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Coronavirus Pandemic

Evolutionary dynamics of SARS-CoV-2 variants under strict non-pharmaceutical interventions – a population-based study

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Abstract

Introduction: China implemented a dynamic zero-COVID strategy to curb viral transmission in response to the coronavirus disease 2019 (COVID-19) pandemic. This strategy was designed to inhibit mutation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for COVID-19. This study explores the dynamics of viral evolution under stringent non-pharmaceutical interventions (NPIs) through real-world observations.

Methodology: Our analysis encompassed all polymerase chain reaction (PCR)-confirmed COVID-19 cases (n = 780) from two consecutive outbreaks occurring in July to August 2021. Epidemiological investigations and in-depth viral genome analyses were conducted to determine the sources of infection and the inter-outbreak linkages.

Results: The outbreaks likely originated via contaminated objects from an imported COVID-19 case to local airport cleaners. Most patients presented clinically mild symptoms. All viral genomes clustered into a single clade, with genomes from the subsequent Yangzhou outbreak forming a distinct branch, diverging from those of the initial Nanjing outbreak. Compared to the Wuhan-Hu-1 strain, the Delta variants isolated from the imported case and early local cases in Nanjing had 35 nucleotide mutations and three deletions. Various single nucleotide variant (SNV) combinations were observed in subsequent transmissions, with NPIs accounting for the termination of 67.2% (92/137) of SNV combinations. Stringent implementation of NPIs resulted in a greater number of terminated SNV combinations than emerging ones. Additionally, vaccination of cases was associated with SNV combination termination.

Conclusions: This study underscores the significant role of NPIs in preventing the accumulation of SARS-CoV-2 mutations.

Key words: SARS-CoV-2; single nucleotide variation; non-pharmaceutical intervention; zero-COVID.

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Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, the causative agent of coronavirus disease 2019 (COVID-19), has an average mutation rate per passage of 3.76×10^{-6} substitutions per site [1], with a yearly rate of approximately 6 synonymous mutations and an estimated 26 non-synonymous amino acid changes [2]. These mutations have the potential to impact the virus's transmissibility; associated disease severity; and the efficacy of vaccines, therapeutic agents, diagnostic tools, as well as other public health and social measures [3]. It is worth noting that vaccines alone may not be sufficient to prevent the emergence of novel immune-evading strains if transmission rates within the population remain high [4]. The evolution of RNA viruses is driven by the accumulation of random mutations and the selective pressure exerted by drugs or immunity [5]. Notably, intra-host SARS-CoV-2 mutation rates are significantly higher than those reported through population-level analyses [6]. Non-pharmaceutical interventions (NPIs), including isolation and quarantine, are considered effective in disrupting viral evolution by breaking its transmission chains [7]. The World Health Organization (WHO) classifies variants of public health or clinical significance into variants of concern (VOC), variants of interest (VOI), or variants under monitoring (VUM) [8]. To date, five VOCs have been named by WHO, including Alpha, Beta, Gamma, Delta, and Omicron [8].

In China, the initial epidemic wave occurred from January to April 2020, primarily driven by the Alpha strain. Following this, the viral transmission was successfully suppressed to a remarkably low level, with daily incidence rates not exceeding 1.03 cases per million individuals, persisting until May 2021. During this period, Beta variants coexisted. The second epidemic wave reached a peak of 2.78 cases per million people daily, and was recorded from the latter half of May to September 2021, with the Delta variants predominating. Subsequently, the Omicron variants emerged as the dominant strain by the end of 2021. China adhered to a dynamic zero-COVID strategy until the end of 2022, effectively maintaining the daily incidence rate below 1 case per million for most of the period prior to 2022. However, a significant surge in incidence rates was observed in 2022, primarily attributed to the predominance of the Omicron variant.

With the emergence of the Delta variant as the dominant strain, China experienced its second-largest outbreak chronologically, occurring in Nanjing and Yangzhou in 2021, after the initial outbreak in Wuhan from 2019 to 2020. In this study, we conducted a comprehensive real-world analysis to systematically elucidate the emergence and persistence of SARS-CoV-2 mutations, particularly within the framework of China's dynamic zero-COVID strategy, during this outbreak.

Methodology

Confirmation of cases and comprehensive epidemiological investigation

All COVID-19 cases that emerged during the outbreaks in Nanjing and Yangzhou between 13 July and 25 August 2021 were confirmed through real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing. The initial positive sample from each case underwent retesting for verification to ensure precision. Additionally, another nasal/pharyngeal swab was collected within 24 hours and tested. Only cases with consistent positive results across all tests were included in our study.

The epidemiological investigation encompassed four key aspects. (1) Clinical manifestations and sampling history: we documented each case's clinical manifestations, including their initial and subsequent symptoms, the onset time of symptoms, disease progression, any complications, and their sampling history along with corresponding test results. (2) Contact history: we thoroughly examined the activities of each case in the 14 days preceding symptom onset; or for asymptomatic cases, the time of their first positive sample. Our investigation focused on interactions with confirmed COVID-19 cases, detailing the date, duration, frequency of contact, and any precautionary measures taken. Additionally, we explored potential exposure to contaminated objects or environments to assess the likelihood of fomite transmission. These insights were crucial for tracing the source of infection, estimating the possible time of infection, and mapping out the transmission chain. (3) Identification of close contacts: our investigation extended to individuals who had contact with confirmed cases or had shared confined spaces with them. This assessment period spanned from four days prior to symptom onset (or the date of the first positive test for asymptomatic cases) until the cases were isolated. (4) Contacts' contacts: We compiled a list of individuals who had interacted with the close contacts, tracing back from the earliest known exposure to a COVID-19 case until the close contact was quarantined. This comprehensive approach ensured an in-depth understanding of the outbreak, facilitating effective contact tracing and mitigation strategies.

Relevant definitions

In this study, the commencement of the infectious period for a COVID-19 case was defined as four days prior to the onset of symptoms; or, for asymptomatic individuals, the date of their initial positive sample collection. In instances where a case was quarantined before the onset of this infectious period and did not result in any secondary infections, the cessation of the viral strain carried by this case was attributed to the efficacy of NPIs. Conversely, if a case was managed after the commencement of the infectious period and did not lead to further infections, the discontinuation of the viral strain was regarded as self-termination.

In the Nanjing outbreak, virus transmission in the initial 10-day period following the cleaners' exposure within the cabin was not detected. This phase was denoted as the "natural epidemic period" (NE). From 21 to 26 July, despite the implementation of intervention measures, such as PCR screening for close contacts and high-risk individuals, hospital treatment of COVID-19 cases, quarantine of close contacts in designated facilities, and partial or complete closure of affected communities; their execution was not immediate. Consequently, this period was categorized as the "incompletely intervened period" (II). From 27 July to 5 August, all aforementioned intervention strategies were promptly and vigorously enforced, and this was defined as the "completely intervened period" (CI). Subsequently, from 6 August onwards, the daily incidence of new COVID-19 cases declined to below 10, with the last case of the Nanjing outbreak identified on 11 August. This latter phase was designated the "epidemic regression period" (ER). Comparable definitions were applied to delineate the various stages of the Yangzhou outbreak.

Non-pharmaceutical intervention (NPI) measures implemented

(1) Management of COVID-19 cases: Confirmed COVID-19 cases were promptly transferred to designated infectious disease hospitals within two hours and received treatment until they met the discharge criteria established by the National Health Commission [9].

(2) Close contact management: Identified close contacts were quarantined in designated facilities within 12 hours, in isolated rooms, except for those needing special care. The quarantine period lasted for 14 days after their final contact with a known COVID-19 case. Respiratory samples were collected on days 1, 4, 7, and 14 for SARS-CoV-2 testing. On day 14, two nasopharyngeal swabs were taken and tested using real-time RT-PCR with two different detection reagents. Those testing negative throughout the quarantine were released to home isolation with medical follow-up for an additional 7 days, requiring PCR tests on days 2 and 7, and avoiding gatherings.

(3) Contacts of contacts management: Identified contacts of contacts were quarantined in designated facilities within 12 hours, in separate rooms, for 7 days. They underwent RT-PCR testing on days 1, 4, and 7. If their related close contacts tested negative for the first 4 days of quarantine and their own tests were negative, they would be discharged.

(4) Community closure: In the event of community transmission or the identification of 5 or more COVID-19 cases within 14 days in a community, the community would be closed. All residents were required to stay home, with life necessities provided by community workers. Residents underwent RT-PCR tests for SARS-CoV-2 on days 1, 4, 7, and 14 of the closure. The closure would be lifted if no new cases were reported.

(5) Community semi-closure: In communities where fewer than five COVID-19 cases occurred within 14 days, residents were required to stay home for 14 days. However, one member of each family was permitted to go out daily for essential shopping. The semi-closure would end if no new cases arose and all residents tested negative for SARS-CoV-2.

(6) Additional social measures: Affected communities' districts or counties were required to close all non-essential businesses, such as chess and card rooms, gyms, museums, karaoke televisions (KTVs), and bars. Essential businesses such as supermarkets had to adhere to COVID-19 safety measures, including wearing masks, maintaining social distance, and shortened business hours.

(7) Population screening measures: In districts where COVID-19 cases had been detected, screening tests for SARS-CoV-2 were conducted based on a thorough risk assessment. If there were new cases that could be traced back to known transmission chains, population screening was intensified, taking place at intervals of 3 to 5 days, to precisely determine the extent of transmission within the community.

Extraction and detection of nucleic acids for SARS-CoV-2 identification

We collected nasopharyngeal or oropharyngeal swabs from suspected COVID-19 patients. Total RNA extraction was performed using a magnetic bead-based nucleic acid extraction system (21011110T014, TianLong Technologies, Xian, China) from 200 µL of each specimen. Subsequently, real-time RT-PCR analysis was conducted using a 2019-nCoV RNA detection kit (20210721D, BioGerm Medical Technologies, Shanghai, China). The reaction conditions were as follows: initial incubation at 50 °C for 10 minutes, followed by 95 °C for 5 minutes, and then 45 cycles of amplification consisting of 95 °C for 10 seconds and 55 °C for 40 seconds. Amplification and detection were performed on the QuantStudio7 Pro Real-Time PCR Systems (Thermo Fisher Scientific, MA, USA), following the manufacturer's guidelines. Data interpretation was facilitated using manufacturer-provided software. Positive samples were determined when the cycling threshold (CT) values were below 37. Samples lacking CT values, or those with CT values exceeding 40, or exhibiting non-repeatable CT values between 37 and 40, were considered negative. A sample was confirmed positive for SARS-CoV-2 only if both the *ORF1ab* and *N* genes tested positive. Detailed information on the Crit. reagents utilized can be found in Supplementary Table 1.

Phylogenetic analysis

We aligned a total of 537 complete or near-complete viral genomes, comprising 167 genomes from the Nanjing outbreak, 353 genomes from the Yangzhou outbreak, 7 genomes from imported Delta variant cases, 4 genomes from the Guangdong outbreak, and 4 genomes from the Yunnan outbreak caused by Delta variants, Wuhan-Hu-1, and the early Delta variant DL-ILBS-22053 (refer to Supplementary Table 2 for details). Alignment was performed using MAFFT v7.487 [10]. We estimated the maximum likelihood (ML) phylogeny utilizing this aligned dataset through IQTree V.2 [11]. Furthermore, a time-resolved phylogenetic tree was constructed with the aid of the Nextstrain pipeline [12].

Statistical analyses

We conducted a comprehensive statistical analysis of pooled demographic and laboratory data from our patient cohort. Initially, descriptive analyses were performed to summarize demographic characteristics. Mean values were calculated for continuous variables, while frequencies and percentages were derived for categorical variables. Univariate logistic regression was employed as a screening tool to identify variables significantly impacting the termination of single nucleotide variation (SNV) combinations. Variables found to be statistically significant in this initial screening underwent further scrutiny using multivariate logistic regression. All statistical analyses were carried out using IBM SPSS version 23.0 (IBM Corp, Armonk, NY, USA) and R (version 9.3) software. The significance level was set at a two-sided α of less than 0.05, indicating statistical significance.

Ethics approval and consent to participate

The study was conducted in strict adherence to the ethical principles outlined in the Declaration of Helsinki. Given the nature of COVID-19 as an emerging infectious disease, the epidemiological investigation, sampling, and testing conducted in this research were classified as part of a public health outbreak response, as determined by the National Health Commission. Consequently, the study was deemed exempt from institutional review board (IRB) assessment requirements.

The Institutional Review Board (IRB) at the Jiangsu Provincial Center for Disease Control and Prevention thoroughly reviewed and confirmed that the study complied with the requirements of relevant laws and regulations. Importantly, the study did not involve any identifiable personal information, thereby further justifying the waiver of the need for informed consent and ethical approval. The IRB at the Jiangsu Provincial Center for Disease Control and Prevention granted this exemption based on the exceptional circumstances surrounding the COVID-19 pandemic.

Results

In July 2021, the Delta variants of SARS-CoV-2 were introduced into Nanjing and subsequently spread to Yangzhou, resulting in local outbreaks that persisted from 20 July to 9 September in these two cities of Jiangsu Province, China. Our study encompassed all 780 cases identified during these outbreaks. The gender ratio was 1:1.42. Individuals aged 60 years and above accounted for 32.6%. Notably, a large proportion of the cases (62.1%) had not received any vaccination against SARS-CoV-2. The majority of the cases (74.2%) exhibited clinically mild symptoms. The comprehensive demographic details of these cases are presented in Supplementary Table 3.

Importation and initial transmission of SARS-CoV-2 Delta variants

On 10 July 2021, a flight originating from Moscow, Russia, arrived in Nanjing, China, carrying 301 passengers. Upon arrival, all passengers underwent RT-PCR testing for SARS-CoV-2 and five individuals tested positive. Notably, while the majority of positive cases exhibited high Ct values, the case identified as Nanjing/Yu had a Ct value of 14.5. Further viral genome analysis revealed that all these cases were infected with the Delta variant of SARS-CoV-2. Interestingly, only the viral genome from the Nanjing/Yu case exhibited the H146Y mutation in the spike protein.

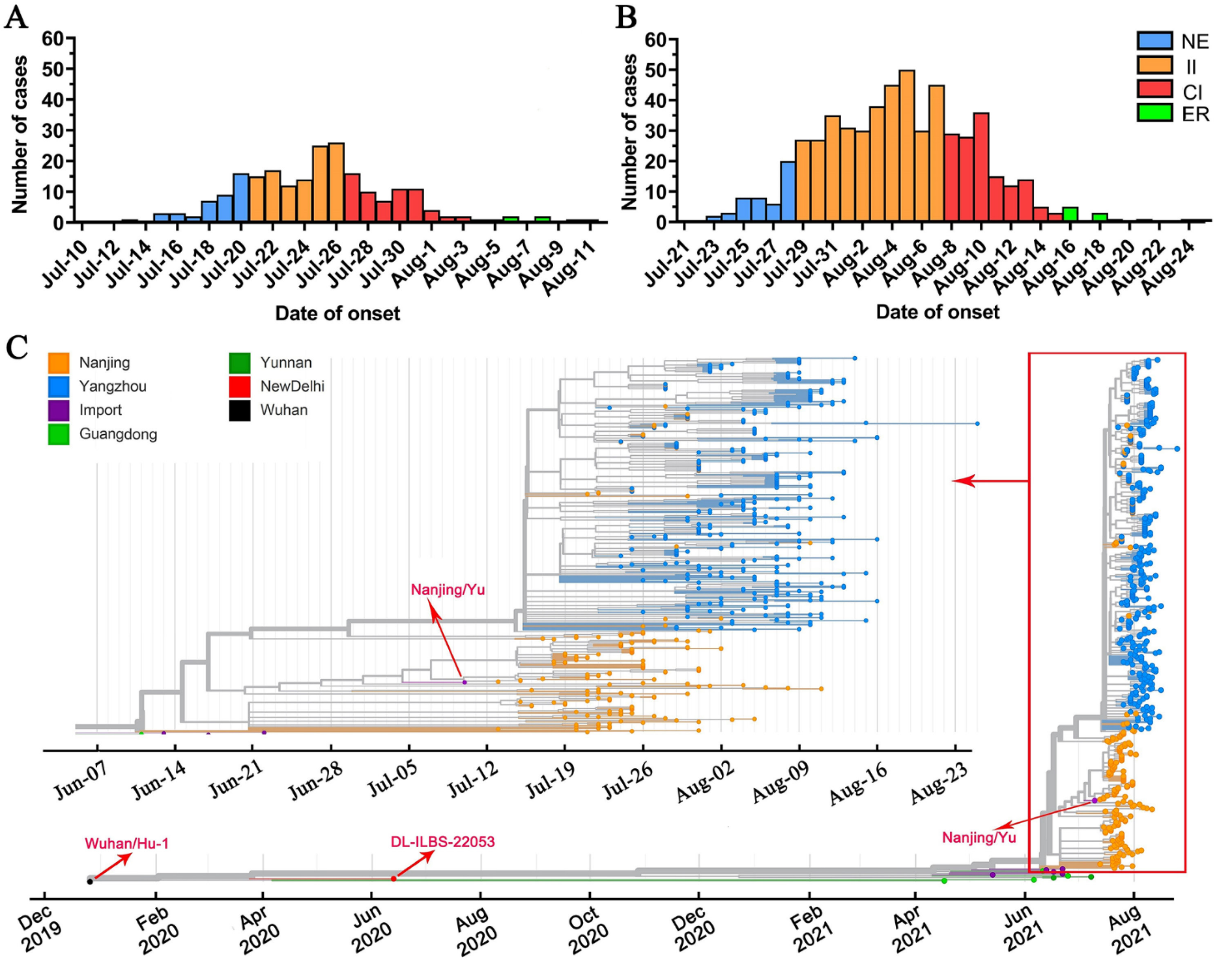
To mitigate the risk of continued transmission originating from potential local sources at the airport, individuals testing negative for SARS-CoV-2 were subjected to a 14-day quarantine at a hotel situated at a considerable distance from the airport following their arrival. During the fifth and seventh days of their quarantine period, two additional cases of COVID-19 were identified.

On the same day, 16 cleaners boarded the aircraft an hour after the passengers and flight crew had disembarked. During the weekly SARS-CoV-2 screening conducted on 20 July, six of these cleaners tested positive for the virus. Subsequent investigations revealed that five of the infected cleaners had direct contact with items contaminated by the Nanjing/Yu case. Specifically, two cleaners sanitized the toilet used by the case, two others swept the aisles traversed by Nanjing/Yu, and one cleaner handled discarded items at the case's seat. Whole-genome sequencing analysis confirmed that the viral genomes of these infected cleaners were identical to those of the Nanjing/Yu case, including the presence of the H146Y mutation in the spike protein.

Between July 1 and July 20, six additional international flights landed in Nanjing, each with confirmed cases of COVID-19. However, none of these cases were infected with the Delta variant. Based on the available evidence, it is highly plausible that transmission of the Delta variant occurred from the Nanjing/Yu case to the airport cleaners via contact with contaminated fomites.

Local outbreaks of SARS-CoV-2 variants in Nanjing and Yangzhou

Figure 1. Distribution of coronavirus disease 2019 (COVID-19) cases and phylogenetic analysis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genome sequences in Nanjing and Yangzhou, 2021.



A and B, Time series and laboratory-confirmed COVID-19 cases in Nanjing and Yangzhou, respectively. Daily number of cases in natural epidemic period (NE), incompletely intervened period (II), completely intervened period (CI), and epidemic regression period (ER) are shown in blue, yellow, red, and green, respectively. C, The time resolved phylogenetic tree was constructed with the Nextstrain pipeline by including early imported COVID-19 cases detected before 10 July 2021 in Jiangsu province, Delta variants of the local cases in Guangdong and Yunnan province detected in the period between March to July 2021, and the early Delta variants DL-ILBS-22053 isolated in New Delhi, India. The sequences from the local COVID-19 cases of Nanjing (orange) and Yangzhou (blue) are highlighted with a red box and shown in panel C (inset).

Nanjing, located on the eastern coast of China, has a permanent resident population exceeding 9 million. Throughout the distinct stages of the outbreak − namely the NE, II, CI, and ER periods − the number of identified COVID-19 cases was 41, 109, 64, and 7, respectively (Figure 1A).

Situated approximately 100 kilometers northeast of Nanjing, Yangzhou encountered a COVID-19 case originating from Nanjing on 21 July. This case was detected in Yangzhou on 27 July, prompting the swift implementation of local control measures on 28 July. The number of COVID-19 cases detected during the subsequent periods were 48, 358, 141, and 12, respectively (Figure 1B).

Phylogenetic analyses unveiled a remarkable resemblance in viral genomes between the Nanjing and Yangzhou outbreaks, clustering them within a single clade. Notably, genomes from the Yangzhou outbreak formed a unique branch, distinguishing them from the majority originating in Nanjing. Moreover, all genomes identified in this study displayed distinct divergence from imported COVID-19 cases detected before 10 July 2021, in mainland China, as well as from the Delta variant (DL-ILBS-22053) isolated in New Delhi, India (Figure 1C).

