

### Summary

The WHO has reported 337 human infections including 66 deaths with onset since February 2013. There are still no signs of ongoing, efficient, or sustained human transmission of this virus.

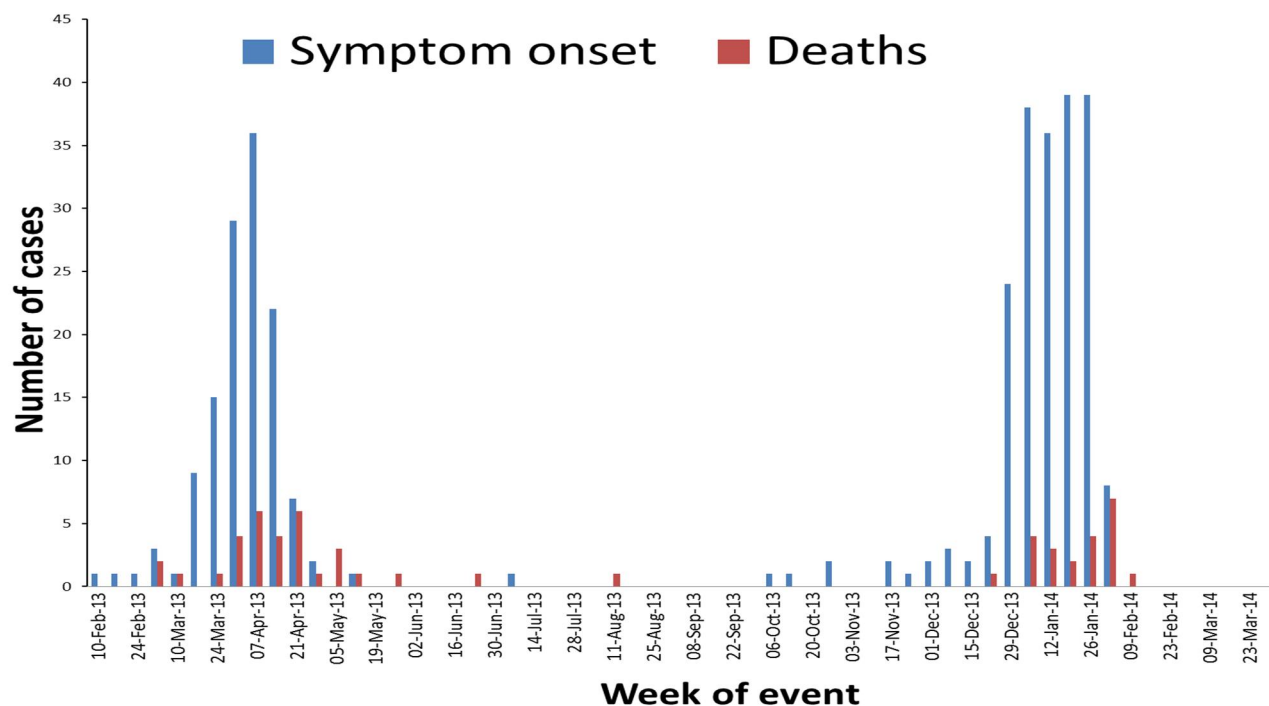
### Key Points

- The H7N9 outbreak in southern China continues unabated, mainly affecting elderly people in contact with domestic poultry.
- No adaptation to efficient person-to-person transmission has been observed so far.
- Since 1 October 2013 there have been 201 cases reported in a 'second wave' of human H7N9 infections (Figure 1, Table 1). All laboratory confirmed human infections have occurred in China (including Hong Kong), with imported cases reported in Taiwan (Figure 2).
- The Chinese government has undertaken the following surveillance measures:
  - screening for avian influenza H7N9 virus in patients with fever attending Tertiary hospitals [1];
  - sentinel surveillance for influenza-like illness [2];
  - individual case investigation; and
  - outbreak surveillance.
- The epidemiology and virology of the second wave is similar to the first with cases and the majority reporting exposure to infected poultry and live market settings.

