HPAI A(H5) Scenario-Based Human Health Risk Assessment

HPAI A(H5) Scenario-Based Human Health Risk Assessment for the United States Center for Outbreak Response Innovation (CORI) Updated as of November 13, 2024

In this update, the Center for Outbreak Response Innovation (CORI) has added a new scenario and formally increased the risk to reflect recent developments.

	Risk to farm workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
NEW Scenario for Increased Potential for Human Adaptation and Increased Human Reports: Increased potential for reassortment and human adaptation, increased reports of human infections, potential early laboratory/epidemiological/sequencing evidence for human-to-human transmission but still no human-to-human transmission confirmed	High	Moderate	Low*	Low*

***While the immediate risk to the general public and healthcare workers is still currently low, the long-term consequences of continued, uncontrolled transmission presents a high risk to all populations.** For this reason, along with the uncertainty and complexity of these events, CORI will continue to monitor the situation and update this risk assessment. For a detailed analysis, including limitations and recommendations see the next page.

This risk assessment adds a new scenario to reflect the heightened risk of H5N1 transmission for farm workers and other people in contact with affected workers and animal populations. CORI makes the judgement to increase the risk level of these two key populations based on 1) continued increases in cases among farm workers, 2) a new H5 case in a Canadian teenager believed to have contact with wild birds, 3) a new serology study showing evidence of undetected H5N1 infection among farm workers, 4) a new laboratory study indicating efficient transmission for direct contact (100%) and inefficient transmission for airborne and fomite transmission (66%), and 5) the recent report of H5N1 in swine, which provides the virus an additional opportunity for reassortment and human adaptation, and may increase the risk of individuals working with pigs to be exposed to H5N1 through this source.

Together, these new developments describe the slow, continued escalation of risk of infection for individuals in direct contact with animals. Although the severity of the H5N1 infections reported thus far have been mild, respiratory symptoms have already been reported among H5 cases and each case presents an opportunity for the virus to better adapt for human transmission. Furthermore, the continued development of this outbreak through the 2024-2025 respiratory virus season presents concerning additional opportunities for the H5N1 virus to mix with the seasonal flu virus and become better adapted for human transmission, potentially escaping targeted and routine surveillance efforts.

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Critical Epidemiological Updates

The following critical epidemiological updates since the last risk assessment have informed the creation of a new scenario and an increase in risk level for farm workers and other people in contact with affected workers and animal populations:

- CDC published the findings of a serology study conducted among 115 farm workers in Colorado and Michigan, which showed that 7% of farmers tested for H5 antibodies were positive. These results support our previous statements that H5N1 cases among farmworkers have been missed, and that testing access should improve. As result of this study, CDC has expanded recommendations for testing to include workers who are exposed to sick cows or poultry but are not experiencing symptoms. Only four of the eight farm workers that tested positive for previous infection recalled symptoms, indicating that asymptomatic infections among humans in contact with infected animals is likely.
- CDC reports additional avian influenza A(H5N1) ferret study results using the H5N1 strain from the first human case in Texas and identified that the virus caused severe illness and death in 100% of ferrets. Researchers also found that the virus spread efficiently between ferrets in direct contact (100%) but did not spread efficiently via respiratory droplets or by fomites (66%). The virus in this study still largely resembles the virus that is currently circulating in cases based on the current data available. The efficient transfer in direct contact raises concern about farm workers in direct contact with affected animals.
- A new pre-print article exploring antibody titers following vaccination with A/Vietnam/1203/2004 H5N1 vaccine shows that both younger and older humans produced H-5 reactive antibodies to the vaccine strain and to the clade 2.3.4.4b isolate currently circulating in cattle, with higher seroconversion rates in young children who had lower levels of antibodies before vaccination. This study may indicate that younger individuals might benefit more from vaccination than older individuals in the event of an H5N1 pandemic.
- Health officials reported a presumptive positive H5 avian flu infection in a Canadian teenager. Confirmation testing and a case investigation are ongoing. According to the British Columbia Health Authority, where the patient is located, the source is expected to be from contact with an infected animal rather than human-to-human transmission, but this has not been confirmed. According to a recent report, the teenager is in critical care and had no prior underlying conditions.

