

# Navigating the complexities of “One Health”

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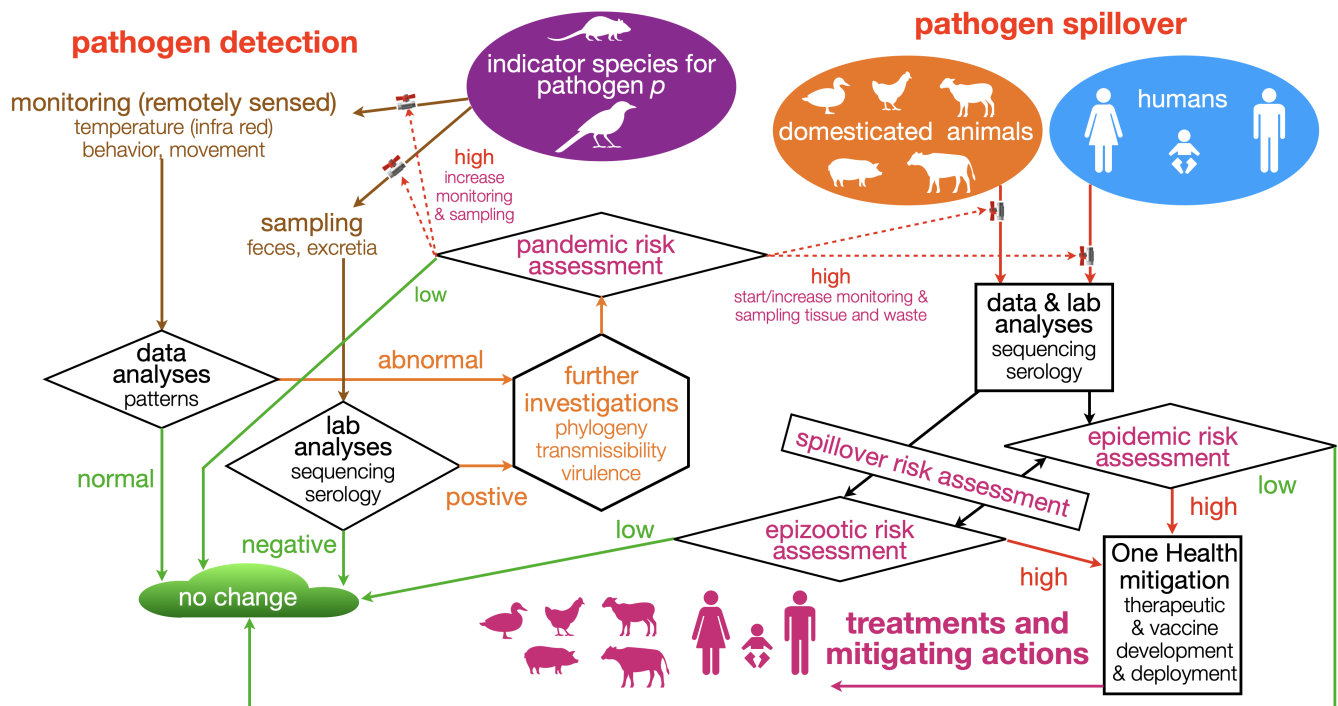
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## Abstract

For two decades, a One Health approach to managing the emergence of novel zoonotic pathogens has been increasingly called for by the animal and public health sectors. One health systems require the integration of data from wildlife indicator species, domesticated animals, and humans into a framework of monitoring and analysis that provides for early warning of impending pathogen spillover and novel strain emergence. Here we provide a graphic description of the elements of a One Health preparedness system and discuss a monitoring framework designed to meet the needs of a well planned One Health approach to pandemic preparedness that includes automated remote sensing of pathogen-specific indicator wildlife species.

## Introduction

Widespread circulation of avian influenza in cattle, with some currently limited spillover infections into humans,<sup>1</sup> and the recent declaration of an mpox global emergency,<sup>2</sup> once again highlight the dramatic risk that zoonoses pose for human health. Additionally, the potential for human-to-animal transmission has been underscored by recent findings of abundant circulation of SARS-CoV-2 in wildlife.<sup>3</sup> Taken together, these case studies reveal the importance of a broad view of pathogen dynamics that includes sylvatic, urban, and human transmission cycles. While the concept of a “One Health” approach<sup>4</sup> can be difficult to conceptualize and daunting to contemplate, we argue here that certain unifying pillars can simplify this task, as in the integrative framework we present



**Figure 1: An integrative “One Health” monitoring framework that consists of the adaptive monitoring of humans, domestic animals, and wildlife, the latter via one or more indicator species, to assess the risk of zoonotic spillover and the possible emergence of a new global pandemic.**

25 in Fig. 1 to detect epizootic or endemic pathogen spillovers (see Figure 1) with Covid-19-like  
 26 pandemic potential.

