

# The Global Challenges of Controlling Coronavirus Disease 2019: A Review Study

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#### Abstract

**Background:** The COVID-19 pandemic is a challenging health problem around the world. At time of this study, the pandemic is still underway, so prevention and control are of great importance. This review provides a comprehensive examination and analysis of the literature related to the challenges of controlling COVID-19.

**Methods:** In this narrative review study, the search was performed on international databases including PubMed, Scopus and Embase, using relevant keywords. The resulting articles and texts were reviewed and screened, and then the relevant information was extracted.

**Results:** The number of patients who are thought to have contracted COVID-19 is much higher than that in the SARS and MERS epidemics. Despite a lower mortality rate, COVID-19 has caused more deaths. One of the challenges that have made the control of the disease more difficult include the emergence of multiple viral mutations. In this review, it was found that the best course of action comprises continuous monitoring of disease-related indicators as part of a series of measures taken together to ensure their effectiveness.

**Conclusion:** It is recommended that governments should form international partnerships in their efforts to overcome the pandemic, and that preventive and control measures should be taken simultaneously.

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**Keywords:** COVID-19, 2019-nCoV infection, SARS-CoV-2 infection, Infection control, Disease management

## Introduction

Coronavirus disease 2019 (COVID-19) started in December 2019 in Wuhan, the capital of Hubei Province, China, and one of China's main transportation hubs, and spread to other parts of the world.<sup>1,2</sup> One of the main reasons for the spread of the disease was the intense migration of Chinese people during New Year celebrations.<sup>1</sup> With the rise of international trade, epidemics of new infectious diseases such as COVID-19 are able to spread more rapidly than ever before.<sup>3</sup> On December 31, 2019, China announced the outbreak of the disease, at the time named 2019-nCoV, to the World Health Organization (WHO).<sup>2,4</sup> On February 11, 2020, the WHO adopted a new name called coronavirus disease (COVID-19). In acknowledgement of the genetic

structure of the virus, the International Committee on Virus Classification renamed 2019-nCoV as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>5</sup>

On January 30, 2020, the WHO announced that the outbreak was a public health emergency of international concern<sup>5,6</sup> and in March 2020 classified it as a pandemic.<sup>7,8</sup> COVID-19 has been declared the sixth international public health emergency and, therefore, requires the public, health professionals and governments to work together to prevent its spread worldwide.<sup>5</sup> Rapid production and sharing of knowledge at the international level is one of the useful measures for disease control that has been done.<sup>9</sup>

One of the greatest fallacies of the 21<sup>st</sup> century is that infectious diseases are disappearing, which is

not the case.<sup>10</sup> The COVID-19 epidemic has become a challenging health problem for many countries around the world,<sup>8</sup> and as of 28 February 2021, it was estimated that there were 113,472,187 cases of the disease, 2,520,653 deaths, and about 91 million cases of recovery reported worldwide.<sup>11,12</sup> Although more than a year has passed since the beginning of this epidemic, the disease has not yet been controlled and no specific treatment has been found for it,<sup>13</sup> so measures related to its prevention and control are very important. The aim of this study was to examine and characterize the global challenges of controlling COVID-19, and to provide comprehensive recommendations for action.

## Methods

### *Literature Search*

In this narrative review, the authors did a comprehensive survey of the published literature in the area of challenges and problems related to the control and management of COVID-19. Literature searches were performed using PubMed, Scopus and Embase databases. The keywords used were “nCoV”, “COVID-19”, “SARSCoV-2”, “coronavirus”, “problem”, “challenge”, “barrier”, “control”, and “management”. The resulting articles and texts were reviewed and screened, and then the relevant information was extracted.

