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Epidemiological and clinical characteristics of COVID-19 in adolescents and young adults

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Public summary

- Adolescents and young adults are more involved in frequent social-activity, overseas studying, and international working and traveling, which might make them susceptible to worldwide spread of the coronavirus disease 2019 (COVID-19).
- Adolescent and younger patients of COVID-19 had a median incubation period of 8 days and 50% of their family contacts could develop illness within 1.4 days after exposure.
- Three asymptomatic patients of COVID-19 have infected their family contacts.
- Although most of the adolescent and young adult patients of COVID-19 have better prognosis outcomes after treatment, few of them showed severe clinical signs and symptoms such as bacterial pneumonia changes by Chest CT findings, fever, and shortness of breath.

Abstract

Background: Adolescents and young adults might play a key role in the worldwide spread of Coronavirus Disease 2019 (COVID-19), because they are more likely to be involved in overseas studying, business, working, and traveling. However, the epidemiological and clinical characteristics of them are still unknown.

Methods: We collected data of 46 confirmed COVID-19 patients aged 10 to 35 years from the Chongqing Three Gorges Central Hospital. The demographic, epidemiological, and clinical data were collected. Several key epidemiological parameters, the asymptomatic cases and transmission to their family members and the clinical characteristics at admission, and during treatment were summarized.

RESULTS: Of 46 confirmed patients, 14 patients (30.4%) were aged from 10 to 24 years, and 24 (52.2%) patients were male. The estimated mean incubation period was 6.6 days (95% confidence interval (CI) 4.4 - 9.6). The median serial interval was 1.9 days (95% CI 0.4 - 6.2). Three of the asymptomatic cases showed the transmission to their family members. Only 1 patient was identified as a severe case at admission. The common symptoms at admission were dry cough (34, 81.0%), and fever (29, 69.1%). Nearly 60% of the patients showed ground-glass opacity by chest CT findings. Three patients developed acute kidney

injury during treatment. Most of the patients (78.3%) were recovered and discharged by the end of the follow-up.

Conclusions:

This single center study with a relatively small sample size showed that the adolescent and young adult patients of COVID-19 had a long incubation period and a short serial interval. The transmission occurred from asymptomatic cases to their family. Fewer patients have developed complications during treatment.

Introduction

The coronavirus disease (COVID-19), a newly emerging infectious pneumonia with unknown causes, was firstly reported in Wuhan, Hubei Province, China in December, 2019. The incidences of COVID-19 were rapidly reported across China because it occurred close to the Chinese spring festival[1]. Early epidemiological and clinical studies depicted that the majority of the patients were middle-aged, or elder individuals, had a mean incubation period of 5.2 days (range 0-14 days), and a serial interval of 7.5 days (95% CI 2-17 days)[2-4]. The most common symptoms were fever, cough, and fatigue[3-5]. Most of the patients presented the abnormalities of chest CT-findings such as ground-glass opacity, and bilateral patchy shadowing[4-6]. The patients aged above 65 years were more likely to be severe cases and developed severe acute complications such as pneumonia, Acute Respiratory Distress Syndrome (ARDS), shock, and acute cardiac injury during treatment[3-5]. These studies provided essential evidence to guide the early medical screen, diagnosis of COVID-19 cases, isolating of the suspected cases, and clinical treatments. However, with the rapid progress of COVID-19, many new characteristics have emerged, which need to update more evidence. One new characteristic is that increasing numbers of younger patients were confirmed across China. One study from the Chinese Center for Disease Control and Prevention indicated that 4168 (9%) of the patients through February 11, 2020 were aged younger than 30 years [7]. In

addition, outbreaks of COVID-19 were reported worldwide. It is reported that the first-generation cases outside China were more likely import from China[8-10]. Several countries, such as South Korea, Japan, and Italy are experiencing a sharp increase in incident COVID-19 confirmed cases. Younger individuals were more likely to be carriers of COVID-19 across countries, since they were more likely to be involved in overseas study, business, work and travel. For example, in South Korea, 178 out of 431 confirmed cases, which were publicly announced on the website of the Ministry of Health and Welfare, were aged ≤35 years through March 1, 2020[11]. However, as far as we know, no study has been specifically conducted to explore the epidemiological and clinical characteristics in younger patients of COVID-19.

In this study, basing on a retrospective case series data, we aimed to estimate the key epidemiological characteristics and describe the clinical symptoms, treatments, and hospital outcomes for COVID-19 patients in adolescents and young adults.

Methods

Study Design and Participants

In this study, we defined the adolescents as 10-24 years of age and young adults as 25-35 years of age according to the World Health Organization's definition. Chongqing, which is the China's fourth municipality after Beijing, Shanghai, and Tianjin, is one of the areas which are adjacent to Hubei Province. Until March 20, 2020, the confirmed cases of COVID-19

have reached to 576, which is the highest in four municipalities of China. According to the Chongqing government, the Chongqing Three Gorges Central Hospital, which is one of the major tertiary teaching hospitals of Chongqing University and locate in Wanzhou district, Chongqing city, was responsible to treat the patients from 10 districts or counties from Chongqing City. Until March 20, 2020, the study hospital treated 248 confirmed cases, which accounted for 43.1% of the patients confirmed in Chongqing. In this study, we retrospectively reviewed the medical records of confirmed COVID-19 cases aged from 10 to 35 years who were hospitalized in the study hospital from January 25, 2020 to February 18, 2020.

Data Collection

Epidemiological data were collected using a standardized questionnaire through face-to-face or telephone interviews with patients or their family members. We firstly collected demographic and social-economic information such as height and weight, educational level, and behavioral characteristics such as smoking, alcohol consumption, and physical activities. Then, we investigated the exposure date and types for each patient during 1 month before the date of symptoms onset. For those who resided in Wuhan, we further collected the histories of exposure to the Huanan Seafood wholesale market or other similar markets. We collected the earliest date of symptoms onset and the specific symptoms. For those who were the first case of developing symptoms out of the family (index patients), we further interviewed their family contacts with exposure histories with the index patient, date of symptoms onset, date of the first medical visit, and date of confirmation. The clinical information for study patients was abstracted from medical records. We collected several key information of date including

date of clinical symptoms onset, date of primary visit to health facilities, and date of confirmation. The typical clinical symptoms and data of the chest CT scan for each patient were collected at admission. The medical histories and treatments such as antiviral therapy, antimicrobial therapy, corticosteroid therapy, and respiratory support were simultaneously recorded. We further collected the data of complications for patients during treatment. Patients were diagnosed with ARDS if they satisfied the berlin definition, and acute kidney injury was defined according to the kidney disease improving global outcomes classification[12 13]. The criteria of diagnosis for cardiac injury was based on the serum levels of cardiac biomarkers (> the 99th percentile upper reference limit) or presenting of the new abnormalities in electrocardiography and echocardiography. We defined types of patients according to the examinations at admission. The mild type was defined as patients who had respiratory symptoms and positive CT findings of pneumonia. The severe type was defined as those who satisfied one of the following criteria: 1) respiratory distress with respiratory frequency ≥30/min; 2) pulse oximeter oxygen saturation ≤93% at rest; and 3) oxygenation index (artery partial pressure of oxygen/inspired oxygen fraction, PaO2/FiO2) ≤300 mm Hg. The clinical outcomes (recovered and discharged, still treatment, or death) were consistently observed until the date of February 23, 2020. The epidemiological data were inputted by Epidata 3.0 (The EpiData Association, Odense Denmark, 2003) with double-checking. To ensure the accuracy of the clinical data, two researchers also independently reviewed the electronic medical records.