Mutation patterns of the virus variant causing the local epidemic

In comparison to the Wuhan-Hu-1 strain, the Delta variant isolated from the Nanjing/Yu case and the initial local cases identified during the Nanjing outbreak exhibited 35 nucleotide mutations and three deletions (Supplementary Table 4). Specifically, the G15451A mutation in the *RdRp* gene mismatched the Charite primer in the 3' primer region, while the G28881T mutation in the *N* gene mismatched the first nucleotide of the 5' primer designed by the Chinese Center for Disease Control and Prevention (China CDC) (Figure 2C) [13]. Notably, no nucleotide mutations were detected in the envelope (*E*) gene.

Some of these nucleotide mutations led to amino acid (aa) substitutions. Specifically, there were four aa substitutions (D63G, R203M, G215C, and D377Y) in the nucleocapsid protein (N), one (I82T) in the membrane protein (M), and 16 substitutions in other ORF regions. These include 11 substitutions in ORF1ab (K261N, A1306S, P2046L, P2287S, V2930L, T3255I, T3646A, P4715L, G5063S, P5401L, A6319V), one in ORF3a (S26L), three in ORF7a (P45L, V82A, T120I), and one in ORF8 (ERF119-120DF) (Figure 2A). Furthermore, eight aa substitutions and one aa deletion were observed in the S protein, encompassing T19R, G142D, H146Y, L452R, T478K, D614G, P681R, D950N, and a deletion at positions 156–157 (Figure 2B, Supplementary Table 4).

Onward mutations of SARS-CoV-2 under a dynamic zero-COVID strategy

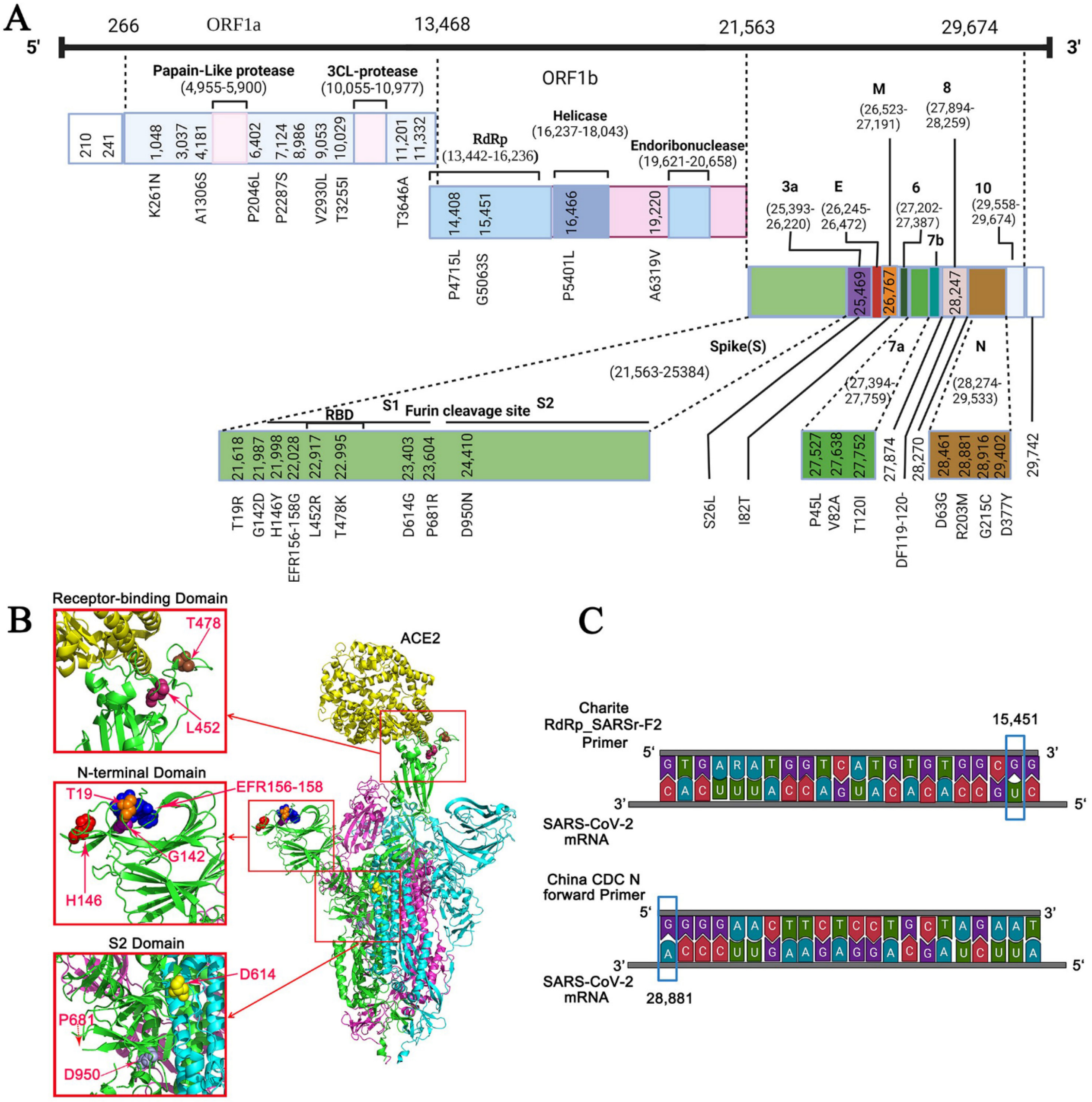
During the Nanjing and Yangzhou outbreaks, we observed a total of 81 amino acid mutations across various domains of the virus. Specifically, these mutations included 1 in the E domain, 3 in the M domain, 5 in the N domain, 11 in the S domain, 53 in the ORF1ab domain, 2 in the ORF3a domain, 3 in the ORF7a domain, and 1 in the ORF10 domain. Among the mutations in the S protein, 11 were novel, namely L5F, P384S, N542K, D574Y, A647S, H655Y, G769V, V951L, Q1005H, T1117I, and Q1208H.

Beyond the 35 baseline mutations of the original virus, there was a broad spectrum of SNVs observed in the onward transmission. Among these, mutations A27010C and A5289T had not been previously identified in existing sequences. In Nanjing and Yangzhou, we identified multiple combinations of SNVs, including those with the 35 baseline mutations alone, combined with C346T, T2803C, T2803C, and T7513C; as well as combinations with rare SNVs. (Figures 3A, 3B)

Out of the 221 COVID-19 cases identified in the Nanjing outbreak, whole-genome sequences were successfully compiled for 167 cases. A total of 48 distinct SNV combinations were observed (Figure 3A, Supplementary Tables 5 and 6). The number of emerging SNV combination types in the NE, II, CI, and ER periods were 16, 17, 13, and 2, respectively (Figure 3C). Of these 48 SNV combination types, 39 (81.25%) terminated during thorough hotel quarantine, while 9 types terminated spontaneously. During the NE period, 16 SNV combination types emerged, but only 5 terminated, including 3 due to NPIs and 2 due to self-termination. Since the II period, the number of terminated SNV combination types exceeded the number of emerging types, paralleling the intensification of NPI measures. Notably, most rare SNV combination types were observed and terminated during the II and CI periods (Figure 3C).

The individual who introduced the SARS-CoV-2 virus from Nanjing to Yangzhou harbored 36 nucleotide mutations in her viral genome. These comprised the 35 baseline mutations present in the original Nanjing strain, along with an additional T2803C mutation. Among the 559 COVID-19 cases recorded in the Yangzhou outbreak, whole-genome sequencing was successfully conducted for 353 cases, revealing 89 distinct SNV combination types (Figure 3B, Supplementary Tables 7 and 8). The distribution of these SNV combination types during the various outbreak periods was as follows: 15 emerged during the NE period, 44 during the II period, 28 during the CI period, and 2 during the ER period. Out of the 89 SNV combination types, 53 (59.55%) were terminated due to rigorous hotel quarantine measures, while 36 types self-terminated. During the NE period, 15 SNV combination types emerged, but only 8 of them terminated, including 2 that were halted due to NPIs and 6 that terminated spontaneously. Notably, in contrast to Nanjing, Yangzhou witnessed a turning point in the number of emerging and terminating SNV combination types during the CI period, rather than the II period. Like

Figure 2. Genomic variance of the Nanjing/Yu case and its impact on diagnosis.

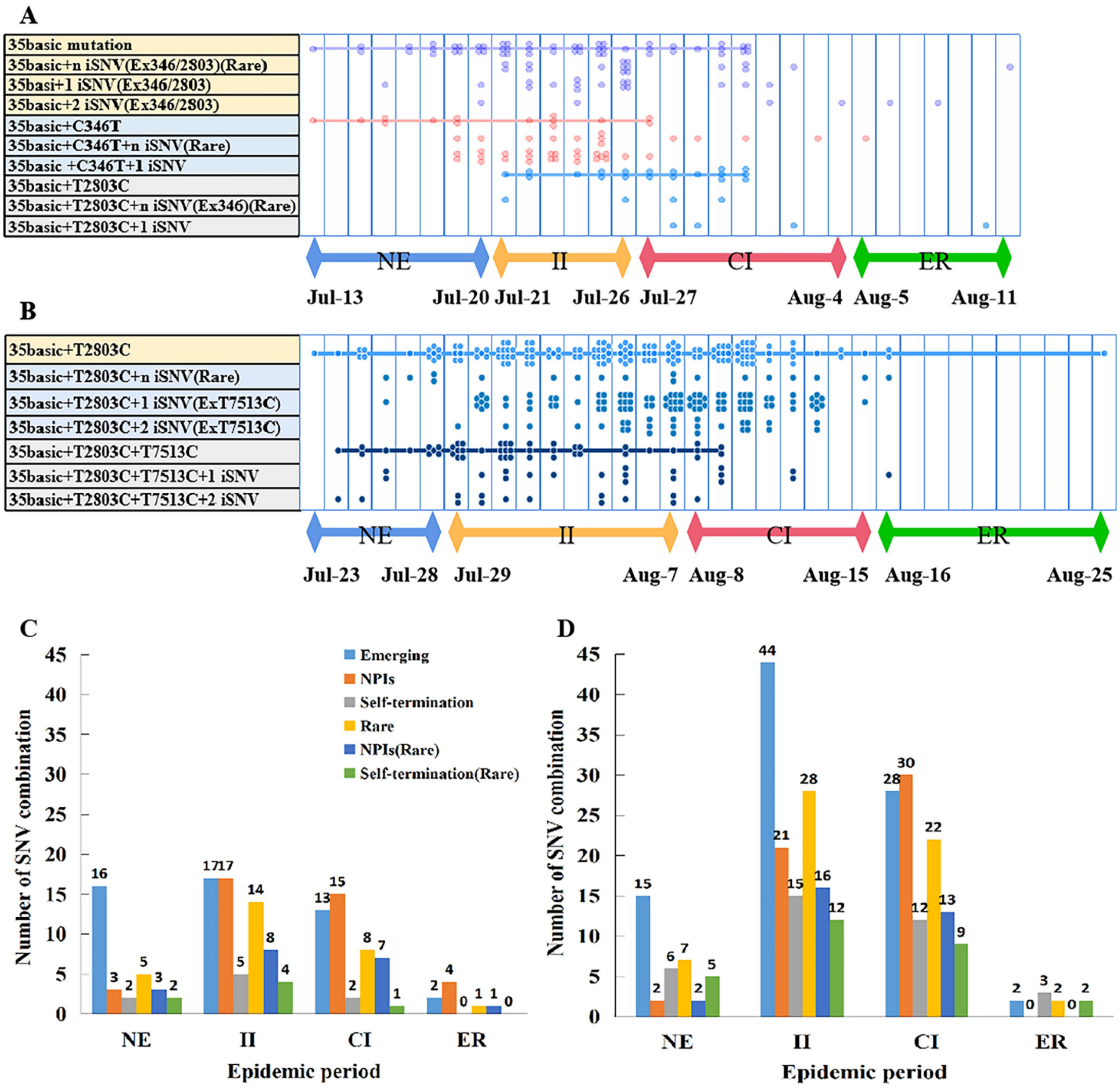


A, The position of 38 variations in the genome. B, Variations in the spike mapped to the spike trimer. Structure made by PyMOL (version 2.6.0a0) using PDBID 7A94. C, Mutations in the real time polymerase chain reaction (RT-PCR) detection primer region. G15451A mutation in RdRp resulted in the mismatch of Charite primer which may have affected its detection efficiency because it mapped to the 3’ primer region. Another G28881T mutation in N gene may have had no effect on the efficiency of China CDC primer since it mapped to the first nucleotide of the 5’ primer region. Figures 2B and 2C were made using Biorender (https://biorender.com/).

Nanjing, most rare SNV combination types were observed and terminated during the II and CI periods in Yangzhou (Figure 3D).

In this study, intra-host single nucleotide variations (iSNVs) were also thoroughly investigated. We gathered sequential respiratory samples from three COVID-19 patients (YZ018, YZ404, and YZ409) at three distinct time points post-infection to track the fluctuations in alternative allele frequencies (AAFs). For YZ409, the AAFs of T12175A, T16392C, and G24410A exhibited an upward trend. Conversely, in YZ404, the AAF of G28916T rose initially but then

Figure 3. Single nucleotide variant (SNV) combinations under zero-COVID strategy.



A, The distribution of different SNV combinations of Nanjing COVID-19 cases in different epidemic periods. The scatter indicates the different SNV combinations among the cases, and the connected line indicates that a certain SNV combination of mutations appeared in related cases. B, The distribution of different SNV combinations of Yangzhou COVID-19 cases in different epidemic periods. The scatter indicates the different SNV combinations among the cases, and the connected line indicates that a certain combination of mutations appeared in related cases. C, The number of SNV combinations formed in the 4 epidemic periods in Nanjing and that only appeared in a single case, the self-terminated number of transmission chain, the number of terminated transmission due to non-pharmaceutical interventions (NPI) measures. D, The number of SNV combinations formed in the 4 epidemic periods in Yangzhou and that only appeared in a single case, the self-terminated number of transmission chain, the number of terminated transmission due to NPI measures. NE, natural epidemic period; II, incompletely intervened period; CI, completely intervened period; ER, epidemic regression period.

declined at the second sampling point, followed by a rebound at the third sampling point. For YZ018, the AAF of G28916T displayed a similar pattern, while the AAF of G21987A also decreased and rebounded. The AAF of C27527T declined in YZ409 and YZ404, whereas in YZ018, it underwent a decrease and subsequent rebound. Furthermore, the AAF of C23604G diminished in both YZ409 and YZ404. Notably, the C7764T mutation spontaneously disappeared during viral replication. Interestingly, in YZ018, the rare allele of T7513C transformed into a homozygous state. This T7513C mutation was detected in over 89 cases during the Yangzhou outbreak, indicating its potential significance (Supplementary Figure 1).

Based on the transmission potential of specific viral mutations, COVID-19 cases were categorized into two groups: non-terminated cases (with onward transmission, n = 371) and terminated cases (without onward transmission, n = 149). To identify factors associated with the termination of SNV combinations, a multivariate logistic regression analysis was performed. The analysis revealed that the epidemic period at which a COVID-19 case was identified and the vaccination status prior to infection were significant predictors of SNV termination. Compared to the NE period, the II, CI, and ER periods had notably higher chances of SNV termination. The odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) are listed below: OR = 2.47 (95% CI, 1.28–4.76) for the II period, OR = 5.77 (95% CI, 2.93–11.37) for the CI period, and OR = 16.12 (95% CI, 3.62–71.84) for the ER period. Additionally, cases who had been fully vaccinated at least 30 days before symptom onset showed a significantly elevated risk of SNV termination in comparison to those who were either unvaccinated or incompletely vaccinated (meaning they had not finished their vaccination course or their final dose was given within 14 days of symptom onset). The OR for this vaccination factor was 2.33 (95% CI, 1.28–4.24) (Supplementary Table 9).

Discussion

Based on epidemiological and virological genomic data, it is evident that the outbreaks in Nanjing and Yangzhou, China, were distinct from those in Guangdong and Yunnan, where local cases of the Delta variant had previously been reported. The Nanjing outbreak was traced back to an aviation passenger, and it was found that the cabin cleaners' protective measures were inadequate. For instance, their gloves did not fully cover the cuffs of their protective suits, and their hands were not adequately sanitized during and after the cleaning process, nor when removing their protective gear. These deficiencies likely contributed to their exposure and subsequent infection.

The Yangzhou outbreak was initiated by a COVID-19 case who had traveled from Nanjing to Yangzhou. Significantly, all viral strains isolated from cases in Yangzhou were traced back to a lineage originating from Nanjing.

Furthermore, mutations in viral genes targeted by detection reagents have the potential to reduce diagnostic efficiency. We have identified two such mutations. One is G15451A in the *RdRp* gene, which mismatches the Charite primer in the 3' primer region. This mutation has been shown to reduce RT-PCR amplification efficiency and significantly increase the median RT-PCR cycle threshold value [14]. The other mutation is G28881T in the *N* gene, which mismatches the first nucleotide of the 5' primer designed by China Centers for Disease Control and Prevention (CDC). This mutation has also been detected in the Delta Variant (B.1.617.2) and the Kappa Variant (B.1.617.1) in Morocco [15].

The S protein of SARS-CoV-2 is crucial in viral infection, and our research revealed several mutations in its sequence with potential functional significance. Specifically, five amino acid substitutions (G142D, H146Y, D614G, L452R, and T478K) and one deletion (157DEL) in the S protein are associated with a reduced ability to bind previously existing neutralizing antibodies, as indicated in Supplementary Table 10 [16–24]. Notably, the H146Y mutation could undermine the efficacy of vaccines and antibody-based interventions, supported by modeling predictions and real-world observations. Our previous studies highlight the importance of the H146 site in the NTD of the S protein, which exhibits strong binding affinity with neutralizing antibodies such as FC05 [20]. Similar properties have been reported for the neutralizing antibody 4A8 [21]. Notably, according to the GISAID database, Delta variants carrying the H146Y mutation in the S protein have been reported in eight countries, including Russia, until 10 July [25].

Furthermore, the P681R mutation, located at the Furin protease cleavage site, is believed to enhance cleavage efficiency, facilitating viral entry into host cells. It has also been associated with promoting viral replication, leading to higher virus loads and increased transmission [26–28]. Additionally, the L5F mutation, found in several other variants, particularly B.1.526, is linked to increased viral transmissibility and was responsible for the second wave of COVID-19 cases in

New York in early 2021 [29]. The H655Y mutation, emerging in B.1.1.529 and P.1 variants, has been proven to evade neutralization by human monoclonal antibodies and can spread rapidly in cats [8,30]. Structural modeling of the T1117I mutation suggests a potential impact on viral oligomerization, crucial for cell infection [31].

Moreover, the G769V mutation, previously found in the R.1 lineage in Japan, remains enigmatic in terms of its functional role [32]. In our study, we initially identified several mutations in the S protein and submitted their information to the GISAID database. These mutations' biological functional impacts have not been previously reported. For instance, the Q1005H and Q1208H substitutions may disrupt intra-protomer hydrogen bonds, leading to the formation of a symmetric histidine triad near the spike's base. Additionally, water-mediated interactions could enhance hydrogen bonding between these histidine residues [33]. The A647S mutation, involving the conversion of a hydrophobic alanine to a hydrophilic serine, may alter the spatial structure between antigens and cells through serine's hydroxyl group binding to the oligosaccharide chain of T645. Similarly, the D574Y mutation is influenced by glycan chains of T572 and T573, potentially mediating immune escape. Notably, in a study in India, vaccine breakthrough infections with the Delta variant exhibited a unique mutation at position S:D574Y [34].

Mutations in other viral regions also possess functional implications. For example, mutations in the ORF1ab region may increase virus load, cause higher cell mortality [35], and reduce lymphocyte (CD3+ T, CD4+ T, CD8+ T, CD19+ B cells, and CD16+ CD56+ NK cells) and cytokine (IL-6 and IL-8) levels [36]. Mutations in ORF3a are likely to affect the viral life cycle, virulence, infectivity, ion channel formation, and virus release [37]. ORF7a mutations alter IFN-I signaling, impacting the virus's ability to suppress the host's immune response [38,39]. The deletion in ORF8 may lead to reduced systemic release of pro-inflammatory cytokines, resulting in decreased virulence and milder infections [40]. The Q27stop mutation, truncating the ORF8 region in the VOC-202012/01 variant, may mediate immune escape and influence transmissibility [41]. Finally, the I82T substitution in the M protein could affect the glucose transport transmembrane helices, contributing to immune evasion [42].

The implementations of NPIs, including mandatory masking, quarantine measures, and social distancing, have been associated with a notable reduction in the effective reproduction number (Rt) of COVID-19 [43]. As the virus transmission slows down, there is a corresponding decrease in the rate of viral mutation. Our study has found that Delta variants (SNV combinations) are capable of spontaneous termination. Nevertheless, the enforcement of NPIs seems to accelerate this termination process. With strict implementation of NPIs, the number of terminated SNV combinations surpasses the number of emerging ones.

In the Nanjing outbreak, strict NPIs were swiftly put into effect, resulting in the number of terminated SNV combinations surpassing the number of emerging ones as early as the second epidemic period. Conversely, in the Yangzhou outbreak, due to a delayed implementation of strict NPIs, it took until the third period for the terminated SNV combinations to outnumber the emerging ones. Reports indicate that chronic infections can lead to immune-evading mutations, potentially giving rise to some VOCs. Therefore, identifying and treating chronic SARS-CoV-2 infections should be deemed a top public health priority [44]. In our study, patients were isolated and treated until their virus nucleic acid tests returned negative, thereby minimizing the generation and dissemination of mutations stemming from chronic infections.

