

A SARS-CoV-2 Omicron outbreak among crew members on a cruise ship in Germany in early 2022

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ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreaks on cruise ships have rarely been investigated. In early 2022, we were informed about a SARS-CoV-2 outbreak on a cruise ship calling Port of Hamburg after 10 infections among crew members were detected. We conducted an outbreak investigation in collaboration between ship owners, the ship physician and Hamburg's Institute for Hygiene and Environment, to identify risk factors and to achieve containment. The aim was to identify risk factors for SARS-CoV-2 infection and SARS-CoV-2 variants in a cohort of 165 crew members.

Materials and methods: For this purpose, we collected data on age, sex, nationality, boarding-time, cabin use (single/shared), work place, and vaccination status of the study participants. Cases were defined as individuals who tested SARS-CoV-2 positive at least once in daily screenings during the outbreak period (10 days) by polymerase chain reaction or antigen test. We investigated risk factors for infection by descriptive, univariable and multivariable analysis. We performed whole genome sequencing to identify SARS-CoV-2 variants. **Results:** We verified 103 SARS-CoV-2 positive cases (attack rate [AR] 62.4%); 39/41 sequenced samples were BA.2.3 Omicron subtype, one BA.1 and one BA.1.1. Among boostered crew members, AR was 38% vs. 65% among those vaccinated once or twice. Among those who stayed < 30 days on board, AR was 31% vs. 72% among those staying on board longer. Among Europeans, the AR was 53% vs. 71% in non-Europeans. Adjusting for age and sex, cases were more likely to have received no booster vaccine (odds ratio [OR]: 2.66, 95% confidence interval [CI]: 0.99–7.13), to have spent more time on board (≥ 30 days, OR: 6.36, 95% CI: 2.81–14.40 vs. < 30 days) and to have a non-European nationality (OR: 2.14, 95% CI: 1.08–4.27). The outbreak stopped shortly after offboard isolation of cases.

Conclusions: This investigation confirms the importance of a booster vaccine against COVID-19. Longer stays onboard could facilitate social mixing. Further studies could investigate the impact of social, cultural/behavioural patterns and public health access on the infection risk. Physical distancing together with screening and isolation can contain SARS-CoV-2 outbreaks on cruise ships.

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Keywords: crew, cruise ship, Omicron, outbreak, SARS-CoV-2

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INTRODUCTION

In the wake of the coronavirus disease 2019 (COVID-19) pandemic, cruise calls were shut down. In summer 2021, industry representatives, politicians, port authorities, municipal and local public health authorities agreed on common guidelines for cruises. As a result, cruise operations reopened stepwise.

The setting on board can be favourable for outbreaks of communicable diseases. Various factors contribute to this circumstance: limited space, gathering and mixing of people from different regions and countries, particular ventilation systems, limited diagnostic resources and isolation/quarantine capabilities on board, to name a few [1, 2]. Influenza-like illness beside gastrointestinal diseases have been the most commonly documented causes for outbreak situations on board of ships, followed by vaccine-preventable diseases such as chickenpox. Bacterial infections caused by Escherichia coli, Salmonella, or Legionella species have also been reported [3-6]. Infectious disease outbreaks on ships often require immediate medical and public health assessment and response. The investigations as well as the communication between all involved people on board and ashore are extremely time- and resource-demanding, and require a high degree of coordination.

Previous outbreak events on cruise ships, such as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak on board of the Diamond Princess in February 2020, underline the importance of conducting early outbreak investigation and public health response [7]. SARS-CoV-2 outbreaks on cruise ships have rarely been investigated [1, 8]. We assume that the absolute number and dimensions of such events are largely underreported. Coordinated scientific research, however, is scarce since public health services are confronted with several challenges [9–11]:

- the pandemic has overstressed the capacity of public health institutions and often did not allow outbreak investigations in selected settings;
- connection and communication barriers between different ent stakeholders and competent authorities in different areas of responsibility and jurisdiction at a national and international level leave limited possibilities for outbreak investigations;
- as passengers and crew members usually travel to their respective homes, they are often difficult to follow-up after disembarkation.

