



Influenza (Flu)

Technical Report: Highly Pathogenic Avian Influenza A(H5N1) Viruses

Updated December 29, 2023

This report provides an update to the [original report](#) posted on March 17, 2023, to include additional sporadic human cases and activity in wild birds, poultry, and other animals. The overall risk to human health associated with the ongoing outbreaks of highly pathogenic avian influenza A(H5N1) viruses in wild birds and poultry has not changed and remains low at this time.

Executive summary

A small number of sporadic human cases of A(H5N1) have been identified since 2022, despite the panzootic of highly pathogenic avian influenza (HPAI) A(H5N1) viruses in wild birds and poultry. Nearly all reported human cases since 2022 were associated with poultry exposures, and no cases of mammal-to-human or human-to-human transmission of HPAI A(H5N1) virus have been identified. In a few cases, the source of exposure to HPAI A(H5N1) virus was unknown. To date, HPAI A(H5N1) viruses currently circulating in birds and poultry, with spillover to mammals, and those that have caused human infections do not have the ability to easily bind to receptors that predominate in the human upper respiratory tract. Therefore, the current risk to the public from HPAI A(H5N1) viruses remains low. However, because of the potential for influenza viruses to rapidly evolve and the wide global prevalence of HPAI A(H5N1) viruses in wild birds and poultry outbreaks, continued sporadic human infections are anticipated. Continued comprehensive surveillance of these viruses in wild birds, poultry, mammals, and people worldwide, and frequent reassessments are critical to determine the public health risk, along with ongoing preparedness efforts.

Key Points

- CDC is actively working on the domestic situation with clade 2.3.4.4b HPAI A(H5N1) viruses in wild birds and poultry outbreaks, including conducting surveillance among people with relevant exposures and preparing for the possibility that contemporary HPAI A(H5N1) viruses gain the ability for increased transmissibility to people.
- CDC, along with our state and local public health partners, continues to actively monitor people in the United States who have been exposed to infected birds and poultry for 10 days after exposure. To date, more than 7,000 people in 52 jurisdictions have been monitored since 2022, and only one human case has been identified.
- H5 candidate vaccine viruses (CVV) produced by CDC are expected to provide good protection against current clade 2.3.4.4b HPAI A(H5N1) viruses in birds and mammals. These H5 CVVs are available and have been shared with vaccine manufacturers.
- Because influenza viruses are constantly changing, CDC performs ongoing analyses of HPAI A(H5N1) viruses to identify changes that might allow for spread more easily to and between people, cause serious illness in people, reduce susceptibility to antivirals, affect the sensitivity of diagnostic assays, or reduce neutralization of the virus by vaccine induced antibodies. To date, few changes in HPAI A(H5N1) viruses of public health concern have been identified and such changes have differed between various HPAI A(H5N1) viruses circulating in wild birds and poultry worldwide or that have sporadically infected humans.
- Currently, HPAI A(H5N1) viruses circulating in birds are believed to pose a low risk to the general public in the United States; however, people who have job-related or recreational exposures to infected birds may be at higher risk of infection and should take appropriate precautions outlined in CDC guidance.

