

Epidemiological characteristics of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China: An overview of vaccine breakthrough infection events

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Author contribution statement

All the authors contributed to the paper presented methodology and conceptualization. They all contributed to data analysis and paper writing.

Keywords

COVID-19 disease, Asymptomatic carrier, Nosocomial infection, Scientific protective strategy, vaccine breakthrough infection

Abstract

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has wreaked havoc to human beings around the world. Although China quickly brought the Coronavirus disease (COVID-19) pandemic under control, there have been several sporadic outbreaks in different regions of China since then. This article describes the chronological nosocomial COVID-19 infection events that related to several sporadic outbreaks of SARS-CoV-2 in different regions of China. We reported epidemiological characteristics and management measures of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China, specially focused on domestic COVID-19 breakthrough infection in China — a vaccinated healthcare professional working in the isolation ward of a designated COVID-19 hospital.

Contribution to the field

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has wreaked havoc to human beings around the world. Although China quickly brought the Coronavirus disease (COVID-19) pandemic under control, there have been several sporadic outbreaks in different regions of China since then. This article describes the chronological nosocomial COVID-19 infection events that related to several sporadic outbreaks of SARS-CoV-2 in different regions of China. We reported epidemiological characteristics and management measures of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China, specially focused on domestic COVID-19 breakthrough infection in China — a vaccinated healthcare professional working in the isolation ward of a designated COVID-19 hospital.

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18

In review

19 **Abstract**

20 The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has wreaked
21 havoc to millions of people around the world. Although China quickly brought the Coronavirus
22 disease (COVID-19) under control, there have been several sporadic outbreaks in different regions
23 of China since June 2020. This article describes the chronological nosocomial COVID-19
24 infection events related to several sporadic outbreaks of SARS-CoV-2 in different regions of
25 China. We report epidemiological characteristics and management measures of sporadic
26 nosocomial COVID-19 infections from June 2020 to June 2021, and specially focused on the
27 domestic COVID-19 breakthrough infection in China including domestic COVID-19
28 breakthrough infection - a vaccinated healthcare professional working in the isolation ward of a
29 designated COVID-19 hospital.

30 **Keywords:** COVID-19 disease; asymptomatic carrier; nosocomial infection; Scientific protective
31 strategy; vaccine breakthrough infection

32

In review

33 **Introduction**

34 The outbreak of the COVID-19 virus was first reported in Wuhan, China, in December 2019. The
35 COVID-19 pandemic led China to quarantine the population in order to protect them ¹. Chinese
36 authorities decided to adopt extraordinary measures to contain and limit the spread of the SARS-
37 CoV-2 virus. From 1 January to 8 April 2020, >8,000 patients with COVID-19 were hospitalized
38 and the Chinese government imposed the Wuhan lockdown on January 23, which ended on April 8,
39 2020.

40
41 With the COVID-19 epidemic quickly under control in the early stages of 2020, importing the
42 SARS-CoV-2 virus could pose great challenges to the control and prevention of nosocomial
43 COVID-19 infection in healthcare settings. Our previous report showed the impact of the novel
44 coronavirus SARS-CoV-2 among healthcare workers in hospitals during the early phase of the
45 COVID-19 epidemic², and suggested that local authorities need to be extremely cautious and
46 implement stringent protective measures to safeguard healthcare workers in order to counteract the
47 threats brought by the pandemic³⁻⁵. Though medical staff belong to the susceptible population to a
48 certain extent, hospitals have practiced cohorting in accordance with recommendations from
49 COVID-19 infection prevention and control professional societies, which has reduced the risk of
50 hospital-acquired COVID-19. Because healthcare workers are at the interface between hospitals and
51 the community, where there is significant COVID-19 transmission, they may be infected by
52 asymptomatic carriers with COVID-19 or COVID-19 patients. Furthermore, in the designated
53 hospital admitting COVID-19 patients or asymptomatic carriers, medical staff are highly exposed
54 to nosocomial COVID-19 acquisition and SARS-CoV-2 transmission. Therefore, healthcare staff
55 may play a key role in initiating or amplifying sporadic COVID-19 outbreaks in healthcare settings
56 including hospitals and other care facilities.

57
58 The importing of the SARS-CoV-2 virus from overseas, induced sporadic outbreaks with COVID-
59 19 from June 2020 to June 2021 in China^{6,7}. This article describes the chronological events that led
60 to several sporadic nosocomial COVID-19 infections in different regions of China from June 2020
61 to June 2021, including domestic COVID-19 breakthrough infection — a vaccinated healthcare
62 professional working in the isolation ward of a designated COVID-19 hospital⁸. Lastly, we provide
63 an overview of local COVID-19 outbreak induced by the B.1.617.2 (Delta) variant of the COVID-
64 19 virus in China.

65
66 **Methods**

67 From the beginning of June 1, 2020, every day, we prospectively focused on the COVID-19
68 epidemic data from the Chinese Center for Disease Control and Prevention. Once we had the new
69 report of nosocomial COVID-19 infection in China, we tracked this epidemic and collected its
70 epidemiological characteristics from announcements by the local Health Commission and presented
71 a narrative research for geographical and epidemiological characteristics of nosocomial COVID-19
72 infection from June 2020 to June 2021.

