

The One Health High-Level Expert Panel

**THE PANZOOTIC SPREAD  
OF HIGHLY PATHOGENIC  
AVIAN INFLUENZA H5N1  
SUBLINEAGE 2.3.4.4b**

A CRITICAL APPRAISAL  
OF ONE HEALTH PREPAREDNESS  
AND PREVENTION



# **THE PANZOOTIC SPREAD OF HIGHLY PATHOGENIC AVIAN INFLUENZA H5N1 SUBLINEAGE 2.3.4.4b**

## **A CRITICAL APPRAISAL OF ONE HEALTH PREPAREDNESS AND PREVENTION**

Authored by the members of the One Health High-Level Expert Panel (OHHLEP):

Marion P. G. Koopmans, Casey Barton Behravesh, Andrew A. Cunningham, Wiku B. Adisasmito, Salama Almuhaire, P  p   Bilivogui, Salome A. Bukachi, Natalia Casas, Natalia Cedi  l Becerra, Dominique F. Charron, Abhishek Chaudhary, Janice R. Ciacci Zanella, Osman Dar, Nitish Debnath, Baptiste Dungu, Elmoubasher Farag, George F. Gao, Margaret Khaitso , Catherine Machalaba, John S. Mackenzie, Wanda Markotter\*, Thomas C. Mettenleiter\*, Serge Morand, Vyacheslav Smolenskiy, Lei Zhou, David T. S. Hayman.

\* Corresponding authors

## INTRODUCTION

**With the world gradually recovering from the COVID-19 pandemic, it is important to think forward when it comes to prevention of infectious disease outbreaks originating from the animal world. There has been a huge body of work on the early detection and response to emerging disease outbreaks following spillover of animal viruses to humans, but far less focus on primary prevention. Primary prevention starts before the first cases of human illness occur, but its implementation is challenging. It requires a focus on understanding underlying principles of disease emergence, and the prevention of spillovers through a One Health approach across human, animal and environmental health sectors [1]. Therefore, in addition to the public health concerns that are currently already widely addressed, One Health requires a focus also on biodiversity conservation and environmental impacts, wildlife health, and livestock production and consumption, and both wild and domestic animal health and welfare concerns. The recent unprecedented shift in the ecology of highly pathogenic avian influenza (HPAI) illustrates this need.**

The recent global shift in the ecology of H5N1 high pathogenic avian influenza (HPAI) is an important case study for the critical need for strengthening the One Health concept into pandemic prevention, preparedness and response and to move away from anthropocentric thinking towards a more holistic approach to emerging diseases [2], [3]. H5N1 HPAI viruses have caused zoonotic infections in humans in close contact with infected poultry, mostly in Asia and Africa, with occasional cases in Europe and recently the Americas [4], [5]. Since the emergence of a new lineage of H5N1 HPAI in 1996, these viruses have evolved into multiple clades and genotypes through genetic and antigenic drift, as well as a complex pattern of reassortments during continued circulation in poultry farms with insufficient biosecurity and recycling of spillovers and spillbacks between poultry and wild bird populations [6]. While the East and Southeast Asia regions have been a source of introductions of H5 HPAI viruses into poultry farms in other regions [7], either directly through the movement of poultry or indirectly via carriage in wild birds, the global expansion that occurred in the past three years is unprecedented. H5 HPAI viruses have spread globally in wild birds to previously uninfected geographic areas [8], infecting an increasing number of wildlife species, including aquatic and terrestrial wild mammals, as well as production animals like farmed mink and pets (cats) [9]–[11]. A recent suspected foodborne incident led to infection of multiple domestic cats across Poland, including deaths, where cats had neurological, respiratory or both neurological and respiratory symptoms [12]–[14], which highlights the risk for other possible routes of exposure among felids, previously reported in captive wild tigers [15], because some cats (5 of 25) had no access to the outdoors. While the risk for infection of humans is still considered low, and there have been only few reported human infections with the current globally spreading H5 HPAI clade from 2020 [5], [16], [17], it is clear that these viruses have infected a wide range of mammalian species efficiently (e.g. seals, sea lions, cetaceans, otters, foxes, bobcats, mountain lions, skunks and mink), most likely attributable to the very high prevalence of the virus in multiple wild bird species [18], [19]. This high prevalence in animals could result in a higher risk for humans as well [20].

