Influenza A(H7N9) virus in China Implications for public health

Seventh update, 3 July 2017

Conclusions and options for response

Since the notification of a novel reassortant influenza A(H7N9) virus on 31 March 2013, 1 548 laboratory-confirmed cases of human infection with avian influenza A(H7N9) virus have been reported. This is the fifth winter season in the northern hemisphere with human cases caused by A(H7N9) infections. During this wave, the number of human cases has been higher than in previous waves and accounts for 48% of the human cases reported so far. The higher number of cases is most likely due to greater environmental contamination in live bird markets and increased circulation of the virus among poultry. In contrast to the situation observed during the summer months in previous years, A(H7N9) viruses are continuously circulating in the poultry population, with transmission to humans causing a substantial number of cases.

In February 2017, a new A(H7N9) virus with mutations in the haemagglutinin gene, indicating a change to high pathogenicity in poultry, was reported. This new variant virus has been detected in 25 of the 750 human cases in the current epidemic wave, but the cases were regionally restricted to three Provinces in China and did not show changes in severity.

Highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI) A(H7N9) viruses co-circulate in the bird population. Although the genetic changes in HPAI viruses may have implications in terms of pathogenicity, surveillance and control strategies for poultry, there is no evidence of increased transmissibility to humans or among humans to date. Data show that the newly emerged HPAI as well as some of the currently circulating LPAI viruses are genetically and antigenically distinct from current A(H7N9) candidate vaccine viruses. To address this, WHO has proposed new A(H7N9) candidate vaccine viruses. Timely characterisation of A(H7N9) viruses and sharing of sequence information remains key for A(H7N9) vaccine virus development.

HPAI A(H7N9) viruses from human cases have been found to have mutations associated with reduced susceptibility to neuraminidase inhibitors. Those mutations may have emerged during antiviral treatment. The proportion of viruses with reduced susceptibility to neuraminidase inhibitors has remained constant during the five recent epidemic waves.

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The continued transmission of A(H7N9) to humans in China poses the risk that sporadic travel-related cases returning from China may be detected in Europe. The options for prevention and control of the infection outlined in the previous Rapid Risk Assessment remain valid:

- People travelling to China should avoid direct exposure to poultry and refrain from visiting live poultry markets or backyard farms.
- Travellers who have visited affected areas should be made aware that if they develop respiratory symptoms and fever upon their return, they should consult a physician and mention their recent travel history to enable early diagnosis and treatment.

In addition, travellers who have visited affected areas should avoid visiting farms after their return from affected areas in China for the entire duration of the 10-day incubation period (and during the symptomatic period in the event that they develop symptoms) in order to prevent a possible virus introduction to poultry in the EU.

It cannot be excluded that humans infected with A(H7N9) return to the EU/EEA and introduce the virus. However, the risk of the disease spreading in Europe via humans is still considered low, as there is no evidence of sustained human-to-human transmission.

EU/EEA Member States and the European Commission should consider relevant options – in terms of preparedness and communication – if sustained human-to-human transmission develops. Such options can include, but are not limited to the:

- development of plans for the identification, testing and follow-up of possible human cases
- continuation of influenza surveillance in poultry and wild birds for avian influenza viruses
- sensitisation of healthcare systems and confirmation of available surge capacity at healthcare facilities
- review of arrangements for delivery of relevant prevention and treatment measures.

Public health authorities need to maintain awareness of the virological and epidemiological features of the current A(H7N9) epidemic, including evidence from monitoring of transmission, severity, virus receptor binding and antiviral susceptibility properties.

Source and date of request

ECDC internal decision on 15 June 2017, following an upsurge of cases in China since December 2016, combined with continuous case reporting and significant geographical spread.

Public health issue

In this risk assessment, ECDC summarises the epidemiological information on human infections with avian influenza A(H7N9) viruses and indicates events which are critical for ECDC's monitoring and reporting efforts.

This rapid risk assessment builds on the sixth update of the ECDC rapid risk assessments on avian influenza, published on 9 March 2017 [1,2].

