

Context

- Avian influenza A(H5Nx) viruses have been reported globally, leading to large outbreaks in poultry and wild birds, and sporadic detections among mammals.
- Recent H5 viruses (clades 2.3.4.4b and 2.3.2.1c) have emerged or re-emerged, causing concern about the potential transmission and spectrum of the burden of disease in humans.
- More recently, a multi-state outbreak of avian influenza A(H5N1) in dairy cows was reported on 25 March 2024 in the U.S., which has been noted as being reflective of the continued spread of clade 2.3.4.4b viruses that entered the U.S. in late 2021.(1; 2)
- As of 17 May 2024, the U.S. Centers for Disease Control and Prevention (CDC) has confirmed one human A(H5N1) infection, and while there is uncertainty about whether the infection was due to exposure to dairy cattle in Texas (with presumed infection or contaminated environment), this is likely the first instance of mammal-to-human transmission.(1-5)
- This living evidence profile (LEP) was originally requested to identify the state of evidence and knowledge gaps from existing evidence syntheses related to the emergence, transmission, and spectrum of the burden of disease in humans of avian influenza as a first step to informing prevention and mitigation interventions.
- A subsequent update (LEP 7.2) was focused on identifying any existing evidence syntheses published since the initial searches conducted on 18 December 2023, as well as single studies that we could identify about transmission involving cattle or other ruminants and transmission risk to livestock workers, given the recent outbreak in the U.S.
- This LEP update (7.3) includes an update to the searches for evidence documents using the same scope as the last version (as outlined in the previous point), and the addition of a new jurisdictional scan to provide more detailed insights from other countries and Canadian provinces and territories about the emergence, transmission, and spectrum of the burden of avian influenza A(H5Nx) subtypes.

Living Evidence Profile

Examining what is known about the emergence, transmission, and spectrum of the burden of disease of avian influenza A(H5Nx) subtypes

17 May 2024

[MHF product code: LEP 7.3]

*Note that this product was previously labeled as LEP 8, but has since been changed to LEP 7 to accompany a complementary LEP (now with the product code LEP 8) about public health strategies that can be used to prevent, reduce, and/or mitigate avian influenza spillover to humans.

+ Global evidence drawn upon



Evidence syntheses selected based on relevance, quality, and recency of search

- Forms of domestic evidence used (🇨🇦 = Canadian)



Evaluation

- Other types of information used



Jurisdictional scan

12 countries (AU, BR, CB, CI, CH, EC, FR, NZ, SP, UK, US, VM), in addition to international organizations and Canadian provinces and territories

* Additional notable features

Prepared in three business days using an 'all hands on deck' approach

Question

- What is known about the emergence, transmission (including spillover potential), and spectrum of the burden of disease in humans of avian influenza A(H5Nx) subtypes currently circulating and emerging in existing evidence documents and from experiences in other jurisdictions?

High-level summary of new key findings

- We identified five new evidence documents (all pre-print single studies) since the last update of this LEP.
 - Building on the last two updates, we've included a total of 33 evidence documents.
- The single studies (pre-print) provided emerging insights on what is known about A(H5Nx) in relation to humans, dairy cattle, and skuas.
- We conducted a jurisdictional scan of select countries (Australia, Brazil, Cambodia, Chile, China, Ecuador, France, New Zealand, Spain, United Kingdom, United States, and Vietnam), international organizations (World Health Organization (WHO), Pan American Health Organization (PAHO), World Organisation for Animal Health (WOAH), European Centre for Disease Prevention and Control (ECDC), and Food and Agriculture Organization (FAO)), and Canadian provinces and territories to identify any relevant publicly available information and experiences with A(H5Nx).
- The WHO, FAO, and WOAHI indicated that 2.3.4.4b is diversifying genetically and spreading geographically, resulting

Box 1: Approach and supporting materials

At the beginning of each living evidence profile and throughout its development, we engage a subject matter expert, who helps us to scope the question and ensures relevant context is taken into account in the summary of the evidence.

