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Strengthening a One Health approach to emerging zoonoses

Samira Mubareka Sunnybrook Research Institute, University of Toronto

John Amuasi Kwame Nkrumah University of Science and Technology, Ghana

Arinjay Banerjee University of Saskatchewan

Hélène Carabin Université de Montréal

Joe Copper Jack Indigenous Knowledge Holder, Whitehorse

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Authors

Samira Mubareka, John Amuasi, Arinjay Banerjee, Hélène Carabin, Joe Copper Jack, Claire Jardine, Bogdan Jaroszewicz, Greg Keefe, Jonathon Kotwa, Susan Kutz, Deborah McGregor, Anne Mease, Lily Nicholson, Katarzyna Nowak, Brad Pickering, Maureen Reed, Johanne Saint-Charles, Katarzyna Simonienko, Trevor Smith, J. Scott Weese, and E. Jane Parmley



Strengthening a One Health approach to emerging zoonoses

Samira Mubareka (Chair)^{a*}, John Amuasi^b, Arinjay Banerjee^c, Hélène Carabin^d, Joe Copper Jack^e, Claire Jardine^f, Bogdan Jaroszewicz^g, Greg Keefe^h, Jonathon Kotwaⁱ, Susan Kutz^j, Deborah McGregor^k, Anne Mease^l, Lily Nicholson^m, Katarzyna Nowak^g, Brad Pickeringⁿ, Maureen G. Reed^c, Johanne Saint-Charles^o, Katarzyna Simonienko^p, Trevor Smith^q, J. Scott Weese^f, and E. Jane Parmley^f

^aSunnybrook Research Institute, University of Toronto; ^bKwame Nkrumah University of Science and Technology, Kumasi, Ashanti Region, Ghana; ^cUniversity of Saskatchewan, Saskatoon, Saskatchewan, Canada; ^dUniversité de Montréal, Montréal, Québec, Canada; ^cIndigenous Knowledge Holder, Whitehorse, Yukon Territory, Canada; ^fUniversity of Guelph, Guelph, Ontario, Canada; ^gUniversity of Warsaw, Warsaw, Warszawa, Poland; ^hUniversity of Prince Edward Island, Charlottetown, Prince Edward Island, Canada; ⁱSunnybrook Research Institute, Toronto, Ontario, Canada; ^jUniversity of Calgary, Calgary, Alberta, Canada; ^kYork University, Toronto, Ontario, Canada; ^lSelkirk First Nation Citizen, Selkirk First Nation, Yukon Territory, Canada; ^mUniversity College London, London, England; ⁿCanadian Food Inspection Agency, Winnipeg, Manitoba, Canada; ^oUniversité du Québec à Montréal, Montréal, Québec, Canada; ^PForest Therapy Center, Białowieża National Park, Poland; ^qGlobal Affairs Canada, Ottawa, Ontario, Canada

*<u>samira.mubareka@sunnybrook.ca</u>

Abstract

Given the enormous global impact of the COVID-19 pandemic, outbreaks of highly pathogenic avian influenza in Canada, and manifold other zoonotic pathogen activity, there is a pressing need for a deeper understanding of the human-animal-environment interface and the intersecting biological, ecological, and societal factors contributing to the emergence, spread, and impact of zoonotic diseases. We aim to apply a One Health approach to pressing issues related to emerging zoonoses, and propose a functional framework of interconnected but distinct groups of recommendations around strategy and governance, technical leadership (operations), equity, education and research for a One Health approach and Action Plan for Canada. Change is desperately needed, beginning by reorienting our approach to health and recalibrating our perspectives to restore balance with the natural world in a rapid and sustainable fashion. In Canada, a major paradigm shift in how we think about health is required. All of society must recognize the intrinsic value of all living species and the importance of the health of humans, other animals, and ecosystems to health for all.

Key words: One Health, zoonoses, policy recommendations, governance, technical leadership, equity, education, research

Executive summary

Time for a paradigm shift

Leading up to the COVID-19 pandemic, there was an acceleration of global zoonotic pathogen activity. It is now abundantly clear that we have established socioecological conditions that favour zoonotic pathogen amplification, spillover, spread, and disease. Yet, we continue to fail to recognize

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the interconnectedness among determinants of health for all animals¹, including humans, and ecosystems; the drivers of pathogen emergence; and the disproportionate impact of emerging zoonoses on racialized or economically disadvantaged people, women, and Indigenous communities.

One Health proposes a paradigm to address issues at the intersection of society, health, and the environment. The One Health view recognizes that the health of living beings and the land are interdependent. A collaborative approach to complex challenges, One Health highlights the need for diverse perspectives to identify potential actions that maximize health for all lands and animals, including humans.

Given the enormous global impact of the COVID-19 pandemic, greatly exacerbated by the intrapandemic emergence of novel variants of concern (VOCs), and multiple, ongoing outbreaks of highly pathogenic avian influenza (HPAI) in Canada (Canadian Food Inspection Agency 2022), there is a pressing need for a deeper understanding of the interface where humans and other animals interact in their shared environment, and the intersecting biological, ecological, and socioecological factors contributing to the emergence, spread, and impact of zoonotic diseases. The SARS-CoV-2 pandemic was heralded by international outbreaks of SARS-CoV in 2003 and Middle East respiratory syndrome coronavirus (MERS-CoV). However, significant pre-pandemic gaps persisted in coronavirus surveillance and research on coronavirus virology, ecology, and the development of medical countermeasures. We also failed to anticipate and mitigate the disproportionate impact of COVID-19 on marginalized populations at higher risk of exposure and severe disease; and, we did not predict the effect non-pharmaceutical interventions would have on health, education, and livelihoods. In brief, we did not embrace or sustain a One Health approach to viral zoonoses. These failures resulted from both a limited understanding of viral biology and drivers of emergence and disease, as well as from a lack of political will.

In Canada, there is a groundswell of One Health initiatives and a burgeoning community of practice. Leadership from the animal health and veterinary medicine sectors has been central to establishing One Health approaches to collaborative research, as well as curriculum and policy development in a range of sectors at regional and national levels. These sectors include academia, often seated in faculties of veterinary medicine; federal government; and the private sector. Organizations focused on wildlife and global health such as the Canadian Wildlife Health Cooperative (CWHC) and the International Development Research Centre (IDRC) have longstanding connections to One Health, and some schools of public health and the environment are also actively engaged in One Health discourse.

A resilient and sustainable structure for a One Health approach must be tied to function and a clear One Health agenda for Canada, accompanied by established tasks, timelines, milestones, and support for execution. There is a need for diverse groups of policymakers and decision-makers to work together with other sectors of society in the design of programs and solutions, with active inclusion of community members and Indigenous knowledge holders and scholars.

Further inaction is not an acceptable option—radical change is desperately needed, beginning by reorienting our approach to health and recalibrating our perspectives to restore balance with the natural world in a rapid and sustainable fashion. In Canada, a major paradigm shift in how we think about health is required. All of society must recognize the intrinsic value of all living species and the importance of health of ecosystems and all animals to health for all. The priorities we set today will determine the future of generations to come; we are directly accountable to them for the decisions we make in this moment, a responsibility we can neither deny nor ignore. While many hope for a return to normal, we must remind ourselves of the predisposing factors that enabled this pandemic. This is a critical opportunity to address

¹Because *Homo sapiens*, or humans, are mammals, we often refer to *other animals* to distinguish them from humans. Where the term *animals* is used alone, we are generally implying non-human animals.





Fig. 1. Framework for interconnected groups of recommendations.

these complex factors. Health must be understood as a shared goal with other animals and the land, to ensure wellness for all.

Recommendations

Here we use a functional framework (Fig. 1) of interconnected, but distinct groups of recommendations to facilitate review and framing for decision and policy makers. Urgent, time-sensitive recommendations are denoted with an asterisk (*).

Strategic Recommendations

By galvanizing and expanding One Health initiatives in Canada, there is excellent potential for a sustainable national strategy on One Health to emerge to ensure that One Health considerations are foregrounded for emerging zoonoses and other pressing issues such as climate change. Currently, there is no obvious government entity responsible for coordinating or supporting One Health in Canada. The following recommendations address current gaps in governance, spanning an interministerial, all-of-government approach, biosecurity, international policy, and meaningful inclusion of an Indigenous knowledge framework.

- 1. ***Establish a One Health Council to develop, coordinate and implement a One Health Action Plan for Canada with immediate focus on emerging zoonotic pathogens.** The Council must include experts and representatives from all relevant academic disciplines and ministries of the Government of Canada, as well as key non-governmental partners. The Council should be tasked with examining the policies, programs, and financial and legislative support of agencies, organizations, and institutions related to One Health at the nexus of Canadian and Indigenous Peoples, domestic and wild animals, plants, ecosystems, and the economy and society, focusing initially on emerging zoonoses and drivers of zoonotic pathogen spillover.
- 2. **Appoint a Special Advisor on One Health** to the federal ministers responsible for health. In addition to providing advice, they would play a key role in the One Health Council.
- 3. ***Establish a Global One Health Security Office** which would be mandated to monitor and mitigate all manner of external biological threats to Canada, and with the Council, incorporate clear objectives for One Health into Canadian foreign policy to position Canada as a global leader and champion for global health and security, as part of a One Health Action Plan.



4. *Develop and implement an Indigenous Engagement and Knowledge Policy Framework for One Health and ensure that the One Health Action Plan accounts for and addresses the United Nations Declaration on the Rights of Indigenous Peoples and the Truth and Reconciliation Commission's Calls to Action. All levels of government must establish frameworks for inclusion of Indigenous Peoples Engagement and Knowledge systems in addressing One Health challenges.

Technical Leadership and Operational Recommendations

One of the principles of One Health is to leverage existing resources, tools, and programs. Many of these exist in Canada but have not been fully developed, implemented, or operated in a sustainable and coordinated fashion to (1) consistently generate accessible data for informed decision-making or (2) actively protect and nurture health and wellness for all animals (including humans) and the land. The following recommendations address technical and operational leadership around surveillance data collection and sharing, as well as critical programs for animal and land health.

- 5. *Implement and sustainably fund the Pan-Canadian Approach to Wildlife Health, as approved by all levels of Government in 2018. The Approach must be put into action immediately.
- 6. *Expand and coordinate existing human, other animal, and environmental emerging pathogens surveillance and biomonitoring activities through Centres of Excellence in One Health to generate health intelligence for decision-making and research by linking teams of scientists, diagnosticians, practitioners, epidemiologists, and public health experts to action surveillance data and other relevant data sources.
- 7. Develop best practices for the collection, analysis, and sharing of surveillance data, and characterization of emerging pathogens. Key activities must be underpinned by principles of biosafety and biosecurity. Scientists, diagnosticians, practitioners, epidemiologists, and public health experts must also collaborate to harmonize and share data, materials, and protocols.
- 8. Commit to Other Effective Conservation Measures, Indigenous Protected and Conserved Areas, and Indigenous-led surveillance activities while applying First Nations' ownership, control, access, and possession principles.

Equity recommendations

The burdens of zoonoses and other challenges such as the climate crisis are not borne equally. When these disproportionately affect different communities, the impacts are often linked to pre-existing and systemic inequities. The exacerbation of various health inequities during the COVID-19 pandemic underscores the need for a comprehensive and inclusive approach, such as One Health. The following recommendations address some gaps in our understanding and commitment to underrepresented and over-affected populations.

- 9. **Engage community groups and communication scholars** to help devise better access to timely, effective, and trustworthy information to populations in situations of vulnerability.
- 10. **Collect consistent and disaggregated social and demographic health data** to identify health inequities to reduce the impact of emerging infectious diseases.
- 11. ***Ensure that Canada's commitment to social equality is advanced by applying gender-based analysis plus (GBA+)** to the analysis of all data, with meaningful inclusion of equity deserving groups, when developing interventions as part of a One Health Action Plan for Canada.

Education and research recommendations

The implementation of One Health curricula has been limited for One Health-related continuing education in medicine and other university faculties, learning environments, and public schools. In



addition, One Health-focused research funding has been sparse in Canada, with few streams or review panels with the multi- or interdisciplinary perspectives and mixed-methods expertise to evaluate One Health research applications. Some priority announcements for One Health-related challenges have been supported, but these are primarily focused on human health, narrow in scope, limited in funding, and do not allow for wider-ranging One Health proposals, particularly for animal and ecosystem health. One Health education and research are essential to promoting awareness, advancing knowledge, and informing policy around complex challenges such as zoonoses. The following recommendations address some of the gaps in existing education and research programs for One Health in Canada.

- 12. **Develop and implement One Health curricula** for accredited health education programs for veterinarians, physicians, and other licensed healthcare providers and public health practitioners in training.
- 13. **Introduce One Health at all stages of education**, from preschool to university. Curricular and extra-curricular learning opportunities must be developed, and One Health topics introduced in professional continuing education programs.
- 14. *Prioritize domestic and international research on emerging zoonoses using a One Health approach as part of Canada's One Health Action Plan. This must include research activities across human, other animal, and ecological health from biological, ecological, epidemiological, social, environmental, Indigenous, governance, and policy perspectives.
- 15. **Provide sustained funding, including through the Tri-Agency, for One Health** through a net increase in available funding that supports collaborative biological, health, ecological, social sciences, and humanities research using a One Health approach through dedicated mechanisms. Panels must be multidisciplinary and capable of assessing projects using a One Health approach.
- 16. Embed research as a critical element of a Centres of Excellence in One Health program (Recommendation 6). These centres would focus on generating scientific knowledge and health intelligence using a collaborative One Health approach, thus also training future One Health scientists, teachers, and decision-makers to inform policy and drive societal change.

1. The SARS-CoV-2 Pandemic: A Shared Crisis

Emerging challenges

The first cases of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were described in humans in late 2019. Rapid global spread ensued and the World Health Organization (WHO) declared a global pandemic on 11 March 2020 (WHO 2020). Two years later, by March 2022, SARS-CoV-2 had been reported to have infected over 470 million people and has led to over 6 million deaths globally (WHO 2022). Many people infected with SARS-CoV-2 also continue to suffer from post-COVID-19 conditions (Davido et al. 2020). In addition to significant impacts on individual health and healthcare systems, there have been direct and profound social and economic impacts (Bonotti and Zech 2021).

SARS-CoV-2-related viruses have been well-described in bat populations, suggesting that SARS-CoV-2 originated in bats before spilling over into humans (Hul et al. 2021; Wacharapluesadee et al. 2021; Zhou et al. 2021). The setting (forest, farm, live animal market, or other) for spillover and the potential role of an intermediate host remain unknown. Shortly after the pandemic was declared, several non-human animal² species were reported to be susceptible to SARS-CoV-2 infection (Hobbs and

²Because *Homo sapiens*, or humans, are mammals, we often refer to *other animals* to distinguish them from humans. Where the term *animals* is used alone, we are generally implying non-human animals.



Reid 2021; OIE 2021). These included captive and companion animals, as well as wildlife, raising the possibility of a secondary animal reservoir for the virus.

Re-emerging challenges

The massive global burden of SARS-CoV-2 in humans has resulted in spillover to naïve animal species (e.g., mink, cats, dogs, deer) (Dhama et al. 2020; Kuchipudi et al. 2022) and to the environment, where viral RNA has been detected in wastewater (Giacobbo et al. 2021). In addition to infecting a broad range of animal species through spillover from humans, variants of concern (VOCs) are broadening the susceptible species range for SARS-CoV-2. For example, the Alpha variant harbouring the N501Y mutation in the viral Spike protein is capable of infecting *Mus musculus* (the house mouse) (Shuai et al. 2021), whereas the parental viral strain is restricted to *Cricetidae* species of rodents, such as hamsters and deer mice. The genomic plasticity of the virus permits rapid and impactful adaptations that are critical to understand; peri-domestic wildlife with host viral receptors most closely resembling the human angiotensin converting enzyme 2 receptor may be at highest risk, meriting surveillance particularly in areas with high rates of human SARS-CoV-2 infection.

