Journal Pre-proof

The epidemiological and clinical features of COVID-19 and lessons from this global infectious public health event

Huilan Tu , Sheng Tu , Shiqi Gao , Anwen Shao , Jifang Sheng

PII: S0163-4453(20)30222-X
DOI: https://doi.org/10.1016/j.jinf.2020.04.011
Reference: YJINF 4551

To appear in: *Journal of Infection*

Accepted date: 11 April 2020

Please cite this article as: Huilan Tu , Sheng Tu , Shiqi Gao , Anwen Shao , Jifang Sheng , The epidemiological and clinical features of COVID-19 and lessons from this global infectious public health event, *Journal of Infection* (2020), doi: https://doi.org/10.1016/j.jinf.2020.04.011

The epidemiological and clinical features of COVID-19 and lessons from this global infectious public health event

Huilan Tu[1], Sheng Tu[1], Shiqi Gao[2], Anwen Shao[2*], Jifang Sheng[1*]

1 State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang Province, China

2 Department of Neurosurgery, The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, Zhejiang Province, China

*Corresponding Author:

Jifang Sheng, Email: jifang_sheng@zju.edu.cn

Anwen Shao, Email: 21118116@zju.edu.cn; anwenshao@sina.com

Running title: Features of COVID-19

Abstract: Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and represents a potentially fatal disease of great global public health importance. As of March 26, 2020, the outbreak of COVID-19 has resulted in 462,801 confirmed cases and 20,839 deaths globally, which is more than those caused by SARS and Middle East respiratory syndrome (MERS) in 2003 and 2013, respectively. The epidemic has posed considerable challenges worldwide. Under a strict mechanism of massive prevention and control, China has seen a rapid decrease in new cases of coronavirus; however, the global situation remains serious. Additionally, the origin of COVID-19 has not been determined and no specific antiviral treatment or vaccine is currently available. Based on the published data, this review systematically discusses the etiology, epidemiology, clinical characteristics, and current intervention measures related to COVID-19 in the hope that it may provide a reference for future studies and aid in the prevention and control of the COVID-19 epidemic.

Keywords: COVID-19; SARS-CoV-2; 2019-nCoV; Epidemiology; Intervention

1. Introduction

In December 2019, a cluster of cases of unexplained viral pneumonia was identified in Wuhan, a metropolitan city in Hubei province, China. Initially, most of the confirmed cases were linked with the Huanan seafood market in Wuhan, where numerous types of live wild animals are sold, including poultry, bats, groundhogs, and snakes. To identify the causative agent of this disease, a large number of tests were conducted, which ruled out several etiological agents that may cause similar symptoms, including the severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), avian influenza virus, and other common respiratory pathogens. Finally, a new coronavirus, putatively named 2019-nCoV by the World Health Organization (WHO) on January 12, 2020, was identified as the causative pathogen of this outbreak. On January 20, after a visit to Wuhan, Professor Zhong Nanshan, a SARS intervention specialist, confirmed that 2019-nCoV was spreading between people [1], which led to increased vigilance by the Chinese government and people. At 10:00 on January 23, Wuhan, the birthplace of the disease, declared a general closure to prevent its further spread. However, Wuhan is a major transportation hub located in the central region of the People's Republic of China with approximately 11 million inhabitants [2], and the period from the end of December 2019 to February 2020 was the time of the "Spring Festival travel rush". Although the Chinese government made great efforts to control the flow of people, the disease spread rapidly from Wuhan to other cities, as well as other countries, likely through asymptomatic carriers [3]. On January 30, 2020, the WHO declared the outbreak of novel coronavirus a public health emergency of international concern, the sixth public health emergency after H1N1 (2009), polio (2014), Ebola in West Africa (2014), zika (2016), and Ebola in the Democratic Republic of Congo (2019) [4]. The International Committee on Taxonomy of Viruses renamed 2019-nCoV as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the related pneumonia as coronavirus disease 2019 (COVID-19) on February 12, 2020 [5]. As the disease is highly infectious, "the law of the People's Republic of China on the prevention and treatment of infectious diseases" lists it as a class B infectious disease, and recommends preventive and control measures similar to those against class A infectious diseases. The outbreak is ongoing, and poses a great global challenge. Health workers, governments, and the public need to co-operate globally to prevent its further spread.

2. Etiological characteristics and origin of COVID-19

Coronaviruses were first described by Tyrell and Bynoe in 1966, who isolated the viruses from patients suffering from the common cold [6]. Tyrell and Bynoe called them coronaviruses because they are spherical virions with a core shell and surface projections resembling a solar corona [7]. Coronaviruses are members of the subfamily *Coronavirinae* in the family *Coronaviridae*, order *Nidovirales*. Members of this subfamily were genetically classified into four major genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus* [8]. Alphacoronaviruses and betacoronaviruses infect only mammals and usually cause respiratory illness in humans and gastroenteritis in animals. The gammacoronaviruses and deltacoronaviruses predominantly infect birds, but some can also infect mammals [9]. Six types of coronavirus have been identified in humans (HCoVs), including HCoV-NL63, HCoV-229E, HCoV-OC43, HCoV-HKU1, SARS-CoV, and MERS-CoV. The first two belong to the *Alphacoronavirus* genus and the latter four to the genus *Betacoronavirus* [10]. SARS-CoV and MERS-CoV can cause severe respiratory syndrome in humans, while the other four human coronaviruses induce only mild upper respiratory diseases in immunocompetent hosts [11, 12]. Coronaviruses did not attract worldwide attention until the 2003 SARS epidemic, followed by the 2012 MERS outbreak and, most recently, the novel coronavirus pandemic.

SARS-CoV-2 was found to be a positive-sense, single-stranded RNA virus belonging to the *Betacoronavirus* B lineage and is closely related to the SARS‐CoV virus [13]. Full-length genome sequences were obtained and indicated that the SARS-CoV-2 genome shares 79.6% sequence identity with that of SARS-CoV [14]. Notably, SARS-CoV-2 infects human lung alveolar epithelial cells through receptor-mediated endocytosis using angiotensin-converting enzyme II (ACE2) as an entry receptor. Attachment to the receptor mediates the subsequent fusion between the viral envelope and host cell membrane, thereby allowing viral entry into the host cell [15, 16].

The origin of the disease has not been determined. As most of the confirmed cases were linked to direct exposure to the Huanan seafood market [17], it was initially believed that the origin of the virus may have been the seafood market. Based on current sequence databases, all human coronaviruses have animal origins: SARS-CoV and MERS-CoV originated in bats, their natural reservoir, but were transmitted to humans via intermediate host civets and camels, respectively [18]. HCoV-NL63 and HCoV-229E are also considered to have originated in bats, while HCoV-OC43 and HKU1 likely originated in rodents [11, 12]. SARS-CoV-2 is closely related to two bat-derived coronavirus strains, bat-SL-CoVZC45 and bat-SL-CoVZXC21 [13, 19] and is 96% identical at the whole-genome level to bat coronavirus TG13 [7, 14]. This suggests that SARS-CoV-2 may also have originated in bats, and was then transmitted to humans *via* an intermediate host in the Huanan seafood market. Analysis of the genome of a coronavirus isolated from pangolins indicated that the isolated strains and SARS-CoV-2 are 99% similar. This suggests that pangolins may be potential intermediate hosts for SARS-CoV-2, and the transmission and evolution path of SARS-CoV-2 may be from bat-CoV to pangolins, and then to humans. However, On February 20, 2020, the website of the Xishuangbanna Tropical Botanical Garden of the Chinese Academy of Sciences published an article that suggested that the seafood market may not have been the source of COVID-19, and that SARS-CoV-2 may have been introduced from elsewhere and then spread rapidly in the market. The symptom onset date for the first patient identified was December 1, 2019, and no epidemiological link was found between the patient and later cases [17]. Based on factors such as the incubation period of the virus, the first new coronavirus infection may have appeared in late November 2019 or even earlier.