Laboratory confirmation and tests

The criteria of diagnosis for COVID-19 cases were based on the national recommendation of the New Coronavirus Pneumonia Prevention and Control Program (6^{th} edition) [14]. Briefly, the throat swab samples or lower respiratory tract were collected and processed at the department of clinical laboratory in the study hospital. Then, the 2019-nCoVRNA were extracted from the patients who were suspected of having the 2019-nCoV infection. Finally, the throat swabs were placed into a collection tube with 150 μL of virus preservation solution, and total RNA was extracted within 2 hours using a respiratory sample RNA isolation kit (Suzhou Tianlong Biotechnology Co. Ltd， Roche's COBASZ480). A Reverse Transcription-Polymerase Chain Reaction (RT-PCR) assay with a cycle threshold value (Ct-value) less than 37 was defined as positive. Asymptomatic cases were defined as those who presented positive results by conducting the nucleic acid test of COVID-19, and had no elevated temperature measured or self-reported fever and no gastrointestinal or respiratory symptoms such as cough and sore reported by physicians at admission. To confirm the validity, we further conducted a face-to-face or telephone interview for each asymptomatic case to collect information on symptoms before 2 weeks of admission. For each patient, the laboratory tests were performed at admission, which included routine blood tests, serum biochemistry, and coagulation function.

Statistical analysis

We described the differences of demographic factors, symptoms at admission, comorbidities, and chest CT findings across age groups. We summarized the distribution of laboratory findings for cases using median and interquartile range(IQR) among total cases, 10-24y, and

25-35y. We defined the incubation period as the time interval from the date of exposure to the date of symptoms onset. We included two types of patients who could recall the exact date of traveling to Wuhan or contacting with other confirmed cases. To ensure accuracy, those who have reported more than one exposure sources (n=1) or contacting periods over 3 days (n=7) were excluded. For patients who reported exposure time in one day, the exposure day was defined as exposure date. The first day was defined as the exposure date for those who reported exposure time within two days. The middle day was defined as the exposure date for those who reported exposure time within three days. We used a parametric survival analysis model with Weibull distribution to estimate the distribution of the incubation period. Since the asymptomatic cases at the first medical visit could develop symptoms during the follow-up, we first treated the incubation period for asymptomatic cases as right-censored data (from the date of exposure to the date of the first medical visit) and performed the estimations. Then, we excluded the asymptomatic cases and repeated the estimations. We defined the family clustered events as those who were the first cases of developing symptoms in their family (index patient), and their family members (secondary cases) had a clear contacting history to the index patient and had no other potential infection sources. We used the date of symptoms onset to measure the date of illness onset. We defined the serial interval as the time interval from the date of illness onset for the index patient to the date of illness onset for the secondary cases. We used a parametric survival analysis model with gamma distribution to estimate the distribution of serial interval. We further calculated the time interval from the date of symptoms onset to the date of the first medical visit using a

parametric survival model with Weibull distribution. We finally compared the differences of treatments, days of persisting fever during treatment, days of transforming to negative results by COVID-19 nucleic acid tests during treatment, and prognosis outcomes by different age groups. We compared proportions of categorical variables using the chi-square test, and using the Fisher exact test when the minimum expected numbers for the variables were less than 1. We used independent group T-tests to compare means of continuous variables following a normal distribution; otherwise, the Mann-Whitney rank tests were used. We performed the summaries and significance tests by SAS 9.4, The parametric survival analyses were conducted by R 3.1.1, The statistically significant level was defined as 0.05 with a 2-side test.

Ethical approval:

Data collection and analyses of cases were approved by the institutional ethnic board of three gorges hospital affiliated with Chongqing University (No.2020-7(讼)).

Since the epidemiological interview for the study case is a part of a continuing public health outbreak investigation, the individual consent was considered exempt.

Results

Of 248 patients registered at the study hospital during the study period, 51 (20.6%) patients were aged from 10 to 35 years. Five patients who did not provide the data of epidemiological outbreak interview were further excluded. The social-economic and symptoms for the study patients were summarized in Table 1. The Majority of them were young adults (n=32), and

the rest were adolescents (n=14). The main exposure types of patients included contacting with other confirmed cases (22, 47.8%) or residing in Wuhan (19, 41.3%). Half of the patients were men (24, 52.2%), had a normal BMI (24, 52.2%), and never conducted physical activity (23, 50.0%). Fewer patients had 1 or more medical disease histories (6, 13.0%). The specific medical diseases included obesity (n=1), diabetes (n=1), Chronic obstructive pulmonary disease (n=1), hyperthyroidism (n=1), kidney stones (n=1), and arthrolithiasis (n=1). Only one (2.2%) patient was identified as a severe case. The individual characteristics for this severe case were summarized in Supplementary Table S1. Four patients were identified as asymptomatic at admission. The most common symptoms at admission were dry cough (34, 81.0%), fever (29, 69.1%), and expectoration (16, 38.1%). The less common symptoms included headache, fatigue, pharyngalgia, chest pain, anorexia, myalgia, dizziness, diarrhea, nausea, and shortness of breath. The common pathological changes of chest CT findings were ground-glass opacity (29, 63.0%), and bilateral patchy shadowing (12, 26.1%). No severe cases were identified in adolescent patients. Compared with young adults, adolescent patients had a lower probability to be asymptomatic (6.3% vs 14.3%). Fewer adolescent patients reported fever, headache, and fatigue. Only 7 (50.0%) adolescent patients showed ground-glass opacity for chest CT scanning, compared with 22 (68.8%) of that in young adults. However, none of these differences reached levels of statistical significance. We displayed the typical patterns of chest CT scan for adolescents and young adults in Figure 1.

