Supplementary Appendix

Appendix Methods

Epidemiological and Clinical Data Collection

The severity of the disease was assessed mainly in accordance with the guideline issued by the Chinese National Health Commission[1] and the guidance of WHO[2].

For the asymptomatic, individuals with positive nucleic acid results but without any symptoms, and /or detectable radiologic abnormality was absent.

The mild case was diagnosed in terms of the following criteria: (1) with mild clinical symptoms, including fever, cough, fatigue, anorexia, shortness of breath, myalgias or other non-specific symptoms; (2) without evidence of viral pneumonia or hypoxia.

For moderate cases, the standards of diagnosis were as follows: (1) with more evident clinical symptoms (such as fever, cough, dyspnea, fast breathing); (2) patients who developed visible pneumonia.

The diagnosis of severe illness was determined according to the following criteria: (1) respiratory distress, RR $\geq$30 times/min in the resting state; (2) oxygen saturation $\leq$93% in the resting state; (3) arterial blood oxygen partial pressure (PaO2)/oxygen concentration (FiO2) $\leq$300 mmHg); (4) rapid aggravation with >50% lung damage progression within 24 to 48 h.

The criteria of critical illness were as follows: (1) respiratory failure requiring mechanical ventilation; (2) shock; (3) combined with other organ failure requiring intensive care.

Patients were categorized into non-severe, severe and critical illness when exploring the differences of viral kinetics and incubation period between the Delta VOC group and the wild-type group. The non-severe cases were consisted of asymptomatic, mild and moderate cases.

Reference:

1. National Health Commission & State Administration of Traditional Chinese Medicine. Diagnosis and treatment protocol for novel coronavirus pneumonia (Trial Version 8). August 19, 2020. Available at:http://www.nhc.gov.cn/xcs/zhengcwj/202008/0a7bdf12bd4b46e5bd28ca7f9a7f5e5a/files/a449a3e2e2c94d9a856d5faea2ff0f94.pdf.
2. World Health Organization. COVID-19 Clinical management: Living guidance, 2021. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1