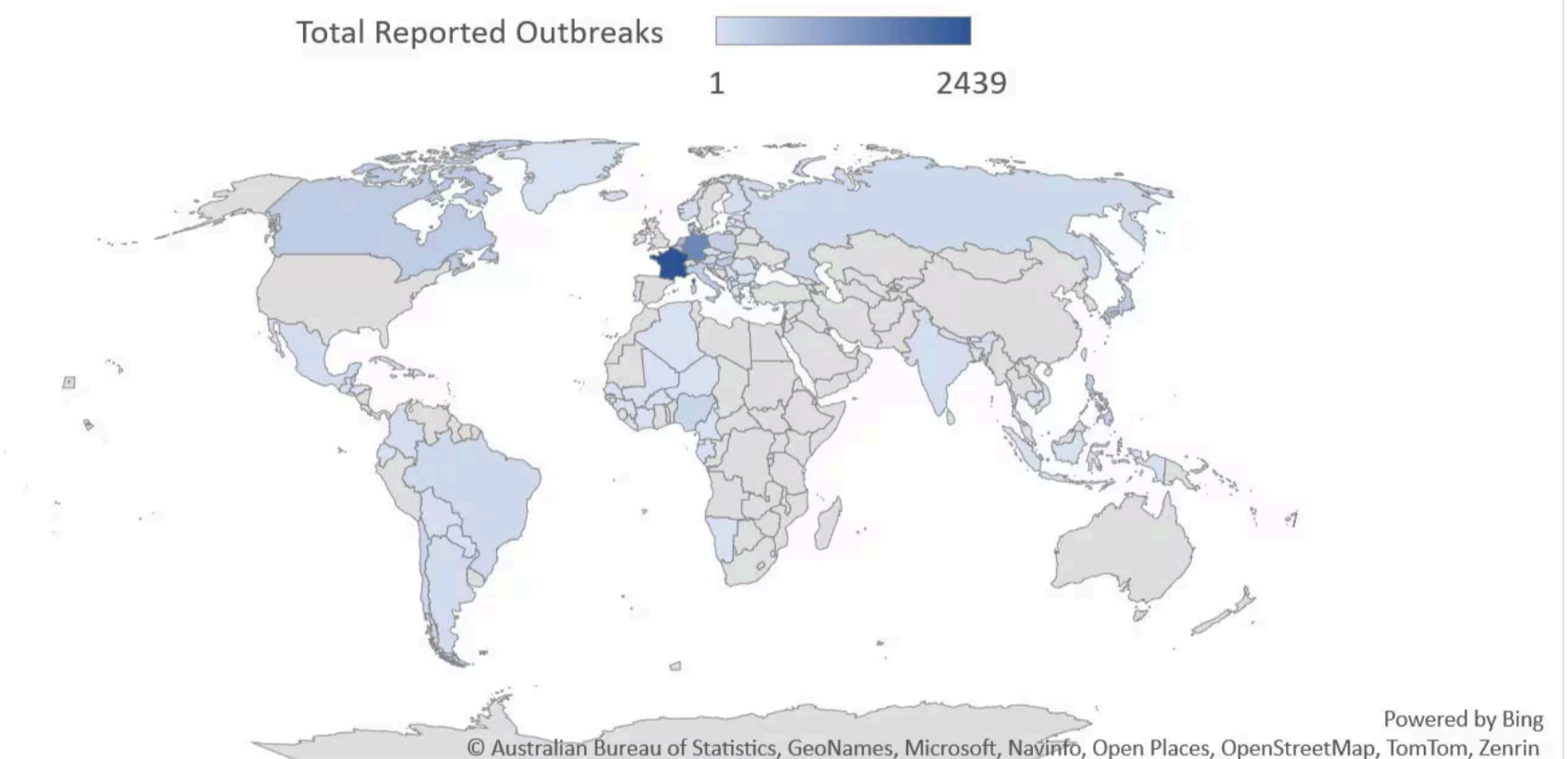
- Comprehensive surveillance and readiness efforts are ongoing, and CDC continually takes preparedness measures to be ready in case the risk to people from HPAI A(H5N1) or other novel influenza A viruses changes.

HPAI A(H5N1) viruses in wild birds and poultry

Since 2005, HPAI A(H5N1) viruses have undergone extensive genetic diversification including the formation of hundreds of genotypes following reassortment with other avian influenza A viruses. Clade 2.3.4.4b HPAI A(H5N1) viruses emerged in 2020 and were introduced into North America in late 2021 [1,2] and spread to Central and South America, resulting in wild bird infections (in terrestrial, seabird, shorebird, and migratory species) and poultry outbreaks in many countries [3-8]. In Fall 2023, the first detections of HPAI A(H5N1) virus in birds in the Antarctica region were reported [9].

Globally, this 2.3.4.4b clade of HPAI A(H5N1) viruses has become widespread causing record numbers of bird outbreaks in wild, backyard, village, and farm birds. Over 11,400 bird outbreaks of HPAI A(H5N1) viruses were reported by 84 member countries to the [World Organisation for Animal Health](#) since January 2022.

Reported HPAI A(H5N1) Bird Outbreaks* Reported to the World Organisation for Animal Health (WOAH), Jan 2022-December 2023



* WOAHA defines an outbreak as an occurrence of one or more cases in a group of animals with a defined epidemiologic relationship therefore outbreak numbers don't reflect the quantity of animals affected.

