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Technical Item

STRATEGIC CHALLENGES IN THE GLOBAL CONTROL OF HIGH PATHOGENICITY AVIAN INFLUENZA

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(90 SG/8)

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Summary

H5N1 2.3.4.4b clade high pathogenicity avian influenza (HPAI) has spread around the world causing an epizootic that has spanned five WOAH regions (Africa, Asia and the Pacific, Americas, Europe, and the Middle East) with continual threat to not only wild and captive birds and poultry, but also to wild, captive and domestic mammals, and humans. H5N1 clade 2.3.4.4b HPAI viruses are the main strains detected globally at present but other H5 clades, H7N3 and H7N9 HPAI viruses, continue to circulate in specific countries and sub-regions. The ecology and epidemiology of Gs/GD Eurasian lineage, especially the 2.3.4.4b clade, has changed with over 374 species of wild birds becoming infected, spreading the virus over established migratory routes, resulting in death of many birds, including endangered species, and serving as a source for transmission to poultry and wild mammals. Improved surveillance and sharing of HPAI information, data and viruses across veterinary, public health, wildlife and the environment sectors is needed to solve this complex One Health issue. The development of appropriate mitigation strategies or changes in husbandry and production practices can reduce the risk of introduction of the virus on farms, its amplification and viral evolution, and any spill-back to wild birds. The approaches to control of HPAI in countries where these 2.3.4.4b viruses remain endemic in poultry or have become endemic across wide geographic areas in some wild bird populations involve measures to reduce the effects of the disease in poultry, including vaccination, and reflect the difficulties encountered in using stamping out alone for virus elimination. The WOAH Terrestrial Animal Health Code allows use of vaccination under specific conditions and without negatively impacting HPAI-free status if appropriate surveillance is conducted. Trade in poultry and poultry products can take place safely in the presence of vaccination. Furthermore, zoning and compartmentalisation of HPAI freedom within a country can facilitate safe trade without unnecessary restrictions.

This Technical Item explores the ecological and epidemiological shift of HPAI observed at global level, by analysing the Members' response to a survey on HPAI control strategies and identifying some of the critical challenges that need to be considered by Members and stakeholders for a global coordinated response.

Keywords: Avian influenza, control, global threat, high pathogenicity, highly pathogenic, H5N1, vaccination, vaccines.

1. Global high pathogenicity avian influenza situation

1.1. Current Situation in the Global, Regional and National outbreak of HPAI

H5 and H7 high pathogenicity avian influenza (HPAI) have been notified to WOAH by 114 Members and non-Members across the WOAH regions of Africa, Asia and the Pacific, Americas, Europe and Middle East between 2005-2023 (as of 26 April) (Figs. 1-3). A total of 38,771 outbreaks were reported (poultry[1], non-poultry domestic birds and wild birds), resulting in over 31 million reported domestic and wild bird deaths, and 448 million domestic birds culled. The reported 129,280 wild bird deaths are likely a gross underestimation.

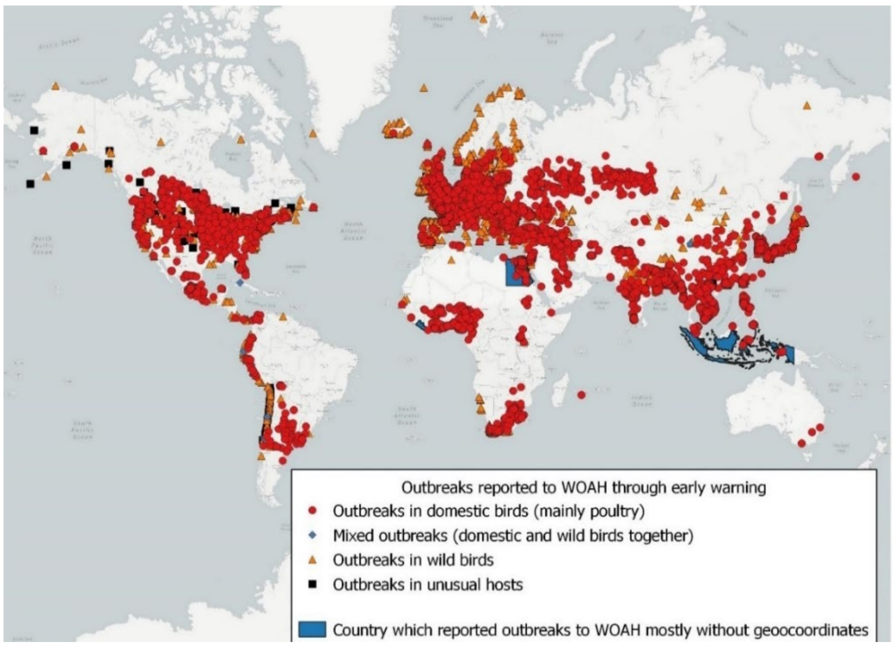

Fig.1. Cumulative reported presence of H5 and H7 HPAI (2005-2023, as of 31 March 2023).

Avian influenza (AI) viruses are classified, based on the surface glycoproteins, into 16 hemagglutinin (H1-16) and 9 neuraminidase (N1-9) subtypes (1). In addition, AI viruses are categorised into two pathotypes, low pathogenicity (LP) and high pathogenicity (HP), based on *in vivo* tests in chickens (intravenous pathogenicity index [IVPI] greater than 1.2) or detection of the genetic correlates for pathogenicity at the proteolytic cleavage site of the hemagglutinin (1; 2). To date, all H1-H4, H6 and H8-H16 viruses have been LPAI while H5 and H7 can be either LPAI or HPAI with HPAI viruses arising by mutation of the gene segment coding for hemagglutinin of LPAI viruses, typically following replication in chicken or turkey hosts. According to Chapter 1.3 of the WOAH Terrestrial Animal Health Code (Terrestrial Code), an infection with HPAI virus needs to be notified to WOAH in poultry, wild birds and non-poultry domestic birds. LPAI viruses that have proven natural transmission to humans with severe consequences or those causing an unexpected increase in virulence in poultry are also notifiable to

[1] For the purpose of the Terrestrial Animal Health Code (2022) 'poultry' refers to all birds reared or kept in captivity for the production of any commercial animal products or for breeding for this purpose, fighting cocks used for any purpose, and all birds used for restocking supplies of game or for breeding for this purpose, until they are released from captivity. Birds that are kept in a single household, the produce? of which are used within the same household exclusively, are not considered poultry, provided that they have no direct or indirect contact with poultry or poultry facilities. Birds that are kept in captivity for other reasons, including those that are kept for shows, racing, exhibitions, zoological collections and competitions, and for breeding or selling for these purposes, as well as pet birds, are not considered poultry, provided that they have no direct or indirect contact with poultry or poultry facilities.

WOAH. In addition, LPAI viruses in wild birds can be reported on a voluntary basis, through the voluntary report on non-WOAH-Listed diseases in wildlife (1; 3). However, Members should not impose bans on international trade of poultry commodities when notified of HPAI in wild birds or non-poultry.