One Health approaches have been applied to prevention and control of HPAI since these viruses were first recorded as a cause of severe zoonotic disease in humans [21]. The inclusion of One Health concepts has also been promoted since the New Delhi intergovernmental meeting on avian influenza [22]. For instance, circulation of H5 HPAI viruses in the poultry production system in Asia has been suppressed through vaccination programs, although its effectiveness is impacted by the emergence of escape variants and the capacity to use vaccines sufficiently in or, ideally, prior to outbreaks [23]. However, the current panzootic is driven by circulation among wild birds, for which vaccination is not an option, except for targeted protection of specific endangered species. Therefore, this novel scenario challenges our current ability to control HPAI [24].

## **BACKGROUND ON INFLUENZA**

Influenza A viruses are common pathogens known to infect humans and a wide range of animal species. They are characterized and named after the subtypes of two surface proteins on the virus particle, the hemagglutinin (H) and the neuraminidase (N). Current seasonal human influenza viruses have H1N1 or H3N2 surface protein subtypes [25]. These surface proteins are key determinants for pathogenicity, host range, and transmissibility, and in combination with additional viral and host factors determine the likelihood and impact of infections in humans.

Wild birds are the natural reservoir of influenza A viruses specifying 16 H and 9 N subtypes. In addition, there is evidence for influenza A virus infection in bats, adding 2 H subtypes and 2 N subtypes (H17N20 and H18N11) to the diversity of influenza A viruses [25].

## EPIDEMICS, EPIZOOTICS AND PANDEMICS

For decades, pandemic preparedness planning has focused on the potential for influenza pandemics following zoonotic spillover of avian influenza viruses, swine influenza viruses, and reassortants thereof into the human population. Influenza viruses are – arguably – the best-known pandemic threats. Influenza pandemics have occurred regularly in human history, with the last example being the H1N1 ‘swine flu’ pandemic in 2009, resulting from viruses that evolved through complex reassortment steps, mixing genes from human, avian and swine influenza viruses. Other pandemics have resulted either from direct spillovers of avian influenza viruses, or following reassortment of avian- and swine- or human influenza virus genes [26], [27]. In the last 100 years there have been four well-documented influenza pandemics, with greatly differing severity.

Avian influenza viruses of subtypes H5 and H7 that circulate naturally in low pathogenic forms (LPAI) in wild birds can acquire mutations that introduce a modified activating proteolytic cleavage site in the H protein resulting in systemic rather than localized infection and disease with high mortality in poultry (HPAI). H5 and H7 HPAI influenza outbreaks have devastated poultry farms, often causing major economic loss and negatively impacting human livelihoods and wellbeing. Sporadic zoonotic infections have occurred throughout the history of H5 HPAI infections, but with varying risk to humans depending on the combination of genes and mutations present in specific virus variants. While some of the factors that determine higher risk for humans are known, it remains difficult to predict which viruses could trigger more widespread human disease outbreaks, and the ongoing process of viral evolution by genomic reassortment requires regular updates of risk assessment.

The H5N1 HPAI virus originated in a commercial goose farm in China in 1996 and likely increased its pathogenicity within commercially farmed poultry in Asia where it spilled over into wild birds. The virus then evolved over years causing epidemic outbreaks with subsequent intercontinental spread with multiple poultry-wild bird host switches in Asia, Africa and Europe, leading to the current situation [28], [29]. This spread has had a significant impact on many wild species, with unprecedented numbers of species impacted [30]. Infections have been confirmed mostly through detections in dead birds in over 400 bird species, including critically endangered species. Local epizootics have led to massive numbers of individuals being killed, with significant proportions of some bird populations, such as 10% of the global Dalmatian Pelican (*Pelecanus crispus*) breeding population and 7% of the critically endangered California Condors (*Gymnogyps californianus*). Many long-lived species have been impacted, whose populations may face multiple threats and will take years to recover [30].

