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Title:

Promising effects of duck vaccination against highly pathogenic avian influenza, France 2023-24

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Abstract

The ongoing panzootic of highly pathogenic avian influenza (HPAI) H5 clade 2.3.4.4b has caused widespread poultry mortality and raised concerns about zoonotic pandemics and wildlife conservation. France recently adopted a preventive vaccination strategy, vaccinating domestic ducks with inactivated and mRNA vaccines. This study evaluates the impact of this campaign on reducing HPAI H5 outbreaks. Using predictive modelling based on previous outbreak data, the expected number of outbreaks in 2023-24 without vaccination was significantly higher than the observed cases, indicating a 95.9% reduction attributable to vaccination. These findings suggest that vaccination effectively mitigated the HPAI H5 outbreak in France.

Text

Highly pathogenic avian influenza (HPAI) H5 viruses of clade 2.3.4.4b continue to affect diverse regions and species worldwide. Since 2020, this ongoing HPAI panzootic has reached an unprecedented scale, leading to the death or culling of over 130 million poultry across 67 countries, substantially threatening food security[1]. Concerns about conservation efforts and zoonotic pandemics are heightened by mass death events reported in multiple wild bird species and by recent spillover events to wild and domestic mammals, affecting more than 48 species across 26 countries[2].

While most countries rely on large-scale poultry depopulation and poultry movement restrictions to control HPAI H5, France has recently adopted a complementary preventive

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vaccination strategy[3]. Since October 2023, all domestic ducks in the production stage are being vaccinated with the inactivated vaccine Volvac B.E.S.T. AI + ND (Boehringer Ingelheim), receiving two doses at 10 and 28 days, and a third dose at 56 days in high-risk zones and high-risk winter periods[4]. Since May 2024, the RESPONS AI H5 vaccine (Ceva Animal Health), a self-amplifying mRNA vaccine, was also added to the vaccination campaign. Vaccination for breeder duck flocks remains optional. As of July 1, 2024, more than 35 million ducks have received two vaccine doses and 1.5 million have received all three vaccine doses[4].

The outcomes of the vaccination campaign seem promising. In 2023-24, HPAI H5 infections have been reported in only 10 poultry farms, representing a substantial reduction from the 1,374 outbreaks detected in 2021-22 and 396 outbreaks in 2022-23 (**Figure 1A**). In contrast, outbreaks continued in non-vaccinating European countries (**Figure 1B** and **1C**). Despite these encouraging results, the question remains whether the significant reduction in outbreaks in France is attributable to the vaccination campaign or to a generally lower level of virus circulation in Europe with a reduced number of detections during this epidemiological season (**Figure 1B** and **1C**).

We addressed this question by predicting the expected number of poultry farm outbreaks in France in 2023-24 if vaccination had not been implemented and compared it to the actual number of outbreaks. Our hypothesis is that the number of poultry farm outbreaks and/or wild bird cases in Europe prior to the first poultry farm outbreak in France can serve as a proxy for predicting the number of outbreaks in France. This is based on migratory wild waterbirds likely being significant vectors of virus spillover into poultry during the fall migration from north to south, but also infected poultry serving as indicators of the presence of infected migratory wild waterbirds[5–7].

Surveillance data on HPAI H5 clade 2.3.4.4b detections in Europe (2016-24) were extracted from the FAO's global animal health database (https://empres-i.apps.fao.org) (**Figure 1A-C**). For each epidemiological season (from September 1 to August 31 of the following year), we retrieved the number of poultry farm outbreaks in France. We defined 24 potential predictors based on combinations of time windows (one, two or three months prior to the first reported poultry farm outbreak in France), geographical regions (region 1: Norway, Sweden, Finland; region 2: Germany, Denmark, The Netherlands, Belgium; region 3: United Kingdom, Ireland; region 4: Bulgaria, Romania, Hungary, Poland, Czech Republic) and infected host types (wild bird or poultry farm). Using quasi-Poisson regressions, we modelled the number of poultry farm outbreaks in France for each epidemiological season in 2016-23 (period without vaccination) in relation to each predictor, and selected those significantly associated with outbreak numbers (p-value < 0.05) and strong model fit (pseudo-$R^2 > 0.80$). These predictors were then used to generate prediction intervals for the expected number of outbreaks in France in 2023-24.

