L2B (WP2) - TAU

Transmission of SARS-CoV-2 in Indoor Settings - Rapid Narrative Review

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1. Introduction

In December 2019, a previously unknown virus was isolated from a cluster of patients presenting with pneumonia with epidemiological link to a seafood and wet animal market in Wuhan, Hubei Province, China (1). Phylogenic analysis showed that the novel virus, named SARS-CoV-2, falls into the beta-CoV genus which includes SARS-CoV, bat-SARS-like CoV, and others. The WHO announced on 11 February 2020 that the disease caused by SARS-CoV-2 would be designated as COVID-19. On 30 January 2020, the outbreak was declared by the Director General of the World Health Organization (WHO) a Public Health Emergency of International Concern (PHEIC) – the sixth declaration since the 2009 Influenza A (H1N1) pandemic. On 12 March 2020, the WHO declared the outbreak a pandemic. As of February 2021, >102 million people were infected with SARS-CoV-2 and 2,200,000 died of COVID-19 (2). A marked variability has been also observed within regions, with fewer countries contributing to the largest observed burden of the outbreak per region. These differences can be explained by variability in case detection/definitions, testing strategies, and reporting practices – including the recognized lag times between case detection and reporting.

Respiratory viruses spread via three main modes of transmission: contact, droplet, and airborne transmission. In contact transmission, infection spreads through direct contact with an infectious person or an article/surface that has become contaminated; the latter is referred to fomite transmission. Second, droplet transmission refers to infection spreading through exposure to virus containing respiratory droplets larger than 100 μm which are exhaled by an infectious person. Transmission via large droplets is likely to occur when someone is within 2-meter distance from the source. The term “close contact” refers to contact or droplet transmission occurring within <2 meters from the source. Evidence suggests the SARS-CoV-2 main mode of transmission is via close contact. SARS-CoV-2 virus can remain infective on surfaces for several days depending on the surface material. In a recently published study, the infective virus was found after 72 h on plastic surfaces and after 48 h on steel surfaces. No infective virus was found on the copper surface after 4 hours (3). For these reasons, surfaces should be disinfected repeatedly; however, this is problematic as most surfaces are not designed to withstand repeated high chemical exposure.

Third, airborne transmission refers to spread though respiratory droplets smaller than 100 μm which can remain suspended in the air over longer distances (>2 meters) and time (typically hours) (4). The term “aerosol” is used to define the size of respiratory droplets (small size and particles) and the cloud of these droplets in the air. Although less likely, airborne transmission of SARS-CoV-2 may occur under special circumstances, including exposure to source in enclosed and/or inadequately ventilated spaces (5). Studies of airborne transmission of SARS-CoV-2 were largely based on experimental or simulation designs (6). Experimental evidence suggested certain activities such as speaking and coughing were more likely to result in aerosols compared to droplets (ratio 100:1, respectively), with infectious, viable SARS-CoV-2 viral particles remaining in aerosols for up to 16 hours (4).

The License to Breath (L2B) project aims to accelerate the utilization of knowledge and experience in corporate business both to contain a pandemic and to anticipate potential new pandemic risks. The L2B project examines coronavirus research and technological development as a whole in producing and ensuring a healthy and safe indoor environment. Ensuring indoor air conditions and human health and safety in different operating environments is important to prevent the spread of SARS-CoV-2. Relatively little is known about the behavior and spread of the virus in indoor environments particularly care-homes, workplaces, and schools, as most of the existing data are related to household and healthcare settings (7). Research data on both the behavior of the virus in indoor conditions and technological solutions in this regard are generated at a rapid pace, but the scientific basis of research results may be partially weak and the results not directly applicable to technology companies. This rapid review was part of Work Package 2 (WP2) of the License to Breath (L2B) project, which aimed to assess the spread of the SARS-CoV-2 virus in indoor environments.