The implications of one or more animal reservoirs for SARS-CoV-2 are significant. A secondary wildlife reservoir introduces the risk of novel coronaviruses re-emerging after adaptation though mutations or recombination with other SARS-CoV-2 or endogenous animal coronaviruses, and may undermine the efficacy of medical countermeasures, including vaccines and antivirals. It is imperative that we understand the fundamental biology of potentially pandemic viruses, considering that the severity of clinical disease, population-level transmission, and social impact are a result of virological determinants (Kirlin 2020). For example, the Alpha VOC drove wave 3 of the pandemic in Canada, resulting in high rates of hospitalizations and further public health measures, and the genomic changes in the Delta variant translated into a 64% increase in household transmission (secondary attack rate) relative to the Alpha VOC, and is associated with increased severity of disease and risk of reinfection. Also, changes in the Delta variant genome contributed to immune escape and reduced efficacy of monoclonal antibody therapy (Allen et al. 2021; Public Health Ontario 2021). The Omicron variant (and sub-lineages) is highly diverged from other SARS-CoV-2 and has been clearly associated with reduced vaccine efficacy against infection, escape from monoclonal antibody therapy, and enhanced transmission (Accorsi et al. 2022; Escalera et al. 2022; Tatham et al. 2022). It is also speculated to have an animal origin, although no Omicron-like virus has been identified in animals prior to emergence in humans. Regardless, the emergence of Omicron and its subsequent impact highlights the significant potential for harm from new VOCs that could spillover from animal populations.

White-tailed deer in Canada and the United States have been screened for SARS-CoV-2 viral RNA and antibodies to establish evidence of infection and exposure. There are high rates of positivity (up to 82.5% by PCR or viral detection) among deer in the United States, and non-VOC, Alpha, Delta, and Omicron viruses have all been reported in this species (Vandegrift et al. 2022; Kuchipudi et al. 2022; Hale et al. 2022; Marques et al. 2022; Kotwa et al. 2022; Pickering et al. in press). Based upon the genomic epidemiology, multiple human-to-deer transmission events have occurred, but the route(s) of transmission remain unknown. Viral RNA has been detected in hunter-harvested Canadian deer as well, raising important questions around wildlife health, country foods, and the potential evolutionary trajectory of SARS-CoV-2 (Kotwa et al. 2022). The highly divergent SARS-CoV-2 variant detected in Ontario deer is unrelated to any other existing SARS-CoV-2 circulating among humans, and there are data supporting deer-to-human spillover in at least one instance (Pickering et al. in press). This is the first evidence of independent, parallel evolution of SARS-CoV-2 in another species, and of deer-to-human transmission.



The environment has also been implicated in the SARS-CoV-2 pandemic, with substantial spillover of viral RNA from humans into wastewater. Environmental monitoring through wastewater surveillance has been an essential public health tool. Although it is unknown whether animal or human exposure to wastewater leads to infection, given the widespread detection of environmental SARS-CoV-2 viral RNA, this possibility must be investigated, particularly considering that the range of host species susceptible to SARS-CoV-2 may be expanding due to VOCs.

Despite heralding events such as the emergence of SARS-CoV in the early 2000s, and the ongoing circulation of Middle East respiratory syndrome coronavirus (MERS-CoV), we were blindsided by the pandemic spread of SARS-CoV-2. Regardless of the clear and present danger posed by highconsequence coronaviruses, we failed to prepare for this coronavirus pandemic. No coronavirus surveillance was in place, research on coronavirus virology and medical countermeasures was scant, and most importantly, limited efforts had been made to mitigate spillover and spread of another highly pathogenic coronavirus in the years since SARS-CoV and MERS-CoV emerged. These failures resulted from a limited understanding of viral biology and the drivers of emergence, on the one hand, and from lack of political will, on the other. It is abundantly clear that the existing pandemic planning was insufficient to address one of the most significant health threats of this century.

Thus, there is a pressing need for a deeper understanding of the interface where all animals, including humans, interact in their shared environments, and the intersecting biological, ecological, and socioecological factors contributing to the emergence, spread, and impact of zoonotic diseases. This is essential to enhance resilience at all scales, gain insights into the connections between animal and land health, and to better understand how human actions are impacting this relationship.

Anthropogenic impact

Because of the interdependence of human, other animal, and ecosystem health, the decisions humans make have consequences beyond human society. National and international travel and trade played important roles in the rapid global spread of SARS-CoV-2, and urbanization, food insecurity, and trade of wild and domestic animals are contributing factors to the emergence of several other high consequence pathogens.

As the human population grows and our cities expand, we encroach further into natural areas and clear land to produce more food for burgeoning populations of people and domestic animals. This expansion not only reduces natural areas providing critical habitat for wild plants and animals, but also creates new intersection points where humans, vectors, domestic animals, and wildlife come into contact. These changes increase opportunities for new pathogens to adapt (emergence) and infect non-traditional hosts (spillover). Environmental factors, such as climate, seasonality, and habitat availability determine the lifecycles and geographic range of different host species, vectors, and microorganisms, thus affecting where and how zoonoses emerge, spillover, and survive. It has been predicted that as the pace of change of these environmental factors becomes even greater, there will be more spillover events and increased incidence of emerging infectious disease (Jones et al. 2008).

Societal impact

Along with the impacts on health and healthcare systems, COVID-19 has worsened many preexisting inequities associated with poverty, race, ethnicity, and gender, both regionally and internationally. Throughout the pandemic, marginalized populations have been the most heavily burdened by both viral infection and policies put in place to prevent the spread of COVID-19 (WHO 2021; Cronin and Evans 2022). The large social and economic costs associated with the control of and response to the COVID-19 pandemic provide a strong and inarguable case for substantial investments in reducing inequities by addressing the structural drivers of inequities. One approach to reduce the



interconnectedness of inequities would be to enact Canada's commitment to implement gender-based analysis plus (GBA+) and the Calls to Action of the Truth and Reconciliation Commission.

The COVID-19 pandemic has highlighted existing societal inequities and continues to degrade health, healthcare, social, and economic well-being. Our shared experience with COVID-19 is sharpening the focus on the urgent need for new ways of tackling and preventing future pandemics in this time of pressing environmental threats.

2. Addressing Complex Challenges with One Health

The history and evolution of One Health

At its core, One Health is about recognizing the connections between all living things and our shared spaces. Others call this concept by different names (e.g., public health, Ecohealth, and traditional ecological knowledge) (Lerner and Berg 2017). One Health is often portrayed as three pillars (or circles): Human health, animal health, and environmental health (World Organisation for Animal Health, n.d.; Centers for Disease Control and Prevention 2021; Destoumieux-Garzón et al. 2018). By recognizing the shared determinants of health (or disease) and interdependencies among these pillars, we highlight the foundational importance of the intrinsic value of all species and generations, and the importance of reciprocal care for each other (as people), animals, and the spaces we all share (Stephen and Gallagher 2021). The importance of equity, value, and reciprocal care are well-described in EcoHealth (Charron 2012). These three critical elements are needed to address sustainability and to build more resilient and equitable systems able to withstand many complex and growing health threats.

One Health encompasses synergies described as One Medicine by Calvin Schwabe (1984) over 40 years ago. Broader concepts of health and the critical consideration of interrelatedness between health and the environment are embodied in the Ottawa Charter for Health Promotion (World Health Organization 1986), which advances the notion of reciprocal care and pledges to "counteract the pressures towards harmful products, resource depletion, unhealthy living conditions, and environments." Caring, holism, and ecology are deemed necessary for health promotion, and the Ottawa Charter called for international action to achieve Health for All by the year 2000. In 2004, the Wildlife Conservation Society hosted a symposium in New York, where the Manhattan Principles underpinning the concept of One World One Health (OWOH) were established (Wildlife Conservation Society 2004). These principles were advanced through a series of consultations on influenza in Beijing (2005), Bamako (2006), New Delhi (2007), and Sharm el-Sheikh, Egypt (2008), as well as International Ministerial Conferences on avian and pandemic influenza. The Beijing Principles were outlined early in this process, and ultimately the OWOH approach was formally adopted by the WHO, the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (OIE), the United Nations Children's Fund, the United Nations System Influenza Coordination, and the World Bank, based on recommendations made at these meetings.

The OWOH approach is summarized in the report entitled *Contributing to One World, One Health: A Strategic Framework for Reducing Risks of Infectious Diseases at the Animal-Human-Ecosystems Interface* (2008) (Food and Agriculture Organization of the United Nations et al. 2008). This foundational document was sparked by outbreaks and the pandemic threat of the highly pathogenic avian influenza virus (HPAI) H5N1, which was causing widespread outbreaks by 2003 (after its initial detection in 1996 in Hong Kong) (Sonnberg et al. 2013). This virus is resurging globally now, with unprecedented levels of activity in Canada. The emergence and spread of HPAI H5N1 virus at that time highlighted an urgent need to understand the drivers of emergence, transmission, and persistence of emerging infectious diseases at the interface where humans interact with other animals and ecosystems. National authorities were encouraged to consider key priorities for surveillance; public health responses; and strategic research through collaboration, multidisciplinary, cross-sectoral



partnerships; integration of governance; and technical and sociocultural aspects of implementation. The current H5N1 situation is an acute reminder of the importance of these key activities.

The OWOH Strategic Framework encouraged decision-makers to reinforce existing mandates, institutions, and programs, and to include all levels of government. Emphasis on technical leadership in surveillance and data sharing, risk assessment, and capacity building helped strengthen national laboratory testing and reporting systems, highlighting gaps in communication and coordination. This focus on improvements included acknowledging the importance of integrating wildlife and ecosystems into surveillance and control programs and the need to establish effective financing frameworks. Key research areas were identified in the OWOH Strategic Framework, including understanding zoonotic pathogen emergence, spread, and persistence; pathogen biology; diagnostics and prevention; sociocultural determinants; and implementation. A range of specific initiatives emerged from an unprecedented orchestration of efforts, stemming from the control of the HPAI H5N1 virus. Building upon the pre-existing Global Framework for the Progressive Control of Transboundary Animal Diseases (2022), these initiatives included FAO's Emergency Centre for Transboundary Animal Diseases (2022), the joint FAO/OIE/WHO Global Early Warning System (GLEWS) (2022), and the Network of Expertise on Avian Influenza (Edwards 2006).

In November of 2012, the World Veterinary and World Medical Associations signed a collaborative Memorandum of Understanding in Bangkok, Thailand (Wilson 2012). The scope of this memorandum included joint educational efforts, cross-species surveillance, the responsible use of antimicrobials, and collaborative research. More recently, the original Manhattan Principles, released in 2005, were updated as the Berlin Principles in 2021 (Gruetzmacher et al. 2021).

Presently, there are a myriad of definitions and descriptions of One Health, but all share common features (Gruetzmacher et al. 2021; Centers for Disease Control and Prevention 2018; One Health Commission 2022; World Organization for Animal Health 2022). First, One Health is about health—the health of people, animals, plants, and ecosystems. It is about how health is the result of the interdependence between species living in shared environments, over time, and across space. One Health is also about collaboration, trust, and sharing of responsibility. By recognizing health interdependencies, One Health calls for more and better inter-, multi-, and transdisciplinary efforts to break down silos and work together to preserve and promote health gains. The UN Sustainable Development Goals (United Nations 2015) are a key example of how upstream drivers can have far-reaching consequences. Building health, promoting resilience, striving for equity, and ensuring capacity to cope and adapt are all hallmarks of holistic health approaches, be they One Health, EcoHealth, Planetary Health, or other.

Indigenous context for One Health

Western notions of One Health were long preceded by traditional forms of knowledge, including Indigenous ways of knowing. Indigenous knowledge recognizes and respects the interconnectedness among all things and is a distinct approach from the Western concept of One Health, using a different set of assumptions than those advanced through Western thought. In Indigenous knowledge systems, the process is often more important than the endpoint itself, and there is no single path or approach for a given process. Based on common principles, Indigenous knowledge differs among Nations and communities. Although Western focus is shifting toward more collaborative, comprehensive, and interdisciplinary approaches through broader incorporation of concepts of land stewardship and health, important gaps remain in listening to Indigenous perspectives and leadership (WHO 2017b; Hillier et al. 2021).

It is also important to recognize the Indigenous context for health and to address the disparities that exist due to colonization and institutional and systemic barriers to good health. First Nations, Inuit,



and Métis peoples living both on and off reserve experience clear disparities in health and wellness (McGregor 2009; Statistics Canada 2015). We cannot consider applying Indigenous models of One Health, on the one hand, while disregarding these inequities, on the other. Good health and clean water are basic human rights and must be ensured for Indigenous Peoples, recognizing Indigenous Peoples' rights to individual, community, and land health. The right to a self-determined future for land, animal, and human health must be recognized in an active, enabling way.

A rapid decline in land health due to human exploitation and climate change also merits focused attention. Cultural genocide and colonialism have coalesced with these anthropogenic drivers, leading to environmental dispossession through direct disruption of land health or the rupture of Indigenous Peoples' relationships with the land. Connection with the land is considered one of the key determinants of health for Indigenous Peoples (Government of Canada 2018). Thus, environmental dispossession has a profound impact on ways of knowing, ways of life, and spiritual, physical, and mental health (Big-Canoe and Richmond 2014; Jones 2019; Mashford-Pringle et al. 2021; Tobias and Richmond 2014). Also, as land health erodes, so does landscape immunity (Ruscio et al. 2015), increasing the risk of zoonoses for those closest to the land and adding to the disproportionate burden of disease incurred by Indigenous Peoples. This issue has been underscored during the pandemic and goes beyond baseline health and severe outcomes associated with COVID-19 and includes hunting and gathering and other key practices for sustenance and wellness, which were severely affected by individual exposure/quarantine or illness, population-level states of emergency and other regional measures (Tobias and Richmond 2014).

The Convention on Biological Diversity clearly underscores the importance of Indigenous knowledge systems in resource management (Plowright et al. 2021). This knowledge is diverse, participatory, and experiential, and not readily defined using static Western frameworks. Supporting Indigenous concepts of One Health includes respecting natural laws and implementing earth-based solutions through land pedagogy (Convention on Biological Diversity n.d.; Learning the Land n.d.). A key element of some Indigenous knowledge systems is using different ways of knowing through collaboration, including Two-Eyed Seeing or *Etuaptmumk* in Mi'kmaq knowledge systems (Bartlett et al. 2012). Incorporation of Indigenous knowledge systems ensures Indigenous leadership and self-determination in One Health solutions to specific challenges; it also increases the impact by applying culturally and environmentally relevant knowledge that is absent or sparse in more Eurocentric approaches to One Health.

One Indigenous approach to One Health, outlined by Joe Copper Jack, has been applied to key activities in land planning, culture, and education in Yukon (One Health Concept Box 1). It is essential that these activities begin with (1) relationship building and (2) the implementation of traditional

Box 1. One Health Concept Box.

Beyond One Health for Indigenous-guided recovery: The Land and Peoples Relationship Model

Joe Copper Jack

Knowledge collaboration is essential to One Health

I use the metaphor of a stream when talking about knowledge collaboration: Traditional knowledge (TK) on one side, Western knowledge (WK) on the other. The knowledges regard and respect each other but do not necessarily meet. If you take away one knowledge system, you get a less healthy stream. We need both stream banks, both ways of knowing. We need to keep both banks healthy, prevent them from eroding. The concept of One Health may be new to Western knowledge systems, but the interdependence of people, other animals, and land, as well as the



Box 1. (continued)

knowledge that the health of other animals and the health of the land is tied to our own, is inherent to most if not all Indigenous knowledge systems (Hueffer et al. 2019; Jack et al. 2020). It is not 'natural' to talk about land and people without each other or the health of one without the health of the other (Fig. 2).

Yukon First Nations' Long-Ago Peoples have always defined themselves as being part of nature and as beings sent here by the Creator to care for Mother Earth. Their key laws centered around the principles of Respect, Care, and Share, which were treated equally and used in combination with other natural laws. Respect is the law applied to all other natural laws. Long-Ago Peoples' laws are applied internally first, and then to others, moving outwards into the broader worldview. For instance, Long-Ago Peoples' laws apply to self, immediate family members, Clan, community, Nation, pets, dwellers, plants, land, water, air, and the universe. Respect is both the greatest consideration given to life and everything created by the Creator. Care is taking care of the land and each other and is the responsibility of all peoples. Share is the passing down and sharing of knowledge openly and in a respectful manner.