73
74 We searched epidemiologic data published on the website of WHO, the China Center for Disease
75 Control and Prevention, National Health Commission, the Health Commission of Qingdao,
76 Shenyang, Shijiazhuang, and Dalian city, Jilin, Shaanxi, and Guangdong Province from June 2020

77 to January 2021. Using the keywords “nosocomial infection”, “COVID-19 variant”, “SARS-CoV-
78 2”, “B1.617.2 (Delta) lineage”, and Boolean operator ‘AND’, we periodically searched the
79 published medical literature using the PubMed service maintained by the U.S. National Library of
80 Medicine of NIH. Confirmed COVID-19 cases are defined as persons who tested positive for SARS-
81 CoV-2 and had clinical symptoms. Asymptomatic carriers refer to persons without clinical
82 symptoms who tested positive for SARS-CoV-2.

83 84 **Results**

85 **Regional distribution of nosocomial COVID-19 infections from June 2020 to June 2021**

86 From June 2020 to June 2021, regional distribution of the sporadic nosocomial COVID-19
87 infections is shown in [Figure 1, 2](#) and [Table 1](#). Most of these cities are located in coastal or airline
88 hub areas, for example, Dalian, Qingdao, Shanghai are coastal cities, and Xi’an, Shenyang,
89 Shijiazhuang, and Guangzhou are airline hub cities.

91 **Occupational distribution of nosocomial COVID-19 infections from June 2020 to June 2021**

92 From June 2020 to June 2021, six cities in China had reported over 45 cases with nosocomial
93 COVID-19 infections, including 39 confirmed cases and 6 asymptomatic cases ([Table 2](#)). Among
94 them, nursing staff (3), doctors (6), patients (12), accompanying staff (22), and laboratorian (2) were
95 diagnosed. The route of these nosocomial infections mainly included workplace accidental exposure
96 to COVID-19, cross infection among healthcare workers, patients, and accompanying staff.

98 **SARS-CoV-2 gene sequencing results of nosocomial COVID-19 infections from June 2020 to 99 June 2021**

100 SARS-CoV-2 gene sequencing is crucial work for nosocomial COVID-19 infections in new
101 sporadic outbreak regions. The virus strain of nosocomial COVID-19 infection found in Qingdao
102 city is the virus strain lineage B.1.1 imported from overseas ([Table 2](#)). Gene sequencing results
103 showed that the coronavirus found in Dalian, Shenyang, and Shijiazhuang cities is similar to the
104 strain imported from Europe; The virus strain found in Xi’an city is a COVID-19 variant B.1.1.7
105 lineage; SARS-CoV-2 strain found in Guangzhou city is the imported virus strain B1.617.2 (Delta)
106 lineage ([Table 2](#)).

107 [A report from Fang et al⁹](#) showed that the strains associated with specific outbreak in Dalian City
108 were as follows: LNDL-BHQ-0722-Y_S12_L001_R1_001, LNDL-SFL-0722-
109 Y_S9_L001_R1_001, LNDL-WY-0722-Y_S11_L001_R1_001, and LNDL-XY-0722-
110 Y_S10_L001_R1_001; The parent strain from Wuhan was
111 NC_045512.2_Severe_acute_respiratory_syndrome_coronavirus_2_isolate_Wuhan-Hu-
112 1_complete_genome. After accessing the public database GISAID and GenBank, 3 Russian strains
113 detected in July were found to share the 10 variation sites with the 2 Hebei strains (GISAID IDs:
114 EPI_ISL_596266, EPI_ISL_569792, and EPI_ISL_569793)¹⁰. Evidence indicates that these the
115 Shijiazhuang strains may have originated from these Russian strains¹⁰.

117 **Discussion**

118 This paper provides us with an inspiring vision regarding the current COVID-19 pandemic. The
119 main findings of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 are listed
120 below: (1) the importance of rolling out an overall nucleic acid test campaign to all staff in healthcare

121 settings, is a crucial part of the COVID-19 surveillance; (2) The case of coronavirus transported
122 onto the workplace warns us that the current hospital disinfection concept urgently requires updating,
123 especially in designated hospitals, and there is an urgent demand of the management of staff
124 accompanying patients in non-designated hospitals ; (3) The phenomenon about COVID-19 vaccine
125 breakthrough infection deserves our great attention.

126 For healthcare workers, patients/accompanying staff, and cleaner, their COVID-19 infection may
127 be from hospital (hospital-acquired infection, also nosocomial infection) or community
128 (community-acquired infection). Distinguishing nosocomial infection and community-acquired
129 infection is an important base to control the epidemic in nosocomial COVID-19 infections. Because
130 healthcare workers are at the interface between hospitals and the community, where there is
131 significant COVID-19 transmission, they may be infected by asymptomatic carriers from the
132 community with COVID-19 or COVID-19 patients. These healthcare workers (infected in the
133 community) do not belong to nosocomial infection (also called hospital-acquired infection). For
134 example, in Figure 1, the infected cases (including healthcare workers, cleaner, etc.) in Beijing,
135 Dalian (27 Dec. 2020) and Shanghai were community-acquired infection, not nosocomial infection.
136 For nosocomial infection of healthcare workers, patients/accompanying staff, and cleaner, as the
137 effective control measures taken by the local government must include: (1) these hospitals imposed
138 lockdown, especially in the designated COVID-19 hospital; (2) rolling out an overall nucleic acid
139 test campaign to all staff is key in healthcare settings.

