

ORIGINAL ARTICLE

Clinical Characteristics of Coronavirus Disease 2019 in China

W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen, C. Tang, T. Wang, P. Chen, J. Xiang, S. Li, Jin-lin Wang, Z. Liang, Y. Peng, L. Wei, Y. Liu, Ya-hua Hu, P. Peng, Jian-ming Wang, J. Liu, Z. Chen, G. Li, Z. Zheng, S. Qiu, J. Luo, C. Ye, S. Zhu, and N. Zhong, for the China Medical Treatment Expert Group for Covid-19*

ABSTRACT

BACKGROUND

Since December 2019, when coronavirus disease 2019 (Covid-19) emerged in Wuhan city and rapidly spread throughout China, data have been needed on the clinical characteristics of the affected patients.

METHODS

We extracted data regarding 1099 patients with laboratory-confirmed Covid-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China through January 29, 2020. The primary composite end point was admission to an intensive care unit (ICU), the use of mechanical ventilation, or death.

RESULTS

The median age of the patients was 47 years; 41.9% of the patients were female. The primary composite end point occurred in 67 patients (6.1%), including 5.0% who were admitted to the ICU, 2.3% who underwent invasive mechanical ventilation, and 1.4% who died. Only 1.9% of the patients had a history of direct contact with wildlife. Among nonresidents of Wuhan, 72.3% had contact with residents of Wuhan, including 31.3% who had visited the city. The most common symptoms were fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). Diarrhea was uncommon (3.8%). The median incubation period was 4 days (interquartile range, 2 to 7). On admission, ground-glass opacity was the most common radiologic finding on chest computed tomography (CT) (56.4%). No radiographic or CT abnormality was found in 157 of 877 patients (17.9%) with nonsevere disease and in 5 of 173 patients (2.9%) with severe disease. Lymphocytopenia was present in 83.2% of the patients on admission.

CONCLUSIONS

During the first 2 months of the current outbreak, Covid-19 spread rapidly throughout China and caused varying degrees of illness. Patients often presented without fever, and many did not have abnormal radiologic findings. (Funded by the National Health Commission of China and others.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Zhong at the State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Health, First Affiliated Hospital of Guangzhou Medical University, 151 Yanjiang Rd., Guangzhou, Guangdong, China, or at nanshan@vip.163.com.

*A list of investigators in the China Medical Treatment Expert Group for Covid-19 study is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Guan, Ni, Yu Hu, W. Liang, Ou, He, L. Liu, Shan, Lei, Hui, Du, L. Li, Zeng, and Yuen contributed equally to this article.

This article was published on February 28, 2020, and last updated on March 6, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2002032

Copyright © 2020 Massachusetts Medical Society.

IN EARLY DECEMBER 2019, THE FIRST PNEUMONIA cases of unknown origin were identified in Wuhan, the capital city of Hubei province.¹ The pathogen has been identified as a novel enveloped RNA betacoronavirus² that has currently been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has a phylogenetic similarity to SARS-CoV.³ Patients with the infection have been documented both in hospitals and in family settings.⁴⁻⁸

The World Health Organization (WHO) has recently declared coronavirus disease 2019 (Covid-19) a public health emergency of international concern.⁹ As of February 25, 2020, a total of 81,109 laboratory-confirmed cases had been documented globally.^{5,6,9-11} In recent studies, the severity of some cases of Covid-19 mimicked that of SARS-CoV.^{1,12,13} Given the rapid spread of Covid-19, we determined that an updated analysis of cases throughout mainland China might help identify the defining clinical characteristics and severity of the disease. Here, we describe the results of our analysis of the clinical characteristics of Covid-19 in a selected cohort of patients throughout China.

METHODS

STUDY OVERSIGHT

The study was supported by National Health Commission of China and designed by the investigators. The study was approved by the institutional review board of the National Health Commission. Written informed consent was waived in light of the urgent need to collect data. Data were analyzed and interpreted by the authors. All the authors reviewed the manuscript and vouch for the accuracy and completeness of the data and for the adherence of the study to the protocol, available with the full text of this article at NEJM.org.

DATA SOURCES

We obtained the medical records and compiled data for hospitalized patients and outpatients with laboratory-confirmed Covid-19, as reported to the National Health Commission between December 11, 2019, and January 29, 2020; the data cutoff for the study was January 31, 2020. Covid-19 was diagnosed on the basis of the WHO interim guidance.¹⁴ A confirmed case of Covid-19 was defined as a positive result on high-

throughput sequencing or real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of nasal and pharyngeal swab specimens.¹ Only laboratory-confirmed cases were included in the analysis.

We obtained data regarding cases outside Hubei province from the National Health Commission. Because of the high workload of clinicians, three outside experts from Guangzhou performed raw data extraction at Wuhan Jinyintan Hospital, where many of the patients with Covid-19 in Wuhan were being treated.

We extracted the recent exposure history, clinical symptoms or signs, and laboratory findings on admission from electronic medical records. Radiologic assessments included chest radiography or computed tomography (CT), and all laboratory testing was performed according to the clinical care needs of the patient. We determined the presence of a radiologic abnormality on the basis of the documentation or description in medical charts; if imaging scans were available, they were reviewed by attending physicians in respiratory medicine who extracted the data. Major disagreement between two reviewers was resolved by consultation with a third reviewer. Laboratory assessments consisted of a complete blood count, blood chemical analysis, coagulation testing, assessment of liver and renal function, and measures of electrolytes, C-reactive protein, procalcitonin, lactate dehydrogenase, and creatine kinase. We defined the degree of severity of Covid-19 (severe vs. nonsevere) at the time of admission using the American Thoracic Society guidelines for community-acquired pneumonia.¹⁵

All medical records were copied and sent to the data-processing center in Guangzhou, under the coordination of the National Health Commission. A team of experienced respiratory clinicians reviewed and abstracted the data. Data were entered into a computerized database and cross-checked. If the core data were missing, requests for clarification were sent to the coordinators, who subsequently contacted the attending clinicians.

