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The research protocol was approved by institutional review board at the Zhejiang Provincial CDC and all human participants gave written informed consent.

Abstract.

Background: Much remains unknown about COVID-19 transmission. We evaluated potential transmission routes from two community COVID-19 outbreaks.

Methods: In the first outbreak, 126 passengers took two buses (59 from Bus #1 and 67 from #2) on a 100-minute round trip to attend a 150-minute worship event. The source patient was a passenger on Bus #2. We compared risks of COVID-19 among individuals taking Bus #1 (n=60) and Bus #2 (n=67), and among all other individuals (n=172) attending the worship event. We also divided seats on the exposed bus into high- and low-risk zones according to distance to the source patient and compared COVID-19 risks in each zone. The second outbreak occurred among 30 trainees attending a 3-day workshop in several conference rooms. In both buses and conference rooms, central air-conditioners were in indoor re-circulation mode.

Results: In the first COVID-19 outbreak, passengers in Bus #2 had a 41.5 (95% confidence interval [CI]: 2.6–669.5) times higher risk of getting COVID-19 compared to those in Bus #1, and 11.4 (95% CI: 5.1–25.4) times higher risk compared to all other individuals attending the worship event. Within Bus #2, passengers in high-risk zones had moderately, but non-significantly, higher risk for COVID-19 compared to those in the low-risk zones. In the second outbreak, the overall attack rate was 48.3%.

Conclusion: Airborne spread of COVID-19 appears to at least partially explain the high attack rates in the exposed bus and conference rooms. Future efforts at prevention and control must consider the potential for airborne spread of the virus.

Introduction.

Human infection by the novel coronavirus disease 2019 (COVID-19) was first reported in late 2019 in Wuhan city of Hubei province in China.[1,2] The World Health Organization (WHO) declared the COVID-19 outbreak a public health emergency of international concern on January 30, 2020. The ongoing epidemic has since affected more than 100 countries and territories. As of March 8, 2020, more than 100,000 cases have been confirmed and thousands have died. Most of the cases are from China, although the number of newly confirmed cases is increasing rapidly in several countries including South Korea, Japan, Italy, and Iran.[3]

Greater efforts are needed to contain and combat the virus; however, much remains unknown about COVID-19 transmission, hampering our ability to implement effective interventions. Several studies have demonstrated transmission through close contact and respiratory droplets produced when an infected person coughs or sneezes[4-6]. Whether COVID-19 can be transmitted as an aerosol (i.e., airborne) through inhalation of virus suspended in the air is unknown. Previous studies have suggested possible airborne routes of transmission for emerging virulent coronaviruses such as the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV)[7-11]. Recent reports suggest that closed environments may facilitate secondary transmission of COVID-19[12,13]. To inform the knowledge gap and investigate potential transmission routes of COVID-19, we present investigations of two outbreaks of COVID-19 among lay Buddhists worshiping in a temple and trainees attending a workshop in Zhejiang province.

Methods.

Brief description of two COVID-19 outbreaks in Zhejiang province

The current study analyzed data collected from two COVID-19 outbreaks in Zhejiang province of China. The first outbreak started on January 19 among 293 lay Buddhists attending an outdoor, worship event held in a temple in Ningbo city of Zhejiang province. The index and source patient was a 64-year old female lay Buddhist. This patient and 66 other passengers took a bus to the event (Figure 1). A second similar bus carried 59 passengers to the same event. Both buses had an air conditioning system on a re-circulating mode (vents below the windows), four openable windows (two on each side), and neither had an attached toilet.

The second outbreak occurred among 30 trainees attending a workshop in Hangzhou city of Zhejiang province. A 45-year-old female trainee from Wuhan was both the source and index patient. The workshop took place between January 12–14, 2020 in two conference rooms. The first day's training was held in a 49m^2 (527.4 sq ft) conference room and the remaining two days of training was done in a 75m^2 (807.3 sq ft) conference room (Figure 2). Both conference rooms were enclosed spaces with central air conditioners on an indoor re-circulating mode with its ventilation system automatically turned on every four hours for a duration of 10 minutes. When on, the ventilation system was able to exchange one-fourth of the air in the rooms.

Data collection

Data on demographics, travel history, and social and family activities were collected by a questionnaire through epidemiologic investigation carried out by local CDC staff.

