

1 **Transmission of SARS-CoV-2 Delta variant among vaccinated**
2 **healthcare workers, Vietnam**

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23 Vietnam

24 **ABSTRACT**

25 **Background:** Data on breakthrough SARS-CoV-2 Delta variant infections are limited.

26 **Methods:** We studied breakthrough infections among healthcare workers of a major
27 infectious diseases hospital in Vietnam. We collected demographics, vaccination history
28 and results of PCR diagnosis alongside clinical data. We measured SARS-CoV-2
29 (neutralizing) antibodies at diagnosis, and at week 1, 2 and 3 after diagnosis. We
30 sequenced the viruses using ARTIC protocol.

31 **Findings:** Between 11th–25th June 2021 (week 7–8 after dose 2), 69 healthcare workers
32 were tested positive for SARS-CoV-2. 62 participated in the clinical study. 49 were
33 (pre)symptomatic with one requiring oxygen supplementation. All recovered uneventfully.
34 23 complete-genome sequences were obtained. They all belonged to the Delta variant, and
35 were phylogenetically distinct from the contemporary Delta variant sequences obtained
36 from community transmission cases, suggestive of ongoing transmission between the
37 workers. Viral loads of breakthrough Delta variant infection cases were 251 times higher
38 than those of cases infected with old strains detected between March-April 2020. Time
39 from diagnosis to PCR negative was 8–33 days (median: 21). Neutralizing antibody levels
40 after vaccination and at diagnosis of the cases were lower than those in the matched
41 uninfected controls. There was no correlation between vaccine-induced neutralizing
42 antibody levels and viral loads or the development of symptoms.

43 **Interpretation:** Breakthrough Delta variant infections are associated with high viral loads,
44 prolonged PCR positivity, and low levels of vaccine-induced neutralizing antibodies,
45 explaining the transmission between the vaccinated people. Physical distancing measures
46 remain critical to reduce SARS-CoV-2 Delta variant transmission.

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48 **RESEARCH IN CONTEXT**

49 **Evidence before this study**

50 We conducted a literature search of PubMed Central for studies or reports of SARS-CoV-2
51 breakthrough infections up to 1st August 2021. We used the terms “breakthrough Delta
52 variant infection”, “Delta variant breakthrough infection” and “SARS-CoV-2
53 breakthrough infections” without language restriction. We identified 14 relevant scientific
54 papers including one published in medRxiv. Of these, only the medRxiv paper described 6
55 cases of breakthrough Delta variant infections. Of the remaining 12, 10 described
56 breakthrough infections associated with non-Delta variants of concerns (Alpha, Beta and
57 Gama variants).

58 None of the above mentioned studies described the transmission between vaccinated
59 people, while one study reported the transmission between vaccinated people and
60 household members. Likewise, there was only one paper comparing the viral loads
61 between fully vaccinated and partially vaccinated individuals with breakthrough Alpha
62 variant infection and found no difference between the two group. And there was one paper
63 comparing the viral load between vaccinated and unvaccinated people infected with the
64 Alpha variant but found no difference in viral load between the two groups. Only one
65 paper had follow-up data on PCR testing after infection and found low viral loads and
66 short duration of viral shedding (2-7 days) in cases of breakthrough infections without
67 information about the causal variant. Most recently, a study in Israel identified a
68 correlation between neutralizing antibody titers after the second dose and at diagnosis and
69 break through infection. The causal variant was the Alpha variant.

70 **Added value of this study**

71 We studied 62 breakthrough cases among healthcare workers of a major hospital for
72 infectious diseases in Ho Chi Minh City (HCMC), Vietnam between 11th-25 June 2021.
73 We captured the infected cases at a very early phase of the infection and carefully followed
74 them up during hospitalization to assess the kinetic of viral loads and neutralizing
75 antibodies, and the development of clinical symptoms. To dissect the epidemiological link
76 and the transmission potential between the vaccinated healthcare workers, we conducted
77 whole genome sequencing of SARS-CoV-2.
78 49/62 case patients were (pre)symptomatic) and all recovered uneventfully. A total of 23
79 complete genome sequences were obtained from the breakthrough cases. The obtained
80 sequences were all belonged to the Delta variant, but distinct from contemporary
81 sequences obtained from cases of community transmission in HCMC, suggesting that the
82 ongoing transmission had occurred between vaccinated healthcare workers. Viral loads
83 peaked at around 2-3 days before and after the development of clinical symptoms with
84 prolonged PCR positivity of up to 33 days. Viral loads were 251 times higher than those in
85 cases infected with old SARS-CoV-2 strains detected in Vietnam between March and
86 April 2020. Vaccine-induced neutralizing antibodies after the second dose and at diagnosis
87 were lower than those in the matched uninfected controls. There was no correlation
88 between vaccine-induced neutralizing antibody levels and viral loads (i.e. infectivity) or
89 the development of symptoms during the course of infection.

90 **Implications of all the available evidence**

91 Our study provided strong evidence demonstrating for the first time the transmission
92 between vaccine breakthrough cases infected with the Delta variant. High viral loads
93 coupled with prolonged PCR positivity and poorly ventilated indoor setting without in-

94 office mask wearing might have facilitated the transmission between vaccinated healthcare
95 workers. The absence of correlation between neutralizing antibody levels and peak viral
96 loads suggested that vaccine might not lower the infectivity of breakthrough cases. Given
97 the rapid spread of the Delta variant worldwide, physical distancing measures remain
98 critical to reduce the transmission of SARS-CoV-2 Delta variant, event in countries where
99 vaccination coverage is high.

100 INTRODUCTION

101 SARS-CoV-2 Delta variant is approximately 60% more transmissible than the Alpha
102 (B.1.1.7) variant, and has rapidly spread worldwide¹, posing a significant threat to global
103 COVID-19 control. The Delta variant possesses mutations in the spike protein (including
104 L452R and T478K) that makes the virus less susceptible to neutralizing antibodies
105 generated by current vaccines or natural infection.^{2,3} This has raised concern about vaccine
106 escape potential.

107 Data on vaccine breakthrough infections, especially those caused by the Delta variant, are
108 limited.⁴ Likewise, it remains unknown regarding the transmission potential of vaccine
109 breakthrough infection cases, especially those infected with the Delta variant. These data
110 however are critical to informing the development and deployment of COVID-19 vaccine,
111 and the implementation of infection control measures. Here, we investigate breakthrough
112 SARS-CoV-2 Delta variant infections among double-vaccinated healthcare workers of a
113 major infectious diseases hospital in Ho Chi Minh City (HCMC), Vietnam.

114 MATERIALS AND METHODS

115 Setting

116 The study was conducted at the Hospital for Tropical Diseases (HTD) in HCMC. HTD is a
117 550-bed tertiary referral hospital for patients with infectious diseases in southern Vietnam.⁵
118 The hospital has around 900 members of staff and 34 departments. All offices, except one,
119 one are equipped with air conditioners that recirculate the air without mechanical
120 ventilation (Supplementary Figure 1).

121 HTD staff members were amongst the first people in Vietnam to be offered the Oxford-
122 AstraZeneca COVID-19 vaccine. The first doses were given on 8th March 2021; the second
123 doses were given in the last two weeks of April 2021.⁶

124 **Data collection**

125 We collected demographics, vaccination history and clinical data alongside the results of
126 SARS-CoV-2 PCR diagnosis from the study participants. For SARS-CoV-2 antibody
127 measurement, we obtained 2ml of EDTA plasma from each study participants at diagnosis
128 and at week 1, 2 and 3 after admission.

