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Review

Management and Treatment of COVID-19: The Chinese Experience

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ABSTRACT

With more than 1,800,000 cases and 110,000 deaths globally, COVID-19 is one of worst infectious disease outbreaks in history. This paper provides a critical review of the available evidence regarding the lessons learned from the Chinese experience with COVID-19 prevention and management. The steps that have led to a near disappearance of new cases in China included rapid sequencing of the virus to establish testing kits, which allowed tracking of infected persons in and out of Wuhan. In addition, aggressive quarantine measures included the

RÉSUMÉ

Avec plus de 1 800 000 cas et 110 000 décès dans le monde, la COVID-19 est l'une des pires éclosions de maladies infectieuses de l'histoire. Ce document présente un examen critique des constats disponibles concernant les leçons tirées de l'expérience chinoise en matière de prévention et de gestion de la COVID-19. Les mesures qui ont conduit à la quasi-disparition des nouveaux cas en Chine comprenaient le séquençage rapide du virus pour établir des trousseaux de tests, ce qui a permis de suivre les personnes infectées à l'intérieur et à

Since mid-December 2019, there has been a worldwide outbreak of coronavirus disease (COVID)–19, caused by SARS-CoV-2 (formerly 2019-nCoV or HCoV-19) and first

detected in Wuhan, China. The incubation period is 1-14 days (mean 5-6 days) in most cases, but can be as long as 24 days.¹ The most commonly seen characteristics of COVID-19 are fever, cough, and abnormal chest computed tomography.^{2,3} At present, the Chinese chrysanthemum bat is thought to be the origin of SARS-CoV-2, based on sequence homology of 96% between SARS-CoV-2 and Bat-CoV-RaTG13.^{4,5} The pangolin has been proposed as an intermediate host, but this has not been confirmed.^{6,7} Human-to-human transmission of SARS-CoV-2 occurs mainly via respiratory droplets,¹ direct contact,¹ asymptomatic transmission,^{8,9} and intrafamilial transmission.³

SARS-CoV-2 can affect any demographic, including senior citizens, children, and pregnant women.^{3,10} According to the World Health Organisation (WHO), the Johns Hopkins Center for Systems Science and Engineering, and the State Council Information Office in Beijing, China, as of April 12, 2020, there have been more than 1,800,000 cases of COVID-19 worldwide,

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complete isolation of Wuhan and then later Hubei Province and the rest of the country, as well as closure of all schools and nonessential businesses. Other measures included the rapid construction of two new hospitals and the establishment of “Fangcang” shelter hospitals. In the absence of a vaccine, the management of COVID-19 included antivirals, high-flow oxygen, mechanical ventilation, corticosteroids, hydroxychloroquine, tocilizumab, interferons, intravenous immunoglobulin, and convalescent plasma infusions. These measures appeared to provide only moderate success. Although some measures have been supported by weak descriptive data, their effectiveness is still unclear pending well controlled clinical trials. In the end, it was the enforcement of drastic quarantine measures that stopped SARS-CoV-2 from spreading. The earlier the implementation, the less likely resources will be depleted. The most critical factors in stopping a pandemic are early recognition of infected individuals, carriers, and contacts and early implementation of quarantine measures with an organised, proactive, and unified strategy at a national level. Delays result in significantly higher death tolls.

with 83,597 cases of COVID-19 confirmed in China, including 2,101 active cases (121 active severe cases), 1378 imported cases, 3351 deaths (mortality rate 3.99%), and 78,145 recovered cases (cure rate 93.5%). Today, normal life is slowly returning in most regions in an orderly and cautious manner, including in Wuhan, the epicenter of the epidemic in China.

To stop transmission of the virus and save lives, China adopted strategies and tactics that included a nationwide directive from the central government, governmental oversight, free testing (nucleic acid assay, gene sequencing, and IgM-IgG serology), free treatment, establishment of “Fangcang” hospitals, travel restrictions, new regulations, diagnostic algorithms, and the transfer of resources to the epicenter of the infection in Hubei Province. Very early, on January 23, 2020, when there were about 800 cases and 17 deaths, the entire city of Wuhan and subsequently Hubei Province were locked down and sealed off.

On March 2, the European Centers for Disease Control and Prevention (CDC) raised the SARS-CoV-2 risk level from moderate to high. On March 11, 2020, WHO declared COVID-19 a pandemic and recommended aggressive action by all countries in the world, warning that most countries were not prepared to handle the spread of SARS-CoV-2. As of April 12, 2020, SARS-CoV-2 has infected 1,770,469 people outside of China, causing 110,867 deaths (mortality rate 6.27%). It has been found in 6 continents, including 212 of 233 (91.0%) countries and international conveyances. The United States (560,402 cases), Spain (166,831 cases), Italy (156,363 cases), Germany (127,854 cases), and Iran (71,686 cases) are among the hardest hit, but cases in other countries are increasing rapidly.¹¹

Managing the Spread of the Epidemic

The most important strategy to combat a pandemic is to prevent it from even happening. This means that the spread of

l'extérieur de Wuhan. En outre, des mesures agressives de quarantaine ont consisté à isoler complètement Wuhan, puis la province de Hubei et le reste du pays, ainsi qu'à fermer toutes les écoles et les entreprises non essentielles. D'autres mesures ont été prises, notamment la construction rapide de deux nouveaux hôpitaux et la création d'hôpitaux provisoires de type « Fangcang ». En l'absence de vaccin, la gestion de la COVID-19 a compris des antiviraux, de l'oxygène à haut débit, de la ventilation mécanique, des corticostéroïdes, de l'hydroxychloroquine, du tocilizumab, des interférons, des immunoglobulines en intraveineuses et des perfusions de plasma de patients convalescents. Ces mesures ne semblent avoir apporté qu'un succès modéré. Bien que certaines mesures aient été soutenues par des données descriptives modestes, leur efficacité n'est pas encore évidente, en attendant de meilleurs essais cliniques contrôlés. En fin de compte, c'est l'application de mesures de quarantaine drastiques qui a permis d'arrêter la propagation du SARS-CoV-2. Plus la mise en œuvre est précoce, moins il est probable que les limites des ressources soient atteintes. Les facteurs les plus critiques pour stopper une pandémie sont l'identification précoce des personnes infectées, des porteurs et des contacts et la mise en œuvre rapide de mesures de quarantaine grâce à une stratégie organisée, proactive et unifiée au niveau national. Tout retard entraîne une augmentation significative du nombre de décès.

a virus needs to be countered as early as possible. The COVID-19 epidemic curves and major intervention measures that were implemented in China are shown in [Figure 1](#). Here is a description of the timeline.

On December 31, 2019, the Wuhan Municipal Health Commission revealed a cluster of cases of pneumonia of unknown etiology. The Chinese CDC sent experts to Wuhan to support the investigation and control effort.¹²

On January 3, 2020, the first genomic sequence of the novel β -genus coronaviruses, now known as SARS-CoV-2, was determined by scientists of the National Institute of Viral Disease Control and Prevention.¹³ China informed the WHO.

On January 10, 2020, the whole genome sequence of the SARS-CoV-2 was shared with the WHO. Several rapid and sensitive detection tests were developed by the China CDC.

On January 16, 2020, the National Health Commission (NHC) issued the first of 7 versions of the protocol for the diagnosis and treatment of COVID-19.