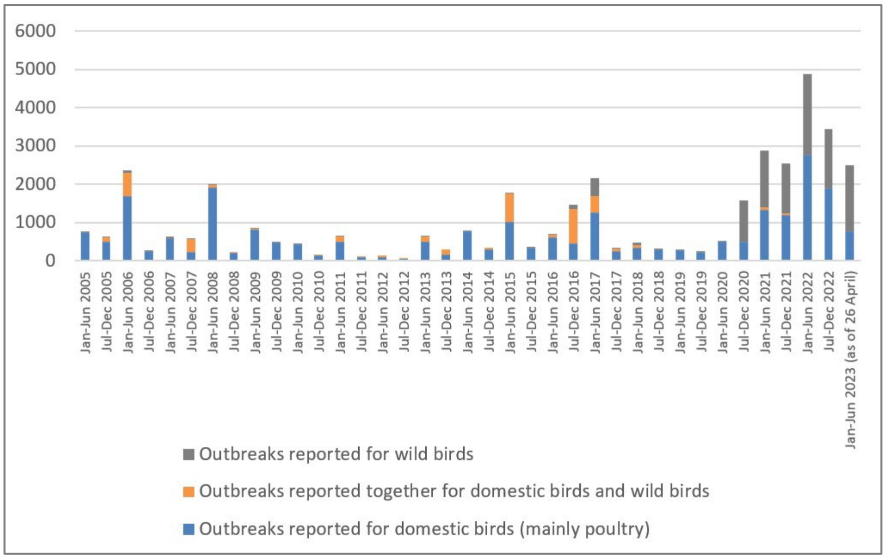

Fig. 2. Number of H5 and H7 HPAI outbreaks reported by animal category (as of 26 April 2023)

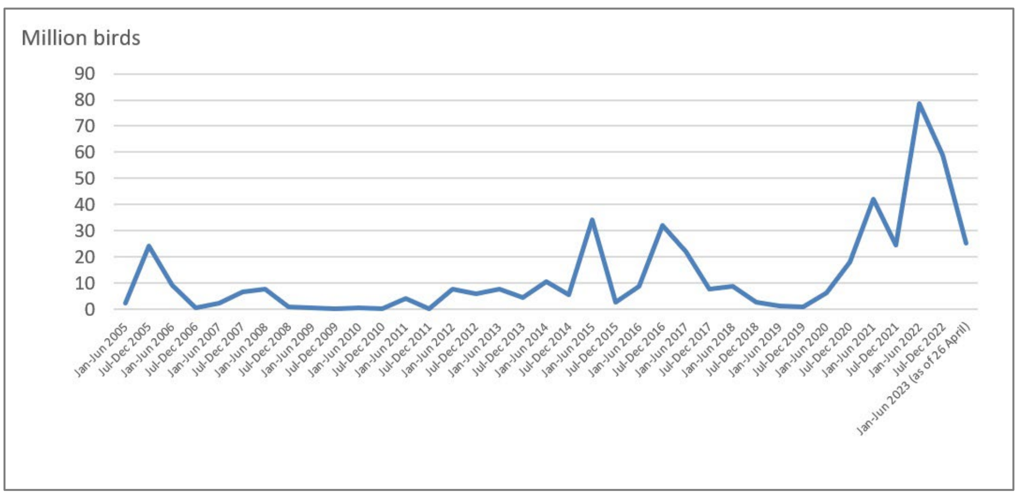

Fig.3 Number of deaths and culling of domestic birds affected by H5 and H7 HPAI from 2005- 2023 (as of 26 April 2023).

Since 1959, 44 distinct H5 and H7 hemagglutinin HPAI virus lineages have been identified with 41 being eliminated through stamping-out programmes, and three remaining lineages being entrenched in some poultry populations as of 2023: 1) H5Nx Goose/Guangdong (Gs/GD) Eurasian lineage (1996-present), spreads globally; 2) H7N9 Anhui1/13 Eurasian lineage (2017-present), restricted to China (People's Rep. of), and 3) H7N3 North American lineage (2012-present), restricted to Mexico (4; 5).

Wild aquatic birds serve as the genetic reservoirs of all LPAI viruses with transfer of these viruses to poultry with adaptation and onward spread within poultry populations (6). Historically, wild aquatic birds have not had significant involvement in epidemiology of HPAI except with the H5Nx Gs/GD Eurasian lineage. The H5Nx Gs/GD virus has genetically diversified through mutations to form multiple hemagglutinin genetic clades and subclades. Since 2005, there have been five intercontinental movements of the H5Nx Gs/GS HPAI virus as emergent virus clades: 2005, clade 2.2; 2008-2010, clades 2.3.2.1 and 2.3.4; 2014-2015, clade 2.3.4.4; 2016-2017, clade 2.3.4.4b; and 2.3.4.4b, 2020-2023 (Figs 2-3) (7-9). Furthermore, Gs/GD viruses were highly active in reassortment processes with various other LPAI viruses. This has led to the emergence of hundreds of different genotypes.

Beginning in October 2020, the 2.3.4.4b virus spread from central Asia to Europe, eastern Asia, Middle East, and Africa (Fig. 4). After crossing the north Atlantic, the virus caused the first cases in North America on the eastern edge of the Avalon Peninsula, Newfoundland, Canada (detected November 2021), triggering the beginning of extensive outbreaks in Canada and USA. In the fall of 2022, the virus moved from Canada and the USA into Mexico and Central and South America. In all geographic locations, the virus has caused extensive infections in diverse species of wild and captive aquatic and non-aquatic birds, extensive infections in poultry and other domestic birds, spill-over infections in wild mammals and farmed mink, and sporadic human infections.

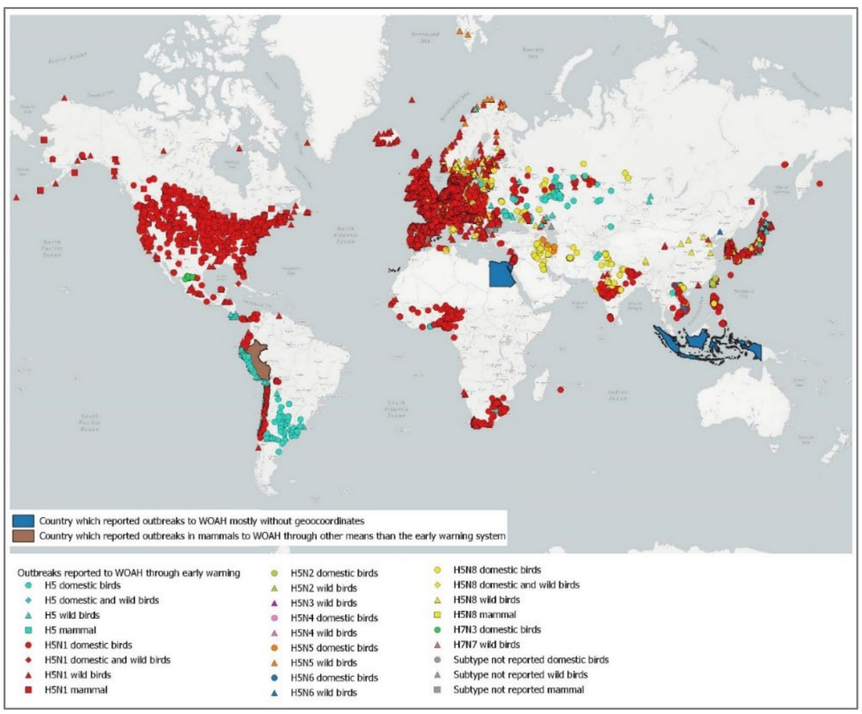

Fig. 4. Geographic spread of the 2.3.4.4b Gs/GD HPAI virus predominantly from October 2020 to 6 April 2023.

1.2. Challenges to HPAI Control in the diverse poultry industries

Poultry is the world's primary source of animal protein, accounting for 40% of global meat production, which in 2020 was 133 million tonnes of meat and 93 million tonnes of eggs (10). Chicken accounts for 90% of poultry meat production with substantial meat production of turkeys (5%), ducks (4%), geese and guinea fowl, and smaller production of quails, ostriches and pigeons. Chickens account for 93% of eggs produced and consumed. Integrated commercial poultry production systems feed not only the human populations of high- and middle-income countries but also billions of people in low-income countries. In addition, 80% of rural households in developing countries raise poultry, many using indigenous breeds, for domestic consumption purposes and for sale in the local markets, which serve as a critical food and income source, especially to women and children. Also, backyard poultry has significant production in middle-income countries and their numbers are rising in high-income countries. In addition to meat and eggs, poultry also provide additional outputs such as manure used as crop fertilizer, specialty food products such as feet, down for clothing and bedding insulation, ostrich leather and feathers for the fashion industry, and offal meal as protein for animal feeds. International trade in poultry, mainly as day-old birds or hatching eggs, and poultry products as listed above, contribute significantly to the global food security and economy. Poultry meat exports account for 11% of total production (15 million tonnes) and US$ 13.5 billion of value (11), and egg exports account for 3% (2.79 million tonnes) of production. Importation of commercial genetic stocks of poultry are critical in supporting meat and egg production systems of all countries. Poultry meat and eggs are a low-cost, high-quality, low-fat protein food source for the global human population, which provide commodity redistribution and economic benefit through trade and support the livelihoods of small farmers. Compared to other proteins of animal origin, poultry production has a lower carbon footprint relative to the amount of methane emissions per kilogram of meat produced (12).

