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REVIEW

COVID-19 pandemic: lessons for global health security

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INTRODUCTION

The COVID-19 has been the worst pandemic in over a hundred years, impacting on the global economy and psyche, far beyond its direct health impacts. In terms of direct virus associated mortality overall, COVID-19 has led to fewer deaths globally than the 1918 "Spanish Flu." It is estimated that the 1918 pandemic (which went on for a few years beyond 1918) was associated with around 50 million deaths world-wide, at a time when the global population was around 1.8 billion people (much smaller than the current global population of 7.9 billion), and thus, the 1918 pandemic killed 2.7% of the global population. It had a major societal impact in many economically advanced countries with many people retaining memories of that event decades later. The Spanish Flu does not appear to have impacted the psyche of the Ceylonese population, but recent studies suggest that approximately 6.7% of the population lost their lives to this pandemic in Sri Lanka (Chandra & Sarathchandra, 2014).

In contrast to the Spanish flu, The World Health Organization (WHO) confirmed COVID-19 deaths as of end of 2021 is approximately 5.5 million, with estimates of COVID-19 associated excess-mortality suggesting that COVID-19 deaths are 2–4 times higher than confirmed deaths (Adam, 2022). Even so, overall global mortality is of the order of 0.28% of the global population, ten-fold lower than the impact of the 1918 Spanish flu. Nevertheless, COVID-19 appears to have had an even greater economic and social impact in most parts of the world, likely because of the globalized economy, supply chains and communications that make the world more inter-dependent than in 1918. Although the full economic impact of COVID-19 cannot yet be estimated, it has been estimated to lead to a reduction of 7.3% of GDP growth overall, with the greatest impact (-8.7%) in middle income countries (Sanchez, 2021). These assessments do not capture the adverse impacts on widening inequalities overall, and particularly so for women, marginalized and vulnerable populations. Social impacts are even more difficult to quantify, ranging from lost educational opportunities and loss of social-skill development in children and long-term psychological and behavioural impacts on a whole generation.

Since neither specific antiviral drugs nor vaccines were available at the early stages of the COVID-19 pandemic, the main counter-measures available were the same "public health and social measures" (PHSM) that were used during the 1918 pandemic. But virologic testing to identify cases for treatment and isolation was also available, an option not available in 1918. Indeed, it was the published data and experience on the efficacy of public health interventions in 1918 that informed the early response to the COVID-19 pandemic in 2020. It is interesting to read some of the recommendations from 1919, viz. avoid needless crowding, smother your coughs and sneezes, open the windows (i.e. ventilation), wash your hands ("your fate may be in your own hands") (Soper, 1919). Similarly, the problems faced in pandemic control in 1918 were also similar, public indifference ("people do not appreciate the risks they run"), "It does not lie in human nature for a man who thinks he has only a slight cold to shut himself up in rigid isolation as a means of protecting others," and "the disease may be transmissible before the patient himself is aware that

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he is attacked" (Soper, 1919). It is humbling that this analysis, written over one hundred years ago, at a time when the causative agent of the 1918 pandemic was yet unknown and the properties of viruses not understood, still remains true now, in a much more technologically advanced setting. In contrast to 1918, the past two years have seen scientific evidence to prove the effectiveness of some of the non-pharmaceutical interventions such as wearing of masks and other public health and social measures (Haug *et al*., 2020; Andrejko *et al*., 2022). It is also a striking contrast with COVID-19 that safe and vaccines were developed and deployed within a year of the emergence of the pandemic in 2020, testament to the scientific and technological advances in the past one hundred years. Large clinical trials identified generic therapeutic interventions (e.g. dexamethasone, IL6 receptor antagonists) that can reduce mortality, and importantly, also identified many that did not (e.g. hydroxychloroquine). Although antiviral therapeutics took longer to develop and be validated, a number of options are now becoming available by early 2022.

Given the impact of the COVID-19 pandemic, it is important to understand the lessons of its emergence and the global response to it, so that we are better prepared to prevent, pre-empt and mitigate similar events in the future. Future pandemics are inevitable, and we need to accept that such pandemics may be even more severe than COVID-19. Key measures that need to be taken have been highlighted in the report of The Independent Panel for pandemic preparedness and response (Table) (The Independent Panel, 2021).

