Prospective Longitudinal Serosurvey of Health Care Workers in the First Wave of the SARS-CoV-2 Pandemic in a Quaternary Care Hospital in Munich, Germany

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Summary: The risk of SARS-CoV-2 infection for front-line health care workers in a hospital setting was increased during the first pandemic wave in Southern Germany. Due to cluster-transmissions, stringent measures for infection control are essential to protect all patient-facing staff.

Abstract

Background: High infection rates among health care personnel in an uncontained pandemic can paralyze health systems due to staff shortages. Risk constellations and rates of seroconversion for health care workers during the first wave of the SARS-CoV-2 pandemic are still largely unclear.

Methods: Health care personnel (n=300) on different organizational units in the LMU Munich University Hospital were included and followed in this prospective longitudinal study in the period of March 24 until July 7, 2020. Participants were monitored in intervals of two to six weeks using different antibody assays for serological testing and questionnaires to evaluate risk contacts. In a subgroup of infected participants, we obtained nasopharyngeal swabs to perform whole genome sequencing for outbreak characterization.

Results: Health care workers involved in patient care on dedicated COVID-19 wards or on regular non-COVID-19 wards showed a higher rate of SARS-CoV-2 seroconversion compared to staff in the emergency department and non-frontline personnel. The landscape of risk contacts in these units was dynamic, with a decrease of unprotected risk contacts in the emergency department and an increase on non-COVID-19 wards. Both, the intensity and number of risk contacts, were associated with higher rates of seroconversion. On regular wards, staff infections tended to occur in clusters, while infections on COVID-19 wards were less frequent and apparently independent of each other.

Conclusion: The risk of SARS-CoV-2 infection for front-line health care workers was increased during the first pandemic wave in Southern Germany. Stringent measures for infection control are essential to protect all patient-facing staff during the ongoing pandemic.

Key words: SARS-CoV-2, serology, seroconversion, health care workers

Introduction

The Coronavirus disease 19 (COVID-19) pandemic caused by the SARS coronavirus 2 (SARS-CoV-2) has brought health care systems all over the globe on the brink of collapse. The spread of SARS-CoV-2 has led to over 54 million infections worldwide and caused the death of over 1.2 million patients [1]. High patient numbers and the high contagiousness of SARS-CoV-2 [2] overwhelmed health care systems and put front-line health care workers (HCWs) at risk of infection: A case series performed in China during the early phase of the pandemic showed that 29% of infected patients were HCWs who were assumed to have acquired the infection at work [3]. A study comparing the general population with front-line HCWs in the UK and the US reported a significantly increased risk of SARS-CoV-2 infections among HCWs [4]. Besides the individual health risk, increasing rates of COVID-19 among HCWs may rapidly result in a bottleneck in patient care with detrimental effects on health care systems, already stretched to the limit under normal, non-pandemic circumstances [5, 6].

Of particular note, not only symptomatic patients, but also pre- or asymptomatic infected individuals can spread SARS-CoV-2 efficiently [7], potentially leading to patients with undiagnosed SARS-CoV-2 infections to act as sources of ongoing transmissions [8]. Similarly, HCWs with asymptomatic infections may increase the risk of nosocomial infections [9], which might be particularly harmful to the elderly and patients at risk for severe COVID-19 [10].

Therefore, protection of HCWs from contracting or spreading a SARS-CoV-2 infection represents an important goal to stabilize health care systems in a pandemic, creating an urgent need to determine which HCWs are at particular infection risk and how they got infected. We hypothesized, that high frequency and intensity of contacts to infected patients on COVID-19 wards would result in more HCW infections reflected by higher frequencies of SARS-CoV-2 seroconversion compared with HCWs on non-COVID-19 wards or those who were not involved in patient-facing care.

To unravel the rate of seroconversion among HCWs in different clinical functions, we performed a longitudinal seroconversion survey in the LMU Munich University Hospital. In four consecutive visits from March 24 until July 7, 2020, covering the complete first wave of the pandemic in Southern Germany, we analyzed risk contacts, rate of seroconversion, and employed whole genome virus sequencing for cluster analysis of perceived outbreaks in a subgroup of HCWs.

Methods

Study design and population

The LMU Munich University Hospital is a large quaternary care hospital in Munich, Germany (approximately 2000 beds, more than 10000 employees). Enrolment was performed on pre-specified organizational units: 1st) Non-frontline HCWs (NF-HCWs), 2nd) Emergency Department (ED-HCWs), 3rd) Intensive Care and General Wards specifically dedicated to care for non-COVID-19 (non-COVID-HCWs) and 4th) for COVID-19 patients (COVID-HCWs) **(Figure 1)**. Participation in the study was voluntarily. After written consent was obtained by the participant, four visits were performed, each consisting of a blood collection (7.5 ml) and a questionnaire **(Figure 1 and 2)**.

Study participant data were collected and pseudonymized for measurements. For virus genome analysis, participants with a RT-PCR-confirmed infection were asked to contact the study team to obtain a swab sample for phylogenic analysis. Data from patients were used in an anonymized fashion. The study was approved by the ethical committee of the Medical Faculty of the Ludwig-Maximilians-University (No: 20-247 and No: 20-245).

Timeline of study and of prophylactic measures implemented

Visits were performed from March 24th to July 7th, starting only few days after the first lockdown decision issued by the responsible authorities on March 21st, 2020 **(Figure 2)**. Organizational measures taken by the hospital in order to prevent disease spread among patients and personnel are depicted in Figure 2.

Personal protective equipment (PPE) was provided to every staff member and included daily supplies of surgical face masks. Care of patients with either suspected or PCR-proven SARS-CoV-2 infection was performed with PPE according to the local hygiene recommendations including eye protection (shield or goggles), filtering face piece (FFP) 2 masks and disposable protective clothing (coats and gloves). Re-use of PPE was strongly discouraged. Videos and posters to educate HCWs to correctly perform donning and doffing were distributed among all HCWs.

Questionnaire

The questionnaire addressed demographic data, medical history, PCR testing for SARS-CoV-2, area of patient care, profession, contact to SARS-CoV-2 infected subjects (patients, colleagues, or private contacts), and intensity of contacts according to the classification of the Robert Koch Institute [11]. Risk categories were self-assessed by the participants using a flow chart **(Supplementary File 1)**. Briefly, contact category 1 was defined as a close contact to an infected patient, colleague, or private person, i.e. less than 2 meters apart for more than 15 minutes, or as contact to potentially infectious aerosols or contaminated fluids (e.g. during intubation) while not wearing PPE. Contact category 2 was defined as an unprotected contact to an infected person (either patient, colleague or private person) who did not fulfill all of the above-mentioned criteria (e.g. a contact under 15 minutes with less than two meters distance or a contact over 15 minutes but with over two meters distance). Category 3 only applied to contacts with positive tested patients and co-workers in the hospital when protection measures (FFP2 mask, protective gown, glasses, gloves) were in worn.