Four human coronaviruses have been identified, namely HKU1, NL63, 229E, and OC43, all causing mild respiratory disease.<sup>2</sup> Prior to the COVID-19 pandemic, there had been two previous coronavirus-related epidemics, both of which featured a virus that originated in bats. In 2002-2003, the epidemic of severe acute respiratory syndrome coronavirus (SARS-CoV) occurred, infecting 8,422 people and causing 916 deaths (11% mortality). The epidemic was ultimately controlled, and the majority of cases were observed in China and Hong Kong.<sup>14</sup> About 10 years later, in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV) first appeared in Saudi Arabia and eventually infected 2,494 people, causing 858 deaths (34.4% mortality).<sup>15</sup>

Research has shown that all people are potentially susceptible to this disease,<sup>16</sup> but those who are in close contact with COVID-19 patients (whether symptomatic or asymptomatic) have a higher risk.<sup>4</sup> Older age and the presence of comorbidities (such as diabetes, hypertension, and cardiovascular disease) are associated with a poor prognosis.<sup>16</sup> In the case of MERS, these factors were also predictors of the disease severity.<sup>17</sup> Most cases of COVID-19 cause a mild illness, with only 15-20% of patients experiencing severe or life-threatening symptoms of the disease.<sup>4</sup> According to a study conducted in Wuhan, China, the incidence of the disease is higher in men,<sup>18</sup> which is

also the case in MERS.<sup>17</sup>

Disease control measures vary from the practice of isolating confirmed and suspected cases to the identification of individuals with whom a symptomatic patient has been in contact. Some effective measures to control the disease include hand washing, taking barrier measures (such as masks and gloves),<sup>19</sup> and restricting unnecessary movements.<sup>20</sup> Experience has shown that these measures alone are not sufficient to control the spread of COVID-19. The interval between infection and the onset of symptoms has been reported as being up to 14 days; as such, the practice of isolating cases and contact tracing will be less effective. Conversely, in the control of epidemics such as SARS, MERS and Ebola, the time of infection and the onset of symptoms were nearly simultaneous or were separated by a short interval.<sup>21</sup>

## Results

### *Epidemiology of COVID-19*

SARS-CoV-2, like SARS-CoV and MERS-CoV, is a zoonotic disease. The spread into humans was most likely caused by Chinese horseshoe bats (*Rhinolophus sinicus*), likely through the intermediate hosts, pangolins.<sup>4</sup> Genetic and epidemiological research has shown that the COVID-19 epidemic was started by animal-to-human transmission and then spread globally through human-to-human transmission.<sup>22</sup>

The incubation period of SARS-CoV-2 varies from 2 to 14 days (average 5 days).<sup>2</sup> Accordingly, the quarantine period imposed following suspected contact with an infected individual is generally two weeks.<sup>4</sup> The incidence of the disease increased exponentially, with mathematical models of disease spread estimating the doubling time to be 7.2 days. In a population where all individuals are considered susceptible to infection, each infected individual has the expectation of infecting 2.2 of other people (basic reproduction number or  $R_0=2.2$ ).<sup>18</sup> According to the WHO initial estimate in January 2020, the  $R_0$  was reported to be between 1.4 and 2.5. However, according to subsequent studies published from January 1 to February 7, 2020, the  $R_0$  range was reported between 1.5 and 6.68.<sup>23</sup> The results of a review of 12 studies showed that the mean and median  $R_0$  were estimated to be 3.28 and 2.79.<sup>24</sup>

The COVID-19 fatality rate in different parts of China varies between 0.39 to 4.05 percent. The mean and median of the case fatality rate of COVID-19 in the world were 3.31 and 2.19 percent, respectively, and Yemen, Western and Northern Europe and North America have the highest fatality rates.<sup>25</sup> The fatality rate of this disease is higher than seasonal influenza (with a fatality rate of between 0.01 and 0.17%) but lower than the previous SARS and

MERS epidemics (fatality rates of approximately 10% and 34%, respectively).<sup>4, 26</sup> In addition to the high transmissibility of COVID-19, the ubiquity of international travel presents the potential for rapid global transmission.<sup>5</sup> Also, one of the recent concerns is related to reactivation or re-infection of cases that have recovered after infection<sup>27, 28</sup> and, therefore, can lead to the spread of the disease.