Our findings suggest a significant and positive association between the number of poultry farm outbreaks in France and the number of infected wild birds reported in region 1 (Norway, Sweden, Finland) one month prior to the first reported outbreak in France. In the absence of vaccination, the expected number of outbreaks in France in 2023-24 was estimated at 487 (95% prediction interval (PI): 273 – 701) (**Figure 1D**), significantly higher than the observed number (n = 10). This discrepancy suggests that the vaccination campaign was

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effective in reducing the number of outbreaks in France in 2023-24, with a relative reduction of the outbreak size of 95.9% (95% PI: 92.7 – 97.2).

While other measures, implemented since 2017, such as enhanced biosecurity, may have also contributed to the observed trends, these measures did not change substantially in 2023-24 and are thus not expected to lead to such a sudden and drastic change in the number of outbreaks. Our results are supported by similar analyses in heavily affected, non-vaccinating European countries, where the predicted number of poultry farm outbreaks aligned with the observed outbreaks (**Figure 1E**). In conclusion, despite the practical challenges associated with vaccination, including high costs, logistic complexities and the intensive surveillance required, the preventive vaccination campaign has shown promising effects by preventing massive HPAI H5 outbreaks in French poultry in 2023-24.

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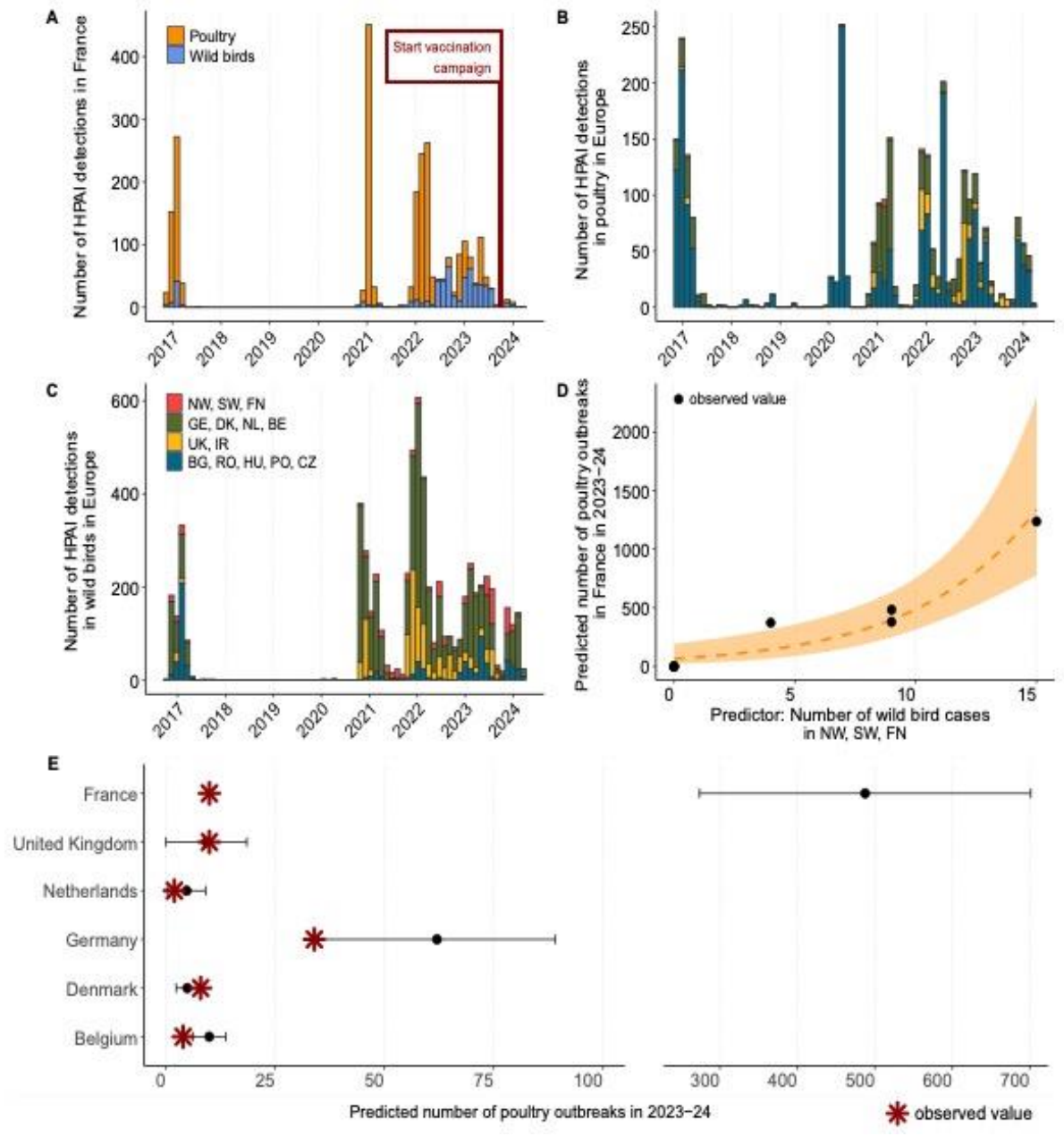

