

Science, not speculation, is essential to determine how SARS-CoV-2 reached humans

On Feb 19, 2020, we, a group of physicians, veterinarians, epidemiologists, virologists, biologists, ecologists, and public health experts from around the world, joined together to express solidarity with our professional colleagues in China.¹ Unsubstantiated allegations were being raised about the source of the COVID-19 outbreak and the integrity of our peers who were diligently working to learn more about the newly recognised virus, SARS-CoV-2, while struggling to care for the many patients admitted to hospital with severe illness in Wuhan and elsewhere in China.

It was the beginning of a global tragedy, the COVID-19 pandemic. According to WHO, as of July 2, 2021, the pandemic has resulted in 182 101 209 confirmed cases and 3 950 876 deaths, both undoubtedly underestimates of the real toll. The impact of the pandemic virtually everywhere in the world has been far worse than even these numbers suggest, with unprecedented additional social, cultural, political, and economic consequences that have exposed numerous flaws in our epidemic and pandemic preparedness and in local and global political and economic systems. We have observed escalations of conflicts that pit many parties against one another, including central government versus local government, young versus old, rich versus poor, people of colour versus white people, and health priorities versus the economy. The crisis has highlighted the urgent need to build a better understanding of how science proceeds and the complex, but critical, links science has with health, public health, and politics.

Recently, many of us have individually received inquiries asking whether we still support what we said in early 2020.¹ The answer is clear: we

reaffirm our expression of solidarity with those in China who confronted the outbreak then, and the many health professionals around the world who have since worked to exhaustion, and at personal risk, in the relentless and continuing battle against this virus. Our respect and gratitude have only grown with time.

The second intent of our original Correspondence was to express our working view that SARS-CoV-2 most likely originated in nature and not in a laboratory, on the basis of early genetic analysis of the new virus and well established evidence from previous emerging infectious diseases, including the coronaviruses that cause the common cold as well as the original SARS-CoV and MERS-CoV.² Opinions, however, are neither data nor conclusions. Evidence obtained using the scientific method must inform our understanding and be the basis for interpretation of the available information. The process is not error-free, but it is self-correcting as good scientists endeavour to continually ask new questions, apply new methodologies as they are developed, and revise their conclusions through an open and transparent sharing of data and ongoing dialogue.

The critical question we must address now is, how did SARS-CoV-2 reach the human population? This is important because it is such insights that will drive what the world must urgently do to prevent another tragedy like COVID-19. We believe the strongest clue from new, credible, and peer-reviewed evidence in the scientific literature³⁻⁶ is that the virus evolved in nature, while suggestions of a laboratory-leak source of the pandemic remain without scientifically validated evidence that directly supports it in peer-reviewed scientific journals.^{7,8}

Careful and transparent collection of scientific information is essential to understand how the virus has spread and to develop strategies to mitigate the ongoing impact of COVID-19, whether it occurred wholly

within nature or might somehow have reached the community via an alternative route, and prevent future pandemics. Allegations and conjecture are of no help, as they do not facilitate access to information and objective assessment of the pathway from a bat virus to a human pathogen that might help to prevent a future pandemic. Recrimination has not, and will not, encourage international cooperation and collaboration.⁹ New viruses can emerge anywhere, so maintaining transparency and cooperation between scientists everywhere provides an essential early warning system. Cutting professional links and reducing data sharing will not make us safer.

We welcome calls for scientifically rigorous investigations.^{10,11} To accomplish this, we encourage WHO and scientific partners across the world to expeditiously move to continue and further extend their initial investigation with experts in China and the Chinese Government. WHO's report from March, 2021,¹² must be considered the beginning rather than the end of an inquiry, and we strongly support the G7 leaders' call for "a timely, transparent, expert-led, and science-based WHO-convened phase 2 COVID-19 origins study".¹³ We also understand that it might take years of field and laboratory study to assemble and link the data essential to reach rational and objective conclusions, but that is what the global scientific community must strive to do.