The HPAI virus is generally highly transmissible, causing severe disease with high mortality in unvaccinated galliform poultry (chickens, turkey, quail, etc.), irrespective of the production system (1; 3). Understanding the poultry value chain of the different production systems is essential to be able to conduct a thorough risk assessment and permit development of effective mitigation of HPAI risks. The design and implementation of a biosecurity plan tailored to the different risk pathways is the principal mitigation strategy that prevents the introduction of the HPAI virus among a naïve population from affected domestic birds or, in relation to the H5Nx Gs/GD Eurasian HPAI virus, from wild bird carriers and their contamination of surrounding environments. This Gs/GD Eurasian lineage HPAI virus, especially the 2.3.4.4b clade, has been spread via wild bird migration and has infected over 375 wild and captive bird species with varying outcomes ranging from asymptomatic infections to individual bird mortality to massive die-offs in breeding colonies of specific bird species, thus negatively impacting avian biodiversity (13). This virus also infects domestic ducks and other waterfowl with many affected flocks having low to no mortality but serve as a local reservoir for the virus replication, shedding, environmental contamination and spread to galliforme poultry and potentially re-exposure and infection of wild birds. The WOAH Terrestrial Code provides recommendations for the recovery of free status after a minimum period of 28 days (two flock-level incubation period) when a stamping-out policy has been completed (i.e. after the disinfection of the last affected establishment) but does not support stamping-out strategies in wild birds (3). Vaccination of poultry is recommended under certain conditions, as a complementary tool to stamping out or to maintain food production and security in HPAI endemic countries, when the probability is high that the disease cannot be rapidly contained by methods based on stamping out, or when existing biosecurity measures along the value chain are insufficient alone to prevent HPAI. Vaccination will not affect the HPAI status of a free country or zone if surveillance supports the absence of infection. The WOAH Terrestrial Code also provides risk-based guidance on trade in poultry and poultry products based on HPAI freedom in country, zone or compartment, and any mitigation strategies used as well as recommendations for effective surveillance in domestic and wild bird population. Guidelines for diagnostic techniques and vaccines for HPAI are covered in the WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (1).

2. Key changes driving the 2.3.4.4b Gs/GD Eurasian lineage HPAI epidemic

2.1. Ecological and epidemiological changes in wild birds and mammals

Wild aquatic birds are the reservoir for LPAI viruses, and such infections are not associated with disease or mortality in their hosts. Over long periods of time, some of these LPAI viruses have moved into galliforme poultry and non-poultry domestic birds through direct or indirect exposure followed by adaptation and circulation. Some of the H5 and H7 LPAI viruses have mutated at the hemagglutinin proteolytic cleavage site to become HPAI viruses, creating unique genetic lineages of HPAI viral hemagglutinin. Historically, HPAI viruses have not been transferred back into wild aquatic birds, and wild aquatic birds have not had significant involvement in the spread of HPAI to poultry or other domestic birds.

The H5Nx Gs/GD Eurasian lineage was first detected in domestic geese in southern China (People's Rep. of) with early infections reported from chickens, ducks, and geese. It caused fatal disease in poultry and humans in Hong Kong in 1997 but that specific strain of the virus was eradicated there. By 2001 it was evident that the virus was causing infection in domestic ducks (14; 15). Beginning in 2002, the Gs/GD Eurasian lineage was causing infections and mortality in a variety of captive waterfowl species in Hong Kong Kowloon Park, and in 2003-2004 moved to nine Asian countries including Indonesia, Japan and Korea. In 2005, the lineage (clade 2.2) was associated with movement of the virus through migration of infected wild waterfowl from Asia to Europe and Africa. Such transregional spread of the Gs/GD Eurasian lineage HPAI has occurred during five time periods (2005 [clade 2.2], 2008-2010 [clade 2.3.2.1 and 2.3.4], 2014-2015 [clade 2.3.4.4 and 2.3.2.1c], 2016-2017 and 2020-2023) with the latter two involving clade 2.3.4.4b (16). The most recent series of wild bird HPAI cases (1 October 2020 - 6 April 2023) has had the widest geographic spread with 72,356 wild bird cases in over 74 countries and territories across Africa, Americas, Asia and Pacific, Europe, and the Middle East (Fig 5.); an unprecedented occurrence without previous historical context. This virus clade is highly infectious for domestic and wild ducks, requiring only small virus doses to produce infections with the virus shedding over more than 14 days (17; 18). This ecological change has led to the HPAI 2.3.3.4b Gs/GD Eurasian lineage being established as an endemic virus in some wild aquatic bird populations and spill-over into scavenger and predatory birds, and wild mammals (19). These infected migratory aquatic birds now serve as a vector of the virus, triggering transmission to outdoor reared domestic birds or indirectly disseminating the virus through breaches in biosecurity from contaminated environments outside of barns. The wild aquatic birds can introduce the HPAI virus to indigenous populations of a variety of wild bird species with independent maintenance and contribution to further virus diversity. Furthermore, mass mortality events have been reported for many wild aquatic and non-aquatic birds species such as common cranes (*Grus grus*) in Israel; African penguins (*Spheniscus demersus*) and Cape cormorants (*Phalacrocorax capensis*) in southern Africa; Peruvian pelicans (*Pelecanus thagus*) and Brown Boobies (*Sula leucogaster*) in South America (20); sandwich terns (*Thalasseus sandvicensis*) in the Netherlands (21); (*Stercorarius skua*) and Northern Gannets (*Morus bassanus*) in Great Britain (22) and turkey vultures (*Cathartes aura*) and black vultures (*Coragyps atratus*) in the USA. Such large mortality events have had a negative impact on wild bird populations, changing the diversity of species in critical ecosystems, and have further endangered some threatened avian species. By contrast, the other two entrenched HPAI viruses, H7N3 North American and H7N9 Eurasian HPAI viruses, have been maintained through lateral premise-to-premise spread in commercial and live bird market system poultry populations, and based on surveillance, wild birds have not been implicated as biological vectors in their maintenance and spread.

Increasing numbers of clade 2.3.4.4b virus infections are being reported in wild and captive mammals[2] including 24 species of carnivores such as red foxes (*Vulpes vulpes*), skunks (*Mephitis mephitis*), common raccoon (*Procyon lotor*), mountain lion (*Puma concolor*), and various bears, and in four species of sea mammals: harbour seals (*Phoca vitulina*) and sea lions (*Otaria flavescens*), and purported evidence of infection in domestic pigs (serology only) and wild boars (artiodactyls) within Europe and the Americas (23). A recent outbreak of 2.3.4.4b clade in a farm of 51,986 mink in northwest Spain had an additional genetic mutation: T271A in the PB2 gene. (24). The mink cases had raised suspicion of mammal-to-mammal transmission, suggesting increased potential public health risk, although changes in the receptor binding site compared to those typical of human pandemic viruses had not occurred. The continued introduction and circulation of these viruses in mammals provides opportunities for stepwise adaptation of HPAI viruses to mammals through mutations, and potential reassortment of gene segments, which could increase the pandemic potential of the viruses for mammals, including humans.