Sample collection and diagnosis of COVID-19

Throat swabs were collected for all individuals exposed to either outbreak. All samples were tested by reverse transcription polymerase chain reaction (RT-PCR) or by viral genome sequencing. Screened individuals were categorized into non-cases, suspected cases, and confirmed cases of COVID-19. Criteria for COVID-19 case definitions and disease severity are provided in the Supplementary Appendix.

Statistical analyses

Attack rates were estimated as the number of diagnosed COVID-19 cases divided by the total number of people at risk, excluding the source patient of each outbreak. In the first outbreak, we compared the risk of COVID-19 between individuals taking the exposed bus (Bus #2) and individuals taking the unexposed bus (Bus #1) as well as the COVID-19 risk between individuals in Bus #2 and all other individuals attending the worship event excluding Bus #2. In addition, we divided seats in Bus #2 into high- and low-risk zones according to the definition of close contact with COVID-19 in travel-associated settings, an area within two meters[14,15] (Classification 1) or two rows[16] (Classification 2) of the source patient. On Bus #2, the distance between two rows was measured at 0.75m, which converts two meters to three rows. Therefore, the high-risk zone includes seats in the same row and within two or three rows (rows 6-10 or rows 5–11) of the index patient (seated in row 8); low-risk zones include seats in other rows (Figure 1). COVID-19 risks in the two types of zones were compared. All comparisons used Chi-squared or Fisher's exact tests. Risk ratios (RRs) and corresponding 95% confidence intervals (CIs) were calculated. For an exposure-disease category with no observations, we imputed a value of 0.5 so that RRs could be computed.[17] A Spearman's

rank correlation test was performed to test the correlation between severity of infected cases and distance to the index patient on Bus #2 (Supplementary appendix S.3).

Results.

Evidence from two outbreaks suggesting airborne transmission of COVID-19 is presented. Other materials related to the transmission dynamics of the two outbreaks are included in supplementary appendix S.4.

Outbreak 1: COVID-19 among lay Buddhists worshiping in the temple

A total of 293 lay Buddhists attended a worship event held in a temple moderated by five monks. Of all the participants, 126 traveled to the temple in two buses, with 59 participants in Bus #1 and the other 67 in Bus #2. All other individuals traveled to the temple through other methods of transportation. Travel duration to and from the temple on the bus was 50 minutes each way (100 minutes total). Passengers remained seated in their own seats during the bus ride and did not change seats on the way back. The worship event lasted 150 minutes in total, beginning at 10:00am and ending at 12:30pm. The event included a lunch with 10 attendees sitting at each round table.

Among all diagnosed cases in this outbreak, the index patient was the only person exposed to residents from Wuhan. The index patient was also the first subject to develop clinical symptoms. As such, the index patient was presumed to be the source of transmission in this outbreak. She was initially asymptomatic during the bus trip but started to have cough, chills, and myalgias on the evening after returning from the temple. The next day, the patient felt better after bathing in a hot tub. However, the patient's husband and daughter started to have fever and cough on January 22, and the entire family went to a hospital seeking treatment. During the hospital visit, the index patient had a normal body temperature. On January 25,

the index patient's daughter was diagnosed as a suspected case of COVID-19, and consequently the entire family was admitted to a hospital for quarantine, where a computed tomography (CT) scan showed exudative inflammation in the lungs of the index patient. All three family members were confirmed COVID-19 positive by RT-PCR assays on January 28. The index patient's husband and daughter did not participate in the worship event on January 19.

Bus #2 carried 67 lay Buddhist passengers and a driver, of whom, 24 passengers (including the index patient) were infected and diagnosed with COVID-19 after the event. No individuals on Bus #1 were subsequently diagnosed with COVID-19. In addition, among the other 172 individuals (167 individuals who traveled to the worship event through other methods of transportation and 5 monks) at the worship event, seven were subsequently diagnosed with COVID-19, and all of them described being in close contact with the index case during the event. Overall, 30 of the 299 individuals at risk during the event developed COVID-19 (excluding the index). Compared to individuals in the non-exposed bus (Bus #1), those in the exposed bus (Bus #2) were 41.5 (95% CI, 2.6–669.5) times more likely to be infected with COVID-19 (Table 1). Compared to all individuals attending the worship event, passengers in Bus #2 had 11.4 (95% CI: 5.1–25.4) times higher chance of being infected by COVID-19 (Table 1).