Appendix Figures

Appendix Figure S1. Phylogenetic tree of delta SARS-CoV-2 virus in Guangzhou. The neighbor-joining (NJ) phylogenetic tree was constructed using the full-length genome sequences by the program MEGA 6.0.6 through the Kimura two-parameter model with 1000 bootstrap replication. The reference sequences of SARS-CoV-2 were downloaded from the GISAID database (http://gisaid.org). The tree was rooted with Wuhan Hu-1 strain NC_045512.2. The local strains G1-G7 were labelled with different color dots. One imported case with 100% identical to G1 was labelled (gray diamond). The scale bar represents 0.01% genetic distance. Bootstrap values >70% are presented at the corresponding nodes of the tree.
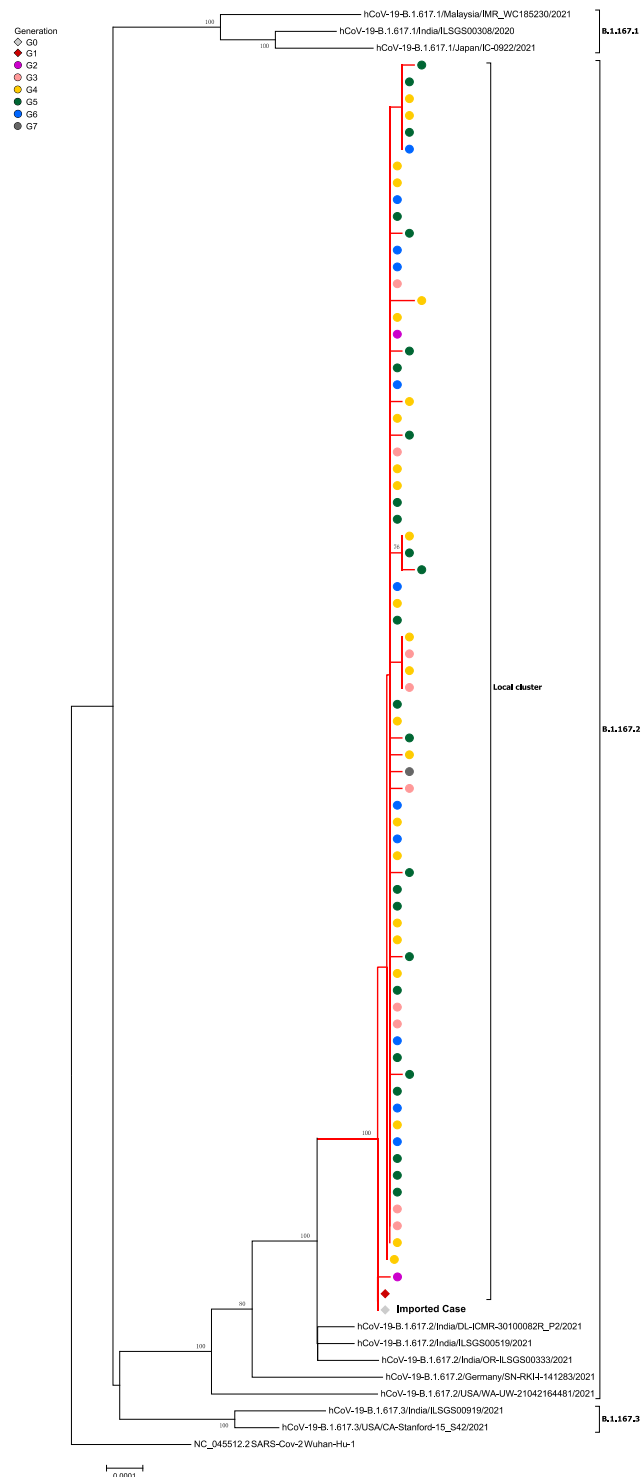
Appendix Figure S2. The highest viral load and dynamics of N gene among hospitalized COVID-19 patients infected with SARS-CoV-2 wild-type or Delta VOC. Refer to Figure 4 for patterns of Ct values of ORF1a/b gene. In the box plot, the boundary of the box closest to zero indicates the 25th percentile, a black line within the box marks