141 Among 9 sporadic nosocomial COVID-19 infections, our results showed that 8 series cases were
142 found by rolling out overall a nucleic acid test campaign to all hospital staff, suggesting the
143 importance of regular screening for all staff in healthcare settings. As part of efforts to control the
144 COVID-19 infections, one of the effective prevention measures taken by local authorities is that all
145 hospital personnel labeled a key population are closely monitored⁷. Whether the epidemic in
146 nosocomial COVID-19 infections can be brought under control depends on how many new
147 infections emerge of their close contacts and secondary close contacts in the next two weeks. If
148 these hospitals imposed lockdown as the effective control measures taken by the local government,
149 then ideally, new confirmed cases with COVID-19 infections will see a downward trend within two
150 weeks. Cases such as hospital-acquired infection in the designated hospital of Qingdao city are a
151 warning that workplace storage and transport could be a hotbed for the coronavirus, or other
152 pathogens. There is an urgent demand for workplace disinfection to protect the health safety of
153 medical staff, patients, and accompanying staff in the current pandemic or into another worse
154 outbreak.

156 Our data also showed that a vaccinated healthcare professional who received inactivated vaccine
157 was infected with COVID-19 while working in the isolation ward of a designated COVID-19
158 hospital, and the coronavirus strain was determined to be the imported COVID-19 variant strain
159 B.1.1.7⁸, suggesting that there exists the domestic COVID-19 vaccine breakthrough infection in
160 China, and this phenomenon deserves our serious attention. Vaccination is well-known to be key to
161 stopping the virus from circulating and more variants from popping up¹¹⁻¹³. The vaccine
162 breakthrough infection case was defined as an individual with positive SARS-CoV-2 nucleic acid
163 amplification tested after receiving at least one dose of a SARS-CoV-2 vaccine¹⁴⁻¹⁶. Jacobson et al¹⁷
164 addressed post-vaccination SARS-CoV-2 infections and the incidence of the B.1.427/B.1.429

165 variant among healthcare personnel at a northern California academic medical center. Hacısuleyman
 166 et al¹⁸ reported two women with vaccine breakthrough infection in a cohort of 417 persons who had
 167 received the second dose of BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) vaccine at
 168 least two weeks previously, and the viral sequencing showed that they were infected with the new
 169 variant virus including E484K in 1 woman and three mutations (T95I, del142–144, and D614G) in
 170 both. These observations revealed a potential risk of COVID infection with the variant virus after
 171 successful vaccination.

172 Vaccine breakthrough cases with SARS-CoV-2 were reported in many countries¹⁹⁻²¹. An analysis
 173 from Israel's vaccination campaign showed that COVID-19-related hospitalizations, severe disease,
 174 and death were reduced in infected cases with SARS-CoV-2 after vaccination, including
 175 symptomatic and asymptomatic infections²¹. Antonelli et al²² identified risk factors for post-
 176 vaccination SARS-CoV-2 infection and describe the characteristics of post-vaccination illness, and
 177 found that Almost all symptoms were reported less frequently in infected vaccinated individuals
 178 than in infected unvaccinated individuals, and vaccinated participants were more likely to be
 179 completely asymptomatic, especially if they were 60 years or older. Our vaccine breakthrough case
 180 from Xi'an supported vaccine effectiveness and cautioned around relaxing physical distancing and
 181 other personal protective measures in the post-vaccination era.

182
 183 SARS-CoV-2 virus delta variants have drawn worldwide attention. The WHO proposed three labels
 184 for global SARS-CoV-2 variants, including variant of concern (VOC), variant of interest (VOI), and
 185 variant under monitoring, to be used alongside the scientific nomenclature in communications about
 186 variants to the public²³. The B.1.617 variant of the COVID-19 virus has been called a triple mutant
 187 variant since it splits into three lineages including the B.1.617.1 (Kappa) variant, the B.1.617.2
 188 (Delta) variant, and the B.1.617.3 variant²⁴. The delta COVID-19 variant, which was first detected
 189 in India in October 2020, had been reported in more than 80 countries on June 20, 2021²⁵. The WHO
 190 declared the delta variant a "variant of concern" on May 10, 2021. In Mid-June 2021, the US Centers
 191 for Disease Control and Prevention upgraded its classification of the delta from a "variant of
 192 interest" to a "variant of concern."²⁶ Our results showed that two medical staff (1 laboratorian and
 193 1 emergency doctor), infected with COVID-19 in the designated hospital, occurred due to workplace
 194 accidental exposure to COVID-19, and the coronavirus strain was determined to be the imported
 195 B.1.617.2 (Delta) variant.

196
 197 To conclude, our findings add to the accumulating evidence regarding the importance of regular
 198 screening for all staff in healthcare settings. Furthermore, our study highlights the need for an update
 199 of the current hospital disinfection procedures in designated hospitals to prevent the nosocomial
 200 spread of SARS-CoV-2 infection. Finally, the epidemiological exposure of vaccinated medical staff
 201 should draw concern in order to minimize the impact of a new outbreak induced by virus mutants.

