Description of document:	Centers for Disease Control and Prevention (CDC) documents regarding the impact and risks to humans of novel avian flu strains 2024
Requested date:	23-June-2024
Release date:	09-August-2024
Posted date:	18-August-2024
Source of document:	FOIA Request CDC FOIA Officer, MS-D54 1600 Clifton Road, N.E. Atlanta, GA 30333 Email: FOIARequests@cdc.gov CDC FOIA web page (PAL) FOIA.gov

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

August 9, 2024

Via email

This letter is our final response to your Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry (CDC/ATSDR) Freedom of Information Act (FOIA) request of June 23, 2024, assigned #24-01281-FOIA, for:

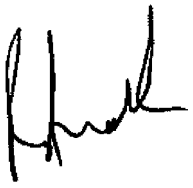
> *A copy of each report, study, model, assessment, white paper, evaluation or other document at CDC regarding the impact and risks to humans of novel avian flu strains such as H5N1 or H7N9, or existing avian flu strains such as H1N1, in causing a potential pandemic, including, for example, impact on cities, our nation, schools, fatalities, hospitalizations, risks to health care workers, shortages of personal protective equipment, etc. I agree to limit this request to records in the Immediate Office of the Director, Office of Readiness and Response, Center for Forecasting and Outbreak Analytics, and OPHDST. I agree to limit this request to records dated between January 1, 2023 and the present.*

You clarified your request per the attached email.

We located 49 pages of responsive records. After a careful review of these pages, no information was withheld from release.

If you need any further assistance or would like to discuss any aspect of the records provided please contact either our FOIA Requester Service Center at 770-488-6399 or our FOIA Public Liaison at 770-488-6246.

Sincerely,



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CDC Avian Influenza A(H5N1) ("H5N1 Bird Flu") Key Points

Date: April 4, 2024

Summary

Against a backdrop of ongoing widespread circulation of influenza A(H5N1) viruses ("H5N1 bird flu") in wild birds with outbreaks in poultry, and sporadic infections in some mammals (most recently cows) and people CDC has confirmed the first human infection with H5N1 virus presumably from a cow. Outbreaks of H5N1 bird flu in cows across several states is ongoing. These are the first known infections of H5N1 bird flu in cattle and only the second human case of A(H5N1) bird flu ever reported in the United States. CDC believes the current public health risk assessment from these recent developments continues to be low; however, people who have job-related or recreational exposures to infected birds and other animals are at higher risk of infection and should take appropriate precautions outlined in CDC updated and expanded interim recommendations.

This is a developing situation and CDC will provide updates as new information becomes available.

In this Document:

Current Situation and Risk Assessment in the United States

- Despite detections of influenza A(H5N1) viruses in U.S. cattle in multiple states, CDC believes the current H5N1 public health risk assessment for the general public remains low; however, risk depends on exposure, and people with more exposure are at greater risk of infection.
- In the United States, ongoing outbreaks of H5N1 bird flu in wild birds and poultry and now cattle have been caused by clade 2.3.4.4b A(H5N1) bird flu viruses. Globally these are the most common A(H5N1) viruses.
- There have been sporadic spillover events into some mammals, including but not limited to, wild or feral animals such as foxes, bears, and seals; stray or domestic animals such as cats and dogs; farmed animals such as mink and foxes, livestock such as goats and cows, and zoo

animals such as tigers and leopards.

- While two human cases of A(H5N1) in people have been reported to CDC since 2022, H5N1 remains mainly an agricultural issue in poultry and now in dairy cows.
- As of April2024, A(H5N1) viruses have been found in wild birds in 50 states and in commercial and backyard poultry in 48 states.
- At this time:
    - More than 9,100 wild birds and more than 82 million commercial and backyard poultry in the United States have been affected by A(H5N1) bird flu.
    - More than 8,000 people in the United States have been or are being monitored following exposure to infected birds/poultry.
    - Cows infected with HPAI A(H5N1) virus have been detected in several states.
- Most infections between 2022 and 2024 have been associated with poultry exposures.
- 26 H5N1 bird flu detections in humans have been reported globally since January 2022.
    - Of these 26 documented cases, seven have died.
    - Of note, eight reported cases were likely due to transient environmental contamination of the upper respiratory tract and not H5N1 virus infection.
- No person-to-person spread has been identified associated with these contemporary A(H5N1) viruses.
- A(H5N1) bird flu viruses detected in the United States since late 2021 are different from earlier A(H5N1) viruses that emerged in 1996 that were associated with hundreds of human cases with a mortality rate of about 50 percent.
- The predominant clade of A(H5N1) virus, called clade 2.3.4.4b, appears well-adapted to spread efficiently among wild birds and poultry in many regions of the world and was first identified in wild birds sampled in the United States in late 2021.
- have ranged from very mild/no signs or symptoms to severe illness, including death in other countries.
- In the United States, the two reported human cases of H5N1 bird flu occurred in 2022 and 2024.
    - The 2022 case only reported fatigue was associated with infected poultry exposure.
    - The2024 case only experienced conjunctivitis and was associated with exposure to cows presumed to be infected with A(H5N1) virus.
    - Both patients had very mild illness and recovered.
- Based on past experience with earlier A(H5N1) viruses and what is known about this group of contemporary A(H5N1) viruses from existing epidemiologic and genetic sequence data, CDC believes the current public health risk from H5N1 bird flu to the general public is low.
- The ongoing spread of HPAI A(H5N1) viruses among wild birds, with outbreaks in commercial and backyard poultry flocks, and in dairy cattle, with sporadic infections of other mammals, are likely to result in increased exposures among people, which may increase the risk, and the number of, human infections.
    - This is especially true for people with work-related or recreational exposures to infected animals (wild birds, poultry, dairy cows), particularly poultry workers, outbreak responders, backyard bird flock owners, livestock farmers and workers, veterinarians and veterinary staff, and waterfowl hunters and anyone else with exposure to infected animals or their contaminated surfaces.
    - There are existing federal recommendations around bird flu exposures for different groups of people, including hunters, poultry producers , farmers, and the general

public, as well as health care providers.
    - CDC also has interim guidance for Prevention, Monitoring, and Public Health Investigations for HPAI H5N1.
        - Specific recommendations for farmers; poultry, backyard flock, and livestock owners; and worker protection are also available.
  - CDC also has guidance documents including recommendations for personal protective equipment and information for people exposed to infected birds and other animals and guidance for testing and treatment of suspected or confirmed human cases to prevent severe illness and spread to other people.
- Given that past human infections with bird flu viruses have resulted mostly from close contact with infected birds/poultry and, to a much lesser extent, other infected animals, some ongoing sporadic human infections with contemporary A(H5N1) viruses would not be surprising, especially among people with exposures who do not take recommended precautions (like wearing personal protective equipment, for example).
- Sporadic human infections in the current context would not significantly change CDC's risk assessment.
- However, identification of multiple simultaneous instances of A(H5N1) viruses spreading from birds or other animals to people or of certain genetic changes in virus specimens could change CDC's risk assessment because they could indicate the virus is adapting to spread more easily from birds or animals to people.
- Additionally, if limited, non-sustained, person-to-person spread with this virus were to occur, that would also raise the public health threat because it could mean the virus is adapting to spread between people.
  - Rare small clusters of limited, non-sustained, human-to-human A(H5N1) virus spread happened in other countries from 2004-2007 without any changes in A(H5N1) viruses.
- Sustained human-to-human spread is needed for a pandemic to occur.
- Because of the potential for influenza viruses to constantly change, continued surveillance and preparedness efforts are critical, and CDC is taking measures to be ready in case the risk assessment changes.

Human Infection with Influenza A(H5N1) in the US

- Most recently, in late March of 2024, a person in Texas tested positive for H5N1 bird flu.
- This infection occurred in a person who had direct exposure to cattle presumed to be infected with H5N1 bird flu.
- The patient reported eye redness as their only symptom (consistent with conjunctivitis) and is recovering.
- This is the second case of H5N1 bird flu ever reported in the United States. The first occurred in 2022 in a person in Colorado who had exposure to infected poultry.
- Human infections with avian influenza viruses are uncommon but have occurred sporadically, mostly from exposure to infected birds, with some reported infections resulting in severe disease in other countries.
- Human infections with bird flu from an intermediary host, are very rare, but have occurred in the United States in 2016 (cat-to-human spread of H7N2 bird flu) and 2024 (cow-to-human spread of H5N1 bird flu.)

- CDC has been monitoring for illness among people exposed to A(H5N1) virus-infected birds since these outbreaks were first detected in U.S. wild birds and poultry.
- CDC continues to work with USDA, FDA, and state health departments to also monitor people exposed to infected birds and sick cattle.
- Because of the potential for influenza viruses to constantly change, continued surveillance and preparedness efforts are critical, and CDC is taking measures to be ready in case the public health risk assessment changes.

Genetic Sequencing of A(H5N1) Specimen from Recent Human Infection

- CDC has sequenced the influenza virus genome identified in a specimen collected from the patient in Texas who was confirmed to be infected with A(H5N1) virus and compared these with A(H5N1) sequences from cattle, wild birds and poultry.
- The virus sequences are HA clade 2.3.4.4b HPAI A(H5N1) with each individual gene segment closely related to viruses detected in dairy cattle available from USDA testing in Texas.
- While minor changes were identified in the virus sequence from the patient specimen compared to the viral sequences from cattle, both cattle and human sequences maintain primarily avian genetic characteristics and for the most part lack changes that would make them better adapted to infect mammals.
- The genome for the human isolate had one change (PB2 E627K) that is known to be associated with viral adaptation to mammalian hosts, and which has been detected before in people and other mammals infected with HPAI A(H5N1) virus and other avian influenza subtypes (e.g., H7N9), but with no evidence of onward spread among people.
- Viruses can undergo changes in a host as they replicate after infection.
- Further, there are no markers known to be associated with influenza antiviral resistance found in the virus sequences from the patient's specimen and the virus is very closely related to two existing HPAI A(H5N1) candidate vaccine viruses that are already available to manufacturers, and which could be used to make vaccine if needed.
- Overall, the genetic analysis of HPAI A(H5N1) viruses in Texas supports CDC's conclusion that the human health risk currently remains low.
- Using next-generation technologies, CDC was able to sequence the influenza viruses directly from clinical specimens collected from the patient in Texas. These technologies also allowed for rapid, detailed analysis of the virus genome sequences, which CDC was able to complete within 24 hours of receiving the samples.
- Read the full report: https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/h5n1-analysis-texas.htm

A(H5N1) Bird Flu in Mammals

- Although A(H5N1) viruses primarily infect different types of wild birds and domestic poultry, A(H5N1) viruses can infect other animals as well.
- Spread of A(H5N1) viruses between birds and mammals have occurred globally, with recent detections in polar bears, elephant seals, goats, and cows. A complete listing of mammalian detections is available.
- Infections in mammals can occur after exposure to sick or dead birds or other animals.
- Sporadic A(H5N1) virus infections of mammals have been reported for 20 years in different

countries that have outbreaks in poultry or wild birds.
- A(H5N1) viruses have previously been known to occasionally infect mammals that eat (presumably infected) birds or poultry and mammals that are exposed to environments contaminated with virus.
- Some limited mammal to mammal transmission has been documented in cattle in the United States.
- The reports of A(H5N1) virus infections in some mammals globally, including in the United States and Canada, may continue to occur as H5N1 bird flu continues to spread widely in wild birds.
- The wide geographic spread of A(H5N1) viruses in wild birds, poultry, and some other mammals could create additional opportunities for people to be exposed to these viruses.
- Therefore, there could also be an increase in sporadic human infections resulting from bird and animal exposures, even if the risk of these viruses spreading from birds or animals to people has not increased.

USDA Reports Recent HPAI Virus Detections in Dairy Cows

- USDA has reported recent detections of highly pathogenic avian influenza (HPAI) in dairy cows and is monitoring the situation.
    - Updated information can be found on the USDA website: Highly Pathogenic Avian Influenza (HPAI) Detections in Livestock | Animal and Plant Health Inspection Service (usda.gov)
- USDA reported that sick cows are experiencing decreased lactation, low appetite, and other symptoms.
- USDA has now also confirmed the presence of HPAI in dairy herds in Michigan and Ohio that had recently received cows from Texas. Spread of symptoms among these herds indicates that spread of HPAI between cattle cannot be ruled out.
- USDA and partners continue to monitor this closely and have advised veterinarians and producers to practice good biosecurity, test animals before necessary movements, minimize animal movements, and isolate sick cattle from the herd.
- Among the dairies whose herds are exhibiting symptoms, the affected animals have recovered after isolation with little to no associated mortality reported.
- Additional information from USDA can be found online:
    - Detection of Highly Pathogenic Avian Influenza in Dairy Herds: Frequently Asked Questions

Genetic Sequencing Information on A(H5N1) Virus from Infected Cattle

- Initial testing has not found changes to the virus that would make it more transmissible to humans.
- Preliminary analysis of the virus from the infected cattle indicates that, current FDA-approved flu antiviral medications are believed to be effective.
- The virus is very closely related to two existing HPAI A(H5N1) candidate vaccine viruses that are already available to manufacturers, and which could be used to make vaccine if needed.
- Seasonal flu vaccines do not provide protection against these viruses. Analysis of virus samples is ongoing.