129 **Nasopharyngeal-throat swab collection, PCR testing and viral load conversion**

130 Nasopharyngeal swabs were collected and placed in 1mL of viral transport medium, and
131 200uL was used for viral RNA extraction using the MagNApure 96 platform (Roche
132 Diagnostics, Germany), according to the manufacturer's instructions. For SARS-CoV-2
133 RNA detection, we used real-time RT-PCR assay with primers and probe targeted at the
134 envelope protein-coding gene (TIB MOLBIOL)⁷. PCR Ct values were converted to RNA
135 loads using an in-house established formula ($y = -0.3092x + 12.553$, $R^2 = 0.9963$, where y
136 is viral load and x is Ct value) based on 10-fold dilution series of in-vitro transcribed
137 RNA^{7,8}.

138 **Whole genome sequencing and sequence analysis**

139 Whole-genome sequences of SARS-CoV-2 were directly obtained from leftover RNA after
140 PCR testing using ARTIC protocol and Illumina reagents on a MiSeq platform with the
141 inclusion of a negative control in every sequencing run. The obtained reads from individual
142 samples were mapped to a SARS-CoV-2 reference genome (GISAID sequence ID:
143 EPI_ISL_1942165) to generate the consensus using Geneious software (Biomatter, New

144 Zealand). SARS-CoV-2 variant assignment was carried out using Pangolin.⁹ Detection of
145 amino acid changes as compared to the original Wuhan strain was done using COV-
146 GLUE.¹⁰ Maximum likelihood phylogenetic tree was reconstructed using IQ-TREE.¹¹

147 **SARS-CoV-2 antibody measurement**

148 We measured antibodies against SARS-CoV-2 nucleocapsid (N) protein using Elecsys
149 Anti-SARS-CoV-2 assay (Diagnostics, Germany), and SARS-CoV-2 neutralizing
150 antibodies using SARS-CoV-2 Surrogate Virus Neutralization Test (sVNT) (GenScript,
151 USA).¹² The experiments were carried according to the manufacturers' instructions.

152 **Additional data for analysis**

153 Because the breakthrough infections coincided with the sampling schedule at month 3 after
154 dose 1 (week 7 after the second dose) of the vaccine study,⁶ we used available data on
155 neutralizing antibodies of the vaccine study for case-control analyses. We matched cases
156 with the controls for age and gender with a matching ratio of 1:3 (when data of the controls
157 are available) or 1:1 (when data of the controls are limited).

158 For viral load comparison, we used previously reported data of SARS-CoV-2 infected
159 cases detected in Vietnam during the early phase of the pandemic in Vietnam between
160 March and April 2020.⁵

161 **Data analysis**

162 Data analysis was carried in Graphpad Prims 9.0.2. For comparisons between groups, we
163 used the Fisher exact test or the Mann-Whitney U test. We performed linear regression
164 analysis to assess the correlation between neutralizing antibody levels at diagnosis and
165 peak viral loads.

166 **Ethics**

167 The study was approved by the Institutional Review Board of HTD and the Oxford
168 Tropical Research Ethics Committee, University of Oxford, UK. Written informed
169 consents were obtained from all the participants.

170 **RESULTS**

171 **The outbreak and initial investigations**

172 On 11th June 2021 (week 7 after the second dose), a 41-year old member of HTD staff
173 (patient 1) complained of body pain and tiredness. Because community transmission of
174 SARS-CoV-2 has been increasing in HCMC since May 2021, he was tested that day and
175 found to be positive for SARS-CoV-2 (PCR Ct value: 18.5 (equivalent to log₁₀ viral load
176 of 8.5 copies per mL)). PCR screening for SARS-CoV-2 was then expanded to all hospital
177 staff and was completed by the end of 12th June 2021. A total of 52 additional members
178 were found positive, including all 6 members sharing an office with patient 1 (Figure 1 and
179 Supplementary Figure 1).

180 Following Vietnamese Government recommendations, HTD was locked down for two
181 weeks (12th-26th June 2021), with no one allowed to enter or leave the hospital. Further
182 PCR testing of all staff during this period identified 16 additional positive cases, totaling
183 69 infected members from 19/34 departments (Figure 1 and Supplementary Table 1).
184 Serological testing for SARS-CoV-2 N protein antibodies was carried out on 683 members
185 (including those stayed in the HTD during the lockdown and the infected cases) between
186 14th and 16th June 2021, but none was positive.

187 **Demographics and clinical features**

188 All the 69 members of HTD staff infected with SARS-CoV-2 were isolated for clinical
189 follow up and management at HTD. Apart from patient 1, one additional member

190 presented with symptoms at diagnosis (15th June 2021). Thus only 1 out of the first 53
191 members tested positive between 11th and 12th June 2021 was symptomatic at diagnosis.
192 Sixty-two consented to have their demographics and clinical features reported. Of these,
193 two received one dose, and 60 (including patient 1) were fully vaccinated. The infected
194 cases (29 females and 33 males) were aged between 24-60 years (median 41.5 years).
195 Forty-seven developed respiratory symptoms between 1-15 days (median: 4) after
196 diagnosis. Three had pneumonia on chest x-ray examination. Of these, one required
197 oxygen supplementation for three days. Otherwise, they all were either asymptomatic or
198 mildly symptomatic (Table 1). All those with symptoms recovered uneventfully.

199 **Viral loads**

200 At diagnosis, median PCR Ct value was 31.7 (range: 37.6–14.0), equivalent to log₁₀ copies
201 per mL of 4.5 (range: 2.6–9.9); eleven (20.8%) of the first 53 cases from 5 different
202 departments had high viral loads, median Ct value (range): 17.9 (14.0–22.6), equivalent to
203 log₁₀ copies per mL of 8.7 (range: 7.3–9.9), including patient 1 and 4/6 members sharing
204 the office with him.

205 The viral loads of the 49 (pre)symptomatic cases peaked within 2-3 days before and after
206 symptom onset, with a median Ct value (range) of 16.8 (13.1–36.9), corresponding to log₁₀
207 copies per mL of 9.1 (range: 2.8–10.2) (Figure 2A). During the course of infection, peaks
208 of viral loads measured at any time point of the symptomatic cases were higher than that of
209 asymptomatic cases; 16.5 (13.6–32) vs. 30.8 (13.1–36.9), equivalent to median log₁₀ viral
210 load of 9.2 copies per mL (range: 4.3–10.1) vs. 4.7 copies per mL (range: 2.8–10.2),
211 p=0.005, respectively (Supplementary Figure 2). The median time from diagnosis to PCR
212 negative prior discharge was 21 days (range: 8–33).

213 Compared with peak viral loads of cases infected with old SARS-CoV-2 strains detected in
214 Vietnam between March and April 2020, peak viral loads of breakthrough cases were
215 significantly higher, median log₁₀ viral load in copies per mL (range): 9.1 (range: 2.8–
216 10.2) vs. 6.7 (1.9–9.5), equivalent to 251 times higher for median viral loads. The
217 differences were more profound among symptomatic cases while there was no difference
218 in viral loads among asymptomatic cases between the two groups (Figure 2B).

219 **Whole genome sequencing**

220 A total of 23 whole genome sequences of SARS-CoV-2 were obtained from 35 samples
221 with sufficient viral loads. The obtained sequences were derived from 23 members
222 (including patient 1) of 10 different departments of HTD (Supplementary Table 1). All
223 were assigned to SARS-CoV-2 Delta variant. They were either identical or different from
224 each other by only 1 to 7 nucleotides, but no novel amino acid changes were identified
225 among them. Phylogenetically, the 23 sequences clustered tightly together but were
226 separated from the contemporary Delta variant sequences obtained from cases of
227 community transmission in HCMC (Figure 3), suggestive of ongoing transmission between
228 the vaccinated people.

