



# The explosive epidemic outbreak of novel coronavirus disease 2019 (COVID-19) and the persistent threat of respiratory tract infectious diseases to global health security

Alimuddin Zumla<sup>a,b</sup> and Michael S. Niederman<sup>c</sup>

Respiratory tract infections remain the top cause of morbidity and mortality from infectious diseases worldwide [1]. The emergence of new pathogens that cause lethal human respiratory illnesses with pandemic potential [2,3] pose major challenges and rapidly focus the attention of global public health authorities and HCWs. Two zoonotic coronaviruses which cause lethal respiratory tract infections in humans feature on the WHO Blueprint list of priority pathogens for research and development [4] because of their pandemic potential. The first human case of severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV) infection which was first reported from Guangdong province China [5], and that of Middle East respiratory syndrome (MERS) coronavirus (MERS-CoV) from Jeddah, Saudi Arabia, in 2012 [5]. In January 2020, another novel zoonotic coronavirus that causes lethal human disease, SARS-CoV-2, was included on the WHO priority Blueprint list [4]. This followed the appearance in December 2019 of a case cluster of patients with pneumonia of unknown origin in Wuhan, capital of Hubei province in China [6–8]. The Chinese Center for Disease Control and Prevention (China CDC) epidemiological investigations implicated the source as Wuhan's Huanan Seafood Wholesale Market [6]. The China CDC took prompt action instituting public health measures including intensive surveillance, epidemiological investigations, and closure of the market on 1 January 2020. A novel coronavirus was identified from patients' samples using whole-genome sequencing [8,9] and was provisionally named 2019-nCoV, now renamed as SARS-CoV-2 [10]. The disease caused by SARS-CoV-2 is abbreviated as COVID-19 (CORonaVirus Disease-2019).

The World Health Organization International Health Regulations Emergency Committee declared COVID-19 outbreak a Global emergency [11] because SARS-CoV has spread rapidly within and outside China at an alarming pace and has caused

considerable consternation and panic among the national, regional, and international public and political communities compounded by news media and social media hype [12]. A specific molecular test for SARS-CoV-2 was developed [13] and a flurry of investigations and research on COVID-19 outbreak rapidly defined the epidemiological, virologic, and clinical features and provided evidence of human-to-human transmission in community, household, and hospital settings [6,8–10,14–19]. These have guided the development of numerous WHO guidelines and recommendation documents related to case definitions, reporting of cases, diagnosis, management, prevention, and control guideline documents [10]. The rapid spread occurring within China despite a 'lock down' of Wuhan resulted in numerous chains of transmission [6,10,14–19], and spread of the virus was facilitated by national and international travel during the January New Year holiday period [20]. The appearance of novel zoonotic diseases is never without controversies [21–23]. Reports of conspiracy theories for the source and sudden appearance of the virus have been negated by phylogenetic studies using sequences of SARS-CoV2–19 obtained from early cases [8,9], which indicate that the novel virus may have been introduced to human populations from the animal kingdom in November 2019 or December

<sup>a</sup>Division of Infection and Immunity, Centre for Clinical Microbiology, University College London, <sup>b</sup>NiHR Biomedical Research Centre, UCL Hospitals NHS Foundation Trust, London, UK and <sup>c</sup>Division of Pulmonary and Critical Care Medicine, Weill Cornell Medical College, New York, New York, USA

Correspondence to: Sir Prof Alimuddin Zumla, MD, PhD, FRCP, Division of Infection and Immunity, Centre for Clinical Microbiology, University College London Royal Free Campus, 2nd floor, Rowland Hill Street, London NW3 2PF, United Kingdom. Tel: +44 2074726402; fax: +44 2077940433; e-mail: a.zumla@ucl.ac.uk.

**Curr Opin Pulm Med** 2020, 26:000–000

DOI:10.1097/MCP.0000000000000676

2019 [21]. As with SARS-CoV [24] and MERS-CoV [25], defining the actual zoonotic source and mode of primary transmission of SARS-CoV-2 to humans remains an enigma, and requires urgent study through ONE-HEALTH collaborations [23].