### Cases

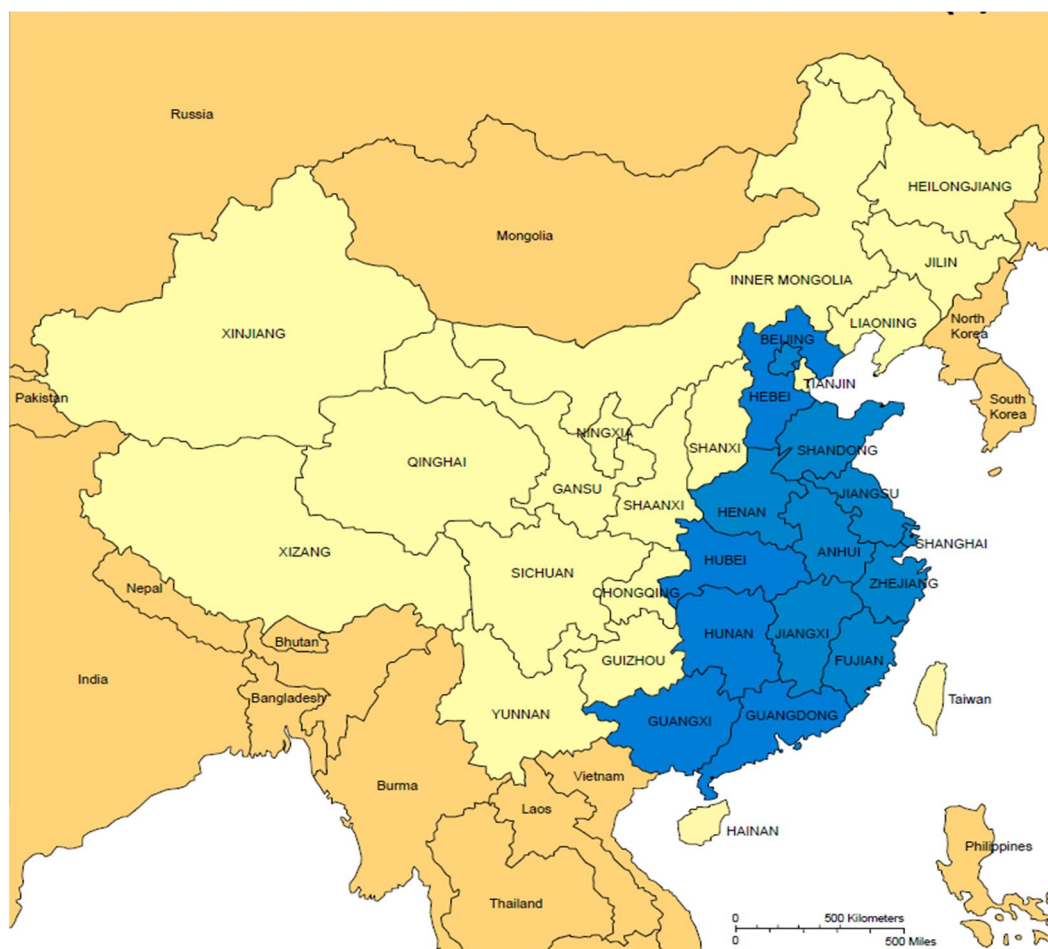
- Accumulation of almost 300 cases in less than a year appears to be unprecedented for human cases of avian flu. For comparison, data from the WHO shows that the most active calendar year for the H5N1 strain, in 2006, saw 115 cases.
- A detailed analysis of the epidemiologic characteristics of avian influenza H7N9 cases in China to 1 Dec 2013[3] has indicated that
  - among 139 persons with confirmed H7N9 virus infection, 71% were male, and 73% were urban residents.
  - Confirmed cases occurred in 12 areas of China.
  - Nine persons were poultry workers, and of 131 persons with available data, 82% had a history of exposure to live animals, including chickens (82%).
  - A total of 137 persons (99%) were hospitalized, 125 (90%) had pneumonia or respiratory failure, and 65 of 103 with available data (63%) were admitted to an intensive care unit.
  - A total of 47 persons (34%) died in the hospital after a median duration of illness of 21 days, 88 were discharged from the hospital, and 2 remain hospitalized in critical condition; 2 patients were not admitted to a hospital.
  - Excluding secondary cases in clusters, 2675 close contacts of case patients completed the seven day monitoring period; respiratory symptoms developed in 28 of them (1%); all tested negative for H7N9 virus.
- The disease caused by the virus is characterized by rapidly progressing severe pneumonia. Common symptoms are not disease specific and those of typical acute respiratory infection, such as fever, cough, and shortness of breath. Complications include the acute respiratory distress syndrome (ARDS), septic shock and multi-organ failure requiring intensive care and mechanical ventilation. A small number of patients with mild clinical illness have been detected through on-going influenza-like illness (ILI) surveillance systems and contact tracing in otherwise healthy children and young adults.

