Received: 22 November 2017

DOI: 10.1111/tbed.12861

ORIGINAL ARTICLE

WILEY Transboundary and Emerging Diseases

Emergence and spread of highly pathogenic avian influenza A(H5N8) in Europe in 2016-2017

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Summary

Circulation of highly pathogenic avian influenza (HPAI) viruses poses a continuous threat to animal and public health. After the 2005–2006 H5N1 and the 2014–2015 H5N8 epidemics, another H5N8 is currently affecting Europe. Up to August 2017, 1,112 outbreaks in domestic and 955 in wild birds in 30 European countries have been reported, the largest epidemic by a HPAI virus in the continent. Here, the main epidemiological findings are described. While some similarities with previous HPAI virus epidemics were observed, for example in the pattern of emergence, significant differences were also patent, in particular the size and extent of the epidemic. Even though no human infections have been reported to date, the fact that A/H5N8 has affected so far 1,112 domestic holdings, increases the risk of exposure of humans and therefore represents a concern. Understanding the epidemiology of HPAI viruses is essential for the planning future surveillance and control activities.

KEYWORDS
domestic birds, epidemiology, H5N8, highly pathogenic avian influenza virus, wild birds

1 | INTRODUCTION

Over the past years, Asian-origin H5 highly pathogenic avian influenza (HPAI) viruses have been responsible for recurrent outbreaks in wild and domestic birds worldwide and have caused occasional infection in humans, posing a continuous threat to both animal and public health. HPAI H5N1 virus was first isolated in 1996 in southern China from a goose (A/goose/Guangdong/1/1996 (Gs/GD/96)) (Xu, Subbarao, Cox, & Guo, 1999), and one year later, it caused the first lethal human infection in Hong Kong (WHO, 2010). Gs/GD/96 has evolved into multiple phylogenetic clades based on the hemagglutinin (HA) gene (WHO, 2014). In fact, 10 distinct genetic clades (0–9) and even more subclades with different antigenic properties were described (WHO, 2008, 2009). H5N1 viruses were separated into four antigenic groups on the basis of hemagglutination inhibition (HI) assay: group A (clades 1, 2.1, 2.4 and 8), group B (clades 1, 2.1, 4, 5, 7 and 9), group C (clades 2.1, 2.2 and 2.3) and group D (clades 2.3 and 5) (Wu et al., 2008). Among these, clade 2.3.4 has continuously circulated in poultry and wild waterfowl with different neuraminidase (NA) subtypes including H5N2 (Zhao et al., 2012), H5N5 (Gu et al., 2011), H5N6 (Bi et al., 2015) and H5N8 (Fan et al., 2014).

On late May–early June 2016, testing of wild birds in the Ubsu-Nur Lake, in the border between Mongolia and the Tyva Republic (Russian Federation), was carried out within the active surveillance activities for the detection of avian influenza (AI) viruses. H5 subtype of AI virus was detected in 17 birds including six black-headed gulls (*Larus ridibundus*), four grey herons (*Ardea cinerea*), four great cormorants (*Phalacrocorax carbo*), one common tern (*Sterna hirundo*), one great crested grebe (*Podiceps cristatus*) and one duck (unidentified species) (FAO, 2016). Sequence analysis of the isolates evidenced that they belonged to the Asian HPAI H5 lineage Gs/GD/96, clade 2.3.4.4 (OIE, 2016), and was later identified as H5N8. Even though some dead birds were found, mortality was not comparable to that caused in 2006 by the H5N1 in the same location when about 4,000 waterbirds died (Food and Agriculture Organization of the United Nations (FAO), 2016). Before the detection of the 2016 H5N8, viruses of the

HPAI H5 lineage Gs/GD/96 had been repeatedly detected in wild migratory birds at the Ubsu-Nur Lake (Food and Agriculture Organization of the United Nations (FAO), 2016). Major wild aquatic bird migration routes overlap in Siberia, and therefore, those novel AI viruses can later spread to the wintering grounds of Europe and Africa during the fall migration (September to December). Overlapping migration routes include the East Atlantic and the Mediterranean/Black Sea flyways connecting with Europe and Africa, and the East Asia/East Africa flyway connecting mainly with Africa (Birdlife international, 2017). Thanks to the early detection of H5N8 and a rapid report by the Russian Federation, the Food and Agriculture Organization of the United Nations (FAO) was able to raise the alarm in relation to the risk of spread of the virus to the south and west of the area where the virus had been detected (Food and Agriculture Organization of the United Nations (FAO), 2016). FAO's concern was based on the previous experience of a repeated pattern whereby detection of HPAI H5 of Gs/GD/96-lineage in wild birds in the southern Russian Federation was followed by detection of similar viruses at distant locations to the west or to the south. In at least three times, detection of AI viruses in wild birds (in particular H5N1 HPAI) in the south-central area of Siberia was followed by detection of the same virus in wild birds or poultry further west and south: clade 2.2 in 2005/06, clade 2.3.2.1c in 2009/10 and clade 2.3.2.1c in 2014/15 (Food and Agriculture Organization of the United Nations (FAO), 2016). Furthermore, in 2014, the spread of HPAI H5N8 virus was also attributed to long-distance flights of infected migratory wild birds, first from South Korea to northern breeding grounds during the spring migration, and then, to Europe and to the west coast of North America during the fall migration, representing an unprecedented transcontinental movement of an Eurasian HPAI virus (Lycett et al., 2016).

FAO's concern in relation to the spread of H5N8 in 2016 was confirmed, as in October 2016, the virus reached Europe. This report describes the main epidemiological findings of the 2016–2017 epidemic of H5N8 in Europe.