Western scientists are beginning to realize the importance of these laws. For example, Arctic researchers Kutz and Tomaselli (2019) assert, "In many ways, Indigenous knowledge provides an ideal example of the 'One Health' approach, in which animals and the complexities of their environment, including the human element, are considered simultaneously." British Columbiabased biologist Eric Balke says, "Natural ecosystems are infrastructure" (Ligeti 2020), adding that many scientists are now talking about "nature-based solutions."

Long-Ago Peoples' approach to their relationship with and care of the land included the perspectives of all affected parties, such as future generations, non-human relations, and land and waters, in planning and decision-making. Key to this approach is the No-Voice perspective, the idea that the views of future generations, non-human relations, and land and water are considered in all decisions with the potential to affect them, either now or in the future.







Box 1. (continued)

The COVID-19 pandemic has reasserted the need for fundamental and monumental change in relationships between human beings and other living entities. The land relationship is an integral part of this recovery. Indigenous Peoples have existed in healthy relationships with land for generations and continue to do so. Care, Share, Respect are our laws for all things created by the Creator.

As a land planner in the Yukon, I promote the collaboration of traditional and Western ways for better planning. Likewise, traditional and Western ways can be used together for One Health (Montesanti and Thurston 2015). Places with co-management have better outcomes for land health. Healthy land can be thought of as an essential service (Copper Jack and Nowak 2020).

The Land and Peoples Relationship Model

The Land and Peoples Relationship Model is a collaborative knowledge-building process that respects both the ways of Yukon First Nations' Long-Ago Peoples and Western knowledge. The model attempts to rebuild equal respect between the land and people, knowing that reconciliation cannot happen if people continue to view themselves as superior to nature and life. The model also aims to rebuild respect between people, where no knowledge system, gender, or group is superior to another.

Collaborative knowledge-building is a process by which participants reach favourable conclusions through the sharing and exchange of knowledge. Participants are asked to show the greatest respect possible during the planning and decision-making stages. The model uses the three key laws (Respect, Care, and Share) combined with two decision-making tools (No-Voice and Knowledge Stream Tree) that include affected parties' viewpoints and long-ago knowledge.

The model includes "those with no voice" in all discussions and decisions made at the roundtable, and their presence is represented with a sign or symbol. Participants are asked to contribute what they feel represents the No-Voice reaction to the issue at hand. The No-Voice reactions are part of the information that is assessed in decision-making. In the event of a stand-off on a particular issue, the No-Voice contribution become a critical factor in the final decision.

In this way, the model guides, directs, and balances the collaborative planning process. The crux of the model is how respect is shown among participants within the planning and decision-making processes. The roundtable experts function as a neutral body focused solely on resolving issues, based on relevancy and usefulness. The model also describes a sacred space.

Rules of engagement

The purpose of the model is to allow issues to be resolved through collaborative planning and consensus building. It is important to recognize and respect that some people communicate through storytelling and animation, while others verbalize and record. Participants of the round-table are responsible for developing their rules of engagement, which include the following requirements:

- 1. Show respect for each other, affected parties, and the land;
- 2. Feel as much as you think;
- 3. Listen to understand what is being said;



Box 1. (continued)

- 4. Clarify what you say and hear; and
- 5. Have patience.

The Knowledge Stream Tree and No-Voice for One Health

The COVID-19 pandemic has wrought significant disruption to health and well-being and will continue to impact future generations through a significant health, environmental, and economic debt. The coronavirus pandemic may also represent the first of many. The SARS-CoV-2 virus existed in balance with its likely host, the bat, until humans intervened to facilitate spillover and spread through activities such as intense global travel. To mitigate future pandemics, we must strive to restore balance through reciprocal care of the land and the plant and animal species it carries. Re-establishing the balance requires an understanding of what constitutes balance and how it can be achieved.

In addition to collaboration, openness to seeing things from a new perspective is an important aspect of land stewardship and the One Health approach. Being open includes seeing from each other's points of view and from the perspective of the land and the animals that inhabit it; what are they saying to us? This openness changes how we understand and feel about those with No-Voice and how they interact, for example, the forest, the bats, and the virus. An open, accepting viewpoint reorients our frames of reference and may lead to novel and more effective avenues of study and implementation.

As well as being based on the principles of Respect, Care, and Share, the Land and Peoples Relationship Model includes the Knowledge Stream Tree (Fig. 2) and the No-Voice. These elements are intrinsically tied together and components cannot be extracted or considered in isolation without losing meaning. Much like a snowshoe that depends on well-crafted bindings, a frame, and meshing to function effectively, one cannot think about the model without all these interdependent parts (Fig. 3).

We propose the following as a means of collaboration and implementation of the Knowledge Stream Tree:



Fig. 3. Interdependent parts of the Land and Peoples Relationship Model.



Box 1. (concluded)

Establish and sustain a Circle of Traditional Knowledge Holders and experts for consultation and knowledge sharing. We propose close and collaborative efforts between federal entities, independent scientists, and traditional knowledge holders to address priority questions using an Indigenous One Health approach. This collaboration begins with a relationship-building phase anchored in humility and mutual respect. This work is possible under knowledge agreements and with the consent of the Elders to share their knowledge for this mutual purpose.

Experts at a roundtable are independent individuals with adequate knowledge who are at arm's length from the government. Content knowledge varies depending on the questions and challenges at hand, so this group may be fluid depending on theme, geographic region, host species, or peoples involved. Fairness and truthfulness guide discussions to reach mutually beneficial paths forward that are useful, relevant, and concrete.

Indigenous knowledge systems and traditional knowledge keepers are critical and essential to effective planning and implementation of projects and interventions aiming to address questions and challenges around zoonoses using a One Health lens. Inclusion puts Indigenous knowledge sharing into action in a participatory and translational manner, enabling ongoing collaboration as challenges arise and providing opportunities for collective post-implementation sustainability and evaluation.

Sustainability is essential and required. Short-term visions and solutions have not met the needs of future generations; we need to maintain a 1,000-year-long view since the implications of decisions made now will have long-term effects. This focus on sustainability requires significant investments now and for generations to come.

knowledge protocols—processes that must be respected. Extracting Indigenous knowledge and using it out of context for convenience or other purposes is harmful and unacceptable. While Western knowledge strives for endpoints independent of relationships, Indigenous knowledge systems revolve around relationships. Relationship building and protocols allow trust and understanding to be established and to evolve over time.

The current reality and health challenges

Avian and swine influenza viruses, human immunodeficiency virus (HIV), Zika virus, SARS-CoV-2, monkeypox, antimicrobial resistance, climate change, pollution, biodiversity loss, economic collapse, and inequality—none of these challenges are independent of the others. Worsening climate change contributes to biodiversity loss, the emergence of new pandemic viruses threatens economies, and responses to disease emergence exacerbate inequities and create vast amounts of waste that pollute waterways and landfills, further threatening biodiversity. In most cases, responsible agencies react after the harm has occurred and work within their own disciplinary silos and mandates to control the problem as best as they can. Despite lessons learned from every new pathogen emergence, we continue to be surprised each time a new threat appears. Even with investments in understanding the emergence and spread of highly pathogenic avian influenza virus, Ebola virus, Zika virus, and SARS-CoV—and even with greater investments in disease control and prevention—we were still caught off guard by the appearance of SARS-CoV-2 in 2019.

Humans are only one of an estimated 7.8 million animal species on earth (Mora et al. 2011). As members of the animal kingdom, humans are just as susceptible to infectious agents as any other animal



species. The likelihood of infection and associated negative impacts of disease depend on health determinants— biological, environmental, social, and economic factors that determine whether a person (or animal) has the resources to stay healthy (World Health Organization 2017a). Although a determinants-of-health approach is less commonly applied to non-human species, several determinants are shared by all species, such as the necessities of daily living (access to food, water, and habitat). A determinants-of-health model is useful for health planning and policy development for different species (Wittrock et al. 2019). However, studying human health and disease separately from animal and ecosystem health and disease is not only reductionist, but also undermines the survival of the human species.

Pathogens differ in their ability to adapt to new host species. The World Health Organization recognizes 200 zoonotic agents, but many more agents with zoonotic potential are discovered every year as genomic technology and molecular biology improve and as conditions such as human encroachment create new opportunities for zoonotic and reverse zoonotic transmission to occur (Grange et al. 2021; Plowright et al. 2021). Disease agents like SARS-CoV-2 are highly adaptable and very difficult to eradicate; agents such as *Mycobacterium bovis*, are linked to food security, and thus introduce other challenges (One Health Case Study 1). The fact that only two infectious agents—smallpox and rinderpest—have been eradicated underscores how difficult it is to control infections, particularly zoonoses. Another aspect of zoonotic disease is that it may cause chronic sequelae in humans and other animal species. For example, *Echinococcus granulosus* (a parasite with life stages in wild carnivores and deer species) can cause protracted liver and lung disease in humans, and SARS-CoV-2 is associated with post-COVID-19 conditions, or 'long-COVID'.

Because zoonoses are challenging to control, greater efforts are needed to prevent the establishment of pathogens in new hosts and to promote and maintain the health of all species and ecosystems and build resilience. Further, the health impacts of changing environmental and economic conditions are becoming increasingly urgent. Adding to current social and environmental stressors are the compounding pressures that are threatening the health of all communities, especially those most vulnerable. Consequently, an approach that recognizes the interdependence of health is needed to better prevent, respond to, and reduce health impacts today without compromising our ability to respond in the future (WHO 2021).

Case Study 1. One Health Case Study.

Mycobacterium bovis in cattle, badgers, deer, and cats

Scott Weese

Mycobacterium bovis is a bacterium that causes bovine tuberculosis (TB) and can also infect various other species. The World Health Organization estimated a burden of 147,000 new cases of zoonotic TB in people globally in 2016, with 12,500 deaths—recognizing that the disease is likely underdiagnosed (who.int/tb/zoonoticTB.pdf). The disease is transmitted to people most often through unpasteurized milk, but direct contact and aerosol transmission are also of concern for people exposed to infected animals.

While the focus of *M. bovis* is its ruminant reservoir, this bacterium can also be harboured and spread by other species, both domestic and wild. There can be complex and surprising transmission patterns. For example, in the United Kingdom, *M. bovis* is widespread in Eurasian badgers (*Meles meles*), complicating control of *M. bovis* in cattle (Clifton-Hadley et al. 1995;



Case Study 1. (concluded)

Corner et al. 2011). Unexpected bridges between wildlife, domestic animals, and humans can be encountered and companion animals such as cats are increasingly infected through contact with wildlife (Gunn-Moore 2014). Unexpected routes of exposure have also been encountered, such as a cluster of infections in pet cats that were fed a commercial raw-meat diet made of venison (O'Halloran et al. 2021). While apparently rare, transmission from cats to humans has been documented (O'Connor et al. 2019). Risks for direct human exposure and spread of *M. bovis* between regions and to wildlife reservoirs can also be created through the widespread and poorly controlled international movement of companion animals, as shown through importation of *M. bovis* into Germany and Italy from cats originating in Ukraine (Attig et al. 2019; Černá et al. 2019). The presence of this bacterium in hunted wildlife also poses a risk to hunters and highlights the need for a One Health approach to hunter education (Wilkins et al. 2003). Therefore, control of this important human and animal pathogen is complicated by its presence in food animals, companion animals, and wildlife; its potential transmission between regions through movement of people or animals; and its interconnected but poorly understood pathways of transmission.

One Health solutions

To get ahead of the ongoing, extraordinary social and environmental changes that are expected, new partnerships, tools, and approaches are urgently needed. One Health offers a pathway towards transformative change. One Health is evolving by enabling all species, places, and generations to achieve their full health potential: Optimal health for all—today and tomorrow and around the world.

One Health can be viewed as a continuum of activities intended to prevent, mitigate, or solve problems occurring where environmental systems and animals, including humans, intersect. The traditional topics of focus have been emerging zoonoses, antimicrobial resistance, and food safety, but expectations for One Health are changing to address other persistent and complex issues including climate change, sustainable development, environmental pollution, and food insecurity (Zinsstag et al. 2011). Behind these changing expectations of One Health, and other holistic approaches to health (e.g., EcoHealth, Planetary Health, Global Health), is a growing recognition that global 21st century pressures (climate change, poverty, biodiversity loss, among many others) are root causes of the traditional problems that One Health has addressed (antimicrobial resistance and zoonoses). One Health needs to address today's challenges and to prepare for future health threats through building community resilience and ecosystem stability. One Health is about the health of animals (including humans), plants, and ecosystems and the interdependencies among them. It is also about filling an increasingly urgent need to change how we do things, to mobilize and co-produce knowledge, to "do better," and to inspire positive change across society in a collaborative and cooperative manner.

A One Health approach is adaptable to a wide range of contexts and purposes including emergency responses to current threats, preventing emerging threats, and preparing and adapting to ongoing, persistent, and future challenges. As an approach, One Health uses methods and tools already developed and in use across different sectors and disciplines. Indigenous knowledge systems, among others, have long recognized the interdependence of all things and the critical importance of balance among them. One Health practitioners and advocates are striving to bring tools and methods together in novel ways and to facilitate conversations between sectors and knowledge holders that do not typically engage with each other. Sharing information and perspectives leads not only to more timely, complete, and accurate information but also to new opportunities for innovation.



The One Health concept underscores that health is the result of the interconnections among humans, other animals, plants, and ecosystems. While the idea is attractive and relatively easy to grasp, practicing One Health can be challenging. The operationalization of One Health requires strong governance, shared responsibility by all sectors and individuals involved, and a commitment to collaboration across sectors that do not always view things the same way or use the same vocabulary or methods, but that have a shared purpose. The siloed infrastructure of government globally, nationally, provincially, and locally is difficult to dismantle, making successful One Health programs and projects challenging to initiate and sustain (Rüegg et al. 2017).

As a zoonotic agent, SARS-CoV-2 is precisely the type of problem to which a One Health approach has been applied. Recent focus has been on discovering viral origins and exploring potential pathways of introduction and mechanisms of transmission and spread of zoonoses (e.g., yellow fever and avian influenza viruses) (Kelly et al. 2020; Mackenzie et al. 2014). However, little emphasis has been placed on identifying key leverage points that could reduce virus spillover in the future and even less on how to reduce the impacts of the inevitable emergence of such viruses. Moreover, most surveillance efforts have focused on human infections, with very little interest or investment in monitoring spread to domestic and wild animal species. However, COVID-19 has shifted the conversation due to the scale and inequitable distribution of the impacts associated with (1) infection and disease and (2) unintended negative consequences of prevention and control measures. The critical yet often indirect connections among all living things, ecosystems, and societies have been highlighted, and calls are being made for a radical change to our approach (Bates et al. 2021; Leach et al. 2021; Thoradeniya and Jayasinghe 2021).

The COVID-19 pandemic, climate change, animal health, food systems, global economy, and biodiversity loss are no longer seen as completely independent issues. Recognition of these connections is changing our expectations for what One Health can offer and where it can be applied. One Health is now being called upon to help prevent future viral emergence and to enable multidisciplinary collaboration to help reduce the impact of future pandemics. If these expectations are to be met, the highest levels of government need to commit to One Health. Practitioners of One Health will also need a new tool kit that includes innovative partnerships, different types of knowledge and expertise, and novel methods.

Although One Health is now globally recognized as a concept and an approach to address environmental and health challenges of the 21st century, there is an urgent need for more and better research on how to practice One Health, to learn from past successes and failures, and to adapt proven strategies to new settings and circumstances. Creating this pathway will require commitment to One Health and a global paradigm shift that promotes health and resilience over economic growth and power.

One Health in practice

Investment is needed to support the development of new tools and forums for respectful discussion and engagement, including with marginalized populations, and new mechanisms to measure health and success, beginning by determining what defines One Health success.

As the traditional focus of One Health projects, infectious diseases such as COVID-19 can be used as a springboard to launch new initiatives. Our shared experiences with SARS-CoV-2 have many people involved in One Health asking not only how to prevent the next pandemic but also how to reduce the impacts while working to build resilient communities and sustainable policies and practices. Participatory methods and a One Health approach are also relevant to the prevention, surveillance, and control of "non communicable diseases," which can be the result of air pollution, chemicals, or heavy metals polluting environments and affecting the health of all living beings.