The clinical and virologic features of SARS-CoV-2 have been defined by several studies [6,10,14–19], and although there are similarities to SARS-CoV and MERS-CoV, some differences have also been observed. COVID-19 appears to replicate efficiently in the upper respiratory tract [14,26] and appears to cause less abrupt onset of symptoms, which are similar to conventional human coronaviruses that are a major cause of common colds and URIs in the winter seasons. Furthermore, during the prodrome and early phase of disease, the upper respiratory tract appears to have large quantity of virus and may be responsible for the rapid person to person spread [26]. In SARS-CoV and MERS-CoV, whereas accurate data are unavailable, the highest viral loads were seen in seriously ill patients. This has implications on infection control measures. COVID-19 also has affinity for cells in the entire respiratory tract.

The time from exposure to onset of symptoms is between 2 and 14 days. As with SARS and MERS, data for COVID-19 available to date [14–19] indicate a spectrum of clinical manifestations occur, from asymptomatic subclinical infection, or mild upper respiratory tract illness to nonlife-threatening pneumonia to severe pneumonia progressing to acute respiratory distress syndrome (ARDS) requiring intensive care, mechanical ventilation, and extracorporeal membrane oxygenation (ECMO). A study of 138 hospitalized patients with COVID-19 the median age was 56 years (interquartile range, 42–68; range, 22–92 years) and 75 (54.3%) were men. Several studies [14–19] show that symptoms of COVID-19 patients are similar to MERS and SARS and fever (92–98%), dry cough (75–82%), fatigue (69–75%), and gastrointestinal symptoms (20–40%) were the most common clinical manifestations. A wide spectrum of clinical disease is being seen from asymptomatic, subclinical, mild, and self-limiting disease to severe disease and ARDS among older people or those with other comorbid diseases such as diabetes, chronic respiratory disease, and hypertension, with men are more likely to die than women. Several of these patients have negative rtPCR tests. Bilateral ground glass or patchy opacity are the most common signs of radiological finding and CT changes [27] have been included as a case definition of COVID-19 by China CDC.

Although COVID-19 appears from currently available data to have a lower death rate [6], it has caused more deaths than SARS and MERS combined. The SARS outbreak in 2003 had rapidly spread from

southern China in 2003 and infected more than 3000 people, killing 774 by 2004 before it ended. For the COVID-19 outbreak, the China CDC recently reported epidemiological features of 44 672 COVID-19 cases across all of China [6], which showed the overall death rate at 2.3%. In China's provinces, the death rate is 2.9% compared with 0.4% in the rest of the country. At least 80% of the cases have been mild, with the sick and elderly most at risk. Worryingly 3019 HCWs have been identified with COVID-19.

The WHO has established a global surveillance system to collect information to describe and monitor COVID-19. Case classifications are based on WHO case definitions for COVID-19 [28]. Active surveillance is taking place globally for possible infections in all countries using the WHO-recommended surveillance case definitions. Since its first discovery in December 2019, the COVID-19 epidemic has progressed relentlessly and there are no indications that the epidemic is slowing down [6,29]. As of March 3, 2020, there were 88948 confirmed cases of COVID-19 reported to the WHO [28]. Of these, 80174 were from China with 2915 deaths; and 8774 cases from 64 countries outside China with 128 deaths. Continued intensive source control is ongoing at the epicenter in China with contact tracing and strict infection prevention and control measures being implemented at hospitals, healthcare centers and quarantine facilities.

With ease of travel, the world has become increasingly susceptible to outbreaks of new and reemerging infectious diseases that can spread quickly because of ease of transportation and rapid movement of people within regions and continents. The virus has spread beyond mainland China to countries around the globe and two cruise ships are now confirmed to have been affected. WHO has recommended that countries with frequent air travel exchange with Wuhan should take precautionary public health measures and undertake screening and infection control activities. The lock-down of Wuhan City seems to have slowed international spread of COVID-19 but many challenges remain before it can be brought under control [30].

A recent Conference (11th and 12th February 2020) held in Geneva hosted by WHO in Geneva [31] delineated priorities for intensified research for development of point of care diagnostic tests, new vaccines, treatments, improved collaborations with the animal and environmental sectors, and community engagement. Although the world awaits the development and evaluation of new vaccines, anti-SARS-CoV-2 specific drugs, antibody, and/or other host-directed interventions [32,33], public health infection control measures remain of prime

importance in limiting human-to-human transmission, especially among close contacts and HCWs, and minimizing risk of international spread by identifying and isolating patients early. However, several questions remain to be answered for optimal infection control measures and management of COVID-19 patients in hospitals: How to limit spread to HCWs especially in light of reports of asymptomatic and minimally symptomatic HCWs with SARS-CoV-2 infection? What is the impact of quarantine after exposure and does this reduce the spread of SARS-CoV-2, or does this add to the risk for those who are quarantined? What are the risks of noninvasive ventilation in COVID-19 patients to HCWs, and when should we intubate and how can we minimize risks to those who do the intubation? What is the role for steroids and of combination antiviral agents for severe lung disease and will they be helpful or harmful? What are the roles for a range of potential host-directed therapies such as cellular therapy with allogeneic stromal cells or repurposed drugs, biologics, convalescent plasma, and combination of antiviral agents for COVID-19 patients with ARDS [33].