Table: Recommendations to ensure that future outbreaks do not become pandemic:

a. Invest in preparedness now to prevent the next crisis
b. Raise new international financing for pandemic preparedness and response
c. A new agile and rapid surveillance system
d. Strengthen the independence, authority and financing of WHO
e. Elevate pandemic preparedness and response to the highest level of political leadership
f. National pandemic coordinators have a direct line to Heads of State or Government
g. Establish a pre-negotiated platform for tools and supplies for emergency health responses

I will summarize the lessons learned from COVID-19 and actions needed for better pandemic responses in the future, pertaining in particular, to points a, b and c of the Independent Panel Recommendations by addressing three inter-related questions. A. Was this pandemic or its severity unexpected? B. Why do we continue to face novel emerging infectious diseases and what can we do about it? C. How can we enhance capacity for surveillance and response?

Was this pandemic or its severity unexpected?

This pandemic was expected, predicted and the potential impacts and challenges highlighted. Even the impact of a pandemic on global supply chains and the adverse impact of disinformation on pandemic response was predicted (Osterholm & Oashaker, 2017). But there was a failure of global leadership to make the investments and preparations needed for a more effective response. What we need going forward, is a dramatic change in prioritization from political and business leaders of preparedness for pandemic threats and their impacts, together with a commitment to develop countermeasures and enhancing resilience of health care systems, economies and societies.

Major advances have been made in combatting infectious diseases over the past hundred years or so, with a scientific understanding of their causes (the germ theory of infectious disease) and modes of development of treatments (antimicrobials) and prevention (vaccines). Feared infectious diseases of the past such as diphtheria or measles have been made preventable and others eradicated (e.g. smallpox) or are close to eradication (e.g. polio). However, novel infectious disease threats continue to emerge. In the past few decades, we have faced HIV/AIDS, Avian influenza viruses H5N1 and H7N9, SARS, the 2009 "swine flu" pandemic, Ebola and Zika, prior to COVID-19. In the words of a recent WHO report, the emergence of antibiotic resistance threatens to lead to a "post-antibiotic era, in which common infections and minor injuries can kill", a scenario "far from being an apocalyptic fantasy – is instead a very real possibility for the 21st century" (WHO, 2014). These emerging infectious disease outbreaks have individually cost billions of US dollars (SARS in 2003–30-50 billion US$; Avian flu H5N1 from 2004-2008 30 billion US$; Ebola in West Africa 53 billion US$). The risk of a sarbecovirus (SARS-CoV related viruses) posing a pandemic threat was identified 5 years prior to the emergence of COVID-19, with the discovery of coronaviruses in bats, distinct but related to SARS-CoV-1, that could infect human cells (Menachery *et al*., 2015). A bat coronavirus also caused an outbreak of diarrhoea in swine in China (Zhou *et al*., 2018).

However, the investments made to address these threats have not matched their observed impact. It appeared that mankind managed to dodge each of these events, as they appeared to be contained (e.g, SARS in 2003; Ebola in 2015) or be relatively mild ("swine flu" pandemic in 2009). Given the frequency with which these zoonotic diseases were emerging, it was inevitable that, sooner or later, one with greater consequence would emerge. That was COVD-19. It is important to recognize that this may not in fact, be the most severe pandemic of the 21st Century. Thus, it is imperative that we learn the lessons from COVID-19, so that we are much better prepared for future pandemic threats.

Why do we continue to face novel emerging infectious diseases and what can we do about it?

The reasons for the increasing frequency of emergence of novel infectious disease are well established and mainly pertain to human activities, viz. intensive livestock production methods (e.g. 80 billion livestock consumed annually, limited genetic diversity of livestock-lines with aim of high levels of production makes it easier for a virus to spread), wild-game animal trade, the bush meat trade, pet animal trade, human population growth and urbanization, antibiotic abuse, breakdown of public health systems, wars, ecological degradation and deforestation and climate change. Microbial factors such as mutation and adaptation also play a role but these have remained the same over millennia. It is the changes in human-drivers that contribute to the progressive increase in emerging infectious diseases over the past 50 years (Jones *et al*., 2008). For example, the SARS outbreak in 2003 emerged via the wild game animal trade (Guan *et al*., 2003). Recent studies add credence to the likely hood that SARS-CoV-2 also arose in a similar manner, from the Huannan seafood market in Wuhan, which also appeared to be selling wild game animals, either live or freshly slaughtered for human consumption (Cohen, 2022). This recognition led to the closing of game animal markets in Southern China in 2004 and prevented the re-emergence of SARS, but this was not extended to other parts of China and Southeast Asia in a sustainable way. If it had, it is very likely that COVID-19 may not have emerged. A recent study of the wild game animal trade in China identified 102 mammalian-infecting viruses, with 65 described for the first time. Twenty-one viruses were considered as potentially high risk to humans and domestic animals (He *et al*., 2022).