Figure 1 Epi-curve of avian influenza A(H7N9) cases and deaths by *Date of Symptom Onset or Death*, as of 13 February 2014



Note: Six confirmed cases are missing from the figure due to incomplete data.

Figure 2 Map of human cases of avian influenza A(H7N9), by province, China, to 13 February 2014.



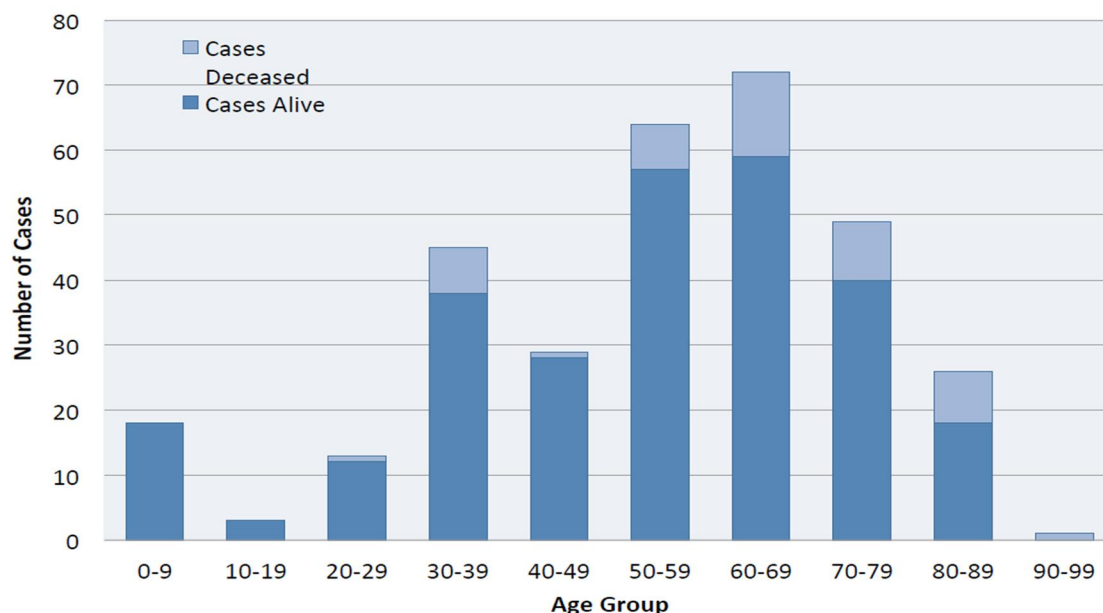
Note: Chinese provinces with reported cases are shaded in blue. This figure includes cases and deaths confirmed by local authorities; some of these cases have not yet been acknowledged by WHO.

Table 1 Summary of avian influenza A(H7N9) laboratory-confirmed human cases and deaths by Province/City and Season.

Province/City	Number of cases (deaths)	
	Wave 1 (19/02/13 to 30/09/13)	Wave 2 (1/10/13 to 13/02/14)
Anhui	4(3)	2(1)
Beijing	2(0)	2(0)
Fujian	5(0)	15(3)
Guangdong	1(0)	58(7)
Guangxi	-	3(0)
Guizhou	-	1(1)
Hebei	1(1)	-
Henan	4(1)	-
Hong Kong SAR	-	4(3)
Huangyan	-	1(0)
Hunan	2(1)	8(1)
Jiangsu	23(8)	11(1)
Jiangxi	6(2)	-
Shandong	2(0)	-
Shanghai	32(15)	8(2)
Zhejiang	46(8)	87(1)
Taiwan	-	2(1)

- Recently, the question of the unusual age and sex profile of H7N9 cases has been discussed with the following offered as contributing factors (Figure 3, 4 and 5) [4]:
  - the elderly generally have weaker health status compared to the young;
  - differential exposure between males and females due to gender-associated practices and norms;
  - biological differences between males and females in the clinical course post exposure/infection;
  - differential healthcare-seeking/access behaviour between male and females, leading to surveillance/detection bias; and
  - the absence of existing immunity to the infection, indicating that avian influenza A(H7N9) is a new infection for the Chinese, compared to swine flu H1N1 in which there was evidence of cross-protective immunity among the elderly that might relate to the low number of cases among that group.