- Additional information on the virus detected in cattle can be found on USDA's website.

Information for People with Potential Exposure to Dead or Sick Animals

- CDC is working with USDA and local public health agencies to monitor worker health and safety, and to identify any health issues directly related to HPAI.
- CDC has updated and expanded recommendations: Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations | Avian Influenza (Flu).People who have job-related exposures to infected birds and other animals are at higher risk of A(H5N1) virus infection and should take appropriate precautions outlined in CDC recommendations.
    - Poultry farmers and poultry workers, backyard bird flock owners, livestock farmers and workers (including dairy workers), veterinarians and veterinary staff, and responders should avoid contact with surfaces that appear to be contaminated with animal feces, raw milk, litter, or materials contaminated by birds or other animals with suspected or confirmed bird flu virus infection.
    - People with relevant exposures should wear recommended PPE such as an N95 filtering facepiece respirator, eye protection, and gloves, and perform thorough hand washing after contact. (e.g., see: PPE recommended for poultry workers) when in direct contact with sick or dead birds or other animals, carcasses, feces, raw milk, or litter from potentially infected birds or other animals, and when going into any buildings with or that have had sick or dead birds or other animals, carcasses, feces, or litter from potentially infected birds or other animals. Additional information on PPE can be found online.
- Hunters should dress game birds in the field when possible and practice good biosecurity to prevent any potential disease spread. Biosecurity information is available on USDA's website
- People with direct or close contact with sick or dead animals, including wild birds (wild birds can be infected with bird flu viruses without appearing sick) with confirmed A(H5N1) virus infection, should be monitored for any signs and symptoms of illness for **10 days** after the last known exposure.

Recommendations for Clinicians

- Clinicians should consider the possibility of HPAI A(H5N1) virus infection in persons showing signs or symptoms of acute respiratory illness who have relevant exposure history.
- If a person is symptomatic, they need to be isolated, and the state/local health department should be notified.
    - Respiratory specimens should be collected for influenza testing using PPE, including for avian influenza A viruses at the state health department.
    - More information is available at: Recommendations for State Health Departments.
- Recommended infection prevention and control measures should be followed when collecting respiratory specimens and evaluating symptomatic persons who have been potentially exposed to novel influenza A viruses associated with severe disease in infected persons, including HPAI A(H5) virus.
- Any symptomatic persons among those being monitored after exposure should be started on empiric oseltamivir treatment as soon as possible even before testing results are available.
- Recommendations for use of antivirals following exposure to HPAI A(H5) virus are available at Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention,

Monitoring, and Public Health Investigations | Avian Influenza (Flu) (cdc.gov)If a person tests positive for influenza A(H5N1) virus, all close contacts should be identified and monitored, and antivirals are recommended for some persons.

Preventive Actions for the General Public

- While the risk to the general public remains low in the United States, there are several actions you can take to protect yourself against getting sick with bird flu:
    - People should avoid contact with poultry, wild birds, and other animals that appear ill or are dead and avoid contact with surfaces that appear to be contaminated with feces from wild birds and other animals or domestic poultry.
    - If you must handle wild birds or sick or dead poultry or other animals, minimize direct contact by wearing proper personal protective equipment (PPE) and following CDC guidance at 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.
    - More information is available at Prevention and Antiviral Treatment of Bird Flu Viruses in People | Avian Influenza (Flu) (cdc.gov).
- It is safe to eat properly handled and cooked poultry and meat and drink pasteurized milk in the United States
    - The U.S. agriculture industry maintains rigorous health and safety standards, including routine monitoring for avian influenza. The proper handling and cooking of poultry, meat, and eggs to the right internal temperature kills bacteria and viruses, including bird flu viruses.
        - Information about safe internal temperatures for different kinds of foods can be found online: Four Steps to Food Safety | CDC
    - People should not prepare or eat uncooked or undercooked food or related uncooked food products.
    - People should not consume unpasteurized (raw) milk, or raw cheeses, from animals with suspected or confirmed A(H5N1) virus infection (avian influenza or bird flu).
    - Choosing pasteurized milk is the best way to keep you and your family safe. More information is available at Fast Facts About Raw Milk.
- Consumers are reminded to handle raw poultry hygienically and cook all poultry and poultry products (including eggs), as well as beef thoroughly before eating.
    - While there is no evidence that any human cases of bird flu virus infection have been acquired by eating properly cooked poultry products, consumption of uncooked poultry and poultry products (like blood) was suspected as the source of highly pathogenic bird flu virus infection in a small number of cases in Southeast Asia.

What to do if you Find a Dead Bird or Other Animal

- State and local agencies have different policies for collecting and testing birds or other animals, so check with your state health department, state veterinary diagnostic laboratory, or state wildlife agency for information about reporting dead birds or other animals in your area.
- If local authorities tell you to simply dispose of the bird or other animal's carcass (body), don't handle it with your bare hands. Use gloves or an inverted plastic bag to place the carcass in a garbage bag, which can then be disposed of in your regular trash.
- To report unusual signs in birds or other animals you have seen in the wild, call 1-866-536-7593.

If You Have Contact with Birds or Animals Infected with Bird Flu and Get Sick

- People who have had direct contact with infected bird(s) or other animals who develop any illness symptoms within 10 days of their last exposure to infected birds or other animals should immediately notify a health care provider about their exposure so they can be evaluated and tested for bird flu virus infection and other possible causes of their symptoms.
- Also, if you have been in contact with sick birds or animals or surfaces contaminated by them and you have not already been in contact with your state or local health department, contact your state or local health department right away.
- Signs and symptoms of bird flu virus infection are non-specific and variable and may include:
    - fever (temperature of 100ºF [37.8ºC] or greater) or feeling feverish,
    - cough,
    - sore throat,
    - runny or stuffy nose,
    - muscle or body aches,
    - headaches,
    - fatigue,
    - eye redness (or conjunctivitis),
    - shortness of breath or difficulty breathing.
- Less common signs and symptoms are:
    - diarrhea,
    - nausea,
    - vomiting, or
    - seizures.
- It is important to remember that infection with influenza viruses, including bird flu viruses, does not always cause fever. Fever may not occur in infected persons of any age, particularly in persons 65 years and older or people who have weakened immune systems due to disease or medications.
    - Respiratory specimens will be collected for influenza testing at a state public health laboratory and may also be tested locally for influenza and other infectious diseases. A health care provider can assess whether testing for other infectious diseases is indicated based upon signs, symptoms, history of exposures, clinical examination findings and the local epidemiology of other pathogens, including other respiratory viruses that may be circulating among people (e.g., SARS-CoV-2).
    - A seasonal flu antiviral medication can be prescribed for treatment of bird flu virus infection. Antiviral treatment works best when taken as soon as possible after symptoms begin.
- People who become sick within 10 days of their exposure to infected birds or other animals should isolate at home away from their household members and should not go to work or school until they are proven not to have bird flu virus infection and have recovered from their illness. The local or state public health department can assist in monitoring and advising when isolation is no longer required.
- Close contacts (family members, etc.) of people who have been exposed to bird flu viruses should monitor their health and report to their health care provider any new symptoms, especially respiratory symptoms, within 10 days of the exposure.

What CDC Is Doing about the Situation in the United States

- CDC is the lead agency for human health.
- The U.S. Department of Interior and USDA are the lead federal departments for outbreak investigation and control in wild birds and agriculture, and USDA APHIS is the lead agency for such activities in domestic birds and agricultural livestock.
- CDC is working closely with USDA to monitor the current H5N1 bird flu situation and will review existing guidance on an ongoing basis to determine if updates are needed.
- CDC also is working with USDA and state partners to monitor for infections in exposed persons in the states where detections in poultry, backyard flocks, or other animals have occurred.
    - People who have been exposed to infected birds, poultry, or other animals are actively monitored for 10 days after exposure.
    - To date, public health departments have monitored more than 8,000 people in 52 jurisdictions who were exposed to birds/poultry or other animals infected with A(H5N1) virus and reported this information to CDC.
    - Of these, 189 people who were being monitored showed symptoms and were subsequently tested for novel influenza A and seasonal flu viruses along with other respiratory viruses.
- CDC will help with surveillance, contact tracing, and other steps to monitor for and reduce spread in jurisdictions where human infections with A(H5N1) virus are identified.
    - CDC's diagnostic tools that are used to detect seasonal influenza viruses also can detect novel influenza A viruses including A(H5N1) viruses.
    - These diagnostic tools are used at more than 100 public health laboratories in all 50 U.S. states and have been shared internationally as well.
- CDC will continue its ongoing assessment of the risk posed by these viruses, including conducting additional laboratory work to further characterize current A(H5N1) viruses.
- CDC is engaged in broad outreach to the public to raise awareness about the current situation and that the current risk to the general public's health is low, but that there are certain groups of people who are at greater risk of infection who should take precautions.
- A jointly conducted audit of CDC and USDA outreach activities was conducted to ensure that all potentially affected groups are being reached through existing channels.
    - All of CDC's current A(H5N1) virus materials are available in Spanish and English, and CDC is working closely with state and local health departments to determine and address if other language or access barriers exist.
- CDC is engaging public health partner organizations to share information and ensure preparedness for any potential human infections.
- CDC has determined that:
    - These bird flu viruses can be detected using CDC's diagnostic tools for seasonal influenza viruses which are used at more than 100 public health laboratories in all 50 U.S. states.
    - Genetic sequencing suggests that currently available FDA-approved antiviral treatments for seasonal flu would work against these viruses.
    - Two existing HPAI A(H5N1) candidate vaccine viruses that are already available to manufacturers, and which could be used to make vaccine if needed.
    - More information on laboratory data is available above in this document.
- CDC will provide updates on this situation as needed on the Avian Influenza Current Situation

Summary or Avian News & Spotlights pages.

Bird Flu Vaccines

- As part of pandemic preparedness activities and as a WHO Collaborating Center, CDC regularly develops candidate vaccine viruses (CVVs)—viruses made for production of vaccine—for novel bird flu viruses with pandemic potential.
- CDC has two HPAI H5N1 CVV that could be used to produce vaccine for people if needed.
    - Further, there are no markers known to be associated with influenza antiviral resistance found in the virus sequences from the patient's specimen and the virus is very closely related to two existing A(H5N1) candidate vaccine viruses that are already available to manufacturers, and which could be used to make vaccine if needed.
    - Because flu viruses are constantly changing, CDC continually analyses viruses to identify genetic changes that suggest these viruses might spread more easily to and between people, and cause serious illness in people, or for changes that suggest reduced susceptibility to antivirals, as well as changes in the virus that might mean a new vaccine virus should be developed.

Antivirals

- There are four commercially available FDA-approved prescription antiviral treatment drugs recommended for influenza.
    - CDC's preliminary genetic analysis of currently circulating A(H5N1) viruses suggests these viruses are susceptible to commercially available, FDA-approved currently recommended, flu antivirals.
- CDC will continue to monitor these viruses and update and adjust guidance as needed.
- If antiviral chemoprophylaxis is initiated, oseltamivir treatment dosing (one dose twice daily) is recommended instead of the antiviral chemoprophylaxis regimen for seasonal influenza. Specific dosage recommendations for treatment by age group is available: Influenza Antiviral Medications: Summary for Clinicians.

Background

- Avian influenza (bird flu) refers to the disease caused by infection with avian (bird) influenza (flu) type A viruses.
- These viruses naturally spread among wild aquatic birds worldwide and can infect domestic poultry and other bird and animal species.
- Avian influenza viruses do not normally infect humans; however, sporadic human infections with avian influenza viruses have occurred.
- Human infections with avian influenza viruses have usually happened after close, prolonged, unprotected exposure to infected birds or an environment that has been contaminated by infected birds (e.g., feces, saliva, or mucous).
- A(H5N1) is one sub-type of bird flu, which is a disease of birds. There are many other subtypes of avian influenza A viruses, including A(H5N6), A(H5N8), A(H7N9), and others.
- There are also different groups of A(H5N1) viruses.
- A(H5N1) virus has been circulating among birds and poultry in different parts of the world for many years and continuing to evolve into different groups that are referred to as

clades.
    - The predominant clade of A(H5N1) virus, called clade 2.3.4.4b, appears well-adapted to spread efficiently among wild birds and poultry in many regions of the world and was first identified in wild birds sampled in the United States in late 2021.
- Wild birds can carry these viruses without getting sick, but domestic poultry get very sick and often die from these viruses.
- CDC has been comparing the properties of current A(H5N1) viruses to past A(H5N1) viruses and has found that current A(H5N1) viruses detected in the United States during late 2021 to the present are different from earlier A(H5N1) viruses.
- So far, current avian influenza A(H5N1) viruses lack changes seen in the past that have been associated with infecting people more easily and causing severe illness in people.
- USDA has publicly posted genetic sequencing for A(H5N1) viruses in the United States.
- These viruses are from clade 2.3.4.4b, which is the predominant A(H5N1) bird flu virus worldwide at this time.
- Current A(H5N1) viruses were first identified in Europe during the fall of 2020 and spread across Europe and into Africa, the Middle East and Asia, becoming the predominant subtype globally by fall of 2021.
- Current A(H5N1) viruses have been spreading in wild birds in much of the world and have caused sporadic poultry infections and poultry outbreaks and sporadic infections in mammals in many countries, including the United States.
- Ancestors of these A(H5N1) viruses first emerged in southern China and led to large poultry outbreaks in Hong Kong in 1997, which resulted in 18 human infections.
    - The bird outbreak was controlled, but the A(H5N1) viruses were not eradicated in birds and re-surfaced in 2003 to spread widely in birds throughout Asia, and later in Africa, Europe, and the Middle East, causing sporadic human infections.
- No known human-to-human spread has occurred with the A(H5N1) virus that is currently circulating in birds in the United States and globally.
- Sporadic human cases of H5N1 bird flu reported with A(H5N1) viruses circulating in birds since 2021 have occurred following exposure to infected poultry, with one case following exposure to infected cattle. Human infections were rare during past A(H5N1) virus outbreaks that have occurred in poultry globally.
- Globally since 2003, countries have reported rare, sporadic human infections with A(H5N1) viruses to the World Health Organization (WHO).
- Monthly case counts are available on the WHO website. Although clade 2.3.4.4b A(H5N1) viruses (H5N6, H5N8) have circulated longer, clade 2.3.4.4b A(H5N1) viruses have only circulated in wild birds and poultry in recent years, after most previous human A(H5N1) cases occurred.