202
 203 **Table 1: Epidemiological characteristics of sporadic nosocomial COVID-19 infections**

Date	City	Number of hospital/ cases	Hospital type	Profession	Classification of infection	Route of infection	Database
19 Jun. 2020	Beijing	1/1	Designated hospital	nurse	Community-acquired infection	family member exposure with COVID-19	Link 1

11 Oct. 2020	Qingdao	1/12	Designated hospital	Patients and accompanying staff	hospital-acquired infection	nosocomial infection	Link 2
29 Oct. 2020	Qingdao	1/1	Designated hospital	nurse	hospital-acquired infection	workplace accidental exposure to COVID-19	Link 3
18 Dec. 2020	Dalian	1/3	Non-designated hospital	Patients	hospital-acquired infection	nosocomial infection	Link 4
27 Dec. 2020	Dalian	1/1	Non-designated hospital	Cleaner	Community-acquired infection	cold-chain environment-to-human transmission	Link 5
3 Jan. 2021	Shenyang	1/12	Non-designated hospital	Medical staff, patients and accompanying staff	hospital-acquired infection	nosocomial infection	Link 6
14 Jan. 2021	Shijiazhuang	2/14	Non-designated hospital	Medical staff, patients and accompanying staff	hospital-acquired infection	nosocomial infection	Link 7
20 Jan. 2021	Shanghai	2/2	Non-designated hospital	Logistics support staff	Community-acquired infection	imported from overseas	Link 8
17 Mar. 2021	Xi'an	1/1	Designated hospital	laboratorian	hospital-acquired infection	Mild Breakthrough Infection	Link 9
14 Jun. 2021	Guangzhou	1/2	Designated hospital	Laboratorian and Emergency doctor	hospital-acquired infection	nosocomial infection	Link 10
27 Jul. 2021	Nanjing	1/4	Non-designated hospital	accompanying staff	hospital-acquired infection	nosocomial infection	Link 11
10 Aug. 2021	Yangzhou	1/3	Non-designated hospital	Doctor	hospital-acquired infection	nosocomial infection	Link 12

204 Designated hospital: a hospital designated for treatment of imported COVID-19 cases

205

206 [Link 1: https://finance.sina.com.cn/china/gncj/2020-06-19/doc-iircuyvi9385332.shtml?r=9&tj=none&tr=9](https://finance.sina.com.cn/china/gncj/2020-06-19/doc-iircuyvi9385332.shtml?r=9&tj=none&tr=9)

207 [Link 2: https://www.zhihu.com/question/425220159](https://www.zhihu.com/question/425220159)

208 [Link 3: https://new.qq.com/omn/20201030/20201030A05GXU00.html](https://new.qq.com/omn/20201030/20201030A05GXU00.html)

209 [Link 4: http://www.xinhuanet.com/politics/2021-01/06/c_1126953634.htm](http://www.xinhuanet.com/politics/2021-01/06/c_1126953634.htm)

- 210 [Link 5: https://new.qq.com/omn/20201229/20201229A0259M00.html](https://new.qq.com/omn/20201229/20201229A0259M00.html)
- 211 [Link 6: https://new.qq.com/omn/20210111/20210111A0DFD500.html](https://new.qq.com/omn/20210111/20210111A0DFD500.html)
- 212 [Link 7: https://news.sina.com.cn/c/2021-01-20/doc-ikftpnnx9631142.shtml](https://news.sina.com.cn/c/2021-01-20/doc-ikftpnnx9631142.shtml)
- 213 [Link 8: https://new.qq.com/omn/20210131/20210131A0071200.html](https://new.qq.com/omn/20210131/20210131A0071200.html)
- 214 [Link 9: https://news.sina.com.cn/c/2021-03-18/doc-ikkntiam4831560.shtml](https://news.sina.com.cn/c/2021-03-18/doc-ikkntiam4831560.shtml)
- 215 [Link 10: https://news.sina.com.cn/c/2021-06-14/doc-ikqcfnc979774.shtml](https://news.sina.com.cn/c/2021-06-14/doc-ikqcfnc979774.shtml)
- 216 [Link 11: http://med.china.com.cn/content/pid/281087/tid/1026](http://med.china.com.cn/content/pid/281087/tid/1026)
- 217 [Link 12: http://news.hexun.com/2021-08-18/204179459.html](http://news.hexun.com/2021-08-18/204179459.html)

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Table 2: Epidemiological characteristics of sporadic nosocomial COVID-19 infections

Date	City	Confirmed/ asymptomatic cases	How to discover the source of infection	Virus type	Database
19 Jun. 2020	Beijing	1/0	Nucleic acid testing for close contacts of people with infection cases	One ancestral virus strain (XFDM strain) ²⁷	Link 1
11 Oct. 2020	Qingdao	6/6	Regular screening for medical staff	Imported virus strain Lineage B.1.1 ²⁸	Link 2
29 Oct. 2020	Qingdao	1/0	Regular screening for medical staff	Imported virus strain Lineage B.1.1 ²⁸	Link 3
18 Dec. 2020	Dalian	3/0	Regular screening for medical staff	European family branch 1 of the L genotype	Link 4
27 Dec. 2020	Dalian	1/0	Regular screening for medical staff	European family branch 1 of the L genotype	Link 5
3 Jan. 2021	Shenyang	12/0	Regular screening for medical staff	Imported virus strain	Link 6
14 Jan. 2021	Shijiazhuang	14/0	Regular screening for medical staff	the strain imported from Europe ²⁹	Link 7
20 Jan. 2021	Shanghai	2/0	Nucleic acid testing for close contacts of people with infection cases	Imported virus strain	Link 8
17 Mar. 2021	Xi'an	1/0	Regular screening for medical staff	Imported virus strain B.1.1.7 ⁸	Link 9
14 Jun. 2021	Guangzhou	2/0	Regular screening for medical staff	Imported virus strain B1.617.2 (Delta) Lineage	Link 10
27 Jul. 2021	Nanjing	4/0	Regular screening for medical staff	Imported virus strain B1.617.2 (Delta) Lineage	Link 11
10Aug. 2021	Yangzhou	3/0	Regular screening for medical staff	Imported virus strain B1.617.2 (Delta) Lineage	Link 12