Although China had cancelled all mass gathering events at the start of the outbreak in Wuhan, mass gathering religious, sporting, and other events continue to attract people from across all continents including China, increasing the risk of spread globally. In this edition of COPM, Petersen *et al.* [34] review recent literature on viral and bacterial infectious diseases with special focus on the Hajj, the largest annually recurring religious pilgrimage in the world attracting 3 million people from 182 countries. Recurring mass gathering religious, sporting, and other events attract people from across all continents increasing the risk of spread of aerosol transmissible respiratory tract infections, and for this year's events, event organizers should be on alert for both lethal coronaviruses, SARS-CoV-2 and MERS-CoV-2 [34].

The COVID-19 epidemic may follow the path of SARS and die out within the next 12 months or will it pan out to be like seasonal influenza or other respiratory tract viral illnesses, manifesting as self-limiting disease and severe disease among older people or those with comorbidities? Only time will tell. In the interim it is critical that although COVID-19 requires intense public health, scientific and political attention currently, the current media hype on the novel COVID-19 outbreak should not detract the attention of health services, frontline physicians, and other HCWs from other respiratory tract infections (RTIs), which cause over 5 million deaths globally annually. This volume of COPM highlights current opinions and new developments on several important issues related the diagnosis, management

and prevention of community acquired pneumonia, bacterial and viral RTIs [34–42].

### Acknowledgements

Sir Alimuddin Zumla is a co-PI of the Pan-African Network on Emerging and Re-Emerging Infections (PANDORA-ID-NET; <https://www.pandora-id.net/>) funded by the European and Developing Countries Clinical Trials Partnership the EU Horizon 2020 Framework Programme for Research and Innovation. Sir Zumla is also in receipt of an National Institutes of Health Research senior investigator award.

### Financial support and sponsorship

None.

### Conflicts of interest

Sir Prof Alimuddin Zumla and Prof Michael Niederman both have a specialist interest in respiratory tract infections and are editors of this volume of COPM.

### REFERENCES

1. WHO. Global Health Observatory. Mortality and global health estimates. [https://www.who.int/gho/mortality\\_burden\\_disease/en/](https://www.who.int/gho/mortality_burden_disease/en/). [Accessed 20 February 2020]
2. Zumla A, Hui DS, Al-Tawfiq JA, *et al.* Emerging respiratory tract infections. *Lancet Infect Dis* 2014; 14:910–911.
3. Zumla A, Hui DSC. Emerging and reemerging infectious diseases: global overview. *Infect Dis Clin North Am* 2019; 33:xiii–xiii10.
4. WHO. A research and development Blueprint for action to prevent epidemics. <https://www.who.int/blueprint/en/>. [Accessed 15 February 2020]
5. Hui DS, Memish ZA, Zumla A. Severe acute respiratory syndrome vs. the Middle East respiratory syndrome. *Curr Opin Pulm Med* 2014; 20:233–241.
6. China CDC Weekly 2020: the epidemiological characteristics of an outbreak of 2019 Novel coronavirus diseases COVID-19-China, 2020. *CCDC Weekly* 2020:2:1–10.
7. Hui DS, I Azhar E, Madani TA, *et al.* The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health: the latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis* 2020; 91:264–266.
8. Zhu N, Zhang D, Wang W, *et al.* A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382:727–733.
9. Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020. [Epub ahead of print] doi:10.1056/NEJMoa2001316.
10. WHO. Coronavirus disease (COVID-19) outbreak. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. [Accessed 15 February 2020]
11. WHO. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). Geneva, Switzerland: World Health Organization. [https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-\(2019-ncov\)](https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)) [Accessed 27 February 2020]
12. Ippolito G, Hui DS, Ntoumi F, *et al.* Toning down the 2019-nCoV hype – and restoring hope. *Lancet Resp Med* 2020. [https://doi.org/10.1016/S2213-2600\(20\)30070-9](https://doi.org/10.1016/S2213-2600(20)30070-9).
13. Corman VM, Landt O, Kaiser M, *et al.* Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020; 25:. doi: 10.2807/1560-7917.ES.2020.25.3.2000045.
14. 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; 395:565–574.
15. Chan JFW, Yuan S, Kok KH, *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; 395:514–523.
16. Chen N, Zhou M, Dong X, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020. [Epub ahead of print]
17. Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020. [Epub ahead of print]