17



To provide a picture of some of the programs and institutions working on topics related to One Health, a network analysis is shown in Figs. 4 and 5 in this section. This network analysis was not exhaustive, as it was not possible to include every program and institution within the area of One Health. However, this program mapping represents a useful starting point.

In Fig. 4, the programs and institutions are mapped based on their topic of focus and colour coded by type of institution. The figure includes international and Canadian institutions that focus on one or more topics within the concept of One Health. Each institution is linked to nodes representing different One Health topics (e.g., food safety, trade, or animal health). Central topics are those that a high number of programs and institutions address: One Health, Human Health, Emerging Infectious Disease, and Animal Health, followed by Environmental Health. These topics are those that One Health has historically used to understand and respond to zoonoses. Other topics that are less central in the figure such as Social Determinants of Health represent topics that are newer additions to One Health.

In Fig. 5, programs and institutions are organized based on their centrality, and the more central organizations are represented by larger squares. In this network analysis, centrality is based on the number of other programs/institutions to which each organization is connected.

The COVID-19 pandemic and climate change are creating new urgency and accelerating longstanding intentions to ensure that the steps taken today to protect well-being are equitable and sustainable so that future generations, other species, and ecosystems can also be healthy. One Health can be a pathway to health security by connecting systems and programs for healthcare and surveillance across species and by providing a mechanism to recognize interdependencies and support reciprocal care for health and our shared future.



Fig. 4. Network analysis by type of institution (black circle = intergovernmental, pale blue circle = governmental, pink circle = academia, green circle = networks, dark blue circle = NGO/NPO); white boxes represent different One Health topics. See supplementary material.

Mubareka et al.





Fig. 5. Institutions linked by topics to show centrality. See supplementary material.

Interconnectedness, value, reciprocal care, multi- and inter-disciplinarity and inclusion underpin the One Health approach, which can be used to address multifaceted challenges such as emerging and zoonotic infectious diseases. These interrelated facets are depicted in Fig. 1 of the Executive Summary and include elements of strategy and governance, operations and technical leadership, equity, and education and research. This framework serves as the foundation for the sections and recommendations that follow, beginning with recommendations addressing an overarching national strategy for One Health in Canada.

Recommendations

Implement a Canadian One Health Action Plan with supporting governance structures and executive functions. Urgent gaps related to the COVID-19 pandemic must be addressed at the highest level of government; these efforts must be leveraged for a One Health approach to all emerging zoonoses through a One Health Council. The Council must include experts and representatives from all relevant academic disciplines and ministries of the Government of Canada, as well as key non-governmental partners. The Council should be tasked with examining the policies, programs, and financial and legislative support of agencies, organizations, and institutions related to One Health and guide implementation of a One Health Action Plan through respective ministries and partners. Reporting on key activities will be essential to ensure accountability.

To ensure One Health priorities are met, a Special Advisor on One Health must be appointed to one or more key ministries overseeing health, which may include human, other animal, and environmental/climate health; this individual would be external to the government and have a key role in a One Health Council. One Health must also be tied to Canadian foreign policy. To promote both national and global health and security, Canada must demonstrate leadership in One Health on the international stage.



Develop and implement an Indigenous Engagement and Knowledge Policy Framework for One Health. This work must be done at municipal, provincial, national, and international levels. First, Canada must address the impacts of colonialism on Indigenous Peoples' health and relationship with the land. Land degradation and cultural genocide are tied to environmental dispossession, impeding the ability of First Nations, Inuit, and Métis Peoples to observe early signs of emerging zoonoses and to protect themselves and others from disease. Important tools such as Other Effective Conservation Measures, Indigenous Protected and Conserved Areas, and Indigenous-led monitoring activities should be included in an Indigenous framework for One Health. Given Canada's commitment to upholding the United Nations Declaration on the Rights of Indigenous Peoples, the One Health Action Plan for Canada must also address the Calls to Action of Canada's Truth and Reconciliation Commission.

3. Human drivers of pathogen emergence

Over recent decades, we have gained substantial knowledge about emerging infectious diseases (EIDs). We know that approximately 60% of EID first-time clusters or outbreaks that infect humans are zoonotic in origin, that more than 70% of these EIDs originate in wildlife, and that EIDs are increasing in frequency (Jones et al. 2008). EIDs include severe acute respiratory syndrome coronavirus (SARS-CoV and SARS-CoV-2), which most likely originated in horseshoe bats (genus *Rhinolophus*; Holmes et al. 2021; Latinne et al. 2020). Global hotspots for disease emergence have been identified, with areas of elevated risk including forested tropical regions experiencing land-use changes (Allen et al. 2017). We also know that RNA viruses may be more likely to emerge as EIDs than other types of pathogens (Woolhouse and Gowtage-Sequeria 2005). Understanding the risk associated with composites of host, pathogen, and environment allows surveillance programs to focus on high-risk scenarios to strengthen global capacity to detect and discover zoonotic viruses with pandemic potential (One Health Institute University of California Davis 2019). As a key step in pandemic preparedness, surveillance is vital (discussed in Section 6). However, given the complex and multifactorial drivers of pathogen emergence and spread, pathogen surveillance alone is insufficient to predict and prevent the next pandemic.

There are a wide number of underlying socioeconomic, environmental, and ecological factors that drive disease emergence (Jones et al. 2008). Twenty years ago, in 2001, the Committee on Emerging Microbial Threats to Health in the 21st Century identified, reviewed, and assessed the state of knowl-edge on factors in the emergence of infectious diseases. In their report, the committee examined 13 factors, all of which still apply today. These include key elements such as pathogen adaptation, host susceptibility, climate and ecosystems, demographics, socioeconomics and inequality, industrial and technical developments, behaviour (including travel), conflict, politics and intentional harm, among others (Smolinski et al. 2003).

Emergence at the human interface with other animals

Zoonotic disease emergence in humans is driven by human activities and behaviour that change human, other animal, and (or) vector interactions. Addressing how humans interact with other animals, including wildlife, is a key component of EID risk management and response (Watsa 2020). Decreased habitat availability, pollution, and climate change impact the health of wildlife and other animals, including humans (One Health Concept **Box 2**). Over the past 50 years, wild animal populations around the globe have declined by 60% on average (Grooten and Almond 2018) and 28% of assessed species are threatened with extinction (IUCN 2021). Ecosystems have been degraded, changing how different species interact and increasing the risk of exposure to novel pathogens. Prevention of EIDs will require us to tackle these underlying factors, including climate change, ecosystem degradation, and land-use change.



We know that ecosystem and land-use change can have dramatic impacts on pathogen transmission patterns. For example, in Malaysia, the development of large-scale swine production facilities near mango orchards where fruit bats roosted is believed to be a driver of Nipah virus transmission from fruit bat reservoirs to pigs, with spillover into humans (Pulliam et al. 2012). Although there are many cases in which land-use change is associated with increased disease transmission, this is not always clear, leading Gottdenker et al. (2014) to suggest that "there is still uncertainty regarding the direction, magnitude, and mechanisms of anthropogenic disturbances on infectious disease transmission and persistence." More research is required to fully understand the impacts of changing landscapes on disease emergence; however, land-use change should be considered as a key risk factor.

Box 2. One Health Concept Box.

Advancing forest health as part of One Health

Katarzyna Nowak, Katarzyna Simonienko, and Bogdan Jaroszewicz

The United Nations 5th Global Biodiversity Outlook has defined eight major transitions needed to stop the decline of nature (Secretariat of the Convention on Biological Diversity 2020). Two of these are "the land and forests transition" and "the biodiversity-inclusive One Health transition." These transitions are inextricably linked in Canada, which harbours more than a quarter of the world's remaining boreal forest. According to the Center for International Forestry Research (CIFOR), connections between forests and One Health require strengthening (CIFOR 2020). We focus here on the benefits of healthy forests to One Health, primary pandemic prevention, and pandemic recovery.

Forests enhance health by providing services such as clean air and cooling effects through the absorption of carbon dioxide and provision of shade from solar radiation. Intact forests are nature-based solutions to slowing down climate warming. Forest biodiversity matters because more biodiverse forest stands are superior at reducing air pollution, diluting disease vectors, and providing people and other animals with plant-derived foods, medicines, and herbs (Wertz-Kanounnikoff and Rodina 2020). Forests also provide therapy that improves our physical and mental well-being and assures high restorativeness (through the landscape's ability to renew the cognitive capacities of forest visitors) (Kortmann et al. 2021; Simonienko 2021).

Being in a forest environment reduces both physiological stress (heart rate, blood pressure, cortisol, and adrenaline levels) and psychological stress (Engemann et al. 2019). A forest environment has been shown to be particularly effective at reducing stress in people with lower socioeconomic status (Marselle et al. 2020). Exposure to the forest environment is associated with greater resistance to future stressors and faster regeneration after a stressful experience, suggesting that forests are important in the prevention of mental and neurodegenerative diseases (Annerstedt et al. 2013). Being in the forest may also strengthen the immune system (Li et al. 2006). People's reliance on access to nature as a source of health during the COVID-19 pandemic was a worldwide phenomenon (Naomi 2020; Weinbrenner et al. 2021).

A challenge related to the mass extinction of species, disappearance of wild areas, and reduction of biodiversity is the phenomenon of negative feedback called the extinction of experience. When wilderness recedes and nature declines, encounters between humans and other free-living animals and plants become less frequent, depriving humans of stimulation. Nature becomes boring, interest in it dwindles, and consequently concern for its protection declines, resulting in further



Box 2. (concluded)

reductions in biodiversity and fewer opportunities to experience nature outside of ourselves. People who know less and experience less also care and act less (Miller 2005).

Mental health and environmental stewardship are closely related and connected to human economies (Buckley et al. 2019). That "the land is a healer" is well-known among Indigenous knowledge holders and societies (Redvers 2020). Canada is well-positioned to support meaning-ful partnerships between Indigenous and Western scientists and knowledge holders in ways that help realize One Health and inform One Health programs around the world, including through forest ecosystem scale thinking.

More than 80% of the world's forests are degraded (Watson et al. 2018). Deforested areas and forest margins have higher risks of disease and a higher likelihood of spillover events (Dobson et al. 2020). For example, in Peru, mosquito bites are significantly more frequent in deforested areas, and in Brazil, the incidence of malaria increases with deforestation. Disease is prevalent in these regions because land clearing often creates pools of stagnant water and because human-induced ecological changes reduce mosquito diversity, favouring those species that transmit malaria (Robbins 2016). Deforestation also contributes to the spread of waterborne pathogens such as giardiasis, cryptosporidiosis, and microsporidiosis through increased contact between people, domestic, and wild animals (Lallo 2012). Research from Cambodia shows that forest loss is associated with an increase in acute respiratory infection and diarrhea (Pienkowski et al. 2017). In fragmented woodlots, where there are fewer predators and competitors (i.e., where food webs are disrupted), there is a higher density of potential disease vectors such as white-footed mice (Ostfeld and Keesing 2000). In areas where small mammal diversity is higher, Lyme disease incidence falls, evidence that biodiversity can buffer us against disease (Ostfeld and Keesing 2000).

Fortunately, there is growing interest in how human health and well-being are linked to biodiversity, nature stewardship, and sustainable development in the public, scientific, and policy spheres (Naeem et al. 2016). A powerful example is the Arramat Project (arramatproject.org/), which supports Indigenous Peoples' whole-environment approaches to the health and well-being of their communities. It is a vital movement to foster transdisciplinary and transboundary cooperation and hybrid knowledge collaboration at the nexus of human health and healthy natural ecosystems, including forests. As forests can act as fortifiers against disease and against vectors of disease and environmental pollutants, they can be "at the heart of a green recovery", and better integrated into One Health approaches (Sen 2020, p. 1; CIFOR 2020).

The wildlife trade also provides opportunities for disease transmission that may affect the health of humans, domestic animals, wildlife, and ecosystems (Karesh et al. 2005). For example, monkeypox emerged in the United States as a consequence of the wildlife pet trade in 2003. Human exposure resulting in 47 confirmed or probable cases in six states was traced to contact with pet prairie dogs that had been co-housed with monkeypox virus-infected rodents imported from Ghana (Prevention 2003). Currently, a global outbreak of monkeypox is being sustained through human-to-human transmission. This serves as a stark reminder of the critical importance of supporting regional efforts for control in endemic regions, and of investing in global health and security. The wildlife trade has been investigated as one of the key factors leading to the emergence of SARS in 2003 and SARS-CoV-2 in 2019 (Mallapaty 2020; World Animal Protection n.d.). International regulation of the legal wildlife trade falls under the Convention on International Trade in Endangered Species of Wild Fauna



and Flora (CITES). Data from imports and exports falling under this agreement reveal that the legal wildlife trade is in the range of 11.5 million wild animals from 1,316 species over a five-year period (2012–16). The United States is the greatest consumer of legal wildlife (Can Ö et al. 2019). The disease risks and conservation concerns associated with the wildlife trade (both legal and illegal) have been well-documented and the COVID-19 pandemic has renewed calls to ban the global wildlife trade (Karesh et al. 2005; Roe and Lee 2021). However, some researchers have been urging caution as wildlife trade bans may have substantial unintended consequences, including socioeconomic impacts on local communities and an increase in the illegal wildlife trade (Roe and Lee 2021; Federal Provincial and Territorial Governments of Canada and Canadian Wildlife Health Cooperative 2018). These issues need to be considered from a One Health perspective, including the assessment of potential unintended consequences such as health impacts on animals from displacement and infectious diseases.

Sustainable development goals

Social determinants of health are also key drivers of pathogen emergence, thus underscoring the relevance of the Sustainable Development Goals (SDGs). The SDGs provide a critical framework to help improve equity, resilience, and sustainability around the world, recognizing the essential linkages among human, other animal, plant, and ecosystem health. Inputs and activities to achieve SDGs directly link with human health (e.g., clean water and sanitation, good health, well-being, zero hunger, and no poverty) and One Health (e.g., climate action, life below water, and life on land). Actions to meet the SDGs and improve the overall health of all animals, including humans, and ecosystems also offer solutions for challenges related to zoonoses. For example, interventions to improve access to water, sanitation, and hygiene can contribute to lower disease rates, enabling marginalized individuals and households more opportunity for employment and better livelihoods. Multiple calls have been made to develop multi-pronged, comprehensive approaches to complex health challenges of the 21st century. This type of health promotion approach would recognize the many factors interacting in different ways to drive emergence of zoonotic diseases, antimicrobial resistance, and climate change, among many other challenges. Many of these root causes are also addressed by actions taken to meet health and equity targets set as part of the global SDG agenda.

Pan-Canadian approach to wildlife health

Moving from our current reactive approach to wildlife health and emerging disease issues to a sustainable, proactive approach will improve our ability to quickly detect emerging threats, promote collaboration, anticipate problems, and sustain healthy populations of all species, including humans. The Pan-Canadian Approach to Wildlife Health (PCAWH), approved in the spring of 2018 by all federal, provincial, and territorial ministers responsible for biodiversity and conservation, promotes a sustained, collaborative One Health approach to wildlife health (Federal, Provincial and Territorial Governments of Canada and Canadian Wildlife Health Cooperative 2018; Stephen 2019). A key goal of PCAWH is to strengthen "Canada's capacity to identify and reduce wildlife health threats that put conservation, public health, or economic and cultural opportunities at risk" (Stephen 2019). Although approved by all levels of government, PCAWH has yet to be implemented, a critical step to ensure that Canada has a sustained, proactive One Health approach to wildlife health.

Recommendations

Develop and implement a One Health Action Plan for Canada to identify and mitigate drivers of zoonotic pathogen spillover. Mitigation of new spillover events is dependent on directly and effectively addressing predisposing conditions, beginning with reciprocal care of land and water. New tools and approaches are urgently needed to address underlying drivers and factors sustaining interspecies



zoonotic disease transmission. There are immediate actions to be taken, which include developing a One Health Action plan that prioritizes identification and mitigation of drivers for infectious diseases spillover. Key drivers of pathogen spillover, endemicity, and spread are not well understood in Canada. Addressing the root causes of emerging zoonotic diseases will support efforts toward the United Nation's Sustainable Development Goals and advance Canada's leadership on a global scale.