Understanding Highly Pathogenic Avian Influenza (HPAI) and Low Pathogenic Avian Influenza (LPAI)

- Avian influenza A viruses are classified into the following two categories: low pathogenic avian influenza (LPAI) A viruses and highly pathogenic avian influenza (HPAI) A viruses.
- The categories refer to molecular characteristics of a virus and the virus's ability to cause disease and mortality in chickens in a laboratory setting.
    - **Low Pathogenic Avian Influenza (LPAI)**: Low pathogenic avian influenza viruses cause either no signs of disease or mild disease in chickens/poultry (such as ruffled feathers

and a drop in egg production).
    - Most avian influenza A viruses are low pathogenic and cause few signs of disease in infected wild birds.
    - In poultry, some low-pathogenic viruses can mutate into highly pathogenic avian influenza viruses.
  - **Highly Pathogenic Avian Influenza (HPAI):** Highly pathogenic avian influenza viruses cause severe disease and high mortality in infected poultry.
    - Only some avian influenza A(H5) and A(H7) viruses are classified as HPAI A viruses, while most A(H5) and A(H7) viruses circulating among birds are LPAI A viruses.
    - HPAI A(H5) or A(H7) virus infections can cause disease that affects multiple internal organs with mortality up to 90% to 100% in chickens, often within 48 hours.
    - However, ducks can be infected without any signs of illness. HPAI A(H5) and A(H7) virus infections in poultry also can spill back into wild birds, resulting in further geographic spread of the virus as those birds migrate. While some wild bird species can be infected with some HPAI A(H5) or A(H7) virus subtypes without appearing sick, other HPAI A(H5) and A(H7) virus subtypes can cause severe disease and mortality in some infected wild birds as well as in infected poultry.
- Both HPAI and LPAI viruses can spread rapidly through poultry flocks.
- HPAI and LPAI designations do not refer to or correlate with the severity of illness in cases of human infection with these viruses.
  - Both LPAI and HPAI A viruses have caused mild to severe illness in infected humans.
  - There are genetic and antigenic differences between the influenza A virus subtypes that typically infect only birds and those that can infect birds and people.
- Wild birds can carry HPAI viruses without showing symptoms, but these viruses can cause illness and death in domestic poultry.
- Infected birds shed bird flu viruses in their saliva, mucous, and feces.
- Human infections with bird flu viruses can happen when enough virus gets into a person's eyes, nose or mouth or is inhaled.
- The greatest risk for infections to occur continues to be among people with close or prolonged unprotected contact with infected birds or contaminated environments.
- Illnesses in humans from avian influenza virus infections have ranged from mild (e.g., eye infection, upper respiratory symptoms) to severe illness (e.g., pneumonia), sometimes resulting in death.
- The spread of avian influenza viruses from one sick person to another is very rare, and when it has happened, it has not led to sustained spread among people.
- People with avian influenza virus infections may have mild to severe illness.

Links for More Information

- CDC is providing the latest bird flu information and updates on the following pages:
  - Current situation page: Avian Influenza Current Situation Summary
  - Bird flu spotlights: Avian Influenza News & Spotlights
  - Bird flu timeline: Highlights in the History of Avian Influenza (Bird Flu) Timeline – 2020-2024.

  - H5N1 Technical reports (for technical audiences): H5N1 Technical Report | Avian Influenza (Flu) (cdc.gov).
- Other agencies are responsible for monitoring for disease in poultry and wild birds and wildlife.
- Backyard Flock Owners: Take Steps to Protect Yourself from Avian Influenza (Bird Flu) | Avian Influenza (Flu) (cdc.gov)
- Bird Flu in Pets and Other Animals | Avian Influenza (Flu) (cdc.gov)

One Health Information for Farms
  - Farm Animals | Healthy Pets, Healthy People | CDC
  - Stay Healthy When Working with Farm Animals

Guidance Documents

- CDC has guidance documents including recommendations for personal protective equipment and information for people exposed to birds or other animals infected with avian influenza viruses.
  - Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations | Avian Influenza (Flu) (cdc.gov)
  - Recommendations for Worker Protection and Use of Personal Protective Equipment (PPE) to Reduce Exposure to Highly Pathogenic Avian Influenza A H5 Viruses | Avian Influenza (Flu) (cdc.gov)
  - Information for People Exposed to Birds Infected with Avian Influenza Viruses of Public Health Concern | Avian Influenza (Flu) (cdc.gov)
  - Self-Observation for Illness for Responders to Poultry Outbreaks of Avian Influenza | Avian Influenza (Flu) (cdc.gov)
- CDC also has guidance for testing and treatment of suspected cases to prevent severe illness and transmission to other people.
  - Interim Guidance on Testing, Specimen Collection, and Processing for Patients with Suspected Infection with Novel Influenza A Viruses with the Potential to Cause Severe Disease in Humans | Avian Influenza (Flu) (cdc.gov)
  - Case Definitions for Investigations of Human Infection with Avian Influenza A Viruses in the United States (cdc.gov)
  - 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 | Avian Influenza (Flu) (cdc.gov)
    - Chemoprophylaxis is not routinely recommended for personnel involved in handling sick birds or decontaminating affected environments (including animal disposal) who used proper personal protective equipment.
  - CDC has guidance for clinicians in a Health Alert Network (HAN) Health Advisory summarizing the agency's recommendations for testing and treatment of patients with possible A(H5N1) virus exposure/infection. (Issued April 29, 2022)
- USDA/APHIS has created guidance for local, state, and federal public health authorities on monitoring of people potentially exposed to avian influenza viruses during official United States Department of Agriculture Animal and Plant Health Inspection Service (APHIS) response activities in the United States. APHIS PH monitoring plan for AI responders

- APHIS Recommendations for Highly Pathogenic Avian Influenza (HPAI) H5N1 Virus in Livestock For State Animal Health Officials, Accredited Veterinarians and Producers : vs-recommendations-hpai-livestock.pdf (usda.gov)

Summary: H5N1 Scenario-Based Human Health Risk Assessment for the United States as of May 22, 2024

Currently, the Center for Outbreak Response Innovation (CORI) judges the H5N1 outbreak in cattle to be between Scenario 2 and Scenario 3, *meaning the virus is transmitting widely in cattle (Scenario 2), but infections in cattle and other animal species (e.g., cats) may offer opportunity for reassortment (Scenario 3), which would increase the potential for a novel influenza virus that could transmit efficiently between humans.*

This judgment is based on the widespread occurrence of H5N1 infections in cattle across the US, the detection of H5 in wastewater in Texas, and high mortality in H5N1-infected cats that live on affected farms. A preprint report released on May 3, 2024, found that cattle may be possible mixing vessels for influenza reassortment because of the existence of both avian and human influenza receptors in cows, which would move the situation into Scenario 3. However, because this study has not yet been peer-reviewed or replicated, we maintain our judgment that we are not yet fully in Scenario 3. If we see additional evidence to support these findings, the study is published in a reputable peer-reviewed journal, or the virus is found in other species such as pigs, we may change our judgment about the risk. To date, no human-to-human transmission has been reported, and we have not seen an increase in human cases.

See the detailed risk assessment analysis beginning on the next page.

	Risk to agricultural workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
Scenario 2 – Widespread transmission in cattle, few human infections, no human-to-human transmission	Moderate	Low	**Very** Low	**Very** Low
Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission	Moderate-High	Moderate	Low	Low

HPAI A(H5N1) Scenario-Based Human Health Risk Assessment for the United States

Center for Outbreak Response Innovation (CORI)

Updated as of May 22, 2024

The recent HPAI A(H5N1) virus outbreak in US dairy cattle has drawn significant attention since the USDA reported detections in dairy herds in Texas and Kansas on March 25, 2024.[1] According to the US Centers for Disease Control and Prevention (CDC), as of **May 22, 2024**, the virus has spread to at least **51 dairy herds in 9 states** (Texas, Kansas, New Mexico, Idaho, Michigan, Ohio, North Carolina, South Dakota, and Colorado).[2,3] There have also been **2** human infections reported in dairy farm workers, the first reported on April 1st, 2024, in Texas and the second reported on May 22nd, 2024, in Michigan, raising concerns about the impact on public health.[4] **No human-to-human transmission** of the virus has been reported to date.

The risks to human health from this outbreak are complex and may change rapidly. They are also highly uncertain because of a current lack of surveillance data and other basic scientific and epidemiological information. Risk assessment can be very helpful in times of significant uncertainty because it enables structured consideration of complex scenarios, likelihoods, and consequences to inform decisions around policy and operational action, as well as implementation of protective measures and future planning for worst-case scenarios. It is important not to wait for perfect information to estimate potential risk, because decisions must be made even in the absence of plentiful data.

Therefore, the Center for Outbreak Response Innovation (CORI) conducted a scenario-based risk assessment to consider human health risks both now and in potential future scenarios. We will update this assessment as additional data become available.

***Please note:** We are evaluating the risks to human health should each scenario occur, **not** the relative risk of any one scenario occurring.

Features that would characterize each scenario include:

Scenario 1 – Minimal spread in cattle: The virus is predominantly infecting cattle and there is minimal spread within herds and to other animals. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk to human health in this scenario is low.

Scenario 2 – Widespread transmission in cattle, few human infections, no human-to-human transmission: The virus is predominantly infecting cattle but spreads widely within herds. There is also occasional cow-to-human transmission but no human-to-human transmission. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk is low, but population-specific risk is increased for agricultural workers.

Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission: The virus begins to infect swine or other animal species that facilitate the

mixing and spreading of influenza viruses. This increases the likelihood that the virus reassorts with other influenza viruses and adapts to humans. In this scenario, we expect that some limited human-to-human transmission could be reported but only among close contacts of agricultural workers and not among healthcare workers. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk of widespread transmission in humans is low, but risk is increased for agricultural workers and close contacts of workers. The relative risk of a future pandemic has increased, but the absolute risk remains low.

Scenario 4 – Increasing reports of human infections, limited human-to-human transmission between close contacts: There are more reports of human infections due to contact with infected animals like cattle or swine. Limited human-to-human transmission is reported among close contacts of infected individuals, including healthcare workers, but there is no efficient human-to-human transmission. Likelihood of widespread human infections is moderate. Population health consequences are low. Overall risk of widespread transmission is low, but population-specific risk is increased for agricultural workers, close contacts of workers, and healthcare workers. The likelihood of a future pandemic is increased.

Scenario 5 – Efficient human-to-human transmission: There are reports of efficient human-to-human transmission. Likelihood of human infections is high because the virus now transmits efficiently and will be very difficult to contain. Population health consequences are high. Overall risk is high for all populations. The likelihood of a pandemic is very high.

Currently, we judge the H5N1 outbreak in cattle to be between Scenario 2 and Scenario 3, *meaning the virus is transmitting widely in cattle (Scenario 2), but infections in cattle and other animal species (eg, cats) may offer opportunity for reassortment (Scenario 3), which would increase the potential for a novel influenza virus that could transmit efficiently between humans.*

This judgment is based on the widespread occurrence of H5N1 infections in cattle across the US, the detection of H5 in wastewater in Texas,[5] and high mortality in H5N1-infected cats that live on affected farms.[6] A preprint report released on May 3, 2024, found that cattle may be possible mixing vessels for influenza reassortment because of the existence of both avian and human influenza receptors in cows,[7] which would move the situation into Scenario 3. However, because this study has not yet been peer-reviewed or replicated, we maintain our judgment that we are not yet fully in Scenario 3. If we see additional evidence to support these findings, the study is published in a reputable peer-reviewed journal, or the virus is found in other species such as pigs, we may change our judgment about the risk. To date, no human-to-human transmission has been reported, and we have not seen an increase in human cases.