Serologic testing

Available samples from visits 1-4 were screened using Anti-SARS-CoV-2 IgG and IgA (EuroImmun, Lübeck, Germany) and Elecsys® Anti-SARS-CoV-2 Ig (Roche, Basel, Switzerland) assays. Subsequently, all samples of volunteers with at least one positive

screening result were tested with LIAISON® SARS-CoV-2 S1/S2 IgG (DiaSorin, Saluggia, Italy) and ARCHITECT SARS-CoV-2 IgG assay (Abbott, Chicago, USA) assays.

Seroconversion was defined as seronegativity at visit 1 and at least two IgG/total Ig-detecting test systems showing reactivity in subsequent visits. In case of low level anti-SARS CoV-2 antibodies at visit 1, a significant increase in antibody titer in at least two test systems at subsequent visits was also considered as seroconversion. All commercial serological tests were performed according to manufacturers' instructions.

Whole virus genome sequencing

In a subgroup of study participants with PCR-confirmed SARS-CoV-2 infection, we obtained nasopharyngeal swabs for phylogenic analysis. Amplicon pools spanning the SARS-CoV-2 genome were prepared for each sample, converted to barcoded sequencing libraries and sequenced on a MinION R9.4.1 flowcell following the ARTIC network nCoV-2019 sequencing protocol v2 (dx.doi.org/10.17504/protocols.io.bdp7i5rn).

Assembly and phylogenetic analyses

The sequenced amplicons were assembled using the Artic bioinformatics protocol (http://artic.network/ncov-2019). Phylogenetic analyses were achieved with the web- and analysis platform Auspice using the SARS-CoV-2 build (https://github.com/nextstrain/ncov) and the bioinformatic toolkit augur (https://github.com/nextstrain/augur). The consensus sequences and meta data for the samples were uploaded to the GISAID repository.

Statistical analysis

Categorical variables were compared between groups using the Pearson's Chi-squared or Fisher's exact test. Paired categorical variables, such as seroconversion rate within one group over time, were compared using McNemar's Chi-squared test. Quantitative variables were tested for normal distribution using Shapiro-Wilk test. Continuous data were compared using Kruskal-Wallis rank sum test and are depicted as mean ± standard deviation or median [interquartile range (IQR)]. A p-value of <0.05 was regarded statistically significant.

Analyses were performed using R (RStudio version 1.2.5033). Prism 8 for mac version 8.4.2 (GraphPad Software, San Diego, USA) and Microsoft PowerPoint 15.12.3 (Microsoft Corporation, Redmond, USA) were used for design of graphs.

Results

Study population and baseline characteristics

We enrolled 338 of 362 invited employees at two sites of LMU Munich University Hospital between March 24th and April 2nd on pre-specified organizational units as described above. 38 subjects were excluded from the study, including 2 HCWs already seroconverted for SARS-CoV-2 at visit 1. The final analysis included 300 subjects (41 non-frontline (NF) HCWs, 29 Emergency-Department (ED) HCWs, 90 non-COVID-HCWs, and 140 COVID-HCWs) **(Figure 2)**. Gender, medical history, or medication did not differ significantly between the four groups, except NF-HCWs were significantly older compared to the other groups **(Table 1)**.

Seroprevalence of antibodies against SARS-CoV-2 differs between organizational units

Seroconversion was detected in 14 of 300 (4.67%) HCWs. No seroconversions were noted among NF-HCWs or ED-HCWs. In HCWs caring for patients either on non-COVID-19 or dedicated COVID-19 wards, we found antibodies against SARS-CoV-2 in 10 (11.1%) and four (2.86%) HCWs, respectively (**Figure 3**). 10 of 14 (71.4%) seroconverted HCWs also had RT-PCR-confirmed and clinically diagnosed COVID-19 **(Figure 4)**. Four (29.6%) HCWs had neither been diagnosed with a SARS-CoV-2 infection nor reported any symptoms in the time between seroconversion and the previous visit. None of the study participants had to be admitted to hospital during the course of their COVID-19. The timeline of antibody development in the seroconverted HCWs showed seroconversion occurring mainly in the period covering the 3rd and 4th visit **(Figure 4B and C, Supplementary Figure 1)**.

Taken together, we found an increased rate of seroconversion in HCWs facing patients on hospital wards in general, which was even more pronounced in the subgroup of HCWs treating patients without suspected SARS-CoV-2 infection. Remarkably, none of the HCWs in the ED, regularly providing the initial care for patients with SARS-CoV-2 infection, seroconverted in our study.

Rate of seroconversion is associated with reported risk contacts

To decipher the role of contacts with SARS-CoV-2-infected subjects in a hospital setting, we analyzed the risk contacts of HCWs to infected patients, colleagues and in their private environment. We found an increased rate of seroconversion among participants, who had reported at least one contact to an infected person. This rate increased with the category of the risk contact reported. Odds ratios (OR) for seroconversion for class 1 (unprotected) and class 2 (unprotected, but less intense) contacts were 3.61 ([95% confidence interval (CI), 1.19-12.4], p=0.02) and 2.41 ([95% CI, 0.75-7.31], p=0.13), respectively (**Figure 5A**). Reporting unprotected (class 1) contacts more often during the study was associated with an increased rate of seroconversion (OR 1.57 [95% CI, 1.07-2.30], p=0.02). Similarly, unprotected (Class 1 and 2 contacts) either to patients, colleagues or private contacts combined, were associated with a significantly higher seroconversion rate (7.97 vs. 1.85%, p=0.012, **Figure 5B**), underlining the importance of adequate PPE for HCWs.

