

BACKGROUND

- A cluster of cases of pneumonia caused by 2019 novel coronavirus (2019-nCoV) was reported in late December 2019, in Wuhan, China¹ which was officially named Coronavirus Disease-2019 (COVID-19) by the World Health Organization (WHO).
- COVID-19 initially spread to other Asian countries, with South Korea being the most affected².
- Following this, a sharp growth in confirmed cases was witnessed in Europe, with many European countries reporting nation-wide community transmission.
- The United States (US) began to report tens of thousands of new cases beginning on March 24th, 2020, exceeding the 123,776 confirmed cases in China recorded on March 29th, 2020³.
- The outbreak seems to be under control in China as several provinces have declared no infected cases remain. However, the rapid expansion of COVID-19 is still ongoing in Europe.

OBJECTIVES

- The review aimed to summarize and share the Chinese experience and what guidelines have been established to control the spread of COVID-19.

- The pharmaceutical guidelines developed in China were identified and described.
- The adjustments in the treatment of COVID-19 over time based on the increasing experience in treating COVID-19 patients were also analysed.

METHODS

- A systematic search of the China National Knowledge Infrastructure (CNKI) database, Yimaitong database, and World Health Organization (WHO) COVID-19 database was conducted on March 20th, 2020 to identify Chinese guidelines relevant to COVID-19.
- Date of publication, source of the guidelines, objectives of the guidelines, and target population of the guidelines, characteristics of included guidelines, were extracted.
- During the analysis, guidelines were classified according to the objectives of the guidelines. The target populations of the COVID-19 guidelines were further categorized. Pharmacological treatments including Traditional Chinese Medicine (TCM) and Western Medicine (WM), were extracted to investigate what medicines were most recommended in the treatment of COVID-19 patients.

