



## LETTER FROM ASIA-PACIFIC AND BEYOND

### Letter from China

**Key words:** coronavirus, COVID-19, laboratory testing, prevention, therapy, transmission.

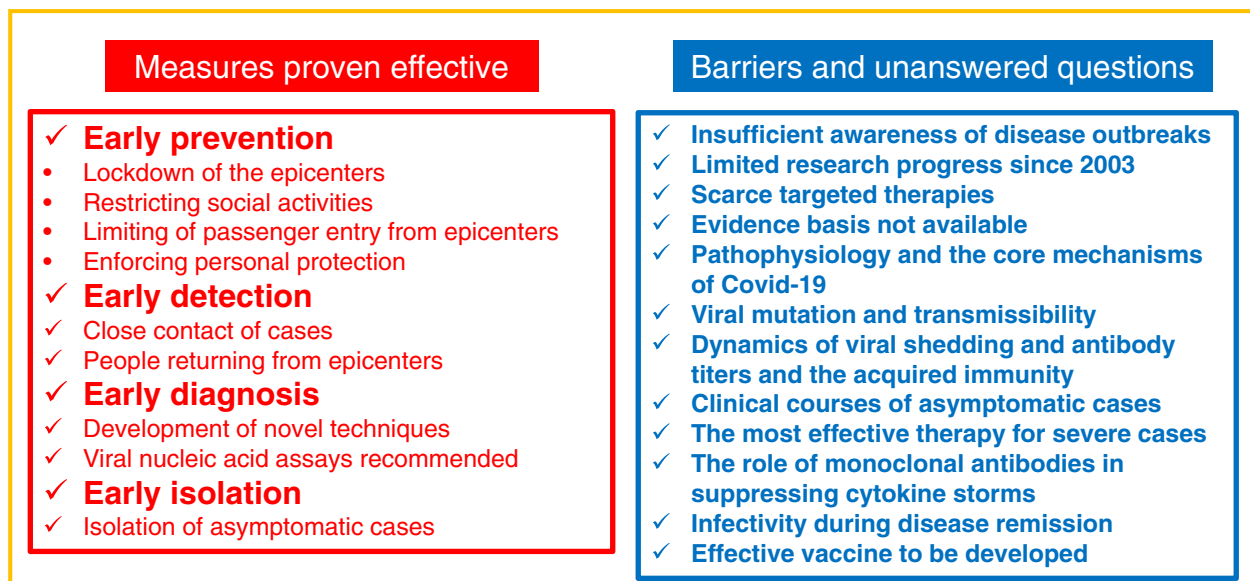
The outbreak of coronavirus disease 2019 (Covid-19) has been rapidly spreading, causing a pandemic globally. More than 180 000 laboratory-confirmed cases have been identified as of 19 March 2020. Hitherto, more than 90 000 cases have been diagnosed outside of China.<sup>1</sup> The rapid spread of Covid-19 has been associated with the ability of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to bind potently with various human tissues (in particular the lungs where angiotensin-converting enzyme is extensively expressed), the readiness of mutations due to the error-prone replication of the viral nucleic acids and the scarcity of evidence indicating the potential of human-to-human transmission at the very initial stages.<sup>2</sup>

As with other communicable diseases such as highly pathogenic avian influenza, the interagency mechanism that has integrated with the principles of early prevention, early detection, early diagnosis and early isolation has now been proven effective for the prevention and control of the Covid-19 outbreak. The focus for containing the Covid-19 outbreak should be shifted upstream—to target at the prevention of the outbreak from further spreading. In light of the lack of vaccines and herd immunity, preventative measures such as the lockdown of Wuhan city, restricting social activities to minimize the crowding (i.e. suspension of school terms and pilgrims) and issuing the travel bans should be initiated pre-emptively. The decision to enforce stringent control of the entry of foreign passengers from the epicentres has been shown to be judicious in curbing the transmission of Covid-19 internationally. Moreover, in some areas where there has been a shortage of medical resources for personal protection, there has been a significantly elevated risk of infection among the healthcare workers, particularly in those who lacked understanding of the protection concept. Thus, timely provision of the medical resources and staff would help alleviate the burn out at the local hospitals. Shortening the time from symptom onset to hospitalization correlated with an improved clinical outcome (Wen-Hua Liang, personal communication). Early detection should be targeted at the close contact of the cases, people returning from the Covid-19 circulating regions and patients with influenza-like illnesses upon consultation at the outpatient clinics. Moreover, detection could be helped by the development of more efficient laboratory techniques such as the chip-based isothermal amplification analyser (CapitalBio Technology, Beijing, China; [www.capitalbiotech.com](http://www.capitalbiotech.com)) which could simultaneously detect a panel of respiratory viruses (including SARS-CoV-2) in less than 1 h as well as the rapid assay kit that could characterize serum immunoglobulin (Ig) M levels with only a drop of blood.<sup>3</sup> Early diagnosis has been the central pillar for the management of disease outbreaks. According to our latest study,<sup>4</sup> nearly

half of the patients remained afebrile on hospital admission and IgM might not be detectable within this period, therefore viral nucleic acid assays remain a valid approach for the early diagnosis of SARS-CoV-2. Identification and isolation of the asymptomatic cases with active viral shedding constitutes a core theme for the early diagnosis of SARS-CoV-2 because recent studies have shown that this population is at high risk of extensive spreading of Covid-19 globally.<sup>5</sup> These interagency mechanisms may be effective under the coordination of the national central government.