Vaccination has been found to reduce the transmission of the Delta variant, though to a lesser degree than the Alpha variant, and its effectiveness diminishes over time [45]. Our findings reveal that fully vaccinated individuals (vaccinated at least 30 days prior to disease onset) are more likely to eliminate their viral SNV combinations compared to the unvaccinated, even in the presence of the H146Y substitution in Delta variants. Nevertheless, the odds ratio (2.33, 95% CI 1.281–4.236) is much lower than that of NPI (16.118, 95% CI 3.616–71.836 for ER period), highlighting the pivotal role of NPIs in terminating SNV combinations.

Since the latter half of 2021, the Delta variants have dominated, succeeded by the Omicron variant, causing multiple global waves of infection. These adaptive mutations confer upon the virus enhanced immune evasion, more efficient transmission, and/or altered clinical presentations. Moreover, the efficacy of diagnostic testing kits has been compromised. In our investigation, we utilized whole-genome sequencing to delineate individual transmission chains, identify sources of infection, and establish the interconnection between the two outbreaks in Jiangsu. The rigorous implementation of NPIs, in conjunction with mass vaccination, facilitated the interruption of Delta variant transmission in Nanjing and Yangzhou in 2021.

Consequently, the distinct SNV combinations arising during the Nanjing and Yangzhou outbreaks did not disseminate further.

There are several limitations to our study. Firstly, the impact of amino acid mutations on the conformation of the spike protein has not been confirmed through cryo-electron microscopy (EM). Additionally, the effect of these mutations on glycosylation is still uncertain. Glycosylation analysis requires a significant amount of virus samples, and glycosylation patterns may vary among hosts. Therefore, we plan to investigate the mechanisms of these mutations further in future studies and present our findings in a separate report.

Conclusions

The rigorous enforcement of NPIs, alongside extensive vaccination efforts, can halt the transmission of Delta variants. Within the contexts of the Nanjing and Yangzhou outbreaks, NPIs demonstrated greater efficacy than vaccination alone in curbing the spread of the virus.

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References

1. Kawasaki Y, Abe H, Yasuda J (2023) Comparison of genome replication fidelity between SARS-CoV-2 and influenza A virus in cell culture. Sci Rep 13: 13105. doi: 10.1038/s41598-023-40463-4.
2. Neher RA (2022) Contributions of adaptation and purifying selection to SARS-CoV-2 evolution. Virus Evol 8: veac113. doi: 10.1093/ve/veac113.
3. Harvey WT, Carabelli AM, Jackson B, Gupta RK, Thomson EC, Harrison EM, Ludden C, Reeve R, Rambaut A, Peacock SJ, Robertson DL (2021) SARS-CoV-2 variants, spike mutations and immune escape. Nat Rev Microbiol 19: 409–424. doi: 10.1038/s41579-021-00573-0.
4. Van Egeren D, Stoddard M, White LF, Hochberg NS, Rogers MS, Zetter B, Joseph-McCarthy D, Chakravarty A (2023) Vaccines alone cannot slow the evolution of SARS-CoV-2. Vaccines 11: 853. doi: 10.3390/vaccines11040853.
5. Lauring AS, Andino R (2010) Quasispecies theory and the behavior of RNA viruses. PLoS Pathog 6: e1001005. doi: 10.1371/journal.ppat.1001005.
6. El-Haddad K, Adhikari TM, Tu ZJ, Cheng Y-W, Leng X, Zhang X, Rhoads D, Ko JS, Worley S, Li J, Rubin BP, Esper FP (2023) Intra-host mutation rate of acute SARS-CoV-2 infection during the initial pandemic wave. Virus Genes 59: 653–661. doi: 10.1007/s11262-023-02011-0.
7. Liu Y, Morgenstern C, Kelly J, Lowe R, CMMID COVID-19 Working Group, Jit M (2021) The impact of non-pharmaceutical interventions on SARS-CoV-2 transmission across 130 countries and territories. BMC Med 19: 40. doi: 10.1186/s12916-020-01872-8.
8. World Health Organization (nd) Tracking SARS-CoV-2 variants. Available: https://www.who.int/activities/tracking-SARS-CoV-2-variants. Accessed: 21 September 2023.
9. National Health Commission of the People's Republic of China (nd) COVID-19 diagnosis and treatment scheme (revised 8th trial version). Available: http://www.nhc.gov.cn/xcs/zhengcwj/202104/7de0b3837c8b4606a0594aeb0105232b.shtml. Accessed: 5 February 2022.
10. Katoh K, Standley DM (2013) MAFFT multiple sequence alignment software version 7: improvements in performance and usability. Mol Biol Evol 30: 772–780. doi: 10.1093/molbev/mst010.
11. Trifinopoulos J, Nguyen L-T, von Haeseler A, Minh BQ (2016) W-IQ-TREE: a fast online phylogenetic tool for maximum likelihood analysis. Nucleic Acids Res 44: W232–235. doi: 10.1093/nar/gkw256.
12. Hadfield J, Megill C, Bell SM, Huddleston J, Potter B, Callender C, Sagulenko P, Bedford T, Neher RA (2018) Nextstrain: real-time tracking of pathogen evolution. Bioinforma Oxf Engl 34: 4121–4123. doi: 10.1093/bioinformatics/bty407.
13. Lopez-Rincon A, Tonda A, Mendoza-Maldonado L, Mulders DGJC, Molenkamp R, Perez-Romero CA, Claassen E, Garssen J, Kraneveld AD (2021) Classification and specific primer design for accurate detection of SARS-CoV-2 using deep learning. Sci Rep 11: 947. doi: 10.1038/s41598-020-80363-5.
14. Valley-Omar Z, Marais G, Iranzadeh A, Naidoo M, Korsman S, Maponga T, Hussey H, Davies M-A, Boulle A, Doolabh D, Laubscher M, Wojno J, Deetlefs JD, Maritz J, Scott L, Msomi N, Naicker C, Tegally H, de Oliveira T, Bhiman J, Williamson C, Preiser W, Hardie D, Hsiao N-Y (2022) Reduced amplification efficiency of the RNA-dependent-RNA-polymerase target enables tracking of the Delta SARS-CoV-2 variant using routine diagnostic tests. J Virol Methods 302: 114471. doi: 10.1016/j.jviromet.2022.114471.
15. Melloul M, Chouati T, Hemlali M, Alaoui Amine S, Touil N, Elannaz H, Ennibi K, Youbi M, Merabet M, Bellefquih AM, Nourlil J, Maaroufi A, El Fahime E (2021) Genome sequences of the Delta variant (B.1.617.2) and the Kappa variant (B.1.617.1) detected in Morocco. Microbiol Resour Announc 10: e00727–21. doi: 10.1128/MRA.00727-21.
16. Shi AC, Xie X (2021) Making sense of spike D614G in SARS-CoV-2 transmission. Sci China Life Sci 64: 1062–1067. doi: 10.1007/s11427-020-1893-9.
17. Suryadevara N, Shrihari S, Gilchuk P, VanBlargan LA, Binshtein E, Zost SJ, Nargi RS, Sutton RE, Winkler ES, Chen EC, Fouch ME, Davidson E, Doranz BJ, Chen RE, Shi P-Y, Carnahan RH, Thackray LB, Diamond MS, Crowe JE (2021) Neutralizing and protective human monoclonal antibodies recognizing the N-terminal domain of the SARS-CoV-2 spike

protein. Cell 184: 2316–2331.e15. doi: 10.1016/j.cell.2021.03.029.

18. Liu J, Liu Y, Xia H, Zou J, Weaver SC, Swanson KA, Cai H, Cutler M, Cooper D, Muik A, Jansen KU, Sahin U, Xie X, Dormitzer PR, Shi P-Y (2021) BNT162b2-elicited neutralization of B.1.617 and other SARS-CoV-2 variants. Nature 596: 273–275. doi: 10.1038/s41586-021-03693-y.
19. Chen RE, Zhang X, Case JB, Winkler ES, Liu Y, VanBlargan LA, Liu J, Errico JM, Xie X, Suryadevara N, Gilchuk P, Zost SJ, Tahan S, Droit L, Turner JS, Kim W, Schmitz AJ, Thapa M, Wang D, Boon ACM, Presti RM, O'Halloran JA, Kim AHJ, Deepak P, Pinto D, Fremont DH, Crowe JE, Corti D, Virgin HW, Ellebedy AH, Shi P-Y, Diamond MS (2021) Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies. Nat Med 27: 717–726. doi: 10.1038/s41591-021-01294-w.
20. Zhang L, Cao L, Gao X-S, Zheng B-Y, Deng Y-Q, Li J-X, Feng R, Bian Q, Guo X-L, Wang N, Qiu H-Y, Wang L, Cui Z, Ye Q, Chen G, Lu K-K, Chen Y, Chen Y-T, Pan H-X, Yu J, Yao W, Zhu B-L, Chen J, Liu Y, Qin C-F, Wang X, Zhu F-C (2021) A proof of concept for neutralizing antibody-guided vaccine design against SARS-CoV-2. Natl Sci Rev 8: nwab053. doi: 10.1093/nsr/nwab053.
21. Chi X, Yan R, Zhang J, Zhang G, Zhang Y, Hao M, Zhang Z, Fan P, Dong Y, Yang Y, Chen Z, Guo Y, Zhang J, Li Y, Song X, Chen Y, Xia L, Fu L, Hou L, Xu J, Yu C, Li J, Zhou Q, Chen W (2020) A neutralizing human antibody binds to the N-terminal domain of the Spike protein of SARS-CoV-2. Science 369: 650–655. doi: 10.1126/science.abc6952.
22. Wang Z, Schmidt F, Weisblum Y, Muecksch F, Barnes CO, Finkin S, Schaefer-Babajew D, Cipolla M, Gaebler C, Lieberman JA, Oliveira TY, Yang Z, Abernathy ME, Huey-Tubman KE, Hurley A, Turroja M, West KA, Gordon K, Millard KG, Ramos V, Da Silva J, Xu J, Colbert RA, Patel R, Dizon J, Unson-O'Brien C, Shimeliovich I, Gazumyan A, Caskey M, Bjorkman PJ, Casellas R, Hatziioannou T, Bieniasz PD, Nussenzweig MC (2021) mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants. Nature 592: 616–622. doi: 10.1038/s41586-021-03324-6.
23. Li Q, Wu J, Nie J, Zhang L, Hao H, Liu S, Zhao C, Zhang Q, Liu H, Nie L, Qin H, Wang M, Lu Q, Li X, Sun Q, Liu J, Zhang L, Li X, Huang W, Wang Y (2020) The impact of mutations in SARS-CoV-2 spike on viral infectivity and antigenicity. Cell 182: 1284–1294.e9. doi: 10.1016/j.cell.2020.07.012.
24. Liu Z, VanBlargan LA, Bloyet L-M, Rothlauf PW, Chen RE, Stumpf S, Zhao H, Errico JM, Theel ES, Liebeskind MJ, Alford B, Buchser WJ, Ellebedy AH, Fremont DH, Diamond MS, Whelan SPJ (2021) Identification of SARS-CoV-2 spike mutations that attenuate monoclonal and serum antibody neutralization. Cell Host Microbe 29: 477–488.e4. doi: 10.1016/j.chom.2021.01.014.
25. Regeneron (nd) Regeneron COVID-19 dashboard. Available: https://covid19dashboard.regeneron.com/?tab=Lineage_Details. Accessed: 22 May 2022.
26. Lopez Bernal J, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, Stowe J, Tessier E, Groves N, Dabrera G, Myers R, Campbell CNJ, Amirthalingam G, Edmunds M, Zambon M, Brown KE, Hopkins S, Chand M, Ramsay M (2021) Effectiveness of COVID-19 vaccines against the B.1.617.2 (Delta) variant. N Engl J Med 385: 585–594. doi: 10.1056/NEJMoa2108891.
27. Cherian S, Potdar V, Jadhav S, Yadav P, Gupta N, Das M, Rakshit P, Singh S, Abraham P, Panda S, Team N (2021) SARS-CoV-2 Spike Mutations, L452R, T478K, E484Q and P681R, in the second wave of COVID-19 in Maharashtra, India. Microorganisms 9: 1542. doi: 10.3390/microorganisms9071542.
28. Zhang Z, Zheng Y, Niu Z, Zhang B, Wang C, Yao X, Peng H, Franca DN, Wang Y, Zhu Y, Su Y, Tang M, Jiang X, Ren H, He M, Wang Y, Gao L, Zhao P, Shi H, Chen Z, Wang X, Piacentini M, Bian X, Melino G, Liu L, Huang H, Sun Q (2021) SARS-CoV-2 spike protein dictates syncytium-mediated lymphocyte elimination. Cell Death Differ 28: 2765–2777. doi: 10.1038/s41418-021-00782-3.
29. West AP, Wertheim JO, Wang JC, Vasylyeva TI, Havens JL, Chowdhury MA, Gonzalez E, Fang CE, Di Lonardo SS, Hughes S, Rakeman JL, Lee HH, Barnes CO, Gnanapragasam PNP, Yang Z, Gaebler C, Caskey M, Nussenzweig MC, Keeffe JR, Bjorkman PJ (2021) Detection and characterization of the SARS-CoV-2 lineage B.1.526 in New York. Nat Commun 12: 4886. doi: 10.1038/s41467-021-25168-4.
30. Braun KM, Moreno GK, Halfmann PJ, Hodcroft EB, Baker DA, Boehm EC, Weiler AM, Haj AK, Hatta M, Chiba S, Maemura T, Kawaoka Y, Koelle K, O'Connor DH, Friedrich TC (2021) Transmission of SARS-CoV-2 in domestic cats imposes a narrow bottleneck. PLoS Pathog 17: e1009373. doi: 10.1371/journal.ppat.1009373.
31. Molina-Mora JA, Cordero-Laurent E, Godínez A, Calderón-Osorno M, Brenes H, Soto-Garita C, Pérez-Corrales C, COINGESA-CR Consorcio Interinstitucional de Estudios Genómicos del SARS-CoV-2 Costa Rica, Drexler JF, Moreira-Soto A, Corrales-Aguilar E, Duarte-Martínez F (2021) SARS-CoV-2 genomic surveillance in Costa Rica: evidence of a divergent population and an increased detection of a spike T1117I mutation. Infect Genet Evol 92: 104872. doi: 10.1016/j.meegid.2021.104872.
32. Hirotsu Y, Omata M (2021) Detection of R.1 lineage severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with spike protein W152L/E484K/G769V mutations in Japan. PLoS Pathog 17: e1009619. doi: 10.1371/journal.ppat.1009619.
33. Gobeil SM-C, Janowska K, McDowell S, Mansouri K, Parks R, Stalls V, Kopp MF, Manne K, Li D, Wiehe K, Saunders KO, Edwards RJ, Korber B, Haynes BF, Henderson R, Acharya P (2021) Effect of natural mutations of SARS-CoV-2 on spike structure, conformation, and antigenicity. Science 373: eabi6226. doi: 10.1126/science.abi6226.
34. Deval H, Nyayanit DA, Mishra SK, Yadav PD, Zaman K, Shankar P, Misra BR, Behera SP, Kumar N, Kumar A, Bhardwaj P, Dwivedi GR, Singh R, Shete AM, Pandit P, Pandey AK, Yadav GK, Gupta S, Kumar M, Kavathekar A, Singh RS, Prajapati S, Kant R (2021) Genome sequencing reveals a mixed picture of SARS-CoV-2 variant of concern circulation in Eastern Uttar Pradesh, India. Front Med 8: 781287. doi: 10.3389/fmed.2021.781287.
35. Yao H, Lu X, Chen Q, Xu K, Chen Y, Cheng M, Chen K, Cheng L, Weng T, Shi D, Liu F, Wu Z, Xie M, Wu H, Jin C, Zheng M, Wu N, Jiang C, Li L (2020) Patient-derived SARS-CoV-2 mutations impact viral replication dynamics and infectivity in vitro and with clinical implications in vivo. Cell Discov 6: 76. doi: 10.1038/s41421-020-00226-1.
36. Zhang X, Tan Y, Ling Y, Lu G, Liu F, Yi Z, Jia X, Wu M, Shi B, Xu S, Chen J, Wang W, Chen B, Jiang L, Yu S, Lu J, Wang J, Xu M, Yuan Z, Zhang Q, Zhang X, Zhao G, Wang S, Chen S, Lu H (2020) Viral and host factors related to the clinical outcome of COVID-19. Nature 583: 437–440. doi: 10.1038/s41586-020-2355-0.

37. Issa E, Merhi G, Panossian B, Salloum T, Tokajian S (2020) SARS-CoV-2 and ORF3a: nonsynonymous mutations, functional domains, and viral pathogenesis. mSystems 5: e00266–20. doi: 10.1128/msystems.00266-20.
38. Cao Z, Xia H, Rajsbaum R, Xia X, Wang H, Shi P-Y (2021) Ubiquitination of SARS-CoV-2 ORF7a promotes antagonism of interferon response. Cell Mol Immunol 18: 746–748. doi: 10.1038/s41423-020-00603-
39. Nemudryi A, Nemudraia A, Wiegand T, Nichols J, Snyder DT, Hedges JF, Cicha C, Lee H, Vanderwood KK, Bimczok D, Jutila MA, Wiedenheft B (2021) SARS-CoV-2 genomic surveillance identifies naturally occurring truncation of ORF7a that limits immune suppression. Cell Rep 35: 109197. doi: 10.1016/j.celrep.2021.109197.
40. Young BE, Fong S-W, Chan Y-H, Mak T-M, Ang LW, Anderson DE, Lee CY-P, Amrun SN, Lee B, Goh YS, Su YCF, Wei WE, Kalimuddin S, Chai LYA, Pada S, Tan SY, Sun L, Parthasarathy P, Chen YYC, Barkham T, Lin RTP, Maurer-Stroh S, Leo Y-S, Wang L-F, Renia L, Lee VJ, Smith GJD, Lye DC, Ng LFP (2020) Effects of a major deletion in the SARS-CoV-2 genome on the severity of infection and the inflammatory response: an observational cohort study. Lancet Lond Engl 396: 603–611. doi: 10.1016/S0140-6736(20)31757-8.
41. Pereira F (2021) SARS-CoV-2 variants combining spike mutations and the absence of ORF8 may be more transmissible and require close monitoring. Biochem Biophys Res Commun 550: 8–14. doi: 10.1016/j.bbrc.2021.02.080.
42. Shen L, Bard JD, Triche TJ, Judkins AR, Biegel JA, Gai X (2021) Emerging variants of concern in SARS-CoV-2 membrane protein: a highly conserved target with potential pathological and therapeutic implications. Emerg Microbes Infect 10: 885–893. doi: 10.1080/22221751.2021.1922097.
43. Bo Y, Guo C, Lin C, Zeng Y, Li HB, Zhang Y, Hossain MS, Chan JWM, Yeung DW, Kwok KO, Wong SYS, Lau AKH, Lao XQ (2021) Effectiveness of non-pharmaceutical interventions on COVID-19 transmission in 190 countries from 23 January to 13 April 2020. Int J Infect Dis 102: 247–253. doi: 10.1016/j.ijid.2020.10.066.
44. Markov PV, Ghafari M, Beer M, Lythgoe K, Simmonds P, Stilianakis NI, Katzourakis A (2023) The evolution of SARS-CoV-2. Nat Rev Microbiol 21: 361–379. doi: 10.1038/s41579-023-00878-2.
45. Eyre David W., Taylor Donald, Purver Mark, Chapman David, Fowler Tom, Pouwels Koen B., Walker A. Sarah, Peto Tim E.A. (2022) Effect of COVID-19 vaccination on transmission of Alpha and Delta variants. N Engl J Med 386: 744–756. doi: 10.1056/NEJMoa2116597.

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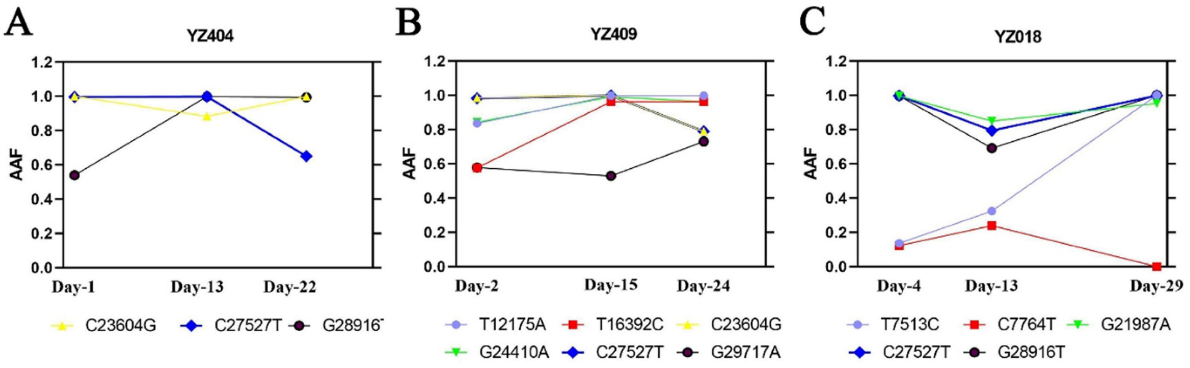
Conflict of interests: No conflict of interests is declared.