#### *Clinical Features and Diagnosis*

Fever and dry cough are the most common symptoms of COVID-19 and are present in the majority of patients.<sup>5, 29</sup> In some cases, shortness of breath, fatigue and other less common symptoms are observed (muscle cramps, confusion, headache, sore throat, nausea and vomiting).<sup>29</sup> However, the results of studies have shown that the most important differential symptoms for COVID-19 include loss of taste and smell.<sup>30, 31</sup>

The diagnosis of COVID-19 requires a combination of epidemiological information (such as residence or travel history of high-risk areas prior to the onset of symptoms), clinical signs, imaging findings, and laboratory tests, based on WHO standards or national guidelines.<sup>4, 32</sup> Any patient with an epidemiological history, COVID-19-associated symptoms, or positive imaging results should be clinically evaluated and precautionary measures should be taken.<sup>4</sup> The information obtained from diagnostic tests alone is not complete because the real false positive/negative rates of these tests are unknown. In order to assess the true accuracy of diagnostic tests and to determine their false positive/negative rates, we need background information (for example, blood samples taken at the time before the onset of the disease that are stored and represent true negatives).<sup>33</sup> In some cases, a positive diagnosis is problematic because there is not always an agreement between laboratory or radiographic findings and clinical characteristics or patient contact history. Therefore, in order to achieve a positive diagnosis of COVID-19, information such as epidemiological history, clinical and radiographic features, and laboratory diagnoses should be combined.<sup>26</sup>

#### *Modes of Transmission*

COVID-19 transmission is predominantly through large respiratory droplets produced during coughing and sneezing of symptomatic patients.<sup>16</sup> However, asymptomatic individuals can also transmit the disease.<sup>34</sup> Infection occurs both by inhalation of these droplets or by touching contaminated surfaces and then touching the nose, mouth and eyes.<sup>2</sup> Of course, virus transmission through surfaces is rare, and in some cases it has been recommended that we should focus on air ventilation instead of disinfecting surfaces;<sup>35</sup> these cases can also be a challenge. The virus is also present in the stool, and contamination

of water can also cause transmission.<sup>2, 36</sup> Vertical transmission from a pregnant woman to a fetus has also been reported.<sup>37, 38</sup>

## **Discussion**

#### *Control Measures*

Because there is currently no approved treatment for COVID-19,<sup>16</sup> it is important to focus on prevention. However, this is difficult for a number of reasons, including the occurrence of asymptomatic transmission either by individuals prior to the onset of symptoms or by those who remain asymptomatic,<sup>34</sup> and the manifestation of a prolonged incubation period.<sup>16</sup> Transmission has been reported to occur through mucosal surfaces such as the conjunctiva. Further, the duration of the illness is prolonged in many cases, with transmission being shown to still occur, even after clinical improvement.<sup>2</sup> Approaches that have been used to control the spread of COVID-19 include controlling the source of infection, prevention and control measures to reduce disease transmission, early diagnosis, and support measures for patients.<sup>4, 5</sup>

One of the factors shown to be effective in controlling the spread of COVID-19 is the provision of sufficient medical equipment such as personal protective equipment (especially fluid resistant masks and medical protective clothing), as adequate access to this equipment has been shown to reduce the number of deaths.<sup>3</sup> Furthermore, it is recommended that several pieces of equipment should be used simultaneously (such as masks and gloves), and to each piece should be disposed of and replaced frequently, potentially using an entirely new set of equipment for each successive patient, thus exacerbating any shortages. The lack of availability of personal protective equipment together with the need to observe hand hygiene and social distancing has made preventing the transmission of COVID-19 more difficult.<sup>39</sup>