In the global spread of SARS-CoV-2, several countries have reported numerous cases that cannot be traced to the putative source of the infection. The first confirmed case of COVID-19 in the United States was a patient who had traveled to Wuhan, China, but reported that he had not visited the seafood market or health care facilities, and had not had any contact with sick people during his stay in Wuhan [20]. The source of his SARS-CoV-2 infection is still unknown. In Italy, meanwhile, where the epidemic is getting worse, "patient zero" has yet to be identified [21]. Greater efforts are required to trace the source of the virus, control it, and clarify its intermediate host, which is of vital importance to controlling the transmission of SARS-CoV-2 [22].

3. Epidemiology

In general, the emergence of an infectious disease comprises three vital elements: infectious source, transmission route, and susceptible population [23]. At present, SARS-CoV-2-infected patients are the main source of infection, producing a large quantity of virus in the upper respiratory tract during a prodrome period [24]. Because of the mild clinical symptoms during the incubation period, patients can remain mobile and carry out routine activities, leading to the spread of infection. Asymptomatic carriers can also be a source of infection [25]. The incubation period of the disease is 1–14 days, usually 3–7 days, and can even reach 24 days, making it difficult to screen for infections. Additionally, the disease is mainly spread by respiratory droplets and contact. Infections among 14 health workers confirmed the disease's high infectivity and raised concerns that some people may be "super spreaders" of the virus [1]. In a relatively closed environment, aerosol transmission can also occur [26].

Nosocomial transmission is also a severe problem. As of February 12, 2020, a total of 3,019 health workers had been infected, and accounted for 3.83% of the total number of infections [27]. Personal protective equipment (PPE), including fluid-resistant gown, gloves, eye protection, full face shield, and fit-tested N95 respirators, is necessary to maximize the safety of healthcare workers who need to be in contact with critically ill patients with confirmed or suspected SARS-CoV-2 infection [28]. A recent study found that SARS-CoV-2 can be detected in the tears and conjunctival secretions of new coronavirus pneumonia patients with conjunctivitis [29], which suggests that ocular infection may be a source of SARS-CoV-2 transmission. The possibility of fecal–oral transmission also needs to be considered, as viral nucleic acids have been found in fecal samples and anal swabs from some COVID-19-infected patients [30]. On February 5, 2020, multiple media outlets also reported that a newborn infant delivered by a woman who had tested positive for SARS-CoV-2 during the epidemic in Wuhan had also tested positive for the virus 30 hours following his/her birth [2]. There is currently no evidence to suggest that SARS-CoV-2 can undergo intrauterine or transplacental transmission [31, 32]; however, when delivering a neonate from an infected patient or a person suspected of being infected, neonatologists should wear suitable protective equipment. Moreover, the newborns must be isolated as soon as they are suspected of being infected.

Although all populations are susceptible to SARS-CoV-2 [26], particular attention and efforts to protect or reduce transmission should be directed at vulnerable groups such as children, health care providers, pregnant women, and the elderly. As of January 29, 2020, a study had obtained data regarding the clinical symptoms and outcomes for 1,099 COVID-19 patients who had been hospitalized at 552 sites. Their median age was 47 years [33]. SARS-CoV-2 has caused severe illness and death primarily in older people, particularly those with pre-existing conditions such as diabetes and heart disease [34], possibly due to a weakened immune system that permits a faster progression of viral infection. Although children are as likely to be infected by the coronavirus as adults, they are less likely to experience severe symptoms [35], which suggests that measures such as school closures may help slow the spread of the virus.

The proportion of pregnant women among the confirmed cases is low; nevertheless, pregnant women are known to be particularly susceptible to respiratory pathogens and severe pneumonia [31]. Furthermore, the occurrence of pneumonia during pregnancy can lead to several adverse obstetric outcomes, such as premature rupture of membranes (PROM) and preterm labor (PTL), intrauterine fetal demise (IUFD), intrauterine growth restriction (IUGR), and neonatal death, and therefore poses great risks to both pregnant women and their unborn children [36, 37]. The mortality rate among pregnant women due to respiratory pathogens is substantially higher than that among ordinary people; for example, the 1918 influenza pandemic resulted in a mortality rate of 2.6% for the overall population, but 37% among pregnant women [38]. Therefore, pregnant women infected with SARS-CoV-2 should be cared for in a health care facility with close maternal and fetal monitoring. In this regard, experiences with illnesses associated with other highly pathogenic coronaviruses, such as SARS and MERS, may also be relevant to SARS-CoV-2, including early isolation, aggressive infection control procedures, oxygen therapy, avoidance of fluid overload, empiric antibiotics, and fetal and uterine contraction monitoring [39].

4. Transmission dynamics and epidemic status of COVID-19

Understanding the transmissibility of SARS-CoV-2 remains crucial for predicting the course of the epidemic and the likelihood of sustained transmission [40]. The reproduction number, R, is used to reflect the transmissibility of a virus, and represents the average number of new infections generated by each infected person, the initial constant of which is called the basic reproduction number, R_0: the larger the R_0 is, the stronger the transmission potential of the virus [41]. An R-value >1 indicates that the outbreak will be self-sustaining unless effective control measures are implemented, while an R-value <1 indicates that the number of new cases will decrease over time and the outbreak will eventually stop [42]. Compared with the R_0 of H1N1 (1.25) [43] and that of SARS (2.2–3.6) [44], the R_0 of SARS-CoV-2 was estimated as 2.2 (95% CI, 1.4 to 3.9) [2], 3.11 (95% CI, 2.39–4.13) [45], and 2.68 (95% CI, 2.47–2.86) [46] by different groups and is significantly larger than 1, indicating that SARS-CoV-2 has a high transmissibility potential and consequently the ability to cause outbreaks. It may be very difficult to contain or control the spread of this virus without adequate prevention and control measures. The effective reproduction number (R_t) quantifies the number of infections caused by each new case occurring at time t. It is typically lower than that of R_0 owing to the effect of control measures in reducing transmission, and the depletion of susceptible individuals during the epidemic; epidemic decay is guaranteed only where R_t is maintained below 1 [47].

The SEIR model, a classic method used to analyze the epidemic trend of an infectious disease, can reflect the flow of people between four states: susceptible (S), exposed (E), infectious (I), and recovered (R), and has been shown to be predictive for a variety of acute infectious diseases such as Ebola and SARS [48, 49]. Based on previous studies and the experience gained from the SARS epidemic, Wang et al. applied this model to estimate the epidemic trend in Wuhan, China. If the prevention and control measures were sufficient in Wuhan, the R_t was assumed to gradually decrease at different phases from a high level of transmission ($R_t = 3.1$, 2.6, and 1.9) to below 1 ($R_t = 0.9$ or 0.5), and the estimated number of infections would peak in late February [42]. Judging from the dwindling number of newly diagnosed cases in China (Fig. 1), the prevention and control measures implemented were indeed effective. However, the global situation remains very serious (Fig. 2), and rigorous measures should be maintained so as to reduce the R_t to an ideal level and control the infection.

