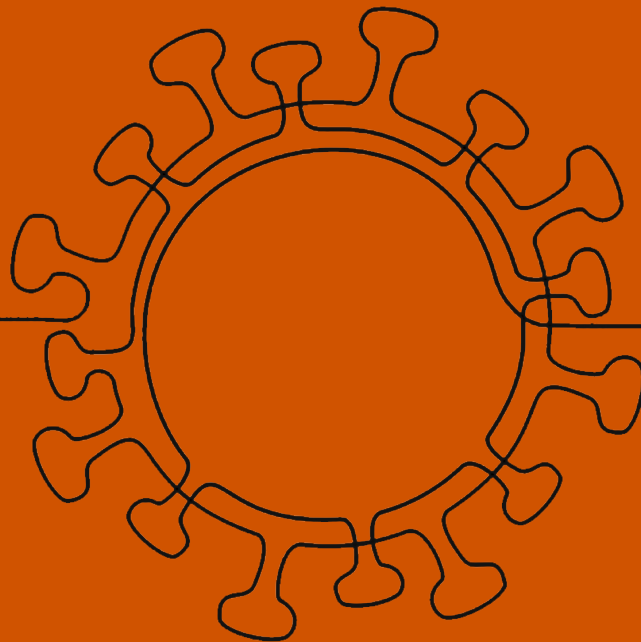


THE *LANCET* COVID-19 COMMISSION

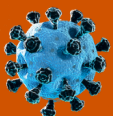
Task Force Statement

DECEMBER 2020



The *Lancet* COVID-19 Commission

Task Force on the Origins and Early Spread of COVID-19
& One Health Solutions to Future Pandemic Threats



THE *LANCET*
COVID-19 COMMISSION

Task Force Members and Staff

TASK FORCE MEMBERS

Peter Daszak, President, EcoHealth Alliance, USA (Chair)

John Amuasi, Leader, Kumasi Center for Collaborative Research in Tropical Medicine, KNUST, Ghana

Danielle Anderson, Scientific Director of ABSL3 Laboratory, Duke-NUS Medical School Singapore, Australia

Carlos das Neves, Director for Research and Internationalisation, President of the Wildlife Disease Association, Portugal/Norway

Isabella Eckerle, Head of the Center for Emerging Viral Diseases, University of Geneva, Switzerland

Hume Field, Adjunct Professor, School of Veterinary Science, University of Queensland, Australia

Gerald Keusch, Professor of Medicine and International Health, Boston University School of Medicine, USA

Sai Kit Lam, Research Consultant, Universiti Malaya, Malaysia

Malik Peiris, Professor of Virology, The University of Hong Kong, China

Stanley Perlman, Professor, Depts of Microbiology and Immunology, and Pediatrics, University of Iowa, USA

Linda Saif, Distinguished University Professor, OARDC/The Ohio State University, USA

Supaporn Wacharapluesadee, Deputy Chief, Thai Red Cross Emerging Infectious Diseases Health Science Centre, Thailand

SECRETARIAT AND TASK FORCE STAFF

Ozge Karadag Caman, Research Scholar, Center for Sustainable Development, Columbia University, USA

Su Yadana, Research Scientist, EcoHealth Alliance, USA

The following report has been posted online by the Commission Secretariat, and has not been peer-reviewed or published in *The Lancet*, nor in any other journal. This reports intends to bring together expert views on key topics as the COVID-19 pandemic unfolds.

The global impact of COVID-19 marks it as the most significant pandemic since the 1918-19 Great Influenza (H1N1). Even though the pandemic is still accelerating its impact in some countries, it has already surpassed most of the other emerging infectious diseases (EIDs) identified since 1918 in the number of known cases, the known mortalities, and its economic impact.

However, despite the deep and broad societal impacts of this disease, its origins remain uncertain, leading to diverse hypotheses, and in the absence of objective investigation and reliable information, considerable controversy and politicization. Likewise, the disease’s ability to evade containment efforts of the public health system in China has the potential to provide lessons for future outbreak control that will have the attention of leaders in many nations.

