SCIENTIFIC REPORT

Avian influenza overview September – November 2017

European Food Safety Authority,
European Centre for Disease Prevention and Control and
European Union Reference Laboratory for Avian influenza

Ian Brown, Thijs Kuiken, Paolo Mulatti, Krzysztof Smietanka, Christoph Staubach, David Stroud, Ole Roland Therkildsen, Preben Willeberg, Francesca Baldinelli, Frank Verdonck and Cornelia Adlhoch

Abstract

Between 1 September and 15 November 2017, 48 A(H5N8) highly pathogenic avian influenza (HPAI) outbreaks in poultry holdings and 9 H5 HPAI wild bird events were reported within Europe. A second epidemic HPAI A(H5N8) wave started in Italy on the third week of July and is still ongoing on 15 November 2017. The Italian epidemiological investigations indicated that sharing of vehicles, sharing of personnel and close proximity to infected holdings are the more likely sources of secondary spread in a densely populated poultry area. Despite the ongoing human exposures to infected poultry during the outbreaks, no transmission to humans has been identified in the EU. The report includes an update of the list of wild bird target species for passive surveillance activities that is based on reported AI-infected wild birds since 2006. The purpose of this list is to provide information on which bird species to focus in order to achieve the most effective testing of dead birds for detection of H5 HPAI viruses. Monitoring the avian influenza situation in other continents revealed the same risks as in the previous report (October 2016-August 2017): the recent human case of HPAI A(H5N6) in China underlines the continuing threat of this avian influenza virus to human health and possible introduction via migratory wild birds into Europe. Close monitoring is required of the situation in Africa with regards to HPAI of the subtypes A(H5N1) and A(H5N8), given the rapidity of the evolution and the uncertainty on the geographical distribution of these viruses. Interactions between EFSA and member states have taken place to initiate discussions on improving the quality of data collections and to find a step-wise approach to exchange relevant (denominator) data without causing an additional resource burden.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Avian influenza is an infectious viral disease in birds, including domestic poultry. Infections with avian influenza viruses in poultry cause two main forms of that disease that are distinguished by their virulence. The low pathogenic (LPAI) form generally only causes mild symptoms, while the highly pathogenic (HPAI) form results in very high mortality rates in most poultry species. That disease may have a severe impact on the profitability of poultry farming.

Avian influenza is mainly found in birds, but under certain circumstances infections can also occur in humans even though the risk is generally very low.

More than a decade ago, it was discovered that virus acquired the capability to be carried by wild birds over long distances. This occurred for the HP AI of the subtype A(H5N1) from South East and Far East Asia to other parts of Asia, Europe and Africa as well as to North America. In the current epidemic the extent of the wild bird involvement in the epidemiology of the disease is exceptional.

From late October 2016 to early February 2017, highly pathogenic avian influenza (HPAI) of the subtype A(H5N8) has been detected in wild migratory birds or captive birds on the territory of 21 Member States, namely Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom. In 17 Member States the virus has spilled over to poultry holdings leading also to lateral spread between holdings in a few Member States, in particular in those with a high density of duck and geese holdings where the poultry cannot be protected sufficiently against contacts with wild birds. A second HP AI subtype A(H5N5) has been detected in wild birds and recently also in poultry holdings in Germany.

The number of infected migratory wild birds found dead and the geographical extent of these findings are posing an immense threat for virus introduction into poultry or captive birds holdings as demonstrated by the high number of outbreaks (~700 as of 08/02/2017).

In the event of an outbreak of avian influenza, there is a risk that the disease agent might spread to other holdings where poultry or other captive birds are kept. As a result it may spread from one Member State to other Member States or to third countries through trade in live birds or their products.

There is knowledge, legislation[1], and technical and financial tools in the EU to effectively deal with outbreaks of avian influenza in poultry and captive birds. However, the very wide virus spread by wild birds and the increased risk of direct or indirect virus introduction into poultry or captive bird holdings has led to the largest HP AI epidemic in the EU so far. This situation calls for a reflection and evaluation of how preparedness, risk assessment, early detection and control measures could be improved.

The Commission and Member States are in need of an epidemiological analysis based on the data collected from the disease affected Member States. The use of the EFSA Data Collection Framework is encouraged given that it promotes the harmonisation of data collection. Any data that is available from neighbouring third countries should be used as well, if relevant.

Therefore, in the context of Article 31 of Regulation (EC) No. 178/2002[2], EFSA should provide the technical and scientific assistance to the Commission based on the following Terms of Reference:

1.   Analyse the epidemiological data on highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI), where co-circulating or linked within the same epidemic, from HPAI disease affected Member States.

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[1] Council Directive 2005/94/EC of 20 December 2005 on Community measures for the control of avian influenza and repealing Directive 92/40/EEC. OJ L 10, 14.1.2006, p. 16.

[2] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.

2. Analyse the temporal and spatial pattern of HPAI and LPAI as appropriate in poultry, captive birds and wild birds, as well the risk factors involved in the occurrence, spread and persistence of the HPAI virus in and at the interface of these avian populations.

3. Based on the findings from the points above, describe the effect of prevention and control measures.

4. Provide for regular quarterly reports updating on the avian influenza situation within the Union and worldwide, in particular with a view to describe the evolution of virus spread from certain regions towards the EU. In case of significant changes in the epidemiology of avian influenza, these reports could be needed more frequently. These reports should in particular closely follow the developments of zoonotic avian influenza viruses (such as HPAI A(H5N6) and LPAI A(H7N9)) in collaboration with the European Centre for Disease Prevention and Control (ECDC).

1.2.   Interpretation of the Terms of Reference

In reply to TORs 1 and 2, this scientific report gives an overview of the HPAI and LPAI outbreaks in poultry and captive birds as well as HPAI events in wild birds detected in Europe between 1 September 2017 and 15 November 2017, mainly based on data submitted by Member States (MSs) and neighbouring countries via the Animal Disease Notification System (ADNS). A phylogenetic characterisation of the circulating viruses is included as well as a brief genetic characterisation to explain how related/distant viruses are. Most outbreaks were located in Italy and Italian representatives submitted additional epidemiological data to EFSA (see Section 2.1.1), which has been used to analyse the characteristics of holdings affected between 1 July and 15 November 2017. Italy also provided information from their epidemiological investigations on the risk factors involved in the spread of highly pathogenic avian influenza virus (HPAIV) between holdings (Annex A).

It was not possible to collect data for a risk factor analysis on occurrence and persistence of HPAIV within the EU. Risk factor analysis requires also data on the susceptible population (e.g. location of holdings, population structure, etc.), which should be collected in a harmonised manner across the EU. Limitations in the performed data collection, reporting and analysis were reported in the first AI overview report (EFSA, ECDC, EURL, 2017).

A description of the applied prevention and control measures (TOR3) is reported based on a case report provided by Italian representatives and attached as Annex B to this report. The main topics covered are increasing awareness, release and repeal of housing order, strengthening biosecurity, preventive culling, implementation of regional stand still, hunting and derogations on restriction zone implementation after a risk assessment.

The monitoring of the avian influenza (AI) situation in other continents (TOR4) focuses on HPAI A(H5N6), HPAI/LPAI A(H7N9), HPAI A(H5N1), HPAI A(H5N8) and LPAI A(H9N2). Background and epidemiology, detections, phenotypic and genetic characterisations are described based on information from confirmed human and poultry cases as well as wild bird events reported between 1 September 2017 and 15 November 2017. Possible actions for preparedness in the EU are discussed.

The report mainly describes information that became available since the publication of the previous report (EFSA, ECDC, EURL, 2017) and that might affect the interpretation of risks related to AI introduction and/or spread.

2.   Data

2.1.   Data on animals

2.1.1. Epidemiological data

The data on the AI outbreaks submitted by MSs between 1 September 2017 and 15 November 2017 to the European ADNS were taken into account for this report. In addition, Italy was asked to provide more detailed epidemiological data (see data dictionary in Table A.1, Appendix A) directly to EFSA on the AI outbreaks that occurred in the same period. The data model has been discussed with representative appointed by the MS during a teleconference. This was carried out by exchanging Excel

files via email to the representative appointed by the MS. The slide presentations, which EU MSs affected by AI presented to the Standing Committee on Plants, Animals, Food and Feed (PAFF Committee), were consulted to extract information on the mortality rates and clinical signs of different species of domestic and wild birds from HPAIV infections, both in single species and multiple species holdings. The PDFs of these slide presentations are available on the European Commission website (European Commission, online). Italy described the dynamics of the AI secondary outbreaks that occurred in summer/autumn 2017 using the template that was generated for the previous report (EFSA, ECDC, EURL 2017). The case report provided to EFSA can be consulted in Annex A.

2.1.2. AI prevention and control measures

Italy expressed the interest in supporting the analysis of the AI outbreaks from 1 July to 15 November 2017 and submitted a case report on the AI prevention and control measures based on the template that was generated for the previous report (EFSA, ECDC, EURL, 2017). The case report provided to EFSA can be consulted in Annex B.

2.2.   Data on humans

The collation of numbers of human cases due to infection with AIVs has been performed by experts at the ECDC. Multiple sources are scanned regularly to collect information about laboratory confirmed human cases, e.g. Disease Outbreak Alert pages at the World Health Organization (WHO)[3], webpages of WHO's Regional offices, Chinese Center for Disease Control, health authorities in Hong Kong, CDC in Taiwan[4] and others (Chinese CDC, online; CHP, online; Taiwan CDC, online; WHO, 2013). Data were extracted and collated in line lists. Double entries and validity of data are continuously checked by ECDC duty experts. Line lists have been developed to collate case-based information on virus type, date of onset of disease, country of reporting, country of exposure, sex, age, exposure, clinical information (hospitalisation, severity.) and outcome. All cases included in the line list and mentioned in the document are laboratory-confirmed cases.

Literature searches were performed continuously until 24 November 2017 in the PubMed database with the key words: 'humans' and 'A(H5N1)'; 'A(H5N6)'; 'A(H5N8)'; 'A(H7N9)'; A(H9N2)'; and narrowed to the most recent available publications as well as using specific search parameters such as 'seroprevalence'; 'risk factors'; 'transmission'. The literature search was not systematic or comprehensive.

3.   Results

3.1.   Overview of HPAI and LPAI outbreaks in Europe between September and November 2017 (TOR 1 and TOR 2)

3.1.1. Phenotypic characterisation of AI viruses circulating in the EU

3.1.1.1.   HPAI in domestic birds

Information extracted from PAFF Committee presentations

Between September and November 2017, there were slide presentations by Italy (18 September and 25 October 2017) and Bulgaria (25 October 2017) at meetings of the Standing Committee on Plants, Animals, Food and Feed. The pdfs of these slide presentations are available at https://ec.europa.eu/food/animals/health/regulatory_committee/presentations_en.

In the report from Italy (18-19 September 2017), a fattening turkey holding of 20,560 birds, HPAI was suspected based on increased mortality rate. In the report from Italy (25 October 2017), HPAI was suspected on one fattening turkey holding of unknown size based on increased mortality, and on another fattening turkey holding of 9,000 birds based on increased mortality and nervous signs. HPAI was suspected in a non-commercial flock of 5 chickens (laying hens) and 6 mute swans based on

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mortality of 2 swans. In another non-commercial flock of 8 domestic geese and 34 domestic ducks, HPAI was suspected based on increased mortality of the ducks. In the report from Bulgaria (25 October 2017), HPAI was suspected on a great-grandparent domestic duck holding of 10,465 birds based on egg drop but no mortality. HPAI was suspected in a non-commercial flock including chickens (hens) and domestic turkeys based on mortality of both species. In all above-mentioned holdings, HPAIV A(H5N8) was diagnosed.

Information extracted from the scientific literature

Between September and November 2017, there were several articles on experimental inoculation of HPAIV A(H5N8) isolates from the 2014/2015 outbreak into domestic birds. Bertran et al. (2017) inoculated HPAIV A(H5N8) (A/Gyrfalcon/Washington/40188-6/2014), which they considered representative of the wholly Eurasian A(H5N8) lineage viruses into different species of minor gallinaceous poultry at 4 week of age: Japanese quail (*Coturnix coturnix japonica*), bobwhite quail (*Colinus virginianus*), pearl guinea fowl (*Numida meleagris*), chukar partridge (*Alectoris chukar*), and ring-necked pheasant (*Phasianus colchicus*). Susceptibility varied among species; the least susceptible birds were Japanese quail, which required 3.2 log10 mean bird infectious doses (BID_{50}) for becoming infected. The most susceptible birds were bobwhite quail, with infection at < 2 log10 BID_{50}. In this study, the BID_{50} and the mean bird lethal dose (BLD_{50}) were the same for each species. Nearly all birds in this study showed mild nonspecific signs prior to death, such as listlessness, or died in the absence of overt clinical signs. The exception was 1 of 12 Japanese quail, which showed neurological signs, consisting of head tremors and leg paralysis at 3 days post challenge. In general, similar gross lesions were observed in the birds of different species. The most characteristic gross lesions were multifocal pancreatic necrosis, and haemorrhages in different organs (proventriculus, duodenum, trachea, skeletal muscle). Histologically, multifocal necrosis with viral antigen staining was widespread in the parenchymal cells of most tissues and was especially prominent in the lungs, heart, brain, spleen, and adrenal glands.

The minor gallinaceous species listed in the previous paragraph were more susceptible than chickens (4.4 log10 BID_{50}; Bertran et al. 2016) or turkeys (5.0 log10 BID_{50}; Spackman et al., 2016) experimentally inoculated with the same virus isolate. However, domestic Pekin ducks and white Chinese geese inoculated with the same virus isolate had <2 to 3.0 log10 BID_{50} (Pantin-Jackwood et al., 2017), underscoring susceptibility similar to those for the tested gallinaceous species listed above.

Kwon et al. (2017a) inoculated two other HPAIV A(H5N8) isolates from the 2014/2015 outbreak into domestic pigeons (Columba livia domestica): A/baikal teal/Korea/2406/2014, which was isolated from a swab sample taken from an affected baikal teal carcass from the 2014 outbreak in Korea, or A/Mallard/Korea/KU3- 2/2015, which was isolated from the fecal sample of a mallard duck from the 2015 outbreak in Korea. The viruses were detected in three out of the five birds inoculated with teal isolate and two out of the five birds inoculated with the mallard isolate. Virus was detected from both oral and cloacal swab samples only for a period up to 8 days post infection. None of them had clinical signs or mortality. Virus antigen was detected in heart, liver, small and large intestines, kidney, and caecal tonsil, and was not co-localized with histological lesions. These results indicate that domestic pigeons can be infected with and shed HPAIV A(H5N8) virus without showing clinical signs. The EFSA opinion on avian influenza concluded that "pigeons are rarely found to be infected during either epizootics or in endemic areas where H5 and H7 viruses circulate, hence they do not play an important role in the spread of AIV" (EFSA AHAW Panel, 2017).

There was one report on the phenotype of HPAIV A(H5N8) in naturally infected poultry, from holdings in Italy affected between December 2016 and February 2017. Fusaro et al. (2017) diagnosed HPAIV A(H5N8) in birds on 6 commercial turkey holdings, 1 chicken (layer) holding, and 3 non-commercial flocks. The onset of clinical signs in all the affected poultry species was generally associated with depression, reluctance to move, and a drop in feed consumption. The clinical condition often evolved into a more severe respiratory and nervous syndrome associated with an increased mortality rate. Average mortality rate was 1.62% (95% CI 1.10%–2.14%).

3.1.1.2. HPAI in wild birds

Pathogenicity in the affected species

Information extracted from the World Organisation for Animal Health (OIE) reports

Between 1 September and 15 November 2017, dead wild birds testing positive for HPAIV A(H5N8) were reported to the OIE by Bulgaria, Cyprus, Germany, and Italy. In all events except one, these were single wild birds found dead. This is in contrast to the winter of 2016/2017, when there were multiple events with high numbers of dead wild birds (see e.g. article by Kleyheeg et al., 2017 summarized below). The wild birds were: one Eurasian buzzard (*Buteo buteo*) in Cyprus; a group of three swans (not specified), two of which were found dead, and one mallard (*Anas platyrhynchos*) in Germany; and three separate mute swans (*Cygnus olor*), one rock pigeon (*Columba livia*), one common kestrel (*Falco tinnunculus*), and one greylag goose (*Anser anser*) in Italy. The pigeon and kestrel were found dead at a poultry holding already with a HPAIV A(H5N8) outbreak.

Information extracted from the scientific literature

Between 1 September and 15 November 2017, there were two articles about wild or zoo birds related to the 2014/2015 outbreak. Globig et al. (2017) investigated an outbreak of HPAIV A(H5N8) in a German zoo in 2014-2015. HPAI was suspected because of 3 of a group of 12 white storks (*Ciconia ciconia*) died suddenly without prior overt clinical signs. These birds were positive for HPAIV A(H5N8) and at autopsy showed multifocal necrosis of liver, spleen, kidney, and/or pancreas. Although the combined cloacal and oropharyngeal swabs of 8 of 9 remaining storks were positive for HPAIV A(H5N8), they showed no clinical signs or lesions, except for one stork with airsacculitis. A group of 19 Chilean flamingos (*Phoenicopterus chilensis*) underwent subclinical HPAIV A(H5N8) infection, based on the combination of high HI titres against A(H5N8) antigen in sera of 15 of 19 flamingos, together with absence of clinical signs. A possible explanation is that these flamingos, some of which were over 20 years old, had had repeated contact with low pathogenic influenza A virus through their mode of filter feeding, and therefore had a degree of immunity to HPAIV A(H5N8).

Kwon et al. (2017b) tested 50 fecal samples from wild birds collected from Jungnangcheon, a stream in the city of Seoul, South Korea, on 6 February 2015, for influenza virus. The mallard (*Anas platyrhynchos*), northern pintail (*Anas acuta*), common pochard (*Aythya ferina*), and tufted duck (*Aythya fuligula*) are typically found there in the winter season. One of the fecal samples, from a mallard, was positive for HPAIV A(H5N8) virus. Mallards may have been subclinically infected by this virus because no wild bird carcasses were found at the sampling site. This study indicates that wild birds in cities can carry HPAIV and may play a role in its introduction into urbanized areas.

There were two articles about wild or zoo birds related to the 2016/2017 outbreak. Kleyheeg et al. (2017) reported on wild bird mortality during a HPAIV A(H5N8) outbreak in the Netherlands, starting in November 2016. To quantify deaths among species groups with known susceptibility or that tested positive for A(H5N8) during the outbreak, they assembled daily mortality data from organizations gathering death reports or removing carcasses in the Netherlands during November 2016–January 2017. After potential double-counts were excluded as much as possible, ≈13,600 wild birds of 71 species were reported dead; 49% of all carcasses were identified by species, most of which were tufted duck (*Aythya fuligula* [39%]) and Eurasian wigeon (*Anas penelope* [37%]). Unidentified waterbird carcasses probably also mostly represented these species. A(H5N8) infection was confirmed in 21 species and not detected among the low numbers of sampled birds representing 13 other species. Because these data are based on numbers of reported carcasses, they provide an underestimation of actual deaths. Although carcass detection rates during daily searches at two outbreak locations (Gouwzee and Wolderwijd) were estimated to be 90%–95%, search efficiency was probably much lower at other outbreak hotspots. Collection rates of waterbird carcasses during typical avian botulism outbreaks are 10%–25%, suggesting that the number of carcasses reported during this A(H5N8) outbreak represented a limited proportion of total deaths. The elevated number of deaths among wild birds raises concern about potential population effects. After accounting for detection probability, they found that up to 5% of the wintering populations of tufted ducks and Eurasian wigeons in the Netherlands might have died. In addition, 2%–10% of the wintering population of great black-backed gulls (*Larus marinus*) and 11%–39% of the wintering population of peregrine falcons (*Falco peregrinus*) were similarly affected. Stronger effects were observed locally. At Gouwzee, ≈6,000 tufted ducks were counted in December after ≈2,000 of them had died in November. Assuming that no migration occurred, it was estimated that up to 25% of the local population of tufted ducks might have died, which might affect population dynamics substantially. These findings indicate that the 2016–2017 A(H5N8) outbreaks in the Netherlands were associated with unprecedented high HPAI-related mortality rates in a wide range of wild bird species. These latest A(H5N8) outbreaks have shifted the paradigm of wild birds as unaffected agents of HPAI

viruses, with increasing concerns about potential effects on their populations. The Netherlands and other important staging areas for migratory waterbirds across Eurasia that have been affected by the 2016–2017 A(H5N8) outbreaks are at risk for substantial numbers of bird deaths during future HPAI outbreaks.

Kleyheeg et al. (2017) also described clinical signs in wild birds thought to be infected with HPAIV A(H5N8). The most specific clinical signs for HPAIV infection were those consistent with neurologic disease. These included paralysis, writhing, rocking their bodies, twisting their heads, loss of balance, and swimming and walking in circles. Other clinical signs were less specific. They included severely weakened impression, apathy, unresponsiveness to threats like human approach or dog attack, retreat into shoreline vegetation, respiratory problems, blood or mucus coming out of the bill, moaning, diarrhoea, falling from the sky and dying within several seconds, and death without showing prior signs of illness or distress.

Kleyheeg et al. (2017) concluded that early HPAI virus detection in wild birds is crucial to contain outbreaks and minimize losses in the poultry sector, and made several recommendations to improve the documentation and management of future outbreaks in wild birds. Monitoring of wild bird deaths could be optimized by timely investigation at sites where migratory birds first arrive, especially when surrounding countries report outbreaks. Awareness of characteristic clinical signs of HPAI in wild birds (see above) would facilitate this effort. Detailed, real-time, active and passive surveillance during outbreaks would help to assess acute risk for infection in poultry. Such surveillance would benefit from central coordination of information exchange during outbreaks, which would also facilitate evaluation afterward. Management of HPAI virus outbreaks in wild birds would benefit from readily available specific guidelines, including protocols about how to handle carcasses (e.g., biosafety and disposal instructions) and what to report (e.g., species, number of birds, demographic parameters, and presence of leg bands), as well as from sufficient financial resources for adequate sampling and testing of specimens to rule out other diseases and to track virus dynamics during an outbreak.

Fusaro et al. (2017) diagnosed HPAIV H5N5 in a Eurasian wigeon (*Anas penelope*) and a gadwall (*Anas strepera*) found dead at Grado Lagoon in northeastern Italy during December 2016–January 2017. This suggests that these species can suffer fatal infection from this virus.

3.1.2. Genetic characterisation of the circulating viruses

The EURL analysed the sequence data availabale for over 380 viruses circulating in Europe from October 2016 to present November 2017 (unpublished results). In addition over 1000 viruses from both Europe and other geographic areas were included in analyses to assess risk to Europe. The HA gene are genetically very similar to each other, but distinguishable phylogenetically from the viruses detected in the Russian Federation in June 2016, and also from the A(H5N8) HPAI viruses present in the EU in 2014/15 (see Figure 1 in supporting information http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.5141/suppinfo/).

Figure 1 represent the maximum likelihood phylogenetic tree of the HA gene. Publically-available and additional sequences contributed by colleagues in Bulgaria and Cyprus from recent H5 HPAI detections were aligned using Mafft and phylogenetic relationships inferred using IQTREE. The maximum likelihood phylogenetic tree shows that the most recent isolates are genetically very similar to other 2017 A(H5N8) 2.3.4.4. viruses in Europe, to other strains from Hungary, and reflect continuing, mostly sporadic detections in both wild birds and poultry.

Co-circulation of LPAI and HPAI viruses in wild birds has led to multiple reassortment events, involving all gene segments with the exception of MP and NS. In particular, the NA gene segment derived from currently circulating LPAI viruses in wild birds has reassorted to result in A(H5N5), A(H5N6) and A(H5N8) subtypes infecting poultry. To date, however, there has not been detection of mammalian adaptation - associated mutations with these viruses still being assessed as having predominantly avian affinity. Although analyses suggest that owing to multiple reassortment events the epizootic H5 strains show significant genotypic variability across the genome, from currently available data, the HA still shows relatively little diversity, with currently circulating viruses closely associated with two separate introduction events in late 2016 and no subsequent statistically supportable evidence of geographic restriction of particular subclades or variants within the EU, except where there is evidence of lateral transmission amongst poultry.

Fusaro et al. (2017) described the introductions of multiple HPAI H5 viral genotypes, all belonging to clade 2.3.4.4, in northern Italy in December 2016-January 2017. Their results confirmed that these strains have a high propensity to reassort with co-circulating LPAI and HPAI viruses, causing the generation of several subtypes and genotypes with unique gene constellations. The genetic variability observed in the viruses identified in domestic birds, the similarity to viruses circulating in Europe and India, and the close proximity of the infected poultry holdings to wetlands all suggest that wild birds played a major role in the multiple and independent introductions of the virus into poultry holdings. Beerens et al. (2018) reported the fast and continued reassortment of HPAI A(H5N8) viruses isolated in the Netherlands in 2016. Both studies highlights the importance of generating complete viral genome sequences in a timely fashion, which may help to monitor the viral spread and define appropriate disease control strategies. This, coupled with intensified wild bird surveillance on wetlands of ecologic importance for avian influenza viruses, can improve our understanding of the virus dissemination routes and support early detection of viruses highly pathogenic to poultry or believed to be of immediate concern to human health.

All of the viruses isolated in Italy since July 2017 resulted belonging to the Poland-like group, previously indicated as present in Europe by Pohlman et al (2017). Poland-like viruses were also reported as circulating in Italy in January-May 2017 (Fusaro et al 2017), and the re-appearance in summer indicates its capacity to likely persist in non migratory wild birds and spread after the nesting period, with the dispersion of juveniles inviduals.

It should be noted that AI NRL's throughout Europe have varying capability to carry out both sequencing and subsequent analyses. During recent emergent virus events the EURL has worked with NRL's to use consistent and robust methods. However, through these collaborations it has become clear that variability in methodology, particularly in phylogenetics, can lead to incomplete, or at times misleading analyses. The EURL is positioned to offer substantive support and advice in these aspects. Robust consistent approaches for the genetic analyses of viruses and interpretation of data to inform decision making for control would be beneficial amongst EU providers.

Furthemore, given recent events, there is also a need for a more consistent approach to evaluating zoonotic risk based on molecular data, both in terms of the scientific methods used and in the subsequent communication of risk results.