Consulted experts

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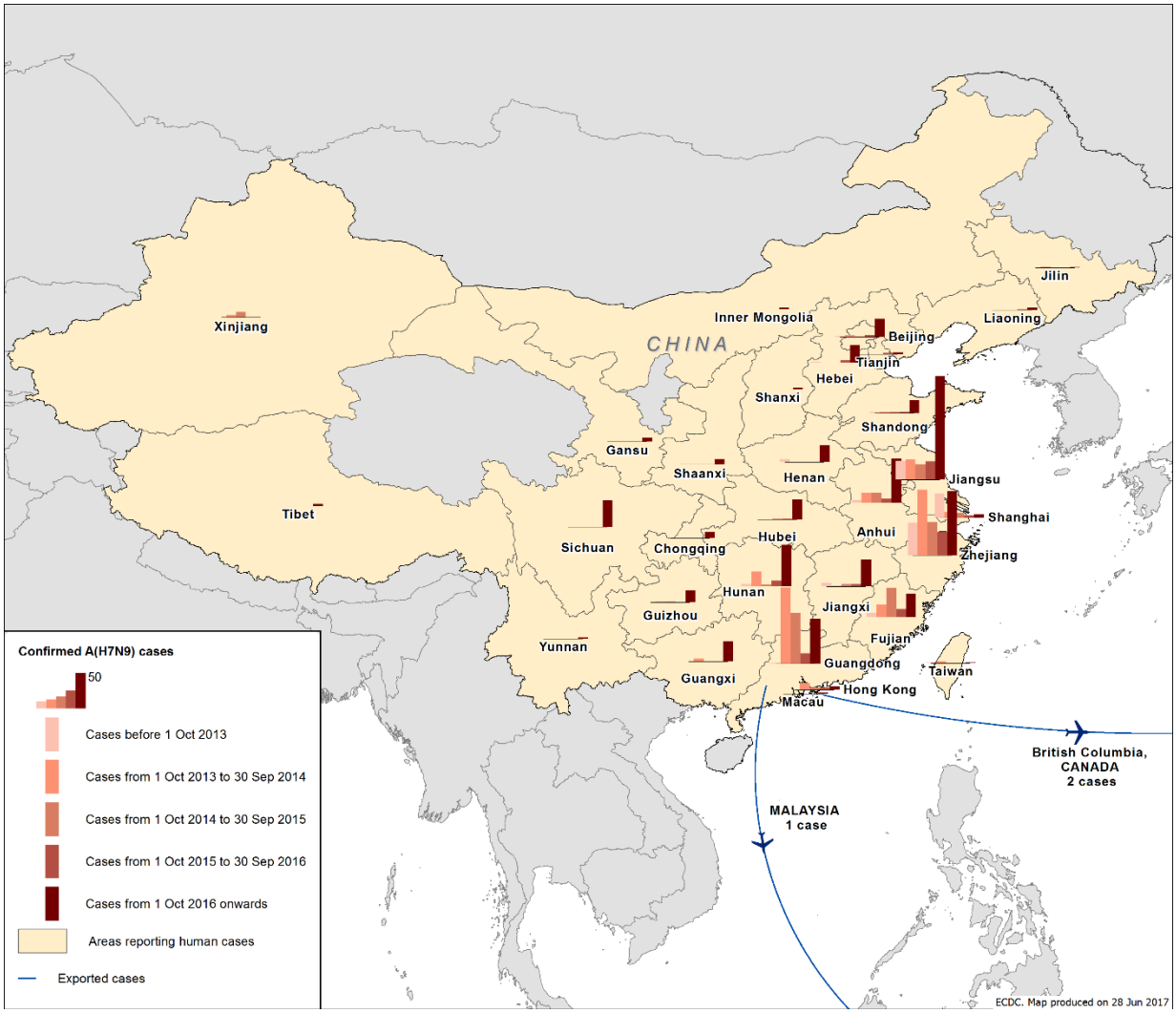
Event information

Update on human cases infected in China

In March 2013, Chinese authorities announced the identification of a reassortant A(H7N9) influenza virus in patients in eastern China. As of 27 June 2017, 1 548 laboratory-confirmed cases were reported as infected in China, including two cases reported from Canada in 2015 and one case from Malaysia in 2014 (Figure 1, Table 1) [3,4].

An interactive ECDC map that shows the number of human cases due to A(H7N9) over time is available from: http://gis.ecdc.europa.eu/influenza/H7N9/

Figure 1. Distribution of confirmed A(H7N9) human cases by place of reporting in China or with recent travel history to China, week 7/2013 to week 25/2017 (N=1 548)



Numbers according to Hong Kong report dated 27 June 2017 [5,8].

Figure 2 shows the five epidemic waves, defined as the period between week 41 of a year until week 40 of the subsequent year, that have been recorded since 2013.The fifth wave started in October 2016 [4], with 750 cases reported as of 27 June 2017. The current wave has the highest number of cases ever reported (Figure 2, Table 1). Compared with earlier waves, which were characterised by only a few sporadic cases, new cases are reported every week. During the first four epidemic waves, the epidemic curve showed a seasonal pattern with a clear peak in January, whereas only a few sporadic cases were reported between weeks 20 and 40. This temporary halt in transmission to humans was assumed to be related to temperatures above 18 °C [6] and solar radiation [7] during the summer months. By contrast, the fifth wave shows continued transmission beyond week 20, although on a lower level, which might reflect a change in the epidemiologic situation in poultry and/or adaptation processes in the virus which could now be more temperature resistant and more stable at higher temperatures.