We updated our original searches conducted on 18 December 2023 and 1 May 2024. For LEP 7.3, we conducted the search on 13 May 2024 for any new evidence since our last update. We searched for evidence addressing the question by screening ACCESSSS, Health Systems Evidence, Health Evidence, and PubMed for full evidence syntheses (or synthesis-derived products such as overviews of evidence syntheses) and protocols for evidence syntheses. We also conducted a search for single studies in PubMed and the U.S. Department of Agriculture National Agricultural Library relevant only to dairy cattle, other non-human mammals (including ruminants), transmission associated with dairy products, and risk to livestock (and not a more comprehensive search for all single studies about avian influenza). The searches were not limited by publication date except in PubMed, which was limited to literature published from the last five years (2019 onwards). In addition, we re-ran searches for pre-prints in medRxiv and bioRxiv from 1 January 2024 to 13 May 2024. The search strategies used are included in Appendix 1.

We hand searched government and stakeholder websites of other select countries (Australia, Brazil, Cambodia, Chile, China, Ecuador, France, New Zealand, Spain, United Kingdom, United States, and Vietnam), international organizations (World Health Organization, Pan American Health Organization, World Organisation for Animal Health, European Centre for Disease Prevention and Control, and Food and Agriculture Organization), and Canadian provinces and territories to identify any publicly available information published since 1 February 2024. A list of sources are included in Appendix 8.

In contrast to synthesis methods that provide an in-depth understanding of the evidence, this profile focuses on providing an overview and key insights from relevant documents. Note that the timing, frequency, and scope of future updates of this LEP will be determined in collaboration with the requestor.

A separate appendix document includes:

- 1) methodological details (Appendix 1)
- 2) details about evidence documents and jurisdiction scans (Appendix 2–7)
- 3) key list of sources for jurisdictions (Appendix 8)
- 4) documents excluded at final stage of review (Appendix 9).

This update to the living evidence profile was prepared in the equivalent of three days of a 'full court press' by all involved staff.

in circulation in wild and migratory birds and poultry, wild carnivorous and scavenging mammals, domestic cats and dogs, and aquatic mammals.

- We also found that there are confirmed human cases in Cambodia (clade 2.3.2.1c of H5N1), China (A(H5N6)), the U.S. (clade 2.3.4.4b of A(H5N1)), and Vietnam (A(H5N1)) in 2024.
- These cases were reported to have had close contact with cattle in the U.S., wild birds (during wild bird trappings), live birds at a live poultry market, or with sick or dead backyard poultry (with some handling or consuming poultry before onset of symptoms) in Cambodia, China, and Vietnam.
- A(H5Nx) viruses continue to circulate among wild birds and poultry, as well as other animals such as wild carnivorous and scavenging mammals, domestic cats and dogs, and aquatic mammals.
- The U.S. dairy cattle outbreak is ongoing and is being monitored by U.S. national agencies such as the U.S. CDC, U.S. Department of Agriculture (USDA), and the U.S. Food and Drug Administration (FDA).
- Samples of retail cow's milk in the U.S. and Canada have been tested recently and all tests conducted in Canada were (PCR) negative for RNA fragments of the A(H5N1) virus and tests in the U.S. for viable A(H5N1) virus were also negative.
- Canada and the other countries scanned (see Box 1 for a list of countries and international organizations scanned) report no evidence of human-to-human transmission and indicate that the overall public health risk for the general public is low and low-to-moderate for those in close contact with the virus.
- International organizations and jurisdictions continue to recommend and emphasize the need for surveillance and collaboration to understand the biology and epidemiology of A(H5Nx) viruses, particularly among priority human populations.

Framework to organize what we looked for

- Biology
 - Circulating clades
 - 2.3.4.4b
 - 2.3.2.1c
 - Other (if new subtypes identified as having emerged)
 - Genomic changes and impacts on:
 - Infectivity/transmission
 - Pathogenicity
 - Virulence/disease severity
 - Mammalian adaptation
 - Antiviral susceptibility
 - Virological characteristics
 - Infectivity/transmission (i.e., likelihood to infect a host)
 - Pathogenicity (i.e., ability to cause disease)
 - Virulence/disease severity
 - Immunological characteristics
 - Innate
 - Adaptive
 - Antigen/antibody and cellular immune responses (including cross-protection and cross-reactivity with other human influenza viruses and seasonal strains)
- Epidemiology (including transmission)
 - Route of transmission
 - Bird to non-human mammal
 - Non-human mammal to mammal (including development of a non-human mammal reservoir, bovines, and other livestock)
 - Bird/non-human mammal to human (i.e., zoonotic transmission)