Those difficulties are illustrated in a study by Gravningen et al. [10]. Four crew members of a Norwegian expedition cruise ship were tested positive for SARS-CoV-2 after the voyage. The majority of the passengers had already disembarked and the public health authorities had difficulties reaching out to the passengers afterwards [10]. We conducted an outbreak investigation among crew members in the Port of Hamburg in collaboration with ship owners, the ship's physician and Hamburg's Institute for Hygiene and Environment (HU), to identify risk factors for infection and to contribute to a better understanding of outbreak situations and containment strategies on board of a cruise ship.

We used epidemiological methods and genome sequencing to map transmission chains and the dynamics of the outbreak. We determined risk factors and their constellations that increase the infectious hazard by statistical methods.

No exact cruise dates can be mentioned in this manuscript as these would make the cruise ship identifiable.

OUTBREAK SITUATION

Early 2022 a cruise ship left the Port of Hamburg to a 14-day voyage along the Norwegian coast with 165 crew members and 175 passengers on board. A rapid antigen test was negative in all passengers prior to boarding. Serial antigen tests of crew members were conducted on a weekly basis, according to the company's regulations. In addition, on day 1 of the voyage, SARS-CoV-2 antigen tests were conducted for all crew members and passengers as it was required by Norwegian entry regulations. All tests were negative.

On day 3 of the journey the ship was informed about positive SARS-CoV-2 tests in two crew members, who had left the ship prior to the ship's departure from Hamburg. As a consequence, all crew members were screened for infection by antigen test on the same day. The results showed 10 positive cases that were further confirmed using an onboard polymerase chain reaction (PCR) device. In the evening, the Hamburg Port Health Centre (HPHC) at the HU was informed about the outbreak. The HPHC is the competent authority for Public Health events on points of entry in Hamburg, Germany, according to International Health Regulations [11]. At this moment the vessel was located in the Norwegian Sea. The ship discontinued its journey and returned to Hamburg.

All positively tested persons were immediately isolated in individual cabins. Furthermore, a total of 7 close contacts to the positive cases were identified by the ship's physician and these were also isolated in individual cabins. For casual contacts, a 'working-quarantine' was ordered which included consistently wearing FFP2-masks (KN95), eating meals separately from others, and daily antigen testing. The number of isolation cabins on board was sufficient at the time of the initial notification.

MATERIALS AND METHODS OUTBREAK INVESTIGATION

The outbreak was investigated in collaboration between ship owners, the ship's physician and Hamburg's Institute

for Hygiene and Environment, including its HPHC, the Division of Hygiene and Infectious Diseases, the Division of Microbiology and the Next-Generation Sequencing (NGS) Laboratory. We collected data on age, sex, nationality, boarding time, cabin use (single/shared), work place, and vaccination status in a cohort of 165 crew members.

Definition of cases

Cases were defined as individuals who tested SARS--CoV-2 positive at least once during daily screenings during the outbreak period (days 1 to 10) by a PCR or antigen test.

Definition of vaccination status

Following the recommendations of the Robert Koch Institute valid at the time [12], crew members were categorised as having received one SARS-CoV-2-vaccination if they had received one dose of an mRNA- or vector-based vaccine. Vaccines without licensure in the European Union were not considered. The term "fully vaccinated" was further defined as having received two doses of an mRNA- or vector-based vaccine (incl. 1 dose Janssen® plus 1 dose mRNA vaccine). A "boostered" person was defined as someone having received two vaccine doses plus an mRNA-based vaccine dose. Shortly before departure and in the early days of the trip (day 0 and day 3), vaccination events were conducted for crew members. The vaccinations administered during these events were excluded from being categorised as "fully vaccinated" or "boostered" due to the short time span between the time of this vaccination and the detection of the outbreak under the presumption that immunisation was not yet achieved [13].