STUDY OUTCOMES

The primary composite end point was admission to an intensive care unit (ICU), the use of mechanical ventilation, or death. These outcomes

were used in a previous study to assess the severity of other serious infectious diseases, such as H7N9 infection.¹⁶ Secondary end points were the rate of death and the time from symptom onset until the composite end point and until each component of the composite end point.

STUDY DEFINITIONS

The incubation period was defined as the interval between the potential earliest date of contact of the transmission source (wildlife or person with suspected or confirmed case) and the potential earliest date of symptom onset (i.e., cough, fever, fatigue, or myalgia). We excluded incubation periods of less than 1 day because some patients had continuous exposure to contamination sources; in these cases, the latest date of exposure was recorded. The summary statistics of incubation periods were calculated on the basis of 291 patients who had clear information regarding the specific date of exposure.

Fever was defined as an axillary temperature of 37.5°C or higher. Lymphocytopenia was defined as a lymphocyte count of less than 1500 cells per cubic millimeter. Thrombocytopenia was defined as a platelet count of less than 150,000 per cubic millimeter. Additional definitions — including exposure to wildlife, acute respiratory distress syndrome (ARDS), pneumonia, acute kidney failure, acute heart failure, and rhabdomyolysis — are provided in the Supplementary Appendix, available at NEJM.org.

LABORATORY CONFIRMATION

Laboratory confirmation of SARS-CoV-2 was performed at the Chinese Center for Disease Prevention and Control before January 23, 2020, and subsequently in certified tertiary care hospitals. RT-PCR assays were performed in accordance with the protocol established by the WHO.¹⁷ Details regarding laboratory confirmation processes are provided in the Supplementary Appendix.

STATISTICAL ANALYSIS

Continuous variables were expressed as medians and interquartile ranges or simple ranges, as appropriate. Categorical variables were summarized as counts and percentages. No imputation was made for missing data. Because the cohort of patients in our study was not derived from random selection, all statistics are deemed to be

descriptive only. We used ArcGIS, version 10.2.2, to plot the numbers of patients with reportedly confirmed cases on a map. All the analyses were performed with the use of R software, version 3.6.2 (R Foundation for Statistical Computing).

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Of the 7736 patients with Covid-19 who had been hospitalized at 552 sites as of January 29, 2020, we obtained data regarding clinical symptoms and outcomes for 1099 patients (14.2%). The largest number of patients (132) had been admitted to Wuhan Jinyintan Hospital. The hospitals that were included in this study accounted for 29.7% of the 1856 designated hospitals where patients with Covid-19 could be admitted in 30 provinces, autonomous regions, or municipalities across China (Fig. 1).

The demographic and clinical characteristics of the patients are shown in Table 1. A total of 3.5% were health care workers, and a history of contact with wildlife was documented in 1.9%; 483 patients (43.9%) were residents of Wuhan. Among the patients who lived outside Wuhan, 72.3% had contact with residents of Wuhan, including 31.3% who had visited the city; 25.9% of nonresidents had neither visited the city nor had contact with Wuhan residents.

The median incubation period was 4 days (interquartile range, 2 to 7). The median age of the patients was 47 years (interquartile range, 35 to 58); 0.9% of the patients were younger than 15 years of age. A total of 41.9% were female. Fever was present in 43.8% of the patients on admission but developed in 88.7% during hospitalization. The second most common symptom was cough (67.8%); nausea or vomiting (5.0%) and diarrhea (3.8%) were uncommon. Among the overall population, 23.7% had at least one coexisting illness (e.g., hypertension and chronic obstructive pulmonary disease).

On admission, the degree of severity of Covid-19 was categorized as nonsevere in 926 patients and severe in 173 patients. Patients with severe disease were older than those with nonsevere disease by a median of 7 years. Moreover, the presence of any coexisting illness was more common among patients with severe disease than among those with nonsevere disease (38.7% vs.