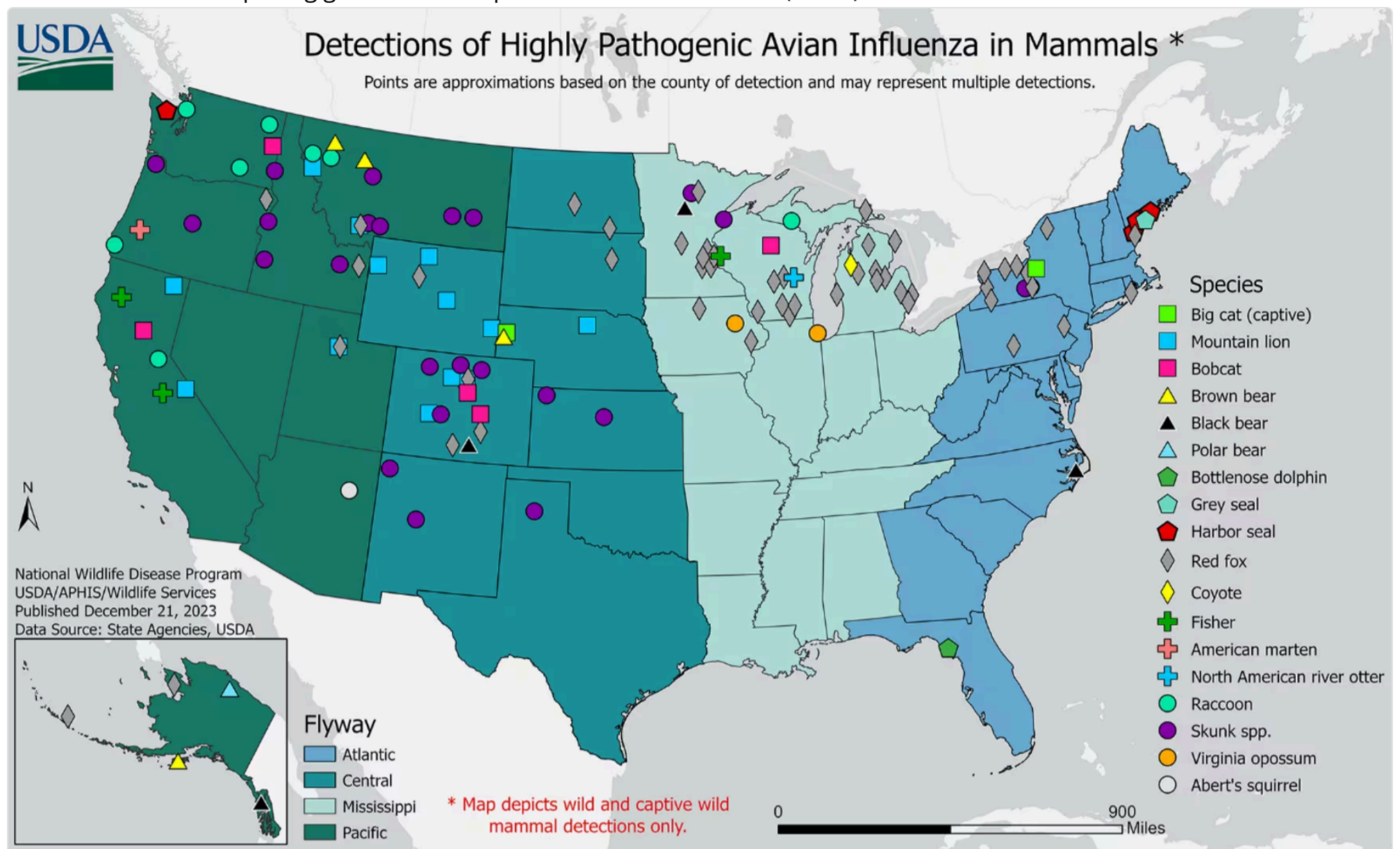
In the United States, [USDA APHIS monitors for avian influenza viruses](#) in wild, commercial, and backyard birds. From January 2022 through December 27, 2023, APHIS reported HPAI A(H5)/A(H5N1) virus detections in more than 8,500 [wild birds](#) in 50 states or territories and more than 1000 [commercial and backyard flocks](#) affecting 77.9 million birds in 47 states.

HPAI A(H5N1) virus infections among mammals

Sporadic HPAI A(H5N1) virus infections of mammals have been reported since 2003-2004 during HPAI A(H5N1) virus outbreaks in poultry or wild birds [10-12]. HPAI A(H5) viruses are known to occasionally infect mammals that eat (presumably infected) birds or poultry and mammals that are exposed to environments with a high concentration of virus.