The trade and consumption of bush meat is responsible for the emergence of Ebola outbreaks in Africa. The trading of live poultry via whole-sale and retail markets and the sale and consumption of live poultry contributes to the emergence of zoonotic avian influenza A viruses such as subtypes H5N1 and H7N9 (Peiris *et al*., 2016). Understanding the pathways of virus emergence can allow interventions that reduce zoonotic and pandemic risk, an example of "risk reduction at source". For example, studies in Hong Kong demonstrated that intermittent closure of live poultry markets (market "rest-days") or even ensuring that the poultry market is emptied of poultry overnight, markedly reduced the maintenance and amplification of avian influenza viruses in these live poultry markets and reduced zoonotic risk. Our studies also show that separation of aquatic and terrestrial poultry, through the wholesale and retail marketing chain, will reduce the emergence of zoonotic threats such as avian influenza H5N1 and H7N9 (Peiris *et al*., 2016).

The pet industry involves the trade of animals across international borders, often involving wild-animal species and even endangered species. For example, this contributed to an outbreak of monkeypox in the USA (Reed *et al*., 2004) and the importation of infected pet hamsters from Europe led to the introduction of the Delta variant of SARS-CoV-2 into Hong Kong in January 2022, at a time when that variant was not present in Hong Kong (Yen *et al*., 2022). The international pet trade is massive; for example, 1.5 billion live-animals were imported into the USA during the period 2000–2009 (Smith *et al*., 2009). It is estimated that change of land-use and environmental habitat for expanding agriculture led to the emergence of Argentine haemorrhagic fever. The misuse and abuse of antibiotics as well as its use as a growth promoter in animal husbandry contributes to increase in antibiotic resistance. Climate change, as well as being inherently disastrous for planetary health, is contributing to the increases of vector-borne diseases. These "man-made" changes lead to planetary dysbiosis and are increasing the rate of emergence of new zoonotic diseases as well as having other undesirable consequences for the sustainability of species diversity, and even the survival of our own species, on planet earth. Given the multi-factorial and multi-disciplinary nature of the challenge, it is imperative that our response should also involve, human health, animal health and the environmental sciences, in a "One Health" response to these challenges.

Enhancing capacity for surveillance and response

Following the SARS epidemic of 2003, it was realized that a novel and unusual epidemic anywhere in the world could be a threat everywhere. In response to this, the WHO developed the International Health Regulations (IHR) which has been ratified by most countries in

2007. This is a binding agreement upon 196 states and the countries are expected to develop capacity to a) detect and report unusual and unexplained outbreaks of disease, b) develop capacity to respond, c) establish effective mechanism for surveillance, and d) develop public health capacity to respond to disease outbreaks when and where they occur. However, a decade later, it was realized that less than half of the countries in the world were confident of achieving these aims, even on their own self-assessment. It was clear that capacities for surveillance, epidemiological analysis, diagnosis and response were far from what is required to meet obligations under IHR. Even those countries that appeared to be well prepared, failed the test of responding adequately to the COVID-19 pandemic. For example, the Johns Hopkins University Global Health Security Index ranked the USA as the best prepared country to respond to a future pandemic. However, by July 2020, with 5% of the global population, it had 25% of confirmed cases worldwide and per-capita deaths were ten times higher than in Europe, with many East Asian countries responding to the pandemic more effectively than either the USA or Europe. As the Independent Panel makes clear, this delayed and inadequate response was not due to a lack of early warning but rather because too many "Developed Countries" under-estimated the risks, even after the WHO declared a Public Health Emergency of International Concern by the 30th January 2020, i.e. within 30 days of hearing about the new outbreak of pneumonia in Wuhan, China. It is clear that all countries need to honestly and realistically learn the lessons of COVID-19 because that would be the best to improve capacity to respond in the future. This includes strengthening capacity for laboratory diagnostics, epidemiology and a science-led leadership. The need for a "One Health"-based response capacity has already been emphasized above. Surveillance should be focused on unusual outbreaks of disease in both humans and animals (both wild and domestic) with active investigation of spill-over of infections across species.