the median, and the boundary of the box farthest from zero indicates the 75th percentile. Whiskers below and above the box indicate the largest and smallest value no further than 1.5 * IQR (inter-quartile range) from 75th percentile or 25th percentile, respectively.
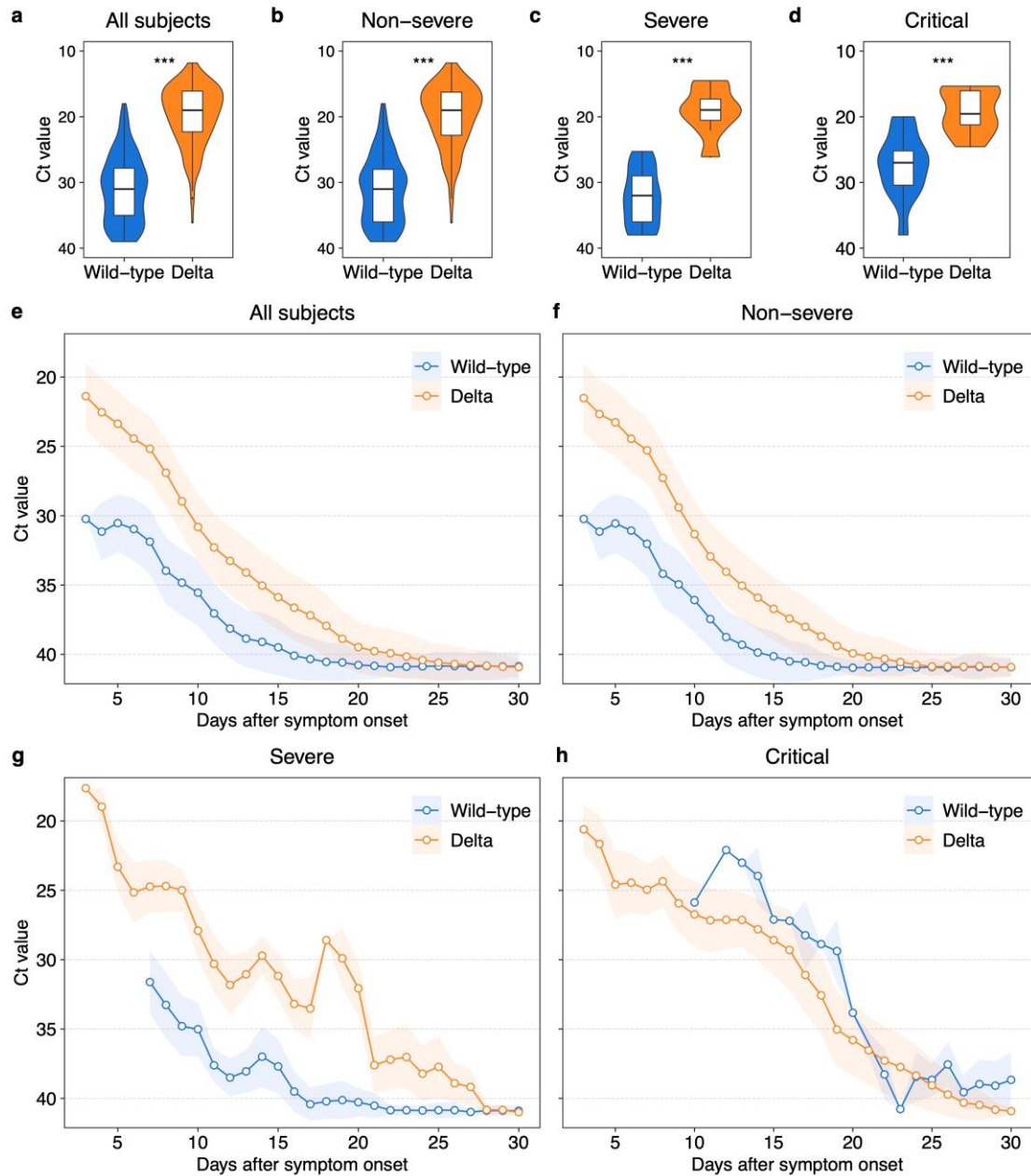
Appendix Figure S3. Time of Ct values from day of first positive testing to negative testing in swab samples. Box/violin plot shows days of Ct values turn to negative for all subjects (a), non-severe (b), severe (c) and critical (d) patients. A negative Ct value is defined by Ct > 40 of the ORF1a/b gene in two consecutive testing. In the box plot, the boundary of the box closest to zero indicates the 25th percentile, a black line within the box marks the median, and the boundary of the box farthest from zero indicates the 75th percentile. Whiskers below and above the box indicate the smallest and largest value no further than 1.5 * IQR (inter-quartile range) from 25th percentile or 75th percentile, respectively.
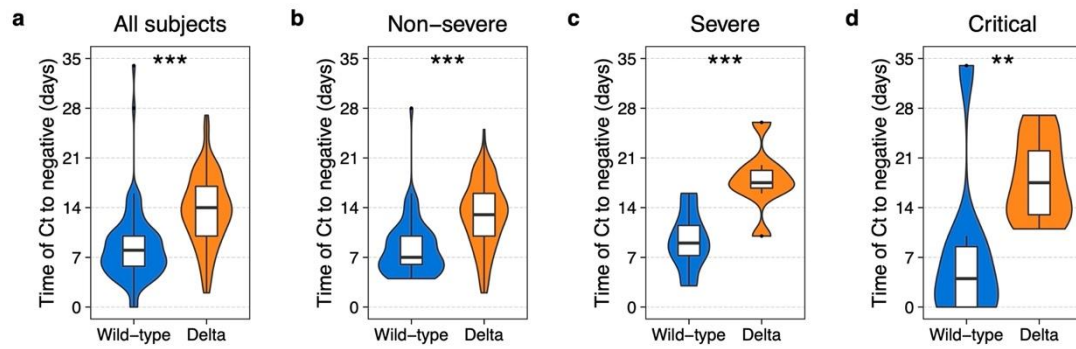
Appendix Tables