2 | MATERIALS AND METHODS

Outbreak data were obtained from the FAO-Global Animal Disease Information System (EMPRES-i) (FAO, 2017). We have used the term outbreak for both domestic and wild birds, as defined by the OIE (World Organization for Animal Health), that is as the occurrence of one or more cases in an epidemiological unit. An epidemiological unit means a group of animals that share a similar risk of exposure to a pathogenic agent with a defined location (i.e., a holding for domestic birds and a relatively small area where animals share approximately the same risk of exposure to the pathogen, for wild birds).

The density of ducks and chickens was obtained from the FAO-Gridded Livestock of the World modelled data for ducks or chickens (Robinson et al., 2014). Temperature anomaly maps were obtained from the National Oceanic and Atmospheric Administration (NOAA). The world temperature anomaly map for a given month is obtained by combining land and sea surface temperatures of that month and comparing it to the average values for that month for the period 1981–2010 (NOAA, 2017). R software was used for both analyses and generation of maps (R Core Team, 2014).

3 | RESULTS

3.1 | Epidemiology of the 2016–2017 epidemic of H5N8 in Europe

According to the data recorded by the FAO-EMPRES-i, between the first H5N8 outbreak in the Ubsu-Nur Lake in June, 2016 up to the 7th of August 2017, 2,067 outbreaks were reported in Europe, of which 1,112 were in poultry and 955 in wild birds (Table 1 and Figure 1). A total of 30 European countries: Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Luxembourg, Macedonia, Netherlands, Poland, Portugal, Romania, the Russian Federation, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, UK and Ukraine, have reported outbreaks of H5N8 HPAI in domestic and/or wild birds within this period (Table 1 and Figure 1). In 19 of those 30 countries, H5N8 HPAI was first detected in wild birds, in six, the virus was first detected in poultry, and in five detections in wild and domestic birds occurred within the same week (Table 1).

3.2 | H5N8 outbreaks in domestic birds

Of the 1,112 outbreaks in poultry, 420 were reported in France and 239 in Hungary, the two most severely affected countries. In France, outbreaks of H5N8 HPAI in poultry were clearly clustered in the south-eastern region of the country (Figure 1). In fact, 415 of the 420 outbreaks occurred in that area (Nouvelle-Aquitaine and Midi-Pyrénées regions). Domestic ducks accounted for more than 90% of the outbreaks, while chickens represented only 9%. The situation forced the French authorities to implement very strict measures to try to control the disease, including preventive culling of all poultry within a radius of 1 km around the outbreaks, as well as outdoor birds of the Anatidae family between 1 and 3 km around an outbreak, and up to 10 km if there was more than one outbreak within the protection zone (EU, 2017a). That resulted in the slaughtering of 5.4 million Anatidae and 1.3 million chickens. Among the 533 holdings preventively depopulated, 139 were actually found to be infected (European Union (EU), 2017a). Other measures included the testing of animals prior to movements within the protection and surveillance zone, which also contributed to the detection of infected premises. In fact, 17% of outbreaks were discovered thanks to pre-movement testing (EU, 2017b).

In Hungary, domestic outbreaks of H5N8 HPAI were clustered in the region of the Southern Great Plain (from south-central to south-western Hungary), where 226 of the 239 of the outbreaks occurred (Food and Agriculture Organization of the United Nations (FAO), 2017). Domestic duck was also the species with most holdings affected (61% of the total), but there were also geese holdings infected (33% of the total) (Food and Agriculture Organization of the United Nations (FAO), 2017). As a consequence of the epidemic,

TABLE 1 Outbreaks of H5N8 detected in both domestic and wild birds in Europe between June, 2016 and August 2017, as well as the month and year of onset of outbreaks in domestic and wild, and whether this first onset occurred in domestic or wild birds (the term same is used when domestic and wild outbreaks occurred within the same week)

Country	Domestic birds	Wild birds	Total	Onset domestic	Onset wild	First onset
Austria	2	24	26	November 2016	November 2016	Same
Belgium	13	4	17	June 2017	February 2017	Wild
Bosnia	1	2	3	February 2017	February 2017	Domestic
Bulgaria	67	13	80	December 2016	December 2016	Domestic
Croatia	7	11	18	December 2016	October 2016	Wild
Czech Republic	43	40	83	January 2017	January 2017	Same
Denmark	2	51	53	November 2016	November 2016	Wild
Finland	0	15	15		November 2016	Wild
France	420	55	475	December 2016	November 2016	Wild
Germany	94	194	288	November 2016	November 2016	Same
Greece	7	8	15	January 2017	December 2016	Wild
Hungary	239	54	293	November 2016	October 2016	Wild
Ireland	0	10	10		December 2016	Wild
Italy	20	8	28	January 2017	December 2016	Wild
Lithuania	0	5	5		February 2017	Wild
Luxembourg	4		4	June 2017		Domestic
Netherlands	9	56	65	November 2016	November 2016	Wild
Macedonia	2		2	January 2017		Domestic
Poland	65	69	134	December 2016	October 2016	Wild
Portugal	0	1	1		January 2017	Wild
Romania	44	90	134	December 2016	November 2016	Wild
Russia	27	1	28	November 2016	June, 2016	Wild
Serbia	4	13	17	January 2017	December 2016	Wild
Slovakia	10	63	73	December 2016	January 2017	Domestic
Slovenia	0	20	20		January 2017	Wild
Spain	10	2	12	February 2017	January 2017	Wild
Sweden	6	37	43	November 2016	November 2016	Same
Switzerland	0	87	87		November 2016	Wild
UK	13	19	32	December 2016	December 2016	Same
Ukraine	3	3	6	December 2016	January 2017	Domestic
Total	1,112	955	2,067			

more than 2 million ducks, 200,000 geese and half million chickens had to be slaughtered (EU, 2017c).