- Environmental viral load (e.g., avian and mammalian viral shedding)
 - Human to human
- Reported cases and other epidemiological indicators of avian influenza A(H5Nx) (e.g., prevalence, case fatality rates, geographic distribution)
- Susceptibility and transmission parameters
 - Incubation period
 - Clinical illness period
 - Latent period
 - Infectious period
 - Virus shedding
- Diagnosis
 - Molecular methods for rapid detection
 - Serological diagnostics (e.g., self-testing, point-of-care diagnostics)
- Clinical presentation
 - Signs and symptoms
 - Risk factors
 - Disease/illness course
- Priority human populations
 - Groups at higher risk of exposure
 - Working on a commercial poultry farm (e.g., producer, seasonal/migrant workers)
 - Working with non-commercial or backyard flocks
 - Livestock farm worker/small herd owner
 - Breeding and handling birds (e.g., dealer, breeder of exotics, falconry, racing pigeons)
 - Hunting and trapping wild birds and mammals (e.g., Indigenous harvesters)
 - Working with live or recently killed poultry, cattle, or other livestock (e.g., butcher, processing plant worker, poultry culler)
 - Working with unpasteurized milk products (e.g., milk processing plant worker, cheesemaker)
 - Veterinarians and veterinary staff
 - Working with wild birds and/or mammals for healthcare, research, and conservation (e.g., laboratory workers, researchers, biologists, wildlife rehabilitators, persons permitted to perform bird branding, capturing, sampling, removal, restoration)
 - Working with non-human mammals that commonly eat wild birds
 - Working or visiting live bird or mammal markets
 - Working with or caretaking of animals that regularly interact with wild birds (e.g., caretakers, pets, guardian dogs, hunting dogs, mink/fur animal farmer)
 - Working in healthcare settings and other contacts of cases (if human-to-human transmission starts)
 - Other equity considerations

What we found

We identified five new evidence documents (all pre-print single studies) since the last update of this LEP. Building on the last two updates, we have included a total of 33 evidence documents that are relevant to the question addressed in this LEP. The single studies (pre-print) provided emerging insights on what is known about A(H5Nx) in relation to humans, dairy cattle, and seabirds.

Gaps in existing evidence documents

There continues to be limited available evidence on the emergence, transmission, and spectrum of the burden of avian influenza A(H5Nx) subtypes, particularly among the priority human populations identified in the organizing framework above. However, the identification of recently published pre-print single studies suggests there is

ongoing research to understand the biology, epidemiology, diagnosis, and clinical presentation of avian influenza A(H5Nx) subtypes among birds, non-human mammals, and humans. Similar to the previous version of this LEP, the evidence documents emphasized the importance of continued surveillance of avian influenza viruses among domestic production animals to understand virus evolution and pathogenesis and to prevent cross-species and mammal-to-mammal transmission.

What existing evidence tells us about the emergence, transmission, and spectrum of the burden of disease in humans of influenza A

General A(H5Nx) subtypes

The identified evidence syntheses described the biology, epidemiology, diagnosis, and clinical presentation of avian influenza A(H5Nx). In terms of biology (virological characteristics), a medium-quality evidence synthesis reported on transmission dynamics largely focusing on domestic poultry as the epidemiological unit and with all of the 46 studies, except five, focusing on highly pathogenic avian influenza (HPAI). The authors suggested that most transmission between poultry farms occurred within a short to medium distance range to each other regardless of subtype or geographical location. The authors reported a reproduction number ranging from 0.03–15.7 for between-farm transmission in poultry of A(H5N1).⁽⁶⁾ A low-quality evidence synthesis found that HPAI virus shedding was higher than that of low pathogenicity avian influenza virus (LPAI). For the introduction routes of HPAI viruses, intranasal, or intraconal routes resulted in no difference in shedding compared to infection by contact. Overall, virus shedding levels among poultry largely depend on the introduction routes (e.g., intranasal, aerosol, oropharyngeal).⁽⁷⁾ Finally, a single study (pre-print) found that avian influenza A(H5N1) virus replicated with high efficacy in precision-cut lung slices from human donors of different ages, with reduced replication among older donors compared to younger donors.⁽⁸⁾