Isolation at home is recommended for confirmed or suspected cases where the illness experienced is mild. Proper ventilation of the house and adequate sunlight are also necessary to kill the virus. Patients and caregivers should wear masks and practice personal hygiene during sneezing and coughing.<sup>2</sup> Reports to health officials are needed to monitor the situation, such that all information relating to the spread of this new virus can be compiled in order to improve the speed and efficacy of the response.<sup>5</sup> Recommended measures at the community level include avoiding entering crowded areas, refraining from unnecessary travel, and practicing hand hygiene regularly.<sup>2</sup>

As to any disease outbreak reported to date, effective vaccines, diagnostic and therapeutic measures are essential.<sup>9</sup> The development and production of vaccines and antiviral treatments are

currently underway.<sup>5</sup> The complete sequence of the SARS-CoV-2 genome was obtained and shared by mid-January 2020, representing a significant and rapid advancement to this end.<sup>1</sup> Although several potential treatments have been suggested so far, no antiviral therapy for COVID-19 has yet been approved. In contrast to the previous two epidemics, vaccination development is still in its infancy. Although different vaccines have been produced around the world so far,<sup>40</sup> the discovery of a vaccine alone is not enough to control the COVID-19 pandemic. These vaccines, in addition to having a high effectiveness, need to be produced on a wide scale and at an appropriate price, and also be available to the whole world in order to hope for herd immunity. In addition, the level of the acceptance of vaccine by the public is also an important issue. The WHO stated that it would take approximately 18 months to develop a vaccine for SARS-CoV-2, but there are challenges in achieving this, including obtaining sufficient funding, and public acceptance if the risk level of the disease is reduced.<sup>9</sup>

### Challenges

The effectiveness of isolation and contact tracing measures depends on two epidemiological parameters; the number of secondary infections resulting from each new infection and the rate of transmission through asymptomatic cases. Due to the high transmission of COVID-19, reducing the delay between the onset of symptoms, together with contact tracing, is critical for success.<sup>21</sup> Because some infected individuals are asymptomatic, and as such do not contribute to mathematical models of disease spread, it is difficult to predict when the disease will peak.<sup>17</sup> Those who do not seek care present a further challenge to control the disease, as they are likely to spread infection without being reported in national figures.

One of the challenges in controlling the COVID-19 epidemic is the limited capacity of governmental and non-governmental organizations to respond with coherent interdisciplinary efforts due to lack of medical equipment and laboratory facilities for disease assessment.<sup>17</sup> Studies show that controlling COVID-19 becomes more difficult and less effective in cases where there are extended delays between the onset of symptoms and isolation, poor diagnosis sensitivity and specificity, as well as availability of tests, and increased transmission before the onset of symptoms through lack of social distancing and use of personal protective equipment.<sup>21</sup> Therefore, implementing isolation of symptomatic patients and contact tracing should be performed to the best degree possible.

During the experiences about MERS epidemic, high-income countries with good healthcare provision were more responsive to preventing the spread of communicable diseases. This was related to such

factors as having access to a stronger surveillance system, having contact tracing abilities, triage, assessing and testing facilities, and further, the availability of rapid tests for use in such laboratories.<sup>41</sup> Conversely, in the COVID-19 epidemic, not just developing countries, but also high-income countries are seriously affected, and are reported to experience high mortalities.<sup>11</sup> However, the problems and challenges associated with the COVID-19 will be greater in low- and middle-income countries.<sup>42</sup> Evidently in the COVID-19 epidemic, unlike the previous two coronavirus epidemics, there are other challenges that need to be investigated and addressed.

Ubiquity of social media and emotional, biased or subjective reporting of the disease are the factors that impact the disease control. Misleading information and theories published on social media cause panic and distrust in the society,<sup>5,9</sup> divert attention away from efficacious measures of controlling the disease, and thwart the efforts of health care workers. Preventing the dissemination of misleading information and countering this by providing credible information repositories for people to access appropriate, timely information (for example the website WHO Actions) can help address this problem and improve and enhance the disease control.

