COVID-19 in Americans aboard the *Diamond Princess* cruise ship

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Summary: The *Diamond Princess* cruise ship was the site of a large outbreak of coronavirus disease 2019 (COVID-19). Our findings highlight the high risk of SARS-CoV-2 transmission on cruise ships

Abstract

Background: The *Diamond Princess* cruise ship was the site of a large outbreak of coronavirus disease 2019 (COVID-19). Of 437 Americans and their travel companions on the ship, 114 (26%) tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Methods: We interviewed 229 American passengers and crew after disembarkation following a ship-based quarantine to identify risk factors for infection and characterize transmission onboard the ship.

Results: The attack rate for passengers in single-person cabins or without infected cabinmates was 18% (58/329), compared with 63% (27/43) for those sharing a cabin with an asymptomatic infected cabinmate, and 81% (25/31) for those with a symptomatic infected cabinmate. Whole genome sequences from specimens from passengers who shared cabins clustered together. Of 66 SARS-CoV-2-positive American travelers with complete symptom information, 14 (21%) were asymptomatic while on the ship. Among SARS-CoV-2-positive Americans, 10 (9%) required intensive care, of whom 7 were ≥70 years.

Conclusion: Our findings highlight the high risk of SARS-CoV-2 transmission on cruise ships. High rates of SARS-CoV-2 positivity in cabinmates of individuals with asymptomatic infections suggest that triage by symptom status in shared quarters is insufficient to halt transmission. A high rate of intensive care unit admission among older individuals complicates the prospect of future cruise travel during the pandemic, given typical cruise passenger demographics. The magnitude and severe outcomes of this outbreak were major factors contributing to the Centers for Disease Control and Prevention's decision to halt cruise ship travel in U.S. waters in March 2020.

Key words:

SARS-CoV-2; risk factor; symptoms; whole genome; cruise ship

Background

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a respiratory virus newly identified in January 2020, is the cause of a large pandemic with substantial global morbidity and mortality (1,2,3). COVID-19 causes respiratory and, less frequently, gastrointestinal symptoms [4]. A substantial minority of infected persons never develop symptoms [5] but may still transmit SARS-CoV-2 infection [6,7,8].

The *Diamond Princess* (DP) cruise ship was the site of the largest outbreak of COVID-19 outside China in February 2020, with 712 (19%) cases among 3,711 passengers and crew [9]. On January 20, 2020, the DP departed Yokohama, Japan, on a round-trip voyage, making stops in Vietnam, Taiwan, and Japan [10]. Of 3,711 persons onboard, 437 were US citizens, residents, and non-American partners of citizens or residents (referred to as Americans below). On January 23, a passenger developed a cough, disembarked on January 25 and was diagnosed with COVID-19 on February 1 [11]. Upon the ship's return to Yokohama on February 3 [12], Japanese authorities did not allow passengers or crew to disembark and initiated SARS-CoV-2 testing of those onboard.

Group activities continued onboard through February 4. On February 5, after testing showed ten passengers with SARS-CoV-2 infection, passengers were told to stay in their cabins for ship-based quarantine [11,13,9]. Asymptomatic crew members continued to perform their work, which included delivering meals to cabins, and symptomatic crew were isolated [12].

On February 7, Japanese authorities set up a ship-based clinic. Anyone who had fever or respiratory symptoms was tested for SARS-CoV-2, along with their close contacts. Anyone testing positive was hospitalized regardless of illness severity [12]. On February 11, testing was expanded to asymptomatic passengers, and eventually included everyone who remained on board [9,14].

During February 16–17, after approximately 11 days of ship-based quarantine, most Americans were repatriated voluntarily to the United States on chartered flights and quarantined under federal authority on US military bases. Those who were identified as SARS-CoV-2-positive were transferred to US medical facilities A total of 108 Americans remained in Japan [9].

We conducted an investigation to describe clinical manifestations, transmission dynamics, and risk factors for SARS-CoV-2 among Americans on the DP cruise ship.

Methods

Data collection

We performed a retrospective cross-sectional survey of American passengers and crew using a standardized form including questions about demographics; symptoms; comorbidities; smoking; participation in group events during February 3–5, the period just before ship-based quarantine; shore excursions during the voyage; and close contacts during the ship-based quarantine. Questionnaires were translated into six languages. Data collected for American passengers and crew, including reverse transcriptase polymerase chain reaction (RT-PCR) results from Japan, passenger

cabin number, and symptom information at time of specimen collection, were combined with RT-PCR results from testing done in the United States.

Survey population

We attempted to survey all Americans on the January 20–February 3 sailing of the DP. Patients who were severely ill at the time of the survey and unable to answer questions were excluded (n=10). Participants were interviewed February 28–March 18, approximately 2–5 weeks after disembarkation from the ship.