2. Methods

Studies focusing on the spread of the SARS-CoV-2 virus in indoor environments were included, including workplace buildings, long-term care facilities, schools, daycare centers, businesses, etc., Observational epidemiological studies, clinical studies, and transmission studies were included, with no restriction as to geographical location or the type of publication. Studies published in languages others than English were excluded, as well as studies on aerosol physics or those on indoor transmission of SARS-CoV-2 in healthcare or residential settings. The search string (annex 1) yielded 2823 results in PubMed. In total, data from 40 articles were extracted, including three studies identified via hand searching (annex 2 - PRISMA flowchart). All records were imported into EndNote for de-duplication. One reviewer (OO) independently reviewed the list of references obtained. Bibliographies of selected papers were also reviewed (hand-searching) to identify additional potential studies of interest. Data extraction from selected references was performed by a single reviewer (OO).

3. Results and discussion

3.1. Long Term Care Facilities (LTCFs)

Broadly, LTCFs comprise assisted living facilities (ALFs) and similar residential care facilities, skilled nursing facilities (SNFs) and other nursing homes, and residential facilities for persons with intellectual and developmental disabilities. The rates of COVID-19 in residents of >15,000 nursing homes in the US increased from 11.5 cases per 1000 resident-weeks in June 2020 to 23.2 cases per 1000 resident-weeks in November 2020. The total number of reported cases exceeded 500,000 by the end of November 2020, of which 48% were among staff members (8). These rates may vary across settings given the differences in predisposing risk factors, including underlying medical conditions and socioeconomic factors (9). The trends observed in nursing homes followed the observed trends in surrounding communities, which highlighted the need to monitor local transmission in mitigation strategies. The overall case fatality was estimated to be >20% among residents - >8 times higher than the general population (10); the case fatality in staff members, however, was significantly lower (0.6%). Higher case fatality rates were observed in SNFs, with one case investigation in Washington reported >33% case fatality among residents (11). Data from a national survey of nursing homes in Ireland indicated the prevalence and case fatality among resident were 44% and 28%, respectively (12). In Brazil, the prevalence in two LTCFs affected by outbreaks ranged from 76%-100%, and the case fatality ranged from 17%-33% (13).

In Canada, a population-based study in Greater Toronto Area estimated the diagnosed cases per capita in LTCFs as 64-fold higher than the general population (14). Consistent with the data from the US, a disproportionate share of deaths in LTCFs was observed by May 2020, with the COVID-19 case fatality among residents in LTCFs estimated at ~27% vs. 4,0% in the general population. The test positivity proportion - a measure of adequacy of testing - in LTCFs resident was 2.4-fold higher than the general population. This is despite a much wider scope of testing in LTCFs, which suggests higher risk of transmission therein.

Similar to most settings, one of the key challenges facing mitigation in LTCFs asymptomatic/presymptomatic transmission. Cross-sectional surveys demonstrated significant number of residents in LTCFs who tested positive for SARS-CoV-2 were asymptomatic at the time of testing, suggesting that a symptom-based screening of residents in LTCFs may not identify infections (15) (16). In another study from Seattle, nearly 70% of staff members in a SNF who tested positive for SARS-CoV-2 were asymptomatic at the time of screening (17). In the UK, 26% and 23% of residents and staff in six care homes across London were symptomatic at the time of screening, respectively, and round half remained asymptomatic throughout the duration of surveillance (18) (19).

A nursing home outbreak in the Netherlands pointed the potential role of aerosol transmission of SARS-CoV-2, with an attack rate of >80% among residents and 50% among staff in a single affected ward out of 7 wards in the facility (20). In this outbreak, the affected ward had a particular ventilation system which recirculating indoor air without filtration, whereas unaffected wards were ventilated with outside air.

3.2. Workplaces

The true magnitude of SARS-CoV-2 transmission in workplaces is likely underestimated. A nationwide study from Singapore applied Bayesian modelling to adjust for differential testing rates and the sensitivity of tests and estimated that symptom-based testing strategy missed more than two thirds of infections in work contacts of COVID-19 cases (21). In the UK, nearly 80% of notified COVID-19 cases in workplaces were in healthcare settings and LTCFs. However, mortality statistics indicated that certain occupational groups such as taxi drivers security guards were disproportionately affected, with 2- and 4-fold increased risk of death, respectively (22).

A study from the US showed construction workers had nearly 5-fold higher risk of COVID-19 hospitalization compared with other occupational groups of the same age, which could be amplified by socioeconomic and health disparities (23). Data from 36 states in the US showed the burden of COVID-19 in workers in food processing, food manufacturing, or agriculture disproportionally affected certain ethnic minorities (24).