Pre-emptive development of countermeasures

Methods for vaccine development of influenza are well known, but it takes over 8 months to develop and distribute a vaccine for a novel pandemic influenza virus. However, influenza pandemics move much faster than vaccine development and vaccines were not in time to mitigate the first wave of the 2009 pandemic of H1N1 influenza (Monto & Webster, 2013). Therefore, a system of proactive surveillance of influenza viruses at the animal-human interface, together with risk assessment of these viruses, has been implemented which can lead to development of pre-pandemic vaccines in advance of the emergence of an epidemic or pandemic (WHO, 2020). Both surveillance and risk assessment tools are now well established for zoonotic and pandemic influenza viruses, with global surveillance data being collected, collated and risk-assessed twice yearly at WHO influenza vaccine strain selection meetings. What is needed is for the global influenza virus program model to be expanded to cover the emergence of SARS- CoV-2 variants, and to cover emerging respiratory viral threats for the future.

In spite of repeated warnings from the scientific community of the threat from coronaviruses from bats, appropriate counter-measures (pre-emptive development of vaccines and antivirals) were not developed, because the coordinated global investment was not forthcoming. In fact, there had been considerable efforts to develop a vaccine for SARS soon after the outbreak in 2003 (Kam *et al.*, 2007) (Gillim- Ross & Subbarao, 2006), but research funding for these efforts rapidly waned with the effective containment of that outbreak. Thus, when COVID-19 emerged in early 2020, the pre-emptive preparedness that should have been in place was sadly lacking.

The pharmaceutical industry, which conventionally develops drugs and antivirals, cannot be expected to invest in development of counter- measures to emerging viruses that may or may not cause an outbreak in future, because such a model is not commercially viable (i.e. a particular virus may never emerge to transmit between humans). Clearly, such investment has to come from Governments and International agencies. This was not forthcoming, until 2017, when a Government-Private partnership, the Coalition for Epidemic Preparedness Initiative (CEPI), was launched at Davos 2017, as the result of an emerging consensus that a coordinated, international and intergovernmental plan was needed to develop and deploy new vaccines to prevent future epidemics, an initiative funded by the Governments of Norway, Japan, Germany and India, together with the Bill and Melinda Gates Foundation and the Wellcome Trust (CEPI). At its inception, it identified pandemic threat disease, including SARS, MERS, Ebola, Rift Valley Fever, Chickungunya, Nipha, Lassa fever and "disease X." If this initiative had a longer time to run, we would have been much better prepared to face COVID-19. As part of this program on emerging viral disease threats, vaccine development was initiated for MERS coronavirus (MERS-CoV). One of the earliest initiatives funded was to University of Oxford and Janssen Pharmaceutical, to fund a vaccine against Lassa and MERS-CoV using a similar adenoviral vaccine viral vector technology. Some of the developments arising from the MERS-CoV vaccine development provided a foundation for the University of Oxford team when they rapidly changed direction to the newly emerged SARS-CoV-2 coronavirus. As COVID-19 emerged, CEPI rapidly changed focus toward SARS-CoV-2 development and also was instrumental, with WHO, in setting up the COVAX facility, to facilitate global distribution of COVID-19 vaccines. This was, and is, a farsighted initiative that took initial steps to respond to the threats posed by emerging viral pathogens. If these steps had been taken earlier, by more organizations and on a larger scale, the world would have been much better prepared for COVID-19. The recent "100 days mission" launched by CEPI to fund development of vaccine technologies that can form the basis for even more rapid development of vaccines is to be applauded.