Appendix Table S1. Initial laboratory findings among hospitalized patients with different strains

	Total (n=419)		Mild (n=62)		Moderate (n=294)		Severe (n=38)		Critical (n=25)	
	WT strain (n=260)	Delta strain (n=159)	WT strain (n=21)	Delta strain[†] (n=41)	WT strain (n=196)	Delta strain (n=98)	WT strain (n=30)	Delta strain (n=8)	WT strain (n=13)	Delta strain (n=12)
Hematologic										
Leukocyte, $\times 10^9/L$	4.7 (3.8,5.9)	5.8 (4.6,6.9) **	5.4 (4.2,6.1)	6.6 (5.6,8.1)*	4.6 (3.7,5.8)	5.6 (4.4,6.3) **	4.5 (4.0,6.3)	5.1 (4.4,6.0)	5.4 (4.6,7.7)	5.9 (5.0,6.4)
Neutrophils, $\times 10^9/L$	2.8 (2.1,3.7)	3.9 (2.9,5.1) **	2.9 (2.2,3.5)	4.3 (3.1,5.7)**	2.6 (2.0,3.5)	3.7 (2.7,4.7) **	3.4 (2.5,5.3)	3.6 (3.4,5.0)	3.7 (3.7,4.4)	4.5 (3.2,5.0)
Neutrophils percentage (%)	59.0 (51.2,68.8)	69.0 (62.2,75.2) **	53.8 (50.3,61.9)	67.6 (61.4,73.7)**	57.5 (50.1,66.9)	68.6 (61.8,74.9) **	72.8 (61.0,79.9)	76.8 (74.3,78.5)	72.9 (58.5,82.6)	74.7 (67.8,77.5)
Lymphocytes, $\times 10^9/L$	1.4 (1.0,2.0)	1.1 (0.9,1.5) **	1.9 (1.4,2.1)	1.3 (1.0,2.0) *	1.4 (1.1,2.0)	1.1 (0.8,1.4) **	1.0 (0.8,1.2)	0.7 (0.6,1.0)	1.0 (0.5,1.2)	1.0 (0.9,1.1)
Lymphocytes percentage (%)	31.4 (23.2,39.2)	19.8 (15.3,27.2) **	34.7 (30.2,40.6)	19.6 (15.5,28.8)**	32.2 (25.0,40.5)	21.1 (15.8,27.9) **	20.2 (14.3,29.2)	14.8 (11.3,17.7)	18.1 (9.9,21.6)	17.2 (14.6,19.8)
Monocytes, $\times 10^9/L$	0.4 (0.3,0.5)	0.5 (0.4,0.6) **	0.4 (0.3,0.5)	0.5 (0.4,0.8) **	0.4 (0.3,0.5)	0.5 (0.4,0.6) **	0.3 (0.2,0.4)	0.4 (0.3,0.5)	0.4 (0.3,0.5)	0.5 (0.4,0.5)
Monocytes percentage (%)	7.7 (5.7,9.4)	8.7 (7.1,11.2) **	7.8 (5.9,8.6)	8.6 (6.2,12.6)	7.8 (6.0,9.5)	8.8 (7.3,10.9)**	6.0 (4.4,9.5)	8.0 (7.6,9.5)	7.8 (4.2,8.5)	8.2 (6.8,10.8)
NLR	1.8 (1.3,3.0)	3.5 (2.3,4.8) **	1.5 (1.3,2.1)	3.5 (1.9,4.4) **	1.8 (1.2,2.6)	3.2 (2.3,4.7) **	3.5 (2.0,5.4)	5.2 (4.4,6.9)	3.9 (3.4,8.2)	4.2 (3.6,5.4)
HGB, g/L	136.0	133.0	132.5	132.0	137.0	134.0	132.5	141.0	128.0	125.5

	(124.0,146.0)	(125.0,145.0)	(123.8,149.2)	(121.0,147.0)	(126.0,148.0)	(127.0,144.0)	(120.8,144.0)	(128.5,148.0)	(121.0,139.0)	(123.8,135.0)
Platelets,	183.0	192.0	197.0	225.0	185.5	183.5	163.0	160.5	149.0	152.5
$\times10^9$/L	(146.5,228.0)	(156.5,240.5)*	(177.5,229.8)	(198.0,279.0)*	(148.0,232.8)	(152.2,227.8)	(141.0,191.8)	(146.5,200.2)	(125.0,186.0)	(134.0,178.0)