The WHO in Geneva declared the coronavirus outbreak to be a pandemic on March 11, 2020. Up to March 26, 2020, at least 82,078 cases of COVID-19 had been confirmed in China, with 3,298 known deaths, representing a fatality rate of approximately 4%. The outbreak in China seems to be slowing, as evidenced by the reduction in the daily number of newly diagnosed cases (Figs 1 and 2). The coronavirus outbreak seems to be spreading faster outside China than inside (Fig. 1B). The WHO reported that more than 462,801 people have been infected worldwide, more than 380,723 of which are outside of China. (WHO; http://2019ncov.chinacdc.cn/2019-ncov/global.html). This does not mean that the outbreak is out of control, and as long as countries take robust action to detect cases early, isolate and care for patients, and track contacts, there is still a chance of containing the virus.

5. Clinical features and diagnosis of COVID-19

Recently, Guan et al. reported that the common clinical manifestations of 2019-nCoV infection among 1,099 laboratory-confirmed cases of COVID-19 included fever (88.7%), cough (67.8%), fatigue (38.1%), sputum production (33.7%), shortness of breath (18.7%), sore throat (13.9%), and headache (13.6%) [33]. In addition, a few

COVID-19 patients also showed gastrointestinal symptoms [30], i.e., diarrhea (3.8%) and vomiting (5.0%) [33]. Although studies have indicated that fever is the dominant symptom (Table 1), some severely or critically ill patients may have moderate, low, or even no significant fever [50, 51]. Therefore, undue emphasis should not be placed on a patient's body temperature for disease evaluation in clinical treatment and daily screening. Most patients have a good prognosis, while a few are in a critical condition, especially the elderly and those with underlying chronic conditions such as cardiac disease and diabetes [52]. Sepsis is the most frequently observed complication, followed by respiratory failure, acute respiratory distress syndrome (ARDS), heart failure, and septic shock [53].

The first symptoms of COVID-19 are nonspecific. Differential diagnosis should include the possibility of a wide range of infectious (e.g., adenovirus, influenza, parainfluenza, respiratory syncytial virus [RSV], human metapneumovirus [HmPV]) and noninfectious (e.g., vasculitis, dermatomyositis) common respiratory disorders [54]. For health care workers, timely differential diagnosis of patients is important for reducing cross-infection and controlling the outbreak.

Computed tomography (CT) has an important role to play in the diagnosis and evaluation of COVID-19. Multiple patchy ground glass opacities in bilateral, multifocal lung lesions, with peripheral distribution, are typical chest CT imaging features in COVID-19 patients, whereas pleural effusion, pericardial effusion, cavitation, thoracic lymphadenopathy, and pulmonary emphysema are uncommon imaging findings [55-58]. Studies have shown that CT has a low rate of missed COVID-19 diagnosis (3.9%, 2/51) [59] and the sensitivity of chest CT was greater than that of RT-PCR (98% *vs*. 71%, respectively, $p < 0.001$) [60], indicating that CT may be useful as a standard method for the diagnosis of COVID-19. However, CT cannot identify specific viruses or distinguish between viruses [59]. Bernheim et al. reported that 20/36 (56%) early-stage patients had a normal CT [61], which suggests that chest CT is unlikely to be a reliable standalone tool to rule out COVID-19 infection, especially for patients with early symptom onset.

To date, the gold-standard method for the clinical diagnosis of COVID-19 is nucleic acid detection in nasal and throat swab samples or other respiratory tract samples by real-time PCR, which is then further confirmed by next-generation sequencing [62, 63]. However, this diagnostic method has several shortcomings, such as a low detection rate and high false-negative rates. Moreover, this method is suitable only for diagnosis, and cannot be used to judge the severity and progression of the disease. Additionally, the supply cannot keep up with the demand, and it takes one day or more to obtain results, which may be detrimental to the timely treatment of patients [64]. The Chinese health authorities have issued the 5th version of the diagnosis and treatment plan for COVID-19 [65]. According to the updated criteria, suspected cases with imaging characteristics of pneumonia can be clinically diagnosed as COVID-19 in Hubei province. In this way, patients can receive standardized treatment as soon as possible, so as to further improve the success rate of treatment and contain the spread of the epidemic. Recently, Li et al. developed a rapid and simple point-of-care lateral flow immunoassay that can simultaneously detect IgM and IgG antibodies against SARS-CoV-2 in human blood within 15 minutes. This rapid test has great potential benefit for the fast screening of SARS-CoV-2 infections to prevent virus transmission and assure the timely treatment of patients [66].

6. Intervention methods

6.1 Potential therapeutic interventions

At present, there is no specific antiviral treatment recommended for COVID-19, and no vaccine is available. For mildly to moderately ill patients, active symptomatic support remains key for treatment, such as maintaining hydration and nutrition and controlling fever and cough. For patients with severe infection or those with respiratory failure, oxygen inhalation through a mask, high nasal oxygen flow inhalation, non-invasive ventilation, or mechanical ventilation is needed. Extracorporeal membrane oxygenation (ECMO) can be implemented if all the above methods do not work [67]. Additionally, hemodynamic support is essential for managing septic shock [54], and antibiotics and antifungals may also be required. As corticosteroid therapy is commonly used among critically ill MERS patients [68], short courses of corticosteroids at low-to-moderate doses can be used with caution [69, 70]. As anxiety and fear are common among COVID-19 patients, dynamic assessment strategies should be established to monitor their mental health [71].

Identifying effective antiviral agents to combat the disease is urgently needed. Current guidelines [26] recommend IFN-alpha, lopinavir/ritonavir, ribavirin, chloroquine phosphate, and arbidol as antiviral therapies. IFN-alpha is a broad-spectrum antiviral drug that can inhibit the replication of animal and human coronaviruses [72, 73], while lopinavir is a proteinase inhibitor used to treat HIV infection, with ritonavir being used as a booster [74, 75]. In Korea, the viral load of one patient was reduced and clinical symptoms improved with combined administration of lopinavir and ritonavir [76]. However, a randomized, controlled, open-label trial in China found that lopinavir/ritonavir cotreatment did not significantly enhance clinical improvement, reduce mortality, or diminish throat viral RNA detectability in seriously ill COVID-19 patients [77]. The efficacy of lopinavir/ritonavir in treating COVID-19 requires further clinical confirmation. Ribavirin, a synthetic guanosine analog and broad-spectrum inhibitor of RNA and DNA viruses, is frequently used for the treatment of SARS and MERS patients [78, 79]. Morgenstern et al. [80] reported that, compared with single treatment, a combination of ribavirin and IFN-beta inhibited SARS-CoV replication when administered at greatly reduced concentrations. However, the use of ribavirin is associated with significant toxicity, including hemolysis and reduced hemoglobin levels [81], indicating that ribavirin should be used with caution as a treatment for COVID-19. Multicenter clinical trials conducted in China indicated that chloroquine phosphate, widely used to treat malaria and autoimmune diseases [82, 83], may have some efficacy against COVID-19 associated pneumonia, with acceptable safety [84-86]. Arbidol, a Russian-made small indole-derivative molecule, is used for prophylaxis and treatment of influenza and other respiratory viral infections [87, 88]. Deng et al. [89] found that arbidol combined with lopinavir/ritonavir might delay the progression of lung lesions and reduce the viral load in COVID-19 patients. Nearly all the above-mentioned drug options are associated with the treatment of SARS, MERS, or other new influenza viruses and additional randomized, prospective studies are still needed to determine their efficacy against COVID-19.