Related to epidemiology, nine evidence syntheses described the prevalence, route of transmission, and susceptibility parameters among birds, non-human mammals, and humans. Three low-quality evidence syntheses (one conducted in 2018, one in 2019, and one did not specify the search date but was published in 2023) described the prevalence in birds from different regions around the world. In Sub-Saharan Africa, the authors reported an overall 3.0% prevalence, with A(H5N1) being the most frequently observed, followed by A(H5N2) and A(H5N8) among both wild and domestic birds (particularly in chickens and ducks).⁽⁹⁾ According to the authors, Indigenous African bird species and migratory water birds from Eurasia keep avian influenza viruses in circulation. Further, they indicated that A(H5N1) HPAI viruses were widespread in this region due to being a major wintering destination for migratory water birds.⁽⁹⁾ In China, it was found that waterfowl were considered the most important transmitters of avian influenza viruses (including the A(H5Nx) subtypes); however, the prevalence in wild birds varied by region.⁽¹⁰⁾ One low-quality evidence synthesis reported a combined global prevalence of 1.6% of A(H5N8) among birds.⁽¹¹⁾ We found one low-quality evidence synthesis that described the prevalence of A(H5N1) in humans. In Egypt, it was found that most A(H5N1) human-infection cases were among children, younger adults, and those with direct exposure to poultry.⁽¹²⁾ Two medium-quality and two low-quality evidence syntheses described other routes of transmission and susceptibility parameters. One evidence synthesis found the movement of birds, humans, and fomites all play a role in transmitting HPAI viruses among birds and between humans and birds during poultry production (e.g., live bird movements between farms, chick movements from hatchery, bird pick-up to slaughter for broiler production, feed delivery, egg collection, human movement such as contact from veterinarians or farm workers).⁽¹³⁾ Another evidence synthesis described the risk of interspecies transmission from backyard farms that involve both domestic poultry and swine.⁽¹⁴⁾ However, one evidence synthesis found that the role of backyard farms in transmission was minimal.⁽⁶⁾ Authors in another evidence synthesis highlighted the importance for studies to contextualize the species and subtypes to have a better understanding of transmission and risk.⁽¹⁵⁾ Finally, a medium-quality evidence synthesis that conducted literature searches in October 2023 indicated that ongoing challenges with A(H5N1) have significantly impacted biodiversity and mammalian health as there are an increasing number of infected mammal species, as well as probable non-human mammal-to-mammal transmission.

The authors of the evidence synthesis underscored the importance of continuous surveillance and international collaboration.(16)

Related to the diagnosis of avian influenza A(H5Nx), three evidence syntheses (one low-quality and two medium-quality) indicated that promising techniques largely involve sample collections from live birds at markets and farms (e.g., swabs, serology), dead birds (e.g., swabs, organ samples), and the environment (e.g., feces, mud, feeding sources, feathers and air and surfaces likely contaminated with viruses such as cages, chopping boards, defeathering machines, trucks, boots).(17-19)

For clinical presentation, a low-quality evidence synthesis indicated that all reported cases of A(H5N6) in humans had prior contact with birds and were found to have a high disease severity, with 95% of cases resulting in hospitalization. Most of reported contact methods included visits to live bird markets, employment as a poultry worker, and direct exposure to recently killed poultry.(20)

One medium-quality evidence synthesis indicated that LPAI A(H5) typically caused mild clinical symptoms among poultry. However, HPAI viruses like A(H5N2), A(H5N6), and A(H5N8) were described to cause severe morbidity and mortality in poultry.(6)