H5N1 Scenario-Based Human Health Risk Assessment

H5N1 Human Health Risk Assessment Scenario Table

	Risk to agricultural workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
Scenario 1 – Minimal spread in cattle	Low	Low	**Very** Low	**Very** Low
Scenario 2 – Widespread transmission in cattle, few human infections, no human-to-human transmission	Moderate	Low	**Very** Low	**Very** Low
Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission	Moderate-High	Moderate	Low	Low
Scenario 4 – Increasing reports of human infections, limited human-to-human transmission between close contacts	High	Moderate-High	Moderate	Low-Moderate
Scenario 5 – Efficient human-to-human transmission	High	High	High	High

Methods: The purpose of this document is to consider possible future developments in this outbreak and describe corresponding risks to human populations should a given scenario occur. In each scenario, we consider the risk to 4 distinct populations: agricultural workers on affected farms, other people in the vicinity of affected animal populations and agricultural workers (eg, household contacts of workers, people living near affected facilities with potential contact with infected animals or farm workers, healthcare providers treating infected individuals), US healthcare workers, and the US general public.

In determining these risks, we consider several factors, including cow-to-cow transmission pathways (eg, respiratory transmission, drinking contaminated water and feeding on contaminated grasslands, aerosolization of the virus through the milking process, etc.), cow-to-human transmission pathways (eg, unprotected and close contact with infected animals, consumption of unpasteurized dairy products, etc.), human-to-human transmission pathways (eg, aerosol, oral, direct contact), and cow-to-other animal transmission. We also consider disease morbidity and mortality, instances of transmission, the level of testing conducted in cattle and other farm animals, the level of testing conducted in humans, existing processes to limit spread from infected animals, genomic surveillance capabilities, and any new mutations showing greater potential for sustained human-to-human transmission. Other factors include events that could increase human-to-human transmission (eg, mass gatherings, seasonal trends, school terms, etc.), treatments available to humans (eg, antivirals), preventative measures for animal-to-worker transmission (eg, use of N95 mask or equivalent, goggles, gloves, gown, head cover, and boot covers) and transmission to the general public, preventative medical countermeasures, preventative nonpharmaceutical interventions for human-to-human transmission, and ongoing response operations to address the outbreak.

H5N1 Scenario-Based Human Health Risk Assessment

Appendix: Additional Details on Process and Recommendations

Scenario 1: H5N1 outbreak stays predominantly in cattle and has minimal spread within herds and to other animals.

In the first scenario, we considered the risk to human health if the H5N1 virus stays in cattle and has minimal spread within herds and to other animals. We determined the health risk to **agricultural workers** to be **low**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **low**, the risk to **healthcare workers to be very low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **very low**.

Our **confidence** in these risk scores is **high** given the current level of information known for each of these factors and the fact that the virus is not actively spreading to humans or within human populations in this scenario. To minimize the spread of H5N1in animals, USDA recommends:

- Increased diagnostic testing in cattle.
- Continued separation of infected cattle from the rest of the herd.
- Enforced cattle import restrictions to limit the movement of infected cattle across state borders.
- Stringent control of potentially infected food products (removal of milk or other infected products).

To minimize the potential for cow-to-human transmission, USDA recommends:

- Agricultural workers and other individuals in close contact with infected cattle or environments use adequate protective equipment and hygienic/sanitation measures.

Scenario 2: H5N1 virus stays predominantly in cattle but spreads widely within herds. There is also a low incidence of cow-to-human transmission but no human-to-human transmission.

In the second scenario, we considered the risk to human health if the H5N1 virus is spreading widely within bovine herds but has minimal spread to other animal species. We determined the health risk to **agricultural workers** in this scenario to be **moderate**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **low**, the risk to **healthcare workers to be very low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **very low**.

Our **confidence** in these risk scores is **low**, as the level of testing conducted in cattle and other farm animals is low. Based on available USDA data, there is considerable cow-to-cow transmission occurring. We do not know precisely how much exposure agricultural workers have to infected cattle, but it is likely sufficient to enable transmission. Furthermore, we do not have details on the routes of transmission to humans, making it difficult to determine the exact risk to agricultural workers. Though we determined the risk of widespread human infection to be low given the low incidence of documented cow-to-human transmission, that could change. As the number of infected cattle increases, so does the risk to agricultural workers. To reduce risk, USDA recommends:

- Agricultural workers diligently use appropriate personal protective equipment (such as masks, goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle and potentially infected environments.
- Increased diagnostic testing in cattle and the continued separation of infected cattle during convalescence.
- Enforced cattle import restrictions to limit the movement of infected cattle across state borders.
- Stringent control of potentially infected food products (removal of milk or other infected products).
- Information sharing between the agriculture and public health sectors to increase transparency and monitor for increases in cow-to-human transmission.

Scenario 3: H5N1 virus begins to infect swine or other animal species that have facilitated the mixing and spreading of influenza viruses. This increases the likelihood that the virus reassorts with other influenza viruses and adapts to humans. Some limited human-to-human transmission is reported, but only among close contacts of human cases. Healthcare workers have not reported infections.

In the third scenario, we considered the risk to human health if the H5N1 virus begins spreading widely in pigs or other potential mixing vessel animals, creating greater opportunity for reassortment with human influenza viruses. In this scenario, we expect some very limited human-to-human transmission would be reported among close contacts of cases. We determined the health risk to **agricultural workers** to be **moderate-high**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **moderate**, the health risk to **healthcare workers** to be **low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low**.

Our **confidence** in these risk scores is **low**, as the level of testing conducted in cattle and other farm animals is low. The jump from cattle to swine poses an increased risk for new mutations that could have a greater potential for sustained transmission within human populations, particularly for agricultural workers and local communities. To decrease risk to human health, we recommend:

- Agricultural workers diligently use personal protective equipment (including masks goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle, infected animals, and potentially infected environments.
- Increased diagnostic testing in cattle and other farm animals, continued genomic surveillance, the separation of infected cattle and other animals, and stringent control of potentially infected food products.
- Information sharing between the agriculture and public health sectors to increase transparency and monitor for increases in human transmission.
- Increased public health surveillance for H5N1 cases in local communities.
- Enhanced communication with the public about the situation and the measures being taken to address it.

Scenario 4: There are more reports of human infections due to contact with infected animals like cattle or swine. Limited human-to-human transmission is reported among close contacts of infected individuals, including healthcare workers, but there is no efficient human-to-human transmission.

In the fourth scenario, we considered the risk to human health if the H5N1 virus begins spreading more readily among close human contacts, including healthcare workers. In this scenario, increased, but still limited, human-to-human transmission is reported among close contacts. Transmission between people is still not efficient. We determined the health risk to **agricultural workers** to be **high**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **moderate-high**, the health risk to **healthcare workers** to be **moderate**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low-moderate**.

Our **confidence** in these risks scores is **low**, as the level of testing conducted in farm animals and humans is generally low. Increased incidence of human-to-human transmission may indicate increased transmission efficiency, but it may also be due to greater prevalence of the virus in communities. There is still significant uncertainty about whether the virus will spread efficiently among people. To reduce risk to human health, we recommend actions including but not limited to:

- Implementing and supporting recommended isolation of human cases and quarantine of close contacts of cases through escalated case finding and contact tracing, Tamiflu prophylaxis for those exposed, compensation for individuals who are isolated/quarantined and cannot report to work, and social support to provide for essential needs of those in isolation/quarantine.
- Increasing focus on sentinel surveillance, wastewater surveillance, and education of clinicians to consider H5N1 as a possible diagnosis for people who present with new respiratory illness.
- Continued development and widespread implementation of antigen and molecular testing in both hospital and outpatient settings.
- Policy preparation for the possibility of a pandemic, including congressional deliberations about emergency funding and emergency planning by healthcare institutions, workplaces, and federal, state, territorial, local, and tribal public health agencies.
- Increased investment and urgent development, testing, and production of vaccines and treatment options.
- Increased risk communication to the public to provide regular updates and prevent mis- and disinformation.

Scenario 5: There are reports of efficient human-to-human transmission. The likelihood of human infections is high because the virus now transmits efficiently and will be very difficult to contain.

In the fifth scenario, we considered the risk to human health if the virus jumps from animals to humans, and we find efficient human-to-human transmission of H5N1. We determined the health risk to **agricultural workers** to be **high**, the health risk to **non-workers in the vicinity of affected workers and**

animal populations to be **high**, the health risk to **healthcare workers** to be **high**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **high**.

Our **confidence** in these risks scores is **high**. The level of H5N1 testing in humans is currently minimal, and we have limited information or evidence available to determine the exact human-to-human transmission pathways. Preventative medical countermeasures to address human-to-human transmission, such as vaccines, are available, but it is unclear how effective they would be. Nonpharmaceutical interventions are not currently in use, and there are no human public health response operations in place. The risk is therefore high for agricultural workers and the local and global communities. To decrease the risk of human-to-human transmission, we recommend actions including, but not limited to:

- Increased diagnostic and surveillance testing in humans (including increased genomic surveillance).
- Implementing and supporting recommended isolation of cases and quarantine of close contacts of cases through escalated case finding and contact tracing, Tamiflu prophylaxis for those exposed, compensation for individuals who are isolated/quarantined and cannot report to work, and social support to provide for essential needs of those in isolation/quarantine.
- Increasing sentinel surveillance, wastewater surveillance, and education of clinicians about how to recognize and treat H5N1 infection.
- Widespread implementation of antigen and molecular testing in both hospital and outpatient settings.
- Congressional approval of supplemental appropriations to fund public health response activities.
- Urgent continued development, testing, and production of vaccines and treatment options.
- Adoption of medical countermeasures and nonpharmaceutical interventions.
- Increased risk communication to the public to provide regular epidemiologic updates, discuss the interventions that may be used, recommend measures that individuals and organizations can take to protect public health, and address mis- and disinformation.
- Monitoring and mitigation of transmission at mass gathering events.

References

1. Avian Influenza A(H5N1) – United States of America. Accessed April 15, 2024. https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON512

2. Highly Pathogenic Avian Influenza (HPAI) Detections in Livestock | Animal and Plant Health Inspection Service. Accessed April 15, 2024. https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock

3. CDC. Avian Influenza A(H5N1) U.S. Situation Update and CDC Activities. Centers for Disease Control and Prevention. Published April 26, 2024. Accessed April 29, 2024. https://www.cdc.gov/flu/avianflu/spotlights/2023-2024/avian-situation-update.htm

4. What's Happening With Dairy Cows and Bird Flu | Johns Hopkins | Bloomberg School of Public Health. Published April 8, 2024. Accessed April 15, 2024. https://publichealth.jhu.edu/2024/whats-happening-with-dairy-cows-and-bird-flu

5. Wolfe MK, Duong D, Shelden B, et al. Detection of hemagglutinin H5 influenza A virus sequence in municipal wastewater solids at wastewater treatment plants with increases in influenza A in spring, 2024. Published online April 29, 2024. doi:10.1101/2024.04.26.24306409

6. Burrough ER, Magstadt DR, Petersen B, et al. Early Release - Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus Infection in Domestic Dairy Cattle and Cats, United States, 2024 - Volume 30, Number 7—July 2024 - Emerging Infectious Diseases journal - CDC. doi:10.3201/eid3007.240508

7. Kristensen C, Jensen HE, Trebbien R, Webby RJ, Larsen LE. The avian and human influenza A virus receptors sialic acid (SA)-α2,3 and SA-α2,6 are widely expressed in the bovine mammary gland. Published online May 3, 2024:2024.05.03.592326. doi:10.1101/2024.05.03.592326

H5N1 Scenario-Based Human Health Risk Assessment

Summary: H5N1 Scenario-Based Human Health Risk Assessment for the United States as of July 8, 2024

Currently, the Center for Outbreak Response Innovation (CORI) judges the H5N1 outbreak in cattle to be between Scenario 2 and Scenario 3, *meaning the virus is transmitting widely in cattle (Scenario 2), but infections in cattle and other animal species (e.g., cats) may offer opportunity for reassortment (Scenario 3), which would increase the potential for a novel influenza virus that could transmit efficiently between humans.*

This judgment is based on the widespread occurrence of H5N1 infections in cattle across the US, the detection of H5 in wastewater 6 states 5 states (California, Idaho, Iowa, Minnesota, Michigan, and Texas), and high mortality in H5N1-infected cats that live on affected farms. A preprint report released on May 3, 2024, found that cattle may be possible mixing vessels for influenza reassortment because of the existence of both avian and human influenza receptors in cows, which would move the situation into Scenario 3. However, because this study has not yet been peer-reviewed or replicated, we maintain our judgment that we are not yet fully in Scenario 3. If we see additional evidence to support these findings, the study is published in a reputable peer-reviewed journal, or the virus is found in other species such as pigs, we may change our judgment about the risk. To date, no human-to-human transmission has been reported, and we have not seen an increase in human cases.

See the detailed risk assessment analysis beginning on the next page.