3.1.3. Description of the AI-detections in time and space

3.1.3.1. HPAI A(H5N8) in poultry holdings and wild birds

Between 1 September and 15 November 2017, 48 HPAI A(H5N8) outbreaks were reported in poultry holdings and 9 wild bird events. These are presented in Table 1 and Figure 2 in relation to the 2016/2017 epidemics that took place across Europe.

Table 1: Number of H5 HPAI outbreaks by country from 1 September to 15 November 2017. The epizootic numbers from 19 October 2016 till 15 November 2017 are provided in parentheses

Country	H5N8			H5N5			H5N6	Total
	Poultry	Wild Birds	Captive Birds	Poultry	Wild Birds	Captive Birds	Poultry	
France	(485)	(51)	(3)	(0)	(0)	(0)	(0)	(539)
Hungary	(238)	(86)	(5)	(0)	(1)	(0)	(0)	(330)
Germany	(89)	1 (742)	(15)	(3)	(1)	(0)	(0)	1 (850)
Bulgaria	4 (75)	(13)	(2)	(0)	(0)	(0)	(0)	4 (90)
Italy	44 (79)	5 (13)	(0)	(0)	(1)	(0)	(0)	49 (93)
Poland	(65)	(66)	(0)	(0)	(2)	(0)	(0)	(133)
Romania	(45)	(93)	(2)	(0)	(0)	(0)	(0)	(140)
Czech Republic	(38)	(39)	(0)	(0)	(0)	(1)	(0)	(78)
United Kingdom	(12)	(23)	(0)	(0)	(0)	(0)	(0)	(35)

Spain	(10)	(2)	(0)	(0)	(0)	(0)	(0)	(12)
Croatia	(9)	(12)	(0)	(2)	(0)	(0)	(0)	(23)
Slovakia	(8)	(58)	(3)	(0)	(0)	(0)	(0)	(69)
Netherlands	(8)	(47)	(10)	(0)	(2)	(0)	(0)	(67)
Greece	(5)	(8)	(0)	(0)	(1)	(0)	(1)	(15)
Sweden	(4)	(30)	(2)	(0)	(0)	(0)	(0)	(36)
Republic of Serbia	(4)	(20)	(0)	(0)	(0)	(0)	(0)	(24)
Austria	(2)	(55)	(1)	(0)	(1)	(0)	(0)	(59)
Belgium	(2)	(3)	(13)	(0)	(0)	(0)	(0)	(18)
Ukraine	(2)	(3)	(1)	(0)	(0)	(0)	(0)	(6)
Denmark	(1)	(49)	(1)	(0)	(0)	(0)	(0)	(51)
Bosnia and Herzegovina	(1)	(1)	(1)	(0)	(0)	(0)	(0)	(3)
FYRO Macedonia	(1)	(1)	(0)	(0)	(0)	(0)	(0)	(2)
Switzerland	(0)	2 (94)	(0)	(0)	(0)	(0)	(0)	2 (94)
Slovenia	(0)	(41)	(0)	(0)	(3)	(0)	(0)	(44)
Finland	(0)	(16)	(1)	(0)	(0)	(0)	(0)	(17)
Ireland	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(10)
Lithuania	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(5)
Portugal	(0)	(1)	(0)	(0)	(0)	(0)	(0)	(1)
Cyprus	(0)	1 (1)	(0)	(0)	(0)	(0)	(0)	1 (1)
Luxembourg	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(4)
Montenegro	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)
Total	**48 (1 183)**	**9 (1 583)**	**(64)**	**(5)**	**(14)**	**(1)**	**(1)**	**57 (2 851)**
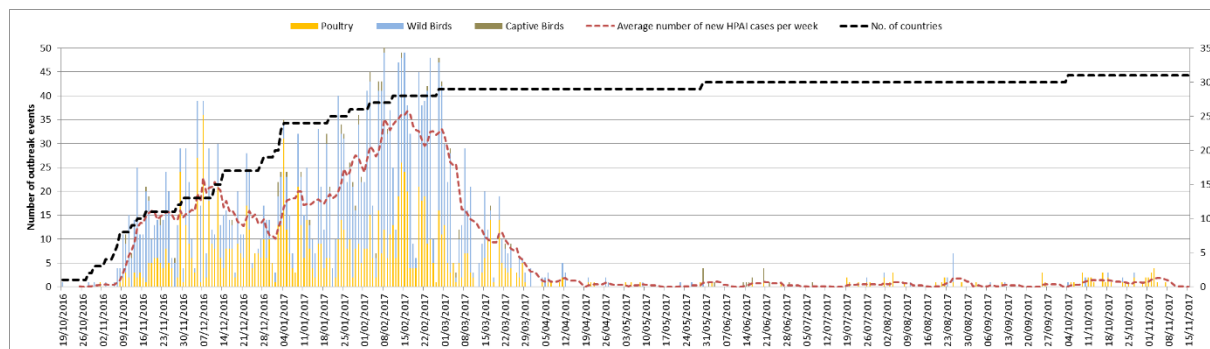
Figure 2: Number of H5 HPAI outbreaks from 19 October 2016 to 15 November 2017[5]

Italy has reported 44 new outbreaks of **HPAI** A(H5N8) in poultry holdings from 1 September to 15 November 2017 (Table 1 and Figure 3). Since 1 September 2017, detections of HPAI A(H5N8) have been reported for the first time in two new Italian provinces. One outbreak was reported in Roma province in a non-commercial holding of layer hens, while three detections were reported in the province of Piedmont; one in a commercial layer hen holding and two in wild birds. All remaining recent poultry outbreaks (detected 1 September to 15 November 2017) have been located within

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[5] Data presented in Figures 2, 3 and 4 do not include six poultry outbreaks occurred before 15 November in Italy that were reported by Italy to the ADNS sfter the date the data were downloaded from the ADNS for generating the figures

three regions where A(H5N8) outbreaks have previously occurred; Lombardy, Veneto and Emilia-Romagna. These northern regions are known to have a high density of poultry holdings (Turkeys).

Bulgaria has reported four new outbreaks in poultry between mid-October and early-November 2017: two in commercial duck holdings and two in non-commercial holdings (Figure 3).

Figure 3: Number of HPAI A(H5N8) detections of in poultry, captive and wild birds by date and country from 1 September 2017 to 15 November 2017[5]

Detections in wild birds

Between 1 September and 15 November 2017 detections of HPAI A(H5N8) in wild birds have been reported by four European countries (Table 1). On the 4 October 2017 a common buzzard (*Buteo buteo*) was found dead in Cyprus and submitted to Veterinary Services for AIV testing. A(H5N8) HPAI was confirmed on 23 October 2017. This was the first report of HPAI A(H5N8) in Cyprus. In Germany, HPAI A(H5N8) was confirmed in a free-living mallard (*Anas platyrhynchos*) on 18th October 2017 in Lower Saxony. In Italy four detections of HPAI A(H5N8) were reported in two mute swans (*Cygnus olor*), one greylag goose (*Anser anser*), and one event comprising both a rock pigeon (*Columba livia*) and a common kestrel (*Falco tinnunculus*). Two wild bird events were reported by Switzerland in September 2017 involving 2 mallards (*Anas platyrhynchos*) and 2 mute swans (*Cygnus olor*).

Timely exchange of HPAI detections in wild birds is very important to increase preparedness. The recent EFSA scientific opinion (2017) concluded that "passive surveillance is an appropriate method for HPAI surveillance in wild birds if the HPAI infections are associated with mortality" and suggested "identification of priority locations in the EU where targeted active wild bird surveillance could be implemented during wild bird migration periods". This principle could be applied at global level to monitor the AI situation.

HPAI A(H5N8) in Italy

The frequency of HPAI A(H5N8) detections in Italy have increased over the summer and autumn period (1 May to 15 November 2017) (Figure 4). Although the number of detections has fluctuated by month in 2017, there has been an increasing trend in the number of new HPAI A(H5N8) events in poultry and wild birds; May (2), June (none), July (6), August (13), September (7), October (27) and November (15). Reporting for the month of November is incomplete.
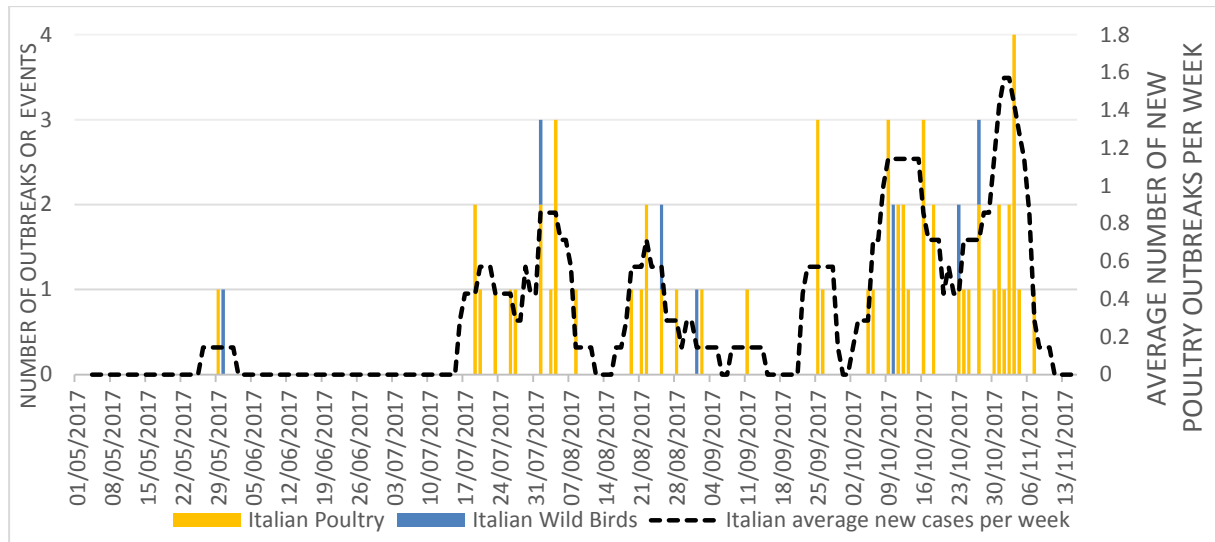
Figure 4: Number of A(H5N8) HPAI outbreaks in poultry and events in wild birds detected in Italy from 1 May 2017 to 15 November 2017[5]

3.1.3.2. LPAI in poultry holdings and wild birds

There have been seven detections of LPAI in Europe between 1 September 2017 and 15 November 2017, four in Italy in farmed anseriformes, one in France in a turkey breeder premises, one in the Netherlands in unidentified poultry, and one in captive birds in Germany (Figure 5).
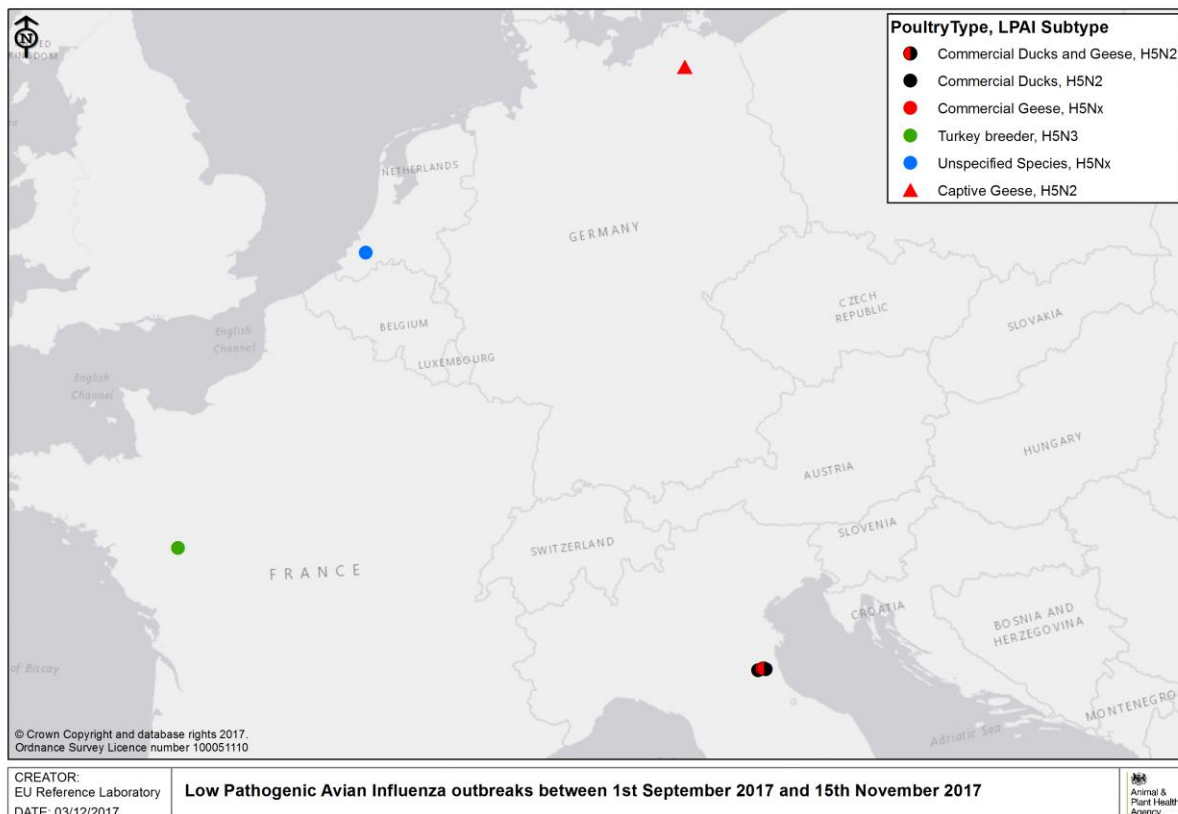
Figure 5: Map of detections of LPAI in Europe between 1 September 2017 and 15 November 2017

3.1.3.3. Target list of wild bird species for HPAI passive surveillance of H5 HPAI viruses in the EU

The list provided in Table 2 is produced as a guide to operators involved in passive wild bird surveillance for early warning of H5 HPAI in their region. The purpose of this list is to provide information on which bird species to focus in order to achieve the most effective testing of dead birds for detection of H5 HPAI viruses. It should be noted that the programmes within countries should be modulated according to demographics of local wild bird populations. Also, this list does not imply that only the carcasses of wild bird species on this list should be examined for H5 HPAI virus; the carcasses other wild bird species also should be examined, if there are reasons to do so.

The list is based on the data on the detection of H5 HPAI viruses in wild bird carcasses reported in the AI passive surveillance system by Member States between 2005 and 2017, excluding data from 2011 to 2013 where no epizootics occurred. Therefore data included are from the A(H5N1) HPAI outbreak starting in 2005, the A(H5N8) HPAI outbreak starting in 2014, and the A(H5Nx) HPAI outbreak starting in 2016. Overall, the list consists of wild bird species associated with an aquatic habitat, or wild bird species that prey on wild waterbirds or scavenge their carcasses. An exception is the fieldfare (*Turdus pilaris*). In principle, the list indicates which free-living wild bird species in the EU are more likely both to be exposed to H5 HPAI virus and to suffer a fatal infection. For this reason Muscovy duck (*Cairina moschata*) and Wood duck (*Aix sponsa*) that are exotic species only present as free-living population in a very few places in EU, were excluded. Some species were included, even if the high rate of positivity was from a single outbreak in one country, because it means that the species in question can be exposed to H5 HPAI virus in the field and can suffer fatal infection.

The list includes all species for which the rate of detection of H5 HPAI virus was 0.4% or greater; that is, a chance of at least 1 in 250 of being detected positive. Careful consideration has been given to the thresholds for inclusion and some species tested at in large numbers but with low rates of detection have been excluded. It may well be that these excluded species would be targeted for active surveillance, i.e., testing apparently healthy wild birds. However, the cut-off point of 0.4% is a pragmatic choice and may be changed up or down by MSs based on local conditions including number of reports of dead wild birds and available funding.

Table 2: Fifty wild bird species targeted for passive surveillance of H5 HPAI viruses in the EU. This list is based on data reported by Member States to the AI EU Reference Laboratory in the AI passive surveillance system between 2005 and 2017 (years 2011, 2012, 2013 excluded). Only those submissions that were identified to species and having a detection rate of 0.4 % or higher were included. The species are arranged in families (for the large family Anatidae also in subfamily, tribe or genus), and ordered according to the species with the highest detection rates

Family	Subfamily, tribe, or genus	Species	% positive (no. positive/no. tested)
Ducks, geese, and swans (Anatidae)	Diving ducks (Aythyini)	Tufted duck (*Aythya fuligula*)	33.4% (338/1011)
		Greater scaup (*Aythya marila*)	12.7% (9/71)
		Common pochard (*Aythya ferina*)	11.4% (26/228)
		Red-crested pochard (*Netta rufina*)	0.9% (1/112)
	Dabbling ducks (Anatinae)	Northern pintail (*Anas acuta*)	5.4% (3/56)
		Eurasian wigeon (*Anas penelope*)	3.7% (8/219)
		Gadwall (*Anas strepera*)	1.7% (3/179)
		Mallard (*Anas platyrhynchos*)	0.5% (96/20672)
		Eurasian teal (*Anas crecca*)	0.4% (5/1145)
	Sea ducks (Mergini)	Goosander (*Mergus merganser*)	6.4% (7/109)
		Common goldeneye (*Bucephala clangula*)	5.7% (3/53)
		Smew (*Mergus albellus*)	5.0% (1/20)
		Common eider (*Somateria mollissima*)	1.3% (3/228)
	Shelducks and sheldgeese (Tadorninae)	Common shelduck (*Tadorna tadorna*)	0.5% (1/218)
		Egyptian goose (*Alopochen aegyptiacus*)	0.4% (1/234)
	True geese (*Anser, Branta,*	Lesser white-fronted goose (*Anser erythropus*)	13% (3/23)

	Chen)	Greylag goose (*Anser anser*)	3.5% (68/1968)
		Taiga bean Goose (*Anser fabalis*)	2.8% (4/143)
		Canada goose (*Branta canadensis*)	1.8% (19/1061)
		Pink-footed goose (*Anser brachyrhynchus*)	1.3% (1/75)
		Brant goose (*Branta bernicla*)	1.2% (1/84)
		Greater white-fronted goose (*Anser albifrons*)	0.6% (2/350)
	Swans (*Cygnus*)	Black swan (*Cygnus atratus*)	9.5% (6/63)
		Whooper swan (*Cygnus cygnus*)	9.3% (169/1818)
		Mute swan (*Cygnus olor*)	7.6% (931/12268)
Grebes (Podicipedidae)		Black-necked grebe (*Podiceps nigricollis*)	79.9% (246/308)
		Great crested grebe (*Podiceps cristatus*)	8.5% (50/588)
		Little grebe (*Tachybaptus ruficollis*)	7.8% (6/77)
Storks (Ciconiidae)		White stork (Ciconia ciconia)	0.5% (5/911)
Herons (Ardeidae)		Eurasian bittern (*Botaurus stellaris*)	2.9% (1/35)
		Little egret (*Egretta garzetta*)	2.9% (2/69)
		Great white egret (*Egretta alba*)	0.9% (4/441)
		Grey heron (*Ardea cinerea*)	0.8% (40/5093)
Pelicans (Pelecanidae)		Dalmatian pelican (*Pelecanus crispus*)	27.5% (11/40)
		Great white pelican (*Pelecanus onocrotalus*)	9.5% (2/21)
Cormorants and shags (Phalacrocoracidae)		Great cormorant (*Phalacrocorax carbo*)	0.6% (12/2090)
Raptors (Accipitridae, Falconidae, Strigidae)		White-tailed eagle (*Haliaeetus albicilla*)	6.6% (28/426)
		Rough-legged buzzard (*Buteo lagopus*)	3.7% (1/27)
		Common buzzard (*Buteo buteo*)	1.1% (72/6307)
		Peregrine falcon (*Falco peregrinus*)	3.4% (10/297)
		Northern goshawk (*Accipiter gentilis*)	1.3% (8/616)
		Eurasian eagle-owl (*Bubo bubo*)	0.9% (3/340)
Coots, crakes, and rails (Rallidae)		Western swamphen (*Porphyrio porphyrio*)	6.7% (1/15)
Sandpipers (Scolopacidae)[b]		Green sandpiper (*Tringa ochropus*)	33.3% (1/3)
Gulls, terns, and allies (Laridae)		Great black-backed gull (*Larus marinus*)	13.8% (22/159)
		European herring gull (*Larus argentatus*)[a]	3.1% (66/2135)
		Mew gull (*Larus canus*)	0.8 (4/481)
		Black-headed gull (*Chroicocephalus ridibundus*)	0.7% (30/4075)
Corvids (Corvidae)		Eurasian magpie (*Pica pica*)	0.6% (7/1232)
Thrushes (Turdidae)		Fieldfare (*Turdus pilaris*)	0.5% (1/192)

(a) This does not include the Caspian gull (Larus cachinnans) or the yellow-legged gull (Larus michahellis), which are considered separate species.
(b) Another wader, Numenius species was not included in this list because it was not identified to species. However, in the EU, the two most likely Numenius species are the Eurasian curlew (N. arquata) and the whimbrel (N. phaeopus).

3.1.3.4. Human cases

No transmission of influenza virus A(H5N8) to a human has been observed in Europe or world-wide. As stated in 3.1.2. molecular data do not indicate a pattern associated with increased risk of transmission to humans. However, the high frequency of reassortment events related to the clade 2.3.4.4 A(H5N8) viruses might pose a risk for A(H5N8) viruses to acquire features for increased transmission to humans (Beerens et al., 2017; Fusaro et al., 2017; Pohlmann et al., 2017).

3.1.4. Characterisation of the HPAI A(H5N8)-affected poultry holdings in Italy (from July to November 2017)

Italy was the most affected MS during the summer and autumn (July-November 2017), therefore this section of the report is focussed on the characterisation of the affected Italian holdings and the lateral spread in the northern Italian regions.

A more detailed characterization of the HPAI A(H5N8) outbreaks in poultry holdings reported by Italy in ADNS between 1 July and 15 November 2017 was done based on additional data provided by the

Italian authorities. There were no cases reported in captive birds or any zoo in this period. The holding was considered to be the epidemiological unit since the implemented biosecurity measures did not guarantee a complete separation at house level.

The additional data (in the following referred to as "EFSA data collection") were obtained by means of a data model designed building on the experience of the HPAI A(H5N8) outbreaks in 2016-2017 (EFSA and ECDC, 2014). A compromise between rapid action and solidity of the data collection methodology had to be found. Italy received an Excel file, pre-filled with ADNS information, with the aim of collecting potentially useful epidemiological information (see Appendix A and section 2.1.1). The data model has been discussed with the Italian representatives, clarifying definitions to obtain the best possible data quality.

It has to be pointed out that the dataset does not include any information related to negative samples and this makes it often impossible to draw firm conclusions. In fact, in order to determine if a feature poses a higher risk to a given holding or species, the reference to the entire population and therefore to the negative cases, is unavoidable: alternatively, a denominator for all these figures should be available to be able to perform a retrospective case-control study and estimate the Odds Ratios, as a proxy for the relative risk for possible risk factors. EFSA will continue discussing this topic with the MSs to find a step-wise approach to exchange relevant (denominator) data without putting an additional burden.