On January 20, 2020, the NHC upgraded the management of the COVID-19 to the highest level pertaining to class A infectious diseases.

On January 21, 2020, the NHC officially started to release daily disease information on the government website.

On January 23, 2020, the Chinese government began to limit movement of people in and out of Wuhan and announced that all public transportation, including city buses, subways, ferries, long-distance coaches, outbound channels at airports, and railway stations in Wuhan had been suspended or closed.

On January 24, 2020, the local government planned 2 new quarantine hospitals with 1000 and 1600 beds to be constructed within 10 days. By March 8, 2020, 42,600 health professionals from outside Hubei and 1,800 epidemiologic teams participated in battling COVID-19 in Hubei.¹⁴

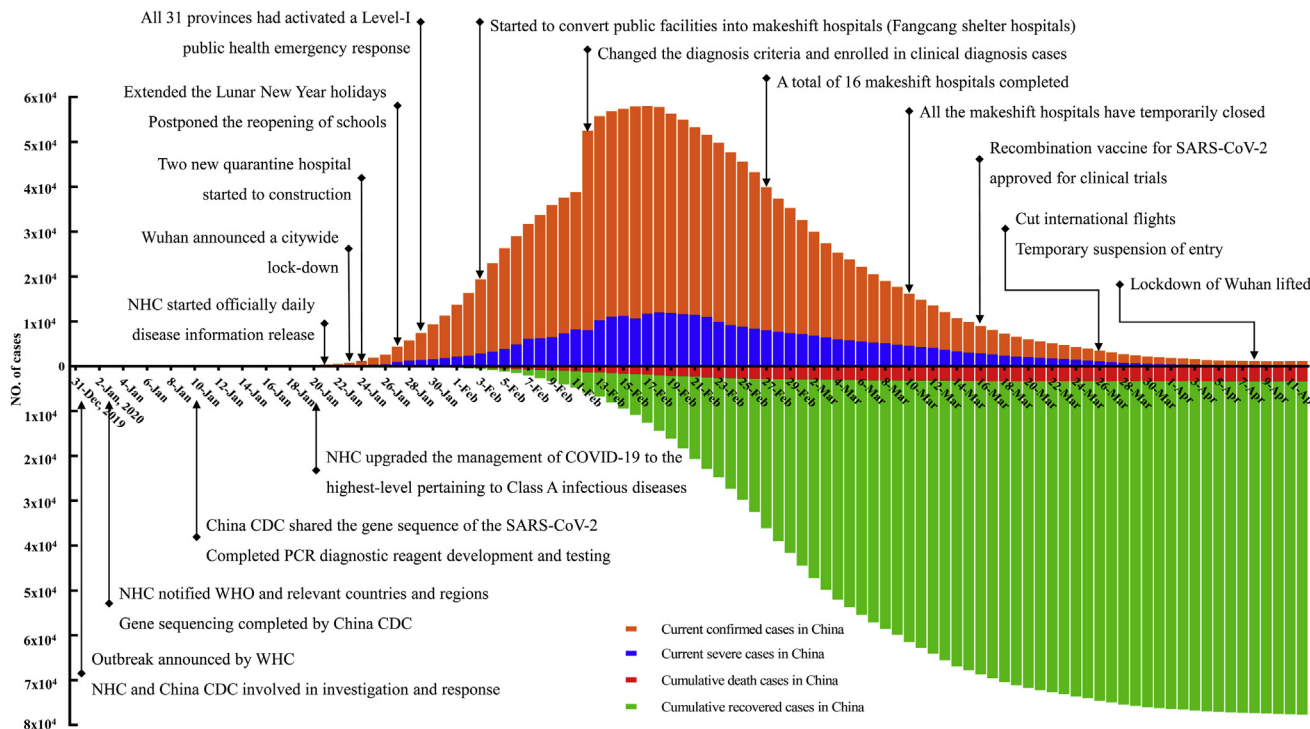


Figure 1. COVID-19 epidemiology curves and major intervention measures implemented in China. China CDC, Chinese Center for Disease Control and Prevention; NHC, National Health Commission of China; WHC, Wuhan Health Commission; WHO, World Health Organization. Data from the NHC, excluding Hong Kong and Macau Special Administrative Regions and Taiwan.

On January 27, 2020, the Chinese government announced the extension of the Lunar New Year holidays, and postponement of reopening of schools and factories.

On January 29, 2020, all 31 provinces on the Chinese mainland had activated a level 1 public health emergency response, the highest in the country, to prevent further spread.

On February 3, 2020, public facilities such as conference venues and sports stadiums were converted into makeshift hospitals to isolate patients with mild to moderate COVID-19 from their families and communities, while providing medical care, disease monitoring, food, shelter, and social activity.¹⁵ As of March 10, 2020, more than 12,000 patients had recovered and all makeshift hospitals were temporarily closed.¹⁶

On February 7, 2020, the Chinese government announced that all medical expenses of confirmed patients would be covered by health insurance or financial compensation.

On February 8, 2020, the Chinese central and local governments began to take measures to ensure the orderly resumption of production by companies to provide material support for the control of the epidemic. These included offering free health check-ups and arranging chartered buses, trains, and airplanes to send migrant workers back to resume work in other regions.

Quarantine Strategies

Quarantine and surveillance are still the most effective means of controlling the spread of infectious diseases. Some of the strategies and tactics are described below.

- 1) Limiting migration—Wuhan city announced a citywide lockdown on January 23, 2020. Subsequently, the Chinese government banned all domestic travel, extended the Lunar New Year holidays, and postponed reopening of schools and factories to reduce the nationwide migration of the population.
- 2) Designated hospitals—In Wuhan, to consolidate patients, medical experts, resources, and treatment, there were 45 COVID-19–designated hospitals: 6 for critical patients and 39 for severe patients and patients > 65 years of age. All regional hospitals established standardized fever clinics to timely screen for fever and strengthen isolation management. Designated hospitals were increased as needed by conversion of public and nonpublic hospitals.
- 3) Community isolation—Travelers from Wuhan and other epidemic areas were required to register at their destination along with their travel history with the use of smartphones and to self-quarantine for 2 weeks to prevent community transmission. Only 1 family member could leave the house to purchase daily living supplies every 2 days.
- 4) Maintaining adequate supply of essential items and revamping supply chains—Express delivery companies conducted “noncontact delivery” in communities. Shelves in stores were kept stocked by criminalizing price gouging and preventing hoarding. Opening green channels and coordinating transportation of supplies helped to ensure the safe delivery of key supplies. In the early stages of the COVID-19 outbreak, there was a shortage of personal protection equipment (PPE), which was mitigated by the use of reserve supplies, acquiring donations, and increases

of production (Supplemental Appendix S1; Supplemental Fig. S1).

- 5) Testing—Early testing provided the basis for tracking and isolation in Wuhan to identify persons who could potentially spread the disease. The numbers of tests performed in Wuhan are shown in Figure 2.
- 6) Tracking—A major part of the success in controlling the spread of COVID-19 was rooted in the tracking strategy. All patients testing positive for COVID-19 were tracked and their contacts isolated. Big data and artificial intelligence (AI) were used to strengthen contact tracing and the management of priority populations.
- 7) Temperature screening—Temperature screening checkpoints were established at supermarkets, residential area entrances, and transportation hubs. Everyone was screened for temperature when entering public areas. Temperature screening is a cheap, easily implemented, and rapid method of screening large numbers of the population for possible COVID-19. Fever is the most common symptom in patients with COVID-19. Persons who had traveled to Hubei or had close contact with COVID-19 patients in the preceding 14 days were required to undergo temperature checks.¹⁰
- 8) Personal protection—All residents were required to wear medical surgical masks or N95 masks when accessing public places. The internet and media were leveraged to publicize the correct knowledge of protection and prevention of spread, such as using masks, daily disinfection, and washing hands correctly.
- 9) Controlling cross-infection—Hospitals offered online consultation and medical services to reduce the frequency that patients visited hospitals. Online work and learning were used to avoid cross-infection.