Specimen collection and laboratory testing

Specimens were collected by nasopharyngeal (NP) swab, oropharyngeal (OP) swab, or both. Specimens were tested by RT-PCR for SARS-CoV-2. Results from RT-PCR testing were provided by the Japanese Ministry of Health, Labour and Welfare (MHLW) and by CDC [15].

Available samples from repatriated Americans testing positive in the United States (n=28) underwent whole genome sequencing for SARS-CoV-2 [16]. A phylogenetic tree was built using the global database of SARS-CoV-2 sequences available before March 20, 2020. A median joining network [17] of observed haplotypes was generated using the subset of sequences from samples collected from those on the DP including 69 previously reported sequences from Japan and Hong Kong and the 28 sequences from this investigation.

Definitions

A case was defined as a positive SARS-CoV-2 RT-PCR test in a specimen collected from passenger or crew while in Japan or in the United States. Attack rate (AR) was defined as the rate of SARS-CoV-2 infection regardless of symptoms. A symptomatic case was defined as a case with documentation of fever or respiratory symptoms either by the Japanese outbreak response team or by the CDC survey. Timing of SARS-CoV-2 infections was dichotomized into early quarantine (a positive test result on or before February 12, the midpoint of quarantine) and late quarantine (a positive result after February 12). Close contact was considered being in a room with someone for a more than 15 minutes without wearing a mask.

Data analysis

Demographic characteristics and case status were tabulated for respondents and non-respondents using information obtained from the ship manifest and MHLW. The proportions were compared using a 2-sided chi-square test or Fisher's exact test.

We used bivariate and multivariable logistic regression models for risk factor analysis. Crew were excluded from this analysis because there were few American crew and their exposures were different from passenger exposures. Risk factors with p-value ≤ 0.10 were included in multivariable models.

We determined the AR for three cabin exposure categories: 1) for passengers in single-person cabins or in multi-person cabins without SARS-CoV-2-positive cabinmates, 2) for passengers in multi-person cabins with at least one asymptomatic SARS-CoV-2-positive cabinmate but no symptomatic SARS-CoV-2 positive cabinmates, and 3) for passengers in multi-person cabins with at least one symptomatic SARS-CoV-2-positive cabinmate. We considered the cabinmate with the earliest positive test date as the index case in the cabin and included them in the first exposure category above. Individuals testing positive on the same date as their cabinmate were counted in the second or third categories. Crew did not undergo cabin quarantine and were excluded from this analysis, as were passengers who were never tested.

We stratified symptoms by SARS-CoV-2 PCR result and compared results using chi-square and Student's t-tests. Due to sample size constraints, risk factors for symptoms among SARS-CoV-2-positive individuals were assessed by bivariate analysis. The prevalence of severe disease, defined as requiring intensive care, was calculated by age group; trends were assessed using the Cochran-Armitage test.

Ethics

The survey was reviewed and determined to be a non-research, public health response activity by the human subjects advisor for the CDC COVID-19 response. Participants provided verbal informed consent.

Results

Of 437 American DP passengers and crew, 114 (26%) tested positive for SARS-CoV-2. This included 98 who had a positive RT-PCR result in Japan before repatriation, 10 who had negative results in Japan but then had a positive result in the United States, and 6 who were never tested in Japan and had a positive result in the United States. The temporal distribution of SARS-CoV-2 infections coincided with changes in testing criteria, with a substantial increase after the initiation of a universal testing policy by the MHLW on February 11 (**Supplemental Figure 1**).

The survey response rate was 229/437 (52%) (**Table 1**). Demographic and clinical characteristics of respondents and non-respondents were similar. Respondents were more likely to be symptomatic at time of sample collection (19.7% vs. 12.5%, P=0.04). Respondents were more likely than non-respondents to have a SARS-CoV-2-positive RT-PCR result (**Table 1**); this was true for those interviewed in Japan (26.6% vs. 17.8%, P<0.001) and in the United States (28.8% vs. 23.1%, P=0.005) .

Among 229 respondents, 66 (28.8%) had a SARS-CoV-2-positive RT-PCR result, including 35 with an identifiable symptom onset date. A peak in onset of first symptoms occurred on February 6, shortly after initiation of cabin quarantine (**Figure 1A**); a second peak occurred one week later. Six (60%) of 10 SARS-CoV-2-positive respondents with symptom onset dates on or after February 12 had a cabinmate already diagnosed with SARS-CoV-2-infection.

Attack rates did not differ by cabin location. There was an association between AR and SARS-CoV-2 status of cabinmate (p-value < 0.01) (**Figure 1B**). Those in single-person cabins or in multi-person cabins without a SARS-CoV-2-positive cabinmate had the lowest AR (58/329, 18%, 95% confidence interval [CI]: 13–22%), followed by passengers with at least one asymptomatic SARS-CoV-2-positive cabinmate but no symptomatic SARS-CoV-2-positive cabinmates (AR 27/43, 63%, 95% CI 50–76%). Passengers with at least one symptomatic SARS-CoV-2-positive cabinmate had the highest AR (25/31, 81%, 95% CI 66–96%).