Figure 1. A) Temporal distribution of highly pathogenic avian influenza (HPAI) H5 (clade 2.3.4.4b) poultry farm outbreaks (orange) and wild bird cases (blue) in France. The start of the vaccination campaign (October 1st, 2023) is displayed with a vertical red line. **B)** Temporal distribution of HPAI H5 (clade 2.3.4.4b) poultry farm outbreaks in four regions: region 1 (red): Norway (NW), Sweden (SW), Finland (FN); region 2 (green): Germany (GE), Denmark (DK), The Netherlands (NL), Belgium (BE); region 3 (yellow): United Kingdom (UK), Ireland (IR); region 4 (blue): Bulgaria (BG), Romania (RO), Hungary (HU), Poland (PO), Czech Republic (CZ). **C)** Temporal distribution of HPAI H5 (clade 2.3.4.4b) wild bird cases in four regions: region 1 (red): Norway (NW), Sweden (SW), Finland (FN); region 2 (green): Germany (GE), Denmark (DK), The Netherlands (NL), Belgium (BE); region 3 (yellow): United Kingdom (UK), Ireland (IR); region 4 (blue): Bulgaria (BG), Romania (RO), Hungary (HU), Poland (PO), Czech Republic (CZ). **D)** Predicted number of HPAI H5 poultry farm outbreaks in France as a function of the predictor variable: number of HPAI H5 wild bird

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cases in region 1: Norway (NW), Sweden (SW), Finland (FN). Black dots represent the observed number of French outbreaks from 2016 to 2023. **E)** Predicted number of HPAI H5 poultry farm outbreaks in France and in heavily affected, non-vaccinating European countries. Horizontal black lines represent the corresponding 95% prediction interval. Red stars represent the observed number of HPAI H5 poultry farm outbreaks in each country in 2023-2024.

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Funding statement

This study was performed in the framework of the Chair for Avian Health and Biosecurity, hosted by the National Veterinary College of Toulouse and funded by the French Ministry of Agriculture and Food, General Directorate for Food.