## **EARLY IDENTIFICATION OF ZOO NOTIC INFLUENZA VIRUS OUTBREAKS AND PANDEMIC RISK ASSESSMENT**

In view of the risk of pandemics, spillover infections of animal influenza viruses to humans need to be tightly monitored. Zoonotic influenza virus infections causing clinical illness in humans are relatively rare, but require careful evaluation with rapid characterization of the virus and contact tracing to assess the extent of spread in people and other animals. The World Health organization (WHO) and the US Centers for Disease Control and Prevention (CDC) have developed risk assessment frameworks in which the pandemic potential of animal influenza viruses is ranked based on ten risk elements [31], [32], using an Influenza Risk Assessment Tool (IRAT) describing:

- properties of the virus (receptor binding properties, genomic characteristics, transmission in animal models, susceptibility to antiviral treatment),
- attributes of viral infection in the human population (human infections, disease severity, population immunity), and
- virus ecology and epidemiology in non-human animal hosts (geographic distribution in animals, infections in animals).

Periodically, new candidate vaccine viruses are defined based on the work of the Global Influenza Surveillance and Response System (GISRS) network and the World Organisation for Animal Health (WOAH)/Food and Agriculture Organization of the United Nations (FAO) Network of Expertise on Animal Influenza (OFFLU). This underscores the importance of a multisectoral One Health approach to inform sufficient understanding of the current and evolving scope of animal influenza viruses, but also highlights the need for continued financial and organizational support and why primary prevention is preferable, by reducing the frequency of spillovers.

## **COMPARING THE CURRENT SITUATION WITH H5N1 HPAI POULTRY OUTBREAKS IN ASIA OVER TIME SINCE 1996**

If we apply the above framework to the current situation, the risk for humans from the properties of the virus and attributes in the human population is not fundamentally different from events over the past decades, and one could argue that the current H5N1 HPAI sublineages dominating globally (based on lineage 2.3.4.4b) are less worrisome than other, less widespread sublineages associated with more frequent zoonotic infections. When looking at virus ecology and epidemiology, however, the situation is very different and the risk of zoonotic emergence has certainly increased [9], [29], [33]. This element of the risk assessment, however, has not been translated into action: while we know of the global geographic and taxonomic expansions of H5N1 HPAI from reports of wild bird mortality incidents, and of related mortalities of seals, sea lions, cetaceans, otters, foxes, mink, and domestic cats along with the occasional human case and efforts such as the WOAHP/FAO Network of Expertise on Animal Influenza (OFFLU) and WOAHP's World Animal Health Information System (WAHIS), there are gaps in international reporting of animal influenza viruses of pandemic potential and these need strengthening. For instance, in some countries, the first evidence of the circulation of H5 HPAI in wild birds may come from human disease reporting and subsequent outbreak investigations. However, currently an important missing component is the systematic collection of data from wild birds and mammals. While this is understandable in terms of costs and priorities for disease detection, OHHLEP strongly recommends exploring the potential of driver based hot spot surveillance (analogous to ecological monitoring) to enhance the level of preparedness. Currently, when viewing this with a One Health lens, there is no fully integrated system in place that allows the systematic monitoring of the evolving situation in a manner that could be used to assess changes in risk.

Frameworks exist for inter-agency collaboration between the FAO, WOAHP and WHO Tripartite, that allow the exchange of information. These include a Tool for Influenza Pandemic Risk Assessment (TIPRA) undertaken after initial assessments, and the Global Early Warning System for transboundary animal diseases (GLEWS+) as a mechanism for sharing information rapidly and conducting risk assessments on threats at the animal environment interface [34]. These could form the basis for further development.