Statistical analysis

We calculated the SARS-CoV-2 attack rates among crew members for different risk factors and compared them by chi-squared test, Fisher's Exact test, or Mann-Whitney U test, as applicable. Logistic regression was used for univariable and multivariable analysis. Three separate multivariable regression models were built for three variables to adjust for age and sex. The three variables were chosen based on their a) statistical significance associated with becoming SARS-CoV-2 positive in the descriptive analysis and in the univariable model; and b) on their epidemiologically most plausible cause for becoming infected. Due to strong collinearity, it was not possible to include all potential risk factors in one final model. Analyses were carried out using Stata/IC 17.0 (Stata Corp, Texas, USA).

Sequencing

For whole-genome sequencing of SARS-CoV-2, only samples with a cycling threshold (Ct) \leq 25 were chosen. RNA and DNA concentration of 45 samples were tested before and after a DNase digestion. The samples were

prepared for sequencing following the Illumina[®] RNA Prep with Enrichment, (L) Tagmentation kit (Illumina, Inc., San Diego, CA, USA) according to the manufacturer's instructions. The sequencing was performed on an Illumina MiSeq with a reading length of 150 bp (paired-end).

The raw paired sequencing reads were quality checked, with a minimum base quality of 30, and aligned with bwa v0.7 [14]. Sorting, duplication and indel realignment were performed by using Samtools v.1.6 [15] and Picard v.2.27.4 [16]. Consensus sequences were built using bcftools v1.15.1. Pangolin v4.1.2 was used for lineage [17]. To detect transmission chains, the resulting consensus sequences were used as input for further analysis with Snippy v4.4.3 and Snippy-snake v1.0.0 [18, 19]. All sequences were uploaded on GISAID (www.gisaid.org, access date 12/2022) and are available under the accession numbers EPI_ISL_16188009 - EPI_ISL_16188049.

ACTIONS AND MEASUREMENTS SARS-CoV-2 testing

Tests on board were performed by the medical staff (ship's physician and nurses). Two types of antigen test were used: SARS-CoV-2 rapid antigen test by Roche and MEDsan. The use of the onboard PCR device was abandoned with an increasing number of cases. As the PCR device turned out to show contradictory results, it was questionable whether it was suitable for use at sea. Furthermore, the device was not purchased for use in large quantities. After the return to the Port of Hamburg, all passengers were tested before disembarkation via SARS-CoV-2 rapid antigen test (MEDsan) in collaboration with the ship's medical staff and the Hamburg Port Health Authority. Serial swab tests and PCR analyses of the entire crew were carried out upon arrival by a shore-based laboratory.

Isolation and quarantine

All passengers disembarked on the return day (day 5) and were tested by rapid antigen test ashore. Crew members who were not essentially needed for the ship's safety on board also disembarked (84 persons in total) on the day of return and were isolated/quarantined in a hotel ashore. In accordance to the German recommendations valid at the time, quarantine and isolation measures were ended for persons remaining asymptomatic, after at least 7 days subject to a negative test result [20].

RESULTS

OUTBREAK MANAGEMENT

On the day of arrival in Hamburg (day 5), 41 of the 165 crew members tested positive cumulatively by antigen test on board; there were no reports of infections among the 175 passengers. In the serial swab of all crew members

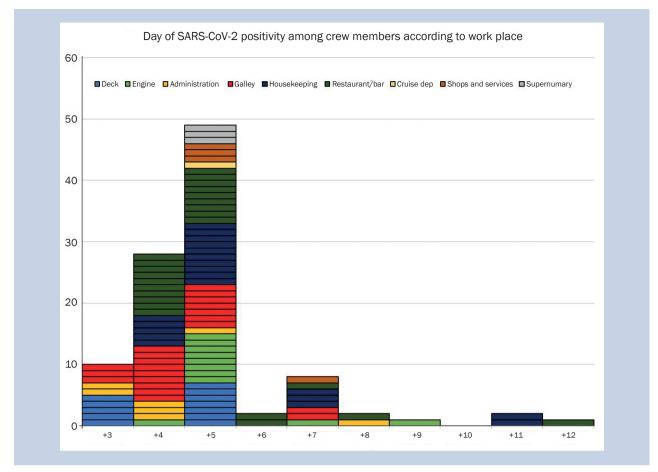


Figure 1. Timeline and number of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive tests among crew members by days and according to workplace during a SARS-CoV-2 outbreak among crew members on a cruise ship in early 2022. Exact dates are not shown for data protection reasons. Antigen-testing of all crew members on day +3 and +4. On arrival at Port of Hamburg (day +5) PCR tests were conducted on all crew members

performed on arrival, 82 of 165 PCR tests were found to be positive for SARS-CoV-2.