There are many other antiviral drugs with potential as treatment options against COVID-19. Remdesivir, a nucleotide analog prodrug currently in clinical trials for the treatment of Ebola virus infections [90], is a promising compound [91], since preclinical studies have suggested that remdesivir may be effective for both prophylaxis and treatment of HCoV infections [54, 92, 93]. Elfiky [94] found that sofosbuvir was a potent inhibitor of COVID-19 RNA-dependent RNA polymerase (RdRp). Oseltamivir is a neuraminidase inhibitor indicated for the treatment of influenza [95, 96]. Nafamostat can block MERS-CoV infection in vitro [97] and is potentially applicable to the treatment of Ebola virus disease [98]. Favipiravir is a broad-spectrum antiviral that has shown promise for treating influenza [99] and may also be effective against the Ebola virus [100]. Nitazoxanide is both an antiprotozoal agent and a first-in-class broad-spectrum antiviral agent [101] that may be useful for the treatment of MERS infections [102].

It has recently been suggested that treatment with angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor 1 (AT1R) inhibitors might reduce the pulmonary inflammatory response in COVID-19 patients [103]. Monoclonal antibody therapy [104] and convalescent plasma [105] also have potential as therapeutic interventions to treat COVID-19. Chinese traditional medicines, such as ShuFengJieDu [106, 107] and Lianhuaqingwen capsules [108, 109] can also aid in the prevention and treatment of infectious respiratory diseases such as influenza A (H1N1). Radix astragali (Huangqi), Radix glycyrrhizae (Gancao), Radix saposhnikoviae (Fangfeng), *Rhizoma Atractylodis Macrocephalae* (Baizhu), *Lonicerae Japonicae Flos* (Jinyinhua), and *Forsythiae Fructus* (Lianqiao) have long been used for the prevention of contagious respiratory viral diseases, indicating that Chinese herbal formulas may also be treatment options for COVID-19 [110, 111]. In addition, fighting viruses with antibiotics is often overlooked [112], and drugs such as teicoplanin [113, 114] and ivermectin [115-117] may also be useful to treat COVID-19 (Table 2).

6.2 Nonpharmaceutical interventions

Currently, the therapeutic strategies employed to deal with COVID-19 are only supportive, and prevention aimed at reducing transmission is another strategy. On January 23, 2020, the local government of Wuhan announced the suspension of public transport services, and closed airports, railway stations, and highways in the city. Since then, many other cities have also begun to regulate traffic [118]. Transportation quarantine has been comprehensively strengthened in passenger stations and other public places, and temperature tests have been carried out to screen for potential cases of COVID-19. In addition, strict monitoring measures have been put in place in various regions for returnees, especially those returning from Hubei province or with suspected exposure to the infection. The Chinese government has also employed numerous other coercive measures to limit population mobility, such as canceling public gatherings, closing schools, encouraging remote work, and extending the Chinese Spring Festival holidays [23]. The Chinese government attached great importance to the COVID-19 outbreak and invested a large amount of manpower and funds for the purchase of medical equipment, drugs, and protective equipment, and fully implement medical treatment [119]. Rapidly sharing scientific information is an effective means of reducing public panic about COVID-19 [120]. However, the internet also has the potential for the dissemination of misinformation [121], and governments should be responsible for providing accurate information and clarifying 'fake news' to help the public to deal with this new infection.

Routine, long-term implementation of some of the measures to interrupt or reduce the spread of SARS-CoV-2 might be difficult. However, many simple and low-cost interventions, such as handwashing [122, 123], may reduce the transmission of epidemic-causing respiratory viruses. Wearing masks as a public health intervention may also help break the transmission link with apparently healthy infectious sources [124-126]. At present, for the public, the most direct and effective way to prevent the spread of the disease is to take protective measures, including improving personal hygiene, wearing a medical mask, having enough rest, maintaining ventilation, and avoiding crowds.

7. Discussion

Coronaviruses have been associated with several outbreaks of infectious disease in humans, including SARS in 2002–2003 and MERS in 2012. According to the WHO, a total of 8,098 people worldwide became sick with SARS during the 2003 outbreak, 774 of whom died. After the SARS outbreak, MERS became the second coronavirus to cause a serious global public health crisis. From 2012 to 2018, the WHO recorded 2,220 laboratory-confirmed cases, resulting in at least 790 deaths [127]. According to the current statistics, the number of COVID-19 infections and deaths far exceeds that of SARS and MERS and is still increasing. The reservoir host of the 2003 SARS virus was thought to be the Asian civet (*Paguma larvata*). The focal point of host-to-human transmission was thought to be the live animal market in Guangdong province in China, much like the ongoing COVID-19 outbreak [128]. The COVID-19 outbreak is another reminder of the ability of viral spill-over from animals to cause severe disease in humans. While it is unclear whether the Huanan seafood market is the source of the current outbreak, a total ban on the illegal wildlife trade is imminent.

The epidemic situation in China has improved. As this is a sudden and new infectious disease, many limitations, such as the lack of administrative capacity, insufficient financial support, low professional quality of some personnel, and inadequate equipment, as well as other inadequacies of the national disease control system, have seriously affected the effective control of COVID-19 [129]. To modernize the disease control system in the future, it is necessary to establish sound public health laws and regulations, and form a disease control system in line with the national conditions, so that it can play a timely and effective role in any future infectious disease outbreak [130].

The SARS-CoV-2 epidemic continues. In the last few months, substantial progress has been made in pathogen monitoring, identifying sources, basic etiology, and clinical treatment. The Chinese government has taken a series of timely and effective measures to contain the spread of the epidemic in China. However, the global situation is very serious, and numerous questions remain unanswered. It will take the combined efforts of all the countries in the world for the epidemic to ultimately subside. However, the coronaviruses identified to date might be only the tip of the iceberg, and other novel and severe zoonotic events may yet occur. Therefore, close monitoring and vigilance remain a top priority for health workers and health authorities. We are not only dealing with the current crisis, but also learning from this experience, so as to establish an effective emergency response system to prevent similar crises in the future.

Acknowledgments

This work was funded by the National Natural Science Foundation of China (81701144, 81670567), and Zhejiang Provincial Natural Science Foundation of China (No.LED20H190003). Wish the global epidemic of 2019 novel coronavirus pneumonia ends soon.

Author contributions

Huilan Tu, Sheng Tu, and Shiqi Gao wrote the paper; Huilan Tu drew the figures and tables; Anwen Shao, and Jifang Sheng revised the paper.

Conflict of interest

The authors state that there was no conflict of interest in the preparation of this review.

Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Li, X., et al., *Potential of large "first generation" human-to-human transmission of 2019-nCoV.* Journal of medical virology, 2020. **92**(4): p. 448-454.
2. Li, Q., et al., *Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia.* The New England journal of medicine, 2020: p. 10.1056/NEJMoa2001316.
3. Wang, C., et al., *A novel coronavirus outbreak of global health concern.* Lancet (London, England), 2020. **395**(10223): p. 470-473.
4. Lai, C.-C., et al., *Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges.* International journal of antimicrobial agents, 2020: p. 105924-105924.
5. Gorbalenya, A.E., et al., *Severe acute respiratory syndrome-related coronavirus: The species and its viruses – a statement of the Coronavirus Study Group.* 2020: p. 2020.02.07.937862.
6. Tyrrell, D.A. and M.L. Bynoe, *Cultivation of viruses from a high proportion of patients with colds.* Lancet (London, England), 1966. **1**(7428): p. 76-77.
7. Velavan, T.P. and C.G. Meyer, *The COVID-19 epidemic.* Tropical medicine & international health : TM & IH, 2020. **25**(3): p. 278-280.
8. Cui, J., F. Li, and Z.L. Shi, *Origin and evolution of pathogenic coronaviruses.* Nat Rev Microbiol, 2019. **17**(3): p. 181-192.
9. Woo, P.C., et al., *Discovery of seven novel Mammalian and avian coronaviruses in the genus deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus.* J Virol, 2012. **86**(7): p. 3995-4008.
10. Tang, Q., et al., *Inferring the hosts of coronavirus using dual statistical models based on nucleotide composition.* Scientific reports, 2015. **5**: p. 17155-17155.
11. Su, S., et al., *Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses.* Trends Microbiol, 2016. **24**(6): p. 490-502.
12. Forni, D., et al., *Molecular Evolution of Human Coronavirus Genomes.* Trends in microbiology, 2017. **25**(1): p. 35-48.
13. Lu, R., et al., *Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding.* Lancet (London, England), 2020. **395**(10224): p. 565-574.
14. Zhou, P., et al., *A pneumonia outbreak associated with a new coronavirus of probable bat origin.* Nature, 2020: p. 10.1038/s41586-020-2012-7.
15. Zu, Z.Y., et al., *Coronavirus Disease 2019 (COVID-19): A Perspective from China.* Radiology, 2020: p. 200490-200490.
16. Wan, Y., et al., *Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS.* Journal of virology, 2020: p. JVI.00127-20.
17. Huang, C., et al., *Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.* Lancet (London, England), 2020. **395**(10223): p. 497-506.
18. Al-Hazmi, A., *Challenges presented by MERS corona virus, and SARS corona virus to global health.* Saudi journal of biological sciences, 2016. **23**(4): p. 507-511.
19. Wu, F., et al., *A new coronavirus associated with human respiratory disease in China.* Nature, 2020: p. 10.1038/s41586-020-2008-3.
20. Holshue, M.L., et al., *First Case of 2019 Novel Coronavirus in the United States.* The New England journal of medicine, 2020. **382**(10): p. 929-936.
21. Carinci, F., *Covid-19: preparedness, decentralisation, and the hunt for patient zero.* BMJ (Clinical research ed.), 2020. **368**: p. bmj.m799-bmj.m799.
22. Cheng, Z.J. and J. Shan, *2019 Novel coronavirus: where we are and what we know.* Infection, 2020: p. 10.1007/s15010-020-01401-y.
23. Yang, Y., W. Shang, and X. Rao, *Facing the COVID-19 outbreak: What should we know and what could we do?* Journal of medical virology, 2020: p. 10.1002/jmv.25720.
24. Zou, L., et al., *SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients.* The New England journal of medicine, 2020: p. 10.1056/NEJMc2001737.
25. Rothe, C., et al., *Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany.* The New England journal of medicine, 2020. **382**(10): p. 970-971.

26. Medicine, G.O.o.N.H.C.O.o.S.A.o.T.C., *The diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (Trial Version 6).* 2020: p. 1-5.
27. Wang, Y., et al., *Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures.* Journal of medical virology, 2020: p. 10.1002/jmv.25748.
28. Wax, R.S. and M.D. Christian, *Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients.* Canadian journal of anaesthesia = Journal canadien d'anesthesie, 2020: p. 10.1007/s12630-020-01591-x.
29. Xia, J., et al., *Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection.* Journal of medical virology, 2020: p. 10.1002/jmv.25725.
30. Gao, Q.Y., Y.X. Chen, and J.Y. Fang, *2019 novel coronavirus infection and gastrointestinal tract.* Journal of digestive diseases, 2020: p. 10.1111/1751-2980.12851.
31. Chen, H., et al., *Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records.* Lancet (London, England), 2020. **395**(10226): p. 809-815.
32. Schwartz, D.A., *An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes.* Arch Pathol Lab Med, 2020.
33. Guan, W.-J., et al., *Clinical Characteristics of Coronavirus Disease 2019 in China.* The New England journal of medicine, 2020: p. 10.1056/NEJMoa2002032.
34. Chen, C., et al., *Analysis of myocardial injury in patients with COVID-19 and association between concomitant cardiovascular diseases and severity of COVID-19.* Zhonghua xin xue guan bing za zhi, 2020. **48**(0): p. E008-E008.
35. Bi, Q., et al., *Epidemiology and Transmission of COVID-19 in Shenzhen China: Analysis of 391 cases and 1,286 of their close contacts.* 2020: p. 2020.03.03.20028423.
36. Schwartz, D.A. and A.L. Graham, *Potential Maternal and Infant Outcomes from (Wuhan) Coronavirus 2019-nCoV Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections.* Viruses, 2020. **12**(2): p. E194.
37. Madinger, N.E., J.S. Greenspoon, and A.G. Ellrodt, *Pneumonia during pregnancy: has modern technology improved maternal and fetal outcome?* American journal of obstetrics and gynecology, 1989. **161**(3): p. 657-662.
38. Gottfredsson, M., *The Spanish flu in Iceland 1918. Lessons in medicine and history.* Laeknabladid, 2008. **94**(11): p. 737-745.
39. Rasmussen, S.A., et al., *Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know.* American journal of obstetrics and gynecology, 2020: p. S0002-9378(20)30197-6.
40. Lipsitch, M., D.L. Swerdlow, and L. Finelli, *Defining the Epidemiology of Covid-19 - Studies Needed.* The New England journal of medicine, 2020: p. 10.1056/NEJMp2002125.
41. Li, X., et al., *Transmission dynamics and evolutionary history of 2019-nCoV.* Journal of medical virology, 2020: p. 10.1002/jmv.25701.
42. Wang, H., et al., *Phase-adjusted estimation of the number of Coronavirus Disease 2019 cases in Wuhan, China.* Cell discovery, 2020. **6**: p. 10-10.
43. Roberts, M.G. and H. Nishiura, *Early estimation of the reproduction number in the presence of imported cases: pandemic influenza H1N1-2009 in New Zealand.* PloS one, 2011. **6**(5): p. e17835-e17835.
44. Lipsitch, M., et al., *Transmission dynamics and control of severe acute respiratory syndrome.* Science (New York, N.Y.), 2003. **300**(5627): p. 1966-1970.
45. Read, J.M., et al., *Novel coronavirus 2019-nCoV: early estimation of epidemiological parameters and epidemic predictions.* 2020: p. 2020.01.23.20018549.
46. Wu, J.T., K. Leung, and G.M. Leung, *Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study.* Lancet (London, England), 2020. **395**(10225): p. 689-697.
47. Riley, S., et al., *Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions.* Science (New York, N.Y.), 2003. **300**(5627): p. 1961-1966.
48. Chowell, G., et al., *The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda.* Journal of theoretical biology, 2004. **229**(1): p. 119-126.

