Interventional Study of Nonpharmaceutical Measures to Prevent COVID-19 Aboard Cruise Ships

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Cruise ships carrying COVID-19–vaccinated populations applied near-identical nonpharmaceutical measures during July–November 2021; passenger masking was not applied on 2 ships. Infection risk for masked passengers was 14.58 times lower than for unmasked passengers and 19.61 times lower than in the community. Unmasked passengers' risk was slightly lower than community risk.

In the summer of 2021, several European Union Member States (EUMS) and European Economic Area (EEA) countries gradually lifted COVID-19 public health measures and reopened borders. The easing of restrictions enabled cruise lines to resume operations, applying guidelines published by the EU Healthy Gateways Joint Action, the European Centre for Disease Prevention and Control, and European Maritime Safety Agency. We assessed the effectiveness of nonpharmaceutical measures (NPMs) by comparing COVID-19 incidence rates among EUMS and EEA communities and populations of cruise ships and applying different sets of measures.

The Study

We conducted an ecologic study in which cruise ships in group 1 (passenger and crew populations on 2 cruise ships, ships A and B) and group 2 (passenger and crew populations of 9 cruise ships) carrying vaccinated populations applied identical NPMs apart from face masking in passengers and physical distancing, which group 1 did not apply (*1*) (Table). The cruise ship company provided epidemiologic data and screening and diagnostic results for group 1 (Appendix, https://wwwnc.cdc.gov/EID/article/30/5/23-1364-App1.pdf). Ship captains or doctors reported epidemiologic data and screening and diagnostic results to competent health authorities and EU Healthy Gateways Joint Action (Appendix). Passenger populations changed in every cruise, but ≈6 passengers remained onboard the ship for >1 voyage. COVID-19 imposed severe crew change restrictions, and most crew remained the same during the study; the percentage of crew disembarking likely represented <0.5% of the crew population. We calculated COVID-19 incidence rates for the period of July–November 2021 for groups 1, 2, and 3 (EUMS communities). We obtained epidemiologic data for EUMS communities from the European Centre for Disease Prevention and Control website (*4*).

We calculated incidence rate ratios, standardized incidence ratios (SIRs), and 95% CI using the epiR package in R (*5*). We used Fisher's exact test to determine statistical significance. We considered $p<0.05$ statistically significant. We calculated SIRs for groups 1 and 2 by using epidemiologic COVID-19 data in EUMS and EEA countries during the study period as a reference population to calculate expected number of cases onboard (*4*) (Appendix).

The group 1 health measures protocol was reviewed and agreed upon by the Hellenic Ministry of Health's national COVID-19 taskforce. The study received approval from the University of Thessaly's Research Ethics Committee (protocol no. 103/16.11317 1.2021; decision no. 103/01.12.2021). Written consent for serologic testing was obtained from all crew members.

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DOI: https://doi.org/10.3201/eid3005.231364

The risk for COVID-19 infection in group 2 (masked passengers of 9 ships) was 14.58 (95% CI 7.799–28.361) times lower than risk for group 1 (unmasked passengers) and 19.61 (95% CI 18.86–34.48) times lower than in group 3 (EUMS community members). Infection risk for unmasked passengers in group 1 was lower than in the community (SIR 0.744, 95% CI 0.512–1.045; p = 0.094) (Appendix).

Conclusions

Our ecologic study demonstrated that COVID-19 infection risk among masked cruise ship passengers was 19.61 times lower than in the community (95% CI 18.86–34.48); the risk for infection among unmasked passengers was lower than in the community but not statistically significant (SIR 0.744, 95% CI 0.512–1.045; p = 0.094). Those findings suggest that NPMs implemented onboard the cruise ships were effective in reducing risk (*1*). Recent vaccination for the circulating variant appeared to contribute to reduced infection risk onboard ships, where vaccination coverage was almost 100%, compared with 66% cumulative vaccine uptake among the EUMS population (*3*). No outbreak occurred during the study period (group 1: median no. cases per voyage 1.00, range 0–15; group 2: median 0 cases per

Table. COVID-19 health measures, laboratory screening, and diagnostic testing for SARS-CoV-2 per comparison population group in interventional study of nonpharmaceutical measures to prevent COVID-19 aboard cruise ships*