229 **Antibody development and case-control analyses**

230 A total of 209 plasma samples were collected from the 62 study participants; 61 at
231 diagnosis and week 1, and 57 at week 2 and 31 at week 3 after admission. At diagnosis, all
232 but three had detectable neutralizing antibodies, with comparable levels between
233 (pre)symptomatic and asymptomatic cases (Supplementary Figure 3). Likewise, there was
234 no correlation between neutralizing antibodies at diagnosis and peak viral loads during the
235 course of infection (Figure 4).

236 At week 2 and 3 after diagnosis, neutralizing antibody levels of the case patients
237 significantly increased, and were higher than neutralizing antibody levels measured at
238 week 2 after the second dose of the 62 matched uninfected controls (Supplementary Figure
239 3).

240 Ten patients had data on neutralizing antibodies measured at both two weeks after the
241 second dose and at diagnosis. Neutralizing antibody levels measured at these two time
242 points of the 10 case patients were significantly lower than those in the 30 matched
243 uninfected controls, median % of inhibition (range): 69.4 (13.7-96.3) vs. 91.3 (57.5-97.6),
244 $p=0.012$ and 59.4 (12.5-95.0) vs. 91.1 (20.9-97.0), $p=0.001$, respectively (Figure 5).
245 Similarly, the 62 case patients had lower levels of neutralizing antibodies measured at
246 diagnosis than those in the 62 matched uninfected controls, median % of inhibition
247 (range): 68.6 (12.5-97.0) vs. 82.3 (19.3-96.7), $p=0.002$.

248 The seroconversion rates for antibodies against N protein steadily increased from 0% at
249 baseline to 65% (20/31) at week 3. Asymptomatic patients had slightly lower
250 seroconversion rates than symptomatic patients (Supplementary Figure 4). There was no
251 difference in neutralizing antibodies between the N protein antibody negative and positive
252 groups (data not shown).

253 **DISCUSSION**

254 We studied Oxford-AstraZeneca vaccine breakthrough infections associated with SARS-
255 CoV-2 Delta variant among healthcare workers of a major hospital for infectious diseases
256 in HCMC, Vietnam between 11th and 25th June 2021 (week 7 and 8 after the second dose).
257 62/69 infected cases participated in the clinical study. One required cannula oxygen
258 supplementation for three days but all made full recovery in line with recent reports

259 regarding the vaccine effectiveness in protecting against severe disease.¹³⁻¹⁵ However, we
260 found strong evidence demonstrating for the first time that fully vaccinated healthcare
261 workers could still pass the virus between each other.

262 Indeed, the 23 whole-genome sequences of SARS-CoV-2 obtained from the infected cases
263 clustered tightly on the phylogenetic tree, but separately from the contemporary Delta
264 variant genomes obtained from cases of community transmission in HCMC. This strongly
265 suggested that these individuals likely caught the virus from a single introduction into the
266 hospital. Additionally, because only 1 out of the first 53 infected cases of the outbreak
267 were symptomatic at diagnosis, presymptomatic and/or asymptomatic transmission had
268 occurred between the vaccinated members of staff of HTD. This was likely attributed to
269 several factors. Firstly, high viral loads, $>7 \log_{10}$ copies per mL, which was strongly
270 correlated with positive culture (i.e. infectiousness),^{8,16} was recorded in 11 of the first 53
271 positive cases of the outbreak at diagnosis. Second, HTD offices are typically equipped
272 with air conditioners without mechanical ventilation systems, a well-known indoor setting
273 that could facilitate the transmission of SARS-CoV-2.¹⁷ Third, mask wearing in the office
274 was not mandatory at the time.

275 Lower levels of neutralizing antibodies after vaccination and at diagnosis were associated
276 with breakthrough infections in a recent report from Israel,¹⁸ supporting findings of the
277 present study. However, we found no correlation between vaccine-induced neutralizing
278 antibody levels at diagnosis and the development of respiratory symptoms or viral loads
279 (i.e. infectivity). Thus, while neutralizing antibodies might be a surrogate of protection,
280 especially against severe diseases as a whole,¹⁹ they might not be good indicators of
281 disease progression and infectiousness for breakthrough Delta variant infection. The rapid

282 increase in neutralizing antibodies after infection among cases of the present study in turn
283 suggested that a third dose may improve the immunity and potentially the protection.

284 At the beginning of the outbreak, none of the HTD members of staff (including the PCR
285 confirmed cases) were tested positive for N-protein antibodies, which only develop in
286 response to whole-virus based vaccine and natural infection. Additionally, between 12th
287 and 14th May 2021, all members of HTD staff were subjected to a periodic testing for
288 SARS-CoV-2 by PCR, but none was positive. The data thus suggested that the infected
289 cases were captured at an early phase of the infection. Therefore, by carefully following up
290 the patients during hospitalization, we have also provided new insights into the natural
291 history of breakthrough Delta variant infections. We found viral loads of breakthrough
292 Delta variant infection cases peaked around 2-3 days before and after the development of
293 symptoms, and were 251 times higher than those of the infected cases detected during the
294 early phase of the pandemic in 2020.⁵ Additionally, there has been only one report
295 showing that 9/11 cases of vaccine breakthrough infection had no detectable RNA when
296 retested within 2–7 days after diagnosis.²⁰ Yet, we found prolonged PCR positivity was up
297 to 33 days in our study participants. These factors might explain the current rapid
298 expansion of the Delta variant, even in the countries with high vaccination coverage.

299 In summary, we report the transmission SARS-CoV-2 Delta variant among vaccinated
300 health care workers. Breakthrough Delta variant infections are associated with high viral
301 loads, prolonged PCR positivity, and low levels of neutralizing antibodies after vaccination
302 and at diagnosis. These factors coupled with poorly ventilated indoor settings and without
303 mask wearing might have facilitated presymptomatic and/or asymptomatic transmission
304 among the vaccinated workers. Physical distancing measures remain critical to reduce

305 SARS-CoV-2 Delta variant transmission, thereby mitigating the impact of the ongoing
306 COVID-19 pandemic.

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396 LEGENDS TO TABLES AND FIGURES

397 **Table 1:** Demographics and clinical characteristics of the study participants

398 **Figure 1:** Flowchart showing timelines and results of SARS-CoV-2 RT-PCR screening
399 before and during the lockdown (11-25 June 2021)

400 **Notes to Figure 1:** *The remaining members of staff were working from home.

401 **Figure 2:** Viral load analyses, A) plot outlining kinetics of viral loads in relation to illness
402 onset of the 49 study participants who were either symptomatic or presymptomatic at
403 admission, B) comparison between peak viral loads of breakthrough infections (cases) and
404 those (controls) infected with old SARS-CoV-2 strains detected between March and April
405 2020 in Vietnam

406 **Notes to Figure 2:** Vertical dashed line indicates the time point of illness onset. Horizontal
407 dashed line indicates detection limit of PCR assay. A) Black lines indicates median viral
408 loads, B) black dots represent for whole groups, red dots represent for symptomatic cases
409 and blue dots represent for asymptomatic cases. Peak viral loads comparison between
410 symptomatic and asymptomatic groups of the cases and controls: median \log_{10} viral load in
411 copies per mL (range): 9.2 (4.3–10.1) vs. 6.9 (3.7–9.5), $p < 0.001$ and 4.7 (2.8–10.2) vs. 4.9
412 (1.9–8.6), $p = 0.511$.