Urgently implement the Pan-Canadian Approach to Wildlife Health. The PCAWH has been approved by the federal government and provincial and territorial partners to close gaps among existing programs and protect wildlife health, particularly during this time of accelerating environmental change. Clear benefits to ecological, human, and other animal health are gained by ensuring health and biodiversity among wildlife. With a focus on threat reduction, program and policy development, and coordination of services, key activities must concentrate on generating health intelligence, responsible management, innovation, and effective governance. Considering the spillover of SARS-CoV-2 into wildlife populations, and the circulation of monkeypox in humans, implementing PCAWH is now an even more pressing matter.

4. Surveillance as a critical tool for response and preparedness

The emergence of novel pathogens, including those with pandemic potential, cannot be completely prevented. Therefore, there is a need both to respond to new challenges quickly and effectively and to reduce impact of emerging infectious diseases (EIDs). Underpinning the response to EIDs is the availability and use of reliable information. Accurate and timely understanding of a situation is critical for the assessment of risk, development of interventions, effective communication, and situational awareness. As a result, surveillance is a core component of pandemic preparedness and response, and is used both proactively and reactively.

A broad term, surveillance encompasses a range of information gathering and assessment activities and includes dissemination of information, so action can be taken to control disease (Thrusfield 2005). Surveillance is a core component of emerging disease identification and control and allows us to: (1) identify and respond to new infectious disease challenges, (2) prevent or mitigate outbreaks, (3) implement pharmaceutical and non-pharmaceutical interventions, (4) guide targeted laboratory and field research, and (5) assess the impact of control measures. Surveillance is important in the context of rare, high-profile events (e.g., the SARS-CoV-2 pandemic), but it is also essential for responding to disease emergence occurring over longer time scales (e.g., the gradual expansion of tickborne disease ranges, the spread of antimicrobial resistance), highlighting the need for a robust, responsive, and comprehensive surveillance structure.

Within these broad aims of surveillance, there is a diverse toolbox that can be used. Active surveillance involves efforts to obtain specific information (e.g., field sampling of dead birds for avian influenza, genomic analysis of viral or bacterial pathogens), while passive surveillance involves the use of data available from other sources (e.g., analysis of clinical diagnostic laboratory data and reportable disease data). Each approach has inherent strengths and weaknesses, but both must be included and used in a coordinated manner. For example, passive surveillance can identify a reportable disease case, and then active surveillance can be used to follow up and check for that reportable disease in a population that would not otherwise have been investigated. Sentinel surveillance is an additional approach used selectively to discern pathogen epidemiology and risk in selected scenarios. For example, the Canadian Lyme Sentinel Network has conducted sentinel surveillance of ticks in seven provinces, establishing baselines for the abundance and prevalence of *Borrelia burgdoferi* (the etiologic agent of Lyme disease) and other tick-borne pathogens (Guillot et al. 2020).

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Many surveillance systems rely on laboratory data, which are best for providing information about known problems. Diseases or pathogens that are not readily identifiable using laboratory-based surveillance may be missed or identified late. In contrast, clinical or syndromic surveillance (e.g., mortality events in wild animals) can provide an early warning of unidentified and new potential threats. Although insensitive, syndromic surveillance is an important tool for identifying new issues that require further investigation, speeding initial detection of problems, and generating significant health intelligence when implemented and coordinated effectively (Dórea and Vial 2016).

Surveillance gaps and challenges

There is a pressing need for an action-oriented, comprehensive plan for One Health surveillance in Canada and for surveillance to be adaptable enough to respond to changes when needed. Key to accomplishing a suitable plan for surveillance is identifying some of the major gaps in current surveillance systems and recognizing the challenges inherent in establishing an ideal One Health surveillance system.

To address emerging zoonoses, One Health surveillance systems need to operate across a range of jurisdictions, and Canada participates in numerous international, national, provincial/territorial, regional, and sector-specific surveillance efforts. However, when one considers that One Health surveillance requires detailed information about diverse human, other animal, and environmental sources, the need for multifaceted and integrated surveillance is apparent. Despite some excellent surveillance efforts and programs (e.g., Canadian Integrated Program for Antimicrobial Resistance Surveillance and the Canadian Wildlife Health Cooperative) (Public Health Agency of Canada 2007), the scope, depth, and connectivity of surveillance efforts in Canada across the One Health spectrum is suboptimal. Optimal surveillance should be standardized, goal-oriented, transparent, comprehensive, adaptable, sustainable, have adequate surge capacity and be integrated within and across human, other animal, and environmental health sectors. It should also be informed by existing knowledge of biological determinants of transmission and disease. For example, surveillance for novel coronaviruses among animals would include advanced genomic sequencing methods and computational biology to examine key determinants of spillover risk and pathogenicity (Mercer and Salit 2021) and biological characterization to assess risk to health.

Data are only useful if they are used. Inadequate effort or ability to access and translate data into action, particularly in real time, can hinder surveillance systems. Some degree of delay is inherent in the surveillance process as time is required to gather, analyze, and transfer information, but when dealing with emerging issues, time lags diminish the value of surveillance as an early identification or intervention tool.

A One Health approach to surveillance necessarily involves integrating the surveillance activities of diverse specialists and stakeholders (One Health Case Study 2). In Canada, surveillance is performed by a wide range of individuals and groups, including governments (Indigenous, federal, provincial, territorial, and local), academic institutions, healthcare facilities for humans and other animals, professional networks, and private diagnostic laboratories. Within government, surveillance is often performed across multiple departments. This intersectionality highlights the complexity of the issues surveillance tries to address and the importance of intersectoral and interdisciplinary work, but it also creates potential barriers (e.g., timely and comprehensive information exchange), inefficiencies, duplications, and gaps.

Communication of surveillance activities is key and should be multidirectional and ongoing. Stakeholders and rights holders need to be included early in surveillance initiatives to ensure that



Case Study 2. One Health Case Study.

Community-led and collaborative surveillance in the Canadian Arctic

Susan Kutz

The communities of Ulukhaktok in Northwest Territories and Kugluktuk and Ekaluktutiak in Nunavut have come together to work with academic and government partners to conduct wildlife health surveillance. Concerns have been raised about the health of local caribou and muskoxen, which are important to these communities (Di Francesco et al. 2022; Hanke et al. 2022; Tomaselli et al. 2018a). To understand caribou and muskox ecology and the population trajectory, hunters' and trappers' organizations use on-the-ground surveillance, bringing together traditional and Western scientific knowledge. Hunters, subsistence harvesters, and guides are provided with sample collection kits, including material for data, tissue, and blood collection (Fig. 6). Hunting and trapping organizations or government monitors liaise with the harvesters, facilitating data recording and sample transfer for analyses after initial processing in the community. Key to establishing Inuit-specific relevant indicators for health and zoonotic disease are group interviews and other participatory methods (Tomaselli et al. 2018b). University partners analyze a range of health indicators related to nutrition and infectious diseases and examine host genetics. Key findings are first presented back to community partners for discussion and verification and then reported through plain language community reports, public presentations, and local social media, as well as co-authored publications. This work is also sustained through annual interviews to understand broader ecological and longer-term trends. Ongoing co-learning from local observation and laboratory analysis makes this approach exceptionally impactful to both scientific and Indigenous communities and facilitates the Indigenous voice in co-management. When relationships and trust are built through ongoing and open communication, there are broad benefits, both at a regional level and for a wider potential community of practice.

needs are met, to identify resources to support surveillance, to identify potential synergies, and to facilitate rapid and effective use of surveillance data. Communication between people involved in surveillance and stakeholders must continue throughout, to ensure that surveillance data are properly used and that emerging issues are identified and acted upon.

How and when surveillance data are communicated is also important. Surveillance reporting should be as granular and timely as possible, but it is limited in some surveillance programs, as the time from data collection to release of results can be many years. This delay reduces or negates the applied use of surveillance data.

Good surveillance is designed to provide an appropriate reflection of the broader population. However, for reasons such as expense, logistics, or lack of knowledge, many surveillance systems collect data that are, in fact, based on specific sub-populations and do not generalize to broader populations. This introduces bias, which limits interpretation and conclusions (Lipsitch et al. 2015). For example, relying on case fatality rate (proportion of deaths among confirmed cases) data obtained from hospitals may lead to an overestimate of the overall case fatality rate of a disease that has a range of presentations, if only severe cases are hospitalized (Lipsitch et al. 2015). These biases can be overcome if they are recognized.

Animal health surveillance in Canada has largely focused on diseases that negatively impact agricultural production and create food safety issues, with less direct attention to broader animal health and welfare issues. Although foodborne and production-limiting diseases are of significant concern,

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Fig. 6. Community-led wildlife health surveillance sample collection kit, allowing ease of collection, transport, and storage.

they do not fully encompass all the risks to animals (especially companion and working animals) and non-foodborne zoonotic diseases. Improved integration of human and other animal clinical and diagnostic data could help to move animal health surveillance toward a One Health system.

Detection of naturally occurring diseases in humans and other animals through routine clinical and diagnostic activities may be the most effective and efficient early response to some threats; however, there are significant gaps in effective use of clinical diagnostic data. One example is *Echinococcus* in dogs (One Health Case Study 3).

At the transection of human and other animal health, pathogens with a wide range of hosts cause many major diseases of public health importance, introducing complex transmission dynamics.

Case Study 3. One Health Case Study.

One Health surveillance: Wild canids as sentinels for Echinococcus multilocularis

Jonathon Kotwa

Alveolar echinococcosis (AE) is a chronic infection caused by consuming larvae of *Echinococcus multilocularis* (tapeworm). In humans and dogs, AE is typically fatal when left untreated. In humans, AE is characterized by a lengthy clinical incubation period of 5–15 years, during which the larvae typically proliferate in the liver, behaving similarly to infiltrative hepatic neoplasia (liver cancer). *E. multilocularis* is usually maintained in a life cycle that involves two mammalian hosts. Wild canids (e.g., foxes and coyotes), dogs, and (less commonly) cats act as definitive hosts, and harbour adult parasites in the small intestine without apparent clinical disease. Wild rodents serve as intermediate hosts, developing AE and spreading the parasite to new definitive hosts when they are consumed. Humans and dogs can act as accidental (intermediate) hosts. Humans and dogs can develop AE when eggs of the parasite, shed by infected definitive hosts, are consumed (Fig. 7).







Fig. 7. (A. Banete and J. Kotwa). Echinococcus multilocularis life cycle.

Given the severity of AE, one important objective of surveillance for *E. multilocularis* is to ensure timely collection of data on the distribution of the parasite to identify areas of risk for human and dog health. AE is a rare diagnosis in both humans and dogs (Corsini et al. 2015; Deplazes et al. 2017). Canine AE is thought to occur primarily in areas with high prevalence among wild canid definitive hosts (Deplazes et al. 2017). As a result, dogs with AE likely represent poor sentinels for the above-mentioned surveillance objective, demonstrated by the following example. Since 2012, several cases of AE in dogs, lemurs, and a chipmunk were reported in the region surrounding the western shores of Lake Ontario (French et al. 2018; Oscos-Snowball et al. 2015; Pinard et al. 2019; Skelding et al. 2014; Turner et al. 2016). These cases were surprising since Ontario was considered to be free of E. multilocularis prior to the first report of canine AE in 2012. A subsequent survey of wild canids across Southern Ontario demonstrated E. multilocularis prevalence of 23%, and infection in wild canids was shown to be widely distributed across the western, central, and eastern regions of Southern Ontario, with a high prevalence hotspot surrounding the western shores of Lake Ontario (Kotwa et al. 2019). Although the occurrence of index cases of AE in animals signaled an underlying health issue and were important to the recognition of E. multilocularis emergence in Southern Ontario, the full extent of the problem was not understood. It was thought that E. multilocularis would be found mainly in the region where the animal cases of AE were diagnosed. However, six years after the first index case of canine AE was reported, in 2018, a dog from the Ottawa area with no known history of travel was diagnosed with AE (A. Peregrine, unpub. data). In the absence of the prevalence and distribution data obtained through wild canid sentinel surveillance of E. multilocularis, this finding would have been surprising, as all previous cases of canine AE were diagnosed several hundred kilometres away from the Ottawa region.

This complexity may pose considerable challenges in understanding certain pathogen systems, but a One Health approach provides opportunities to use a wide range of species for potential surveillance purposes.

Implementing a One Health surveillance system is undoubtedly a complex and costly endeavor and would require adequate long-term funding to cover surveillance of human health (acute care,



community care), other animal health (wildlife, food animals, companion animals), and the environment (air, soil, water). Funding would also be necessary to integrate these surveillance data into a One Health system and to develop the necessary expertise, infrastructure, and coordination. Although expensive, investing in effective and sustainable One Health surveillance programs would be less costly than responding to future disease emergences (see Section 5).

Recommendations

Expand and coordinate existing human, other animal, and environmental emerging pathogen and syndromic surveillance activities at provincial, territorial, and federal levels. These activities should be linked to academic and private sector surveillance efforts, human and other animal diagnostic testing, and other relevant sources of data (e.g., wastewater and other environmental testing). Overall, there must be better coordination of surveillance programs across the One Health spectrum, with designation of responsibility for ongoing cataloguing and communicating surveillance activities in Canada. Existing surveillance programs and groups should be coordinated to facilitate rapid and effective exchange of information. The programs should work together to reduce barriers to information exchange through data privacy and sharing agreements and to establish a rapid approach to information sharing, when needed. Initiatives should be funded to harmonize data collection and electronic data systems and facilitate efficient and rapid collection of data across the One Health spectrum. Also essential is centralized, consistent, curated, ongoing, and timely public and private reporting of selected surveillance activities, as well as coordinated, sustained, and adequate funding of existing and future surveillance activities for public health and academic partners. A companion animal disease surveillance network should be funded, and links should be established between academic and private veterinary facilities and diagnostic laboratories. This should have integrated communication and data sharing with human, wildlife, and food animal surveillance networks and work closely with a proposed United States Companion Animal Disease Surveillance Network. Data would be centralized and linked to data from surveillance activities outlined in the Pan-Canadian Approach to Wildlife Health and the Pan Canadian Action Plan on Antimicrobial Resistance, both of which have been developed and approved, but not yet implemented.

Establish Centres of Excellence in One Health to link teams of scientists, diagnosticians, practitioners, epidemiologists, and public health experts to action surveillance data and other relevant data sources. Surveillance data are useful only when transformed into health intelligence. This process requires contextual characterization of the pathogens from biological and epidemiological perspectives, which is essential to informing risk and impacts of emerging zoonotic pathogens. To assign risk based on the likelihood of spillover and potential severity of impact, this process requires coordinated and collaborative efforts among community practitioners, academic biomedical, human and other animal health scientists (including immunologists, virologists, and microbiologists), public health agencies, modellers, computational biologists, and genomic and clinical epidemiologists.

5. Crossing borders: Transboundary transmission, international trade, global health, and security

Since the onset of the COVID-19 pandemic, it has been said often and by many that "infectious diseases know no boundaries." The fact that this phrase has become cliché does not make it any less true. We live in an ever more-populous world, in which our planet's nearly 8 billion inhabitants increasingly interface with domestic and wild animals. This heightened interaction between humans and other animals increases the possibility that diseases of animal origin will spillover to humans, causing new infectious diseases with epidemic or pandemic potential. The extraordinary global mobility of both humans and animals significantly enhances the possibility of transboundary spread. Travel and transportation that once took months can now be accomplished in hours, thus steepening the



upward epidemiologic curve by rapidly enabling new and emerging pathogens to spread to vulnerable hosts in new jurisdictions. We must also confront serious threats posed both by the accidental release and the deliberate use of pathogens as biological weapons by terrorists or states. The breadth of these challenges requires a comprehensive One Health response, in which the skills, resources, and expertise of a multisectoral community are required to mitigate health security threats on a global scale.