Variable	Comparison population groups		
	Group 1: cruise ships A and B sailing in EUMS waters	Group 2: 9 cruise ships sailing in EUMS waters	Group 3: EUMS/EEA community populations
Mask wearing	Unmasked passengers, masked crew†	Masked passengers and crew	Policies varied
Physical distancing‡	N	Y	Policies varied
Daily body temperature measurement for passengers and crew	Y	Y	NA
Pre-embarkation health screening questionnaire for passengers and crew§	Y	Y	NA
Quarantine measures for close contacts of SARS-CoV-2–positive passengers and crew members	Y	Y	Yes
Buffet line allowed in food service areas¶	Y	N	NA
>95% passengers and crew members vaccinated#	Y	Y	Vaccine coverage varied in EUMS
Serologic testing for crew members	Y	N	NA
End of voyage reporting by cruise line to competent authorities for COVID-19 surveillance data	Y	Y	NA
Other NPMs: education and training; restrictions for population density, excursions, and port visit; policy enforcement	Y	Y	Policies varied**
Screening/diagnostic testing for crew members			
All crew members already onboard the cruise ship tested by RADT within 1 wk before resuming operations	Y	Y	NA
Day of embarkation RADT	Y	Y	NA
Routine RADT	Every 7 d	Every 7 d	Varied among EUMS
Screening/diagnostic testing for passengers			
Day of embarkation RADT	Y	Y	NA
RADT before disembarkation	Y	Y	NA
Nonvaccinated (or not fully vaccinated) passengers tested by RADT on day 3 or 4 of cruise††	Y	Y	NA

*See Appendix (https://wwwnc.cdc.gov/EID/article/30/5/23-1364-App1.pdf) for more detailed information about definitions and methods used in the study. EEA, European Economic Area; EUMS, European Union member states; NA, not applicable; NPM, nonpharmaceutical measures; RADT, rapid antigen detection test.
†All passengers wore masks on 1 voyage in which elevated number of cases occurred in cruise ship A.
‡Physical distancing of 1.5 m.
§Information collected included demographic information (name, date/time of itinerary, port of disembarkation, cabin number, contact telephone number for 14 d after disembarkation), health questions regarding the past 14 d (presence of COVID-19 compatible symptoms, close contact of COVID-19 case, and whether person provided care was in close proximity, traveled on conveyance, or shared household with SARS-CoV-2–positive person).
¶Group 1 ships provided meals as sitting service and in a buffet line with strict hand hygiene measures, sneeze-guards, replacement of serving utensils, and food service by crew. Group 2 ships provided meals in a sitting service and not in a buffet line. Both groups applied the same rules about handwashing, maximum number of persons in food service areas, and distancing of tables and chairs.
#Persons were considered fully vaccinated 14 d after the last dose of a COVID-19 vaccine.
**Other measures applied in the community: gathering restrictions with maximum capacities, masking and physical distancing in indoor public spaces (theaters, gyms), hybrid policies for education and workplace settings, and proof of vaccination or negative tests to attend events (*2*).
††During the study period, the cumulative vaccine uptake (%) in the total population in EUMS/EEA (group 3) was ≈66% for the primary course (*3*).

voyage, range 0–4). Of 44 close contacts of SARS-CoV-2–positive persons, 10 tested positive during quarantine, which could be attributed to protective effects of up-to-date vaccination for the circulating SARS-CoV-2 Delta variant. No deaths or severe cases were reported among the 11 cruise ships, despite the highly pathogenic nature of the Delta variant and older average age of cruise passengers.

Experimental studies in confined spaces demonstrated that masking is one of the most effective NPMs to prevent aerosol infection transmission (*6*). However, a systematic review of clinical trials in community settings and healthcare facilities demonstrated that wearing masks in the community likely makes little difference to outcomes compared with not wearing a mask (*7*). Masking in different settings (ships, hospitals, communities) might have different effects, however, the effectiveness of masking measures is likely influenced by how strictly those measures are enforced. During the pandemic, an absence of mask-wearing measures resulted in large outbreaks onboard ships (*8*,*9*). Our study demonstrated reduced COVID-19 incidence rates because of the protective effect of masking onboard ships. We suggest integrating use of high-filtration masks into routine case management, outbreak response measures, and preparedness and contingency planning for future public health emergencies of international concern. Crew members presented a lower infection risk than passengers and community populations, possibly because of mandatory mask use, recent vaccination, the strict enforcement of masking and vaccination policies, and reinforced education on symptoms and reporting requirements.