At this point in the pandemic’s trajectory, a great deal of knowledge has been generated from ecological and phylogenetic studies of CoVs in bats and a few other mammal species in China and southeast Asia, suggesting that the progenitor of SARS-CoV-2 is a wildlife-origin (likely bat-origin) CoV. COVID-19 is a “Disease X” event¹ – a disease caused by a previously unknown microbe that emerged and spread – resulting in a rapidly spreading high consequence pandemic, in the absence of vaccines or drugs to fight it. However, we now know a lot about the SARS-CoV-2 virus, the causative agent of COVID-19. It is a β -coronavirus (CoV) closely related to the virus that caused 2002-2003 Severe Acute Respiratory Syndrome (SARS-CoV), and the 2012-present Middle East Respiratory Syndrome (MERS-CoV) outbreaks. Both originated in bats with the involvement of intermediate hosts (civets and related mammals for SARS, camels for MERS) before host-shifting into humans. Other bat-origin CoVs have caused disease in livestock, e.g. Swine Acute Diarrhea Syndrome coronavirus (SADS-CoV) which has the potential to emerge in people, but has not yet been shown to do so. Indeed, SARS-CoV-2 joins a series of CoVs and related viruses that have emerged into

people or livestock, from bats or other wildlife, and with the involvement of amplifier hosts.

This connection to animals gives COVID-19 a great deal of commonalities with most other EIDs and just about all prior pandemics – that they are caused by animal-origin (zoonotic) microbes. Thus, efforts to reduce the risk of future emergence of novel viruses like SARS-CoV-2 require an understanding of the interactions between animals and humans, and their microbial flora, and the environmental changes (e.g. land use change, agricultural expansion, climate change) that drive transmission among and between these populations. This is the essential premise of the One Health concept, a paradigm that we will explore in detail as we seek to identify potential measures to learn to better predict and prevent future pandemics.

OUR GOALS

The overarching aim of this taskforce is to identify the critical components and illuminate a pathway towards pandemic prevention. This is a strategic approach whereby we anticipate the future emergence of novel Disease X candidates, identify their likely geographic origins, the likely pathways through which they will emerge, and the underlying drivers of their emergence. This is essential to the goal of identifying measures to block the spillover of novel agents from animals to people, reduce the chance of short transmission chains becoming local and regional outbreaks, and bolster international collaboration in One Health. It is also necessary for education on the linkages among the environmental changes that drive pandemic risk to improve our early actions and resilience to the emergence and spread of novel agents. Notably, disease outbreaks among food animals important for human nutrition, and the potential of human origin pathogens host-shifting to animals with devastating consequences are both intrinsic concerns of a fully informed One Health approach.

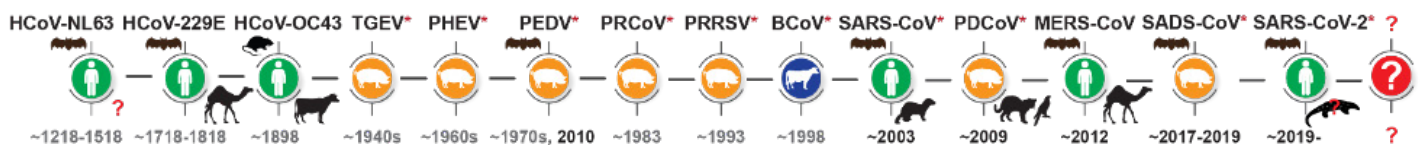


Fig. 1: Based on molecular clock analysis, coronaviruses and other nidoviruses have emerged repeatedly in people or livestock, especially since 2000 (bold dates)²⁻¹². Red star = origins in Asia, Europe or USA; black animals = likely reservoir (above) or intermediate host (below). Red question mark = The next potential future CoV pandemic that we need to focus on preventing.

In the broader context of One Health, the potential for spillover of SARS-CoV-2 from people into wildlife, food animals, or pets is of public health concern because of the risk of establishing secondary host reservoirs leading to further cases in people, or due to its impact on these animal populations. Our main charge, however, is to examine the evidence regarding the spillover of SARS-CoV-2 to humans, the need to understand the origins of COVID-19 in the context of other emerging infectious diseases, and the drivers of its early spread by which it escaped initial control and became pandemic.

Our taskforce therefore has three distinct goals:

1. **Identifying the most likely origin of SARS-CoV-2** and the pathway by which it emerged in people, based on the preponderance of evidence. The closest known relatives of SARS-CoV-2 are found in *Rhinolophus* spp. horseshoe bats in Southern China (Yunnan province), yet the first cases of COVID-19 were recognized in people over 1,000 miles away, in the city of Wuhan. We seek clarity on the putative animal species and the location and time when related coronaviruses have been identified in bats and other mammalian species. We also seek clarity on when the virus first infected people and on whether an intermediate host was involved. Some origin hypotheses propose that the wildlife trade acted as a pathway for this virus to move across China, whether it was native to or introduced from outside China. Others postulate that the virus was isolated, genetically manipulated, or accidentally released from a biosecurity laboratory in Wuhan. Additionally, there are a number of reports suggesting the presence of SARS-CoV-2 earlier than December in China and prior to January in other countries. It is unclear how well-supported these findings are, and what they imply about the origins of the virus and the initiation of the Wuhan outbreak.