Among 31 passengers sharing a cabin with a symptomatic cabinmate, 21 (68%) tested SARS-CoV-2-positive within 5 days of their cabinmate (**Figure 2**). Four (40%) of the remaining 10 tested positive more than 5 days after the index case of the cabin; the longest time lag between cabinmates testing positive was 11 days.

All 28 SARS-CoV-2 genome sequences from samples from Americans on the DP clustered in the B group of the global phylogenetic tree, a group dominated by early sequences from China and containing all previously reported genome sequences from the DP (**Supplemental Figure 2**). All 28 genome sequences carried the G11083T mutation reported in the presumed Hong Kong index case [18]. Among 28 sequences, 12 were from six pairs of individuals who had close contact. In all instances, pairs of linked genomes grouped closely to one another within the haplotype network (**Figure 3**). Linked sequences were separated by only 0–2 single nucleotide variants (SNVs) compared with 0–9 SNVs among all DP sequences. Two pairs (Link E and Link C) had identical sequences, while four pairs (Links A, B, D, and F) had unique sequences with 1-2 SNVs separating the pairs.

Age ≥70 years compared with <60 years was significantly associated with SARS-CoV-2-infection in bivariate analysis (**Table 2)**. There was no association between SARS-CoV-2 infection and sex, smoking history, or comorbidities. Close contact with an individual who was SARS-CoV-2-positive was a risk factor for being SARS-CoV-2-positive (OR 3.4, 95% CI: 1.8,6.7). Participation in certain activities and excursions was significantly associated with SARS-Cov-2 infection in bivariate analysis (**Table 2**). In multivariable models, only close contact with an individual who tested positive for SARS-CoV-2 was significantly associated with SARS-CoV-2 infection (**Table 2**).

In our survey cohort, 21% (14/66) of respondents reported being completely symptom-free while on the ship. The remaining 52, including some who were initially classified as asymptomatic at time of sampling in Japan, reported symptoms (**Table 3**). Among 66 SARS-CoV-2-positive respondents, the most common symptoms reported were fever (45%), cough (36%), headache (26%), diarrhea (19%), and chills (17%). Fever and cough were often the earliest symptoms reported, whereas diarrhea, headache, and chills often occurred later in the course and had a wide distribution of onset times. Age, sex, comorbidities, and smoking were not significantly associated with having symptoms (**Table 4**).

Rates of SARS-CoV-2 infection varied by age (**Supplementary Figure 3**). Severe disease was not reported in those <60 years old. Rates of severe disease were 8% (3/39) in 60-69 year-olds, 10% (5/48) in 70-79 year-olds, and 14% (2/14) in those ≥80 years. Overall, 10 (9%) American travelers required intensive care. The age trend was not statistically significant (p=0.17). No Americans died, and the last American was discharged in July.

Discussion

One in four Americans onboard the DP tested positive for SARS-CoV-2; 21% of their infections were asymptomatic. Attack rates increased from 17% in cabins without infected cabinmates to 81% in cabins with a symptomatic infected cabinmate. Higher rates of severe illness were found among older individuals.

The AR of 26% among Americans was similar to the rate of the entire ship's population of 19% [9]. Cruise ships are environments that are conducive to efficient and rapid spread of respiratory infections such as influenza [20–24]. The DP outbreak highlights two key factors related to SARS-Cov-2 transmission on cruise ships: the intermingling of passengers and crew from different geographic locations that facilitates introduction of the virus, and the highly interactive closed environment that facilitates spread.

Our results suggest that substantial SARS-CoV-2 transmission occurred on the ship before implementation of quarantine, followed by intra-cabin transmission among cabinmates during cabin quarantine. The association between reported participation in certain events, for example the bus excursion in Cai Rang, Vietnam, and group activities on February 3–4, suggests several common mass exposure events. This finding is similar to earlier reports showing high rates of infection among DP passengers on a bus tour in Kagoshima, Japan[11].

Close contact with a confirmed case, regardless of symptoms, was a risk factor for SARS-CoV-2 infection. The AR among cabinmates of asymptomatic infected persons was elevated compared to persons in single-person cabins or with uninfected cabinmates but lower than among those sharing a cabin with a symptomatic infected person, a pattern suggestive of intra-cabin transmission. Recent cohort studies of secondary transmission have reported ARs among household members of 11.2% [25], 16.3% [26] and 19.3% [27]. The ARs observed among cabinmates on the DP (56–83%) were higher than these and may indicate more frequent and sustained exposure in small cabins compared to larger residences. This difference may also be a reflection of the older age of passengers on the DP (median age, 69 years) compared to those in households with children and young adults [27]. The cabinmate AR observed in our investigation may also be higher because it is a conflation of exposures in congregate settings before quarantine and intra-cabin exposure. To differentiate between the two, we used the median incubation period of 5 days as the separation point between exposures in congregate settings pre-quarantine and intra-cabin secondary transmission [28]. Even after excluding cabinmates who tested positive within 5 days of their cabinmate, the AR in those with a positive cabin-mate was still 40%, suggesting intra-cabin transmission.