Degree and amount of risk contacts differ between HCW groups and show a dynamic course during the first pandemic wave

All HCWs had limited risk exposure outside the hospital and reported only a low level of risk contacts in their private environment **(Figure 5C, 6D)**. Among frontline HCWs, ED-HCWs (93.1%, n=27, p=0.003) and COVID-HCWs (94.3%, n=132, p<0.001) reported significantly more contacts to SARS-CoV-2-infected individuals throughout the whole study period compared to non-COVID-HCWs (64.4%, n=58) **(Figure 5C)**. COVID-HCW had a higher rate of fully protected (class 3) contacts (52.9%, n=74) compared to ER-HCW (6.9%, n=2,

p<0.001) and non-COVID-HCW (10.0%, n=9, p<0.001). On the other hand, ED-HCWs and non-COVID-HCWs had a higher percentage of unprotected (class 1) contacts (55.2%, n=16, p=0.02 and 41.1%, n= 37, p=0.20 respectively), compared to COVID-HCWs (32.9%, n=46) (**Figure 5C)**. In fact, working on a non-COVID-19 ward was associated with a significantly higher rate of unprotected (class 1) contact to infected patients compared to COVID-19 HCWs (OR 2.29 [95% CI, 1.25-4.25]; p=0.008).

Overall, 50% of seroconverted HCWs (n=7) had a known unprotected class 1 contact before seroconversion **(Figure 5D)**. Seroconverted HCWs, working on regular wards or COVID-19 wards, reported unprotected contacts with an infected colleague more often (40% vs. 0%; **Supplementary Figure 2**). Unprotected private contacts, although small in number, showed a trend to be associated with a higher rate of seroconversion (OR 5.99 [95% CI, 0.76-28.2], p=0.08). However, unprotected risk contacts in the hospital, either to an infected patient (OR 3.45 [95% CI, 1.12-10.6], p=0.03) or colleague (OR 3.38 [95% CI, 1.05-10.3], p=0.04) had a statistically significant association with seroconversion **(Figure 5A)** and were reported more frequently **(Figure 6)**.

Considering the dynamic situation in hospitals during the first wave of the pandemic, we analyzed the different risk contacts over time reported at the individual visits **(Figure 6, Supplementary Figure 3)**. ED-HCWs reported the highest amount of unprotected risk contacts in the initial phase of the study, which, however, declined with the progression of the pandemic **(Figure 6A)**. In contrast, non-COVID-HCWs reported a marked increase of risk contacts over the study period, mainly driven by unprotected contacts to colleagues or patients **(Figure 6B-D)**. HCWs caring for COVID-19 patients reported a substantial, yet stable rate of unprotected contacts during the study period **(Figure 6A)**.

Nosocomial infection clusters drive higher seroprevalence in HCWs on non-COVID-wards

Next, we aimed to analyze factors influencing the seroprevalence among HCWs in different organizational units. Focused analysis of the timeline of seroconverted HCWs showed that 10 of 14 HCWs (71.4%) had RT-PCR-proven and clinically diagnosed SARS-CoV-2 infection. Interestingly, 9/10 PCR-proven infections had occurred in two short time-periods (five infections from 4/2/20-4/10/20 and four infections from 5/21/20-5/25/20) suggesting a clustering of infections **(Figure 7A)**.

Previously, whole virus genome sequencing has been reported to help unravel unknown routes of hospital-acquired infections [12]. In our study, SARS-CoV-2 RNA for genome sequencing was available from nasopharyngeal swabs of four HCWs with RT-PCR-confirmed infection (**Figure 7A**). Phylogenetic analyses found that three samples obtained in the second period represented a cluster of nosocomial infections, starting from an initially undiagnosed infected patient, who was treated for a COVID-19-unrelated disease on a regular ward (patient 0) **(Figure 7B)**. Two of the seropositive HCWs worked on the ward where patient 0 was treated. Another HCW who got infected in this cluster had been visiting a hospitalized relative **(Figure 7C)**.

Discussion

This prospective longitudinal serological analysis provides detailed information on risk exposure to SARS-CoV-2 and seroconversion rates of HCWs of different organizational units during the first wave of the pandemic in Munich, Germany. We report that frontline HCWs are at an increased risk of infection compared to non-frontline HCWs, who have been reported to show a similar risk of infection as the general public [13]. Unprotected contact to an infected person was associated with a higher rate of seroconversion. The seroconversion rate was not only influenced by the degree but also by the frequency of reported risk contacts. Surprisingly, non-COVID-HCWs showed a higher rate of unprotected exposure to

SARS-CoV-2-infected patients compared to COVID-HCWs. The higher rate of seroconversion in HCWs caring for patients initially classified as “non-COVID-19” seemed to be mainly influenced by the two infection clusters. We found that unprotected risk contacts shifted from the ED to non-COVID-19 wards with progression of the first pandemic wave. This may, at least partly, be explained by the occurrence of clusters of infections on non-COVID-19 wards and the stringent use of PPE in the ED and on COVID-19 wards. While private risk contacts showed an association with seroconversion similar to occupational contacts, these contacts were infrequent compared to contacts at work, underlining the increased work-related risk of frontline HCWs. No clusters explaining contamination in the private life of study participants were identified.

Interestingly, despite many class 1 contacts, no ED-HCW developed antibodies against SARS-CoV-2. This may be explained by the fundamentally different working methods of a HCWs in the ED compared to inpatient wards. ED-HCWs are confronted with a high number of patients each day but with very short time periods, while HCWs on inpatient wards are involved with patient care over days to weeks. The aforementioned differences in the type of care and the influence on contact intensity are not reflected in the classification used and the difference of working methods itself might render them more likely to contract a SARS-CoV-2 infection from an infected, yet undetected patient. Of note, in a study comparing the infection risk of inpatient and outpatient HCWs to the general public in a multivariate analysis, outpatient HCWs showed a lower risk increase (11-fold) compared to inpatient HCWs (24-fold) [4]. Furthermore, patients with a false-negative PCR-test and no obvious clinical COVID-19-related symptoms, can spread the infection in the hospital [14, 15]. A decrease of protective measures in these patients after admission to the hospital might represent a “trojan-horse” effect, adding to the observed increase of risk contacts on normal wards during the first pandemic wave.

In line with our results, previous seroprevalence studies have reported an increased frequency of seroconversion not only among COVID-HCWs but also among HCWs caring

for non-COVID-19 patients [13, 16]. However, there is controversial data on the risk differences of HCWs in specific areas. Some studies show an increase risk for COVID-HCWs [13, 16, 17], while others did not find relevant differences in risk compared to HCWs on regular wards [18, 19]. Another study reported a reduced risk for HCWs on intensive care units compared to regulars wards, all providing providing care for COVID-19 patients [20]. One explanation for the increased risk for seroconversion in non-COVID-HCWs in our study might be the occurrence of two infection clusters. Only sporadic infections were observed in COVID-HCWs. Further, reuse or inappropriate use of PPE has been reported to be associated with an increased SARS-CoV-2 infection risk [4]. Reuse of PPE was strongly discouraged in our hospital and sufficient PPE was available for all HCWs at all times. This may explain the relatively small number of seroconverted HCWs on COVID-19 wards compared to other studies, where, especially at the beginning of the pandemic, a shortage of PPE made the reuse of protective equipment more common [13].

