 never tested positive.

The attack rate for each scenario was

- 86% at the boxing stadiums
- 18.2% at the nightclubs
- 16.5% within households
- 4.9% within workplaces
- 1.4% at other places

The characteristics of the participants during exposure were evaluated by phone interviews that included questions about whether participants wore a mask during the contact with the infected individual, the type of mask worn, and the frequency of wearing a mask during the contact. Other questions included the frequency of handwashing while with the infected individual, if they practiced social distancing, or if they had physical contact with the infected person.

Wearing a mask at all times during contact with an infected individual was found to be associated with a lower risk for infection with SARS-CoV-2.

Wearing a mask sometimes during contact with an infected person did not lower the infection risk. The type of mask worn was not associated with the risk of infection, and both medical grade masks and cloth masks were found to reduce the risk. The authors also reported that handwashing and social distancing were associated with a lower risk of infection in the settings investigated in the study.

The researchers conclude that the evidence from the study supports recommendations to wear a mask correctly and at all times while in public in order to reduce the risk of infection with SARS-CoV-2 after contact with an infected person.

One important component of wearing a mask is protecting all points of potential infection. Researchers have found that there is a large number of the ACE-2 receptors that the virus uses to gain entry to infect a cell located in the upper respiratory tract (Chen et al., 2020). Access to the upper respiratory tract occurs through the mouth and nose, and as might be expected, inhalation of infected particles leads to exposure that can result in infection. Conversely, exhalation releases infectious particles from the nose and mouth from people who are ill. The cardinal symptom of loss of smell associated with COVID-19 indicates that cells in the nasal passages may be directly targeted by the virus. Measurement of the density of ACE-2 receptors in the nasal passages and trachea show that there is a much higher amount of ACE-2 in the tissues of the nose.

In fact, the increased ACE-2 expression in olfactory (nasal) versus respiratory (trachea) tissue was found to be similar across all individuals tested, which indicates that this characteristic does not vary considerably between different people and would apply to the infectivity of everyone.

The potential of the nasal cavity as the main site of infectivity and production of virus indicates that covering the nose with a mask is as important, if not more, as having adequate covering of the mouth.

Can targeting shelter-in-place recommendations to specific groups reduce transmission?

Until there is a highly effective treatment or vaccine, the transmission of COVID-19 can only be controlled through non-pharmacological methods. However, while the use of broad, community wide lockdowns are extremely effective at slowing the spread of COVID-19, they also have a negative effect, and public health officials have been watching for evidence of smaller forms of physical distancing that can still have a large effect on the transmission of the virus without large disruptions in the community.

In one study, researchers modeled whether sheltering of different age groups during another wave of infection would have an effect on transmission (Wilder et al., 2020). There were two extremes of a second wave that were calculated based on the level of physical distancing by the population as a whole. The authors define **physical distancing** as reducing the amount of contacts through staggered work schedules, increasing spacing in restaurants, and prescribing times to use the gym or grocery store.

If the physical distancing is high, at 25% of the original level of contacts within a community, a second wave is not experienced. If the amount of physical distancing is low, at 75% of the original level of contact, then the second wave of the outbreak would infect a large fraction of the population (30% or more) and overwhelm local healthcare facilities regardless of whether any particular group engages in sheltering.

If it is possible to limit physical contact to 50% of the original levels, a middle ground, sheltering of one particular group can have an effect on the total number of infections. There are two patterns of sheltering that have been shown to have an effect, sheltering of those who have the most daily contacts within a community or sheltering of those who are most vulnerable. The two age groups that have the largest number of daily contacts are those between the ages of 20 to 40 and 40 to 60. If both these groups were to shelter-in-place, there would be a sharp reduction in the fraction of the population infected in a second wave.

> **Based on the calculations, the authors found that sheltering people in the age groups from 20 to 60 helps shield older groups from infection more effectively than if an equivalent fraction of the older group engaged in sheltering themselves.**

There are also local differences in populations that can affect the outcome observed from sheltering of certain groups. For example, because the average age of residents in the Lombardy region of Italy is higher than New York or Hubei, sheltering by those over the age of 60 reduces deaths much more substantially in Lombardy than in the other two regions. The increased benefit due to the age of the population actually makes sheltering those over the age of 60 more effective in Lombardy than sheltering of the middle-aged groups (from age 20 to 60).

The outcomes of the calculations suggest that a population-wide sheltering in place can be avoided during a possible second wave of infection while still achieving a substantial reduction in the transmission of SARS-CoV-2 by sheltering of specific age groups combined with adherence to physical distancing by the rest of the population.

Can interventions less stringent than a full lockdown reduce transmission?

Researchers are able to use computer models that are based on variables that have been measured during the first months of the pandemic. They can then alter the variables in the model to simulate how changes in behavior will affect the transmission and use rate of health care resources. In one modeling study, the researcher used data from Kings County, Washington, which is the area that includes Seattle (Jackson et al., 2020).

The interventions assessed in the simulations were

- **Voluntary work-from-home**: employers are encouraged to use telecommuting or other remote work for as many employees as possible. In this model, 33% of workers were assigned to telecommuting when the practice was voluntary
- **Cocoon seniors**: nursing homes are closed to persons with COVID-19 symptoms (including both visitors and staff), and that seniors in the community reduce their community contacts by 90%.
- **Community social distancing**: the general public is encouraged to reduce voluntary contacts outside of the home (not counting workplaces), and a 25% reduction in community contacts is used in the model.
- **Self-isolation for symptoms**: members of the general public are encouraged to stay home if they are experiencing symptoms of COVID-19, and the model assumes that symptomatic people self-isolate 33% of the time, or an average of 2.3 days per individual.
- **Test-and-quarantine**: identify persons with SARS-CoV-2 infection, isolate the cases, and quarantine their household contacts. Cases are isolated until the end of symptoms, and household contacts are quarantined for 14 days, and a 20% rate of detection of new cases was used for the model with 33% of the households complying with quarantine.