The fifth wave shows an extended geographical spread, with nine new provinces having reported human cases since the ECDC rapid risk assessment published on 9 March 2017 [2] (Figure 1, Table 1). However, most human

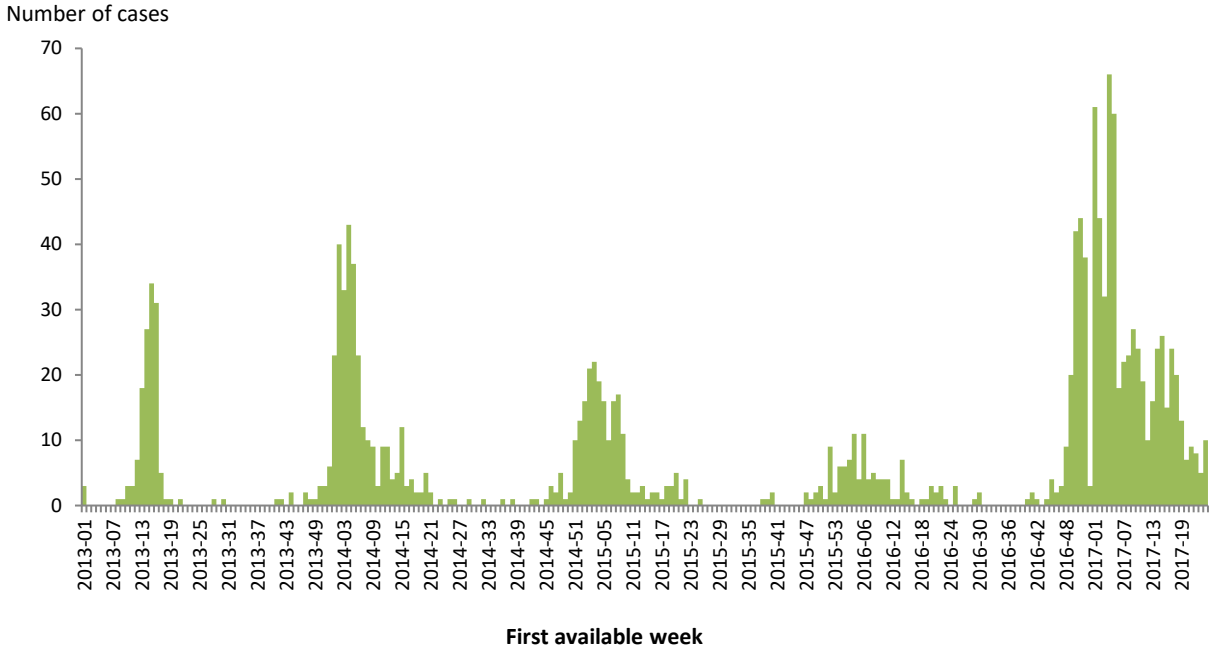
cases and poultry outbreaks continue to be reported in areas with high poultry and human population densities (Figure 3).

Table 1. Number of reported cases due to A(H7N9) infection by place and time of reporting

Place of reporting	First wave (weeks 7/2013–40/2013)	Second wave (weeks 41/2013–40/2014)	Third wave (weeks 41/2014–40/2015)	Fourth wave (weeks 41/2015–40/2016)	Fifth wave (weeks 41/2016–25/2017	Total
Zhejiang	46	93	47	33	91	310
Guangdong	1	108	72	14	63	258
Jiangsu	27	29	22	26	146	250
Fujian	5	17	41	11	33	107
Anhui	4	14	14	6	63	99
Hunan	3	21	2	8	59	93
Shanghai	34	8	6	3	6	57
Jiangxi	5	1	3	3	38	52
Sichuan	0	0	0	0	38	38
Beijing	2	3	1	3	26	35
Guangxi	0	4	0	0	28	31
Hubei	0	0	1	1	29	31
Hebei	1	0	0	3	25	29
Henan	4	0	0	0	24	28
Shandong	2	2	2	2	19	28
Hong Kong	0	10	3	3	5	21
Guizhou	0	1	1	0	17	19
Xinjiang	0	3	7	0	0	10
Chongqing	0	0	0	0	9	9
Shaanxi	0	0	0	0	7	7
Gansu	0	0	0	0	5	5
Taiwan	1	3	0	0	1	5
Liaoning	0	0	0	1	3	4
Tianjin	0	0	0	2	3	5
Jilin	0	2	0	0	1	3
Tibet	0	0	0	0	3	3
Macau	0	0	0	0	2	2
Shanxi	0	0	0	0	2	2
Yunnan	0	0	0	0	2	2
Inner Mongolia	0	0	0	0	2	2
Canada	0	0	2	0	0	2
Malaysia	0	1	0	0	0	1
Total	**135**	**320**	**223**	**120**	**750**	**1 548**

Source: [5,8]

Figure 2. Distribution of reported human influenza A(H7N9) cases in China by week, week 1/2013 to week 25/2017 (N=1 548)



* If week of onset was not available. the week of reporting was used

Source: [5,8]

Fourteen clusters with limited human-to-human transmission, mainly consisting of two cases each, were investigated during the current wave. Two clusters involved transmission among patients admitted to the same hospital ward; one cluster was in an admitted patient and a visitor; one cluster was among co-workers selling poultry; and ten other clusters involved transmission among family members. For several family clusters, common exposure to poultry could not be ruled out. Similar clusters were also identified during previous waves, and there are still no indications of sustained chains of human-to-human transmission [3,9-12]

Among the 1 548 cases notified since the beginning of this epidemic in 2013, 565 have been reported to have died (case–fatality ratio=36%; Table 2). The observed case–fatality ratio does not appear to have changed during the fifth wave. These estimates are based on the currently available information and might change as deaths among current and recent cases occur and are reported.