## WEAKNESSES IN PANDEMIC PREPAREDNESS AND PREVENTION

With this, we note a weakness in pandemic preparedness, where public health action is typically triggered only by human cases, and action on protecting animal health and associated consequences for biodiversity is mostly focused on the early detection and control of outbreaks in poultry involving culling and/or regional poultry vaccination. However, these actions do not address the fundamentally different pandemic risk to humans in the current situation arising from a panzootic wildlife infectious disease. Although spillover to mammals by H5N1 HPAI is still a rather rare event, mutations are observed in these viruses associated with an increase in the risk of human infection. Moreover, although definitive proof is lacking, a recent outbreak on a mink farm in Spain indicated possible direct mink to mink transmission [11]. These events are not routinely captured by the existing surveillance systems, stressing the need for adaptiveness. The COVID-19 pandemic taught us that the world was far from optimally prepared, and that by the time the circulation among humans had been detected, the window of opportunity for containment had closed. So, what is next? The fast expansions of H5 HPAI and the resulting spillover infections in fur animals and wild carnivores can be used as preparedness scenarios, asking for instance: are we able to detect emerging circulation among pigs, fur animals and humans in a sufficiently timely manner to allow for early containment? We now have a better understanding of what the global fur animal industry looks like, but surveillance is still patchy despite such farms being a potential pandemic threat. Similarly, if we see an increasing list of spillover to mammals, what is being done to enhance surveillance in pigs? Initial experimental infections with H5 HPAI viruses (e.g., H5N1, H5N2, and H5N8 clade 2.3.4.4 viruses) suggested pigs are not highly susceptible to viruses of sublineage 2.3.4.4 [35]–[37], but the ongoing genetic changes should be a warning sign that we cannot consider this “one virus” and we cannot be complacent about pandemic potential [38].

There is also an unprecedented but difficult to quantify ecological impact of this virus. Populations of wild birds have been severely affected by introduction from poultry and subsequent cross- and trans-continental spread. The massive die-offs of wild sea birds and waterfowl in multiple continents, most recently in South America endangering Antarctica as well, has also affected birds of prey, and terrestrial and marine mammals [39]. Oceania is the only region with no infections recorded so far. However, the lack of systematic tracking of wildlife and broader ecological impacts from this major event underscores a massive global gap in surveillance for early spillover events as well as for equity for the wildlife health sector. There are major gaps in our understanding of the impact of this panzootic on wildlife and the environment on short and longer time scales.

## SUGGESTIONS MOVING FORWARD

Improving efforts to prevent transmission between and among wild and domestic animal species is one of the best ways to avoid animal to human transmission [2], [3]. Although extremely challenging, this preventative approach is essential in complementing the current focus on early detection and response in poultry and in the human population [24], [40], [41].

Based on this, we suggest using this ongoing panzootic to further assess where H5N1 HPAI surveillance and AI influenza surveillance more generally can be improved at all levels (international, regional, national, and local) using a One Health approach [42]. This may address the other possible blind spots that focus on specific viruses and clades that have historically been an issue for animal, but not human health or vice versa. This includes exploring the potential expansion of the existing systems to driver-based surveillance to identify hot spots for increased spillover risk, including the role of large-scale farming of susceptible mammals and multi species animal holdings, of wild birds, and of pets [18], [30]. Given barriers to implementation of enhanced surveillance in general, which will be even more complex when expanding to driver-based surveillance, innovative approaches are needed, for instance including environmental sampling (e.g., water, dust, food sources, slaughterhouse waste) and data collection involving citizen scientists [40]. Information collected should be easily accessible internationally following good data governance principles and in compliance with relevant legal terms and agreements. This would include an agreed set of metadata using standards that have been developed in the field of big data analytics (for driver data), and for the current surveillance. Important barriers for sharing of data include concerns about data privacy and security, intellectual property and data misuse, lack of incentives, lack of data quality standards, technical and capacity resource challenges, as well as concerns about priority and competition for publication. Other barriers could include fear for repercussions, including for instance preemptive culling of wildlife, loss of income, and stigmatization.

To promote global preparedness, we also suggest to careful evaluation of current incidents (H5 HPAI infection of different mammals) with regards to the timeliness of their detection, and the completeness of the follow-up, for scenario exercises.

