



Early View

Original article

Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China

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Articles (Fast-track)

Clinical characteristics and outcomes of hospitalized patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China

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Abstract

BACKGROUND: During the outbreak of coronavirus disease 2019 (COVID-19), consistent and considerable differences in disease severity and mortality rate of patients treated in Hubei province compared to those in other parts of China has been observed. We sought to compare the clinical characteristics and outcomes of patients being treated inside and outside Hubei province, and explore the factors underlying these differences.

METHODS: Collaborating with the National Health Commission, we established a retrospective cohort to study hospitalized COVID-19 cases in China. Clinical characteristics, the rate of severe events and deaths, and the time to critical illness (invasive ventilation or intensive care unit admission or death) were compared between patients in and outside of Hubei. The impact of Wuhan-related exposure (a presumed key factor that drove the severe situation in Hubei, as Wuhan is the epicenter as well the administrative center of Hubei province) and the duration between symptom onset and admission on prognosis were also determined.

RESULTS: Upon data cut-off (Jan 31st, 2020), 1,590 cases from 575 hospitals in 31 provincial administrative regions were collected (core cohort). The overall rate of severe cases and mortality was 16.0% and 3.2%, respectively. Patients in Hubei (predominantly with Wuhan-related exposure, 597/647, 92.3%) were older (mean: 49.7 vs. 44.9 years), had more cases with comorbidity (32.9% vs. 19.7%), higher symptomatic burden, abnormal radiologic manifestations, and, especially, a longer waiting time between symptom onset and admission (5.7 vs. 4.5 days) compared with patients outside Hubei. Patients in Hubei [severe event rate 23.0% vs. 11.1%, death rate 7.3% vs. 0.3%, hazards ratio (HR) for critical illness 1.59, 95%CI 1.05-2.41] have a poorer prognosis compared with patients outside of Hubei after adjusting for age and comorbidity. However, among patients outside of Hubei, the duration from symptom onset to hospitalization (mean: 4.4 vs. 4.7 days) and prognosis (HR 0.84, 95%CI 0.40-1.80) were similar between patients with or without Wuhan-related exposure. In the overall population, the waiting time, but neither treated in Hubei nor Wuhan-related exposure, remained an independent prognostic factor (HR 1.05, 1.01-1.08).

CONCLUSION: There were more severe cases and poorer outcomes for COVID-19 patients treated in Hubei, which might be attributed to the prolonged duration of symptom onset to hospitalization in the epicenter. Future studies to determine the reason for delaying hospitalization are warranted.

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Key words: SARS-CoV-2; COVID-19; Hubei; Wuhan; clinical characteristics; prognosis

Short title: COVID-19 inside and outside Hubei

Introduction

A rapid outbreak of coronavirus disease 2019 (COVID-19) that arises from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, originates in Wuhan city, Hubei province in China and has become a global threat.^{1,2} COVID-19 can result in severe illnesses such as acute respiratory distress syndrome (ARDS), multiorgan dysfunction syndrome (MODS), and resultant death.¹⁻³ The World Health Organization (WHO) declared the SARS-CoV-2 a public health emergency of international concern on 30th Jan. As of February 16th, 2020, 58,873 laboratory-confirmed cases and 1,699 deaths have been documented globally.⁴

Considerable differences in disease severity and patient mortality in Hubei province with other parts of China have been documented.⁵ Most primarily infected patients have been identified and treated in Hubei province, predominantly have close exposure to Wuhan. This is because Wuhan, the epicenter of COVID-19, is the administrative center of Hubei province and the majority of the population displaced from Wuhan have temporarily relocated to other areas of Hubei. But contrary to the initial wave of cases, an increasing number of patients have been diagnosed outside Wuhan and/or Hubei province, many of whom did not have close contact with people from Wuhan. These patients were more likely to have been infected by secondary or tertiary transmission of SARS-CoV-2. Other investigators have assumed that the high percentage of patients with Wuhan-related exposure (indicating potentially higher virulence) drove the severe situation in Hubei.⁶

Exploring the difference between patients in and outside the highly endemic area, as well as by primary and progeny virus, may help clinicians better appreciate the evolution of SARS-CoV-2, and lead to more efficient allocation of healthcare resources. In addition, the exploration of the driving forces underlying these observations such as virus virulence and temporary shortage of health resources may help inform clinical practice and disease prevention. In this nationwide study, we sought to compare the clinical characteristics and outcomes of patients with COVID-19 between these populations, and explore the factors contributing to these differences.

Methods

Data sources

On behalf of the National Clinical Research Center for Respiratory Disease, and collaborating with the National Health Commission of the People's Republic of China, we have established a retrospective cohort to study the COVID-19 cases throughout China. We obtained medical records and compiled the data from laboratory-confirmed hospitalized cases with COVID-19 reported to the China National Health Commission between November 21st, 2019 and January 31st, 2020. The National Health Commission requested that all hospitals submit clinical records to the database. Hospitals whose clinical records had not been submitted by this deadline were requested again by the National Health Commission. Confirmed cases of COVID-19 were defined as patients who tested positive by high-throughput sequencing or real-time reverse-transcription polymerase-

chain-reaction (RT-PCR) assay for nasal and pharyngeal swab specimens. Only laboratory-confirmed cases were included in our analysis.

Data extraction and processing

A team of experienced respiratory clinicians reviewed and abstracted the data. Data were entered into a computerized database and cross-checked. In the surveillance cohort, we included all patients in the daily report, with only the location and patient's clinical status (severity, live and discharge status). In the core cohort, baseline, examination and treatment information was available and collected. The recent exposure history, clinical symptoms and signs, and laboratory findings upon admission were extracted from electronic medical records. Radiologic assessments, including chest X-ray or computed tomography (CT), were performed based on the documentation/description in medical charts or combined with, if imaging films were available, a review by our medical staff. Major disagreement between two reviewers was resolved by consultation with the third reviewer. We defined the severity of COVID-19 (severe vs. non-severe) based on the American Thoracic Society guidelines for community-acquired pneumonia given its extensive acceptance.⁷

Patients with Wuhan-related exposure were defined as patients who lived in or recently traveled to Wuhan, or had recent close contact with people from Wuhan, confirmed by China centers for disease control and prevention (CDC) according to the self-report by patients and survey by the local CDC staff. We compared the differences in clinical characteristics and treatments. In terms of prognosis, the primary endpoint was critical illness including admission to the intensive care unit (ICU), or invasive ventilation, or death. We adopted this endpoint because admission to ICU, invasive ventilation, and death are serious outcomes of COVID-19 that have been adopted in a previous study to assess the severity of other serious infectious diseases, such as the avian influenza H7N9 virus.⁸ Secondary endpoints consisted of the mortality rate, and the time from symptom onset to the critical illness and each of its components. We specifically examined the duration from symptom onset to admission.

Due to the great confounding impact of age and comorbidity on the prognosis of COVID-19, we sought to evaluate the prognostic effect of each candidate variable based on adjustment for age and comorbidity [including chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, coronary heart disease, cerebrovascular disease, viral hepatitis type B, malignant tumor, chronic kidney disease and immunodeficiency]. Therefore, we pre-planned several Cox regression analyses to evaluate the prognostic impact of 1) Hubei location alone; 2) Wuhan-related exposure alone; and 3) Wuhan-related exposure in patients outside Hubei. In addition, we planned to test a hypothesis that the time from symptom onset to hospitalization might underly the difference in prognosis between the location and contact history. Thus, we included Hubei location, Wuhan-related exposure, time from symptom onset to hospitalization, age and comorbidity in a Cox model.

Statistical analysis

Continuous variables were expressed as the means and standard deviations or medians and interquartile ranges (IQR) as appropriate. Categorical variables were summarized as the counts and percentages in each category. Wilcoxon rank-sum tests were applied to continuous variables, chi-square tests and Fisher's exact tests were used for categorical variables as appropriate. The risk of reaching to the critical illness and the potential risk factors were analyzed using proportional hazard (PH) Cox regression models when PH assumption was not violated. We tested the PH assumption by modeling the log-log of survival curve using each variable included as strata, if the curve did not cross at all time points, the PH assumption was considered not violated. The hazards ratio (HR) along with the 95% confidence interval (95%CI) were reported. To visualize the probability of reaching critical illness of different categories, we presented the hazard function curves estimated by Cox regression model which have adjusted for all included confounders. The significance of the difference between the curves were obtained from the Cox regression model. Significance level was set at P value <0.05. All analyses were conducted with SPSS software version 23.0 (Chicago, IL, USA).

Role of the funding source

The funder had no role in the study design, data collection, analysis and interpretation, or writing of the report. The corresponding authors had full access to all data and had the final responsibility for the decision to submit for publication.

Results

Nationwide Epidemiology Surveillance of COVID-19

Up to January 31st, 2020, a total of 11,791 patients with laboratory-confirmed COVID-19 were identified in China. The flowchart of cohort establishment was shown in **Figure S1**. Of these, 7,153 (60.7%) patients were identified in Hubei province. The severe cases accounted for 15.9% of the whole cohort, and 19.2% and 11.0% within and outside Hubei province, respectively. The overall mortality was 2.20% throughout China (3.48% in Hubei province, 0.22% outside Hubei province) (**Figure 1**). The latest data has shown a similar trend as of February 15, 2020 (**Figure S1&2**).