After the quarantine/isolation off-board, the number of new cases decreased considerably (Fig. 1). In total, the outbreak among crew members included 103 cases and lasted 10 days.

All passenger tests were negative and the passengers were able to continue their journey home after they were advised to monitor themselves for symptoms and report them to their regional public health administration.

OUTBREAK INVESTIGATION Statistical analysis

One hundred and three SARS-CoV-2 cases among crew members were identified over a course of 10 days (attack rate [AR] 62.4%; Table 1). The majority (n = 87) of cases tested positive on 3 consecutive days: 3 to 5 of the journey (Fig. 1). Day 5 was the day of return to the Port of Hamburg, and represents the shore-side laboratory PCR test results. The median age was comparable in SARS-CoV-2 positive and SARS-

-CoV-2 negative crew members (36 vs. 38 years, p = 0.45; Table 1). The AR did not differ significantly between males and females (65.3% vs. 53.7%, p = 0.18).

Among crew members who had received a vaccine booster dose, the AR was 38% vs. 66% among those who had only been vaccinated once or twice (p = 0.014). Among those with a stay of less than 30 days on board, the AR was 31% vs. 72% among those staying on board 30 days or longer (p < 0.001). The AR was 53% in Europeans vs. 71% in non-Europeans (p = 0.016). Between work places, the AR differed significantly (p = 0.003), with a notably low AR in the cruise department (9%). In univariable analysis, the risk of infection was only significantly lower in the cruise department compared to working on deck, which was defined as the reference category (odds ratio [OR]: 0.06, 95% confidence interval [CI]: 0.01-0.56, p = 0.014; Table 2). There was no significant difference for all other work places (Table 2). Crew members working in the cruise department also had high coverage of vaccine booster doses, they were all European and predominantly stayed less than 30 days on board (data not shown).

Characteristics		N	SARS-CoV-2 positive	SARS-CoV-2 negative	Attack rate (%)	P value
Crew members overal	I	165	103	62	62.4	
Sex	Male	124	81	43	65.3	0.18*
	Female	41	22	19	53.7	
Age median (range)		NA	36 (23-61)	38 (20-66)	NA	0.45#
Nationality	Europe	76	40	36	52.6	0.016§
	Other	89	63	26	70.8	
Work place	Deck	19	12	7	63.2	0.003 [§]
	Engine	20	11	9	55.0	
	Administration	9	7	2	77.8	
	Galley	27	21	6	77.8	
	Housekeeping	26	20	6	76.9	
	Restaurant/bar	38	24	14	63.2	
	Cruise department	11	1	10	9.1	
	Shops and services	6	4	2	66.7	
	Supernumerary	9	3	6	33.3	
Cabin use	Alone	55	29	26	52.7	0.069*
	With a cabin mate	110	74	36	67.3	
Vaccination status	One or two doses**	144	95	49	66.0	0.014*
	Booster**	21	8	13	38.1	
Time on board in	< 30 days	39	12	27	30.8	< 0.001
categories	≥ 30 days	126	91	35	72.2	

 Table 1. Baseline characteristics in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive and SARS-CoV-2 negative crew members in a SARS-CoV-2 outbreak on a cruise ship in early 2022

[#]Mann Whitney U test; [§]Fisher Exact test; ^{*}Chi-squared test; ^{**}One dose: one dose of any mRNA or vector-based vaccine, two doses: two doses of any mRNA or vectorbased vaccine (incl. 1 dose Janssen plus 1 dose mRNA vaccine), booster (two doses plus an mRNA-based vaccine). Vaccines without licensure in the EU (e.g. Sinovac) were not considered; NA – not available

There was some evidence that the AR was higher in crew members sharing a cabin than in those with a cabin of their own (67% vs. 53%, p = 0.069). Also, among those sharing a cabin, 95% had not received a booster vaccine dose, 73% had a non-European nationality, and 83% stayed 30 or more days on board.