Efforts to understand better the origin of SARS-CoV-2 may:

- Help assess the continued risk of re-emergence or emergence of future CoVs, including SARS-related CoVs (SARSr-CoVs), SADS-related CoVs, and MERS-related CoVs (MERSr-CoVs).
- Provide a strategy to heighten biosecurity, improve identification of early case clusters of Disease X scenarios, design human behavior change programs, and introduce legislation/policies to reduce risk of future emergence in China, Southeast Asia and beyond.

- Inform and potentially alleviate a politically-divisive strategy to 'blame' countries for the outbreak.
 - Provide clues from nature regarding the capacity of other SARSr-CoVs to emerge.
 - Identify natural reservoir host ranges and reservoir host populations with potentially ongoing circulation of SARS-CoV-2 ancestors or pre-pandemic strains.
 - Examine the molecular clock evidence for the evolutionary path of SARS-CoV-2 to determine the probable timeline of acquisition of important virulence genes.
2. **Assessing the early spread of COVID-19** and the reasons control measures were unable to contain the initial outbreak. The first case of COVID-19 in people was reported in early December in Wuhan. The Wuhan and Hubei authorities were actively working to suppress a growing outbreak by mid-December, and the Federal CDC (China CDC) was involved at the end of December. It is important, however, to assess evidence of unexplained clusters of severe pneumonia in 2019 in Wuhan or other areas of China prior to December 2019. Despite rapid identification of a causative agent prior to January 2020, and perhaps unprecedented travel bans during the Chinese New Year, the virus spread internationally, with the first report from Thailand on January 12, 2020 and possibly in Europe and North America around the same time. Recent literature reports retrospective syndromic surveillance with evidence that the virus may have been present in various countries prior to this, albeit that these results have yet to be independently verified.

Assessing all of the factors that explain the different outbreak trajectory between SARS and SARS-CoV-2 may help to:

- Identify specific points at which future epidemics can be contained more effectively before amplification and international spread.
- Identify specific strategies, agencies, and/or policies to improve future control of pandemics as close as possible to initial spillover event.
- Assess the plausibility of SARS-CoV-2 circulation elsewhere in China in relation to the earliest evidence of its presence in Wuhan City or Hubei province.

- Define strategies for a more systematic system for identifying clusters of severe respiratory disease, including radiological markers, and the early application of sequencing methodologies to identify the presence of new or novel variant pathogens.
3. **Identifying One Health solutions to future pandemic threats.**

All prior pandemics, and most known emerging diseases have originated in non-human animals, usually wildlife, and emerged due to environmental and socioeconomic changes like land use change, agricultural expansion, the wildlife trade, and increased international travel. These drivers bring people, our livestock, and wildlife into closer contact across large areas of the planet, and are the factors behind the emergence and spread of HIV/AIDS, pandemic influenza, Ebola, SARS, Nipah virus, and likely COVID-19. In particular, the identification of the first large case cluster of COVID-19 at a seafood and wildlife market mirrors the emergence of SARS in the live animal markets of Guangdong in 2003, but some data suggest that earlier cases occurred. Likewise, the rapid environmental changes with declines in biodiversity in rural China mirror those across tropical and subtropical regions that have led to spillover of a number of novel bat-origin diseases. The COVID-19 pandemic has led to occasional spillover into pet and zoo animals and further involvement of farmed animals, with large scale outbreaks and high transmissibility of SARS-CoV-2 in mink farms in Europe and the USA. This virally-mediated connection among the environment, animals and people is a One Health problem that underpins pandemic risk.

In this taskforce, we will use our findings to identify One Health approaches to controlling future pandemics that will:

- Identify potential synergistic effects and return-on-investments of taking a multisectoral approach to outbreak investigation and pandemic prevention that includes human health, animal health, and environmental health aspects.
- Identify key strategies, policies, organizations and mechanisms to fund and deliver a coordinated One Health approach to preventing future pandemics at the national, regional, and international level.
- Recommend public information programs focused on key messages to raise awareness in the general population and build support for relevant policies that can facilitate a transformative change of behaviors and actions.
- Identify the sustainable development benefits of One Health solutions to prevent pandemics.