In the United States, from May 2022 through December 27, 2023, [USDA APHIS reported](#) HPAI A(H5N1) virus detections in 207 mammals comprising 21 different species in 27 states. Globally, sporadic HPAI A(H5N1) virus infections in mammal species number over 300 outbreaks. These outbreaks have occurred in 29 different mammal species and were reported by 13 member countries to the [World Organisation for Animal Health](#) since January 2022. Mammal outbreaks included farmed mink in [Spain](#) and [farmed foxes and other mammals in Finland](#), [harbor and gray seals in the United States](#), [sea lions in](#)

Peru [↗](#), Argentina, and Chile [↗](#), elephant seals in the Antarctic region [↗](#), and domesticated pets such as cats in Poland [↗](#), France, South Korea, and the United States [↗](#), and dogs in Italy [↗](#). The reports of HPAI A(H5N1) virus infections in mammals are not surprising given the widespread outbreaks of HPAI A(H5N1) virus infections in wild birds worldwide.



Source: USDA APHIS | 2022-2023 Detections of Highly Pathogenic Avian Influenza in Mammals

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Genetic data have revealed that when some mammals are infected with HPAI A(H5N1) virus, the virus may undergo intra-host evolution resulting in genetic changes that allow the virus to replicate more efficiently in the lower respiratory tract [13-15]. Some HPAI A(H5N1) viruses that have infected humans in 2023 have also revealed the same or similar genetic changes as those identified in wild and captive mammals. For example, sequencing of viruses from specimens collected from human cases identified in Cambodia during October and November 2023 revealed the presence of the polymerase basic protein 2 (PB2) 627K marker, which is often associated with mammalian adaptation during infection. Similarly, the HPAI A(H5N1) virus sequenced from the human case in Chile identified in March 2023 had markers of mammalian adaptation (PB2 591K and 701N) [16].

Although these genetic changes may impact mammalian disease outcome, they have not been associated with enhanced transmissibility of the virus to humans. HPAI A(H5N1) viruses do not currently have the ability to easily infect and bind to α 2,6-linked sialic acid receptors that are predominant in the human upper respiratory tract [2], which would be needed to increase the risk of transmission to people [17,18].

Human cases of A(H5N1)

While HPAI A(H5N1) viruses are currently circulating widely in wild birds and poultry in many geographic regions, relatively few human cases of A(H5N1) have been reported in recent years [Figure 1]. From January 2022 through December 27, 2023, nineteen sporadic human cases of A(H5N1) were reported from eight countries, including nine cases of severe disease and five deaths, three cases of mild illness, and seven asymptomatic cases [Table 1].

One human case of A(H5N1) was reported in the United States in April 2022. The individual reported fatigue without other symptoms and a low level of A(H5N1) viral RNA was detected in a single upper respiratory tract specimen. It is possible that detection of A(H5N1) viral RNA resulted from deposition of non-infectious viral material in the upper respiratory tract of the individual and did not represent true infection, similar to the environmental contamination that was attributed to the two

asymptomatic cases in poultry workers reported in Spain [19]. Transient environmental deposition may also explain the detection of A(H5N1) viral RNA in cases of A(H5N1) reported in asymptomatic poultry workers in the U.K. that were investigated as part of a surveillance study [20-22].

Nearly all cases reported since January 2022 had recent exposure to sick or dead poultry, and no cases of human-to-human HPAI A(H5N1) virus transmission were identified. Nine cases (four children, five adults) had severe disease, and five died. Twelve cases were associated with clade 2.3.4.4b HPAI A(H5N1) virus, and six cases were associated with clade 2.3.2.1c HPAI A(H5N1) viruses. The clade of the single case reported by Vietnam was not reported. None of the HPAI A(H5N1) virus genetic sequences contained any known markers of reduced susceptibility to currently recommended FDA-approved influenza antiviral medications.

Table 1. Global reported A(H5N1) human cases, January 2022 through December 27, 2023