All genome sequences of SARS CoV-2 viruses from the American travelers carried the same G11083T mutation reported in the presumed Hong Kong index case, consistent with a single index case leading to this cruise ship outbreak. SARS-CoV-2 genome sequences from samples from six pairs of individuals with known close contact differed by two or fewer mutations. Two links (A and B) showed evidence of intra-cabin transmission, given unique genotypes that showed accumulation of SNVs from the initial index case genotype to the first cabinmate and then the second cabinmate. The accumulation of 0-2 SNVs between consecutive passages of the virus within this investigation and

the overall diversity of sequences from the outbreak suggest that genotypic data can be used to support epidemiological investigations of transmission events during SARS-CoV-2 outbreaks [18].

The role of surface contamination in SARS-Cov-2 transmission could not be determined. A DP environmental sampling investigation showed high rates of SARS-CoV-2 RNA contamination on surfaces inside cabins occupied by passengers with COVID-19 regardless of symptoms, and low rates in common areas [29]. However, no viable virus was isolated. The same study found no evidence of airborne transmission.

The contribution that asymptomatic infected passengers played in the perpetuation of the COVID-19 outbreak on the DP could not be fully determined. Asymptomatic transmission of SARS-CoV-2 has been well-characterized in other outbreaks where timing of exposure to asymptomatic individuals was known [8]. During our survey, nearly two-thirds of SARS-CoV-2-positive persons who were originally classified as asymptomatic at the time of specimen collection reported having symptoms while onboard the ship. High rates of asymptomatic infection could be due to sampling after resolution of symptoms when virus was still detectable, sampling in the pre-symptomatic phase, or true asymptomatic cases [30]. Systematic cross-sectional testing regardless of symptoms will detect more asymptomatic or pre-symptomatic infections compared to strategies where symptomatic individuals are prioritized for testing. Longitudinal follow-up of asymptomatic individuals can help determine the true asymptomatic rate. In a cross-sectional survey at a long-term care facility, 57% of individuals were initially asymptomatic when positive for SARS-CoV-2 [5], but most ultimately developed symptomatic disease, consistent with our findings. Notably, the rate of asymptomatic infection we report (21%) closely matches early modeling estimates of 18% [31].

There were several study limitations. Our survey response rate was 52% ; respondents and non-respondents were similar, but respondents were more likely to be symptomatic and SARS-CoV-2-positive, thereby possibly more motivated to participate. Respondents knew SARS-CoV-2 test results at the time of their interview, possibly introducing recall bias among those with positive results. Patients who were severely ill at the time of the survey were not eligible for the questionnaire. A small subset (< 5%) of our population was never tested for SARS-CoV-2; therefore, the true AR may be higher than we reported. We were unable to determine the precise timing of incident cases because we used sampling date as a proxy for infection date, complicating our ability to assess patterns of transmission and determine directionality of transmission in cabinmates. Finally, Americans comprised only 12% of the ship's population; therefore, this investigation focused on Americans was unable to assess complete transmission dynamics onboard the ship.

The DP outbreak was an early harbinger of the global spread of SARS-CoV-2 that followed [9] and the largest COVID-19 cruise ship outbreak to date. A massive, month-long public health response involving international, federal, state, and local authorities was launched to address this outbreak and to repatriate passengers and crew to multiple countries. Repatriated Americans were managed in one of the largest US federal quarantine activities of the last 50 years [9].

The ship-based cabin quarantine eliminated intermingling of passengers and likely helped avert many new cases; however, it was not effective at halting transmission within cabins [32]. Quarantine of repatriated Americans after they arrived in the United States and restriction of travel of those who remained in Japan were necessary to prevent introduction of SARS-CoV-2 into U.S. communities at a

time when there was no reported community spread. Over 10% of the repatriated Americans were positive for SARS-CoV-2 at time of repatriation, and the U.S.-based quarantine likely prevented further spread from this cohort.

Our findings highlight the high risk of COVID-19 transmission on cruise ships. High ARs in cabinmates of individuals with asymptomatic infections suggest that triage by symptom status is not enough to halt transmission and that broad testing of asymptomatic individuals including cabinmates is warranted, especially before the end of a 14-day quarantine period. A high rate of severe disease in older individuals complicates the prospect of cruise travel, especially on cruises with older populations. The magnitude of the outbreak and severity of the illnesses among many infected on the DP were major factors contributing to CDC's decision to halt cruise ship travel in U.S. waters with a No Sail Order initiated during March 2020 [33].