Figure 1 Percentage of the source of guidelines related to COVID-19 in China

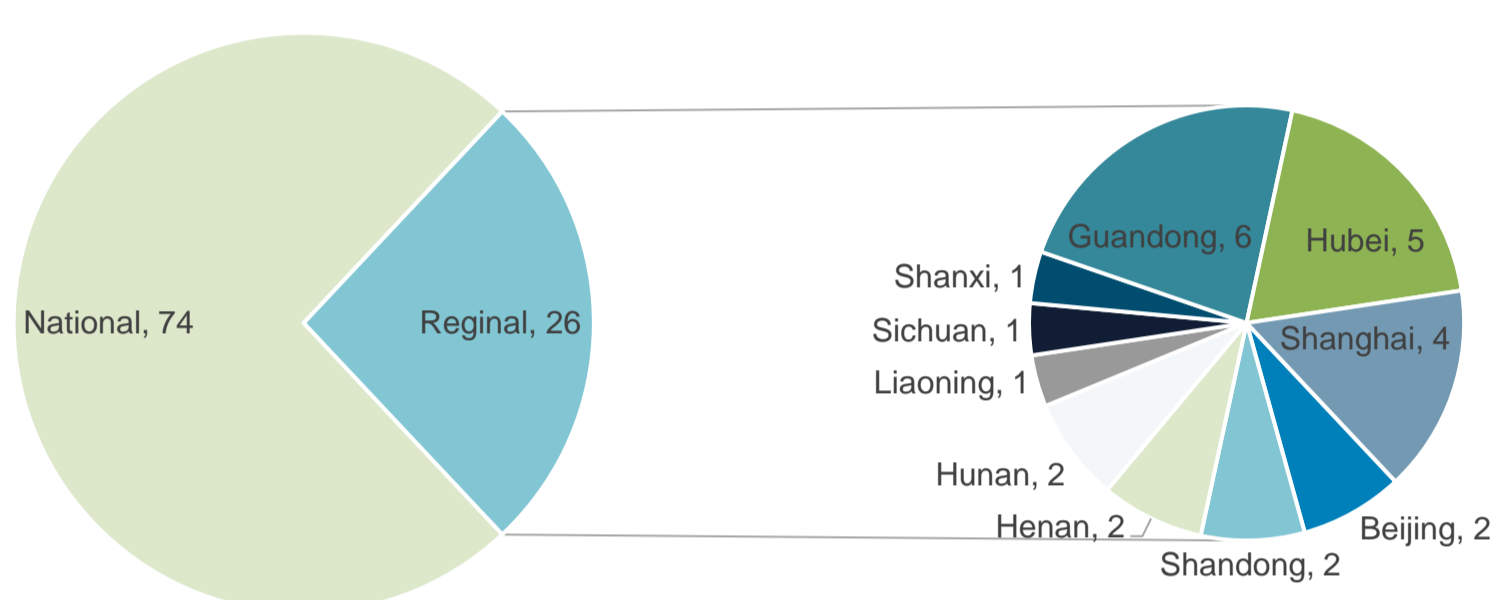


Figure 2 Percentage of the objective of included guidelines related to COVID-19

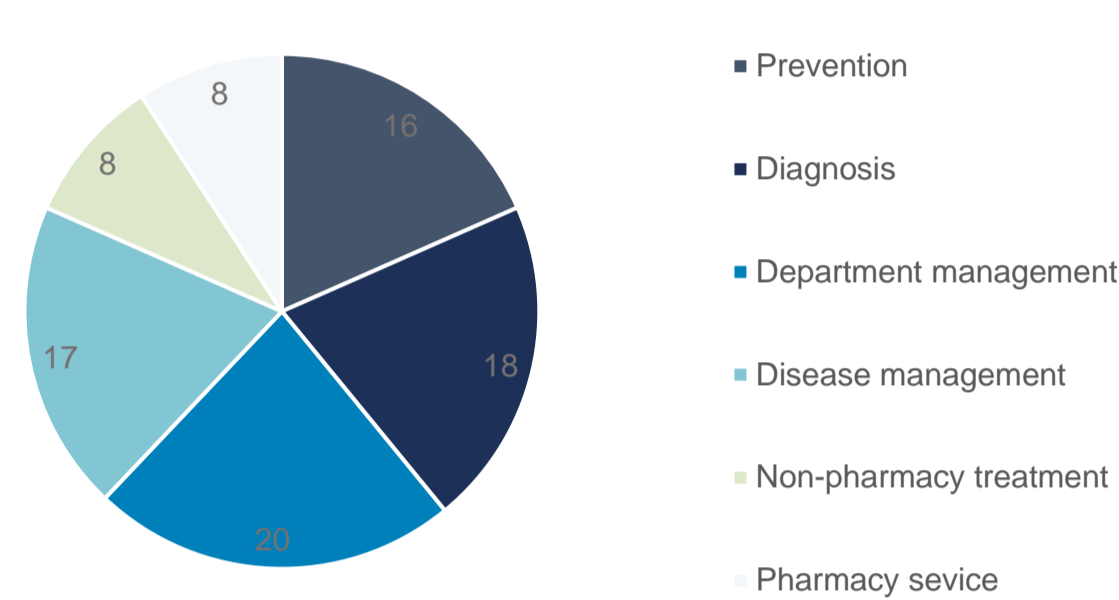


Figure 3. Percentage of the target patient populations of included guidelines related to COVID-19