We were able to identify seats for each passenger in the exposed bus (Figure 1). The bus had 15 rows of seats. Starting from the 3rd row, each row had three seats on one side of the aisle and two seats on the other side of the aisle. The index patient sat in the middle seat on the 3-seat side of the 8th row. Besides the passengers sitting close to the index patient, the seats of other cases were scattered in the bus. Passengers in the high-risk zones had

moderately but non-significantly higher risk of getting COVID-19 than those in the low-risk zones using either classification 1 (RR, 1.6, 95% CI, 0.8–3.2) or classification 2 (RR, 1.8, 95% CI, 0.9–3.3) (Table 1). Of note, on the 3-seat side of the bus, except for the passenger sitting next to the index patient, none of the passengers sitting in seats close to the bus window were infected. In addition, the driver and passengers sitting close to the bus door were not infected either, and only one passenger sitting close to an openable window got infected.

The index patient developed moderate symptoms (Figure 1). Among passengers who eventually developed COVID-19 on Bus #2, three were asymptomatic, three had mild symptoms, and the remaining seventeen cases had moderate symptoms. The severity of secondary cases was not associated with their proximity to the index patient on the bus (correlation, 0.00; P=0.99). In a further contact investigation of the 23 infected cases on Bus #2, numbers of tertiary cases transmitted by each of them were reported (Figure 1).

Outbreak 2: COVID-19 Outbreak during a workshop

The workshop was attended by 30 trainees from different cities between January 12–14. They booked hotels on their own and had meals outside the training building by themselves. Therefore, the transmission mostly occurred during the workshop. Some workshop trainees reported poor air quality in the conference rooms. The training was broken down into half-day sessions (about four hours each) composed of lectures by invited trainers, discussions among trainees, and presentations by trainees. Trainees voluntarily took seats before each of the half-day sessions and could not recall their seat orders for all sessions.

Among the trainees, only the index patient traveled from Wuhan. She reported no fever during the training, however, her colleagues observed her taking unknown medications throughout the workshop. The index patient returned to Wuhan on January 15. She developed a fever (38℃) and cough on January 17 and was diagnosed with COVID-19. Between January 16–22, a total of 15 trainees who attended the workshop, including the index patient, were diagnosed with COVID-19. The attack rate was 48.3% (95% CI, 31.4–65.6).

Discussion.

Previous investigations have reported respiratory droplets, either through close contact or touching of inanimate objects (i.e., fomites), as the major transmission route for COVID-19. As a result, washing hands using soap under running water for 20 seconds and masking mouth and noses when coughing or sneezing is widely suggested for disease prevention.[14,15] Through detailed epidemiologic analysis, airborne spread of the virus appears to explain these two community COVID-19 outbreaks in eastern China.

Our data strongly suggest that airborne transmission contributed to the COVID-19 outbreak among lay Buddhists in Zhejiang province. The index patient was the only person exposed to individuals from Wuhan and the first at the event to be diagnosed with COVID-19 suggesting a high probability that she was the source of the outbreak. The two buses mimicked a quasi-experiment and the second unexposed bus, which left and arrived at the temple at similar times with similar individuals, provided a credible control group. Both buses had an air conditioning system on a re-circulating mode, which may have facilitated the spread of the virus in the exposed bus. Attack rates on the exposed and unexposed buses were sharply distinct (34.3% versus 0%) suggesting that the exposure and the environment in which the exposure took place contributed to this outbreak. Additionally, passengers sitting closer to the index case on the exposed bus did not have statistically higher risks of COVID-19 as those sitting further away. If COVID-19 transmission occurred solely through close contact or respiratory droplets during this outbreak, risk of COVID-19 would likely be related to distance from the index case and ‘high-risk’ zones on the bus would have more infected cases. Our findings suggesting airborne transmission of COVID-19 is in line with a past report of a SARS outbreak on a plane.[18] Both SARS and COVID-19 are caused by coronaviruses and both

outbreaks occurred in enclosed spaces. It should be noted that, except for a passenger sitting next to the index, all passengers sitting close to a window on the left side of the bus remained healthy. This may be related to airflow within the bus; however, we were unable to empirically test this hypothesis. Similarly, transmission at the worship event between the bus rides only led to few infections, and all of those reported close contact with the index case. These data suggest that forced, circulating air might play an important role in airborne spread of the virus.