Clade 2.3.4.4b

We identified limited insights about clade 2.3.4.4b from evidence syntheses. Relevant evidence identified is primarily based on epidemiological findings in China, the Western Pacific Region, and North America. In terms of biology, a medium-quality evidence synthesis indicated that the increasing presence of influenza A viruses among poultry and wild bird habitats within various water environments warrants the need for standardized protocols and increased research in underrepresented regions.(21) In terms of epidemiology, one medium-quality evidence synthesis found that the overall seroprevalence of A(H5N1) infection among humans was 2.45% in China, with a higher seroprevalence in Central China (7.3%).(22) A low-quality evidence synthesis indicated that the risk of zoonotic transmission is low in Western Pacific Region, despite changes in primary subtypes and frequency of reported cases.(23) Another low-quality evidence synthesis found that this particular clade was found among wild birds in Alaska, and the authors concluded that these wild birds likely contributed to outbreaks among wild and domestic birds in Canada and the United States in recent years.(24)

We also identified one low-quality evidence synthesis that found that people with poultry exposures (e.g., poultry workers and cullers) had higher seroprevalence of A(H5N1) antibodies than non-poultry exposed people. There were low frequencies of antibodies detected among close contacts of confirmed A(H5N1) cases.(25)

One newly identified single study (pre-print) confirmed that the A(H5N1) clade 2.3.4.4b caused the deaths of five south polar skuas (a type of seabird) in Antarctica.(26) Another new single study reported the circulation of a new genotype B3.13 of clade A(H5N1) 2.3.4.4b among dairy cattle after amino acid mutations associated with mammalian adaptations indicated approximately four months of evolution with limited local circulation in dairy cattle in the United States.(27) The study highlighted that the detection of low-frequency sequence variants could pose a potential zoonotic threat of increased interspecies transmission.

Clade 2.3.2.1c

We found limited information on clade 2.3.2.1c in the identified evidence syntheses. Two medium-quality evidence syntheses reported that this particular clade was found in domestic poultry and dead birds in Cameroon in addition to African pigs in Nigeria.(28; 29) The authors indicated that there could be potential transmission to other mammals, emphasizing the need for improved surveillance in Africa. Additionally, clade 2.3.2.1c was mentioned briefly in a low-quality evidence synthesis, where they described the low risk of zoonotic transmission in the Western Pacific Region.(23)

In terms of the biology of avian influenza A(H5Nx), a low-quality evidence synthesis reported that the evolution and host adaptation of influenza A viruses in bovine species had been hindered until the emergence of novel influenza D virus in cattle, as some bovine host factors with potential anti-influenza properties may have provided influenza A virus resilience for bovines.(30) In addition, a new single study (pre-print) reported that influenza A virus receptors found in humans, ducks, and chickens were widely expressed in the bovine mammary gland and respiratory tract, which may explain the high levels of A(H5N1) virus in infected bovine milk. The authors expressed their concerns regarding the possibility of new genomic changes occurring within influenza A virus.(31) The authors of another single study (pre-print) concluded that infected cows may shed virus for two to three weeks. The study also found amino acid mutations associated with mammalian adaptation, indicating four months of evolution with limited local circulation in dairy cattle. Low-frequency sequence variants were also detected, which may lead to the increased probability of phenotypes that may increase interspecies transmission.(27)

Epidemiological features of avian influenza A(H5Nx) transmission were discussed in the four single studies that we identified from our focused search on outbreaks in cattle and other ruminants. According to one study by the U.S. CDC, dairy cattle farms reported cow-to-cow transmission of A(H5N1).(1) The reported incidence was four to six days after the first animals were affected and then tapered off between 10 and 14 days in March 2024. The affected cows experienced apparent systemic illness, an abrupt drop in milk production, reduced feed intake and rumination, and the production of thick, yellow milk. The study indicated that ingestion of feed contaminated with feces from wild birds is presumed to be the most likely initial source of infection in the dairy cows. The study concluded that A(H5N1) can be shed in milk, which could lead to cross-species and mammal-to-mammal transmission via unpasteurized milk. While the study indicated that the exact source of the virus is unknown, migratory birds (Anseriformes and Charadriiformes) were considered potential sources. Wild waterfowl were identified in another study as a potential transmission pathway for avian influenza in livestock (including cows) on commercial facilities, and it was noted that natural or artificial water and food sources in or near facilities reportedly increased the likelihood of attracting these birds.(32) A newly identified single study (pre-print) indicated that non-waterfowl species had the highest dairy farm exposure, and additional factors such as livestock trade, the use of poultry litter that may contain excrement and/or feathers along with bedding from poultry farms, and contaminated milking machinery may have led to the amplification of the outbreaks in the United States.(33) The outbreak in the U.S. has been reportedly clustered within the clade 2.3.4.4b new genotype B3.13 and a recent single study (pre-print) suggests that this new genotype could pose as a potential zoonotic threat, requiring continued monitoring to inform epidemiological risk and early warning for any interspecies transmission. The new genotype B3.13 may have resulted from the recent reassortment events.(27)