We recorded family clustered events from 6 symptomatic index patients at admission (Figure 2). According to the definition of the serial interval, we only included 12 secondary cases out of these family cluster data to estimate the distribution of serial interval (Figure 3 Panel A). The estimated median serial interval was 1.9 days (95% CI 0.4 - 6.2). The estimated 95th percentile of serial interval could reach as long as 28.6 days (95% CI 10.6 -76.9). Among 14 patients who provided the exact date of traveling to Wuhan or contacting other confirmed cases, the estimated median incubation period was 8.3 days (95% CI 5.0 -13.4) (Figure 3 Panel B). The estimated 95th percentile of the incubation period could reach as long as 24.8 days (95% CI 14.9 - 47.6). After excluding 3 asymptomatic cases, the estimated median incubation period decreased to 6.6 days (95% CI 4.4 - 9.6) (Figure 3 Panel C). The estimated 95th percentile of the incubation period decreased to 14.8 days (95% CI 10.4 - 22.0). Based on 42 symptomatic cases, we estimated the median days from symptom onset to the first medical visit to be 1.4 days (95% CI 0.8 - 2.4) (Figure 3 Panel D). The estimated 95th percentile days from symptom onset to the first medical visit was 13.2 days (95% CI 8.3 - 20.9).

On admission, 10 (21.7%) patients were leucopenia (white blood cell count $< 4\times10^{9}/\mathrm{L}$), and 29 (63.0%) patients were lymphopenia (Table 2). Ten patients (21.7%) had decreased levels of platelet count ($< 150\times10^{9}/\mathrm{L}$). The other elevated levels of laboratory indicators for study patients were lactate dehydrogenase (9, 19.6%), C-reactive protein (9, 19.6%), D-dimer levels (7, 15.2%), alanine aminotransferase (7, 15.2%), and total bilirubin (7, 15.2%). Several

differences were observed in laboratory findings between adolescent and young adult patients. For example, 8 (25.0%) young adult patients presented elevated levels of c-reactive protein, while only 1 adolescent patient showed a similar pattern.

The treatments and prognosis outcomes were summarized in Table 3. During the treatment periods, all patients received antiviral therapy, 39 (84.8%) patients received oxygen inhalation, and 43 (93.5%) patients received an interferon alpha inhalation. Few patients (5, 10.9%) received antifungal treatment. Three (6.5%) patients have developed acute kidney injury during the treatment. The median days from the date of admission to the date of consecutively negative results for COVID-19 nucleic acid tests were 12.5 days (IQR 8.0 – 16.0). The median days of persistent fever during admission were 5 days (IQR 1- 8). Until the date of 25th February 2020, 36 patients had recovered and discharged, 10 patients were hospitalized, and no patients died. Compared with young adults, adolescent patients received less therapy of oxygen inhalation.

We observed 4 asymptomatic cases at admission and both of them were consistently confirmed as asymptomatic cases by our face-to-face or telephone interviews. The disease progress for asymptomatic patients during treatment periods was showed in Figure 4. Two asymptomatic cases (case 2 and case 3) still did not show any symptoms until February 23, 2020. Asymptomatic case 1 has developed symptoms of shortness of breath, difficulty breathing, and chest tightness in the 17 days after admission. Asymptomatic case 4 has

developed symptoms of dry cough, phlegm, and nausea in the 6 days after admission and his COVID-19 nucleic acid has transformed into negative in the 14 days after admission. We detected family-clustered events from 3 asymptomatic cases, which indicated that the transmission during their asymptomatic periods occurred between asymptomatic cases and their family close contacts. For example, two relatives of the asymptomatic case 1 who lived with him, and did not report other potential infection sources, have developed illness on January 17, 2020.

Discussion

This study, to the best of our knowledge, is the first to assess the epidemiological and clinical characteristics of COVID-19 in adolescent and young adult patients. We added new knowledge to understand the characteristics of COVID-19 in the younger population. We detected 4 asymptomatic cases out of 46 patients at admission. We reported a mean incubation period of 7.2 days in symptomatic cases and could reach as long as 10 days with allowing for the truncated time to event data for asymptomatic cases. We estimated a median serial interval of 1.9 days from the dates of illness onset in index patients to the date of developing illness in their family close contacts. We found that the most common symptoms were dry cough, fever, and expectoration. Only 29 (63.0%) of the patients showed the ground-glass opacity by chest CT scan. The typical changes of laboratory indicators were decreased white blood cell count, decreased lymphocyte count, decreased platelet count, increased lactate dehydrogenase, and elevated C-reactive protein. During the treatment, we

found only 3 patients occurred acute kidney injury, and no other medical complications were reported. Nearly 80% of the patients were recovered and discharged at the end of follow-up.

Our study suggests that the incubation period of COVID-19 in adolescents and young adults might longer than elder patients. A retrospective study reported the mean incubation period was 5.2 days (95% CI: 4.1-7.0) and the 95th percentile of the incubation period was 12.5 days based on early COVID-19 patients from Wuhan [2]. A later study, which used the data of travelers from Wuhan, estimated the mean incubation period to be 6.4 days (95% CI 5.6-7.7) and ranged from 2.2 to 11.1 days[15]. The similar studies reported a shorter incubation period (median = 4 days) for patients outside Wuhan[6 16]. However, most of these studies were based on patients aged over 50 years. Knowledge gaps persisted for the incubation period in younger COVID-19 patients. In this study, we used patients with exact information for exposure time intervals and reported a mean incubation period of 7.2 days (95% CI 5.2-10.1) for patients aged under 35 years. The 95th percentile of the incubation period was 14.8 days (95% CI 10.4-22.00). With allowing for the right truncated periods for asymptomatic cases, the estimated mean incubation period was 10.0 days (95% CI 6.4-16.1) and the estimated 95th percentile could reach as long as 24.8 days (95% CI 14.9 - 47.6). Our findings highlighted the importance of extending medical observing or quarantining periods for adolescent and young adult patients of COVID-19.

Our study suggests that the person-to-person transmission has occurred rapidly from adolescent and young adult infected cases of COVID-19 to their family contacts. We recorded 6 family-cluster events of COVID-19 in asymptomatic patients. We estimated the mean serial interval to be 6.5 days (95% CI 2.5 -17.4), which is shorter than that (7.5 days, 95% CI 5.3-19.0) estimated from early Wuhan patients [2]. Most importantly, we estimated the median serial interval to be 1.9 days (95% CI 0.4 - 6.2), which was still lower than that (4.0 days, 95% CI 3.1-4.9) estimated in a recent modeling study[17].