## 27 Framework basics and concept of ‘indicator’ wildlife species

28 At the crux of One Health programs is the monitoring of three classes of populations: humans,  
 29 domesticated animals, and wildlife. The difficulty of monitoring each of these is highly variable  
 30 and high quality data is paramount. Certain forms of pathogen surveillance among humans have  
 31 dramatically improved since their initial deployment, especially wastewater,<sup>5</sup> and infection sur-  
 32 veys<sup>6</sup> during and after the COVID-19 pandemic. Further, important recent calls have been made  
 33 for a Global Immunological Observatory<sup>7,8</sup> that would identify changes in immunological signa-  
 34 tures at the population level and more rapidly reveal cryptic pathogens spreading among humans.  
 35 Comparably less surveillance among farm animals or wildlife is ongoing, however, and this may  
 36 be necessary to anticipate and prevent future pandemics. To address this gap, a pillar of our con-  
 37 ceptual framework is the identification and detailed monitoring of one or more wildlife ‘indicator’  
 38 species for each pathogen of concern.

39 Tracking and monitoring of temperature, behavior, and movement patterns,<sup>9</sup> in addition to  
40 sampling feces and excreta, should be ongoing in a manner designed to reveal disease-induced  
41 changes. While detecting disease via the behavior and movement of individuals is a relatively  
42 new concept, we see this (see Dougherty et al.<sup>9</sup> for further discussion) as central to a One Health  
43 approach (Fig. 1). In particular, areas of spatio-temporal overlap among wildlife, domesticated ani-  
44 mals, or humans are ideal regions of focus for monitoring indicator species. In the case of pathogens  
45 with durable environmental persistence, these regions can form ‘Local Infectious Zones’<sup>10</sup> or infec-  
46 tious ‘hot spots’. An additional general benefit of monitoring regions of spatio-temporal overlap  
47 is that their size can also be observed for changes (*e.g.*, due to urbanization or climate change)  
48 that may increase the likelihood of pathogen spillover. In tandem, monitoring may facilitate the  
49 implementation of mitigating actions such as measures to reduce human-animal or animal-animal  
50 contacts on temporary or permanent basis to reduce the probability of zoonotic spillovers in hot  
51 spots.

52 A key benefit of movement monitoring is that sampling can be automated, continuous, and  
53 fed immediately into AI systems using state-of-the-art machine learning algorithms for real-time  
54 analysis. Then One Health program managers and scientists need only be alerted when changes  
55 in movement and behavior are detected. In turn, active monitoring can be deployed (*e.g.*, with  
56 serology and sequencing), and further investigations used to reveal the causative agent, and the  
57 degree to which such a pathogen has the potential to ignite either a localized epidemic or a new  
58 global pandemic. Finally, risk assessment of the potential for local versus a global outbreak could  
59 be used to inform the policies needed for the rapid deployment of mitigation strategies in at-risk  
60 domesticated animal populations and human communities.

61 While deploying monitoring systems in humans and domesticated animals is relatively straight-  
62 forward, identifying an indicator species in wildlife is more difficult. A pathogen with pandemic  
63 potential, however, may already be established (or emergent) in either the sylvatic, urban, or  
64 human transmission cycles. In these cases, some of its details would already be known, and diffi-  
65 culties associated with deploying surveillance should be partially alleviated. For example, current  
66 global circulation of H5N1 avian influenza was first in birds and is now circulating abundantly in  
67 domesticated cattle, with a few spillover infections in humans to date.<sup>1</sup> Further, SARS-CoV-2 is  
68 now circulating widely in humans and animals;<sup>3</sup> and in the latter, pathogens variants with the  
69 potential to give rise to future pandemics may well emerge.

70 In systems where novel pathogens have the potential to emerge, it is possible that close relatives  
71 of these pathogens have been identified and are currently circulating in humans, domestic animals,  
72 or wildlife. These pathogens may then be monitored in a One Health program to see rates of new  
73 variant emergence and evaluate these new (now circulating) variants in highly regulated (biosafety  
74 level 3) labs that study their transmission and pathogenicity in appropriate animal model systems.

75 For example, multiple coronaviruses and influenza viruses are known to circulate in humans<sup>11</sup> and  
76 animals.<sup>12</sup> Finally, it is possible that a pathogen with pandemic potential has no known relatives  
77 in current circulation. To anticipate these, large-scale indicator species monitoring is required,  
78 particularly across the sylvatic transmission cycle, to detect their emergence before they spill over.  
79 If changes in organism temperature, behavior, or movement are detected, further investigation and  
80 genome identification should occur.