Managing Human and Equipment Resources

Physician scheduling was optimized.¹⁷ This scheduling is shown in Supplemental Table S1. Emergency staffing was arranged as needed within half an hour.

Nurses 1-3 jointly completed all of the nursing work for patients, including daily care, disinfecting the isolation areas, etc. Nurse 4 was the team leader, who was mainly responsible for counting supplementary materials, delegating resources, and completing nursing records.

Workflow was optimized and the correct use of protective equipment, cleaning, and disinfection measures was ensured.¹⁸

During the outbreak, many elective surgeries were not performed. In addition, surgery may accelerate and exacerbate disease progression of COVID-19.¹⁹

Treatment of COVID-19

Suspected and confirmed patients were quarantined and treated in designated hospitals. High-risk patients were hospitalized to proactively prevent complications and secondary infections, treat underlying diseases, and provide organ function support according to the patients' conditions.¹⁰

Clinical classification

Physicians classified the disease severity of patients with SARS-CoV-2 infection according to the “Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia” issued by NHC (trial version 7)²⁰ or “Clinical Management of Severe Acute Respiratory Infection When Novel Coronavirus (2019-nCoV) Infection Is Suspected” from WHO.²¹ The severity definitions in the Chinese guidance were more widely used in clinical practice in China owing to its simplicity. According to the Chinese guidelines,^{20,89} the clinical classification of COVID-19 patients includes 4 levels of severity: mild, moderate, severe, and critical (Table 1). So far, there is no special COVID-19 clinical classification criteria for pregnant women, which may be due to the fact that clinical characteristics of COVID-19-infected pregnant women are generally similar to those of nonpregnant women with COVID-19 infection.²²

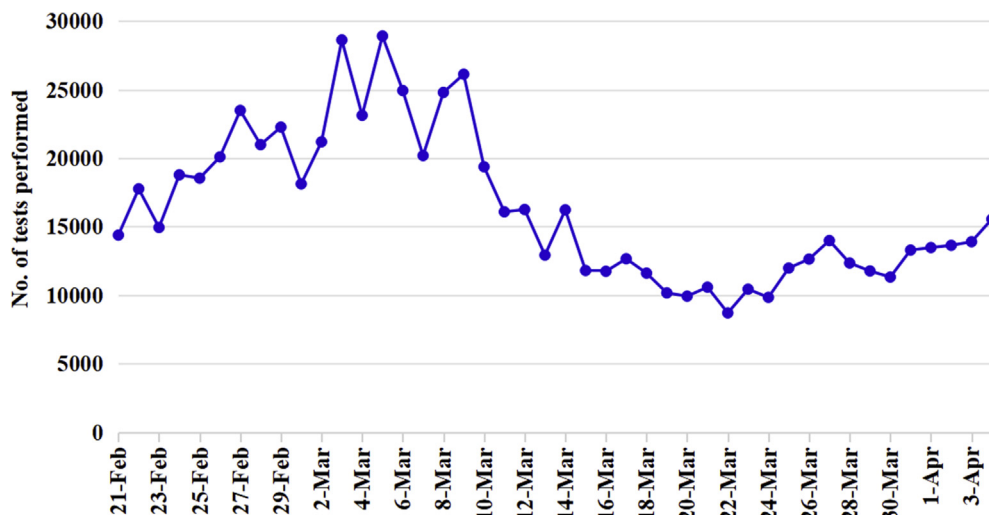


Figure 2. The daily number of nucleic acid tests performed in Wuhan. Data from the Wuhan Municipal Health Commission.

Table 1. COVID-19 clinical classification and treatment recommendations

Classification	WHO interim guidance ²¹		Chinese clinical guideline ^{20,89}		Treatment recommendations
	Adult	Child	Adult	Child	
Asymptomatic infection	NA	NA	NA	Laboratory-confirmed patients without any clinical symptoms or radiologic findings	Monitoring
Mild	Patients with nonspecific symptoms, such as fever, fatigue, cough, anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache. Rarely, patients may also present with diarrhea, nausea, and vomiting [*]		Patients with mild clinical symptoms and no sign of pneumonia on imaging		General treatment, symptomatic treatment, antiviral treatment
Moderate	Adult with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen	Child with nonsevere pneumonia who has cough or difficulty breathing plus fast breathing, [†] and no signs of severe pneumonia	Patients who have fever and respiratory symptoms with radiologic findings of pneumonia		Same as above, and supplemental oxygen therapy
Severe	Adolescent or adult with fever or suspected respiratory infection, plus respiratory rate > 30 breaths/min, severe respiratory distress, or oxygen saturation ≤ 93% on room air	Child with cough or difficulty breathing, plus at least one of the following: 1) central cyanosis or oxygen saturation < 90%; 2) severe respiratory distress (eg, grunting, very severe chest retractions); or 3) signs of pneumonia with a general danger sign [‡] : inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. Although the diagnosis is made on clinical grounds, chest imaging may identify or exclude pulmonary complications.	Adult who meets any of the following criteria: 1) respiratory distress (≥ 30 breaths/min); 2) oxygen saturation ≤ 93% at rest; 3) PaO ₂ /FiO ₂ ≤ 300 mm Hg (1 mm Hg = 0.133 kPa) [§] or chest imaging shows obvious lesion progression > 50% within 24-48 hours	Child who meets any of the following criteria: 1) tachypnea independent from fever and crying; 2) oxygen saturation ≤ 92% according to finger pulse oximeter taken at rest; 3) laboured breathing, [¶] cyanosis, and intermittent apnea; 4) lethargy and convulsion; 5) difficulty feeding and signs of dehydration; 6) HRCT shows infiltration in both lungs or multiple lobes, lesion progress in a short time, or pleural effusion	Same as above (for mild), and respiratory support (high-flow nasal oxygen and noninvasive ventilation or invasive mechanical ventilation)
Critical ARDS	Adults who meet the ARDS diagnostic criteria of the Berlin definition ³⁴ (oxygenation impairment identified according to the Berlin definition ³⁴)	Children who meet the ARDS diagnostic criteria of the Berlin definition ³⁴	Patients who meet any of the following criteria: 1) respiratory failure and requiring mechanical ventilation; 2) shock; 3) with other organ failure that requires ICU care		Same as above (for mild), and respiratory support (invasive mechanical ventilation, extracorporeal membrane oxygenation)
Sepsis	Adults with life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection ^{**}	Children with suspected or proven infection and ≥ 2 age-based systemic inflammatory response syndrome criteria, of which one must be abnormal temperature or white blood cell count			

Continued

Table 1. Continued.

