

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 January 15, 2025

In this update, the Center for Outbreak Response Innovation (CORI) reports the latest developments in the H5N1 outbreak; the risk levels remain unchanged.

Recent developments highlight the importance of enhanced surveillance as well as coordinated containment and prevention activities but do not immediately change the current risk level. For the risk scenario to increase, human-to-human transmission would need to be confirmed, and/or evidence of increasing severity of disease would need to be confirmed. For the risk level to decrease, there would need to be a decline in human cases and a reduction in opportunities for reassortment (eg widespread utilization of PPE by farm workers and others in contact with animals and/or a decline in animal cases).

	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 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 present 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.

Critical Updates:

- A California child is presumed positive for H5N1. The child is located in San Francisco and had red eyes and a fever, according to the [city health department](#), was not hospitalized, and has fully recovered. The case was detected through enhanced surveillance by the public health laboratory. CDC confirmatory testing is ongoing.
- [The case study for the British Columbia severe H5N1 case](#) has now been published. The publication highlights the clinical progression of the disease over time, diagnostic and medical interventions used, and genetic sequence information of the virus.
- A new study, published in [Emerging Infectious Diseases](#), investigates the potential mechanisms of severe human H5N1 disease using strains circulating in US cattle that caused mild human illness and a Vietnam strain known to cause more severe disease. They compared these strains by looking at the key drivers of severe respiratory disease, virus replication and host cell damage in the alveolar epithelium. US strains from the current dairy cattle outbreak showed reduced replication in lung organoids compared to the Vietnam isolate, offering one potential reason that recent human clade 2.3.4.4b cases with exposure to cattle have resulted in mild illness; however, it is crucial that the virus continues to be monitored for changes in pathogenicity or transmissibility.

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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

- CDC [human case numbers](#) are updated on Mondays, Wednesdays, and Fridays, while the [number of tests conducted](#) by each exposure category (poultry, dairy cows) are based on weekly counts, this can lead to some fluctuations in positivity rates

Recommendations

In the current scenario, it is vital to:

1. Prevent reassortment opportunities, especially during the current flu season

- Members of the general public are vaccinated against seasonal flu
- Individuals consume only pasteurized dairy products (milk, cheeses, etc.)
- Farm workers diligently use personal protective equipment (PPE; including masks, goggles, gloves, gowns, head covers, and boot covers) when working directly with or closely to cattle and poultry, other infected or potentially infected 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
- [Individuals planning agricultural or other events that bring together birds, cattle, and swine, should consider](#) testing animals before exhibits or events, promoting good hygiene at events, and taking extra steps to ensure that sick animals remain at home, and animals who become sick at or recently following an event are seen by a veterinarian

2. Ensure timely, accurate surveillance and prevention of H5N1 in agricultural animals

- Increase diagnostic testing and genomic surveillance in cattle and poultry.
- Separation of infected cattle during convalescence
- Enforce 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

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- Increase 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
 - Continue development and widespread implementation of antigen and molecular testing in both hospital and outpatient healthcare settings
 - Increase 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
 - Increase 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.* The likelihood of widespread human infections is low. Population health consequences are low. The overall risk to human health in this scenario is low.

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Scenario for Widespread Transmission in Cattle: *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. There are few human infections and no human-to-human transmission. The likelihood of widespread human infections is low. Population health consequences are low. The 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 which 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, or laboratory or epidemiological evidence to indicate that the virus has adapted for human-to-human transmission. The likelihood of widespread human infections is low. Population health consequences are low. The overall risk of widespread transmission in humans is low, but the 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, and 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 to the ongoing seasonal respiratory virus season (October to April), which increases 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 and 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. The 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, and 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. The likelihood of widespread human infections is moderate. Population health consequences are low. The overall risk of widespread

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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.* The 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 for Potential Human Adaptation: Increased potential for reassortment and human adaptation, still no human-to-human transmission	Moderate-High	Low	Low	Low
CURRENT- 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	High	Moderate-High	Moderate	Low-Moderate

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reassortment, increasing reports of human infections, limited human-to-human transmission between close contacts				
Scenario for Sustained Human Transmission: Efficient human-to-human transmission	High	High	High	High

References

- Flagg, Meaghan, Brandi N. Williamson, Johan A. Ortiz-Morales, Tessa R. Lutterman, and Emmie de Wit. “Early Release - Comparison of Contemporary and Historic Highly Pathogenic Avian Influenza A(H5N1) Virus Replication in Human Lung Organoids - Volume 31, Number 2—February 2025 - Emerging Infectious Diseases Journal - CDC.” Accessed January 14, 2025. <https://doi.org/10.3201/eid3102.241147>.
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