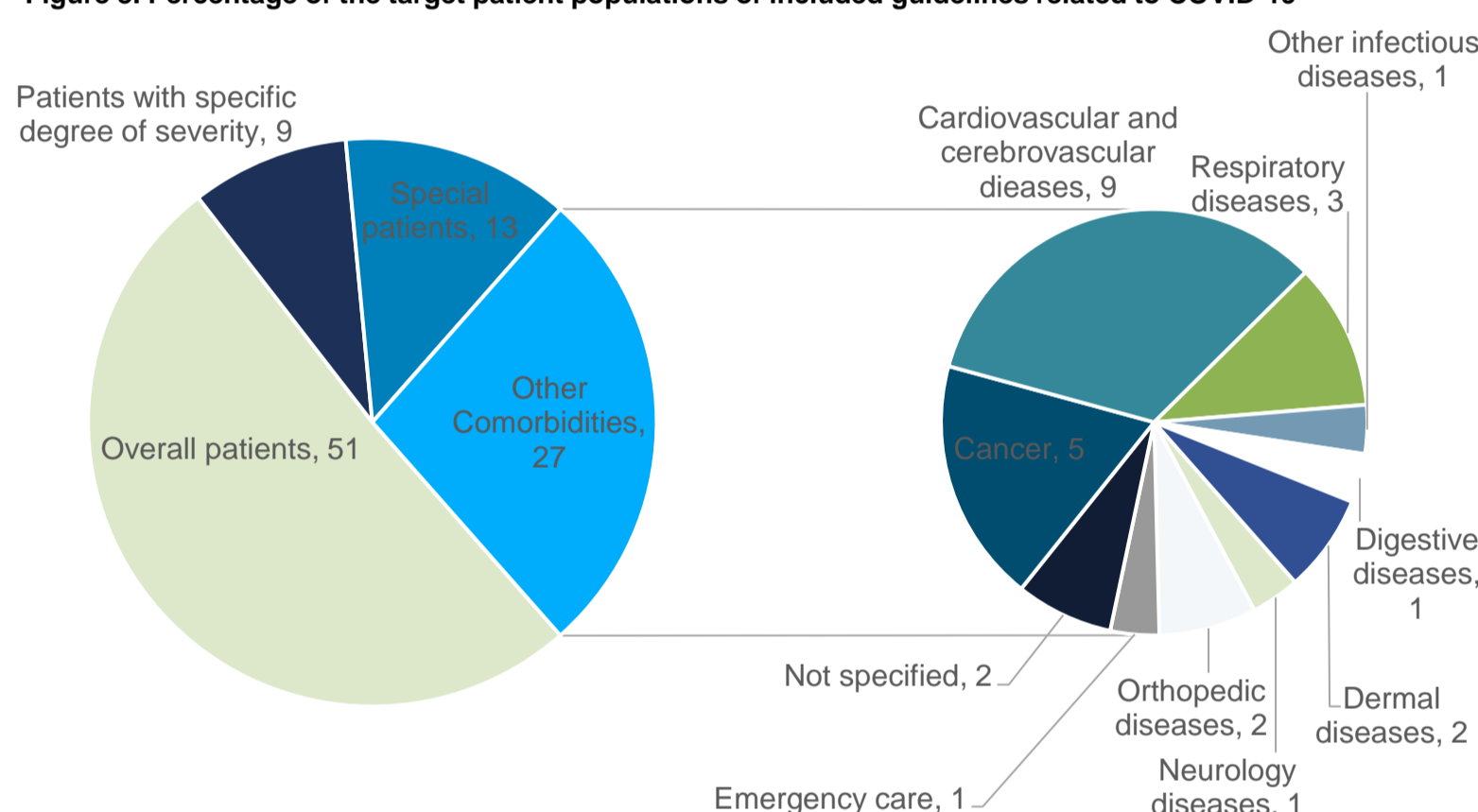


Figure 4. Percentage of the recommended pharmacological treatment in Chinese guidelines of COVID-19