From 1 July to 15 November 2017 a total of 63 HPAI A(H5N8) outbreaks occurred in the Italian poultry holdings (Figure 6**: Map of detections of A(H5N8) HPAI in poultry in Italy by holding species between 1 July and 15 November 2017**Figure 6). A diverse range of poultry holding types have been affected over this time period (Figure 7), with detections most commonly reported in fattening turkeys (n=29), followed by laying hens (n=12), holdings with mixed species and production (n=7), broilers (n=5), fattening ducks (n=4) and geese (n=2), mixed production of chicken (n=1) and ducks (n=1), fattening mixed species (n=1) and breeding chicken (n=1).
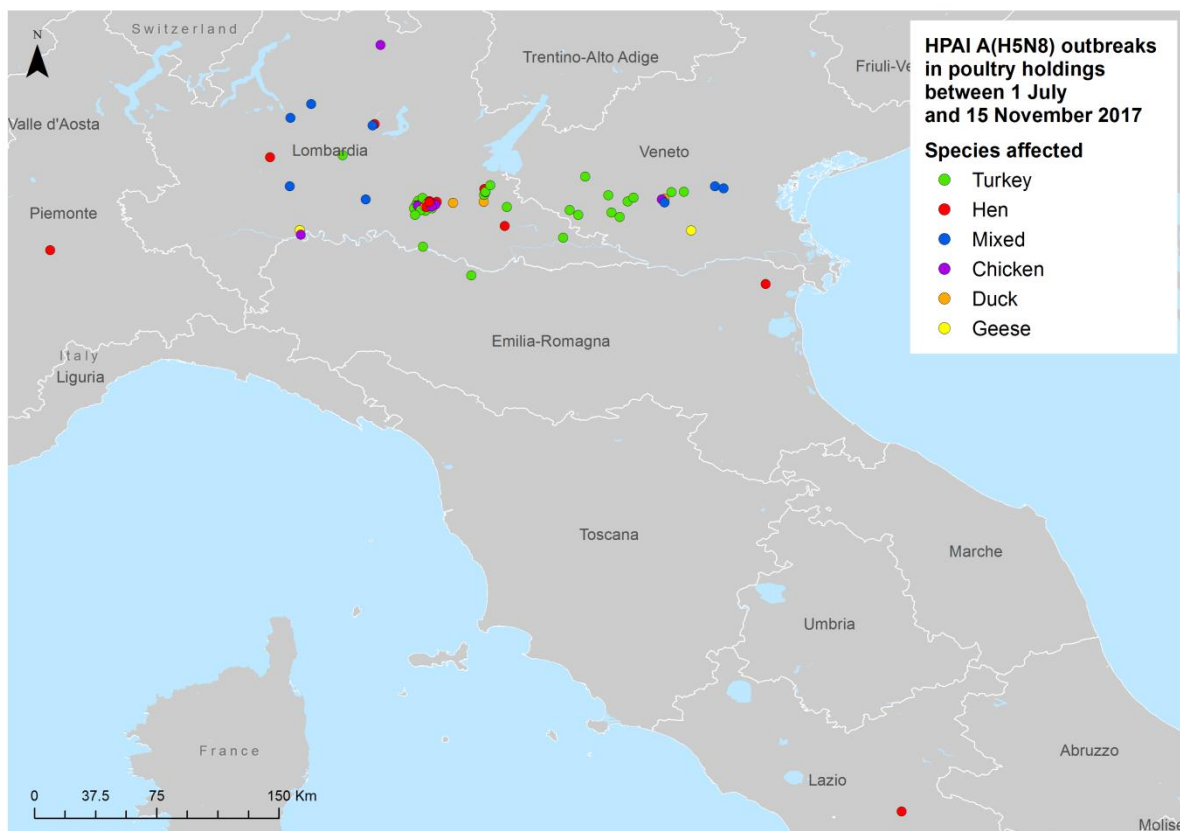

Figure 6: Map of detections of A(H5N8) HPAI in poultry in Italy by holding species between 1 July and 15 November 2017
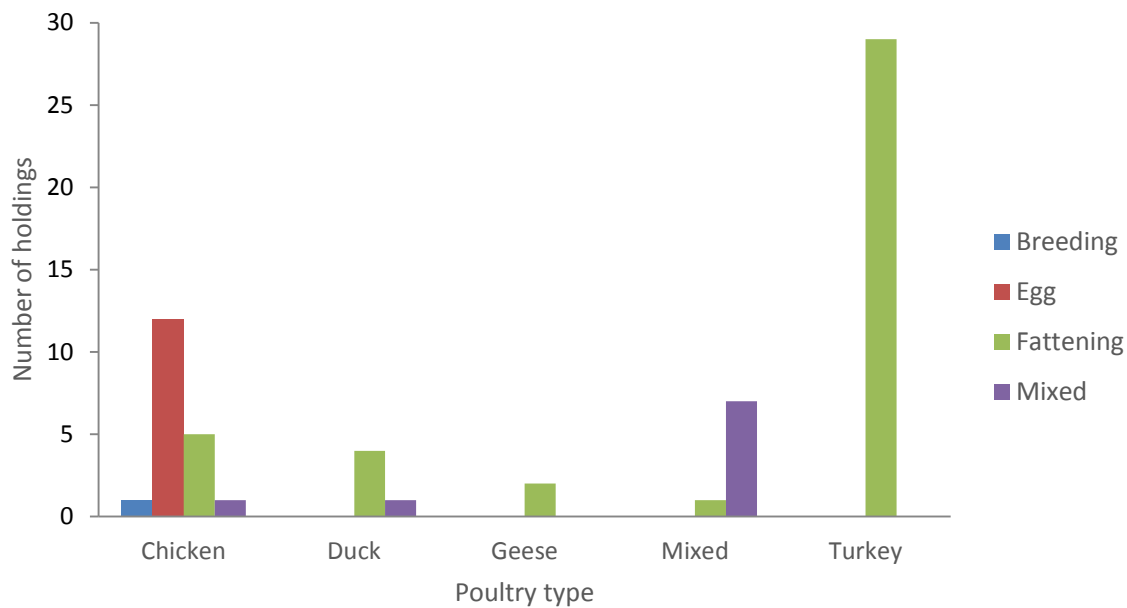
Figure 7: Number of HPAI A(H5N8) affected holdings by poultry species and production type in Italy from 1 July to 15 November 2017 (n=63)

3.1.4.1. Size of affected commercial and non-commercial holdings

The size of the affected holdings was analysed using the number of susceptible birds reported in ADNS. The analysis was performed for both holding production categories, commercial (n=50) versus non-commercial (n=13), using the definitions used in the EU legislation[6]. Figure 8 and Figure 9 show that all 50 affected **commercial holdings** have more than 1,000 susceptible birds on its premises, whereas 12 of the 13 (92%) affected **non-commercial holdings** has less than 200 birds (even with 9 (69%) having 50 or less birds). These data confirm the difference in size between affected commercial and non-commercial holdings. One affected commercial holding had three game bird species on its premises (clinical signs in pheasants but not in partridges and mallards) but all other affected commercial holdings had only one bird species. Around half of the affected non-commercial holdings (n=7) had more than one bird species.

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[6] 'commercial poultry holding' means a holding where poultry are kept for commercial purposes; 'non-commercial holding' means a holding where poultry or other captive birds are kept by their owners: (a) for their own consumption or use; or (b) as pets (Council Directive 2005/94/EC of 20 December 2005 on Community measures for the control of avian influenza and repealing Directive 92/40/EEC (OJ L 10, 14.1.2006, p. 16))
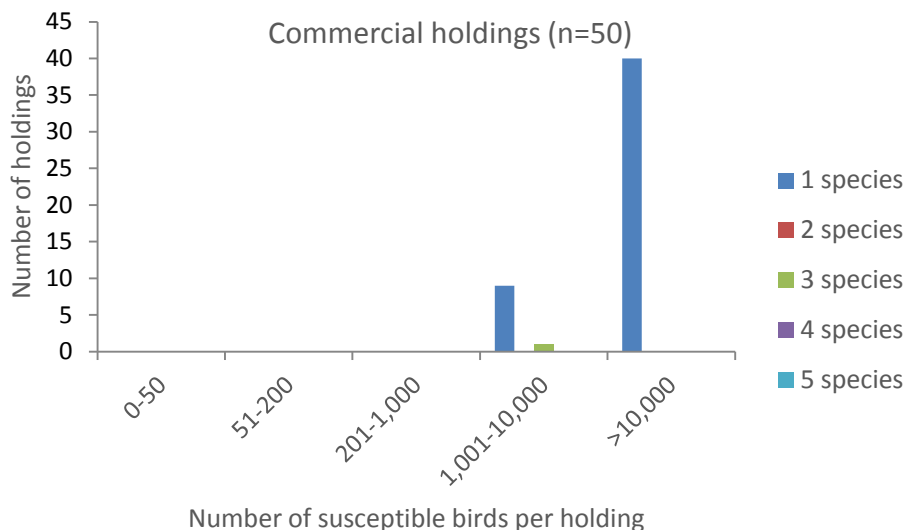
Figure 8: Number of HPAI A(H5N8) affected commercial holdings by class of number of susceptible birds per holding and by number of species bred per holding, in Italy from 1 July to 15 November 2017
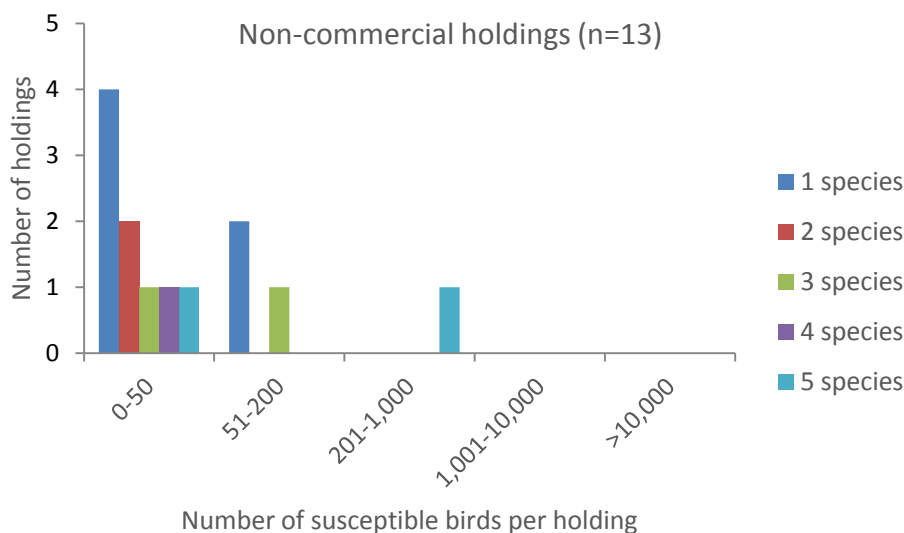
Figure 9: Number of HPAI A(H5N8) affected non-commercial holdings by class of number of susceptible birds and by number of species bred per holding, in Italy from 1 July to 15 November 2017

3.1.4.2.   Secondary HPAI H5 outbreaks (from July to November 2017)

Submission of information on secondary outbreaks

Among 63 outbreaks occurred in Italy between 19 July and 15 November, 31 were identified as secondary[7], which related to only four primary outbreaks that mainly occurred after the first week of October 2017 (Annex A). Three of these clusters were very limited and involved a maximum of four secondary outbreaks. In the fourth outbreak, the lateral spread has led to a larger cluster which is still ongoing as of 15 November 2017.

The first cluster was observed in relation to a large laying hen facility, hosting about 450,000 birds. The primary outbreak was confirmed on 21 July, at the time of confirmation two meat turkey holdings

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[7] 'Secondary outbreak' means an outbreak not epidemiologically linked with a previous outbreak in the same region of a Member State

were indicated as candidates for preventive slaughtering. Nevertheless, due to the number of poultry in the farm, and to extreme weather conditions (with temperatures higher than 40°C for prolonged time, with consequential increase in natural death of birds during the heat wave, in many Italian regions and the subsequent saturation of the rendering premises), it took 15 days to conclude the culling measures. In the mean time, four fattening turkey holdings in the Protection Zone of the outbreak, were confirmed as infected with HPAI A(H5N8) virus. No evident contacts were identified, however, the close proximity to the infected laying hen farm, and the results of phylogenetic analyses (which indicated genetic similarities between 99.2 and 99.5%) lead the conclusion that the four turkey holdings were to be considered as secondary outbreaks.

The cluster in Vicenza province (Veneto region) included only two secondary outbreaks, one related to proximity (less than 1 km) and the second one likely due to risk contacts with a non-commercial holding that introduced birds from the infected holding in the same municipality.

Later on, in October 2017, secondary spread was detected in relation to a live bird market (LBM) in the Bergamo province. The LBM was held outside the further restricted zone[8] (FRZ), so no restrictions were enforved on exhibitions and gathering of rural/backyard flocks. The cluster in the Bergamo province indicated also the first noteworthy spread to the rural/backyard sector, which raised concern as it could have represented a potential source of maintenance of the virus in non-commercial holdings. Nevertheless, only 4 secondary outbreaks were detected in non-commercial flocks, after which the spread to other non-commercial holdings seemed to have faded out.

The most important cluster of secondary-outbreaksis the one still ongoing as of November 15 in the Brescia province (Lombardy region). In this case contact tracing indicated potential spread via sharing of vehicles. The compartmentalisation measures applied in the Lombardy region, while they achieved limiting/avoiding the spread of the disease to adjoining regions, were probably related to the circulation of the virus in the Brescia province. Functional separation of Lombardy from the adjoining regions requires that vehicles for feed and animal movements cannot be used in other regions.However, due to the shortage of lorries for feed distribution, vehicles were shared among farms, including also holdings rearing different species/production types.

When considering the total number of outbreaks which occurred between July and November 2017 in Italy (n=63), it is evident that secondary cases represent a high proportion of the total outbreaks (n=31, 49.21%). The proportion is even more striking when accounting for the industrial poultry sector alone, with 50 total outbreaks out of which 26 were secondary outbreaks (52%). Of these 26 outbreaks, 80.77% (n=21) are represented by secondary outbreaks detected in the Brescia province from the second half of October) (Annex A, Figure 3). The secondary spread between July and November is very similar to what was observed in the large HPAI epidemic of 1999-2000, and in the 2002-2003 LPAI epidemic in the same area in Italy. In fact, when looking at the first epidemic wave (January – May 2017) and the first part of the second wave (July – September 2017), the number of weekly outbreaks was lower, and more temporally separated than those observed since October 2017, suggesting multiple point-introductions from infected wild-birds, while the large numbers of weekly outbreaks since October are more typical of a *classic* epidemic of infectious diseases in domestic birds.

3.1.4.3. Sampling strategy leading to outbreak detection at holding level

Italy was asked to report the context of the sampling which resulted in detection of the outbreak by selecting the most relevant category out of the following three options:
- 'Active surveillance': background screening of apparently healthy populations;
- 'Passive surveillance': notifications of disease suspicion;
- 'Outbreak related surveillance': as part of outbreak response i.e. control zones, tracings.

Data on both the undertaken type of surveillance linked to the first positive case of the outbreaks and the species were received from all the 63 affected holdings (Figure 10). Infection was detected via passive surveillance in 47 (75%) of the holdings, whereas outbreak-related surveillance and active surveillance revealed infection in 15 (24%) and 1 (1%) of the reported houses, respectively. When

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[8] 'the further restricted zones' are zones around or adjacent to the protection and surveillance zones as provided for in Article 16(4) of Council Directive 2005/94/EC of 20 December 2005 on Community measures for the control of avian influenza and repealing Directive 92/40/EEC. OJ L 10, 14.1.2006, p. 16–65.

analysing the data at species level, it can be observed that **passive surveillance** is the category that records the highest number of detection (positive samples) in basically all the species.
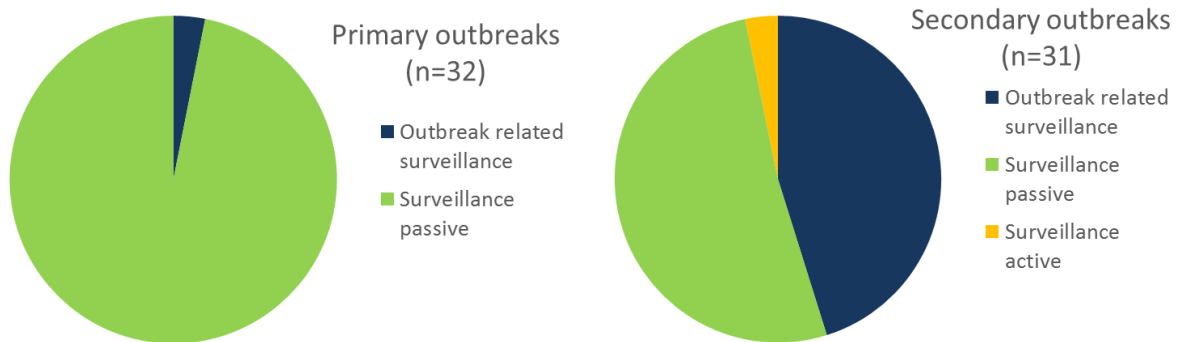

Figure 10: Number of HPAI A(H5N8) primary and secondary outbreaks by sampling strategy leading to outbreak detection in Italy from 1 July to 15 November 2017

3.1.4.4. Signs observed at species level

Italy was requested to report the sign(s) observed in the outbreaks by indicating 'yes' or 'no' for increased mortality, clinical signs, drop in feed and/or water intake, drop in egg production, and other non-clinical indicators (which can be any sign that is not covered by the four specific options listed, for instance serology, link with another outbreak, etc.) by species present, compared to a normal situation. More than one signs might be observed in the species at holding level, therefore more than one parameter could have been indicated when collecting the data.

For the only affected holding identified by active surveillance none of the above parameters were reported, whereas the observations from outbreaks identified by passive surveillance and outbreak related surveillance are reported in Figure 11 and Figure 12, respectively.

Increased mortality was the most reported observation of HPAI A(H5N8) infections in chickens, ducks, geese and turkeys. Also **clinical signs** were observed in many affected holdings at the moment of outbreak detection, ranging from 4% to 50% depending on the species. **Drops in feed and/or water intake** were reported only in few outbreaks.

A **drop in egg** production was reported in 1 out of 15 affected holdings with hens.

Other non-clinical signs[9], such as serology or links with other outbreaks, were not reported.

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[9] it can be everything that is not covered by 'increased mortality', 'presence of clinical signs', 'drop in egg production' or 'drop in feed and/or water intake'
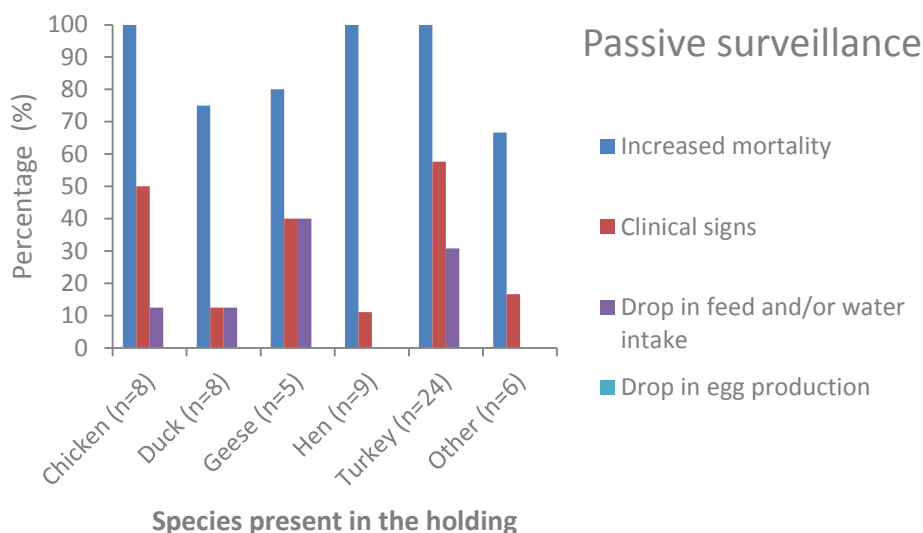
Figure 11: Percentage of signs observed by species identified to be infected with HPAI A(H5N8) by passive surveillance in Italy from 1 July till 15 November 2017 (more than one species might be present in a holding and more than one parameter might be indicated per species)
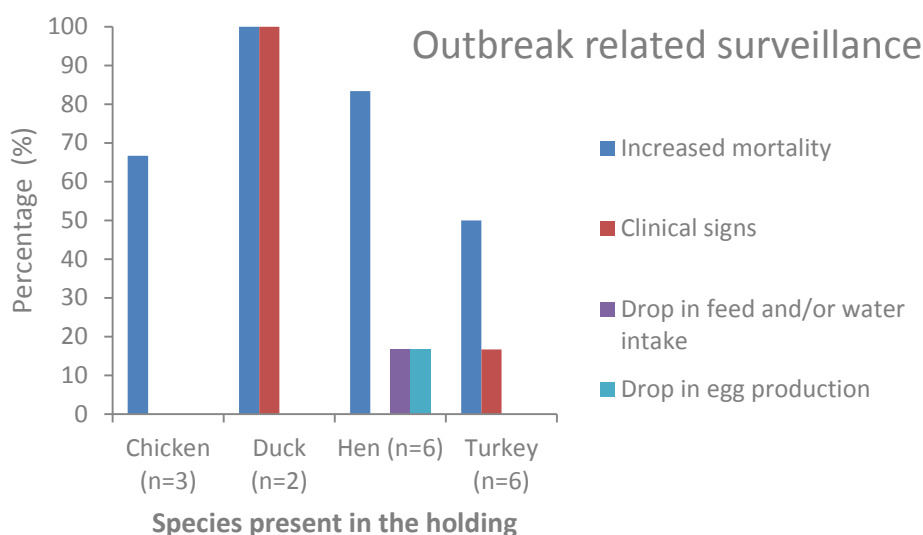
Figure 12: Percentage of signs observed by species identified to be infected with HPAI A(H5N8) by outbreak related surveillance in Italy from 1 July till 15 November 2017 (more than one species might be present in a holding and more than one parameter might be indicated per species)

3.1.4.5. Outdoor access of poultry in affected holdings

Italy reported if the domestic birds had outdoor access in the 21 days before the outbreak by selecting whole day, part of the day, no outdoor access or unknown. A time period was specified in the question to take the implementation of housing orders into account as it would change the outdoor access of domestic birds. Analysing outdoor access has been done in relation to (i) the number of susceptible birds present on the affected holding and (ii) the holding production category (commercial versus non-commercial).

All 63 HPAI A(H5N8) affected holdings reported information about outdoor access (Figure 13). Only 1 out of 50 **affected commercial holding** (breeding mallards, partridges and pheasants) had part of the day outdoor access whereas the 49 others had no outdoor access. All the **affected non-**

commercial holdings had outdoor access for at least part of the day. On two non-commercial holdings, outdoor access was part of the day or the whole day depending on the species.
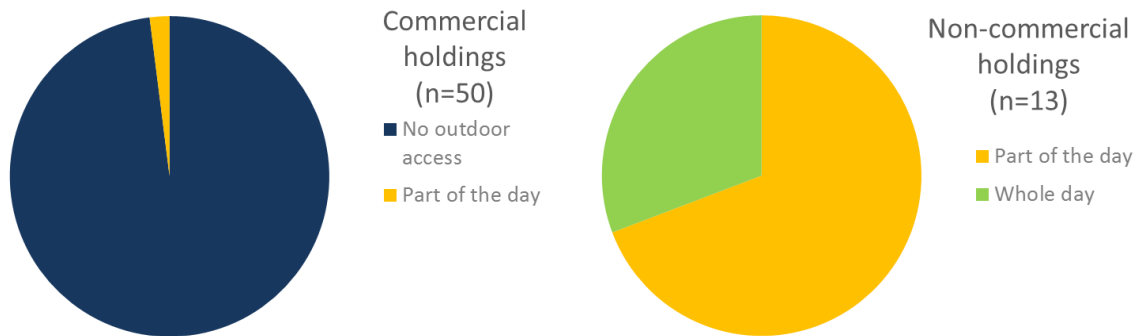
Figure 13: Information on outdoor access of birds in HPAI A(H5N8) affected commercial and non-commercial holdings in Italy from 1 July 2017 till 10 November 2017

3.1.4.6.   Most likely source of indirect virus introduction

Italy reported the most likely source of the virus based on the epidemiological investigation. One of the following options could be selected:
- Direct wild birds: direct contact with wild birds or their secretions.
- Indirect wild birds: transfer of wild bird faeces into the premises by personnel, equipment, vehicles, feed/bedding.
- Direct poultry: movement of infected poultry onto premises.
- Indirect poultry: transfer of poultry faeces/products from another infected premises by personnel, equipment, vehicles, feed/bedding.

For all the primary outbreaks indirect contact with wild birds has been identified as the only most likely source of infection, whereas for secondary outbreaks the most likely source of virus introduction was direct or indirect contact with poultry (Figure 14). More information on the secondary outbreaks and the available evidence underpinning the most likely source of virus introduction is provided in section 3.1.4.2 and Annex A.
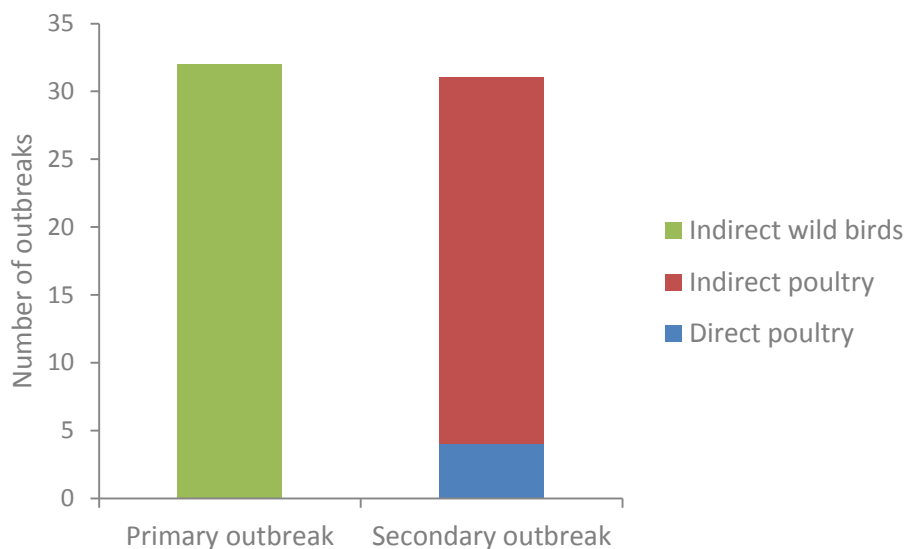
Figure 14: Number of HPAI A(H5N8) primary and secondary outbreaks by sampling strategy leading to outbreak detection in Italy from 1 July to 15 November 2017 (n=63)

3.2. Applied prevention and control measures (TOR3)

3.2.1. In Italy

Italy has been the most largely affected MS in the period of reference (July-November 2017), hence the description of control measures will focus on the Italian situation only. A detailed description of control and prevention measures is provided in Annex B; here only the most important measures are reported.

Biosecurity measures enforced during the second HPAI epidemic wave in Italy (July 2017 till present) were already provided for in the Ministerial Decree of 30 March 2017. The Provision indicated the criteria to define high-risk areas which would be subjected to more severe measures including:

- housing order,
- ban on using superficial water supplies,
- ban on using live-decoy birds, and on rearing them in conditions that could put the reared birds in close contact with wild birds,
- need to stock bedding materials and feed, protected from wild birds or other animals.

Criteria for defining high-risk areas included the same factors already accounted for in National Risk Based Surveillance plan for Avian Influenza, which represent risk factors for the introduction and spread of disease:

- proximity to wetlands that are used as wintering/nesting sites for migratory/residential birds,
- wild water bird population density,
- density of poultry farms, weighted by the susceptibility of reared species (i.e. higher susceptibility of turkeys, and laying hens with respect to short-lived production types as broilers),
- history of Avian Influenza outbreaks in the past,
- current epidemiological situation,
- results of the past Surveillance plans (potentially indicating circulation of AI viruses).

Also measures for early detection/warning were included in the Ministerial provision of 30 March 2017, indicating the need to promptly (and mandatorily) report any productive or sanitary changes observed in farms:

- decrease in feed and/or water consumption,
- decreased production of eggs,
- clinical signs,
- increased mortality rate.

A FRZ was designed outside of the Protection and Surveillance Zones of the outbreaks (see Annex B). The extension of the FRZ was varied in accordance to the epidemiological situation and the risk of spreading to the Densely Populated Poultry Area. A first FRZ was proposed, for the second epidemic wave in Italy, on 28 July 2017, eight days after the confirmation of the first outbreak in July. Measures applied in the FRZ included:

- request of keeping birds inside closed buildings,
- measures to reduce the risk of direct/indirect contacts with wild birds,
- enforcement of increased biosecurity measures regarding vehicles and personnel entering and exiting farms,
- ban on exhibitions, fairs, and live bird markets,
- pre-movement clinical inspection and virological testing of birds,
- ban on restocking fattening turkey farms,
- ban on releasing game for hunting.

A waiver on the ban on restocking meat-type turkey could be obtained, only after authorization by an official veterinarian. The evaluation included: compliance to high biosecurity standards (assessed by using a pre-defined checklist that collected information on structural and managerial biosecurity measures); and assessment of the geographical risk, which accounted for the poultry density in the area, and the proximity to other poultry premises.