	Risk to agricultural workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
Scenario 2 – Widespread transmission in cattle, few human infections, no human-to-human transmission	Moderate	Low	**Very** Low	**Very** Low
Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission	Moderate-High	Moderate	Low	Low

H5N1 Scenario-Based Human Health Risk Assessment

HPAI A(H5N1) Scenario-Based Human Health Risk Assessment for the United States

Center for Outbreak Response Innovation (CORI)
Updated as of July 8, 2024

Since the last update on June 18, 2024:

- CDC has reported a fourth human case of H5N1 associated with the outbreak in U.S. dairy cows. All human cases (1 Texas, 2 Michigan, 3 Michigan, 4 Colorado) have been among dairy workers exposed to sick cows.
- The risk assessment scenarios remain unchanged; CORI judges that the H5N1 outbreak in cattle is still between Scenario 2 and Scenario 3, meaning that the risk to the general public and healthcare workers is low to very low, the risk to agricultural workers is moderate to high, and the risk to other people in contact with affected workers and animal populations is low to moderate.
- US Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) is now reporting a total of 140 confirmed cases in cattle, 48 of which have occurred in the last 30 days.

The risks to human health from this outbreak are complex and may change rapidly. They are also highly uncertain because of a current lack of surveillance data and other basic scientific and epidemiological information. Risk assessment can be very helpful in times of significant uncertainty because it enables structured consideration of complex scenarios, likelihoods, and consequences to inform decisions around policy and operational action, as well as implementation of protective measures and future planning for worst-case scenarios. It is important not to wait for perfect information to estimate potential risk, because decisions must be made even in the absence of plentiful data.

Therefore, the Center for Outbreak Response Innovation (CORI) conducted a scenario-based risk assessment to consider human health risks both now and in potential future scenarios. We will update this assessment as additional data becomes available.

***Please note:** We are evaluating the risks to human health should each scenario occur, **not** the relative risk of any one scenario occurring.

Features that would characterize each scenario include:

Scenario 1 – Minimal spread in cattle: The virus is predominantly infecting cattle and there is minimal spread within herds and to other animals. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk to human health in this scenario is low.

Scenario 2 – Widespread transmission in cattle, few human infections, no human-to-human transmission: The virus is predominantly infecting cattle but spreads widely within herds. There is also occasional cow-to-human transmission but no human-to-human transmission. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk is low, but population-specific risk is increased for agricultural workers.

Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission: The virus begins to infect swine or other animal species that facilitate the mixing and spreading of influenza viruses. This increases the likelihood that the virus reassorts with other influenza viruses and adapts to humans. In this scenario, we expect that some limited human-to-human transmission could be reported but only among close contacts of agricultural workers and not among healthcare workers. Likelihood of widespread human infections is low. Population health consequences are low. Overall risk of widespread transmission in humans is low, but risk is increased for agricultural workers and close contacts of workers. The relative risk of a future pandemic has increased, but the absolute risk remains low.

Scenario 4 – Increasing reports of human infections, limited human-to-human transmission between close contacts: There are more reports of human infections due to contact with infected animals like cattle or swine. Limited human-to-human transmission is reported among close contacts of infected individuals, including healthcare workers, but there is no efficient human-to-human transmission. Likelihood of widespread human infections is moderate. Population health consequences are low. Overall risk of widespread transmission is low, but population-specific risk is increased for agricultural workers, close contacts of workers, and healthcare workers. The likelihood of a future pandemic is increased.

Scenario 5 – Efficient human-to-human transmission: There are reports of efficient human-to-human transmission. Likelihood of human infections is high because the virus now transmits efficiently and will be very difficult to contain. Population health consequences are high. Overall risk is high for all populations. The likelihood of a pandemic is very high.

Currently, we judge the H5N1 outbreak in cattle to be between Scenario 2 and Scenario 3, *meaning the virus is transmitting widely in cattle (Scenario 2), but infections in cattle and other animal species (eg, cats) may offer opportunity for reassortment (Scenario 3), which would increase the potential for a novel influenza virus that could transmit efficiently between humans.*

This judgment is based on the widespread occurrence of H5N1 infections in cattle across the US, the detection of H5 in wastewater in 6 states, and high mortality in H5N1-infected cats that live on affected farms. A preprint report released on May 3, 2024, found that cattle may be

possible mixing vessels for influenza reassortment because of the existence of both avian and human influenza receptors in cows, which would move the situation into Scenario 3. However, because this study has not yet been peer-reviewed or replicated, we maintain our judgment that we are not yet fully in Scenario 3. If we see additional evidence to support these findings, the study is published in a reputable peer-reviewed journal, or the virus is found in other species such as pigs, we may change our judgment about the risk. To date, no human-to-human transmission has been reported, and we have not seen an increase in human cases.

H5N1 Human Health Risk Assessment Scenario Table

	Risk to agricultural workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
Scenario 1 – Minimal spread in cattle	Low	Low	**Very** Low	**Very** Low
Scenario 2 – Widespread transmission in cattle, few human infections, no human-to-human transmission	Moderate	Low	**Very** Low	**Very** Low
Scenario 3 – Increased potential for reassortment and human adaptation, still no human-to-human transmission	Moderate-High	Moderate	Low	Low
Scenario 4 – Increasing reports of human infections, limited human-to-human transmission between close contacts	High	Moderate-High	Moderate	Low-Moderate
Scenario 5 – Efficient human-to-human transmission	High	High	High	High

Methods: The purpose of this document is to consider possible future developments in this outbreak and describe corresponding risks to human populations should a given scenario occur. In each scenario, we consider the risk to 4 distinct populations: agricultural workers on affected farms, other people in the vicinity of affected animal populations and agricultural workers (eg, household contacts of workers, people living near affected facilities with potential contact with infected animals or farm workers, healthcare providers treating infected individuals), US healthcare workers, and the US general public.

In determining these risks, we consider several factors, including cow-to-cow transmission pathways (eg, respiratory transmission, drinking contaminated water and feeding on contaminated grasslands, aerosolization of the virus through the milking process, etc.), cow-to-human transmission pathways (eg, unprotected and close contact with infected animals, consumption of unpasteurized dairy products, etc.), human-to-human transmission pathways (eg, aerosol, oral, direct contact), and cow-to-other animal transmission. We also consider disease morbidity and mortality, instances of transmission, the level of testing conducted in cattle and other farm animals, the level of testing conducted in humans, existing processes to limit spread from infected animals, genomic surveillance capabilities, and any new mutations showing greater potential for sustained human-to-human transmission. Other factors include events that could increase human-to-human transmission (eg, mass gatherings, seasonal trends, school terms, etc.), treatments available to humans (eg, antivirals), preventative measures for animal-to-worker transmission (eg, use of N95 mask or equivalent, goggles, gloves, gown, head cover, and boot covers) and transmission to the general public, preventative medical countermeasures, preventative nonpharmaceutical interventions for human-to-human transmission, and ongoing response operations to address the outbreak.

Appendix: Additional Details on Process and Recommendations

Scenario 1: H5N1 outbreak stays predominantly in cattle and has minimal spread within herds and to other animals.

In the first scenario, we considered the risk to human health if the H5N1 virus stays in cattle and has minimal spread within herds and to other animals. We determined the health risk to **agricultural workers** to be **low**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **low**, the risk to **healthcare workers to be very low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **very low**.

Our **confidence** in these risk scores is high given the current level of information known for each of these factors and the fact that the virus is not actively spreading to humans or within human populations in this scenario. To minimize the spread of H5N1in animals, USDA recommends:

- Increased diagnostic testing in cattle.
- Continued separation of infected cattle from the rest of the herd.
- Enforced cattle import restrictions to limit the movement of infected cattle across state borders.
- Stringent control of potentially infected food products (removal of milk or other infected products).

To minimize the potential for cow-to-human transmission, USDA recommends:

- Agricultural workers and other individuals in close contact with infected cattle or environments use adequate protective equipment and hygienic/sanitation measures.

Scenario 2: H5N1 virus stays predominantly in cattle but spreads widely within herds. There is also a low incidence of cow-to-human transmission but no human-to-human transmission.

In the second scenario, we considered the risk to human health if the H5N1 virus is spreading widely within bovine herds but has minimal spread to other animal species. We determined the health risk to **agricultural workers** in this scenario to be **moderate**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **low**, the risk to **healthcare workers to be very low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **very low**.

Our **confidence** in these risk scores is low, as the level of testing conducted in cattle and other farm animals is low. Based on available USDA data, there is considerable cow-to-cow transmission occurring. We do not know precisely how much exposure agricultural workers have to infected cattle, but it is likely sufficient to enable transmission. Furthermore, we do not have details on the routes of transmission to humans, making it difficult to determine the exact risk to agricultural workers. Though we determined the risk of widespread human infection to be low given the low incidence of documented cow-to-human transmission, that could change. As the number of infected cattle increases, so does the risk to agricultural workers. To reduce risk, USDA recommends:

- Agricultural workers diligently use appropriate personal protective equipment (such as masks, goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle and potentially infected environments.

- Increased diagnostic testing in cattle and the continued separation of infected cattle during convalescence.
- Enforced cattle import restrictions to limit the movement of infected cattle across state borders.
- Stringent control of potentially infected food products (removal of milk or other infected products).
- Information sharing between the agriculture and public health sectors to increase transparency and monitor for increases in cow-to-human transmission.

Scenario 3: H5N1 virus begins to infect swine or other animal species that have facilitated the mixing and spreading of influenza viruses. This increases the likelihood that the virus reassorts with other influenza viruses and adapts to humans. Some limited human-to-human transmission is reported, but only among close contacts of human cases. Healthcare workers have not reported infections.

In the third scenario, we considered the risk to human health if the H5N1 virus begins spreading widely in pigs or other potential mixing vessel animals, creating greater opportunity for reassortment with human influenza viruses. In this scenario, we expect some very limited human-to-human transmission would be reported among close contacts of cases. We determined the health risk to **agricultural workers** to be **moderate-high**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **moderate** the health risk to **healthcare workers** to be **low**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low**.

Our **confidence** in these risk scores is low, as the level of testing conducted in cattle and other farm animals is low. The jump from cattle to swine poses an increased risk for new mutations that could have a greater potential for sustained transmission within human populations, particularly for agricultural workers and local communities. To decrease risk to human health, we recommend:

- Agricultural workers diligently use personal protective equipment (including masks goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle, infected animals, and potentially infected environments.
- Increased diagnostic testing in cattle and other farm animals, continued genomic surveillance, the separation of infected cattle and other animals, and stringent control of potentially infected food products.
- Information sharing between the agriculture and public health sectors to increase transparency and monitor for increases in human transmission.
- Increased public health surveillance for H5N1 cases in local communities.

- Enhanced communication with the public about the situation and the measures being taken to address it.

Scenario 4: There are more reports of human infections due to contact with infected animals like cattle or swine. Limited human-to-human transmission is reported among close contacts of infected individuals, including healthcare workers, but there is no efficient human-to-human transmission.

In the fourth scenario, we considered the risk to human health if the H5N1 virus begins spreading more readily among close human contacts, including healthcare workers. In this scenario, increased, but still limited, human-to-human transmission is reported among close contacts. Transmission between people is still not efficient. We determined the health risk to **agricultural workers** to be **high**, the health risk to **other people in the vicinity of affected workers and animal populations** to be **moderate-high**, the health risk to **healthcare workers** to be **moderate**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **low-moderate**.

Our **confidence** in these risks scores is low, as the level of testing conducted in farm animals and humans is generally low. Increased incidence of human-to-human transmission may indicate increased transmission efficiency, but it may also be due to greater prevalence of the virus in communities. There is still significant uncertainty about whether the virus will spread efficiently among people. To reduce risk to human health, we recommend actions including but not limited to:

- Implementing and supporting recommended isolation of human cases and quarantine of close contacts of cases through escalated case finding and contact tracing, Tamiflu prophylaxis for those exposed, compensation for individuals who are isolated/quarantined and cannot report to work, and social support to provide for essential needs of those in isolation/quarantine.
- Increasing focus on sentinel surveillance, wastewater surveillance, and education of clinicians to consider H5N1 as a possible diagnosis for people who present with new respiratory illness.
- Continued development and widespread implementation of antigen and molecular testing in both hospital and outpatient settings.
- Policy preparation for the possibility of a pandemic, including congressional deliberations about emergency funding and emergency planning by healthcare institutions, workplaces, and federal, state, territorial, local, and tribal public health agencies.

- Increased investment and urgent development, testing, and production of vaccines and treatment options.
- Increased risk communication to the public to provide regular updates and prevent mis- and disinformation.

Scenario 5: There are reports of efficient human-to-human transmission. The likelihood of human infections is high because the virus now transmits efficiently and will be very difficult to contain.

In the fifth scenario, we considered the risk to human health if the virus jumps from animals to humans, and we find efficient human-to-human transmission of H5N1. We determined the health risk to **agricultural workers** to be **high**, the health risk to **non-workers in the vicinity of affected workers and animal populations** to be **high**, the health risk to **healthcare workers** to be **high**, and the health risk to the **US general public** (and the consequent risk of a pandemic) to be **high**.

