16TH SCIENTIFIC CONFERENCE OF THE BULGARIAN FOCAL POINT OF EFSA
SOFIA, 16 MAY 2024

EFSA OPINIONS ON THE USE OF VACCINATION TO PREVENT AND CONTROL HPAI

VACCINATION OF POULTRY AGAINST HPAI

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EUROPEAN FOOD SAFETY AUTHORITY

TERM OF REFERENCES – OUTLINE

1. Update on the available vaccines against HPAI for poultry
2. Vaccination strategies

→ **available at:**

https://www.efsa.europa.eu/en/efsajournal/pub/8271

3. Surveillance in the vaccinated zone and/or vaccinated establishments
4. Restrictions and risk mitigation measures to be applied in a vaccinated establishment or a vaccination zone

→ **available at:**

http://www.efsa.europa.eu/en/efsajournal/pub/8755

TOR 1 – AVAILABLE VACCINES

TOR 1 – VACCINE CHARACTERISTICS

The only authorised in the EU

Technology	Poultry species (experimental data)	Administration route	Vaccine name	Estimated antigenic distance (AU)	Lineage, clade	Predicted efficacy of a vaccine to stop sustained HPAIV transmission in a vaccinated population (VE_T)
Inactivated full virus	Chickens (Pekin ducks, turkeys)	Subcutaneous or intramuscular	Nobilis Influenza H5N2[NL]	4.37	Eurasian H5	< 0.5 in chickens after 1 dose
Inactivated full virus	Poultry (Muscovy ducks)	Subcutaneous	Vaxigen Flu H5N8[IT]	2.32	2.3.4.4b	in chickens >0.9; in Muscovy ducks <0.5 after 1 dose, >0.9 after 2 doses
Subunit	Chickens (Muscovy, Pekin, mule ducks, turkeys)	Subcutaneous	Volvac B.E.S.T. AI + ND[FR, IT]	4.18	2.3.2	In mule duck > 0.9 (after 2 doses); in Muscovy ducks 0.8-0.9 after 1 dose, >0.9 after 2 doses; in Pekin ducks >0.9
Live vector	Chickens (ducks, turkeys)	In ovo or subcutaneous	Vectormune AI[IT, NL]	4.18	2.2	in chickens > 0.9; in turkeys 0.5-0.8
Replicon	(ducks, geese, chickens, zoo birds)	Intramuscular	Duck H5-SRV vaccine®[FR, HU]	2.32	2.3.4.4b	> 0.9 in mule ducks
Nucleic acids (DNA)	(chickens, turkeys)	Intramuscular	ExactVac – Vaxliant ENABLE adjuvant[IT, NL]	2.51	2.3.4.4a	<0.5 in chickens after 1 dose

TOR 1 - RECOMMENDATIONS

- Generate **suitable and harmonised data on**:
  - the **onset and duration of immunity** particularly for long living poultry types
  - the **impact of maternal immunity**
  - the indications of vaccines for **poultry species other than chickens** and considering **different poultry production types**
  - **VE** to reduce $R_0<1$ under **experimental** condition and to assess **effectiveness in field trials** taking into account regional differences

- The development of **mass applicable** AI vaccines
- The **rapidly update** if required based on the antigenic match; for this purpose, continuous surveillance efforts to **monitor virus evolution** are needed