To the best of our knowledge, this is the first study reporting prospective and longitudinal data on seroconversion of HCWs covering the complete first pandemic wave of COVID-19. Most of the available studies are based on self-reporting [13] data or are of retrospective nature [13, 16, 21-24].

Our study also has limitations. Due to the novelty of the disease, there were only limited study resources available, resulting in a small number of HCWs included in this study. Together with the reported cluster infections, the small number of study subjects makes a comparison between HCWs on COVID-19 and non-COVID-19 wards difficult. Prospective studies with larger study cohorts addressing this question are needed.

Conclusion

This study demonstrates that increased frequencies and intensities of contacts to SARS-CoV-2-infected individuals are associated with a higher seroconversion rate among front-line HCWs. Our findings underline the importance of stringent hygiene measures on COVID-19 wards as well as all other patient-facing HCWs.

NOTES

Author contributions

T.W., J.S., A.O., T.M., K.A., P.R. W., P.S. and M.M. contributed to sample and data collection. M.M., A.G., S.K. and C.S. contributed to sequencing and data analysis. O.T.K, H.B. and M.K provided supervision. T.W., J.S., A.O., O.T.K. and M.K. contributed to data interpretation. B.G. provided guidance regarding hospital hygiene measurements. T.W., J.S., A.O., M.K. and O.T.K. wrote the manuscript. T.W., A.O. and J.S. produced the figures. All authors reviewed the manuscript.

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Competing interests

The authors declare no competing interests.

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Figure legends

Figure 1: Study flow chart

Study flow chart illustrating the recruitment process and the study samples analyzed. After invitation, 338 HCWs from COVID-19 wards, from non-COVID-19 wards, from the hospital's emergency departments as well as non-frontline HCW were recruited to the study. 36 participants were excluded due to withdrawal of consent (n=6), terminated work contracts (n=15) or other reasons (n=4). In total, seven participants were lost to follow up. 302 samples underwent serologic testing. Due to seropositivity at the start of the study, two participants were excluded before data analysis. Participants were stratified for working area. 47% (n=140) of participants were working on wards with contact to COVID-19 patients, 30% (n=90) of participants were working on wards without COVID-19 patients. 10% (n=29) of participants were part of the emergency room team with potential contact to COVID-19 patients (ED HCW). 41 participants (14%) were non-frontline HCWs.

Figure 2: Infection control and prophylactic measures during study time

Number of COVID-19 patients hospitalized in our quaternary care hospital (red) and number of new PCR-proven infections with SARS-CoV-2 in the Munich Metropolitean area during the study period are shown [25] . Visit periods (V1-V4) are depicted in dashed lines. Measures regarding infection control are shown in green boxes and prophylactic measures are shown in orange boxes. ✂represents start of the government-imposed lockdown (including closure of schools, childcare, restaurants). * either when being transported inside the hospital or when HCW present in the room. & patients were screened for COVID-19-related symptoms, contact to infected persons, visit of a region defined at risk area. # including PCR-testing of all admitted patients.

Figure 3: SARS-CoV-2 seroconversion in HCWs during the first pandemic wave

Percentage bars showing the fraction of study participants tested seropositive for SARS-CoV-2 antibodies by the end of the study. In total, 14 out of 300 participants developed antibodies throughout the study period (4.67%). Four out of 140 (2.86%) HCWs from COVID-19 wards and 10 out of 90 (11.1%) HCWs from non-COVID-19 wards were seropositive at end of the study. No participants of the non-frontline HCWs (no patient contact) and none of the ED-HCW seroconverted.

Figure 4: Detailed timeline of seroconverted HCWs

(A) Timeline of the 14 study participants with positive SARS-CoV-2 antibody tests by the end of the study. Lines indicate weekly intervals. Symbol positions denote exact time-points of serological testing, PCR tests and quarantine periods. Almost all of the HCWs had a respiratory swab taken at least once during the study period and 10 had a tested SARS-CoV-2 PCR-positive followed by 14 day-quarantine. At this time, quarantine was prolonged until PCR was negative, (B) Time-course of antibody development of HCWs of different organizational units showing that seroconversion mainly occurs on patient-facing inpatient wards dedicated to either care for COVID-19 or non-COVID19 patients, Green bars are indicating non-COVID-HCWs, purple bars COVID-HCWs. (C) time-course of antibody titers in seroconverted HCWs with one line representing each study subject (green, non-COVID-HCWs; purple, COVID-HCWs; Euroimmun SARS-CoV-2 IgG is shown as 1 of 4 different commercially available ELISAs, which were performed to determine seroconversion) Red shaded horizontal areas indicate borderline results.

Figure 5: Influence of degree and number of risk contacts on SARS-CoV-2 seroconversion

At each visit, study participants completed a questionnaire exploring contacts to patients, colleagues, or in the private setting with risk of SARS-CoV-2 infection. Classification was adapted from national health authorities (Robert Koch Institute, Berlin, Germany; for details see Methods section). (A) Odds ratios according to the degree and type of risk contact in the overall study cohort (B) nine out of 103 HCWs (8.7%) developed antibodies compared to only five out of 197 (2.5%) participants without unprotected contacts (p=0.012). (C) Percentage of risk contacts according to the different deployment of HCW at the end of the study (D) Percentage of different risk contacts in seroconverted HCWs prior to seroconversion

Figure 6: Time-course of the proportion of class 1 risk contacts in different HCW groups during the first pandemic wave.