The first limitation of our study is that direct, individual observation of passenger and crew compliance was impossible in the uncontrolled environments of live cruises. The estimated case underreporting rates applied (1:4) were based on US data (February 2020–September 2021), but our study was implemented in Europe (July–November 2021), so differences could apply (*10*). The practice of 14-day quarantine and monitoring for disembarking passengers was applied only for close contacts of SARS-CoV-2–positive persons, so secondary cases could have been unidentified. We did not collect data on vaccination type, cabin occupancy, shore-based excursions, and onboard activities for the entire study population, so incidence rate differences for those factors could not be tested. Previous research of a COVID-19 cruise outbreak demonstrated that involvement in certain group activities (e.g., shows) and shore-based bus excursions were associated with infection, as well as a consistent dose-response relationship between number of cabinmates and attack rates in which attack rates decreased as passenger occupancy per cabin decreased (*11*,*12*). Alternative exposures, such as preembarkation queuing, social activities, contaminated surface contact, and common area use, deserve attention. Incubating passengers might not have been identified, but daily fever screening and diagnostic testing before boarding, during voyage, and before disembarking enhanced surveillance, reducing the possibility of undetected incubating COVID-19 cases (*1*). Strategies guaranteeing study protocol adherence were unfeasible on active voyages; however, enforcing company protocols and competent authority inspections maintained the intervention's fidelity. Use of buffet lines in group 1 might be a confounder, but both groups applied identical food service occupancy limits; fomite transmission was unlikely given strict hand hygiene measures, replacement of serving utensils, sneeze-guards, and food service by crew. The ship company uniformly applied and enforced clear policies in groups 1 and 2. That uniform application was impossible in group 3 (communities) because implementation policies varied: full or partial; national, regional, or local; mandatory or voluntary; and groups targeted (i.e., at-risk persons, healthcare workers, travelers). Topics for further research include cost-effectiveness of NPMs on cruise ships in the context of pandemics, public health emergencies of international concern or during respiratory illness outbreaks.

In conclusion, our ecologic study demonstrated the safe restart of cruise ship sector operations and indicated that mask use added an extra layer of protection; further studies should be conducted to verify the results. Masking should be considered in future public health emergencies when making decisions regarding NPMs and other measures that could interfere with international traffic and trade.

Acknowledgments

We wish to acknowledge the contribution of the Hellenic Ministry of Health's COVID-19 taskforce, the National Public Health Organization of Greece and the Biomedical Research Foundation, Academy of Athens, for the next-generation sequencing (NGS) analysis of positive samples. Moreover, we thank the ships' medical doctors and all ship officers and crew members for their contributions. We express our sincere thanks to the National Public Health Organization of Greece and to the President of the Biomedical Research Foundation, Academy of Athens, Dimitrios Thanos for the NGS analysis of positive samples.

Part of this research was conducted in the framework of the Healthy Sailing project which received funding from the European Union's Horizon Framework Programme under grant agreement no. 101069764. Moreover, part of this research was conducted in the framework of the EU Healthy Gateways Joint Action, which received funding from the European Union's Health Programme (2014–2020) under grant agreement no. 801493. The cost of laboratory testing (serological tests and rapid antigen detection tests conducted onboard ships) was covered by the cruise lines.

About the Author

Dr. Mouchtouri, an associate professor of hygiene and epidemiology at the University of Thessaly, is scientific manager of the European Union project Healthy Sailing and led the maritime transport work package of the European Union Joint Action Healthy Gateways. Her primary research interests include the prevention and control of cross-border health threats and public health aspects in maritime transport.

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Article DOI: https://doi.org/10.3201/eid3005.231364

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Appendix

Definitions and Methods

EU Healthy Gateways guidelines allowed medical mask or properly fitting respirator (FFP2) and, if unavailable, a non-medical "community" mask. When crew members or passengers were outside of their individual cabins, they had to use a facemask, exceptions included during eating and drinking. All crew members wore KN95/FFP2 facemasks (or equivalent) during the study period onboard Group 1 and 2 cruise ships. Passengers in Group 2 wore a medical mask or properly fitting respiratory protection (KN95/FFP2); however, if elevated numbers of COVID-19 cases were detected onboard, then all passengers were also provided with KN95/FFP2 (or equivalent) masks by the shipping company.