Figure 3 Distribution of confirmed avian influenza A(H7N9) cases by age, to 13 February 2014 (n=336).



- The age distribution among H7N9 cases is both older and wider than that of H5N1 cases, whereas the case fatality ratio for H7N9 (34%) is lower than that for H5N1 (globally approximately 60%) (Figure 4).

Figure 4 Distribution of confirmed avian influenza A (H5N1) and (H7N9) cases by age, to 13 February 2014, China

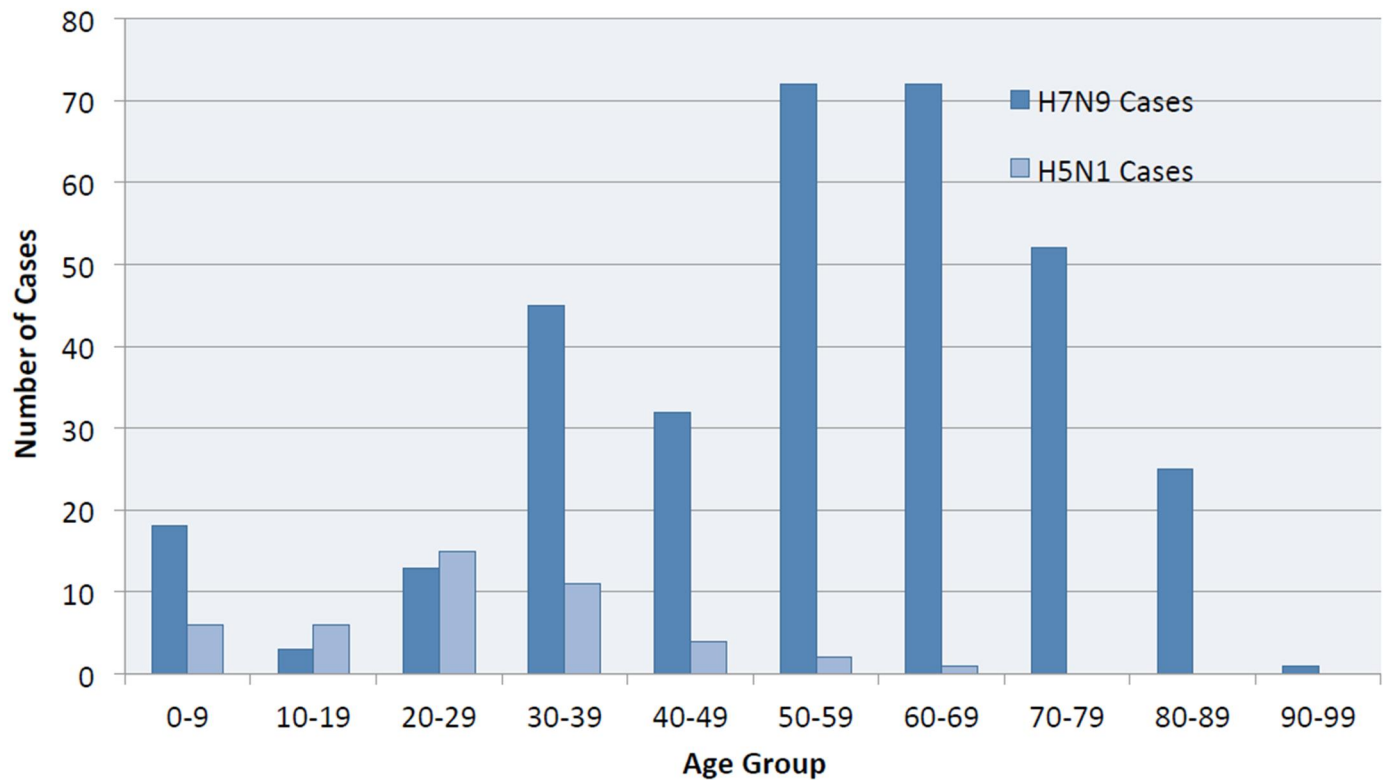
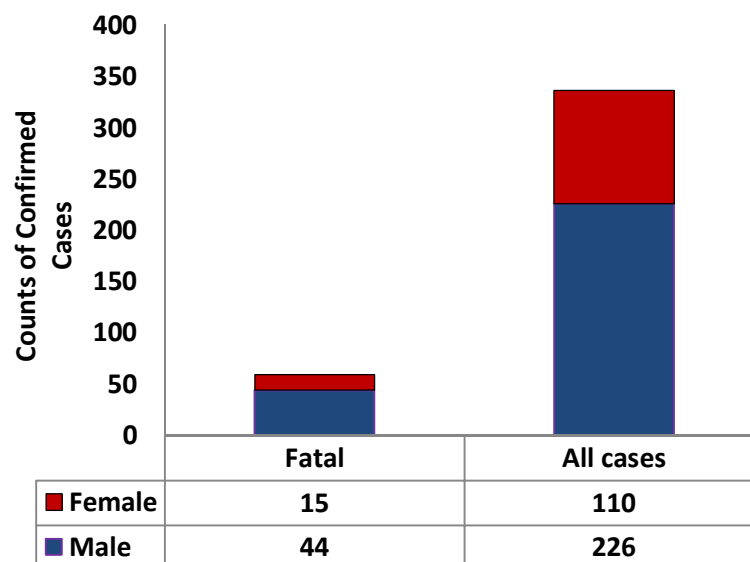