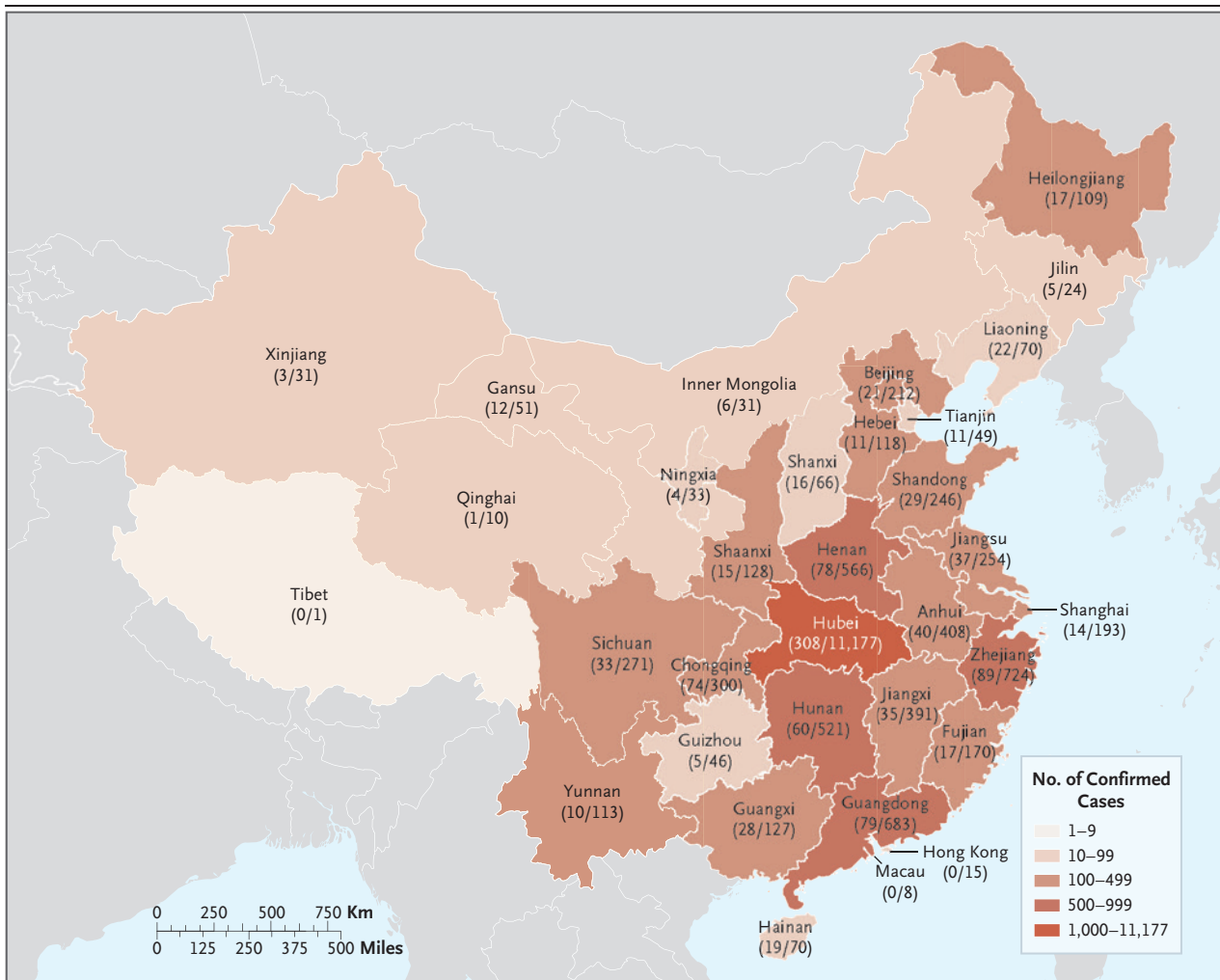


Figure 1. Distribution of Patients with Covid-19 across Mainland China.

Shown are the official statistics of all documented, laboratory-confirmed cases of coronavirus disease 2019 (Covid-19) throughout China, according to the National Health Commission as of February 4, 2020. The numerator denotes the number of patients who were included in the study cohort and the denominator denotes the number of laboratory-confirmed cases for each province, autonomous region, or provincial municipality, as reported by the National Health Commission.

21.0%). However, the exposure history between the two groups of disease severity was similar.

RADIOLOGIC AND LABORATORY FINDINGS

Table 2 shows the radiologic and laboratory findings on admission. Of 975 CT scans that were performed at the time of admission, 86.2% revealed abnormal results. The most common patterns on chest CT were ground-glass opacity (56.4%) and bilateral patchy shadowing (51.8%). Representative radiologic findings in two patients with nonsevere Covid-19 and in another

two patients with severe Covid-19 are provided in Figure S1 in the Supplementary Appendix. No radiographic or CT abnormality was found in 157 of 877 patients (17.9%) with nonsevere disease and in 5 of 173 patients (2.9%) with severe disease.

On admission, lymphocytopenia was present in 83.2% of the patients, thrombocytopenia in 36.2%, and leukopenia in 33.7%. Most of the patients had elevated levels of C-reactive protein; less common were elevated levels of alanine aminotransferase, aspartate aminotransferase,

creatinine kinase, and D-dimer. Patients with severe disease had more prominent laboratory abnormalities (including lymphocytopenia and leukopenia) than those with nonsevere disease.

CLINICAL OUTCOMES

None of the 1099 patients were lost to follow-up during the study. A primary composite end-point event occurred in 67 patients (6.1%), including 5.0% who were admitted to the ICU, 2.3% who underwent invasive mechanical ventilation, and 1.4% who died (Table 3). Among the 173 patients with severe disease, a primary composite end-point event occurred in 43 patients (24.9%). Among all the patients, the cumulative risk of the composite end point was 3.6%; among those with severe disease, the cumulative risk was 20.6%.

TREATMENT AND COMPLICATIONS

A majority of the patients (58.0%) received intravenous antibiotic therapy, and 35.8% received oseltamivir therapy; oxygen therapy was administered in 41.3% and mechanical ventilation in 6.1%; higher percentages of patients with severe disease received these therapies (Table 3). Mechanical ventilation was initiated in more patients with severe disease than in those with nonsevere disease (noninvasive ventilation, 32.4% vs. 0%; invasive ventilation, 14.5% vs. 0%). Systemic glucocorticoids were given to 204 patients (18.6%), with a higher percentage among those with severe disease than nonsevere disease (44.5% vs. 13.7%). Of these 204 patients, 33 (16.2%) were admitted to the ICU, 17 (8.3%) underwent invasive ventilation, and 5 (2.5%) died. Extracorporeal membrane oxygenation was performed in 5 patients (0.5%) with severe disease.

The median duration of hospitalization was 12.0 days (mean, 12.8). During hospital admission, most of the patients received a diagnosis of pneumonia from a physician (91.1%), followed by ARDS (3.4%) and shock (1.1%). Patients with severe disease had a higher incidence of physician-diagnosed pneumonia than those with nonsevere disease (99.4% vs. 89.5%).

DISCUSSION

During the initial phase of the Covid-19 outbreak, the diagnosis of the disease was complicated by the diversity in symptoms and imaging

findings and in the severity of disease at the time of presentation. Fever was identified in 43.8% of the patients on presentation but developed in 88.7% after hospitalization. Severe illness occurred in 15.7% of the patients after admission to a hospital. No radiologic abnormalities were noted on initial presentation in 2.9% of the patients with severe disease and in 17.9% of those with nonsevere disease. Despite the number of deaths associated with Covid-19, SARS-CoV-2 appears to have a lower case fatality rate than either SARS-CoV or Middle East respiratory syndrome-related coronavirus (MERS-CoV). Compromised respiratory status on admission (the primary driver of disease severity) was associated with worse outcomes.