Classification	WHO interim guidance ²¹		Chinese clinical guideline ^{20,89}		Treatment recommendations
	Adult	Child	Adult	Child	
Septic shock	Adults with persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP (≥ 65 mm Hg) and serum lactate level > 2 mmol/L	Children who have any hypotension (SBP < 5 th percentile or > 2 SD below normal for age) or 2 or 3 of the following: altered mental state; tachycardia or bradycardia (HR < 90 beats/min or > 160 beats/min in infants and HR < 70 beats/min or > 150 beats/min in children); prolonged capillary refill (> 2 s) or feeble pulse; tachypnea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia			

ARDS, acute respiratory distress syndrome; FiO₂, fraction of inspired oxygen; HR, heart rate; HRCT, high-resolution computed tomography; ICU, intensive care unit; MAP, mean arterial pressure; NA, not available; PaO₂, arterial partial pressure of oxygen; SBP, systolic blood pressure.

* The elderly and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as dyspnea, fever, gastrointestinal symptoms, or fatigue, may overlap with COVID-19.

[†] Fast breathing: age < 2 months ≥ 60 breaths/min; age 2-11 months: ≥ 50 breaths/min; age 1-5 years: ≥ 40 breaths/min.

[‡] Other signs of pneumonia may be present: chest retractions, fast breathing (in breaths/min[†]).

[§] In high-altitude areas (> 1000 metres above sea level), PaO₂/FiO₂ should be corrected by the following formula: PaO₂/FiO₂ \times [atmospheric pressure (mm Hg)/760].

^{||} Respiratory rate: age < 2 months: ≥ 60 breaths/min; age 2-12 months: ≥ 50 breaths/min; age 1-5 years: ≥ 40 breaths/min; age > 5 years: ≥ 30 breaths/min.

[¶] Moaning, nasal fluttering, and infrasternal, supraclavicular, and intercostal retractions.

** Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia.

Nonpharmacologic Treatment—Supportive and Symptomatic Care

General treatment. Symptomatic and supportive treatment is essential and the main treatment for COVID-19.²⁰ General supportive measures for SARS-CoV-2–infected patients include bed rest, adequate nutrition, water and electrolyte balance, and intensively monitoring vital signs (blood pressure, respiratory rate, heart rate, and oxygen saturation). Laboratory markers of disease progression and clinical outcomes, such as D-dimer, C-reactive protein, procalcitonin, neutrophil count, lymphocyte count, and inflammatory cytokines, were monitored.^{1,23–25}

Symptomatic therapy. Fever is the most common symptom of SARS-CoV-2 infection.^{1,23–25} Continuous high fever may cause metabolic disorders and system dysfunction. Therefore, WHO guidance advocates the use of antipyretics and cooling measures.²¹ Multiple studies have shown that COVID-19 patients have underlying diseases, including hypertension and diabetes, leading to higher mortality.^{1,26} For these patients, blood pressure and blood sugar must be monitored, and if abnormal, it should be promptly treated. The onset of severe disease leading to liver, kidney, or cardiac injury should be anticipated and treated appropriately.

Respiratory support. Studies have shown that in severe cases, 66.7% of patients (124/186) received oxygen therapy, 44.7% (63/141) received high-flow nasal cannula (HFNC), 39.4% (108/274) received noninvasive mechanical ventilation, and 24.1% (66/274) required invasive mechanical ventilation. Only 6.2% (17/274) patients received extracorporeal membrane oxygenation (ECMO) (Table 2).^{1,23,24,27,28}

Supplemental oxygen. In a study of 1099 patients in China, 41.3% of confirmed COVID-19 patients (454/1099) and 35.7% of nonsevere patients (331/926) received oxygen therapy.¹ WHO guidelines recommend that supplemental oxygen therapy be given to patients with severe acute respiratory infection (SARI), respiratory distress, hypoxemia, or shock.²¹ However, there are no restrictions on which patients can receive supplemental oxygen therapy in the Chinese guidelines,²⁰ which may have resulted in the overuse of

oxygen therapy. In general, patients with blood oxygen saturation (SPO₂) ≥ 93% do not require supplemental oxygen, and hyperoxemia may induce further respiratory injury and even higher mortality.²⁹ The indications for supplemental oxygen should be carefully applied in patients with COVID-19.²¹

High-flow nasal cannula oxygen therapy and noninvasive mechanical ventilation. HFNC and noninvasive positive-pressure ventilation (NIPPV) was used as step-up therapy in patients who failed to improve on supplemental oxygen.²⁰ A Chinese expert consensus released in 2019 recommends that physicians can consider providing HFNC to mild or moderately ill patients (arterial oxygen partial pressure [PaO₂]/fractional inspired oxygen [FiO₂] 100–300 mm Hg). The clinical application of NIPPV on hypoxemic respiratory failure caused by severe pneumonia has long been controversial.^{30,31} WHO²¹ and Chinese²⁰ guidelines both recommend using HFNC and NIPPV with extreme care and closely monitoring the condition of patients treated with HFNC or NIPPV for deterioration. Failure of a short trial (1 hour) of NIPPV may require proceeding to invasive mechanical ventilation.

Invasive mechanical ventilation. According to Guan et al.,¹ 14.5% of severe patients (25/173) received invasive mechanical ventilation and 32.4% (56/173) received noninvasive mechanical ventilation. If standard oxygen therapy fails, Chinese guidelines recommend a trial of HFNC or noninvasive ventilation, but WHO guidelines recommend escalating to invasive mechanical ventilation.²¹ It is generally accepted that timely use of invasive mechanical ventilation is an important component of the treatment of severe respiratory failure and acute respiratory distress syndrome (ARDS).³² Based on a Chinese expert consensus,³³ it is recommended that invasive mechanical ventilation be the first choice for moderate or severe ARDS patients (PaO₂/FiO₂ ≤ 150 mm Hg)³⁴ or for patients after failure of HFNC and NIPPV. Lung-protective ventilation strategy, ie, low tidal volumes (6–8 mL/kg of predicted body weight) and low inspiratory pressures (platform pressure < 30 cm H₂O) should be incorporated to prevent ventilator-related lung injury.³²

Extracorporeal membrane oxygenation. ECMO is a form of extracorporeal life support for very ill patients that circulates blood

Table 2. Treatment, oxygen support, and death in severe cases with COVID-19

Outcome	Guan et al. ¹	Liu et al. ²⁸	Yang et al. ²⁷	Wang et al. ²⁴	Huang et al. ²³
ICU/severe cases, n*	173	53	52	36	13
Treatment, n (%)					
Antiviral treatment	80 (46.2)	52 (98.1)	23 (44.2)	34 (94.4)	12 (92.3)
Antibiotic treatment	139 (80.3)	53 (100)	49 (94.2)	NA	13 (100)
Corticosteroid treatment	77 (44.5)	37 (69.8)	30 (57.7)	26 (72.2)	6 (46.2)
Intravenous immunoglobulin	58 (33.5)	29 (54.7)	28 (53.8)	NA	NA
CRRT	9 (5.2)	NA	9 (17.3)	2 (5.6)	3 (23.1)
Oxygen support, n (%)					
Oxygen therapy	123 (71.1)	NA	NA	NA	1 (7.7)
High-flow nasal cannula	NA	26 (49.1)	33 (63.5)	4 (11.1)	NA
Noninvasive mechanical ventilation	56 (32.4)	NA	29 (55.8)	15 (41.7)	8 (61.5)
Invasive mechanical ventilation	25 (14.5)	NA	22 (42.3)	17 (47.2)	2 (15.4)
ECMO	5 (2.9)	NA	6 (11.5)	4 (11.1)	2 (15.4)
Death, n (%)	14 (8.1)	26 (49.1)	32 (61.5)	6 (16.7)	5 (38.5)

CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; NA, not available.