## 81 Risk assessments

82 For general One Health approaches to succeed, there must be continual pandemic, epizootic, and  
83 epidemic risk assessment using the latest quantitative methods, with an additional assessment of  
84 spillover to evaluate the risk of zoonoses (Fig. 1). In our framework, we propose that each of these  
85 specific assessments follows from data collected from either the indicator species (pandemic poten-  
86 tial), domesticated animals (epizootic potential) and human populations (epidemic potential). For  
87 epizootic and epidemic potential, data should be routinely monitored, and appropriate mitigation  
88 measures consequently taken. Most importantly, if the risk of a potential zoonotic pandemic is  
89 evaluated to be high, monitoring and sampling of the indicator species should be increased. If  
90 these measurements remain abnormal, domesticated animals and humans need to be monitored  
91 closely, including via sequencing and serology. With those data, risk assessments for epizootic  
92 and epidemic potentials should be performed using the best available quantitative methods, and  
93 appropriate therapeutics and vaccines developed and deployed according to cost-benefit analyses.

94 In our framework, we view animal vaccination primarily as a treatment strategy when epizootic  
95 risks are high. However, such strategies could themselves affect risk assessments, creating an  
96 important feedback loop between intervention and epidemiology. The magnitude of these effects  
97 could be quantitatively captured with our proposed conceptual monitoring framework. While  
98 animal vaccination is currently underutilized, there have been recent calls to develop and deploy  
99 mass animal vaccination globally.<sup>13</sup> With mass vaccination, our proposed monitoring approach  
100 would also enable detailed cohort studies for the effects of such vaccines in wild and domesticated  
101 animal populations. For example, epidemiological characteristics, such as vaccine efficiency for  
102 both transmission-blocking and severity-reduction capacities, could be determined. Further, the  
103 effects of animal vaccination on pathogen evolution could be monitored, and the vaccinal reductions  
104 in cross-species transmission (and risk of spillover) determined. Finally, these cohort studies would  
105 also clarify basic immunology (*e.g.*, strength and duration of immune response) and host-pathogen  
106 interactions in these organisms (in humans, see Saad-Roy<sup>14</sup> for a perspective on potential cohort  
107 studies for immuno-epidemiology and evolution).

## 108 **Future outlooks**

109 For a One Health program to be successful, many regional, national, and global challenges must  
110 be overcome. Locally, laboratory capacity must be sufficient to process a constant flow of samples.  
111 In tandem, local computational availability is required to perform the necessary data analyses for  
112 monitoring. While both already exist in some regions, the COVID-19 pandemic revealed that there  
113 remains high inequity across the world. Further, since a One Health monitoring framework would  
114 ideally span large physical areas, regional coordination of efforts is required. Finally, regional  
115 policies should be synergized, and data shared immediately. These challenges are only magnified  
116 at the global level, but resolving them is key for rapid identification and proper mitigation.

117 Importantly, climate change is poised to dramatically alter the landscape of infectious disease  
118 transmission and spillover within the next decades. For example, recent phylogeographic modelling  
119 suggests that such changes in climate will significantly accelerate animal-to-human zoonoses.<sup>15</sup>  
120 Since the details of where and when these events will occur remains unknown, it is imperative to  
121 deploy One Health monitoring mechanisms widely and rapidly. As the regions of contact between  
122 wildlife and domestic animals, or between wildlife and humans, grow, surveillance mechanisms  
123 should be enhanced to increase data collection at these critical junctions. In turn, these data  
124 could also provide valuable insights on the effects of climate change on pathogen spillover and  
125 evolution.

126 While the specifics of our framework hinge on a variety of factors, ranging from pathogen-  
127 specific details to regional and national policies, the key elements of our framework make complex-  
128 ities that are often associated with One Health more coherent and comprehensible. While many  
129 One Health programs currently exist, none seamlessly integrate across domestic animals, wildlife,  
130 and humans. Our proposed framework accomplishes this, as well as identifies the kinds of data  
131 that require collection at each scale. If our framework was deployed in conjunction with a poten-  
132 tial Global Immunological Observatory and ongoing wastewater surveillance, our societies would  
133 have a very robust multi-pronged approach to pathogen detection. This could both anticipate and  
134 prevent the next pandemic.

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138 Ecology.