221 Delta Lineage: the highly contagious Covid-19 variant first identified in India

222

223 [Link 1: http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.246](http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.246)

224 [Link 2: http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.224](http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.224)

- 225 Link 3: <https://new.qq.com/omn/20201030/20201030A05GXU00.html>
226 Link 4: http://www.xinhuanet.com/politics/2021-01/06/c_1126953634.htm
227 Link 5: <https://new.qq.com/omn/20201229/20201229A0259M00.html>
228 Link 6: <https://new.qq.com/omn/20210111/20210111A0DFD500.html>
229 Link 7: <http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2021.006>
230 Link 8: <https://new.qq.com/omn/20210131/20210131A0071200.html>
231 Link 9: <http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2021.094>
232 Link 10: <https://news.sina.com.cn/c/2021-06-14/doc-ikqcfncA0979774.shtml>
233 Link 11: <http://med.china.com.cn/content/pid/281087/tid/1026>
234 Link 12: <http://news.hexun.com/2021-08-18/204179459.html>

235

236 **Authors contribution**

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238 contributed to data analysis and paper writing.

239

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247

248 **References**

- 249 1. Feng M, Li Z, Xiong J, Xu W and Xiang B. Geographical and Epidemiological
250 Characteristics of 3,487 Confirmed Cases With COVID-19 Among Healthcare Workers in
251 China. *Frontiers in Public Health*. 2021;8.
252 2. Xiang B, Li P, Yang X, Zhong S, Manyande A and Feng M. The impact of novel
253 coronavirus SARS-CoV-2 among healthcare workers in hospitals: An aerial overview.
254 *American Journal of Infection Control*. 2020;48:915-917.
255 3. Abbas M, Nunes TR, Martischang R, Zingg W, Iten A, Pittet D and Harbarth S.
256 Nosocomial transmission and outbreaks of coronavirus disease 2019: the need to
257 protect both patients and healthcare workers. *Antimicrobial Resistance and Infection*
258 *Control*. 2021;10.
259 4. O'Leary N, Kingston L, Griffin A, Morrissey A-m, Noonan M, Kelly D, Doody O,
260 Niranjana V, Gallagher A, O'Riordan C and Lynch A. COVID-19 healthcare policies in
261 Ireland: A rapid review of the initial pandemic response. *Scandinavian Journal of*
262 *Public Health*. 2021.
263 5. Ran L, Chen X, Wang Y, Wu W, Zhang L and Tan X. Risk Factors of Healthcare
264 Workers With Coronavirus Disease 2019: A Retrospective Cohort Study in a Designated
265 Hospital of Wuhan in China. *Clinical Infectious Diseases*. 2020;71:2218-2221.
266 6. Feng M, Ling Q, Xiong J, Manyande A, Xu W and Xiang B. Geographical and
267 Epidemiological Characteristics of Sporadic Coronavirus Disease 2019 Outbreaks From
268 June to December 2020 in China: An Overview of Environment-To-Human Transmission

269 Events. *Front Med.* 2021;8: 654422.

270 7. Feng M, Ling Q, Xiong J, Manyande A, Xu W and Xiang B. Occupational
271 Characteristics and Management Measures of Sporadic COVID-19 Outbreaks From June
272 2020 to January 2021 in China: The Importance of Tracking Down "Patient Zero".
273 *Frontiers in Public Health.* 2021;9.

274 8. Outbreak Reports: Mild Breakthrough Infection in a Healthcare Professional
275 Working in the Isolation Area of a Hospital Designated for Treating COVID-19 Patients
276 — Shaanxi Province, China, March, 2021. *China CDC Weekly.* 2021, 3(19): 397-400.
277 <http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2021.094>.

278 9. Fang FH, Song Y, Hao LP, Nie K and Sun XD. A Case of COVID-19 Detected in a
279 Cargo Worker at Pudong Airport - Shanghai Municipality, China, November 8, 2020.
280 *China Cdc Weekly.* 2020;2:910-911.

281 10. Qi S, Zhao X, Hao P, Liu N, Gao GF, Song Y, Xu W and Li Q. Two Reemergent Cases
282 of COVID-19-Hebei Province, China, January 2, 2021. *China Cdc Weekly.* 2021;3:25-27.

283 11. Kashte S, Gulbake A, El-Amin Iii SF and Gupta A. COVID-19 vaccines: rapid
284 development, implications, challenges and future prospects. *Hum Cell.* 2021.

285 12. Inchingolo AD, Inchingolo AM, Bordea IR, Malcangi G, Xhajanka E, Scarano A,
286 Lorusso F, Farronato M, Tartaglia GM, Isacco CG, Marinelli G, D'Oria MT, Hazballa D,
287 Santacroce L, Ballini A, Contaldo M, Inchingolo F and Dipalma G. SARS-CoV-2 Disease
288 through Viral Genomic and Receptor Implications: An Overview of Diagnostic and
289 Immunology Breakthroughs. *Microorganisms.* 2021;9.