Patient characteristics in the core cohort

In the core cohort, we have collected 1,590 cases from 575 hospitals in 31 provincial administrative regions (full list in online supplement p4-9) upon data cut-off on Jan 31st. Our dataset covered 13.4% (1,590/11,791) of all cases being reported and covered 91.2% of regions (31/34) that had confirmed cases (**Figure 2**). Overall, the mean age was 48.9 years; 904 patients (57.3%) were males and 399 (25.1%) had coexisting conditions, including hypertension (269 [16.9%]), diabetes (130 [8.2%]), and cardiovascular disease (59 [3.7%]). Fever (88.0%), dry cough (70.2%), fatigue (42.8%), productive cough (36.0%), and shortness of breath (20.8%) were the most common symptoms. Most patients (71.1%) had abnormal chest CT manifestations. The overall rate of severe cases and mortality was 16.0% and 3.2%, respectively. Details were summarized in **Table 1**.

Patients treated inside Hubei and outside Hubei

As shown in **Table 1**, 40.7% of the patients from the core dataset were hospitalized in Hubei province (647/1590). Most patients (597/647, 92.3%) in Hubei province had Wuhan-related exposure. Patients in Hubei province were older (mean: 55.1 vs. 44.6 years) and had more cases with comorbidity (32.9% vs. 19.7%). Patients in Hubei province had a higher symptomatic burden including fatigue (46.4% vs. 40.3%), productive cough (40.2% vs. 33.1%), shortness of breath (36.3% vs. 10.2%), myalgia or arthralgia (20.3% vs. 15.5%), nausea or vomiting (8.1% vs. 4.2%), hemoptysis (2.3% vs. 0.5%), and unconsciousness (2.7% vs. 0.5%), but not pharyngalgia (11.3% vs. 17.0%) compared to non-Hubei patients. Moreover, patients in Hubei province were more likely to have abnormal chest radiograph (18.1% vs. 13.4%) and CT (74.7% vs. 68.6%) manifestations. Patients in Hubei province also had a longer duration from symptom onset to hospitalization (5.7 vs. 4.5 days) compared with patients outside of Hubei province.

Patient with vs. without Wuhan-related exposure

The majority of patients (1,334/1,590, 83.9%) in this dataset had Wuhan exposure history (18.1% lived in Wuhan, 36.7% recently traveled to Wuhan, and 45.1% had recent contact with people from Wuhan). Compared with those that had no exposure to Wuhan, Wuhan-exposed patients were significantly older (mean: 49.7 vs. 44.9 years) and had more cases with comorbidity (26.3% vs. 18.8%, $P=0.012$), including hypertension (18.1% vs. 10.5%), diabetes (8.8% vs. 4.7%), and malignancy (1.3% vs. 0%); fever (88.0% vs. 87.7%), fatigue (43.2% vs. 40.7%), and shortness of breath (21.8% vs. 15.6%). Furthermore, abnormal manifestation in chest radiograph (16.2% vs. 10.5%) and CT (71.9% vs. 66.8%) were more commonly seen in patients with Wuhan-related exposure than their counterparts. **Table 1** summarized detailed information.

Patient with vs. without Wuhan-related exposure outside Hubei

Of 943 patients outside of Hubei province, 737 (78.2%) reported Wuhan-related exposure. There were no differences in patient's clinical characteristics, signs, comorbidities, the rate of abnormal chest images, and most symptoms between patients with and without Wuhan-related exposure. However, Wuhan-related patients reported less productive cough (30.5% vs. 43.8%) and shortness of breath (8.7% vs. 15.5%) than their counterparts. See details in **Table 2**. The duration from symptom onset to hospitalization was similar between patients with and without Wuhan-related exposure (mean: 4.4 vs. 4.7 years) treated outside of Hubei province.

Prognostic analyses

As shown in **Figure 3**, both patients treated in Hubei province (23.0% vs. 11.1%, $P<0.001$) and those with Wuhan-related exposure (16.9% vs. 11.3%, $P=0.026$) had more severe or fatal cases compared to their counterparts. Similarly, Hubei patients (7.3% vs. 0.3%, $P<0.001$) and patients with Wuhan-related exposure (3.6% vs. 0.8%, $P=0.017$) had a higher mortality rate. After adjusting for age and comorbidity, the Cox regression model without PH assumption violation revealed that patients in Hubei province (HR 1.59, 95%CI 1.05-2.41; $P=0.027$, **figure 4A**) and those with Wuhan exposure history (HR 1.34, 95%CI 0.70-2.57; $P=0.385$, **figure 4B**) were more likely to reach critical illness. Details were

summarized in **Table S1-3**.

We further subdivided patients with Wuhan-related exposure according to the location of hospitals. Patients with Wuhan exposure history who underwent treatment outside of Hubei province had a better prognosis compared with those treated in Hubei (HR 0.57, 95%CI 0.36-0.91, $P=0.018$, **Figure 4C**), and yielded similar outcomes compared with patients with no Wuhan exposure history (HR 0.84, 95%CI 0.40-1.80, $P=0.653$, **Figure 4C&D**). Most importantly, after being included in the Cox regression model, the duration from symptom onset to hospitalization, but not Hubei or Wuhan-related exposure, remained an independent factor of the prognosis among the general population (HR 1.05, 1.01-1.08, $P=0.005$) (**Table 3**).

Discussion

Although the pandemic has lessened in China and the results reported here focused on the early stage of the outbreak, an increasing number of patients have been diagnosed outside China and some other areas have become new epicenters, such as Lombardia, Italy and Madrid, Spain. Summarizing the experience from China and providing in-depth understanding of the situation in the previous epicenter can help to improve the strategy in the current epicenters. For the situation outside of the epicenter Hubei, two studies presented characteristics and outcomes among patients outside Hubei in Shenzhen and Zhejiang, however, the sample size is small therefore, comparison to Hubei patients cannot be performed.^{9,10} To our knowledge, this is the first nationwide study in China investigating the differences in the clinical characteristics and the prognosis of patients with COVID-19 between both those in and outside of Hubei province, and those with and without Wuhan-related exposure. We believe that our core cohort could partially represent the overall situation as of Jan 31st, taking into account the patient number (13.4% of all cases) and the broad coverage (covering almost all major provinces/cities/autonomous regions). Moreover, this dataset showed consistent epidemiological characteristics with the surveillance dataset, indicating that it represented the real-world conditions.

Compared with those with contact history with people from Wuhan or living in Hubei province, patients without Wuhan-related exposure or living outside of Hubei were younger, had fewer comorbidities, less abnormal chest radiographic manifestations, and slightly lower symptom burden. These findings suggested a potentially augmented infectivity in the general population beyond fragile individuals (i.e., the elderly). This is in agreement with the median reproduction number (R_0), which has increased from 2.0 in early studies to 3.8 in more recent studies.^{11,12} In addition, viral genome sequencing of cases from Hubei province and other regions/countries has also lent support to the continuous evolution in the viral functional regions that facilitates its transmission among the human population (self-adaptation).¹³ However, we should be cautious about the bias resulting from the undiagnosed cases in the early phase of transmission when most people were not aware of this disease.

It has been believed that the onward transmission of a virus might result in attenuated

disease.^{14,15} Our results showed fewer severe events and a lower mortality rate among patients outside of Hubei province and patients that had no history of Wuhan-related exposure. However, these results might have been biased by the temporary shortage of health resources, such as the limited hospital performance and detection capacity, that resulted from the sudden outbreak of COVID-19 in Hubei. After the surge of cases in January 2020, hospitals in Hubei province were heavily overloaded and managed an overwhelming increase in the number of patients. These shortages could have led to a delay in the diagnosis and treatment of patients, which further contributed to the worsening of overall status upon admission and an increased risk of death.

In this study, we have included the duration from symptom onset to admission to evaluate the impact of the healthcare capacity on the difference between Hubei and other regions in China. Significantly longer waiting time was observed among patients in Hubei province, whereas patients with or without Wuhan-related exposure shared similar waiting time outside of Hubei province. Importantly, we have found that the prolonged waiting time, rather than the geographic location or the Wuhan-related exposure history, predicted the clinical prognosis of COVID-19. We speculated that some patients from Wuhan traveled to other cities outside of Hubei province seeking more timely treatment. These patients reported a similar waiting time and medical care records, which translated into a similar prognosis with the local residents. Consistently, the incidence of severe cases and mortality continuously decreased (**figure S1**) since clinicians, nurses, and medical instruments have been dispatched to Hubei province. On the other hand, timely screening of candidates with suspected symptoms or contact with confirmed cases might help promptly initiate medical care, thus preventing further spreading of the disease.

There are some limitations of this study. First, although we made every effort to collect data from all patients, some hospitals did not answer our request. Thus, although the dataset had a broad coverage of all patients and regions, the non-responsive bias cannot be fully excluded. Second, the date of symptom onset is self-report based, bias from patient recall might exist. Third, we cannot evaluate the exact healthcare capacity of each hospital but used a duration from symptom onset to admission as an indirect measure. Fourth, only a small proportion of patients had Wuhan exposure history, which may give a non-balanced result with some possible bias. Fifth, some other factors that may have impact on the prognosis, e.g. secondary infection, cannot be evaluated in this study. In addition, a significant proportion of people infected by the SARS-CoV-2 are asymptomatic and were not included in this study of hospitalized patients, the situation in the general infected population requires further studies.

Our findings indicate that the temporary shortage in health capacity in the outbreak epicenter, rather than the transmission history, has resulted in the large number of severe cases or deaths in Hubei province. These results have expanded our understanding of patients infected by secondary or tertiary transmission which will account for the majority of patients that are infected worldwide, and provided timely and important implications for basic research and establishing public health policy. Adequate management of health care

resources as well as the public's response is important to mitigate the impact of the outbreak. This study highlights the necessity of urgent and vigorous support of healthcare resources and increased public awareness during the early stages of an outbreak of COVID-19 or similar diseases.

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Figure legends

Figure 1. Severe and deaths cases in China, inside Hubei and outside Hubei as of Jan 31, 2020. * The severe events and death events were reported by different statistic sources so that presented slight difference in total number.