Approximately 2% of the patients had a history of direct contact with wildlife, whereas more than three quarters were either residents of Wuhan, had visited the city, or had contact with city residents. These findings echo the latest reports, including the outbreak of a family cluster,⁴ transmission from an asymptomatic patient,⁶ and the three-phase outbreak patterns.⁸ Our study cannot preclude the presence of patients who have been termed “super-spreaders.”

Conventional routes of transmission of SARS-CoV, MERS-CoV, and highly pathogenic influenza consist of respiratory droplets and direct contact,¹⁸⁻²⁰ mechanisms that probably occur with SARS-CoV-2 as well. Because SARS-CoV-2 can be detected in the gastrointestinal tract, saliva, and urine, these routes of potential transmission need to be investigated²¹ (Tables S1 and S2).

The term Covid-19 has been applied to patients who have laboratory-confirmed symptomatic cases without apparent radiologic manifestations. A better understanding of the spectrum of the disease is needed, since in 8.9% of the patients, SARS-CoV-2 infection was detected before the development of viral pneumonia or viral pneumonia did not develop.

In concert with recent studies,^{1,8,12} we found that the clinical characteristics of Covid-19 mimic those of SARS-CoV. Fever and cough were the dominant symptoms and gastrointestinal symptoms were uncommon, which suggests a difference in viral tropism as compared with SARS-CoV, MERS-CoV, and seasonal influenza.^{22,23} The absence of fever in Covid-19 is more frequent than in SARS-CoV (1%) and MERS-CoV infection

Table 1. Clinical Characteristics of the Study Patients, According to Disease Severity and the Presence or Absence of the Primary Composite End Point.*

Characteristic	All Patients (N = 1099)	Disease Severity		Presence of Primary Composite End Point†	
		Nonsevere (N = 926)	Severe (N = 173)	Yes (N = 67)	No (N = 1032)
Age					
Median (IQR) — yr	47.0 (35.0–58.0)	45.0 (34.0–57.0)	52.0 (40.0–65.0)	63.0 (53.0–71.0)	46.0 (35.0–57.0)
Distribution — no./total no. (%)					
0–14 yr	9/1011 (0.9)	8/848 (0.9)	1/163 (0.6)	0	9/946 (1.0)
15–49 yr	557/1011 (55.1)	490/848 (57.8)	67/163 (41.1)	12/65 (18.5)	545/946 (57.6)
50–64 yr	292/1011 (28.9)	241/848 (28.4)	51/163 (31.3)	21/65 (32.3)	271/946 (28.6)
≥65 yr	153/1011 (15.1)	109/848 (12.9)	44/163 (27.0)	32/65 (49.2)	121/946 (12.8)
Female sex — no./total no. (%)	459/1096 (41.9)	386/923 (41.8)	73/173 (42.2)	22/67 (32.8)	437/1029 (42.5)
Smoking history — no./total no. (%)					
Never smoked	927/1085 (85.4)	793/913 (86.9)	134/172 (77.9)	44/66 (66.7)	883/1019 (86.7)
Former smoker	21/1085 (1.9)	12/913 (1.3)	9/172 (5.2)	5/66 (7.6)	16/1019 (1.6)
Current smoker	137/1085 (12.6)	108/913 (11.8)	29/172 (16.9)	17/66 (25.8)	120/1019 (11.8)
Exposure to source of transmission within past 14 days — no./total no.					
Living in Wuhan	483/1099 (43.9)	400/926 (43.2)	83/173 (48.0)	39/67 (58.2)	444/1032 (43.0)
Contact with wildlife	13/687 (1.9)	10/559 (1.8)	3/128 (2.3)	1/41 (2.4)	12/646 (1.9)
Recently visited Wuhan‡	193/616 (31.3)	166/526 (31.6)	27/90 (30.0)	10/28 (35.7)	183/588 (31.1)
Had contact with Wuhan residents‡	442/611 (72.3)	376/522 (72.0)	66/89 (74.2)	19/28 (67.9)	423/583 (72.6)
Median incubation period (IQR) — days§	4.0 (2.0–7.0)	4.0 (2.8–7.0)	4.0 (2.0–7.0)	4.0 (1.0–7.5)	4.0 (2.0–7.0)
Fever on admission					
Patients — no./total no. (%)	473/1081 (43.8)	391/910 (43.0)	82/171 (48.0)	24/66 (36.4)	449/1015 (44.2)
Median temperature (IQR) — °C	37.3 (36.7–38.0)	37.3 (36.7–38.0)	37.4 (36.7–38.1)	36.8 (36.3–37.8)	37.3 (36.7–38.0)
Distribution of temperature — no./total no. (%)					
<37.5°C	608/1081 (56.2)	519/910 (57.0)	89/171 (52.0)	42/66 (63.6)	566/1015 (55.8)
37.5–38.0°C	238/1081 (22.0)	201/910 (22.1)	37/171 (21.6)	10/66 (15.2)	228/1015 (22.5)
38.1–39.0°C	197/1081 (18.2)	160/910 (17.6)	37/171 (21.6)	11/66 (16.7)	186/1015 (18.3)
>39.0°C	38/1081 (3.5)	30/910 (3.3)	8/171 (4.7)	3/66 (4.5)	35/1015 (3.4)
Fever during hospitalization					
Patients — no./total no. (%)	975/1099 (88.7)	816/926 (88.1)	159/173 (91.9)	59/67 (88.1)	916/1032 (88.8)
Median highest temperature (IQR) — °C	38.3 (37.8–38.9)	38.3 (37.8–38.9)	38.5 (38.0–39.0)	38.5 (38.0–39.0)	38.3 (37.8–38.9)
<37.5°C	92/926 (9.9)	79/774 (10.2)	13/152 (8.6)	3/54 (5.6)	89/872 (10.2)
37.5–38.0°C	286/926 (30.9)	251/774 (32.4)	35/152 (23.0)	20/54 (37.0)	266/872 (30.5)
38.1–39.0°C	434/926 (46.9)	356/774 (46.0)	78/152 (51.3)	21/54 (38.9)	413/872 (47.4)
>39.0°C	114/926 (12.3)	88/774 (11.4)	26/152 (17.1)	10/54 (18.5)	104/872 (11.9)