Table 2. Distribution of reported A(H7N9) cases and fatalities by epidemic wave, weeks 7/2013 to 25/2017

	First wave (weeks 7/2013–40/2013)	Second wave (weeks 41/2013–40/2014)	Third wave (weeks 41/2014–40/2015)	Fourth wave (weeks 41/2015–40/2016)	Fifth wave (weeks 41/2016-24/2017)	Cumulative number of cases (weeks 7/2013–25/2017)
Cases	135	320	223	120	750	1548
Deaths	43	134	98	45	245	565
CFR (%)	32%	42%	44%	38%	33%	36%

Source: [5,8]

Virological characteristics

Phylogenetic analyses have shown that two separate lineages evolved in China – the Yangtze River Delta (YRD) lineage and the Pearl River Delta (PRD) lineage, both of which show spatial distribution in China. Further viral adaptation processes have occurred, i.e. the emergence of highly pathogenic strains within the YRD lineage as well as two distinct sub-lineages, YRD-1 and YRD-2, with the latter being the dominant circulating virus [13]. Viral evolution and adaptation processes involved sites relevant for receptor-recognition and/or antigenicity with YRD-2 viruses showing low cross-reactivity to current candidate vaccine virus (CVV) strains [14].

Following the OIE notification, the Ministry of Agriculture in China published an emergency notice to strengthen national A(H7N9) surveillance, prevention and control on 18 February 2017 [15]. On 19 February 2017, China's Centre for Disease Control and Prevention reported the first description of human infections related to a highly

pathogenic A(H7N9) avian influenza (HPAI) virus* in Guangdong. Gene sequencing analysis revealed mutations in the cleavage site of the haemagglutinin (HA) gene with the insertion of basic amino acids known to confer increased pathogenicity in chickens [16,17]. The conversion of low pathogenic avian influenza (LPAI) A(H7N9) into HPAI virus has been already described in a previously published ECDC Public Health Development and Rapid Risk Assessment [18,19]. A new real-time assay has been developed for the rapid detection of this highly pathogenic variant of A(H7N9) [20].

Twenty-five human cases caused by HPAI A(H7N9) virus were reported, with onset of illness before April 2017, from Guangxi, Guangdong and Hunan Provinces; one case was reported from Taiwan, with travel history to Guangdong [21]. The clinical disease is severe, and 13 of the cases died [22].

So far, detailed clinical and epidemiological data are available for eight patients infected with HPAI viruses. These cases are associated with exposure to sick and dead poultry in rural areas. These eight patients were hospitalised earlier than those patients who were infected with LPAI A(H7N9) and showed similar epidemiologic characteristics and disease severity [23]. In order to further assess the impact of HPAI viruses on, for example, severity and transmissibility to humans, better data are needed.

The HPAI virus has a slightly increased binding preference for human airway receptors compared with the low-pathogenic form, which may facilitate circulation in poultry and possible transmission among humans [14]. However, studies have shown that at least three further mutations are needed to switch the receptor specificity of LPAI or HPAI H7N9 viruses for human-type receptors and promote binding to human trachea epithelial cells [24]. In addition to the three identified mutations, further adaptations relevant for the stability of the virus are necessary for it to be able to transmit to and between mammals.

Simultaneously to the findings of highly pathogenic viruses in humans, HPAI A(H7N9) viruses were detected in poultry in Guangdong in a small subset of environmental and poultry specimens. Following these initial detections, the Veterinary Bureau of the China Animal Disease Control Centre notified the OIE about 48 outbreaks or detections of HPAI A(H7N9) in poultry or environmental samples in other Provinces (37 chickens, 1 duck and 10 environmental samples). These samples were taken from 23 live bird markets in Fujian, Guangdong, Hunan and Guangxi Provinces, and from 10 farms in Guangxi, Hebei, Henan, Hunan, Shaanxi, Heilongjiang, Inner Mongolia and Tianjin [25]. Outbreaks of HPAI A(H7N9) were reported from backyard and chicken layer farms where the animals showed clinical signs and high mortality [26]. Within four months after the detection, a wide geographic spread of the HPAI A(H7N9) virus with a co-circulation of high and low pathogenic viruses in poultry occurred. HPAI A(H7N9) might have higher infectiousness in poultry than LPAI strains, which might be visible in the rapid spread across China [14].

WHO reports that the viruses isolated from three reported human cases of infection with avian influenza A(H7N9) showed an amino acid substitution in the neuraminidase gene known to be associated with reduced sensitivity to neuraminidase inhibitors [27,28]. However, the three patients received antiviral treatment with neuraminidase inhibitors before samples were collected, which could have induced the antiviral resistance in the patients as observed before in other patients [28,29]. Analyses have previously shown that 7% to 9% of the viruses analysed have known or suspected markers for reduced susceptibility to one or more types of neuraminidase inhibitor antiviral treatment. Reduced susceptibility was observed during all waves [30]. As most of the analysed sequences derived from patients under treatment, the resistance might have been acquired during treatment.