OUR APPROACH

We have assembled an international group of experienced specialists trained in multiple relevant fields to review scientific evidence on key theories of COVID-19 origins & control. Our taskforce includes leaders in the fields of:

- Virology, with capacity to examine viral sequences to assess the evolutionary origins of SARS-CoV-2, relationships to other viruses, and potential evidence of laboratory manipulation or natural recombination.
- Ecology of viral emergence, with a deep understanding of the causes of other emerging diseases, including the wildlife trade, land use change including intensive farming and animal production, and human behaviors that increase wildlife contact.
- Outbreak investigation, epidemiology, and surveillance, with capacity to compare how the COVID-19 outbreak trajectory developed with other recent spillover events.
- Human medicine and infectious diseases, including epidemiology, pathogenesis, diagnosis, pathology, and clinical care, encompassing treatment, prevention, and public health implications.
- One Health, with leadership in developing policy options at national, regional and intergovernmental scales.
- Lab biosafety, with deep experience in working in BSL-3, and -4 laboratories, including within China.
- Experience of working in China, with a large network of collaborators in key agencies and laboratories from which we can seek further information.
- Experience of working with international organizations with responsibilities for pandemic preparedness and outbreak management on the animal, human, and environmental dimensions.

We will collate all available evidence on each of the three goals below. We will conduct analyses of available data, perform interviews with key leaders in diverse fields, and use other approaches to assess the validity of evidence, the weight of evidence, and the gaps in our understanding for each key question and issue. We will do this from a neutral, science- and evidence-based, hypothesis-testing perspective, with a rigorous systematic process that will assess all hypotheses on why COVID-19 emerged, why it was able to become pandemic, factors that affected spread, and how to predict and prevent future outbreaks. We will build a detailed timeline of the COVID-19 outbreak, stretching from the end of the SARS outbreak (2003) to present. We will use this to 1) visualize the key discoveries of relevance to each issue; 2) identify scientific and media reports that should have acted as 'red flag' warnings and calls for preventative action prior to COVID-19; 3) assess how different disciplines and agencies within the "One Health arch" collaborated on surveillance and emergency preparedness before and during the outbreak, and 4) identify policy actions that were taken to reduce pandemic risk, and reports or actions that politicized our understanding of COVID-19's origins and early spread.

On the origin question, we will use a 'Preponderance of Evidence' approach to analyze data on all leading hypotheses for origin. We will:

- Work backwards from the Huanan Market cluster, as well as forwards from the rural Yunnan sites of nearest known SARS-CoV-2 relatives in wildlife.
- Interview key members of the outbreak investigation teams and virological labs analyzing early cases in China to seek further support or lack thereof for each theory.
- Weigh the evidence for and against each theory on COVID-19 origins and identify critical gaps in data and recommend strategies that can be adopted to address them.
- Analyze data on the earliest reported cases in China and outside of China, and assess the validity of these reports.
- Use the expertise of Task Force members to evaluate the findings and draw reasonable and rational conclusions to guide informed changes in surveillance and pandemic preparedness.

We will examine multiple hypotheses including:

1. Yunnan bat→ hunter→ Wuhan. The virus evolved in S. China from a bat SARSr-CoV lineage and infected a person directly – e.g. a bat hunter – and this person transmitted it to others in their social network, including people in the wildlife trade, which allowed the virus to move through the trade network to Wuhan. We will consider all potential pathways of human exposure by bats in the region, keeping in mind it could have happened more than once with limited spread and no recognition signal of the event until 2019.
2. Yunnan bat→ traded/farmed wildlife intermediate host→ Wuhan. A bat infected by SARS-CoV-2 was captured by a hunter, or flew into a farm where wildlife are kept in cages and infected animals that the hunter/farmer ultimately sold into the wildlife trade. Alternatively, carnivorous animals could have consumed SARS-CoV-2 contaminated meat or feed. The animals carried the virus to the Wuhan market as they were trucked into Wuhan. These animals could have been civets, porcupines, raccoon, dogs, or another animal commonly raised for food or fur in China. The Wuhan Huanan Market served to spread infection and amplify the signal to the point of recognition.
3. Hubei bat→ via hunter or intermediate host, or direct to Wuhan market. The virus is from a bat endemic to Hubei (the province where Wuhan is), and either of the above two pathways began there. This scenario needs to take into account the timing of spillover vs. the first cluster of cases, and assess whether and when bats hibernate in that region.
4. Origin in another region in China or neighboring countries. This happened in another part of China, e.g., Guangdong, or even in countries bordering on Yunnan where the same bats and probably similar viruses circulate, or where essential intermediate hosts are found.
5. Origin in another more distant country. Assess hypotheses of USA or European origin with subsequent introduction into Wuhan. Analyze data on proposed first findings of evidence of COVID-19 outside China (e.g., patient in France, sewage in Spain, blood samples in USA, etc.).
6. Role of pangolins as intermediate hosts. The virus moved from bats into pangolins in the wildlife trade and then into people. Assess sequence data from all closely related CoVs isolated from pangolins, assess volume of live or frozen pangolins traded,