Symptoms — no. (%)	9 (0.8)	5 (0.5)	4 (2.3)	0	9 (0.9)
Conjunctival congestion	53 (4.8)	47 (5.1)	6 (3.5)	2 (3.0)	51 (4.9)
Nasal congestion	150 (13.6)	124 (13.4)	26 (15.0)	8 (11.9)	142 (13.8)
Headache	745 (67.8)	623 (67.3)	122 (70.5)	46 (68.7)	699 (67.7)
Cough	153 (13.9)	130 (14.0)	23 (13.3)	6 (9.0)	147 (14.2)
Sore throat	370 (33.7)	309 (33.4)	61 (35.3)	20 (29.9)	350 (33.9)
Sputum production	419 (38.1)	350 (37.8)	69 (39.9)	22 (32.8)	397 (38.5)
Fatigue	10 (0.9)	6 (0.6)	4 (2.3)	2 (3.0)	8 (0.8)
Hemoptysis	205 (18.7)	140 (15.1)	65 (37.6)	36 (53.7)	169 (16.4)
Shortness of breath	55 (5.0)	43 (4.6)	12 (6.9)	3 (4.5)	52 (5.0)
Nausea or vomiting	42 (3.8)	32 (3.5)	10 (5.8)	4 (6.0)	38 (3.7)
Diarrhea	164 (14.9)	134 (14.5)	30 (17.3)	6 (9.0)	158 (15.3)
Myalgia or arthralgia	126 (11.5)	100 (10.8)	26 (15.0)	8 (11.9)	118 (11.4)
Chills					
Signs of infection — no. (%)					
Throat congestion	19 (1.7)	17 (1.8)	2 (1.2)	0	19 (1.8)
Tonsil swelling	23 (2.1)	17 (1.8)	6 (3.5)	1 (1.5)	22 (2.1)
Enlargement of lymph nodes	2 (0.2)	1 (0.1)	1 (0.6)	1 (1.5)	1 (0.1)
Rash	2 (0.2)	0	2 (1.2)	0	2 (0.2)
Coexisting disorder — no. (%)					
Any	261 (23.7)	194 (21.0)	67 (38.7)	39 (58.2)	222 (21.5)
Chronic obstructive pulmonary disease	12 (1.1)	6 (0.6)	6 (3.5)	7 (10.4)	5 (0.5)
Diabetes	81 (7.4)	53 (5.7)	28 (16.2)	18 (26.9)	63 (6.1)
Hypertension	165 (15.0)	124 (13.4)	41 (23.7)	24 (35.8)	141 (13.7)
Coronary heart disease	27 (2.5)	17 (1.8)	10 (5.8)	6 (9.0)	21 (2.0)
Cerebrovascular disease	15 (1.4)	11 (1.2)	4 (2.3)	4 (6.0)	11 (1.1)
Hepatitis B infection¶	23 (2.1)	22 (2.4)	1 (0.6)	1 (1.5)	22 (2.1)
Cancer	10 (0.9)	7 (0.8)	3 (1.7)	1 (1.5)	9 (0.9)
Chronic renal disease	8 (0.7)	5 (0.5)	3 (1.7)	2 (3.0)	6 (0.6)
Immunodeficiency	2 (0.2)	2 (0.2)	0	0	2 (0.2)

* The denominators of patients who were included in the analysis are provided if they differed from the overall numbers in the group. Percentages may not total 100 because of rounding. Covid-19 denotes coronavirus disease 2019, and IQR interquartile range.

† The primary composite end point was admission to an intensive care unit, the use of mechanical ventilation, or death.

‡ These patients were not residents of Wuhan.

§ Data regarding the incubation period were missing for 808 patients (73.5%).

¶ The presence of hepatitis B infection was defined as a positive result on testing for hepatitis B surface antigen with or without elevated levels of alanine or aspartate aminotransferase.

|| Included in this category is any type of cancer.