Recommendations for facemask use in communities and at points of entry (ports and airports) during the study period were as follows: ECDC recommended face mask use and physical distancing be continued when indoors (*1*). The US Centers for Disease Control and Prevention (CDC) advised that face mask use and physical distancing measures can be relaxed in indoor and outdoor settings applying to persons who are fully vaccinated if national/local regulations allow, but these measures should still be practiced by unvaccinated persons (*2*). At ports and airports during the study period, ECDC and EU HEALTHY GATEWAYS joint action recommended face mask use and physical distancing be continued when indoors (*1*,*3*). The use of face masks was mandated by the CDC at points of entry (e.g., airports) and on conveyances (aircrafts, rail, bus and public transportation) traveling inside, out of or into the U.S., with

exceptions for outdoor settings on conveyances. For any unvaccinated travelers, it was advised to maintain face mask use and physical distancing during travel (*2*).

Pre-embarkation questionnaires were administered by cruise line staff. Specific information collected included: demographic information (name, date/time of itinerary, port of disembarkation, cabin number, contact telephone number for 14 d after disembarkation), health questions regarding the past 14 d (presence of COVID-19 compatible symptoms, close contact of COVID-19 case, if provided care for COVID-19 case, if have been in close proximity or traveled on conveyance or shared household with a COVID-19 case).

A close contact of a COVID-19 case was defined as any person who had contact with a COVID-19 case within a timeframe ranging from 48 h before the onset of symptoms, of the case, or date of collection of a positive COVID-19 sample for an asymptomatic case, to 10 d after the onset of symptoms or date of collection of positive sample if asymptomatic. A: If a single or more cases sharing the same cabin have been identified onboard, then the following definitions of contacts should be applied: High-risk exposure (close) contact: A person who has stayed in the same cabin with a COVID-19 case. A person who had direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on). A crew member who entered the cabin of a case while they were inside the cabin, without wearing appropriate PPE. For example, a crew member who cleaned the cabin of a case or who delivered food to the cabin. A person who has had face-to-face contact (on-board or on-shore) within 1.5 m for more than 15 min or who was in a closed environment for more than 15 min with a case. For passengers this could include, but is not limited to, participating in common activities, attending a class or sharing the same social space such as at a restaurant. This also includes contact with intimate partners. For crew this may include working in the same area as a case or socializing with a case (including fellow crew members), waiting on a table where a case was dining or leading a social activity where the case was participating. Healthcare workers or other persons providing direct care for a case without wearing appropriate PPE. Low-risk exposure (casual) contact: Risk assessment of individual cases and their contacts will be conducted by the ship's medical staff and/or public health authorities to identify the low-risk exposure (casual) contacts. Any data available from contact tracing technologies should also be considered. B. If three or more confirmed cases who are staying in two or more different cabins and who are not traveling together (excluding the cases identified the day of embarkation): Risk assessment of individual cases and their contacts

will be conducted by the public health authorities and the ship as part of contact tracing. Risk assessments could identify additional contacts who are not under the categories listed in part "A" of the definition. Any data available from contact tracing technologies will also be considered. Local/national regulations, definitions and procedures could also apply as part of the contact tracing.

Cruise ship A and B crew members were tested with SARS-CoV-2 IgG II assay (Abbott, Illinois, USA) which is a chemiluminescent microparticle immunoassay (CMIA) for the semiquantitative measurement of IgG antibodies that target the receptor binding domain (RBD) of the S1 subunit of the spike (S) protein of SARS-CoV-2. In addition, for cruise ship B serum samples were analyzed for the qualitative detection of IgG antibodies with the same method, (CMIA), using the ABBOTT SARS-CoV-2 IgG assay (Abbott, Illinois, USA), that targets the nucleocapsid (N) virus protein.

The shipping company provided education and training for crew members in Groups 1 and 2 when joining the ship, and then regularly via refresher trainings. Content included recognizing COVID-19 signs and symptoms, procedures and importance of reporting symptoms and appropriate implementation of NPMs. Information strategies were applied onboard for passengers' education. Both Group 1 and 2 cruise ships applied the same restrictions about the maximum capacities of passengers and crew onboard, as well as the same restrictions for maximum occupancy of specific ship spaces (e.g., dining rooms, theaters). The maximum capacity per cabin was two crew members. The number of passengers was restricted to a maximum of four per cabin during the study period. Furthermore, the overall population allowed to travel on cruise ships was restricted. Group 1 and 2 cruise ships applied the same rules for the dining room setting regarding distancing of tables and chairs. During the study period, NPMs were incorporated into the shipping company policy, and were a condition for crew members to work and passengers to voyage. NPMs policy was fully enforced by the companies for both crew members and passengers through security staff, while for crew members there were penalties, and if non-compliant they were asked to disembark. Both passengers and crew members were instructed on proper use of facemasks by security staff. Shows, films in the cinema and other social events for passengers were allowed onboard, with precautions to prevent overcrowding by limiting numbers of participants.

