STRENGTHENING SCIENTIFIC UNDERSTANDING OF PRIMARY PANDEMIC PREVENTION AND BUILDING INTERVENTIONS TO ADDRESS PRE-SPILLOVER AND SPILLOVER OF ZOONOTIC PATHOGENS

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As a result of COVID-19, the World Health Organization (WHO) has called on society to, 'protect and preserve the source of human health: nature' (WHO 2020). That bold vision will require evidence-based science to support fundamentally new decision-making, policies, and interventions paired with greater multilateral and trans-sectoral cooperation.

The Wildlife Conservation Society has convened an array of experts to recommend three critical interventions needed to mitigate the threat of new, emerging pandemics. Each of these interventions have short, medium, and long-term targets that will require dedicated effort and investment in order to be effective in reducing the overall risk of future pandemics. To effectuate these targets, we have identified key actions and research gaps that are prime for private philanthropic investment and can ultimately help guide and leverage significant, and growing, public funding commitments through national, bi-lateral, and multi-lateral agencies worldwide.

This paper briefly describes the three overall interventions and the associated research gaps as an overview.

Understanding Mechanisms of Disease Emergence in Changing Landscapes

The Lancet editorial board recently highlighted that the One Health approach inherently necessitates the reduction of human impact on the environment, which is a significant medical intervention in its own right.[1] Land-use change has been identified as one of the biggest drivers of zoonotic disease emergence. However, our current knowledge of disease ecology and ecological degradation is insufficient to pinpoint and mitigate the specific anthropogenic drivers. To societally engineer effective interventions that stop spillover, we must first establish a stronger understanding of the component parts, their interactions, and how the entire system responds to environmental stressors. Transformative change in our approach to study environmental degradation and disease ecology is needed.

Degradation and associated environmental stressors can influence infection dynamics in various ways that increase the zoonotic disease spillover risk (Loh et al. 2015). New interfaces and edges between people, livestock, and wildlife increase contact rates (Faust et al. 2018; Bloomfield et al. 2020) and alter types of contact. Environmental stressors can directly affect wildlife hosts (Plowright et al. 2021), for example altered environments can favor hosts that are good reservoirs of zoonotic pathogens and loss of diversity can lead to amplification of zoonotic pathogens and more human exposure. Ecological

[1] Lancet, T. One Health: a call for ecological equity. Lancet 401, 169 (2023).

degradation processes that increase the risk of pathogen spillover are happening at rates never before seen and are likely to accelerate further (Steffen et al. 2015; Bradshaw et al. 2021). For example, from 2001 to 2021, 437 million hectares of tree cover was lost globally, which represents an 11% decrease in tree cover since 2000. Basically, we are using up 50% more natural ressources than the Earth can provide. Currently, we need 1.5 Earths which we do not have.

Our present understanding of how landscape change drives zoonotic disease emergence is almost entirely based on correlational and observational studies (Gottendenker et al. 2014). It is only very recently that a long-term (25 years!) study has identified the mechanistic connections between habitat loss, climate and increased spillover risk (Eby et al. 2022). Numerous studies indicate associations between environmental change and pathogen emergence—such as the increased incidence of Ebola and malaria seen with the increase in deforestation. However, they are context specific and often do not reveal the mechanisms driving the process.

More long-term, multi-scale, systematic, replicated studies are required to truly assess links between environmental change and disease emergence. Study design must investigate drivers that influence attributes and behaviors of individuals, populations, and ecosystems, and address the problem at scales from molecules (e.g., reservoir host immune systems) to landscapes (e.g., patterns of pathogen prevalence and host aggregation) utilizing a transdisciplinary and cross-sectoral One Health framework. Research should be conducted in consultation across local sectoral stakeholders, using methods like participatory epidemiology with government policy makers and administrations, civil society, Indigenous Peoples, and local communities. Combining scientific and Indigenous Ways of Knowing to better understand local ecology and spillover threats is critical. Combining extensive field data with laboratory analyses, mechanistic modeling, and artificial intelligence will establish a strong, co-created evidence base on spillover and mechanisms of disease emergence to inform and guide stakeholders, decision-makers and donor organisations. Understanding the mechanisms will allow adaptation and mitigation of the drivers. This can be achieved through a modular tiered approach: systems need to be put in place to collect, analyse, and share harmonized data (e.g. new platforms in development, such as SMART for Health and WildHealthNet) in tandem with cross-sectoral funding streams that allow the analysis and, more importantly, the structures and mandates to actually act on this information.