[2] https://www.woah.org/en/disease/avian-influenza/#ui-id-2

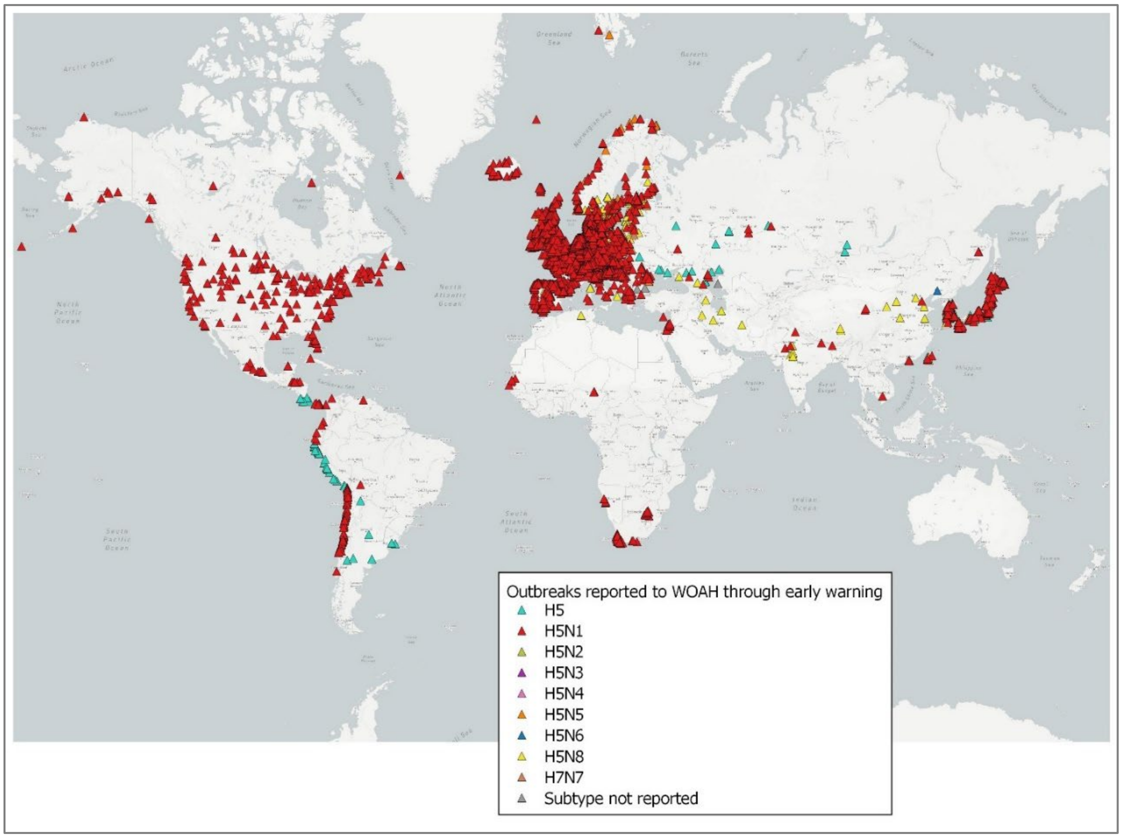

Fig. 5. Reported outbreaks of HPAI in wild birds between 1 October 2020 and 6 April 2023.

2.2. Epidemiological changes in poultry and other domestic birds

The original epidemiology of HPAI followed H5 or H7 LPAI virus direct or indirect exposure to wild bird reservoir and transfer to poultry with mutation within galliforme poultry to a HPAI virus and circulation in poultry with premises-to-premises spread of the virus on fomites through human activity and possibly some contribution by aerosols (25; 26). Typically, the farm gate was the point of control and the process uniformly used was stamping-out strategies through a combination of diagnosis and surveillance to locate the virus, quarantine of affected premises, movement controls of poultry within the infected zone, culling of poultry on affected premises and cleaning and disinfection to destroy the virus in the affected barns. Of the 44 unique HPAI epizootics since 1959, 41 have been eliminated, usually within less than one year through stamping-out programmes. As an example, an H7N7 LPAI-infected chicken layers on two farms in Germany during 2015 (27). The H7N7 LPAI and HPAI viruses were eliminated by stamping-out programmes on the two farms and surveillance did not identify any additional cases. Historically, migratory aquatic birds have not been involved with the epidemiology of HPAI epizootics.

The change in the epidemiology of HPAI in poultry occurred with the H5Nx Gs/GD Eurasian lineage as a result of the continued exposure to, infection of and transmission to domestic waterfowl of a HPAI virus, many of which have been asymptomatic, as well as the expansion with infection and spread by migratory waterfowl species beginning in 2002 (7). The clades 2.2, 2.3.2.1, 2.3.4.4c and 2.3.4.4b have been associated with transregional movement of the Gs/GD Eurasian lineage though migration of infected aquatic birds. As a case study of the changing epidemiology, in 2014, the 2.3.4.4c clade was introduced across the Bering Strait into North America by migrating waterfowl from Asia (28). The first cases in domestic birds in the USA were as a result of transmission from wild birds to captive hunting raptors, backyard galliforme and anseriforme birds (28; 29). This initial wild bird 2.3.4.4b HPAI virus was highly adapted to mallard and domestic ducks with easy transmission, but was poorly adapted to chickens and turkeys, requiring high challenge doses to produce infection; it was also poorly transmissible in experimental studies (30-32). The initial cases in commercial poultry were in California, Arkansas, Missouri and Minnesota without farm-to-farm spread but were point-source introductions by indirect contact with wild waterfowl (28; 29). However, in late spring until June 2015, most of the poultry cases resulted from farm-to-farm spread and the role of wild birds in the spread to poultry ended (29). The infection pressure and environmental contamination by wild aquatic birds was low based on 73 confirmed wild bird cases in 4,879 bird surveillance samples from the Pacific flyway for 2014-2015 (33). When including passive surveillance samples, 98 confirmed wild bird cases across 20 species in 15 States in the USA were reported in the 2014-2015 outbreak, as well as 211 commercial and 21 affected backyard poultry premises in 21 States, with the last case on 17 June 2015. The wild bird detections declined in the USA, with just two detections in the 2015-2016 season, one in the 2016-2017 season and none in subsequent surveillance seasons up to 2020-2021 (34). However, in 2022, the 2.3.4.4b HPAI virus entered North America via the Atlantic Ocean from Europe and the epidemiology changed compared to the 2014-2015 outbreak with the majority of backyard and commercial farm cases resulting from wild bird introductions or movement from contaminated environments into the farms. Onward spread from farm to farm was less than 15%. In 2022, over 6,000 detections of the 2.3.4.4b virus in over 140 wild bird species and more than 100 wild mammals in 49 USA States occurred. This higher wild bird infection rate and broader geographic footprint was associated with the higher 60% case rate in backyard birds (493 cases) and lower 40% case rate in commercial poultry (323 cases).

The biosecurity measures needed to keep HPAI out of premises because of environmental contamination have now moved from the farm gate to the barn door as the 'line of separation' from the contaminated environment around the barn (curtilage) and the poultry inside the barn. Stamping-out measures have been effective at eliminating the virus from affected farms and thus reducing farm-to-farm transmission, but the continual threat from introductions from wild birds, especially through the contaminated environment around the barns, creates the risk of reintroduction as an ongoing threat. This process threatens the socioeconomics of stamping-out programmes as the main outbreak management tool for dealing with 2.3.4.4b Gs/GD virus. There are mounting consumer concerns and political resistance to a blank check for eradication and compensation costs in support of a process that is deemed non-sustainable. The ongoing outbreaks have a negative impact on the sustainability of commercial production as well as the livelihoods of farmers, especially those in low-income countries and dealing with culling of healthy birds (over 50 million in the USA alone); this loss of income has led to psychological stress and illness. In addition, the consumer has seen the cost of goods increase; for example in the USA and the European Union egg prices increased by 155% and 62% since the first quarter of 2022, respectively[3]. The welfare of birds is a concern not only in terms of death and suffering, but also the depopulation of large numbers of seemingly healthy poultry, loss of high-quality protein from this food supply and lack of free-range outdoor production.

2.3. Zoonotic features

Before 1996, human cases of avian influenza viruses were exceedingly rare, but with the appearance of H5N1 Gs/GD Eurasian lineage in Hong Kong in 1997, human infections have increased, and many with fatal outcomes. This began a new era in influenza A biology with a focus on preparing and assessing the risk of animal influenza viruses as potential human pandemic viruses. The H5Nx Gs/GD Eurasian lineage HPAI viruses have resulted in sporadic human infections (H5N1: 868 known cases with 457 fatalities since 2003; H5N6: 84 cases with 33 fatalities since 2014) and similarly, the H7N9 Eurasian LPAI and HPAI viruses (1,568 known cases with 616 fatalities since 2013) have caused sporadic human infections (35). Some molecular markers have been reported for H5Nx Gs/GD HPAI viruses suggesting a certain level of adaptation to mammals, including humans, but neither virus lineage has exhibited sustained human-to-human transmission. Enhanced One Health activities are needed, by cooperation with public health officials and wildlife authorities, to provide continued surveillance and monitoring of avian and mammalian populations and sharing of viruses and data to maximise preventive and control measures in animal and human populations. Isolated human cases of 2.3.4.4b HPAI infections have been reported from Asia, North and South America, and Europe. However, since 2016, the number of H5N1 HPAI cases in humans has declined, but an increase has

[3] https://www.foodingredientsfirst.com/news/rabobank-analysis-forecasts-eggflation-to-remain-high-in-2023.html

been seen in sporadic cases with H5N6 2.3.4.4b viruses (36). WOAH Members are obliged to report to WOAH infections of domestic and captive wild birds with LPAI viruses, including H9N2, having proven natural transmission to humans associated with severe consequences (3). A human infection with avian influenza is reportable to the World Health Organization under the International Health Regulations (2005)[4].