Use of facemasks was not used in this model because there were not specific values available at the time of the study that could be input into a model to simulate their use. Testing of the model showed that is was able to accurately reproduce conditions where the outcomes were already known, e.g. March and early April.

Removing all interventions within the model for the King County region led to 42,000 COVID-19 hospitalizations between June 2020 and January 2021, and the expected hospital occupancy was 6-times the available beds at the peak of the outbreak. When the above interventions were used individually, they only had modest impacts on the simulated course of an outbreak. The most effective strategy when used alone was testing and quarantining individuals, and implementation of this strategy led to a 12.7% reduction in hospitalizations. Having seniors shelter in place was the least effective stand-alone intervention, which resulted in only a 1.5% reduction in hospitalizations.

The effect of voluntary work from home with the sequential addition of the other measures is shown in Figure 1. The target for occupancy of hospital beds by people with COVID-19 is 35% in this study, and even with all of the measures in place, this target is not reached during the majority of the time period in the simulation. There would be a 48% reduction in the total number of people hospitalized when compared to not implementing any of the strategies. At the peak of the outbreak, the simulation suggests that 70% of the available beds in King County would be in use by people with COVID-19 even with use of all of the strategies.

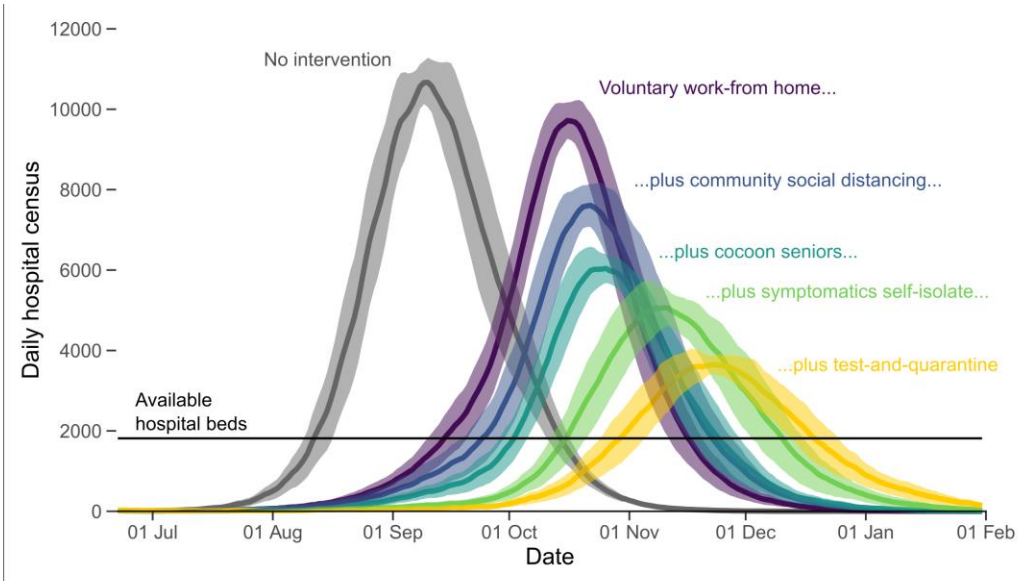

Figure 1. Graph of the expected number of hospital beds occupied by COVID-19 patients under with a cumulative use of intervention scenarios in King County between June 2020 and January 2021. (From Jackson, 2020)

The researchers had not initially included school closure as an intervention because it is highly disruptive for both children and parents when schools are closed. A separate simulation was performed to determine the impact on hospital occupancy if schools were closed on top of the other strategies. If school were closed the first week of October through December, there is a reduction in the number of people hospitalized, and the number of beds occupied remains at below 35% for most of the outbreak because there is a slower increase in the number people hospitalized compared to not closing schools, but at the peak the hospital occupancy increases to 58%.

Summary

- The infection fatality rate of SARS-CoV-2 has not changed since the start of the pandemic, making it necessary to continue to reduce transmission of the virus to prevent large numbers of deaths and long-term complications.
- SARS-CoV-2 spreads mainly through clustering and superspreading events.
- Under certain circumstances SARS-CoV-2 can spread in an airborne-like manner, but outside of these circumstances, the virus is transmitted via droplets during close contact with an infected individual.
- The circumstances where airborne-like transmission is more likely are indoor spaces with little ventilation where large numbers of people are in close contact.
- All people with COVID-19 are infectious before the onset of symptoms, and some individuals never develop symptoms.
- The combination of an infectious period before symptoms are apparent and airborne-like transmission during indoor events leads to superspreading events, where a single person can infect 80% of those in attendance.
- Children and young adults can spread SARS-CoV-2 to adults even though they themselves are at low risk for severe symptoms.
- The large amount of transmission that occurs from superspreading events suggests that preventing events with these conditions can reduce transmission in the community.
- Increasing ventilation may allow for removal of infectious particles in the air if systems use high air-exchange rates with a fresh air source and have more than one ventilation site.
- There is conclusive evidence that masks reduce the amount of particles emitted into the air and prevent inhalation of particles already in the environment, which reduces the risk of transmission.
- Targeting shelter-in-place orders for age groups who have the most contacts rather than those with the highest risk of severe symptoms may be more effective for reducing transmission in most communities.

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