Annex – Supplementary Items

Supplementary Figure S1. Temporal dynamics of intra-host populations in patients YZ404, YZ409 and YZ018. Alternative allele frequencies (AAFs) among sampling dates in patients YZ404 (A), YZ409 (B) and YZ018 (C). Days post the first symptom date are shown in the abscissa. Colors represent different iSNVs.



Supplementary Table 1. Key reagents.

Reagent	Source	Identifier
SuperScript™ IV First-Strand Synthesis System	Thermo Fisher, Vilnius, Lithuania	Cat# 18091050
Q5® Hot Start High-Fidelity 2X Master Mix	NEB, Ipswich, MA, USA	Cat# M0494S
Long Fragment Target Capture Kit for SARS-CoV-2 Whole Genome	BAIYITECH, Hangzhou, China	Cat# BK-LFWCoV024
Target Capture Kit for SARS-CoV-2 Whole Genome	BAIYITECH, Hangzhou, China	Cat# BK-WCoV024
TruePrep DNA Library Prep Kit V2 for Illumina	Vazyme, Nanjing, China	Cat# TD502-02
TruePrep index Kit V2 for Illumina	Vazyme, Nanjing, China	Cat# TD202
PhiX Control v3 Support	Illumina, Hayward, CA, USA	Cat# FC-110-3001
MiSeq™ Reagent Kit v2 (300-cycles)	Illumina, Hayward, CA, USA	Cat# MS-102-2002
ATOPlex RNA Multiplex PCR-based Library Preparation Set V3.0	MGI, Shenzhen, China	Cat# 940-000133-00
MGIEasy Fast PCR-FREE FS Library Prep Set	MGI, Shenzhen, China	Cat# 940-000021-00
DNBSEQ one-step	MGI, Shenzhen, China	Cat# 1000026466
MGISEQ-2000RS High-throughput Sequencing Set (FCS SE100)	MGI, Shenzhen, China	Cat# 1000020570
CPAS Barcode Primer 4 Reagent Kit	MGI, Shenzhen, China	Cat# 1000014048
Agilent High Sensitivity DNA Kit	Agilent, Waldbronn, Germany	Cat# 5067-4626
NGS Reverse Transcription Kit	Thermo Fisher, Carlsbad, CA, USA	Cat# A45003
Ion AmpliSeq SARS-CoV-2 Insight Research Assay - GS Chef-Ready	Thermo Fisher, Carlsbad, CA, USA	Cat# A51306
Ion Torrent™ Ion Library TaqMan™ Quantitation Kit	Thermo Fisher, Vilnius, Lithuania	Cat# 4468802
Ion 530™ Chip Kit (2 × 4-pack)	Thermo Fisher, Carlsbad, CA, USA	Cat# A27764
Ion 510™ & Ion 520™ & Ion 530™ Kit – Chef (200bp, 2 sequencing run per initialization)	Thermo Fisher, Carlsbad, CA, USA	Cat# A34461
High Pure PCR Product Purification Kit	Roche, Mannheim, Germany	Cat# 11732668001
Agencourt AMPure XP	Beckman, Beferly, MA, USA	Cat# A63881
Qubit™ dsDNA HS Assay Kit	Thermo Fisher, Eugene, USA	Cat# Q32851
Qubit™ dsDNA BR Assay Kit	Thermo Fisher, Eugene, USA	Cat# Q32850
Qubit RNA HS Assay Kit	Thermo Fisher, Eugene, USA	Cat# Q32852
ULSEN Ultra-sensitive Novel Coronavirus Whole-genome capture Kit	MicroFuture, Beijing, China	Cat# V-090418-1
Nextera DNA Flex Library Prep	Illumina, Hayward, CA, USA	Cat# 20018704
NXTR® XT DNA SMP Prep Kit	Illumina, Hayward, CA, USA	Cat# 15032785
IDT® for Illumina DNA/RNA Unique Dual Indexes Set B	Illumina, Hayward, CA, USA	Cat# 20027214
IDT® for Illumina DNA/RNA Unique Dual Indexes Set D	Illumina, Hayward, CA, USA	Cat# 20027216
NextSeq2000 P2 reagent (300 cycle)	Illumina, Hayward, CA, USA	Cat# 20046813
iseq100 Reagent V2 (300 cycle)	Illumina, Hayward, CA, USA	Cat# 20031371
MiniSeq Mid Output Kit (300-cycles)	Illumina, Hayward, CA, USA	Cat# 15073757
Nextera DNA CD Indexes (24 Indexes)	Illumina, Hayward, CA, USA	Cat# 20018707

Supplementary Table 2. Samples and sequencing information.

Patient_id	Sample_id	Symptom onset_date	Collection_date	Periods	Symptom	Sample_type	Prefecture	Experiment_type	Sequencing_atform	Ct-ORF	Ct-N	Mapped_reads	Coverage (%)	Depth
NJ001	NJ001	2021/7/19	2021/7/21	NE	Mild	OPS[a]	NJ[c]	m-pcr	BGI	26.9	26.1	5,893,109	100.00	19715.99
NJ002	NJ002	2021/7/16	2021/7/21	NE	Mild	OPS	NJ	m-pcr	BGI	20.55	19.24	5,891,515	100.00	19710.66
NJ003	NJ003	2021/7/20	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	27.3	26.6	1,414,576	99.56	5493.016
NJ004	NJ004	2021/7/15	2021/7/21	NE	Mild	OPS	NJ	m-pcr	Illumina	35.4	35.3	1,021,122	99.94	2583.658
NJ005	NJ005	2021/7/20	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	33	33	741,008	99.02	1782.179
NJ006	NJ006	2021/7/17	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	30.4	28.6	765,024	99.79	1936.053
NJ007	NJ007	2021/7/18	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	33.3	32.1	856,100	99.41	2360.713
NJ009	NJ009	2021/7/20	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	BGI	31.4	32.1	5,395,751	100.00	18052.03
NJ010	NJ010	2021/7/15	2021/7/21	NE	Mild	OPS	NJ	m-pcr	Illumina	21	20	620,017	99.94	1597.72
NJ011	NJ011	2021/7/18	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	14	12	566,054	99.94	1478.998
NJ012	NJ012	2021/7/18	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	18	19	1,040,647	99.77	4054.291
NJ013	NJ013	2021/7/20	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	BGI	31.6	28.3	1,906,595	100.00	6359.526
NJ014	NJ014	2021/7/19	2021/7/21	NE	Mild	OPS	NJ	m-pcr	BGI	32	34	5,908,269	100.00	19766.71
NJ015	NJ015	2021/7/20	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	18	16	458,247	99.91	1205.087
NJ020	NJ020	2021/7/13	2021/7/23	NE	Mild	OPS	NJ	m-pcr	Illumina	14	16	1,491,423	99.94	4594.292
NJ021	NJ021	2021/7/20	2021/7/23	NE	Mild	OPS	NJ	m-pcr	Illumina	26	26	1,467,781	99.84	4613.42
NJ022	NJ022	2021/7/20	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	20	22	1,558,870	99.93	4787.205
NJ023	NJ023	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	31	31	1,070,088	99.43	3439.416
NJ026	NJ026	2021/7/20	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	BGI	30	30	2,991,657	99.90	9992.143
NJ027	NJ027	2021/7/20	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	24	24	1,903,657	99.84	5739.518
NJ028	NJ028	2021/7/20	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	BGI	33	33	1,199,864	99.87	2009.471
NJ031	NJ031	2021/7/16	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	33	30	2,167,484	99.79	6598.661
NJ032	NJ032	2021/7/13	2021/7/21	NE	Mod.	OPS	NJ	m-pcr	Illumina	29	26	2,073,507	99.65	6357.679
NJ033	NJ033	2021/7/19	2021/7/23	NE	Mild	OPS	NJ	m-pcr	Illumina	22	22	1,348,934	99.93	4229.287
NJ034	NJ034	2021/7/19	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	BGI	28	28	2,622,422	99.88	4391.188
NJ035	NJ035	2021/7/15	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	BGI	30	31	1,929,804	99.90	3230.667
NJ036	NJ036	2021/7/19	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	19	20	1,108,812	99.89	3555.446
NJ037	NJ037	2021/7/17	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	28	30	1,279,287	99.72	4013.909
NJ039	NJ039	2021/7/22	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	27	28	1,313,571	99.83	4214.173
NJ040	NJ040	2021/7/19	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	18	18	1,107,193	99.94	3582.698
NJ041	NJ041	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	25	25	1,347,369	99.92	4295.82
NJ042	NJ042	2021/7/21	2021/7/23	NE	Mild	OPS	NJ	m-pcr	Illumina	34	34	21,798,793	99.94	67072.8
NJ043	NJ043	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	34	34	4,516,308	99.70	13911.44
NJ044	NJ044	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	17	18	3,198,293	99.87	9750.579
NJ045	NJ045	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	BGI	18	21	3,572,903	99.90	11934.04
NJ046	NJ046	2021/7/22	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	29	29	1,491,545	99.75	4432.82
NJ047	NJ047	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	25	25	1,133,726	99.70	3595.7
NJ048	NJ048	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	27	28	2,209,793	99.89	6822.537
NJ049	NJ049	2021/7/16	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	22	23	840,602	99.84	2390.311
NJ050	NJ050	2021/7/19	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	22	24	1,007,111	99.74	2937.674
NJ051	NJ051	2021/7/21	2021/7/23	NE	Mod.	OPS	NJ	m-pcr	Illumina	22	24	1,077,943	99.77	3129.545
NJ052	NJ052	2021/7/19	2021/7/24	NE	Mod.	OPS	NJ	m-pcr	Illumina	20	21	824,837	99.93	2389.559
NJ053	NJ053	2021/7/21	2021/7/24	II	Mod.	OPS	NJ	m-pcr	Illumina	22	22	1,184,305	99.94	3440.324
NJ054	NJ054	2021/7/23	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	28	28	56,997,748	99.91	172081.2
NJ055	NJ055	2021/7/23	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	26	26	62,093,487	99.83	188204
NJ056	NJ056	2021/7/22	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	25	25	72,371,458	99.91	218513.8
NJ058	NJ058	2021/7/23	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	26	25	50,849,240	99.91	154657.7
NJ059	NJ059	2021/7/18	2021/7/25	NE	Mod.	OPS	NJ	m-pcr	Illumina	26	26	46,140,680	99.94	140927.6
NJ061	NJ061	2021/7/22	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	28	28	64,503,228	99.93	194482.5
NJ062	NJ062	2021/7/23	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	14	14	49,430,285	99.94	151133.8
NJ063	NJ063	2021/7/24	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	19	19	76,804,846	99.94	232420.8
NJ064	NJ064	2021/7/24	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	22	22	59,360,876	99.94	180672.5
NJ065	NJ065	2021/7/23	2021/7/25	II	Mild	OPS	NJ	m-pcr	Illumina	26	26	64,107,364	99.94	194675.3
NJ066	NJ066	2021/7/23	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	16	16	43,046,948	99.94	132379.2
NJ067	NJ067	2021/7/22	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	20	21	60,190,823	99.94	183448.2
NJ068	NJ068	2021/7/22	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	20	22	46,339,293	99.94	140256.7
NJ070	NJ070	2021/7/22	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	18	20	71,347,296	99.94	216842.6
NJ071	NJ071	2021/7/24	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	17	17	47,620,887	99.94	145410.3
NJ073	NJ073	2021/7/22	2021/7/25	II	Mod.	OPS	NJ	m-pcr	Illumina	33	33	1,716,750	99.94	5737.751
NJ074	NJ074	2021/7/22	2021/8/8	NE	Mod.	OPS	NJ	m-pcr	Illumina	30	30	435,812	99.65	1766.879
NJ075	NJ075	2021/7/21	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	24	26	15,848,415	99.91	58279.28
NJ078	NJ078	2021/7/23	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	32	34	8,925,398	99.88	31245.42
NJ079	NJ079	2021/7/25	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	34	36	10,381,604	99.92	32105.38
NJ080	NJ080	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	22	24	26,219,270	99.94	100515
NJ082	NJ082	2021/7/22	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	17	23	16,428,932	99.94	64312.04
NJ084	NJ084	2021/7/23	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	17	23	28,543,584	99.94	111964.9
NJ085	NJ085	2021/7/21	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	17	22	18,836,610	99.94	73941.13
NJ086	NJ086	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	23	25	32,857,352	99.94	127995.6
NJ087	NJ087	2021/7/22	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	19	21	49,255,674	99.94	190979.2
NJ088	NJ088	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	15	17	38,257,880	99.94	150158.5
NJ089	NJ089	2021/7/23	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	32	23	5,358,593	99.88	19284.6
NJ090	NJ090	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	21	25	29,846,203	99.94	116494.4
NJ091	NJ091	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	21	24	9,941,793	99.94	39078.62
NJ092	NJ092	2021/7/24	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	24	27	12,788,936	99.94	49801.79
NJ093	NJ093	2021/7/23	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	22	24	15,893,058	99.94	57446.12
NJ094	NJ094	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	22	22	8,984,801	99.94	34554.35
NJ095	NJ095	2021/7/25	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	16	18	15,173,624	99.94	58000.42
NJ096	NJ096	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	14	17	9,733,624	99.94	36982.72

NJ097	NJ097	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	23	24	11,363,700	99.94	42677.63
NJ098	NJ098	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	32	34	12,737,216	99.93	46090.27
NJ099	NJ099	2021/7/25	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	18	21	10,816,901	99.91	41025.49
NJ100	NJ100	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	28	29	23,993,151	99.88	92676.05
NJ101	NJ101	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	15	18	9,730,420	99.94	36687.12
NJ102	NJ102	2021/7/25	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	17	17	12,225,834	99.94	47861.34
NJ103	NJ103	2021/7/19	2021/7/26	NE	Mod.	OPS	NJ	m-pcr	BGI	22	22	2,618,222	99.94	5256.675
NJ104	NJ104	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	19	21	8,980,819	99.94	34307.58
NJ105	NJ105	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	30	32	15,530,829	99.85	53571.21
NJ106	NJ106	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	16	16	14,215,135	99.94	52387.41
NJ107	NJ107	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	16	19	12,906,137	99.94	47243.8
NJ110	NJ110	2021/7/25	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	31	31	10,273,633	99.88	30893.7
NJ114	NJ114	2021/7/24	2021/7/27	II	Mild	OPS	NJ	m-pcr	Illumina	20	19	4,177,539	99.94	11840.62
NJ115	NJ115	2021/7/26	2021/7/27	II	Mild	OPS	NJ	m-pcr	Illumina	34	32	1,381,603	99.75	3748.584
NJ120	NJ120	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	28.8	25.9	933,030	99.55	3555.006
NJ121	NJ121	2021/7/22	2021/7/31	II	Mod.	OPS	NJ	m-pcr	BGI	38.7	35.9	94,759	99.65	316.3816
NJ124	NJ124	2021/7/22	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	18.2	15.3	368,032	99.80	12.33765
NJ125	NJ125	2021/7/23	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	20.4	17.5	640,625	99.61	1929.753
NJ126	NJ126	2021/7/26	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	15.7	13.2	347,775	99.59	1013.313
NJ127	NJ127	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	30	29	18,652,075	99.94	67441.5
NJ129	NJ129	2021/7/26	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	23.4	20.7	1,265,743	99.52	4981.298
NJ131	NJ131	2021/7/25	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	17.7	14.7	956,763	99.64	2587.101
NJ132	NJ132	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	25	25	16,835,744	99.94	62428.16
NJ133	NJ133	2021/7/26	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	29	29	15,810,833	99.94	57493.49
NJ137	NJ137	2021/7/26	2021/8/10	II	Mod.	OPS	NJ	m-pcr	Illumina	26	26	2,232,338	99.85	7913.897
NJ138	NJ138	2021/7/26	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	23.1	22	264,942	99.54	1040.55
NJ141	NJ141	2021/7/26	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	18.8	15.6	980,602	99.52	2828.862
NJ142	NJ142	2021/7/26	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	31	31	5,402,126	99.92	8195.749
NJ143	NJ143	2021/7/26	2021/8/10	II	Mild	OPS	NJ	m-pcr	TF[g]	34	34	220,922	99.73	1464.925
NJ145	NJ145	2021/7/26	2021/7/31	II	Mild	OPS	NJ	m-pcr	Illumina	22.9	19.5	738,808	99.59	2284.6
NJ146	NJ146	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	24	20.5	494,037	99.61	1530.478
NJ152	NJ152	2021/7/26	2021/8/10	II	Mod.	OPS	NJ	m-pcr	TF	25	25	2,030,437	99.80	13709.94
NJ156	NJ156	2021/7/26	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	24.8	23.4	950,238	99.64	2868
NJ157	NJ157	2021/7/27	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	33.5	32	1,036,888	99.43	3196.759
NJ158	NJ158	2021/7/25	2021/7/31	II	Mod.	OPS	NJ	m-pcr	Illumina	33.3	31.5	758,709	99.46	2321.692
NJ159	NJ159	2021/7/27	2021/7/28	CI	Mod.	OPS	NJ	m-pcr	Illumina	12	13	7,972,661	99.94	22378.86
NJ160	NJ160	2021/7/26	2021/7/27	II	Mod.	OPS	NJ	m-pcr	BGI	18	22	4,165,046	99.88	8368.15
NJ162	NJ162	2021/7/27	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	21.2	19.4	930,888	99.73	2839.635
NJ164	NJ164	2021/7/26	2021/8/10	II	Mod.	OPS	NJ	m-pcr	Illumina	26	27	206,891	99.45	811.6303
NJ165	NJ165	2021/7/28	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	20.3	19.3	207,893	99.31	614.5542
NJ166	NJ166	2021/7/27	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	BGI	36.1	36.7	170,059	99.78	567.0518
NJ167	NJ167	2021/7/27	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	28.6	29.5	1,994,734	99.56	7735.701
NJ168	NJ168	2021/7/27	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	29.2	28	1,981,999	99.57	7442.95
NJ175	NJ175	2021/7/27	2021/7/31	CI	Mild	OPS	NJ	m-pcr	Illumina	25.4	23.9	1,148,512	99.68	3378.314
NJ176	NJ176	2021/7/27	2021/7/31	CI	Mild	OPS	NJ	m-pcr	Illumina	29.4	27.8	1,615,010	99.52	6120.011
NJ177	NJ177	2021/7/28	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	29.1	28.1	915,298	99.54	3627.126
NJ179	NJ179	2021/7/28	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	20.4	18.3	1,348,116	99.78	4041.57
NJ182	NJ182	2021/7/29	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	27.2	24.6	2,025,271	99.56	7723.182
NJ184	NJ184	2021/7/28	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	BGI	36.4	35.2	327,835	99.89	1093.516
NJ186	NJ186	2021/7/29	2021/8/10	CI	Mod.	OPS	NJ	m-pcr	Illumina	33	33	24,917	98.92	100.0977
NJ187	NJ187	2021/7/29	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	21.8	20.8	1,040,421	99.67	3154.95
NJ188	NJ188	2021/7/28	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	27.9	26.5	1,326,499	99.55	5174.659
NJ189	NJ189	2021/7/30	2021/7/31	CI	Mild	OPS	NJ	m-pcr	Illumina	27.9	26.4	1,061,889	99.62	3186.831
NJ192	NJ192	2021/7/30	2021/7/31	CI	Mod.	OPS	NJ	m-pcr	Illumina	25.4	23.9	1,508,078	99.60	5824.268
NJ193	NJ193	2021/7/30	2021/8/10	CI	Mild	OPS	NJ	m-pcr	TF	30	30	2,329,786	99.75	15682.61
NJ195	NJ195	2021/7/24	2021/7/31	II	Mod.	OPS	NJ	m-pcr	TF	39	39	2,139,455	99.86	14813.98
NJ196	NJ196	2021/7/28	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	32	30	2,686,673	99.88	15400.34
NJ197	NJ197	2021/7/30	2021/8/3	CI	Mild	OPS	NJ	m-pcr	TF	25	27	3,707,905	99.89	25547.63
NJ198	NJ198	2021/7/30	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	26	27	647,062	99.82	4427.391
NJ199	NJ199	2021/7/31	2021/8/10	CI	Mod.	OPS	NJ	m-pcr	TF	30	30	1,365,684	99.78	9089.513
NJ200	NJ200	2021/7/31	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	22	24	5,636,384	99.83	39085.66
NJ201	NJ201	2021/7/31	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	25	27	2,350,858	99.83	16234.55
NJ203	NJ203	2021/7/30	2021/8/10	CI	Mod.	OPS	NJ	m-pcr	TF	33	33	1,372,493	99.78	9263.599
NJ204	NJ204	2021/7/28	2021/8/3	CI	Mild	OPS	NJ	m-pcr	TF	23	25	4,055,842	99.85	28033.93
NJ205	NJ205	2021/7/31	2021/8/3	CI	Mild	OPS	NJ	m-pcr	TF	26	28	1,019,838	99.79	7040.493
NJ206	NJ206	2021/7/31	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	18	20	5,428,442	99.92	29739.42
NJ207	NJ207	2021/7/31	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	14	16	5,778,873	99.83	37018.06
NJ208	NJ208	2021/7/22	2021/8/3	II	Mild	OPS	NJ	m-pcr	TF	32	33	1,654,095	99.82	10618.64
NJ209	NJ209	2021/7/30	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	24	27	4,016,786	99.84	25074.3
NJ210	NJ210	2021/7/30	2021/8/3	CI	Mild	OPS	NJ	m-pcr	TF	17	20	3,074,352	99.78	17238.55
NJ211	NJ211	2021/7/29	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	23	24	3,905,947	99.82	26785.25
NJ212	NJ212	2021/7/31	2021/8/3	CI	Mild	OPS	NJ	m-pcr	TF	17	15	3,038,581	99.83	15513.77
NJ213	NJ213	2021/7/31	2021/8/3	CI	Mild	OPS	NJ	m-pcr	TF	37	36	1,195,453	99.56	5174.975
NJ215	NJ215	2021/7/31	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	31	33	2,874,080	99.87	18781.26
NJ217	NJ217	2021/7/31	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	13	15	4,053,568	99.92	24870.71
NJ218	NJ218	2021/8/1	2021/8/10	CI	Mod.	OPS	NJ	m-pcr	TF	28	29	2,451,953	99.79	16057.24
NJ220	NJ220	2021/7/31	2021/8/3	CI	Mod.	OPS	NJ	m-pcr	TF	15	19	4,713,137	99.84	30434.29
NJ221	NJ221	2021/8/2	2021/8/10	CI	Mod.	OPS	NJ	m-pcr	TF	30	30	1,979,837	99.78	13042.76
NJ222	NJ222	2021/7/30	2021/8/6	CI	Mod.	OPS	NJ	m-pcr	TF	18	20	2,912,071	99.67	16475.41
NJ223	NJ223	2021/7/26	2021/8/6	CI	Mild	NPS[b]	NJ	m-pcr	Illumina	30	30	335,666	98.79	1037.277
NJ224	NJ224	2021/8/2	2021/8/6	CI	Mod.	NPS	NJ	m-pcr	Illumina	16	19	736,787	99.59	2887.592
NJ226	NJ226	2021/8/1	2021/8/4	CI	Mod.	OPS	NJ	m-pcr	Illumina	35	33	2,021,475	99.76	7442.81