3. Global control strategies

3.1. Country-based HPAI eradication programmes.

The XXXII WOAH General Conference (May 1964) included HPAI (i.e., fowl plague) in the List A of diseases that require compulsory notification to WOAH on a monthly or fortnightly basis to facilitate Members' efforts to prevent the introduction of the disease via international trade in birds and their products. However, HPAI was discussed at WOAH beginning in the late 1920s. Traditionally, the principal control strategy for HPAI has been eradication of the virus through stamping-out programmes. In confronting the first HPAI outbreak in the USA in 1924-25, Dr E.L. Stubbs stated, '…(HPAI is) capable of causing such destruction of the poultry population as to be of economic importance in diminishing the food supply…the dangerous character of the disease warranted the radical methods for complete eradication within a few months…' (37; 38). The use of stamping-out programmes led to the eradication of HPAI in Europe and Asia, North and South America by the mid-1930s (39; 40). Since 1959, scientific and technological advances have improved the stamping-out process in most of the high-income countries, thus shortening the timeframe between detection and elimination. These have relied largely on mechanisms including a single incident command system with electronic communication that has enabled unified and coordinated response on national and State levels with various entities involved, data collection and analysis capabilities, processes that supported HPAI management and response decisions, and importantly, strong public-private partnerships between national and State governments and private sector companies to develop cooperation and response activities. Notably, compensation and indemnification mechanisms, when used, have supported the early reporting of HPAI and eased response activities. The development and deployment of rapid molecular diagnostics and surveillance assays, coupled with commercial courier systems to rapidly move samples from field to diagnostic laboratories, has accelerated the molecular detection of highly pathogenic avian influenza. Novel methods are continuously being developed and improved to facilitate mass depopulation with a 24-hour goal for completion on a single farm, including improved and environmentally sound methods for disposal such as composting and rendering, as well as new methods for wet and dry virus elimination within barns and environments and on equipment. These improvements have been incorporated in the stamping-out programmes of many countries, but the H5Nx Gs/GD Eurasian lineage has shown that elimination by stamping-out programmes alone is costly and not sustainable with continual pressure from reintroduction from wild birds. In most low-middle income countries, the nature of the poultry production and selling systems, capacity issues with Veterinary Services, weak signals of infection in domestic ducks, and limited incentives to report disease including the unavailability of compensation, means that stamping out is not sufficient to eliminate the virus. Most low-middle income countries in Asia and Africa have not been able to eliminate the virus once it became established in poultry. Zoning (regionalisation) and compartmentalisation of HPAI infection have eased the country-wide geographic restrictions to smaller risk areas or low risk premises in some countries, allowing continued safe supply and even export of poultry and poultry products.

3.2. Country-based HPAI vaccination programmes reported through WAHIS

Vaccination has been used in a limited number of countries as either a preventive, emergency or routine measure to protect poultry or other captive bird populations from H5 and H7 HPAI. In 1995, both Mexico and Pakistan faced emergent HPAI outbreaks, and they were unable to accomplish eradication by enhanced biosecurity and stamping-out programmes (41). The HPAI viruses became endemic in their poultry populations and vaccination was added as a complementary tool to assist in

[4] https://www.who.int/publications/i/item/9789241580410

elimination of the viruses. The vaccination programme allowed maintenance of rural livelihood and food security for the countries while the eradication process was underway through stamping-out with Mexico achieving elimination by the end of 1995, and Pakistan reporting its last H7N3 cases in 2004. Beginning in 1996, the Gs/GD Eurasian lineage HPAI virus began causing outbreaks on mainland China (People's Rep. of) and spread to Hong Kong SAR in 1997 with the virus becoming endemic in China (People's Rep. of) and extending from 2002 to neighboring Asian countries. Once the HPAI virus was endemic in poultry populations, routine vaccination was implemented to maintain food security and rural livelihoods in China (People's Rep. of), and soon thereafter in Indonesia, Egypt, Vietnam and Bangladesh (41; 42). In the case of Vietnam, vaccination was introduced in 2005 after some 30 million poultry had been destroyed using a stamping-out policy but the virus had not been eliminated (7). Vaccination was also introduced to reduce zoonotic spillover. In the mid-2000s, a few countries used emergency vaccination (Cote d'Ivoire, Sudan, Korea (Dem People's Rep. of), Israel, Russia, and Pakistan) and were able, in combination with stamping-out in poultry, to eradicate the virus from their country. In addition, preventive targeted vaccination was used in a few flocks (Mongolia, France and Netherlands) to many commercial flocks (Kazakhstan and Guatemala) to protect poultry at high risk (41). Poultry vaccination has been used successfully in China (People's Rep. of) since 2017 to reduce the zoonotic threat posed by H7N9 HPAI viruses. In addition, successful HPAI vaccination programmes were undertaken in 13 European Union countries in zoo birds (non-poultry) in the mid-2000s (43). WOAH Members that have declared official vaccination in WAHIS since 2005 are: Armenia, Belarus, Bangladesh, China (People's Rep. of) including Hong Kong (SAR), Egypt, El Salvador, Germany, Indonesia, Jordan, Korea (Dem People's Rep. of), Kuwait, Laos, Mexico, Niger, Nigeria, Pakistan, Peru, Russia, Sudan, Turkmenistan and Vietnam. In addition, Guatemala has a poultry vaccination programme for H7N3 HPAI[5].

3.3. Survey results of WOAH Members

Early in 2023, to support this Technical Item, WOAH launched a survey titled, 'Strategic Challenges to the Global Control of High Pathogenicity Avian Influenza' (SCGC-HPAI survey) with the purpose of collecting information on the most relevant challenges Members face in the implementation of HPAI control strategies and to explore options for better national, regional and global coordination.

Out of 182 WOAH Members, 133 Members responded to the questionnaire (73% response rate), with each WOAH region having a response rate of 50% or greater. Due to the design of the survey, not all the respondents answered all the questions, therefore, the denominator per question varied.

The primary focus of concern among 92% (122 out of 133 Members) of the respondents was the impact of HPAI on domestic animal health, ranging from 'Very concerned' to 'Extremely concerned' for most of the Members. Other areas such as wildlife health, public health and social impact were also considered a concern for a smaller number of respondents, with most of those Members answering 'Very concerned' or 'Extremely concerned' (Fig. 6).