While other European countries such as Bulgaria or Spain also evidenced a clustered distribution of domestic H5N8 HPAI outbreaks, in Northern European countries (i.e., the Netherlands, Germany, Poland, the Czech Republic or Slovakia), the distribution of outbreaks was much more homogeneous throughout the territory.

In chickens, mortality rate differed among holdings, but often mortalities over 30% were observed (EFSA, 2017b). Clinical signs were variable and included from non-specific signs such as depression or diarrhoea to nervous signs such as head shaking or ataxia. Lesions included haemorrhagic pneumonia and catarrhal or haemorrhagic enteritis (European Food Safety Authority (EFSA), 2017b). In contrast, domestic ducks infected with H5N8 frequently showed neither morbidity nor mortality (European Food Safety Authority (EFSA), 2017b).

Furthermore, domestic bird H5N8 infections in Europe did not seem to be linked to a specific size of holding. In fact, of the domestic herds affected in Europe, 37% had less than 100 birds, 8% between 100 and 500, 4% between 500 and 1,000, 28% between 1,000 and 1,000, and 23% more than 10,000 (Table 2). The pattern seemed to differ among countries. While in some countries such as the Czech Republic or Romania, the epidemic mainly affected small holdings, in others such as Germany, Hungary or Poland, it mainly affected large-size holdings, and in France, the large majority were either large or small (Table 2).

In relation to the species affected, available data indicate that 69% of the domestic outbreaks in European countries were in

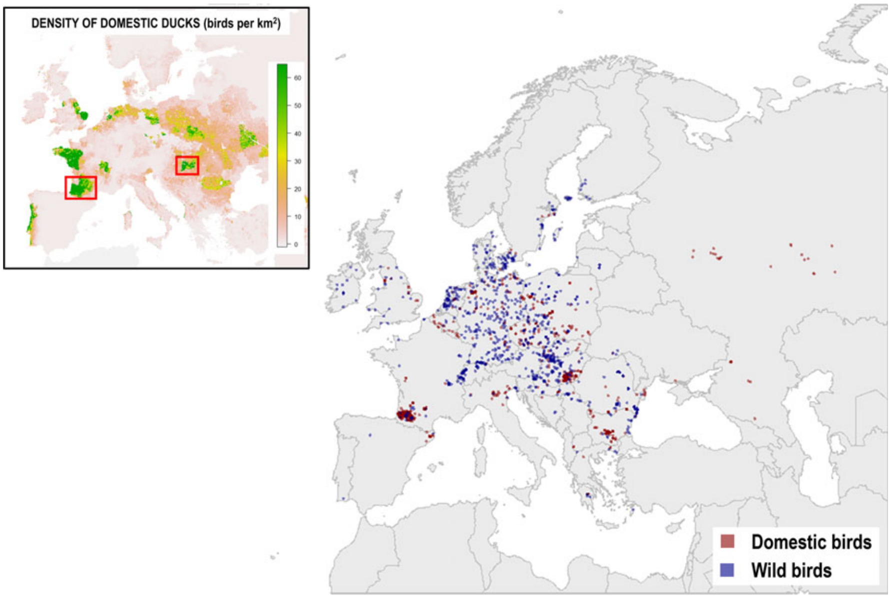

FIGURE 1 Spatial distribution of outbreaks of H5N8 HPAI in domestic (red dots) and wild (blue dots) birds in Europe. Box in the upper left corner represents the density of domestic ducks (birds per km^2) in Europe (from Robinson et al., 2014). Red squares mark the areas of high density of ducks in France and Hungary, where clustering of H5N8 outbreaks in poultry occurred [Colour figure can be viewed at wileyonlinelibrary.com]

domestic ducks, 12% in chickens, 10% in geese, 9% in turkeys and 1% in pheasants.

3.3 | Evaluation of the association between poultry density and domestic outbreaks of H5N8

To evaluate whether domestic H5N8 outbreaks in Europe were associated with the density of ducks or chickens, we obtained the density of ducks and chickens for each of the locations where domestic outbreaks occurred using the FAO-Gridded Livestock of the World modelled data for ducks or chickens (Robinson et al., 2014). Then, we estimated for each country the mean density of ducks and chicken in the areas affected by the H5N8. The results indicate that in France and Hungary, the countries in which poultry was more severely affected, and where the disease showed evidences of clustering, H5N8 domestic outbreaks occurred in areas where the average density of ducks was extremely high. The mean number of ducks per square kilometre in the affected areas of France and Hungary was 187 and 140, respectively, as compared with a mean value of only 11 ducks per square kilometre in the remaining countries affected. In contrast, when H5N8 domestic outbreaks occurred in areas of high chicken density, as in the cases of Italy and the Netherlands (mean number of chicken per square kilometre 2,135 and 1,816, respectively), this did not seem to result in extensive spread of H5N8 HPAI (only 13 domestic outbreaks occurred in Italy and nine in the Netherlands).