One of the major challenges in addressing the COVID-19 pandemic is related to the methods of gathering and disseminating statistics across different countries and regions. For example, the basic reproduction number ( $R_0$ ) for COVID-19 is typically reported to be between 2 and 3.5.<sup>18, 26, 41</sup> However, studies conducted by the US centers for disease control and prevention (CDC) reported this range between 3.8 to 8.9, with a median of 5.7.<sup>43</sup> That the rate of disease transmission may be considerably faster than previously thought. In another study, which reported  $R_0$  changes in six countries with the highest cumulative numbers of infected people until September 2020,<sup>44</sup> the highest  $R_0$  was in Brazil at 22.6. In all cases, the  $R_0$  peak was seen in March 2020. It is necessary to assess infection transmission rates in many other countries in order to better use these statistics to inform necessary pandemic control measures.

In many countries and regions with poor economic status, non-therapeutic prevention measures have become challenging, such as maintaining social distancing.<sup>45</sup> Also, diagnostic tests<sup>46</sup> and protective and therapeutic facilities are typically unhomogeneously distributed throughout different regions of a country.<sup>47</sup> Another challenge is insufficient attention to the degree of obedience of individuals and factors affecting this obedience,<sup>48</sup> and the co-occurrence of COVID-19 with other diseases such as cancer,<sup>49</sup> cardiovascular disease,<sup>50</sup> diabetes<sup>51</sup> and mental illness<sup>52</sup> which

increases the morbidity and mortality of COVID-19.

One of the other challenges that have made the control of COVID-19 more difficult includes the emergence of multiple viral mutations, such as those in the United Kingdom, South Africa, and Brazil (B.1.1.7, B.1.135, and P. 1, respectively).<sup>53</sup> Some of these mutations even have more transmissibility<sup>54</sup> and can, therefore, cause other problems, such as problems in the efficacy of producing vaccines.

The results of this comprehensive literature review have indicated that in order to better control the COVID-19 pandemic, a series of measures should be taken synchronously to maximize their effectiveness. These measures include increasing and improving the level of cooperation between organizations and governments at national and international levels, potentially even temporarily halting commonplace international restrictions imposed on some countries that act to restrict transfer of information and resources. Publishing information in a timely manner is of paramount importance. Sophisticated use of social networks, isolation of symptomatic patients and better contact tracing should be employed to facilitate mapping the infection status across wide areas, so that this information can also be shared in a timely manner. Social networks, social media platforms, and smartphone applications should enable the agencies to focus on susceptible populations including children, the elderly, healthcare providers, and people with comorbidities making them vulnerable. Finally, future studies must be supported, where possible, to develop effective vaccines and antiviral drugs to manage the disease. Of course, it should be noted that the impact of the measures and policies mentioned also depends on the degree of public obedience. The degree of compliance and obedience of individuals may depend on their behavior, attitudes, and beliefs about the disease that have not received sufficient attention.

## Conclusion

Studies show that the number of people infected with COVID-19 is much higher than that of the SARS and MERS coronavirus epidemics. Despite the lower mortality rate of COVID-19, compared to the previous two epidemics, it has led to more deaths. At the time of this study, the COVID-19 pandemic is still much large, so prevention and control measures are very important, and all indicators related to the spread of COVID-19 should be constantly monitored. The global outbreak of COVID-19 can have various endings. At best, the disease may be controlled, as was the case in the SARS and MERS epidemics, if necessary international measures are taken. Alternatively, COVID-19 could impose heavy death tolls and impact quality of life in countries around the world, akin to the situation that followed the Spanish flu in 1918. It is recommended that allied international

efforts should be made to overcome this pandemic, and that preventive and control measures should be taken simultaneously. Due to the limited time available to respond to the COVID-19 pandemic, decision-making around disease control, management and prevention must be undertaken promptly.

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