A comprehensive holistic approach to disease ecology research helps build capacity from local to national to regional scales. Long-term studies are critical to establishing and robust building partner relationships, growing One Health capacity, and conducting rigorous science. Building trust and subsequent integration, across sectors, of One Health government partners (e.g., agriculture, environment, infrastructure and public health agencies), is fundamental to knowledge generation and sharing that will drive policy change and mitigation actions.

Long-term spillover-focused mega-studies beyond Eby et a. 2022 are generally lacking. Such studies would improve global health security and address the existing knowledge gaps on how land use change elevates the risk of disease emergence and which type of land use changes in which locations are higher risk than others. This evidence will support and strengthen Health Impact Assessments and the design of measures to mitigate spillover associated with high-risk land use change activities. Results will provide the foundation for mechanism-based global indicators and biosecurity assessments of spillover threats due to land use change. Such indicators are commonly used by multilateral agencies and donor organizations to establish monitoring programs, economically evaluate development opportunities, and incentivize better land use decisions (e.g., Global Environment Facility, World Bank). A clearer understanding of

spillover mechanisms will inform evaluations of the economic impact and return on investment of mitigation measures and nature-based interventions.

The Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES) Workshop Report on Biodiversity and Pandemics has called for, 'Improving understanding of the relationship between ecosystem degradation and restoration and landscape structure, and the risk of emergence of disease' (2020). Under a biosecurity imperative, the G7 on 19 February 2021 stated 'stronger defenses against future risks to global health security' are needed (European Council 2021).

Significant investments are needed to jump-start such transformative research (Coulson et al. 2020; Plowright 2021) that would bring together a consortium of the world's leading experts in spillover, disease ecology, conservation, immunology, movement ecology, and virology. This science is foundational to nature-based solutions (i.e. environmental management and conservation efforts) that reduce the risk of global pandemics and benefit the health of all.

Reducing The Trade in Live Wild Animals

The commercial wildlife trade can present a high risk for the evolution, emergence, amplification, and transmission of zoonotic pathogens. Addressing these risks requires urgent consideration of wildlife trade chains – from the source where the animal is killed or captured, right through to market, where it is prepared, consumed or sold for other purposes – and of the varied forms of trade: formal and informal, legal, and illegal.

In order to inform more effective behavior change and demand reduction campaigns, we must more effectively identify and better understand key target audiences (e.g., poachers, traders, retailers, not just consumers) and their behaviors and practices. This is essential to achieve true impact and change, and requires a shift from traditional tactics that have been designed around meeting monitoring and evaluation metrics (e.g., assessing how many wildlife trade campaign posters were produced) as has previously been the focus of many funding commitments.

Research to identify key challenges to achieving successful prosecution of wildlife crime is essential to guide effective support and interventions to help strengthen processes in individual countries and for transnational trafficking cases. Examples of such challenges might include poor coordination between NGOs, police, and prosecutors; poor management of evidence chain of custody; poor collation or presentation of wildlife crime evidence by enforcement agents/police for prosecutors to effectively present a strong case; a lack of appropriate sentencing guidelines; barriers to information sharing across agencies and across countries. We need to understand which of these barriers exist in different key trafficking nations/regions in order to break them down.