TABLE 2 Number and percentage of domestic outbreaks affected by the H5N8 according to the size of the holding for different European countries

	Size of domestic holdings affected according to the number of birds				
	<100	100–500	500–1,000	1,000–10,000	>10,000
Czech Republic	30 (70%)	6 (14%)	2 (5%)	2 (5%)	3 (7%)
France	183 (46%)	8 (2%)	27 (7%)	140 (35%)	40 (10%)
Germany	20 (22%)	8 (9%)	0 (0%)	23 (25%)	41 (45%)
Hungary	15 (7%)	24 (10%)	10 (4%)	100 (44%)	80 (35%)
Poland	21 (33%)	5 (8%)	2 (3%)	8 (13%)	28 (44%)
Romania	38 (86%)	6 (14%)	0 (0%)	0 (0%)	0 (0%)
Total Europe	375 (37%)	82 (8%)	43 (4%)	283 (28%)	229 (23%)

3.4 | Sources of infection in domestic holdings

To evaluate whether the origin of infections of domestic holdings may have been linked to contact with wild birds, we calculated, for each domestic outbreak, the distance to the closest outbreak in wild birds. The results evidence that 25% of the domestic outbreaks had a wild bird outbreak within a distance of 12.1 km, 50% within a distance of 21.3 km and 80% within a distance of 33.0 km. However, there are also evidences that other sources of infection were also relevant. In Spain, of the 10 domestic holdings affected, in two, direct or indirect contact with wild birds was considered the most likely source of infection, while in the other eight, infection was attributed to having received animals from the two primary outbreaks (*Department of Agriculture of Catalonia, personal communication*). In Belgium, of the 13 outbreaks in domestic holdings, seven were attributed to indirect transmission in markets, two to purchase of infected animals and only three to contact with wild birds (EU, 2017d).

3.5 | H5N8 outbreaks in wild birds

Of the 955 outbreaks in wild birds, Germany was the country most severely affected with 194, followed by Romania with 90, and Switzerland with 87. There were many species of wild birds involved, in particular swans, including the mute swan (*Cygnus olor*), the species most commonly affected with 270 outbreaks, but also the Whooper swan (*Cygnus cygnus*) with 62 outbreaks and swans of unidentified species, involved in 44 further outbreaks. Other relevant wild bird species were mallards (*Anas platyrhynchos*) with 91 outbreaks and tufted ducks (*Aythya fuligula*) involved in 58 outbreaks. Interestingly, 47 of the 58 outbreaks in tufted ducks occurred at the beginning of the epidemic (in the second half of November, between weeks 46 and 48, see Figure 2) and affected several different countries (Austria, Denmark, Finland, Germany, the Netherlands and Switzerland). In contrast, 229 of the 270 (85%) outbreaks in mute swans, 51 of the 62 (82%) outbreaks in Whooper swans and 36 of the 46 (78%) outbreaks in mallards occurred between weeks 1 and 8 (January and February 2017).

Clinical signs observed in wild birds, especially in mute swans, included neurological signs, such as torticollis, incoordination and ataxia, as well as sudden death. Macroscopic and microscopic lesions were similar to those already described for poultry (European Food Safety Authority (EFSA), 2017b).

3.6 | Spatio-temporal distribution of outbreaks (October 2016–August 2017)

After detection of H5N8 at the Ubsu-Nur Lake in June, 2016, the virus was not detected again until October (weeks 42–44), when it was reported in wild birds in Hungary, Poland and Croatia (Figures 2 and 3). In November (weeks 44–48), H5N8 expanded further west reaching Austria, Switzerland, Germany, Sweden, Finland, Denmark, the Netherlands and France. December 2016 (weeks 48–52) marks the expansion of H5N8 to Bulgaria, Italy, Slovakia, the UK and Ireland. In January 2017 (weeks 1–5), H5N8 expanded also to the Czech Republic, Slovenia, Macedonia, Spain and Portugal. February (weeks 5–9) was the month with the highest number of outbreaks, with expansion to Belgium, Bosnia and Lithuania (Figures 2 and 4). March (weeks 9–13) marked a clear decrease in the number of outbreaks in both domestic and wild birds, which continued in April (weeks 13–17). However, H5N8 transmission has not ceased, and between May and August (weeks 18–30), H5N8 continued its spread, although at low levels, in some specific areas (Figures 2 and 4).

Severe cold conditions are known to influence both long-distance migration of water birds and movements between the wintering sites during winter periods (Ottaviani et al., 2010). Therefore, we evaluated whether temperatures may have played a role in the spread of H5N8 during 2016–2017 using temperature anomaly maps, which were obtained from the National Oceanic and Atmospheric Administration (NOAA). The world temperature anomaly map for a given month is created by combining land and sea surface temperatures on that month and comparing it to the average values for that month for the period 1981–2010 (National Oceanic and Atmospheric Administration (NOAA), 2017). A positive anomaly indicates that the observed temperature was warmer than the average, and a negative anomaly, cooler than the average. The results show that during October, November and December 2016 (Figure 5), the areas of central Russia, but also further west, up to the eastern European region were affected by a negative anomaly, with temperatures up to 5 degrees below average (National Oceanic and Atmospheric Administration (NOAA), 2017). In January 2017, most of Europe was also affected by a negative anomaly, which was even more severe in the eastern regions of Europe.

4 | DISCUSSION

In recent years, Europe has been affected by several HPAI epidemics. The 2005–2006 H5N1 epidemic caused 356 and 637 outbreaks in domestic and wild birds, respectively, and affected 23 European countries (Food and Agriculture Organization of the United Nations (FAO), 2017). The 2014–2015 H5N8 epidemic caused only 13 outbreaks in domestic birds and five in wild birds and affected only seven countries (Food and Agriculture Organization of the United Nations (FAO), 2017). However, the H5N8 subtype, which reached Europe in 2016, has caused, up to August 2017, 1,112 outbreaks in domestic birds and 955 in wild birds in 30 countries, the largest epidemic by a HPAI in the continent, and more than a year after its introduction into Europe continues causing outbreaks.