Our **confidence** in these risks scores is high. The level of H5N1 testing in humans is currently minimal, and we have limited information or evidence available to determine the exact human-to-human transmission pathways. Preventative medical countermeasures to address human-to-human transmission, such as vaccines, are available, but it is unclear how effective they would be. Nonpharmaceutical interventions are not currently in use, and there are no human public health response operations in place. The risk is therefore high for agricultural workers and the local and global communities. To decrease the risk of human-to-human transmission, we recommend actions including, but not limited to:

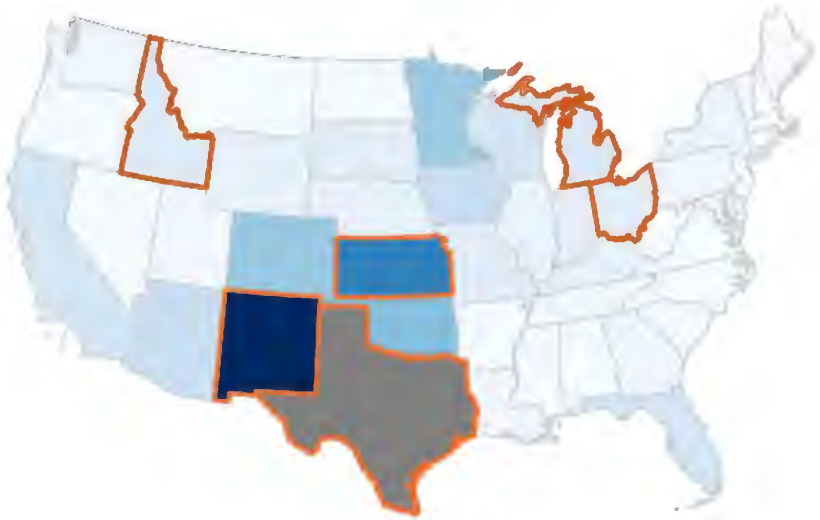
- Increased diagnostic and surveillance testing in humans (including increased genomic surveillance).
- Implementing and supporting recommended isolation of cases and quarantine of close contacts of cases through escalated case finding and contact tracing, Tamiflu prophylaxis for those exposed, compensation for individuals who are isolated/quarantined and cannot report to work, and social support to provide for essential needs of those in isolation/quarantine.
- Increasing sentinel surveillance, wastewater surveillance, and education of clinicians about how to recognize and treat H5N1 infection.
- Widespread implementation of antigen and molecular testing in both hospital and outpatient settings.
- Congressional approval of supplemental appropriations to fund public health response activities.

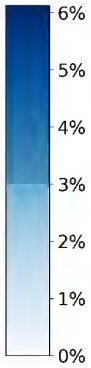
- Urgent continued development, testing, and production of vaccines and treatment options.
- Adoption of medical countermeasures and nonpharmaceutical interventions.
- Increased risk communication to the public to provide regular epidemiologic updates, discuss the interventions that may be used, recommend measures that individuals and organizations can take to protect public health, and address mis- and disinformation.
- Monitoring and mitigation of transmission at mass gathering events.

References

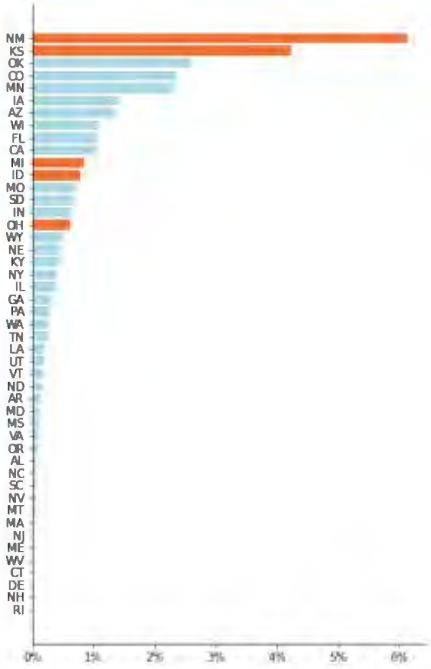
- Burrough ER, Magstadt DR, Petersen B, et al. Early Release - Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus Infection in Domestic Dairy Cattle and Cats, United States, 2024. Emerg Infect Dis. April 29, 2024. doi:10.3201/eid3007.240508
- Kristensen C, Jensen HE, Trebbien R, Webby RJ, Larsen LE. The avian and human influenza A virus receptors sialic acid (SA)-α2,3 and SA-α2,6 are widely expressed in the bovine mammary gland. bioRxiv. May 3, 2024. doi:10.1101/2024.05.03.592326
- US Department of Agriculture Animal and Plant Health Inspection Service. Highly Pathogenic Avian Influenza (HPAI) Detections in Livestock. Updated June 13, 2024. Accessed July 8, 2024. https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/livestock
- US Centers for Disease Control. CDC A(H5N1) Bird Flu response Update. Published July 5, 2024. Accessed July 8, 2024. https://www.cdc.gov/bird-flu/spotlights/h5n1-response-07052024.html#:~:text=Four%20human%20cases%20of%20A,had%20exposure%20to%20sick%20cows
- US Centers for Disease Control. CDC Confirms Second Human H5 Bird Flu Case in Michigan; Third Case Tied to Dairy Outbreak. Published May 30, 2024. Accessed July 8, 2024. https://www.cdc.gov/media/releases/2024/p0530-h5-human-case-michigan.html
- US Centers for Disease Control. CDC reports Second Human Case of H5 Bird Flu Tied to Dairy Cow Outbreak. Published May 22,2024. Accessed July 8, 2024. https://www.cdc.gov/media/releases/2024/s0522-human-case-h5.html
- US Centers for Disease Control. Update: Human Infection with Highly Pathogenic Avian Influenza A(H5N1) Virus in Texas. Published April 5, 2024. Accessed July 8, 2024 https://www.cdc.gov/ncird/whats-new/human-infection-H5N1-bird-flu.html
- Wolfe MK, Duong D, Shelden B, et al. Detection of hemagglutinin H5 influenza A virus sequence in municipal wastewater solids at wastewater treatment plants with increases in influenza A in spring, 2024. medRxiv. April 29, 2024. doi:10.1101/2024.04.26.24306409

Relative importation risk of introduction of H5N1 in cow livestock





Origin assumption: Texas
States that have already signalled presence of H5N1 in cow farms: Texas, Kansas, Idaho, New México, Michigan, Ohio



Ref data: Sellman, Stefan, et al. "Modeling US cattle movements until the cows come home: Who ships to whom and how many?." *Computers and Electronics in Agriculture* 203 (2022): 107483
Data Access: April 3rd 2024
Notes: cattle movements reconstructed by sampled Q12009 (first quarter) dairy CVI interstate shipment data

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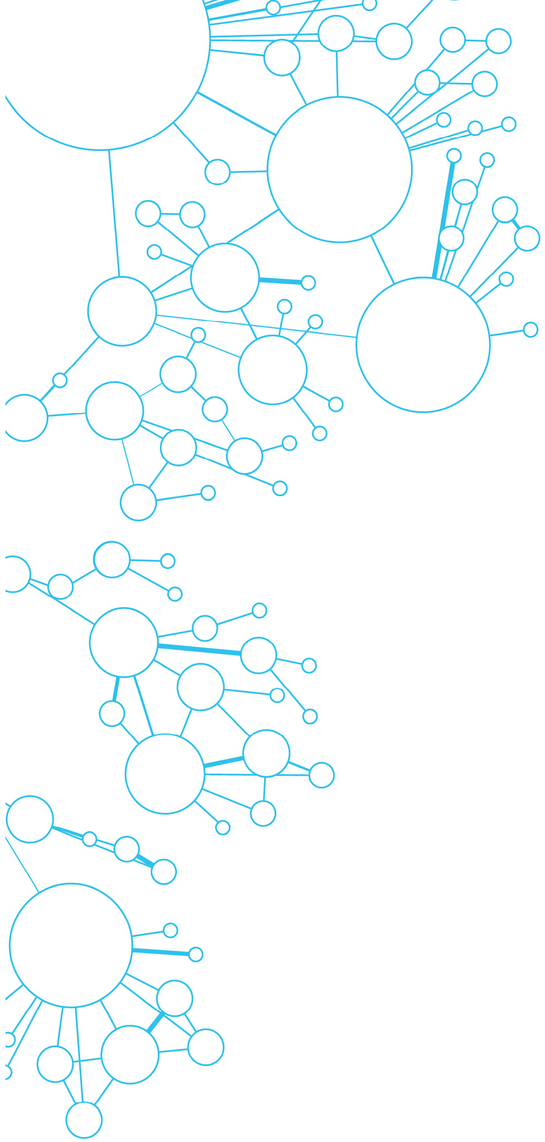

@alexvespi

Northeastern

H5N1 & dairy cow mobility

(Updated 04/27/2024)

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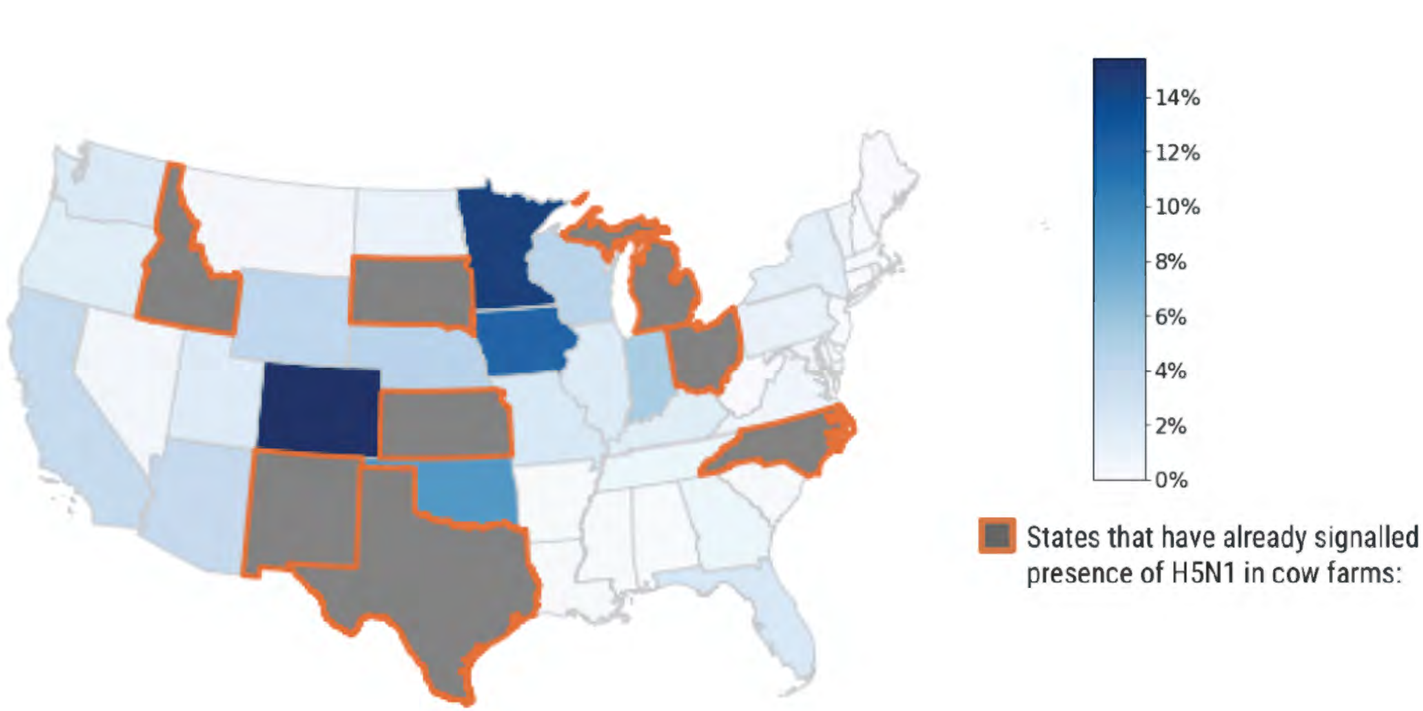
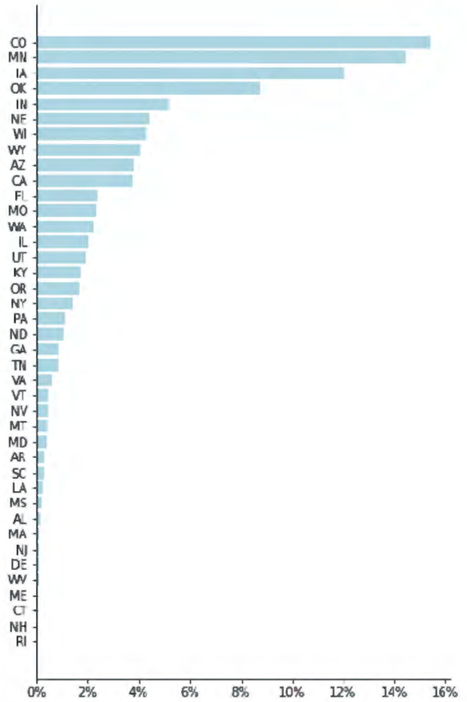
AND SOCIO-TECHNICAL SYSTEMS

Multi-source relative importation risk of introduction of H5N1 in dairy cow livestock April 16, 2024





Multisource relative importation risk of introduction of H5N1 in **dairy** cow livestock update. As of **April 16, 2024**, detection already occurred among dairy livestock in Texas, Kansas, Idaho, New Mexico, Michigan, Ohio, South Dakota and North Carolina.