Table 2. Radiographic and Laboratory Findings.*

Table 2. Radiographic and Laboratory Findings.*					
Variable	All Patients (N = 1099)	Disease Severity		Presence of Composite Primary End Point	
		Nonsevere (N = 926)	Severe (N = 173)	Yes (N = 67)	No (N = 1032)
Radiologic findings					
Abnormalities on chest radiograph — no./total no. (%)	162/274 (59.1)	116/214 (54.2)	46/60 (76.7)	30/39 (76.9)	132/235 (56.2)
Ground-glass opacity	55/274 (20.1)	37/214 (17.3)	18/60 (30.0)	9/39 (23.1)	46/235 (19.6)
Local patchy shadowing	77/274 (28.1)	56/214 (26.2)	21/60 (35.0)	13/39 (33.3)	64/235 (27.2)
Bilateral patchy shadowing	100/274 (36.5)	65/214 (30.4)	35/60 (58.3)	27/39 (69.2)	73/235 (31.1)
Interstitial abnormalities	12/274 (4.4)	7/214 (3.3)	5/60 (8.3)	6/39 (15.4)	6/235 (2.6)
Abnormalities on chest CT — no./total no. (%)	840/975 (86.2)	682/808 (84.4)	158/167 (94.6)	50/57 (87.7)	790/918 (86.1)
Ground-glass opacity	550/975 (56.4)	449/808 (55.6)	101/167 (60.5)	30/57 (52.6)	520/918 (56.6)
Local patchy shadowing	409/975 (41.9)	317/808 (39.2)	92/167 (55.1)	22/57 (38.6)	387/918 (42.2)
Bilateral patchy shadowing	505/975 (51.8)	368/808 (45.5)	137/167 (82.0)	40/57 (70.2)	465/918 (50.7)
Interstitial abnormalities	143/975 (14.7)	99/808 (12.3)	44/167 (26.3)	15/57 (26.3)	128/918 (13.9)
Laboratory findings					
Median PaO ₂ :FiO ₂ ratio (IQR)†	3.9 (2.9–4.7)	3.9 (2.9–4.5)	4.0 (2.8–5.2)	2.9 (2.2–5.4)	4.0 (3.1–4.6)
White-cell count					
Median (IQR) — per mm ³	4700 (3500–6000)	4900 (3800–6000)	3700 (3000–6200)	6100 (4900–11,100)	4700 (3500–5900)
Distribution — no./total no. (%)					
>10,000 per mm ³	58/978 (5.9)	39/811 (4.8)	19/167 (11.4)	15/58 (25.9)	43/920 (4.7)
<4000 per mm ³	330/978 (33.7)	228/811 (28.1)	102/167 (61.1)	8/58 (13.8)	322/920 (35.0)
Lymphocyte count					
Median (IQR) — per mm ³	1000 (700–1300)	1000 (800–1400)	800 (600–1000)	700 (600–900)	1000 (700–1300)
Distribution — no./total no. (%)					
<1500 per mm ³	731/879 (83.2)	584/726 (80.4)	147/153 (96.1)	50/54 (92.6)	681/825 (82.5)

Lymphocytopenia was defined as a lymphocyte count of less than 1500 per cubic millimeter. To convert the values for creatinine to milligrams per deciliter, divide by 88.4. Data regarding the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$) were missing for 894 patients (81.3%). Data regarding hemoglobin were missing for 226 patients (20.6%). Data were missing for the measurement of sodium in 363 patients (33.0%), for potassium in 349 patients (31.8%), and for chloride in 392 patients (35.7%).

Table 3. Complications, Treatments, and Clinical Outcomes.

Variable	All Patients (N = 1099)	Disease Severity		Presence of Composite Primary End Point	
		Nonsevere (N = 926)	Severe (N = 173)	Yes (N = 67)	No (N = 1032)
Complications					
Septic shock — no. (%)	12 (1.1)	1 (0.1)	11 (6.4)	9 (13.4)	3 (0.3)
Acute respiratory distress syndrome — no. (%)	37 (3.4)	10 (1.1)	27 (15.6)	27 (40.3)	10 (1.0)
Acute kidney injury — no. (%)	6 (0.5)	1 (0.1)	5 (2.9)	4 (6.0)	2 (0.2)
Disseminated intravascular coagulation — no. (%)	1 (0.1)	0	1 (0.6)	1 (1.5)	0
Rhabdomyolysis — no. (%)	2 (0.2)	2 (0.2)	0	0	2 (0.2)
Physician-diagnosed pneumonia — no./total no. (%)	972/1067 (91.1)	800/894 (89.5)	172/173 (99.4)	63/66 (95.5)	909/1001 (90.8)
Median time until development of pneumonia (IQR) — days*					
After initial Covid-19 diagnosis	0.0 (0.0–1.0)	0.0 (0.0–1.0)	0.0 (0.0–2.0)	0.0 (0.0–3.5)	0.0 (0.0–1.0)
After onset of Covid-19 symptoms	3.0 (1.0–6.0)	3.0 (1.0–6.0)	5.0 (2.0–7.0)	4.0 (0.0–7.0)	3.0 (1.0–6.0)
Treatments					
Intravenous antibiotics — no. (%)	637 (58.0)	498 (53.8)	139 (80.3)	60 (89.6)	577 (55.9)
Oseltamivir — no. (%)	393 (35.8)	313 (33.8)	80 (46.2)	36 (53.7)	357 (34.6)
Antifungal medication — no. (%)	31 (2.8)	18 (1.9)	13 (7.5)	8 (11.9)	23 (2.2)
Systemic glucocorticoids — no. (%)	204 (18.6)	127 (13.7)	77 (44.5)	35 (52.2)	169 (16.4)
Oxygen therapy — no. (%)	454 (41.3)	331 (35.7)	123 (71.1)	59 (88.1)	395 (38.3)
Mechanical ventilation — no. (%)	67 (6.1)	0	67 (38.7)	40 (59.7)	27 (2.6)
Invasive	25 (2.3)	0	25 (14.5)	25 (37.3)	0
Noninvasive	56 (5.1)	0	56 (32.4)	29 (43.3)	27 (2.6)
Use of extracorporeal membrane oxygenation — no. (%)	5 (0.5)	0	5 (2.9)	5 (7.5)	0
Use of continuous renal-replacement therapy — no. (%)	9 (0.8)	0	9 (5.2)	8 (11.9)	1 (0.1)
Use of intravenous immune globulin — no. (%)	144 (13.1)	86 (9.3)	58 (33.5)	27 (40.3)	117 (11.3)
Admission to intensive care unit — no. (%)	55 (5.0)	22 (2.4)	33 (19.1)	55 (82.1)	0
Median length of hospital stay (IQR) — days†	12.0 (10.0–14.0)	11.0 (10.0–13.0)	13.0 (11.5–17.0)	14.5 (11.0–19.0)	12.0 (10.0–13.0)

Clinical outcomes at data cutoff — no. (%)					
Discharge from hospital	55 (5.0)	50 (5.4)	5 (2.9)	1 (1.5)	54 (5.2)
Death	15 (1.4)	1 (0.1)	14 (8.1)	15 (22.4)	0
Recovery	9 (0.8)	7 (0.8)	2 (1.2)	0	9 (0.9)
Hospitalization	1029 (93.6)	875 (94.5)	154 (89.0)	51 (76.1)	978 (94.8)

* For the development of pneumonia, data were missing for 347 patients (31.6%) regarding the time since the initial diagnosis and for 161 patients (14.6%) regarding the time since symptom onset.