Figure 2. Shown are the official statistics of all documented laboratory-confirmed cases throughout China according to the National Health Commission (as of Jan 31st, 2020). The numerator denoted the number of patients being finally included in the data analysis for each province/autonomous region/provincial municipalities, while the denominator denoted the number of laboratory-confirmed cases for each province/autonomous region/provincial municipalities as reported by the National Health Commission.

Figure 3. Severe and deaths cases in Hubei and outside Hubei, Wuhan-related exposure vs. no Wuhan-related exposure

Figure 4. A, The time-dependent risk of reaching to the critical illness between patients in and outside Hubei province; B, The time-dependent risk of reaching to the critical illness between patients with and without Wuhan-related exposure; C, The time-dependent risk of reaching to the critical illness among patients in Hubei province who had Wuhan-related exposure, patients outside Hubei province who had Wuhan-related exposure, and patients outside Hubei province who did not have a Wuhan-related exposure; D, The time-dependent risk of reaching to the critical illness between patients treated outside Hubei with and without Wuhan-related exposure.

Table 1. Clinical characteristics and outcomes of patients with COVID-19 stratified by Hubei hospitalization and Wuhan-related exposure.

	Total (n=1590)	In Hubei (n=647)	Outside Hubei (n=943)	P Value	No Wuhan-related exposure (n=256)	Wuhan-related exposure (n=1334)	P Value
Characteristics							
Age, years	48.9±16.3	55.1±15.4	44.6±15.5	<0.001	44.9±14.6	49.7±16.5	<0.001
Sex				0.756			0.782
Male	904/1578 (57.3%)	369/638 (57.8%)	535/940 (56.9%)		148/254 (58.3%)	756/1324 (57.1%)	
Female	674/1578 (42.7%)	269/638 (42.2%)	405/940 (43.1%)		106/254 (41.7%)	568/1324 (42.9%)	
Smoking status				0.367			0.505
Never/unknown	1479 (93.0%)	597 (92.3%)	882 (93.5%)		241 (94.1%)	1238 (92.8%)	
Former/current	111 (7.0%)	50 (7.7%)	61 (6.5%)		15 (5.9%)	96 (7.2%)	
Comorbidities							
Any	399 (25.1%)	213 (32.9%)	186 (19.7%)	<0.001	48 (18.8%)	351 (26.3%)	0.012
COPD	24 (1.5%)	14 (2.2%)	10 (1.1%)	0.094	2 (0.8%)	22 (1.6%)	0.408
Diabetes	130 (8.2%)	79 (12.2%)	51 (5.4%)	<0.001	12 (4.7%)	118 (8.8%)	0.025
Hypertension	269 (16.9%)	156 (24.1%)	113 (12.0%)	<0.001	27 (10.5%)	242 (18.1%)	0.003
Cardiovascular disease	59 (3.7%)	38 (5.9%)	21 (2.2%)	<0.001	7 (2.7%)	52 (3.9%)	0.471
Cerebrovascular disease	30 (1.9%)	24 (3.7%)	6 (0.6%)	<0.001	2 (0.8%)	28 (2.1%)	0.210
Hepatitis B infection	28 (1.8%)	9 (1.4%)	19 (2.0%)	0.439	6 (2.3%)	22 (1.6%)	0.436
Malignancy	18 (1.1%)	12 (1.9%)	6 (0.6%)	0.030	0 (0%)	18 (1.3%)	0.097
Chronic kidney disease	21 (1.3%)	16 (2.5%)	5 (0.5%)	0.001	3 (1.2%)	18 (1.3%)	1.000
Immunodeficiency	3 (0.2%)	2 (0.3%)	1 (0.1%)	0.570	0 (0%)	3 (0.2%)	1.000
Symptoms							
Any	1517 (95.4%)	621 (96%)	896 (95.0%)	0.395	237 (92.6%)	1280 (96.0%)	0.023
Fever	1351/1536	552/623 (88.6%)	799/913 (87.5%)	0.576	213/243 (87.7%)	1138/1293 (88.0%)	0.914

	(88.0%)						
Conjunctival congestion	10/1345 (0.7%)	3/554 (0.5%)	7/791 (0.9%)	0.538	3/192 (1.6%)	7/1153 (0.6%)	0.161
Nasal congestion	73/1299 (5.6%)	24/535 (4.5%)	49/764 (6.4%)	0.144	11/185 (5.9%)	62/1114 (5.6%)	0.863
Headache	205/1328 (15.4%)	94/540 (17.4%)	111/788 (14.1%)	0.105	30/191 (15.7%)	175/1137 (15.4%)	0.914
Dry cough	1052/1498 (70.2%)	450/617 (72.9%)	602/881 (68.3%)	0.058	167/233 (71.7%)	885/1265 (70.0%)	0.640
Pharyngalgia	194/1317 (14.7%)	60/530 (11.3%)	134/787 (17.0%)	0.004	31/194 (16.0%)	163/1123 (14.5%)	0.584
Productive cough	513/1424 (36.0%)	234/582 (40.2%)	279/842 (33.1%)	0.007	94/218 (43.1%)	419/1206 (34.7%)	0.021
Fatigue	584/1365 (42.8%)	255/549 (46.4%)	329/816 (40.3%)	0.026	85/209 (40.7%)	499/1156 (43.2%)	0.544
Hemoptysis	16/1315(1.2%)	12/533 (2.3%)	4/782 (0.5%)	0.008	2/189 (1.1%)	14/1126 (1.2%)	1.000
Shortness of breath	331 (20.8%)	235 (36.3%)	96 (10.2%)	<0.001	40 (15.6%)	291 (21.8%)	<0.029
Nausea/vomiting	80/1371 (5.8%)	46/568 (8.1%)	34/803 (4.2%)	0.003	12/200 (6.0%)	68/1171 (5.8%)	0.871
Diarrhea	57/1359 (4.2%)	28/559 (5.0%)	29/800 (3.6%)	0.218	9/195 (4.6%)	48/1164 (4.1%)	0.701
Myalgia/arthralgia	234/1338 (17.5%)	112/551 (20.3%)	122/787 (15.5%)	0.024	32/195 (16.4%)	202/1143 (17.7%)	0.760
Chill	163/1333 (12.2%)	77/547 (14.1%)	86/786 (10.9%)	0.090	35/191 (18.3%)	128/1142 (11.2%)	0.008
Signs							
Throat congestion	21/1286 (1.6%)	7/525 (1.3%)	14/761 (1.8%)	0.655	1/181 (0.6%)	20/1105 (1.8%)	0.343
Tonsil swelling	31/1376 (2.3%)	16/589 (2.7%)	15/787 (1.9%)	0.360	4/184 (2.2%)	27/1192 (2.3%)	1.000
Lymphadenectasis	2/1375 (0.1%)	2/588 (0.3%)	0/787 (0%)	0.183	0/189 (0%)	2/1186(0.2%)	1.000
Rash	3/1378 (0.2%)	2/583 (0.3%)	1/795 (0.1%)	0.577	0/191(0%)	3/1187(0.3%)	1.000
Unconsciousness	20/1421 (1.4%)	16/595 (2.7%)	4/826 (0.5%)	0.001	1/199 (0.5%)	19/1222 (1.6%)	0.342
Abnormal chest images							
Radiograph	243 (15.3%)	117 (18.1%)	126 (13.4%)	0.011	27 (10.5%)	216 (16.2%)	0.023
Computed tomography	1130 (71.1%)	483 (74.7%)	647 (68.6%)	0.010	171 (66.8%)	959 (71.9%)	0.114
Outcomes							
Critical illness	131 (8.24%)	95 (14.7%)	36 (3.8%)	<0.001	10 (3.9%)	121 (9.1%)	0.004

ICU admission	99 (6.23%)	68 (10.5%)	31 (3.3%)	<0.001	7 (2.7%)	92 (6.9%)	0.010
Invasive ventilation	50 (3.14%)	39 (6.0%)	11 (1.2%)	<0.001	4 (1.6%)	46 (3.4%)	0.168
Death	50 (3.14%)	47 (7.3%)	3 (0.3%)	<0.001	2 (0.8%)	48 (3.6%)	0.017

Data are mean± standard deviation, n (%), or n/N (%), where N is the total number of patients with available data. p values are calculated by χ^2 test, Fisher's exact test, or Mann-Whitney U test. COPD=chronic obstructive pulmonary disease.