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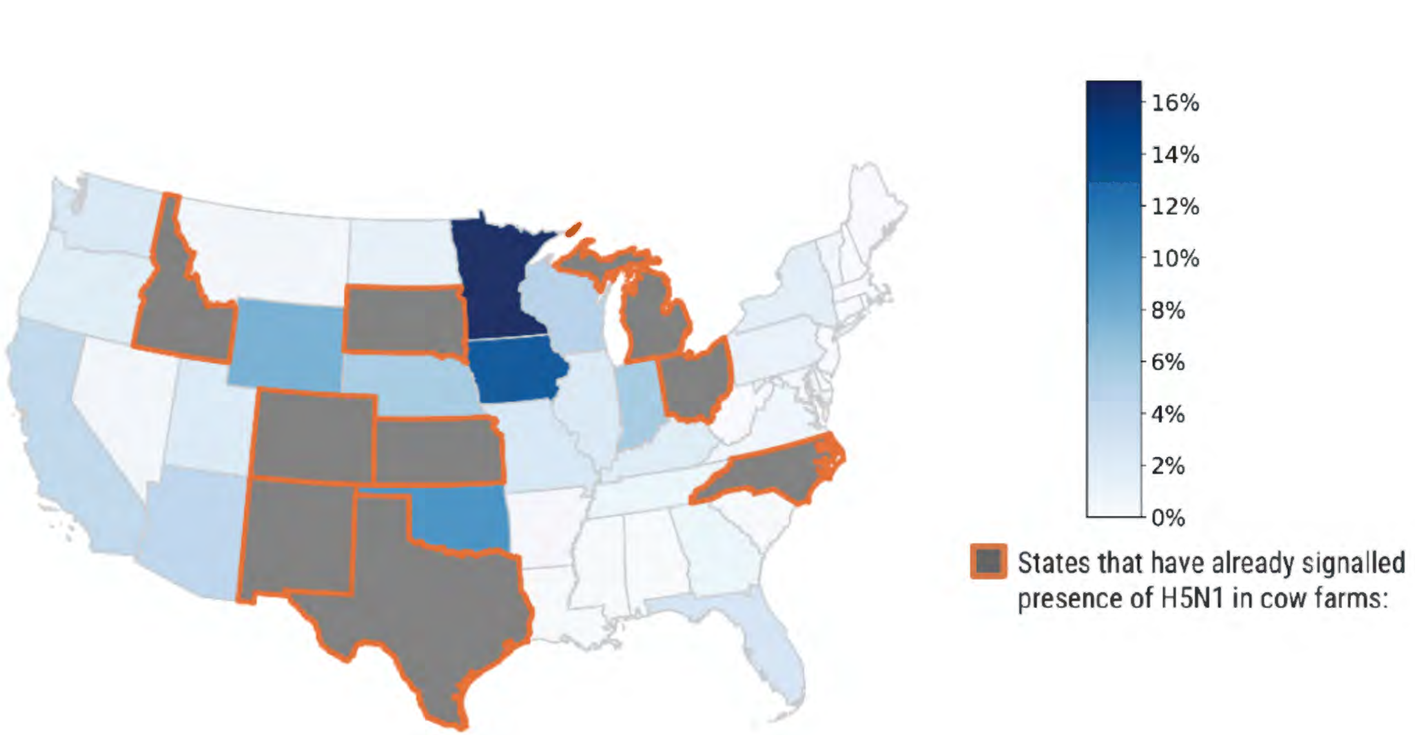
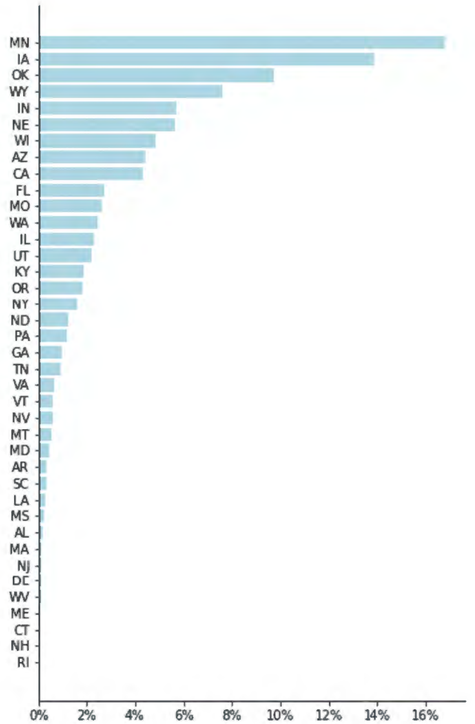
Multi-source relative importation risk of introduction of H5N1 in dairy cow livestock April 26, 2024





Multisource relative importation risk of introduction of H5N1 in **dairy** cow livestock update. As of **April 26, 2024**, detection already occurred among dairy livestock in Texas, Kansas, Idaho, New Mexico, Michigan, Ohio, South Dakota, North Carolina and Colorado.

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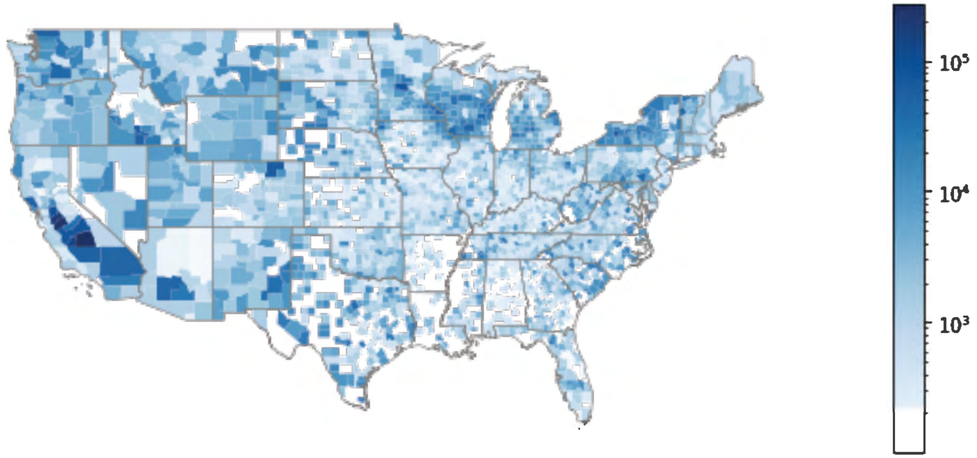
Data & Methods

Distribution of the binned means size of dairy farm across counties.



Ref data:
[1] Sellman, Stefan, et al. "Modeling US cattle movements until the cows come home: Who ships to whom and how many?." *Computers and Electronics in Agriculture* 203 (2022): 107483
Data Access: April 3rd 2024

Notes on the data generation as described in [1]:
Goal: county-level shipment size reconstruction
Input: veterinary inspections (CVIs), official documents issued by accredited state veterinarians when cattle and other livestock species are being shipped across state borders for non-slaughter purposes

For each state Y, the model estimates the probability P(Y) that a single infected cow travels from the set of states S that have confirmed H5N1 in dairy cows to that specific state Y . In other words, given the occurrence of one exported case, P(Y) is the probability that the diseased cow will be reported in location Y, with respect to any other possible location.

The relative risk of importation is calculated directly from the flow of cattle between the states. With wij the number of animals transferred from state i (the source) to state j, the relative risk of importation in state j.

The multi-source calculation has the following assumptions:

- The outbreak size is comparable in states that have reported cases
- No difference in screening or testing for cows movement across different states

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Technical Report on highly pathogenic avian influenza A(H5N1) viruses

Executive summary

Since 2022, despite the wide geographic spread of highly pathogenic avian influenza (HPAI) A(H5N1) viruses in wild birds and to poultry worldwide, with sporadic spillover to mammals, only a small number of sporadic human cases of A(H5N1) have been identified. All reported human cases to date were associated with recent poultry exposures, and no cases of human-to-human transmission have been identified. 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 6,300 people in 52 jurisdictions have been monitored since 2022, and only one human case has been identified
- An H5 candidate vaccine virus (CVV) produced by CDC is nearly identical or, in many samples, identical to the hemagglutinin (HA) protein of recently detected clade 2.3.4.4b HPAI A(H5N1) viruses in birds and mammals (including the recent outbreak in farmed mink in Spain) and could be used to produce a vaccine for people, if needed, and would provide good protection against the clade 2.3.4.4b HPAI A(H5N1) viruses circulating in birds. This H5 CVV is available and has been shared with vaccine manufacturers.
- Because influenza viruses are constantly changing, CDC performs ongoing analyses of A(H5N1) viruses to identify genetic 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, no such concerning changes have been identified in HPAI A(H5N1) viruses circulating in wild birds and poultry worldwide or that have sporadically infected humans.
- Currently, HPAI A(H5N1) viruses are believed to pose a low risk to the health of 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.

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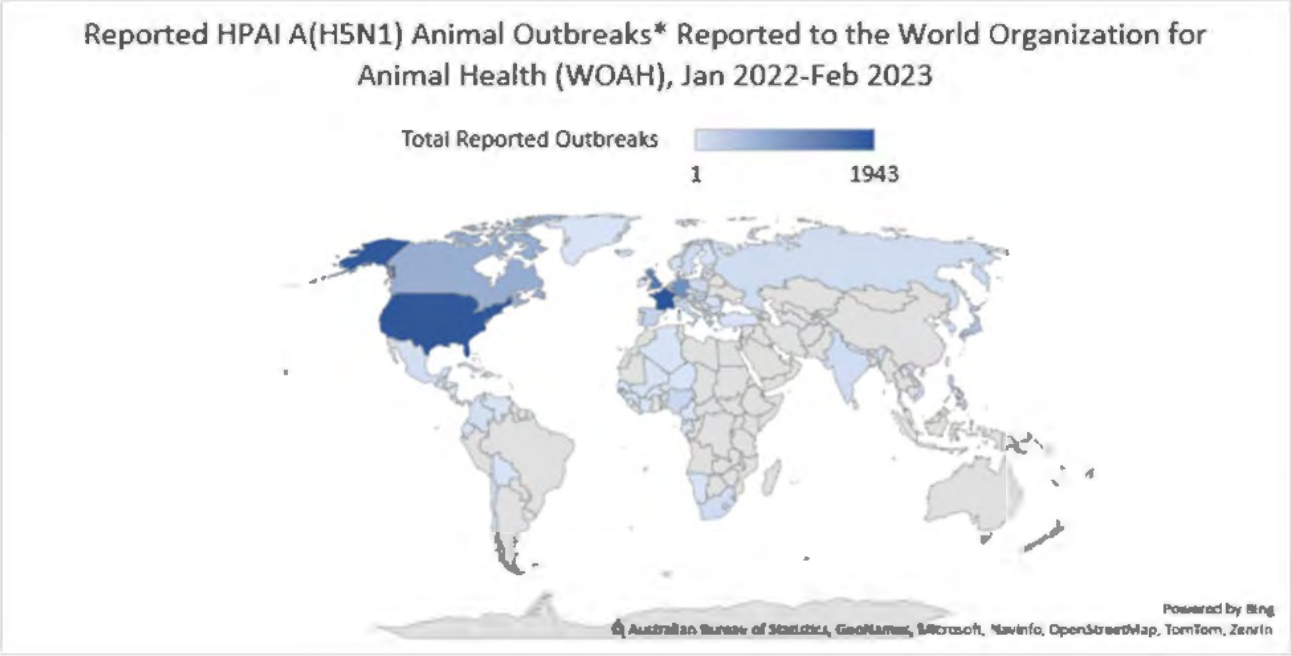
HPAI A(H5N1) viruses in wild birds and poultry

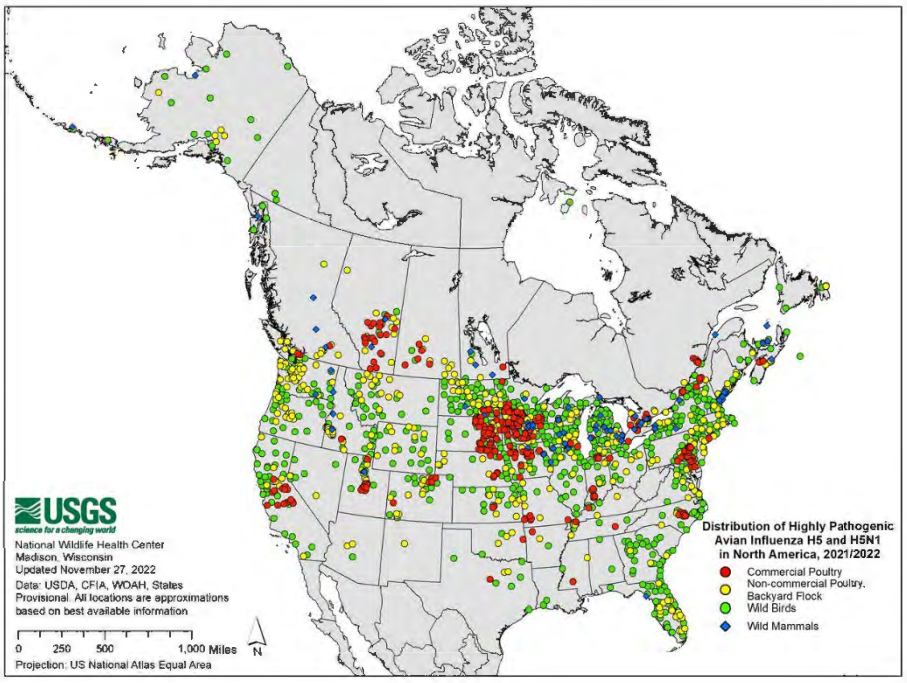
Since 2005, HPAI A(H5N1) viruses have undergone extensive genetic diversification including the formation of hundreds of genotypes following reassortment with other avian influenza A viruses. Clade 2.3.4.4b HPAI A(H5N1) viruses emerged in 2020 and were introduced into North America in late 2021 [1] and have spread to Central and South America, resulting in wild bird and poultry outbreaks in many countries [2].