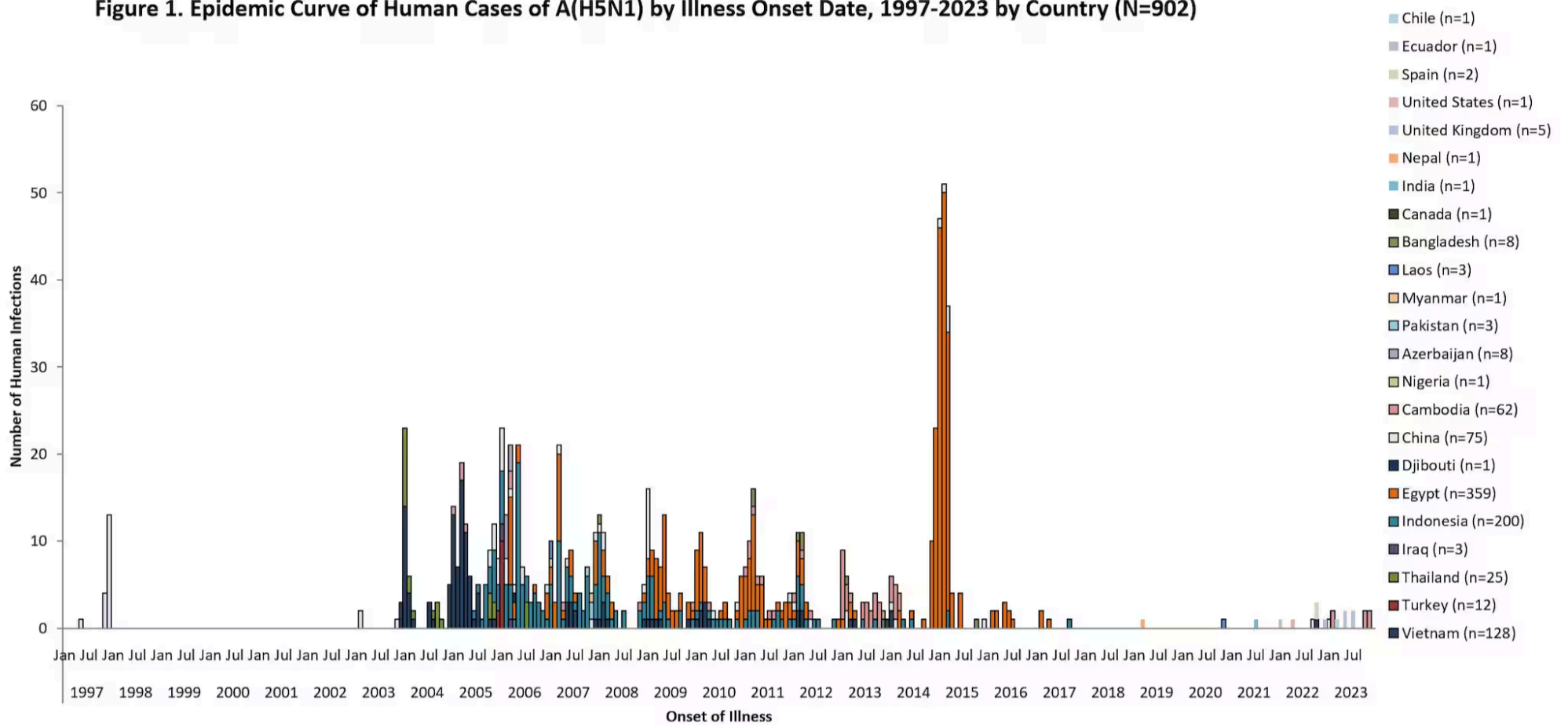
Country of Case	Month of illness onset or case detection	Disease Severity and Outcome	Virus Clade by sequencing or associated poultry outbreaks
Cambodia	February 2023	Critical illness, died	Clade 2.3.2.1c
	February 2023	Mild illness, survived	Clade 2.3.2.1c
	October 2023	Critical illness, died	Clade 2.3.2.1c
	October 2023	Critical illness, died	Clade 2.3.2.1c
	November 2023	Critical illness, died	Clade 2.3.2.1c
	November 2023	Mild illness, survived	Clade 2.3.2.1c
Chile	March 2023	Critical illness	Clade 2.3.4.4b
China	September 2022	Critical illness, died	Clade 2.3.4.4b
	January 2023	Hospitalized, outcome not reported	Clade 2.3.4.4b
Ecuador	December 2022	Critical illness, survived	Clade 2.3.4.4b
Spain	September 2022	Asymptomatic	Clade 2.3.4.4b
	October 2022	Asymptomatic	Clade 2.3.4.4b
United Kingdom	January 2022	Asymptomatic	Clade 2.3.4.4b
	May 2023	Asymptomatic	Clade 2.3.4.4b
	May 2023	Asymptomatic	Clade 2.3.4.4b
	July 2023	Asymptomatic	Clade 2.3.4.4b
	July 2023	Asymptomatic	Clade 2.3.4.4b
United States	April 2022	Fatigue only, survived	Clade 2.3.4.4b

Country of Case	Month of illness onset or case detection	Disease Severity and Outcome	Virus Clade by sequencing or associated poultry outbreaks
Vietnam	October 2022	Critical illness, survived	Not reported

Since 1997, a total of 902 sporadic human A(H5N1) cases have been reported from 23 countries, caused by different HPAI A(H5N1) virus clades [23,24], with a cumulative case fatality proportion of greater than 50%. Human A(H5N1) cases peaked in 2006 (115 cases, 9 countries) and 2015 (145 cases, 4 countries) primarily due to a large epidemic in Egypt with 136 cases [Figure 1].