49. Fang, H., J. Chen, and J. Hu, *Modelling the SARS epidemic by a lattice-based Monte-Carlo simulation.* Conference proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference, 2005. **2005**: p. 7470-7473.

50. Chen, N., et al., *Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.* Lancet, 2020. **395**(10223): p. 507-513.

51. Wang, D., et al., *Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China.* Jama, 2020.

52. Li, B., et al., *Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China.* Clin Res Cardiol, 2020.

53. Zhou, F., et al., *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.* Lancet, 2020.

54. Cascella, M., et al., *Features, Evaluation and Treatment Coronavirus (COVID-19)*, in *StatPearls*. 2020, StatPearls Publishing

Copyright © 2020, StatPearls Publishing LLC.: Treasure Island (FL).

55. Xu, X., et al., *Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2.* Eur J Nucl Med Mol Imaging, 2020.

56. Wang, Y., et al., *Temporal Changes of CT Findings in 90 Patients with COVID-19 Pneumonia: A Longitudinal Study.* Radiology, 2020: p. 200843.

57. Zhou, S., et al., *CT Features of Coronavirus Disease 2019 (COVID-19) Pneumonia in 62 Patients in Wuhan, China.* AJR Am J Roentgenol, 2020: p. 1-8.

58. Han, R., et al., *Early Clinical and CT Manifestations of Coronavirus Disease 2019 (COVID-19) Pneumonia.* AJR Am J Roentgenol, 2020: p. 1-6.

59. Li, Y. and L. Xia, *Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management.* AJR Am J Roentgenol, 2020: p. 1-7.

60. Fang, Y., et al., *Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR.* Radiology, 2020: p. 200432.

61. Bernheim, A., et al., *Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection.* Radiology, 2020: p. 200463.

62. Wang, Y., et al., *Combination of RT-qPCR Testing and Clinical Features For Diagnosis of COVID-19 facilitates management of SARS-CoV-2 Outbreak.* Journal of medical virology, 2020: p. 10.1002/jmv.25721.

63. Corman, V.M., et al., *Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR.* Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin, 2020. **25**(3): p. 2000045.

64. Dai, W.-C., et al., *CT Imaging and Differential Diagnosis of COVID-19.* Canadian Association of Radiologists journal = Journal l'Association canadienne des radiologistes, 2020: p. 846537120913033-846537120913033.

65. Medicine, G.O.o.N.H.C.O.o.S.A.o.T.C., *The diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (Trial Version 5).* 2020. **52**(02): p. 96+95.

66. Li, Z., et al., *Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis.* Journal of medical virology, 2020: p. 10.1002/jmv.25727.

67. She, J., et al., *2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies.* Clin Transl Med, 2020. **9**(1): p. 19.

68. Arabi, Y.M., et al., *Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome.* Am J Respir Crit Care Med, 2018. **197**(6): p. 757-767.

69. Shang, L., et al., *On the use of corticosteroids for 2019-nCoV pneumonia.* Lancet, 2020. **395**(10225): p. 683-684.

70. Zhou, W., et al., *Potential benefits of precise corticosteroids therapy for severe 2019-nCoV pneumonia.* Signal Transduct Target Ther, 2020. **5**: p. 18.

71. Xu, K., et al., *[Management of corona virus disease-19 (COVID-19): the Zhejiang experience].* Zhejiang Da Xue Xue Bao Yi Xue Ban, 2020. **49**(1): p. 0.

72. Pei, J., et al., *Chicken interferon type I inhibits infectious bronchitis virus replication and associated respiratory illness.* J Interferon Cytokine Res, 2001. **21**(12): p. 1071-7.

73. Turner, R.B., et al., *Prevention of experimental coronavirus colds with intranasal alpha-2b interferon.*

J Infect Dis, 1986. **154**(3): p. 443-7.
74. Yao, T.T., et al., *A systematic review of lopinavir therapy for SARS coronavirus and MERS coronavirus-A possible reference for coronavirus disease-19 treatment option.* J Med Virol, 2020.
75. Cvetkovic, R.S. and K.L. Goa, *Lopinavir/ritonavir: a review of its use in the management of HIV infection.* Drugs, 2003. **63**(8): p. 769-802.
76. Lim, J., et al., *Case of the Index Patient Who Caused Tertiary Transmission of COVID-19 Infection in Korea: the Application of Lopinavir/Ritonavir for the Treatment of COVID-19 Infected Pneumonia Monitored by Quantitative RT-PCR.* J Korean Med Sci, 2020. **35**(6): p. e79.
77. Cao, B., et al., *A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19.* N Engl J Med, 2020.
78. Koren, G., et al., *Ribavirin in the treatment of SARS: A new trick for an old drug?* Cmaj, 2003. **168**(10): p. 1289-92.
79. Arabi, Y.M., et al., *Ribavirin and Interferon Therapy for Critically Ill Patients With Middle East Respiratory Syndrome: A Multicenter Observational Study.* Clin Infect Dis, 2019.
80. Morgenstern, B., et al., *Ribavirin and interferon-beta synergistically inhibit SARS-associated coronavirus replication in animal and human cell lines.* Biochem Biophys Res Commun, 2005. **326**(4): p. 905-8.
81. Booth, C.M., et al., *Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area.* Jama, 2003. **289**(21): p. 2801-9.
82. Golden, E.B., et al., *Quinoline-based antimalarial drugs: a novel class of autophagy inhibitors.* Neurosurg Focus, 2015. **38**(3): p. E12.
83. Savarino, A., et al., *Effects of chloroquine on viral infections: an old drug against today's diseases?* Lancet Infect Dis, 2003. **3**(11): p. 722-7.
84. Gao, J., Z. Tian, and X. Yang, *Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies.* Biosci Trends, 2020. **14**(1): p. 72-73.
85. Touret, F. and X. de Lamballerie, *Of chloroquine and COVID-19.* Antiviral Res, 2020. **177**: p. 104762.
86. Devaux, C.A., et al., *New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?* Int J Antimicrob Agents, 2020: p. 105938.
87. Blaising, J., S.J. Polyak, and E.I. Pécheur, *Arbidol as a broad-spectrum antiviral: an update.* Antiviral Res, 2014. **107**: p. 84-94.
88. Kadam, R.U. and I.A. Wilson, *Structural basis of influenza virus fusion inhibition by the antiviral drug Arbidol.* Proc Natl Acad Sci U S A, 2017. **114**(2): p. 206-214.
89. Deng, L., et al., *Arbidol combined with LPV/r versus LPV/r alone against Corona Virus Disease 2019:a retrospective cohort study.* J Infect, 2020.
90. Tchesnokov, E.P., et al., *Mechanism of Inhibition of Ebola Virus RNA-Dependent RNA Polymerase by Remdesivir.* Viruses, 2019. **11**(4).
91. Martinez, M.A., *Compounds with therapeutic potential against novel respiratory 2019 coronavirus.* Antimicrob Agents Chemother, 2020.
92. Wang, M., et al., *Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro.* Cell Res, 2020. **30**(3): p. 269-271.
93. Khan, S., et al., *The emergence of a novel coronavirus (SARS-CoV-2), their biology and therapeutic options.* J Clin Microbiol, 2020.
94. Elfiky, A.A., *Anti-HCV, nucleotide inhibitors, repurposing against COVID-19.* Life Sci, 2020. **248**: p. 117477.
95. McQuade, B. and M. Blair, *Influenza treatment with oseltamivir outside of labeled recommendations.* Am J Health Syst Pharm, 2015. **72**(2): p. 112-6.
96. Jefferson, T., et al., *Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments.* Bmj, 2014. **348**: p. g2545.
97. Yamamoto, M., et al., *Identification of Nafamostat as a Potent Inhibitor of Middle East Respiratory Syndrome Coronavirus S Protein-Mediated Membrane Fusion Using the Split-Protein-Based Cell-Cell Fusion Assay.* Antimicrob Agents Chemother, 2016. **60**(11): p. 6532-6539.
98. Nishimura, H. and M. Yamaya, *A Synthetic Serine Protease Inhibitor, Nafamostat Mesilate, Is a Drug Potentially Applicable to the Treatment of Ebola Virus Disease.* Tohoku J Exp Med, 2015. **237**(1): p. 45-50.
99. Goldhill, D.H., et al., *The mechanism of resistance to favipiravir in influenza.* Proc Natl Acad Sci U S A,