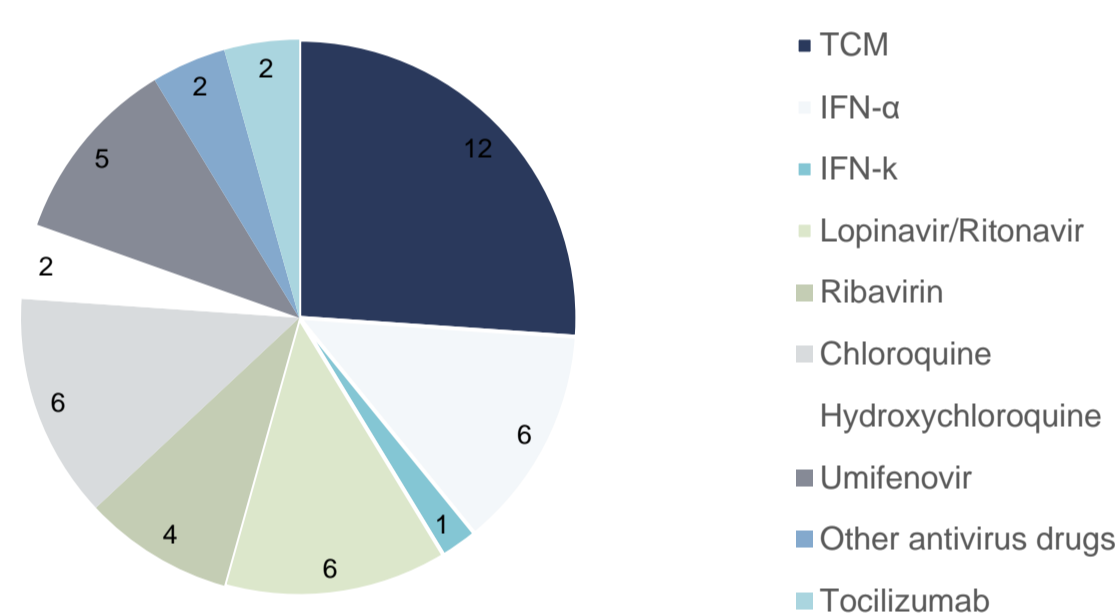


Table 1. The inclusion of Chloroquine (CQ) and Hydroxychloroquine (HCQ) in guidelines for the treatment of COVID-19

Publish date	Guideline name	Publishing organization	Key information related to chloroquine and Hydroxychloroquine
2020-02-20	Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia ⁴	Health Commission of Guangdong Province for chloroquine in the COVID-19 treatment	It recommended chloroquine phosphate tablet, 500 mg bid for 10 days for patients diagnosed as mild, moderate and severe cases of novel coronavirus pneumonia and without contraindications to chloroquine. Contraindicated to use combined with macrolide antibiotics including azithromycin.
2020-02-21	Close monitoring the adverse effects of chloroquine phosphate for the treatment of novel coronavirus pneumonia ⁵	Health Commission of Hubei Province	Chloroquine phosphate can cause acute death. Lethal dose for adults is 2-4 g.
2020-02-28	Notifications on the adjustment of dosage of chloroquine phosphate for the treatment of novel coronavirus pneumonia ⁶	National Health Commission	Chloroquine phosphate (500 mg bid for 7 days for adults aged 18-65 with body weight over 50 kg; 500 mg bid for Days 1-2 and 500 mg qd. for Days 3-7 for adults with body weight below 50 kg) Contraindicated to use combined with macrolide antibiotics including azithromycin.
2020-03-02	Shanghai expert consensus on the integrated treatment for novel coronavirus pneumonia ⁷	Shanghai expert panel on the clinical treatments for COVID-19	Hydroxychloroquine Sulphate and Chloroquine phosphate were both recommended.
2020-03-04	The Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (7 th version) ⁸	National Health Commission	Chloroquine phosphate (500 mg bid for 7 days for adults aged 18-65 with body weight over 50 kg; 500 mg bid for Days 1-2 and 500 mg qd. for Days 3-7 for adults with body weight below 50 kg)
2020-03-05	Guangdong expert consensus on the Chinese integrative medicines for the prevention and treatment of COVID-19 ⁹	Guangdong association of integrative medicine	Chloroquine phosphate (500 mg bid for 7 days for adults aged 18-65 with body weight over 50 kg; 500 mg bid for Days 1-2 and 500 mg qd. for Days 3-7 for adults with body weight below 50 kg)
2020-03-15	Shandong expert consensus on the Diagnosis and Treatment for Novel Coronavirus Pneumonia ¹⁰	Shandong expert panel on the clinical treatments for COVID-19	Hydroxychloroquine Sulphate (200 mg tid).