While some transmission through close contact cannot be ruled out in the second outbreak, we believe that airborne transmission of COVID-19 is also likely for several reasons. First, the 48% attack rate is much higher than those reported in other exposure settings. For example, in a study of 445 contacts from the United States, two close contacts developed COVID-19. This study reported an attack rate of 0.5% among all close contacts and 10.5% among household familial members,[19] much lower than this workshop outbreak. Second, although a ventilation system was equipped in each conference room, it was turned on every four hours and only for a duration of 10 minutes. This suggests airflow within the conference room was largely contained, continually exposing workshop participants. However, other routes of transmission are possible because we were unable to identify seat arrangements on each day of the workshop. In addition, we did not have an available unexposed control group for this outbreak. Regardless, the particularly high attack rate, approaching 50%, is alarming and suggests large community gatherings, especially those in enclosed settings with minimal air ventilation, should be limited.

Our study has important strengths. First, the two outbreaks in this report had clear index and source patients and we were able to collect detailed information on the environment in which

the outbreaks occurred and exposure opportunities. The data allowed us to identify and exclude potential routes of transmission. Second, the bus outbreak mimicked a quasi-experiment, in which two buses, one with an individual with disease and one without, carried similar passengers at similar times, providing a credible unexposed control group. The same outbreak also included both an indoor (bus ride) and outdoor component (the worship event) of similar lengths, allowing a comparison between those settings. The result showed a much higher attack rate in a closed environment with re-circulating air. The potential role of mechanical air-circulation for COVID-19 spread is also supported by a recent study which observed virus contaminated air exhaust outlets.[20] Third, the two outbreaks, a social outdoor event with public transportation and a workshop within an enclosed space, are common daily events, providing potentially greater generalizability to our results.

Our study also has limitations. In the worship event outbreak, seven other lay Buddhists not travelling with Bus #2 were also infected, so we cannot fully rule out that infected passengers in bus #2 may have been infected through alternative sources. However, the absence of individuals in the control bus with COVID-19 and the very high attack rate in the exposed bus (34%) suggests alternative sources are unlikely. Our sample size of infected cases within the exposed bus was somewhat limited, which could have contributed to the non-significant results regarding the impact of distance to the index case on infection risk. However, given that there were infected subjects sitting in the last row, airborne transmission is likely to be at least a partial transmission route. Finally, in the workshop outbreak, transmission through close contact cannot be fully ruled out as we were not able to obtain more detailed information on seating and a control group was not available.

In conclusion, we investigated two COVID-19 outbreaks in Zhejiang Province and found that airborne transmission at least partially explains the extraordinary attack rate seen. Both investigations suggest that, in closed environments with air re-circulation, COVID-19 is a highly transmissible pathogen. Our finding of likely airborne transmission has important public health significance and future efforts at prevention and control should consider the potential for airborne spread of COVID-19, particularly in enclosed spaces with re-circulating air conditioning systems.

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Tables and Figures.

Table 1. COVID-19 risk assessment of different sections of the exposed bus and between the exposed bus and unexposed controls.

Figure 1. Schematic diagram of Bus #2.

Figure 2. Outlines of the conference rooms for the first day (top) and the other two days (bottom).

Table 1. COVID-19 risk assessment of different sections in the exposed bus and between the exposed bus and unexposed controls.

	Cases	Total	Attack rate (95% CI)	Relative Risk (95% CI), P-value	
Exposed Bus and Other Attendees of Temple					
Bus #1	0	60	0 (0–6.0)	1 (Reference)	…
All Individuals Attending Temple except Bus #2	7	232	3.0 (1.3–6.2)	…	1 (Reference)
Bus #2	23	67	34.3 (24.1–46.3)	41.5 (2.6–669.5), <0.01	11.4 (5.1–25.4), <0.01
Overall	30	299	10.0 (7.1–14.0)	…	…
Different Sections of Exposed Bus					
Classification 1[14,15]					
Low-risk zones (rows 1-4, 12-15)	9	34	26.5 (14.4–43.3)	1 (Reference)	…
High-risk zone (rows 5-11)	14	33	42.4 (27.2–59.2)	1.6 (0.8–3.2), 0.17	…
Classification 2[16]					
Low-risk zones (rows 1-5, 11-15)	12	44	27.3 (16.2–42.0)	1 (Reference)	…
High-risk zone (rows 6-10)	11	23	47.8 (29.2–67.0)	1.8 (0.9–3.3), 0.09	…

Abbreviations: CI, confidence interval.