All of these activities need political support and appropriate funding [43] and a careful translation to possible actions. Recommendations include more immediate measures such as improved communication regarding risk (e.g. including feed sources like raw meat diet for domestic and farmed wild animals, roaming cats), farm biosecurity, risk-based surveillance and early warning systems involving poultry and potential bridging hosts (e.g., mink, pigs, domestic cats) with more medium-term approaches such as reducing poultry farm sizes and stocking densities, carefully regulating, managing and monitoring certain production systems in high-risk areas and species, such as legal trade in and farming of wildlife, reducing the illegal trade in domestic and wild birds, and the implementation of vaccination programs coupled with AI vaccine stewardship. Longer-term solutions likely require understanding and reducing the broad, upstream drivers that foster conditions conducive to such outbreaks, such as the demand for poultry products, while considering the need for high quality and safe food, produced in environmentally sustainable and ethical ways [1], [2], [44], [45]. Measures may require appropriate compensatory mechanisms, the funding of which might require new global funding schemes. Many of the approaches will require local community level work, e.g., working with small producers such as local duck farmers for whom HPAI might not seem a threat, to help mitigate risk[46], [47]. These measures need to parallel actions that directly mitigate human health risk and will help change behaviour and social norms and reduce political barriers, that together are more effective and sustainable.

Measures that reduce short-, medium-, and long-term risks to wildlife species are also required. Reducing pressure on wildlife includes addressing direct drivers such as land/sea use change, direct exploitation, pollution, invasive species and climate change, as well as indirect drivers which include demographic and sociocultural changes related to values and behaviors, and encompass economic, technical, institutional and governance changes [48], all of which are linked to changes required for infectious disease control as well. Given the human, domestic and wild animal health issues and environmental impacts, all One Health sectors need to advocate for further funding and improved responses, including a focus on prevention.

## **IMPLICATIONS FOR THE DRAFT PANDEMIC INSTRUMENT**

WHO Member States established an Intergovernmental Negotiating Body (INB) to “draft and negotiate a WHO convention, agreement, or other international instrument on pandemic prevention, preparedness and response”, whose work is underway. The One Health Joint Plan of Action [49], a framework to guide implementation of a prevention-focused, One Health approach, developed and agreed upon by the Quadripartite, will be relevant in the negotiation of this new instrument, as it focuses on understanding the drivers of (re-)emerging zoonotic diseases and related processes and pathways, developing risk mitigation measures, and enhancing sustainable and targeted One Health surveillance [3], [42], [50].

## **CONCLUSION**

The unprecedented change in the epidemiology and ecology of H5N1 HPAI exerts a devastating impact on wild birds, poultry farms, farmers and their communities, and wild mammals globally. These viruses evolved in poultry farming, and now are globally dispersed in wild birds. With this, a novel global challenge is to understand and reduce the impact of this disease risk on health of wildlife, ecosystems, domestic animals, and humans now and in the years to come. H5N1 HPAI also stresses the need for integrating One Health as the basis for pandemic prevention and preparedness planning, and thus the importance of multisectoral collaborations among the animal, environmental, and public health sectors in conducting risk assessments and developing countermeasures to prevent disease and to control spread [33]. To reduce the future pandemic risk, urgent action is required. This should focus on improving efforts to prevent transmission between and among wild and domestic animal species, with emphasis on upstream drivers that foster conditions conducive to such outbreaks as well as rapid response and risk assessment of each and every zoonotic outbreak. Political commitment and sustainable funding are needed to implement and maintain One Health prevention programs, surveillance and timely and efficient response to outbreaks.

## **DISCLAIMER**

This publication was prepared by OHHLEP members who serve in their personal capacity. The opinions expressed in this article are the author's own and do not necessarily reflect the view of the employer or affiliated institution or agency.

