COVID-19 pneumonia and elevated IL-6 in China (ChiCTR2000029765). Janus kinase (JAK) inhibition could affect both inflammation and cellular viral entry in COVID-19. Janus

All patients with severe COVID-19 should be screened for hyperinflammation using laboratory trends (eg, increasing ferritin, decreasing platelet counts, or erythrocyte sedimentation rate) and the HScore¹¹ (table) to identify the subgroup of patients for whom immunosuppression could improve mortality. Therapeutic options include steroids, intravenous immunoglobulin, selective cytokine blockade (eg, anakinra or tocilizumab) and JAK inhibition.

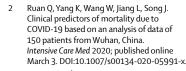
PM is a clinical training fellow within the Experimental Medicine Initiative to Explore New Therapies network and receives project funding unrelated to this Correspondence. PM also receives co-funding by the National Institute for Health Research (NIHR) University College London Hospitals Biomedical Research Centre. DFM chairs the NIHR and Medical Research Council funding committee for COVID-19 for therapeutics and vaccines. DFM reports personal fees from consultancy for ARDS for GlaxoSmithKline, Boehringer Ingelheim, and Bayer; in addition, his institution has received funds from grants from the UK NIHR, Wellcome Trust, Innovate UK, and others, all unrelated to this Correspondence. DFM also has a patent issued to his institution for a treatment for ARDS. DFM is a Director of Research for the Intensive Care Society and NIHR Efficacy and Mechanism Evaluation Programme Director. All other authors declare no competing interests.

Puja Mehta, Daniel F McAuley, Michael Brown, Emilie Sanchez, Rachel S Tattersall, *Jessica J Manson, on behalf of the HLH Across Speciality Collaboration, UK

jessica.manson@nhs.net

Centre for Inflammation and Tissue Repair, UCL Respiratory, Division of Medicine, University College London, London, UK (PM); Department of Rheumatology (JJM), Hospital for Tropical Diseases (MB), and Department of Clinical Virology (ES), University College London Hospital, London NW1 2PG, UK; Wellcome-Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, UK (DFM); Regional Intensive Care Unit, Royal Victoria Hospital, Belfast, UK (DFM); Department of Rheumatology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK (RST); and Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK (RST)

1 WHO. Coronavirus disease 2019 (COVID-19) situation report – 52. March 12, 2020. https://www.who.int/docs/default-source/ coronaviruse/20200312-sitrep-52-covid-19. pdf?sfvrsn=e2bfc9c0_2 (accessed March 13, 2020).



- 3 Ramos-Casals M, Brito-Zeron P, Lopez-Guillermo A, Khamashta MA, Bosch X. Adult haemophagocytic syndrome. Lancet 2014; 383: 1503–16.
- 4 Karakike E, Giamarellos-Bourboulis EJ. Macrophage activation-like syndrome: a distinct entity leading to early death in sepsis. Front Immunol 2019; 10: 55.
- 5 Seguin A, Galicier L, Boutboul D, Lemiale V, Azoulay E. Pulmonary involvement in patients with hemophagocytic lymphohistiocytosis. Chest 2016; 149: 1294–301.
- 6 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497–506.
- Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet 2020; 395: 473-75.
- 8 Shakoory B, Carcillo JA, Chatham WW, et al. Interleukin-1 receptor blockade is associated with reduced mortality in sepsis patients with features of macrophage activation syndrome: reanalysis of a prior phase iii trial. Crit Care Med 2016; 44: 275-81.
- 9 Chinese Clinical Trial Registry. A multicenter, randomized controlled trial for the efficacy and safety of tocilizumab in the treatment of new coronavirus pneumonia (COVID-19). Feb 13, 2020. http://www.chictr.org.cn/ showprojen.aspx?proj=49409 (accessed March 6. 2020).
- 10 Richardson P, Griffin I, Tucker C, et al. Baricitinib as potential treatment for 2019-nCoV acute respiratory disease. Lancet 2020; 395: e30-31.
- 11 Fardet L, Galicier L, Lambotte O, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. Arthritis Rheumatol 2014: 66: 2613-20.

Did the hesitancy in declaring COVID-19 a pandemic reflect a need to redefine the term?

WHO's declaration that the global spread of coronavirus disease 2019 (COVID-19) is a pandemic¹ has contributed greatly to clearing up confusion in the terminology in the professional literature and the media. Discussions on when wide geographical spread of a disease becomes a pandemic tend to recur when the world is confronted with an emerging infectious disease.²³ The debate around the terminology used for COVID-19 raises two important questions.

The first question is why there was reluctance to call the COVID-19 outbreak a pandemic, and the second question is whether the terminology is of any practical importance.

In almost all good textbooks, an epidemic becomes a pandemic when there is widespread geographical distribution of the disease. For some weeks, the COVID-19 epidemic, which had spread to over 100 countries, seemed to fit the classical definition of a pandemic. One could reasonably ask whether the use of the term pandemic would change any of the actions necessary to control the spread of the virus.

There are several situations in which it could be helpful to use well defined terminology to control the spread of an infectious disease. The resources for controlling a pandemic are both different, substantially larger, and generally much more far-reaching than for a localised outbreak or epidemic. Thus the terms used for the different situations could be restricted according to the control measures that are necessary. Perhaps unique to pandemics, these include considerable international coordination and collaboration in providing aid to affected countries, recruiting the necessary resources for promoting research on medications and vaccines, and developing complex risk communication. In particular, travel restrictions become a major issue and, although these are guided by the International Health Regulations, countries have the option to adopt unilaterally their own barriers to international travel. This was clearly the case for COVID-19. If the term pandemic is clearly defined, it can communicate much more clearly the seriousness of the situation and help justify the extreme measures instituted. It can also provide the international health community with a common term to enlist the cooperation of the general public and convey the necessary sense of urgency to decision makers. This should stimulate rapid



Published Online March 12, 2020 https://doi.org/10.1016/ S0140-6736(20)30630-9

For the **International Health Regulations** see https://www.
who.int/ihr/en/

introduction of preventive measures such as social distancing to reduce the pace of the spread, providing valuable time for upgrading of the medical services, and preparing the community.