A critical balance is maintained by important relationships and interdependencies among species. Human impact on rich, biodiverse regions provides opportunities for pathogen spillover from animals; thus, many emerging infectious disease events are zoonotic (Jones et al. 2008; Salyer et al. 2017). Throughout history, most significant international outbreaks and pandemics have animal origins. These outbreaks and pandemics include the Black Death (estimated 200 million deaths due to *Yersinia pestis*), the 1918-1920 influenza pandemic (25–50 million deaths due to H1N1 influenza virus), HIV, Rift Valley fever (One Health Case Study 4) and, more recently, high consequence coronaviruses (SARS-CoV, MERS-CoV, and SARS-CoV-2) (Acharya et al. 2021; DeLeo and Hinnebusch 2005). In addition, there are common but less well-recognized zoonotic pathogens bearing significant health impacts. For example, salmonellosis is estimated to cause 1.2 million human illnesses a year in the United States, resulting in 450 deaths. Although most of these infections are foodborne, roughly 11% can be attributed to animal exposure (Sharp and Hahn 2011). Close to 14% of all salmonellosis in the early 1970s were attributed to pet turtles; however, regulations on the sale of these animals have significantly decreased infections (Bosch et al. 2016). West Nile fever, influenza and bovine tuberculosis are further examples of diseases of animal origin that infect humans.

When examining infectious diseases through a One Health lens, we must appreciate that species spillover is not unidirectional; humans may also transmit pathogens to animals. Many examples exist,

Case Study 4. One Health Case Study.

Rift Valley Fever

Samira Mubareka

Rift Valley fever (RVF) is caused by Rift Valley fever virus, a phlebovirus first discovered in 1931. The RVF virus is endemic in Africa and parts of the Middle East, where it is transmitted to humans and ruminants (cattle, goats, and sheep) by *Culex* and *Aedes* mosquitoes. Humans may also become infected through direct contact with infected animals and animal products. Illness in humans is characterized by fever and headache and, less commonly, nausea, vomiting, abdominal pain, and diarrhea. Bleeding, miscarriage, or death occur in <10% of cases. In ruminants, infection is complicated by fetal malformations, abortion, and death, with a case fatality rate of 16%–18% among sheep and goats. The virus has a predilection for the liver (hepatotropic) and is associated with high viral loads and dissemination to other organ systems, such as the brain in severe cases. High levels of viremia (presence of virus in the blood) also contribute to viral transmission by enabling arthropod vector (mosquito) infection and spread. Disease control measures require a One Health approach that addresses all three host populations (human, ruminant, and mosquito vector) and includes public awareness, surveillance, and reporting for each host population; animal vaccination; biosecurity; vector control; and policies around animal movement and slaughtering.



Case Study 4. (continued)

Drivers and impact of Rift Valley fever

Large outbreaks of RVF have been described and associated with significant health and economic consequences. Given its threat to public health and safety, RVF is on the World Health Organization's list of priorities for research and development (R&D Blueprint) (World Health Organization, n.d.). Amplification of RVF has been attributed to industrialization and animal movement through international trade or internal displacement. In recent decades, the geographic range of RVF virus has expanded to previously Rift Valley fever-free areas, including Egypt (1977), Madagascar (1990), and the Arabian Peninsula (2000). Genomic epidemiology suggests common ancestry, underscoring the likelihood of undetected, smoldering inter-pandemic viral activity (Dar et al. 2013). Outbreaks are often triggered by rainfall, flooding, and other conditions, favouring mosquito population growth. Regional armed conflict has also played a role in driving RVF outbreaks both through human and other animal displacement and by compromising pathogen detection and control efforts (Fig. 8). For example, an atypical outbreak in Sudan occurred outside of the rainy season in 2019. One of the key drivers was thought to be the targeting of health professionals by military forces, impeding capacity to respond early in the outbreak (Ahmed et al. 2020). Animal exportation was also thought to play a significant role (Ahmed et al. 2020). RVF virus is a potential biothreat, thus epidemic activity may a) destabilize regional health and security, and b) increase the risk of spread to non-endemic areas.



Fig. 8. (A. Banete). Multiple invertebrate and vertebrate species involved in Rift Valley Fever virus transmission and infection, and potential drivers.



Case Study 4. (concluded)

A One Health approach to the control of RVF was instrumental in managing viral activity in East Africa through the establishment of a Global Disease Detection Division (now the Division of Global Health Protection) through collaborations between the United States Centers of Disease Control (CDC), CDC Kenya, the Kenya Medical Research Institute (KEMRI), and the Kenya Ministry of Health (Munyua et al. 2019). This approach involved building diagnostic and research capacity, including a biocontainment level 3 laboratory at KEMRI and formalizing inter-sectoral collaboration for outbreak management through the establishment of the Zoonotic Disease Unit with support from the United States Cooperative Biological Engagement Program of the Department of Defense and Biological Engagement Program of the Department of State. In addition, Kenya's Field Epidemiology and Laboratory Training Program (FELTP) was established for workforce development to support outbreak response and mitigation using a One Health approach. Gaps in One Health have been noted and continue to be addressed at a regional level through a 10-year Strategic Action Plan for health and environment interventions in Africa from 2019 to 2029, which is further supported by the International Livestock Research Institute, the Africa One Health University Network, and the Africa Centers for Disease Control and Prevention's One Health Program (Otu et al. 2021).

such as the transmission of influenza virus from humans to pigs during the 2009 influenza pandemic, and more recently, the transmission of SARS-CoV-2 to domestic, farmed, and wild animal species. Recent work in Canada and by the United States Department of Agriculture (USDA) has identified evidence of exposure to SARS-CoV-2 in white-tailed deer. This new information heightens awareness of the potential role wildlife may play in the epidemiology of the COVID-19 pandemic (Chandler et al. 2021; Kotwa et al. 2022; Pickering et al. in press). Could these animals establish a natural reservoir, or are they simply a dead-end host with no role in driving viral activity and impact? In 2020, numerous farmed minks in Europe were depopulated because of the SARS-CoV-2 outbreak, and surveillance efforts were put into place to understand the risk from mink farming. In Denmark, mink-derived mutations were identified in the SARS-CoV-2 genome and fears were raised following evidence of transmission of these variants back to humans and then subsequently between humans in the community (Fenollar et al. 2021; Hammer et al. 2021). Concerns about the potential for this new SARS-CoV-2 strain to escape vaccines under production ultimately contributed to the mass culling of mink in Denmark, significantly impacting the global mink industry. The ebb and flow of viral transmission between humans and other animals may drive adaptive viral evolution among potential hosts. It has therefore become critical to better understand this evolutionary plasticity and its implications.

External threats need internal solutions

The COVID-19 pandemic has challenged Canadians and the international community in many ways. It has offered difficult yet important lessons. To ensure the health and wellness of Canadians, we can no longer simply look inward and focus domestically. SARS-CoV-2 did not originate in Canada; like most novel pathogens, it emerged outside our borders. However, unlike MERS-CoV and Ebola virus, community transmission became rapidly established shortly after international spread occurred. The lesson is clear— to protect Canadians from emerging and reemerging disease threats, a sustainable program must be established through collaborative efforts, and supported by reliable government policy to make a global One Health approach an integral component of Canada's national and foreign policies.



Governments traditionally prioritize issues that require immediate, urgent responses and that capture the electorate's attention. Whether dealing with a pandemic, natural disasters, social programming, health care, or education issues, governments tend to focus on the "here and now" and to announce and deliver near-term responses that align with electoral cycles. Although it is understandable and important that governing parties invest political and financial capital to extinguish raging fires, too often too little attention is paid to investing in risk reduction that could have prevented the blaze from taking hold in the first place.

The prioritization of the here and now is evident when it comes to investments in One Health and global health security, as demonstrated by the staggering costs of the pandemic. Although the ultimate cost of responding to the pandemic for Canada and the world may never be known, preliminary estimates highlight unprecedented global financial and social damage. When factoring in direct expenditures, financial stimuli, lost productivity, trade disruption, healthcare, and mental health (both short and long-term), and the myriad of other resulting costs, the pandemic's price tag has no contemporary equivalent. One recent analysis concluded that the pandemic is costing Canada \$1.5 billion per day (Lorinc 2021). Globally, the International Monetary Fund (IMF) has projected that "the loss of global economic output between 2020 and 2025 as a consequence of the pandemic would total \$28 trillion and that 120 million jobs would be lost permanently in the tourism industry alone" (Jackson et al. 2021, p. 9). The cumulative economic impact from COVID-19 in the United States is estimated to be more than \$16 trillion, or approximately 90% of annual gross domestic product, a sum more than four times the economic impact of Great Recession, and more than double the monetary value for all the wars fought by the United States since 11 September 2001 (Global Health Security Agenda 2018). Investing in One Health initiatives will foster improved policies and actions from Canada and its global partners, but also bear cost savings that will economically benefit all Canadians and establish Canadian leadership on the global stage.

The ongoing COVID-19 pandemic—like so many outbreaks and infectious disease events in the past—offers important lessons for Canada and the international community. Perhaps the most critical is the imperative to adopt a global One Health approach to support national health-security interests. Although it is understandable and essential that the primary preoccupation of Canadian health professionals and scientists is infectious diseases already circulating within our borders, we must enhance our efforts and be proactive to prevent, detect, and respond to global biological threats—both known and unknown to Canada. While there are many critical differences between SARS-CoV, H1N1, and SARS-CoV-2, and most recently, highly pathogenic avian influenza virus (H5N1), one element of commonality among these pathogens is that each came to Canada from abroad (in 2003, 2009, 2020, and 2021, respectively). As these examples illustrate, it is impossible in the modern age to fully insulate our nation from a highly contagious, new, or emerging infectious disease that emerges anywhere on our interconnected planet. In this context, it is in Canada's direct national interest to engage and invest more in global health security.

While the concept of Global Health Security (GHS) has been around for several decades, it has gained momentum and adherents in recent years. A key milestone in the maturation of GHS was the creation in 2014 of the Global Health Security Agenda (GHSA), a group that now comprises some 70 countries, international organizations, non-government organizations, and private-sector companies that "have come together to achieve the vision of a world safe and secure from global health threats posed by infectious diseases" (Global Health Security Agenda 2018). Launched in the shadow of the devastating Ebola outbreak that ravaged West Africa in 2014–15, the GHSA recognizes the diverse range of health security threats posed by infectious diseases—whether naturally occurring, deliberate, or accidental—and underscores the need for "strong multisectoral engagement, including human and



animal health, agriculture, security, defense, law enforcement, development assistance, foreign affairs, research, and finance sectors, among others" (Global Health Security Agenda 2018).

Unfortunately, the GHSA has yet to achieve its full potential, in part because the commitment to multisectoral engagement and collaboration remains more aspirational than real. A key reason for this is the persistence of sector-specific silos, a backward- and inward-looking approach that is anathema to the One Health objective at the core of the GHSA. The reluctance of many traditional health partners to engage fully with GHS stakeholders from the defence, military, and security sectors is but one example of this unworkable approach (Carlin et al. 2021)

Canada is uniquely positioned to demonstrate the efficacy and utility of a multisectoral One Health approach. For decades, Canada has been at the forefront of several One Health efforts, with the Canadian Science Centre for Human and Animal Health in Winnipeg, home to both the Public Health Agency of Canada's (PHAC) National Microbiology Laboratory and the Canadian Food Inspection Agency's (CFIA) National Centre for Foreign Animal Disease, and the first facility in the world to house both human and animal containment level 4 labs in the same complex. The long-time collaborative relationship between PHAC and CFIA is complemented by their respective partnerships with Global Affairs Canada's Weapons Threat Reduction Program (WTRP). The WTRP, which is Canada's contribution to the G7-led Global Partnership Against the Spread of Weapons and Materials of Mass Destruction (GPWMD, n.d.), has been spearheading efforts for nearly two decades to strengthen Global Health Security and mitigate threats posed by the deliberate use of disease as a weapon.

Importantly, the WTRP and the broader Global Partnership community have long recognized that the tools best suited to combat deliberate disease are the same ones required for natural or accidental outbreaks, and they therefore have been proactive in engaging partners from the public and animal health sectors to tackle shared threats and priorities. The expertise and facilities resident in PHAC and CFIA, when combined with the financial resources and international networks of Global Affairs Canada's Weapons Threat Reduction Program, have proven a powerful combination, with the demonstrated ability to deliver tangible, mutually beneficial health-security results.

However, as novel threats emerge and pandemic-associated capacity shrinks, there are widening gaps in program support and coverage, with an urgent need to address these pre-emptively through effective and rapid coordination, prioritization, and mitigation. As the world recovers from the worst pandemic in a century, instruments for preparedness and response are being developed at the international level to incorporate lessons learned. Consideration is being given to revision of the International Health Regulations, which are currently devoid of a framework to prevent pathogen spillover into humans and a Pandemic Treaty to address prevention and response, which includes equitable vaccine distribution (Labonté et al. 2021). Canadian leadership in these and other international efforts is currently lacking—a significant concern from both domestic and global perspectives.

Recommendations

Position Canada as a leader in Global Health Security. Taking a leadership role includes contributing to global efforts—such as the proposed World Health Organization Pandemic Treaty and the proposed Global Health Threats Board (G20)—and enhancing ongoing contributions to the Coalition for Epidemic Innovations (CEPI).



Incorporate clear objectives for One Health into Canadian foreign policy. Doing so will position Canada as a global leader in One Health and a champion of efforts to ensure global health and security.

Establish a Global One Health Security Office. This office must be mandated both to monitor and mitigate all manner of external biological threats to Canada and to serve as a nexus for Canadian contributions to international efforts. Reporting or coordination mechanisms with the National Security Advisor, a One Health Council, and any Special Advisors to ministers are also needed.

6. Social inequities and determinants from a one health perspective

It is an unfortunate fact that our world is riddled with social inequities. In times of crisis, more than any other, these inequities are accentuated. The COVID-19 crisis is an accelerated version of the heightened inequities that other crises, such as the climate crisis, sustained on a more protracted timescale. The inequities related to exposure to and impacts of zoonoses, such as COVID-19, and climate issues share the same roots. Originating upstream, problems disproportionately affect people already suffering from pre-existing and systemic inequities.

The exacerbation of health inequities during the COVID-19 pandemic underscores the need for a comprehensive and inclusive approach, such as One Health. As with many of the approaches in the Ecosystem Approaches to Health (Bunch and Waltner-Toews 2021), One Health operates under a complex-systems framework. However, initial One Health initiatives did not have "equity ingrained as a core principle in its approach" (Harrison et al. 2019). Things are changing, however, and One Health practitioners are increasingly considering equity, or rather inequities (Friedson-Ridenour et al. 2019). For example, the Global 1 Health Network has four Research Enabling Platforms, one of which is ensuring equity in the COVID-19 policy response. Adopting this perspective invites us to appreciate the existence of different pathways of exposure based on sex/gender, socioeconomic and other inequities affecting a complex system of interrelations at various temporal and spatial scales. These considerations are essential with the COVID-19 syndemic (two or more epidemics enhancing the burden of disease; Singer et al. 2017). In this section, we outline the web of factors that lead to health inequities, including how intersectionality plays a role, and how crises and responses to crises exacerbate pre-existing inequities.

Health inequities

Social inequity is rooted in the dominance of one group over another. Social inequities—including gender, ethnic, territorial, and economic inequities—lead to marked inequities in health and wellbeing across populations. Gender inequity is ubiquitous but not uniform as it combines with other health inequities such as homelessness, poverty, or structural racism (Abrams and Szefler 2020; Bailey et al. 2017; Craig 2020; van Daalen et al. 2020; Yaya et al. 2020). This interaction has been variously termed and analyzed: Matrix of oppression (Hill Collins 1990), co-constitution (Bilge 2015), co-substantiality (Kergoat 1982) and intersectionality (Cho et al. 2013; Crenshaw 1989; Crenshaw 2019). Attention to this can illustrate how people's experiences of hazards differ across multiple intersections such as location, ethnicity, gender, and age and how these differences are influenced by broader social structures and power relationships, such as histories of colonization and gendered norms and expectations (Walker et al. 2021). In Canada, the economic repercussions of social inequities highlight the vulnerability with which certain populations, including women, youth, recent immigrants, and racialized people, live (Bastien et al. 2020).