It is time to turn down the heat of the rhetoric and turn up the light of scientific inquiry if we are to be better prepared to stem the next pandemic, whenever it comes and wherever it begins. Meanwhile, people around the world continue to be infected by SARS-CoV-2, many are suffering severe disease and long-term sequelae, and too many are dying. Too many populations lack access to SARS-CoV-2 testing, COVID-19 treatments, and safe and effective vaccines, which will inevitably perpetuate the pandemic and its consequences. At the very least,



Published Online
July 5, 2021
[https://doi.org/10.1016/S0140-6736\(21\)01419-7](https://doi.org/10.1016/S0140-6736(21)01419-7)

Submissions should be made via our electronic submission system at <http://ees.elsevier.com/thelancet/>

we owe it to all who have suffered from COVID-19, as well as our families and the global community, to work collaboratively to end the pandemic and support international efforts to ensure vaccine equity, even as we prepare for the next pandemic.¹⁴

Having robust surveillance and detection systems in place across the globe is essential to detect and report new or evolving pathogens that can potentially unleash the next local or global threat, as required by the International Health Regulations. Equally essential will be ensuring that the field workforce, laboratory facilities, and the health-care community can all work under the safest conditions. Until this pandemic ends, we ask, as we did in February, 2020,¹ for solidarity and rigorous scientific data.

PD's remuneration is paid solely in the form of a salary from EcoHealth Alliance, a 501(c)(3) non-profit organisation. EcoHealth Alliance's mission is to develop science-based solutions to prevent pandemics and promote conservation. Funding for this work comes from a range of US Government funding agencies and non-governmental sources. All past and current funders are listed publicly, and full financial accounts are filed annually and published. EcoHealth Alliance's work in China was previously funded by the US National Institutes of Health (NIH) and the United States Agency for International Development (USAID). Neither PD nor EcoHealth Alliance have received funding from the People's Republic of China. PD joined the WHO-China joint global study on the animal origins of SARS-CoV-2 towards the end of 2020 and is currently a member. As per WHO rules, this work is undertaken as an independent expert in a private capacity, not as an EcoHealth Alliance staff member. The work conducted by this study was published in March, 2021. EcoHealth Alliance's work in China includes collaboration with a range of universities and governmental health and environmental science organisations, all of which are listed in prior publications, three of which received funding from US federal agencies as part of EcoHealth Alliance grants or cooperative agreements, as publicly reported by NIH. EcoHealth Alliance's work in China is currently unfunded. All federally funded subcontractees are assessed and approved by the respective US federal agencies in advance and all funding sources are acknowledged in scientific publications as appropriate. EcoHealth Alliance's work in China involves assessing the risk of viral spillover across the wildlife-livestock-human interface, and includes behavioural and serological surveys of people, and ecological and virological analyses of animals. This work includes the identification of viral sequences in bat samples, and has resulted in the isolation of three bat SARS-related coronaviruses that are now used as reagents to test therapeutics and vaccines. It also includes the

production of a small number of recombinant bat coronaviruses to analyse cell entry and other characteristics of bat coronaviruses for which only the genetic sequences are available. NIH reviewed the planned recombinant virus work and deemed it does not meet the criteria that would warrant further specific review by its Potential Pandemic Pathogen Care and Oversight (P3CO) committee. All of EcoHealth Alliance's work is reviewed and approved by appropriate research ethics committees, the Institutional Animal Care and Use Committee, institutional review boards for biomedical research involving human subjects, P3CO oversight administrators, and biosafety committees, as listed on all relevant publications. JMH is a member of the board of directors of EcoHealth Alliance. JL is a former Chief Veterinary Officer of the UN Food and Agriculture Organization. JSM is a member of the WHO International Health Regulations Emergency Committee for COVID-19, a member of the One Health High Level Expert Panel that advises the Food and Agriculture Organization of the UN, the World Organisation for Animal Health, the United Nations Environment Programme, and WHO, and a past member of the scientific advisory committee for the Center for Emerging Infectious Diseases of the Wuhan Institute of Virology (2008–11). JKM receives funding from USAID to the University of California at Davis, where she is a Principle Investigator, for the PREDICT Project, which funded viral detection and discovery capacity strengthening, One Health education, and global health capability strengthening around the world, including China and the Wuhan Institute of Virology. JKM is also a voluntary board member, with no compensation or financial interest, for the following not-for-profit collaborative consortia advocating for social and environmental equity, conservation, and global viral discovery in order to mitigate risks from viral spillover and pandemics: Global Virome Project, Gorilla Doctors, Bay Area Global Health Alliance, and UC Global Health Institute. JKM has reviewed for and consulted with numerous US state and federal agencies, including the NIH, Department of Defence, USAID, Food and Drug Administration, as well as non-governmental organisations such as the National Academies of Science, Engineering & Medicine and the American Association of Academic Medical Centers. JKM has ongoing collaborations with organisations, scientists, and other professionals in at least 40 countries, including China and the Wuhan Institute of Virology. JKM declares that her spouse owns and operates BHM Construction and A&J Investments, is an investor in VSP, and is a board member for San Francisco Achievers. SMP receives funding from an NIH grant for a project about SARS-CoV and host cell interactions and vaccine development. LE, HF, AEG, JKM, JSM, SMP, and LP have past or ongoing academic and scientific collaborations on coronavirus biology with colleagues in China and several other countries. LP directs a WHO COVID-19 Reference Laboratory. PD, HF, GTK, SKL, SMP, and LS are members of the *Lancet* Task Force on the Origins and Early Spread of COVID-19 & One Health Solutions to Future Pandemic Threats. JL is a member of the *Lancet* One Health Commission. All authors contributed to the 2020 Correspondence in *The Lancet* in support of the scientists, public health professionals, and medical professionals of China combatting COVID-19.