*ICU/severe cases included severe and critical cases as defined in Table 1.

flow through an artificial lung for gas exchange and then back into the bloodstream. It provides a period of pulmonary rest, artificially supports critical ill patients while their heart or lungs recover, and plays a role in the care of heart or lung transplant patients. ECMO has rarely been used in China owing to limited resources.^{1,23} Moreover, there are no published studies about the efficacy and safety of ECMO with severely ill COVID-19 patients. Previously, the experience of using ECMO in Middle East Respiratory Syndrome (MERS) and influenza has been controversial.³⁵

Pharmacologic agents. We summarize the treatment of 327 pooled cases of severe cases with COVID-19 in Table 2.^{1,23,24,27,28} In severe cases, 87.3% of patients (254/291) received antibiotic treatment, 61.5% (201/327) received antiviral treatment, 53.8% (176/327) received corticosteroid treatment, and 41.3% (115/278) received intravenous immunoglobulin. Only 8.4% of patients (23/274) received continuous renal replacement therapy. The mortality rate of the 327 pooled severe cases was 25.4% (83/327) (Table 2).

Despite the use of various medications, the consensus of Chinese experts is that neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc) and ganciclovir are not generally recommended. Routine prophylactic antibiotics, especially combined wide-spectrum antibiotics, are also not typically recommended.³³ However, because of the widespread use of the medications, as indicated in the previous paragraph, ongoing trials are being conducted to clarify which medications may or may not be helpful in treating COVID-19.

Antiviral treatment. At present, there is no evidence to support the effectiveness of antiviral drugs for COVID-19, although these are commonly used in the treatment of COVID-19 in China. The guidelines of the NHC recommend interferon- α 2b inhalation, lopinavir/ritonavir, ribavirin, chloroquine, and arbidol as antiviral therapy and does not recommend using more than 2 antiviral drugs at the same time (Table 3).^{10,36}

Xu et al. reported that of 55 of 62 confirmed COVID-19 patients in Zhejiang province received antiviral treatment. Twenty-one patients (34%) received lopinavir/ritonavir and interferon- α 2b inhalation, 17 (28%) received arbidol and lopinavir/ritonavir, and 8 (13%) received interferon- α 2b by inhalation.³⁷ Chen et al. reported that 75 of 99 confirmed patients in Wuhan received antiviral treatment, including oseltamivir, ganciclovir, and lopinavir/ritonavir.³⁸ The duration of antiviral treatment was 3-14 days.³⁸ However, the results of a clinical trial of lopinavir/ritonavir in China showed no clear benefit beyond standard care in hospitalized adult patients with severe COVID-19.³⁹ Remdesivir may have the greatest potential for the successful treatment of SARS-CoV-2, but efficacy and safety in COVID-19 need further evaluation.^{40,41} Remdesivir has been studied in clinical trials to treat COVID-19 in China.

Favipiravir was approved for treatment of influenza on February 15, 2020, in China and is being studied in COVID-19 clinical trials. The preliminary results indicate that favipiravir has significantly more potent antiviral action and fewer adverse effects than lopinavir/ritonavir ($P < 0.001$).⁴² One of the clinical trials was conducted in Shenzhen, and the results showed that the median time to viral clearance was 4 days in

the favipiravir treatment group compared with 11 days in the lopinavir/ritonavir treatment group ($P < 0.001$). In terms of chest imaging, the improvement rates of the favipiravir treatment group and the lopinavir/ritonavir treatment group were 91.4% and 62.2%, respectively. No significant adverse reactions were noted in the favipiravir treatment group, and there were significantly fewer adverse effects than in the lopinavir/ritonavir group.⁴³

In early *in vitro* studies, chloroquine and hydroxychloroquine were found to inhibit SARS-CoV-2 infection efficiently,^{40,44} and several clinical trials have been quickly conducted in China to evaluate the efficacy and safety of chloroquine and hydroxychloroquine. Gao et al. summarized that compared with the control treatment, chloroquine phosphate was effective in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course.⁴⁵ The expert consensus on chloroquine phosphate recommends 500 mg twice daily for 10 days for patients diagnosed with COVID-19. Adverse effects of chloroquine and hydroxychloroquine must be carefully monitored.⁴⁶

Zhou et al. proposed that hydroxychloroquine could serve as a better therapeutic agent than chloroquine, owing to reduced toxicity, fewer side-effects, lower cost, and relative safety in pregnancy.⁴⁷ Yao et al. used physiologically based pharmacokinetics models and found that hydroxychloroquine was more potent than chloroquine at inhibiting SARS-CoV-2 *in vitro*. They recommended 400 mg hydroxychloroquine sulfate twice daily for 1 day, followed by 200 mg twice daily for 4 days to treat SARS-CoV-2 infection.⁴⁸ The efficacy and safety data of chloroquine or hydroxychloroquine from high-quality clinical trials are urgently needed.

Glucocorticoid therapy. Russell et al. recommended that corticosteroids should not be used in SARS-CoV-2-induced lung injury or shock.⁴⁹ However, Shang et al. suggested using short courses (≤ 7 days) of corticosteroids at low to moderate dose (≤ 0.5 -1 mg/kg/d methylprednisolone or equivalent) for critically ill patients with COVID-19.⁵⁰ According to a Chinese experts' consensus statement, the following criteria should be met before using corticosteroids in patients with COVID-19: 1) adults (≥ 18 years old), 2) laboratory-confirmed cases, 3) symptoms occurring within 10 days, 4) radiographic imaging consistent with COVID-19 pneumonia and progressing rapidly, and 5) SPO₂ $\leq 93\%$, shortness of breath (respiratory rate ≥ 30 /min), or oxygenation index ≤ 300 mm Hg at rest and with no oxygen therapy.⁵¹

A retrospective study found that low- to moderate-dose glucocorticoid therapy had no effect on the time to viral clearance in patients with COVID-19. Glucocorticoids are not recommended in mild cases, because there was no improvement in the rate of radiographic recovery.⁵² However, a single center in Wuhan shared that early low-dose and short-term corticosteroids (1-2 mg/kg/d for 5-7 days) was associated with a faster improvement of clinical symptoms and absorption of focal lung lesions in severe cases of COVID-19.⁵³ Another study analyzed 15 critical cases and suggested that a low dose and short duration of corticosteroids (methylprednisolone < 1 mg/kg, < 7 days) may be beneficial for critically ill patients with COVID-19.⁵⁴ Zhou et al. analyzed 10 patients with COVID-19 who received corticosteroids and