Investigations of transmission in workplaces demonstrated the potential role of aerosols, particularly super spreading events where a large number of cases were epidemiologically linked to a single source. A large outbreak among workers in a meat processing plant in Germany indicated that transmission from the index case occurred within a 8-meter area under of conditions of low air exchange rate and constant recirculation of unfiltered air (25). Aerosol transmission was suggested as potential route of transmission in an outbreak among meeting attendees in Germany, where none of them wore face masks throughout the meeting (26).

3.3. Schools

Most countries mandated varying degrees of school closure during the course of pandemic, which affected more than 200 million children globally (27). However, the question remains as to whether school closure or reopening had contributed to the control or resurgence of the epidemic, respectively (28) (29). A living systematic review of showed the risk of transmission among school children was generally low, based on data from both longitudinal and cross-sectional studies (30). In Sweden where upper secondary schools were closed whereas lower secondary schools remained open, parents of children in the latter settings had a slightly increased risk of infection (31); teachers in open schools had relatively higher risk of infection, which spilled over to their partners. A population-level study in New South Wales, Australia, reported that opening of schools during first epidemic did not contribute significantly to SARS-CoV-2 transmission (32).

Following school reopening in England, the majority (64%) of 177 confirmed COVID-19 events which were reported by educational settings were single cases, and >50% of the confirmed 55 outbreaks involved a single secondary case (33). In reopened educational settings, the outbreaks affected only 0.04% of kindergartens and 0.17% each of primary and secondary schools. Of note, the risk of outbreaks appeared to be strongly associated with increase in community transmission, which highlights the importance of control measures at the population-level.

National data from South Korea showed school reopening did not result in an increase in the number of pediatric case or school outbreaks, and the most common infection source was believed to be family members (34). In a study from Singapore, the was no evidence of infection in children attending pre-school and secondary schools who had been exposed to confirmed cases – the majority of whom were school staff, which suggested lower susceptibility and/or infectiousness (35). Consistent findings were reported in a study of two school complexes in Rome with a prevalence of SARS-CoV-2 of 1.3%, which was lower than the observed prevalence in the general population during the same 3-month period (late September to early December 2020) (36).

3.4. Restaurants and bars

Based on our search, few studies assessed the transmission of SARS-CoV-2 in restaurants and bars. An analysis of COVID-19 superspreading events in Hong Kong identified a large cluster,

which comprised 106 cases, was linked to a collection of four bars with the likely source being musicians who performed therein (37). Another outbreak investigation involving a restaurant in Jeonju, South Korea, provided important insights onto the potential role of airborne transmission (38). The Korean Disease Control and Prevention Agency (KDCA) conducted a thorough investigation which included analysis of data from multiple sources, including CCTV images, and a live simulation under similar climatic conditions in the same restaurant. An index case is believed to had infected two out of 13 close contacts who were dining/working in the restaurant around the same time (attack rate of 15.4%). The restaurant had no windows or a ventilation system with two ceiling-type air conditioners. The distance between the infector case and one of the infectees was 6.5 m, who left the restaurant after shortly after (exposure time of 5 minutes). Measuring the air velocity indicated that droplets transmission could occur within relatively short exposure time and over distances greater than the widely used cutoff of 2 meters. Similarly, an outbreak investigation in a restaurant in Guangzhou, China, showed that poor ventilation and air flow from air-conditioning were key in facilitating transmission of droplets, potentially aerosols, from infector to infectees (39).
A study from Japan which compared persons who worked at or visited nightlife business (i.e., bars, nightclubs, live music clubs, etc.) to those who did not showed the proportion of SARS-CoV-2-positive tests was 3-fold higher in the former group (40).