Additional control measures included differentiated protocols of tests to be performed for moving birds from holdings within the FRZ. Furthermore, strict functional separation was required between the affected regions (Lombardy, Veneto, Piedmont, Emilia-Romagna). This meant that personnel and vehicles operating in a region, could not be used in different regions, allowing the spread of the disease via direct and indirect contacts among farms.

3.2.2. In a zoo

Globig et al. (2017) provide a reminder that there are exceptions to the requirement of culling all birds of a holding where HPAI has been confirmed. The holding in question was the zoo of Rostock, Mecklenburg-Western Pomerania, Germany, where zoo birds were found infected with HPAIV A(H5N8). Suspicion of HPAI was based on clinical signs in a few white storks (*Ciconia ciconia*) at the zoo. Subsequent in-depth diagnostic investigation showed that other birds kept in the same compound as the white storks were or had been infected with HPAIV A(H5N8), and the birds from this compound were culled. However, an exception from culling the 500 remaining zoo birds was granted by the competent authority in order to preserve as large of a fraction of the avian zoo collection as possible. A risk assessment was perfomed, the remaining zoo birds were grouped into eight epidemiological units avoiding contact with the possible source of infection, and 60 birds of each unit were tested repeatedly for HPAIV. All eight units were sampled consecutively three times with negative results. Therefore, the exemption from obligatory culling of all birds proved useful in this case.

3.3. AI situation in other continents between 1 September and 15 November 2017 (TOR4)

3.3.1. HPAI A(H5N1)

3.3.1.1. Domestic and wild birds

Detections

Outbreaks of the Asian lineage HPAI A(H5N1) in poultry have been observed in several African countries, the Middle East and Asia throughout the year 2017. Bangladesh and Nepal informed about two events in wild birds in early 2017. Between 1 September and 15 November 2017, several oubreaks of HPAIV A(H5N1) in non-commercial poultry were reported from Kelantan province in Malaysia (see Figure 15).
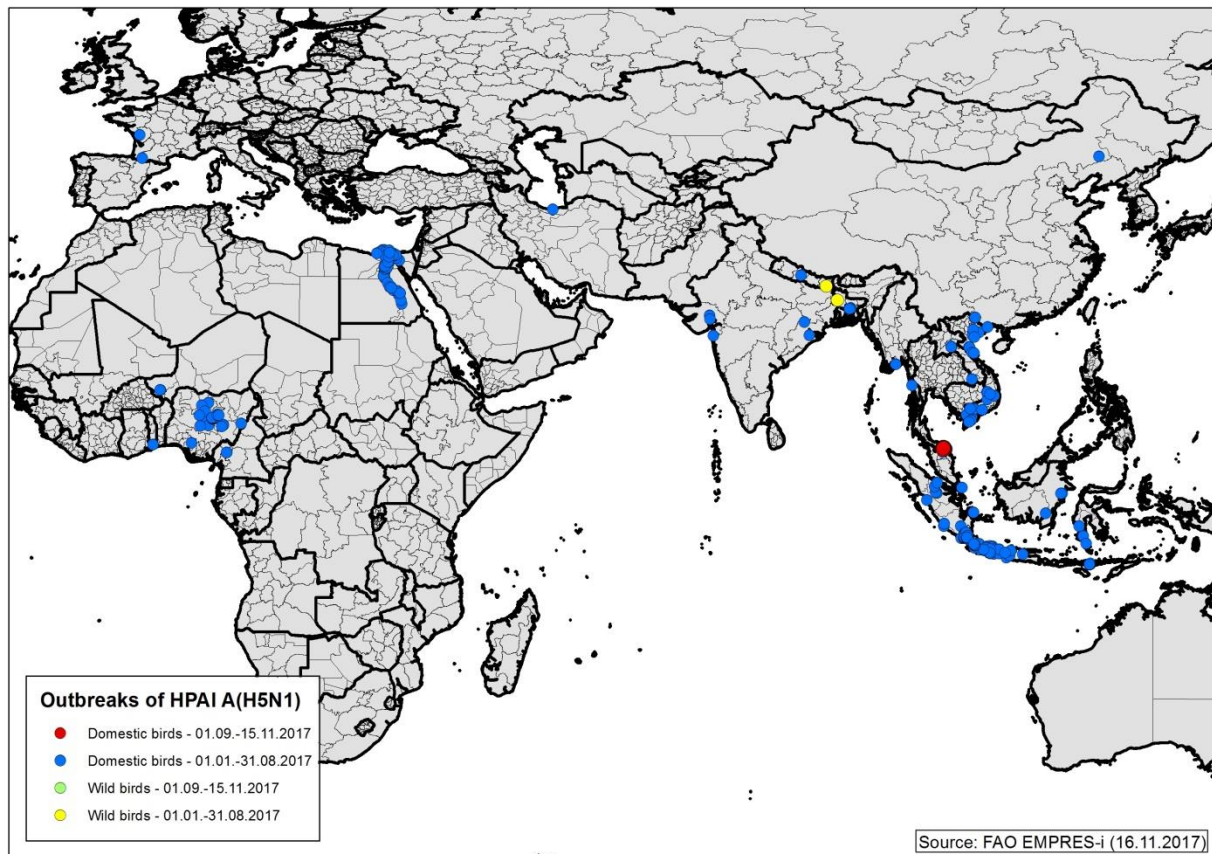
Figure 15: Distribution of confirmed HPAI A(H5N1) outbreaks in birds by place of reporting between 1 January and 15 November 2017 (data source: Food and Agriculture Organization (FAO) EMPRES-i; status: 16.11.2017)

Phenotypic characterisation

HPAIV of the A(H5N1) subtype responsible for the ongoing outbreaks worldwide continue to exhibit high pathogenicity for gallinaceous poultry and moderate to low pathogenicity for waterfowl (Azab et al., 2017, Liu et al., 2016) . Comparative assessment of pathogenicity of A(H5N1) HPAIV belonging to clades 2.3.2.1b, 2.3.2.1c, 2.3.4 and 2.3.4.1 for mallards provided evidence for efficient infection, with varied clinical course: relatively mild for 2.3.4 and lethal for 2.3.2.1b (Ducatez et al., 2017). Mandarin ducks (*Aix galericulata*) inoculated with clade 2.3.2.1 A(H5N1) isolated in South Korea in 2010 remained healthy throughout the experiment and shedding of the virus was minimal (Kang et al., 2017). Infection of ferrets with selected avian-derived A(H5N1) isolates of clade 2.3.2.1 b and 2.3.2.1 c led to severe disease, systemic replication and death (Pearce et al., 2017).

Genetic characterisation

Since the first detection of Gs/Gd/96 'Guangdong' lineage of A(H5N1) HPAIV in 1996, the HA of the virus has undergone an extensive evolution with the continuous emergence (and disappearance) of multiple genetic clades. The following clades were detected between 2013 and 2017 (Smith et al., 2015; Liu et al., 2016; Marinova-Petkova et al., 2016a; Bhat et al., 2017; El Romeh et al., 2017; Ghafouri et al., 2017a; Rashid et al., 2017; Salaheldin et al., 2017; Shittu et al., 2017):

- 2.1.3.2a (Indonesia)
- 2.2.1.1 (Egypt)
- 2.2.1.2 (Egypt)
- 2.2.1.2a (Egypt, Israel and Occupied Palestinian Territories)
- 2.3.2.1.a (Bangladesh, India)
- 2.3.2.1.b (China and Hong Kong SAR)

- 2.3.2.1.c (Cambodia, China, Laos, Indonesia, India, Vietnam, Iraq, Iran, Lebanon, Nigeria, Burkina Faso, Niger, Ghana, Ivory Coast, Romania and Bulgaria)

- 7.2 (China).

The A(H5N1) HPAIV virus that was detected in North America in December 2014 should be treated separately as it was a reassortant that contained the HA of the Gs/Gd/96 lineage (clade 2.3.4.4), but four segments (including NA) from the North American lineage LPAIV (Torchetti et al., 2015).

A separate event was also associated with the emergent A(H5N1) virus from France (2015/2016) that turned out to belong to the European avian lineage and was clearly distinguishable genetically from the Gs/Gd/96-like lineage (Briand et al., 2017).

Intraclade and interclade reassortants of Gs/Gd/96-like A(H5N1) have been described (Marinova-Petkova et al., 2016a). Recently, a novel genotype containing HA, NA and M genes from the A(H5N1) clade 2.3.2.1a and the remaining genes of the Eurasian-origin LPAIV has been described in Bangladesh (Barman et al., 2017). There is also evidence of the intersubtype reassortments (including A(H5N1)/A(H9N2)) of clades 2.3.2.1a (Marinova-Petkova et al., 2016b) or 7.2 (Liu et al., 2016). The analysis of the whole-genome sequences from the (A)H5N1 virus clade 2.3.2.1c detected in poultry in Nigeria in 2014-2016 showed the dynamic nature of the epidemic in this country, demonstrated by the emergence and co-circulation of different genotypes (Laleye et al., 2017).

A(H5N1) viruses circulating worldwide continue to exhibit markers for increased zoonotic potential (Arafa et al., 2015) but so far no definite mutations have occurred that would enable sustained human-to-human transmission. The receptor-binding site of the HA in the A(H5N1) virus from France (2015/2016) was 'avian-like' and no major host adaptation or transmission markers indicative of the increased affinity to mammalian species were found (Briand et al., 2017).

3.3.1.2. Human infections due to A(H5N1)

Human infections with influenza A(H5) viruses have been caused by influenza A(H5N1) virus in several non-EU/EEA countries.

Since 2003 and as of 4 December 2017, 860 laboratory-confirmed cases of human infection with avian influenza A(H5N1) virus (Figure 16), including 454 deaths, have been reported from 16 countries (World Health Organization (WHO), 2017a). The latest case was reported in September 2017 by Indonesia. This was the first case reported in Indonesia since 2014 (WHO, 2017b).
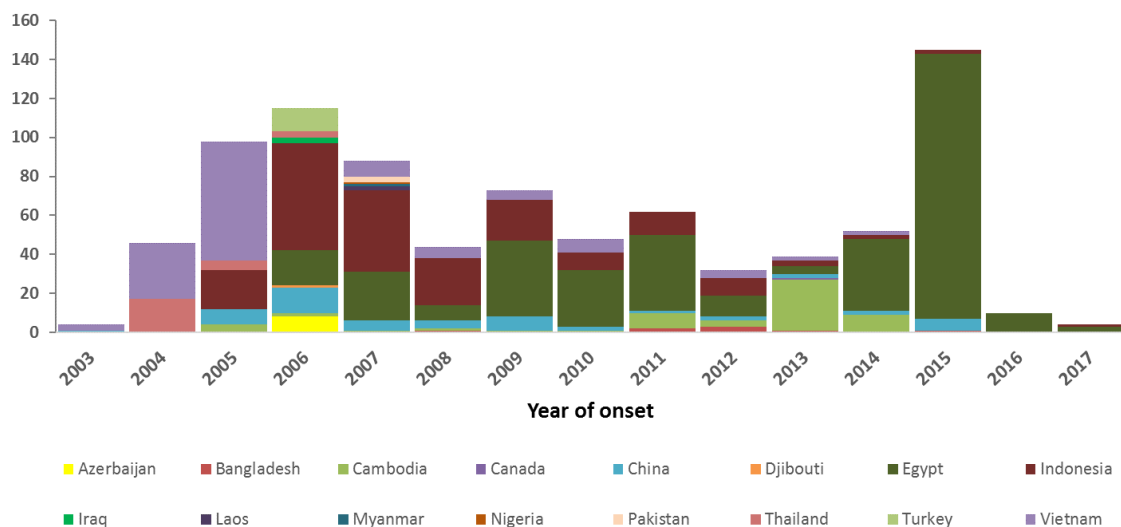
Figure 16: Distribution of confirmed human cases of A(H5N1) by country of reporting 2003 – 2017 (n=860)

3.3.2. HPAI A(H5N6)

3.3.2.1. Domestic and wild birds

Detections

The novel reassortant H5N6 HPAIV (clade 2.3.4.4c) was detected in domestic birds in China, Japan, Myanmar, the Philippines, Taiwan and Vietnam in 2017, but most of the outbreaks were reported from the Republic of South Korea. In the relevant time period for this report, China and Vietnam confirmed outbreaks of A(H5N6) HPAIV in large poultry holdings in September and October 2017 (see Figure 17). The detections in wild birds were largely confined to Japan including cases in black-headed gulls (*Chroicocephalus ridibundus*), tufted ducks (*Aythya fuligula*) and mute swans of November 2017 in Simane province (see Figure 18).
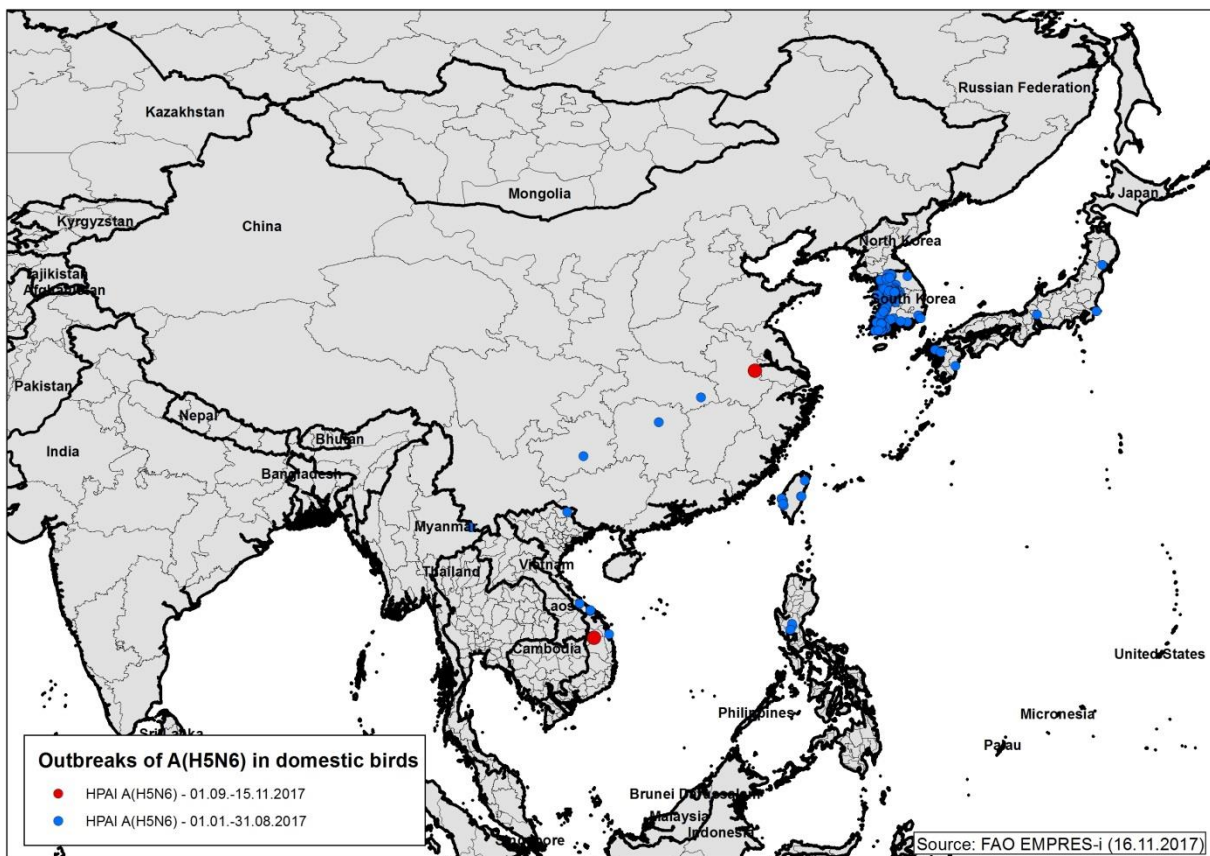
Figure 17: Outbreaks of A(H5N6) HPAIV in domestic birds between 1 January and 15 November 2017 (data source: FAO EMPRES-i; status: 16.11.2017)
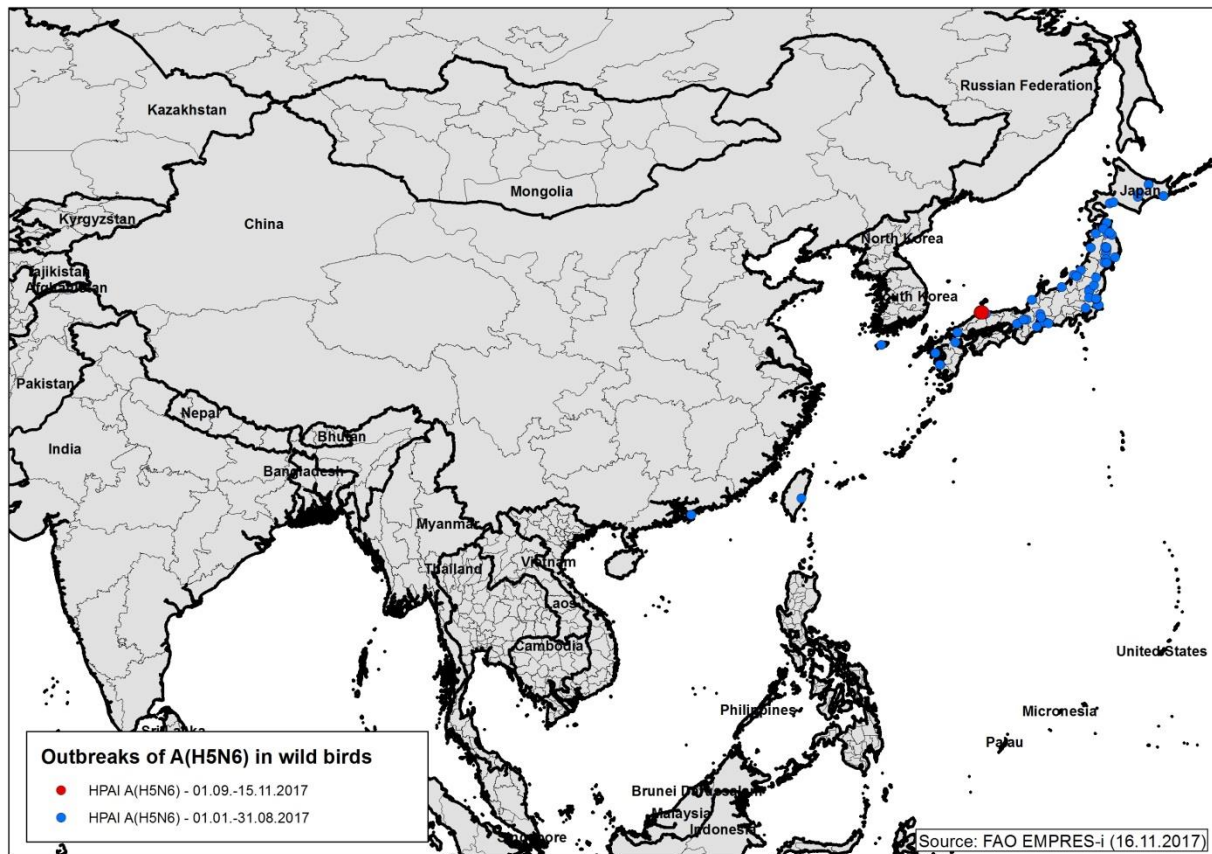
Figure 18: Outbreaks of A(H5N6) HPAIV in wild birds between 1 January and 15 November 2017 (data source: FAO EMPRES-i; status: 16.11.2017)

Phenotypic characterisation

The phenotype of the recent A(H5N6) viruses from Asia seems similar to that of the 2016–2017 A(H5N8) viruses: highly virulent for chickens, less virulent for domestic ducks, and variable virulence for wild birds. Increased mortality in galliforms as well as increased mortality and neurological signs (torticollis, ataxia) in domestic ducks were reported from the Republic of Korea (OIE reports). However, virus isolation from apparently healthy ducks and geese in live bird markets in China was also described (Jiao et al., 2016; Sun et al., 2016). A Korean A(H5N6) isolate was tested in 6-week-old SPF chickens inoculated intravenously and the IVPI value was 2.66 (Si et al., 2017). Another South Korean A(H5N6) isolate, detected in 2016, had the IVPI value of 2.94 and the mean death time (MDT) for embryos was 36 h (Kim et al., 2017). The IVPI value of two avian-origin A(H5N6) viruses isolated from swine in China was 2.8 and 2.99 (Li et al., 2015). All IVPI values meet the criteria for high virulence according to OIE Diagnostic Manual. Experimental infection of 6-week-old chickens infected via the intranasal route (10^6EID_{50}) with A(H5N6) HPAIV isolated from apparently healthy ducks in Southern China resulted in the quick progression of clinical signs, including depression, anorexia, and death of 100% birds within 6–7 days post infection. The virus replicated in a wide range of organs and was successfully transmitted to naïve chickens that also died (Jiao et al., 2016).

Field observations of clinical manifestation in wild birds are rare. There was detection of A(H5N6) HPAIV in South Korea in three whooper swans (*Cygnus cygnus*) in 2016, one with neurological signs and two found dead. It is possible that whooper swans brought HPAIV A(H5N6) into Korea. However, it is also possible that whooper swans, which are highly susceptible to HPAI A(H5N1) infection, may have been exposed locally through direct or indirect contact with other A(H5N6)-infected but asymptomatic migratory species, such as mallards or spot-billed ducks (*Anas poecilorhyncha*), or perhaps through exposure to infected poultry (Jeong et al., 2017). In winter 2016–2017 in Japan, 230 cases of HPAI caused by A(H5N6) viruses were reported from wild birds, captive birds and poultry holdings throughout the country. The Japanese A(H5N6) isolate differed slightly from that of HPAIVs isolated previously in Japan and China. The virus exhibited high pathogenicity and a high replication

capacity in chickens, whereas virus growth was slightly lower in ducks compared with an A(H5N8) HPAIV isolate collected in Japan in 2014 (Hiono et al., 2017).

Conversely, the A(H5N6) virus was detected in apparently healthy Northern pintails (*Anas acuta*) sampled during active surveillance in Hong Kong SAR.

Genetic characterisation

    i)   Phylogenetic analysis

Phylogenetic studies showed that the A(H5N6) viruses have been generated through multiple reassortment events. The primary A(H5N6) virus (detected at the end of 2013 in China) contained the HA gene of the A(H5N1) HPAIV clade 2.3.4.4, the internal genes of A(H5N1) clade 2.3.2.1, and the NA gene from the H6N6 LPAIV (Qi et al., 2014). Since that time, subsequent reports have provided evidence about growing genetic diversity caused by multiple reassortment events, mostly with Eurasian-origin AIV, including local HPAIV and LPAIV strains circulating in wild birds and poultry. However, the vast majority of HA genes still belong to the 2.3.4.4 lineage, although there are reports of an A(H5N6) virus with the HA derived from the 2.3.2 clade (Du et al., 2017).

In a recently published paper by Yang et al. (2017), three events have been suggested to explain the generation of novel A(H5N6) reassortants. In the first event, the 'reassortant A-type' acquired HA gene segment from H5N2 clade 2.3.4.4 virus, NA gene segment (non-truncated) from H6N6 virus and internal gene segments from A(H5N1) clade 2.3.2.1.c. In the second event, the 'reassortant B-type' was generated by the acquisition of HA gene segment from A(H5N8) clade 2.3.4.4 virus, NA gene segment (truncated) from H6N6 virus and internal gene segments from A(H5N1) clade 2.3.2.1.c. The 'reassortant C-type' was generated as a result of the reassortment between reassortant B (HA and NA genes) and poultry-adapted A(H9N2) virus (internal genes). Notably, A(H5N6) viruses with an insert of internal A(H9N2)-like genes seemed to prevail in live poultry markets (LPMs) in different regions of China (Chen et al., 2017).

Studies carried out in China on 175 A(H5N6) AIVs isolated between 2014 and 2015 in LPMs in Hunan Province provided evidence for the existence of at least six genotypes arising from segment reassortment, including a variant that possessed an HA from A(H5N1) clade 2.3.2 (Du et al., 2017). In the surveillance in LPM in Eastern China in 2016, a novel subtype H7N6 was described in chicken. The virus possessed gene segments derived from A(H5N6), A(H9N2) and A(H7N9) viruses (Wu et al., 2017).

The A(H5N6) AIVs detected in Japan in November 2016 were classified into the genetic clade 2.3.4.4 c and were genetically closely related to A(H5N6) HPAIVs that had been recently isolated in South Korea and China (Okamatsu et al., 2017). The A(H5N6) viruses found in wild birds and poultry in Korea in 2016 seem to be closely related A(H5N6) viruses circulating in Guangdong province in China. Reassortment events with Eurasian LPAIV were also detected (Kwon et al., 2017b; Lee et al., 2017). In another study, the A(H5N6) from faecal samples was proved to contain genes derived from H4N2 and H1N1 (Si et al., 2017). (Jeong et al., 2017) characterised genetically two novel reassortants A(H5N6) AIVs detected in November 2016 in whooper swans in South Korea and found them to be distinguishable from the A(H5N8) and A(H5N1) HPAIVs previously isolated in Korea. Kim et al. (2017) subjected for analysis five A(H5N6) isolates from faecal wild bird samples in South Korea and found that they were reassortants generated from numerous Eurasian AI virus subtypes, including A(H5N8) highly pathogenic viruses.

    ii)   Molecular marker analysis

Two predominant HA cleavage site amino acid motifs found in A(H5N6) viruses from Asia are: PLREKRRKRGLF, PLRERRRKRGLF, occasionally also PLKEKRRKRGLF, PQRERRRKRGLF, and PLREKRRRRGLF (Influenza Virus Database, NCBI), all consistent with high virulence.

The available studies on the genetic markers of virulence and host adaptation show that although most of A(H5N6) viruses exhibit preferential binding to sialic acid receptors joined to sugar through an α-2,3 sialic acid linkage (Kim et al., 2017), a feature typical of avian influenza viruses, a change towards human receptor-binding preference (α-2,6 sialic acid linkage) has also been described (Sun et al., 2016; Guo et al., 2017). For example, the A(H5N6) Chinese isolates from poultry had lost the glycosylation site at residue 158 of HA, bound both α2,6-resialylated and α2,3-resialylated chicken red blood cells (cRBCs), showed extensive binding to human tracheal epithelial and alveolar cells,

replicated in the lungs of mice, and were transmissible through direct contact between ferrets (Sun et al., 2016).