290 13. van der Lubbe JEM, Huber SKR, Vijayan A, Dekking L, van Huizen E, Vreugdenhil J,
291 Choi Y, Baert MRM, Feddes-de Boer K, Gil AI, van Heerden M, Dalebout TJ, Myeni SK,
292 Kikkert M, Snijder EJ, de Waal L, Stittelaar KJ, Tolboom J, Serroyen J, Muchene L,
293 van der Fits L, Rutten L, Langedijk JPM, Barouch DH, Schuitemaker H, Zahn RC and
294 Wegmann F. Ad26.COV2.S protects Syrian hamsters against G614 spike variant SARS-CoV-
295 2 and does not enhance respiratory disease. *npj Vaccines.* 2021;6:12.

296 14. Ioannou P, Karakonstantis S, Astrinaki E, Saplamidou S, Vitsaxaki E, Hamilos G,
297 Sourvinos G and Kofteridis DP. Transmission of SARS-CoV-2 variant B.1.1.7 among
298 vaccinated health care workers. *Infectious diseases (London, England).* 2021:1-4.

299 15. Blachere NE, Hacisuleyman E and Darnell RB. Vaccine Breakthrough Infections with
300 SARS-CoV-2 Variants REPLY. *New England Journal of Medicine.* 2021.

301 16. Kustin T, Harel N, Finkel U, Perchik S, Harari S, Tahor M, Caspi I, Levy R,
302 Leshchinsky M, Ken Dror S, Bergerzon G, Gadban H, Gadban F, Eliassian E, Shimron O,
303 Saleh L, Ben-Zvi H, Keren Taraday E, Amichay D, Ben-Dor A, Sagas D, Strauss M, Shemer
304 Avni Y, Huppert A, Kepten E, Balicer RD, Netzer D, Ben-Shachar S and Stern A. Evidence
305 for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2-mRNA-
306 vaccinated individuals. *Nature Medicine.* 2021.

307 17. Jacobson KB, Pinsky BA, Rath MEM, Wang H, Miller JA, Skhiri M, Shepard J, Mathew
308 R, Lee G, Bohman B, Parsonnet J and Holubar M. Post-vaccination SARS-CoV-2 infections
309 and incidence of the B.1.427/B.1.429 variant among healthcare personnel at a northern
310 California academic medical center. *medRxiv : the preprint server for health sciences.*
311 2021.

312 18. Hacisuleyman E, Hale C, Saito Y, Blachere NE, Bergh M, Conlon EG, Schaefer-

313 Babajew DJ, DaSilva J, Muecksch F, Gaebler C, Lifton R, Nussenzweig MC, Hatzioannou
314 T, Bieniasz PD and Darnell RB. Vaccine Breakthrough Infections with SARS-CoV-2
315 Variants. *New England Journal of Medicine*. 2021;384:2212-2218.

316 19. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, Sudre CH, Nguyen LH,
317 Drew DA, Merino J, Hu C, Selvachandran S, Antonelli M, Murray B, Canas LS, Molteni
318 E, Graham MS, Modat M, Joshi AD, Mangino M, Hammers A, Goodman AL, Chan AT, Wolf J,
319 Steves CJ, Valdes AM, Ourselin S and Spector TD. Vaccine side-effects and SARS-CoV-
320 2 infection after vaccination in users of the COVID Symptom Study app in the UK: a
321 prospective observational study. *Lancet Infectious Diseases*. 2021;21:939-949.

322 20. Bernal JL, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, Simmons R,
323 Cottrell S, Roberts R, O'Doherty M, Brown K, Cameron C, Stockton D, McMenamin J and
324 Ramsay M. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on
325 covid-19 related symptoms, hospital admissions, and mortality in older adults in
326 England: test negative case-control study. *BMJ-British Medical Journal*. 2021;373.

327 21. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, Brooks N, Smaja M,
328 Mircus G, Pan K, Southern J, Swerdlow DL, Jodar L, Levy Y and Alroy-Preis S. Impact
329 and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-
330 19 cases, hospitalisations, and deaths following a nationwide vaccination campaign
331 in Israel: an observational study using national surveillance data. *Lancet*.
332 2021;397:1819-1829.

333 22. Antonelli M, Penfold RS, Merino J, Sudre CH, Molteni E, Berry S, Canas LS, Graham
334 MS, Klaser K, Modat M, Murray B, Kerfoot E, Chen L, Deng J, Osterdahl MF, Cheetham
335 NJ, Drew DA, Nguyen LH, Pujol JC, Hu C, Selvachandran S, Polidori L, May A, Wolf J,
336 Chan AT, Hammers A, Duncan EL, Spector TD, Ourselin S and Steves CJ. Risk factors
337 and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID
338 Symptom Study app: a prospective, community-based, nested, case-control study. *The
339 Lancet Infectious diseases*. 2021.

340 23. Hao Y, Guan XH, Liu TT, He ZG and Xiang HB. Hypothesis: the central medial
341 amygdala may be implicated in sudden unexpected death in epilepsy by
342 melanocortiner-gic-sympathetic signaling. *Epilepsy Behav*. 2014;41:30-2.

343 24. Liu TT, He ZG, Tian XB and Xiang HB. Neural mechanisms and potential treatment
344 of epilepsy and its complications. *Am J Transl Res*. 2014;6:625-30.