413 **Figure 3:** Maximum likelihood tree illustrating the relatedness between SARS-CoV-2
414 Delta variant strains obtained from cases of vaccine breakthrough infection (red) and
415 contemporary Delta variant sequences obtained from cases of community transmission in
416 Ho Chi Minh City (blue) and other provinces in Vietnam or countries (black).

417 **Note to Figure 3:** Cases of vaccine breakthrough infections were derived from 12/19
418 affected department of the Hospital for Tropical Diseases

419 **Figure 4:** Correlation between neutralizing antibodies at diagnosis and peak viral loads
420 during the course of infection

421 **Figure 5:** Comparison between neutralizing antibody levels of case patients (red) and
422 uninfected controls (grey green). A) between the 10 case patients whose data on
423 neutralizing antibodies at both week 2 after the second doses (8 weeks after the first dose)
424 abd at diagnosis were available and the uninfected controls, B) between the 62 case
425 patients and the uninfected controls for data at diagnosis

Table 1: Demographics and clinical characteristics of the study participants

Signs/Symptoms	All cases (n=62)	Male (n=33)	Female (n=29)
Age, y, median (range)	41.5 (24-60)	41 (27-60)	43 (24-59)
Occupation, n (%)			
Nurse	13	5	8
Pharmacist	10	3	7
IT	7	7	0
Clinician	7	5	2
Accountant	4	0	4
Technical staff	3	3	0
Cleaner	2	2	0
Others	16	8	8
Symptomatic, n (%)	49 (79.0)	24 (72.7)	25 (86.2)
PCR diagnosis to illness onset, d, (median; range)*	4 (0-15)	3 (0-8)	5 (0-15)
Comorbidity [#] , n (%)	17 (27.4)	9 (27.3)	8 (27.6)
COVID-19 vaccination [‡] , n (%)	62 (100)	33 (100)	29 (100)
Two doses	60 (96.7)	33 (100)	27 (93.1)
One dose	2 (3.3)	0	2 (6.9)
Fever, n (%)	17 (27.4)	9 (27.3)	8 (27.6)
Cough, n (%)	23 (37.1)	19 (57.6)	14 (48.3)
Sore throat, n (%)	21 (33.9)	9 (27.3)	12 (41.4)
Runny nose, n (%)	22 (35.5)	9 (27.3)	13 (44.8)
Loss of smell, n (%)	24 (38.7)	14 (42.4)	10 (34.5)
Loss of taste, n (%)	5 (8.1)	3 (9.1)	2 (6.9)
Muscle pain, n (%)	17 (27.4)	13 (39.4)	4 (13.8)
Headache, n (%)	12 (19.4)	6 (18.2)	6 (20.7)
Chest pain, n (%)	2 (3.2)	0	2 (6.9)
Nausea, n (%)	5 (8.1)	3 (9.1)	2 (6.9)
Others, n (%) [§]	5 (8.1)	1 (3.0)	4 (13.8)
Pneumonia, n (%) ^{**}	3 (4.8)	0	3 (10.3)

Notes to Table 1:

*Symptomatic cases only

[‡]All receiving AstraZeneca vaccine; The second doses were given in last 2 weeks of April 2021.[#]Overweight (n=6), obese (n=3), hypertension (n=3), hepatitis B (n=2), diabetes (n=1), pregnancy (n=1), diabetes and hepatitis B (n=1).[§]Chills (n=2), sweating (n=1), giddiness (n=1), red eyes (n=1), and diarrhea (n=1)^{**}One requiring oxygen supplementation via cannula route for 3 days.

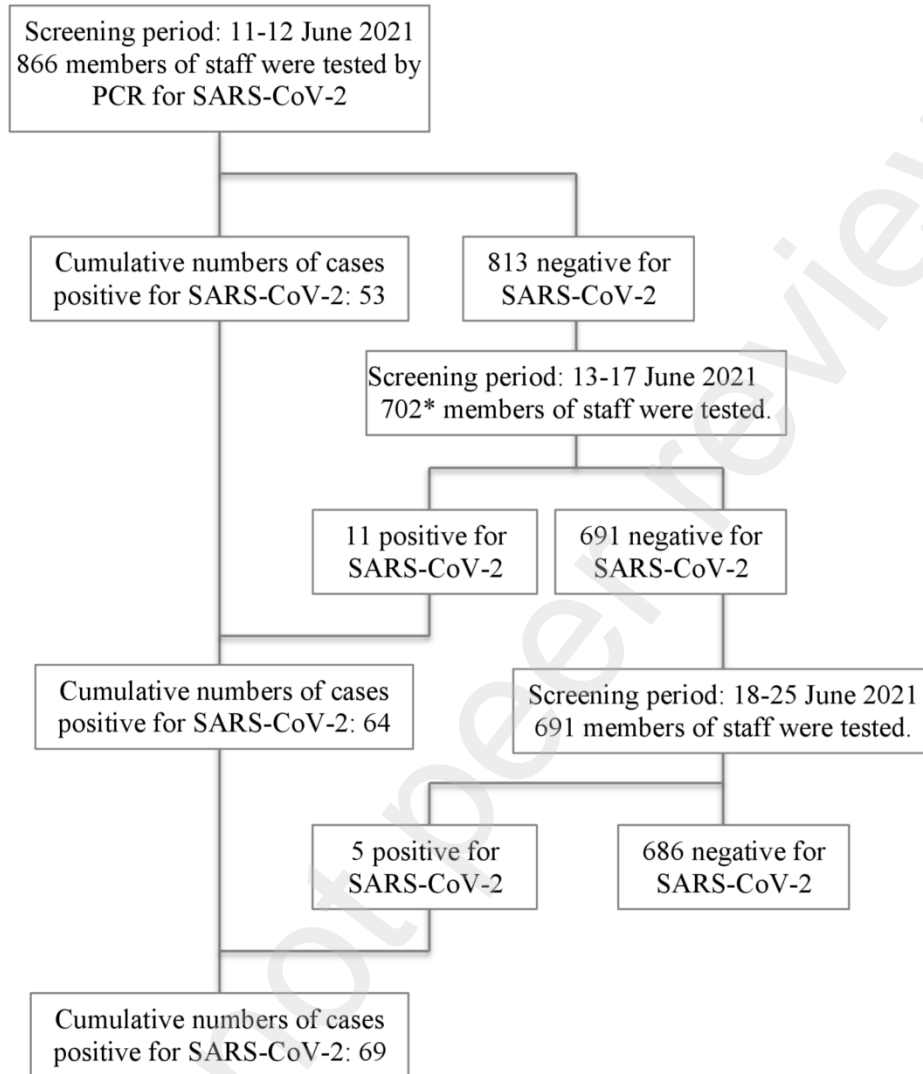


Figure 1: Flowchart showing timelines and results of SARS-CoV-2 RT-PCR screening before and during the lockdown (11-25 June 2021)

Notes to Figure 1: *The remaining members of staff were working from home.