Animal infections and environmental detection

The Food and Agriculture Organization of the United Nations (FAO) reported additional samples positive for high and low pathogenic A(H7N9) virus from bird or environment specimens. Since 2013, approximately 2 500 specimens have tested virologically positive. Samples were mainly taken from live bird markets, vendors and some commercial or breeding farms [31,32]. The 11 newly affected provinces and cities since the last ECDC update are Fujian, Henan, Hubei, Liaoning, Sichuan, Inner Mongolia, Beijing, Heilongjiang, Tibet, Tianjin and Shaanxi [2]. Only chickens, pigeons, geese, ducks and a tree sparrow tested positive for A(H7N9) [31,32]. FAO references 12 peer-reviewed articles reporting an overall positivity rate of 2.4% for A(H7N9) in nearly 72 000 environmental and bird samples [31,32].

* 1. 'Avian influenza' means an infection of poultry or other captive birds caused by any influenza A virus: a) of the subtypes H5 or H7; or b) with an intravenous pathogenicity index (IVPI) in six-week old chickens greater than 1.2.

2. 'Highly pathogenic avian influenza (HPAI)' means an infection of poultry or other captive birds caused by: a) avian influenza viruses of the subtypes H5 or H7 with genome sequences codifying for multiple basic amino acids at the cleavage site of the haemagglutinin molecule similar to that observed for other HPAI viruses, indicating that the haemagglutinin molecule can be cleaved by a host ubiquitous protease; or b) avian influenza viruses with an intravenous pathogenicity index in six-week old chickens greater than 1.2;2.

3. 'Low pathogenic avian influenza (LPAI)' means an infection of poultry or other captive birds caused by avian influenza viruses of subtypes H5 or H7 that do not come within the definition in paragraph 2.

The 2017 figures show an increase in virological positive and serological reactive specimens compared to previous years, and the number of tested sites and specimens increased significantly over time (Table 3).

Table 3: Examples of testing results by type of test and period, China, November 2014 to May 2017

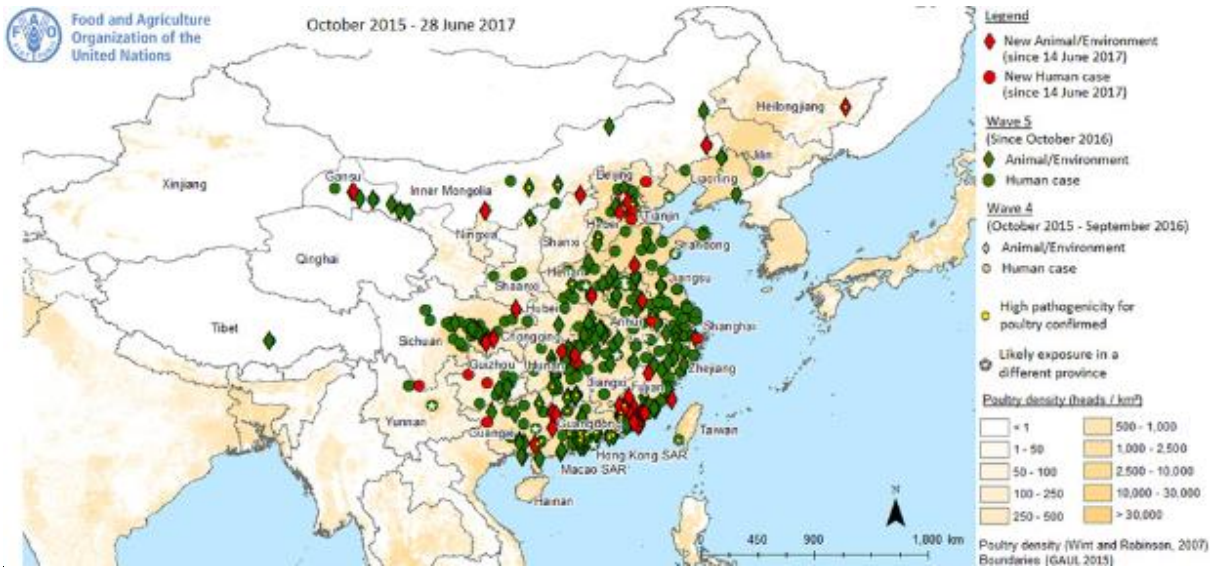
Period	Surveillance sites	Virological testing			Serological testing		
		Tested	Positive	%	Tested	Positive	%
May 2017 [30]	16 042	74 365	107	0.14	316 685	1 182	0.37
April 2017 **[33]**	8 183	53 503	14	0.03	156 933	764	0.49
March 2017 **[34]**	21 978	163 115	55	0.03	290 486	1 533	0.53
September 2016 **[35]**	3 596	23 187	0	0.00	84 808	147	0.17
March 2016 **[36]**	5 875	10 733	1	0.01	102 412	16	0.02
September 2015 **[37]**	2 480	23 116	0	0.00	57 171	29	0.05
February 2015 **[38]**	4 409	149 486	86	0.06	27 307	18	0.07
November 2014 **[39]**	5 326	48 533	3	0.01	103 050	19	0.02

Source: Chinese ministry of agriculture, monthly surveillance report

The geographical range and the number of detections in poultry increased, as did the number of case detections in humans over the same time period. This is noteworthy, because the surveillance system for low pathogenic viruses in birds is hampered by the fact that the animals do not show symptoms, and detections are based on surveillance systems that target LPAI A(H7N9) in bird populations. The detection of human cases served as sentinels for the presence of LPAI A(H7N9) in poultry. Surveillance of HPAI A(H7N9) viruses is facilitated by the fact that infected poultry show symptoms in addition to the usually high mortality observed in affected holdings.