We provided evidence supporting the transmission of adolescent and young adult asymptomatic patients of COVID-19 to their family or close contacts. In this study, four out of 46 patients were identified as asymptomatic cases. Three of them were identified as the index patients in their families. The two asymptomatic primary cases had neither any symptoms nor chest CT findings during the treatment. One asymptomatic primary case has suffered from difficulty and shortness of breath, and chest tightness in the 17 days during treatment. Most importantly, all of their family contacts have developed symptoms before the admission date for the asymptomatic index patients. Our findings were consistent with the existing evidence. Camilla Rothe et al. firstly reported an asymptomatic Chinese woman might be the transmission source for her two German business partners[18]. Zhen-Dong Tong et al. reported a 2-family cluster of COVID-19 patients in Zhejiang Province after each family's primary case contacted with an asymptomatic case of COVID-19 from Wuhan[19]. Recently, a

similar study has identified a 20-years age Chinese woman as an asymptomatic carrier who has infected five individuals in her family[20].

Compared with the early evidence from Wuhan patients, the adolescent and young adult patients of COVID-19 presented different patterns of symptoms and fewer abnormalities of laboratory indicators at admission. The most common symptoms were fever (83%), cough (82%), and shortness of breath (31%) in early elder patients from Wuhan[3]. Later studies with more case series reported other common symptoms including fatigue, gastrointestinal symptoms, upper airway congestion, myalgia, and headache[4 6 21]. The results of chest CT scanning indicated that nearly 80% of the early patients showed bilateral pneumonia, and ground glass opacity[3 4 21 22]. Laboratory examinations indicated that over 70% of the patients emerged lymphocytopenia, elevated lactate dehydrogenase, and elevated C reactive protein[3 4 23]. In this study, the most common symptoms at admission were dry cough (81.0%), fever (69.1%), and expectoration (38.1%). Only 1 patient reported shortness of breath at admission. The proportion of reporting fever at admission decreased to 58.3% in adolescent patients. Nearly 60% of the patients showed ground-glass opacity changes by chest CT findings, which decreased to 50% in adolescent patients. Only 26.09% and 13.04% of all patients showed the bilateral patchy shadowing or consolidation by chest CT findings. In terms of laboratory examinations, 63.0% of the patients had lymphocytopenia, which was close to the existing evidence. However, fewer patients had elevated levels of lactate dehydrogenase

(19.6%), and C-reactive protein (19.6%). Both of these abnormalities of laboratory findings were less pronounced in adolescent patients.

Our study indicated that younger patients have better prognosis outcomes during the treatment. Early studies reported that nearly 40% of the patients have at least one medical chronic disease at admission and the common complications during the treatment included acute respiratory distress syndrome, shock, acute cardiac injury, arrhythmia, kidney injury, and liver dysfunction[3 4 6 24]. Most of the patients received antiviral therapy and oxygen inhalation. Part of them received glucocorticoid therapy or antifungal treatment. Nearly 20% of the patients were identified as severe cases and received mechanical ventilation and Extracorporeal Membrane Oxygenation (ECMO). In our study, only 1 (2.2%) patients were identified as severe cases at admission. After received treatments of antiviral therapy, interferon-alpha inhalation, and oxygen inhalation, nearly 80% of the patients recovered and discharged at the end of the follow-up. Three patients developed severe kidney injury during treatment. Although a significant difference was observed in the treatment of oxygen inhalation for adolescent and young adult patients, this difference was largely caused by personal selection. Therefore, this difference has no clinical significance.

This study provided initial evidence for the epidemiological and clinical characteristics of COVID-19 in adolescents and young adults. Compared with early evidence from middle-aged or elder patients, the adolescent and young adult patients had a longer incubation period

which indicated that a longer period for medical observation or isolation is needed for these patients. The shorter serial interval indicated that the transmission could occur rapidly from younger patients to their close contacts. Compared with elder patients, younger patients had fewer typical signs and symptoms, and fewer abnormalities of laboratory findings. Fewer of them developed severe complications during treatment. Our results suggest that adolescents and young adults might be the key subpopulation in the later stage for preventing the worldwide spread of COVID-19.

The study has some limitations. Firstly, we conducted this study only based on 46 patients. The relatively small sample size limited us to obtain sound evidence concerning differences in most characteristics between subgroups, so the interpretation of the study findings should be made with caution. Secondly, at the end date of this study, nearly 20% of the patients still hospitalized, which limited us to fully illuminate the prognosis outcomes for the study patients. Finally, our conclusions should be explained with caution in the general population, because the study patients are only from a single hospital from Chongqing city.

Conclusions

This single-center study with a relatively small sample size suggested that the adolescent and young adult COVID-19 patients had a longer incubation period, a shorter serial interval, and a higher odd to be asymptomatic, in comparison to reports for the elderly patients in the

literature. The transmission to their family contacts occurred in several asymptomatic cases. Fewer patients have developed complications during treatment.

Competing interests:

All authors declare no competing interests.

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Figure legends

Figure 1. Chest computed tomographic (CT) images for study patients infected with COVID-19.

Panel A-B depicted the chest CT images of lung window and mediastinum window for a patient aged 21 years on day 10 after illness onset, and Panel C-D depicted the chest CT images of lung window and mediastinum window for a patient aged 33 years on day 14 after illness onset.

Figure 2. Information on exposures and dates of illness onset in 6 symptomatic cases and their family close contacts.

Numbers in boxes are calendar dates. Data from the 12 secondary cases (close contacts were defined as those who had clear exposure to only one index case and had no other potential source of infection) were used to estimate the distribution of serial interval.

Figure 3. Key distributions of epidemiological characteristics for study patients.

The estimated serial interval distribution is depicted in Panel A. The estimated incubation period distribution for symptomatic cases and asymptomatic cases truncated at hospitalization is depicted in Panel B. The estimated incubation period distribution only for asymptomatic cases is depicted in Panel C. The estimated distributions of times from illness onset to first medical visit is depicted in Panel D.

Figure 4. The progresses of clinical symptoms and chest CT findings during treatment periods for 4 asymptomatic cases and their family contacts.

Numbers in boxes are calendar dates. The symptoms and the chest CT-findings related to COVID-19 were marked in onset dates by black arrows.

Tables

Table 1. Baseline characteristics of study patients infected with COVID-19.