Nearly all reported human A(H5N1) cases had poultry exposures, such as to sick or dead poultry or visiting live poultry markets. Rare, limited, and non-sustained instances of human-to-human HPAI A(H5N1) virus transmission likely occurred in a small number of family members following prolonged, close unprotected exposure with a symptomatic case-patient during 2004-2007 in multiple countries [25-28].

Figure 1. Epidemic Curve of Human Cases of A(H5N1) by Illness Onset Date, 1997-2023 by Country (N=902)



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Active monitoring of persons exposed to HPAI A(H5N1) virus in the United States

Although few human cases have occurred recently, given widespread infection among poultry and wild birds, people who have job-related or recreational exposures to infected birds or sick or dead mammals might be at higher risk of infection.

CDC, in collaboration with state, territorial, and local public health partners, actively monitors people exposed to infected birds and poultry for 10 days after their last exposure, from February 2022 through December 27, 2023:

- Total monitored: more than 7,000 people in 52 jurisdictions.
- Total illnesses reported among monitored persons: more than 175 people.
- Number positive for influenza A(H5N1) virus: 1 person.

Of the more than 175 people showing symptoms who were tested for novel influenza A and seasonal influenza viruses along with other respiratory viruses, HPAI A(H5N1) virus genetic material was detected in a respiratory specimen from one person in Colorado who experienced fatigue without any other symptoms while participating in poultry culling activities. [See above section on "Human cases of A(H5N1)."]

U.S. influenza surveillance for human infections with novel influenza A viruses, including HPAI A(H5N1) virus

Human infection with a novel influenza A virus, including HPAI A(H5N1) virus, is a nationally notifiable condition (case definition: [Novel Influenza A Virus Infections 2014 Case Definition | CDC](#))

Influenza testing is widely available in clinical laboratories and healthcare facilities. Assays in these settings would detect A(H5N1) virus infections as influenza A positive and a subset of assays would be able to also determine that they are not influenza A virus subtypes H1 or H3 that commonly circulate among humans. Specimens from persons possibly exposed to H5N1 virus or that test positive for an influenza A virus but negative for A(H1) and A(H3) subtypes should be forwarded to the appropriate state or local public health laboratory for further testing. Very few specimens have been submitted to CDC for H5 testing since January 2022.

- Seasonal influenza virus detection assays that can also detect novel influenza A viruses are used in 128 public health laboratories in all 50 U.S. states.
- Specific diagnostic assays to detect current A(H5) viruses are available at 99 public health laboratories in all 50 states.

Per long-standing protocols, upon detection of a virus that tests positive for influenza A but is negative for human H1 or H3 genes the public health laboratory will rapidly contact CDC and ship the specimen to CDC. Samples that are influenza A positive but negative for human H1 or H3 genes may also be tested for H5 by state public health laboratories and are rapidly sent to CDC for a diagnostic result. An investigation of the case will be initiated, and a case report form submitted to CDC through the novel influenza A reporting module.

CDC and U.S. Government Preparedness Activities

Activity

Global surveillance and rapid response to human infections

Summary

CDC's Influenza Division supports surveillance in live bird markets, backyard farms, and wild birds and/or their environments in Bangladesh, Cambodia, China, Guatemala, Kenya, Lao PDR, Peru, Thailand, and Vietnam. Surveillance data highlight the high prevalence and wide range of avian influenza A viruses in birds and help to describe the changing epidemiology of avian influenza A viruses.

In 2022, the Influenza Division tracked more than 50 human infections with avian influenza A viruses reported to the WHO from seven countries in four WHO regions. Most recently, [CDC Influenza Division field staff assisted in the rapid response investigations of two human H5N1 cases in Cambodia in 2023](#).