345 25. Liu TT, He ZG, Tian XB, Liu C, Xiang HB and Zhang JG. Hypothesis: Astrocytes in
346 the central medial amygdala may be implicated in sudden unexpected death in epilepsy
347 by melanocortiner-gic signaling. *Epilepsy Behav*. 2015;42:41-3.

348 26. Xiang HB, Liu C, Liu TT and Xiong J. Central circuits regulating the sympathetic
349 outflow to lumbar muscles in spinally transected mice by retrograde transsynaptic
350 transport. *Int J Clin Exp Pathol*. 2014;7:2987-97.

351 27. Pang X, Ren L, Wu S, Ma W, Yang J, Di L, Li J, Xiao Y, Kang L, Du S, Du J, Wang
352 J, Li G, Zhai S, Chen L, Zhou W, Lai S, Gao L, Pan Y, Wang Q, Li M, Wang J, Huang Y,
353 Wang J, Grp C-FR and Grp C-LT. Cold-chain food contamination as the possible origin
354 of COVID-19 resurgence in Beijing. *National Science Review*. 2020;7:1861-1864.

355 28. Liu P, Yang M, Zhao X, Guo Y, Wang L, Zhang J, Lei W, Han W, Jiang F, Liu WJ,
356 Gao GF and Wu G. Cold-chain transportation in the frozen food industry may have

357 caused a recurrence of COVID-19 cases in destination: Successful isolation of SARS-
358 CoV-2 virus from the imported frozen cod package surface. *Biosafety and health*.
359 2020;2:199-201.

360 29. Liu C, Liu TT, He ZG, Shu B and Xiang HB. Inhibition of itch-related responses
361 by selectively ablated serotonergic signals at the rostral ventromedial medulla in
362 mice. *Int J Clin Exp Pathol*. 2014;7:8917-21.

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367 **Figure 1: Geographical distribution of sporadic nosocomial COVID-19 infections from June**
368 **2020 to June 2021 in China.** Seven cities (Dalian, Beijing, Qingdao, Shijiazhuang, Xi'an,
369 Guangzhou, and Shanghai) reported the nosocomial COVID-19 infections. Medical staff, patients
370 and accompanying staff (12) in Shenyang (Jan 3, 2021), patients (3) in Dalian (Dec 18, 2020),
371 patients and accompanying staff (6) in Qingdao (Oct 11, 2020), laboratory personnel (1) in Xi'an
372 (Mar 17, 2021), medical staff, patients and accompanying staff (14) in Shijiazhuang (Jan 14, 2021),
373 and Medical staff (2) in Guangzhou (Jun 14, 2021) were diagnosed as infected cases.

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376 **Figure 2: The graph's left-right axis is used as a timeline of the key events and dynamic profile**
377 **of sporadic nosocomial COVID-19 infections from June 2020 to June 2021 in China.**

378 From June 2020 to June 2021, five cities in China had reported 10 series cases with nosocomial
379 COVID-19 infections, including 39 confirmed cases and 6 asymptomatic cases.

380 The delta COVID-19 variant was first detected in India in October 2020. The World Health
381 Organization designated Delta as a variant of interest in April and a variant of concern on 11 May
382 2021. In Mid-June 2021, the US Centers for Disease Control and Prevention upgraded its
383 classification of delta from a "variant of interest" to a "variant of concern."