Adjusting for age and sex, cases were more likely to have received no booster vaccine (OR: 2.66, 95% CI: 0.99-7.13), to have spent more time on board (\geq 30 days, OR: 6.36, 95% CI: 2.81–14.40 vs. < 30 days) and to have a non-European nationality (OR: 2.14, 95% CI: 1.08–4.27).

Laboratory analysis

A shore-based laboratory performed SARS-CoV-2 PCR analysis of the 165 swab samples taken from the crew members after the arrival in Hamburg. The extracted nucleic acids of 82 SARS-CoV-2 positive tested samples were sent to the NGS Laboratory (Institute for Hygiene and Environment, Hamburg, Germany) to identify SARS-CoV-2 variants and possible transmission chains by sequencing. Hence, 45 samples were sequenced and only 41 samples showed high quality reads which then were further analysed. The Pangolin classification revealed that 39 consensus sequences are related to Omicron subtype BA.2.3, one sequence to BA.1.1 and one sequence to BA.1.18. The BA.2.3-related sequences show a high similarity in a single nucleotide polymorphism analysis (Fig. 2).

DISSCUSION

OUTBREAK INVESTIGATION

The majority of cases on board were related to a larger Omicron subtype BA.2.3 outbreak. However, other smaller outbreaks cannot be ruled out (as two sequences were classified as subtypes of BA.1). However, BA.1 is less transmissible compared to BA.2.3, which might have an effect on the outbreak situation on the ship [21].

Due to the possibility to analyse only half of the positive samples by sequencing, transmission chains and sources cannot be completely verified.

Characteristics		Odds ratio (95% CI)	P value
Sex	Male	1.63 (0.79-3.33)	0.18
	Female	Baseline	
Age [years]		0.98 (0.95-1.01)	0.26
Nationality	Europe	Baseline	
	Other	2.18 (1.15-4.14)	0.017
Work place	Deck	Baseline	
	Engine	0.71 (0.20-2.57)	0.61
	Administration	2.04 (0.33-12.69)	0.44
	Galley	2.04 (0.56-7.50)	0.28
	Housekeeping	1.94 (0.53-7.17)	0.32
	Restaurant/bar	1 (0.32-3.13)	0.99
	Cruise department	0.06 (0.01-0.56)	0.014
	Shops and services	1.17 (0.17-8.09)	0.88
	Supernumerary	0.29 (0.06-1.55)	0.15
Cabin use	Alone	Baseline	
	With a cabin mate	1.84 (0.95-3.57)	0.070
Vaccination status	One or two doses*	Baseline	
	Booster*	0.32 (0.12-0.82)	0.017
Time on board in categories	< 30 days	Baseline	
	≥ 30 days	5.85 (2.67-12.81)	< 0.001

 Table 2. Association of different risk factors with becoming severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive during a SARS-CoV-2 outbreak among crew members on a cruise ship in early 2022

Univariate analysis – logistic regression; ^{*}One dose: one dose of any mRNA or vector-based vaccine, two doses: two doses of any mRNA or vector-based vaccine (incl. 1 dose Janssen plus 1 dose mRNA vaccine), booster (two doses plus an mRNA-based vaccine). Vaccines without licensure in the EU (e.g. Sinovac) were not considered; CI – confidence interval

Our investigation shows that not receiving a COVID-19 vaccine booster dose, longer stays on board and a non-European nationality were associated with a higher risk of SARS-CoV-2 infection during an Omicron outbreak among crew members of a cruise ship. A longer stay on board could be an indicator for more social contacts and therefore mixing on board.