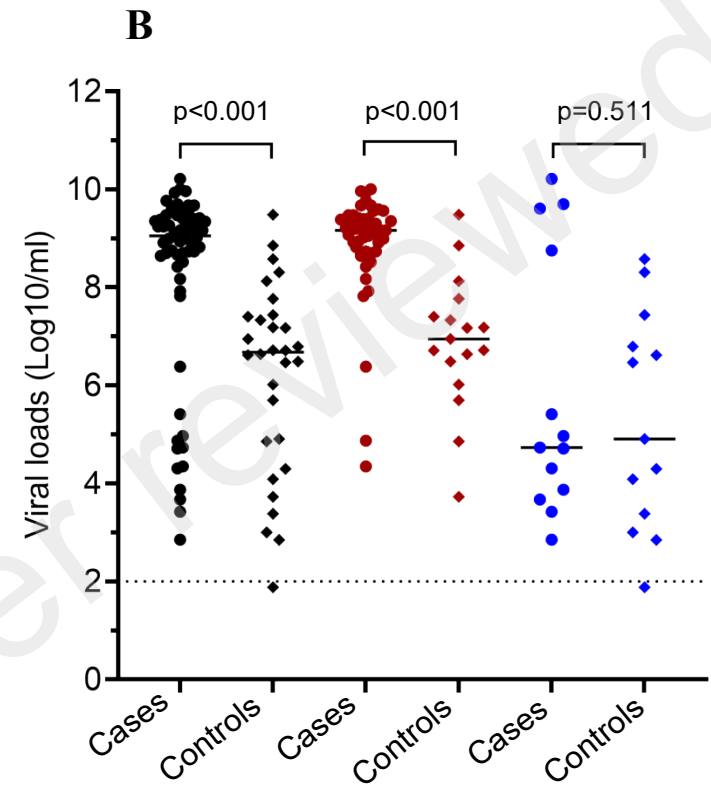
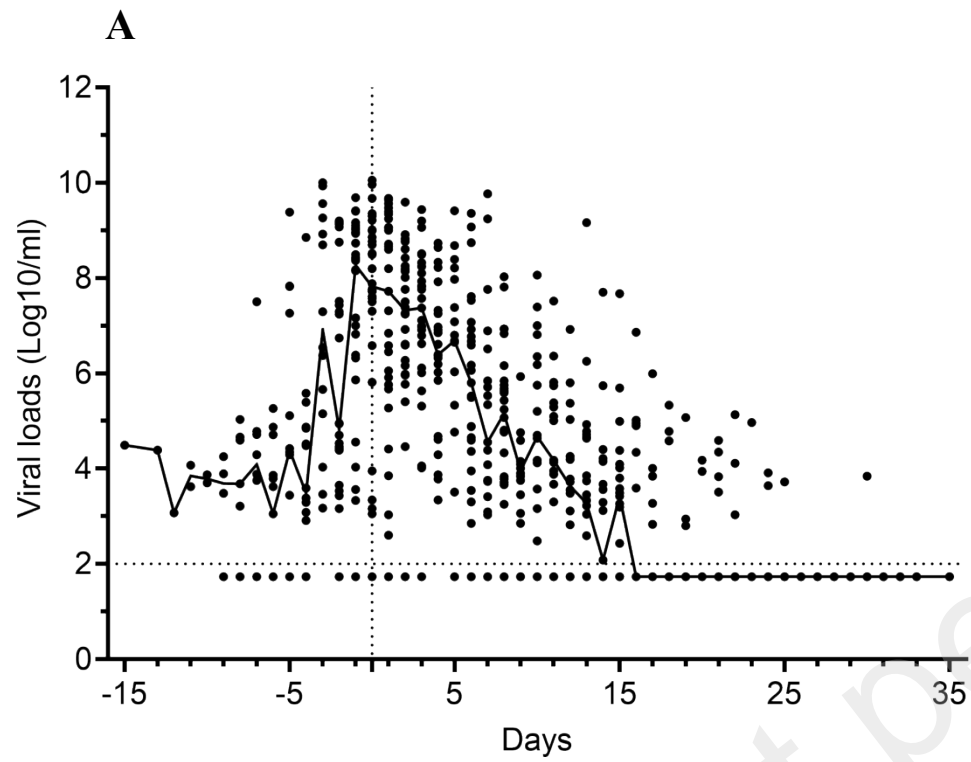


Figure 2: Viral load analyses, A) plot outlining kinetics of viral loads in relation to illness onset of the 49 study participants who were either symptomatic or presymptomatic at admission, B) comparison between peak viral loads of breakthrough infections (cases) and those (controls) infected with old SARS-CoV-2 strains detected between March and April 2020 in Vietnam

Notes to Figure 2: Vertical dashed line indicates the time point of illness onset. Horizontal dashed line indicates detection limit of PCR assay. A) Black lines indicates median viral loads, B) black dots represent for whole groups, red dots represent for symptomatic cases and blue dots represent for asymptomatic cases. Peak viral loads comparison between symptomatic and asymptomatic groups of 1.1E+10 (1.1E+10) vs 1.1E+10 (1.1E+10) (0.03 (1.2E+10) vs 0.03 (2.7E+05) vs 0.001 (1.1E+10) vs 1.1E+10 (-10.2)

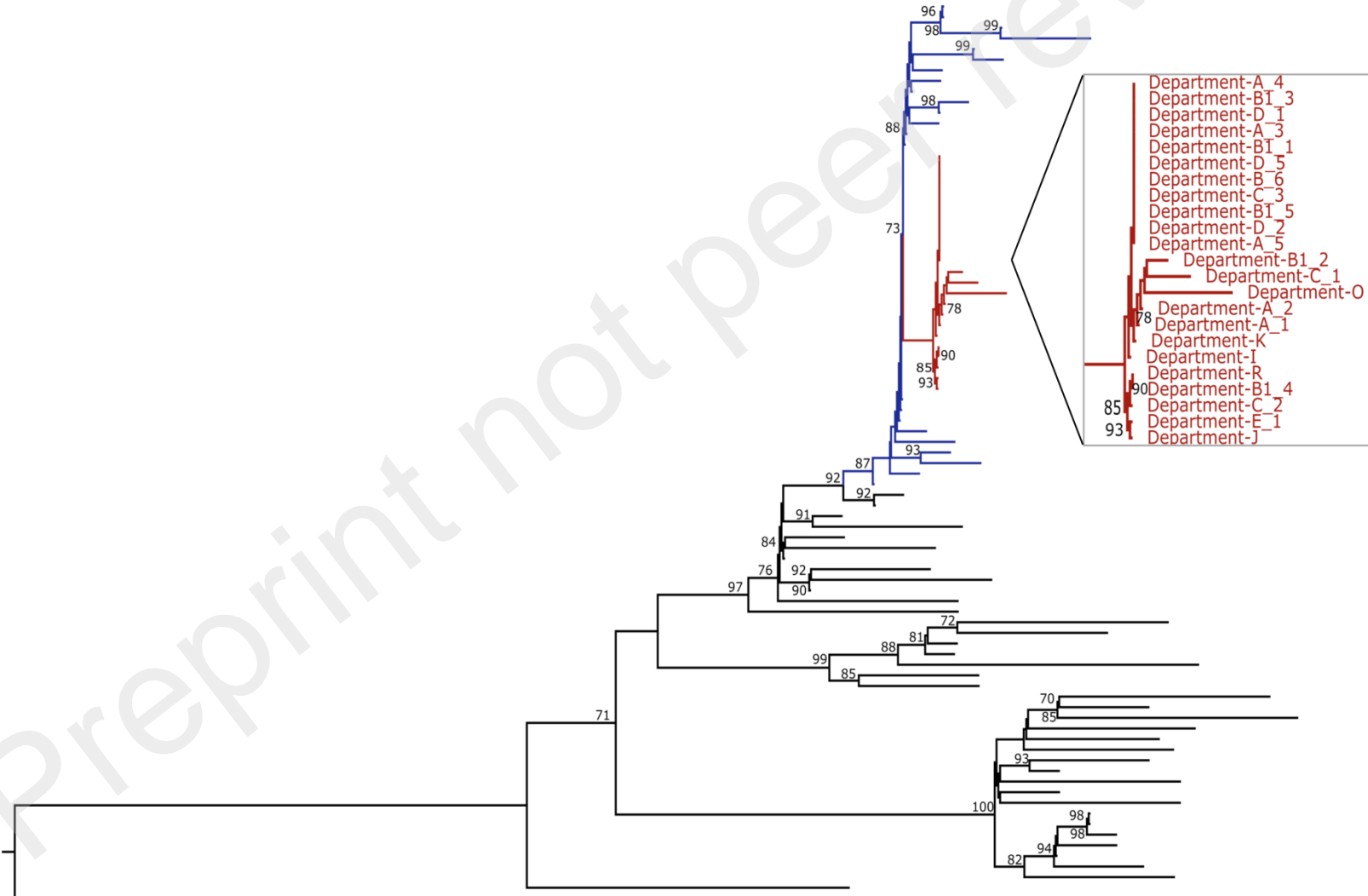


Figure 3: Maximum likelihood tree illustrating the relatedness between SARS-CoV-2 Delta variant strains obtained from cases of vaccine breakthrough infection (red) and contemporary Delta variant sequences obtained from cases of community transmission in Ho Chi Minh City (blue) and other provinces in Vietnam or countries (black).