3.5. Other public places

Public Transport

Analysis of data during the early phase of the epidemic in Wuhan, China, showed significant association between the frequency of flights, trains, and buses from Wuhan and the rates of COVID-19 cases in other cities (41). This highlighted the role of inter-regional public transport in the spread of the SARS-CoV-2, particularly between epicenters and nearby cities/regions. A notable outbreak investigation in Zhejiang province, China, highlighted the potential role of airborne transmission of SARS-CoV-2 in public transport (42). In late January 2020, 128 persons traveled in 2 buses on a 100-minute round trip to attend 150-minute outdoor worship event in a Buddhist temple. The attack rate among the 67 passengers who rode with the source patient was ~35%, whereas none of the passengers in the other bus were infected. None of the passengers wore masks at the time. Sharing the bus with the index case was implicated in transmission given the relatively low attack rate among those who attended the event but traveled via different means (7/172 persons = 4.1%). Hence, passengers in the implicated bus were nearly 12-times more likely to be infected with SARS-CoV-2 as compared to all others. The likelihood of airborne transmission in the affected bus, where air conditioner was in indoor recirculation mode, was corroborated by the similarity in infection risk in those who sat closer to the index case compared to those who sat farther away. In another study from China, long exposure time on trains was associated with infection risk and came second to transmission in residential buildings (43).

With many countries imposing strict travel restrictions, data on transmission of SARS-CoV-2 on aircrafts are scarce. An outbreak during early phase of the epidemic was linked to a flight carrying 325 passengers and crew members from Singapore to Zhejiang in late January 2020 (44). None of the passengers were symptomatic upon boarding the plane, and only crew members reportedly wore masks. Upon arrival, one passenger was found to have fever and later tested positive for

SARS-CoV-2 – which led to isolation of all passengers and crew members for 14 days. A total of 12 cases were confirmed eventually, none of whom were crew members. Although an aircraft-associated infection rate of 3.7% may seem small, the actual rate could be higher as only symptomatic passengers and crew members were tested.

Places of Worship

In April 2020, two out of three clusters in Singapore occurred in Churches, both were linked to a single case who travelled from Wuhan, China, at the time (45). Transmission in places of worship is likely given close contact over prolonged repeated activities, including droplet-generating singing which is a common practice in Churches. A cluster of 52 COVID-19 cases with an attack rate of 53.3% among choir members in Washington indicated the potential role of aerosols in transmission of SARS-CoV-2 via singing (46). An outbreak in a LTCF located in the southwest of the Netherlands was traced back to 39 residents who attended a 50-minute church service which included singing and sharing supper by passing a serving bowl with bread (47). The attacks rate was significantly higher (85%) for residents who attended the service vs. those who did not (18%). Although this suggested a strong link to the service, genomic analyses indicated at least 17 separate introductions, some of which preceded the church service and coincided with community transmission, which ruled out the service as a single superspreading event.

Ships

A notable example of SARS-CoV-2 transmission aboard cruise ships was the Diamond Princess, where an outbreak resulted in 712 COVID-19 cases out of 3713 passengers (19%). The attack rates in passengers who shared cabins with symptomatic or asymptomatic COID-19 cases were 3-4 times higher than those who were in single cabins or shared cabins with uninfected passengers (48). Environmental samples showed SARS-CoV-2 RNA was detectable from cabins of COVID-19 cases, and the detection proportion was similar in symptomatic compared to asymptomatic cases (49). The viral RNA was most detected on the floor around the toilet in bathrooms and bed pillows, however, no viable viruses were isolated from any of the samples.

In another outbreak which involved 1271/4779 (~27%) of crew members on the U.S.S. Theodore Roosevelt aircraft carrier, 43% of SARS-CoV-2 infections remained asymptomatic throughout the outbreak (50). An association between infection positivity and working in confined places was observed compared to those who worked in a combination of open-air and confined places, suggesting potential role of aerosol transmission. Some of the potential risk factors suggested by the investigators include sleeping in bays packed with adjacent bunks, working in densely populated areas, and dense gatherings at gyms and galleys.