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 11,300 animal outbreaks of HPAI A(H5N1) viruses were reported by 73 member states to the World Organization for Animal Health since January 2022.



* WOAH 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 animal affected.

In the United States, USDA APHIS monitors for avian influenza viruses in wild, commercial, and backyard birds. From January 2022 to February 2023, APHIS reported HPAI A(H5)/A(H5N1) virus detections in 6,284 wild birds in 49 states and 777 commercial and backyard flocks in 47 states.

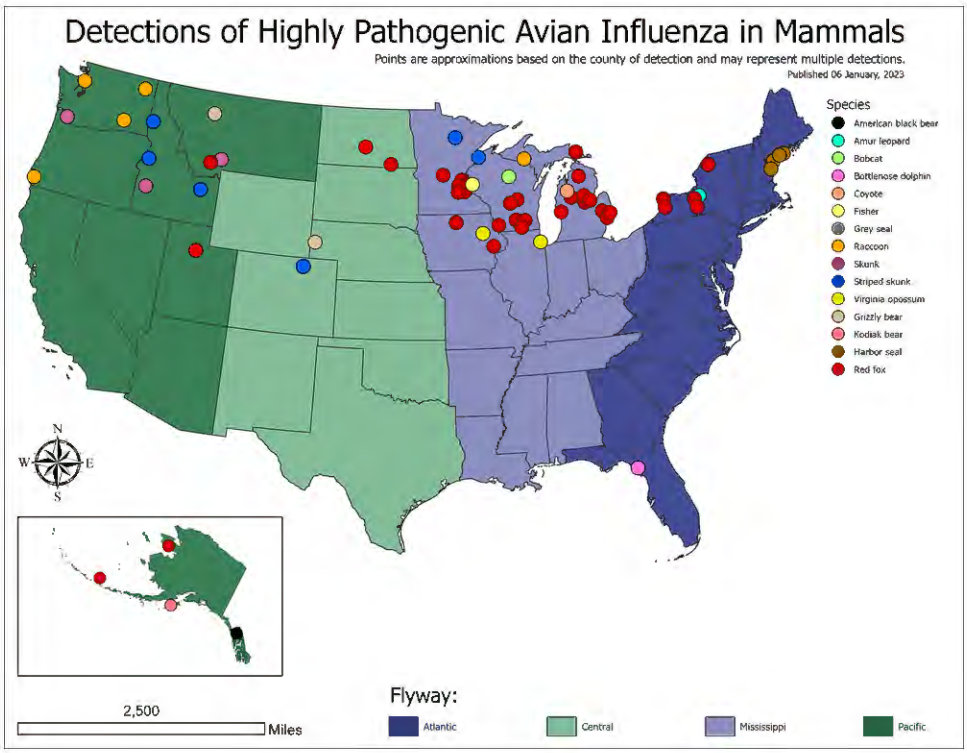


Source: Distribution of Highly Pathogenic Avian Influenza in North America, 2021/2022 | U.S. Geological Survey (usgs.gov)

HPAI A(H5N1) virus infections among mammals

Sporadic HPAI A(H5N1) virus infections of mammals have been reported for 20 years in countries that have experienced HPAI A(H5N1) virus outbreaks in poultry or wild birds. 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 to February 2023, USDA APHIS reports HPAI A(H5N1) virus detections in 131 mammals in 23 states. Globally, sporadic HPAI A(H5N1) virus infections have been reported in farmed mink in Spain, sea lions in Peru and Chile, and foxes in Canada, France, and other countries. 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.



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

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 [3-5].

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 an ability to easily infect and bind to α2,6-linked sialic acid receptors that are predominant in the human upper respiratory tract [6], which would be needed to increase the risk of transmission to people [7,8].

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]. Between January 2022 and March 7, 2023, ten sporadic human cases of A(H5N1) were reported from seven countries [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 reported in Spain [9].

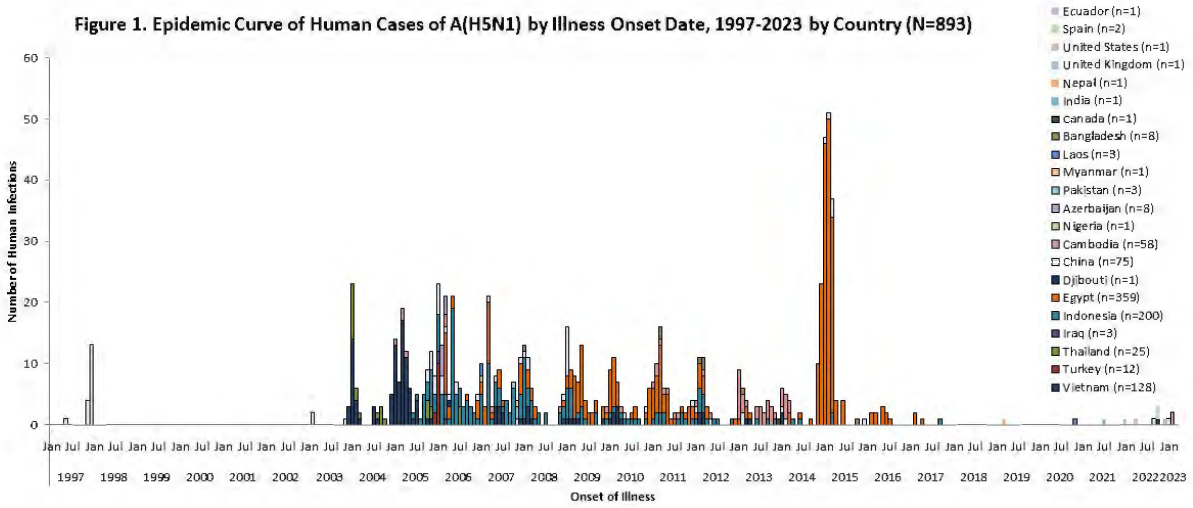
All reported cases had recent exposure to sick or dead poultry, and no cases of human-to-human HPAI A(H5N1) virus transmission were identified. Five cases (3 children, 2 adults) were hospitalized, and 2 died. Seven cases were associated with clade 2.3.4.4b HPAI A(H5N1) viruses, and two cases were associated with clade 2.3.2.1c HPAI A(H5N1) viruses; 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. Reported A(H5N1) human cases, January 2022 to March 6, 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
Cambodia	February 2023	Mild illness, survived	Clade 2.3.2.1c
China	September 2022	Critical illness, died	Clade 2.3.4.4b
China	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
Spain	October 2022	Asymptomatic	Clade 2.3.4.4b
United Kingdom	January 2022	Asymptomatic	Clade 2.3.4.4b
United States	April 2022	Fatigue only, survived	Clade 2.3.4.4b
Vietnam	October 2022	Critical illness, survived	Not reported

Since 1997, a total of 893 sporadic human A(H5N1) cases have been reported from 21 countries [Figure 1], caused by different HPAI A(H5N1) virus clades [10], 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 probable, limited, non-sustained human-to-human HPAI A(H5N1) influenza 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 [11-14].



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. As of March 7, 2023:

- Total monitored: more than 6,300 people in 52 jurisdictions since February 2022
- Total illnesses reported among monitored persons: more than 160 people
- Number positive for influenza A(H5N1) virus: 1

Of the approximately 160 people showing symptoms who were tested for novel influenza A and seasonal flu 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 currently circulating seasonal influenza A virus subtypes (H1 or H3). 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 standard protocols, upon detection of a virus that tests positive for H5, or a virus that cannot be subtyped as currently circulating H1 or H3, the public health laboratory will contact CDC and ship the specimen to CDC for confirmation. 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	Summary
Global surveillance and rapid response to human infections	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.
Virological assessments	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.
Diagnostics	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.

Candidate vaccine virus development	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). A/Astrakhan/3212/2020-like CVVs closely related 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 U.S. FDA (CBER-RG8A) encode a hemagglutinin (HA) protein that is 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. Two additional clade 2.3.4.4b H5N1 CVVs have been recommended for development as part of pandemic preparedness.
Vaccines	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 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), 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.

References

1. Bevins SN, Shriner SA, Cumbee JC Jr, Dilione KE, Douglass KE, Ellis JW et al. Intercontinental Movement of Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4 Virus to the United States, 2021. Emerg Infect Dis. 2022 May;28(5):1006-1011.

2. World Health Organization. Antigenic and genetic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness. February 2023. https://cdn.who.int/media/docs/default-source/influenza/who-influenza-recommendations/vcm-northern-hemisphere-recommendation-2023-2024/20230224_zoonotic_recommendations.pdf?sfvrsn=38c739fa_4

3. Gabriel G, Czudai-Matwich V, Klenk HD. Adaptive mutations in the H5N1 polymerase complex. Virus Res. 2013 Dec 5;178(1):53-62. doi: 10.1016/j.virusres.2013.05.010.

4. Bogs J, Kalthoff D, Veits J, Pavlova S, Schwemmle M, Mänz B et al. Reversion of PB2-627E to -627K during replication of an H5N1 Clade 2.2 virus in mammalian hosts depends on the origin of the nucleoprotein. J Virol. 2011 Oct;85(20):10691-8. doi: 10.1128/JVI.00786-11.

5. Agüero M, Monne I, Sánchez A, Zecchin B, Fusaro A, Ruano MJ et al. Highly pathogenic avian influenza A(H5N1) virus infection in farmed minks, Spain, October 2022. Euro Surveill. 2023 Jan;28(3):2300001. doi: 10.2807/1560-7917.ES.2023.28.3.2300001.

6. Kandeil A, Patton C, Jones J, Jeevan T, Harrington W, Trifkovic S et al. Rapid evolution of A(H5N1) influenza viruses after intercontinental spread to North America. Research Square; 2022. DOI: 10.21203/rs.3.rs-2136604/v1.

7. van Riel D, den Bakker MA, Leijten LM, Chutinimitkul S, Munster VJ, de Wit E et al. Seasonal and pandemic human influenza viruses attach better to human upper respiratory tract epithelium than avian influenza viruses. Am J Pathol. 2010 Apr;176(4):1614-8. doi: 10.2353/ajpath.2010.090949.

8. Shinya K, Ebina M, Yamada S, Ono M, Kasai N, Kawaoka Y. Avian flu: influenza virus receptors in the human airway. Nature. 2006 Mar 23;440(7083):435-6. doi: 10.1038/440435a.

9. Aznar E, Casas I, González Praetorius A, Ruano Ramos MJ, Pozo F, Sierra Moros MJ et al. Influenza A(H5N1) detection in two asymptomatic poultry farm workers in Spain, September to October 2022: suspected environmental contamination. Euro Surveill. 2023 Feb;28(8):2300107. doi: 10.2807/1560-7917.ES.2023.28.8.2300107. https://pubmed.ncbi.nlm.nih.gov/36820643/

10. Lai S, Qin Y, Cowling BJ, Ren X, Wardrop NA, Gilbert M et al. Global epidemiology of avian influenza A H5N1 virus infection in humans, 1997-2015: a systematic review of individual case data. Lancet Infect Dis. 2016 Jul;16(7):e108-e118. doi: 10.1016/S1473-3099(16)00153-5. https://pubmed.ncbi.nlm.nih.gov/27211899/

11. Ungchusak K, Auewarakul P, Dowell SF, Kitphati R, Auwanit W, Puthavathana P et al. Probable person-to-person transmission of avian influenza A (H5N1). N Engl J Med. 2005 Jan 27;352(4):333-40. doi: 10.1056/NEJMoa044021. https://pubmed.ncbi.nlm.nih.gov/15668219/

12. Wang H, Feng Z, Shu Y, Yu H, Zhou L, Zu R et al. Probable limited person-to-person transmission of highly pathogenic avian influenza A (H5N1) virus in China. Lancet. 2008 Apr 26;371(9622):1427-34. doi: 10.1016/S0140-6736(08)60493-6. https://pubmed.ncbi.nlm.nih.gov/18400288/

13. WHO Disease Outbreak News. 2006 – Indonesia. 31 May 2006. Accessed at: https://www.who.int/emergencies/disease-outbreak-news/item/2006_05_31-en

14. World Health Organization. Human cases of avian influenza A (H5N1) in North-West Frontier Province, Pakistan, October-November 2007. Wkly Epidemiol Rec. 2008 Oct 3;83(40):359-64. Accessed at: https://reliefweb.int/report/guinea/weekly-epidemiological-record-wer-3-october-2008-vol-83-no-40-pp-357-364-enfr

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

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

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