NOTES

Author contributions

MP, CHB, and CRF designed the investigation. NTP, FAT, RLW, and MT supervised data collection. MP, MW, EVK, and ZDS analyzed the data. MP, MW, EVK, FAT, ESH and CRF wrote the first draft of the manuscript. CHB, CTAH, AI, and AMM contributed to the writing of the manuscript. CAE and XL oversaw PCR testing. AU, MRM, JZ, YL and ST generated and analyzed genome sequence data. MP, AMA, AS, BK, PTC, RM, FAT, RLW, MT, CTAH, RM, RN, AI, MK, LFM, ESH, BJM, MSC, and CRF assisted with the *Diamond Princess* public health response and scientific implementation of the investigation. All authors read and approved the final version of the manuscript.

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NONE OF THE AUTHORS HAS ANY POTENTIAL CONFLICTS TO DISCLOSE.

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Figure 1: Date of first symptom onset SARS-CoV-2-positive Americans aboard the *Diamond Princess* cruise ship in subset of 35 SARS-CoV-2-positive Americans who were interviewed and had identifiable symptom onset dates, stratified by presence of SARS-CoV-2-positive cabinmates (**A**). Attack rates stratifying by presence of known symptomatic and asymptomatic SARS-CoV-2+ cabinmates in American *Diamond Princess* passengers (**B**).

Figure 2. Time in days between positive test results among cabinmates (N=31). Grey arrows represent cabinmates that never tested positive.

Figure 3. Median joining haplotype network of 97 SARS-CoV-2 genomes generated from confirmed cases from the *Diamond Princess* cruise ship and other published sequences. Each circle indicates a unique sequence (haplotype), circle size indicates number of genomes with that sequence. Tick marks on lines represent the number of single nucleotide variants (SNVs) between haplotypes. Subsets identified by color and pattern are previously published genomes, the first identified case of a passenger (Hong Kong), and 28 genomes from this investigation, including genomes from six pairs of individuals with epidemiological links (Links A-F) and those with no reported links. Pairs of linked sequences differed by 0–2 SNVs; all sequences differed by 0–9 SNVs.

Table 1. Demographic characteristics of Americans aboard the *Diamond Princess* during the COVID-19 outbreak, January-March, 2020 (N=437)

Characteristic	Category	Total N=437	Interviewed n (%) N=229	Not interviewed n (%) N=208	p-value
Age median (interquartile range), years			69 (62-73)	68 (61-74)	0.08
Age group, years	0-19	3	0 (0)	3 (1.4)	0.22
	20-39	31	13 (5.7)	18 (8.7)	
	40-59	51	23 (10.0)	28 (13.5)	
	60-69	159	89 (38.9)	70 (33.7)	
	70-79	161	88 (38.4)	73 (35.1)	
	80 and older	32	16 (7.0)	16 (7.7)	
Sex	Male	203	107 (46.7)	96 (46.2)	0.90
	Female	234	122 (53.3)	112 (53.8)	
Passenger or crew	Passenger	425	223 (97.4)	202 (97.1)	0.87
	Crew	12	6 (2.6)	6 (2.9)	
Location after leaving the ship	Japan (quarantined or hospitalized)	108	60 (26.2)	48 (23.1)	0.75
	Texas	145	78 (34.1)	67 (32.2)	
	California	165	82 (35.8)	83 (39.9)	
	Nebraska	19	9 (3.9)	10 (4.8)	
Presumed close contact of a COVID-19 case	Yes	128	76 (33.2)	52 (25)	0.06
	No	309	153 (66.8)	156 (75)	
Symptomatic at time of sampling*	Symptomatic	71	45 (19.7)	26 (12.5)	**0.04**
	Asymptomatic	366	184 (80.3)	182 (87.5)	
SARS-CoV-2 test result in Japan	Positive	98	61 (26.6)	37 (17.8)	**<0.001**
	Negative	280	150 (65.5)	130 (62.5)	
	Not tested	59	18 (7.9)	41 (19.7)	
Any SARS-CoV-2 test result	Positive	114	66 (28.8)	48 (23.1)	**0.005**
	Negative	302	159 (69.4)	143 (68.8)	
	Not tested	21	4 (1.7)	17 (8.2)	

Note. *As defined and reported by Japanese authorities.