Figure 5 Sex distribution of avian influenza A(H7N9) cases and deaths, to 13 February 2014



### Human Diagnosis and Treatment

- An analysis of the kinetics of serological responses to H7N9 infection has demonstrated that early and rapid induction of neutralizing antibodies correlated significantly with improved clinical outcome [5]. The implication of this finding is that a H7N9 vaccine which induces a neutralizing antibody titre of  $\geq 1:40$  is likely to provide some protection against severe disease.
- Thus far the H7N9 viruses detected in China are nearly identical at a genetic level.

- Sequence analyses have shown that the genes of the H7N9 viruses from China are of avian origin, but with signs of adaptation to mammalian species. The adaptation includes increased ability to bind to mammalian cell receptors, and to grow at temperatures close to the normal body temperature of mammals, which is lower than that of birds.
- Antigenically, the H7N9 viruses are different from seasonal influenza viruses infecting humans, but closely related to A/Anhui/1/2013 (H7N9), the recommended virus for H7N9 vaccine development.
- Early information from China suggests that when oseltamivir was given early in the course of illness, it has been found to be effective against H7N9 virus infection in reducing severe illness and deaths. Oseltamivir resistance has been reported in several patients with severe illness shortly after the initiation of the antiviral treatment and concluded in unfavourable outcomes.

## Animal infections and environment detection

- Preparedness activities include identification of critical points of entry where surveillance should be targeted and management measures enhanced. Such measures could include cleaning and disinfection of live bird markets and introducing market rest days with no poultry, among others. The highest risk of spread is associated with legal or illegal trade of live birds through humans, and the avian species most implicated so far are chickens, quail, and pigeons.
- Recently announced control measures include-
  - Guangdong Province: Shenzhen City announced the market rest period for consecutive 2 weeks from 31 January 2014 (the Lunar New Year Day) to 13 February 2014 (Lunar 14 January). During the rest period, all live bird markets (including wholesale and retail markets) are closed and poultry are not allowed to stay in the market.
  - Shanghai City started its seasonal live bird trade suspension from 31 January 2014 (Lunar New Year day) until 30 April 2014. During the suspension period, all live poultry wholesale markets and retail vendors are prohibited to trade live poultry.
  - Zhejiang Province closed live bird markets until 15 February 2014 in the main districts of the municipalities and the counties (cities) where cases are found for three months. Further from 1 July 2014, local authorities plan to permanently close live poultry trading markets in the province's main municipalities.

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