However, successful prosecution in terms of the process of law enforcement is not the only key factor to understand and support. We also need to establish whether this is actually a deterrent to prevent further crime. Studies are needed to clarify the effectiveness (or not) of criminal sentencing and punishments of wildlife traders in terms of deterring return to this illegal activity, and whether it actually results in a reduction in volume, scale, and breadth of wildlife trade associated with the prosecuted individual and their wider network. For example, anecdotal evidence has identified other family members replacing and even expanding the involvement in wildlife trade following the incarceration of a key breadwinner; custodial sentences can negatively impact an individual's ability to attain legal employment on release,

necessitating a return to illicit activities e.g., back to wildlife trade crimes, unless alternatives are facilitated.

A greater body of research characterizing wildlife trade criminal networks, and including all actors, is greatly needed: prior efforts have often overlooked the inclusion of financiers who never "get their hands dirty" but have the connections and economic power to easily replace traders on the ground and middle-men across trans-national networks to perpetuate illegal activities if original actors are caught and prosecuted.

There already exists a substantial body of scientific evidence demonstrating zoonotic pathogens in wildlife trade, including SARS and SARS-Cov-2-related viruses and others of pandemic potential, which highlight the clear risk that commercial trade in live and fresh-dead wildlife poses to human health. Given continuous viral evolution and the vast number of unknown viruses estimated to exist in wild mammals and birds alone, surveillance approaches that capture both known but also emerging and unknown pathogens through Next Generation Sequencing (NGS), multiplex serology, and implementation of continually evolving novel screening technologies need particular focus. Investments in improved cross-sectoral early-warning systems and the continued surveillance of potential pathogens in traded wildlife along trade chains — and associated humans — are essential. For example, WCS developed SMART-Health to identify potential spillover events before they become outbreaks. This cell-phone-based tool enables frontline rangers to report significant health events in wildlife into a surveillance system [WildHealthNet] and then deploys innovative technologies, such as carcass-side testing in the Congolese jungle for Ebola. This surveillance system is being successfully piloted in Asia and Latin America. Rural communities in Cambodia and Laos have used it to prevent outward spread of avian influenza and African Swine Fever from wildlife to livestock and people.

Affecting Policy Change for Pandemic Prevention

Two major multilateral processes and opportunities that focus on the upstream solutions needed to prevent future pandemics are currently taking place, with the World Health Organization in the process of drafting a new accord to strengthen pandemic prevention, preparedness and response and the Convention on Biological Diversity nearing the final stage of adopting its post-2020 Global Biodiversity Framework.[2] However, issues related to mandates and sectoral/interministerial silos have hampered efforts to recognize prevention at source (or primary prevention) in these global processes.

A deeper understanding of the baseline policies and governance structures already in place at the international level is needed. Key research areas include:

- Mapping the international governance framework for pandemic prevention at source with a focus on key drivers, such as climate change, land use change, as well as the wildlife trade for multiple purposes (e.g., meat consumption, pet trade, traditional medicine). This will require an identification of the intersection of the governance of issue areas that have been traditionally siloed, such as biodiversity conservation, international trade, public health, and food security.

2 Update: On December 19, 2022, the 15th Conference of Parties (CoP) of the Convention on Biological Diversity (CBD) came to an end with the adoption of the Kunming-Montreal Global Biodiversity Framework, a set of targets to reverse the trend of biodiversity loss and protect wildlife and ecosystems. To address health concerns, the text provides that "the framework is to be implemented with consideration of the One Health approach", therefore recognising the interlinkages between the health of the environment, animals and humans. In addition, target 5 that aims to ensure that wildlife exploitation and trade is conducted in a sustainable way, emphasises that this is a prerequisite to reduce "the risk of pathogen spill-over".

This particular area of research has the potential to unveil where the specific governance gaps are.

- Identification of the capabilities and barriers to advance policy and governance approaches that break down silos across issue areas with a particular focus on the Global South.

- Developing prioritization frameworks for enacting policy in places with high priority due to high zoonotic spillover risk, such as the tropics and sub-tropics where there is high biodiversity and increasing land-use changes that facilitate spillover.

- Strengthen governance mechanisms to better integrate and value civil society and the private sector.

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