Percentage of participants reporting class 1 risk contacts throughout the study period are shown stratified by groups and visits. Contact class 1 for each visit is given for (A) all contacts, (B) infected patients, (C) infected colleague, and (D) for infected persons in the private environment. Differences of each visit compared to baseline (visit 1) were analysed per group. * $p<0.05$; ** $p<0.01$; *** $p<0.001$ (McNemar's test)

Figure 7: Whole virus genome sequencing for identification of a cluster of infection

(A) Timeline of all (10) PCR-proven SARS-CoV-2 infections shows temporal clustering during two short time-periods (red arrow indicates begin of the study; green (non-COVID HCW) and purple (COVID-HCW) arrows represent first positive PCR test; subjects with nucleic acid eluates available for sequencing are indicated with letters A-D) (B) Maximum likelihood phylogeny of SARS-CoV-2 sequences from COVID and non-COVID HCWs (green and purple circles), patients (blue circle) and the index person (patient 0, blue with red border) involved in the outbreak in relation to two reference genomes from Wuhan, China. The number of mutations in relation to the reference sequence Wuhan/Hu-1/2019 is shown on the x-axis axis. Nextstrain nomenclature clades are indicated above the main branches. (C) Distribution of all seroconverted HCWs on the different pre-specified wards (circles represent individual wards; number represent number of seroconverted HCWs; colors represent phylogeny of SARS-CoV-2 sequences depicted in B)

Table 1

	NF-HCW (N=41)	ED-HCW (N=29)	Non-COVID HCW (N=90)	COVID-HCW (N=140)	Total (N=300)	p value
Female sex	34 (82.9%)	19 (65.5%)	60 (66.7%)	87 (62.1%)	**200 (66.7%)**	0.10
Age (years)	41.5 [30.2-53.7]	32.0 [26.9-37.0]	34.2 [28.7-41.4]	36.6 [28.7-44.7]	**35.1 [28.7-45.1]**	0.02
Age group						< 0.01
<20	0 (0.0%)	1 (3.4%)	0 (0.0%)	1 (0.7%)	**2 (0.7%)**	
20-29	10 (24.4%)	12 (41.4%)	28 (31.1%)	46 (32.9%)	**96 (32.0%)**	
30-39	10 (24.4%)	10 (34.5%)	35 (38.9%)	38 (27.1%)	**93 (31.0%)**	
40-49	5 (12.2%)	4 (13.8%)	16 (17.8%)	36 (25.7%)	**61 (20.3%)**	
50-59	11 (26.8%)	1 (3.4%)	7 (7.8%)	16 (11.4%)	**35 (11.7%)**	
60-69	5 (12.2%)	1 (3.4%)	4 (4.4%)	3 (2.1%)	**13 (4.3%)**	
Body mass index (kg/m2)	22.2 [19.7-26.1]	23.8 [22.2-24.9]	24.2 [20.9-27.4]	23.7 [22.1-26.1]	**23.7 [21.7-26.4]**	0.28
Occupation						< 0.01
Administration staff	23 (56.1%)	0 (0.0%)	0 (0.0%)	0 (0%)	**23 (7.7%)**	
Laboratory staff	18 (43.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**18 (6%)**	
Nursing staff	0 (0.0%)	15 (51.7%)	46 (51.1%)	85 (60.7%)	**146 (48.7%)**	
Physicians	0 (0.0%)	14 (48.3%)	38 (42.2%)	44 (31.4%)	**96 (32.0%)**	
Other frontline HCW	0 (0.0%)	0 (0.0%)	6 (6.7%)	11 (7.9%)	**17 (5.6%)**	
Medical history						
Smoker (past or active)	6 (14.6%)	10 (34.5%)	16 (18.0%)	35 (25.4%)	**67 (22.6%)**	0.14
Cardiovascular disease	4 (9.8%)	2 (6.9%)	6 (6.7%)	14 (10.0%)	**26 (8.7%)**	0.81
Pulmonary disease	3 (7.3%)	3 (10.3%)	8 (8.9%)	10 (7.1%)	**24 (8.0%)**	0.92
Other diseases	11 (26.8%)	6 (20.7%)	16 (17.8%)	35 (25.0%)	**68 (22.7%)**	0.55
Medication						
Antihypertensive medication	4 (9.8%)	1 (3.4%)	8 (8.9%)	6 (4.3%)	**19 (6.3%)**	0.36
Immunomod-ulatory drugs	0 (0.0%)	0 (0.0%)	4 (4.4%)	5 (3.6%)	**9 (3.0%)**	0.40
Other drugs	15 (36.6%)	4 (13.8%)	25 (27.8%)	25 (17.9%)	**69 (23.0%)**	0.03

Data are given as number (percentage of category total) or median [interquartile range].

