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The importance of rapid and robust availability of epidemiological data for real-time mapping of the risk of avian influenza a (H5N1) spread

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When the world human population was small and sparsely distributed, infectious diseases were deadly but local. Globalization and the constant movement of people have turned viruses and bacteria into mass killers. Advances in medicine and living conditions have recently reduced infectious disease burden, but the severe social and economic impact of the recent Coronavirus disease (COVID-19) outbreak has opened a wide debate on the zoonotic spread of pathogens from animals to humans, the so-called spillover process. The equation is simple: the more we destroy nature, the more we risk triggering recurrent and emerging infectious diseases. When we cut down forests, drain freshwater habitats, wipe out natural ecosystems, push animals into increasingly fragmented areas, hunt and stress them, we alter natural balances by promoting the species hopping of viruses and the transmission of other pathogen, the so-called spillover process. Experts who authored the recent IPBES report [1] estimate that there are about 1.7 million viruses circulating among mammals and birds and of these about half may have the ability to transfer to humans. An effective global strategy to reduce the risk of spillover should focus on three actions [2]: (i) banning or strictly regulating commercial markets and trade in live wild animals that pose a public health risk, both domestically and internationally; (ii) protecting tropical and subtropical forests; and (iii) improving pathogen surveillance. Regarding the latter, recent epidemiological events related to avian influenza make it urgent to address the challenges of data sharing and exploitation using a One Health approach based on cross-sectoral collaboration for animal, human and environmental health. Typically, avian influenza causes little or no clinical signs in infected poultry, and in these cases, it is named low-pathogenic influenza (LPAI). Low-pathogenic viruses can be 'transported' by migratory reservoir birds and arrive in various regions of the world. It is very common for migratory wild birds to have contact with domestic birds, especially on poultry farms as they are attracted to the food supply. Transmission to poultry, especially if

it occurs on intensive farms, leads to replication of the virus a considerable number of times, with high risk of mutation. On some occasions, therefore, a new virus characterized by high-pathogenicity (HPAI) may emerge during the infectious process. The identified and still predominant HPAI is H5N1 [3], but unlike in the past, the current virus appears to spread to previously unreached places, such as South America [4]. As noted by Marion P G Koopmans and colleagues [5], coordinated and up-to-date real-time surveillance systems are needed, particularly the species most at risk must be monitored (e.g. poultry, pigs, and mink) and the people who handle them and the farm environment.

Rapid access to sequencing and data-sharing mechanisms, such as the availability of open data, along with genomic surveillance, become crucial to quickly take informed policy actions, improve communication on current epidemiological status, perform scientific analysis of a dynamic threat, and understand its social and economic impact. To provide a public, comprehensive, and timely epidemiological update with respect to the spread of HPAI globally, we collected data on outbreaks that have occurred in recent years and made available via our GitHub repository [6], with the Creative Commons Attribution 4.0 International (CC BY 4.0) license, which allows the user to share, copy, and redistribute the material in any format. The database contains a folder for each continent, namely *Africa*, *Americas*, *Asia* and *Europe*, containing a CSV file describing the outbreaks that occurred in the respective countries from 2021 to 28 April 2023 per virus subtype and typology of animal (i.e. wild birds and domestic poultry). The information was extracted from reports released in pdf format from European Food Safety Authority (EFSA), European Centre for Disease Prevention and Control (ECDC), and European Union Reference Laboratory for Plant parasitic nematodes (EURL) [7]. In addition, depending on the reference continent, it is possible to find files describing the epidemiological situation of specific countries such as Italy [8] and the United States [9]

that provide more granular information on each outbreak, including the province in which it occurs and the number of animals that tested positive. This is important information because it helps to estimate the spread of the epidemic curve of the virus with detailed graphical outputs, as shown in Figure 1, which summarizes the geographical distribution of the outbreaks in Italy.