Characteristics	No. (%)			*P* value
	Total (n=46)	Adolescents (n=14)	Young adults (n=32)	
Exposure types				0.58
Resided in Wuhan	19 (41.3)	7 (50.0)	12 (37.5)	
Travel to Wuhan	3 (6.5)	2 (14.3)	1 (3.1)	
Contact with confirmed cases	22 (47.8)	5 (35.7)	17 (53.1)	
None	2 (4.4)	0 (0.0)	2 (6.3)	
Gender				0.93
Male	24 (52.2)	7 (50.0)	17 (53.1)	
Female	22 (47.8)	7 (50.0)	15 (46.9)	
Education, years				0.94
1-9	18 (39.1)	6 (42.9)	12 (37.5)	
10-12	10 (21.7)	3 (21.4)	7 (21.9)	
≥13	18 (39.1)	5 (35.7)	13 (40.6)	
BMI, kg/m^2				0.51
Under weight	4 (8.7)	1 (7.1)	3 (9.4)	
Normal	24 (52.2)	8 (57.1)	16 (50.0)	
Overweight/obesity	17 (37.0)	4 (28.6)	13 (40.6)	
Smoke status				0.99
Never	41 (89.1)	13 (92.9)	28 (87.5)	
Ever or now	5 (10.9)	1 (7.1)	4 (12.5)	
Physical activity				0.23
Never	23 (50.0)	6 (42.9)	17 (53.1)	
Rare	14 (30.4)	3 (21.4)	11 (34.4)	
Often	9 (19.6)	5 (35.7)	4 (12.5)	
Alcohol consumption				0.72
Never	32 (71.1)	11 (78.6)	21 (67.7)	
Rare or often	13 (28.9)	3 (21.4)	10 (32.3)	
Chronic diseases history				0.65
None	40 (87.0)	13 (92.9)	27 (84.4)	
At least one[a]	6 (13.0)	1 (7.1)	5 (15.6)	
Severity				0.40
Asymptomatic	4 (8.7)	2 (14.3)	2 (6.3)	
Mild	41 (89.1)	12 (85.7)	29 (90.6)	
Severe	1 (2.2)	0 (0.0)	1 (3.1)	
Symptoms at administration				
Dry cough	34 (81.0)	11 (91.7)	23 (76.7)	0.40
Fever	29 (69.1)	7 (58.3)	22 (73.3)	0.46
Expectoration	16 (38.1)	6 (50.0)	10 (33.3)	0.48

Headache	8 (19.1)	2 (16.7)	6 (20.0)	0.99
Fatigue	8 (19.1)	2 (16.7)	6 (20.0)	0.65
Pharyngalgia	7 (16.7)	3 (25.0)	4 (13.3)	0.39
Chest pain	3 (7.1)	1 (8.3)	2 (6.7)	0.99
Chest stuffiness	3 (7.1)	2 (16.7)	1 (3.3)	0.99
Anorexia	4 (9.5)	0 (0.0)	4 (13.3)	0.31
Myalgia	3 (7.1)	1 (8.3)	2 (6.7)	0.99
Dizziness	3 (7.1)	2 (16.7)	1 (3.3)	0.19
Diarrhea	2 (4.8)	2 (16.7)	0 (0.0)	0.08
Nausea	1 (2.4)	0 (0.0)	1 (3.3)	0.99
Rhinobyon	1 (2.4)	0 (0.0)	1 (3.3)	0.99
Shortness of breath	2 (2.4)	0 (0.0)	2 (6.7)	0.99
CT findings for lung				
Ground-glass opacity	29 (63.0)	7 (50.0)	22 (68.8)	0.23
Bilateral patchy shadowing	12 (26.1)	5 (35.7)	7 (21.9)	0.47
Consolidation	6 (13.0)	2 (14.3)	4 (12.5)	0.99
Local patchy shadowing	2 (4.4)	0 (0.0)	2 (6.3)	0.99

[a]The specific medical diseases included obesity (1), diabetes (1), Chronic lung disease (1), hyperthyroidism (1), kidney stones (1), and arthrolithiasis (1).

Table 2. Laboratory findings of study patients on admission. Values are medians (interquartile ranges) unless stated otherwise.

Variables	Total (N=46)	Adolescents (n=14)	Young adults (n=32)	P value
White blood cell count ($\times 10^9$/L)	5.0 (4.1- 6.7)	5.4 (4.5- 6.7)	4.8 (3.9- 6.7)	0.37
<4 (No(%))	10.0 (21.74)	1.0 (7.1)	9 (28.1)	0.21
>10 (No(%))	2.0 (4.4)	0 (0.0)	2 (6.3)	
Neutrophil count ($\times 10^9$/L)	3.4 (2.5- 4.4)	3.8 (3.1- 5.6)	3.2 (2.4- 4.4)	0.16
Lymphocyte count ($\times 10^9$/L)	1.3 (1.0- 1.8)	1.4 (1.1- 2.3)	1.3 (0.9- 1.8)	0.34
< 1.5 (No(%))	29 (63.0)	8 (57.1)	21 (65.6)	0.59
Platelet count ($\times 10^9$/L)	192.5 (156.0- 237.0)	183 (156.0- 227.0)	194.5 (152.0- 248.0)	0.16
< 150 (No(%))	10 (21.7)	2 (14.3)	8 (25.0)	0.70

Haemoglobin (g/L)	139.5 (130.0- 151.0)	147 (133.0- 151.0)	137.5 (128.5- 150.5)	0.29
Prothrombin time (S)	11 (10.6- 11.4)	11.25 (10.7- 11.9)	11 (10.5- 11.1)	0.07
Activated partial thromboplastin time (S)	27 (25.9- 30.3)	28.2(26.1- 30.4)	26.9 (25.0- 30.3)	0.39
D-dimer (mg/L)	0.3 (0.2- 0.4)	0.2 (0.1- 0.3)	0.3 (0.2- 0.4)	0.16
≥ 0.5 (No(%))	7 (15.2)	3 (21.4)	4 (12.5)	0.66
Alanine aminotransferase (U/L)	17.9 (11.6- 32.5)	16.3 (7.1- 24.3)	20 (11.7- 32.7)	0.25
>40 (No(%))	7 (15.2)	1 (7.2)	6 (18.8)	0.41
Aspartate aminotransferase (U/L)	18.3 (14.5- 26.9)	16.6 (12.4- 23.6)	19.3 (15.8- 28.6)	0.09
>40 (No(%))	3 (6.5)	0 (0.0)	3 (9.4)	0.54
Total bilirubin, μmol/L	8.7 (5.9- 14.6)	9 (5.9- 24.8)	8.3 (6.1- 13.5)	0.38
>17.1 (No(%))	7 (15.3)	4 (28.6)	3 (9.4)	0.18
Blood urea nitrogen, mmol/L	3.4 (2.6- 4.8)	3.9 (2.6- 4.9)	3.15 (2.6- 4.6)	0.32
Creatine (μmol/L)	61.5 (52.0- 79.0)	62.5 (53.0- 81.0)	61.5 (51.5- 77.0)	0.61
Creatine kinase (U/L):	57 (41.0- 73.0)	53 (42.0- 73.0)	57.6 (36.0- 74.9)	0.84
≥200 (No(%))	2 (4.4)	0 (0.0)	2 (6.3)	1.00
Lactate dehydrogenase (U/L):	195.5 (145.0- 240.0)	180 (152.0- 220.0)	200 (144.0- 244.0)	0.43
≥250 , (No(%))	9 (19.6)	2 (14.3)	7 (21.9)	0.70
Procalcitonin, ng/ml	0.03 (0.0- 0.1)	0.04 (0.0- 0.1)	0.03 (0.0- 0.1)	0.47
≥ 0.1(No(%))	2 (4.4)	0 (0.0)	2 (6.3)	1.00
C-reactive protein, mg/L	2.6 (0.8- 9.4)	3.2 (0.3- 5.6)	3.0 (1.0- 10.0)	0.42
≥10 (No(%))	9 (19.6)	1 (7.1)	8 (25.0)	0.16