2018. **115**(45): p. 11613-11618.
100. Guedj, J., et al., *Antiviral efficacy of favipiravir against Ebola virus: A translational study in cynomolgus macaques.* PLoS Med, 2018. **15**(3): p. e1002535.
101. Rossignol, J.F., *Nitazoxanide: a first-in-class broad-spectrum antiviral agent.* Antiviral Res, 2014. **110**: p. 94-103.
102. Rossignol, J.F., *Nitazoxanide, a new drug candidate for the treatment of Middle East respiratory syndrome coronavirus.* J Infect Public Health, 2016. **9**(3): p. 227-30.
103. Sun, M.L., et al., *[Inhibitors of RAS Might Be a Good Choice for the Therapy of COVID-19 Pneumonia].* Zhonghua Jie He He Hu Xi Za Zhi, 2020. **43**(0): p. E014.
104. Shanmugaraj, B., et al., *Perspectives on monoclonal antibody therapy as potential therapeutic intervention for Coronavirus disease-19 (COVID-19).* Asian Pac J Allergy Immunol, 2020.
105. Cunningham, A.C., H.P. Goh, and D. Koh, *Treatment of COVID-19: old tricks for new challenges.* Crit Care, 2020. **24**(1): p. 91.
106. Li, Y., et al., *Anti-inflammatory effects of Shufengjiedu capsule for upper respiratory infection via the ERK pathway.* Biomed Pharmacother, 2017. **94**: p. 758-766.
107. Ji, S., et al., *Unique synergistic antiviral effects of Shufeng Jiedu Capsule and oseltamivir in influenza A viral-induced acute exacerbation of chronic obstructive pulmonary disease.* Biomed Pharmacother, 2020. **121**: p. 109652.
108. Ding, Y., et al., *The Chinese prescription lianhuaqingwen capsule exerts anti-influenza activity through the inhibition of viral propagation and impacts immune function.* BMC Complement Altern Med, 2017. **17**(1): p. 130.
109. Duan, Z.P., et al., *Natural herbal medicine Lianhuaqingwen capsule anti-influenza A (H1N1) trial: a randomized, double blind, positive controlled clinical trial.* Chin Med J (Engl), 2011. **124**(18): p. 2925-33.
110. Luo, H., et al., *Can Chinese Medicine Be Used for Prevention of Corona Virus Disease 2019 (COVID-19)? A Review of Historical Classics, Research Evidence and Current Prevention Programs.* Chin J Integr Med, 2020.
111. Lu, H., *Drug treatment options for the 2019-new coronavirus (2019-nCoV).* Biosci Trends, 2020. **14**(1): p. 69-71.
112. Colson, P. and D. Raoult, *Fighting viruses with antibiotics: an overlooked path.* Int J Antimicrob Agents, 2016. **48**(4): p. 349-52.
113. Shea, K.W. and B.A. Cunha, *Teicoplanin.* Med Clin North Am, 1995. **79**(4): p. 833-44.
114. Baron, S.A., et al., *Teicoplanin: an alternative drug for the treatment of coronavirus COVID-19?* Int J Antimicrob Agents, 2020: p. 105944.
115. Varghese, F.S., et al., *Discovery of berberine, abamectin and ivermectin as antivirals against chikungunya and other alphaviruses.* Antiviral Res, 2016. **126**: p. 117-24.
116. Laing, R., V. Gillan, and E. Devaney, *Ivermectin - Old Drug, New Tricks?* Trends Parasitol, 2017. **33**(6): p. 463-472.
117. Lee, Y.J. and C. Lee, *Ivermectin inhibits porcine reproductive and respiratory syndrome virus in cultured porcine alveolar macrophages.* Arch Virol, 2016. **161**(2): p. 257-68.
118. Lau, H., et al., *The positive impact of lockdown in Wuhan on containing the COVID-19 outbreak in China.* J Travel Med, 2020.
119. Wang, W., J. Tang, and F. Wei, *Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China.* Journal of medical virology, 2020. **92**(4): p. 441-447.
120. Song, P. and T. Karako, *COVID-19: Real-time dissemination of scientific information to fight a public health emergency of international concern.* Bioscience trends, 2020: p. 10.5582/bst.2020.01056.
121. The, L., *COVID-19: fighting panic with information.* Lancet (London, England), 2020. **395**(10224): p. 537-537.
122. Rabie, T. and V. Curtis, *Handwashing and risk of respiratory infections: a quantitative systematic review.* Tropical medicine & international health : TM & IH, 2006. **11**(3): p. 258-267.
123. Mbakaya, B.C., P.H. Lee, and R.L.T. Lee, *Hand Hygiene Intervention Strategies to Reduce Diarrhoea and Respiratory Infections among Schoolchildren in Developing Countries: A Systematic Review.* International journal of environmental research and public health, 2017. **14**(4): p. 371.
124. Cowling, B.J., et al., *Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial.* Annals of internal medicine, 2009. **151**(7): p. 437-446.

125. MacIntyre, C.R. and A.A. Chughtai, *Facemasks for the prevention of infection in healthcare and community settings.* BMJ (Clinical research ed.), 2015. **350**: p. h694-h694.

126. Leung, C.C., T.H. Lam, and K.K. Cheng, *Mass masking in the COVID-19 epidemic: people need guidance.* Lancet (London, England), 2020: p. S0140-6736(20)30520-1.

127. Al-Omari, A., et al., *MERS coronavirus outbreak: Implications for emerging viral infections.* Diagnostic microbiology and infectious disease, 2019. **93**(3): p. 265-285.

128. Peeri, N.C., et al., *The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned?* International journal of epidemiology, 2020: p. dyaa033.

129. Wang, X., X. Zhang, and J. He, *Challenges to the system of reserve medical supplies for public health emergencies: reflections on the outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic in China.* Biosci Trends, 2020. **14**(1): p. 3-8.