One of the lessons from COVID-19 must be to scale up initiatives such as CEPI, to address, not only vaccine development, but also, to address the challenge of equitable distribution of vaccines. COVID-19 vaccines were both one of the triumphs and disappointments of the pandemic SAGA. On one hand they were developed, licensed and deployed faster than most people believed possible and were effective and safe. But although over 8 billion vaccine shots have been given worldwide, sufficient to vaccinate all the priority groups needing vaccine world-wide, a large part of the less developed world remains unvaccinated. In the developed world, in spite of adequate vaccine supplies to give two, three of even four doses of vaccine per individual, conspiracy theories and rumours derailed vaccination campaigns. Taken together, these have resulted in thousands of needless deaths world-wide.

Vaccine inequity involved intellectual property issues and also involved the lack of vaccine manufacturing capacity in large parts of the world, e.g. Africa, together with the infrastructure to mount a rapid vaccination campaign in some parts of the world with associated cold-chain facilities. It will be important to address these gaps for the future. This also involves a greater investment in bio-medical research and in judicious efforts to set up capacity of local vaccine manufacturing in countries such as Sri Lanka. Indeed, the speed and collaborative nature of biomedical research during COVID-19 were one of the positive aspects to emerge from the pandemic, with vaccines being developed within a year, therapeutic interventions identified and rapid sharing of data on the emergence of novel viral variants (e.g. South Africa).

There are also other social issues that we need to be better prepared to counter. For example, we need better strategies to counter the significant spread of misinformation via social media that seriously cripples public health and control measures, (for example, false anti-vaccine propaganda). It became clear that the relative emphasis of "individual" rights vs. the "collective good" became a major tension in pandemic response in some so-called "developed countries".

CONCLUSION

Having just come through the heavy impacts of the COVID-19 pandemic, it would be a travesty if we do not learn its lessons and prepare to respond better, to future pandemics. The responses we take toward better pandemic preparedness are linked to our response to the other existential crises we face, such as the biodiversity loss and climate change. We need to move towards a trajectory for "economic development" that is not solely driven by "Gross Domestic Product". As Hinchliffe *et al*. (2021) recently eloquently put it, "The politics of planetary public health demand a shift away from (relying exclusively on) the biomedical, technological, and behavioural fixes and the economic imperatives of market capitalism, towards forms of governance and organisation where the health of the planet is assessed openly in terms of its equitability and sustainability".

Conflict of interest

The author has no conflicts of interest to declare.

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REFERENCES

Adam D. (2022). The pandemic's true death toll: millions more than official counts. *Nature* **601** (7893): 312–315. DOI: https://doi.org/10.1038/d41586-022-00104-8

Andrejko K.L., Pry J.M., Myers J.F., Fukui N., DeGuzman J.L., Openshaw J., Watt J.P., Lewnard J.A., Jain S. & California COVID-19 Case-Control Study Team. (2022). Effectiveness of face mask or respirator use in indoor public settings for prevention of SARS-CoV-2 infection-California, February-December 2021. *Morbidity and Mortality Weekly Report (MMWR)* **71**(6): 212–216. DOI: https://doi.org/10.15585/mmwr.mm7106e1

Chandra S. & Sarathchandra D. (2014). The influenza pandemic of 1918–1919 in Sri Lanka: its demographic cost, timing, and propagation. *Influenza and Other Respir Viruses* **8**(3): 267–273. DOI: https://doi.org/10.1111/irv.12238

Coalition for Epidemic Preparedness Initiative (CEPI) (2017). Available at *https://cepi.net/*

Cohen J. (2022). Studies bolster pandemic origin in Wuhan animal market. *Science* **375**
DOI: https://doi.org/10.1126/science.adb1760

Gillim-Ross L. & Subbarao K. (2006). Emerging respiratory viruses: challenges and vaccine strategies. *Clinical Microbiology Reviews* **19**(4): 614–636.
DOI: https://doi.org/10.1128/CMR.00005-06

Guan Y. *et al*. (18 authors) (2003). Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. *Science* **302**(5643): 276–278.
DOI: https://doi.org/10.1126/science.1087139

Haug N., Geyrhofer L., Londei A., Dervic E., Desvars-Larrive A., Loreto V., Pinior B., Thurner S. & Klimek P. (2020). Ranking the effectiveness of worldwide COVID-19 government interventions. *Nature Human Behaviour* **4**(12): 1303–1312.
DOI: https://doi.org/10.1038/s41562-020-01009-0