## REFERENCES

1. W. B. Adisasmito et al., "One Health: A new definition for a sustainable and healthy future," *PLoS Pathog*, vol. 18, no. 6, Jun. 2022, doi: 10.1371/journal.ppat.1010537.
2. OHHLEP et al., "PREVENTION OF ZOO NOTIC SPILLOVER: FROM RELYING ON RESPONSE TO REDUCING THE RISK AT SOURCE PREVENTION OF ZOO NOTIC SPILLOVER Whitepaper/ Opinion piece CONTENTS."
3. W. Markotter et al., "Prevention of zoonotic spillover: From relying on response to reducing the risk at source," *PLoS Pathogens*, vol. 19, no. 10 October. Public Library of Science, Oct. 01, 2023. doi: 10.1371/journal.ppat.1011504.
4. World Health Organization (WHO), "Human infection caused by avian influenza A(H5) – Ecuador ," <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON434>, Jan. 18, 2023.
5. A. Bruno et al., "First case of human infection with highly pathogenic H5 avian Influenza A virus in South America: A new zoonotic pandemic threat for 2023?" *J Travel Med*, vol. 30, no. 5, Jul. 2023, doi: 10.1093/jtm/taad032.
6. Y. Cui et al., "Evolution and extensive reassortment of H5 influenza viruses isolated from wild birds in China over the past decade," *Emerg Microbes Infect*, pp. 1793–1803, 2020, doi: 10.1080/22221751.2020.1797542.
7. J. H. Verhagen, R. A. M. Fouchier, and N. Lewis, "Highly pathogenic avian influenza viruses at the wild–domestic bird interface in europe: Future directions for research and surveillance," *Viruses*, vol. 13, no. 2. MDPI AG, Feb. 01, 2021. doi: 10.3390/v13020212.
8. A. Kandeil et al., "Rapid evolution of A(H5N1) influenza viruses after intercontinental spread to North America," *Nat Commun*, vol. 14, no. 1, Dec. 2023, doi: 10.1038/s41467-023-38415-7.
9. T. Kuiken, R. A. M. Fouchier, and M. P. G. Koopmans, "Being ready for the next influenza pandemic?," *The Lancet Infectious Diseases*, vol. 23, no. 4. Elsevier Ltd, pp. 398–399, Apr. 01, 2023. doi: 10.1016/S1473-3099(23)00117-2.
10. A. Günther et al., "Iceland as Stepping Stone for Spread of Highly Pathogenic Avian Influenza Virus between Europe and North America," *Emerg Infect Dis*, vol. 28, no. 12, pp. 2383–2388, Dec. 2022, doi: 10.3201/eid2812.221086.
11. M. Agüero et al., "Highly pathogenic avian influenza A(H5N1) virus infection in farmed minks, Spain, October 2022," *Eurosurveillance*, vol. 28, no. 3, Jan. 2023, doi: 10.2807/1560-7917.ES.2023.28.3.2300001.
12. L. Rabalski et al., "Emergence and potential transmission route of avian influenza A (H5N1) virus in domestic cats in Poland, June 2023," *Eurosurveillance*, vol. 28, no. 31, Aug. 2023, doi: 10.2807/1560-7917.ES.2023.28.31.2300390.
13. K. Domańska-Blicharz et al., "Outbreak of highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in cats, Poland, June to July 2023," *Eurosurveillance*, vol. 28, no. 31, Aug. 2023, doi: 10.2807/1560-7917.ES.2023.28.31.2300366.