Two types of A(H5N6) can be distinguished based on the length of NA: with- and without truncated NA stems (deletions at amino acid positions 59–69), a signature of adaptation to terrestrial poultry ((Bi et al., 2016; Sun et al., 2016; Yang et al., 2017).

The A(H5N6) viruses that acquired the internal gene cassette from A(H9N2) viruses have been shown to carry mutations related to transmissibility and virulence in mammals or Adamantine resistance in PB1, PA, M1 and M2. The A(H5N6) reassortant viruses that derived NS1 from A(H5N1) viruses possess mutations indicating increased virulence in mice (Yang et al., 2017).

3.3.2.2. A(H5N6) in mammals (excluding humans)

No detections reported between 1 September and 15 November 2017.

3.3.2.3. Human infections due to A(H5N6)

Since 2014 and as of 4 December 2017, 16 laboratory-confirmed cases of human infection with avian influenza A(H5N6) virus, including six deaths, have been reported globally by WHO (WHO, 2016a). All cases occurred in mainland China. The latest case was reported on 1 December 2016. In a recent publication, 17 cases including 12 deaths due to A(H5N6) have been reported since 2014 (Jiang et al., 2017). With a current case reported on 20 November, this adds up to 18 reported human cases in total (CHP, online) (Figure 19).
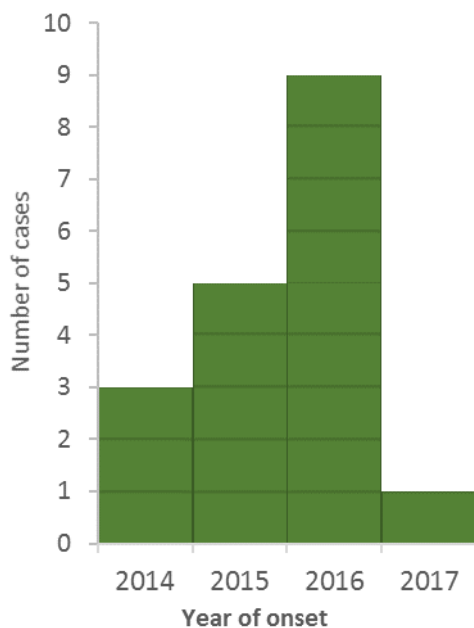
Figure 19: Number of human cases due to A(H5N6) infection by year of onset, 2014–2017. Data used from the Centre for Health Protection of the Department of Health of the Government of Hong Kong SAR and Jiang et al. 2017 (CHP, online; Jiang et al., 2017)

3.3.3. HPAI A(H5N8)

3.3.3.1. Domestic and wild birds

Detections

Between 1 September and 15 November 2017, further outbreaks of HPAI A(H5N8), clade 2.3.4.4b, were reported from Nigeria and South Africa only, despite the widespread detection in domestic and wild birds in several African countries and the Middle East until summer 2017. Besides, several poultry

outbreaks including ostrichholdings in South Africa, HPAI A(H5N8) was reported in Egyptian goose, (*Alopochen aegyptiaca*), peregrine falcons (*Falco peregrinus*), house sparrows (*Passer domesticus*), pied crow (*Corvus albus*), and laughing doves (*Spilopelia senegalensis*) (see Figure 20).
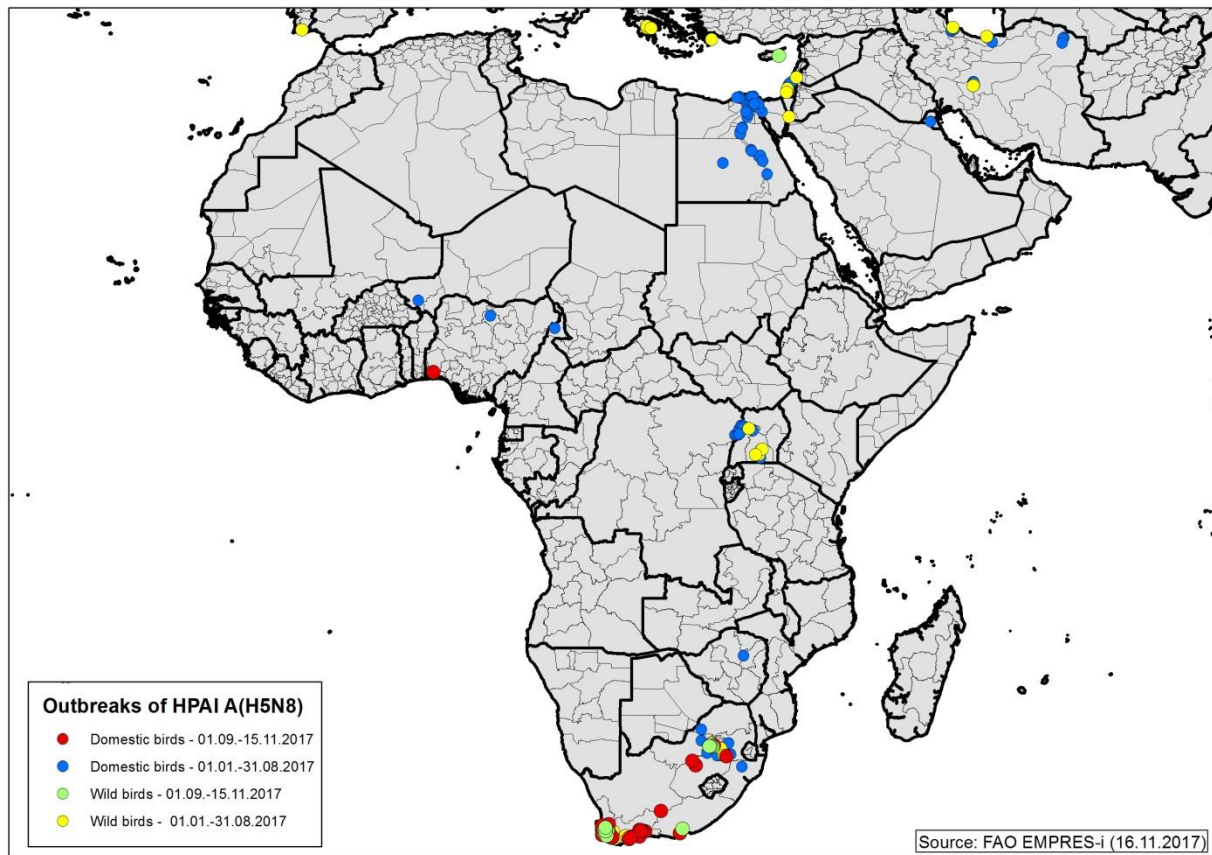
Figure 20: Distribution of confirmed HPAI A(H5N8) outbreaks in birds by place of reporting in Africa and the Middle East between 1 January and 15 November 2017 (data source: FAO EMPRES-i; status: 16.11.2017)

Outbreaks of HPAI A(H5N8) in Asia were notified by China, India, Nepal, South Korea and Taiwan and several subtypes of HPAI H5 viruses are co-circulating in the domestic and wildlife populations of these countries (see also Section 3.3.1 and 3.3.2). Since September 2017, only Taiwan reported outbreaks in non-commercial chicken and duck hodlings, but no cases in wild birds were confirmed during this time period (see Figure 21).

Figure 21: Distribution of confirmed HPAI A(H5N8) outbreaks in birds by place of reporting in Asia and the Middle East between 1 January and 15 November 2017 (data source: FAO EMPRES-i; status: 16.11.2017)

Phenotypic characterisation

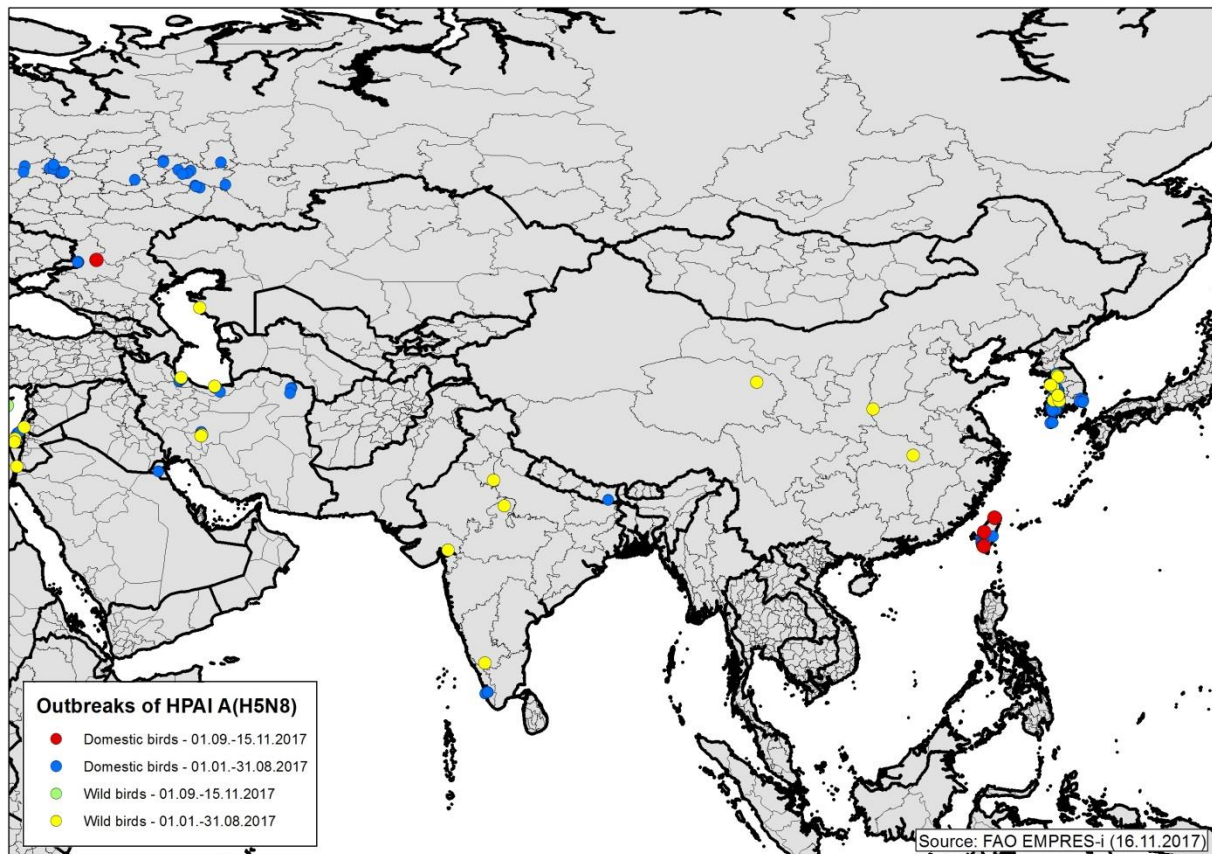Data on the phenotypic characteristics of the current A(H5N8) HPAIV clade 2.3.4.4 (2016/2017) virus from outside Europe are scarce. Conversely, a large amount of data has been published recently on the pathogenicity of the A(H5N8) clade 2.3.4.4 (2014/2015) virus detected in Asia and North America. The major conclusions are briefly summarised below. However, caution is recommended when extrapolating these results on the properties of the recent A(H5N8) viruses, as despite some similarities, the recent A(H5N8) virus seems to evoke higher mortality for certain species, especially wild birds.

In general, the A(H5N8) clade 2.3.4.4 (2014/2015) virus seemed to be less virulent for domestic waterfowl than gallinaceous poultry. Despite its high lethality for chickens, its apparent virulence and transmissibility for this species was lower in comparison with A(H5N1) HPAIV (Bertran et al., 2016; Lee et al., 2016a). Intraclade-dependent differences in virulence were also observed (Tanikawa et al., 2016). Higher resistance of some local breeds/lineages of chickens has been reported from South Korea (Lee et al., 2016a; Lee et al., 2016b).

Experimental inoculation of Pekin ducks with an A(H5N8) virus from North America resulted in no mortality, lack or only mild clinical signs (conjunctivitis, diarrhoea) but virus shedding and transmission to contact-exposed ducks was observed (Pantin-Jackwood et al., 2017). Experimentally infected Muscovy ducks survived infection and seroconverted (Lee et al., 2016a). Mild clinical signs but occasionally nervous symptoms were observed following experimental inoculation of Chinese geese (*Agnes cygnoides*) (Pantin-Jackwood et al., 2017). Absence of clinical signs but replication of A(H5N8) strains isolated in Korea in 2014 was reported in pigeons. Transmission to contact birds was not observed (Kwon et al., 2017a).

The A(H5N8) clade 2.3.4.4 (2014/2015) was detected from a variety of wild bird species in Asia/North America but few studies have addressed the pathogenicity of the isolates for wild birds in the experimental setting. In one of these, the absence of clinical signs but efficient replication and

transmition to co-housed birds was reported after experimental infection of Mandarin ducks (*Aix galericulata*) with a South Korean A(H5N8) isolate (Kwon et al., 2017a). Mallards (*Anas platyrhynchos*) inoculated with an A(H5N8) HPAIV from North America exhibited fever, decreased body weight, shed low titers of the virus to contact ducks and had moderate lesions at necropsy (Pantin-Jackwood et al., 2016).

Genetic characterisation

i)   Phylogenetic analysis

In May, 2016, a novel reassortant A(H5N8) HPAIV belonging to clade 2.3.4.4 was identified in Tyva Republic in Russia near the border with Mongolia and in Qinghai Lake in China. Phylogenetic analysis showed that three genes (HA, NA and NS) of novel Russian and Chinese isolates were derived from clade 2.3.4.4 B, whereas the remaining segments (PB2, PB1, PA, NP, M) clustered with LPAIV detected in wild birds in Mongolia, China and Vietnam (Lee et al., 2017, Li et al., 2017). Since then, further A(H5N8) clade 2.3.4.4 B reassortants have been identified across Europe and Asia.

In October, 2016, two slightly different genotypes of A(H5N8) viruses were detected at two zoos in India, with most of the gene segments closely related to the A(H5N8) sequences from Tyva Republic, Qinghai Lake and Uvs-Nuur Lake. However, the NP and PA genes (first genotype) or only NP gene (second genotype) showed the highest similarities to the Eurasian LPAIV sequences (Nagarajan et al., 2017). Similar observations were also made for the Korean A(H5N8) isolates obtained in December 2016 and January 2017, which were proved to be reassortants generated from A(H5N8) clade 2.3.4.4B and Eurasian LPAI viruses (Kim et al., 2017; Woo et al., 2017). Novel reassortants were also detected in December 2016 in Egypt (Kandeil et al., 2017a) The analysis of partial sequences of HA genes from outbreaks in Iran in November 2016 also showed that they belonged to clade 2.3.4.4B (Ghafouri et al., 2017b). The data suggests that multiple genotypes were generated in the summer of 2016 in central Asia, and then were disseminated to the Far East, Middle East, Africa and Europe.

ii)   Molecular analysis

Most of A(H5N8) isolates identified in Asia and Africa show the avian-like receptor specificity as indicated by presence of glutamine (Q) at amino acid position 226 of HA protein. However, Marchenko et al. (2017) reported N94S and T123P substitutions in the HA protein, associated with increased interactions with human-type sialic acid receptors. All available studies indicate that analysed isolates are susceptible to amantadine and neuraminidase inhibitors. The most prominent mutations responsible for increased pathogenicity for mammals such as PB2 E627K and D701N were not detected. However, markers of mammalian host specificity were observed in other genes, e.g. PB1 L13P in isolates from India and Egypt (Nagarajan et al., 2017; Kandeil et al., 2017a). Variability in PB1-F2 protein length was also observed, isolates from India possessed truncated PB1-F2 protein (11 amino acids), whereas in isolates from South Korea this protein was of full length.

3.3.3.2.   A(H5N8) in mammals (excluding humans)

So far natural and experimental infections in dogs have been observed with virus transmission from infected to contact animals (Yuk et al., 2017)

In swine, replication in the lower respiratory tract was demonstrated after high titre inoculation of North American clade 2.3.4.4. A(H5N8) viruses, however, replication seemed not feasible in nasal epithelium or ex vivo tracheal explants also no transmission between experimentally infected pigs and contact pigs occurred (Kaplan et al., 2017).

No human A(H5N8) cases have been reported world-wide, however an increase of mutations characterised as human-like signatures contributing to increased binding of the virus to human–type receptors has recently been observed in Asian viruses (Xu et al., 2017). This increase of pathogenicity was shown in a study substituting gene segments of the A(H5N8) virus by A(H5N1) segments in a ferret model (Park et al., 2017).

3.3.4. HPAI-LPAI A(H7N9)

3.3.4.1. Domestic and wild birds

Since January 2017, the Chinese authorities reported the detection of 204 LPAI A(H7N9) and 27 HPAI A(H7N9) positive samples from poultry, and wild birds or the environment. Between 1 September and 15 November 2017, one duck sample of LPAIV A(H7N9) from a live bird market was reported from Fujian province and one chicken holding tested positive from Liaoning Province in the framework of the active surveillance campaigns (see Figure 22, 23 and 24) (FAO, online-b). No HPAI A(H7N9) was detected during the relevant time period of this report. Altogether 23 156 virological samples of birds and the environment were collected in 23 provinces in September 2017 (FAO, online-b). The results of the surveillance campaigns are monthly published by the Chinese Ministry of Agriculture (MoA, online) and also available on the EMPRES-i website of the FAO (FAO, online-b). Furthermore, Japan reported about isolation and genetic sequencing of HPAI A(H7N9) virus from an illegally imported duck meat product confiscated from a flight passenger (GenBank [https://www.ncbi.nlm.nih.gov/nuccore/1233835231]; FAO, online-b). The Chinese Ministry of Agriculture started a H7 vaccination programme for poultry in early July 2017 in Guangdong and Guangxi provinces. The nationwide A(H7N9) vaccination campaigns of poultry with influenza A(H5) and A(H7) bivalent vaccines started extensively in September 2017. With exception of poultry in AI-free zones and export farms, all domestic birds will be vaccinated (FAO, online-b; MoA, online).
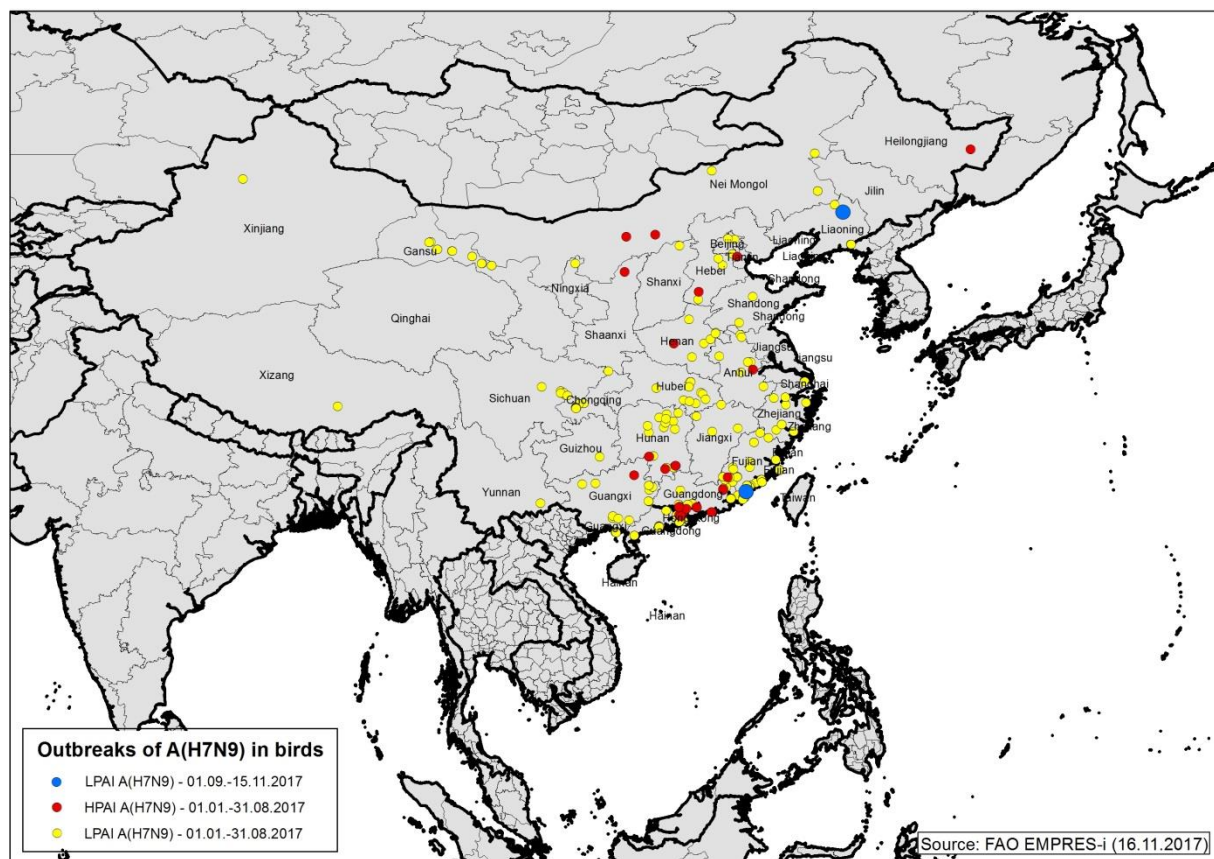
Figure 22: Distribution of confirmed LPAIV and HPAIV A(H7N9) in birds and environmental samples by place of reporting between 1 January and 15 November 2017 (data source: FAO EMPRES-i; status: 16.11.2017)
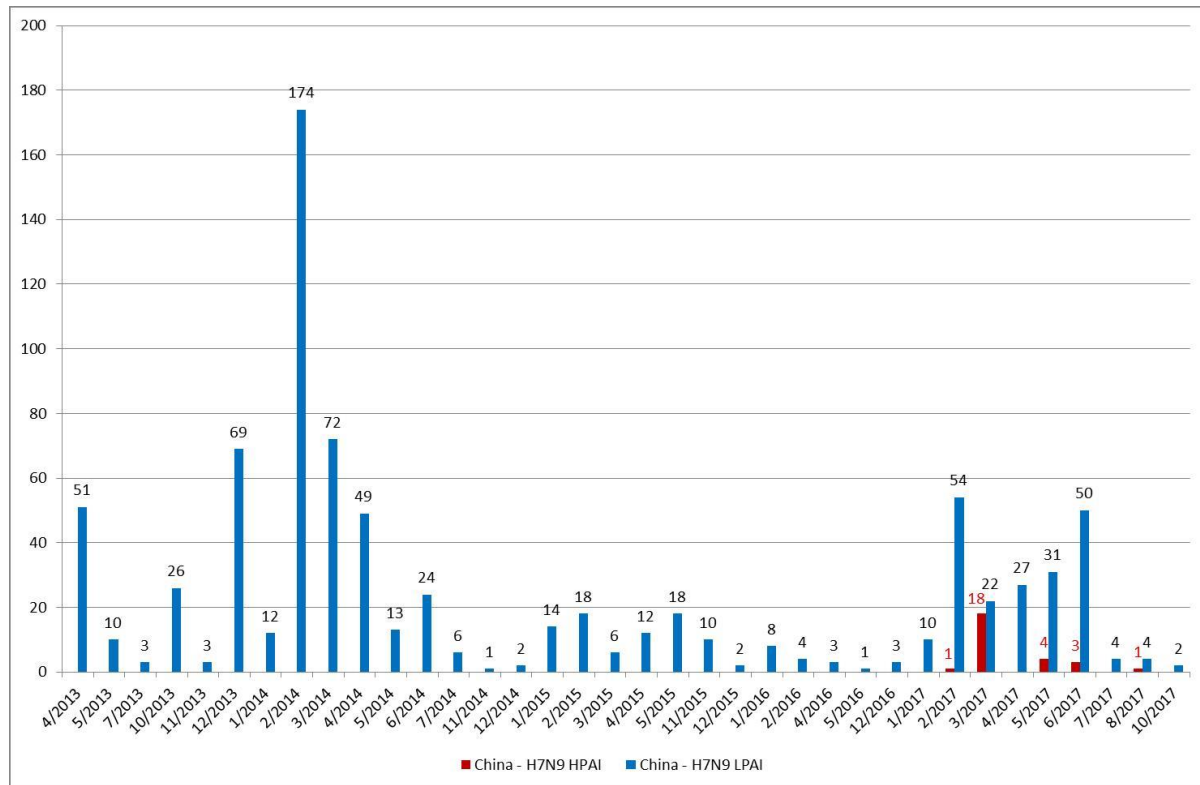
Figure 23: Number of confirmed LPAI and HPAI A(H7N9) outbreaks in birds and environmental samples in China since March 2013 (status: 16.11.2017)
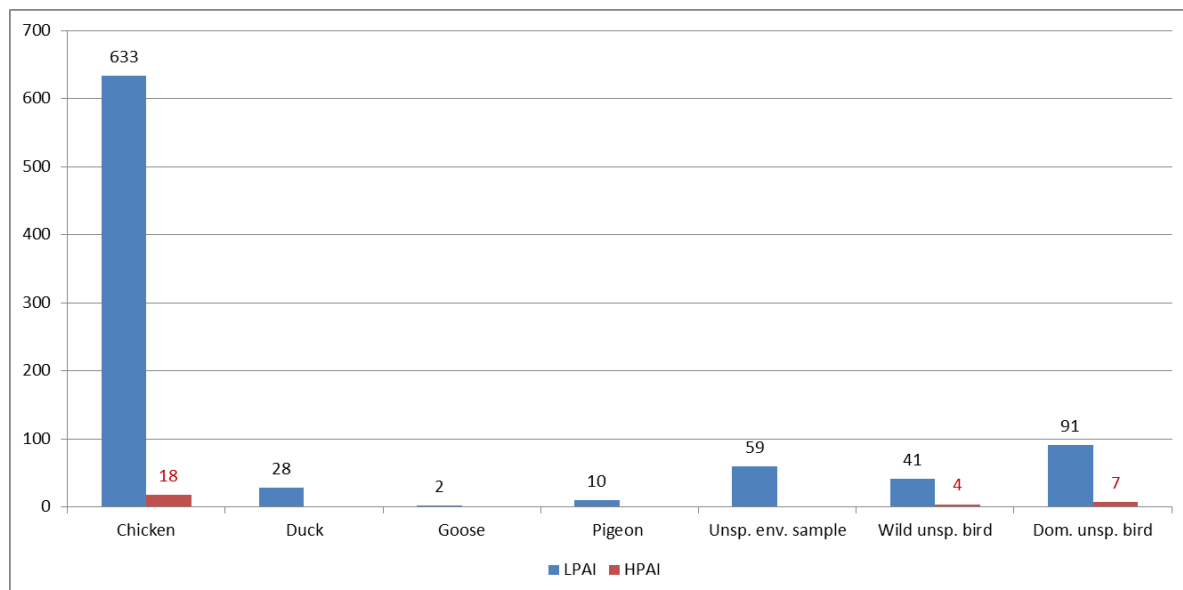
Figure 24: Number of confirmed LPAI and HPAI A(H7N9) outbreaks by species and environmental sample type in China since March 2013 (status: 16.11.2017)

3.3.4.2. Human infections due to A(H7N9)

In March 2013, a novel avian influenza A(H7N9) virus was detected in patients in China. Since then and up to 4 December 2017, 1 565 cases have been reported, including 568 deaths (Table 3). The latest case reported from China on 2 December 2017 represents also the first case of the sixth wave (CHP, 2017). No autochthonous cases have been reported outside China. Most cases are isolated, and sporadic zoonotic transmission from poultry to humans is the most likely explanation for the outbreak. The outbreak shows a seasonal pattern (Figure 25 and Figure 26). The first wave in spring 2013 (weeks 2013-7 to 2013-40) resulted in 135 cases, the second wave (weeks 2013-41 to 2014-40) led

to 320 cases, the third wave (weeks 2014-41 to 2015-40) caused 223 cases, 120 cases were reported as a result of the fourth wave (weeks 2015-41 to 2016-40), 766 cases were reported as part of the fifth wave (weeks 2016-41 to 2017-40). The first case of the likely sixth seasonal wave is a 64-year-old male from Yunnan and has been reported 2 December 2017. This case had onset of symptoms on 21 November after contact with dead poultry and was in serious condition (CHP, 2017).