Table 2. Clinical characteristics and outcomes of patients with COVID-19 with or without Wuhan-related exposure outside Hubei.

	no Wuhan-related exposure (n=206)	Wuhan-related exposure (n=737)	P Value
Characteristics			
Age, years	44.2±14.8	44.7±15.6	0.717
Sex			0.690
Male	119/204 (58.3%)	416/736 (56.5%)	
Female	85/204 (41.7%)	320/736 (43.5%)	
Smoking status			
Never/unknown	196 (95.1%)	686 (93.1%)	0.338
Former/current	10 (4.9%)	51 (6.9%)	
Comorbidities			
Any	46 (22.3%)	140 (19.0%)	0.322
COPD	2 (1.0%)	8 (1.1%)	1.000
Diabetes	11 (5.3%)	40 (5.4%)	1.000
Hypertension	25 (12.1%)	88 (11.9%)	0.904
Cardiovascular disease	7 (3.4%)	14 (1.9%)	0.190
Cerebrovascular disease	2 (1.0%)	4 (0.5%)	0.617
Hepatitis B infection	6 (2.9%)	13 (1.8%)	0.275
Malignancy	0 (0%)	6 (0.8%)	0.349
Chronic kidney disease	2 (1.0%)	3 (0.4%)	0.301
Immunodeficiency	0 (0%)	1 (0.1%)	1.000
Disease severity			
Non-severe	197 (95.6%)	710 (96.3%)	0.681
Severe	9 (4.4%)	27 (3.7%)	
Symptoms			
Any	188 (91.3%)	708 (96.1%)	0.010
Fever	168/194 (86.6%)	631/719 (87.8%)	0.713
Conjunctival congestion	2/148 (1.4%)	5/643 (0.8%)	0.621
Nasal congestion	7/140 (5.0%)	42/624 (6.7%)	0.568
Headache	21/145 (14.5%)	90/643 (14.0%)	0.895
Dry cough	134/184 (72.8%)	468/697 (67.1%)	0.154
Pharyngalgia	25/145 (17.2%)	109/642 (17.0%)	0.903
Productive cough	74/169 (43.8%)	205/673 (30.5%)	0.001
Fatigue	68/162 (42.0%)	261/654 (39.9%)	0.655
Hemoptysis	2/143 (1.4%)	2/639 (0.3%)	0.155
Shortness of breath	32 (15.5%)	64 (8.7%)	0.006
Nausea/vomiting	10/153 (6.5%)	24/650 (3.7%)	0.121

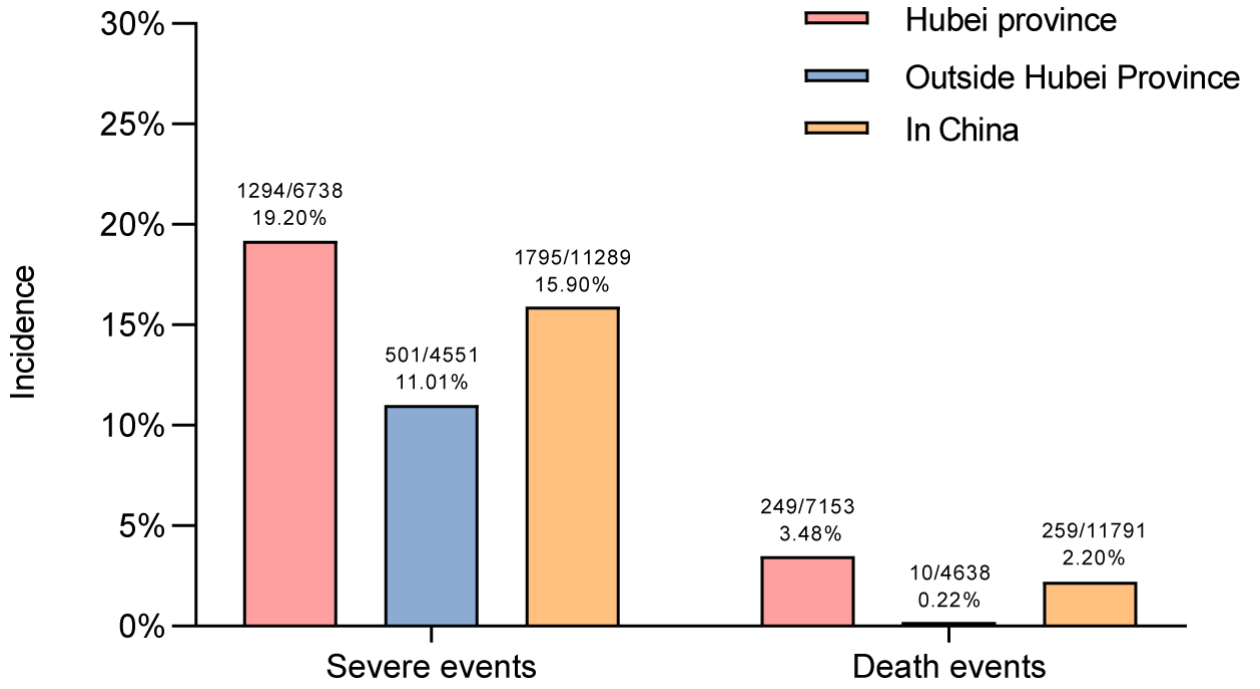
Diarrhea	8/148 (5.4%)	21/652 (3.2%)	0.221
Myalgia/arthralgia	21/148 (14.2%)	101/639 (15.8%)	0.706
Chill	23/146 (15.8%)	63/640 (9.8%)	0.055
Signs			
Throat congestion	1/135 (0.7%)	13/626 (2.1%)	0.484
Tonsil swelling	4/140 (2.9%)	11/647 (1.7%)	0.321
Lymphadenectasis	0/141(0%)	0/646(0%)	-
Rash	0/142 (0%)	1/653 (0.2%)	1.000
Unconsciousness	1/152 (0.7%)	3/674 (0.4%)	0.557
Abnormal chest images			
Radiograph	22 (10.7%)	104 (14.1%)	0.246
Computed tomography	136 (66.0%)	511 (69.3%)	0.396
Outcomes			
Critical illness	9 (4.4%)	27 (3.7%)	0.681
ICU admission	7 (3.4%)	24 (3.3%)	1.000
Invasive ventilation	4 (1.9%)	7 (0.9%)	0.269
Death	1 (0.5%)	2 (0.3%)	0.523

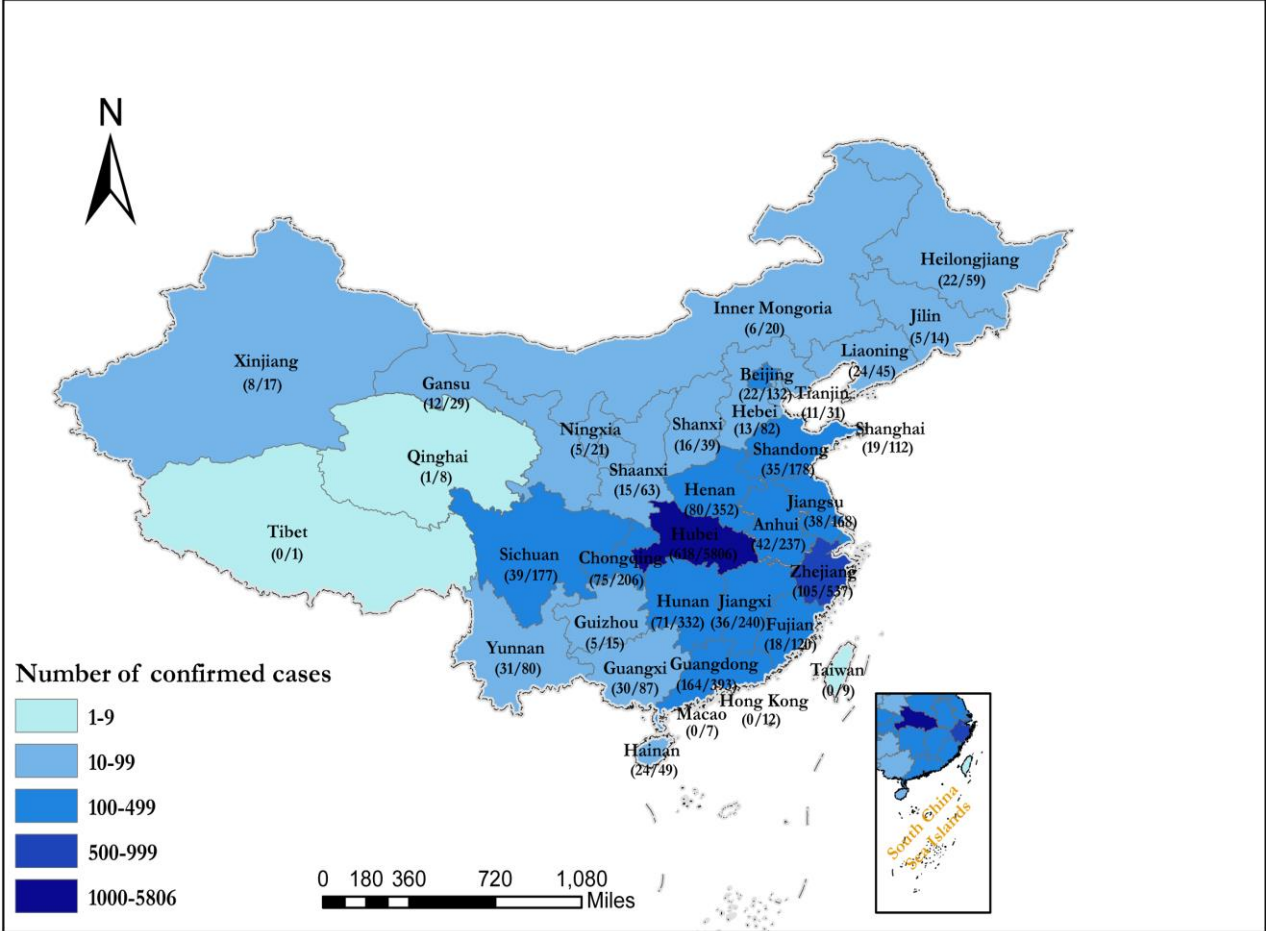
Data are mean± standard deviation, n (%), or n/N (%), where N is the total number of patients with available data. p values are calculated by χ^2 test, Fisher's exact test, or Mann-Whitney U test. COPD=chronic obstructive pulmonary disease.