Even though in Europe the density of chickens is much higher than the density of ducks, 70% of the domestic outbreaks occurred in duck holdings and only 12% in chicken holdings. The fact that the majority of domestic outbreaks in Europe occurred in ducks may be linked to the particularities of the production in ducks as compared to other poultry species, in particular in the case of foie gras production. The foie gras production occurs in several phases (EFSA,

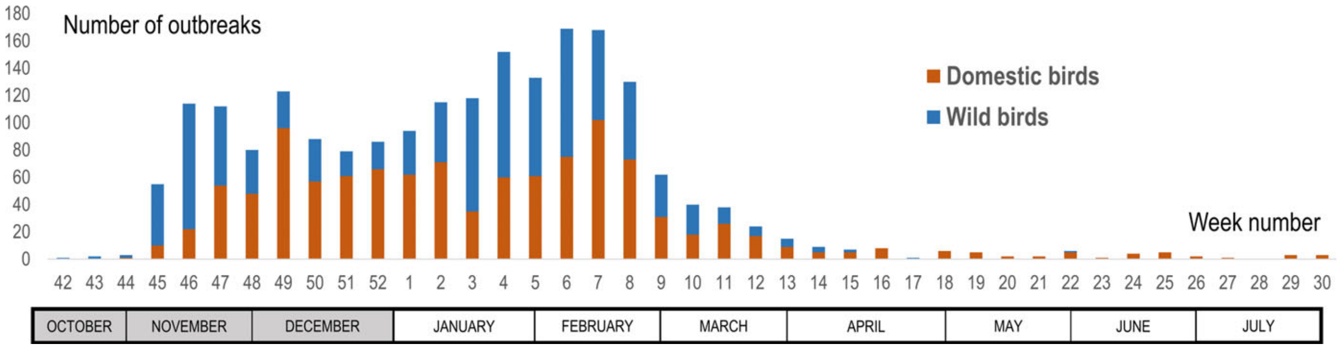

FIGURE 2 Number of outbreaks of H5N8 in both domestic and wild birds in Europe by week [Colour figure can be viewed at wileyonlinelibrary.com]

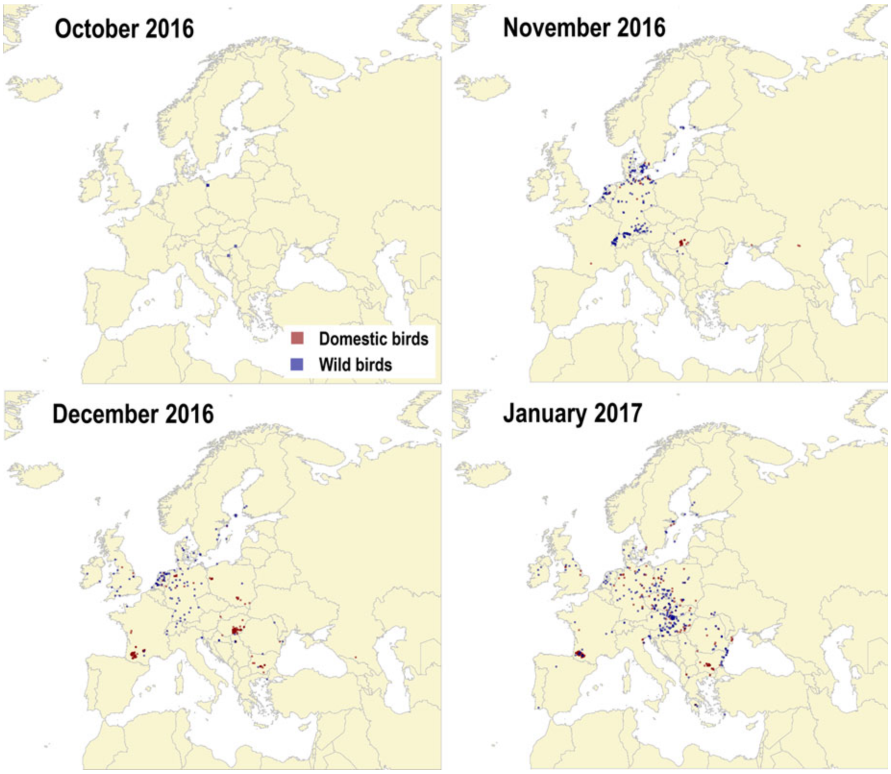

FIGURE 3 Location of outbreaks of H5N8 in both domestic and wild birds in Europe from October 2016 to January 2017 [Colour figure can be viewed at wileyonlinelibrary.com]