The societal roles attributed to genders and the life experiences of individuals, marked by their differing economic, social, and physical conditions, bring people into contact with their environment, including zoonosis, differently. For example, in many parts of the world, girls and women are



responsible for raising household livestock, shopping at wet markets, and preparing animal-derived food for household consumption. This proximity to animals can put them at greater risk of exposure to zoonosis (Bagnol et al. 2015). Further, as primary food providers, girls and women can be disproportionately affected by food insecurity. They must care for malnourished family members and work extra hours to make up the shortfall. For example, depending on the region, women farmers are responsible for a substantial proportion of all food production in developing countries. Due to climate change, traditional food sources are increasingly difficult to predict, making it a challenge for women to feed and provide for their families. In situations like this, some people are at higher risk for various diseases, and by seeking non-traditional food sources, they may be more likely to contract zoonoses (Keatts et al. 2021).

Story Box 1. One Health Story Box.

Mining and One Health in the Yukon during the COVID-19 pandemic

Anne Mease

At the onset of COVID-19 in 2020, the Yukon Territory went into total lockdown. Although we had only five cases by June 2021, our state of emergency lasted until 4 August 2021. Our borders were closed, our gatherings were limited to small bubbles, and 14-day quarantine measures were strictly enforced. Those exempt from these restrictions included essential service employees, including healthcare workers and supermarket staff. Mining was included as an essential service on the premise that mining contributes to a strong and healthy Yukon economy (Gignac 2020a), yet other industries that provide the same economic benefits, such as tourism or hospitality, were not considered essential.

While other mining companies across Canada were able to go into care and maintenance mode to protect the miners and nearby communities, major mines in the Yukon were either unable or unwilling to do this. First Nations communities affected by mining, such as Mayo (First Nation of Nacho Nyak Dun), Pelly Crossing (Selkirk First Nation), or Dawson City (Tr'ondek Hwech'in First Nation), took matters into their own hands by setting up check stops outside their communities, thus mainly prohibiting mine workers from entering their communities.

Because the Yukon Government supported and encouraged mining activity during this time, leaders such as Chief Simon Mervyn of the Nacho Nyak Dun First Nation in Mayo, Yukon passed Resolution #044-2020, which reads as follows: "We direct that any mining or other industrial or commercial activity currently underway on NND settlement land cease immediately" (Gignac 2020a). In addition, former Chief Angela Demit of the White River First Nation asked the Yukon Government (YTG) to "suspend all Mining Activity During COVID-19 State of Emergency to protect Elders and most Vulnerable" (Rudyk 2020; Bernauer and Slowey 2020). These requests were made under the autonomy of self-government; however, they went unheeded as the Yukon government maintained that mining was essential to the economy, and consequently mining in the Yukon would be "open for business" (Bernauer and Slowey 2020).

What was not considered in allowing the mines to operate and mining exploration to proceed was the overall health of the people, wildlife, and habitat. During the pandemic, people have grown increasingly dependent on the land for food security and well-being (Elliot 2021a). As a result, throughout the pandemic, we became more reliant on the land for subsistence—to make sure there was enough food because we had no clue what this virus was or how long it would last. In turn, we increased our harvesting of ungulates, fish, and berries—while at the same time



Story Box 1. (concluded)

adhering to our traditional laws of not hunting cow moose for any reason and reducing our salmon catch limit, not an easy task because our diets rely on these foods for sustenance and medicine. However, this need for added food security also put pressure on the environment because more hunters disturbed the land with all-terrain and other mechanized vehicles, putting our flora and fauna in danger in the coming years and placing our food security—and thus our health—at risk.

The challenges posed by COVID-19 in the Yukon only compound pre-existing issues, including controversy over a mine in the territory of the Kaska and in the range of Finlayson caribou, which matters to the culture and food security of the Kaska (Gignac 2021). Additional critical concerns included the degrading treatment of Indigenous women in the Yukon and discrimination and personal safety concerns in British Columbia's mining sector (Gignac 2020b). At the same time, some companies announced increased gold production during the pandemic period, also marked by a cyanide spill (Elliot 2021b; Victoria Gold Corp 2021).

We must also consider longer-term land health when resource roads, mining, and other landdisturbing projects are proposed, because of the links between permafrost thaw and diseases such as anthrax. An outbreak of anthrax in Russia in 2016 resulted in the death of a child, hospitalization of over a hundred people, and decimation of reindeer. The outbreak was associated with melting permafrost and the release of bacteria from animals buried centuries earlier (Ezhova et al. 2021).

Many Indigenous people plan for the next seven generations to ensure the well-being for those yet to be born and for the natural world—a concept that others can learn from.

Lessons from COVID-19

The dynamics of dominance regularly place certain populations in different health situations (One Health **Story Box 1**). When a crisis hits, people who are already disadvantaged are at higher risk than others. In addition, the decisions made about solutions to the crisis often impact these same populations more severely. The COVID-19 crisis exposed a weakness built into the healthcare system: Because healthcare workers in assisted-living facilities, who are mostly women, work in multiple facilities, they are exposed to more outbreaks and risk severe illness and (or) transmitting SARS-CoV-2 to others. Furthermore, these low-paid jobs are often occupied by racialized women or immigrants, whose living conditions do not always permit physical distancing (Statistics Canada 2020). Over half of all female workers (56%) in Canada are employed in occupations involving the '5 Cs': caring, clerical, catering, cashiering, and cleaning (Statistics Canada 2017). These are precisely the types of jobs that are directly involved in containing pandemics and providing needed care and support. In Montréal, 46% of women of working age who have been diagnosed with COVID-19 by June of 2020 were healthcare workers, whereas the proportion for men is 19% (Springmann 2020).

Women tend to occupy lower paid positions in the service and care sectors. For example, in assisted living facilities, 89% of attendants, who do most of the care requiring close contact with patients, are women, and 46% of these women are visible minorities. These jobs are characterized by atypical schedules, placement agencies cobbling together schedules in different facilities, inadequate protective equipment, use of public transportation to get from one placement to another, and home situations that render physical distancing difficult (Springmann 2020; Germain 2016). The greater infection rate among women can be explained by the fact that women more often occupy jobs that require them to

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be in close contact with other people. This is not only the case in the health sector. Women comprise nearly all daycare providers and most community workers, grocery tellers, and restaurant attendants—all jobs where physical distancing is difficult (Springmann 2020).

Evidence is emerging that disadvantaged groups have suffered disproportionately from COVID-19. According to a study in New York State, Black and Hispanic people die more from COVID-19 than white people, overall, but this is not the case when they are admitted to acute care, where Black and Hispanic populations have "lower in-hospital case-fatality rates than white populations" (Ogedegbe et al. 2020). Disaggregated COVID-19 data have not been consistently collected across Canada; however, Statistics Canada (2021) has reported that COVID-19 mortality rates were two times higher in neighbourhoods with the largest proportion of visible minorities compared to neighbourhoods with the smallest proportion. These examples point to inequities in access to health care as a critical determining factor in COVID-19 survival rates in both the United States and Canada. Although, people's health status is dependent upon social determinants of health, access to health care also plays an important role, especially where access is scarce and dependent upon one's financial situation. There are important disparities in healthcare access in Canada, where healthcare is provided by brick-and-mortar institutions, and through community programs for both individual patient care (community access programs for outpatient clinics and in-home care) and public health. The unevenness in the delivery of these services may in turn potentiate further socioeconomic stress where barriers exist.

Another impact of COVID-19 has been the toll it has taken on people's mental health. A metaanalysis looked at the psychological impacts (anxiety, depression, panic attacks, post-traumatic stress) of COVID-19 around the world. It concluded that the groups most at risk of developing mental health problems are women, nurses (who are often women), people with less financial means, individuals with deteriorating health, and people living in isolation (Bastien et al. 2020). This anxiety is related to the risks of contracting the disease, but it is also a response to changes brought on by decisions made to minimize the impact of COVID-19. These solutions often had differing impacts on distinct sectors of society. For example, research has shown that women across the globe bore the brunt of government decisions to close schools. Following pre-COVID trends, women have contributed more than men to the extra tasks brought on by mitigation measures (Kantamneni 2020). Twice as many women as men reported having challenges balancing paid work and childcare in October 2020 (Yavorsky et al. 2021). The extra burden of caring for and schooling children translated into reduced productivity in the paid work sphere for women. This effect is demonstrated in the decline in women's scientific output: a study of approximately 50,000 articles published in medRxiv, a major preprint repository for the health sciences, found that the gap between the number of male and female authors increased from 23% in January 2020 to 55% in April 2020 (Andersen et al. 2020).

Work in crisis settings has shown that more violence against women (including sexual violence) is reported after disasters (WHO Department of Injuries Violence Prevention 2005). An international report by the United Nations highlighted that one in five women who are refugees or who have been displaced because of a natural disaster has experienced sexual violence (UN Climate Change 2019). This escalation of violence toward women has occurred during the COVID-19 crisis, as well. Women who suffer from domestic violence can escape constant exposure by going to work, but during shutdowns, women are constantly exposed to the risk of violence in the home. As well, the stress of losing family revenue can increase tension and violence. In Ontario, "the Violence Against Women Hotline saw a 60% increase in calls during the second wave of the epidemic, compared to the same period in 2019" (Ici.Radio-Canada.ca 2021). The consequences of the lockdown on violence against women was anticipated by people working in the field and should have been anticipated and mediated by governments implementing non-pharmaceutical interventions.



Recommendations

Engage community groups and communication scholars to help devise better access to timely, effective, and trustworthy information for populations in situations of vulnerability. To reduce health inequities, the information and guidance related to zoonoses needs to be communicated in a way that ensures that marginalized people can both trust and understand (Corbie-Smith 2021; Razai et al 2021; Bloom et al. 2021). The information provided needs to be easily accessible to all vulnerable populations, and the language used needs to be easily understood. Clear guidance, including on how to access care, will reduce health inequities related to education level and language barriers, as well as reduce any stigma which arises from misinformation.

Collect consistent and disaggregated social and demographic health data to identify health inequities. High-risk populations should be prioritized; however, there is a large gap in data collected in Canada on social determinants in health care. Very few provinces have collected this information during the COVID-19 pandemic (Blair et al. 2021). There is a need for consistent and disaggregated social/demographic data collection on health across the country so that health inequities, including those related to access to care, can be properly identified, and equitable policies can be implemented. Similar recommendations on the need for race- or ethnicity-based data have been provided in previous RSC briefings: Impacts of COVID-19 in Racialized Communities and The Epidemiology of COVID-19 in Canada in 2020.

Ensure that Canada's commitment to social equality is advanced by applying gender-based analysis plus (GBA+) to the analysis of all data, with meaningful inclusion of equity deserving groups in a One Health Action Plan for Canada. Gender-based analysis plus (GBA+) is a tool that can be used to evaluate what the impacts of certain initiatives, such as policies and services, might be on diverse groups of women, men, and people with other gender identities. Represented by the 'plus,' factors such as age, sexual orientation, disability, education, language, geography, culture, indigeneity, and income are considered to intersect. Quebec and Canada have already adopted the principle of GBA+, but its application is inconsistent. It is not new policies that are needed but their effective implementation. A standardized screening process, whereby a certain set of questions are asked of each potential policy, could be developed to facilitate implementation.

7. The fundamentals: Education and research

A one health curriculum

The challenges of human, other animal, and ecosystem health are complex and increasingly interrelated. Issues related to zoonotic pathogens, antimicrobial resistance, and climate change do not respect species or geopolitical divides. Professionals across the diverse disciplines related to animal and human health need a firm academic grounding beyond narrow professional constructs, including an understanding of the interface among their disciplines and with areas of ecology, social science, and Indigenous knowledge.

To achieve this holistic knowledge base, programs in veterinary, medical, and other health professional education should include core competencies related to One Health in their curricula. Already used by leading medical and veterinary education organizations, existing frameworks can become the basis to establish education programs using accreditation standards within their respective jurisdictions. Establishing One Health education programs within accreditation standards will assure consistent and more universal adoption of One Health curricula.

To successfully tackle the complex and urgent health and environmental challenges of the 21st century, a strong workforce of skilled individuals and leaders is needed. Critical knowledge and skills



are required to apply integrated and collaborative approaches, foster knowledge and resource sharing across disciplines, knowledge traditions and communities, and maximize the likelihood of creating proactive, effective, and sustainable solutions (Barrett et al. 2019; Cleaveland et al. 2017; Parkes et al. 2020; Togami et al. 2018; Whitmee et al. 2015).

To meet this growing need, institutions across the world have been developing One Health training programs, however, only recently have efforts been made to develop shared competencies and learning outcomes for One Health to help ensure consistent and robust training across institutions. Competency-based education has been used for decades, including in, but not limited to, human and veterinary medicine and public health (AAVMC Working Group on Competency-Based Veterinary Education et al. 2018), ensuring that, regardless of the institution, students leave their respective programs with the specific skills, attributes, and knowledge needed for successful practice (Public Health Agency of Canada 2021). Following the establishment of competencies, specific learn-ing outcomes are identified that provide a scaffold for students to ultimately achieve the desired competency (Albanese et al. 2008; Hooper et al. 2014). Efforts are underway in Canada to develop core competencies for One Health, which will likely include competency in health knowledge and understanding, problem solving and critical thinking, leadership and collaboration, communication, and professional and ethical behaviour.

Emerging zoonoses research: the road to recovery and preparedness

Because of the complexity of the research questions at hand and the interdisciplinarity essential to research programs focused on One Health, it may be challenging to finitely define what constitutes One Health research. Here we consider research examining multiple (but not necessarily all) facets of health, including that of ecosystems, humans, and other animals to be applying a One Health approach. In this policy report we focus on zoonotic disease research, but evidently there is an expanse of research beyond this area that merits deeper consideration, including equally pressing questions around health and climate change, pollution, forest degradation, biodiversity, social and political ecology, socioeconomics, geopolitics, food security, and armed conflict, among others.

One Health zoonotic disease research is expansive and may include hypothesis-driven research, translational research and development, implementation, and evaluative sciences (One Health **Case Study 5**). For example, examining the effect of artificial light on bird immunity and susceptibility to infection by West Nile virus is as much a One Health project as is looking at the impact of pasteurization of water buffalo milk on *Brucella* control and farmer health and livelihood. Both examine health from more than one perspective and stand to improve it.

Case Study 5. One Health Case Study.

Bats and their ability to coexist with their viruses

Arinjay Banerjee

Chiroptera—bats—is the only true flying mammalian order. With 1400 different species, bats represent a diverse group of mammals. Bats perform essential ecological roles, such as pollination, insect control, and seed dispersal, all of which are critical for the sustenance of our ecosystem and planetary health. Despite the important ecological role of bats, studies have now identified that some bat species are reservoirs of emerging viruses that can cause significant disease in humans and livestock.



Case Study 5. (continued)

Over 150 different viruses have been detected in multiple bat species globally. Viruses that cause severe disease in humans, such as the Marburg, Nipah, Hendra, and rabies viruses, have been clearly linked to bats, and Ebola-like viruses have been detected in some bat species (Goldstein et al. 2018). Studies have found that bats harbour several emerging and re-emerging viruses such as coronaviruses (CoVs), filoviruses, and paramyxoviruses-causative agents of important and often severe human and agricultural animal infections (Fig. 9; Huang et al. 2013; Li et al. 2005; Memish et al. 2013; Moratelli and Calisher 2015; Schountz 2014). A recent study found that global bat species are reservoirs of coronaviruses (Grange et al. 2021; PREDICT Consortium 2020; PREDICT Consortium, n.d.) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is thought to have evolved in Rhinolophus bats (Banerjee et al. 2021; Banerjee et al. 2019, Hul et al. 2021; Wacharapluesadee et al. 2021; Zhou et al. 2021). Despite evidence that they harbour these viruses, infected bats do not show visible signs of disease (O'Shea et al. 2014). Indeed, multiple species of bats can coexist with multiple families of viruses without demonstrating disease symptoms, including coronaviruses. Intriguingly, bats that are naturally or experimentally infected with some of these viruses do not demonstrate classical signs of disease (Guito et al. 2021; Munster et al. 2016; Seifert et al. 2020,). In addition, bats can also rid themselves of the virus (Amman et al. 2015; Schuh et al. 2017). But bats are not immune to all virus infections. For example, Tacaribe virus causes disease, and sometimes death, in bats (Cogswell-Hawkinson et al. 2012). And because Chiroptera is a diverse order, information from studies on one genus or species may not apply to all bats. However, observations of bat immunity have convinced researchers to investigate the immune responses in bats against these highly pathogenic viruses (Banerjee et al. 2020).