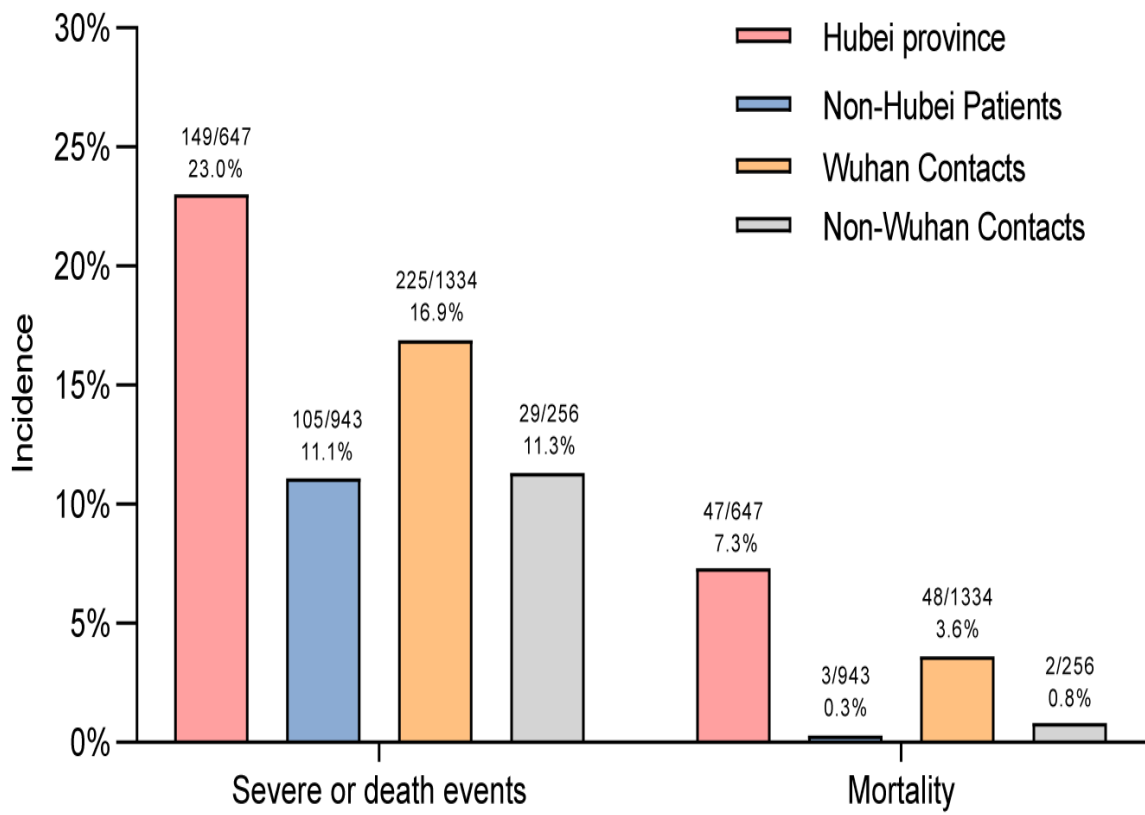
Table 3. Hazard ratios estimated by multivariate proportional hazard Cox model

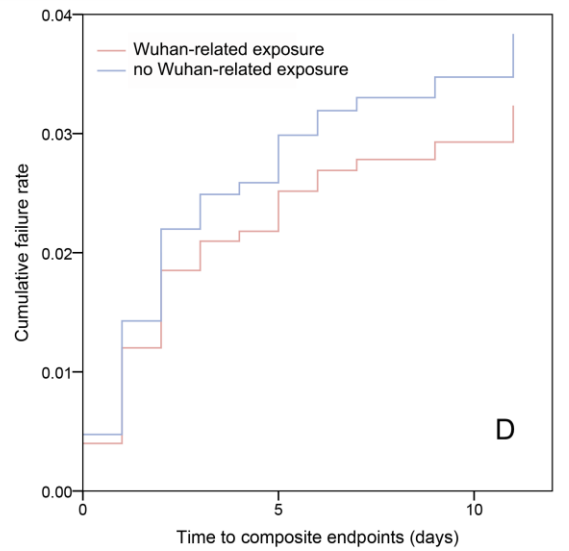
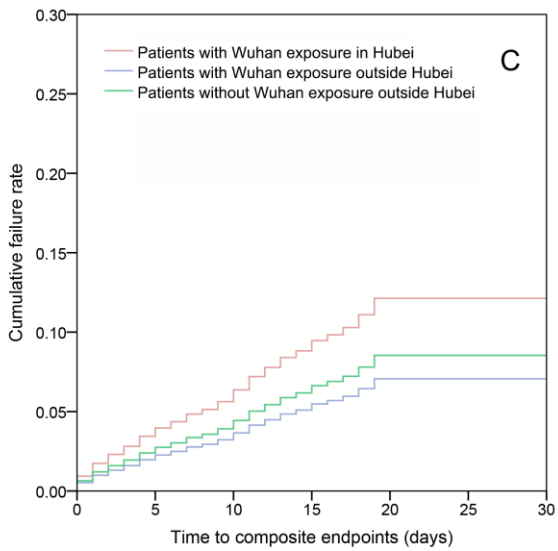
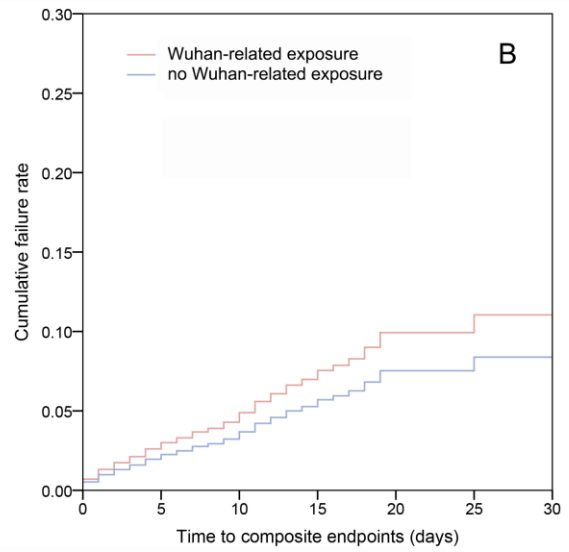
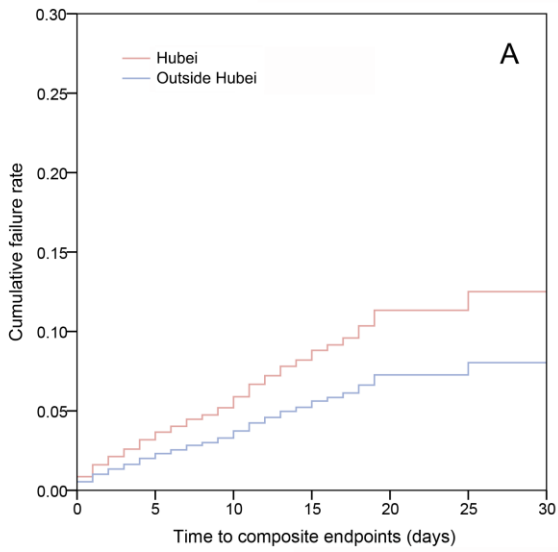
Variables	HR	LL	UL	P value
Age (continuous)	1.036	1.021	1.052	<0.001
Any comorbidity (yes vs. no)	2.132	1.393	3.261	<0.001
Wuhan-related exposure (yes vs. no)	1.13	0.556	2.296	0.735
Hubei location (yes vs. no)	1.333	0.86	2.065	0.198
From symptom onset to hospitalization (continuous)	1.045	1.013	1.078	0.005

HR: hazards ratio; LL: lower limit of the 95% confidence interval; UL: upper limit of the 95% confidence interval. Comorbidity included chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, coronary heart disease, cerebrovascular disease, viral hepatitis type B, malignant tumor, chronic kidney disease and immunodeficiency









Clinical characteristics and outcomes of hospitalized patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China

Online Supplement

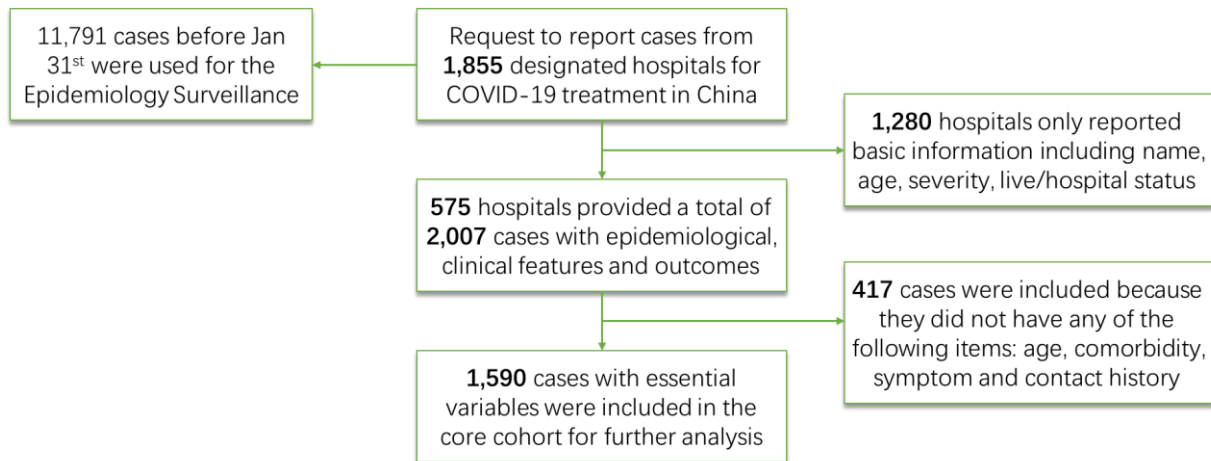


Figure S1. The flowchart of cohort establishment

As of February 15th, 2020, a total of 68,500 laboratory-confirmed cases have been identified in China. The largest percentage (82.12%) of cases were diagnosed in Hubei province (56,249 patients). The percentage of cases with severe pneumonia in Hubei province (21.20%) was higher than that outside of Hubei province (10.45%). The mortality was also higher in Hubei province (2.84% vs. 0.56%). (**Figure S3**). **Figure S2** shows the change of mortality rate in Hubei province, regions outside of Hubei province and the overall population who had laboratory-confirmed COVID-19.