A Chinese investigation team identified a greater contamination of the environment in live poultry markets or other live poultry-related environments with A(H7N9) viruses. Higher exposure levels are thought to be the reason and driver behind the increase in human cases reported since December 2016 [40]. A higher number of infected poultry at live bird markets and broader distribution of infected poultry across different Provinces might be the driver for the higher contamination of the environment and therefore higher risk of exposure for humans.

Figure 3. Distribution of human cases of influenza A(H7N9) and positive avian and environmental samples, China, 1 October 2015 to 28 June 2017



Source: Food and Agriculture Organization of the United Nations (FAO), Emergency Prevention System for Transboundary Animal Diseases (EMPRES), Rome, Italy [25].

Control measures in China

A known risk factor for infection with influenza A(H7N9) for humans is handling poultry at live bird markets or in backyard farms [41]. Since 2013, closures of live bird markets in major Chinese cities has been effective in preventing transmission to humans. The closure of live bird markets is recommended as a rapid measure for the control of the disease [42,43]. Market rest days and other measures to clean markets with live bird trade were suggested and implemented in some areas to control A(H7N9) infections. In Guangdong, a new policy was introduced to centrally slaughter live poultry although attitudes of consumers, live-poultry traders, and poultry farm

workers showed that these measures were not very well accepted due to various reasons, such as the fear of decreased trade [44]. These measures were also applied during the current wave and in December 2016 and January 2017. According to FAO and the Chinese authorities, several cities in affected areas temporarily closed live bird markets, poultry wholesale markets, and farmers' poultry markets, or suspended all live poultry trade either for the season or until further notice. Other cities implemented centralised slaughtering [15,40].

However, the closure of live bird markets and the measures affecting trade chains might have involuntarily contributed to the further spread of the virus, e.g. when infected poultry was moved to previously unaffected regions, returned to the (backyard) farms they originated from, or when infected poultry was sold in sites without standard regulations. This hypothesis is supported by the increase of infected humans during the current fifth wave – often farmers and those who reported exposure to backyard poultry – in rural areas in an increasing number of Provinces [31,32,40,45].

The Centre for Health Protection's (CHP) Port Health Office in Hong Kong conducts health surveillance measures at all boundary control points. Thermal imaging systems are in place for body temperature checks on inbound travellers. Suspected cases will be immediately referred to public hospitals for follow-up [46].

Following the detection of HPAI A(H7N9) viruses, measures to control A(H7N9) in the poultry population were initiated. The Ministry of Agriculture in China published an emergency notice to strengthen national A(H7N9) prevention and control. It will also start a H7 vaccination programme for poultry in early July 2017 in Guangdong and Guangxi Provinces, where both LP and HP A(H7N9) viruses are co-circulating. A recombinant bivalent (H5 + H7) inactivated vaccine will be used. Breeding farms in other provinces may carry out H7 vaccination, pending approval by the local veterinary authorities; provincial veterinarians are authorised to conduct emergency H7 vaccination to facilitate outbreak control [32]. Culling activities with compensation of affected farmers were initiated by the Chinese agriculture and finance ministries [47].

Legal framework for surveillance and control in the EU/EEA

Surveillance and control among humans

Human infections with A(H7N9) and other novel influenza strains are notifiable under EU legislation and the International Health Regulations* (IHR) through the Early Warning and Response System (EWRS) and the IHR notification system [48,49]. ECDC has developed an interim case-finding algorithm and a case definition for disease surveillance. Patients infected with avian influenza A(H7N9) virus in EU/EEA Member States are reported in accordance with this case definition [50].

Infectious disease protocols for case investigations are available from the Consortium for the Standardization of Influenza Sero-Epidemiology (CONSISE) [51] and national authorities. Agreed protocols for clinical investigations have been prepared by the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) [52]. Contacts of confirmed cases should be followed-up and tested. International recommendations for the use of post-exposure prophylaxis differ.

Surveillance and control measures in birds

The surveillance and control of pathogenic avian influenza viruses in poultry and wild birds is laid down in EU legislation detailed in Council Directive 2005/94/EC and Commission Decision 2010/367/EU. In addition, official notifications have to be reported in accordance with the Terrestrial Animal Health Code of the World Organisation for Animal Health (OIE).