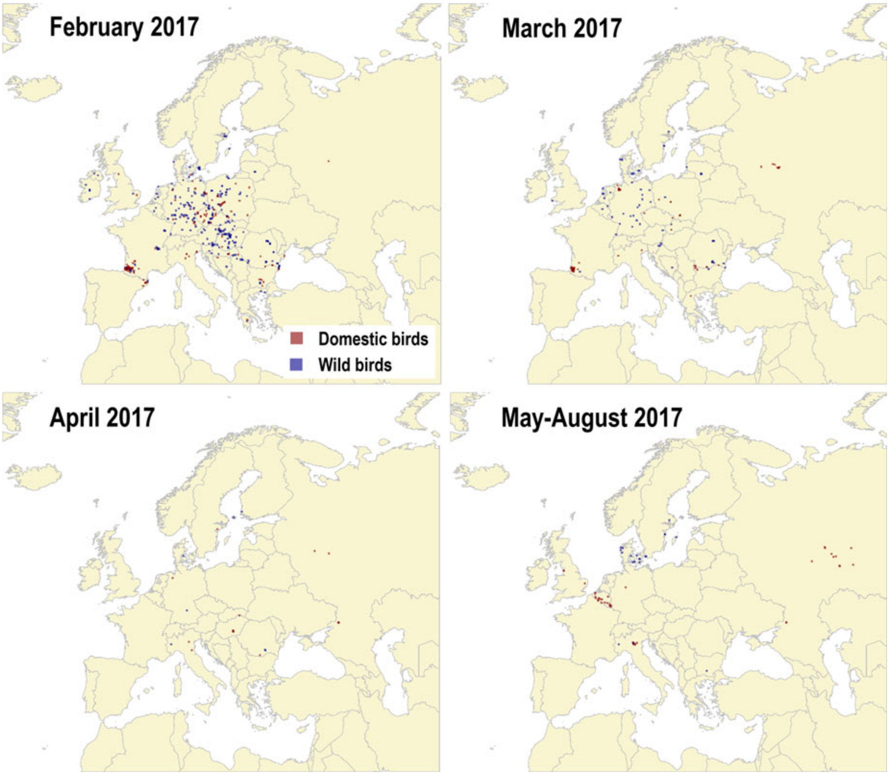

FIGURE 4 Location of outbreaks of H5N8 in both domestic and wild birds in Europe from February 2017 to August 2017 [Colour figure can be viewed at wileyonlinelibrary.com]

2017a): during the growing phase, due to its long duration (12 weeks), and the fact that ducks are usually maintained in large free-range flocks, preventing direct or indirect contact with wild birds contact is often not feasible and that increases the risk of HPAI infection. Then, the fattening phase, which lasts for 2 weeks, is carried out indoors and in small flocks (because it is labour intensive). Therefore, at the end of the growing phase, a large growing flock may be separated into many small fattening flocks leading to

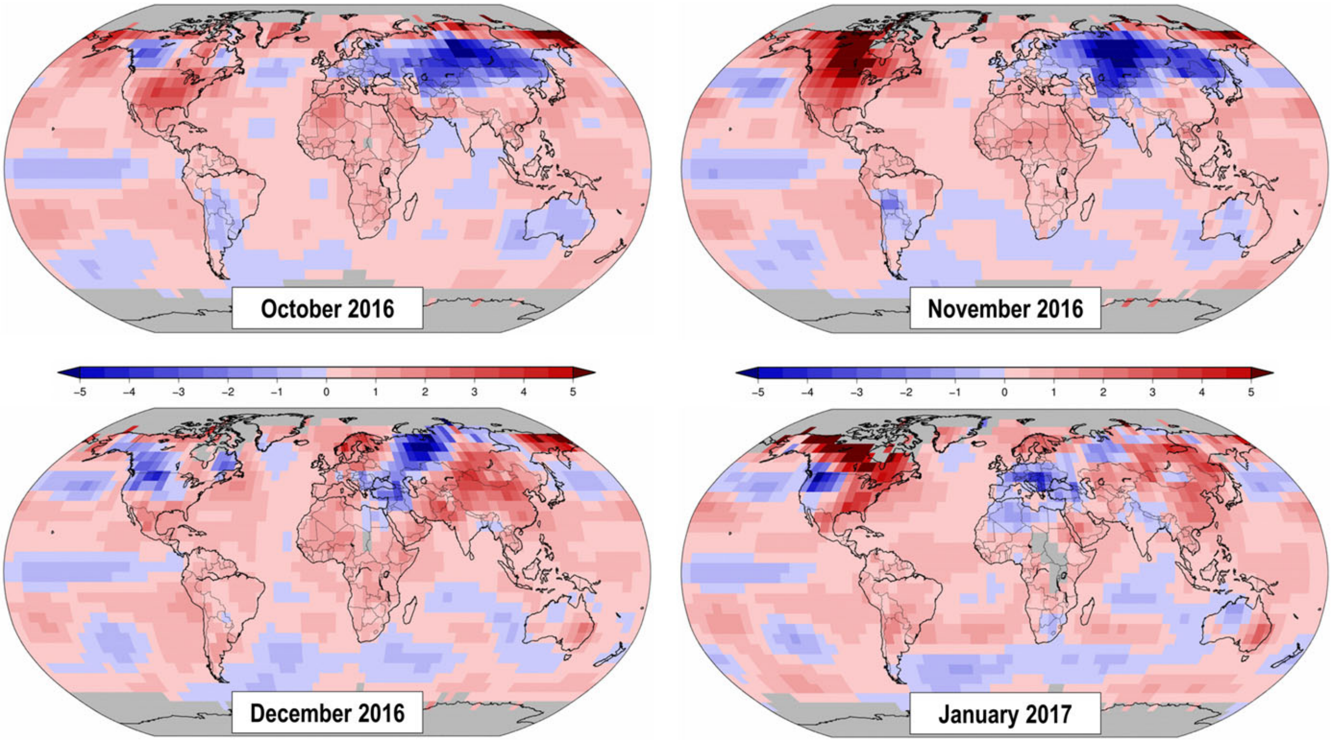

FIGURE 5 Temperature (in degrees Celsius) anomaly maps for the months of October, November and December 2016 and January 2017 obtained from the National Oceanic and Atmospheric Administration (NOAA): https://www.ncdc.noaa.gov/sotc/global/201709 [Colour figure can be viewed at wileyonlinelibrary.com]

intensive animal movements to different locations and facilitating HPAI viruses spread.