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Routine Surveillance Updates

- The Centers for Disease Control and Prevention (CDC) is reporting 46 confirmed human cases of H5 in the United States as of November 13, 2024.
- The United States Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS) has reported 189 new infected herds across four states (OR, ID, CA, UT) in the last 30 days, bringing the total for the outbreak to 494.
- CDC reports that for the duration of the outbreak, 240 tests for poultry workers and 121 tests for dairy workers have been sent to CDC for H5 testing, resulting in a positivity rate since March 2024 of 8.3% (20/240) and 20.6% (25/121), respectively.

Cattle Worker Positivity Rate: 20.6%
Poultry Worker Positivity Rate: 8.3%

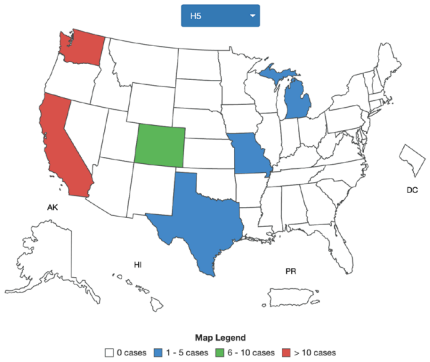

Figure 1: 2024 Map of Human H5 Infections (available from CDC)

Total Cattle Herds Affected: 494 in 16 states
Total Swine Affected: 1 in 1 state

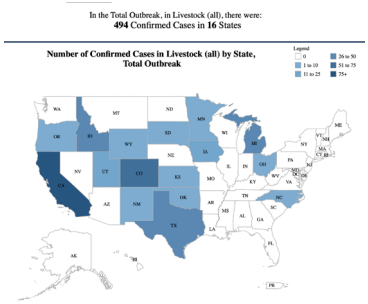

Figure 2: HPAI Confirmed Cases in All Livestock (available from USDA APHIS)

Critical Limitations

- Information on the true prevalence and incidence of affected animals remains limited because testing is only required by USDA when moving cattle across state lines. This gap in information may be ameliorated in part by new efforts for bulk milk testing.
- Testing for humans remains limited due to many factors: 1) commercial testing is unavailable, 2) testing must first be completed for seasonal flu, and then tests that are positive for influenza A but cannot be subtyped must be sent to CDC for H5N1 confirmation, 3) targeted surveillance efforts are limited to commercial farms that are aware of the infection in their animals, and are open to health department involvement, 4) symptom reporting by affected farm workers is likely vastly underreported due to the complex relationship between farm workers and owners, and may be impacted by stigma, fear of government involvement, and concerns about missing work.

Recommendations

In the current scenario, it is vital to:

1. **Prevent reassortment opportunities, especially during the current flu season**
    - Farm workers diligently use personal protective equipment (PPE; including masks goggles, gloves, gowns, head covers, and boot covers) when working directly with or close to cattle and poultry, other infected or potentially animals, and potentially infected environments.
    - Farm workers receive the seasonal flu vaccine as early as possible in the current flu season.
    - Individuals working with agricultural animals who are sick do not report to work, especially if they exhibit respiratory or flu-like symptoms, and seek medical care for diagnosis.
    - Individuals working with agricultural animals who are sick and unable to stay home wear a KN95 mask when in contact with animals.
2. **Ensure timely, accurate surveillance and prevention of H5N1 in agricultural animals**
    - Increased diagnostic testing and genomic surveillance in cattle and poultry.
    - 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).
3. **Continue enhanced public health activities to prevent H5N1 transmission to and among humans**
    - Increased 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.
    - Implementation of and support for recommended isolation of human cases and quarantine of close contacts of cases through escalated case finding and contact tracing, antiviral (eg, 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.
    - Continued development and widespread implementation of antigen and molecular testing in both hospital and outpatient healthcare settings.
    - Increased public health surveillance for H5N1 cases in local communities.
4. **Continue enhanced, open communication about the current situation and potential risks**
    - Information sharing between the agricultural and public health sectors to increase transparency and monitor for increases in animal-to-human or human-to-human transmission.