Vaccine development

Due to the antigenic and genetic evolution of A(H7N9) viruses, new vaccines for the circulating A(H7N9) viruses were developed; clinical trials are ongoing. Evidence presented at the latest WHO influenza vaccine composition consultation showed that the recent highly pathogenic viruses (and some of the currently circulating low pathogenic A(H7N9) ones) are genetically and antigenically distinct from the current A(H7N9) candidate vaccine viruses. To address this, new A(H7N9) candidate vaccine viruses were proposed [53]. Sequences were shared through the GISAID EpiFlu sequence database, and a few viruses containing these new mutations were shared with all WHO Collaborating Centres and other partners in order to improve diagnostics and the development of

* Case definitions for the four diseases that require notification in all circumstances under the International Health Regulations (2005) are available at http://www.who.int/ihr/Case_Definitions.pdf.

candidate vaccines [54]. The timely characterisation of A(H7N9) viruses and the sharing of sequence information remain crucial for A(H7N9) vaccine virus development.

ECDC threat assessment for the EU

Influenza A(H7N9) remains a widespread zoonotic disease in several provinces in China. The virus is transmitted sporadically to humans exposed to infected poultry or contaminated environments (e.g. live bird markets or backyard farms). Human-to-human transmission is rare.

The reporting of human cases of influenza A(H7N9) in China has followed a seasonal pattern, with peaks in the winter months and sporadic cases in summer. The fifth wave in 2017 is characterised by a significantly larger magnitude, by increased duration and an expanded geographical spread. Also, case numbers are higher than during the first four waves. This may suggest that the virus has become more widespread in its domestic bird reservoir and that environmental contamination has increased, which, in turn, has led to increased human exposure to the virus. It is of concern that there is substantial circulation of the virus in bird populations, giving rise to human cases during the summer months. The age and sex distribution has remained comparable throughout all five waves. The change in the epidemiological pattern of the disease coincides with the emergence of an HPAI strain in 2017. However, data suggest that the HPAI strain has not yet spread extensively among poultry. It has not been detected in wild birds and has not contributed to a major increase in human cases.

Risk of increased A(H7N9) transmissibility among poultry, captive birds and wild birds

LPAI A(H7N9) viruses were detected in resident wild birds on a very few occasions, e.g. in doves and a sparrow. However, recent work suggests that the newly emerged HPAI A(H7N9) viruses have higher infectiousness in poultry than the related low pathogenicity strains. HPAI viruses are associated with a high inferred rate of molecular adaptation. Such adaptation processes might lead to infections of resident and migratory water fowl, with the risk of global dissemination through bird migration. This has previously been observed for HPAI A(H5N1) viruses [13,14,55,56].

Data are too limited to assess whether infection with the HPAI A(H7N9) strain results in increased viral shedding and transmissibility among birds, which would result in a wider spread of the virus and more infections in birds. Following the initial detection of HPAI A(H7N9) viruses in poultry in January in Guangdong, HPAI viruses rapidly spread to other provinces. However, the vast majority of the viruses detected during the fifth wave were LPAI A(H7N9) viruses. This virus appears to be well adapted to gallinaceous animals, suggesting a limited transmission to wild birds.

Risk of increased exposure of humans

An increase in poultry cases and a higher contamination of the environment in the fifth epidemic wave resulted in an increase of exposure, which in turn led to additional reports of human infections. The emergence of an HPAI strain among poultry might lead to a higher number of systemically infected poultry that also shed more viruses, which would increase the contamination of the environment and increase the risk of exposure to birds with high virus load. However, poultry infected with HPAI strains will be symptomatically ill or die rapidly, which might decrease or limit the risk for human exposure if precautionary measures like wearing personal protective equipment or avoiding contact are applied.

Risk of increased A(H7N9) transmissibility to humans

The increase in human infections reported in the current epidemic wave does not seem to be related to a change in transmissibility of the A(H7N9) virus to humans; rather, it seems to be related to the geographical extension of the epizooty. In particular, the emergence of an HPAI A(H7N9) strain did not contribute significantly to the increase in human cases in the fifth epidemic wave. So far, eight cases were reported.

There is evidence of HPAI A(H7N9) viruses retaining dual receptor binding properties, with slightly increased binding preference for both receptors compared with LPAI H7N9. The persisting preference for both avian- and human-type receptors of HPAI H7N9 viruses may result in their circulation in poultry and possible transmission among humans [14]. Exposure to HPAI-virus-infected birds harbouring high virus concentrations might increase the risk of transmission to humans, particular in outbreak situations in farms with a high number of affected birds.

Risk of person-to-person transmission

To date, only a few clusters with possible human-to-human transmission of the LPAI A(H7N9) viruses have been reported. There have been no reports of clusters of HPAI A(H7N9) virus infections. There is currently no evidence that the transmissibility among humans has changed. ECDC concurs with the WHO assessment that the likelihood of sustained human-to-human transmission is low [29].

Risk of increased HPAI H7N9 pathogenicity in humans

The multi-basic amino acid insertion at the cleavage site of HA, consistent with the evolution from low to high pathogenicity, relates to increased pathogenicity only in poultry. There is some evidence of unchanged severity of illness in humans infected by LPAI and HPAI A(H7N9) viruses [57]. However, data are only available from eight cases and thus very limited.