He W.T. *et al*. (22 authors) (2022). Virome characterization of game animals in China reveals a spectrum of emerging pathogens. *Cell* **185**(7): 1117–1128.e8.
DOI: https://doi.org/10.1016/j.cell.2022.02.014

Hinchliffe S., Manderson L. & Moore M. (2021). Planetary healthy publics after COVID-19. *Lancet Planet Health* **5**(4): e230–e236.
DOI: https://doi.org/10.1016/S2542-5196(21)00050-4

Jones K.E., Patel N.G., Levy M.A., Storeygard A., Balk D., Gittleman J.L. & Daszak P. (2008). Global trends in emerging infectious diseases. *Nature* **45**1(7181): 990–993.
DOI: https://doi.org/10.1038/nature06536

Kam Y.W. *et al*. (14 authors) (2007). Antibodies against trimeric S glycoprotein protect hamsters against SARS-CoV challenge despite their capacity to mediate FcgammaRII-dependent entry into B cells *in vitro*. *Vaccine* **25**(4): 729–740.
DOI: https://doi.org/10.1016/j.vaccine.2006.08.011

Menachery V.D. *et al*. (15 authors) (2015). A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. *Nature Medicine* **21**(12): 1508–1513.
DOI: https://doi.org/10.1038/nm.3985

Monto A.S. & Webster R.G. (2013). Influenza pandemics: History and lessons learned. In: *Textbook of Influenza*, 2nd edition (eds. R.G. Webster, A.S. Monto, T.J. Braciale & R.A. Lamb), pp. 20–34. Wiley Online Library.
DOI: https://doi.org/10.1002/9781118636817.ch2

Osterholm MT & Oshaker M. (2017). *Deadliest Enemy*. Little Brown and Company, New York, USA.

Peiris J.S.M., Cowling B.J., Wu J.T., Feng L., Guan Y., Yu H. & Leung G.M. (2016). Interventions to reduce zoonotic and pandemic risks from avian influenza in Asia. *The Lancet Infectious Diseases* **16**(2): 252–258.
DOI: https://doi.org/10.1016/S1473-3099(15)00502-2

Reed K.D. *et al*. (12 authors) (2004). The detection of monkeypox in humans in the Western Hemisphere. *The New England Journal of Medicine* **350**(4): 342–350.
DOI: https://doi.org/10.1056/NEJMoa032299

Sanchez J.M. (2021). *COVID-19's Economic Impact around the World*. Available at https://www.stlouisfed.org/publications/regional-economist/third-quarter-2021/covid19s-economic-impact-world

Smith K.F., Behrens M., Schloegel L.M., Marano N., Burgiel S. & Daszak P. (2009). Reducing the risks of the wildlife trade. *Science* **324**(5927): 594–595.
DOI: https://doi.org/10.1126/science.1174460

Soper G.A. (1919). The lessons of the pandemic. *Science* **49**(1274): 501–506.
DOI: https://doi.org/10.1126/science.49.1274.501

The Independent Panel for Pandemic Planning and Response (2021). *Covid-19: Make it the Last Pandemic.* Available at *https://theindependentpanel.org/wp-content/uploads/2021/05/COVID-19-Make-it-the-Last-Pandemic_final.pdf*

World Health Organization (2014). *Antimicrobial Resistance Global Report on Surveillance*. Available at *https://www.who.int/publications/i/item/9789241564748*

World Health Organization (2020). Tool for Influenza Risk Assessment (TIPRA). Available at *https://www.who.int/publications/i/item/tool-for-influenza-pandemic-risk-assessment-(tipra)-2nd-edition*

Yen H.L. *et al*. (11 authors) (2022). Transmission of SARS-CoV-2 delta variant (AY.127) from pet hamsters to humans, leading to onward human-to-human transmission: a case study. *Lancet* **399**: 1070–1078.
DOI: https://doi.org/10.1016/S0140-6736(22)00326-9

Zhou P. *et al*. (45 authors) (2018). Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. *Nature* **556**(7700): 255–258.
DOI: https://doi.org/10.1038/s41586-018-0010-9