Although working in the cruise department appears to be associated with a lower risk of infection in the univariable analysis — and one may hypothesize that this group worked and socialised separately from the other groups — we could not confirm this theory in interviews. It was reported that social mixing occurred between crew members working in different places. Furthermore, the low infection risk in the cruise department group could also be explained by the high booster vaccine coverage, all members of the crew department being European and their short stays on board. We therefore believe that different work places were not an independent risk factor for SARS-CoV-2 infection on this cruise ship. Why would non-Europeans have a higher risk of SARS--CoV-2 infection? We found statistical correlations between the nationality, boarding-time, cabin use (single/shared), work place, and vaccination status, which may all influence the risk of an infection but also have an influence on each other.

The vaccination rate with a booster dose (which was 2% among non-European vs. 25% among European crew), for example, could be a reason for a higher risk of an infection among the non-European crew members. It is unknown whether social, cultural and behavioural patterns or a limited access to relevant public health information may be associated with different infection risks in Europeans and non-Europeans.

A reason for the differences in vaccination rates might be different access to COVID-19 vaccines for those crew members staying on board for a longer period (non-European crew members usually have longer contracts compared

5A.	ID	1	2	3	4	5		6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	REF
2.3	1		0	0	0	0	(0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	2	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	64
2.3	3	0	0		0	0	(0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	64
2.3	4	0	0	0		0	(0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	64
2.3	5	0	0	0	0		(0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	6	0	0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	7	0	0	0	0	0	(0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	8	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	9	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	10		0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	11	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	12		0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	13		0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	Ó	0	Ó	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	14		0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	64
2.3	15		0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	16		0	0	0	0	(0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	17		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
.3	18		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
.3	19		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	20		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	21		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	22	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	23		0	0	0	0	9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	1.00
2.3	24		0	0	0	0	(0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	25		0	0	0	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	100
2.3	26		0	0	0	0	9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	27		0	0	0	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	0	0	0	0	0	0	0	0	1	1	1	1	45	44	
.3	28		0	0	0	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	1	1	1	1	45	44	
2.3	29 30		0	0	0	0	9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	0	0	0	0	0	0	1	1	1	1	45	44	5
.3	30		0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	1	1	1	1	45 45	44 44	50
2.3	31		0	0	0	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45 45	44	
2.3	32	0	0	0	0	0	-	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	45 45	44	
2.3	33		0	0	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		1	1		45 45	44	1.51
2.3	34		0	0	0	0			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		1	1	1	45 45	44	
2.3	35		0	0	1	0		1	1	1	1	0	1	1	0	0	0	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	4	1	2	2	1	45	44	
2.3	36		1	1	1	1			4	1	1	1	1	-	1	1	1	1	1	-	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	46	45	
2.3	37		1	1	1	1		4	4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	-		1	1	1		1	1	1		-	1	1	2	2	2	2	46	45	
2.3	38		1	1	1			4	4	1	1	1	1	1	1	1	1		1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	-	2	46	45	
	39		45	45	1	1		1	45	45	45	1	1	1	45	45	1	1	45	45	45	45	1	45	45	45	45	45	45	45	45	45	45	45	45	45	45	46	46	2 46	46	46	45	64
.1	40				45	45	4	- Gi	40	40	45	40	45	45			45	40					45					40				45	45	45	45 44	45	40		46 45	46 45	46 45	9	9	64
.18	41 REF		44 64		44 64				44 64	45 65	45 65	45 65	45 65	57	56																													
	REF	64	64	64	64	64	6	94	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	64	65	65	65	65	5/	26	<u>. </u>

Figure 2. Single nucleotide polymorphism (SNP) matrix of the sequenced samples during a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak among crew members on a cruise ship in early 2022. Consensus sequences were used as input for further analysis with Snippy v4.4.3 and Snippy-snake v1.0.0 with default settings. Each sample is compared to every sample and reference sequence (NC_045512) concluding in a matrix with SNPs differences. Colours were depicted by the authors describing sequences with 0 SNP differences (green), with low SNP differences (yellow) and high SNP differences (orange, red). Pangolin lineage declaration is shown for each sample.

to European crew members) and for those coming from non-European countries (mRNA vaccines were not available in all countries).