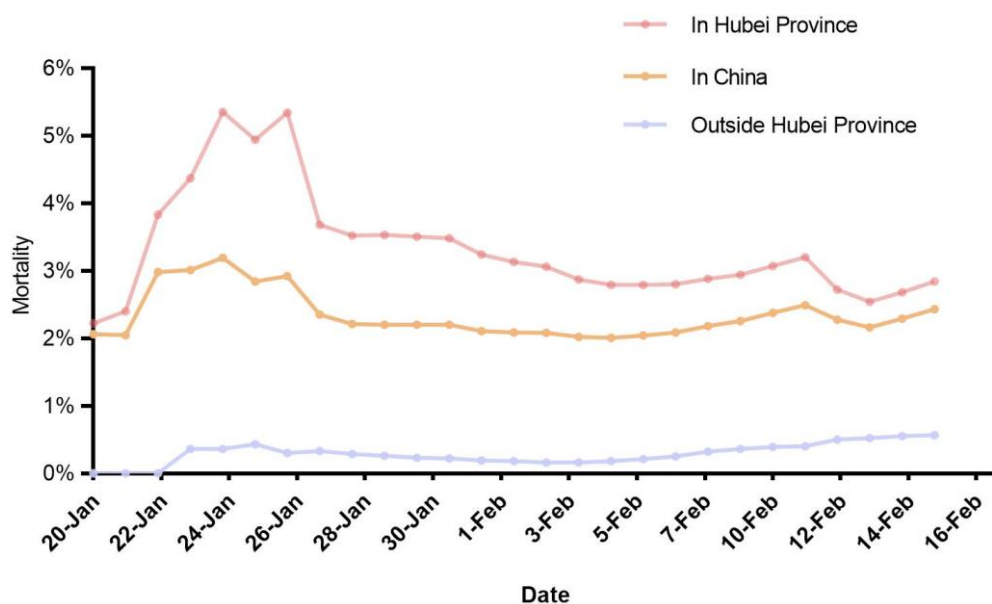


Figure S1. Trends of daily mortality stratified by the geographic location where patients with COVID-19 were diagnosed and managed. COVID-19: coronavirus disease 2019

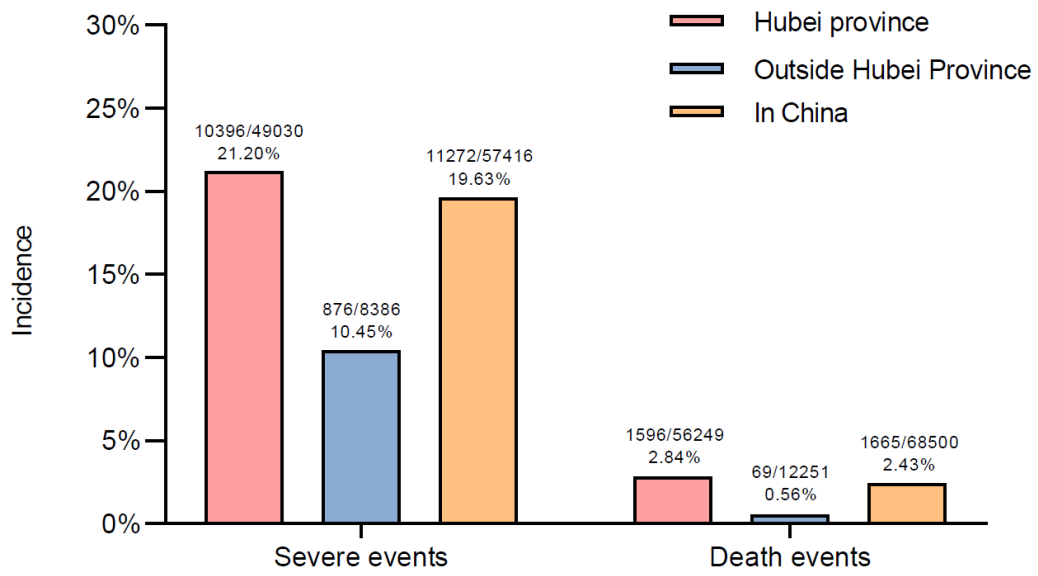


Figure S2. Severe and deaths cases in China, in Hubei and outside Hubei province as of Feb 15th, 2020

Table S1. Hazard ratios for patients treated in Hubei estimated by multivariate proportional hazard Cox model

Variables	HR	LL	UL	P value
Age (continuous)	1.036	1.021	1.05	<0.001
Any comorbidity (yes vs. no)	2.095	1.419	3.093	<0.001
Hubei location (yes vs. no)	1.594	1.054	2.412	0.027

HR: hazards ratio; LL: lower limit of the 95% confidence interval; UL: upper limit of the 95% confidence interval

Table S2. Hazard ratios for Wuhan-contacts estimated by multivariate proportional hazard Cox model

Variables	HR	LL	UL	P value
Age (continuous)	1.039	1.025	1.053	<0.001
Any comorbidity (yes vs. no)	2.114	1.433	3.119	<0.001
Wuhan contacts (yes vs. no)	1.336	0.695	2.57	0.385

HR: hazards ratio; LL: lower limit of the 95% confidence interval; UL: upper limit of the 95% confidence interval. Comorbidity included chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, coronary heart disease, cerebrovascular disease, viral hepatitis type B, malignant tumor, chronic kidney disease and immunodeficiency

Table S3. Hazard ratios for Wuhan-contacts vs. non-contacts outside Hubei province, estimated by multivariate proportional hazard Cox model

Variables	HR	LL	UL	P value
Age (continuous)	1.029	1.004	1.055	0.021
Any comorbidity (yes vs. no)	2.529	1.235	5.178	0.011
Wuhan contacts (yes vs. no)	0.841	0.395	1.79	0.653

HR: hazards ratio; LL: lower limit of the 95% confidence interval; UL: upper limit of the 95% confidence interval. Comorbidity included chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, coronary heart disease, cerebrovascular disease, viral hepatitis type B, malignant tumor, chronic kidney disease and immunodeficiency

List of hospitals reporting the included cases

Wuhan Jinyintan hospital, Union Hospital Affiliated to Tongji Medical College of Huazhong University of science and technology, Wuhan Central Hospital, Wuhan first hospital, Chengdu Public Health Clinical Medical Center, Huangshi Central Hospital, Shenzhen Third People's Hospital, Wuhan Pulmonary Hospital, Tianyou Hospital Affiliated to Wuhan University of science and technology, Changsha First Hospital, The third people's Hospital of Hainan Province, Huanggang Central Hospital, Wenling first people's Hospital, Yichang Third People's Hospital, Taihe Hospital Affiliated to Hubei Medical College, Xiantao first people's Hospital, Wuhan Huangpi District People's Hospital, Jingzhou Chest Hospital, Jingzhou first people's Hospital, Shanghai Public Health Clinical Center, Beijing You'an Hospital Affiliated to Capital Medical University, Zhengzhou Sixth People's Hospital, Chongqing Three Gorges Central Hospital, The ninth Affiliated Hospital of Guangxi Medical University, Hangzhou Xixi hospital, Nanjing Second Hospital, Suzhou Fifth People's Hospital, The first hospital of Zhejiang Province, The Fifth Affiliated Hospital of Zhongshan University, Huangshi traditional Chinese medicine hospital, Yangjiang people's Hospital, Zhongxian hospital, the First Affiliated Hospital of Chongqing Medical University, Anqing Municipal Hospital, Changzhou Third People's Hospital, Guangzhou first people's Hospital, Harbin infectious diseases hospital, Tianmen first people's Hospital, Wuxi People's Hospital, Wuhan fifth hospital, Xishuangbanna Dai Autonomous Prefecture People's Hospital, Chongqing Iron and Steel General Hospital, Daye people's Hospital, Nanxishan Hospital of Guangxi Zhuang Autonomous Region, Jiaying First Hospital, Jiangling people's Hospital, Jinzhong infectious disease hospital, Lanzhou Pulmonary Hospital, Liuzhou people's Hospital, Ma'anshan He county people's Hospital, The First Affiliated Hospital of Nanchang University, Ningbo Yinzhou people's hospital medical community, Shaoxing people's Hospital, Shijiazhuang fifth hospital, Taizhou Enze Medical Center, Xinyang Central Hospital, Yueyang No.1 People's Hospital, Zhanjiang Central People's Hospital, The First Affiliated Hospital of Zhengzhou University, Shenzhen Hospital of Chinese Academy of Sciences, Chongqing Kaizhou District People's Hospital, Chongqing Changshou District People's Hospital, Chongqing Yunyang County People's Hospital, Ankang Central Hospital, Chenzhou Second People's Hospital, Datong Fourth People's Hospital, Dengzhou people's Hospital, Fengjie people's Hospital, Foshan first people's Hospital, Fuyang Second People's Hospital, Gongyi people's Hospital, Guangshan people's Hospital, Guoyao Dongfeng General Hospital, Hainan people's Hospital, The Second Affiliated Hospital of Hainan Medical College, The first people's Hospital of Xiaoshan District, Hangzhou, Huaihua first people's Hospital, Jiashan first people's Hospital, Lu'an people's Hospital, Affiliated Hospital of Qingdao University, Qingyuan people's Hospital, Quanzhou County People's Hospital, Rizhao people's Hospital, Shaodong people's Hospital, Shiyan Xiyuan Hospital, Tongling people's Hospital, Wenzhou People's Hospital, Wenzhou Central Hospital, The Second Affiliated Hospital of Wenzhou Medical University, Wuxi Fifth People's Hospital, Wuhan Youfu hospital, Xi'an eighth hospital, Xinxiang infectious disease hospital, Yangxin County People's Hospital, Yuebei Second People's Hospital, Yunnan infectious diseases hospital, Zhaoqing first people's Hospital, Zhaozhou County People's Hospital, Shao Yifu Hospital Affiliated to Zhejiang University School of Medicine, Zhijiang people's Hospital, People's Hospital of Dianjiang County, Chongqing, Chongqing Jiulongpo first people's Hospital, Chongqing Shizhu Tujia Autonomous County People's Hospital, The first people's Hospital of Wanzhou District, Chongqing, Yongchuan Hospital Affiliated to Chongqing Medical University, Anguo hospital, The Third Hospital of Peking University, peking university shenzhen hospital , BOLUO people's Hospital, Changde Lixian people's Hospital, Changde Second People's Hospital, Chenzhou Central Hospital, Chengjiang