Table 3. Antiviral drugs for COVID-19 recommended in the guidelines of the NHC

Medication instruction	Alpha-interferon	Lopinavir/ritonavir	Ribavirin	Chloroquine	Arbidol
Recommended dosage and course	5 million units or equivalent dose per time for adults, adding 2 mL of sterile water, aerosol inhalation, twice per day. For children,* 100,000-200,000 IU/kg in mild cases, 200,000-400,000 IU/kg in severe cases, twice per day for 5-7 days.	200 mg/50 mg per capsule, 2 capsules each time, twice per day for adults. The course of treatment should be ≤ 10 days. For children,* weight 7-15 kg, (12 mg/3 mg)/kg; weight 15-40 kg, (10 mg/2.5 mg)/kg; weight > 40 kg, same as adults.	Combining with alpha-interferon or lopinavir/ritonavir, 500 mg for adults per time, intravenous injection 2-3 times per day. The course of treatment should be ≤ 10 days. For children,* 10 mg/kg per time (maximum 500 mg per time), intravenous injection 2-3 times per day.	Only for adults aged 18-65 y. Weight > 50 kg, 500 mg per time, twice per day for 7 days. Weight < 50 kg, 500 mg per time, twice per day for 2 days and then 500 mg per time, once per day for 5 days.	200 mg for adults, 3 times per day. The course of treatment should be ≤ 10 days.
Medication for special populations					
Children	Recommended	Recommended for children > 2 y old	Recommended	Not recommended	Unclear
Pregnant/lactating women	Prudent use	Recommended	Forbidden	Prudent use in lactating women	Unclear
Elderly	Recommended	Safety unclear; prudent use	Not recommended	Unclear	Unclear
Liver dysfunction patients	Prudent use	Prudent use	Prudent use	Prudent use	Unclear
Renal dysfunction patients	Prudent use	Recommended	CCR < 50 mL/min: not recommended	Prudent use	Prudent use in severe renal dysfunction
Contraindication	Patients with severe liver/renal dysfunction	Patients with severe liver dysfunction	Pregnant/lactating women	Pregnant women	Unclear
Approved indications	Broad-spectrum antiviral, immunomodulatory, and antitumor	HIV-1 infection	Respiratory syncytial virus pneumonia	Malaria	A and B influenza viruses
Adverse reactions	†	†	†	†	†
Off-label drug use		Yes	Yes	Yes	Yes
Clinical trials [‡]	6	9	1	16	3

CCR, creatinine clearance rate; NHC, National Health Commission; HIV, human immunodeficiency virus.

*The guidelines of the NHC did not recommend the dosage and course for children. The recommended dosage and course of the drugs for children in the table are from Chen et al.'s studies.³⁶

† Refer to product guidelines for specific information.

‡ The number of clinical trials of COVID-19 in China as of April 3, 2020. Data from <http://www.chictr.org.cn/>.

found that short-term moderate-dose corticosteroids (160 mg/d) plus immunoglobulin (20 g/d) were effective for reversing the continued deterioration of COVID-19 patients who failed to respond to the low-dose therapy (40-80 mg/d corticosteroids and 10 g/d immunoglobulin).⁵⁵ An open-label randomized controlled trial has been conducted to investigate the effectiveness of glucocorticoid therapy in patients with severe COVID-19.⁵⁶

Convalescent plasma. Previous studies in MERS suggested that convalescent plasma may be effective.⁵⁷ Mair-Jenkins et al. further suggested that convalescent plasma may reduce mortality in patients with SARI of viral etiology.⁵⁸ The NHC (trial version 2) includes convalescent plasma as a potential treatment in severe cases, critical cases, and cases of rapidly worsening clinical status.⁵⁹ Donors and recipients should be carefully selected, and serum-specific IgG antibodies for SARS-CoV-2 should be tested to guarantee the quality of convalescent plasma. Critical patients who received convalescent plasma showed significant improvement in clinical symptoms and laboratory findings.⁶⁰ Multiple clinical trials have been registered in the Chinese Clinical Trial Registry to study the safety and efficacy of convalescent plasma treatment in COVID-19 patients.⁶¹

Intravenous immunoglobulin. In Guan et al.'s study¹ of 173 severe COVID-19 cases, 58 patients (33.4%) received intravenous immunoglobulin treatment (IVIg). IVIg was considered as a potential therapy for immunologic injury in COVID-19 in clinical practice because of its anti-inflammatory action in treating conditions such as hemophagocytic lymphohistiocytosis and cytokine storm. Similarly, two reviews recommended IVIg based on mechanisms of SARS-CoV-2-mediated inflammatory responses.^{62,63} However, further investigation and more clinical studies are needed.

Biologic modulators. The results of laboratory findings of COVID-19 patients in China showed an increase in plasma inflammatory cytokine levels, especially interleukin (IL) 6.^{23,38} Therefore, the anti-IL6 monoclonal antibody tocilizumab was considered as a potential drug for some COVID-19 cases with extensive lung lesions and elevated IL-6 levels.²⁰ Three clinical trials have been initiated and registered in the Chinese Clinical Trial Registry (<http://www.chictr.org.cn/index.aspx>), but no results or data have been released at this time.

Other pharmaceutical measures

Traditional Chinese medicine treatment. The potentially beneficial role of traditional Chinese medicine is described in the guidelines of the NHC, and some Chinese patent medicines (CPMs) have been used to treat COVID-19.¹⁰ However, the experience with most of these treatments is anecdotal. Gu et al. reviewed 93 Chinese medicine prescriptions and 157 forms of constituent medicines for COVID-19 treatment and found that they may be effective in reducing fever, mucous production, cough, and asthma symptoms.⁶⁴ Yan et al. discovered that 10 antiviral components from CPMs can directly bind to both host cell target angiotensin-converting enzyme (ACE) 2 receptor and viral target main protease, suggesting their potential for COVID-19 treatment.⁶⁵

Other treatment measures. According to the guidelines of the NHC,¹⁰ vasoactive drugs may be required to supplement fluid resuscitation and to improve microcirculation. Continuous renal replacement therapy has been used in acute kidney injury.⁶⁶ Apheresis methods, including plasma exchange, adsorption, perfusion, and filtration, were used in critical cases with severe inflammatory reactions.⁶⁷

In addition to the treatment of the patients' physical condition, psychologic support was provided to address the anxiety and fear that occurs in patients who are suffering from COVID-19 as well as in their loved ones and health workers. During the quarantine, mental health intervention provided online was especially recommended. According to Hu et al., the use of hypnotics can significantly improve clinical outcomes of COVID-19 patients. These improvements may be attributable to decreased oxygen consumption resulting from reduced periods of anxiety and improved immunity from experiencing high-quality sleep.⁶⁸

Vaccine development. The development of a vaccine for SARS-CoV-2 has been accelerated as a priority project. On January 23, the Coalition for Epidemic Preparedness Innovations (CEPI) announced a \$12.5 million grant to fund vaccine development by Queensland University in Australia, the National Institutes of Health in the United States, and the pharmaceutical companies Inovio and Moderna. On January 24, a virus strain of SARS-CoV-2 was successfully isolated from patients' samples in China to provide the basis for vaccine development.⁶⁹ On February 3, CEPI and GlaxoSmithKline announced collaboration to strengthen the global effort to develop a vaccine. Vaccine safety is a priority. Currently, strategies for SARS-CoV-2 vaccine development include recombinant proteins, DNA vaccines, mRNA vaccines, traditional live vaccines, and recombinant adenovirus vaccines. These are in various phases of development, ranging from nonhuman animal studies to clinical trials.^{3,70,71} On March 13, mRNA-1273 vaccine clinical trials began in the United States.⁷⁰ On March 16, recombination vaccines for SARS-CoV-2 entered into phase I clinical trials.⁷¹ Although these are significant strides, the prospects for a commercially available vaccine are at least 6 months away, and probably much longer.