Table 2. Factors associated with a positive SARS-CoV-2 test result regardless of symptom status among interviewed American *Diamond Princess* passengers (N=223) as assessed in bivariate and multivariable models

	SARS-CoV-2+			
Risk factor	Unadjusted Odds Ratio (OR) (95% Confidence Interval)	Adjusted OR (aOR) 1* (95% CI)	aOR2** (95% CI)	aOR3*** (95% CI)
Male Sex	0.90 (0.58, 1.39)	0.81 (0.41, 1.59)	0.73 (0.32, 1.64)	0.78 (0.14, 4.33)
Age				
0-59	Ref	Ref	Ref	Ref
60-69	2.05 (0.99, 4.58)	1.86 (0.63, 6.34)	1.41 (0.42, 5.25)	3.19 (0.16, 126.50)
70-79	**2.68 (1.31, 5.94)**	1.42 (0.47, 4.01)	0.82 (0.24, 3.09)	5.00 (0.39, 175.90)
80+	**4.90 (1.88, 13.23)**	3.73 (0.85, 17.78)	2.23 (0.42, 12.72**)**	44.25 (1.10, 4694.17)
Underlying Conditions				
Type II diabetes	1.49 (0.67, 3.21)			
Heart disease	1.41 (0.57, 3.29)			
High blood pressure	0.72 (0.39, 1.30)			
Lung disease	1.61 (0.70, 3.60)			
Immunosuppressive condition	1.94 (0.67, 5.31)			
High cholesterol	0.60 (0.22, 1.39)			
Any underlying condition	1.28 (0.81, 2.01)			
Current/Former Smoking	1.59 (0.82, 3.07)			
Kind of Exposure				
Close Contact	**3.43 (1.80, 6.65)**	**3.37 (1.73, 6.64)**	**2.87 (1.31, 6.42)**	**31.07 (5.29, 360.20)**
Asymptomatic Contact	**2.53 (1.11, 5.78)**			
Symptomatic Contact	1.99 (0.86, 4.47)			

Deck				
A	Ref			
B	1.02 (0.52, 1.95)			
C	1.03 (0.53, 1.96)			
D	0.75 (0.38, 1.46)			
E	0.69 (0.29, 1.55)			
L	0.62 (0.17, 1.81)			
P	1.50 (0.55, 3.82)			
Cabin				
Exterior	Ref	Ref	Ref	Ref
Interior	0.65 (0.39, 1.05)	0.91 (0.43, 1.87)	0.83 (0.33, 1.98)	0.72 (0.10, 4.33)
Excursions				
Kagoshima – 1/22/2020				
Tour	0.59 (0.31, 1.09)			
Bus	0.69 (0.30, 1.62)			
Hong Kong – 1/25/2020				
Tour	0.91 (0.49, 1.68)			
Bus	1.37 (0.62, 3.07)			
Chan May – 1/27/2020				
Tour	1.35 (0.71, 2.64)			
Bus	2.03 (0.85, 5.39)			
Cai Rang – 1/28/2020				
Tour	1.72 (0.88, 3.52)			
Bus	**2.45 (1.18, 5.36)**		2.28 (0.95, 5.82)	
Keelung – 1/31/2020				
Tour	0.87			

	(0.47, 1.59)		
Bus	0.87		
	(0.42, 1.83)		
Transition period			
2/3/2020			
Participatory event	0.86		
	(0.18, 3.20)		
Music show	**0.20**		0.49
	(0.06, 0.56)		(0.06, 3.69)
Other show	**4.00**		**10.15**
	(1.46, 11.35)		**(1.12, 167.17)**
2/4/2020			
Participatory event	1.03		
	(0.05, 9.33)		
Music show	**0.08**		
	(0.01, 0.37)		
Other show	**5.25**		
	(1.29, 24.67)		

CI: confidence interval

*The first multivariable model included sex, age, underlying health conditions, and close contact with a COVID-19 case.

**The second model included all risk factors from the first model plus participation in cruise excursions that were identified as potential risk factors for SARS-CoV-2 infection in bivariate analysis.

***The third model included all risk factors from the first model plus cruise activities that were identified as potential risk factors for SARS-CoV-2 infection in bivariate analysis

Table 3. Reported clinical characteristics of American passengers and crew on the *Diamond Princess* cruise ship, stratifying by SARS-CoV-2 infection status

	SARS-CoV-2-positive		SARS-CoV-2-negative		p-value*
	N=66		N=146		
No symptoms while on cruise	14/66 (21%)		109/146 (75%)		<0.01
Reported symptoms	n/N	Duration in days (median, IQR)	n/N	Duration in days (median, IQR)	
Fever	29/65 (45%)	4 (1-6)	7/146 (5%)	2 (1-3)	**<0.01**
Cough	24/66 (36%)	5 (2-15)	12/146 (8%)	5 (4-5)	**<0.01**
Headache	17/65 (26%)	2 (1-3)	11/146 (8%)	4 (2-8)	**<0.01**
Diarrhea	12/64 (19%)	2 (2-4)	8/146 (5%)	2 (1-3)	**<0.01**
Chills	11/66 (17%)	2 (1-2)	3/145 (2%)	2 (2-2)	**<0.01**
Nasal congestion	10/65 (15%)	5 (4-20)	8/146 (5%)	2 (1-3)	**0.03**
Runny nose	9/65 (14%)	2 (2-4)	10/145 (7%)	3 (2-4)	0.17
Sore throat	8/65 (12%)	8 (6-8)	5/146 (3%)	4 (4-7)	0.03
Muscle ache	7/65 (11%)	4 (2-5)	9/146 (6%)	2 (1-2)	0.38
Nausea	4/66 (6%)	1 (1-1)	4/146 (3%)	1 (1-2)	0.43
Vomiting	4/66 (6%)	1 (1-1)	4/146 (3%)	1 (1-1)	0.43
Shortness of Breath	3/64 (5%)	1 (1-1)	1/144 (0.7%)	1 (1-1)	0.17
Abdominal Pain	2/65 (3%)	4 (4-4)	2/146 (1%)	1 (1-1)	0.77
Other symptoms	13/65 (20%)	3 (2-7)	7/146 (5%)	5 (4-8)	**<0.01**
Number of symptoms (median, range)	2 (1-3)		0 (0-0.8)		**<0.01**