people's Hospital, Dalian Central Hospital, Danzhou people's Hospital, Dengzhou Central Hospital, Feidong County People's Hospital, Fuzhou Nanfeng County Hospital, Ganzhou Fifth People's Hospital, Gao'an people's Hospital, Public Security County People's Hospital, Affiliated Hospital of Guangdong Medical University, The Sixth Affiliated Hospital of Guangzhou Medical University, Affiliated Hospital of Guizhou Medical University, Hangzhou first people's Hospital, Hangzhou Lin'an District People's Hospital, Nanpi County Hospital of traditional Chinese medicine of Hebei Province, Henan people's Hospital, Hefeng County Central Hospital, Hohhot First Hospital, Huludao Central Hospital, The First Affiliated Hospital of Hunan Medical College, Shenzhen Union Hospital of Huazhong University of science and technology, Huaibei people's Hospital, Huangshi Second Hospital, Huangchuan people's Hospital, Huizhou Zhongda Huiya hospital, Huizhou Central People's Hospital, Jining first people's Hospital, Jianshi County People's Hospital, Fengcheng people's Hospital of Jiangxi Province, Jiangyou infectious diseases hospital, Jieyang people's Hospital, Jinhua Central Hospital, Jinzhong Pingyao people's Hospital, Jingjiang people's Hospital, The Second Affiliated Hospital of Kunming Medical University, Laifeng County Central Hospital, Yueqing people's Hospital, Lijiang people's Hospital, Lixin people's Hospital, The Fourth People's Hospital of Lianyungang, Linqu County People's Hospital, Linyi people's Hospital, Longxi first people's Hospital, Min Da Hospital, Minqing County General Hospital, Nantong Third People's Hospital, Nanyang Central Hospital, The First Affiliated Hospital of Nanyang Medical College, Nanyang Oilfield General Hospital, Ningbo First Hospital, The Fourth People's Hospital of Ningxia, Pingxiang Second People's Hospital, Quzhou Kecheng District People's Hospital, Qujing maternal and child hospital, Ruian people's Hospital, The First Affiliated Hospital of Xiamen University, Shangcheng County People's Hospital, Shanghai Baoshan Dachang hospital, Shanghai Pudong New Area Gongli Hospital , People's Hospital of Yushan County, Jiangxi Province, Shangrao City, Xuanwu Hospital of Capital Medical University, Sichuan Mianyang 404 hospital, Sixian Hospital of traditional Chinese Medicine, Suihua First Hospital, Suiping County People's Hospital, Tianjin Fourth Central Hospital, Tianjin Haihe hospital, Tiantai County People's Hospital, Tongchuan Mining Bureau Central Hospital, Tongren people's Hospital, Weihai Central Hospital, The First Affiliated Hospital of Wenzhou Medical University, Wuzhou Third People's Hospital, Armed police Hubei provincial general team hospital, Xixian people's Hospital, Longshan County People's Hospital in Western Hunan, Xiangcheng first people's Hospital, The Sixth People's Hospital of Xinjiang Uygur Autonomous Region, The First Affiliated Hospital of Xinjiang Medical University, Xinmi Hospital of traditional Chinese Medicine, Xinxiang County People's Hospital, Xinye people's Hospital, Xinyang first people's Hospital, Xinyang Hospital of traditional Chinese Medicine, Xuanen County People's Hospital, Xinhua Hospital, Yili Prefecture, Yongzhou Central Hospital, Yuyao people's Hospital, Changchun infectious disease diagnosis and treatment center, Changsha eighth hospital, Changsha first people's Hospital, 921st Hospital of the joint service support force of the Chinese people's Liberation Army, Central theater General Hospital of the Chinese people's Liberation Army, The First Affiliated Hospital of China Medical University, The Third Affiliated Hospital of Zhongshan University, Zhongshan Second People's Hospital, Chongqing Chengkou people's Hospital, Chongqing Hechuan District People's Hospital, Chongqing Red Cross Hospital, Zhoushan women's and children's Hospital, Zhoukou infectious diseases hospital, Zhuzhou first people's Hospital, Zhumadian Central Hospital, Anlong people's Hospital, Anxi County Hospital, Anyang Fifth People's Hospital, Anyang People's Hospital, Anyuan people's Hospital, Badong County Ethnic hospital, Wuyuan County People's Hospital of Bayannur City, Baise people's Hospital, The First Affiliated Hospital of Bengbu Medical College, Baoding first Central Hospital, Changping District Hospital of Beijing Municipality, Changping District Hospital of traditional Chinese and Western medicine of Beijing, Beijing Chuiyangliu Hospital , Beijing Center for Disease Control and Prevention, Mentougou District Hospital of

Beijing Municipality, Shunyi District Hospital of Beijing Municipality, Beijing Xicheng District Guangwai hospital, Oriental Hospital of Beijing University of traditional Chinese Medicine, Benxi Sixth People's Hospital, Binzhou Central Hospital, Bozhou people's Hospital, Cangnan Third People's Hospital, People's Hospital of Anxiang County, Changde City, Changde first people's Hospital, Chaoyang Second Hospital, Chengdu Handan people's Hospital, Chengde Third Hospital, Chizhou people's Hospital, Chongxin County People's Hospital, Chongyi people's Hospital, Affiliated Hospital of North Sichuan Medical College, Dazhou Central Hospital, Dali first people's Hospital, The Second Affiliated Hospital of Dalian Medical University, The First Affiliated Hospital of Dalian Medical University, Danyang people's Hospital, Daocheng people's Hospital, Deqing people's Hospital, Dezhou Second People's Hospital, Dezhou people's Hospital, Dezhou Qingyun people's Hospital, Dingyuan County General Hospital, Dongfang people's Hospital, Dongguan Ninth People's Hospital, Dongguan Nancheng hospital, Dongyang people's Hospital, Enshi Central Hospital, Erlianhot hospital, Fangchenggang first people's Hospital, Nanzhuang hospital, Chancheng District, Foshan City, Foshan Nanhai District Third People's Hospital, Lishui hospital, Nanhai District, Foshan City, The First Affiliated Hospital of Fujian Medical University, Zhangzhou Hospital Affiliated to Fujian Medical University, Fuzhou Changle district hospital, Fuzhou Anle County Hospital, Fuzhou Fifth People's Hospital, Fuzhou Dongxiang District People's Hospital, Fuyang District First People's Hospital, Ganzhou Longnan County People's Hospital, Gaolan County People's Hospital, Gongcheng Yao Autonomous County People's Hospital, Gushi people's Hospital, Guang'an people's Hospital, Guangdong Hospital of traditional Chinese Medicine, Guangzhou Eighth People's Hospital, Guangzhou 12th people's Hospital, Shenzhen Hospital of Guangzhou University of traditional Chinese Medicine, People's Hospital of Guiding County, Hanjiang Hospital of Sinopharm, Harbin Acheng District People's Hospital, Nangang District People's Hospital of Harbin, The First Affiliated Hospital of Harbin Medical University, Haikou People's Hospital, Hainan West Central Hospital, Handan Sixth Hospital, Handan Central Hospital, Hanshan people's Hospital, Hangzhou Dingqiao hospital, The third people's Hospital of Yuhang District, Hangzhou, The first people's Hospital of Yuhang District, Hangzhou, Minzhou people's Hospital, Hefei Sixth People's Hospital (Hefei infectious diseases hospital), He Xian Memorial Hospital, Hebei Chest Hospital, Hechi people's Hospital, Hejin people's Hospital, The First Affiliated Hospital of Henan University of science and technology, Zhangye people's Hospital Affiliated to Hexi University, Heyuan people's Hospital, Heze Municipal Hospital, Heilongjiang provincial hospital , South Yunnan Central Hospital of Honghe Prefecture, Hulunbuir Manzhouli hospital, Hunan Youxian people's Hospital, The First Affiliated Hospital of Hunan University of traditional Chinese Medicine, China Resources WISCO General Hospital, Huaihua Chenxi County People's Hospital, Huai'an Fourth People's Hospital, Huainan Mashan infectious disease hospital, Huangshan people's Hospital, Huangshi fifth hospital, Huichang people's Hospital, Huining County People's Hospital, Huizhou first people's Hospital, Jixi people's Hospital, Qianan County People's Hospital of Jilin Province, Jinan Fourth People's Hospital, Jining second people's Hospital, Affiliated Hospital of Jining Medical College, Shunde Hospital Affiliated to Jinan University, Jiamusi Fujin Central Hospital, Huachuan County People's Hospital of Jiamusi, Jiahe County People's Hospital, Jianshi County Hospital of traditional Chinese Medicine, Jiangshan people's Hospital, People's Hospital of Le'an County, Jiangxi Province, Jiangxi Provincial People's Hospital, Jinxian County People's Hospital, Jingmen Chest Hospital, Kunming Second People's Hospital, Laixi people's Hospital, The second hospital of Lanzhou University, Lancang Second People's Hospital, Leping people's Hospital, Leshan people's Hospital, Lengshuijiang people's Hospital, Lianjiang county hospital, The first people's Hospital of Lianyungang, Liaoning Chaoyang Disease Control Center Hospital, Liaocheng people's Hospital, Linshui people's Hospital, Linhai Second People's Hospital, Linxia people's Hospital, Linyi Lanshan District