Activity

Virological assessments

Summary

Because influenza viruses have a high error rate during replication and rapidly evolve, CDC continually conducts genetic analyses of viruses to identify changes that may impact virus phenotypes such as antigenicity, antiviral susceptibility, transmissibility, and/or pathogenesis. Genetic analysis is also performed to assess changes that may impact diagnostic test performance.

Activity

Diagnostics

Summary

Various CDC influenza virus diagnostic real time RT-PCR tests detect typical human (seasonal) viruses or novel influenza A viruses (e.g., H5, H7) that may infect people through zoonotic transmission. These diagnostic tests are used in all 50 U.S. states and globally. Additionally, there are CDC diagnostic tests that specifically detect the current H5 viruses, which are available in public health laboratories in all 50 U.S. states and international laboratories.

Most commercial assays used for human influenza virus testing are likely to detect HPAI A(H5N1) viruses because they target conserved proteins.

Activity

Candidate vaccine virus development

Summary

The development of influenza candidate vaccine viruses (CVVs), coordinated by WHO, remains an essential component of the overall global strategy for influenza pandemic preparedness. A library of H5 candidate vaccine viruses (CVV) has been produced with additional recommendations for development during bi-annual vaccine consultation meetings (See Table and <https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations/zoonotic-influenza-viruses-and-candidate-vaccine-viruses> [↗](#)). The [CDC Influenza Risk Assessment Tool](#) is also used to help [prioritize HPAI A\(H5\) viruses for development of CVVs](#).

A/Astrakhan/3212/2020-like and A/American wigeon/South Carolina/22-000345-001/2021-like CVVs closely related HPAI A(H5N1) (clade 2.3.4.4b) viruses circulating in North America have been developed and are available for vaccine manufacturers. The two CVVs produced by the U.S. CDC (i.e., IDCDC-RG71A and IDCDC-RG78A) and one CVV produced by U.S. FDA (CBER-RG8A) encode hemagglutinin (HA) proteins that are nearly identical or identical to the HA of most recent clade 2.3.4.4b H5N1 viruses detected in birds and mammals and could be used to produce a vaccine for people if needed. One additional clade 2.3.4.4b H5N1 CVV has been recommended for development as part of pandemic preparedness. In addition to CVVs targeting clade 2.3.4.4b viruses, CVVs have been developed for clade 2.3.2.1c viruses, such as those that have infected humans in Cambodia during 2023. Antigenic testing demonstrates that two existing clade 2.3.2.1 CVVs, NIBRG-301 (A/duck/Vietnam/NCVD-1584/2012-like) and IDCDC-RG75A (A/chicken/Ghana/20/2015-like), will offer protection against the viruses identified in Cambodia in 2023.

Activity

Vaccines

Summary

Influenza virus strains of pandemic potential change over time and multiple new strains circulate in animals every year without leading to sustained human-to-human transmission. The U.S. government has a preparedness program that enables a rapid response to influenza virus strains as the strains evolve. As part of this program, the Biomedical Advanced Research and Development Authority (BARDA) works with private industry partners to make and test small quantities of updated vaccines that match new strains of influenza viruses with pandemic potential as they emerge in case any of them result in sustained human-to-human transmission, while at the same time, supporting manufacturing capacity to allow for large-scale vaccine production when needed.

Limitations of the Report



This report is subject to the following limitations. First, the number of reported human infections with currently circulating clade 2.3.4.4b HPAI A(H5N1) viruses is small. Conclusions regarding virus characterization analyses, transmissibility from animals to people, transmissibility among people, and clinical spectrum of illness in people should be interpreted in light of this small number. Second, detailed exposure information was not available for all persons actively monitored for illness after exposure to HPAI A(H5N1) virus-infected birds and poultry in the United States. Thus, we were not able to assess the impact of exposure variables such as duration of exposure, nature of exposure (e.g., direct vs. indirect contact), and use of personal protective equipment on infection risk.












Conclusions



- To date, CDC analyses of clade 2.3.4.4b HPAI A(H5N1) viruses detected in wild birds, poultry, and sporadically in mammals since late 2021 indicate that these viruses all have a high degree of genetic identity with each other and no significant mammalian adaptive substitutions, insertions, or deletions have been identified, particularly in the HA gene, which is important for zoonotic and subsequent human-to-human transmission.
- Considering the high prevalence of HPAI A(H5N1) viruses detected in wild birds and poultry worldwide, spill over into mammals (particularly carnivores that may feed on infected avian species) and additional sporadic zoonotic infections among people with exposures to sick or dead poultry or wild birds are anticipated.
- HA clade 2.3.4.4b A(H5N1) viruses currently circulating in wild birds and poultry worldwide lack the ability to preferentially bind to the types of sialic acid receptors that are predominant in the upper respiratory tract of humans and therefore do not currently have the ability to easily infect or transmit among people.
- Despite extensive worldwide spread of influenza A(H5N1) viruses in wild birds and poultry in recent years, only a small number of sporadic human infections with 2.3.4.4b or clade 2.3.2.1c H5N1 viruses have been reported since 2022; all cases had recent exposure to poultry and no cases of human-to-human influenza A(H5N1) virus transmission were identified.