Liver and renal function

ALT, U/L	19.6	14.0	20.0	12.6	18.6	14.3	27.0	20.0	13.0	15.1
	(13.8,28.1)	(9.9,20.0) **	(14.2,30.6)	(9.8,17.4)**	(13.5,27.0)	(10.1,20.6)**	(20.6,48.1)	(11.4,34.8)	(11.0,23.0)	(12.7,18.4)
AST, U/L	20.2	20.0	19.1	18.3	19.3	19.9	32.6	25.6	27.5	20.4
	(16.6,28.4)	(15.7,27.6)	(15.7,26.2)	(15.0,27.7)	(16.2,25.3)	(16.2,26.1)	(26.2,49.6)	(20.1,36.0)	(19.0,47.0)	(18.1,23.8)
TB, umol/L	9.4 (6.6,13.6)	6.7 (4.5,8.8) **	10.7 (6.8,17.0)	6.2 (4.8,8.3) **	9.3 (6.6,13.1)	6.5 (4.3,8.8)**	10.4 (7.1,14.0)	7.7 (6.7,8.2)	6.7 (6.5,25.8)	7.9 (6.4,12.0)
Alb, g/L	40.0	43.8	40.3	46.2	40.5	43.2	34.8	41.5	32.6	39.2
	(36.6,42.7)	(40.3,46.3) **	(36.6,45.3)	(45.2,47.6)**	(37.7,42.9)	(40.3,46.0) **	(33.0,36.5)	(38.9,43.8)**	(31.5,34.7)	(36.5,40.9)*
Urea	3.8 (3.2,4.5)	3.8 (3.3,4.7)	4.0 (3.2,4.5)	4.1 (3.5,4.6)	3.8 (3.2,4.5)	3.7 (3.1,4.5)	NA (NA,NA)	5.3 (4.4,6.9)	NA (NA,NA)	5.3 (4.0,6.3)
Cr, umol/L	58.5	67.3	49.0	62.9	58.8	66.0	64.8	75.9	65.2	81.0
	(47.6,75.6)	(55.8,79.5)**	(40.2,73.3)	(48.6,80.4)	(48.2,74.9)	(56.0,75.5)*	(52.4,77.1)	(69.1,86.1)	(51.3,106.7)	(72.1,102.3)
Cys-C, mg/L	0.9 (0.7,1.0)	1 (0.8,1.1) **	0.8 (0.7,1.1)	0.9 (0.8,1.0)	0.8 (0.7,1.0)	1.0 (0.8,1.1)**	0.9 (0.8,1.1)	1.3 (1.2,1.5)*	1.4 (1.0,2.0)	1.2 (1.1,1.4)

Myocardial enzyme

LDH, U/L	185.0	199.0	170.0	178.5	176.0	199.0	305.5	232.5	229.0	215.0
	(151.0,230.0)	(167.5,237.5)*	(137.0,223.0)	(160.0,229.5)	(150.0,215.0)	(174.0,235.5)**	(224.2,391.0)	(210.8,338.2)	(151.0,466.0)	(199.5,238.5)
CK, U/L	74.0	103.5	78.0	100.0	67.0	100.0	121.0	106.5	114.0	116.0
	(50.0,112.0)	(76.2,149.2)**	(65.0,97.0)	(85.5,139.0)**	(48.0,103.0)	(71.0,153.0)**	(91.5,205.8)	(76.2,216.0)	(60.0,443.0)	(90.5,194.5)
CK-MB, ng/ml	10.3 (7.6,15.0)	13.8(11.4,17.9) **	9.7 (2.1,15.0)	14.2 (12.1,20.0) **	10.6 (8.2,15.5)	13.4 (11.5,17.1)**	9.1 (6.3,13.3)	16.9 (12.0,23.0)*	9.3 (3.2,14.4)	11.9 (9.6,16.4)
LAC, mmol/L	1.8 (1.3,2.2)	1.5 (1.2,2.0) **	2.0 (1.6,2.9)	1.6 (1.3,2.1)	1.7 (1.3,2.1)	1.4 (1.2,2.0)*	1.6 (1.3,2.6)	1.7 (1.3,1.9)	2.2 (1.7,2.4)	1.3 (1.1,1.6)*