[5] https://rr-americas.woah.org/wp-content/uploads/2023/02/110_experiencias-de-campo-de-guatemala-sobre-ia-_eng.pdf

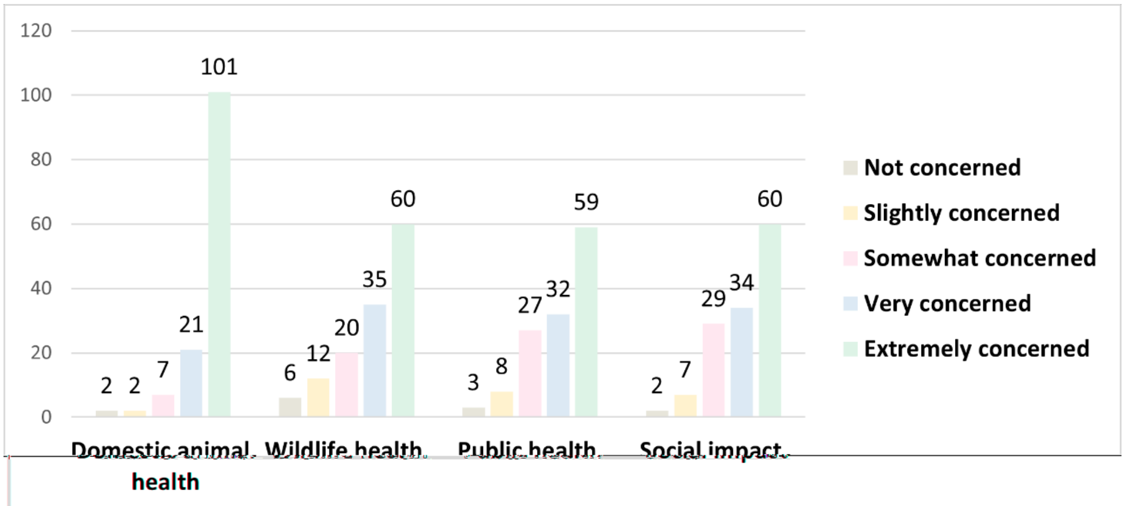

Figure 6. Level of concern regarding the various sectors impacted by HPAI.

Most of the respondents mentioned that the current HPAI control measures implemented in their countries were considered insufficient, from a technical (55%, 73 out of 132 Members) and financial (61%, 80 out of 131 Members) perspective. In the Americas, most respondents mentioned the lack of technical capacity to face HPAI (e.g., surveillance, biosecurity, quarantine, movement control, separation of domestic and wild birds, stamping out, etc.), with 85% (22 out of 26 Members) reporting concerns. Globally, the top three technical areas that respondents believe require capacity development are risk-based surveillance, epidemiology and data analysis, and strategic planning. Financial concerns exist across all five WOAH regions, with Africa and the Americas expressing the highest levels of concern at 76% (29 out of 38 Members) and 78% (21 out of 27 Members) respectively.

According to the survey, the public's and poultry sector's reception to the implementation of disease control measures in their country varied. Approximately 62% (80 out of 130 Members) were either neutral or supportive of the measures, while 35% (46 out of 130 Members) expressed some level of resistance, but generally accepted them. Only 3% (4 out of 130 Members) strongly resisted most of the control measures. The main reasons for strong resistance were the economic costs associated with implementing the measures

4. Emerging strategic national challenges in the global control of HPAI

WOAH provides science-based recommendations for the prevention, control and elimination of HPAI through the Terrestrial Code, Manual of Diagnostic Tests and Vaccines for Terrestrial Animals and other WOAH publications and conferences based on the collective inputs of WOAH Avian Influenza Reference Laboratories, several WOAH Collaborating Centres and avian influenza experts in OFFLU. These outputs were used by Members to develop national control and eradication strategies for HPAI. However, the changing ecology and epidemiology of the Gs/GD Eurasian lineage, especially the 2.3.4.4b but also other clades, and its socioeconomic impact have challenged the old paradigm of eradication through current stamping-out strategies.

4.1. Avian influenza intelligence: surveillance and monitoring for early detection and prevention

Detection of HPAI virus (mostly 2.3.4.4b) in migratory, scavenging, predatory and resident birds in 72 countries and territories across Africa, Americas, Asia and the Pacific, Europe and Middle East since October 2020, has highlighted the emerging concern. Parts of the wild aquatic bird populations are endemically infected, creating a reservoir resulting in the virus being spread over vast distances and contaminating the environment and creating high infection pressure. This, in turn, leads to the HPAI virus spreading to animal agriculture, establishing a reservoir of infection. Repeated spill-back transmissions of HPAI viruses from infected poultry into wild bird habitats and populations have significantly added to the status. This changing ecological and epidemiological situation has resulted in infections and deaths in terrestrial and sea mammals, and sporadic human infections, some of which occurred in countries that had not experienced human cases previously. Furthermore, the impact on a wide range of bird species, including those acting as spill-over hosts, has resulted in significant mortality events and the decline of breeding colonies of various endangered or threatened bird species, particularly seabirds. To better comprehend and mitigate the changing ecology of wild birds in relation to 2.3.4.4b HPAI and its effects on domestic birds and wildlife, nations must strengthen their monitoring and surveillance of wild bird populations, which serves as a basis for closing crucial knowledge gaps concerning affected species.

According to Members' responses to the SCGC-HPAI survey, almost 75% (95/129 Members) reported that they were conducting surveillance in wild bird populations. Respondents reported that they are implementing more than one type of surveillance within their jurisdiction (85% of the Members: 81/95), utilise passive surveillance as their primary surveillance approach, followed by risk-based surveillance (59%: 56/95 Members), enhanced passive surveillance (42%: 40/95 Members) and only 24% (23/95 Members) have implemented an active surveillance strategy across their territory (Fig. 7). Nonetheless, implementing HPAI surveillance activities in wild birds comes with challenges. Respondents identified insufficient budget allocation as the primary challenge, with 64% (76/118 Members) reporting this as an issue. Additionally, 51% (60/118 Members) cited the technical complexity of the task as a challenge.

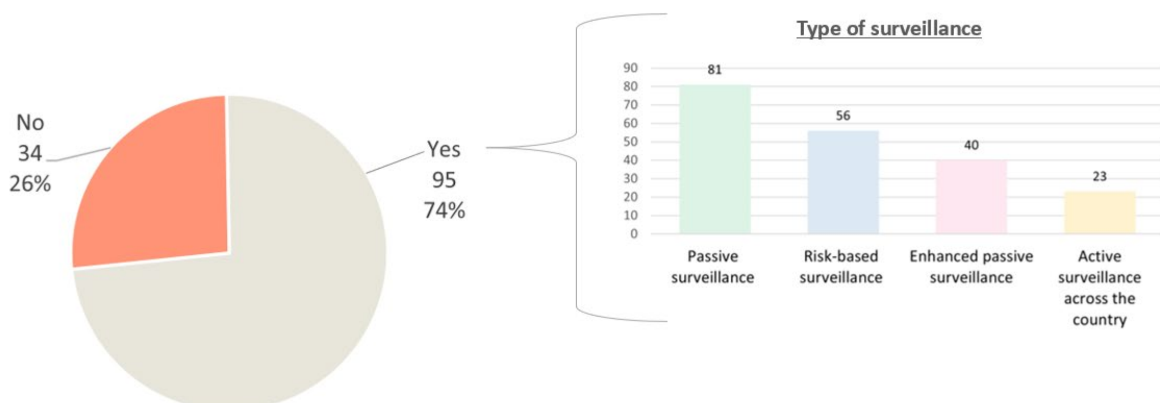

Fig. 7. Number of Members implementing wild bird surveillance as part of the national avian influenza early detection system.

For 86% of the Members (109/127 Members) a regular mechanism for disseminating wild bird, domestic bird and poultry surveillance outcomes related to avian influenza with their respective national public health authorities exists. Additionally, 58% (71/123 Members) reported sharing surveillance results on AI with national public health authorities on a regular basis; 36% (44/123 Members) share the information when there is evidence of potential human health risk, and 7% (8/123 Members) only share the surveillance information upon request. Similarly, 56% (71/126 Members) mentioned systematically sharing the AI sequences detected in their countries or territory. However, most of the Members (57%, 43/75 Members) responded that they had not deposited the sequences in a public repository but shared it with other national or international reference laboratories. Nevertheless, 43%

(32/75 Members) reported they deposited sequences in public databases such as Genbank, GISAID or BV-BRV, etc.

a. Considering the current epidemiological situation and the results of the survey, the following strategic challenges require reflection by WOAH Delegates and stakeholders With the overarching aim of improving One Health, how can we improve HPAI virus intelligence by optimising wild bird and mammal surveillance by combining this with domestic bird surveillance for HPAI early warning, as well as fostering information sharing on viral sequence and viruses among veterinary services, and wildlife, environmental, and public health networks/professionals'?

b. Given the evolving ecology and epidemiology in wild birds, what risk assessment tools are needed to evaluate, inform and manage the increased risk of HPAI to animal health?

c. How can production processes be revisited to improve farm biosecurity and reduce risks to poultry and the risk of spill-back to wild birds (e.g., housing, density, geographical location of the farms, deterrents for wild birds, farm management practices, etc.)?