The index patient was removed from the table. For exposure-disease categories with no observations, we imputed a value of 0.5 so that RRs could be computed

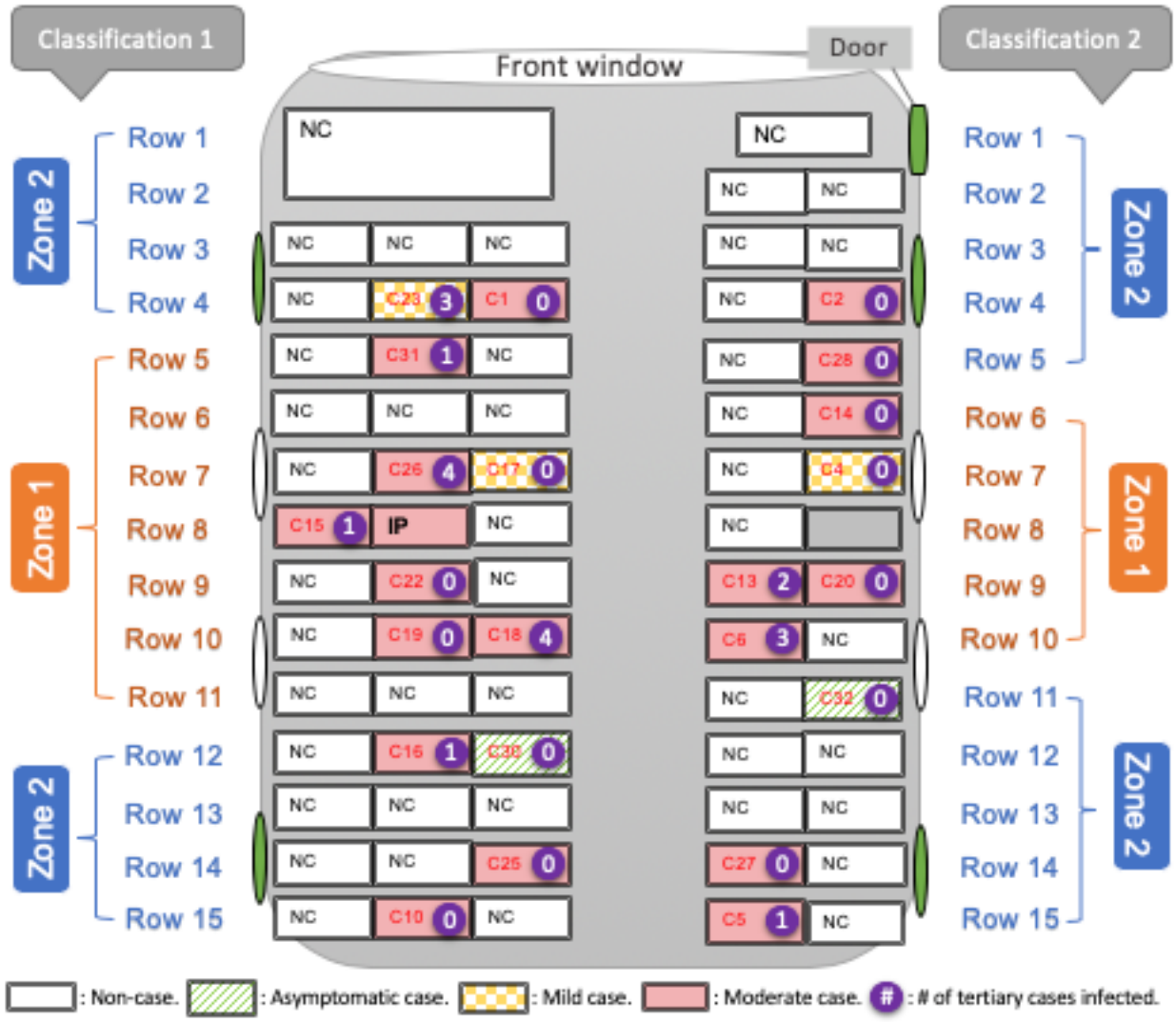

Figure 1: Schematic diagram of Bus #2. IP: Index patient; NC: Non-case; C#: Case number with texts colored in red; Classification 1[14,15] and 2[16]: Two different approaches to define high-risk and low-risk zones; Zone 1 (high-risk zone); Zone 2 (low-risk zones); Severity levels of cases were indicated: Asymptomatic cases: seats marked in green diagonal stripes; Mild cases: marked in yellow checkerboard; Moderate cases: marked in light pink; IP – Index patient; NC – Non-case; Seats marked with a numbered circle indicates the number of tertiary cases infected by the corresponding case; Green window and door: Four side windows and the door that can be opened for fresh air.