The 1 564 cases were reported from Zhejiang (310), Guangdong (258), Jiangsu (253), Fujian (108), Anhui (101), Hunan (95), Shanghai (56), Jiangxi (50), Sichuan (38), Beijing (35), Guangxi (32), Hubei (31), Hebei (29), Henan (28), Shandong (27), Hong Kong SAR (21), Guizhou (20), Xinjiang (13), Chongqing (9), Yunnan (8), Shaanxi (7), Gansu (5), Taiwan (5), Tianjin (5), Liaoning (5), Jilin (3), Tibet (3), Shanxi (3), Inner Mongolia (2), and Macau SAR (2). Three imported cases were reported in Canada (2) and Malaysia (1) (Figure 27).

An interactive map with the distribution of cases by place of reporting over time can be accessed here: https://gis.ecdc.europa.eu/influenza/H7N9/

After the emergence of HPAI A(H7N9) virus (changes in the hemagglutinin gene indicating a change to high pathogenicity in poultry) in the Chinese poultry population during the fifth wave 2016/17, also transmission to humans has been observed. On 5 September 2017, China CDC reported one additional human case HPAI A(H7N9) virus during the fifth wave (since October 2016), bringing the number of human cases with HPAI A(H7N9) virus to 28. These 28 cases were from Guangdong, Guangxi, Hebei, Hunan, Shaanxi and Taiwan (the case had travel history to Guangdong) with illness onset date before July 2017. No increased transmissibility or virulence to human cases has been detected related to the HPAI A(H7N9) virus (Chinese National Influenza Center, 2017).

A study comparing transmission of LPAI and HPAI A(H7N9) viruses in ferrets showed, the HPAI viruses were able to replicate in mice, ferrets and non-human primates (Imai et al., 2017). Pathogenicity in mice and ferrets were higher in HPAI than LPAI viruses. The tested neuraminidase-inhibitor sensitive viruses transmitted airborne via ferrets and several of the infected and exposed animals died. A neuraminidase-resistant virus showed lower pathogenicity. Limited effectiveness of antiviral drug of neuraminidase inhibitors was shown.

Altogether 40 clusters of human-to-human transmission cases were identified over the whole period, 14 of them were defined as probable human-to-human transmission and 26 as possible. An analysis comparing the characteristics of human-to-human transmission across the first five waves showed that the characteristics of cases within clusters in the fifth wave 2016/17 was comparable to the previous waves (Zhou et al., 2018). The secondary infections were related to household exposures or exposures in healthcare settings. No difference regarding the case-fatality ratio was observed comparing clusters (35%) with all sporadic cases (see table 3) were identified.
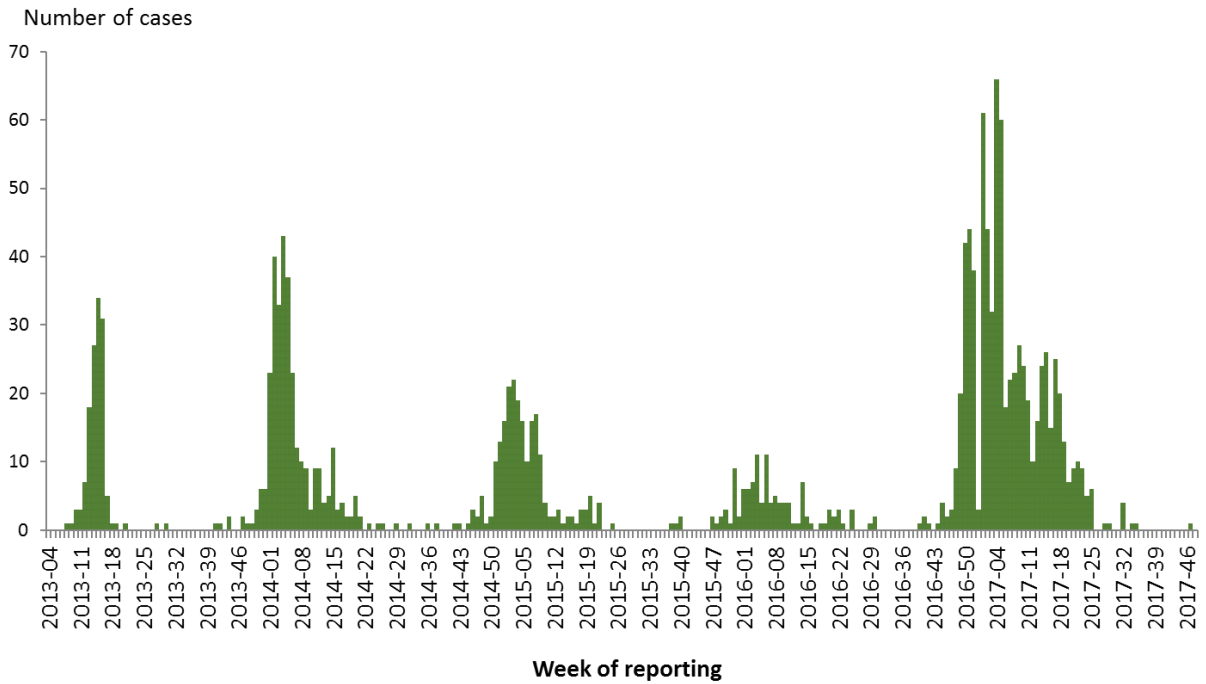
Source: WHO and Hong Kong Centre for Health Protection (CHP, 2017; WHO, 2017a)

Figure 25: Distribution of confirmed human cases of A(H7N9) by first available week* of onset of disease, February 2013 – 4 December 2017 (n=1 565)
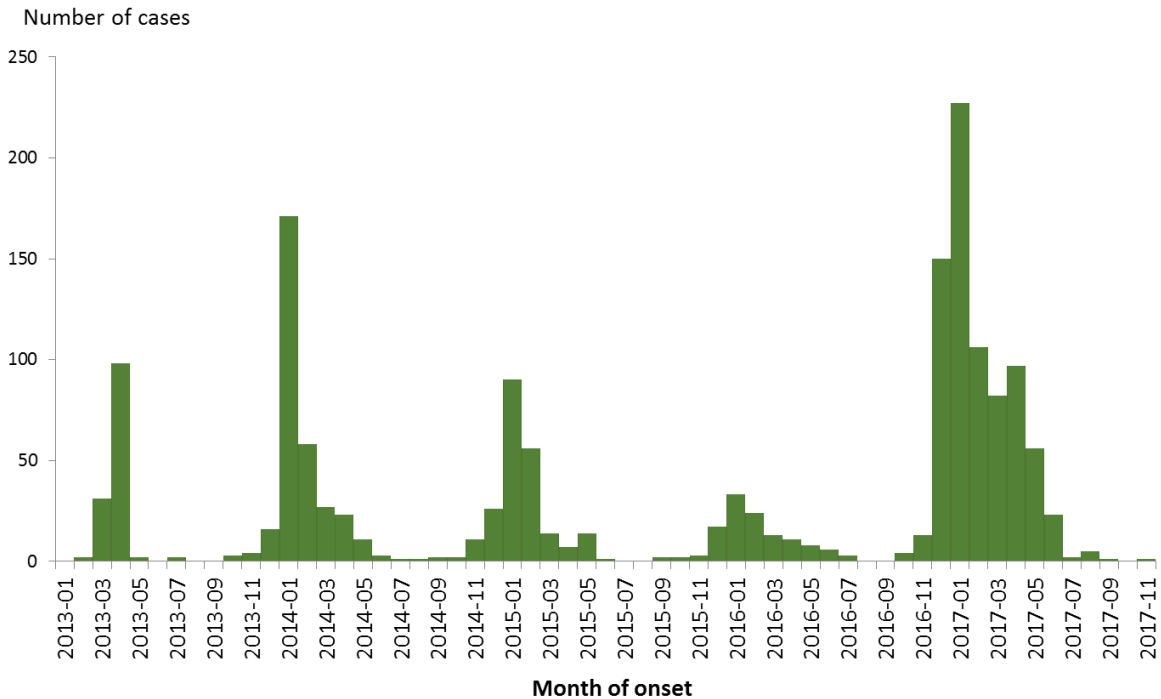
Source: WHO and Hong Kong Centre for Health Protection (CHP, 2017; WHO, 2017a)

Figure 26: Distribution of confirmed human cases of A(H7N9) by first available month*of onset of disease, February 2013 – 4 December 2017 (n= 1 565)

Table 3: Number of reported human cases and fatalities due to A(H7N9) infection up to 4 December 2017

	First wave (02/2013–09/2013)	Second wave (10/2013–09/2014)	Third wave (10/2014–09/2015)	Fourth wave (09/2015–10/2016)	Fifth wave (10/2016-10/2017)	Sixth wave (since 10/2017, week 41)	Cumulative number of cases
Cases	135	320	223	120	766	1	1 565
Deaths*	43	134	98	45	248	-	568
CFR (%)	32%	42%	44%	38%	32%	-	36%

Source: WHO and Hong Kong Centre for Health Protection (CHP, 2017; WHO, 2017a)

*The estimates in the table are based on the information available at the time of notification. Therefore, CFR may be affected by completeness of information about outcome at time of notification.
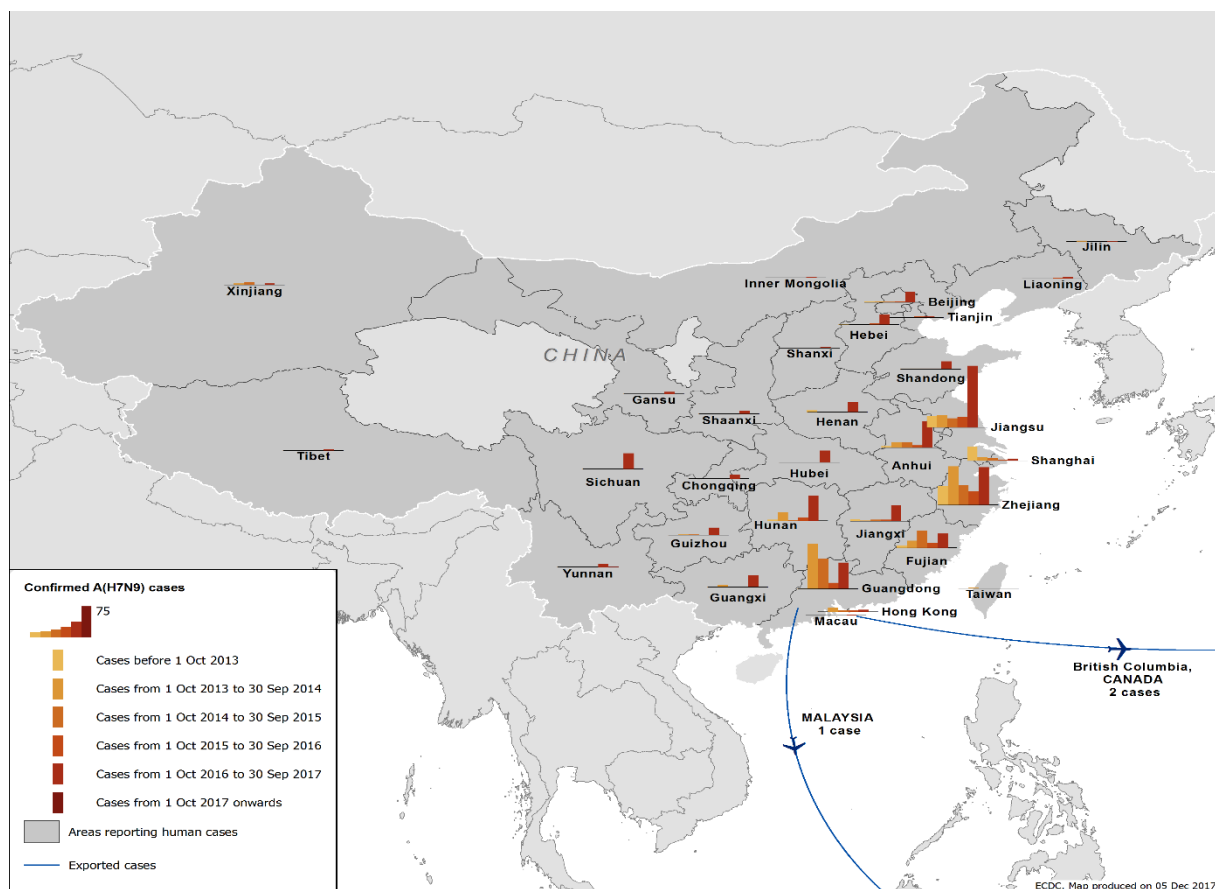
Source: WHO and Hong Kong Centre for Health Protection (CHP, 2017; WHO, 2017a)

Figure 27: Distribution of confirmed human cases of A(H7N9) by first available month, February 2013 to 4 december 2017

3.3.5. LPAI A(H9N2)

3.3.5.1. Domestic and wild birds

A(H9N2) remains the most commonly detected non-notable subtype of influenza viruses in poultry in Asia, Middle East and North Africa. The endemic status of these regions continued between 1 September and 15 November 2017 while there is no information to report that would affect any risk estimation.

3.3.5.2. Human infections due to A(H9N2)

Since 1998 and as of 4 December 2017, 43 laboratory-confirmed cases of human infection with avian influenza A(H9N2) virus, including one death, have been reported globally. Cases occurred in China (36), Egypt (4) and Bangladesh (3) (Figure 28). The latest case was reported in November 2017 from Hunan Province in China with exposure to poultry (Government Information Bureau of the Macao health authorities, 2017). This is the fifth case reported in 2017 from China.
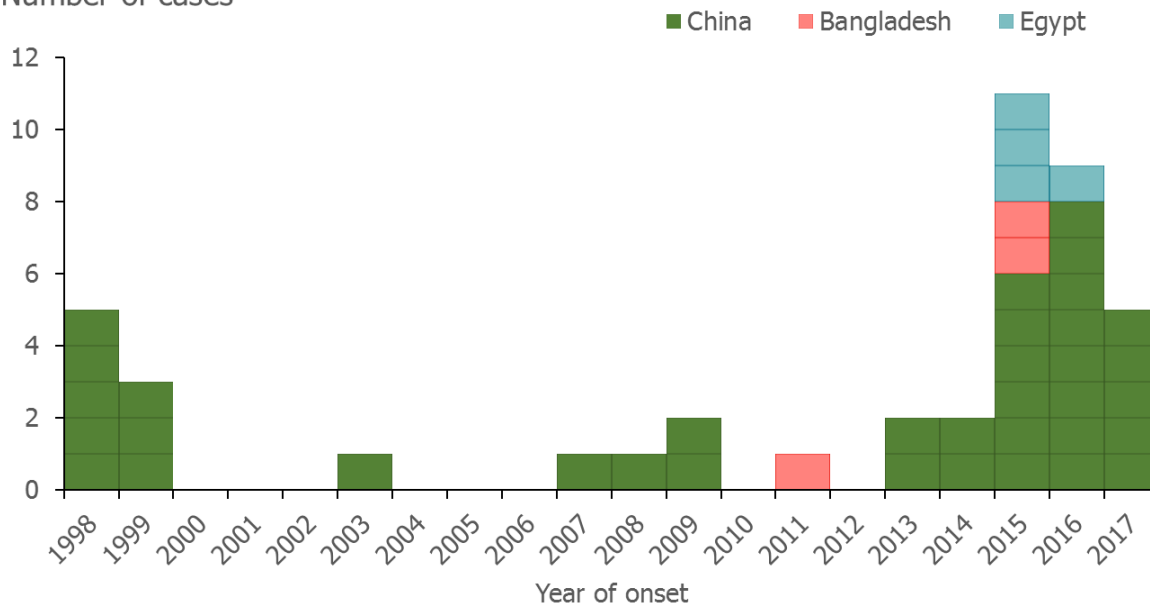
Figure 28: Distribution of confirmed human cases of A(H9N2) by country of reporting 1998 – 2017 (n=42)

A recent study analysed A(H9N2) viruses from Egypt and identified a tendency for increased binding with erythrocytes expressing α 2,6-linked sialic acid that correlates with the Q226L amino acid substitution at the receptor binding unit of the hemagglutinin (Q234L, H9 numbering). Further analyses of the hemadsorption site of the NA of the N2 showed substitutions that are similar to the N2 of prepandemic A(H3N2)/1968 virus. However, for the NA no increased zoonotic potential was identified related to distinct antigenic or functional characteristics (Naguib et al., 2017).

3.3.6. Scientific analysis AI spread from Third countries to poultry in the EU

Sections 3.3.1–3.3.5 showed in the time period of the report from 1 September until 15 November 2017 a lower number of reported outbreaks in poultry and wild birds in Asia, Northern Africa and the Middle East. The outbreaks of clades 2.3.2.1c, A(H5N1), and 2.3.4.4b, A(H5N8), in Africa and the current human case of clade 2.3.4.4, A(H5N6), in China, despite low number of cases in birds, demonstrated the necessity of close monitoring. There is considerable uncertainty regarding the real geographical distribution of these viruses. The environmental stability of AIV will increase with the lower temperatures and reduced UV radiation in the coming months. Aggregation as well as mixing of wild birds from different geographic origins during migration and winter time will increase the risk of spreading the infection. The A(H7N9) virus has not been detected on a large scale in wild waterfowl. This might be attributable by the high degree of adaptation to gallinaceous poultry. The risk associated with the incursion of this subtype by means of wild birds is currently low but constant monitoring is warranted. The multiple pathways through which AIV can be brought to the EU include trade and illegal movements of poultry and poultry products, contaminated fomites and wild birds.

The risk of avian influenza viruses being transported to Europe through poultry trade is negligible as live poultry, day-old chicks and semen have been identified as the only non-wild bird pathways via which AIV introduction is non-negligible and suitable risk management measures are in place, such as testing and quarantine (EFSA AHAW Panel, 2017). EU legislation (Regulation EC/798/200815) prohibits the importation of live poultry, day-old chicks and hatching eggs, semen and other birds (captive birds such as parrots, finches and ornamental birds for trade) from countries which cannot provide suitable health guarantees to comply with the certification. The list of approved countries is therefore limited (for reference see Table F5 of Appendix F, EFSA AHAW Panel, 2017).

Illegal movement of captive birds (in particular passerines) is a viable pathway for spread of the viruses, in particular H5Nx, but the risk is difficult to assess due to the paucity of data.

3.3.7. Surveillance and diagnosis of human infections and public health measures for prevention and control

3.3.7.1. Surveillance in the EU

As in the previous report already outlined, human infections with A(H7N9), AH(H5N6), A(H5N8) and other novel influenza strains are notifiable under EU legislation and the International Health Regulations (IHR) through the Early Warning and Response System (EWRS)[10] and the IHR notification system (WHO, 2016b). Infectious disease protocols for case investigations are available from the Consortium for the Standardization of Influenza Sero-Epidemiology (CONSISE) and national authorities (CONSISE, 2013; Laurie et al., 2013; Van Kerkhove et al., 2013). Agreed protocols for clinical investigations have been prepared by the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) (International Severe Acute Respiratory and Emerging Infection Consortium, 2013). Contacts of confirmed cases should be followed-up and tested. International recommendations for the use of post-exposure prophylaxis differ. Evidence of the effectiveness of contact tracing on board airlines in limiting spread of infection is limited and should only be considered upon a risk assessment on a case-by-case basis (ECDC, 2014).

Public health measures

Contacts of confirmed cases should be followed-up and tested. International recommendations for the use of post-exposure prophylaxis differ. Evidence of the effectiveness of contact tracing on board airlines in limiting spread of infection is limited and should only be considered upon a risk assessment on a case-by-case basis (ECDC, 2014).

Protective measures have been recommended in accordance with national guidelines for HPAI, including personal protection equipment and oseltamivir prophylaxis for up to 10 days after the last contact. A tutorial on the safe use of personal protective equipment can be found at ECDC website:

https://ecdc.europa.eu/en/publications-data/tutorial-safe-use-personal-protective-equipment

Information on the protection and management of exposed people during HPAI virus outbreaks in Europe is avialble for some countries (Adlhoch et al., 2016).

Diagnosis

With routine diagnostic laboratory assays, the novel A(H5Nx) or A(H7Nx) viruses should be detected as positive for influenza A virus, and negative for influenza B, A(H1), A(H1)pdm09 and A(H3) viruses.

Influenza A(H5Nx) or A(H7N9) viruses are expected to be classified as un-subtypeable influenza A if no-specific A(H5) or A(H7) diagnostic test is performed. It is standard procedure in diagnostic laboratories to send influenza A virus isolates or clinical samples that cannot be subtyped to the national reference laboratory (National Influenza Centres; NICs), and further to a WHO Collaborating Centre for Reference and Research on Influenza for characterisation, as was undertaken in China for the first influenza A(H7N9) isolates.

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[10] Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC Text with EEA relevance

In October 2017, WHO reviewed and updated the recommendations regarding RT-PCR testing (WHO, 2017c).

3.3.7.2. Public health control measures (in relation to the EU)

3.3.7.3. Vaccines

The most important intervention in preparing for the pandemic potential of influenza viruses is the development and use of human vaccines, therefore the situation is constantly monitored and assessed by WHO. No human vaccines against A(H7N9), A(H5N1) or other avian influenza are currently authorised or stockpiled for use in the EU.

Following the vaccine composition meeting in March and October 2017, WHO published an updated overview of recommended candidate vaccine viruses (CVVs) and the status of development (WHO, 2017d, e). Currently 32 different CVVs for different A(H5) clades are listed as available, for five CVVs with the most recently circulating viruses including A(H5N1) clade 2.3.2.1c and A(H5N6) clade 2.3.4.4 availability is pending. The most recent circulating avian influenza viruses have been reviewed and based on the current antigenic, genetic and epidemiologic data, no new CVVs were proposed (WHO, 2017d)

CVVs based on an attenuated influenza A/Puerto Rico/9/1934 virus backbone showed less severe disease and reduced virulence without extrapulmonary spread in the ferret model compared to wild type viruses (Belser et al., 2017).

3.3.8. ECDC risk assessment for the general public in the EU

The risk of zoonotic transmission to the general public in EU/EEA countries is considered to be low. Monitoring and testing of wild birds and domestic poultry in the EU plays an important role in the detection of further virus spread among birds and consequently the reduction of the possible risk for exposure of humans to infected birds.

It is important to remain vigilant, identify any possible early transmission events to humans and ensure active surveillance of exposed workers at the affected holdings for human health complaints, particularly during and after culling operations. Additionally, persons with direct exposure to wild birds should be monitored and as a minimum, exposed persons e.g. involved in culling activities, should be instructed to report health complaints (passive monitoring).

Currently the risk of travel-related importation of human cases due to avian influenza virus infection, particularly from Asia is low. This is based on the fact that a low number of human cases are currently reported from China indicating a low level of human exposure to A(H7N9) viruses in poultry markets and the environment. This could also serve as an indicator for low level circulation in poultry. With the decrease of the ambient temperature over the winter months the situation could, however, change very rapidly as it has been the case during the previous waves during the months of November and December. The fact that clusters of cases with likely human-to-human transmission have been observed and the identified potential of HPAI A(H7N9) viruses to transmit between mammals via droplets is concerning. Specific caution should be taken if humans are identified to be infected with HPAI viruses to avoid and control further transmission events.

Outbreaks of A(H5N8) continue in Europe and with the high capability of the virus to reassort with other local avian influenza viruses, the threat of avian influenza viruses of A(H5N8) to transmit to humans after adaptation processes or through the acquisition of new characteristics via reassortment remain.

Protective measures have been recommended in accordance with national guidelines for HPAI, including personal protection equipment and oseltamivir prophylaxis for up to 10 days after the last contact. Information about national recommendations regarding avian influenza can be found at the ECDC website (ECDC, online). Persons exposed to the virus are asked to report any symptoms to the municipal health service and in the event that they develop conjunctivitis or influenza-like-illness, sampling material will be obtained for diagnostic testing. These measures have also been recommended by the US Centers for Disease Control and Prevention (CDC) during HPAI A(H5N1), A(H5N2) and A(H5N8) outbreaks in the US in 2015 (CDC, online). The FAO also raised awareness

regarding HPAI A(H5N8) providing general recommendations as well as those pertaining to poultry producers, hunters and national authorities (FAO, online-a).