assess the prevalence of SARS-CoV viruses in pangolins, analyze ability of pangolin scales to transmit virus.

7. It was bioengineered in the Wuhan BSL-4 lab. The virus was a product of genetic manipulation of one or more than one virus as part of a pathogenesis, bioweapon, or other program.
 8. It is the SARS-CoV-2 virus present in a previously collected bat sample that was accidentally released from Wuhan Institute of Virology (WIV), Wuhan CDC, or a Wuhan University lab. This theory suggests it was cultured in the lab and could have accidentally infected a lab worker, or was discarded with animals used in experiments, or had infected researchers sampling bats in caves. This scenario would require an assessment of the samples stored in these labs, what the routine protocols were, the number of people with access to samples or bat caves for sampling, decontamination procedures and evidence of safety violations or lack of biosecurity, as well as systematic serological study of collected serum samples from laboratory personnel, if such samples are available.
 9. The involvement of RaTG13 and the Mojiang miners or similar scenarios. This hypothesis proposes that pneumonia cases in a small group of miners in 2013 were due to SARS-CoV-2 or a closely related virus (RaTG13) and that the virus was then studied in WIV and subsequently released in some manner.
 10. Frozen seafood or other cold-chain origin. The virus was spread via frozen seafood, packaging, or other cold-chain fomites within China, and may have initially been introduced to China through this pathway.
- Identify how and when the criteria for case reporting were determined, and whether or not that could have led to an underestimation of the number of cases and the lethality of COVID-19.
 - Attempt to identify when clarity was first achieved on the ability of SARS-CoV-2 to spread efficiently among people, including mildly infected or asymptomatic individuals in the community, and when and how this was reported.
 - Recommend strategies for future efforts for control.

On the issue of One Health and Preventing Future Pandemics, we will identify One Health approaches that would have benefits to preventing future pandemics, how this would be funded, and what organizations and agencies would be involved. We will:

- Review common features among COVID-19 and other pandemics that have origins in wildlife, livestock and are driven to emerge by underlying changes in population density and human travel, environmental changes and biodiversity loss.
- Identify potential synergistic effects and return-on-investment of taking a multisectoral approach to pathogen surveillance, outbreak investigation, and pandemic prevention that includes human health, animal health, and environmental health aspects.
- Identify key strategies, organizations and mechanisms to fund, restructure or develop de novo and implement a coordinated One Health approach to preventing future pandemics at the intergovernmental and national levels.
- Identify how policy platforms for conservation of biodiversity, sustainable development, and health can be reinforced by programs that aim to prevent pandemics.

INITIAL CONSENSUS

Although our work is in its very early stages, we have already reached consensus on the following key points:

ON THE ORIGINS OF COVID-19

One Health outbreak investigation teams: It is clear that the lack of data on potential animal origins of this likely zoonotic pathogen is a key challenge. We recommend that outbreak investigation teams in emerging disease

On the early spread issue, we will document and review all available data on the spread of cases from the ones that were first identified, and on the outbreak investigation and control efforts from China, World Health Organization (WHO), and other countries within the timeline up to Jan 30th 2020, just after the declaration of a Public Health Emergency of International Concern (PHEIC) by WHO. We will:

- Compare trajectories and control efforts with other recent emerging diseases (e.g. Nipah virus, H1N1, West Africa Ebola, H7N9).
- Identify critical points in the investigation and control efforts for which alternative strategies could have been adopted.

hotspot countries adopt a One Health approach as soon as possible and include veterinary scientists, ecologists, social scientists, and field staff equipped and skilled in the investigation of animal origins in testing wildlife and livestock and in doing the viral characterization necessary to identify close relatives of known agents. Outbreak teams should begin assessing the animal origins and human behavioral risk pathways at the same time as medical staff conduct quarantine, testing, disease control measures, and contact tracing. This will require that high throughput sensitive and specific virologic tests be validated for use in humans and animals. In this way, necessary sampling can be identified and critical data on a disease's origin will not be lost.