In contrast to the low mortality observed in domestic ducks during the H5N8 epidemic in Europe in 2014–2015, the 2016–2017 H5N8 was able to cause clinical disease and mortality in domestic ducks. However, there are also evidences that some H5N8 infections occurred without evident mortality or clinical symptoms. Preventive slaughtering of apparently healthy duck farms in France revealed that many of them were actually infected. Furthermore, infected holdings without symptomatology were also discovered through pre-movement testing in France or through epidemiological investigations in Spain. While in domestic chicken, passive surveillance based on clinical signs/mortality may be considered the most efficient method for the early detection of H5N8 outbreaks, in domestic ducks, passive surveillance would need to be combined with some sort of active surveillance (EU, 2017e). Further research is needed to identify the determinants of clinical disease in domestic ducks and in other species.

The spatial pattern of domestic outbreaks varied between countries, with some countries where the disease was clustered within some areas and others where outbreaks had a more homogeneous distribution throughout the territory. France and Hungary were the two countries with the most domestic outbreaks, and in both cases, the vast majority of outbreaks affected ducks and were clustered in very specific areas, which had the particularity of having an extremely high density of ducks. In those two countries, the epidemic resulted in hundreds of holdings infected and the slaughtering of millions of birds to control the epidemic, which evidences that HPAI may have devastating consequences for the poultry sector. In other countries such as Spain and Bulgaria, even though the number of holdings affected was much lower, clustering of disease was also observed. In those two countries, ducks represented the majority (if not all of the holdings affected), and the local spread to other holdings, resulting in clustering, may have been related to the specificities of the production system in ducks. In contrast, in countries such as Germany or the Netherlands, where domestic outbreaks involved mainly other poultry species rather than ducks, H5N8 infections did not result in extensive spread, even when domestic outbreaks occurred in areas of high chicken density.

In Europe, H5N8 infections in domestic birds did not seem to be associated with a specific size of holding. In fact, in some countries, infections seemed to affect smallholdings, while in others, infections occurred mainly in large-size holdings. Whether those observed patterns are the result of differences in the characteristics (size) of the poultry holdings in the country, or there were other epidemiological factors, which influenced the size of the flocks infected, deserves further attention.

In the majority of European countries affected by the H5N8, infection was detected before in wild than in domestic birds. That evidences that the surveillance systems implemented in wild birds, mainly based on passive detection, were efficient for the early detection of H5N8. The mortality observed in ducks, swans and geese indicated that the contemporary H5N8 was more virulent than the 2014–2015 H5N8 (European Food Safety Authority (EFSA), 2017a). However, further research would be needed on how the susceptibility to H5N8 2016–2017 varies among and within wild bird species. The absence of clinical signs and/or mortality in wild birds does not necessarily mean the absence of HPAI circulation, as evidenced by the detection, by active surveillance, of H5N8 HPAI in two Eurasian wigeons (*Anas penelope*) in the Netherlands in 2014 (Verhagen et al., 2015), or in one mallard (*Anas platyrhynchos*) and one European Herring Gull (*Larus argentatus argentatus*) in Germany in 2015 (EU, 2015).

It seems clear that wild birds have played a role in the arrival of the H5N8 to Europe and its subsequent spread to the domestic bird population (Food and Agriculture Organization of the United Nations (FAO), 2016). The fact that 25% of the domestic outbreaks had a wild bird outbreak reported within a distance of 12.1 km, 50% within a distance of 21.3 km and 80% within a distance of 33.0 km suggests a possible link between outbreaks in domestic and wild birds. However, the mechanism by which domestic birds would get the infection from wild birds is not clear. In the 2014 H5N8 epidemic in Europe, indirect introduction of the virus into poultry holdings via humans, vehicles, equipment or fomites contaminated with virus was considered more likely than direct contact between wild birds and domestic birds (EFSA, 2014). Therefore, biosecurity measures to prevent direct contact and indirect contact with wild birds are considered essential to prevent HPAI infections of domestic holdings. However, besides infection from wild birds, once the H5N8 infection was established in the domestic population, a significant number of new infections in domestic holdings seemed to have occurred because of epidemiological relationships with other domestic holdings, as was evidenced in France, Spain and Belgium.

In relation to wild birds, there were significant differences among countries in the number of outbreaks reported, with Germany as the country with the most outbreaks (194). Some of the variation among countries may be explained by differences in their wild bird populations or the level of circulation of the virus, but also by differences in the intensity of surveillance of HPAI in wild birds (including the level of awareness of the general population to report wild birds found dead). For example, Germany accounted for 47% of the total samples of wild birds from passive surveillance tested in the EU in 2016 (European Union (EU), 2017e).

The most frequently affected wild bird species was the mute swan (*Cygnus olor*), but other swans, Whooper swan (*Cygnus cygnus*) and swans of unidentified species were also commonly affected. In 2006, around 70% of all H5N1 outbreaks in wild birds in Europe were swans, almost 90% of which were mute swans (Hesterberg et al., 2009). Experimental infections carried out with HPAI (H5N1 of Asian lineage) in mute swans evidenced they were both highly susceptible to infection, and efficient spreaders of the virus given the duration and concentration of viral shedding (Brown, Stallknecht, & Swayne, 2008). Besides, frequent detection in swans may also be related to their higher size as compared to other species, whose carcasses may be rapidly removed by predators and scavengers and to the fact that they are frequently found near inhabited areas, which might further facilitate detection (Hesterberg et al., 2009).