18. Wang D, Hu B, Hu C, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020. [Epub ahead of print]
19. Zhang JJ, Dong X, Cao YY, *et al.* Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China. *Allergy* 2020. [Epub ahead of print] doi:10.1111/all.14238.
20. Haider N, Yavilinsky A, Simons D, *et al.* Passengers' destinations from China: low risk of Novel Coronavirus (2019-nCoV) transmission into Africa and South America. *Epidemiol Infect* 2020; 148:e41. doi:10.1017/S0950268820000424.
21. Calisher C, Carroll D, Colwell R, *et al.* Statement in support of the scientists, public health professionals, and medical professionals of China combatting COVID-19. *Lancet* 2020. [Epub ahead of print]
22. Vetter P, Eckerle I, Kaiser L. Covid-19: a puzzle with many missing pieces. *BMJ* 2020; 368:m627.
23. Kock RA, Karesh WB, Veas F, *et al.* 2019-nCoV in context: lessons learned? *Lancet Planet Health* 2020. [Epub ahead of print]
24. WHO. SARS (Severe Acute Respiratory Syndrome); 2020. <https://www.who.int/ith/diseases/sars/en/>. [Accessed 14 February 2020]
25. WHO. 2020. Middle East respiratory syndrome coronavirus (MERS-CoV); 2020. <https://www.who.int/emergencies/mers-cov/en/>. [Accessed 12 February 2020]
26. Zou L, Ruan F, Huang M, *et al.* SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med* 2020. [Epub ahead of print]
27. Pan Y, Guan H, Zhou S, *et al.* Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. *Eur Radiol* 2020. [Epub ahead of print]
28. Global Surveillance for human infection with coronavirus disease (COVID-2019). <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/> [Accessed 3 March, 2020]
29. WHO. Coronavirus disease 2019 (COVID-19) Situation Report – 32 [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200221-sitrep-32-covid-19.pdf?sfvrsn=4802d089\\_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200221-sitrep-32-covid-19.pdf?sfvrsn=4802d089_2) [Accessed 22 February 2020]
30. Heymann DL, Shindo N. WHO Scientific and Technical Advisory Group for infectious hazards. COVID-19: what is next for public health? *Lancet* 2020. [Epub ahead of print]
31. GloPID-R facing the COVID-19 emergency with its members and partners. <https://www.glopid-r.org/glopid-r-facing-the-covid-2019-emergency-with-its-members-and-partners/> [Accessed 20 February 2020].
32. WHO. Global research on coronavirus disease (COVID-19) <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov> [Accessed 20 February 2020].
33. Zumla A, Hui DS, Azhar EI, Maani AA. Reducing mortality from 2019-nCoV: host-directed therapies should be an option. *Lancet* 2020; 395:e35–e36.
34. Petersen E, Memish ZA, Zumla A *et al.* Transmission of respiratory Tract infections at mass gathering events. *COPM* 2020.
35. Metlay J, Waterer G. Update in adult community-acquired pneumonia: key points from the new ATS/IDSA 2019 Guideline. *COPM* 2020.
36. Arnold F, Fuqua JL. Viral respiratory infections: a cause of CAP, or a predisposing factor? *COPM* 2020.
37. O'Sullivan S, Torres A, Rodrigues A, Martin-Loesch I. Influenza management with new therapies. *COPM* 2020.
38. Feldman C, Anderson R. Pneumococcal virulence factors. *COPM* 2020.
39. Povoia P, Coelho L, Bos LDJ. New biomarkers for respiratory infections. *COPM* 2020.
40. Cilloniz, Liapikou A, Torres A. Advances in molecular diagnostic tests for pneumonia. *COPM* 2020.
41. Gil R, Webb BJ. Strategies for prediction of drug-resistant pathogens and empiric antibiotic selection in community-acquired pneumonia. *COPM* 2020.
42. Waterer G. Beyond antibiotics for pulmonary nontuberculous mycobacterial disease. *COPM*-2020.