Case Study 5. (concluded)

Understanding how bats control infection with viruses that cause severe disease in humans will provide important insights for the development of new drugs or drug targets to control and manage human infections. In recent research, we have shown that cells from *Pteropus alecto* and *Eptesicus fuscus* have evolved the ability to strictly control virus infection-mediated inflammatory responses, which may contribute to the lack of overt disease symptoms in bats (Ahn et al. 2019; Banerjee et al. 2017; Pavlovich et al. 2018). Pathology observed in patients with SARS, COVID-19, and Middle East respiratory syndrome (MERS) is largely driven by an excessive inflammatory response generated upon infection with these CoVs (Blanco-Melo et al. 2020; DeDiego et al. 2014; Lau et al. 2013; McDermott et al. 2016). Thus, understanding virus-host interactions in bats is not only an intriguing biological question but perhaps also important in controlling detrimental disease outcomes in other mammals.

All mammals, including humans, are infected by viruses. Some viruses cause severe disease in humans, such as Ebola virus, whereas other viruses, such as herpes viruses, can cause long-term persistent infection with limited disease symptoms. However, the detection of viruses in wildlife, such as bats, does not necessarily mean that these viruses will actively cross the species barrier to infect humans. A multitude of factors must align to cause spillover of a virus from a wildlife species into humans (Plowright et al. 2017). It is important to acknowledge that bats are no more likely to infect humans with a novel virus than are other known mammalian reservoirs of viruses, such as rodents (Mollentze and Streicker 2020), and to examine the anthropogenic behaviour that is responsible for the spillover of bat- or other wildlife-borne pathogens into the human population.

Clear challenges exist with a One Health approach to research. Fragmented, ineffective research outcomes may be secondary to persistent silos, competition (for financial support or recognition), conflicting priorities, poor planning and coordination, differing values, short-term and limited support, and a myriad of other impediments. Mutual goal and scope-setting at the outset is helpful. Starting conditions, including investigator experience, the research context, and relational dynamics between researchers can set the tone for process and influence outcomes; one study examining health events (97% related to infectious diseases) found several determinants of productive One Health research collaborations, including education and training, prior experience and existing relationships, organizational structures, organizational culture, human resources, communication, network structures and relationships, leadership, management, available and accessible resources, and the political environment (Errecaborde et al. 2019).

COVID-19 has inarguably revealed the interconnectedness between key domains of human and other animal health, with strong links to habitat and ecosystem health through possible knock-on, if not causative, effects. Thus, the Chairs of the Lancet One Health Commission have called for a One Health research coalition for COVID-19 (Amuasi et al. 2020). Unfortunately, research efforts remain loosely coordinated where they exist, with vast lacunae where they are absent. These gaps are present within the conventional framework of One Health research encompassing all animals, including humans, and ecosystems. They also exist across disciplines, where biological (virology, bacteriology, mycology, parasitology, immunology, computational biology), epidemiological (disease ecology, modelling, and clinical epidemiology), environmental (ecosystems, climate, landscape immunity), and social (human populations structures, cultures, economics, geopolitics, and governance) research suffers from important omissions in substance and collaboration. Finally, ensuring that public health and academia engage with each other is essential to high quality, relevant, and immediately actionable



research to guide decision-making; while some examples exist, there were many missed opportunities over the course of the pandemic in Canada.

Substantial challenges exist with One Health research funding in Canada. Tri-Agency—Canadian Institutes for Health Research (CIHR), Natural Sciences and Engineering Research Council (NSERC), and Social Sciences and Humanities Research Council (SSHRC) funding has occasionally supported projects with One Health aspects. However, there are scant sustained and truly multidisciplinary funding schemes focusing on One Health approaches to emerging pathogens and zoonoses or other aspects of One Health. CIHR's Institute of Infection and Immunity (III) has supported zoonotic disease research networks, but these remain narrow in pathogen scope (e.g., Lyme Disease Network, antimicrobial resistance). The recently released Institute of Infection and Immunity Strategic Plan, identified priorities, including global infectious disease threats, climate change-related zoonoses, and One Health approaches for antimicrobial resistance. These represent welcome progress provided there are substantial and sustained commitments to building the expertise, networks, workforce, and infrastructure (both physical and regulatory) required to execute this and broader work.

To date, there have been few, if any, panels with the combined expertise to consider One Healthrelated proposals. Because most One Health proposals overlap with multiple funding agencies, these tend to fall in between agency priorities for funding, and are left unfunded. The Canadian Safety and Security Program (Defence Research and Development Canada) and the Public Health Agency of Canada's Infectious Diseases and Climate Change fund have supported One Health-oriented projects, which have catalyzed several regional and national initiatives. However, without long-term prospects for support, there are high opportunity costs due to unsustainability, and One Health research does not lend itself to one- to two- year timeframes. The lack of pre-existing intramural and other executive research bodies (e.g., equivalents of the National Institute of Allergy and Infectious Diseases Laboratory of Virology; Rocky Mountain Laboratories, Montana; Centers for Research in Emerging Infectious Diseases; National Biocontainment Laboratories and Fogarty International Center) put Canada at a clear disadvantage, both domestically and internationally during the pandemic. It was also not immediately evident with whom partnerships were possible, with public health and academic research at arm's length from each other and many government scientists seconded to operational tasks, particularly early in the pandemic. Canada has also not invested in programs to tackle zoonotic diseases in the same manner as other leading initiatives, such as the EcoHealth Alliance in the United States or the Friedrich Loeffler Institute in Europe.

There have been some regional initiatives, such as Quebec's Multi-Party Observatory on Zoonoses and Adaptation to Climate Change, part of the Government of Quebec's 2020 Climate Action Plan supported by the Green Fund (Germain et al. 2019). However, there are no national observatories to support research prioritization. In addition, regional initiatives cannot be conducted effectively or meaningfully in Canada unless they involve Indigenous scholars, health organizations, knowledge holders, and governments, particularly in areas around Arctic One Health, wildlife surveillance, and Indigenous Peoples' health. The Institute of Indigenous Peoples' Health at CIHR has funded several Indigenous COVID-19 rapid-response grants, but like so much other catalyst COVID-19 funding, there are no clear plans to leverage these investments for long-term projects around zoonotic disease and Indigenous health.

In addition, limited investment has been made in international One Health research. Meaningful participation by Canadian scientists is essential to (1) contribute to global efforts to combat infectious diseases (most importantly) and (2) enable efforts to protect Canadians from transboundary novel and emerging pathogens. Initiatives such as the Global Governance Research Network on Infectious Disease (GGRID) are commendable but limited and require further investment and expansion. It is critical to also support international One Health research integrating natural sciences. Without



foundational knowledge of non-endemic etiologic agents, we will continue to have too few experienced scientists able to competently work on special pathogens. There is also limited coordination among high level (3 and 4) containment laboratories in Canada—each function as a silo and has limited capacity to collaborate nationally, let alone internationally, and there is an excess of both overlap and gaps in emerging zoonoses projects. Also, few academic centres have the capacity to focus on zoonotic diseases for animal health (e.g., there is limited work on pathogens such as *Brucella canis*). Finally, from an ecological perspective, without understanding the drivers of pathogen emergence outside our borders, we cannot anticipate predisposing conditions within.

Knowing where to begin with One Health-related research will require thoughtful prioritization over both short- and long-term time scales across national and international domains. There are both urgent needs that potentially overlap with public and animal health mandates and longer-term, systems-based questions that merit attention. Work in the United States indicates that several wildlife species are susceptible to SARS-CoV-2, but we have a very limited line of sight on this in Canada since this research falls between academic research and public health and between natural sciences and health, meaning it has limited support from public health current peer-reviewed funding mechanisms. Fortunately, Defence Research and Development Canada, the Public Health Agency of Canada, Environment and Climate Change Canada, the Canadian Food Inspection Agency and provinces (ministries of natural resources) have stepped in to temporarily and partially address this important gap with short-term, modest targeted investments for limited surveillance (leading to the detection of SARS-CoV-2 in Canadian wildlife; Kotwa et al. 2022; Pickering et al. in press), but fulsome research programs are not currently in view.

In summary, there are currently no robust, sustained funding streams for One Health research in Canada. Past investment in emerging zoonoses is either limited or virtually nonexistent, compared to other areas of health, and there are few established mechanisms to access funding for rapid, effective collaborative research in times of acute need for those with existing expertise and capacity. These become urgent and critical challenges as new threats such as highly pathogenic avian influenza virus rapidly emerge. This, at least in part, may be attributed to the absence of a national One Health Action Plan. In the same fashion that climate change policy and planning has been driven by science, so must One Health-related policy and decision-making be supported by robust data, which at the moment, are very sparse in Canada.

Recommendations

Implement One Health curricula and learning opportunities. One Health curricula must be incorporated into accredited programs for veterinarians, physicians, and other licensed healthcare providers and public health practitioners in training. Inclusion of One Health education frameworks in accredited and board-certified programs and institutions will assure consistent and more universal adoption of One Health curricula. Also, One Health education should be introduced at all stages of education, from preschool to university. Curricular and extracurricular learning opportunities must be developed and supported, with an emphasis on interdisciplinary approaches. Introduction of One Health topics in professional continuing education programs delivered by professional associations must also be considered.

Prioritize domestic and international research in emerging zoonoses using a One Health approach. Canada must prioritize excellence in emerging zoonoses research to fill key knowledge gaps at regional and national levels and actively contribute at the global level to advance mitigation and preparedness for novel, high-consequence pathogens. This prioritization must be done by incorporating expertise across human, other animal, and ecosystem health from biological, social, and environmental perspectives. Key priorities in the near term are pathogen and host biology, ecosystem stressors and landscape



immunity, drivers of spillover, and determinants of the impact of emerging zoonotic diseases. In addition to generating knowledge, these research activities will train future One Health researchers, teachers, and decision-makers to ultimately inform policy and drive societal change. Training requires both nimble catalyst and **sustained Tri-Agency and other funding for One Health**, ideally through partnered One Health funding programs that include the health of all living beings and ecosystems. Panels must be multidisciplinary and capable of assessing One Health projects using integrative approaches from the biological, social, and environmental sciences and that incorporate Indigenous ways of knowing. Partnership grants must be sufficiently unrestricted to enable investigator-driven research and collaboration at national and international levels. These recommendations are also linked to the recommendation for **Centres of Excellence in One Health and emerging pathogen response** (Section 4), enabling research funding to be rapidly flowed to existing, productive collaborations with the appropriate content expertise during public health emergencies, and to build research capacity between outbreaks and pandemics.

8. Summary

The COVID-19 pandemic has foregrounded the acute need for a global One Health strategy. People, Planet, and Prosperity are the three G20 pillars for action, and building One Health resilience is a key action identified by the G20 Health Ministers during a meeting in Rome in September of 2021:

We call for collaborative multisectoral action to increase surveillance, strengthen prevention, preparedness and response for improved health outcomes and enhanced well-being for all, sustainable food systems, water and sanitation, and environmental protection. We highlight the need to build a strong, trans-disciplinary, holistic One Health approach with political commitment for long-term investment. This would enable us to strengthen and support resilient and sustainable health, social protection and food systems, and to address risks emerging from the human-animal-environment interface, leveraging the technical leadership and coordinating role of the WHO, FAO, OIE and UNEP. We will consider identifying key actions and calling upon relevant international organisations, partners in the health and private sectors, civil society, academia, philanthropic and research institutions to follow through on these actions... **We commit to operationalizing the One Health approach at all levels** (G20 Italia 2021 2021).

In Canada, a major paradigm shift in how we think about health is needed. All of society must recognize the intrinsic value of all living species and the importance of human, other animal, and ecosystem health to health for all. All of society must also recognize that Indigenous ways of knowing have long been based on the interconnectedness of all animals, including humans, and the land, and the benefit of balance to all. Importantly, there must be broad acceptance of efforts and directives to strengthen societal responsibility and improve human, other animal, and ecosystem health. We must also recognize that human activities leading to habitat destruction, biodiversity loss, and climate change contribute to zoonotic pathogen spillover, and that understanding the drivers of spillover is fundamental to mitigation.

Communication and collaboration among sectors and peoples are needed to understand the web of factors that lead to the emergence of zoonoses, including biological, environmental, and social determinants. This approach is also required to identify and prioritize populations at risk of contracting zoonoses, including those who rely on the hunting, trading, and consumption of wild animals to survive. There is a need for diverse groups of policymakers and decision-makers to work together with other sectors of society in the design of solutions and community members and Indigenous scholars must be actively included. To develop sustainable policies, inequities in health and the policies put in place to reduce these inequities need to be constantly assessed and improved.

One Health approaches do not require each component across the land-animal-plant spectrum to be included for each challenge-solution dyad, but a means to engage various elements is at the core of the



One Health approach. For multidisciplinary, multisectoral cooperation, collaboration, and coordination, not all sectors (human, other animal, plant, and environmental health) need necessarily be engaged, but all must be considered and involved as appropriate to the challenge at hand. Collaborating across agencies and disciplines is a key feature of a One Health approach, and coordination to meet important challenges is a means to effectively implement a One Health solution. These principles transcend borders and enable global engagement. Threats to health constitute threats to security. Critical relationships and trust between national and international agencies are essential. The Quadripartite Zoonoses Guide (QZG) from the FAO, OIE, UNEP, and WHO provides an excellent framework to begin addressing One Health challenges from technical and operational perspectives at a global scale (World Health Organization et al. 2019).

A resilient and sustainable structure for a One Health approach must be tied to function. In section two, we outlined a myriad of organizations, institutions, and programs that are part of a loose community of practice of One Health in Canada. Any gains from these efforts have been made organically, and although laudable, they remain tenuous in the absence of a clear One Health agenda for Canada, accompanied by established timelines and support for execution. Of course, this agenda should leverage existing activities, but important gaps require timely filling if we are to mitigate impending zoonotic threats. Also essential is a national action roadmap or plan for One Health, with responsible agencies, programs, and positions tied to key milestones and tasks. This roadmap would hold the One Health community of practice to account. Furthermore, key performance indicators will be critical to evaluating the efficacy and impact of One Health initiatives. Since these are often broad, early identification of key performance indicators at the outset of proposed work will ensure that investments made in One Health result in concrete deliverables.

Inaction risks ongoing loss of life in the face of the current pandemic, the climate crisis, and new biothreats. Doing nothing may cost in the range of hundreds of thousands to millions of lives, considering the knock-on effects at all levels of society, on both domestic and international fronts. The need for action is no longer a matter for debate. It is time for Canada to stand up and be counted as a key contributor to global pandemic recovery, health, and security.

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Author contributions

SM, JA, AB, HC, JCJ, CJ, BJ, GK, JK, SK, DM, AM, LN, KN, BP, MGR, JS-C, KS, TS, JSW, and EJP conceived and designed the study. SM, JA, AB, HC, JCJ, CJ, BJ, GK, JK, SK, DM, AM, LN, KN, BP, MGR, JS-C, KS, TS, JSW, and EJP performed the experiments/collected the data. SM, JA, AB, HC, JCJ, CJ, BJ, GK, JK, SK, DM, AM, LN, KN, BP, MGR, JS-C, KS, TS, JSW, and EJP analyzed and interpreted the data. SM, JA, AB, HC, JCJ, CJ, BJ, GK, JK, SK, DM, AM, LN, KN, BP, MGR, JS-C, KS, TS, JSW, and EJP contributed resources. SM, JA, AB, HC, JCJ, CJ, BJ, GK, JK, SK, DM, AM, LN, KN, BP, MGR, JS-C, KS, TS, JSW, and EJP contributed resources. SM, JA, AB, HC, JCJ, CJ, BJ, GK, JK, SK, DM, AM, LN, KN, BP, MGR, JS-C, KS, TS, JSW, and EJP drafted or revised the manuscript.

Competing interests

The authors have declared that no competing interests exist.



Supplementary material

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Supplementary Material 1

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FACETS | 2023 | 8: I-64 | DOI: 10.1139/facets-2021-0190 facetsjournal.com