Certain measures were recommended to be in place during port visits, shore-based activities and excursions including rigorous hand hygiene, use of facemasks, health screening and contactless temperature measurement upon re-boarding the ship and measures to reduce overcrowding and maintain appropriate physical distancing during embarkation/disembarkation and ashore. Shore/excursions staff were recommended to be trained in procedures if a possible COVID-19 case was identified. While traveling in groups it was to be ensured that passenger groups maintained physical distancing from other tour groups and that disembarking and embarking travellers (from different ships or from the same ship but different voyages) did not occupy the same enclosed or semi-enclosed areas (e.g., gangways, terminal waiting spaces, check-in areas) at the same time.

The type of RADT used could be any type of RADT listed in the document "Common list of COVID-19 rapid antigen tests, including those of which their test results are mutually recognized, and a common standardized set of data to be included in COVID-19 test result certificates" (*4*). All ships in both groups 1 and 2 used the same types of RADT. The standards for RADT selection that were used in the community (Group 3) were the same as the cruise ships, since all EU MS had agreed on the common list for RADT. In Group 1 cruise ships, specimens that tested positive with RADT were sent for reverse transcription polymerase chain reaction r (RT-PCR) analysis and for Next Generation Whole Genome Sequencing.

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Appendix Table 1. Results of statistical analysis among comparison Groups 1 and 2 for COVID-19 data, incidence rates and standardized incidence ratios using EUMS/EEA communities as a reference population*

Population and voyage characteristic	Group 1			Group 2, 9 cruise ships
	Cruise ship A	Cruise ship B	Total	
No. voyages	17	5	22	58
Median voyage duration, d (min, max)	7.00 (7.00, 14.0)†	7.00 (6.00, 12.0)†	7.00 (6.00, 14.0)	7.00 (3.00, 11.0)†
Total person-days (min, max)	96,194 (4,459, 11,312)	66,359 (9,486, 21,924)	162,553 (4,459, 21,924)	881,811 (5,379, 19,866)
Total passenger-days (min, max)	42,427 (1,561, 4,914)	32,428 (4,416, 11,676)	74,855 (1,561, 11,676)	529,029 (3,540, 13,419)
Total crew-days (min, max)	53,767 (2,884, 6,398)	33,903 (5,070, 10,248)	87,670 (2,884, 10,248)	352,740 (1,764, 12,768)
Median no. travelers, passengers and crew (min, max)	755 (637, 890)	1581 (1531, 1827)	786 (637, 1827)	2,097.5 (1,331, 2,838)
Median no. crew (min, max)	420 (412, 457)	845 (842, 854)	423.5 (412, 854)	875 (524, 1824)
Median no. passengers (min, max)	341 (223, 459)	736 (684, 973)	350.5 (223, 973)	1,204.5 (513, 1917)
Median percentage of vaccinated travelers onboard, crew and passengers (min, max)‡	100 (99.72, 100)	100 (100, 100)	100 (99.72, 100)	100 (NA, NA)
Median percentage vaccinated crew (min, max)	100 (99.27, 100)	100 (76.25, 100)	100 (76.25, 100)	92.57 (41.61, 100)
Median percentage vaccinated passengers (min, max)	100 (100, 100)	100 (100, 100)	100 (100, 100)	100 (100, 100)
SARS-CoV-2 Spike IgG–positive, (<50 AU/mL)/ total tested (%)	434/436 (99.50)	225/225 (100.00)	659/661 (99.70)	NT
Antinucleocapsid IgG–positive (>1.40 index)/ total tested (%)	Not tested	36/225 (16)	36/225 (16)	NT
SARS-CoV-2–positive by RT-PCR (next generation whole genome sequencing result)	21/27 (9 Delta variant [AY lineages])			NT
Epidemiologic rates				
Total no. cases	31§	5¶	36	21#
Cases among crew (%)	3 (9.68)	0 (0)	3 (8.33)	5 (23.81)
Cases among passengers (%)	28 (90.32)	5 (100)	33 (91.67)	16 (76.19)
Median no. cases (min, max)	1.00 (0, 15.0)**	1.00 (0, 4.00)	1.00 (0, 15.0)	0 (0, 4.00)
Median no. cases in crew (min, max)	0 (0, 2.00)	0 (0, 0)	0 (0, 2.00)	0 (0, 2.00)
Median no. cases in passengers (min, max)	1.00 (0, 13.0)	1.00 (0, 4.00)	1.00 (0, 13.0)	0 (0, 4.00)
Total no.voyages with ≥1 case (%)	12 (70.59)	2 (40)	14 (63.64)	13 (22.41)
Incidence rate (95% CI)	0.322 (0.219–0.457)	0.075 (0.024–0.176)	0.221 (0.155–0.307)	0.024 (0.015–0.036)
Passenger incidence rate (95% CI)	0.660 (0.439–0.954)	0.154 (0.050–0.360)	0.441 (0.303–0.619)	0.030 (0.017–0.049)
Crew incidence rate (95% CI)	0.056 (0.012–0.163)	0 (0.000–0.110)	0.034 (0.007–0.100)	0.014 (0.005–0.033)