Authors' contributions

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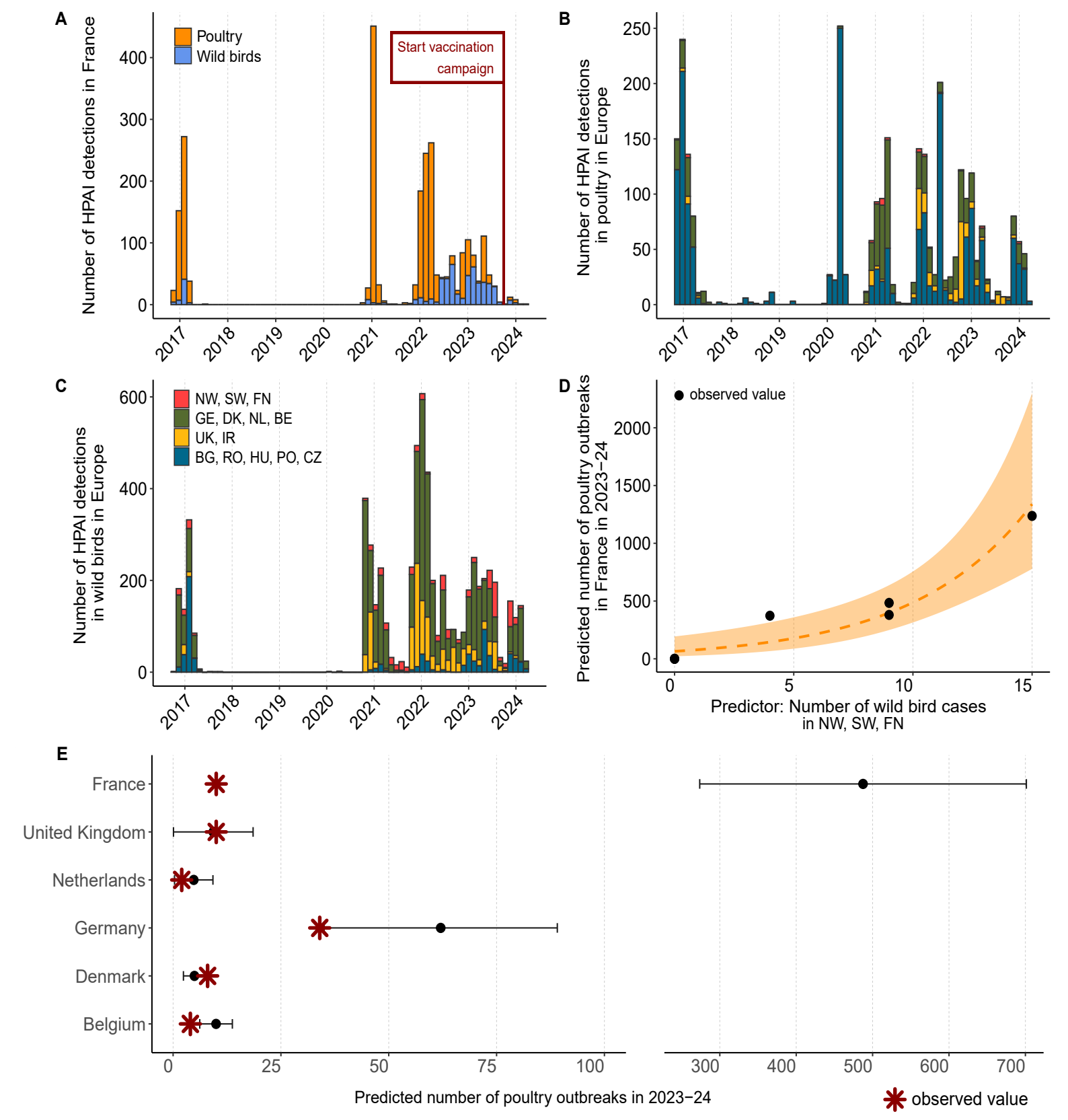
Study design: C.G., L.F., T.V. Data resources: L.F. Data analysis: C.G., L.F., E.M. Analysis guidance: S.L., T.V. Manuscript preparation: C.G. Review and approval of final manuscript: all authors

Competing interests

The authors declare no competing interests.


A
Number of HPAI detections in France
Poultry
Wild birds
Start vaccination campaign
0
100
200
300
400
2017
2018
2019
2020
2021
2022
2023
2024
B
Number of HPAI detections in poultry in Europe
0
50
100
150
200
250
C
Number of HPAI detections in wild birds in Europe
NW, SW, FN
GE, DK, NL, BE
UK, IR
BG, RO, HU, PO, CZ
0
200
400
600
D
Predicted number of poultry outbreaks in France in 2023–24
observed value
0
500
1000
1500
2000
0
5
10
15
Predictor: Number of wild bird cases in NW, SW, FN
E
France
United Kingdom
Netherlands
Germany
Denmark
Belgium
0
25
50
75
100
300
400
500
600
700
Predicted number of poultry outbreaks in 2023–24
observed value