Note to Figure 3: Cases of vaccine breakthrough infections were derived from 12/19 affected department of the Hospital for Tropical Diseases

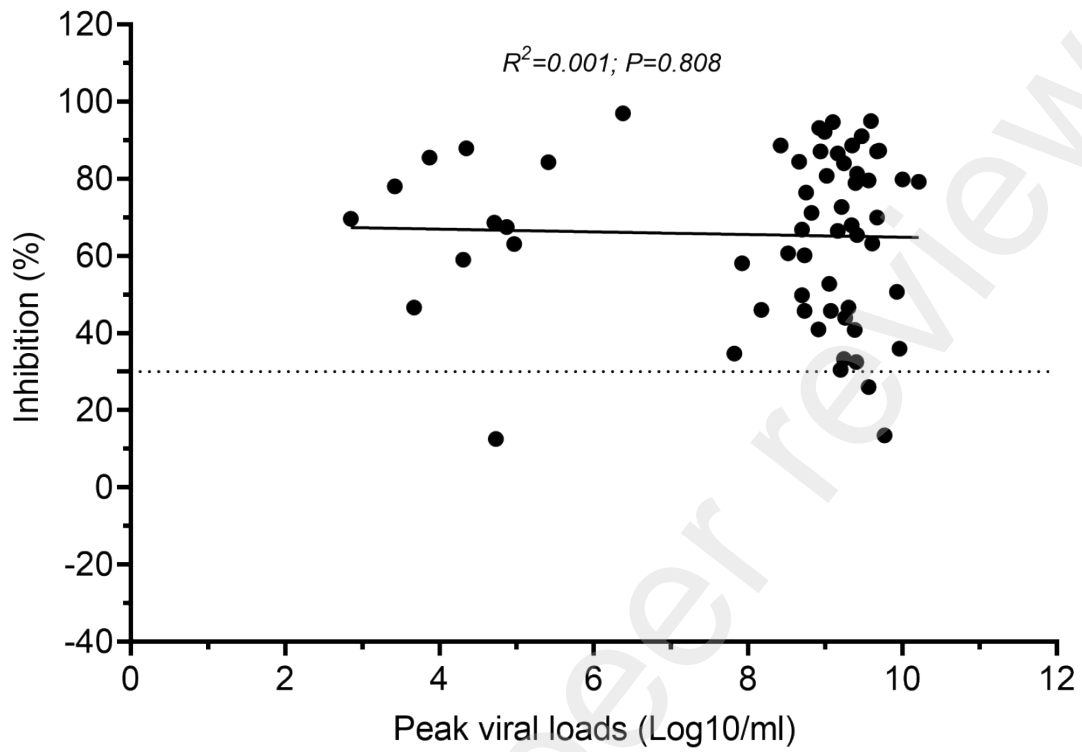


Figure 4: Correlation between neutralizing antibodies at diagnosis and peak viral loads during the course of infection

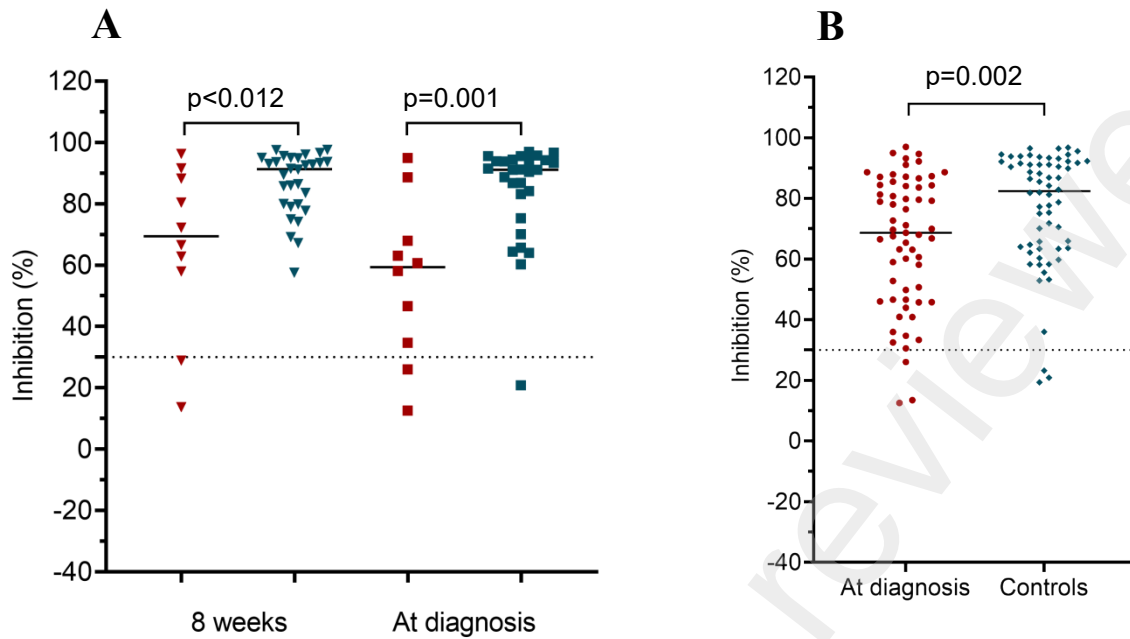
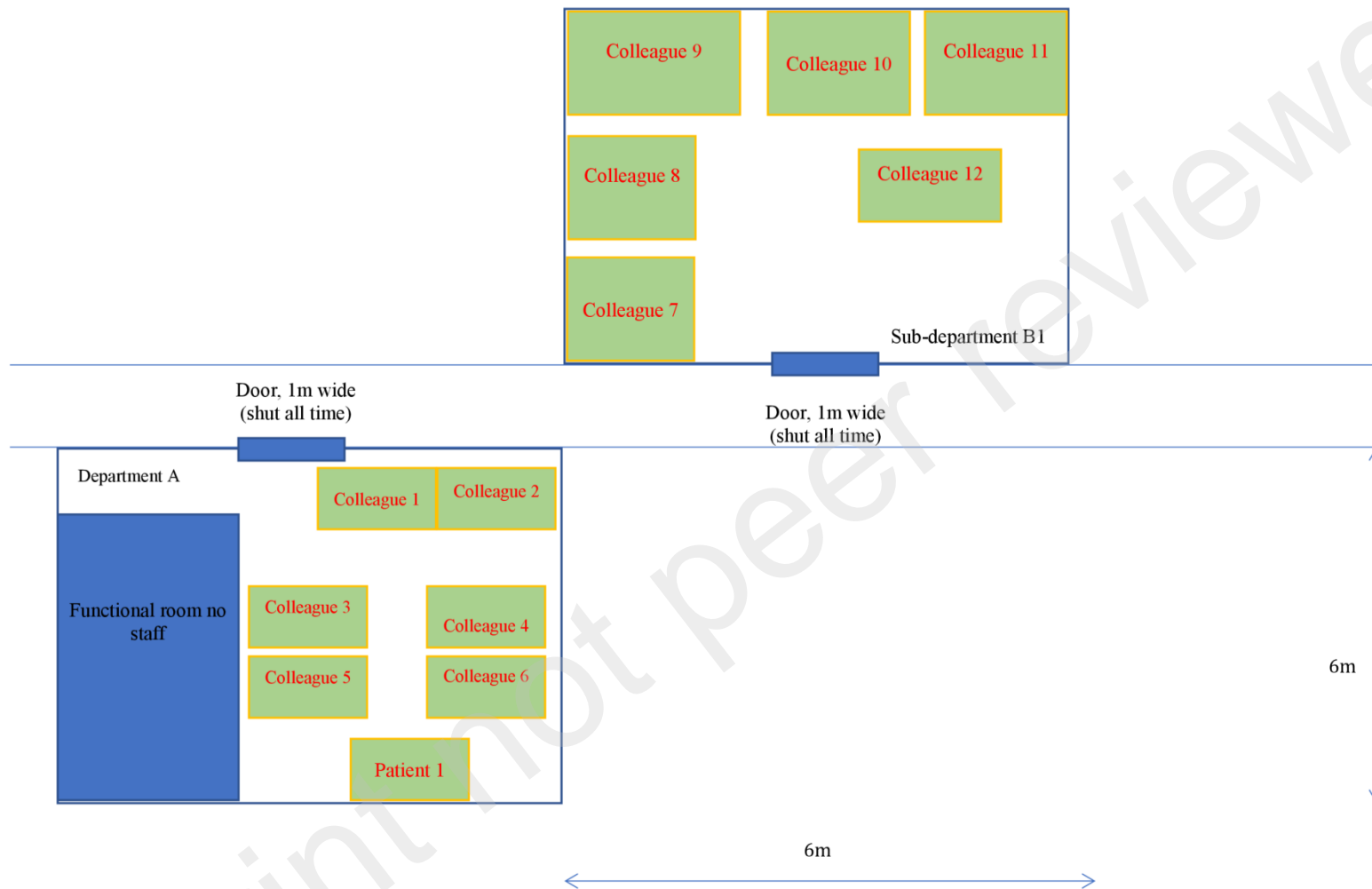