People's Hospital, Linying County People's Hospital, Liuyang people's Hospital, Loudi first people's Hospital, Loudi Central Hospital, Luzhou people's Hospital, Lushan County People's Hospital, The Third Affiliated Hospital of Army Medical University, The First Affiliated Hospital of Army Medical University, Luoping County People's hospital official website, Luoyuan County Hospital, Luohe Sixth People's Hospital, MAANSHAN Fourth People's Hospital, MAANSHAN Hospital of traditional Chinese Medicine, Coal Industry General Hospital, The first people's Hospital of Mengcheng County, Mianyang people's Hospital, People's Hospital of Mianchi County, Mudanjiang Second People's Hospital, The Second Affiliated Hospital of Nanchang University, Fuzhou Fifth Hospital Affiliated to Fuzhou Medical College of Nanchang University, Nanchong Central Hospital, Southern Hospital of Southern Medical University, The First Affiliated Hospital of Nanhua University, Public Health Hospital of Nanhua University, Nanhua Hospital Affiliated to Nanhua University, Xiangtan Hospital Affiliated to Nanhua University, Nanning Fourth People's Hospital, People's Hospital of Neihuang County, Ningbo Second Hospital, Community health service center, Baihe street, Jiangdong District, Ningbo City, Li Huili Hospital of Ningbo Medical Center, Mindong Hospital of Ningde City, Ningde Xiapu County Hospital, Ningdu County People's Hospital, Ningguo people's Hospital, People's Hospital of Ninglang Yi Autonomous County, Ouhai District Third People's Hospital, Pingdingshan infectious diseases hospital, Pingguo people's Hospital, Qiqihar seventh hospital, The First Affiliated Hospital of Qiqihar Medical College, Qidong Third People's Hospital, Qingdao Chengyang people's Hospital, Qingdao Huangdao District People's Hospital, The Fourth People's Hospital of Qinghai Province, Qingyuan people's Hospital, Quanjiao people's Hospital, Luojiang District Hospital of Quanzhou City, Queshan County People's Hospital, Renshou people's Hospital, Wulian people's Hospital of Rizhao, Rongcheng people's Hospital, Runan people's Hospital, Rushan people's Hospital, Sanming integrated hospital of traditional Chinese and Western Medicine, Zhongshan Hospital Affiliated to Xiamen University, Shandong Provincial Hospital , Shandong Chest Hospital, Shanxi Bethune hospital, Ruicheng County People's Hospital of Shanxi Province, The second hospital of Yuncheng City, Shanxi Province, The First Affiliated Hospital of Shantou University Medical College, Shantou Central Hospital, Shangluo Luonan people's Hospital, The Second Affiliated Hospital of Fudan, Shanghai, Renji Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai 10th people's Hospital, Shanghai Fengxian District Central Hospital, Anting hospital, Jiading District, Shanghai, Shanghai Tongren Hospital, Shangrao Guangxin District People's Hospital, Shangrao people's Hospital, Shangrao Wannian County People's Hospital, Shangrao Yongxiu people's Hospital, Shenzhen Bao'an District Hospital of traditional Chinese Medicine, Shenzhen Sixth People's Hospital, Shenzhen Longgang District People's Hospital, Shenzhen Pingshan people's Hospital, Shenyang hospital, Shiyan people's Hospital, Shiyan integrated traditional Chinese and Western Medicine Hospital, The First Affiliated Hospital of Shihezi University Medical College, Shishi General Hospital, Shishou people's Hospital, Shuangfeng County People's Hospital, West China Hospital of Sichuan University, Sihui people's Hospital, Songzi people's Hospital, Suichuan County People's Hospital, Taizhou Second People's Hospital, Taizhou first people's Hospital, Taiyuan Fourth People's Hospital, Tanghe County People's Hospital, Tianjin Third Central Hospital, Tianjin Fifth Central Hospital, Tianjin First Central Hospital, Tianjin People's Hospital, Tianjin Xiqing hospital, Tianjin Medical University General Hospital , tianjin hospital, Tianquan Tianyuan hospital, Tieling Central Hospital, Tonghua people's Hospital, Tongbai County Central Hospital, Wanning people's Hospital, Weixin County People's Hospital, Weishan people's Hospital, Wenzhou Longwan District First People's Hospital, Wenzhou Yongjia hospital, Wenzhou Hospital of traditional Chinese Medicine, People's Hospital of Woyang County, Wuwei people's Hospital, Wuxi Fourth People's Hospital, Wuzhong people's Hospital, Wuhan Caidian District People's Hospital, People's

Hospital of Wuhan University, Wuhan Pulmonary Hospital, Caidian District People's Hospital of Wuhan, Wuhan Sixth Hospital, Wuhan Dongxihu District People's Hospital, Wuhan commercial staff hospital, Wuhan Wuchang hospital, Wuhan hospital of traditional Chinese Medicine, Wuyang County People's Hospital, The First Affiliated Hospital of Xi'an Jiaotong University, Central Hospital of Xi'an Mining Bureau, Xiping County People's Hospital, Xishuangbanna mental health center, Xilingol League hospital, Xilinhot, Xianyang Qianxian people's Hospital, Xianyang Central Hospital, Xianyang Wugong County People's Hospital, Xiangtan Xiangtan County People's Hospital, Xinhuang people's Hospital, The seventh division hospital of Xinjiang production and Construction Corps, Xinyu people's Hospital, Xinyang Third People's Hospital, Xinyang Fifth People's Hospital, Suqian infectious disease control center, Affiliated Hospital of Xuzhou Medical University, Xuyong County People's Hospital, Haiyang people's Hospital of Yantai, Yantai Qishan hospital, Yan'an University Affiliated Hospital, Yancheng Dafeng people's Hospital, Yan Fen clinic, Yangzhou Third People's Hospital, Yangquan Third People's Hospital, Yangshuo people's Hospital, Yichang first people's Hospital, Yichang Central People's Hospital, People's Hospital of Zigui County, Yichang, Yimen people's Hospital, Yiyang Anhua people's Hospital, South County People's Hospital of Yiyang, People's Hospital of Datong Lake District, Yiyang City, Yinchuan first people's Hospital, Yingkou Third People's Hospital, Yingcheng people's Hospital, Yongfu people's Hospital, Yongjia people's Hospital, Yongtai County Hospital, Yuzhong first people's Hospital, Yulin Red Cross Hospital, People's Hospital of Jiangchuan District, Yuxi City, Yuxi people's Hospital, Yueyang Second People's Hospital, The third people's Hospital of Yunnan Province, Affiliated Hospital of Changchun Beihua University, Changjiang Shipping General Hospital, Changzhi Changzhi people's Hospital, Zhao'an County Hospital, The First Affiliated Hospital of Zhejiang University Medical College, Taizhou Hospital of Zhejiang Province, Zhenjiang first people's Hospital, Zhengzhou Central Hospital, Ningbo Huamei Hospital of Chinese Academy of Sciences, PLA Navy General Hospital, 985th Hospital of the joint service support force of the Chinese people's Liberation Army, 924th Hospital of the joint service support force of the Chinese people's Liberation Army, Aviation General Hospital of China Medical University, Xiangya Third Hospital of Central South University, Huiya hospital, the First Affiliated Hospital of Zhongshan University, Zhongwei people's Hospital, Zhongxiang people's Hospital, Chongqing Liangjiang New Area first people's Hospital, Chongqing Bishan District People's Hospital, Fengdu County People's Hospital of Chongqing, Chongqing Fuling Central Hospital, Chongqing public health medical treatment center, Chongqing Liangping District People's Hospital, Chongqing Tongnan District People's Hospital, Chongqing Wanzhou District Shanghai hospital, Central Hospital of Wuling Town, Wanzhou District, Chongqing, Chongqing Xiushan people's Hospital, The Third Affiliated Hospital of Chongqing Medical University, The First Affiliated Hospital of Chongqing Medical University, Zhoukou Central Hospital, Zhuhai People's Hospital, Zibo Central Hospital, Zigong Rongxian people's Hospital, Zigong first people's Hospital, Zhuhai integrated traditional Chinese and Western Medicine Hospital, Tianhe District Center for Disease Control and Prevention, Shanwei people's Hospital, Shantou Chenghai District People's Hospital, The Second Affiliated Hospital of Shantou University Medical College, Shantou Chaonan Minsheng hospital, Luocun hospital, Nanhai District, Luhe County People's Hospital, The first naval hospital of the southern theater of the PLA, Jianghai work station of Jiangmen disease control and Prevention Center, Huizhou Third People's Hospital, Huadu District People's Hospital, The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou Chest Hospital, Guangzhou Haizhu Center for Disease Control and Prevention, Guangning people's Hospital, Zhuhai Hospital of Guangdong Hospital of traditional Chinese Medicine, Guangdong hydropower hospital Co. Ltd, Guangdong Provincial People's Hospital, The second people's Hospital of Guangdong Province, Panyu District Central Hospital, Dongguan Dalang hospital, Chaozhou Central Hospital