Table 3. Treatments and prognosis outcomes in patients with COVID-19. Values are No. (%) unless stated otherwise.

Treatments and prognosis outcomes	Total patients (N=46)	Adolescents (N=14)	Young adults (N=32)	P value
Complications				
Acute kidney injury	3 (6.5)	1 (7.1)	2 (6.3)	0.99
Treatments				0.63
Antiviral therapy	46 (100.0)	14 (100.0)	32 (100.0)	-
Antifungal treatment	5 (10.9)	2 (14.3)	3 (9.4)	0.63
Oxygen inhalation	39 (84.8)	9 (64.3)	30 (93.8)	0.02
Atomization inhalation treatment				
Interferon alpha	43 (93.5)	13 (92.9)	30 (93.8)	0.67
N-acetylcysteine + interferon alpha	1 (2.2)	0 (0.0)	1 (3.1)	
N-acetylcysteine + budesonide + interferon alpha	2 (4.4)	1 (7.1)	1 (3.1)	
Days of persistent fever during admission, Median (IQR)	5 (1.0-8.0)	4.5 (0.0-7.0)	5 (2.0-9.0)	0.43
Days from date of admission to date of presenting negative result of COVID-19 nucleic acid test, Median (IQR)	12.5 (8.0-16.0)	13.0 (8.0-16.0)	12.50 (8.5-15.5)	0.87
Prognosis				0.07
Hospital admission	10 (21.7)	2 (14.3)	8 (25.0)	
Recovered and Discharged	36 (78.3)	12 (85.7)	24 (75.0)	

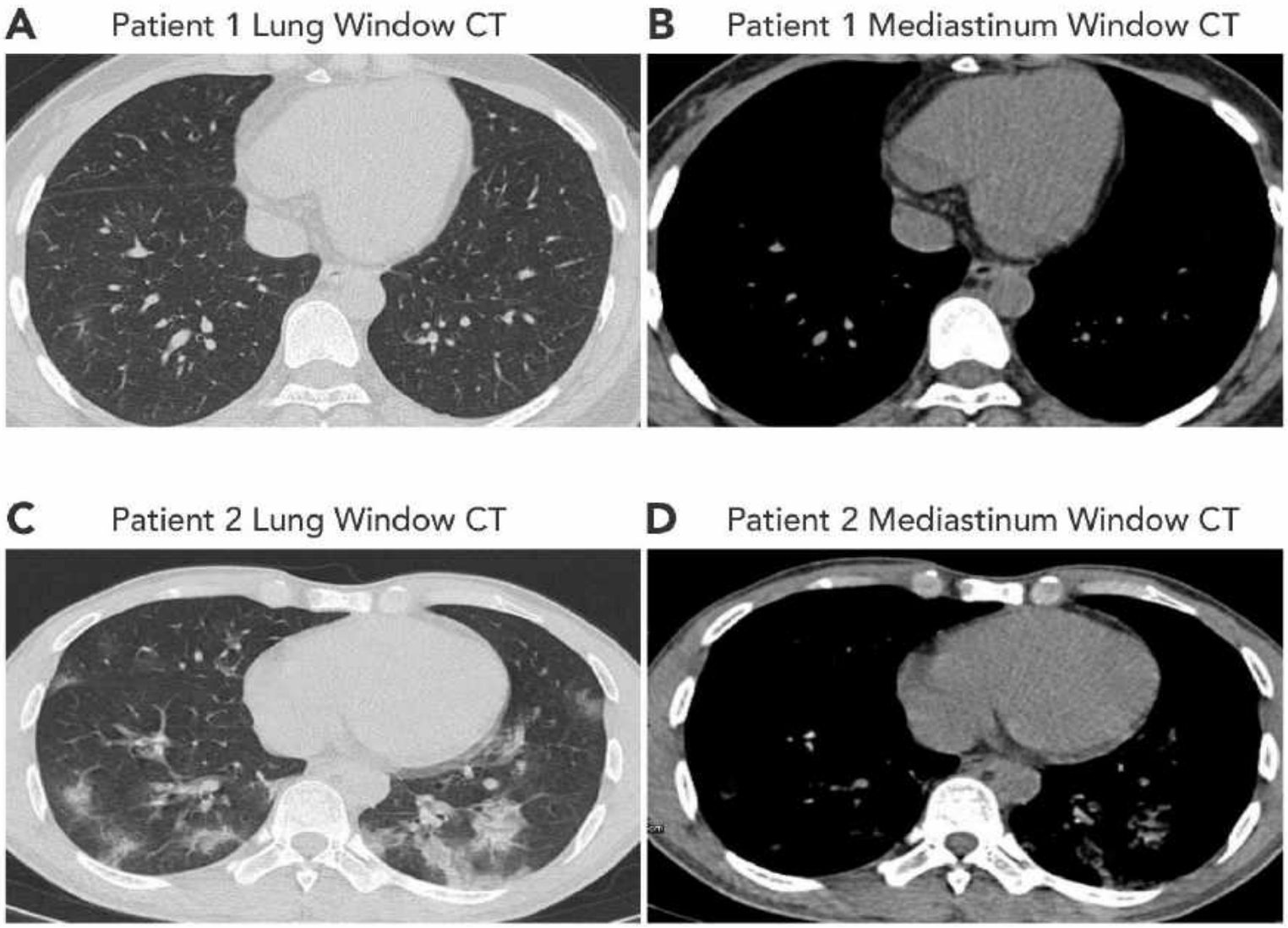
A
Patient 1 Lung Window CT
B
Patient 1 Mediastinum Window CT
C
Patient 2 Lung Window CT
D
Patient 2 Mediastinum Window CT