Respiratory nursing support. Studies have shown that prone positioning was associated with improved oxygenation and a decrease in CO₂ retention, leading to reduced mortality, in patients with influenza, MERS, or ARDS.^{72,73} As a result, a Chinese expert consensus recommends that patients be prone for ≥ 12 hours a day when PaO₂/FiO₂ < 150 mm Hg.⁷⁴ Before placing the patient in prone position, oral secretions should be suctioned regularly to help keep the artificial airway open. In addition, COVID-19 patients suffer from copious proteinaceous exudates in their lungs and airways.^{75,76} Aspiration of sputum can help to keep the airway intact and potentially improve sample collection and the accuracy of SARS-CoV-2 nucleic acid detection.⁷⁷ The patient's position should be assessed and changed regularly to avoid decubitus skin injury. Elevating the head of the bed 30-45 degrees,⁷⁸ suctioning out oropharyngeal secretions, and monitoring the pressure of a rebreathing bag can help to prevent ventilator-associated pneumonia.

Cardiac complications. Cardiac abnormalities were found to be present in a high proportion of patients who died of COVID-19 and may be more associated with severe disease. Based on current studies, COVID-19 patients with cardiovascular diseases are more likely to develop into critical cases and have higher mortality.^{1,23,24,38,79} Clinicians should be alert to the manifestations of heart injury by closely monitoring patients' vital signs (blood pressure and heart rate), laboratory tests including creatine kinase, lactate dehydrogenase, high-sensitivity cardiac Troponin I, creatine kinase MB, B-type natriuretic peptide (BNP) and N-terminal proBNP, and electrocardiography. Antiviral drugs, such as ribavirin and lopinavir/ritonavir, have been widely used in cardiac patients, although there no well-designed trials to support that. The hypothesis that COVID-19 directly causes myocardial injury may support the usage of antiviral drugs, but the side-effects of these drugs on the cardiovascular system, such as sudden cardiac death and bradycardia, should be carefully considered.⁸⁰

Owing to the fact that cardiac insufficiency can lead to a coagulation disorder and that severe COVID-19 patients were reported to have increased level of D-dimer, low-molecular-weight heparin was recommended to treat COVID-19 patients in the early phase of disease.⁶² As with SARS-CoV, ACE2 has been identified as the receptor for SARS-CoV-2 to enter cells.⁸¹ The use of ACE inhibitors (ACEIs) may not be of any benefit, because they does not bind to the ACE2 receptor. This also means that discontinuing ACEIs in patients with COVID-19 is not necessary. Regarding angiotensin receptor blockers (ARBs), there is evidence that ARBs could lead to increased expression of ACE2, thus worsening disease, but this remains controversial. There is no current recommendation to discontinue ARBs during treatment of COVID-19 in China. Monteil et al. found that SARS-CoV-2 infection in engineered human blood vessel organoids and human kidney organoids could be inhibited by human recombinant soluble ACE2.⁸² Further investigations are required to shed light on the role of ACE2 in cardiac manifestations of COVID-19.

Regarding acute myocardial infarction in COVID-19 patients, Peking Union Medical College Hospital and Zhongnan Hospital of Wuhan University provided the following experience.^{83,84} For acute ST-segment-elevation myocardial infarction (STEMI) in patients with confirmed COVID-19, strict isolation should start immediately and thrombolytic contraindications should be evaluated. Patients with thrombolytic contraindications should be transferred to the local infectious disease specialist hospitals immediately for further treatment. Patients without thrombolytic contraindications should first be started on intravenous thrombolysis and then transferred to the local infectious disease specialist hospitals for further treatment.⁸³ Considering the increased risk of exposure due to the lack of negative-pressure catheterization chambers and shortages of PPE, and the greater difficulty of finely manipulating the guidewires under level 3 protection, fibrinolysis is preferred when both percutaneous coronary intervention (PCI) and fibrinolysis are available. Once PCI is required, all medical workers should be under level 3 protection and thorough environmental disinfection must be given after each PCI.⁸⁴

Effectiveness and Importance of Public Health Interventions

The WHO-China joint mission report reported that China's vigorous public health measures to prevent the COVID-19 are the most "ambitious, agile, and aggressive disease containment effort in history."⁸⁵ The drastic measures taken are listed in Table 4. If not for a national strategy that incorporated all of these measures simultaneously, it was estimated there would have been 744,000 COVID-19 cases outside Wuhan on day 50 of the epidemic, compared with the actual number of fewer than 20,000.⁸⁶

As of April 13, 2020, COVID-19 has spread to 6 continents and 212 countries and regions. We compare the epidemiologic characteristics among China, Italy, South Korea, and the United States in Figure 3. The data from China show that the daily number of infected patients has been less than 50 for the past week. However, there are a steady daily number of imported cases. Similarly, in South Korea, the strategy that worked also included early testing, tracking, and isolation. Unfortunately, lessons learned in China have not been universally adopted, and the numbers of cases in many countries are rapidly increasing.

The lessons learned in China and South Korea are that in these times of crises, the earlier the intervention from a societal perspective the better. China had implemented an electronic monitoring system for infectious disease outbreaks after

Table 4. Specific lockdown measures in Wuhan later extended to the entire country

Measure	Content
Specific limitations	<ul style="list-style-type: none"> • Strict travel restriction • Mandatory quarantine • Restrict public transportation • Close schools and entertainment venues • Shutdown of all nonessential companies • Cancel conferences • Cease all public gatherings • Stay at home
Enforcement measures	<ul style="list-style-type: none"> • COVID-19 belongs to class B infectious disease but managed as the highest-level class A infectious disease. • Building the Joint Prevention and Control Mechanism of the State Council to issue the COVID-19 development • Delivering the Prevention and Control Headquarters Notice of COVID-19 • Enforcement laws including "Law of the People's Republic of China on the prevention and treatment of infectious diseases," "Surveillance protocol for pneumonia cases from novel coronavirus (second edition)," "Preventive measures against infectious diseases in business and service business sites," "Provisions on the emergency handling of entry-exit inspection and quarantine for public health emergencies at border ports," etc.
Required measures	<ul style="list-style-type: none"> • Temperature screening on the public occasions, such as hospitals, supermarkets • Purchasing daily necessities on a regular schedule • Delivering food and disinfectants for every family • Real-time disinfection of public areas.