† Data regarding the median length of hospital stay were missing for 136 patients (12.4%).

(2%),²⁰ so afebrile patients may be missed if the surveillance case definition focuses on fever detection.¹⁴ Lymphocytopenia was common and, in some cases, severe, a finding that was consistent with the results of two recent reports.^{1,12} We found a lower case fatality rate (1.4%) than the rate that was recently reportedly,^{1,12} probably because of the difference in sample sizes and case inclusion criteria. Our findings were more similar to the national official statistics, which showed a rate of death of 3.2% among 51,857 cases of Covid-19 as of February 16, 2020.^{11,24} Since patients who were mildly ill and who did not seek medical attention were not included in our study, the case fatality rate in a real-world scenario might be even lower. Early isolation, early diagnosis, and early management might have collectively contributed to the reduction in mortality in Guangdong.

Despite the phylogenetic homogeneity between SARS-CoV-2 and SARS-CoV, there are some clinical characteristics that differentiate Covid-19 from SARS-CoV, MERS-CoV, and seasonal influenza infections. (For example, seasonal influenza has been more common in respiratory outpatient clinics and wards.) Some additional characteristics that are unique to Covid-19 are detailed in Table S3.

Our study has some notable limitations. First, some cases had incomplete documentation of the exposure history and laboratory testing, given the variation in the structure of electronic databases among different participating sites and the urgent timeline for data extraction. Some cases were diagnosed in outpatient settings where medical information was briefly documented and incomplete laboratory testing was performed, along with a shortage of infrastructure and training of medical staff in non-specialty hospitals. Second, we could estimate the incubation period in only 291 of the study patients who had documented information. The uncertainty of the exact dates (recall bias) might have inevitably affected our assessment. Third, because many patients remained in the hospital and the outcomes were unknown at the time of data cutoff, we censored the data regarding their clinical outcomes as of the time of our analysis. Fourth, we no doubt missed patients who were asymptomatic or had mild cases and who were treated at home, so our study cohort may represent the more severe end of Covid-19. Fifth,

many patients did not undergo sputum bacteriologic or fungal assessment on admission because, in some hospitals, medical resources were overwhelmed. Sixth, data generation was clinically driven and not systematic.

Covid-19 has spread rapidly since it was first identified in Wuhan and has been shown to have a wide spectrum of severity. Some patients with Covid-19 do not have fever or radiologic abnormalities on initial presentation, which has complicated the diagnosis.

Supported by the National Health Commission of China, the National Natural Science Foundation, and the Department of Science and Technology of Guangdong Province.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank all the hospital staff members (see Supplementary Appendix for a full list of the staff) for their efforts in collecting the information that was used in this study; Zong-jiu Zhang, Ya-hui Jiao, Xin-qiang Gao, and Tao Wei (National Health Commission), Yu-fei Duan and Zhi-ling Zhao (Health Commission of

Guangdong Province), and Yi-min Li, Nuo-fu Zhang, Qing-hui Huang, Wen-xi Huang, and Ming Li (Guangzhou Institute of Respiratory Health) for facilitating the collection of patients' data; the statistical team members Zheng Chen, Dong Han, Li Li, Zhi-ying Zhan, Jin-jian Chen, Li-jun Xu, and Xiao-han Xu (State Key Laboratory of Organ Failure Research, Department of Biostatistics, Guangdong Provincial Key Laboratory of Tropical Disease Research, School of Public Health, and Southern Medical University, respectively); Li-qiang Wang, Wei-peng Cai, Zi-sheng Chen (the Sixth Affiliated Hospital of Guangzhou Medical University) and Chang-xing Ou, Xiao-min Peng, Si-ni Cui, Yuan Wang, Mou Zeng, Xin Hao, Qi-hua He, Jing-pei Li, Xu-kai Li, Wei Wang, Li-min Ou, Ya-lei Zhang, Jing-wei Liu, Xin-guo Xiong, Wei-juna Shi, San-mei Yu, Run-dong Qin, Si-yang Yao, Bo-meng Zhang, Xiao-hong Xie, Zhan-hong Xie, Wan-di Wang, Xiao-xian Zhang, Hui-yin Xu, Zi-qing Zhou, Ying Jiang, Ni Liu, Jing-jing Yuan, Zheng Zhu, Jie-xia Zhang, Hong-hao Li, Wei-hua Huang, Lu-lin Wang, Jie-ying Li, Li-fen Gao, Cai-chen Li, Xue-wei Chen, Jia-bo Gao, Ming-shan Xue, Shou-xie Huang, Jia-man Tang, and Wei-li Gu (Guangzhou Institute of Respiratory Health) for their dedication to data entry and verification; Tencent (Internet-services company) for providing the number of hospitals certified to admit patients with Covid-19 throughout China; and all the patients who consented to donate their data for analysis and the medical staff members who are on the front line of caring for patients.

APPENDIX

The authors' full names and academic degrees are as follows: Wei-jie Guan, Ph.D., Zheng-yi Ni, M.D., Yu Hu, M.D., Wen-hua Liang, Ph.D., Chun-quan Ou, Ph.D., Jian-xing He, M.D., Lei Liu, M.D., Hong Shan, M.D., Chun-liang Lei, M.D., David S.C. Hui, M.D., Bin Du, M.D., Lan-juan Li, M.D., Guang Zeng, M.Sc., Kwok-Yung Yuen, Ph.D., Ru-chong Chen, M.D., Chun-li Tang, M.D., Tao Wang, M.D., Ping-yan Chen, M.D., Jie Xiang, M.D., Shi-yue Li, M.D., Jin-lin Wang, M.D., Zi-jing Liang, M.D., Yi-xiang Peng, M.D., Li Wei, M.D., Yong Liu, M.D., Ya-hua Hu, M.D., Peng Peng, M.D., Jian-ming Wang, M.D., Ji-yang Liu, M.D., Zhong Chen, M.D., Gang Li, M.D., Zhi-jian Zheng, M.D., Shao-qin Qiu, M.D., Jie Luo, M.D., Chang-jiang Ye, M.D., Shao-yong Zhu, M.D., and Nan-shan Zhong, M.D.