Risk of resistance to antivirals

Acquired resistance during or after antiviral treatment is common, and some HPAI A(H7N9) viruses were detected with mutations harbouring reduced susceptibility to neuraminidase inhibitors. However, these resistant viruses were identified in patients already under antiviral treatment and might have been induced under therapy. Analyses have shown that 7%–9% of the viruses analysed have known or suspected markers for reduced susceptibility to one or more antiviral treatments with neuraminidase inhibitors, which has been similar during all waves so far [30]. Continued genetic testing (pre- and post-treatment) is needed to exclude the possibility of a wider circulation of viruses with NA-resistant mutations in humans. It is also essential for public health authorities to continue monitoring the antiviral susceptibility of bird populations.

Risk of emergence of new reassortants in humans

As other avian influenza viruses are circulating in the bird population in China, the likelihood of reassortment of those viruses in animals is high, with a risk of transmission to pigs or to humans. The risk of reassortment between seasonal and avian influenza viruses in humans is possible, particularly during the influenza season. In several patients, co-infections of A(H7N9) with seasonal influenza viruses were observed, either with A(H1N1)pdm09, A(H3N2), or B viruses. Moreover, a nosocomial cluster of a co-infection of A(H7N9) and a seasonal A(H1N1)pdm09 influenza virus was observed in two patients with severe underlying immunocompromised conditions [58].

The increasing circulation of the virus, resulting in increased human and animal exposure, heightens the risk of reassortment events and increases the risk of viruses with a higher human transmission potential. This also increases the likelihood that a pandemic strain emerges.

Risk of spread outside of China

There is a risk of spread outside of China because the virus can be exported through infected wild birds, poultry trade, or infected travellers.

So far, the virus is adapted to poultry and not to migratory waterfowl. Only a few detections were made in resident local birds, e.g. in doves or a sparrow. The risk of introduction into the EU through migratory birds can be considered very low at the moment, although it cannot be excluded that current adaptation processes of the A(H7N9) viruses might enable transmission to migratory waterfowl in the future. The continuous circulation of A(H7N9) in poultry in China poses the small risk that people who had contact with poultry in China might introduce the virus to EU poultry farms.

The risk of avian influenza viruses being imported from China to Europe through legal trade of poultry or poultry products is negligible. EU regulations do not permit importation of live poultry, day-old chicks, hatching eggs or other birds (captive birds such as parrots, finches and ornamental birds) from China. The only poultry commodities authorised for import from China into the EU are sterilised meat products, heat-treated poultry meat from Shandong, and heat-treated egg products. Given the very heat-sensitive nature of all influenza viruses, these commodities are not considered to pose a risk of influenza virus transmission to consumers.

Illegal trade of infected poultry to neighbouring countries might be a possible scenario although so far no virus detections in areas close to national borders have been reported.

The increasing number of cases in both poultry and humans in China represents a risk for the spread of the virus from China to Central Asia or Europe or even farther. Currently, the likelihood of detecting human cases in Europe is mainly related to the number of people who were exposed in China and travel to Europe. This likelihood increases in the summer months when most people travel (Figure 4). With the ongoing transmission to humans and the expansion of affected areas, the importation of A(H7N9) through travellers to the EU/EEA cannot be ruled out.

Travel-related cases to Malaysia and Canada were reported previously, and additional cases can be expected with the ongoing epidemic in China.

Figure 4. Distribution of international air travellers from EU/EEA countries to and from China, by month, October 2011 to December 2015

Source: International Air Transport Association (IATA)

Risk to public health in the EU/EEA and to EU/EEA citizens

The increasing geographic spread and intensity of A(H7N9) virus in China increases exposure and heightens the risk of the virus being introduced through infected travellers returning to Europe. However, over the last five seasons no introduction of the virus into Europe has been observed, and the transmission of this virus has so far been confined to China. The risk of the disease spreading in Europe via humans is still considered low, as there is no evidence of sustained human-to-human transmission.

ECDC critical events

Influenza A(H7N9) cases in humans and poultry continue to be reported. Case numbers are higher than during previous seasons, and the geographical spread has increased. ECDC decided to reassess the risk associated with this event and has established a list of critical events that would indicate a significant change in the epidemiology of the disease and trigger a reassessment of the situation:

- An increase in the size of human-to-human clusters beyond three cases
- An increase in the number and size of clusters related to nosocomial transmission in hospital settings
- An increase in the number of generations of human-to-human transmission beyond one
- An increase in the severity of reported cases, e.g. an increased case–fatality ratio
- Increase in the proportion of human cases infected with highly pathogenic A(H7N9) virus compared to low pathogenic virus
- A change in the epidemiology of A(H7N9) of infected human cases, e.g. different age groups
- The emergence of local transmission of A(H7N9) among poultry outside of China
- The emergence of locally infected human cases outside of China
- The detection of a human case in an EU/EEA healthcare facility
- Detection of A(H7N9) in wild birds
- Increasing, large and geographically widespread outbreaks or detections of highly pathogenic A(H7N9) virus in poultry
- Reassortment with other avian or seasonal viruses
- Molecular modification of viruses with markers for human adaptation
- Increase in antiviral resistance of viruses, also in humans without antiviral treatment.

ECDC actively monitors the situation, with a special focus on the occurrence of any of the above events.

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