14. World Health Organization (WHO), "Influenza A(H5N1) in cats – Poland," <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON476>, Jul. 16, 2023.
15. R. Thanawongnuwech et al., "Probable Tiger-to-Tiger Transmission of Avian Influenza H5N1." [Online]. Available: [www.cdc.gov/eid](http://www.cdc.gov/eid)
16. European Centre for Disease Prevention and Control (ECDC), "Public health situation for avian influenza A(H5) viruses," <https://www.ecdc.europa.eu/en/infectious-disease-topics/z-disease-list/avian-influenza/threats-and-outbreaks/situation-ah5>.
17. World Health Organization (WHO), "Global Influenza Programme," <https://www.who.int/teams/global-influenza-programme/avian-influenza>.
18. J. A. Harvey, J. M. Mullinax, M. C. Runge, and D. J. Prosser, "The changing dynamics of highly pathogenic avian influenza H5N1: Next steps for management & science in North America," *Biol Conserv*, vol. 282, Jun. 2023, doi: 10.1016/j.biocon.2023.110041.
19. OFFLU, "First documented case of avian influenza (H5N1) virus infection in a lion," Network of Expertise on Avian Influenza. Nature Publishing Group, Jun. 28, 2023. doi: 10.1038/emi.2016.127.
20. Food and Agriculture Organization (FAO), World Health Organization (WHO), and World Organisation for Animal Health (WOAH), "Ongoing avian influenza outbreaks in animals pose risk to humans: Situation analysis and advice to countries from FAO, WHO, WOAH," <https://www.who.int/news/item/12-07-2023-ongoing-avian-influenza-outbreaks-in-animals-pose-risk-to-humans>.
21. L. D. Sims and M. Peiris, "One Health: The Hong Kong Experience with Avian Influenza," 2012, pp. 281–298. doi: 10.1007/82\_2012\_254.
22. "New Delhi International Ministerial Conference On Avian and Pandemic Influenza," [https://www.cdc.gov/onehealth/pdf/delhi/chair\\_summary.pdf](https://www.cdc.gov/onehealth/pdf/delhi/chair_summary.pdf).
23. I. BROWN and World Organisation for Animal Health (WOAH), "High pathogenicity avian influenza and vaccination: application in Europe Region," Oct. 2022. doi: 10.20506/TT.3335.
24. World Organisation for Animal Health (WOAH), "WOAH Resolution N. 28 Strategic challenges in the global control of high pathogenicity avian influenza CONSIDERING THAT," May 2023.
25. W. J. Liu et al., "Emerging HxNy Influenza A Viruses," *Cold Spring Harb Perspect Med*, vol. 12, no. 2, Mar. 2022, doi: 10.1101/cshperspect.a038406.
26. Y. Guan, D. Vijaykrishna, J. Bahl, H. Zhu, J. Wang, and G. J. D. Smith, "The emergence of pandemic influenza viruses," *Protein and Cell*, vol. 1, no. 1. Higher Education Press, pp. 9–13, 2010. doi: 10.1007/s13238-010-0008-z.
27. F. Krammer et al., "Influenza," *Nature Reviews Disease Primers*, vol. 4, no. 1. Nature Publishing Group, pp. 1–21, Dec. 01, 2018. doi: 10.1038/s41572-018-0002-y.

28. T. Kuiken and R. Cromie, "Protect wildlife from livestock diseases," *Science*, vol. 378, no. 6615. American Association for the Advancement of Science, p. 5, Oct. 07, 2022. doi: 10.1126/science.adf0956.
29. R. Xie et al., "The episodic resurgence of highly pathogenic avian influenza H5 virus," *Nature*, vol. 622, no. 7984, pp. 810–817, Oct. 2023, doi: 10.1038/s41586-023-06631-2.
30. Convention on the Conservation of Migratory Species of Wild Animals (CMS) and Food and Agriculture Organization (FAO), "Scientific Task Force on Avian Influenza and Wild Birds statement on H5N1 high pathogenicity avian influenza in wild birds - Unprecedented conservation impacts and urgent needs," <https://www.cms.int/en/workinggroup/scientific-task-force-avian-influenza-and-wild-birds>.
31. N. J. Cox, S. C. Troock, and S. A. Burke, "Pandemic Preparedness and the Influenza Risk Assessment Tool (IRAT)," *Curr Top Microbiol Immunol*, vol. 385, pp. 119–136, Aug. 2014, doi: 10.1007/82\_2014\_419.
32. World Health Organization (WHO), "Tool for Influenza Pandemic Risk Assessment-version 2 Tool for Influenza Pandemic Risk Assessment (TIPRA)," Jan. 2020. [Online]. Available: <http://apps.who.int/bookorders>.
33. R. Yamaji et al., "Pandemic potential of highly pathogenic avian influenza clade 2.3.4.4 A(H5) viruses," *Reviews in Medical Virology*, vol. 30, no. 3. John Wiley and Sons Ltd, May 01, 2020. doi: 10.1002/rmv.2099.
34. Food and Agriculture Organization (FAO), World Organisation for Animal Health (WOAH), and World Health Organization (WHO), "FAO, OIE, WHO. 2013 GLEWS+ The Joint FAO–OIE–WHO Global Early Warning System for health threats and emerging risks at the human–animal–ecosystems interface. A concept paper," 2013. [Online]. Available: [www.glews.net/wp-content/uploads/2011/04/FINAL\\_CON-](http://www.glews.net/wp-content/uploads/2011/04/FINAL_CON-)
35. A. Graaf-Rau et al., "Emergence of swine influenza A virus, porcine respirovirus 1 and swine orthopneumovirus in porcine respiratory disease in Germany," *Emerg Microbes Infect*, vol. 12, no. 2, 2023, doi: 10.1080/22221751.2023.2239938.
36. B. S. Kaplan, M. K. Torchetti, K. M. Lager, R. J. Webby, and A. L. Vincent, "Absence of clinical disease and contact transmission of HPAI H5NX clade 2.3.4.4 from North America in experimentally infected pigs," *Influenza Other Respir Viruses*, vol. 11, no. 5, pp. 464–470, Sep. 2017, doi: 10.1111/irv.12463.
37. F. Rosone et al., "Seroconversion of a Swine Herd in a Free-Range Rural Multi-Species Farm against HPAI H5N1 2.3.4.4b Clade Virus," *Microorganisms*, vol. 11, no. 5, May 2023, doi: 10.3390/microorganisms11051162.
38. N. S. Lewis et al., "Emergence and spread of novel H5N8, H5N5 and H5N1 clade 2.3.4.4 highly pathogenic avian influenza in 2020," *Emerging Microbes and Infections*, vol. 10, no. 1. Taylor and Francis Ltd., pp. 148–151, 2021. doi: 10.1080/22221751.2021.1872355.