Figure 5: Comparison between neutralizing antibody levels of case patients (red) and uninfected controls (grey green). A) between the 10 case patients whose data on neutralizing antibodies at both week 2 after the second doses (8 weeks after the first dose) and at diagnosis were available and the uninfected controls, B) between the 62 case patients and the uninfected controls for data at diagnosis

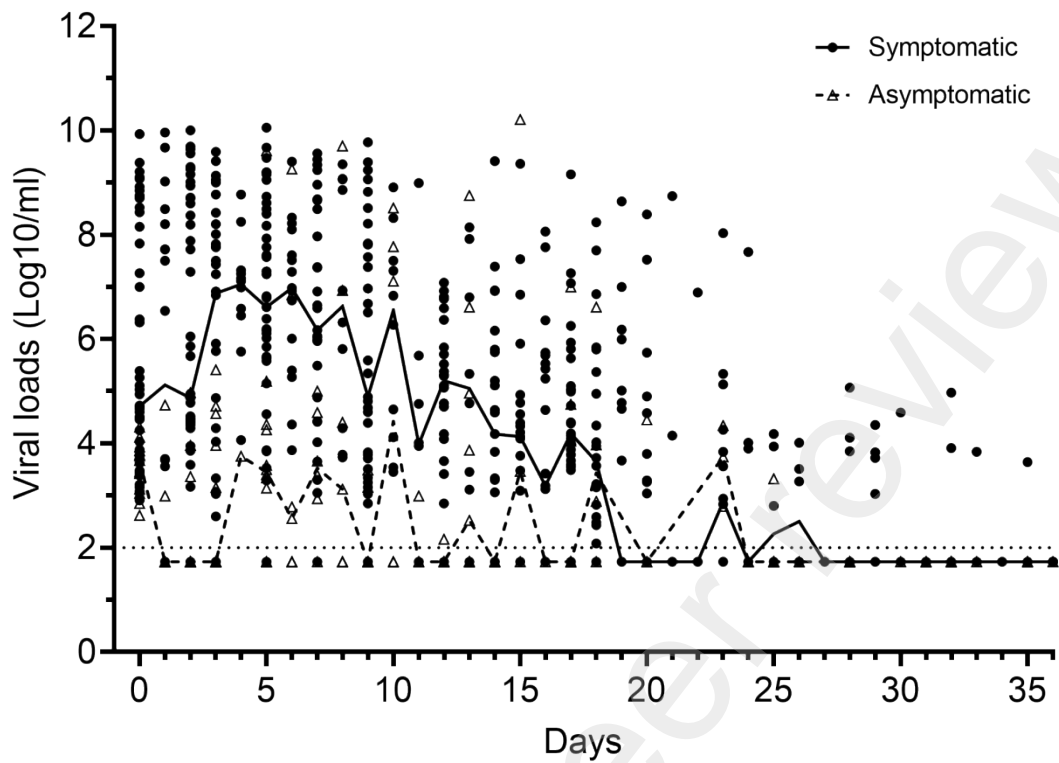
SUPPLEMENTARY MATERIALS

Supplementary Table 1: Numbers of PCR confirmed cases detected per department

Name of department*	Functions	Number of staff	Number of staff tested positive (%)	Numbers genomes obtained
Department A	Supportive service	7	7 (100)	5
Department B	Supportive service	56	16 (29)	6
Sub-department B1	Supportive service	8	7 (88)	6
Sub-department B2	Supportive service	7	4 (57)	0
Sub-department B3	Supportive service	8	3 (38)	0
Sub-department B4	Supportive service	9	2 (22)	0
Department C	Supportive service	3	3 (100)	3
Department D	Supportive service	60	12 (20)	3
Department E	Patient care	75	6 (8)	1
Department F	Supportive service	36	4 (11)	0
Department G	Patient care	50	3 (6)	0
Department H	Supportive service	20	3 (15)	0
Department I	Supportive service	6	2 (33)	1
Department J	Patient care	28	1 (4)	1
Department K	Patient care	31	1 (3)	1
Department L	Patient care	32	1 (3)	0
Department N	Patient care	28	1 (4)	0
Department O	Patient care	19	1 (5)	1
Department P	Patient care	29	1 (3)	0
Department Q	Supportive service	11	1 (9)	0
Department R	Supportive service	15	1 (7)	1
Department S	Patient care	17	1 (5.9)	0
Department T	Patient care	18	1 (5.6)	0