Routine vaccination with seasonal influenza vaccine is recommended in most countries for workers having contact with birds and poultry to minimise the possibility of co-infection with human and avian influenza viruses thereby reducing the theoretical risk of reassortment.

Persons in direct contact with infected poultry before or during culling and disposal, including poultry workers, should be monitored for 10 days, in order to identify possible related influenza-like symptoms, fever or conjunctivitis. Local health authorities may consider actively monitoring these groups. Administration of antiviral prophylaxis for exposed persons (as recommended for A(H5N1)) can be considered as a precautionary measure depending on the local risk assessment (i.e. intensity of exposure) and in the context of the start of seasonal influenza in the EU to minimise the likelihood of reassortment events (ECDC, 2006). Considering the severity of the disease, the fact that limited human-to-human transmission cannot be excluded in some clusters, that no vaccine is available on the market against A(H5Nx) or A(H7N9) and the favourable safety profile of the anti-viral drugs of choice, it is likely that the benefits of post-exposure chemoprophylaxis of close contacts with neuraminidase inhibitors outweigh the risks (European Centre for Disease prevention and Control, 2017).

Healthcare workers managing symptomatic exposed (or possible) cases should follow standard, contact and respiratory precautions, depending on the local risk assessment.

4. Conclusions

HPAI and LPAI outbreaks in Europe between 1 September and 15 November 2017 (TOR 1 and TOR 2)

Main observations:

- To date, no human infections with HPAI or related LPAI viruses have been reported in the EU.

- In the EU, between 1 September and 15 November 2017 (based on ADNS):
  - 48 HPAI A(H5N8) outbreaks were reported in poultry: 44 in Italy and 4 in Bulgaria,

  - there were no H5 HPAI outbreaks in captive birds,

  - 7 H5 HPAI events were reported in wild birds in 3 MSs (1 in Cyprus, 1 in Germany and 5 in Italy) and in 2 events in Switzerland,

  - 6 H5 LPAI outbreaks were reported in poultry in 3 MSs (4 in Italy, 1 in France, 1 in the Netherlands) and 1 H5 LPAI outbreak in captive birds in Germany.

- A second epidemic wave started in Italy on the third week of July and is still ongoing as of 15 November 2017; 63 outbreaks in poultry (mainly turkey) holdings and 7 events in wild birds were confirmed as caused by HPAI viruses of A(H5N8) subtype. Around half of the outbreaks were caused by secondary spread.

- HPAI A(H5N8) induced high mortality in chickens and turkeys but variable (low to high) mortality in ducks, geese and game birds.

Conclusions:

- The risk of zoonotic transmission to the general public in the EU/EEA countries is considered to be very low.

- Despite the ongoing human exposures to infected poultry during the outbreaks, no transmission to humans has been identified.

- The HPAI A(H5N8) virus persisted during winter into the late summer at least and still results in wild bird infections and in primary introductions in poultry holdings. It suggests that the virus is able to persist in the EU in wild bird populations, the environment, or both, during the period between two winters.

- An update of the list of wild bird target species for passive surveillance activities is provided based on the reported AI-infected wild birds since 2006.

Applied prevention and control measures (TOR3)

Main observations:

- Italy performed a detailed analysis of the outbreaks occurring during summer and autumn 2017, which provided the insights to primary/secondary outbreaks and to the most likely sources of virus introduction and spread.

- Strengthening of control measures by the Italian competent authority has been applied and includes an enlarged restriction zone.

Conclusions:

- The Italian epidemiological investigations indicated the more likely sources of secondary spread in a densely populated poultry area: sharing of vehicles (especially feed lorries), sharing of personnel (including also holdings belonging to the same owner or relatives), and close proximity to infected holdings (neighborhood spread).

AI situation in other continents between October 2016 and August 2017 (TOR4)

Conclusions:

- The current epidemiology of HPAIV A(H5N6) in Asia, with widespread occurrence in migratory birds of the order *Anseriformes*, and continued detection in the period under review, indicates a risk of long-distance spread of this virus to wintering grounds westwards to western Asia, Europe, Africa, and the Middle East and eastwards to western North America, similar to that of HPAIV A(H5N8) and HPAIV A(H5N1) in previous years.

- The current human case of HPAI A(H5N6) in China underlines the continuing threat of this avian influenza virus to human health.

- Close monitoring is required of HPAI of the subtypes A(H5N1) and A(H5N8) situation in Africa, given the rapidity of the evolution and the uncertainty on the geographical distribution of these viruses.

- No human case has ever been reported in the EU due to avian influenza viruses subtypes A(H5N1), A(H5N6), A(H7N9) or A(H9N2). Small human clusters have been identified in countries where these viruses are endemically circulating in poultry, but no sustained human-to-human transmission has been observed although sporadic human-to-human transmission, especially with A(H7N9) have been identified.

5. Suggestions

- Interactions between EFSA and MSs has taken place to initiate discussions on improving the quality of data collections and the exchange of denominator data, but further efforts are required. This includes data on poultry population structure, housing and management to facilitate data and risk factor analysis, and hence to strengthen science-based advice to risk managers. There is a need to promote a common understanding and application of definitions related to control activities and their reporting across MSs.

- Continued surveillance for avian influenza virus in wild birds and poultry combined with timely data sharing among MSs as well as between animal and human health sectors is crucial to detect and respond early to threats relevant for animal and public health.

- Timely generation of complete viral genome sequences, coupled with intensified wild bird surveillance on wetlands of ecologic importance for avian influenza viruses, is important to improve our understanding of the virus dissemination routes and support early detection of viruses highly pathogenic to poultry or believed to be of immediate concern to human health.

- Robust consistent approaches for the genetic analyses of viruses and interpretation of data to inform decision making for control would be beneficial amongst EU providers. Additionally there is a need for a more consistent approach to evaluating zoonotic risk based on molecular data.

- Alternatives to culling need to be kept in mind to rescue valuable avifaunistic collections after incursions of AI. These alternatives are based on specific risk assessment, intensive clinical surveillance and sampling and proper housing and quarantine of remaining birds.

- In the case of AI detection in wild birds in a MS, detailed, real-time (active and passive) surveillance of wild birds is valuable to help assess acute risk for infection in poultry. Detection of morbidity and mortality from AI in wild birds can be optimized by timely investigation at sites where migratory birds first arrive, and facilitated by awareness of characteristic clinical signs of AI. Wild bird surveillance may benefit from central coordination of information exchange during outbreaks, readily available specific guidelines, and adequate resources for adequate sampling and testing of specimens.

- There is a need for strengthening collaboration at national, EU and global levels to monitor the AI situation in order to increase preparedness. Targeted wild bird surveillance programmes at a few priority locations within the EU should be considered, modulated and pro-active in relation to risk factors and uncertainties at a global scale (e.g. taking into account temporal and geospatial events).

- Addressing AI in a One Health Approach should be stimulated at national and international levels.

- There is a need to improve the collection and reporting of information on exposure events of people to AI.

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Abbreviations

AI	Avian Influenza
CDC	Center for Disease Control
CHP	Centre for Health Protection
CONSISE	Consortium for the Standardization of Influenza Sero-Epidemiology
CRBCs	Chicken red blood cells
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority
EURL	European Union Reference Laboratory for Avian Influenza
EWRS	Early Warning and Response System
FAO	Food and Agriculture Organization
HPAI	Highly pathogenic avian influenza
IHR	International Health Regulations
ISARIC	International Severe Acute Respiratory and Emerging Infections Consortium
LBM(s)	Live bird market(s)
LPAI	Low pathogenic avian influenza
LPM(s)	Live poultry market(s)
MS(s)	Member State(s)
OIE	World Organisation for Animal Health
PAFF Committee	The Standing Committee on Plants, Animals, Food and Feed
Q	Glutamine
WHO	World Health Organization
FRZ	Further restriction zone

Appendix A –Additional data on characterisation of affected holdings

Table A1: Additional epidemiological data (complementing ADNS) requested by EFSA (EFSA data collection)

Variable	Question	Possible answers	Definitions and clarifications
Sampling programme type	In which context the samples were collected?	- Outbreak-related surveillance - Surveillance active - Surveillance passive	'Outbreak-related surveillance', as part of outbreak response i.e. control zones, tracings; 'Surveillance passive', notifications of disease suspicion. 'Surveillance active', background screening of apparently healthy populations outside mandatory EU programme but part of early warning mechanisms. Early detection of outbreaks can be reported under 'surveillance passive', unless it was performed under an active/outbreak-related surveillance activity
Outbreak detection - mortality	Was the outbreak detected based on increased mortality?	- Y - N - NA	Report the first/main signs that triggered the detection of the outbreak; multiple 'Yes' (Y) are allowed in case more than one sign triggered the detection of the outbreak. For mix production systems, report the information for the first affected species. In case a sign has been checked, but did not trigger the detection, choose 'NO' (N). In case the sign has not been checked or the information is missing, leave 'Not Available' (NA)
Outbreak detection - clinical signs	Was the outbreak detected based on presence of clinical signs?	- Y - N - NA	Report the first/main signs that triggered the detection of the outbreak; multiple 'Yes' (Y) are allowed in case more than one sign triggered the detection of the outbreak. For mix production systems, report the information for the first affected species. In case a sign has been checked, but did not trigger the detection, choose 'NO' (N). In case the sign has not been checked or the information is missing, leave 'Not Available' (NA)
Outbreak detection - drop egg production	Was the outbreak detected based on a drop in egg production?	- Y - N - NA - NR	Report the first/main signs that triggered the detection of the outbreak; multiple 'Yes' (Y) are allowed in case more than one sign triggered the detection of the outbreak. For mix production systems, report the information for the first affected species. In case a sign has been checked, but did not trigger the detection, choose 'NO' (N). In case the sign has not been checked or the information is missing, leave 'Not Available' (NA). In case the outbreak refers to non-egg production, mark 'Not Relevant' (NR).
Outbreak detection - drop feed/water intake	Was the outbreak detected based on a drop in feed and/or water intake?	- Y - N - NA	Report the first/main signs that triggered the detection of the outbreak; multiple 'Yes' (Y) are allowed in case more than one sign triggered the detection of the outbreak. For mix production systems, report the information for the first affected species. In case a sign has been checked, but did not trigger the detection, choose 'NO' (N). In case the sign has not been checked or the information is missing, leave 'Not Available' (NA)

Outbreak detection - non-clinical indicators	Was the outbreak detected based on other non-clinical indications?	- Y - N - NA	Report the first/main signs that triggered the detection of the outbreak; multiple 'Yes' (Y) are allowed in case more than one sign triggered the detection of the outbreak. For mix production systems, report the information for the first affected species. In case a sign has been checked, but did not trigger the detection, choose 'NO' (N). In case the sign has not been checked or the information is missing, leave 'Not Available' (NA). Other non-clinical indications refer for instance to serology, link with another outbreak, etc. In fact, it can be everything that is not covered by 'increased mortality', 'presence of clinical signs', 'drop in egg production' or 'drop in feed and/or water intake'.
Secondary outbreak data	Are there convincing data available supporting that the outbreak in the affected holding is a secondary outbreak?	- Y - N - NA	To be filled ONLY for secondary outbreaks. Insert 'NO' (N) if the information is not present. Insert 'Not Available' (NA) if you don't know whether the information exists or not. 'Primary outbreak' means an outbreak <u>not epidemiologically linked</u> with another outbreak in domestic birds (including poultry and/or captive birds, commercial and/or non-commercial holding); 'secondary outbreak' means an outbreak <u>epidemiologically linked</u> with another outbreak in domestic birds.
Holding ID	EFSA will generate a unique holding ID	Text/Number	Dummy identifier. The geo-coordinates might not be sufficient to identify the same holding. 'Holding' means any agricultural or other premises, including hatcheries, circuses, zoos, pet bird shops, bird markets, backyards and aviaries, where poultry or other captive birds are being bred or kept. However, this definition does not include slaughterhouses, means of transport, quarantine facilities and centres, border inspection posts and laboratories authorised by the competent authority to hold avian influenza virus.
Holding production category	What is the category of affected holding?	- Commercial - Non-commercial	'Commercial holding' means a holding where poultry are kept for commercial purposes; 'Non-commercial holding' means a holding where poultry or other captive birds are kept by their owners: (a) for their own consumption or use; or (b) as pets[1].
Zoo	Was the affected unit a zoo?	- Y - N	'Zoos' means all permanent establishments where animals of wild species are kept for exhibition to the public for 7 or more days a year, with the exception of circuses, pet shops and establishments on the grounds that they do not exhibit a significant number of animals or species to the public[2]
Total number of epidemiological units	Number of epidemiological unit in the holding	Number	There can be more than 1 epidemiological unit in a holding. In this case each unit should be separated from the other unit by adequate and well implemented biosecurity measures (upon official veterinary judgement) so that it can be considered independent.
Epi Unit ID	Provide a unique identifier for each epidemiological unit in the	Text/Number	Dummy identifier. There must be as many Flock ID as the number reported in the "total number of epidemiological unit".

	holding		
Epi Unit affected	Is the epidemiological unit affected by the virus at the time of outbreak confirmation?	- Y - N	It can be that, e.g., only 2 out of 5 epidemiological units in a holding might be affected by the virus at the time of outbreak confirmation
Epi unit Genus of the birds present	What is the Genus of the domestic birds present in the epidemiological unit (Linnaeus)?	Free text	Genus of the present birds in the epidemiological unit. All genus gathered by the 4 orders (Anseriformes, Galliformes, Columbiformes, Passeriformes) Note: the same Epi Unit ID can be repeated (inserting new rows) in case in the same epidemiological unit more than one genus is present. E.g. a backyard is likely to be considered as one flock and therefore it will be associated to a single Epi Unit ID. However, in case, e.g., chickens and ducks are bred together, the database should have two rows with the same Epi Unit ID, but different genus.
Epi unit Species of the birds present	What is the Species of the domestic birds present in the epidemiological unit (Linnaeus)	Free text	Species of the present birds in the epidemiological unit. All species gathered by the 4 orders (Anseriformes, Galliformes, Columbiformes, Passeriformes) Note: the same Epi Unit ID can be repeated (inserting new rows) in case in the same epidemiological unit more than one species is present. E.g. a backyard is likely to be considered as one flock and therefore it will be associated to a single Epi Unit ID. However, in case, e.g., chickens and ducks are bred together, the database should have two rows with the same Epi Unit ID, but different species.
Epi unit Common name of the birds present	What is the common name of the domestic birds present in the epidemiological unit	Free text	Common name of the present birds in the epidemiological unit Note: the same Epi Unit ID can be repeated (inserting new rows) in case in the same epidemiological unit more than one species is present. E.g. a backyard is likely to be considered as one epidemiological unit and therefore it will be associated to a single Epi Unit ID. However, in case, e.g., chickens and ducks are bred together, the database should have two rows with the same Epi Unit ID, but different species.
Epi unit - production type	What is the production type (per epidemiological unit)?	- Breeding - Fattening - Egg - Fois gras - Mixed - Other	'Breeding' refers to any breeding programme for the production of poultry, including for restocking of game birds
Epi unit - Susceptible population size	How many susceptible domestic birds were present at the time of the	Number	Number of susceptible birds (i.e. all birds present) in the epidemiological unit

	outbreak (per epidemiological unit)?		
Epi unit – clinical signs	How many clinically affected domestic birds were present at the time of the outbreak (per epidemiological unit)?	Number	Number of clinically affected birds (i.e. a fraction of all birds present) in the epidemiological unit
Epi unit - deads	How many dead domestic birds were present at the time of confirmation of the outbreak (per epidemiological unit)?	Number	Number of dead birds (i.e. a fraction of all birds present) in the epidemiological unit
Epi unit - Outdoor access	Had the domestic birds outdoor access in the 21 days before the outbreak (per epidemiological unit)?	- Whole day - Part of the day - No outdoor access - Unknown	Indicate for each epidemiological unit if there was outdoor access
Most likely source	What is the most likely source of the virus (per epidemiological unit)?	- Direct wild birds - Indirect wild birds - Direct poultry - Indirect poultry - Not applicable - Unknown	Direct wild birds: direct contact with wild birds or their secretions. Indirect wild birds: transfer of wild bird faeces into the premises by personnel, equipment, vehicles, feed/bedding. Direct poultry: movement of infected poultry onto premises. Indirect poultry: transfer of poultry faeces/products from another infected premises by personnel, equipment, vehicles, feed/bedding. Not applicable: for epidemiological units that are not affected Only one answer is possible since the idea is to identify the most likely source. If there are no data supporting a selection of the most likely source, then it is better to select 'unknown'. If there is indication that relevant wild bird species particularly including waterbirds or infected poultry have access to the epidemiological unit, then select the DIRECT route as most likely. Only select the INDIRECT route if wild birds or infected poultry cannot access the epidemiological unit
Most likely source_explanation	What are the convincing evidences supporting the indicated most likely source?	Free text	Describe and explain what are the convincing evidence supporting the 'most likely source' of the virus in the affected epidemiological unit
Exposed people	How many people were exposed to the	Number	A rough estimate is fine, if this would be available.

	virus during culling and destruction?		

[1] According to the definition provided in Article 2 of the Council Directive 2005/94/EC

[2] According to the definition provided in Article 2 of the Council Directive 1999/22/CEE

Annex to:

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Annex A –   Secondary spread of HPAI during July – November 2017 epidemic in Italy

Mulatti Paolo, Alessandra Azzolini, Giovanni Cunial, Diletta Fornasiero, Lebana Bonfanti, Stefano Marangon

Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro (Padua) - Italy

- **Epidemiological Situation**

Since the end of 2016, Italy has been experiencing circulation of Highly Pathogenic Avian Influenza (HPAI) A(H5N8) both in wild birds and domestic poultry. A first epidemic wave was observed in December 2016 – May 2017, with 16 outbreaks in poultry holdings and 7 cases in migratory birds. A second wave started on the third week of July and is still ongoing as of 15 November 2017; 63 outbreaks in poultry holdings and 7 in wild birds were confirmed as caused by HPAI viruses of A(H5N8) subtype (Figure 1). A total of 79 outbreaks have been confirmed in poultry between 21 January and 10 November, 2017.
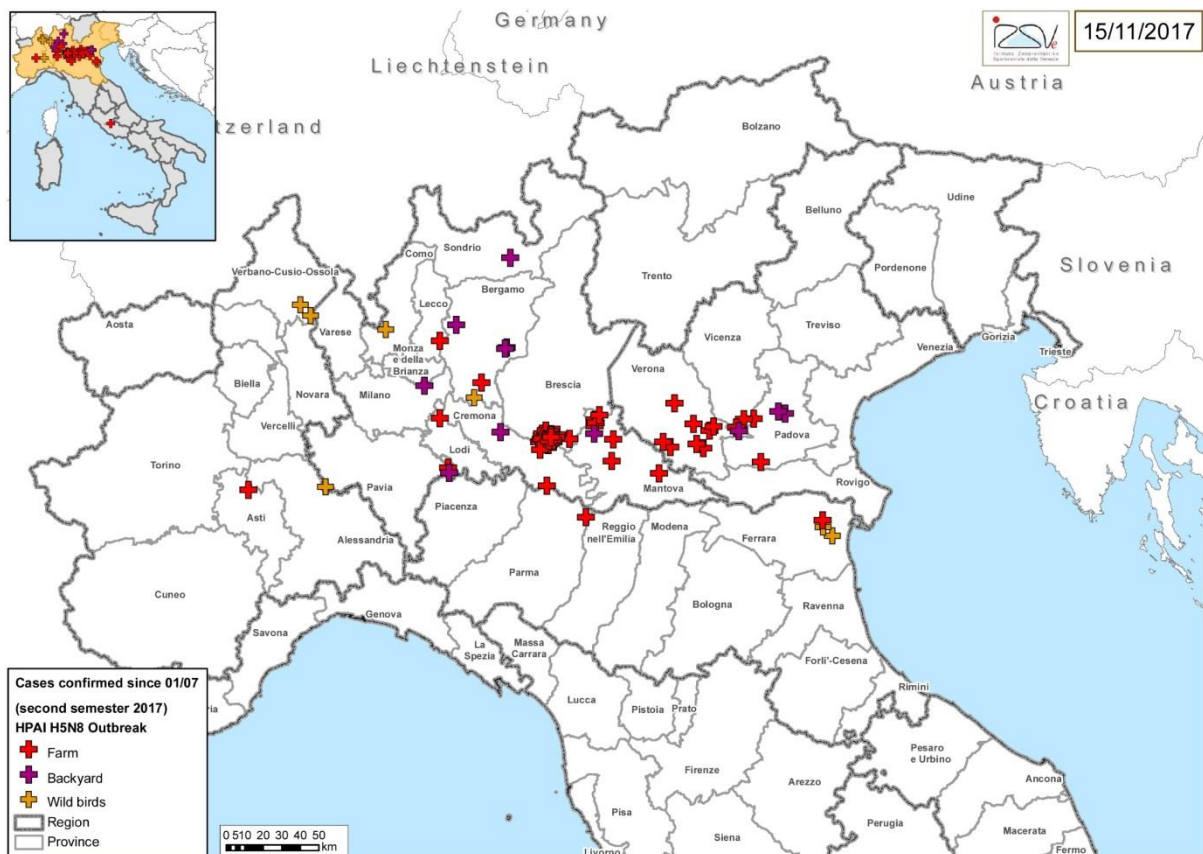

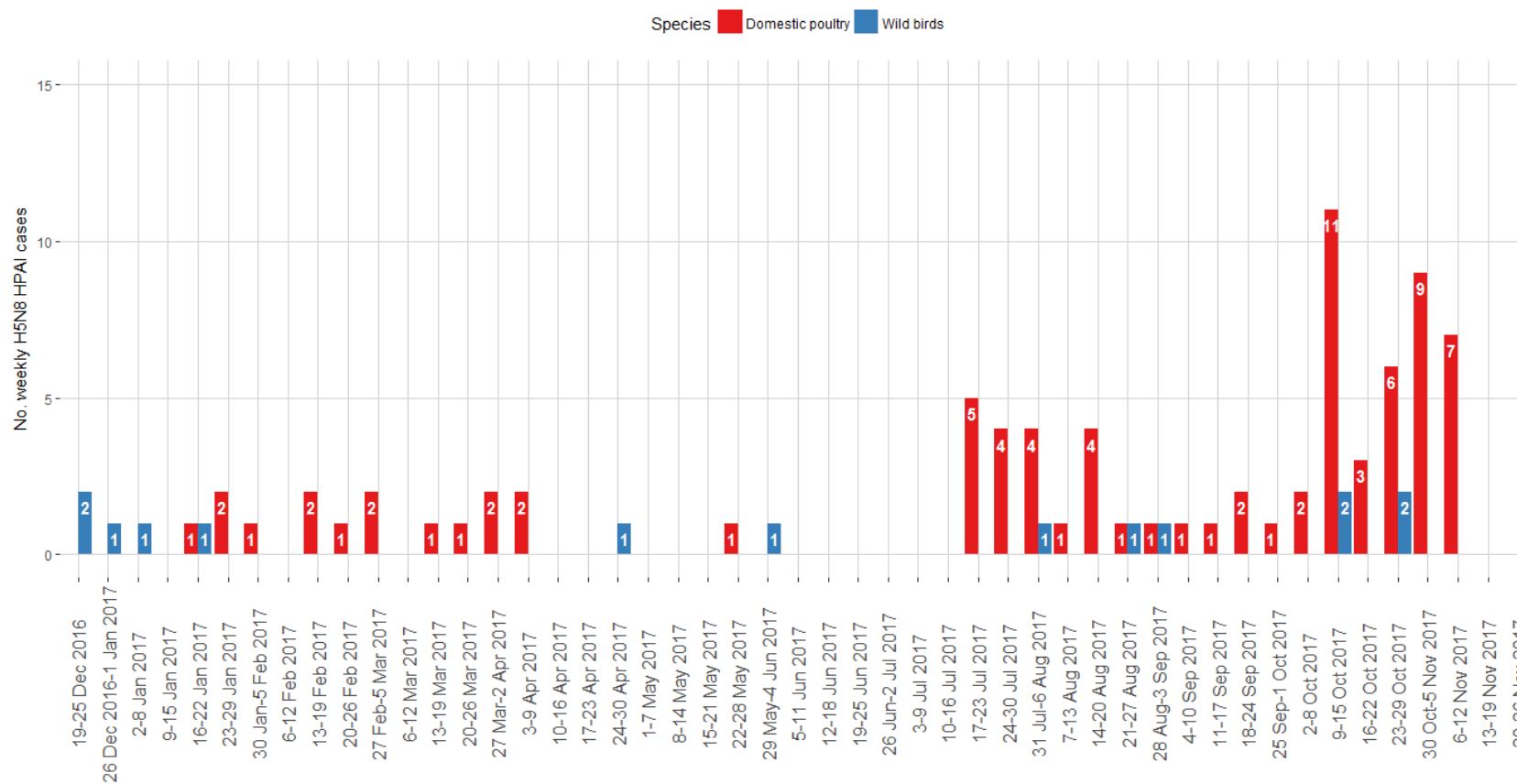**Figure 1:** Geographical distribution of HPAI A(H5N8) outbreaks in the second semester 2017 in Italy

Figure 2: Temporal evolution of the HPAI A(H5N8) epidemic in Italy; Red: outbreaks in domestic poultry, Blue: events in wild birds

- **Chronological overview of HPAI secondary spread**

Most of the affected holdings were located in proximity to wetlands used as nesting and wintering sites by residential and migratory wild birds. Up to the end of September, epidemiological and genomic analyses suggested that the majority of the outbreaks were compatible with multiple direct or indirect introductions from the wild reservoir. Nevertheless, lateral spread became more frequent starting from the first half of October, leading to a large cluster of secondary outbreaks in Brescia province between October and November 2017.

Lateral spread was observed in relation to four outbreaks; three of these were rapidly resolved with a maximum of 4 secondary outbreaks, the fourth is still ongoing as of 15 November.