Coagulation function

PT, s	13.5	12.8	13.6	12.9	13.4	12.8	13.4	12.9	13.2	12.8
	(13.1,14.0)	(12.4,13.5) **	(13.3,14.3)	(12.5,13.7)*	(13.1,14.0)	(12.3,13.3)**	(13.0,13.9)	(12.4,13.3)	(12.4,13.6)	(12.5,13.4)
PTA, %	96.0	84.9	90.5	84.4	96.0	85.4	94.0	84.1	74.5	85.7
	(87.0,101.5)	(79.1,89.5) **	(76.8,96.0)	(77.6,87.9)	(87.0,102.0)	(80.6,90.2)**	(88.0,102.0)	(80.7,89.6)	(65.8,98.2)	(79.3,88.1)
Fib, g/L	3.6 (2.8,4.4)	2.9 (2.6,3.4) **	2.8 (2.3,3.4)	2.6 (2.3,2.8)	3.6 (2.9,4.3)	3.0 (2.7,3.5)**	4.6 (3.6,5.8)	3.5 (3.3,3.7)	3.9 (3.2,4.3)	3.3 (2.8,3.5)

Inflammatory indicator

SAA, mg/L	49.1	12.3	NA	7.8	14.4	14.0	192.6	66.8	44.5	58.3
	(4.0,146.4)	(6.1,52.2)	(NA,NA)	(4.0,13.5)	(4.0,71.5)	(6.6,49.9)	(150.8,258.5)	(21.1,124.4)**	(44.5,44.5)	(19.4,144.6)
CRP, g/L	9.0	9.0	9.0	9.0	9.0	9.0	36.5	12.6	31.9	24.7
	(9.0,22.0)	(9.0,13.4) *	(9.0,9.0)	(9.0,9.0)	(9.0,15.0)	(9.0,12.9)	(17.0,63.4)	(11.0,22.9)*	(20.4,47.7)	(12.2,41.1)
PCT, ng/ml	0 (0,0.1)	0.1 (0,0.1) **	0 (0,0.1)	0.1 (0,0.1)	0 (0,0.1)	0.1 (0,0.1)**	0.1 (0.1,0.2)	0.1 (0.1,0.1)	0.1 (0.1,0.2)	0.1 (0.1,0.1)

Radiologic findings, n/N (%)

Bilateral pneumonia	177/258 (69)	71/157 (45) **	5/21 (24)	4/40 (10)	133/195 (68)	50/97 (52)**	30/30 (100)	6/8 (75)	9/12 (75)	11/12 (92)
Unilateral pneumonia	39/258 (15)	34/157 (22)	1/21 (5)	4/40 (10)	36/195 (18)	28/97 (29)	0/30 (0)	1/8 (12)	2/12 (17)	1/12 (8)
Ground glass opacity	153/258 (59)	48/156 (31)**	4/21 (19)	3/40 (7)	121/195 (62)	40/97 (41)**	22/30 (73)	2/8 (25)*	6/12 (50)	3/11 (27)
Multiple mottling	181/258 (70)	65/156 (42)**	5/21 (24)	5/40 (12)	139/195 (71)	51/97 (53)**	28/30 (93)	2/8 (25)**	9/12 (75)	7/11 (64)
Pleural effusion	17/258 (7)	5/157 (3)	0/21 (0)	0/40 (0)	9/195 (5)	1/97 (1)	6/30 (20)	0/8 (0)	2/12 (17)	4/12 (33)
Pleural thickening	21/258 (8)	7/156 (4)	0/21 (0)	0/40 (0)	14/195 (7)	3/96 (3)	6/30 (20)	1/8 (12)	1/12 (8)	3/12 (25)

1. Data are median (IQR) and n/N (%). N is the total number of patients with available data.

2. *$p<0.05$, ** $p<0.01$ compared with the wild type strain. p values were calculated by Mann-Whitney U test, χ^2 test or Fisher's exact test, as appropriate.