Population and voyage characteristic	Group 1			Group 2, 9 cruise ships
	Cruise ship A	Cruise ship B	Total	
Passenger SIR (observed/expected cases) (95% CI)††	–	–	0.744 (33/44) (0.512–1.045)	0.051 (16/313) (0.029–0.083)
Crew SIR (observed/expected cases) (95% CI)††	–	–	0.058 (3/52) (0.012–0.169)	0.024 (5/209) (0.008–0.056)
Characteristics of cases				
Fully vaccinated cases (%)	31 (100.00)	7 (100.00)	38 (100.00)	13 (61.90)
Symptomatic at time of diagnosis (%)	20 (64.51)	1 (14.29)	21 (55.26)	5 (23.81)
Symptomatic after diagnosis (%)	NA	1 (14.29)	1 (2.63)	4 (19.05)
Day case was detected				
Day of embarkation testing (%)‡‡	0	2 (28.57)	2 (5.26)	5 (23.81)
Mid-cruise/before disembarkation testing (%)	20 (64.52)	4 (80.00)	24 (63.16)	6 (28.57)
Tested after showing symptoms (%)	10 (32.26)	1 (20.00)	11 (28.95)	1 (4.76)
Crew routine 7-d testing (%)	1 (3.23)	0	1 (2.63)	5 (23.81)
Crew initial testing (%)	0	0	0	0
Close contact testing (%)	0	0	0	0
Close contacts				
Close contacts identified (crew)	3	14	17	24
Close contacts identified (passengers)	21	6	27	36
Mean no. close contacts per case (min, max)	0.797 (0, 1.0)	3.875 (3.75, 4.00)	1.308 (0, 4.0)	2.85 (0, 10.0)
Close contacts quarantined ashore (crew)	0	0	0	7
Close contacts quarantined ashore (passengers)	1	3	4	23
Close contacts that became positive (crew)	0	0	0	0
Close contacts that became positive during quarantine (passengers)	0	0	0	10

*NT, not tested; SIR, standardized incidence ratio; –, not applicable.
†Cruise ship A: 16 voyages had 7-d duration, 1 voyage had 15-d duration. Cruise ship B: 1 voyage had 6-d duration, 2 voyages had 7-d duration, 1 voyage had 8-d duration, and 1 voyage had 14-d duration. Group 2: 1 voyage had 3-d duration, 1 voyage had 4-d duration, 2 voyages had 6-d duration, 48 voyages had 7-d duration, 3 voyages had 10-d duration, and 3 voyages had 11-d duration.
‡During the study period, all passengers and crew members were required to be vaccinated as a condition to board cruise ships.
§1 voyage with 15 cases, 1 voyage with 3 cases, 3 voyages with 2 cases, and 7 voyages with 1 case.
¶1 voyage with 4 cases, 1 cruise with 1 case.
#1 voyage with 4 cases, 1 voyage with 3 cases, 3 voyages with 2 cases, and 8 voyages with 1 case.
**In response to the voyage with an elevation in case counts (n = 15), face masking by all passengers onboard during the voyage was required as a response measure.
††Reference population: COVID-19 incidence rate in European Union Member States/European Economic Area countries during the study period multiplied by 4 to reflect the actual incidence rate (assuming that 1 in 4 cases were reported).
‡‡Two cases in cruise ship B and 5 cases in Group 2 cruise ships were diagnosed on day of embarkation testing. These persons were not allowed to embark, and therefore were not included in the analysis.