Finally, one report noted that while Europe and North America continued to see widespread outbreaks of avian influenza A(H5Nx) in domestic and wild birds between December 2023 and March 2024, North America remained a hotspot for outbreaks in poultry.(34) The report also noted that goat kids in the U.S. were infected with influenza A(H5N1) virus, which represents the first reported infection in any ruminant species worldwide.

Key findings from the jurisdictional scan

Key findings from the jurisdictional scan are summarized below according to each of the categories in the organizing framework.

Biology

Some international organizations and countries reported on the circulating clades. In a joint assessment released on [23 April 2024](#) by the WHO, FAO, and WOAH, the entities indicated that clade 2.3.4.4b is diversifying genetically and spreading geographically, resulting in circulation in wild and migratory birds and poultry, wild carnivorous and scavenging mammals, domestic cats and dogs, and aquatic mammals. A [technical report](#) updated on 26 April 2024

notes that the U.S. CDC is actively working on clade 2.3.4.4b viruses and is performing ongoing analyses of the virus to identify genetic changes, especially given that this [genetic clade was found](#) in dairy cattle in Texas. To date, few genetic changes of public health concern have been identified in viruses circulating in wild birds and poultry. The [clade 2.3.2.1c of A\(H5N1\)](#) was identified through genetic sequencing in two confirmed human cases in Cambodia. This clade has been circulating in birds and poultry in Cambodia and Vietnam for several years. In [France](#), they confirmed A(H5N1) infection among farmed Muscovy ducks that had two doses of vaccination. The second dose was given 41 days prior to the infection. The [European Food Safety Authority](#) indicated that the humoral immune response and virological protection data suggest that vaccine protection was reduced post-second dose with increasing age of the ducks.

Epidemiology

Avian influenza A(H5Nx) is currently being monitored across international organizations, countries, and Canadian provinces and territories analyzed in our jurisdiction scans. An updated situation summary from the U.S. CDC from [16 May 2024](#), an ECDC weekly bulletin from [4 May 2024](#), and a joint assessment by the WHO, FAO, and WOAH released on [23 April 2024](#) reported that the overall risk for the public is low and those at risk of exposure to infected animals is low-to-moderate. The joint assessment and a WHO report from [28 March 2024](#) stated that there is currently no indication that the virus could cause an increased binding to receptors in the human upper respiratory tract, therefore human-to-human transmission of the currently circulating virus is unlikely without further genetic changes. This conclusion was echoed in a [rapid risk assessment](#) from the Public Health Agency of Canada on 19 April 2024.

There have been confirmed human cases in the [U.S.](#), [Cambodia](#), [Vietnam](#), and [China](#) in 2024. These cases were reported to have had close contact with cattle (clade 2.3.4.4b of A(H5N1) in the United States), and wild birds (during wild bird trappings), live birds at a live poultry market, or with sick or dead backyard poultry (with some handling or consumption of poultry before onset of symptoms in Cambodia, Vietnam, and China. In Cambodia, the five confirmed cases of clade 2.3.2.1c of A(H5N1) (including one death) had contact with sick or dead backyard poultry in their villages. In China, the two confirmed human cases of A(H5N6) (including one death) both had previous exposure to live birds at live poultry markets. The person who died of A(H5N6) had underlying conditions and died 26 days after developing symptoms. In Vietnam, it was documented that the confirmed single human case of A(H5N1) (and subsequent death) had been trapping wild birds and had no reported contact with dead or sick poultry. The U.S. CDC is [working with the Cambodian government](#), the Wildlife Conservation Society of Cambodia, and the WHO in a One Health approach to respond to human infections of avian influenza in Cambodia. The ECDC released an avian influenza overview report from [December 2023–March 2024](#) that highlights virus detections in Europe and outside of Europe. While avian influenza A(H5Nx) has circulated in Spain and France, there have been no reported human cases in 2024 as of the time of writing. Finally, [Australia](#), [Ecuador](#), [New Zealand](#), and the [United Kingdom](#) have not reported any human cases as of 13 May 2024, but all countries have reported they are continuing to be vigilant given the emerging global risk. In Canada, there have been no reported cases in humans.