NJ227	NJ227	2021/8/3	2021/8/4	CI	Mod.	OPS	NJ	m-pcr	Illumina	34	33	1,193,633	99.70	4344.945
NJ228	NJ228	2021/8/4	2021/8/6	CI	Mod.	OPS	NJ	m-pcr	Illumina	38	36	862,254	99.87	3436.348
NJ229	NJ229	2021/8/5	2021/8/6	ER	Mod.	NPS	NJ	m-pcr	Illumina	36	36	670,441	99.41	2329.684
NJ230	NJ230	2021/8/6	2021/8/7	ER	Mod.	NPS	NJ	m-pcr	Illumina	19	18	544,726	99.82	1882.677
NJ232	NJ232	2021/8/8	2021/8/9	ER	Mod.	OPS	NJ	m-pcr	Illumina	24	25	23,233,671	99.93	90935.46
NJ234	NJ234	2021/8/10	2021/8/14	ER	Mod.	OPS	NJ	m-pcr	Illumina	20	21	1,643,699	99.94	6532.425
NJ235	NJ235	2021/8/11	2021/8/13	ER	Mod.	OPS	NJ	m-pcr	BGI	28	26	12,826,523	99.93	40712.12
YZ001	YZ001	2021/7/23	2021/7/28	NE	Mod.	OPS	YZ[d]	m-pcr	Illumina	19	20	2,712,182	99.92	7319.275
YZ002	YZ002	2021/7/25	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	16	16	58,468,029	99.93	165219.4
YZ003	YZ003	2021/7/25	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	18	18	36,241,018	99.92	100101.2
YZ004	YZ004	2021/7/27	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	18	18	8,596,632	99.92	17094.83
YZ005	YZ005	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	18	18	32,763,885	99.94	90837.97
YZ006	YZ006	2021/7/25	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	18	19	9,629,323	99.87	23400.49
YZ007	YZ007	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	30	30	52,444,838	99.93	137320
YZ009	YZ009	2021/7/25	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	18	14	69,834,847	99.92	177166.5
YZ010	YZ010	2021/7/27	2021/8/10	NE	Severe	OPS	YZ	m-pcr	Illumina	26	26	1,347,834	99.30	5408.447
YZ012	YZ012	2021/7/26	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	20	18	44,594,971	99.92	113449
YZ013	YZ013	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	18	18	57,395,337	99.92	153102.3
YZ014	YZ014	2021/7/29	2021/8/2	NE	Crit.	OPS	YZ	m-pcr	Illumina	36	34	64,707,878	99.92	176122.7
YZ015	YZ015	2021/7/28	2021/8/2	NE	Crit.	OPS	YZ	m-pcr	Illumina	28	28	26,392,447	99.92	54900.49
YZ016	YZ016	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	17	17	2,917,680	99.94	10812.31
YZ018	YZ018	2021/7/29	2021/8/2	NE	Mod.	NPS	YZ	m-pcr	Illumina	16	16	15,010,240	99.87	55382.95
YZ019	YZ019	2021/7/29	2021/8/4	NE	Severe	OPS	YZ	m-pcr	TF	30	31	1,779,230	99.75	12514.63
YZ020	YZ020	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	18	18	2,227,180	99.94	8663.303
YZ021	YZ021	2021/7/24	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	30	30	16,018,498	99.94	62475.28
YZ023	YZ023	2021/7/26	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	14	12	13,963,501	99.94	54454.75
YZ025	YZ025	2021/7/29	2021/8/2	NE	Mild	OPS	YZ	m-pcr	Illumina	26	26	2,812,766	99.93	10640.39
YZ026	YZ026	2021/7/24	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	28	26	2,584,161	99.94	9893.152
YZ029	YZ029	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	16	16	21,371,244	99.94	82914.15
YZ030	YZ030	2021/7/30	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	30	30	611,093	99.77	1479.57
YZ031	YZ031	2021/7/30	2021/8/2	II	Crit.	OPS	YZ	m-pcr	BGI	28	27	7,674,117	99.87	18306.22
YZ032	YZ032	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	30	28	1,875,242	99.82	4569.217
YZ033	YZ033	2021/7/30	2021/8/4	NE	Mod.	OPS	YZ	m-pcr	TF	30	29	3,253,177	99.81	19820.28
YZ034	YZ034	2021/7/30	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	24	25	9,561,798	99.87	23011.31
YZ035	YZ035	2021/7/28	2021/8/2	NE	Crit.	OPS	YZ	m-pcr	BGI	33	33	4,420,638	99.76	10363.18
YZ036	YZ036	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	11	13	3,511,111	99.87	8343.174
YZ037	YZ037	2021/7/30	2021/8/2	II	Mod.	OPS	YZ	m-pcr	Illumina	24	24	21,821,627	99.94	85312.91
YZ038	YZ038	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	20	20	2,683,209	99.94	10163.03
YZ039	YZ039	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	Illumina	36	32	17,285,078	99.94	66818.34
YZ041	YZ041	2021/7/30	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	16	14	9,218,644	99.90	35912.87
YZ043	YZ043	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	20	20	10,396,251	99.93	39480.57
YZ044	YZ044	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	22	22	15,465,439	99.94	60372.59
YZ045	YZ045	2021/7/28	2021/8/2	NE	Crit.	OPS	YZ	m-pcr	Illumina	22	22	11,045,899	99.93	42928.45
YZ046	YZ046	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	26	26	8,661,265	99.94	34165.79
YZ047	YZ047	2021/7/30	2021/8/2	II	Mod.	OPS	YZ	m-pcr	Illumina	26	26	8,709,930	99.94	33456.66
YZ048	YZ048	2021/7/29	2021/8/2	NE	Mild	OPS	YZ	m-pcr	BGI	35	34	128,185	99.75	305.8903
YZ049	YZ049	2021/7/26	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	18	16	9,749,776	99.94	37718.75
YZ050	YZ050	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	30	28	10,313,725	99.94	40392.38
YZ051	YZ051	2021/7/25	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	15	16	8,365,427	99.87	19913.8
YZ052	YZ052	2021/7/30	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	30	24	15,001,500	99.94	57833.11
YZ053	YZ053	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	26	24	12,749,496	99.94	49413.07
YZ054	YZ054	2021/7/30	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	32	32	10,703,647	99.94	42188.11
YZ056	YZ056	2021/7/31	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	29	29.6	1,760,781	99.81	12293.7
YZ057	YZ057	2021/7/31	2021/8/2	II	Crit.	OPS	YZ	m-pcr	BGI	33	33	2,299,706	99.82	5468.761
YZ058	YZ058	2021/7/31	2021/8/2	II	Severe	OPS	YZ	m-pcr	TF	10	9	6,754,215	99.94	42702.32
YZ059	YZ059	2021/7/29	2021/8/2	II	Mod.	OPS	YZ	m-pcr	TF	30.8	29.5	366,294	99.82	2137.946
YZ060	YZ060	2021/7/28	2021/8/10	NE	Mod.	OPS	YZ	m-pcr	TF	26	26	1,989,538	99.81	12870.68
YZ061	YZ061	2021/7/31	2021/8/4	II	Mod.	OPS	YZ	m-pcr	Illumina	24	25	382,249	99.61	1520.48
YZ062	YZ062	2021/7/31	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	16	14	5,822,047	99.84	37460.54
YZ063	YZ063	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	18	20	8,266,380	99.86	19679.56
YZ064	YZ064	2021/7/31	2021/8/2	II	Mild	OPS	YZ	m-pcr	BGI	12	15	1,059,825	99.47	2518.665
YZ065	YZ065	2021/8/1	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	37	30	100,167	99.56	701.6162
YZ066	YZ066	2021/8/1	2021/8/2	II	Mild	OPS	YZ	m-pcr	BGI	25	25	9,546,646	99.87	23531.25
YZ067	YZ067	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	14	18	8,243,515	99.94	19534.97
YZ069	YZ069	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	22	23	8,357,344	99.86	20053.69
YZ070	YZ070	2021/7/28	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	Illumina	20	20	2,417,562	99.94	9297.844
YZ074	YZ074	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	32	31	1,327,834	99.75	3175.667
YZ076	YZ076	2021/7/30	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	20	21	11,193,272	99.86	26883.59
YZ077	YZ077	2021/7/30	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	23	23.5	941,026	99.79	5562.444
YZ079	YZ079	2021/7/31	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	24.5	25	713,348	99.72	4244.41
YZ080	YZ080	2021/7/24	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	17	19	18,803,063	99.87	45081.26
YZ081	YZ081	2021/7/26	2021/8/2	NE	Crit.	OPS	YZ	m-pcr	BGI	12	14	7,317,739	99.94	17501.15
YZ082	YZ082	2021/7/28	2021/8/2	NE	Severe	OPS	YZ	m-pcr	Illumina	37	27	5,224,634	99.94	20784.64
YZ083	YZ083	2021/7/29	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	28	27	2,795,146	99.83	19406.64
YZ084	YZ084	2021/7/31	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	14	14	3,967,031	99.89	25247.41
YZ085	YZ085	2021/8/1	2021/8/10	II	Mod.	OPS	YZ	m-pcr	Illumina	25	26	126,134	99.51	509.782
YZ086	YZ086	2021/8/1	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	29.8	29.1	1,669,001	99.73	11025.46
YZ087	YZ087	2021/7/29	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	11	14	3,896,582	99.82	9265.278
YZ089	YZ089	2021/7/30	2021/8/4	NE	Mod.	OPS	YZ	m-pcr	TF	11.6	15.6	1,036,643	99.78	6065.386
YZ091	YZ091	2021/8/1	2021/8/18	II	Crit.	OPS	YZ	m-pcr	Illumina	33	29	2,361,315	99.86	9001.676
YZ092	YZ092	2021/7/31	2021/8/4	II	Mild	OPS	YZ	m-pcr	TF	24	24	2,527,051	99.77	17389.03
YZ094	YZ094	2021/8/1	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	22.8	25	5,262,546	99.77	36825.15

YZ095	YZ095	2021/7/27	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	15	15	8,457,881	99.86	20202.7
YZ096	YZ096	2021/7/31	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	28	28	2,439,837	99.68	14895.12
YZ097	YZ097	2021/7/31	2021/8/2	II	Mild	OPS	YZ	m-pcr	BGI	31	32	868,847	99.79	2075.863
YZ098	YZ098	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	32	30	533,844	99.76	1278.872
YZ099	YZ099	2021/8/1	2021/8/4	NE	Mod.	OPS	YZ	m-pcr	TF	26	26	3,620,921	99.77	23267.64
YZ100	YZ100	2021/8/1	2021/8/4	II	Severe	OPS	YZ	m-pcr	TF	21.5	21	4,584,156	99.83	26154.21
YZ102	YZ102	2021/7/25	2021/8/2	NE	Severe	OPS	YZ	m-pcr	Illumina	14	15	7,330,743	99.87	17581.64
YZ103	YZ103	2021/7/31	2021/8/2	II	Severe	OPS	YZ	m-pcr	Illumina	11	13	4,579,104	99.85	10873.22
YZ104	YZ104	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	Illumina	24	24	8,290,978	99.87	19951.34
YZ105	YZ105	2021/7/28	2021/8/4	NE	Crit.	OPS	YZ	m-pcr	Illumina	21.7	21.9	2,408,982	99.94	9570.654
YZ106	YZ106	2021/8/2	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	28.7	29	534,516	99.56	3070.922
YZ108	YZ108	2021/8/1	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	20	20	10,261,348	99.89	24982.77
YZ109	YZ109	2021/7/31	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	11	11	5,216,616	99.92	32975.43
YZ110	YZ110	2021/7/30	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	14	15	13,716,800	99.93	32766.8
YZ112	YZ112	2021/7/31	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	22	23	15,651,848	99.87	38105.87
YZ115	YZ115	2021/7/31	2021/8/10	II	Mod.	OPS	YZ	m-pcr	Illumina	25	25	326,364	99.58	1282.524
YZ118	YZ118	2021/8/2	2021/8/4	II	Mild	OPS	YZ	m-pcr	TF	32.5	29	883,515	98.34	4288.538
YZ121	YZ121	2021/8/1	2021/8/4	II	Mild	OPS	YZ	m-pcr	Illumina	27.8	27.8	677,644	99.84	2645.484
YZ124	YZ124	2021/8/1	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	32.7	29	1,820,038	99.38	7518.475
YZ125	YZ125	2021/7/29	2021/8/2	NE	Mild	OPS	YZ	m-pcr	Illumina	24	24	2,693,751	99.94	10449.46
YZ126	YZ126	2021/7/30	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	29	28	534,362	99.76	1323.141
YZ128	YZ128	2021/8/2	2021/8/10	II	Mild	OPS	YZ	m-pcr	TF	23	24	2,725,696	99.77	18569.52
YZ129	YZ129	2021/8/2	2021/8/10	II	Mild	OPS	YZ	m-pcr	Illumina	20	20	4,735,926	99.94	18633.52
YZ131	YZ131	2021/8/2	2021/8/19	II	Mild	OPS	YZ	m-pcr	Illumina	15	15	11,921,156	99.94	47331.99
YZ134	YZ134	2021/8/2	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	25.7	25.4	2,613,281	99.82	11572.27
YZ135	YZ135	2021/8/3	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	25.4	24.2	2,113,210	99.84	11769.19
YZ137	YZ137	2021/8/3	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	24	23.4	3,481,957	99.83	21265.62
YZ140	YZ140	2021/8/2	2021/8/10	II	Crit.	OPS	YZ	m-pcr	Illumina	27	27	291,450	99.58	1163.023
YZ143	YZ143	2021/7/31	2021/8/10	II	Crit.	OPS	YZ	m-pcr	Illumina	30	30	355,622	98.97	1424.866
YZ146	YZ146	2021/8/2	2021/8/10	II	Mod.	OPS	YZ	m-pcr	Illumina	29	30	342,842	99.62	1364.552
YZ149	YZ149	2021/8/1	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	13	12	3,476,175	99.85	8265.455
YZ155	YZ155	2021/8/4	2021/8/18	II	Mod.	OPS	YZ	m-pcr	Illumina	30	30	2,870,743	99.59	10956.42
YZ156	YZ156	2021/8/3	2021/8/4	II	Mod.	OPS	YZ	m-pcr	TF	28.5	27	4,516,139	99.78	25690.52
YZ159	YZ159	2021/8/3	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	37	37	2,132,592	99.87	7965.675
YZ160	YZ160	2021/8/3	2021/8/11	II	Mod.	NPS	YZ	m-pcr	BGI	35	35	47,442	99.15	156.0289
YZ161	YZ161	2021/8/2	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	25	28	2,338,350	99.88	9279.92
YZ162	YZ162	2021/8/3	2021/8/11	II	Mod.	OPS	YZ	m-pcr	Illumina	23	24	14,624,517	99.93	56873.11
YZ163	YZ163	2021/8/1	2021/8/2	II	Mod.	OPS	YZ	m-pcr	BGI	26	24	19,885,750	99.87	49195.98
YZ168	YZ168	2021/7/30	2021/8/6	II	Mild	OPS	YZ	m-pcr	Illumina	30	31	1,766,729	99.78	7074.892
YZ169	YZ169	2021/8/4	2021/8/6	II	Mod.	OPS	YZ	m-pcr	Illumina	31	33	711,115	99.70	2651.302
YZ170	YZ170	2021/7/30	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	27	29	1,816,118	99.91	7103.912
YZ171	YZ171	2021/8/4	2021/8/6	II	Mod.	OPS	YZ	m-pcr	Illumina	37	35	13,927,942	99.89	52769.75
YZ172	YZ172	2021/8/3	2021/8/14	II	Mod.	OPS	YZ	m-pcr	Illumina	36	37	2,395,738	98.56	8997.583
YZ175	YZ175	2021/8/4	2021/8/5	II	Mod.	OPS	YZ	m-pcr	Illumina	27	29	1,858,767	99.88	7435.49
YZ178	YZ178	2021/8/3	2021/8/4	II	Mod.	NPS	YZ	m-pcr	TF	25.5	24	2,195,424	99.85	9906.395
YZ181	YZ181	2021/8/1	2021/8/11	II	Mild	OPS	YZ	m-pcr	BGI	33	33	175,226	99.89	570.4045
YZ182	YZ182	2021/7/29	2021/8/11	NE	Mod.	NPS	YZ	m-pcr	Illumina	26	28	21,147,871	99.90	83632.72
YZ187	YZ187	2021/8/3	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	34	34	11,843,814	99.82	41502.75
YZ188	YZ188	2021/7/31	2021/8/11	II	Severe	NPS	YZ	m-pcr	Illumina	32	32	6,387,839	99.82	23724.33
YZ192	YZ192	2021/7/31	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	28	28	40,771,872	99.87	156992.8
YZ196	YZ196	2021/8/2	2021/8/6	II	Mod.	NPS	YZ	m-pcr	Illumina	37	39	520,905	98.99	1957.041
YZ198	YZ198	2021/7/26	2021/8/2	NE	Crit.	NPS	YZ	m-pcr	BGI	20	21	13,806,372	99.85	33115.98
YZ200	YZ200	2021/7/31	2021/8/2	II	Severe	NPS	YZ	m-pcr	BGI	34	32	128,528	99.74	310.6324
YZ202	YZ202	2021/8/4	2021/8/6	II	Mod.	NPS	YZ	m-pcr	Illumina	34	35	1,748,828	99.79	6504.53
YZ204	YZ204	2021/7/31	2021/8/6	II	Severe	NPS	YZ	m-pcr	Illumina	38	37	28,064,559	99.94	107814.6
YZ210	YZ210	2021/8/4	2021/8/6	II	Mod.	OPS	YZ	m-pcr	Illumina	26	26	1,057,775	99.56	3941.723
YZ211	YZ211	2021/8/1	2021/8/6	II	Mod.	OPS	YZ	m-pcr	Illumina	33	34	1,008,907	99.36	3957.272
YZ212	YZ212	2021/8/4	2021/8/6	II	Mod.	OPS	YZ	m-pcr	Illumina	28	27	1,902,567	99.71	7617.377
YZ214	YZ214	2021/8/5	2021/8/6	II	Mild	OPS	YZ	m-pcr	Illumina	32	33	1,111,334	99.44	4294.378
YZ215	YZ215	2021/8/3	2021/8/6	II	Mod.	OPS	YZ	m-pcr	Illumina	34	34	2,035,002	99.50	7912.416
YZ224	YZ224	2021/8/5	2021/8/11	II	Mod.	OPS	YZ	m-pcr	Illumina	33	33	2,073,165	99.52	8037.804
YZ227	YZ227	2021/8/4	2021/9/23	NE	Mod.	NPS	YZ	m-pcr	Illumina	32	33	2,045,507	99.74	6873.464
YZ229	YZ229	2021/7/30	2021/8/2	NE	Crit.	NPS	YZ	m-pcr	BGI	27	26	12,727,899	99.87	31022.64
YZ230	YZ230	2021/8/3	2021/8/11	II	Severe	NPS	YZ	m-pcr	Illumina	30	30	8,289,250	99.88	32209.97
YZ232	YZ232	2021/8/5	2021/8/6	II	Mod.	NPS	YZ	m-pcr	Illumina	34	34	1,143,673	99.83	4428.969
YZ234	YZ234	2021/8/4	2021/8/6	II	Mod.	NPS	YZ	m-pcr	Illumina	27	24	981,941	99.76	3879.749
YZ235	YZ235	2021/8/5	2021/8/6	II	Crit.	NPS	YZ	m-pcr	Illumina	25	23	482,974	99.57	1908.759
YZ236	YZ236	2021/8/4	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	33	32	1,218,309	99.85	4509.005
YZ240	YZ240	2021/8/5	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	33	33	6,920,826	99.84	22568.44
YZ242	YZ242	2021/8/5	2021/8/11	II	Mild	NPS	YZ	m-pcr	Illumina	24	24	23,152,212	99.94	92512.51
YZ249	YZ249	2021/8/4	2021/8/6	II	Mod.	OPS	YZ	m-pcr	Illumina	22	21	1,351,732	99.56	5197.615
YZ251	YZ251	2021/8/5	2021/8/18	II	Mild	OPS	YZ	m-pcr	Illumina	30	32	1,862,987	99.90	6984.405
YZ254	YZ254	2021/8/5	2021/8/11	II	Severe	NPS	YZ	m-pcr	Illumina	31	31	10,806,436	99.93	40182.28
YZ256	YZ256	2021/8/4	2021/8/18	II	Mod.	OPS	YZ	m-pcr	Illumina	33	34	295,292	99.24	1116.229
YZ265	YZ265	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	BGI	30	30	373,658	99.89	1246.48
YZ266	YZ266	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	BGI	18	18	352,353	99.94	1147.764
YZ268	YZ268	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	BGI	35	35	62,419	99.47	204.7944
YZ271	YZ271	2021/8/5	2021/8/19	II	Mild	OPS	YZ	m-pcr	Illumina	31	31	3,604,361	99.87	13824.5
YZ272	YZ272	2021/8/5	8/18/2021	II	Mild	OPS	YZ	m-pcr	Illumina	32	34	18,416,391	99.93	68807.29
YZ275	YZ275	2021/8/6	2021/8/7	II	Mod.	NPS	YZ	m-pcr	Illumina	19	19	643,515	99.93	2149.275
YZ278	YZ278	2021/8/1	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	26	27	10,281,151	99.93	39609.08
YZ279	YZ279	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	33	33	273,118	99.56	1024.564