RESULTS

- A total of 100 guidelines were identified, including 74 national guidelines, were mainly published by the National Medical Association of China and 26 regional guidelines, which were released by 8 provinces and 2 municipalities (Figure 1).
- The included guidelines focused on the prevention and control measurements, as well as clinical diagnosis and treatment strategies of COVID-19 (Figure 2).
- More than half of the guidelines targeted general COVID-19 patients, and the rest 49 guidelines focused on specific populations, such as paediatric population, geriatric population, and patients with comorbidities (Figure 3).
- A total of 15 guidelines proposed recommendations for pharmacological treatments. Interferon, lopinavir/ritonavir, ribavirin, chloroquine (CQ), and umifenovir were mainstream western medical therapies being most recommended in the included guidelines (Figure 4).
- CQ, as one of the drugs generating lots of discussions, has been first recommended in the 6th version of National Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia¹¹.
- The detailed instructions on dosage adjustment and adverse events management of CQ have also been updated in subsequent 7 Chinese guidelines with the accumulations of preclinical and preliminary clinical evidence (Table 1).

CONCLUSIONS

During COVID-19 pandemic, China proactively generated guidelines addressing all aspects of COVID-19 management. Such endeavours secured China to react and coordinate all the available resources to cope with COVID-19 promptly and efficiently. These guidelines may have been insufficiently disseminated but led to widening CQ use across the world.

Although the guidelines provide limited information on the rational for their updates, it is considered that they were updated based on the development of clinical experience in treating patients and the evidence emerging from the large range of ongoing open studies.

REFERENCES

- Lu, R., Zhao X., Li J., et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020; 395(10224): 565-574.2. Cherny Ni et al. *Ann Oncol*. 2017 Oct 1;28(10):2340-2366.
- Shim, E., Tariq A., Choi W., et al. Transmission potential and severity of COVID-19 in South Korea. *LJID*. 2020; 93:339-344.
- Worldometer. Number of COVID-19 cases in United States. 2020 [cited 2020 29 March]; Available from: <https://www.worldometers.info/coronavirus/country/us/>.
- Health Commission of Guangdong Province. Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia. *CJTRD*. 2020; 43(3): 185-188.
- Hubei Health Commission. Close monitoring the adverse effects of chloroquine phosphate for the treatment of novel coronavirus pneumonia. [cited 2020 March 25]; Available from: <http://www.hubei.gov.cn/>.
- Notifications on the adjustment of dosage of chloroquine phosphate for the treatment of novel coronavirus pneumonia. [cited 2020 March 25]; Available from: <http://www.nhc.gov.cn/yzygj/s7653p/202002/0293d017621941f6b2a4890035243730.shtml>
- Shanghai medical aid expert group for novel coronavirus pneumonia. Shanghai expert consensus on the integrated treatment for novel coronavirus pneumonia. *Chinese Journal of Infectious Diseases*. 2020; 38. Epub ahead of print.
- National Health Commission. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (7th trial version). [cited 2020 March 25]; Available from: <http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eaae415350a8ce964.pdf>.
- Guangdong expert group of integrated Chinese Medicine. Guangdong expert consensus on the Chinese integrative medicines for the prevention and treatment of novel coronavirus pneumonia. *WJTCM*. 2020; 5: 805-812.
- Shandong medical aid expert group for novel coronavirus pneumonia. Shandong expert consensus on the diagnosis and treatment for novel coronavirus pneumonia. *J Shandong Med*. 2020; 60(7): 1-5.
- National Health Commission. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (6th trial version). [cited 2020 March 25]; Available from: <http://www.nhc.gov.cn/yzygj/s7653p/202002/8334a8326d94d329d9f351d7da8aefc2/files/b218cfebf1bc54639af227f9226f6b817.pdf>.