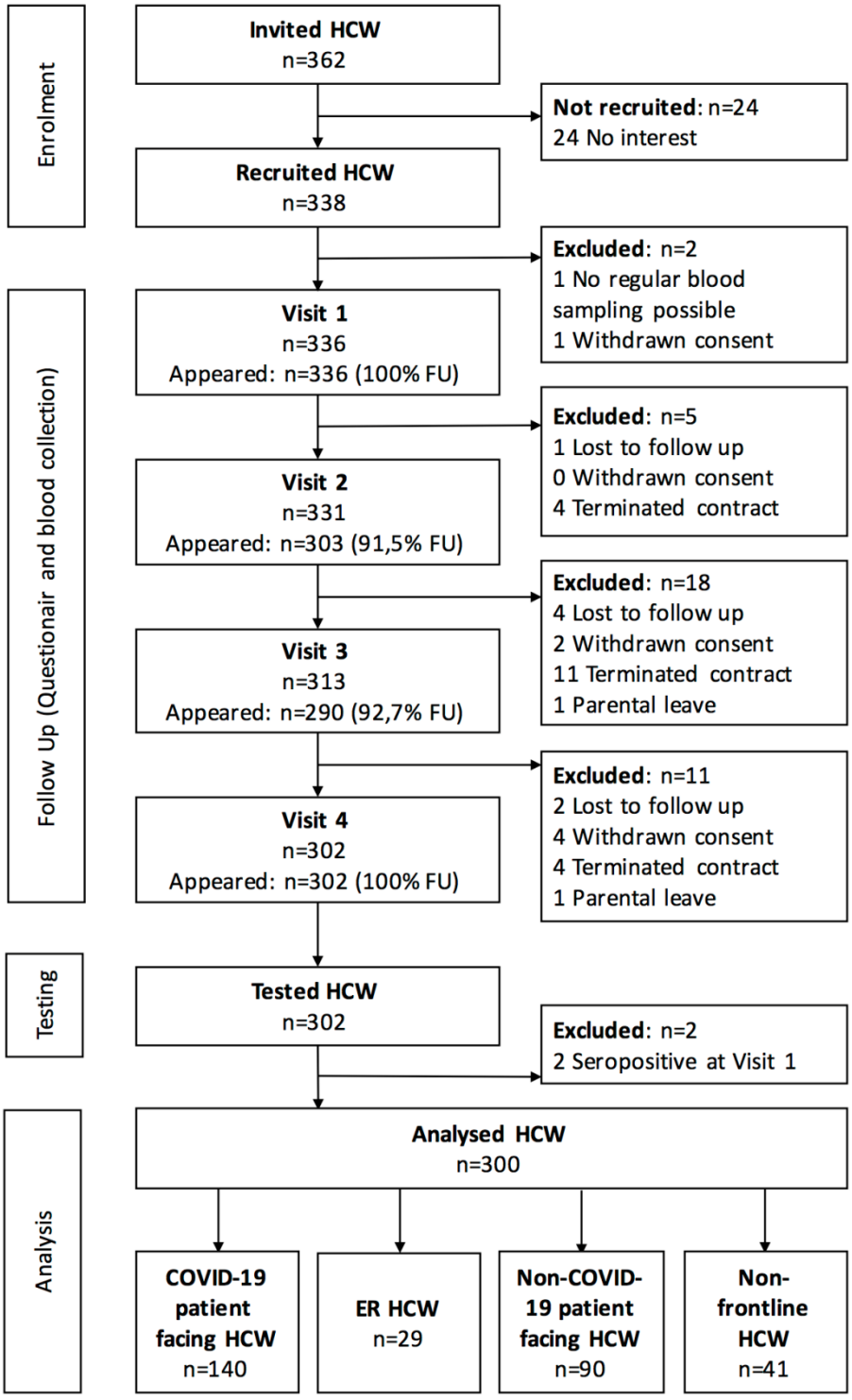
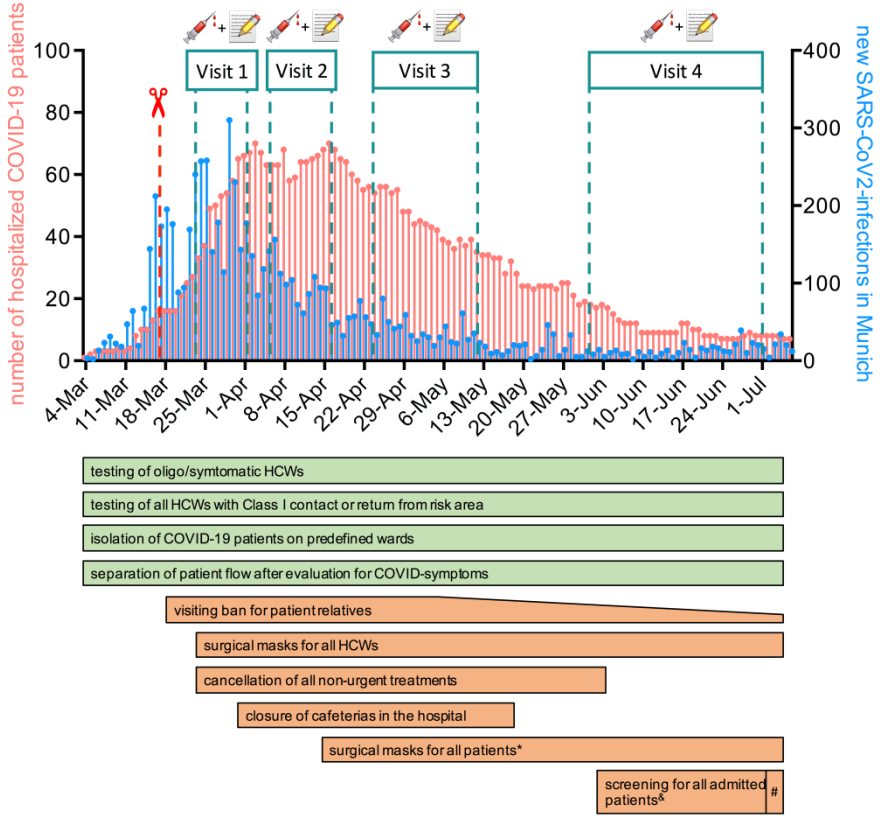


Figure 1. Study flow chart

Figure 2


number of hospitalized COVID-19 patients
new SARS-CoV2-infections in Munich
Visit 1
Visit 2
Visit 3
Visit 4
100
80
60
40
20
0
400
300
200
100
0
4-Mar
11-Mar
18-Mar
25-Mar
1-Apr
8-Apr
15-Apr
22-Apr
29-Apr
6-May
13-May
20-May
27-May
3-Jun
10-Jun
17-Jun
24-Jun
1-Jul
testing of oligo/symtomatic HCWs
testing of all HCWs with Class I contact or return from risk area
isolation of COVID-19 patients on predefined wards
separation of patient flow after evaluation for COVID-symptoms
visiting ban for patient relatives
surgical masks for all HCWs
cancellation of all non-urgent treatments
closure of cafeterias in the hospital
surgical masks for all patients*
screening for all admitted patients&
#