YZ280	YZ280	2021/8/5	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	23	25	17,762,709	99.94	66302.55
YZ281	YZ281	2021/8/5	2021/8/18	II	Mod.	NPS	YZ	m-pcr	Illumina	29	29	11,088,918	99.94	41678.39
YZ282	YZ282	2021/8/6	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	14	14	16,938,798	99.94	64715.86
YZ283	YZ283	2021/8/5	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	17	17	14,419,736	99.94	56103.2
YZ284	YZ284	2021/8/5	2021/8/18	II	Mod.	NPS	YZ	m-pcr	Illumina	16	17	21,164,008	99.94	73816.79
YZ285	YZ285	2021/8/6	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	33	33	1,530,147	99.85	5789.582
YZ286	YZ286	2021/8/7	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	19	19	14,431,679	99.93	55292.96
YZ288	YZ288	2021/8/5	2021/8/11	II	Severe	NPS	YZ	m-pcr	Illumina	32	32	2,394,309	99.83	9104.587
YZ289	YZ289	2021/8/5	2021/8/7	II	Mod.	NPS	YZ	m-pcr	Illumina	31	28	684,518	99.68	2284.642
YZ290	YZ290	2021/8/6	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	27	27	3,446,589	99.68	12361.52
YZ291	YZ291	2021/8/6	2021/8/18	II	Mod.	NPS	YZ	m-pcr	Illumina	29	29	2,274,406	99.59	8934.633
YZ298	YZ298	2021/8/6	2021/8/11	II	Severe	NPS	YZ	m-pcr	Illumina	31	31	19,327,073	99.94	73727.15
YZ303	YZ303	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	33	33	33,984,348	99.88	121622.1
YZ304	YZ304	2021/8/6	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	26	28	24,080,266	99.87	95047.11
YZ307	YZ307	2021/8/2	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	24	25	13,970,217	99.93	52657.07
YZ308	YZ308	2021/8/4	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	23	24	2,005,515	99.86	7927.65
YZ309	YZ309	2021/8/6	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	27	28	1,890,571	99.84	7555.75
YZ310	YZ310	2021/8/6	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	22	23	1,891,507	99.93	6243.864
YZ311	YZ311	2021/8/7	2021/8/18	II	Mod.	NPS	YZ	m-pcr	Illumina	27	28	6,626,249	99.88	25058.76
YZ315	YZ315	2021/8/5	2021/8/11	II	Mod.	OPS	YZ	m-pcr	Illumina	28	28.2	5,013,865	99.90	18425.42
YZ319	YZ319	2021/8/7	2021/8/8	II	Mild	NPS	YZ	m-pcr	Illumina	27	26	193,330	99.74	784.58
YZ323	YZ323	2021/8/7	2021/8/8	II	Mod.	NPS	YZ	m-pcr	Illumina	26	26	369,023	99.74	1455.258
YZ326	YZ326	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	29	30	3,056,235	99.93	11225.91
YZ328	YZ328	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	21	22	1,731,558	99.94	6924.178
YZ329	YZ329	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	32	35	350,607	99.75	1320.504
YZ330	YZ330	2021/8/4	2021/8/19	II	Mod.	NPS	YZ	m-pcr	Illumina	29	29	16,093,247	99.86	60984.61
YZ331	YZ331	2021/8/2	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	30	30	1,533,060	99.86	5568.201
YZ334	YZ334	2021/8/7	2021/8/8	II	Mod.	NPS	YZ	m-pcr	Illumina	25	25	189,594	99.56	759.6693
YZ338	YZ338	2021/8/4	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	20	22	31,980,006	99.94	124808.9
YZ339	YZ339	2021/8/1	2021/8/11	II	Mild	NPS	YZ	m-pcr	Illumina	32	32	7,882,454	99.82	29740.9
YZ340	YZ340	2021/8/7	2021/8/8	II	Mild	NPS	YZ	m-pcr	Illumina	22	20	576,961	99.77	2322.174
YZ341	YZ341	2021/8/8	2021/8/8	CI	Mod.	NPS	YZ	m-pcr	Illumina	22	21	607,944	99.58	2444.163
YZ342	YZ342	2021/8/5	2021/8/18	II	Mod.	NPS	YZ	m-pcr	Illumina	30	30	7,351,180	99.88	27594.85
YZ343	YZ343	2021/7/25	2021/8/2	NE	Mod.	OPS	YZ	m-pcr	BGI	32	30	395,850	99.83	954.9447
YZ345	YZ345	2021/8/7	2021/8/9	II	Mod.	NPS	YZ	m-pcr	Illumina	34	38	1,336,398	99.94	5253.582
YZ348	YZ348	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	20	20	2,809,689	99.94	11277.17
YZ350	YZ350	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	17	19	16,273,985	99.94	64186.88
YZ351	YZ351	2021/8/8	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	33	34	2,479,611	99.07	9487.248
YZ352	YZ352	2021/8/8	2021/8/11	CI	Mild	NPS	YZ	m-pcr	Illumina	30	30	30,167,034	99.85	115703.4
YZ353	YZ353	2021/8/6	2021/8/9	II	Mod.	NPS	YZ	m-pcr	Illumina	28	28	2,774,725	99.94	11161.65
YZ354	YZ354	2021/8/7	2021/8/9	II	Mod.	NPS	YZ	m-pcr	Illumina	34	34	2,138,256	98.99	7975.334
YZ355	YZ355	2021/8/6	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	17	20	23,935,317	99.94	91840.22
YZ356	YZ356	2021/8/7	2021/8/9	II	Mild	NPS	YZ	m-pcr	Illumina	32	32	5,717,220	99.90	19674.22
YZ357	YZ357	2021/8/4	2021/8/11	II	Mild	OPS	YZ	m-pcr	Illumina	32	33	1,362,037	99.81	5324.623
YZ358	YZ358	2021/8/6	2021/8/9	II	Mod.	OPS	YZ	m-pcr	Illumina	27	27	3,313,288	99.92	13348.19
YZ360	YZ360	2021/8/7	2021/8/9	II	Mod.	OPS	YZ	m-pcr	Illumina	30	32	1,670,497	99.82	5663.923
YZ362	YZ362	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	24	24	30,911,678	99.99	123339.4
YZ363	YZ363	2021/8/4	2021/8/11	II	Crit.	NPS	YZ	m-pcr	Illumina	20	20	21,990,916	99.94	84499.94
YZ364	YZ364	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	30	31	2,473,670	99.93	9687.334
YZ365	YZ365	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	21	23	1,407,252	99.90	5587.949
YZ366	YZ366	2021/8/7	2021/8/9	II	Mod.	NPS	YZ	m-pcr	Illumina	30	30	2,858,406	99.74	11499.21
YZ367	YZ367	2021/8/7	2021/8/9	II	Mild	OPS	YZ	m-pcr	Illumina	30	30	3,016,439	99.93	12120.94
YZ368	YZ368	2021/8/8	2021/8/9	CI	Mod.	NPS	YZ	m-pcr	Illumina	33	33	3,379,807	99.83	13612.13
YZ374	YZ374	2021/8/7	2021/8/11	II	Mild	OPS	YZ	m-pcr	Illumina	32	33	3,008,852	99.86	11601.56
YZ375	YZ375	2021/8/6	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	24	24	37,152,195	99.94	140957.5
YZ376	YZ376	2021/8/7	2021/8/12	II	Mild	OPS	YZ	m-pcr	Illumina	26	26	1,456,716	99.29	5837.734
YZ378	YZ378	2021/8/8	2021/8/11	CI	Mod.	OPS	YZ	m-pcr	Illumina	36	35	1,734,739	99.72	6971.058
YZ380	YZ380	2021/8/4	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	20	20	19,612,173	99.94	75911.87
YZ381	YZ381	2021/8/8	2021/8/11	CI	Mild	OPS	YZ	m-pcr	Illumina	27	28	1,963,325	99.90	7867.678
YZ383	YZ383	2021/8/4	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	24	24	23,052,751	99.94	91010.4
YZ385	YZ385	2021/8/8	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	19	20	14,918,001	99.94	58514.6
YZ386	YZ386	2021/8/8	2021/8/11	CI	Severe	NPS	YZ	m-pcr	Illumina	26	28	24,948,522	99.94	97426.32
YZ387	YZ387	2021/8/7	2021/8/12	II	Mod.	OPS	YZ	m-pcr	Illumina	29	28	1,225,594	99.13	4899.398
YZ388	YZ388	2021/8/8	2021/8/10	CI	Mild	OPS	YZ	m-pcr	TF	29	28	763,636	99.77	4627.807
YZ391	YZ391	2021/8/8	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	16	18	17,871,746	99.94	70134.84
YZ392	YZ392	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	26	27	20,039,407	99.94	79100.37
YZ393	YZ393	2021/8/8	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	24	26	26,345,467	99.84	103677.7
YZ394	YZ394	2021/8/2	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	32	33	38,343,842	99.88	134896.5
YZ395	YZ395	2021/8/9	2021/8/11	CI	Mild	NPS	YZ	m-pcr	Illumina	22	25	22,988,304	99.93	88592.28
YZ396	YZ396	2021/8/8	2021/8/11	CI	Severe	NPS	YZ	m-pcr	Illumina	24	25	23,320,978	99.86	87800.49
YZ397	YZ397	2021/8/8	2021/8/10	CI	Mod.	OPS	YZ	m-pcr	TF	20	20	2,652,447	99.91	17511.01
YZ398	YZ398	2021/8/8	2021/8/11	CI	Mod.	OPS	YZ	m-pcr	Illumina	30	31	1,515,258	99.93	5865.973
YZ399	YZ399	2021/8/7	2021/8/10	II	Mod.	OPS	YZ	m-pcr	TF	21	20	2,529,031	99.89	16709.9
YZ400	YZ400	2021/8/8	2021/8/10	CI	Mod.	OPS	YZ	m-pcr	TF	20	20	2,231,102	99.87	14778.87
YZ401	YZ401	2021/8/2	2021/8/10	II	Mod.	OPS	YZ	m-pcr	TF	30	30	357,172	99.77	2278.9
YZ402	YZ402	2021/8/9	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	27	29	4,306,711	99.93	15569.48
YZ403	YZ403	2021/8/6	2021/8/10	II	Mod.	OPS	YZ	m-pcr	TF	25	25	1,156,317	99.77	7172.973
YZ404	YZ404	2021/8/10	2021/8/11	CI	Mod.	OPS	YZ	m-pcr	BGI	25	25	1,224,800	99.90	4085.871
YZ405	YZ405	2021/8/9	2021/8/11	CI	Mild	OPS	YZ	m-pcr	BGI	26	26	1,453,957	99.89	4852.018
YZ406	YZ406	2021/8/7	2021/8/11	II	Mod.	OPS	YZ	m-pcr	BGI	27	27	1,214,804	99.89	4052.508
YZ407	YZ407	2021/8/4	2021/8/10	II	Mild	NPS	YZ	m-pcr	TF	32	30	412,336	99.77	2489.916
YZ408	YZ408	2021/8/10	2021/8/11	CI	Severe	NPS	YZ	m-pcr	Illumina	16	18	28,494,535	99.94	112487.6

YZ409	YZ409	2021/8/8	2021/8/10	CI	Mod.	OPS	YZ	m-pcr	TF	27	25	2,508,870	99.81	15970.54
YZ410	YZ410	2021/8/7	2021/8/10	II	Mod.	OPS	YZ	m-pcr	TF	25	24	1,824,349	99.85	12249.53
YZ411	YZ411	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	BGI	31	31	617,533	99.89	2060.022
YZ412	YZ412	2021/8/8	2021/8/10	CI	Mod.	NPS	YZ	m-pcr	TF	24	24	1,734,326	99.84	11104.85
YZ413	YZ413	2021/8/6	2021/8/10	II	Mod.	NPS	YZ	m-pcr	TF	32	30	214,632	99.77	1359.505
YZ414	YZ414	2021/8/9	2021/8/10	CI	Mild	NPS	YZ	m-pcr	TF	27	27	1,667,594	99.78	10742.46
YZ415	YZ415	2021/8/9	2021/8/10	CI	Mild	NPS	YZ	m-pcr	TF	28	28	1,153,930	99.82	7174.557
YZ416	YZ416	2021/8/9	2021/8/10	CI	Mod.	NPS	YZ	m-pcr	TF	20	22	2,983,963	99.82	20091.1
YZ417	YZ417	2021/8/8	2021/8/10	CI	Mild	NPS	YZ	m-pcr	TF	18	20	1,775,859	99.83	11657.68
YZ418	YZ418	2021/8/8	2021/8/11	CI	Mild	NPS	YZ	m-pcr	Illumina	18	19	1,899,110	99.94	7672.136
YZ419	YZ419	2021/8/9	2021/8/11	CI	Mild	NPS	YZ	m-pcr	Illumina	33	34	507,801	98.89	2010.902
YZ420	YZ420	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	23	25	1,942,947	99.84	7820.37
YZ422	YZ422	2021/8/4	2021/8/8	II	Mod.	NPS	YZ	m-pcr	Illumina	30	29	102,863	99.47	417.3331
YZ424	YZ424	2021/8/9	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	20	21	2,281,297	99.93	8413.484
YZ425	YZ425	2021/8/9	2021/8/10	CI	Mod.	NPS	YZ	m-pcr	TF	31	32	2,101,102	99.78	14234.28
YZ426	YZ426	2021/8/8	2021/8/10	CI	Mod.	OPS	YZ	m-pcr	TF	30	29	2,229,780	99.81	14772.75
YZ427	YZ427	2021/8/9	2021/8/10	CI	Mod.	NPS	YZ	m-pcr	Illumina	35	30	3,730,192	99.88	13639.17
YZ428	YZ428	2021/8/10	2021/8/10	CI	Mild	NPS	YZ	m-pcr	Illumina	24	24	1,656,503	99.81	6658.233
YZ429	YZ429	2021/8/9	2021/8/10	CI	Mod.	NPS	YZ	m-pcr	Illumina	35	34	3,354,830	99.94	12838.89
YZ430	YZ430	2021/8/9	2021/8/10	CI	Mild	NPS	YZ	m-pcr	TF	26	26	1,974,665	99.85	13287.63
YZ431	YZ431	2021/8/9	2021/8/10	CI	Mod.	NPS	YZ	m-pcr	TF	31	30	2,288,925	99.79	15475.22
YZ433	YZ433	2021/8/7	2021/8/10	II	Mod.	NPS	YZ	m-pcr	TF	22	24	2,458,768	99.82	15928.28
YZ434	YZ434	2021/8/9	2021/8/10	CI	Mod.	NPS	YZ	m-pcr	TF	25	25	2,354,189	99.75	15823.29
YZ435	YZ435	2021/8/9	2021/8/10	CI	Severe	OPS	YZ	m-pcr	TF	25	26	2,017,316	99.77	13390.97
YZ436	YZ436	2021/8/7	2021/8/10	II	Mild	NPS	YZ	m-pcr	Illumina	30	30	2,467,858	99.91	9915.299
YZ438	YZ438	2021/8/4	2021/8/18	II	Mod.	NPS	YZ	m-pcr	Illumina	24	25	1,854,648	99.59	6975.67
YZ439	YZ439	2021/8/9	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	30	30	697,645	98.89	2372.728
YZ440	YZ440	2021/8/7	2021/8/18	II	Severe	NPS	YZ	m-pcr	Illumina	23	24	9,925,468	99.94	38033.45
YZ441	YZ441	2021/8/5	2021/8/10	II	Mod.	NPS	YZ	m-pcr	TF	30	30	2,011,151	99.78	13634.75
YZ442	YZ442	2021/8/7	2021/8/10	II	Mod.	NPS	YZ	m-pcr	TF	25	26	2,190,698	99.78	14740.3
YZ443	YZ443	2021/8/4	2021/8/10	II	Mod.	NPS	YZ	m-pcr	TF	21	24	2,462,431	99.79	16727.03
YZ444	YZ444	2021/8/9	2021/8/12	CI	Mod.	NPS	YZ	m-pcr	Illumina	31	31	2,265,480	99.58	9028.512
YZ446	YZ446	2021/8/6	2021/8/11	II	Mod.	OPS	YZ	m-pcr	Illumina	24	25	2,061,177	99.86	8270.156
YZ448	YZ448	2021/8/10	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	25	26	25,731,971	99.87	98132.75
YZ450	YZ450	2021/8/9	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	18	20	17,833,578	99.94	71029.37
YZ451	YZ451	2021/8/9	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	18	20	21,514,559	99.94	85342.05
YZ452	YZ452	2021/8/8	2021/8/10	CI	Mild	NPS	YZ	m-pcr	TF	27	27	1,573,036	99.80	10191.64
YZ453	YZ453	2021/8/5	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	24	26	19,218,774	99.79	74832.61
YZ454	YZ454	2021/8/10	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	32	33	16,456,867	99.83	60148.29
YZ455	YZ455	2021/8/10	2021/8/11	CI	Mild	NPS	YZ	m-pcr	Illumina	20	20	20,465,691	99.94	81403.3
YZ456	YZ456	2021/8/10	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	28	29	641,400	99.55	2597.14
YZ458	YZ458	2021/8/9	2021/8/11	CI	Mild	NPS	YZ	m-pcr	Illumina	18	20	1,880,124	99.94	7588.175
YZ459	YZ459	2021/8/10	2021/8/12	CI	Mod.	OPS	YZ	m-pcr	Illumina	0	33	3,311,557	99.77	12476.32
YZ460	YZ460	2021/8/10	2021/8/11	CI	Mild	NPS	YZ	m-pcr	Illumina	29	28	802,102	99.57	3080.047
YZ461	YZ461	2021/8/9	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	31	27	388,093	99.48	1579.776
YZ462	YZ462	2021/8/11	2021/8/19	CI	Mod.	OPS	YZ	m-pcr	Illumina	28	29	8,306,466	99.24	28682.06
YZ463	YZ463	2021/8/11	2021/8/11	CI	Mod.	NPS	YZ	m-pcr	Illumina	33	33	818,577	99.60	3196.083
YZ465	YZ465	2021/8/5	2021/8/12	II	Mod.	OPS	YZ	m-pcr	BGI	29	30	5,972,548	99.90	19055.78
YZ466	YZ466	2021/8/8	2021/8/12	CI	Mod.	OPS	YZ	m-pcr	BGI	24	25	14,110,668	99.94	44831.1
YZ467	YZ467	2021/8/10	2021/8/12	CI	Mild	OPS	YZ	m-pcr	BGI	24	25	11,518,392	99.94	36399.24
YZ468	YZ468	2021/8/10	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	23	24	10,467,360	99.94	40308.7
YZ469	YZ469	2021/8/10	2021/8/12	CI	Mild	OPS	YZ	m-pcr	Illumina	28	27	1,136,282	99.60	4600.826
YZ470	YZ470	2021/8/10	2021/8/12	CI	Mod.	NPS	YZ	m-pcr	Illumina	31	30	1,097,410	99.58	4439.936
YZ471	YZ471	2021/8/10	2021/8/12	CI	Mild	NPS	YZ	m-pcr	Illumina	29	28	1,287,959	99.45	5133.955
YZ472	YZ472	2021/8/10	2021/8/11	CI	Mild	OPS	YZ	m-pcr	Illumina	31	32	2,297,388	99.78	9165.181
YZ473	YZ473	2021/8/10	2021/8/12	CI	Mild	OPS	YZ	m-pcr	Illumina	36	35	1,794,043	99.86	7218.252
YZ475	YZ475	2021/8/10	2021/8/11	CI	Mild	OPS	YZ	m-pcr	Illumina	30	30	762,025	99.57	2980.38
YZ478	YZ478	2021/8/7	2021/8/11	II	Mod.	NPS	YZ	m-pcr	Illumina	22	22	24,686,913	99.94	95555.85
YZ480	YZ480	2021/8/10	2021/8/12	CI	Mod.	OPS	YZ	m-pcr	BGI	22	24	13,775,207	99.94	43777.45
YZ481	YZ481	2021/8/10	2021/8/12	CI	Severe	OPS	YZ	m-pcr	BGI	30	30	184,753	99.72	593.9336
YZ484	YZ484	2021/8/11	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	30	31	6,065,307	99.72	23073.52
YZ485	YZ485	2021/8/10	2021/8/12	CI	Mild	NPS	YZ	m-pcr	Illumina	33	34	26,732,537	99.93	105802.9
YZ486	YZ486	2021/8/10	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	25	25	6,361,492	99.89	24114.53
YZ488	YZ488	2021/8/10	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	23	24	11,791,744	99.94	44919.96
YZ489	YZ489	2021/8/11	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	25	25	6,090,301	99.94	23121.42
YZ492	YZ492	2021/8/10	2021/8/12	CI	Mod.	OPS	YZ	m-pcr	Illumina	30	30	2,829,372	99.63	11461.95
YZ494	YZ494	2021/8/9	2021/8/12	CI	Mod.	OPS	YZ	m-pcr	Illumina	19	20	1,579,525	99.61	6290.944
YZ497	YZ497	2021/8/11	2021/8/12	CI	Mod.	OPS	YZ	m-pcr	Illumina	20	21	1,100,006	99.60	4457.015
YZ498	YZ498	2021/8/6	2021/8/18	II	Mild	OPS	YZ	m-pcr	Illumina	28	29	10,672,340	99.93	41085.47
YZ499	YZ499	2021/8/12	2021/8/13	CI	Mod.	OPS	YZ	m-pcr	Illumina	26	27	1,679,771	99.86	6713.408
YZ500	YZ500	2021/8/11	2021/8/18	CI	Mild	OPS	YZ	m-pcr	Illumina	24	25	10,123,903	99.91	38797.16
YZ504	YZ504	2021/8/10	2021/8/18	CI	Mild	OPS	YZ	m-pcr	Illumina	29	29	1,131,290	99.45	3987.386
YZ505	YZ505	2021/8/12	2021/8/18	CI	Mild	OPS	YZ	m-pcr	Illumina	25	26	399,825	98.99	1495.327
YZ506	YZ506	2021/8/11	2021/8/13	CI	Mild	OPS	YZ	m-pcr	Illumina	25	32	358,592	99.02	1394.056
YZ507	YZ507	2021/8/11	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	32	33	4,194,722	99.93	16049.52
YZ509	YZ509	2021/8/10	2021/8/18	CI	Mild	OPS	YZ	m-pcr	Illumina	32	33	2,897,692	99.86	10708
YZ510	YZ510	2021/8/10	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	27	27	8,878,686	99.94	33662.13
YZ512	YZ512	2021/8/11	2021/8/13	CI	Mod.	OPS	YZ	m-pcr	Illumina	23	27	1,423,963	99.88	5715.885
YZ514	YZ514	2021/8/12	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	25	25	2,730,071	99.64	10381.09
YZ515	YZ515	2021/8/12	2021/8/16	CI	Mod.	OPS	YZ	m-pcr	Illumina	31	34	701,680	99.75	2625.356
YZ516	YZ516	2021/8/9	2021/8/16	CI	Mod.	OPS	YZ	m-pcr	Illumina	25	26	1,578,775	99.83	6312.204
YZ517	YZ517	2021/8/12	2021/8/16	CI	Mild	OPS	YZ	m-pcr	Illumina	30	28	1,689,086	99.84	6751.423