130. Heymann, D.L., et al., *COVID-19: what is next for public health?* Lancet (London, England), 2020. **395**(10224): p. 542-545.

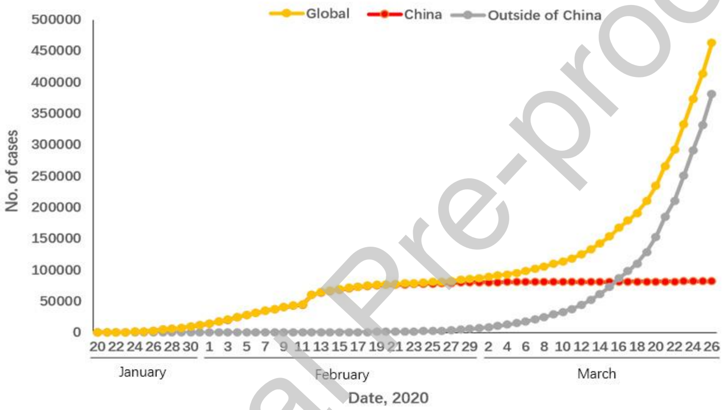

Fig. 1. New daily cases of laboratory-confirmed coronavirus disease 2019 (COVID-19) as of March 26, 2020. (A) Daily numbers of new cases globally and (B) daily numbers of new cases from China (including the Hong Kong Special Administrative Region [SAR] and Macau SAR) and outside of China.

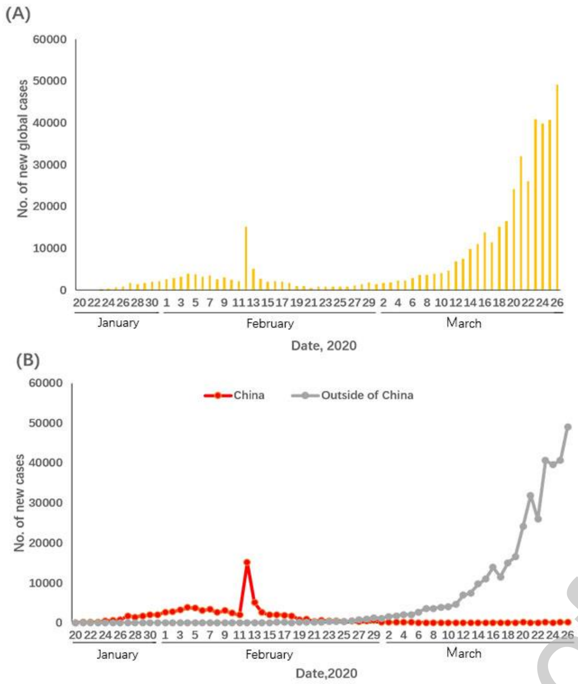

Fig. 2. Daily cumulative laboratory-confirmed cases of coronavirus disease 2019 (COVID-19) as of March 26, 2020. Daily numbers of global cases and daily numbers of cases from China (including Hong Kong Special Administrative Region [SAR] and Macau SAR)] and outside of China.

Table 1 Demographics, clinical characteristics, and clinical outcomes of patients infected with COVID-19.

	Guan et al.[33] (n=1099) n (%)	Huang et al.[17] (n=41) n (%)	Chen et al.[50] (n=99) n (%)	Wang et al.[51] (n=138) n (%)
Age, years	47.0 (35.0-58.0)	49.0 (41.0-58.0)	55.5 (13.1)	56.0 (42.0-68.0)
Female sex	459/1096 (41.9)	11/41 (27)	32 (32)	63 (45.7)
Current smoking	137/1085 (12.6)	3 (7)	NA	NA
Any comorbidity	261 (23.7)	13 (32)	50 (51)	64 (46.4)
Diabetes	81 (7.4)	8 (20)	NA	14 (10.1)
Hypertension	165 (15.0)	6 (15)	NA	43 (31.2)
Cardiovascular disease	42 (3.9)	6 (15)	40 (40)	20 (14.5)
COPD	12 (1.1)	1 (2)	NA	4 (2.9)
Malignancy	10 (0.9)	1 (2)	1 (1)	10 (7.2)
Chronic liver disease	23 (2.1)	1 (2)	NA	4 (2.9)
Presentation				
Fever	975 (88.7)	40 (98)	82 (83)	136 (98.6)
Cough	745 (67.8)	31 (76)	81 (82)	82 (59.4)
Fatigue	419 (38.1)	18 (44)	NA	96 (69.6)
Myalgia	164 (14.9)	NA	11 (11)	48 (34.8)
Sputum production	370 (33.7)	11/39 (28)	NA	37 (26.8)
Short of breath	205 (18.7)	22/40 (55)	31 (31)	43 (31.2)
Sore throat	153 (13.9)	NA	5 (5)	24 (17.4)
Headache	150 (13.6)	3/38 (8)	8 (8)	9 (6.5)
Diarrhea	42 (3.8)	1/38 (3)	2 (2)	14 (10.1)
Nausea or Vomiting	55 (5.0)	NA	1 (1)	19 (13.7)
Chills	126 (11.5)	NA	NA	NA
Haemoptysis	10 (0.9)	2/39 (5)	NA	NA
Outcome				
Discharged	55 (5.0)	28 (68)	31 (31)	47 (34.1)
Remained hospitalized	1029 (93.6)	7 (17)	57 (58)	85 (61.6)
Died	15 (1.4)	6 (15)	11 (11)	6 (4.3)

Data are median (IQR), mean (SD), n (%), or n/N (%), where N is the total number of patients with available data. COPD, chronic obstructive pulmonary disease; NA, not available.

Table 2 Common and potential treatment options of COVID-19.

Classes	Drugs	Action mode	Target diseases	Reference
Anti-viral	Lopinavir/Ritonavir	Protease inhibitors	HIV/AIDS, SARS, MERS	[74, 75]
	Ribavirin	Synthetic guanosine nucleoside	HCV, SARS, MERS	[78, 79]
	Arbidol	Broad-spectrum antiviral compound	Influenza virus	[87, 88]
	Remdesivir	Nucleotide analogue prodrug	A wide array of RNA virus including Ebola	[54, 90, 92, 93]
	Oseltamivir	Neuraminidase inhibitor	Influenza virus	[95, 96]
	Sofosbuvir	Nucleotide Inhibitor	Hepatitis C	[94]
	Nafamostat	Synthetic serine protease inhibitor	MERS, Ebola	[97, 98]
	Favipiravir	Nucleoside analog	Ebola, Influenza A(H1N1)	[99, 100]
	Nitazoxanide	Antiprotozoal agent	A wide range of viruses including human/animal coronaviruses	[101, 102]
Anti-malarial	Chloroquine phosphate	9-aminoquinolin	Malaria, Autoimmune disease	[82, 83]
Anti-biotic	Teicoplanin	Glycopeptide antibiotic	Gram-positive infections	[113, 114]
	Ivermectin	Broad-spectrum anti-parasitic compound	Chikungunya virus and other Alphaviruses, Parasitic infection	[115-117]
Herbal treatments	Chinese traditional medicine like ShuFengJieDu Capsules, Lianhuaqingwen Capsule, Huangqi, Gancao, Fangfeng, Baizhu, Jinyinhua, and Lianqiao.		Upper respiratory tract infection including Influenza virus	[106-109, 111]