There have been three waves of coronavirus outbreaks in the 21st century—the severe acute respiratory syndrome that occurred in 2003, the Middle East respiratory syndrome that took place in 2015 and the Covid-19 that emerged in 2019. Unlike the other two outbreaks, the Covid-19 has resulted in a global pandemic that significantly exceeded the total number of cases and the affected geographic regions of the previous outbreaks. Because of the substantially greater infectivity and higher fatality ratio, Covid-19 should be managed proactively in a manner that should be distinct from the management of the avian influenza pandemic. The rapid spreading would have become catastrophic should Covid-19 not be contained pre-emptively given the notable infectivity (basic reproductive number being around 3.0).<sup>6,7</sup> This is also in keeping with a recent modelling study that indicated the ability of the pathogens with a basic reproductive number being 3.5 or greater to elicit a global pandemic regardless of the active measures to be undertaken to contain the global human-to-human transmission. More than 90% of the contacts should be traced, should the basic reproductive number of SARS-CoV-2 be 3.5 or greater.<sup>8</sup>


Development of the effective therapeutic approaches is indispensable to effectively manage the patients, in particular, the severe cases. Apart from convalescent plasma which has been proven effective in a pilot study,<sup>9</sup> there has not been other targeted therapy for Covid-19. A latest trial indicated that lopinavir-ritonavir did not confer additional benefits in shortening the course of Covid-19.<sup>10</sup> We are still keenly awaiting the results from randomized clinical trials with chloroquine, remdesivir, hydrogen and oxygen mixed gas inhalation and other repurposed traditional Chinese medicines such as the Lianhuaqingwen capsules, which will provide further rationales for the clinical management of Covid-19. However, it should be stressed that research progress on coronavirus has not been very fruitful to date, as insufficient attention has been paid since the severe acute respiratory syndrome outbreak in 2003. There would have been a handful of therapeutic approaches if efforts towards new drug development had been expedited much earlier and on a longer term basis. We must ensure opportunities to develop targeted therapies to Covid-19 and other coronavirus diseases do not cease when the current outbreak is over.



**Figure 1** Key effective measures, major research barriers and important unanswered questions.

As we are living inside the village of planet earth, no one is immune to the Covid-19 and hence active preventive measures will be vital to combat the current global pandemic. To help readers better digest the status quo and the uncharted territories of medical practice or research, the keys of the successful strategies and the unanswered questions have been summarized in Figure 1. By incorporating the interagency mechanisms, a concerted effort of the whole society is needed to effectively curb the further outbreak of Covid-19 worldwide.

**Acknowledgements:** We thank Wen-hua Liang (State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Health, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou, China) for assistance with preparation of the draft. This study is supported by the National Health Commission, National Natural Science Foundation, Department of Science and Technology of Guangdong Province.

Wei-jie Guan, MD  and Nan-shan Zhong, MD  
*State Key Laboratory of Respiratory Disease, National Clinical Research Center for Respiratory Disease, Guangzhou Institute of Respiratory Health, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou, China*

## REFERENCES

- 1 World Health Organization. Novel coronavirus (2019-nCoV) situation reports. 2020. [Accessed 19 Mar 2020.] Available from URL: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>
- 2 Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Yip CC, Poon RW *et al.* A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020; **395**: 514–23.
- 3 State Key Laboratory of Respiratory Disease. The State Key Laboratory has jointly developed an assay kit for the rapid detection of novel coronavirus IgM (article in Chinese). 2020. [Accessed 19 Mar 2020.] Available from URL: <http://www.skldr.cn/show.php?id=1376>
- 4 Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC *et al.* Clinical characteristics of coronavirus disease 2019 in China. *N. Engl. J. Med.* 2020. <https://doi.org/10.1056/NEJMoa2002032>.
- 5 Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W *et al.* Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N. Engl. J. Med.* 2020; **382**: 970–1.
- 6 Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N. Engl. J. Med.* 2020; **382**: 1199–207.
- 7 Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, Lou Y, Gao D, Yang L, He D *et al.* The basic reproduction number of novel coronavirus (2019-nCoV) estimation based on exponential growth in the early outbreak in China from 2019 to 2020: a reply to Dhungana. *Int. J. Infect. Dis.* 2020. <https://doi.org/10.1016/j.ijid.2020.02.025>.
- 8 Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, Munday JD, Kucharski AJ, Edmunds WJ, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group *et al.* Feasibility of controlling Covid-19 outbreaks by isolation of cases and contacts. *Lancet Glob. Health* 2020. [https://doi.org/10.1016/S2214-109X\(20\)30074-7](https://doi.org/10.1016/S2214-109X(20)30074-7).
- 9 Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, Wang F, Li D, Yang M, Xing L *et al.* Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA*. Published online March 27, 2020. <https://doi.org/10.1001/jama.2020.4783>.
- 10 Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, Ruan L, Song B, Cai Y, Wei M *et al.* A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N. Engl. J. Med.* 2020. <https://doi.org/10.1056/NEJMc2001282>.