3. [†]: mild cases in Delta group consisted of 12 asymptomatics.

4. Abbreviations: WT strain, wild-type strain; NLR, neutrophils-to-lymphocytes ratio; HGB, hemoglobin; ALT, alanine transaminase; AST, aspartate aminotransferase; TB, total bilirubin; Alb, albumin; LDH, lactate dehydrogenase; CK, creatine kinase; LAC, lactic acid; PT, prothrombin time; PTA, prothrombin activity; Fib, fibrinogen; SAA, serum amyloid A protein; CRP, C-reactive protein; PCT, procalcitonin.

Appendix Table S2. Demographics and baseline characteristics of cases infected with the wild-type strain with and without exact exposure times

Covariate	Total (n=260)	Cases without exact exposure times (n=53)	Cases with exact exposure times (n=207)	p-value
Demographics				
Sex, n (%)				1
Male	119 (46)	24 (45)	95 (46)	
Female	141 (54)	29 (55)	112 (54)	
Age (years)				
Median (Min, Max)	49 (1, 90)	49 (1, 90)	49 (5, 84)	0.75
< 18, n (%)	7 (3)	3 (6)	4 (2)	0.28
18-59, n (%)	170 (65)	32 (60)	138 (67)	
≥ 60, n (%)	83 (32)	18 (34)	65 (31)	
Atopic, n (%)	22 (8)	5 (9)	17 (8)	0.99
Smoking history, n (%)	21 (8)	3 (6)	18 (9)	0.66
Drinking history, n (%)	11 (4)	2 (4)	9 (4)	1
Disease severity				0.72
Mild, n (%)	21 (8)	3 (6)	18 (9)	
Moderate, n (%)	196 (75)	40 (75)	156 (75)	
Severe, n (%)	30 (12)	6 (11)	24 (12)	
Critical, n (%)	13 (5)	4 (8)	9 (4)	
PCR cycle threshold values				
N gene (peak) Median (IQR)	31.2 (28.0, 36.0)	32.0 (27.2, 37.0)	31.0 (28.0, 36.0)	0.70
ORF1a/b gene (peak) Median (IQR)	34.0 (30.0, 38.0)	34.0 (29.0, 38.5)	34.0 (30.0, 37.0)	0.51

Data are median (IQR), median (min, max) and n (%).

Appendix Table S3. Demographics and baseline characteristics of cases infected with the Delta VOC with and without exact exposure times.

Covariate	Total (n=159)	Cases without exact exposure times (n=32)	Cases with exact exposure times (n=127)	*p*-value
Demographics				
Sex, n (%)				0.80
Male	64 (40)	14 (44)	50 (39)	
Female	95 (60)	18 (56)	77 (61)	
Age (years)				
Median (Min, Max)	47 (1, 92)	58.5 (4, 85)	46 (1, 92)	0.32
< 18, n (%)	26 (13)	5 (16)	21 (17)	0.14
18-59, n (%)	81 (55)	12 (38)	69 (54)	
≥ 60, n (%)	52 (33)	15 (47)	37 (29)	
Atopic, n (%)	5 (3)	1 (3)	4 (3)	1
Smoking history, n (%)	12 (8)	4 (12)	8 (6)	0.42
Drinking history, n (%)	1 (1)	0 (0)	1 (1)	1
Disease severity				0.24
Mild, n (%)	41 (26)	11 (34)	30 (24)	
Moderate, n (%)	98 (62)	15 (47)	83 (65)	
Severe, n (%)	8 (5)	3 (9)	5 (4)	
Critical, n (%)	12 (8)	3 (9)	9 (7)	
PCR cycle threshold values				
N gene (peak) Median (IQR)	19.0 (16.1, 22.3)	18.2 (17.1, 23.6)	19.1 (16.1, 22.1)	1
ORF1a/b gene (peak) Median (IQR)	20.6 (17.7, 23.6)	19.6 (18.6, 23.5)	20.6 (17.6, 23.6)	0.88

Data are median (IQR), median (min, max), n (%).