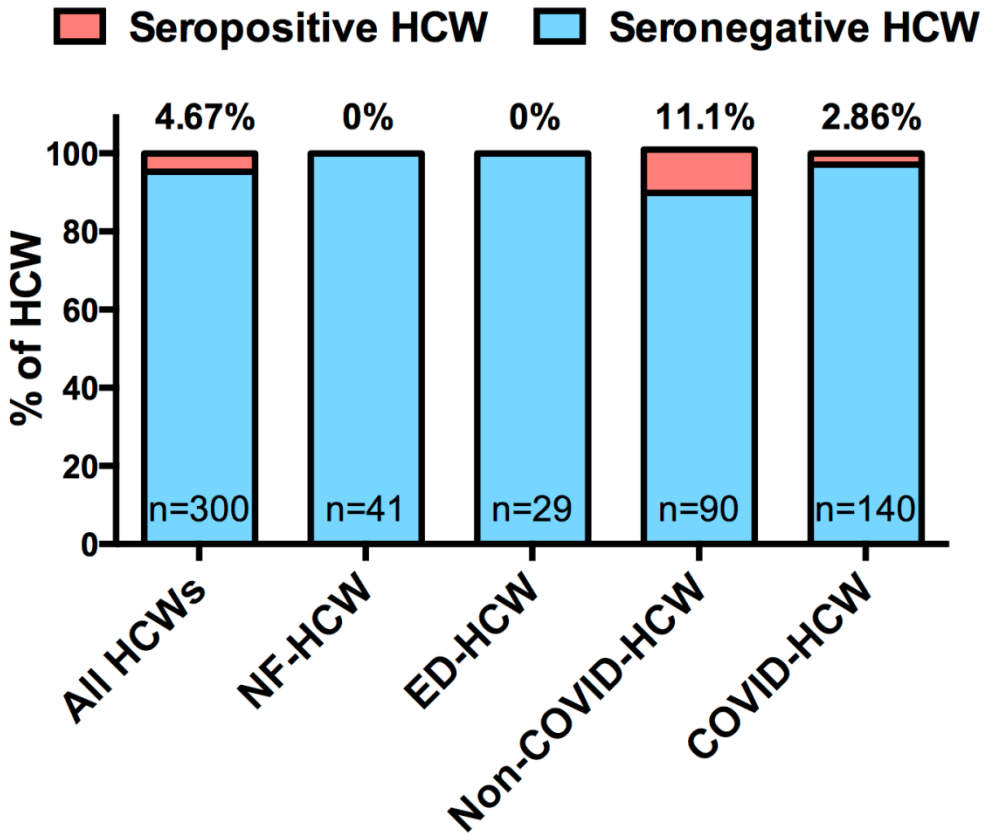


Figure 3. Seroconversion in HCWs during the first wave of the COVID-19 pandemic

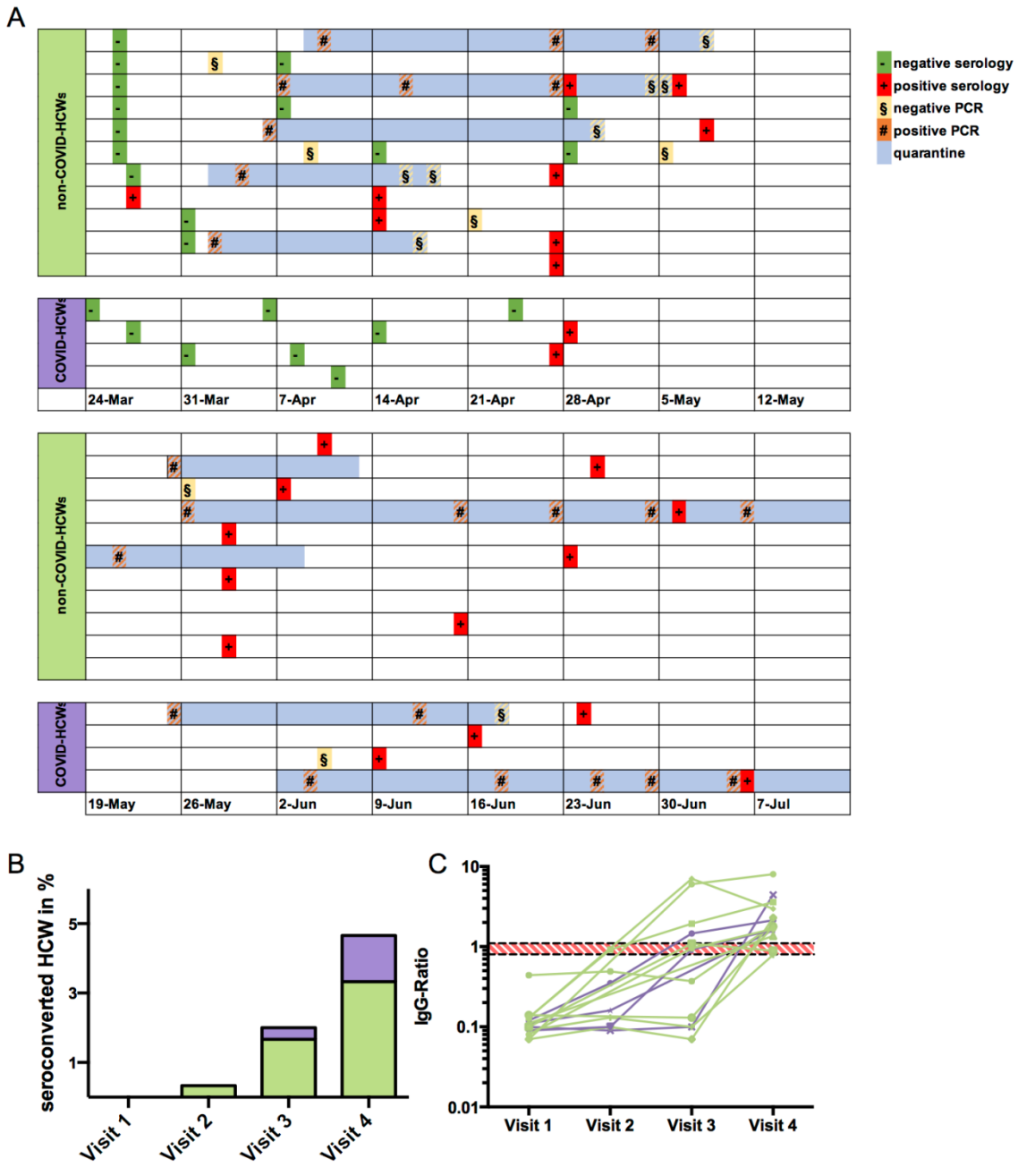


Figure 4. Detailed timeline of seroconverted HCWs

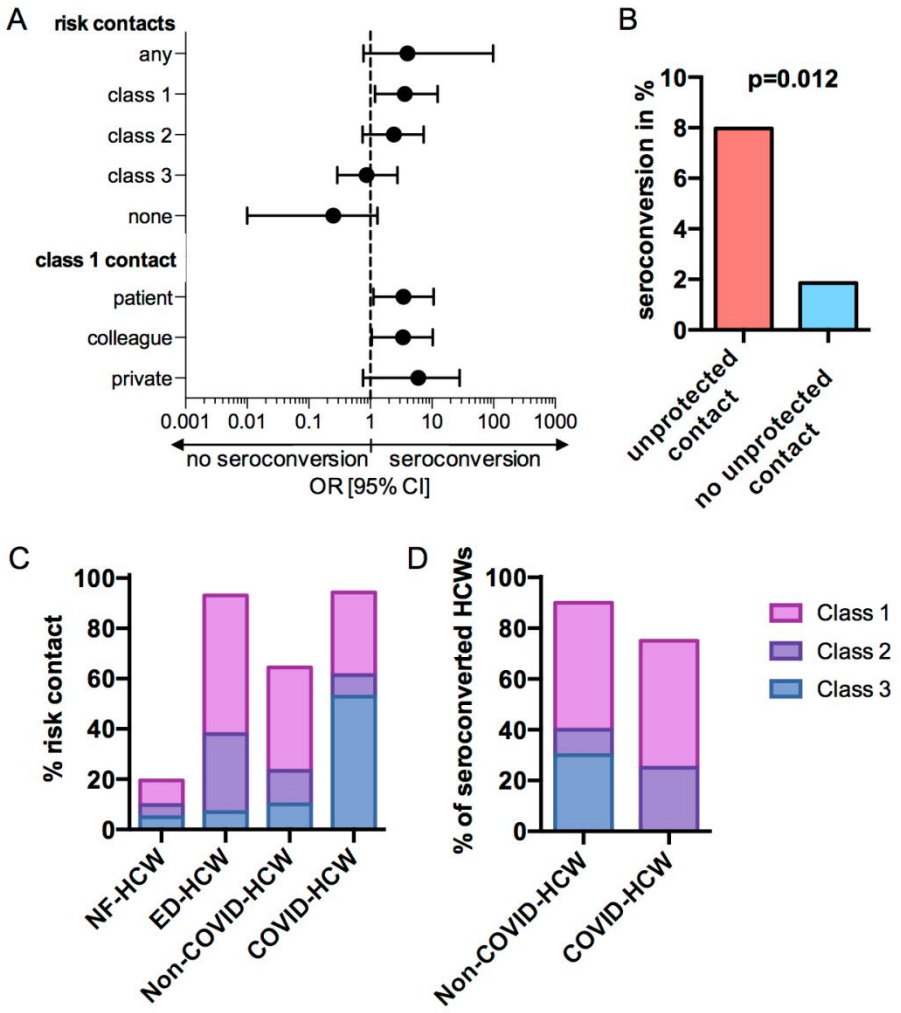


Figure 5. Influence of degree and number of risk contacts on seroconversion