YZ518	YZ518	2021/8/12	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	18	19	10,403,785	99.93	36565.65
YZ519	YZ519	2021/8/12	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	23	24	1,383,281	99.88	4847.055
YZ522	YZ522	2021/8/12	2021/8/13	CI	Mod.	OPS	YZ	m-pcr	Illumina	23	24	980,260	99.76	3782.601
YZ523	YZ523	2021/8/12	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	28	29	889,943	99.59	3267.013
YZ524	YZ524	2021/8/13	2021/8/14	CI	Mod.	OPS	YZ	m-pcr	Illumina	24	25	1,437,113	99.90	5781.894
YZ525	YZ525	2021/8/12	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	19	20	11,534,996	99.91	44240.5
YZ526	YZ526	2021/8/10	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	29	30	15,000,466	99.94	55482.26
YZ531	YZ531	2021/8/13	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	17	18	10,735,438	99.94	40623.74
YZ532	YZ532	2021/8/13	2021/8/15	CI	Mod.	NPS	YZ	m-pcr	Illumina	16	18	1,704,304	99.55	6373.416
YZ534	YZ534	2021/8/13	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	22	23	4,891,887	99.93	18559.2
YZ535	YZ535	2021/8/13	2021/8/15	CI	Mod.	OPS	YZ	m-pcr	Illumina	31	27	508,379	99.58	2033.586
YZ536	YZ536	2021/8/14	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	19	20	26,301,042	99.94	99605.61
YZ537	YZ537	2021/8/13	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	21	22	11,139,714	99.94	42842.83
YZ539	YZ539	2021/8/11	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	27	27	13,756,097	99.92	51334.64
YZ540	YZ540	2021/8/4	2021/8/14	CI	Mod.	OPS	YZ	m-pcr	Illumina	23	24	790,282	99.82	3174.38
YZ541	YZ541	2021/8/13	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	30	30	8,803,186	99.94	33754.01
YZ542	YZ542	2021/8/13	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	19	20	6,817,804	99.91	25319.28
YZ545	YZ545	2021/8/13	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	26	27	12,309,648	99.94	47530.96
YZ546	YZ546	2021/8/13	2021/8/15	CI	Mod.	OPS	YZ	m-pcr	Illumina	30	30	165,921	99.70	668.936
YZ547	YZ547	2021/8/14	2021/8/18	CI	Mild	OPS	YZ	m-pcr	Illumina	31	32	11,897,197	99.94	45605.08
YZ548	YZ548	2021/8/13	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	18	19	11,881,278	99.94	45815.42
YZ549	YZ549	2021/8/10	2021/8/15	CI	Mod.	NPS	YZ	m-pcr	Illumina	33	31	385,667	99.41	1536.305
YZ551	YZ551	2021/8/15	2021/8/19	CI	Mild	NPS	YZ	m-pcr	Illumina	29	30	12,026,776	99.91	45284.34
YZ552	YZ552	2021/8/15	2021/8/18	CI	Mild	NPS	YZ	m-pcr	Illumina	22	23	1,599,325	99.63	5909.415
YZ553	YZ553	2021/8/15	2021/8/18	CI	Mod.	NPS	YZ	m-pcr	Illumina	27	28	12,219,751	99.94	46040.41
YZ554	YZ554	2021/8/5	2021/8/17	II	Mod.	OPS	YZ	m-pcr	Illumina	29	30	1,866,221	99.92	7289.246
YZ559	YZ559	2021/8/16	2021/8/17	ER	Mod.	OPS	YZ	m-pcr	Illumina	22	24	2,026,302	99.92	7550.223
YZ560	YZ560	2021/8/16	2021/8/16	ER	Mild	OPS	YZ	m-pcr	Illumina	33	33	779,946	99.89	2702.612
YZ561	YZ561	2021/8/16	2021/8/18	ER	Mild	OPS	YZ	m-pcr	Illumina	32	33	6,410,587	99.85	25273.11
YZ562	YZ562	2021/8/10	2021/8/18	CI	Mod.	OPS	YZ	m-pcr	Illumina	29	30	6,127,909	99.85	24298.09
YZ564	YZ564	2021/8/16	2021/8/18	ER	Mod.	OPS	YZ	m-pcr	Illumina	29	31	5,532,590	99.90	21918.26
YZ570	YZ570	2021/8/25	2021/8/18	ER	Mild	OPS	YZ	m-pcr	Illumina	28	29	6,392,719	99.71	22901.38
NJ/Yu	NJ/Yu	2021/7/10	2021/7/10	NA	Asym	OPS	NJ	m-pcr	Illumina					
	XB		2021/5/14				Jiangsu import							
	XSG		2021/6/13				Jiangsu import							
	GSF		2021/6/17				Jiangsu import							
	ZYC		2021/6/22				Jiangsu import							
	CXJ		2021/6/22				Jiangsu import							
	BN		2021/6/22				Jiangsu import							
	IVDC-06-01		2021/6/6				GD[e]							
	IVDC-0610-39		2021/6/25				GD							
	IVDC-0610-01		2021/6/11				GD							
	IVDC-05-01		2021/4/17				GD							
	Ruili-IVDC-04-01		2021/3/31				YN[f]							
	Ruili-IVDC-04-02		2021/3/30				YN							
	YN-01		2021/6/17				YN							
	YN-47		2021/7/8				YN							
	DL-ILBS-22053		2020/6/13				New Delhi							

a: oropharyngeal swab; b: nasopharyngeal swab; c: Nanjin; d: Yangzhou; e: Guangdong; f: Yunnan; g: Thermo Fisher. Mod., Moderate; Crit., critical; Asym., asymptomatic; m-pcr, multiplex-pcr.

Supplementary Table 3. Demographic characteristics of coronavirus disease 2019 (COVID-19) cases in Nanjing and Yangzhou.

Demographic data		**Cases in Nanjing (n=221)**	**Cases in Yangzhou (n=559)**
Age	< 30	42 (19.00%)	125 (22.36%)
	30–40	34 (15.38%)	65 (11.63%)
	40-50	68 (30.77%)	57 (10.20%)
	50-60	48 (21.72%)	87 (15.56%)
	≥ 60	29 (13.12%)	225 (40.25%)
Sex	Man	85 (38.50%)	237 (42.40%)
	Woman	136 (61.50%)	322 (57.60%)
CT Value	< 20	57 (25.79%)	91 (16.28%)
	20-30	100 (45.25%)	276 (49.37%)
	≥ 30	51 (23.08%)	190 (33.99%)
	Unknown	13 (5.88%)	2 (0.36%)
Clustering	Nonclustered	189 (85.52%)	109 (19.50%)
	Clustered	32 (14.48%)	450 (80.50%)
Vaccination	No	105 (47.51%)	379 (67.80%)
	Vaccined<30days	16 (7.24%)	38 (6.80%)
	Vaccined≥30days	100 (45.25%)	142 (25.40%)
Clinical type	Mild	160 (72.40%)	419 (74.96%)
	Moderate	51 (23.08%)	85 (15.21%)
	Severe	1 (0.45%)	19 (3.40%)
	Crit.	9 (4.07%)	36 (6.44%)

Results are expressed as median (minimum and maximum values) and n (%).

Supplementary Table 4. Mutation sites of Delta variants from case Nanjing/Yu.

Mutation site	Protein (number of substitutions)	INFO
2019-nCoV_210	ORF1ab (16)	VEP=upstream gene variant, DISTANCE=56, QHD43415.1,gene-orf1ab
2019-nCoV_241		VEP=upstream gene variant, DISTANCE=25, QHD43415.1,gene-orf1ab
2019-nCoV_3037		VEP=synonymous_variant,QHD43415.1:p.924F,gene-orf1ab:c.2772ttC>ttT
2019-nCoV_8986		VEP=synonymous_variant,QHD43415.1:p.2907D,gene-orf1ab:c.8721gaC>gaT
2019-nCoV_11332		VEP=synonymous_variant,QHD43415.1:p.3689V,gene-orf1ab:c.11067gtA>gtG
2019-nCoV_1048		VEP=missense_variant,QHD43415.1:p.261K>N,gene-orf1ab:c.783aaG>aaT
2019-nCoV_4181		VEP=missense_variant,QHD43415.1:p.1306A>S,gene-orf1ab:c.3916Gct>Tct
2019-nCoV_6402		VEP=missense_variant,QHD43415.1:p.2046P>L,gene-orf1ab:c.6137cCa>cTa
2019-nCoV_7124		VEP=missense_variant,QHD43415.1:p.2287P>S,gene-orf1ab:c.6859Cct>Tct
2019-nCoV_9053		VEP=missense_variant,QHD43415.1:p.2930V>L,gene-orf1ab:c.8788Gta>Tta
2019-nCoV_10029		VEP=missense_variant,QHD43415.1:p.3255T>I,gene-orf1ab:c.9764aCc>aTc
2019-nCoV_11201		VEP=missense_variant,QHD43415.1:p.3646T>A,gene-orf1ab:c.10936Act>Gct
2019-nCoV_14408		VEP=missense_variant,QHD43415.1:p.4715P>L,gene-orf1ab:c.14144cCt>cTt
2019-nCoV_15451		VEP=missense_variant,QHD43415.1:p.5063G>S,gene-orf1ab:c.15187Ggt>Agt
2019-nCoV_16466		VEP=missense_variant,QHD43415.1:p.5401P>L,gene-orf1ab:c.16202cCa>cTa
2019-nCoV_19220		VEP=missense_variant,QHD43415.1:p.6319A>V,gene-orf1ab:c.18956gCt>gTt
2019-nCoV_21618	Spike (8)	VEP=missense_variant,QHD43416.1:p.19T>R,gene-S:c.56aCa>aGa
2019-nCoV_21987		VEP=missense_variant,QHD43416.1:p.142G>D,gene-S:c.425gGt>gAt
2019-nCoV_21998		VEP=missense_variant,QHD43416.1:p.146H>Y,gene-S:c.436Cac>Tac
2019-nCoV_22917		VEP=missense_variant,QHD43416.1:p.452L>R,gene-S:c.1355cTg>cGg
2019-nCoV_22995		VEP=missense_variant,QHD43416.1:p.478T>K,gene-S:c.1433aCa>aAa
2019-nCoV_23403		VEP=missense_variant,QHD43416.1:p.614D>G,gene-S:c.1841gAt>gGt
2019-nCoV_23604		VEP=missense_variant,QHD43416.1:p.681P>R,gene-S:c.2042cCt>cGt
2019-nCoV_24410		VEP=missense_variant,QHD43416.1:p.950D>N,gene-S:c.2848Gat>Aat
2019-nCoV_25469	ORF3a (1)	VEP=missense_variant,QHD43417.1:p.26S>L,gene-ORF3a:c.77tCa>tTa
2019-nCoV_26767	Membrane (1)	VEP=missense_variant,QHD43419.1:p.82I>T,gene-M:c.245aTc>aCc
2019-nCoV_27527	ORF7a (3)	VEP=missense_variant,QHD43421.1:p.45P>L,gene-ORF7a:c.134cCa>cTa
2019-nCoV_27638		VEP=missense_variant,QHD43421.1:p.82V>A,gene-ORF7a:c.245gTt>gCt
2019-nCoV_27752		VEP=missense_variant,QHD43421.1:p.120T>I,gene-ORF7a:c.359aCa>aTa
2019-nCoV_27874	ORF8 (1)	VEP=upstream gene variant, DISTANCE=20,QHD43422.1,gene-ORF8
2019-nCoV_28461	Nucleocapsid (4)	VEP=missense_variant,QHD43423.2:p.63D>G,gene-N:c.188gAc>gGc
2019-nCoV_28881		VEP=missense_variant,QHD43423.2:p.203R>M,gene-N:c.608aGg>aTg
2019-nCoV_28916		VEP=missense_variant,QHD43423.2:p.215G>C,gene-N:c.643Ggt>Tgt
2019-nCoV_29402		VEP=missense_variant,QHD43423.2:p.377D>Y,gene-N:c.1129Gat>Tat
2019-nCoV_29742	ORF10 (1)	VEP=downstream gene variant, DISTANCE=68,QHI42199.1,gene-ORF10

Supplementary Table 5. Mutation combinations observed in the Nanjing outbreak.

Combination of Mutation[a]	**Date of onset of first case**[b]	**Date of onset of last case**[c]	**Total number of cases (controlled/un-controlled)**[d]	**Number of cases in control period**[e]	**Number of cases in uncontrolled period**[f]
Basic Mutation (same with Nanjing/Yu)	2021/7/13	2021/7/31	51 (28/23)	26	25
C8819T	2021/7/26	2021/7/26	1 (0/1)	0	1
T2803C	2021/7/29	2021/7/31	19 (14/5)	11	8
T2803CC15738T	2021/7/28	2021/7/28	1 (1/0)	1	0
T2803CG16968T	2021/7/28	2021/8/2	2 (1/1)	2	0
A27133T	2021/7/31	2021/7/31	1 (1/0)	1	0
C1060TC14573TC14576GT14562C	2021/7/26	2021/7/26	1 (1/0)	0	1
C1385T	2021/7/22	2021/7/22	1 (1/0)	0	1
C16289T	2021/7/31	2021/7/31	1 (1/0)	1	0
C16289TA2467G	2021/8/1	2021/8/4	2 (2/0)	2	0
C17402T	2021/8/2	2021/8/2	1 (1/0)	1	0
C18828T	2021/7/20	2021/7/26	6 (5/1)	0	6
C22642T	2021/7/22	2021/7/24	2 (1/1)	0	2
C22642TC9165T	2021/7/30	2021/7/30	1 (1/0)	1	0
C346T	2021/7/13	2021/7/27	14 (8/6)	2	12
C346TA6411G	2021/7/20	2021/7/23	2 (2/0)	0	2
C346TC1060T	2021/7/20	2021/7/25	9 (7/2)	0	9
C346TC1060TC14708T	2021/7/25	2021/7/25	1 (1/0)	0	1
C346TC1060TT2803C	2021/7/25	2021/7/25	1 (1/0)	0	1
C346TC18828TC1060T	2021/7/25	2021/7/25	1 (1/0)	0	1
C346TC2623T	2021/7/23	2021/7/23	1 (0/1)	0	1
C346TC28687T	2021/7/20	2021/7/20	1 (1/0)	0	1
C346TC8772T	2021/7/19	2021/7/27	6 (3/3)	1	5
C346TG11083T	2021/7/20	2021/7/26	5 (3/2)	0	5
C346TG28209T	2021/7/19	2021/7/25	2 (1/1)	0	2
C346TG28209TA25934C	2021/7/22	2021/7/29	3 (2/1)	1	2
C346TG28209TA25934CC17822T	2021/8/3	2021/8/5	2 (2/0)	2	0
C346TG28209TA25934CT7513C	2021/7/31	2021/7/31	1 (1/0)	1	0
C346TC8772TG5629T	2021/7/28	2021/7/28	1 (1/0)	1	0
C398T	2021/7/26	2021/7/26	1 (1/0)	0	1
G167T	2021/7/26	2021/7/26	1 (1/0)	0	1
G20995T	2021/7/26	2021/7/26	1 (1/0)	0	1
G6865T	2021/7/25	2021/7/25	1 (1/0)	0	1
T15567C	2021/7/23	2021/7/30	3 (2/1)	1	2
T20751C	2021/7/26	2021/8/1	3 (3/0)	3	0
T22738C	2021/7/21	2021/7/21	1 (1/0)	0	1
T26259C	2021/7/16	2021/7/22	2 (0/2)	0	2
T26259CC1385T	2021/7/20	2021/7/24	2 (1/1)	0	2
T26259CG472A	2021/8/6	2021/8/8	2 (2/0)	2	0
T26259CG472AC16192A	2021/8/11	2021/8/11	1 (1/0)	1	0
T26259CG246T	2021/7/21	2021/7/21	1 (1/0)	0	1
A13566G	2021/7/22	2021/7/22	1 (0/1)	0	1
C22642TT2803CA15201GC14573TC14576GG26951CT14562C	2021/7/21	2021/7/21	1 (0/1)	0	1
C346TC22642T	2021/7/19	2021/7/19	1 (0/1)	0	1
T2803CC25452TC25433TC25572T	2021/7/30	2021/7/30	1 (0/1)	1	0
T2803CG23868T	2021/7/26	2021/7/26	1 (1/0)	0	1
T2803CT7513C	2021/7/29	2021/8/10	2 (2/0)	2	0
C13517T	2021/7/26	2021/7/26	1 (0/1)	0	1

a: The emergence of combination of mutation in Nanjing. b: Date of the earliest case among the cases with the combination of mutation. c: Date of the last case among the cases with the combination of mutation. d: Total number of cases of this mutation combination in Nanjing. e: Number of cases with onset dates in completely intervened (CI) and epidemic regression (ER) stage. f: Number of cases with onset dates in natural epidemic period (NE) and incompletely intervened period (II). Controlled number: onset date of cases after non-pharmaceutical interventions (NPI) measures (include same date). uncontrolled number: onset date of cases before NPI measures.

Supplementary Table 6. Major mutation combinations in the Nanjing outbreak.