4. Conclusions and policy implications

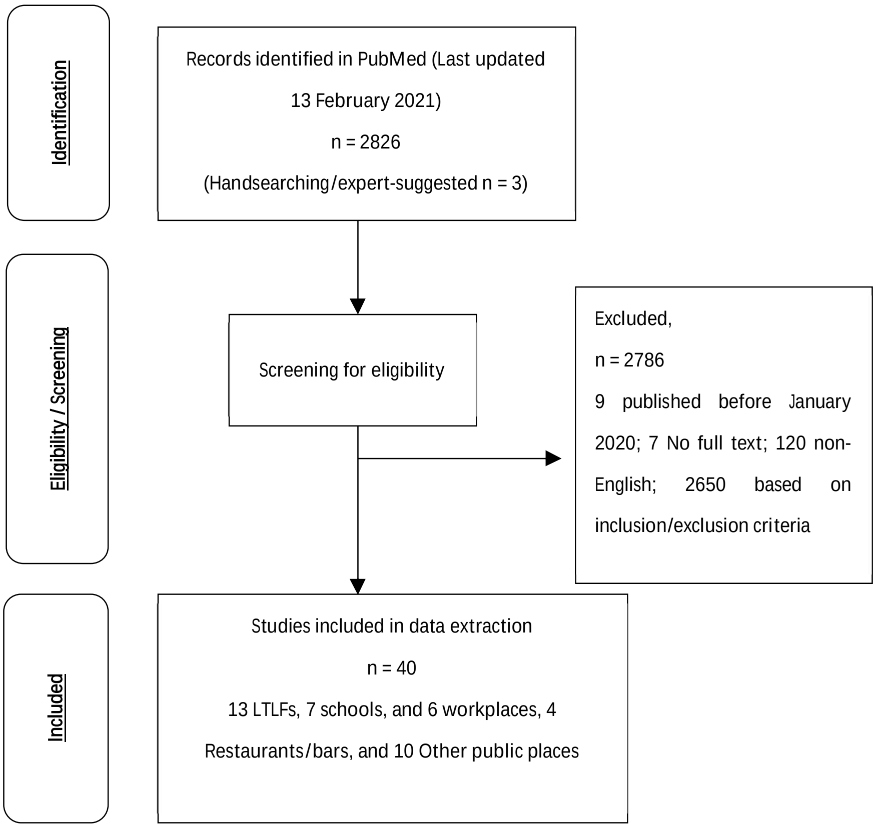
Epidemiological evidence which accumulated throughout the course of the SARS-CoV-2 pandemic consistently pointed to indoor transmission as corner stone in the spread of infection. The risk of transmission, however, varied across indoor environments. While settings such as long-term care facilities have been disproportionately affected by the pandemic, the evidence of transmission in schools was less clear. Mitigation strategies should take into consideration the potential role of airborne transmission in indoor settings, including workplaces and public transport. Exposure to droplets and/or aerosols is affected by both environmental and behavioral factors, many of which are modifiable (4). The totality of evidence summarized in this review indicate that crowded and/or poorly ventilated environments were more likely to result in superspreading events of SARS-CoV-2, in which both droplets and longer-range aerosols could be involved in transmission. Therefore, improving building ventilation by means of exchange of indoor air with outdoor air, air filtration, and possibly cleaning by ultraviolet light ¨would decrease the risk of indoor transmission. Given that exposure to infectious aerosols is associated with proximity to source, limiting the number the number of persons in indoor environments would also reduce the chances of transmission. Considering a systems approach, these measures and policies are not contingent on behavioral factors and are therefore less sensitive to public outrage and stigma (51). Some of the outbreak investigations included in this review suggested masks (face coverings) could reduce the risk of indoor transmission of SARS-CoV-2, however, evidence from population studies is lacking. The infectious dose of SARS-CoV-2, its relationship to phenotype and severity of COVID-19, and the contributions of host-specific factors to pathogenesis are also less understood.

Annexes

Annex 1. Search string (PubMed)

(((SARS-CoV-2[Text Word]) OR (COVID-19[Text Word])) AND (transmission[Text Word])) AND ((((((((((((((workplace[Text Word]) OR (work*place*[Text Word])) OR (workspace*[Text Word])) OR (work*space*[Text Word])) OR (work*environment*[Text Word])) OR (meeting*[Text Word])) OR (office*[Text Word])) OR (building*[Text Word])) OR (long-term care[Text Word])) OR (nursing home*[Text Word])) OR (long*term care[Text Word])) OR (restaurant*[Text Word])) OR (bars[Text Word])) OR (public place*[Text Word])) OR (school*[Text Word]))*

Annex 2. PRISMA Chart



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