Another wild bird species frequently involved in the 2016–2017 H5N8 epidemic was the tufted duck (*Aythya fuligula*), with the particularity that 81% of the outbreaks in this species occurred in the second half of November (i.e., early in the epidemic) and affected six different countries (Austria, Denmark, Finland, Germany, the Netherlands and Switzerland). That, and the fact that 600,000–800,000 pairs breed in Russia and that they have a migratory behaviour (BTO, 2017), suggest that they may have played a role in the introduction of the H5N8 into Europe from Russia. Most of the outbreaks in swans occurred later in the epidemic, which may be suggestive of secondary infections from other species. Of the three species of swans present in the EU, the mute swan is mostly sedentary, and movements seldom exceed tens of kilometres (Waldenström, Kuiken, & Wille, 2017). In contrast, Whooper swans are mainly migratory, with the populations breeding in Scandinavia and Russia, west of the Urals, wintering mainly in Denmark and Germany, and the populations breeding east of the Urals wintering in the Black and the Caspian seas. In the case of the Bewick's Swan (*Cygnus columbianus bewickii*), there are populations which migrate from Siberia to wintering areas in Denmark, Germany, The Netherlands and Britain. A large number of other bird species have been found positive for avian influenza viruses, in particular within the order Anseriformes. However, the role played by the different species in HPAI spread to Europe, in particular in the case of the 2016–2017 H5N8 epidemic, is not clear. Bird migration is a complex phenomenon with considerable variation between regions, species or years depending on ecological (e.g., abundance of food resources) or climatic factors (e.g., cold weather) (Waldenström et al., 2017). There are still many unknown factors in relation to the role of wild birds in HPAI spread. They include susceptibility of the different species, pathogenicity of the virus in the wild bird host, efficiency of transmission, survival of virus in the environment or the influence of behavioural factors such as gregariousness.

Ottaviani and collaborators concluded that the H5N1 introduction, spread and persistence in Europe in 2006 may have been enhanced by the cold 2005–2006 winter (Ottaviani et al., 2010). Similarly, temperature anomaly maps evidence that, between October 2016 and January 2017, the areas of central Russia and Eastern Europe were affected by a negative anomaly, with temperatures up to 5 degrees below average for those months. That may have been driven the unprecedented southern and western expansion of the H5N8 in Europe in 2016–2017. Low temperature not only influences HPAI spread through its role in bird movements, but also favouring bird aggregation and by enhancing virus persistence in the environment (Ottaviani et al., 2010).

The spatial and temporal pattern of outbreaks in the 2016–2017 H5N8 epidemic had similarities with previous HPAI epidemics in Europe. In the 2005–2006 H5N1 epidemic, after the detection of the virus in Russia in July 2005, the virus was reported in wild birds in Romania and Croatia in October, the peak was reached in February–March 2006, affecting 22 European countries, and then there was a progressive decrease in the number of outbreaks until the epidemic was extinguished. In the 2014–2015 H5N8 epidemic, even though the size was much smaller, the temporal pattern had some similarities: after the detection of the virus in Russia, the H5N8 was first detected in Germany in November 2014, although in that case, the peak and the extinction of the epidemic occurred earlier, in November and February, respectively. The emergence of the H5N8 in 2016 followed a repeated pattern whereby HPAI viruses are first detected in Siberia, and a few months later, after the fall migration of wild birds, they are detected in Europe. One difference with previous epidemics has been the capacity of the 2016–2017 H5N8 to persist during the summer of 2017 and continue to circulate at low level causing sporadic outbreaks, and that raises concern about the possibility of the virus becoming endemic in Europe. Determination of the mechanism by which the virus was able to persist would be essential. Possible hypotheses include the existence of a bird reservoir (domestic or wild) or the maintenance of the environment.

Concerning the zoonotic potential, while the H5N1 subtype has caused, up to June 2017, 859 human cases worldwide, with 453 deaths (WHO, 2017), no human infections with H5N8 have been reported to date. The analysis of the genome of the current H5N8 indicated that this subtype is primarily a bird virus without increased affinity for humans (ECDC, 2016).

Besides H5N8, within the last year, other HPAI of H5 subtype has circulated or is currently circulating in Europe. H5N5 has caused only 17 outbreaks between domestic and wild birds, but it is widely distributed affecting Serbia, Croatia, Montenegro, Slovenia, Greece, the Netherlands, Germany, the Czech Republic and Italy. In December 2017, H5N6 was detected in domestic and wild birds in the Netherlands and Switzerland and was found to be related to an H5N6 detected in February 2017 in Greece (EU, 2017f). The AI EU Reference Laboratory concluded that H5N5 and H5N6 viruses are the result of further reassortment involving H5N8 HPAI and are still predominantly bird viruses without any specific increased affinity for humans. However, the widespread circulation of HPAI (in particular those of the H5 subtype) in animal populations may result in reassortments of the viruses, which represents a risk of human influenza pandemics in the long term (European Centre for Disease Prevention and Control (ECDC), 2016). The recent emergence of A (H5N6) viruses in China causing severe disease in humans is indicative of the risk of infection of humans with reassorted viruses from clade 2.3.4.4 originating from birds (European Centre for Disease Prevention and Control (ECDC), 2016).

Given the repeated pattern of HPAI viruses emergence in Europe, new incursions are likely to occur in the future. Therefore, understanding the epidemiology of previous HPAI incursions in Europe is essential for the early detection of new HPAI viruses, which may help to prevent their transmission within the birds' populations and ultimately to humans.

ACKNOWLEDGEMENT

IRTA is supported by CERCA Programme / Generalitat de Catalunya.

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How to cite this article: Napp S, Majó N, Sánchez-Gónzalez R, Vergara-Alert J. Emergence and spread of highly pathogenic avian influenza A(H5N8) in Europe in 2016-2017. *Transbound Emerg Dis*. 2018;65:1217–1226. https://doi.org/10.1111/tbed.12861