In terms of birds, poultry continue to remain at risk from the continued circulation and spillover of A(H5N1) viruses from wild birds. The [ECDC weekly bulletin](#) reported new recurrences of A(H5N1) in poultry and non-poultry birds. The U.K. has self-declared [zonal freedom from highly pathogenic avian influenza](#) since 29 March 2024. The U.K. does not currently have outbreaks of avian influenza in poultry or other captive birds and the current [risk is low](#), however A(H5N1) continues to be found in wild birds in the U.K. and across Europe. Since 1 February 2024, there have been [eight cases of avian influenza](#) found in wild birds across the U.K., which include a mix of A(H5N1) and A(H5N5). [France](#) confirmed A(H5N1) in a vaccinated Muscovy duck-housing establishment, affecting 8,700 ducks in January 2024. Additionally, another [outbreak](#) was detected in January 2024, causing the death of 40 ducks and presenting clinical signs of neurological disorders, and decreased food and water intake. According to [PAHO](#), there were seven outbreaks of avian influenza A(H5) in wild birds in Brazil but no outbreaks in production birds or human cases between 1 January 2024 to 18 March 2024. Since then, an [outbreak of A\(H5N1\)](#)

[in non-poultry birds](#) was detected in Brazil between 6 April 2024 to 3 May 2024. The [Canadian Food Inspection Agency](#) reports on the number of infected poultry flocks where A(H5N1) has been detected in Canada. They reported that British Columbia, Alberta, Saskatchewan, Ontario, and Nova Scotia currently have infected premises.

According to the joint assessment by the WHO, FAO, and WOA, spillover from birds to non-human mammals have been reported in the Americas and Europe, resulting in severe infection with neurological symptoms in some non-human mammals. For example, the assessment reported that infection in ferrets has led to severe disease. The Canadian Food Inspection Agency in collaboration with Environment and Climate Change Canada and the Canadian Wildlife Health Cooperative have a [dashboard](#) where they monitor A(H5Nx) in different types of wildlife. As of February 2024, there have been confirmed cases of either A(H5N1), A(H5), A(H5N5), or a combination across all the provinces and territories.

In terms of cattle and other ruminants, the [joint assessment](#) by the WHO, FAO, and WOA reported A(H5N1) detection in dairy cattle in the U.S and in neonatal goats (that shared space on a farm with A(H5N1) infected poultry). The U.S. CDC reported that there has been one reported human case following exposure to dairy cattle. The outbreak in [dairy cows is multi-state](#) and was first reported on 25 March 2024 and resulted in the first presumed mammal to human transmission of avian influenza. Lateral transmission among dairy cattle on affected premises in the U.S. is likely occurring. Currently, there are [reports](#) that A(H5N1) has spread from dairy cattle back into some poultry premises; however, the transmission route and frequency of cattle-to-bird transmission is unknown. As of 20 April 2024, no markers of mammalian adaptation have been found in the avian influenza A(H5N1) virus isolated from infected dairy cattle. While public health risk is low, the ongoing multi-state outbreak among dairy cattle and widespread influenza infection among wild birds and sporadic outbreaks among poultry flocks and mammals are concerning. The [USDA Animal and Plant Health Inspection Service](#) provides regular updates on detections in dairy cattle and updated epidemiological reports and guidance for farmers and veterinarians. The [U.S. FDA](#) completed 297 retail dairy samples, and all were found negative as of 10 May 2024. The [ECDC weekly bulletin](#) reported no cases in cattle in Europe as of 3 May 2024. According to the [Public Health Agency of Canada](#), as of 16 May 2024, highly pathogenic avian influenza A(H5N1) has not been detected in cattle or livestock (apart from poultry) in Canada, and the risk of transmission to humans remains low. Additionally, the [Canadian Food Inspection Agency](#) in collaboration with Health Canada and the Public Health Agency of Canada have been proactively [testing commercial milk samples](#) across Canada to detect fragments of the A(H5N1) virus. As of 14 May 2024, all tested samples have been negative.

