



PRESS RELEASE

Avian Flu, from 'FluWarning' early alerts for virus spillovers

A system developed by Researchers at the Politecnico di Milano and the University of Milan detects changes that may indicate cross-species transmission and anticipate possible epidemics

Milan, 20 November 2025 – How can we monitor the cross-species transmission of avian flu? The answer is *FluWarning*, a digital system that reports abnormal changes in flu viruses, developed by a research team from the *Politecnico* di Milano and the *University* of Milan. The system analyses the genetic code of flu viruses, looking for subtle but significant changes that could indicate cross-species transmission (for example, from birds to cattle or to humans), a process known as *spillover*.

The study, which was recently published in the prestigious journal *Science Advances*, was developed under the NRRP-funded PRIN 2022 – SENSIBLE project (*Small-data Early warNing System for viral pathogens In puBLic hEalth*). The *FluWarning* research team includes three members from **DEIB – Department of Electronics, Information and Bioengineering** at the Politecnico di Milano, SENSIBLE's Principal Investigator **Anna Bernasconi**, Professor **Stefano Ceri** and Researcher **Tommaso Alfonsi**, along with **Matteo Chiara**, Professor in the **Department of Biosciences** at the University of Milan.

The study relied on data from GISAID, a platform for sharing virus sequences and the related metadata produced by laboratories all around the world. *FluWarning* was developed using data from the H1N1 swine flu pandemic in 2009, a well-documented example of a virus being transmitted from animals to humans. It was then applied to H5N1 bird flu, a highly pathogenic strain among birds, which in the past year has also begun to spread among US cattle.

The system uses a statistical method to recognise anomalies. Depending on the settings, it can be used to recognise individual anomalous sequences or groups of anomalous sequences. FluWarning learns the normal sequences of influenza viruses and issues an alert whenever the code of the sequences changes significantly. For each alert, virologists analyse the corresponding sequences and confirm or reject the presence of spillover.

'With its simple installation and analysis that can be done for specific locations and over specific time periods, the *FluWarning* software can potentially be used by many laboratories or regional genomic surveillance institutions, enabling important discoveries on both small and large scales,' **Anna Bernasconi** notes. 'In fact, the system is perfectly operational. It can give feedback on these changes day by day.'

In 2024–2025, **two H5N1 genotypes were linked to independent outbreaks in the US**, where numerous heads of dairy cattle were found to be infected with bird flu. *'FluWarning* identified clusters of viral activity in several US states, particularly in California, where a state of emergency was declared on 18 December 2024 due to the risk of bird flu contamination in cattle. Surprisingly,

some *FluWarning* **alerts appeared before official reports were published**. The system also detected specific mutations in the haemagglutinin (HA) gene, a key protein that affects the way the virus infects the host cells,' **Matteo Chiara** says. The tool monitored the evolution of the virus and identified characteristic markers of the California strains.

'FluWarning is an important step towards more effective detection of viral changes that could pose a risk to animals or humans. **By making this technology widely available, we hope to strengthen global surveillance** on a health issue of global significance' **Stefano Ceri** concludes.

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