While CDC's assessment is that the overall threat of HA clade 2.3.4.4b A(H5N1) viruses to public health is currently low, the widespread geographic prevalence of infected birds and poultry raises the potential for exposures of humans and other mammals that could result in viral evolution or reassortment events which might change the current risk assessment. Vigilance and ongoing surveillance of HPAI A(H5N1) viruses circulating in wild birds, poultry, and in sporadic infections of mammals and people worldwide is critical to monitor the public health risk and to detect genetic changes (particularly in the HA gene) that would change CDC's risk assessment.

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Resources

[Case Definitions for Investigations of Human Infection with Avian Influenza A Viruses in the United States](#)

[Interim Guidance on Influenza Antiviral Chemoprophylaxis of Persons Exposed to Birds with Avian Influenza A Viruses Associated with Severe Human Disease or with the Potential to Cause Severe Human Disease](#)

[Interim Guidance on Follow-up of Close Contacts of Persons Infected with Novel Influenza A Viruses and Use of Antiviral Medications for Chemoprophylaxis](#)

[Brief Summary for Clinicians: Evaluating and Managing Patients Exposed to Birds Infected with Avian Influenza A Viruses of Public Health Concern](#)

[Interim Guidance on Testing and Specimen Collection for Patients with Suspected Infection with Novel Influenza A Viruses with the Potential to Cause Severe Disease in Humans](#)

[Interim Guidance for Infection Control Within Healthcare Settings When Caring for Confirmed Cases, Probable Cases, and Cases Under Investigation for Infection with Novel Influenza A Viruses Associated with Severe Disease | Avian Influenza \(Flu\) \(cdc.gov\)](#)

[Interim Guidance on the Use of Antiviral Medications for Treatment of Human Infections with Novel Influenza A Viruses Associated with Severe Human Disease](#)

Previous H5N1 Technical Reports

[Technical Report: Highly Pathogenic Avian Influenza A\(H5N1\) Viruses \(cdc.gov\) – October 27, 2023](#)

[Technical Report: Highly Pathogenic Avian Influenza A\(H5N1\) Viruses \(cdc.gov\) – October 5, 2023](#)

[Technical Report: Highly Pathogenic Avian Influenza A\(H5N1\) Viruses \(cdc.gov\) – July 7, 2023](#)

[Addendum: Human Infection with highly pathogenic avian influenza A\(H5N1\) virus in Chile \(cdc.gov\) – April 17, 2023](#)

[Technical Report: Highly Pathogenic Avian Influenza A\(H5N1\) Viruses \(cdc.gov\) – March 17, 2023](#)

Additional Information

[Bird Flu Current Situation Summary | Avian Influenza \(Flu\) \(cdc.gov\)](#)

[Novel Influenza A Virus Infections \(cdc.gov\): An interactive dashboard of all novel influenza A virus infections in humans reported in the United States since 2010](#)

[Reported Human Infections with Avian Influenza A Viruses](#)

[Past Examples of Probable Limited, Non-Sustained, Person-to-Person Spread of Avian Influenza A Viruses](#)



[Highlights in the History of Avian Influenza \(Bird Flu\) Timeline – 2020-2023](#)

[Information for People Exposed to Birds Infected with Avian Influenza Viruses](#)

[Prevention and Antiviral Treatment of Bird Flu Viruses in People](#)

[Recommendations for Worker Protection and Use of Personal Protective Equipment \(PPE\) to Reduce Exposure to Novel Influenza A Viruses Associated with Severe Disease in Humans](#)

[CDC Health Advisory, April 29, 2022 – Highly Pathogenic Avian Influenza A\(H5N1\) Virus: Recommendations for Human Health Investigations and Response](#)

[Public Health Monitoring Plan for USDA/APHIS Responders to Detections of Avian Influenza Virus in Poultry](#) 
[353 KB, 18 pages] 

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