Diagnosis

There are common testing methods such as RT-PCR and ELISA methods that are being applied across the jurisdictions for A(H5Nx). For example, there is updated guidance on testing, reporting, and lab information on the use of RT-PCR assay using H5-specific primers and probes from the [U.S. CDC](#). The USDA released recommendations on [14 May 2024](#) related to A(H5N1) virus in livestock for state animal health officials, veterinarians, and producers. The [WOAH](#) indicated that A(H5Nx) in non-avian species (including cattle and other livestock populations) should be a differential diagnosis especially among animals that are showing clinical symptoms, sick or dead domestic animals near affected areas, and suspected animals that may be exposed or linked to suspected or confirmed A(H5Nx) in birds or cattle. In [Australia](#), diagnostic efforts involve PCR and ELISA methods, with avian influenza being a nationally notifiable disease. The French Agency for Food, Environmental and Occupational Health & Safety ([ANSES](#)) is committed to combating the spread of the disease by coordinating the diagnosis of avian influenza in animals and conducting research to improve virus detection. The [B.C. Centre for Disease Control \(BCCDC\)](#) uses nucleic acid testing and [Public Health Ontario](#) uses RT-PCR to detect the presence of A(H5N1).

Clinical presentation

There are existing reports on the clinical presentation of A(H5Nx) in humans, birds, and non-human mammals. Symptoms and conditions ranged from asymptomatic to severe illness in humans such as fever, fatigue, cough, abdominal pain, diarrhea, pneumonia, sepsis, and acute respiratory distress syndrome. Some countries such as [Cambodia](#), [Vietnam](#), and [China](#) reported deaths due to complications. In Cambodia, all confirmed human cases were hospitalized with symptoms, and the person who died was admitted when their condition worsened. The report by ECDC only reported the symptoms of one case in Cambodia, including cough, fever, difficulty breathing, and fever, who was eventually treated with the antiviral, oseltamivir. In Vietnam, the human case who was eventually admitted had fever, cough, abdominal pain, and diarrhea. The patient's conditions worsened to severe pneumonia, severe sepsis, and acute respiratory distress syndrome. The patient eventually died eight days after being admitted to the hospital in March 2024. The two cases in China developed severe symptoms, with one death 26 days after developing symptoms. In the case with exposure to dairy cattle in the [U.S.](#), the patient reported eye redness (consistent with conjunctivitis) as their only symptom.

In terms of [birds](#), clinical signs can include a lack of energy or food intake, decreased egg production, shell-less or soft-shelled eggs, swelling in extremities, respiratory and neurological issues, diarrhea, and sudden death. For example, in the January 2024 outbreak in [France](#), ducks presented neurological disorders, decreased food and water intake, and reported death. According to the [USDA](#), dairy cattle may experience a sudden drop in food intake, marked or acute drop in milk production, thickened milk or no milk, and respiratory signs such as clear nasal discharge.

Priority populations

We found limited publicly available information about priority populations. However, as mentioned in the epidemiology section, confirmed human cases were those in close contact with or handling suspected or confirmed infected cattle and birds (e.g., poultry markets and backyard poultry, wild birds).

Next steps

Additional next steps should focus on efforts to fill gaps in the literature, which include:

- evidence syntheses on the biology (genomic changes, virological characteristics) with clear descriptions of the circulating clades (including different characteristics)
- evidence syntheses on susceptibility and transmission parameters among birds, non-human mammals (e.g., cattle or other livestock), and humans
- evidence syntheses on diagnosis and clinical presentation of avian influenza A(H5Nx) categorized by birds, non-human mammals, and humans
- evidence syntheses with clear descriptions of the population groups and regions, particularly among those at higher risk of exposure
- primary studies that further investigate transmission of avian influenza in cattle and other livestock species, as well as to livestock workers, given the recent outbreak in the U.S. and limited number of primary studies identified from our searches on this topic
- jurisdictional scans that continue to monitor and understand the current state of A(H5Nx) around the world, especially to identify technical reports on the emerging biology and priority populations.

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