Nanjing–Major combinations of mutations	**Number of cases**	**Date (First case[c])**	**Date（Last case）[d]**
35basic mutation (Common[a])	51	2021/7/13	2021/7/31
35basic mutation+1 iSNV(Ex346/2803)(Rare[b])	12	2021/7/20	2021/8/2
35basic mutation+2 iSNV(Ex346/2803)(Rare)	2	2021/7/20	2021/7/30
35basic mutation+3 iSNV(Ex346/2803)(Rare)	1	2021/8/11	2021/8/11
35basic mutation+4 iSNV(Ex346/2803)(Rare)	1	2021/7/26	2021/7/26
35basic mutation+1 iSNV(Ex346/2803)(Common)	16	2021/7/16	2021/8/1
35basic mutation+2 iSNV(Ex346/2803)(Common)	6	2021/7/20	2021/8/8
35basic mutation+C346T(Common)	14	2021/7/13	2021/7/27
35basic mutation+C346T+1 iSNV(Ex2803)(Rare)	3	2021/7/19	2021/7/23
35basic mutation+C346T+2 iSNV(Rare)	4	2021/7/25	2021/7/29
35basic mutation+C346T+3 iSNV(Ex2803)(Rare)	1	2021/7/31	2021/7/31
35basic mutation+C346T+C1060T(Common)	9	2021/7/20	2021/7/25
35basic mutation+C346T+C8772T(Common)	6	2021/7/19	2021/7/27
35basic mutation+C346T+G28209T(Common)	2	2021/7/19	2021/7/25
35basic mutation+C346T+G11083T(Common)	5	2021/7/20	2021/7/26
35basic mutation+C346T+A25934C(Common)	3	2021/7/22	2021/7/29
35basic mutation+C346T+A6411G(Common)	2	2021/7/20	2021/7/23
35basic mutation+C346T+G28209T+A25934C+C17822T(Common)	2	2021/8/3	2021/8/5
35basic mutation+T2803C(Common)	19	2021/7/29	2021/7/31
35basic mutation+T2803C+1 iSNV(Ex346)(Rare)	2	2021/7/26	2021/7/28
35basic mutation+T2803C+3 iSNV(Ex346)(Rare)	1	2021/7/30	2021/7/30
35basic mutation+T2803C+6 iSNV(Ex346)(Rare)	1	2021/7/21	2021/7/21
35basic mutation+T2803C+G16968T(Common)	2	2021/7/28	2021/8/2
35basic mutation+T2803C+T7513C(Common)	2	2021/7/29	2021/8/10

a: Indicates that the same mutation combination occurs in multiple cases. b: Indicates that the same mutation combination occurs in only one case. c: is the onset time of the first case of this mutation combination. d: is the onset time of the last case of this mutation combination.

Supplementary Table 7. Mutation combinations observed in the Yangzhou outbreak.

Combination of mutation[a]	**Date of onset of first case[b]**	**Date of onset of last case[c]**	**Total number of cases (controlled /uncontrolled)[d]**	**Number of cases in control period[e]**	**Number of cases in uncontrolled period[f]**
T2803CC2939T	2021/7/26	2021/8/1	6(4/2)	6	0
C22642TT2803CG5629T	2021/8/9	2021/8/9	1(0/1)	0	1
G11083TT2803C	2021/8/10	2021/8/10	1(0/1)	0	1
G11083TT2803CC23525T	2021/8/10	2021/8/11	2(1/1)	0	2
G11083TT2803CT7513CC18486TG10533T	2021/7/30	2021/7/30	1(0/1)	1	0
T2803CC5497T	2021/8/6	2021/8/6	1(1/0)	1	0
T2803CG3880A	2021/8/9	2021/8/10	3(1/2)	0	3
T2803C	2021/7/23	2021/8/25	140(75/65)	95	45
T2803CA15201GG26951C	2021/8/5	2021/8/13	4(3/1)	2	2
T2803CA15201GG26951CG26754T	2021/8/10	2021/8/10	1(0/1)	0	1
T2803CA15201GG26951CG26754TG28514T	2021/8/16	2021/8/16	1(0/1)	0	1
T2803CA3908GC19955TA156G	2021/8/11	2021/8/11	1(1/0)	0	1
T2803CA5289T	2021/8/8	2021/8/8	1(1/0)	0	1
T2803CA3908G	2021/7/31	2021/8/13	11(8/3)	5	6
T2803CA3908GG4399T	2021/8/4	2021/8/7	2(1/1)	2	0
T2803CA3908GG5953T	2021/8/7	2021/8/7	1(1/0)	1	0
T2803CA7300T	2021/7/30	2021/8/6	4(3/1)	4	0
T2803CC13329T	2021/8/8	2021/8/11	3(3/0)	0	3
T2803CC13329TC28313T	2021/8/10	2021/8/10	1(1/0)	0	1
T2803CC14573TC14576GC2939T	2021/7/27	2021/7/27	1(0/1)	1	0
T2803CC14573TC14576GT7513CA27156T	2021/7/28	2021/7/28	1(0/1)	1	0
T2803CC14573TC14576GT14562C	2021/7/26	2021/7/26	1(0/1)	1	0
T2803CC14573TC14576GT14562CC23188GC16114TC23300TC25339TG24413T	2021/7/28	2021/7/28	1(0/1)	1	0
T2803CC14573TC14576GT14562CT7513CC18486TG10533TC23188G	2021/8/4	2021/8/4	1(0/1)	1	0
T2803CC14573TC14576GT14562CT7513CC18687T	2021/8/12	2021/8/12	1(1/0)	0	1
T2803CC14573TC14576GT14562CT7513CC23188GC11663A	2021/8/5	2021/8/5	1(1/0)	1	0
T2803CC14708TC14805T	2021/8/5	2021/8/5	1(1/0)	1	0
T2803CC14805T	2021/8/4	2021/8/12	2(2/0)	1	1
T2803CC14805TG558T	2021/8/13	2021/8/13	1(1/0)	0	1
T2803CC14922T	2021/8/8	2021/8/8	1(1/0)	0	1
T2803CC14922TC17444T	2021/7/31	2021/8/1	2(0/2)	2	0
T2803CC14922TC17444TC21772T	2021/8/2	2021/8/2	1(1/0)	1	0
T2803CC14922TC17444TC23525T	2021/8/8	2021/8/8	1(1/0)	0	1
T2803CC17336T	2021/8/6	2021/8/10	3(1/2)	2	1
T2803CC17410T	2021/8/2	2021/8/10	2(1/1)	1	1
T2803CC1758T	2021/8/13	2021/8/13	4(4/0)	0	4
T2803CC19263T	2021/8/8	2021/8/8	1(1/0)	0	1
T2803CC19488T	2021/8/5	2021/8/6	4(0/2)	4	0
T2803CC19955T	2021/8/4	2021/8/4	1(0/1)	1	0
T2803CC2106T	2021/8/4	2021/8/12	6(6/0)	3	3
T2803CC21575T	2021/8/5	2021/8/10	4(4/0)	2	2
T2803CC22712TC7169T	2021/7/29	2021/7/29	1(0/1)	1	0
T2803CC23248T	2021/8/1	2021/8/10	6(5/1)	3	3
T2803CC23525T	2021/8/2	2021/8/2	1(0/1)	1	0
T2803CC23525TC8616T	2021/8/7	2021/8/8	2(2/0)	1	1
T2803CC23525TT23248A	2021/8/6	2021/8/6	1(0/1)	1	0
T2803CC24912T	2021/8/5	2021/8/10	2(1/1)	1	1
T2803CC2523TC2676T	2021/8/8	2021/8/10	2(1/1)	0	2
T2803CC25452TC12809TC15222T	2021/8/3	2021/8/3	1(1/0)	1	0
T2803CC2571T	2021/7/30	2021/7/30	1(1/0)	1	0
T2803CC27641T	2021/8/8	2021/8/8	1(1/0)	0	1
T2803CC2939TG27703T	2021/8/3	2021/8/3	1(1/0)	1	0
T2803CC29614T	2021/8/13	2021/8/13	1(1/0)	0	1
T2803CC29738T	2021/8/4	2021/8/4	1(0/1)	1	0
T2803CC4901T	2021/8/9	2021/8/9	1(0/1)	0	1
T2803CC5079T	2021/8/7	2021/8/7	1(1/0)	1	0
T2803CC5849T	2021/8/3	2021/8/15	5(3/2)	4	1
T2803CC9170TG1729A	2021/8/5	2021/8/5	1(0/1)	1	0
T2803CG12798A	2021/8/7	2021/8/7	1(1/0)	1	0
T2803CG23282T	2021/8/2	2021/8/2	1(0/1)	1	0
T2803CG23501T	2021/8/8	2021/8/8	1(0/1)	0	1
T2803CG23501TG21372T	2021/8/10	2021/8/10	1(0/1)	0	1
T2803CG26389T	2021/7/30	2021/7/30	1(1/0)	1	0
T2803CG26389TG942A	2021/8/6	2021/8/8	2(2/0)	1	1
T2803CG26951C	2021/8/2	2021/8/2	1(0/1)	1	0
T2803CG26951CA27010C	2021/8/6	2021/8/6	1(1/0)	1	0

T2803CG295T	2021/8/11	2021/8/11	1(0/1)	0	1
T2803CG3109T	2021/8/11	2021/8/11	1(1/0)	0	1
T2803CG558T	2021/8/7	2021/8/7	1(1/0)	1	0
T2803CT25518G	2021/8/10	2021/8/10	1(0/5)	0	1
T2803CT7378C	2021/8/7	2021/8/7	1(0/1)	1	0
T2803CT7513C	2021/7/24	2021/8/9	47(28/19)	42	5
T2803CT7513CA27156T	2021/8/12	2021/8/12	1(1/0)	0	1
T2803CT7513CA5458GC2143T23641AT26972C	2021/8/7	2021/8/7	1(0/1)	1	0
T2803CT7513CA655G	2021/8/5	2021/8/5	1(1/0)	1	0
T2803CT7513CC1758T	2021/8/2	2021/8/2	1(1/0)	1	0
T2803CT7513CC18486TG10533T	2021/7/24	2021/8/8	8(5/3)	7	1
T2803CT7513CC18486TG10533TC13176T	2021/8/7	2021/8/7	1(1/0)	1	0
T2803CT7513CC18687T	2021/8/5	2021/8/5	1(1/0)	1	0
T2803CT7513CC22735T	2021/8/9	2021/8/9	1(0/1)	0	1
T2803CT7513CC275A	2021/7/30	2021/7/31	2(2/0)	2	0
T2803CT7513CC2947T	2021/7/26	2021/7/26	1(0/1)	1	0
T2803CT7513CC5147TC5385TG1018A	2021/8/13	2021/8/15	2(2/0)	0	2
T2803CT7513CC6807T	2021/7/26	2021/8/4	4(3/1)	4	0
T2803CT7513CG23282TC29358T	2021/8/4	2021/8/7	2(0/2)	2	0
T2803CT7513CG24577TG25186T	2021/7/29	2021/8/1	4(3/1)	4	0
T2803CT7513CG29645T	2021/8/16	2021/8/16	1(0/1)	0	1
T2803CT7513CG29781T	2021/8/7	2021/8/12	5(2/1)	2	3
T2803CT7513CT694A	2021/8/5	2021/8/5	1(1/0)	1	0

a: The emergence of combination of mutation in Yangzhou. b: Date of the earliest case among the cases with the combination of mutation. c: Date of the last case among the cases with the combination of mutation. d: Total number of cases of this mutation combination in Yangzhou. e: Number of cases with onset dates in completely intervened (CI) and epidemic regression (ER) stage. f: Number of cases with onset dates in natural epidemic (NE) and incompletely intervened (II) periods. Controlled number: onset date of cases after non-pharmaceutical interventions (NPI) measures (include same date). uncontrolled number: onset date of cases before NPI measures).

Supplementary Table 8. Major mutation combinations in the Yangzhou outbreak.

Yangzhou–major combinations of mutations	**Number of cases**	**Date (First case)[c]**	**Date (Last case)[d]**
35basic mutation+T2803C (Common[a])	137	2021/7/23	2021/8/25
35basic mutation+T2803C+1 iSNV(Rare[b])	23	2021/7/30	2021/8/13
35basic mutation+T2803C+2 iSNV(Rare)	19	2021/7/26	2021/8/16
35basic mutation+T2803C+3 iSNV(Rare)	6	2021/7/26	2021/8/10
35basic mutation+T2803C+4 iSNV(Rare)	5	2021/7/27	2021/8/16
35basic mutation+T2803C+5 iSNV(Rare)	3	2021/7/28	2021/8/12
35basic mutation+T2803C+6 iSNV(Rare)	1	2021/8/5	2021/8/5
35basic mutation+T2803C+7 iSNV(Rare)	1	2021/8/4	2021/8/4
35basic mutation+T2803C+8 iSNV(Rare)	1	2021/7/28	2021/7/28
35basic mutation+T2803C+C14805T(Common)	2	2021/8/4	2021/8/12
35basic mutation+T2803C+C17336T(Common)	2	2021/8/6	2021/8/10
35basic mutation+T2803C+C17410T(Common)	2	2021/8/2	2021/8/10
35basic mutation+T2803C+G3880A(Common)	3	2021/8/9	2021/8/9
35basic mutation+T2803C+C13329T(Common)	3	2021/8/8	2021/8/11
35basic mutation+T2803C+A7300T(Common)	4	2021/7/30	2021/8/6
35basic mutation+T2803C+C1758T(Common)	4	2021/8/13	2021/8/13
35basic mutation+T2803C+C19488T(Common)	4	2021/8/5	2021/8/6
35basic mutation+T2803C+C21575T(Common)	4	2021/8/5	2021/8/10
35basic mutation+T2803C+C5849T(Common)	5	2021/8/3	2021/8/15
35basic mutation+T2803C+C2106T(Common)	6	2021/8/4	2021/8/12
35basic mutation+T2803C+C23248T(Common)	6	2021/8/1	2021/8/10
35basic mutation+T2803C+C2939T(Common)	6	2021/7/26	2021/8/1
35basic mutation+T2803C+A3908G(Common)	11	2021/7/31	2021/8/13
35basic mutation+T2803C+T7513C(Common)	45	2021/7/24	2021/8/9
35basic mutation+T2803C+A21987G(Common)	3	2021/7/29	2021/8/9
35basic mutation+T2803C+C24912T(Common)	2	2021/8/5	2021/8/10
35basic mutation+T2803C+T7513C+C275A(Common)	2	2021/7/30	2021/7/31
35basic mutation+T2803C+T7513C+C6807T(Common)	4	2021/7/26	2021/8/4
35basic mutation+T2803C+T7513C+A21987G(Common)	2	2021/7/28	2021/8/3
35basic mutation+T2803C+T7513C+G29781T(Common)	5	2021/8/7	2021/8/12
35basic mutation+T2803C+G11083T+C23525T(Common)	2	2021/8/10	2021/8/11
35basic mutation+T2803C+A15201G+G26951C(Common)	4	2021/8/5	2021/8/13
35basic mutation+T2803C+A3908G+G4399T(Common)	2	2021/8/4	2021/8/7
35basic mutation+T2803C+C14922T+C17444T(Common)	2	2021/7/31	2021/8/1
35basic mutation+T2803C+C23525T+C8616T(Common)	2	2021/8/7	2021/8/8
35basic mutation+T2803C+C2523T+C2676T(Common)	2	2021/8/8	2021/8/10
35basic mutation+T2803C+G26389T+G942A(Common)	2	2021/8/6	2021/8/8
35basic mutation+T2803C+T7513C+C18486T+G10533T(Common)	8	2021/7/24	2021/8/8
35basic mutation+T2803C+T7513C+G23282T+C29358T(Common)	2	2021/8/4	2021/8/7
35basic mutation+T2803C+T7513C+G24577T+G25186T(Common)	4	2021/7/29	2021/8/1
35basic mutation+T2803C+T7513C+C5147T+C5385T+G1018A(Common)	2	2021/8/13	2021/8/15

a: Indicates that the same mutation combination occurs in multiple cases. b: Indicates that the same mutation combination occurs in only one case. c: is the onset time of the First case of this mutation combination. d: is the onset time of the last case of this mutation combination.

Supplementary Table 9. Factors associated with single nucleotide variant (SNV) combinations termination.

Variables	Non-last Patient (case/total) n=371	Last Patient (case/total) n=149	Univariable analysis		Multivariable analysis	
			Odds ratio (95% CI)	*p* value	Odds ratio (95% CI)	*p* value
Onset Period						
NE	90 (24.3%)	13 (8.7%)	Ref	..	Ref	..
II	188 (50.7%)	62 (41.6%)	2.283 (1.194-4.367)	0.013	2.467 (1.277–4.764)	0.007
CI	90 (24.3%)	67 (45%)	5.154 (2.659-9.991)	< 0.001	5.774 (2.931–11.374)	< 0.001
ER	3 (0.8%)	7 (4.7%)	16.154 (3.706-70.413)	< 0.001	16.118 (3.616–71.836)	< 0.001
Vaccination[a]						
No	235 (63.3%)	83 (55.7%)	Ref	..	Ref	..
Vaccined<30days	98 (26.4%)	40 (26.8%)	1.156 (0.741-1.803)	0.524	1.113 (0.701–1.769)	0.649
Vaccined≥30days	38 (10.2%)	26 (17.4%)	1.937 (1.109-3.385)	0.02	2.33 (1.281–4.236)	**0.006**
Age						
< 18	48 (12.9%)	21 (14.1%)	Ref	..	..	..
(18–30)	32 (8.6%)	12 (8.1%)	0.857 (0.371-1.983)	0.719	NI†[b]	
(30–40)	44 (11.9%)	22 (14.8%)	1.143 (0.554-2.358)	0.718	NI†	
(40–50)	55 (14.8%)	32 (21.5%)	1.33 (0.679-2.607)	0.406	NI†	
(50–60)	66 (17.8%)	26 (17.4%)	0.9 (0.454-1.786)	0.764	NI†	
≥ 60	126 (34%)	36 (24.2)	0.653 (0.347-1.229)	0.187	NI†	
Gender						
Woman	220 (59.3%)	77 (51.7%)	Ref	..	..	..
Man	151 (40.7%)	72 (48.3%)	1.362 (0.93-1.997)	0.113	NI†	
CT						
< 20	72 (19.4%)	36 (24.2%)	Ref	..	..	..
(20–30)	194 (52.3%)	74 (49.7%)	0.763 (0.471-1.235)	0.271	NI†	
≥ 30	105 (28.3%)	39 (26.2%)	0.743 (0.431-1.279)	0.284	NI†	
Clustering						
Non-clustered	149 (40.2%)	66 (44.3%)	Ref	..	..	..
Clustered	222 (59.8%)	83 (55.7%)	0.844 (0.575-1.239)	0.387	NI†	
Clinical						
Mild	71 (19.1%)	31 (20.8%)	Ref	..	..	..
Moderate	269 (72.5%)	114 (76.5%)	0.971 (0.603-1.561)	0.902	NI†	
Severe or Crit.	31 (8.4%)	4 (2.7%)	0.296 (0.096-0.909)	0.033	NI†	
Termination codon				..	..	..
No	367 (98.9%)	145 (97.3)	Ref		NI†	
Yes	4 (1.1%)	4 (2.7%)	2.531 (0.625-10.255)	0.193	NI†	

Univariable and multivariable analysis of factors affecting the termination of iSNV mutation combinations. a: No = Unvaccinated persons were defined as those who had not been vaccinated and those who had less than 14 days between the time of last vaccination and the time of illness. Yes = Vaccinations were defined as those who were vaccinated and the interval between the last dose of vaccination and the onset of illness was 14 days or more. b: These factors were not included in the multivariable analysis. CI, completely intervened period; ER, epidemic regression period; II, incompletely intervened period; NE, natural epidemic period.

Supplementary Table 10. Mutations and deletions in spike protein and their reported effect.

Mutation site	Effects	Ref.
T19R	——	——
G142D	G142D reducing neutralization by the BNT162b2 immune sera [4] and the mAb 2489 [5].	[4] Nature. 2021;10.1038/s41586-021-03693-y. [5] Nat Med. 2021;27(4):717-726.
H146Y	H146Y reducing neutralization by the mAb FC05 [6] and 4A8 [7].	[6] National Science Review. 2021; nwab053. [7] Science. 2020; 369(6504):650-655.
△E156	——	——
△F157	F157A reducing neutralization by the mAb 2489 [8].	[8] Cell. 2021;184(9):2316-2331.
R158G	——	——
L452R	L452R reducing neutralization by the mAb FC08 [8], COV2-2096 [9], SARS2-01, SARS2-02 and SARS2-32 [10], C643 and C628 [11], and convalescent plasma [12].	[8] National Science Review. 2021; nwab053. [9] Cell Host Microbe. 2021;29(1):44-57. [10] Cell Host Microbe. 2021;29(3):477-488. [11] Nature. 2021;592(7855):616-622. [12] Cell. 2020;182(5):1284-1294.
T478K	T478I reducing neutralization by the mAb SARS2-16, SARS2-19 and and convalescent plasma (13 and 35#) [10].	[10] Cell Host Microbe. 2021;29(3):477-488.
D614G	D614G could enhance virus infectivity and thermal stability, D614G does not significantly affect the effectiveness of existing vaccines but may weaken the neutralizing activity of certain specific antibodies [13].	[13] Sci China Life Sci. 2021;64(7):1062-1067.
P681R	P681R may have increased replication, which leads to higher viral loads and increased transmission [14].	[14] N Engl J Med. 2021; 385(7): 585-594.
D950N	——	——