4.2. Vaccination as a supplemental disease control strategy for business continuity

Poultry vaccination can be used to prevent infections in regions exposed to the virus and assist in stamping-out programmes leading to eradication in infected regions; it can also be used when eradication is not currently feasible. Vaccination against HPAI, when using high potent vaccines with sufficient antigenic match to the field viruses, can increase resistance to infection from HPAI virus exposure such that a 3-4log10 increase in virus exposure is required to produce infection; when infections occur, the birds excrete 2-5log10 less of the virus, thus providing clinical protection against illness and mortality. This reduced susceptibility to and infectivity upon infection translates into reduced transmission, to an extent that the reproduction ratio R0 is below 1 in transmission experiments applying high quality vaccines (44). As a result, onward transmission is prevented and environmental contamination by HPAIV and exposure of humans at interfaces is minimised. In the case where R is reduced, but not to the extent of R<1, vaccination still may have benefits due to its effectiveness to reduce clinical disease and production losses and, depending on the achieved value of R, the extent of outbreaks will be reduced with its consequential reduction in environmental contamination and potential reduction in the probability of onward spread to other farms provided adequate biosecurity and surveillance are in place, and benefit from reduction of risk of further virus evolution and potential consequential changes in risk profile (45). It is technically feasible to design and implement appropriate surveillance systems for vaccinated poultry to demonstrate freedom from infection, and if infection should be detected in vaccinated flocks, they would be subject to a stamping-out strategy. However, despite the global threat, vaccination is not extensively used as a disease control measure, mostly due to the potential impact on international trade.

The SCGC-HPAI survey sheds light on the vaccination practices of WOAH Members: 81% (107/133 Members) did not use any sort of vaccination for HPAI or LPAI in the past five years. However, 19% (25/133 Members) reported using at least one type of vaccination, either for HPAI or LPAI, and whether it was administered as a systematic practice or during emergency situations. The 25 members who implemented vaccination as a control measure for avian influenza reported 34 cases where these measures were implemented. In 65% of these cases (22/34 responses), vaccination was implemented systematically, primarily for low-pathogenic avian influenza (LPAI) at 59% (13/22 responses) and for highly pathogenic avian influenza (HPAI) at 41% (9/22 responses). Notably, the Middle East region had a 63% implementation rate (7/11 responding Members from the Middle East region) for systematic vaccination against LPAI as an AI control measure. Emergency vaccination represented 35% (12/34 responses) of cases where vaccination was used as a control measure. Emergency vaccination was mostly used for LPAI (75%, 9/12 responses) and only in three cases, one each in the Middle East, Europe, and Africa, for emergency HPAI vaccination (Fig. 8).

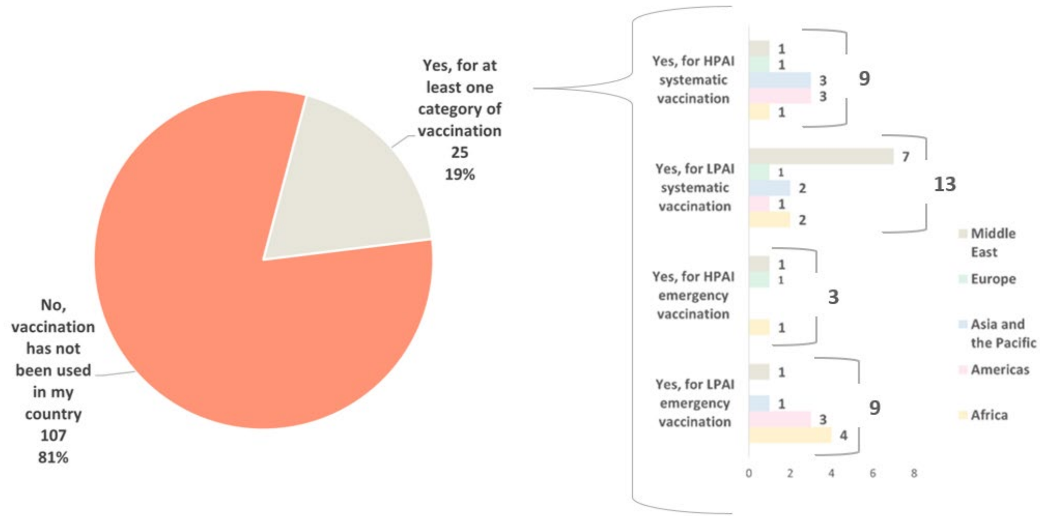

Fig. 8. Respondents informing that vaccination has been used as one of the control measures for Low Pathogenicity Avian Influenza (LPAI) or High Pathogenicity Avian Influenza (HPAI).

The European (56%, 23/41 Members), American (60%, 18/30 Members), and African (61%, 25/41 Members) regions had a similarly high percentage of respondents supporting the potential use of vaccines as a tool for controlling infectious diseases. Half of the respondents are not considering vaccination as a complementary tool for controlling HPAI, citing? concerns about its impact on surveillance, international trade, and silent infections that could jeopardise early warning systems.

Nevertheless, most of the Members (57%, 73/128 Members) considered it feasible to implement WOAH-recommended surveillance in vaccinated poultry flocks, while 32% (41/128 Members) are unsure of its feasibility. Out of 128 Members, only 11% (14 respondents) believed that implementing WOAH-recommended surveillance is not possible, and their reason for this is mainly due to constraints in human and financial resources.

The use of vaccination as a complementary tool for the control of HPAI is being discussed in different scientific and political fora as a response to the global threat. WOAH Delegates and stakeholders are invited to reflect on the following strategic challenges associated with the use of vaccination:

a. Explore how vaccines can be used as a supplemental tool to support prevention of poultry infections and eliminate transmission of viruses, especially in places where biosecurity measures have not prevented incursions of viruses, thus reducing the number of flocks infected and needing culling.

b. Determine which poultry and other bird populations are the best candidates for targeted vaccination as well as the best programme for individual country use (e.g. emergency, systematic).

c. Develop public-private partnerships to develop vaccination programmes that are risk-based, logistically feasible and cost-effective.

d. Determine the availability of registered vaccines and how they would fit into a vaccination programme and also, which tools in the research and development pipeline, such as mass application technologies, could address current vaccine weaknesses.

e. Determine the time to availability of vaccines from manufacturers and explore how regulatory processes can be accelerated to antigenically update seed strains or hemagglutinin inserts.

f. Develop science-based surveillance programmes for vaccinated populations to detect HPAI virus circulation and to substantiate freedom.

g. Develop an ongoing process to assess the antigenic matching of hemagglutinin of non-replicating vaccines to field viruses in order to provide and maintain optimal protection. Such a process would support continual updates of vaccine antigens and seed strains to field viruses at the national and global level.

4.3. International standards to facilitate safe trade, including in the presence of vaccination

The Terrestrial Code provides outcome- and risk-based provisions to prevent the international spread of HPAI while avoiding unjustified international movement restrictions. It contains specific considerations for defining a country or zone free from HPAI, considering the possible use of vaccination, as well as for the establishment of free compartments. It also stipulates that an outbreak of HPAI can be localised to a containment zone and provides specific recommendations for the recovery of the free status of a country or zone after an incursion.

The Terrestrial Code presents specific provisions for the safe importation of various poultry commodities, with science-based recommendations according to the animal health status of the population at the origin. It also includes a list of commodities considered safe irrespective of HPAI status of the exporting country or zone. Those commodities can be traded without any HPAI-related control measures (11).

The Terrestrial Code specifies that 'The use of vaccination against avian influenza may be recommended under specific conditions. Any vaccine used should comply with the standards described in the Terrestrial Manual. Vaccination will not affect the high pathogenicity avian influenza status of a free country or zone if surveillance supports the absence of infection, in accordance with Terrestrial Code Article 10.4.28.2, which states vaccination can be used as an effective complementary control tool when a stamping-out policy alone is not sufficient.'