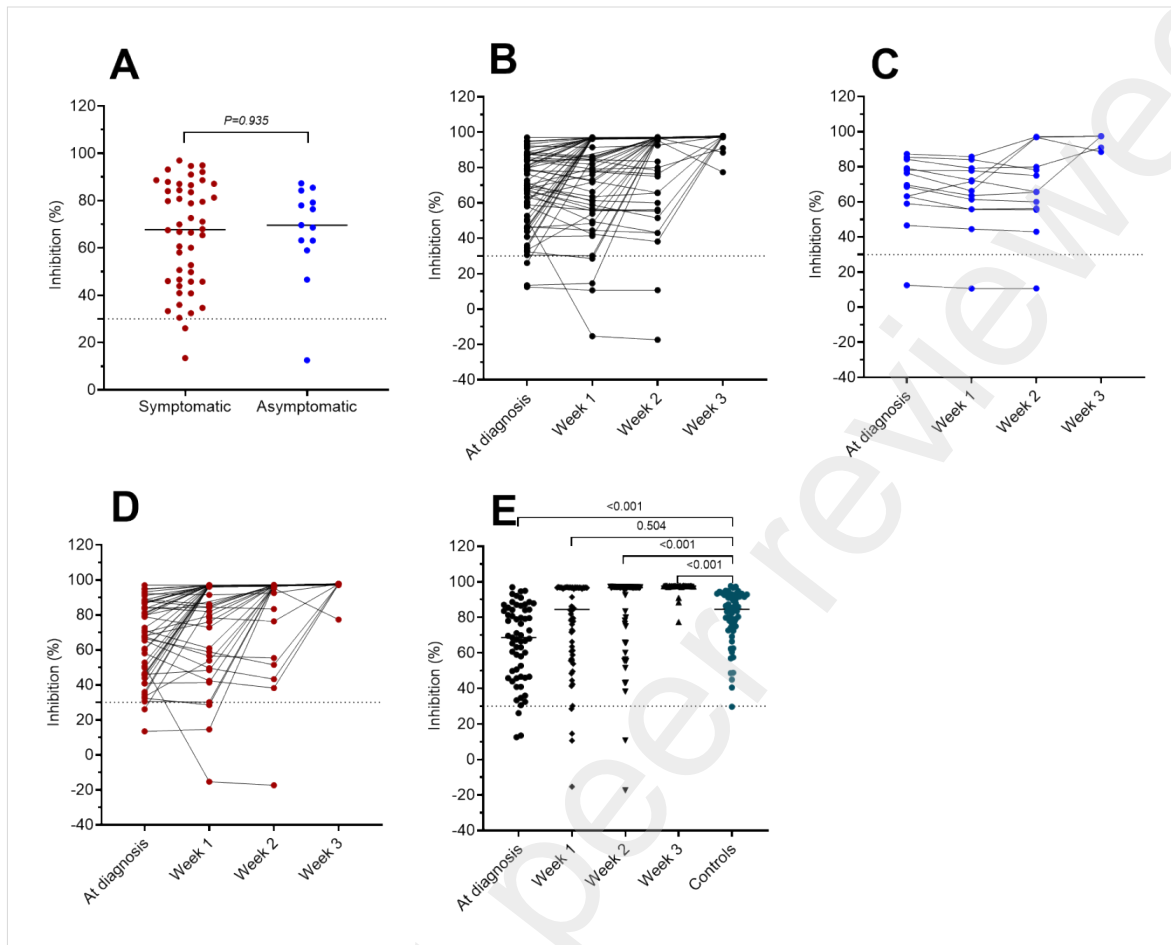


Supplementary Figure 1: Layout of office of patient 1 and a close office where 7/8 members were tested positive on 11th-12th June 2021. Office names are linked with Supplementary Table 1. Offices are equipped with air conditioners without mechanical ventilation. During working hours, doors are kept closed to maintain cooling air.



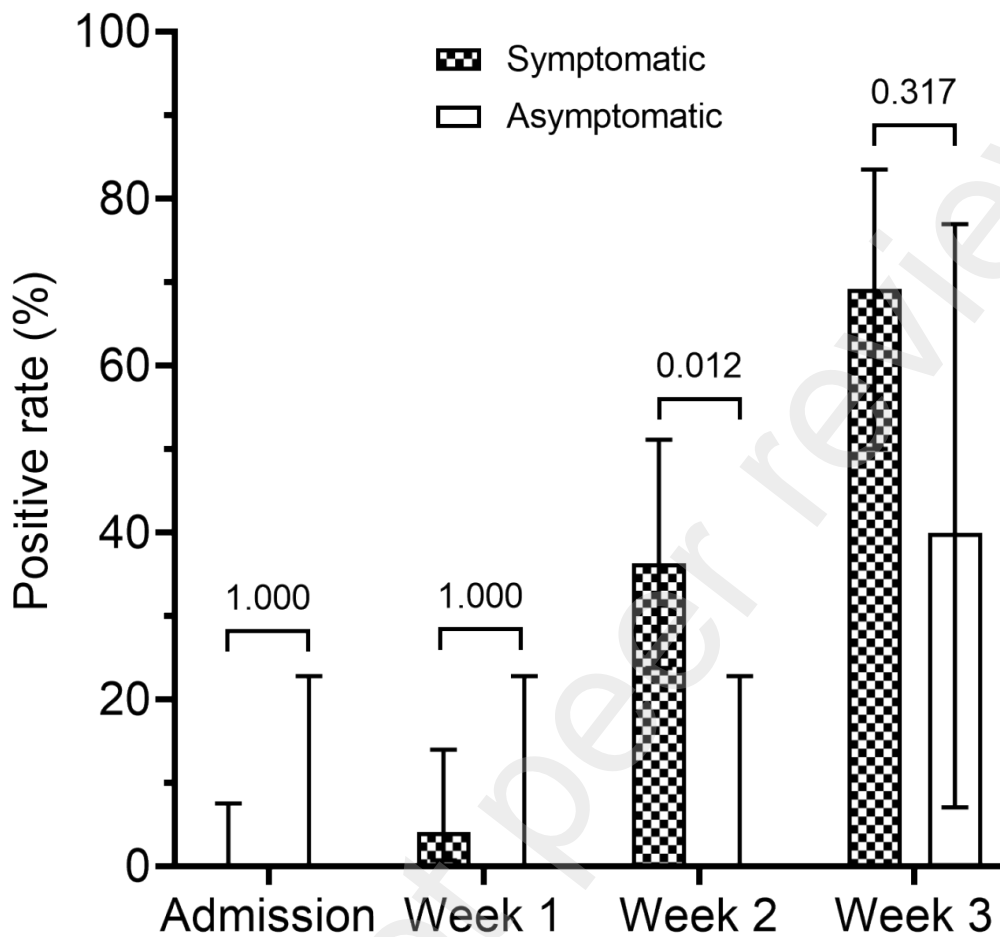
Supplementary Figure 2: Plot outlining kinetics of viral loads since PCR diagnosis during the course of hospitalization of the asymptomatic and symptomatic cases

Notes to Supplementary Figure 2: (Dashed) lines indicate median viral loads.



Supplementary Figure 3: Results of neutralizing antibody measurement, A) at diagnosis of symptomatic (including those developed symptoms after diagnosis) and asymptomatic cases, and kinetics of neutralizing antibodies at admission and at week 1, 2 and 3 after admission of B) the whole group, C) the asymptomatic group, D) the symptomatic group, and E) in comparison with the control group

Supplementary Notes to Figure 3: Dashed line indicates assay cut-off (30%). The asymptomatic case (panel C) who remained seronegative during infection did not respond to the vaccine (data not shown). Neutralizing antibody measurement were repeated twice for the symptomatic case who became seronegative at week 1 and week 2. Age and gender comparison between cases and controls: median in years (range): 41.5 (24-60) vs. 37.5 (24-58), $p=0.47$, and male/female 33/29 vs. 23/29, $p=0.07$.



Supplementary Figure 4: Seroconversion rates against N protein at admission, and week 1, 2 and 3 after admission.

Note to Supplementary Figure 4: For the whole group, the seroconversion rates for antibodies against N protein increased from 0% at baseline to 3.3% (2/61) at week 1, 28.1% (16/57) at week 2 and 65% (20/31) at week 3.