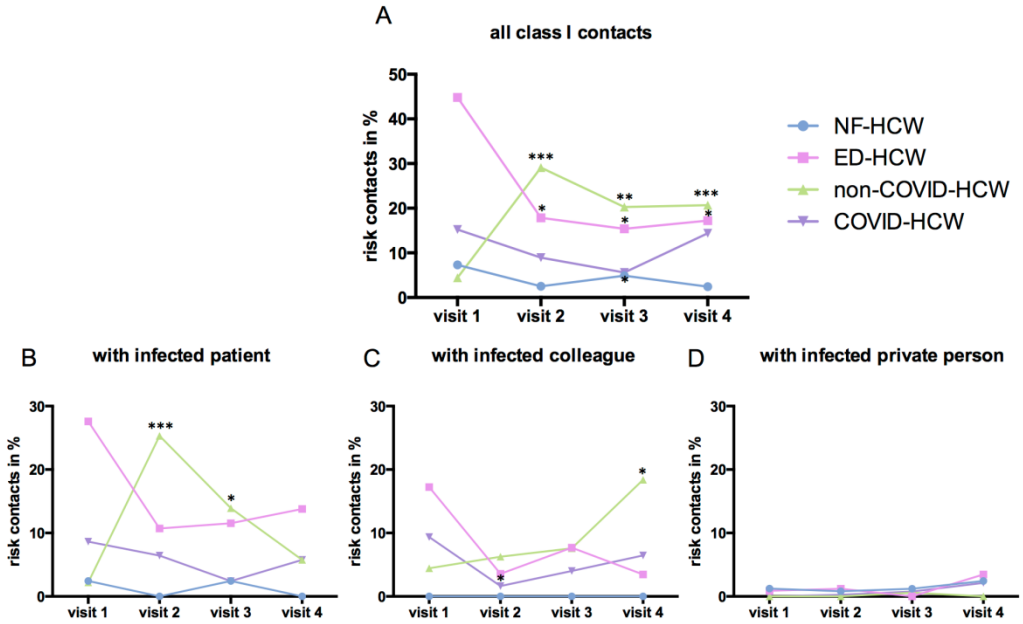


Figure 6. Class I risk contacts in different HCW groups during the first COVID-19 pandemic wave

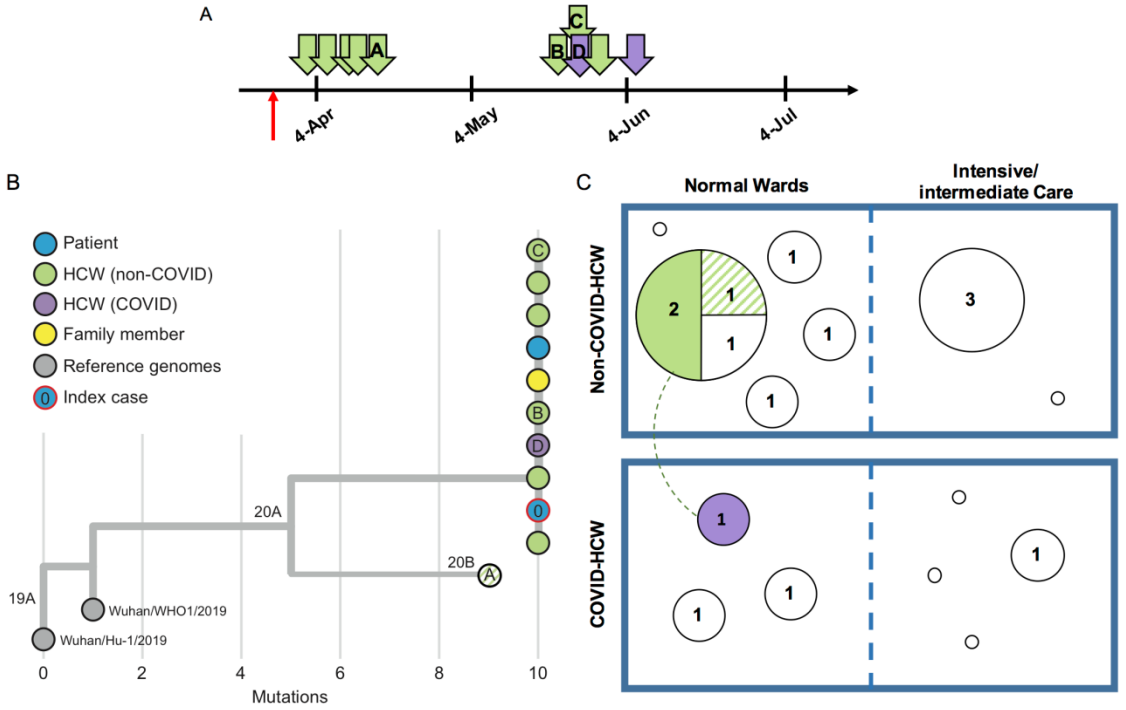


Figure 7. Whole virus genome sequencing for identification of a cluster of infection