To comprehend the Member's position in the SCGC-HPAI survey on trade, the poultry and poultry product sectors were characterised by import and export activities. Among the respondents to the survey, 43% (56/129 Members) identified themselves as mostly importers, while 12% (16/129 Members) were mostly exporters. A significant portion of the respondents, 40% (52/129 Members), reported engaging in both importing and exporting activities. Only a small proportion of respondents, 4% (5/129 Members), reported not being involved in either importing or exporting poultry and poultry products.

However, despite the internationally adopted Terrestrial Code recommendations, trade partners reported challenges to trade in vaccinated animals and to recognise the use of compartmentalisation and zoning including containment zone when outbreaks occur in HPAI-free country.

The SCGC-HPAI survey gathered responses from 127 Members indicating under what circumstances they would be willing to accept the importation of poultry products from HPAI-vaccinated poultry that comply with WOAH Standards. From the survey responses, 25% of respondents would import poultry products from both vaccinated and non-vaccinated animals, 19% would only accept them from flocks located in non-vaccinated compartments, 16% would only accept them from flocks located in non-vaccinated zones, 5% would only accept them from certain non-vaccinated poultry species, regardless of their geographical location, and 18% would not be willing to import any type of poultry product into their territory if the exporting country implements vaccination to control HPAI, even if it follows WOAH standards. Sixteen per cent of respondents had no opinion on the matter (Fig. 9).

To ensure safe trade in poultry and poultry products in a country that practices vaccination, the respondents of the SCGC-HPAI survey highlighted two equally important measures: evidence showing the effectiveness of vaccination programmes and proof that all vaccinated flocks are tested to ensure the absence of virus transmission.

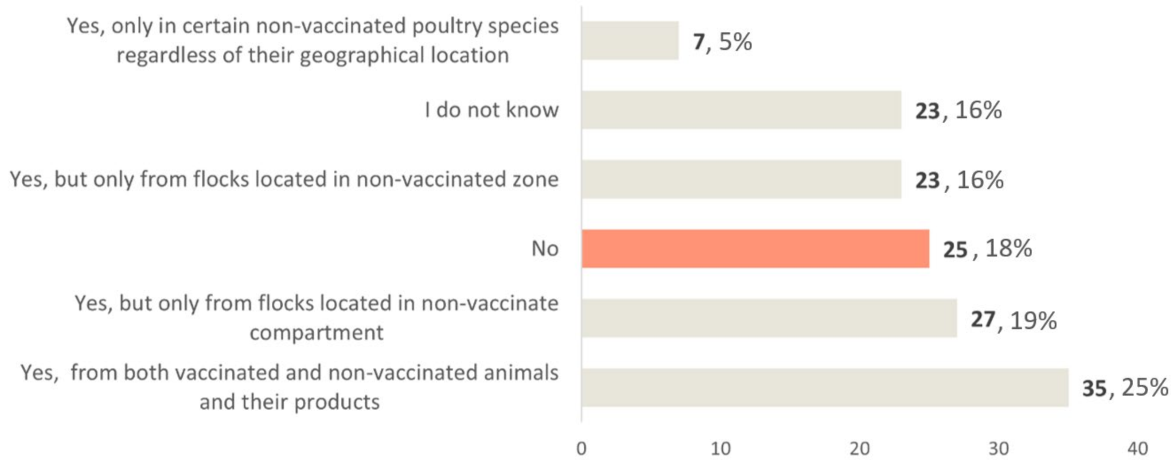

Fig. 9. Acceptance to import poultry products in compliance with WOAH Standards if the exporting partner implemented vaccination against HPAI.

WOAH science-based standards, correctly applied, protect animal health and welfare during production and trade in animals and animal products, as well as protecting wildlife health and biodiversity. Veterinary Authorities should use the standards to set up measures to prevent the spread of HPAI via international trade in animals and animal products, while avoiding unjustified sanitary barriers to trade. To ensure the correct implementation of the international standards related to avian influenza, WOAH Delegates and stakeholders should consider the following strategic challenges:

a. How can WOAH promote harmonisation of national regulations in line with updated WOAH international standards for HPAI on vaccination, zoning and compartmentalisation?

b. What are the concerns and expectations of importing and exporting countries with regard to ensuring safe trade in vaccinated animals?

c. What tools are needed by trade partners to assess the risks associated with combined vaccination and surveillance programmes?

d. How can other tools like zoning and compartmentalisation be used to facilitate trade and what practical guidance is needed to implement the WOAH standards?

5. Global coordinated strategy for the progressive control of avian influenza

The response to the global avian influenza threat must involve coordinated actions by international organisations, governmental agencies, poultry producers, scientific institutions, development partners and other stakeholders to prevent further spread of this virus.

The response must aim to ensure the wellbeing of farmers, protect animal welfare and biodiversity, prevent economic losses, reduce poverty, ensure consumer confidence and allow further contribution of the poultry sector to global health, wealth, equity and sustainability.

Regional and national avian influenza control strategies should be based on best practices, appropriate enforcement of the legislation and close coordination with stakeholders from public and private sectors. Members should increase their technical capacities and expertise, identify and use the relevant scientific knowledge, and engage in risk communication with relevant stakeholders.

The OFFLU network[6] of expertise on animal influenza and the WOAH Avian Influenza Reference Laboratories and Collaborating Centres are following closely the changes in the epidemiology of the disease and virus evolution. Significant research has been conducted and important lessons have been learned at national, regional and global level. The STAR-IDAZ International Research Consortium on Animal Health Research[7] has identified and prioritised knowledge gaps with the aim to maximise funding and accelerate the delivery of disease control tools and strategies.

In this context, FAO and WOAH launched the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TADs) in 2004 to achieve the prevention, detection and control of transboundary animal diseases, including avian influenza. The initiative combines the strengths of both international organisations to achieve agreed common objectives and serves as a facilitating mechanism to empower regional alliances in the fight against TADs.

In 2022, under the umbrella of the GF-TADs, the review and update of the 2007 FAO/WOAH avian influenza strategy was initiated (46). GF-TADs technical teams are collaborating with various stakeholders including global, regional and subregional GF-TADs Secretariats, national Veterinary Services, public and private sector, non-governmental organisations, scientific institutions, regional economic communities and the quadripartite partners WHO and UNEP to collect feedback through consultations, surveys, and workshops. This is an important opportunity to strengthen regional engagement and ownership of the global avian influenza strategy by drawing upon the varied experiences and resources available from each country, sub-region and region using a ground-up approach and to provide a pathway to operationalise the strategy at national, regional and global levels.

In response to recent outbreaks in the Americas and Europe, the GF-TADs Regional Steering Committee for the Americas and Europe approved the creation of the Standing Group of Experts on Avian Influenza (SGE-AI) to advise the GF-TADs Regional Steering Committee on preventive actions, preparedness, and emergency response to the disease. In the Asia-Pacific region, annual regional workshops on avian diseases have been organised under the regional GF-TADs umbrella to review progress in prevention and control of various avian diseases, especially avian influenza, and to define the way forward to further strengthen multi-sectoral and international coordination and collaboration. In the Africa region, Joint Risk Assessment (JRA) workshops, tripartite technical meetings and Incident Coordination Group (ICG) for Economic Community of West African States (ECOWAS) have been conducted to strengthen management of avian influenza.

Those global, regional, and subregional efforts demonstrate the importance of reviewing achievements, identifying collective challenges in multi-sectoral collaboration and coordination, and recommending further actions to improve collaboration and coordination across human-animal-environmental health and other relevant sectors related to AI prevention and control.

6. Conclusions

The ecological and epidemiological changes resulting from the H5Nx 2.3.4.4b HPAI over the past two years have challenged the exclusivity of stamping-out programmes and are requiring that WOAH Delegates work closely with wildlife and public health officials and other stakeholders to solve this global One Health crisis. This Technical Item has identified critical strategic challenges associated with surveillance and monitoring for early detection and prevention; disease control strategies, including vaccination; implementation of international standards and global coordination for the global control of HPAI. The Animal Health Forum, a format being introduced for the first time at the WOAH General Session, will be an opportunity for Delegates and stakeholders to have open discussion, explore those challenges in depth and agree on how best to tackle HPAI at national, regional and global level.

[6] Home - Offlu
[7] Coordinating animal health research globally to accelerate delivery of disease control tools and strategies - STAR-IDAZ

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