*Chi-square test for proportions and Student's T-test for counts

Table 4. Presumptive risk factors for presence of symptoms* among SARS-CoV-2-positive American Diamond Princess passengers N=66)

Characteristic	Category	Total N=66	Symptomatic n (%) N=52	Asymptomatic n (%) N=14	Odds Ratio (95% CI)	p-value*
Age group, years						
	0-39	3	3 (5.7)	0 (0)	Referent	
	40-59	5	5 (9.6)	0 (0)	Undefined	Undefined
	60-69	27	19 (36.5)	8 (57.1)	Undefined	0.54
	70-79	22	17 (32.7)	5 (35.7)	Undefined	1.00
	80 and older	9	8 (15.4)	1 (7.1)	Undefined	1.00
Age group, years						
	≥60	58	44 (84.6)	14 (100)	Undefined	0.19
	<60	8	8 (15.4)	0 (0)		
Sex	Male	28	24 (46.2)	4 (28.6)	2.14 (0.6, 7.72)	0.36
	Female	38	28 (53.8)	10 (71.4)		
Diabetes	Yes	12	10 (19.2)	2 (15.4)	1.31 (0.25, 6.87)	1.00
	No	53	42 (80.8)	11 (84.6)		
Heart problems	Yes	9	8 (16.0)	1 (7.1)	2.48 (0.28, 21.69)	0.67
	No	55	42 (84.0)	13 (92.9)		
High blood pressure	Yes	24	16 (32.0)	8 (57.1)	0.35 (0.1, 1.19)	0.12
	No	40	34 (68.0)	6 (42.9)		
High cholesterol	Yes	5	4 (7.7)	1 (7.1)	1.08 (0.11, 10.54)	1.00
	No	61	48 (92.3)	13 (92.9)		
Chronic lung disease	Yes	11	9 (17.3)	2 (14.3)	1.26 (0.24, 6.61)	1.00
	No	55	43 (82.7)	12 (85.7)		
Chronic kidney disease	Yes	1	1 (1.9)	0 (0)	Undefined	1.00
	No	65	51 (98.1)	14 (100)		
Chronic liver disease	Yes	2	2 (3.8)	0 (0)	Undefined	1.00
	No	64	50 (96.2)	14 (100)		
Taking immunosuppressive medications	Yes	3	3 (5.9)	0 (0)	Undefined	1.00
	No	61	48 (94.1)	13 (100)		
Immunosuppressive conditions	Yes	7	5 (10.2)	2 (15.4)	0.63 (0.11, 3.66)	0.63
	No	55	44 (89.8)	11 (84.6)		
Other health conditions	Yes	31	27 (54)	4 (33.3)	2.35 (0.63, 8.81)	0.34
	No	31	23 (46)	8 (66.7)		
Current/past smoking	Yes	21	18 (34.6)	3 (21.4)	1.94 (0.48, 7.86)	0.52
	No	45	34 (65.4)	11 (78.6)		

Note. Symptomatic is defined as symptoms at time of testing in Japan (fever≥37.5C and/or respiratory symptoms) or/and any self-reported symptoms. *Fisher's exact test.