39. British Antarctic Survey, "First confirmed cases of Avian Influenza in the Antarctic region," <https://www.bas.ac.uk/media-post/first-confirmed-cases-of-avian-influenza-in-the-antarctic-region/>.
40. H. Tian et al., "Avian influenza H5N1 viral and bird migration networks in Asia," *Proc Natl Acad Sci U S A*, vol. 112, no. 1, pp. 172–177, Jan. 2015, doi: 10.1073/pnas.1405216112.
41. Longini Ira M Jr et al., "Formation of regulatory patterns during signal propagation in a mammalian cellular network," *Science* (1979), vol. 309, no. 5737, pp. 1078–1083, Aug. 2005, doi: 10.1126/science.1108876.
42. D. T. S. Hayman et al., "Developing One Health surveillance systems," *One Health*, vol. 17. Elsevier B.V., Dec. 01, 2023. doi: 10.1016/j.onehlt.2023.100617.
43. W. B. Adisasmito et al., "One Health action for health security and equity," *The Lancet*, vol. 401, no. 10376. Elsevier B.V., pp. 530–533, Feb. 18, 2023. doi: 10.1016/S0140-6736(23)00086-7.
44. M. A. Clark, M. Springmann, J. Hill, and D. Tilman, "Multiple health and environmental impacts of foods," *Proc Natl Acad Sci U S A*, vol. 116, no. 46, pp. 23357–23362, Nov. 2019, doi: 10.1073/pnas.1906908116.
45. M. van Dijk, T. Morley, M. L. Rau, and Y. Saghai, "A meta-analysis of projected global food demand and population at risk of hunger for the period 2010–2050," *Nat Food*, vol. 2, no. 7, pp. 494–501, Jul. 2021, doi: 10.1038/s43016-021-00322-9.
46. N. A. Rimi et al., "A decade of avian influenza in Bangladesh: Where are we now?," *Tropical Medicine and Infectious Disease*, vol. 4, no. 3. MDPI AG, 2019. doi: 10.3390/tropicalmed4030119.
47. E. Høg, G. Fournié, M. A. Hoque, R. Mahmud, D. U. Pfeiffer, and T. Barnett, "Avian Influenza Risk Environment: Live Bird Commodity Chains in Chattogram, Bangladesh," *Front Vet Sci*, vol. 8, Sep. 2021, doi: 10.3389/fvets.2021.694753.
48. IPBES, E. S. Brondízio, J. Settele, S. Díaz, and H. T. Ngo, *The global assessment report of the intergovernmental science-policy platform on biodiversity and ecosystem services*. 2019.
49. FAO, UNEP, WHO, and WOA, *One Health Joint Plan of Action, 2022–2026*. FAO; UNEP; WHO; World Organisation for Animal Health (WOAH) (founded as OIE);, 2022. doi: 10.4060/cc2289en.
50. Hayman DT and Woolaston K., "Pandemic treaty: incorporate a One Health framework," *Nature*, vol. 613, no. (7942):27, Jan. 2023.





# The One Health High-Level Expert Panel