Figure 1


Cluster 1
(JAN. 2020)
Index Patient
January 7th Contact With Other Cases
Date Of Illness Onset
Patient 1-1 (Relative 1)
Date Of Illness Onset
Cluster 2
(JAN. 2020)
Index Patient
January 16th Return Home
Date Of Illness Onset
Patient 2-1 (Relative 1)
Date Of Illness Onset
Cluster 3
(JAN. 2020)
Index Patient
January 16th Return Home
Date Of Illness Onset
Patient 3-1 (Relative 1)
Date Of Illness Onset
Patient 3-2 (Relative 2)
Date Of Illness Onset
Cluster 4
(JAN. 2020 - FEB. 2020)
Index Patient
January 16th Return Home
Date Of Illness Onset
Patient 4-1 (Relative 1)
Date Of Illness Onset
Cluster 4
(JAN. 2020 - FEB. 2020)
Patient 4-2 (Relative 2)
Date Of Illness Onset
Patient 4-3 (Relative 3)
Date Of Illness Onset
Cluster 5
(JAN. 2020 - FEB. 2020)
Index Patient
January 21th Contact With Other Case
Date Of Illness Onset
Patient 5-1 (Relative 1)
Date Of Illness Onset
Patient 5-2 (Relative 2)
Date Of Illness Onset
Asymptomatic Patient 5-3 (Relative 3)
No Clinical Symptoms, Normal CT Findings
Date Of nucleic acid test postive
Cluster 6
(JAN. 2020 - FEB. 2020)
Index Patient
January 21th Contact With Other Case
Date Of Illness Onset
Patient 6-1 (Relative 1)
Date Of Illness Onset
Patient 6-2 (Relative 2)
Date Of Illness Onset
Patient 6-3 (Relative 3)
Date Of Illness Onset
Resided In Wuhan
Contact With Confirmed Cases
Travel to Wuhan

Figure 2

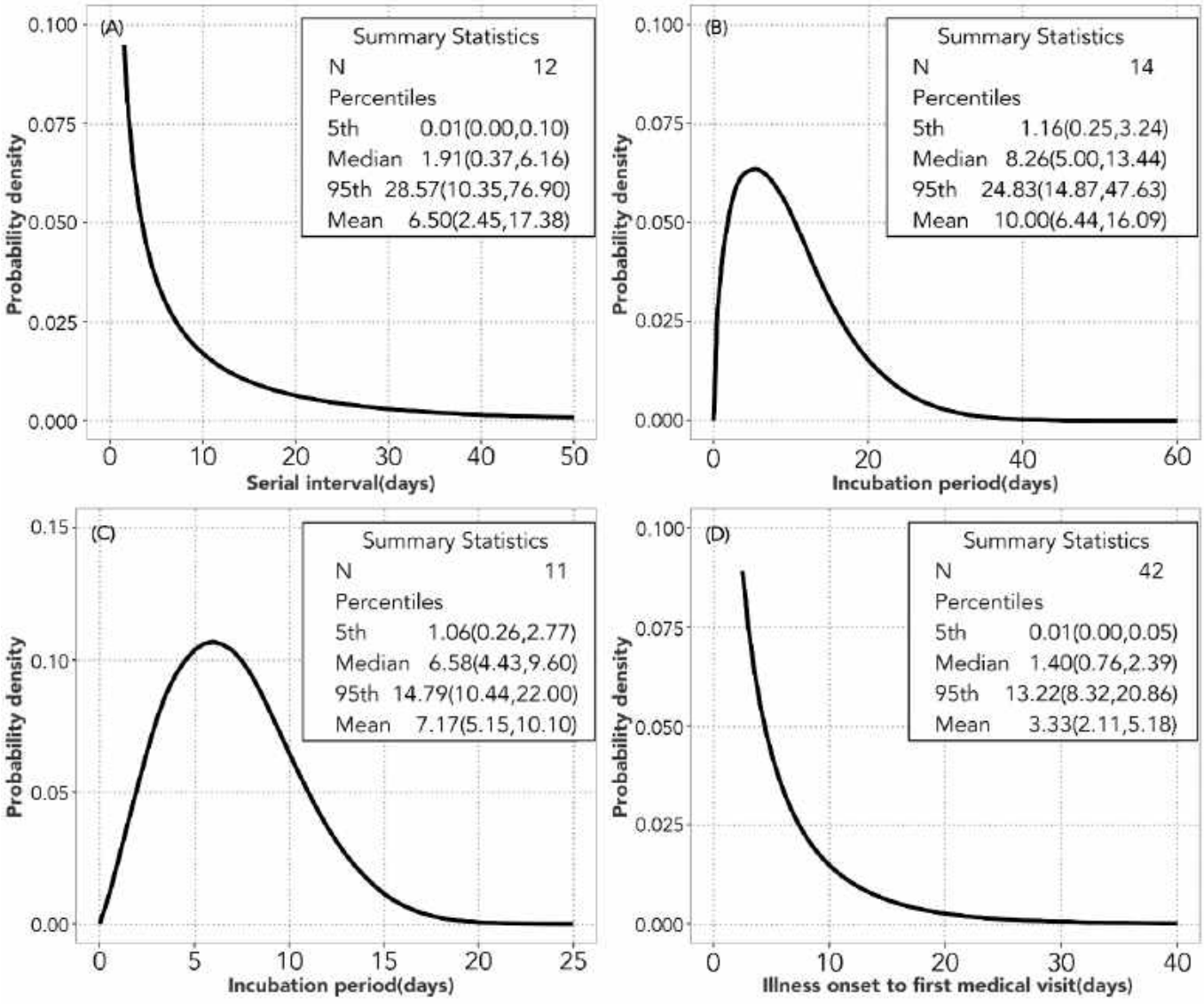
(A)
Summary Statistics
N 12
Percentiles
5th 0.01(0.00,0.10)
Median 1.91(0.37,6.16)
95th 28.57(10.35,76.90)
Mean 6.50(2.45,17.38)
Probability density
Serial interval(days)
(B)
Summary Statistics
N 14
Percentiles
5th 1.16(0.25,3.24)
Median 8.26(5.00,13.44)
95th 24.83(14.87,47.63)
Mean 10.00(6.44,16.09)
Probability density
Incubation period(days)
(C)
Summary Statistics
N 11
Percentiles
5th 1.06(0.26,2.77)
Median 6.58(4.43,9.60)
95th 14.79(10.44,22.00)
Mean 7.17(5.15,10.10)
Probability density
Incubation period(days)
(D)
Summary Statistics
N 42
Percentiles
5th 0.01(0.00,0.05)
Median 1.40(0.76,2.39)
95th 13.22(8.32,20.86)
Mean 3.33(2.11,5.18)
Probability density
Illness onset to first medical visit(days)