There is an inconsistent international definition of the term "fully vaccinated", which results in an incongruent vaccination status of the crew on board. The company's regulations define the receipt of a single Janssen vaccine dose as being "fully vaccinated". This practice reflects the broad routine in the maritime sector. However, German requirements based on the Robert Koch Institute recommendations specify an additional mRNA vaccine for completion of the vaccination protection.

This investigation indicates that the number of vaccinations may affect the individual risk of infection. One important intervention to avoid future SARS-CoV-2 outbreaks among crew members could be to make sure that all crew members are up-to-date with their vaccination status well before starting their contract.

OUTBREAK MANAGEMENT

After the sudden emergence of 10 positive cases, the ship's master decided to interrupt the voyage and re-

turn to the Port of Hamburg. Even though immediate actions were taken by the ship's physician (isolation of positive cases, quarantine of close contacts) a sharp increase of new cases within the following 48 hours was observed.

In the morning of day 5 on board, antigen testing revealed 41 crew members positive for SARS-CoV-2. Series swab tests and PCR analysis carried out by a shore-based laboratory on the same day after the arrival uncovered a total number of 82 out of 165 crew members positive for SARS-CoV-2. The considerable discrepancy of the results underlines that serial PCR testing is superior to antigen testing. However, PCR devices, since they are sensitive for vibration and shock, are in general not validated and therefore not unrestrictedly applicable for the use on ocean-going vessels.

After disembarkation and isolation of positive cases and contacts in a shore side facility, only a small number of further cases occurred and the outbreak was soon declared over. Consistent surveillance and consequent separation of positive and suspected cases from others are crucial for an outbreak control. In addition to the already cramped conditions on board of a ship, space and resources (i.e. treatment rooms, quarantine or isolation cabins, medical personnel, testing capacity, etc.) are also limited. These factors can promote spreading of diseases.

CONCLUSIONS

This investigation confirms the importance of a booster vaccine against COVID-19 for crew members on cruise ships. Longer stays on board could facilitate social mixing and thus the risk for SARS-CoV-2 infections. Non-Europeans appear to be at higher risk for SARS-CoV-2 infections. Further studies could investigate the impact of social, cultural and behavioural patterns as well as access to relevant public health information on the individual infection risk. For containing outbreaks of airborne diseases on cruise ships, physical distancing together with screening and isolation are crucial.

The results and lessons learned from this investigation are also relevant for other respiratory infections and future pandemic situations. They are not limited to the maritime sector or to cruise ship settings. We are convinced that our evaluation of the outbreak situation allows transferable conclusions for informed public health and disease preventing measures in similar settings of cohorts in confined environments.

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REFERENCES

- Guagliardo SA, Prasad PV, Rodriguez A, et al. Cruise ship travel in the era of coronavirus disease 2019 (COVID-19): a summary of outbreaks and a model of public health interventions. Clin Infect Dis. 2022; 74(3): 490–497, doi: 10.1093/cid/ciab433, indexed in Pubmed: 33978720.
- Moriarty LF, Plucinski MM, Marston BJ, et al. Public health responses to COVID-19 outbreaks on cruise ships - Worldwide, February-March 2020. MMWR Morb Mortal Wkly Rep. 2020; 69(12): 347–352, doi: 10.15585/mmwr.mm6912e3, indexed in Pubmed: 32214086.
- Bert F, Scaioli G, Gualano MR, et al. Norovirus outbreaks on commercial cruise ships: a systematic review and new targets for the public health agenda. Food Environ Virol. 2014; 6(2): 67–74, doi: 10.1007/ s12560-014-9145-5, indexed in Pubmed: 24838574.
- Kordsmeyer AC, Mojtahedzadeh N, Heidrich J, et al. Systematic review on outbreaks of SARS-CoV-2 on cruise, navy and cargo ships. Int J Environ Res Public Health. 2021; 18(10), doi: 10.3390/ ijerph18105195, indexed in Pubmed: 34068311.