Figure 2 indicates the timeframe of primary and secondary outbreaks during the second HPAI A(H5N8) epidemic in northern Italy. The graph reveals a first part with very low number of primary outbreaks, which is compatible with multiple point-introductions from wild birds. Contrarily in the last few weeks almost the totality of observed outbreaks was related to lateral spread, which represents a situation often observed during infectious disease epidemics.
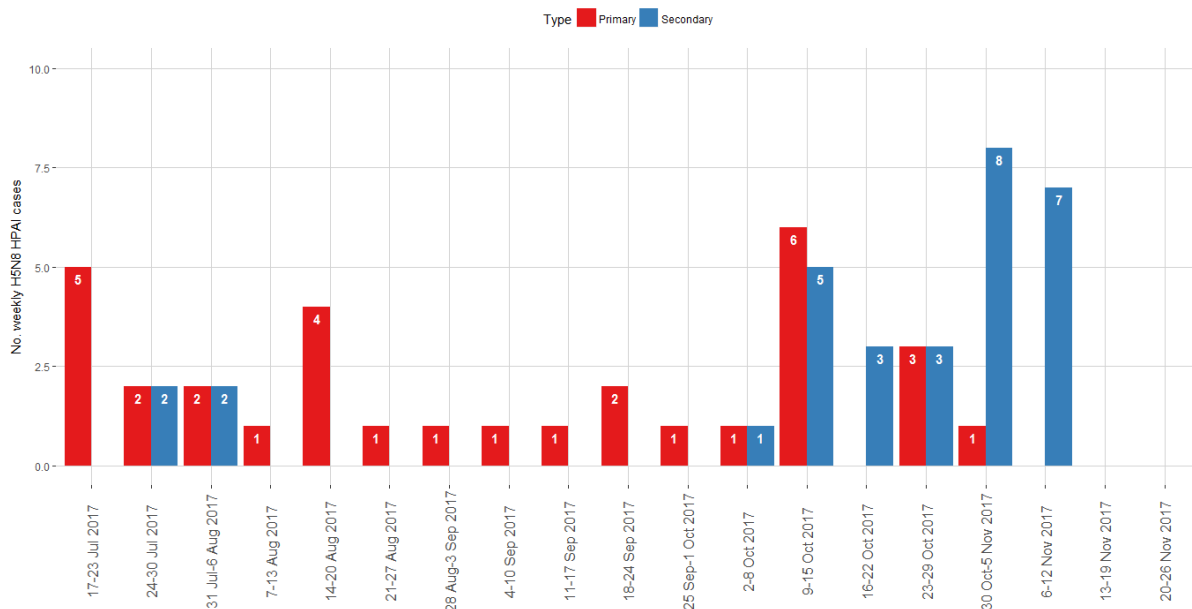

Figure 2: Temporal trend of primary and secondary outbreaks during the second HPAI epidemic wave in Italy (July-November 2017); Red: Primary outbreaks, Blue: Secondary outbreaks

- **Description of the production sector(s) that have been affected by secondary spread**

(i) Cluster in Mantova province (Lombardy Region)

The 19th outbreak was confirmed on 21 July at Castiglione delle Stiviere municipality in Mantova province (Lombardy region) in a large layer operation, which reared about 480,000 birds, in modified cages. The massive number of birds reared and the type of housing, together with the extreme climatic conditions that struck Italy in Summer 2017 (temperature above 40°C for extended periods, leading to increased mortality in birds due to the heat wave, and consequent saturation of the rendering premises), lead to a delay in the culling activities.

Depopulation required 15 days to be finalized, leading to the lateral spread of the virus to four neighboring meat turkey holdings (outbreaks 25, 26, 27 and 29), two of which were indicated to be preventively culled due to proximity to outbreak 19, but the stamping out procedures were not implemented due to the reasons described above.

Phylogenetic analyses corroborated the hypothesis of inter-holding spread, as the viruses showed a high percentage of similarity (ranging from 99.92% to 99.95% for the eight concatenated gene segments), with only 6 to 10 nucleotide differences distributed along the entire genome.

(ii) Cluster in Vicenza province (Veneto Region)

On 26 September, a fattening duck holding was confirmed positive for HPAI A(H5N8) virus in Vicenza province (Veneto region). In the same courtyard there were also other poultry sheds containing rural poultry to be sold to non-commercial holdings (grower holding).

On 6 October, a HPAI A(H5N8) virus was confirmed in a broiler holding, located at about 1 km from the previous outbreak in the same municipality. The holding showed not sufficient biosecurity, both at the managerial and at the structural level.

On 10 October a third HPAI A(H5N8) outbreak was confirmed in the same municipality, in a non-commercial holding that, a week before the appearance of AI signs, introduced birds from the grower holding belonging to the same epidemiological unit of the affected duck holding.

Phylogenetic analyses indicated that viruses isolated in these holdings resulted having a level of similarity between 99.9% and 100% both for HA and NA genes, confirming the hypothesis of lateral spread.

(iii) Cluster in the rural poultry sector (Lombardy Region)

On 10 October a non-commercial holding in Bergamo province (Lombardy region) tested positive for HPAI A(H5N8) virus. About ten days before the beginning of mortality in this holding, four laying hens were introduced from a live bird market in Bergamo. The epidemiological investigation traced-back to a grower holding which sold the four hens to the affected non-commercial holding at the market. Official controls confirmed the presence of the HPAI A(H5N8) virus also in this grower holding. Another HPAI A(H5N8) virus was detected in a rural holding in Bergamo province on 13 October, where birds were introduced from the same grower. Finally, another outbreak, confirmed on 16 October in a rural holding in Sondrio province (Lombardy region), resulted connected to the same grower.

The hypothesis of virus transmission from the grower to the non-commercial holdings is supported by the results of phylogenetic analyses, which indicated the viruses as strictly correlated (100% of similarity for both HA and NA genes).

(iv) Cluster in Brescia province (Lombardy region)

A fourth noteworthy episode of lateral spread occurred in Brescia province, and outbreaks related to this cluster represent the largest fraction of HPAI virus infected poultry holdings identified in Italy between October and November. The primary outbreak was confirmed in a fattening turkey holding (48th outbreak) located in the southern part of Brescia province (Lombardy region). On 8 October the birds were clinically inspected before loading for slaughter and, on the same night, the first load of turkeys was moved to a slaughterhouse located in Cesena (Emilia-Romagna region). Nevertheless, the following day an increase in mortality was observed in another shed, and HPAI A(H5N8) virus was detected.

A fattening turkey holding belonging to the same owner was identified in proximity (about 1 km away) to this outbreak and the decision to pre-emptively stamp out the birds was taken. Unfortunately, the presence of the HPAI virus was detected before the beginning of the killing operations (50th

outbreak). Other two outbreaks were confirmed on 19 October in two fattening turkey holdings in Brescia province (55th and 56th outbreaks), located respectively at a distance of about 100 m and 1 km from the roads used for transporting the birds from the 48th outbreak to the slaughterhouse. The owner of one of these turkey holdings had two other turkey operations that were preventively killed. Contact tracing activities also indicated another turkey holding located in a neighboring municipality managed by the son of the owner. In this case, preventive culling was not applied, as no contacts with the 55th outbreak were demonstrated. The holding resulted infected on 31 October (62nd Outbreak).

Other secondary outbreaks occurred in the following weeks, reaching a total of 21 outbreaks related to the same cluster (the last 5 outbreaks were detected on 10 November), in a group of 9 municipalities situated within a radius of approximately 7 km (**Error! Reference source not ound.**). Epidemiological investigations indicated the more likely sources of spread in: sharing of vehicles (especially feed lorries), sharing of personnel (including also holding belonging to the same owner or relatives), and closed proximity to infected holdings (neighborhood spread).
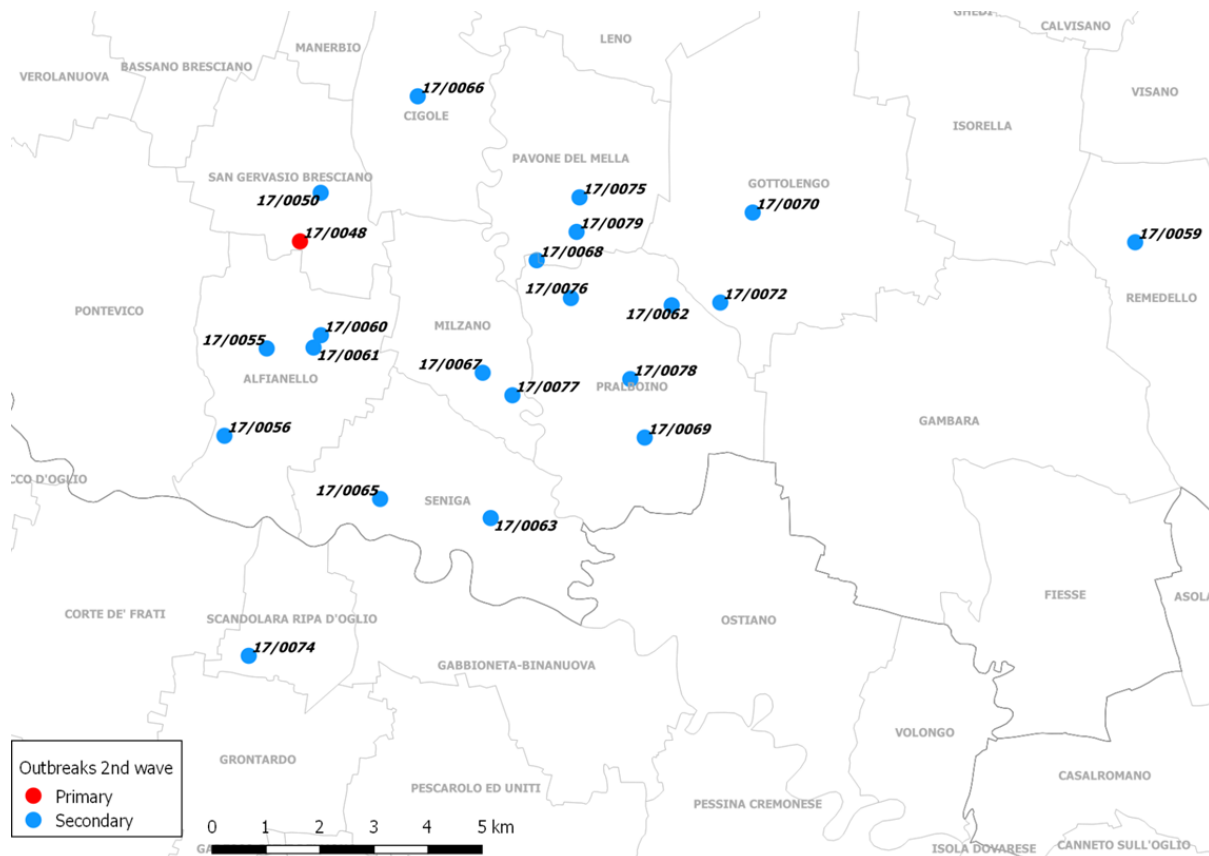

Figure 4: Geographical distribution of the secondary outbreaks in Brescia province

The production types affected by lateral spread of Avian Influenza are summarized in Table 1.

Table 1: Details of production types involved in the secondary outbreaks

Cluster	Conf. date Primary outbreak	Primary outbreaks	Secondary outbreaks						
			Broilers	Ducks	Chicken breeders	Meat turkeys	Laying hens	Non-commercial	Total Secondary outbreaks
Mantua	21/07/2017	Laying hens	0	0	0	4	0	0	4
Vicenza	26/09/2017	Fattening ducks	1	0	0	0	0	1	2
Bergamo	12/10/2017	Grower	0	0	0	0	0	4	4
Brescia	9/10/2010	Meat turkeys	3	3	1	9	5	0	21
Total			4	3	1	13	5	5	31

- ## Detection of the secondary outbreaks and Risk factor analysis

Highly pathogenic avian influenza outbreaks are usually reported after increases in mortality, or when other symptoms clearly referable to Avian Influenza are observed (e.g. neurological symptoms or sharp decreases in the productivity parameters).

In the clusters of Mantua, Vicenza and Bergamo provinces, outbreaks were detected via passive surveillance, with reported increased mortality. Epidemiological investigation and contact tracking activities allowed to identify the related primary outbreak. Results of phylogenetic/genomic analyses were also taken into account when assessing the potential lateral spread occurrence.

As for the cluster of secondary outbreaks in Brescia province, both passive surveillance measures and active monitoring activities related the occurrence of outbreaks lead to the detection of secondary outbreaks. More detailed contact tracking activities of the secondary outbreaks in Brescia, allowed to identify the potential risk contacts for 15 outbreaks out of 21 (71.43%) (Table 2). For the remaining 6 outbreaks phylogenetic analyses indicated high genetic similarities, strongly supporting the hypothesis of transmission between holdings, although no contacts were clearly reported.

Table 2: Contact tracking for the secondary outbreaks in Brescia Province.

Type of contacts	Number of potential risk contacts
Sharing of personnel	2
Sharing of vehicles	21 (9 holdings)
Proximity (within 1 000 m)	9

The high number of contacts at-risk through sharing of vehicles for feed, is mainly related to the functional compartmentalisation of Lombardy region. It has been requested, by veterinary authorities, that poultry holdings in Lombardy region shall not have contacts with free areas and in particular with premises outside this region. As such, vehicles used for feed transport need to circulate only within the area at risk or at least the regional territory of Lombardy. Feed was delivered to single holdings, without stopping by multiple premises, and vehicles were cleaned and disinfected both when entering and when exiting the serviced holdings. Cleaning and disinfection measures were applied also at the return of the lorries to the feed mill premises. However, due to the limited availability of vehicles, it was not possible to guarantee long stops between consecutive services; furthermore, some transport companies used the same lorries to visit holdings rearing different poultry species.

The identification of these risk factors, led to intensifying the cleansing operations on vehicles, prolonging the length of the stops before ensuing services, and to re-organise the feed transport activities in the region.

Annex B – Applied prevention and control measures on avian influenza ITALY

Mulatti Paolo, Giovanni Cunial, Alessandra Azzolini, Diletta Fornasiero, Lebana Bonfanti, Stefano Marangon

Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro (Padua) - Italy

1. Scope

This document provides a brief overview of specific prevention and control measures applied in Italy during the July-November 2017 in relation to avian influenza. This document is made to support the EFSA working group in generating an overview on the application of the selected measures at EU level.

2. Increasing awareness of the stakeholders and the general public

Details on Avian Influenza outbreaks occurred in Italy and on the epidemiological situation at the European level are provided and updated through the website of Istituto Zooprofilattico Sperimentale delle Venezie, where the National Reference Laboratory for Avian Influenza and Newcastle Disease has dedicated sections: http://www.izsvenezie.it/temi/malattie-patogeni/influenza-aviaria/situazione-epidemiologica-HPAI/; http://www.izsvenezie.it/temi/malattie-patogeni/influenza-aviaria/situazione-epidemiologica-hpai-europa/.

Other websites at the local/national level from various stakeholder groups and association (e.g. associations of poultry farmers, National and Regional veterinary associations, etc) link directly to the IZSVe website for updates on AI epidemiological situation, allowing to reach a broader audience.

Official communications by Competent Authority (Ministry of Health) on a new outbreak is forwarded for information to poultry farmer unions, poultry production companies, and veterinary associations.

Updates on the epidemiological situation are also forwarded to the Directorate for Health and Food Safety of the European Commission, and the World Organisation for Animal Health (OIE).

3. Biosecurity measures in high-risk areas

In accordance with Ministerial provision n° 8246 of 30 March 2017, high-risk areas for the introduction of H5/H7 HPAIV have been identified (Figure 3), by taking into account:

- Evolution of the HPAI A(H5N8) epidemiological situation;
- Risk factors for HPAIV introduction, accounting for the presence of wetlands and of wild waterfowl (with a particular focus on mallard ducks);
- Risk factors for HPAIV spread, including poultry population density and accounting for potentially different susceptibility according to the production type of reared birds;
- Outcomes of AI surveillance plan, indicating where notifiable AI viruses were detected in the past five years.

Figure 3: High risk areas for introduction and spread of HPAI in Italy

The risk factor for HPAIV introduction was based on the location of wetlands systems, according to the RAMSAR Convention (Figure 4).
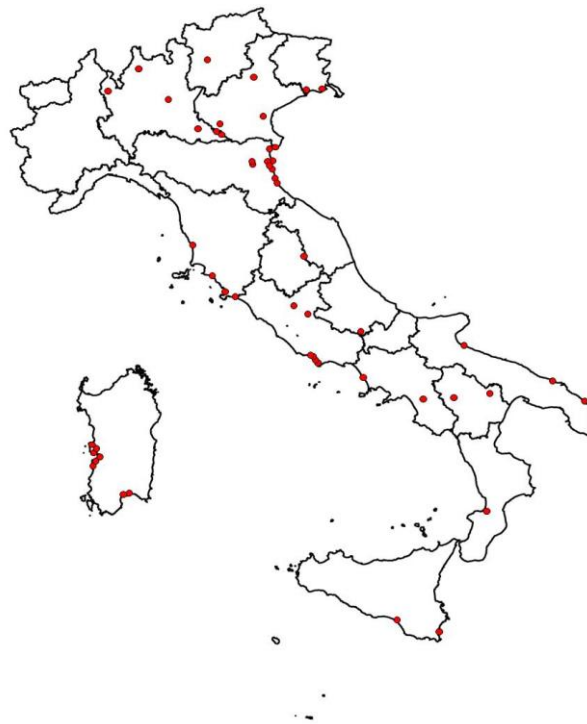

Figure 4: Distribution of wetlands systems in Italy

Data on consistency and distribution of waterbird populations wintering in Italy were available from the waterbird census which is undertaken as part of the IWC (International Waterbird Census) agreed at the European level. Censussed wintering Anatidae species included: European mallard (*Anas platyrhynchos*), Eurasian teal (*Anas crecca*), northern shoveler (*Anas clypeata*), Eurasian wigeon (*Anas penelope*), northern pintail (*Anas acuta*), garganey (*Anas querquedula*), gadwall (*Anas strepera*), common pochard (*Aythya ferina*) and tufted duck (*Aythya fuligula*).

The censuses number of wintering mallard ducks was used to define the population density throughout the Italian wetlands, by using spatial interpolation algorithms (Figure 5).
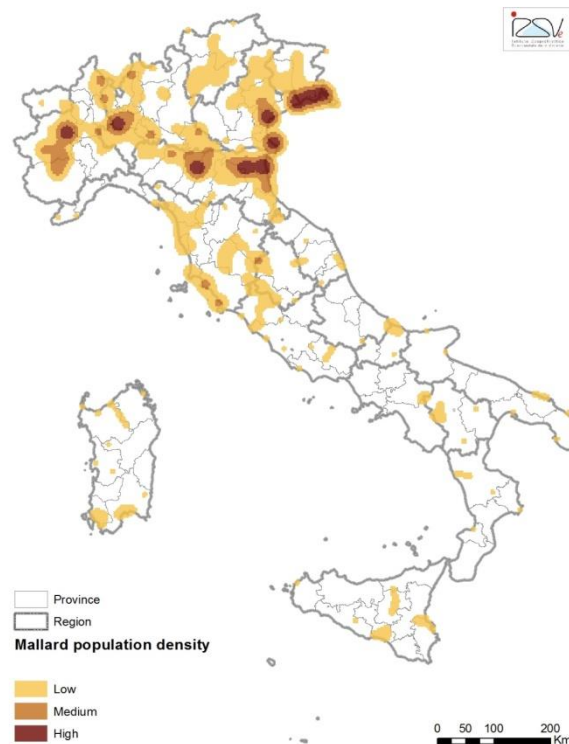

Figure 5: Density of wintering mallard ducks in the Italian wetlands

The density map is updated as soon as new census data are available, and it is accounted for in the risk-based approach for the National Surveillance Plan for avian influenza.

Within the high-risk areas, specific biosecurity measures were applied by means of:
- ban of free-range poultry rearing,
- ban on using superficial water reservoirs (sources that can be accessed by wild birds),
- feed and bedding materials stocks must be protected from wild birds or other animals,
- ban on exhibitions, fairs, and live-bird markets,
- ban on using live-decoy birds and/or rearing them in such conditions that allow them to have contact with wild birds.

4. Early detection

In accordance with Ministerial provision n° 8246 of 30 March 2017, significant productive or sanitary changes observed in holdings must be reported immediately to the Veterinary Services, such as:

- decrease in feed and/or water consumption,
- decreased production of eggs,
- clinical symptoms,
- increased mortality rate.

5. Establishment of a Further Restricted Zone

In view of the epidemiological situation and taking into consideration both the location of the HPAI A(H5N8) outbreaks (inside densely populated poultry areas) and the geographical distribution of poultry holdings, the Ministry of Health issued a provision to establish a Further Restricted Zone (FRZ) to prevent the further spread of the infection (Ministerial provision n°18012 of 28 July, as amended).

Measures applied at holding-level within the Further Restricted Zone:

- Census of industrial poultry holdings
- Birds shall be kept inside closed buildings and measures should be taken to reduce the risk of direct/indirect contact with wild birds
- Pre-movement clinical inspection and virological testing
- Enforcement of increased biosecurity measures regarding the vehicles and the personnel entering and exiting holdings
- Gathering of domestic birds for fairs, exhibitions and live-bird markets is banned
- Re-stocking of meat turkey holdings is prohibited - A derogation to this measure can be authorized only whether an official veterinarian has verified the compliance with new biosecurity standards (these requirements have been recently defined and applied to strengthen the level of biosecurity considering also the risk of AIV introduction from the wild reservoir) and IZSVe has evaluated the geographical risk of the holding according to the poultry density in the area and the proximity to other poultry premises.

The FRZ has been further updated accordingly to the epidemiological situation, increasing the territorial coverage. Figure 6 reports the most up-to-date FRZ (Ministerial Provision n°26651 of 21 November 2017).
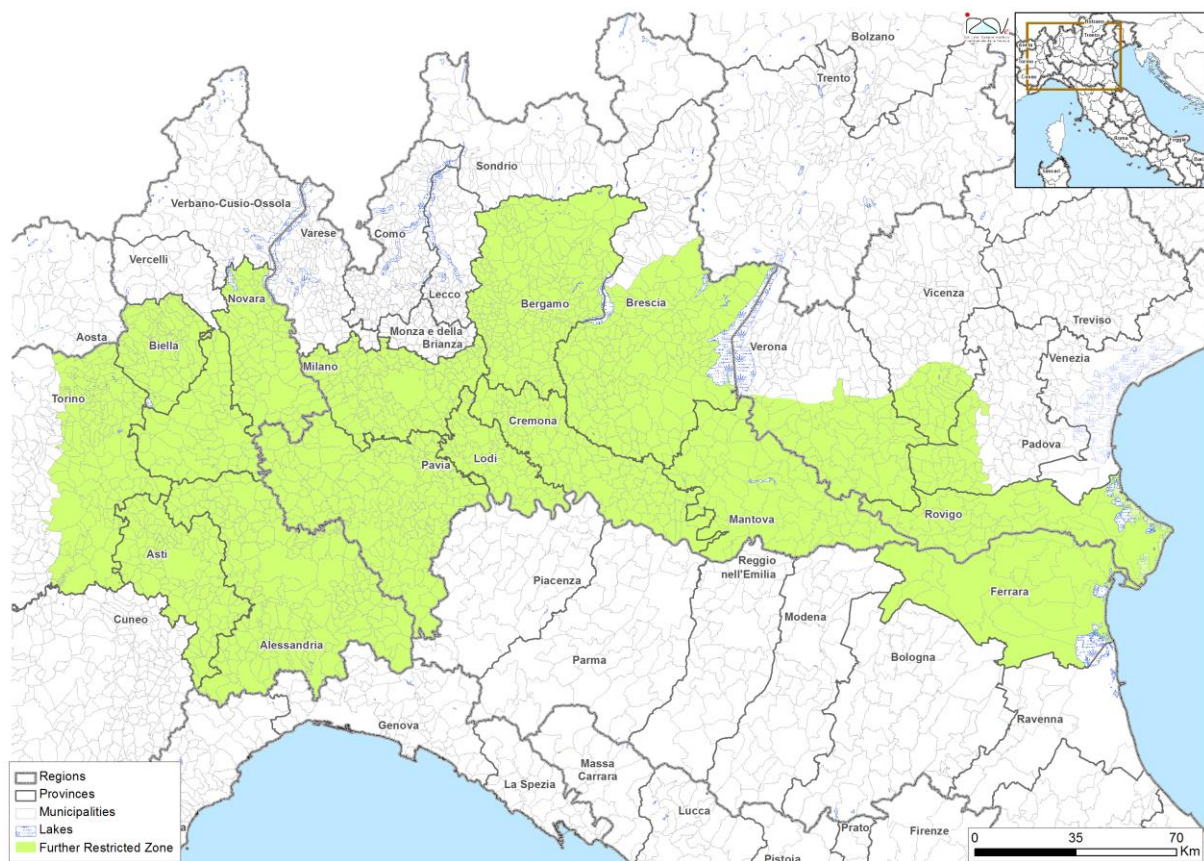
Figure 6: Further Restricted Zone active in Italy, as of 21 November 2017

6. Additional control measures

In accordance with Ministerial provision n°18012 of 28 July, as amended, additional control measures have been established:

- Transportation to slaughter of turkeys, ducks, geese, and of spent lay hens from holdings within the Further Restricted Zone is allowed if a clinical inspection is carried out 24 hours before the first transportation load. Moreover, turkeys have to be tested by tracheal swabs (20 birds per shed, up to a maximum of 60 samples per holding) 48 hours before the first transportation load. Clinical inspection has to be repeated every 48 hours up to the end of loading for slaughter. Whether during inspection any mortality is noticed, further samplings are needed on dead birds. For poultry slaughtered on Monday, samplings carried out the preceding Friday can be considered as valid;
- Spent hens have to be tested by tracheal swabs (20 animals per shed, up to a maximum of 60 samples per holding) 72 hours before loading for slaughter;
- Ducks and geese have to be tested by 30 tracheal and 30 cloacal swabs 48 hours before loading for slaughter;
- In laying hen/pullet holdings of the major producer regions (Lombardy, Piedmont, Emilia-Romagna, Veneto, Lazio) official veterinarians will test at least 20 animals per shed (up to a maximum of 60 samples per holding) by tracheal swabs every 21 days;
- Poultry companies operating in Lombardy, Piedmont, Emilia-Romagna, Veneto must ensure that there is a functional separation of activities, personnel and facilities between at-risk regions;
- Fairs, exhibitions and live-bird markets are banned within the Further Restricted Zone;
- Release of game for hunting is prohibited within the Further Restricted Zone.