Figure 3

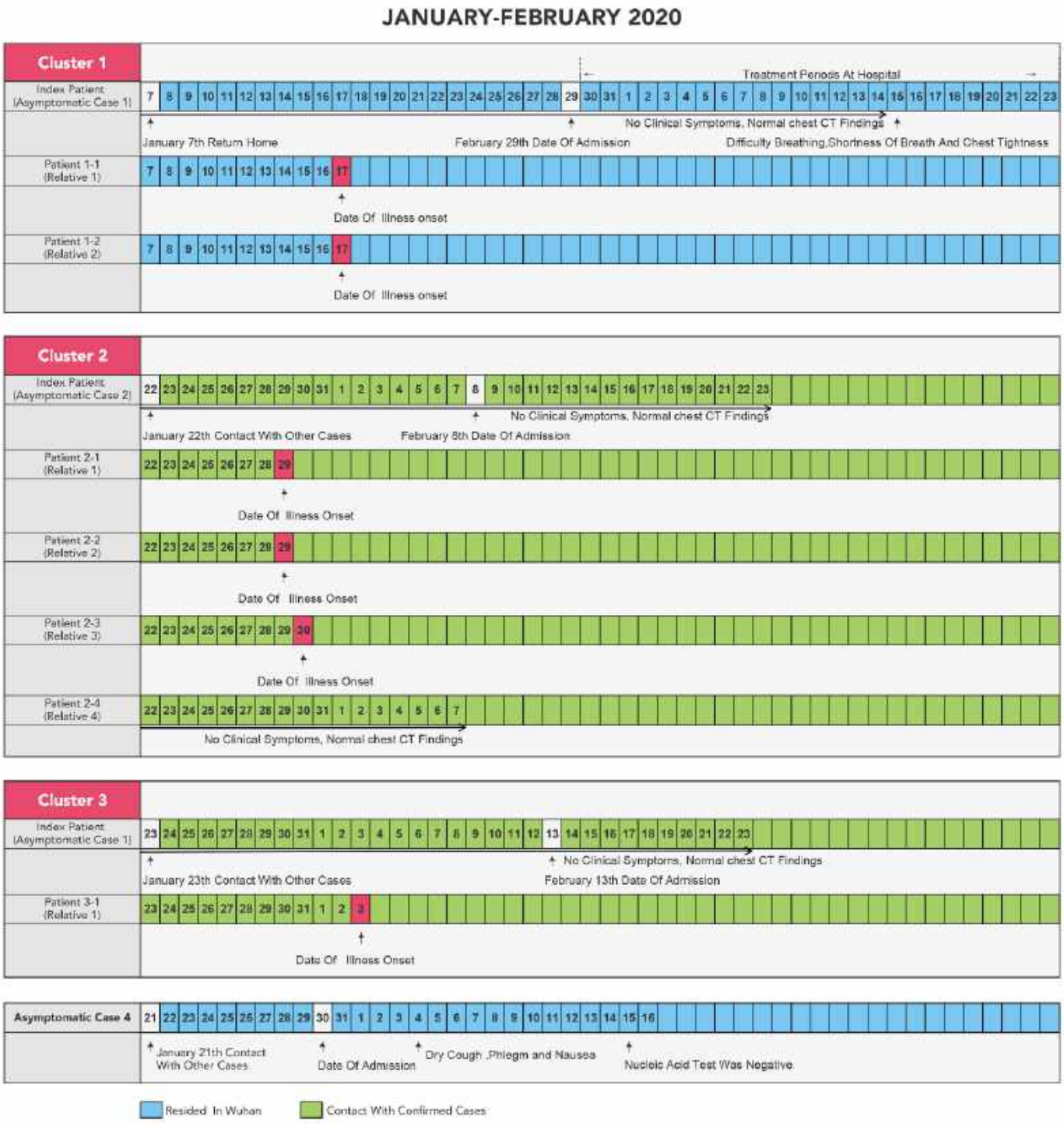
JANUARY-FEBRUARY 2020
Cluster 1
Index Patient (Asymptomatic Case 1)
Treatment Periods At Hospital
January 7th Return Home
February 29th Date Of Admission
No Clinical Symptoms, Normal chest CT Findings
Difficulty Breathing,Shortness Of Breath And Chest Tightness
Patient 1-1 (Relative 1)
Date Of Illness onset
Patient 1-2 (Relative 2)
Date Of Illness onset
Cluster 2
Index Patient (Asymptomatic Case 2)
January 22th Contact With Other Cases
February 8th Date Of Admission
No Clinical Symptoms, Normal chest CT Findings
Patient 2-1 (Relative 1)
Date Of Illness Onset
Patient 2-2 (Relative 2)
Date Of Illness Onset
Patient 2-3 (Relative 3)
Date Of Illness Onset
Patient 2-4 (Relative 4)
No Clinical Symptoms, Normal chest CT Findings
Cluster 3
Index Patient (Asymptomatic Case 1)
January 23th Contact With Other Cases
February 13th Date Of Admission
No Clinical Symptoms, Normal chest CT Findings
Patient 3-1 (Relative 1)
Date Of Illness Onset
Asymptomatic Case 4
January 21th Contact With Other Cases
Date Of Admission
Dry Cough ,Phlegm and Nausea
Nucleic Acid Test Was Negative
Resided In Wuhan
Contact With Confirmed Cases

Figure 4

Supplementary material

Epidemiological and clinical characteristics of COVID-19 in adolescents and young adults

Jiaqiang Liao, Shibing Fan, Jing Chen Jianglin Wu, Shunqing Xu, Yuming Guo, Chunhui Li, Xianxiang Zhang, Chuansha Wu, Huaming Mou, Chenxi Song, Feng Li, Guicheng Wu, Jingjing Zhang, Lian Guo, Huawen Liu, Jinglong Lv, Lixin Xu, Chunhui Lang

Supplementary Table S1. Characteristic of several patient.

Characteristic	Several patient
Gender	Male
Age	31
Chronic diseases history	None
Symptoms at administration	
Dry cough	Yes
Fever	Yes
Fatigue	Yes
Shortness of breath	Yes
White blood cell count ($\times 10^9$/L)	3.5
Neutrophil count ($\times 10^9$/L)	2.45
Lymphocyte count ($\times 10^9$/L)	0.66
Platelet count ($\times 10^9$/L)	125
Haemoglobin (g/L)	147
C-reactive protein, mg/L	116.92
Procalcitonin, ng/ml	0.045
CT findings for lung	

Ground-glass opacity	Yes
Bilateral patchy shadowing	Yes
Treatments	
Lopinavir / litonavir	Yes
interferon	Yes
Complications	None
Prognosis	Discharge home