## 139 References

- 140 [1] Garg S, Reed C, Davis T, Uyeki TM, Behravsh CB, Kniss K, et al. Outbreak of highly  
141 pathogenic avian influenza A (H5N1) viruses in US dairy cattle and detection of two human  
142 cases—United States, 2024. *Morbidity and Mortality Weekly Report*. 2024;73:501-5.
- 143 [2] Taylor L. WHO and African CDC declare mpox a public health emergency. *BMJ*.  
144 2024;386:q1809. Available from: <https://www.bmj.com/content/386/bmj.q1809>.
- 145 [3] Goldberg AR, Langwig KE, Brown KL, Marano JM, Rai P, King KM, et al. Widespread  
146 exposure to SARS-CoV-2 in wildlife communities. *Nature Communications*. 2024;15(1):6210.  
147 Available from: <https://doi.org/10.1038/s41467-024-49891-w>.
- 148 [4] Mackenzie JS, Jeggo M. The One Health Approach—Why Is It So Important? *Tropical*  
149 *Medicine and Infectious Disease*. 2019;4:88.
- 150 [5] Fang Z, Roberts AMI, Mayer CD, Frantsuzova A, Potts JM, Cameron GJ, et al. Wastewater  
151 monitoring of COVID-19: a perspective from Scotland. *Journal of Water and Health*. 2022  
152 12;20(12):1688-700. Available from: <https://doi.org/10.2166/wh.2022.082>.
- 153 [6] Pouwels KB, House T, Pritchard E, Robotham JV, Birrell PJ, Gelman A, et al. Commu-  
154 nity prevalence of SARS-CoV-2 in England from April to November, 2020: results from the  
155 ONS Coronavirus Infection Survey. *The Lancet Public Health*. 2021 2024/08/19;6(1):e30-8.  
156 Available from: [https://doi.org/10.1016/S2468-2667\(20\)30282-6](https://doi.org/10.1016/S2468-2667(20)30282-6).
- 157 [7] Metcalf CJE, Farrar J, Cutts FT, Basta NE, Graham AL, Lessler J, et al. Use of serological  
158 surveys to generate key insights into the changing global landscape of infectious disease. *The*  
159 *Lancet*. 2016;388:728-30.
- 160 [8] Mina MJ, Metcalf CJE, McDermott AB, Douek DC, Farrar J, Grenfell BT. A Global Im-  
161 munological Observatory to meet a time of pandemics. *eLife*. 2020;9:e58989.
- 162 [9] Dougherty ER, Seidel DP, Carlson CJ, Spiegel O, Getz WM. Going through the motions:  
163 incorporating movement analyses into disease research. *Ecology Letters*. 2018;21(4):588-604.  
164 Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1111/ele.12917>.
- 165 [10] Blackburn JK, Ganz HH, Ponciano J, Turner WC, Ryan SJ, Kamath P, et al. Modeling R0  
166 for Pathogens with Environmental Transmission: Animal Movements, Pathogen Populations,  
167 and Local Infectious Zones. *International Journal of Environmental Research and Public*  
168 *Health*. 2019;16(6).

- 169 [11] Ghai RR, Carpenter A, Liew AY, Martin KB, Herring MK, Gerber SI, et al. Animal reser-  
170 voirs and hosts for emerging alphacoronaviruses and betacoronaviruses. *Emerging Infectious*  
171 *Diseases*. 2021;27(4):1015-22.
- 172 [12] Webster RG. The importance of animal influenza for human disease. *Vaccine*.  
173 2002;20:S16-20. Available from: [https://www.sciencedirect.com/science/article/pii/](https://www.sciencedirect.com/science/article/pii/S0264410X02001238)  
174 [S0264410X02001238](https://www.sciencedirect.com/science/article/pii/S0264410X02001238).
- 175 [13] Laxminarayan R, Gleason A, Sheen J, Saad-Roy CM, Metcalf CJ, Palmer GH, et al. Un-  
176 lock the potential of vaccines in food-producing animals. *Science*. 2024;384(6703):1409-11.  
177 Available from: <https://www.science.org/doi/abs/10.1126/science.adj5918>.
- 178 [14] Saad-Roy CM, Metcalf CJE, Grenfell BT. Immuno-epidemiology and the predictability of  
179 viral evolution. *Science*. 2022;376(6598):1161-2. Available from: [https://www.science.](https://www.science.org/doi/abs/10.1126/science.abn9410)  
180 [org/doi/abs/10.1126/science.abn9410](https://www.science.org/doi/abs/10.1126/science.abn9410).
- 181 [15] Carlson CJ, Albery GF, Merow C, Trisos CH, Zipfel CM, Eskew EA, et al. Climate change  
182 increases cross-species viral transmission risk. *Nature*. 2022;607(7919):555-62. Available from:  
183 <https://doi.org/10.1038/s41586-022-04788-w>.