Appendix Table 2. Incidence rate ratios (Group 1 vs Group 2) for passengers

Starting month of voyage	Number of cases		Time at risk, d		Incidence rate, cases/1,000-person days (95% CI)		Incidence rate ratio (95% CI)	p value
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
July	2	4	10,402	100,437	0.192 (0.023–0.695)	0.040 (0.011–0.102)	4.828 (0.437–33.686)	0.102
August	8	8	25,302	221,986	0.316 (0.137–0.623)	0.036 (0.016–0.071)	8.773 (2.870–26.817)	<0.001
September–October	23	4	40,957	218,646	0.562 (0.356–0.843)	0.018 (0.005–0.047)	30.696 (10.488–122.109)	<0.001
July–October	33	16	74,855	529,029	0.441 (0.303–0.619)	0.030 (0.017–0.049)	14.576 (7.799–28.361)	<0.001

Appendix Table 3. Incidence rate ratios (Group 1 vs. Group 2) for crew members*

Starting month of voyage	Cases		Time at risk, d		Incidence rate (95% CI)†		Incidence rate ratio (95% CI)	p value
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2		
July	0	2	14,630	112,252	0.000 (0.000–0.252)	0.018 (0.002–0.064)	NaN	0.999
August	1	3	32,363	141,674	0.031 (0.001–0.172)	0.021 (0.004–0.062)	1.459 (0.028–18.174)	0.561
September–October	2	0	43,589	117,826	0.046 (0.006–0.166)	0.000 (0.000–0.031)	NaN	0.073
July–October	3	5	87,670	352,740	0.034 (0.007–0.100)	0.014 (0.005–0.033)	2.414 (0.375–12.408)	0.201

*NaN, not a number (indicating number of cases was 0 in 1 of 2 groups).
†Incident rate = cases/1,000-person days.

Appendix Table 4. Standardized Incidence Ratios using the European Union Member States/ European Economic area countries as the reference population*

Population group	Observed cases	Expected cases	Standardized incidence ratio (95% CI)	p value
Group 1 passengers	33	44.344	0.744 (0.512–1.045)	0.094
Group 1 crew members	3	51.936	0.058 (0.012–0.169)	<0.001
Group 2 passengers	16	313.399	0.051 (0.029–0.083)	<0.001
Group 2 crew members	5	208.965	0.024 (0.008–0.056)	<0.001
Groups 1 and 2	57	618.68	0.092 (0.067–0.119)	<0.001

*During the study period, 8,455,007 COVID-19 cases were reported in EUMS/EEA countries. The EUMS/EEA countries' total population was 453,090,377 and the study duration was 126 d, which corresponds to 57,089,387,502 person-days. Thus, incidence in the EUMS/EEA community population for the study period was 0.148 per 1,000 person-days. COVID-19 case detection methods in the cruise ship populations (Groups 1 and 2) were intensified through regular, documented RADT screening conducted by healthcare staff, which did not take place in the community (Group 3). Therefore, undetected and underreporting of COVID-19 cases in the community population was expected. To overcome underestimation of COVID-19 incidence rates in the community due to undetected or unreported cases, the number of reported COVID-19 cases in the community was multiplied by four, as the US Centers for Disease Control and Prevention estimated that from February 2020–September 2021, one in four COVID–19 infections were reported (95% uncertainty interval 3.4–4.7) (*5*). In our study, SIR was calculated using 33,820,028 as the total number of COVID-19 cases in EUMS/EEA countries (estimated community incidence rate: 0.592 per 1,000). EUMS/EEA, European Union Member States/European Economic Area; RADT, rapid antigen detection test.

Appendix Table 5. Type of vaccines for crew members for group 1

Type of Vaccine	Ship A no. crew members (%), n = 437	Ship B no. crew members (%), n = 864
Pfizer	382 (87.4)	39 (4.5)
AstraZeneca	37 (8.5)	314 (36.3)
Johnson & Johnson	6 (1.4)	371 (42.9)
Sinopharm	3 (0.7)	1 (0.1)
Moderna	2 (0.5)	13 (1.5)
CoronaVac (SinoVar)	3 (0.7)	124 (14.5)
Pfizer AZ	4 (0.8)	2 (0.2)