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- 1 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; **395**: E42–43.
- 2 Forni D, Cagliani R, Clerici M, Sironi M. Molecular evolution of human coronavirus genomes. *Trends Microbiol* 2017; **25**: 35–48.
- 3 Wacharapluesadee S, Tan CW, Maneerom P, et al. Evidence for SARS-CoV-2 related coronaviruses circulating in bats and pangolins in southeast Asia. *Nat Commun* 2021; **12**: 972.
- 4 Zhou H, Ji J, Chen X, et al. Identification of novel bat coronaviruses sheds light on the evolutionary origins of SARS-CoV-2 and related viruses. *Cell* 2021; in press. <https://doi.org/10.1016/j.cell.2021.06.008>.
- 5 Garry RF. Early appearance of two distinct genomic lineages of SARS-CoV-2 in different Wuhan wildlife markets suggests SARS-CoV-2 has a natural origin. May 12, 2021. <https://virological.org/t/early-appearance-of-two-distinct-genomic-lineages-of-sars-cov-2-in-different-wuhan-wildlife-markets-suggests-sars-cov-2-has-a-natural-origin/691> (accessed June 15, 2021)

- 6 Latinne A, Hu B, Olival KJ, et al. Origin and cross-species transmission of bat coronaviruses in China. *Nat Comms* 2020; **11**: 4235.
- 7 Maxmen A, Mallapaty S. The COVID lab-leak hypothesis: what scientists do and don't know. *Nature* 2021; **594**: 313-15.
- 8 Ling H. The lab leak theory doesn't hold up. The rush to find a conspiracy around the COVID-19 pandemic's origins is driven by narrative, not evidence. June 15, 2021. <https://foreignpolicy.com/2021/06/15/lab-leak-theory-doesnt-hold-up-covid-china/> (accessed June 15, 2021).
- 9 Nature. Protect scientific collaboration from geopolitics. *Nature* 2021; **593**: 477.
- 10 Bloom JD, Chan YA, Baric RS, et al. Investigate the origins of COVID-19. *Science* 2021; **372**: 694.
- 11 McNutt M, Anderson JL, Dzau VJ. Let scientific evidence determine origin of SARS-CoV-2, urge Presidents of the National Academies. June 15, 2021. <https://www.nationalacademies.org/news/2021/06/let-scientific-evidence-determine-origin-of-sars-cov-2-urge-presidents-of-the-national-academies> (accessed June 15, 2021).
- 12 Joint WHO-China study. WHO-convened global study of origins of SARS-CoV-2: China part. March 30, 2021. <https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part> (accessed June 15, 2021).
- 13 G7 Cornwall UK 2021. Carbis Bay G7 Summit communiqué. Our shared agenda for global action to build back better. June 13, 2021. <https://www.g7uk.org/wp-content/uploads/2021/06/Carbis-Bay-G7-Summit-Communique-PDF-430KB-25-pages-3.pdf> (accessed June 15, 2021).
- 14 Lurie N, Keusch GT, Dzau VJ. Urgent lessons from COVID 19: why the world needs a standing, coordinated system and sustainable financing for global research and development. *Lancet* 2021; **397**: 1229-36.