Finally, our team created a line list to provide reliable, synthesized individual information on laboratory-confirmed cases, as described in Table 1. It is an Excel-based tool in order to collect key epidemiological variables such as (a) dates of symptom onset, hospitalization, and possibly confirmed death; b) demographic (i.e. age and sex) and c) geographic information at the highest available resolution (i.e. state, province, and city); d) additional information that can most accurately describe the infections (i.e. symptoms, clade, source of exposure, and clinical outcome). A description of the main fields of the line list is provided below, whereas for the complete data schema, please refer to the GitHub repository (https://github.com/fbranda/avian-flu/blob/main/data_dictionary.yml):

- **Pathogen:** Name of the subtype of influenza A virus.
- **Country:** Country where the case was reported.
- **Province/Region:** Country subdivision where case was reported.
- **District/City:** City where case was reported.
- **Age:** Age of the reported case.
- **Gender:** Gender of the reported case.
- **Case_status:** Status of a case (e.g. not a case, suspect, probable, or confirmed).

- **Date_onset:** Date when the reported case developed symptoms.
- **Date_confirmation:** Date when the reported case was confirmed using RT-PCR.
- **Date_hospitalization:** Date when the confirmed case was admitted to the hospital.
- **Date_death:** Date when the confirmed case died.
- **Symptoms:** List of symptoms of the confirmed case.
- **Outcome:** Clinical outcome of the confirmed case.
- **Contact_comment:** Detailed description of the contact that caused the infection in the case.
- **Source:** Reference of the source describing the reported case.

The information is first collected from various sources, including news aggregators (e.g. <https://bnonews.com/>, <https://www.cidrap.umn.edu/avian-influenza-bird-flu/>); then it is enriched with official WHO reports [10] and finally saved in the database folder called *Line-lists*. For simplicity, the data have been sorted according to the virus subtype and date the case was reported.

The epidemiological situation of avian influenza evolves rapidly, and reports soon become outdated. The COVID-19 pandemic has reinforced the notion that access to information is critical to ensuring public trust in governments through greater transparency and better communication. At the same time, it revealed weaknesses in the way countries collect, analyze, and use data. A key question remains: will synthesizing multiple data streams in a shareable and sustainable way also improve countries' ability to respond to non-COVID-19 threats? The world will likely face the continued threat of new and emerging infections and