Figure 1

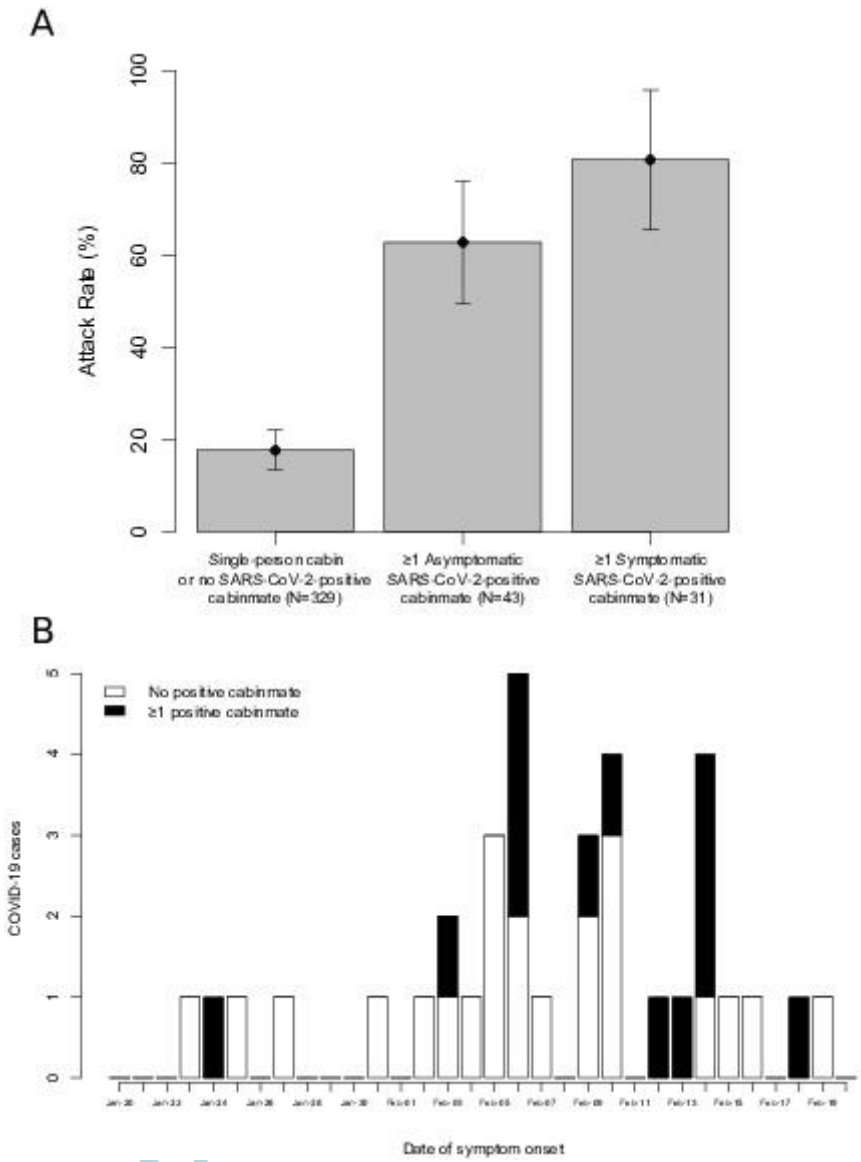

Figure 2

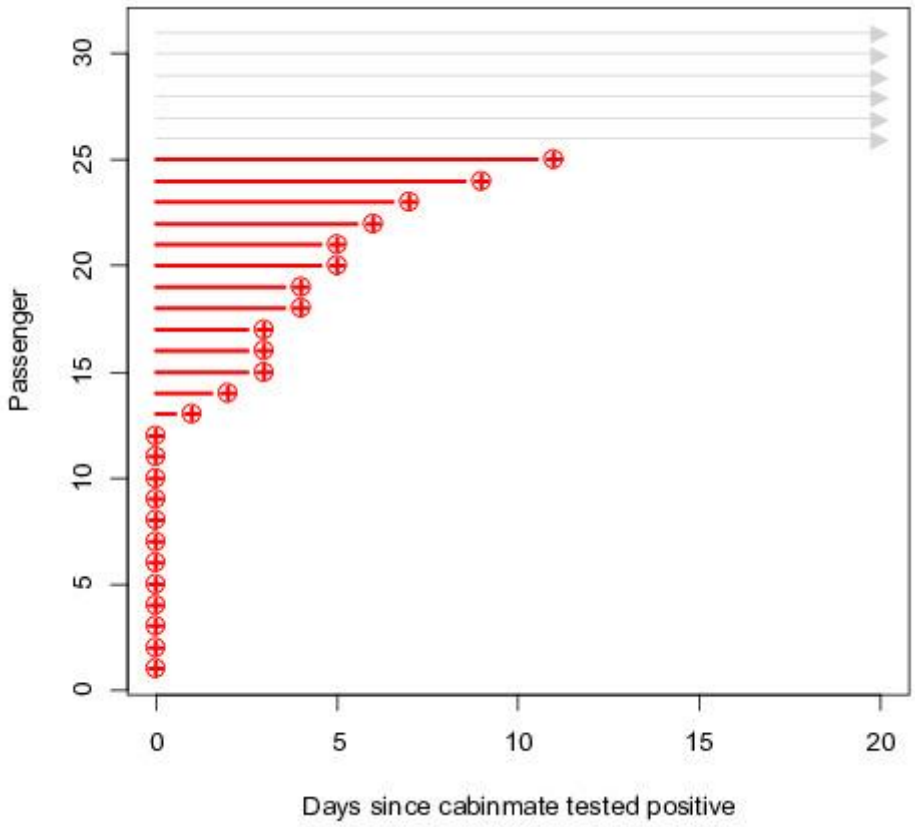

Figure 3