- Kak V. Infections on cruise ships. Microbiol Spectr. 2015; 3(4), doi: 10.1128/microbiolspec.iol5-0007-2015.
- Acevedo F, Diskin AL, Dahl E. Varicella at sea: a two-year study on cruise ships. Int Marit Health. 2011; 62(4): 254–261, indexed in Pubmed: 22544501.
- Rocklöv J, Sjödin H, Wilder-Smith A. COVID-19 outbreak on the Diamond Princess cruise ship: estimating the epidemic potential and effectiveness of public health countermeasures. J Travel Med. 2020; 27(3), doi: 10.1093/jtm/taaa030, indexed in Pubmed: 32109273.
- Rosca EC, Heneghan C, Spencer EA, et al. Transmission of SARS--CoV-2 associated with cruise ship travel: a systematic review. Trop Med Infect Dis. 2022; 7(10), doi: 10.3390/tropicalmed7100290, indexed in Pubmed: 36288031.
- Zhang Hu, Wang Q, Chen J, et al. Cruise tourism in the context of COVID-19: Dilemmas and solutions. Ocean Coast Manag. 2022; 228: 106321, doi: 10.1016/j.ocecoaman.2022.106321, indexed in Pubmed: 35990780.
- Gravningen K, Henriksen S, Hungnes O, et al. Risk factors, immune response and whole-genome sequencing of SARS-CoV-2 in a cruise ship outbreak in Norway. Int J Infect Dis. 2022; 118: 10–20, doi: 10.1016/j.ijid.2022.02.025, indexed in Pubmed: 35189341.
- Gesetz zur Durchführung der Internationalen Gesundheitsvorschriften (2005). 2013. www.gesetze-im-internet.de/igv-dg (cited 2023 May 23).
- Hecht J, Reichert F, Suwono B, et al. COSIK COVID-19-Surveillance in Krankenhäusern. Epidemiologisches Bulletin. 2022; 2: 19–28.
- Barda N, Dagan N, Cohen C, et al. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. Lancet. 2021; 398(10316): 2093–2100, doi: 10.1016/S0140-6736(21)02249-2, indexed in Pubmed: 34756184.
- Li H, Durbin R. Fast and accurate short read alignment with Burrows-Wheeler transform. Bioinformatics. 2009; 25(14): 1754–1760, doi: 10.1093/bioinformatics/btp324, indexed in Pubmed: 19451168.
- Li H, Handsaker B, Wysoker A, et al. The Sequence Alignment/ Map format and SAMtools. Bioinformatics. 2009; 25(16): 2078– -2079, doi: 10.1093/bioinformatics/btp352, indexed in Pubmed: 19505943.
- Broadinstitute. Picard. A set of command line tools (in Java) for manipulating high-throughput sequencing (HTS) data and formats such as SAM/BAM/CRAM and VCF. http://broadinstitute.github. io/picard/.
- Pangolin. Software package for assigning SARS-CoV-2 genome sequences to global lineages. https://github.com/cov-lineages/ pangolin (cited 2023 May 23).
- Snippy. Rapid haploid variant calling and core genome alignment. https://github.com/tseemann/snippy (cited 2023 May 23).
- SnippySnake. Variant calling pipeline with snippy. https://gitlab. com/bfr_bioinformatics/snippySnake (cited 2023 May 23).
- Robert Koch Institut. Quarantäne- und Isolierungsdauern bei SARS--CoV-2-Expositionen und -Infektionen entsprechend dem Beschluss der Ministerpräsidentenkonferenz vom 7. und 24. Januar 2022. https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/ Quarantaene/Absonderung-Archiv.html (cited 2022 June 18).
- Kumar S, Karuppanan K, Subramaniam G. Omicron (BA.1) and Sub-Variants (BA.1, BA.2 and BA.3) of SARS-CoV-2 spike infectivity and pathogenicity: a comparative sequence and structural-based computational assessment. J Med Virol. 2022; 94(10): 4780–4791, doi: 10.1101/2022.02.11.480029.