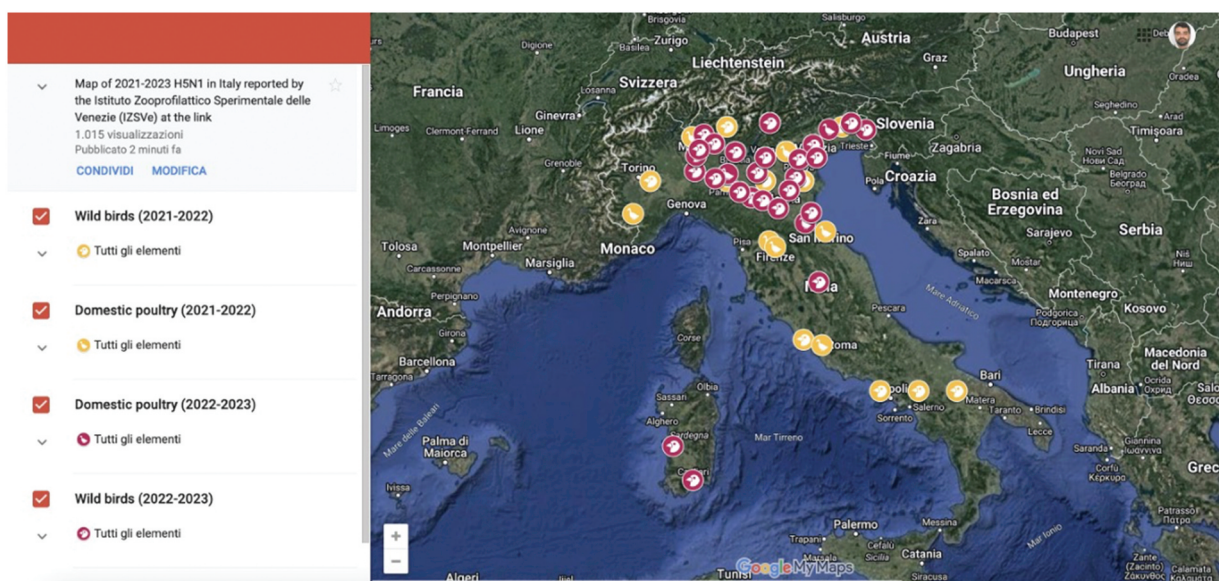


Figure 1. The main outbreaks detected during the HPAI 2021–2023 epidemic in Italy by typology of animal (source: <https://www.izsvenezie.com/reference-laboratories/avian-influenza-newcastle-disease/italy-update/>, accessed on 3 April 2023). The map is available at the link: <https://tinyurl.com/avian-italy-map>.

Table 1. Clinical characteristics of the reported A(H5N1) human cases, January 2022 to April 6, 2023.

Country of case	Province	Age	Gender	Month of illness onset or case detection	Days from onset of illness to hospitalization	Days from onset of illness to death	Virus clade	Symptoms	Outcome	Exposure note
Cambodia	Prey Veng	11	Female	February 2023	5	6	2.3.2.1c	Severe pneumonia	Died	Ducks and chickens at her home died suddenly
	Prey Veng	49	Male	February 2023	Not reported	None	2.3.2.1c	None	Asymptomatic	Not reported
	Antofagasta	53	Male	March 2023	9	None	Not reported	Cough, sore throat, and hoarseness	Serious	The man may have had environmental exposure in areas close to his house where either sick birds or mammals were found
China	Guangxi	38	Female	September 2022	3	26	Not reported	Not reported	Died	Live domestic poultry
Ecuador	Jiangsu	53	Female	January 2023	4	None	2.3.4.4b	Not reported	Not reported	Poultry
	Bolivar	9	Female	December 2022	5	None	2.3.4.4b	Conjunctival pruritus and coryza; nausea, vomiting and constipation	Survived	Poultry
South West England	Bolivar	Not reported	Not reported	January 2022	None	None	2.3.4.4b	None	Asymptomatic	The case lived with a large number of domestically kept birds which had onset of illness
Spain	Guadalajara	19	Male	September 2022	None	None	2.3.4.4b	None	Asymptomatic	Working on an infected poultry farm
	Guadalajara	27	Male	September 2022	None	None	2.3.4.4b	None	Asymptomatic	Working on an infected poultry farm
United States of America	Colorado	Not reported	Male	April 2022	Not reported	None	2.3.4.4b	Fatigue	Survived	The case was involved in culling of poultry at a farm where influenza A (H5N1) virus was confirmed in the poultry
Vietnam	Phu Tho	5	Female	October 2022	3	None	Not reported	Seriously ill	Survived	She ate the meat of sick chickens and ducks

known risks such as the zoonotic diseases that could pose a threat to animals, humans, and general public health. Therefore, there is a unique and rare opportunity to potentially translate the successes and shortcomings of digital tools in COVID-19 into meaningful, sustainable, and equitable tools for change.

Currently, to the best of our knowledge, there is no centralized, comprehensive archive in machine-readable format on avian influenza like the one we have created. There is a need for similar initiatives to set an example for developing a forward-looking policy that can empower professionals to work and do analysis on the data to try to understand the evolving dynamics of this highly changeable pathogen. We need to make sure that different surveillance systems not only manage the same processes but do so by speaking the same language through the use of shared standards. Moreover, there is an urgent need for governments to invest in local and global initiatives that focus on the human-animal-environment interface of diseases. One such investment includes funding for higher education programs in One Health. These programs will prepare the next generation of researchers to address society's grand challenges by enabling the formation of teams whose expertise transcends disciplinary boundaries. We hope that these data can be used to build solid evidence for modeling and conducting epidemiological studies to plan the most appropriate prevention and control measures for each geographic context.

Authors' contributions

Francesco Branda: Conceptualization, Data curation, Formal Analysis, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. Sandra Mazzoli: Investigation, Supervision, Validation, Writing – original draft, Writing – review & editing.

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