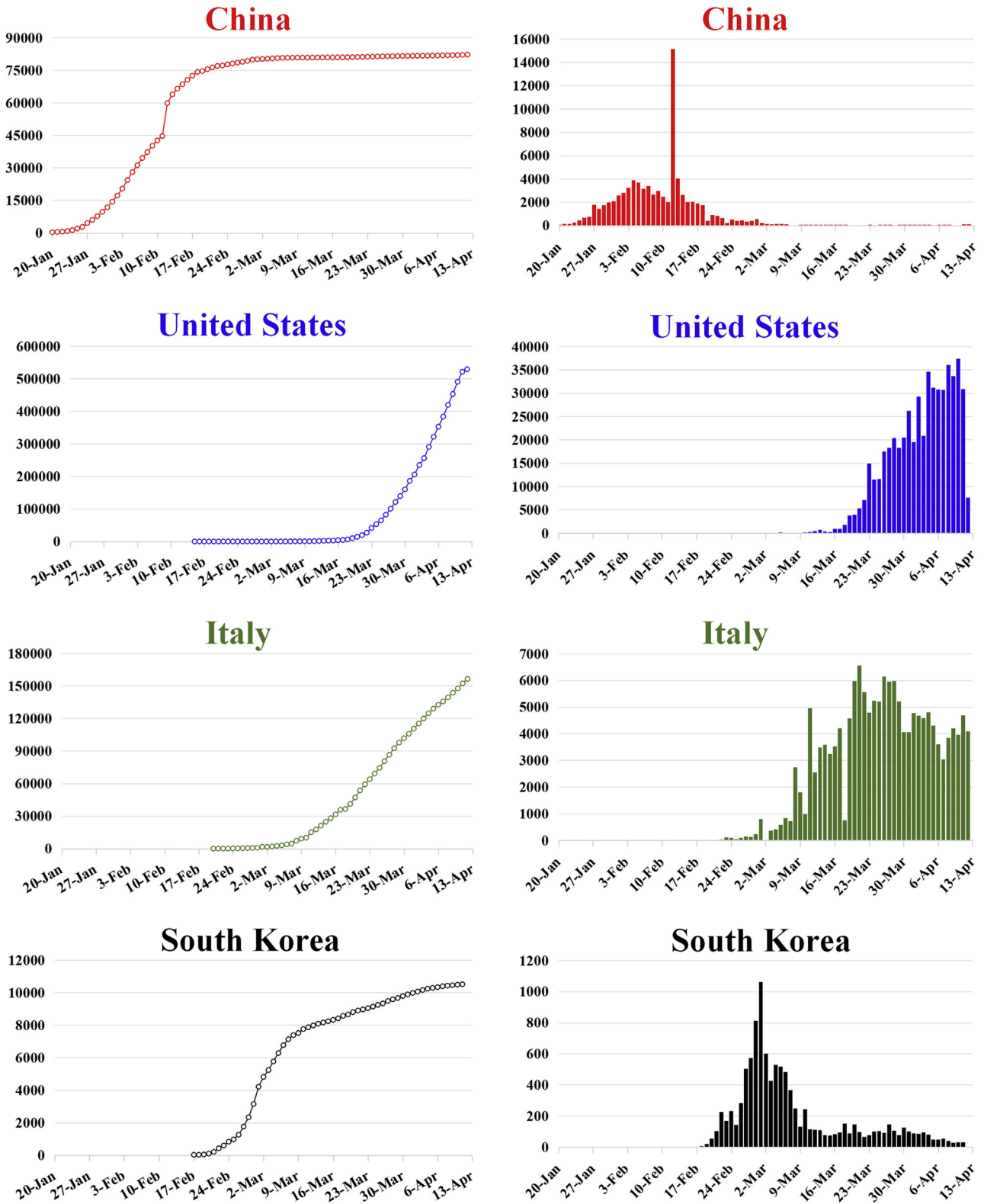


Figure 3. Epidemic curves of the confirmed cases of COVID-19 in various countries. **Left**, timeline of breakouts of SARS-CoV-2. **Right**, daily numbers of increasing cases. Data for China were obtained from the National Health Commission of China, which excluded Hong Kong and Macau Special Administrative Regions and Taiwan. Data for the remaining countries were obtained from the World Health Organisation.

SARS in 2003. The question is how early one can reasonably expect to determine that something is out of the ordinary. People die of respiratory failure due to many causes, including influenza, every day. When should there be suspicion that something like a new virus is involved? The lesson here is that one should always have a high index of suspicion, but this must be balanced against causing mass hysteria and panic.

Once it is recognized that there is a new, potentially lethal, virus, the virus needs to be isolated, the genome sequenced, and testing kits validated and released for rapid distribution. Infected individuals and their contacts need to be tracked and isolated. The earlier this is done, the less impact there will be on the personal and professional lives of people and the economy, and the fewer resources will be needed. When more people are infected, the drastic measures including shutting down cities and restricting travel will need to be more widespread, health care resources will be exhausted, and the economy will take a bigger hit.

It is perhaps significant to evaluate the number and distribution of cases in China as a basis for aggressive testing, tracking, and quarantining. In the early days of the epidemic, the genomic sequence of the virus was determined and tests kits that would deliver results within hours were developed. It should be emphasized that the lockdown in Wuhan was a complete lockdown, other than bringing in necessary medical personnel, ventilators, and PPE, as well as everyday goods and supplies. The difference between this type of lockdown and the shelter in place recommendations that have been put forward in many Western countries is that the lockdown in Wuhan was strictly enforced. Laws in Wuhan limited grocery shopping to 1 person per household once every 2 days, with identity checks when leaving and returning. This type of enforced lockdown was later extended to the rest of the country, so that even in cities of more than 7 million and only 200 cases, the population experienced the same restrictions (Table 4). The entire country stayed on lockdown for more than 2 months. When lockdown measures were eased over the past few weeks, temperature checks were still being performed and one had to show electronic medical data on one's electronic device. The lesson here is that if effective quarantine is what needs to occur, these measures must be supported by personnel to enforce them, and they cannot be voluntary or simply recommended.

Downgrading After the Epidemic or Pandemic Has Been Brought Under Control

According to relevant laws and regulations in China, when the number of confirmed cases has a steady decline and the risk of the spread of the epidemic is effectively controlled, each province should reduce the emergency response levels accordingly. In fact, local governments adjust emergency response levels according to the local epidemic situation. Provincial governments use counties as a unit to divide different regions into high-risk, medium-risk, and low-risk areas and implement different prevention and control measures in the different risk areas.⁸⁷

Low-risk districts have no confirmed cases or no new confirmed cases for 14 consecutive days. Medium-risk districts have new confirmed cases within the previous 14 days but the cumulative number does not exceed 50 confirmed cases, or

there are cumulatively more than 50 confirmed cases but no clustered epidemics within the previous 14 days. High-risk districts have a cumulative number of more than 50 confirmed cases, with clustered epidemics within the previous 14 days.⁸⁸ Even so, there is always a risk of a second wave if restrictions are relaxed too soon and too drastically.

Different prevention and control measures were implemented in different risk areas. In low-risk areas the main focus was to prevent import of outside cases with the economy restored back to normal. In medium-risk areas, both preventing internal and external spread was implemented, and screening of body temperature and disinfection of public facilities was continued. The entertainment industry remained closed, but other business activities resumed. In high-risk areas, strict quarantine and control measures were continued, with continued closure of nonessential businesses.

Conclusion

The experience in China is unique in that it was the first country to implement drastic measures to combat COVID-19. The strategy in China was early testing, diligent tracking, and strict isolation of patients and contacts, first in Wuhan and then nationwide. Even with this, there were more than 80,000 cases in China and more than 3000 deaths. All countries, even China, can learn from this. Although the drastic measures that China implemented appear for now to have stopped the viral spread, earlier implementation could have reduced the number of cases and deaths even more.

Viral epidemics need to be countered with a unified national strategy that can be implemented quickly on a very large scale. The ability to mobilize and to stay nimble in adapting to these challenges is paramount. Public buy-in is crucial for all citizens to abide by the rules and recommendations. Rules must be mandatory and cannot be simply recommended and voluntary. Designated officers must be deployed to enforce these rules. The negative short-term public and economic consequences that may result from shutting down services, restricting travel, and aggressive quarantining must be accepted or the virus will keep spreading. Collaboration and sharing among countries are imperative to establish more effective policies to control the spread of future epidemics and minimize mortality and morbidity.

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Supplementary Material

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