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Figure 1.TIF

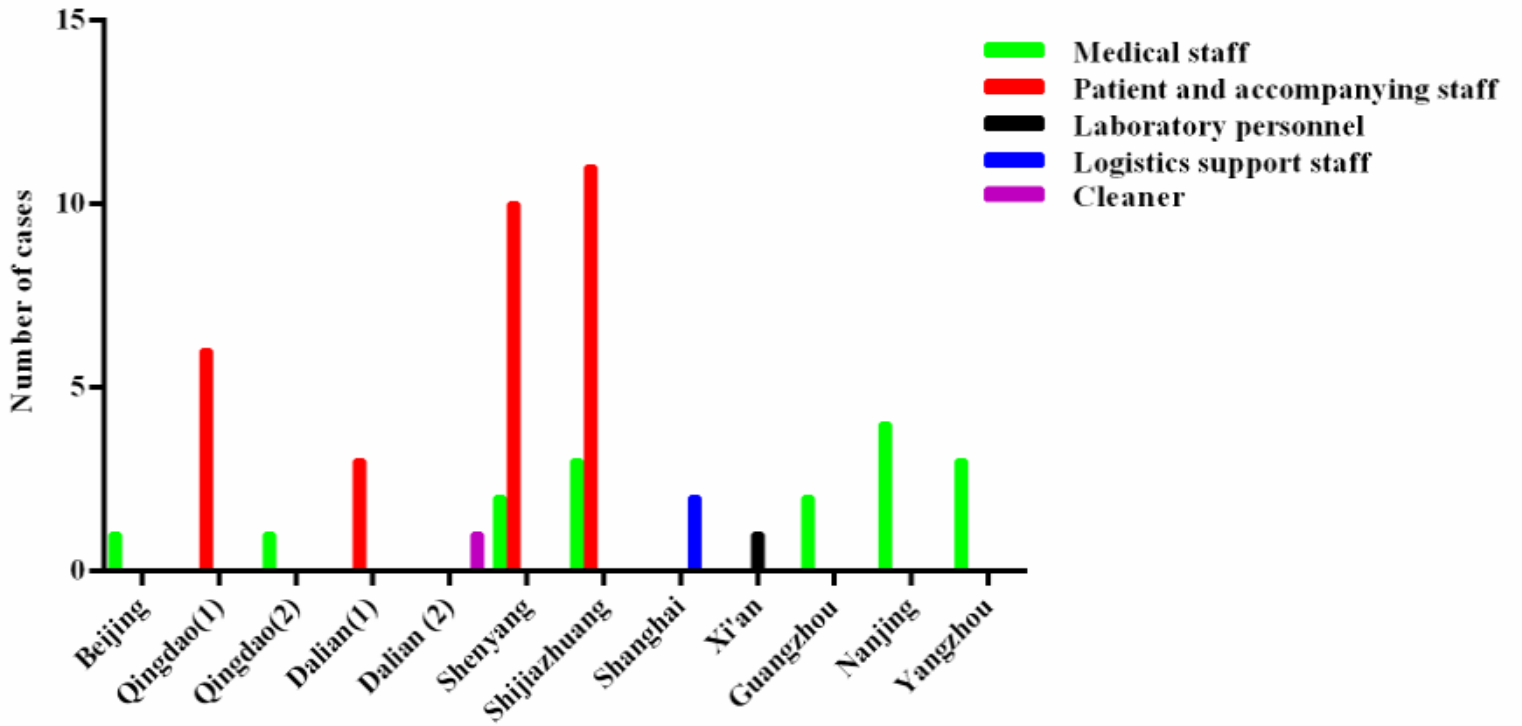
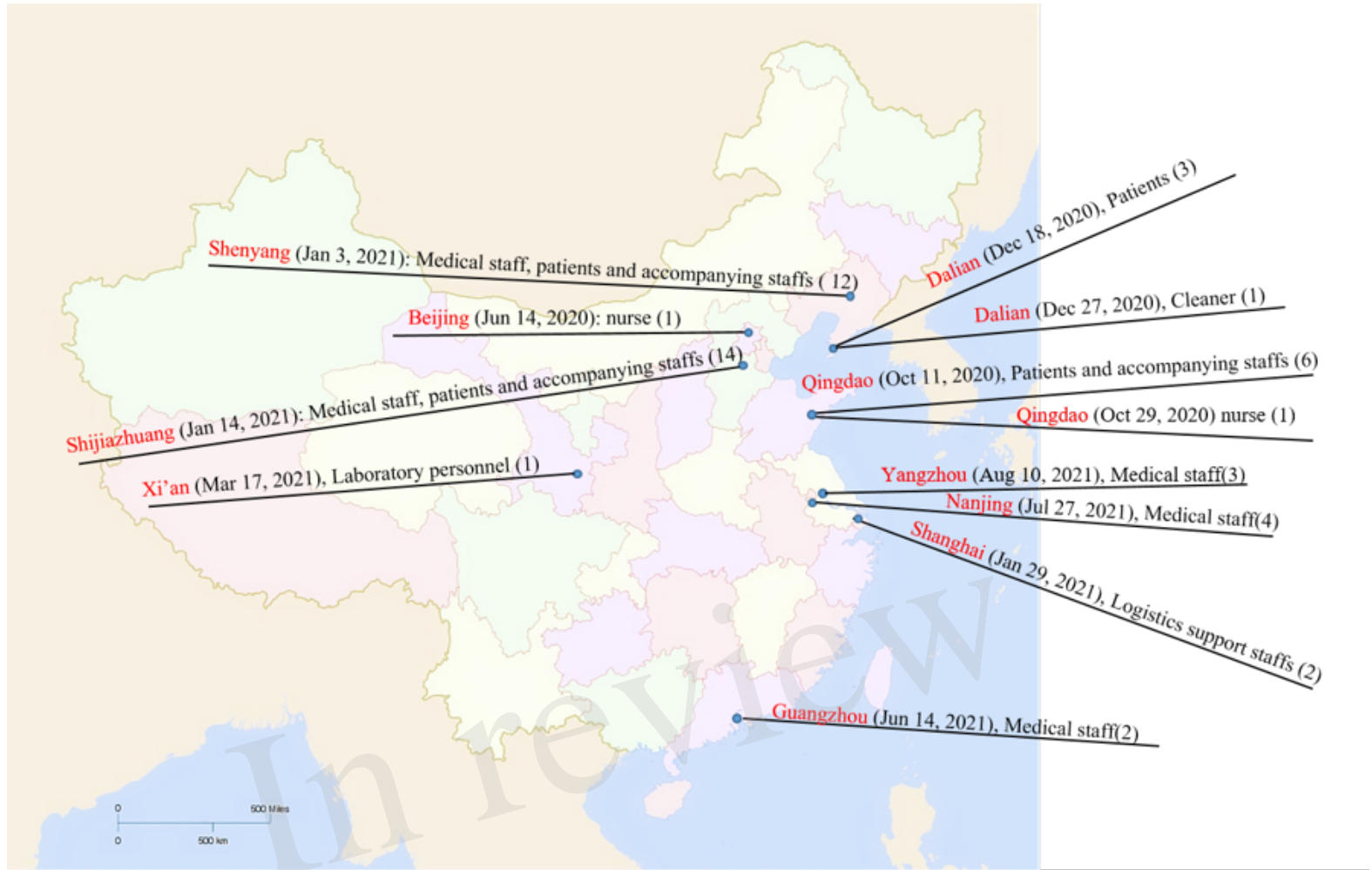


Figure 2.TIF