Post-mortem and archival samples to determine the origin of the outbreak: China has already started examining archival samples from early pneumonias and pneumonia-like illnesses to determine whether COVID-19 appeared before the outbreak in Wuhan. Similar retrospective studies have been conducted in other countries, and should also be conducted in USA, UK, and EU countries, especially in Spain, Italy and France, which have reported detection of SARS-CoV-2 ahead of the pandemic. Other countries can be encouraged to do so if wildlife trade is implicated in virus spread. Besides blood samples, stored pathological samples can be tested for SARS-CoV-2 by PCR. In many countries (including predominantly Muslim countries, China, and others) autopsies are often prohibitive because of religious and cultural reasons, however, biopsy or broncho-alveolar lavage samples may have been obtained and still exist. Culturally-sensitive efforts could also be made to inform populations about respectful post-mortem examination and how important such samples and data can be to unraveling and controlling disease, particularly when and where an outbreak is beginning.

ON THE EARLY SPREAD OF COVID-19

Build trust through international collaboration on emerging diseases: We believe the key to preventing rapid spread of future Disease X scenarios is to build international collaboration around frameworks like the Global Health Security Agenda, develop international research alliances to identify potential future pathogens currently in wildlife, assess risk of emergence, and conduct joint surveillance programs that monitor (using serological tests) the spillover of these novel viruses into people (or animals) in EID hotspots. By building trusted coalitions, openness during the chaos of an outbreak will allow better control, and better sharing of information and data, t

all countries will be better protected from the ravages of the next COVID-19-like event.

ON ONE HEALTH SOLUTIONS FOR FUTURE PANDEMICS

A number of proposals have been put forward by other organizations and review panels. We will deliberate on all of these, and identify which would likely be most effective considering the lessons from COVID-19. However, three key recommendations made by the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES) Pandemics Workshop³³ are a high priority for this taskforce:

Launch a high-level intergovernmental council on pandemic prevention: This council would provide a platform for cooperation among governments and work at the crossroads of the three Rio conventions to:

1. Provide policy-relevant scientific information on the emergence of diseases, predict high-risk areas, evaluate economic impact of potential pandemics, highlight research gaps; and
2. Coordinate the design of a monitoring framework and possibly lay the groundwork for an agreement on goals and targets to be met by all partners for implementing the One Health approach (i.e., one that links human health, animal health, and environmental sectors).

Build a new intergovernmental health and trade partnership: To reduce zoonotic disease risks in the international wildlife trade, it is essential to promote and expand collaborations among the World Organisation for Animal Health (OIE), Convention on International Trade in Endangered Species (CITES), Convention on Biological Diversity (CBD), WHO, Food and Agriculture Organization (FAO), International Union for Conservation of Nature (IUCN), and other relevant entities. This partnership would also work with the High-Level Council to identify policies to reduce or remove species in wildlife trade that are identified by expert review as high-risk reservoirs of potential zoonoses; establish regulatory standards; test the efficacy of establishing market clean-out days, increased cold chain capacity, biosafety, biosecurity and sanitation in markets; and conduct disease surveillance of wildlife in the wildlife trade, and of wildlife hunters, farmers, and traders.

Enact bold transformative policies to protect biodiversity and reduce the role of land-use change in pandemic emergence: These policies should include:

- Developing and incorporating pandemic and emerging disease risk health impact assessments in major development and land-use projects;
- Reforming financial aid for land-use so that benefits and risks to biodiversity and health are recognized and explicitly targeted.
- Better integrating Indigenous knowledge into decision processes and strengthening education initiatives to raise awareness for biodiversity loss and pandemic emergence.
- Assessing how effective habitat conservation measures including protected areas, habitat restoration programs, and nature-based solutions can reduce pandemics and trade-offs where disease spillover risk may increase, and developing programs based on these assessments.
- Enabling transformative change to promote sustainable development, and to reduce the types of consumption, globalized agricultural expansion, and trade that have led to pandemics (e.g., exotic wood, products requiring mine extraction, transport infrastructures, meat and other products of globalized livestock production). This could include modifying previous calls for taxes or levies on meat consumption, livestock production, or other forms of high pandemic risk consumption.

Endnotes

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