If the use of the term pandemic is delayed too long, the declaration of the pandemic could convey a message to the public that the authorities have lost control, generating irrational panic reactions. Since it is expected, and even perhaps desirable, that the public experience some fear during a pandemic, an early declaration of a pandemic might be helpful in mitigating panic. Recruiting public cooperation is much more feasible when the society in general and the health services in particular are not yet under considerable pressure, and there is time for appropriate explanations to the public as to how the pandemic will be controlled. The question remains as to what is the optimal timing for declaring a pandemic. Following the 2009 H1N1 pandemic, Morens and colleagues4 provided useful criteria for defining a pandemic. They included the following components: the cause should be a new virus that has not circulated in humans previously, the disease should be widespread geographically, there should be clear person-to-person spread, and outbreaks should be explosive in nature, with a relatively high casefatality rate. It seems to me that for some time, the COVID-19 outbreak met all these criteria.

Since there continues to be a lack of consensus about when it is appropriate to use the term pandemic, I suggest that a multi-disciplinary group of epidemiologists, infectious disease specialists, risk communicators and health administrators be convened to create new, clearer, expanded definitions of the terms outbreak, epidemic, and pandemic.

I declare no competing interests.

Manfred S Green manfred.s.green@gmail.com

School of Public Health, University of Haifa, Haifa 3498838, Israel

- WHO. WHO Director-General's opening remarks at the media briefing on COVID-19 -11 March 2020. March 11, 2020. https://www. who.int/dg/speeches/detail/who-directorgeneral-s-opening-remarks-at-the-mediabriefing-on-covid-19---11-march-2020 (accessed March 11. 2020).
- Cohen J, Enserink M. Swine flu. After delays, WHO agrees: the 2009 pandemic has begun. Science 2009; 324: 1496–97.
- 3 Doshi P. The elusive definition of pandemic influenza. Bull World Health Organ 2011; 89: 532-38.
- 4 Morens DM, Folkers GK, Fauci AS. What is a pandemic? *J Infect Dis* 2009; **200:** 1018–21.

COVID-19 battle during the toughest sanctions against Iran

Coronavirus disease 2019 (COVID-19) has spread rapidly throughout the world. WHO declared the outbreak a global pandemic on March 11, 2020. In Iran, the first official announcement of deaths from COVID-19 was made on Feb 19, 2020. As of March 16, 2020, 14 991 people have been infected with severe acute respiratory syndrome coronavirus 2, and 853 people have died from COVID-19. 4996 people have recovered.²

The economic loss caused by the spread of COVID-19 in Iran coincides with the ever-highest politically induced sanctions against the country. Although various sanctions have been in place for the past four decades, since May, 2018, the unilateral sanctions imposed by the USA against Iran have increased dramatically to an almost total economic lockdown, which includes severe penalties for non-US companies conducting business with Iran. The Iranian health sector, although among the most resilient in the region,3 has been affected as a consequence.4 All aspects of prevention, diagnosis, and treatment are directly and indirectly hampered, and the country is falling short in combating the crisis.5 Lack of medical, pharmaceutical, and laboratory equipment such as protective gowns and necessary medication has been scaling up the burden of the epidemic and the number of casualties. Despite WHO and other international humanitarian organisations dispatching supplies and medical necessities,⁶ the speed of the outbreak and the detrimental effects of sanctions have resulted in reduced access to life-saving medicines and equipment, adding to the health sector's pre-existing requirements for other difficult health conditions.⁷ It is shameful that besides the lives lost to this deadly virus, extreme sanctions limit access to necessary materials and therefore kill even more Iranian people.

Although sanctions do not seem to be physical warfare weapons, they are just as deadly, if not more so. Jeopardising the health of populations for political ends is not only illegal but also barbaric. We should not let history repeat itself; more than half a million Iraqi children and nearly 40 000 Venezuelans were killed as a result of UN Security Council and US sanctions in 1994 and 2017–18, respectively.⁸ The global health community should regard these sanctions as war crimes and seek accountability for those who impose them

Given the COVID-19 pandemic and its alarming outcomes in Iran,⁹ the international community must be obliged to stand against the sanctions that are hurting millions of Iranians. It is essential for the UN Security Council and the USA to ease, albeit temporarily, the barriers to providing life-saving medical supplies to Iran. In the future, the global community must anticipate possible impacts of sanctions on humanitarian aid and move to prevent further disasters from happening.⁴ Viruses do not discriminate, nor should humankind.

We declare no competing interests.

*Amirhossein Takian, Azam Raoofi, Sara Kazempour-Ardebili takian@tums.ac.ir

Department of Global Health & Public Policy, School of Public Health (AT), Department of Health Economics & Management, School of Public Health (AT, AR), and Health Equity Research Center (AT), Tehran University of Medical Sciences, Tehran 1416753955, Iran; and Consultant Endocrinologist, Tehran, Iran (SK-A)





Published Online March 17, 2020 https://doi.org/10.1016/ S0140-6736(20)30668-1

This online publication has been corrected. The corrected version first appeared at thelancet.com on April 16, 2020

For details of the Iran sanctions see https://www.treasury.gov/ resource-center/sanctions/ Programs/Pages/iran.aspx