The authors' affiliations are as follows: the State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Health, First Affiliated Hospital of Guangzhou Medical University (W.G., W.L., J.H., R.C., C.T., T.W., S.L., Jin-lin Wang, N.Z., J.H., W.L.), the Departments of Thoracic Oncology (W.L.), Thoracic Surgery and Oncology (J.H.), and Emergency Medicine (Z.L.), First Affiliated Hospital of Guangzhou Medical University, and Guangzhou Eighth People's Hospital, Guangzhou Medical University (C.L.), and the State Key Laboratory of Organ Failure Research, Department of Biostatistics, Guangdong Provincial Key Laboratory of Tropical Disease Research, School of Public Health, Southern Medical University (C.O., P.C.), Guangzhou, Wuhan Jinyintan Hospital (Z.N., J.X.), Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (Yu Hu), the Central Hospital of Wuhan (Y.P.), Wuhan No. 1 Hospital, Wuhan Hospital of Traditional Chinese and Western Medicine (L.W.), Wuhan Pulmonary Hospital (P.P.), Tianyou Hospital Affiliated to Wuhan University of Science and Technology (Jian-ming Wang), and the People's Hospital of Huangpi District (S.Z.), Wuhan, Shenzhen Third People's Hospital and the Second Affiliated Hospital of Southern University of Science and Technology, National Clinical Research Center for Infectious Diseases (L. Liu), and the Department of Clinical Microbiology and Infection Control, University of Hong Kong-Shenzhen Hospital (K.-Y.Y.), Shenzhen, the Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai (H.S.), the Department of Medicine and Therapeutics, Chinese University of Hong Kong, Shatin (D.S.C.H.), and the Department of Microbiology and the Carol Yu Center for Infection, Li Ka Shing Faculty of Medicine, University of Hong Kong, Pok Fu Lam (K.-Y.Y.), Hong Kong, Medical ICU, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences (B.D.), and the Chinese Center for Disease Control and Prevention (G.Z.), Beijing, the State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou (L. Li), Chengdu Public Health Clinical Medical Center, Chengdu (Y.L.), Huangshi Central Hospital of Edong Healthcare Group, Affiliated Hospital of Hubei Polytechnic University, Huangshi (Ya-hua Hu), the First Hospital of Changsha, Changsha (J. Liu), the Third People's Hospital of Hainan Province, Sanya (Z.C.), Huanggang Central Hospital, Huanggang (G.L.), Wenling First People's Hospital, Wenling (Z.Z.), the Third People's Hospital of Yichang, Yichang (S.Q.), Affiliated Taihe Hospital of Hubei University of Medicine, Shiyan (J. Luo), and Xiantao First People's Hospital, Xiantao (C.Y.) — all in China.

REFERENCES

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
- Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020; 395:565-74.
- Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382:727-33.
- Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with

- the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514-23.
5. Phan LT, Nguyen TV, Luong QC, et al. Importation and human-to-human transmission of a novel coronavirus in Vietnam. *N Engl J Med*. DOI:10.1056/NEJMc2001272.
 6. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med*. DOI:10.1056/NEJMc2001468.
 7. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020 January 31 (Epub ahead of print).
 8. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. DOI:10.1056/NEJMoa2001316.
 9. World Health Organization. Coronavirus disease (COVID-19) outbreak (<https://www.who.int>).
 10. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. DOI:10.1056/NEJMoa2001191.
 11. National Health Commission of the People's Republic of China home page (<http://www.nhc.gov.cn>).
 12. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507-13.
 13. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020 February 7 (Epub ahead of print).
 14. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. January 28, 2020 (<https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf>).
 15. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia: an official clinical practice guideline of the American Thoracic Society and Infectious Disease Society of America. *Am J Respir Crit Care Med* 2019;200(7):e45-e67.
 16. Gao H-N, Lu H-Z, Cao B, et al. Clinical findings in 111 cases of influenza A (H7N9) virus infection. *N Engl J Med* 2013;368:2277-85.
 17. World Health Organization. Coronavirus disease (COVID-19) technical guidance: laboratory testing for 2019-nCoV in humans (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance>).
 18. Lei H, Li Y, Xiao S, et al. Routes of transmission of influenza A H1N1, SARS CoV, and norovirus in air cabin: comparative analyses. *Indoor Air* 2018;28:394-403.
 19. Otter JA, Donskey C, Yezli S, Douthwaite S, Goldenberg SD, Weber DJ. Transmission of SARS and MERS coronaviruses and influenza virus in healthcare settings: the possible role of dry surface contamination. *J Hosp Infect* 2016;92:235-50.
 20. Zumla A, Hui DS, Perlman S. Middle East respiratory syndrome. *Lancet* 2015;386:995-1007.
 21. Minodier L, Charrel RN, Ceccaldi PE, et al. Prevalence of gastrointestinal symptoms in patients with influenza, clinical significance, and pathophysiology of human influenza viruses in faecal samples: what do we know? *Virology* 2015;12:215.
 22. Leung WK, To KF, Chan PK, et al. Enteric involvement of severe acute respiratory syndrome-associated coronavirus infection. *Gastroenterology* 2003;125:1011-7.
 23. Assiri A, McGeer A, Perl TM, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med* 2013;369:407-16.
 24. World Health Organization. Coronavirus disease (COVID-2019) situation reports (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>).

Copyright © 2020 Massachusetts Medical Society.