- Enhanced communication with the public about the situation and the measures being taken to address it, as well as efforts to mitigate the spread of rumors and disinformation.

5. **Continue and consider strengthening political support for public health response**
   - 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.

Appendix

Scenarios

*__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 for Minimal Spread in Cattle: *The virus is predominantly infecting cattle but 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 for Widespread Transmission in Cattle: *Widespread transmission in cattle, few human infections, and no human-to-human transmission*. The virus is predominantly infecting cattle but spreads widely within herds. There is also occasional cow-to-human transmission. There are few human infections 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 farm workers.

Scenario for Potential Human Adaptation: *There is increased potential for reassortment and human adaptation, but still no human-to-human transmission*. The virus begins to infect swine or other animal species that could facilitate the mixing and spreading of influenza viruses. This increases the likelihood that the virus reassorts with other influenza viruses and adapts to humans. Although the opportunities for reassortment are present, there are no specific mutations, laboratory or epidemiological evidence indicate that the virus has adapted for human-to-human transmission. 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 farm workers. The relative risk of a future pandemic has increased, but the absolute risk remains low.

Scenario for Increased Potential for Human Adaptation and Increased Human Reports: *There is increased potential for reassortment and human adaptation, increased reports of human infections, potential early laboratory/epidemiological/sequencing evidence for human-to-human transmission but still no human-to-human transmission confirmed*. The virus has been observed in animal mixing vessels, including pigs, and additional reassortment opportunities are present, such as mixing of the H5N1 virus with the seasonal flu virus, due the ongoing seasonal respiratory virus season (October to April), that increase the risk of human adaptation. There are more reports of human infections due to contact with infected animals like cattle, swine, and/or poultry. Viral mutations, laboratory or epidemiological evidence may be reported that indicate the potential for human-to-human transmission, but there are no

confirmed reports of human-to-human transmission. Population health consequences are low. Overall risk of widespread transmission in humans is low, but risk is increased for farm workers and individuals who work with animals, and close contacts of those workers. The relative risk of a future pandemic has increased, but the absolute risk remains low.

Scenario for Limited Human Transmission: *There is continued potential for reassortment, 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, swine, and/or poultry. 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 farm workers, close contacts of farm workers, and healthcare workers. The likelihood of a future pandemic is increased.

Scenario for Sustained 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.

H5N1 Human Health Risk Assessment Scenario Table

	Risk to farm workers	Risk to other people in contact with affected workers and animal populations	Risk to healthcare workers	Risk to the US general public
Scenario for Minimal Spread in Cattle: The virus is predominantly infecting cattle but there is minimal spread within herds and to other animals	Low	Low	Low	Low
Scenario for Widespread Transmission in Cattle: Widespread transmission in cattle, few human infections, no human-to-human transmission	Moderate	Low	Low	Low
Scenario Potential Human Adaptation: Increased potential for reassortment and human adaptation, still no human-to-human transmission	Moderate-High	Low	Low	Low

NEW Scenario for Increased Potential for Human Adaptation and Increased Human Reports: Increased potential for reassortment and human adaptation, increased reports of human infections, potential early laboratory/epidemiological/sequencing evidence for human-to-human transmission but still no human-to-human transmission confirmed	High	Moderate	Low	Low
Scenario for Limited Human Transmission: Continued potential for reassortment, increasing reports of human infections, limited human-to-human transmission between close contacts	High	Moderate-High	Moderate	Low-Moderate
Scenario for Sustained Human Transmission: Efficient human-to-human transmission	High	High	High	High

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