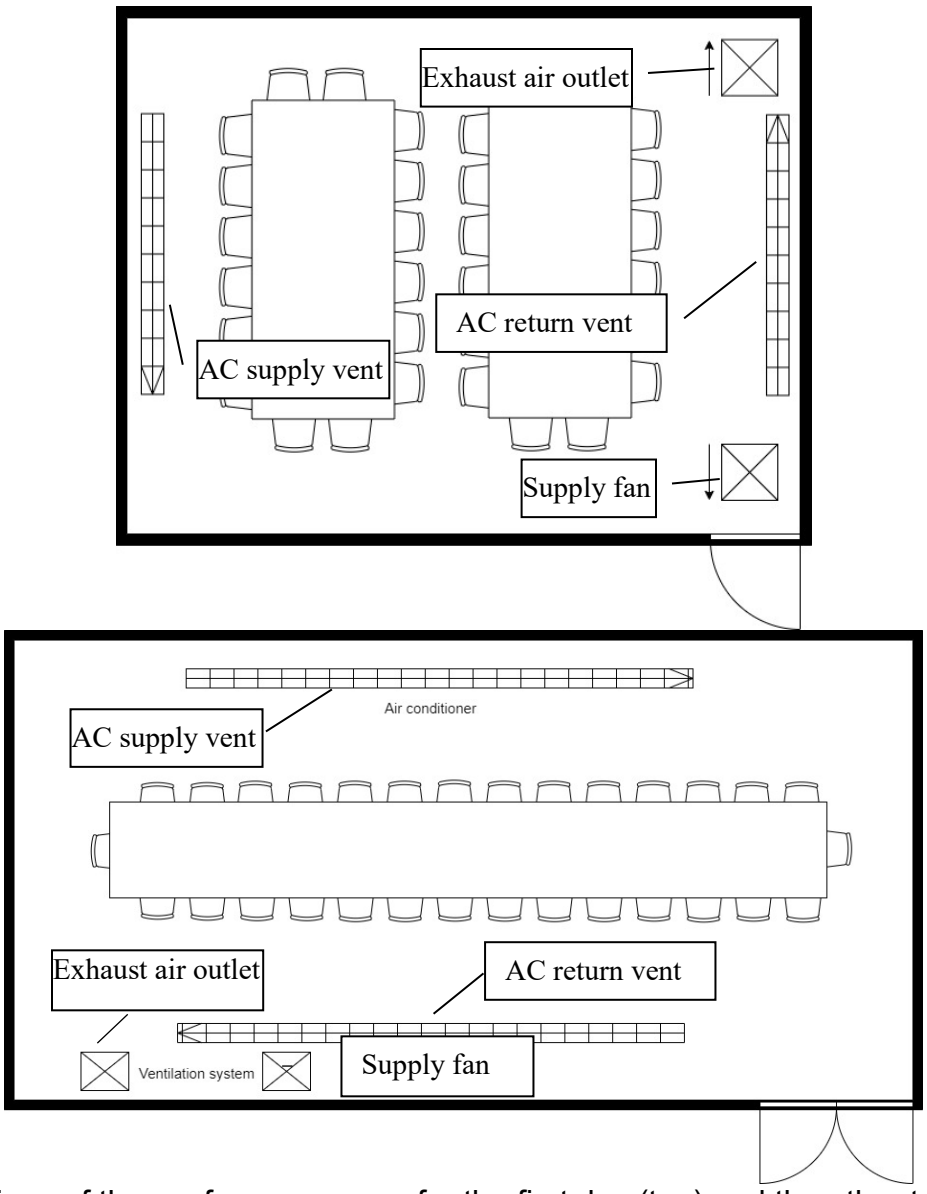

Figure 2: Outlines of the conference rooms for the first day (top) and the other two days (bottom).