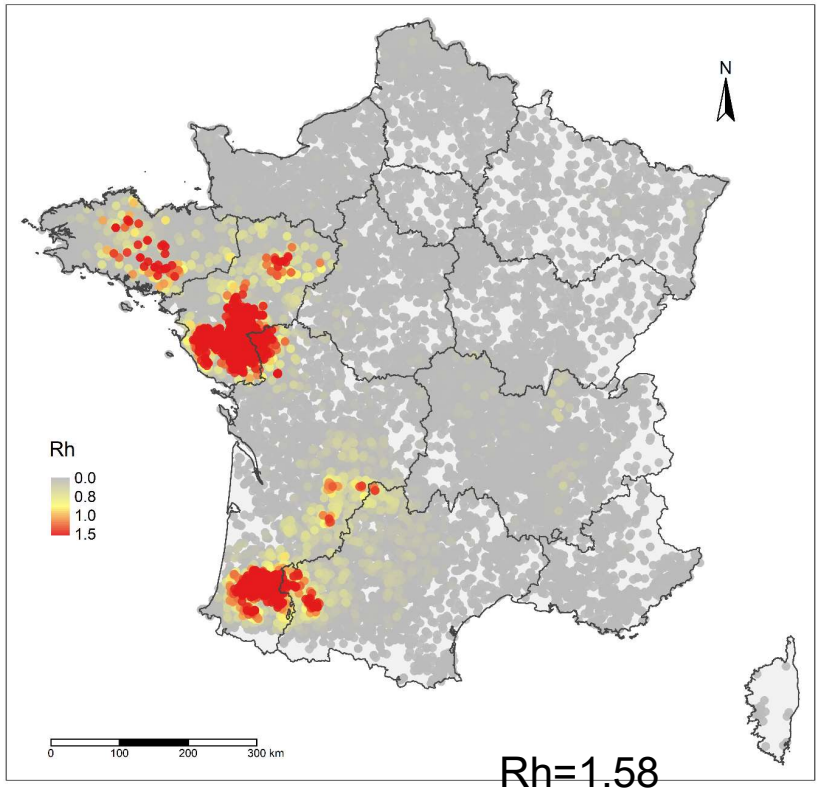
TOR 2 – VACCINATION STRATEGIES

TOR 2 – VACCINATION SCENARIOS

Scenario 0 (S0)	**No vaccination** Culling in all infected poultry farms
Scenario 1 (S1)	**No vaccination** Culling in all infected poultry farms Preventive ring **culling** in all poultry farms within **1-km** radius of infected poultry farms

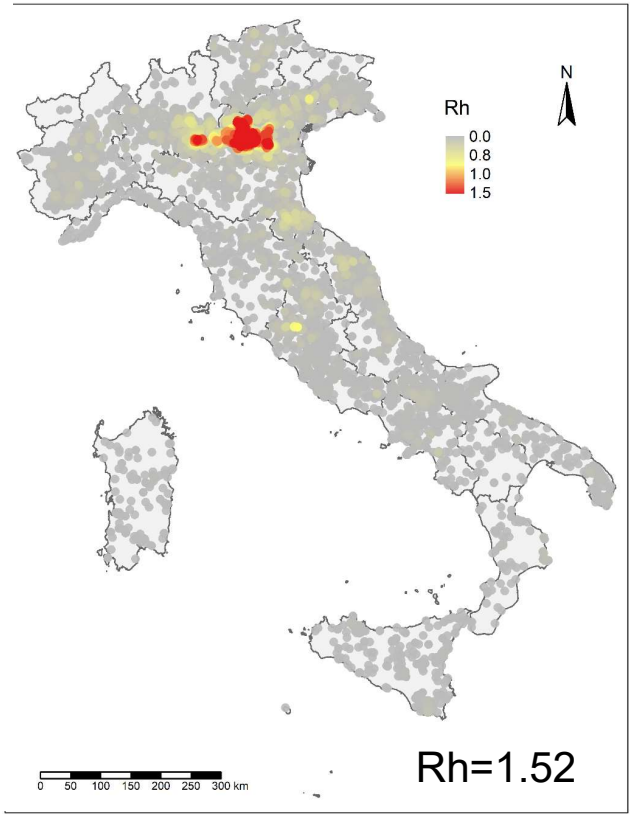
TOR 2 – TRANSMISSION MAPS

Rh are the between-farm reproduction numbers quantified using the kernel. Areas where Rh > 0.8 are considered high-risk areas for transmission



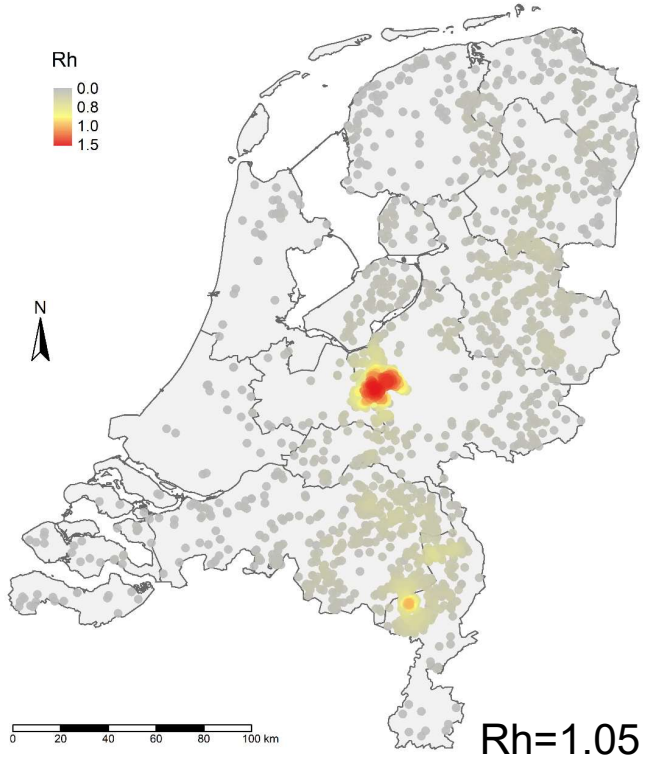
Rh=1.58

(farm density > 0.54 farm/km2)



Rh=1.52

(farm density > 0.52 farm/km2)

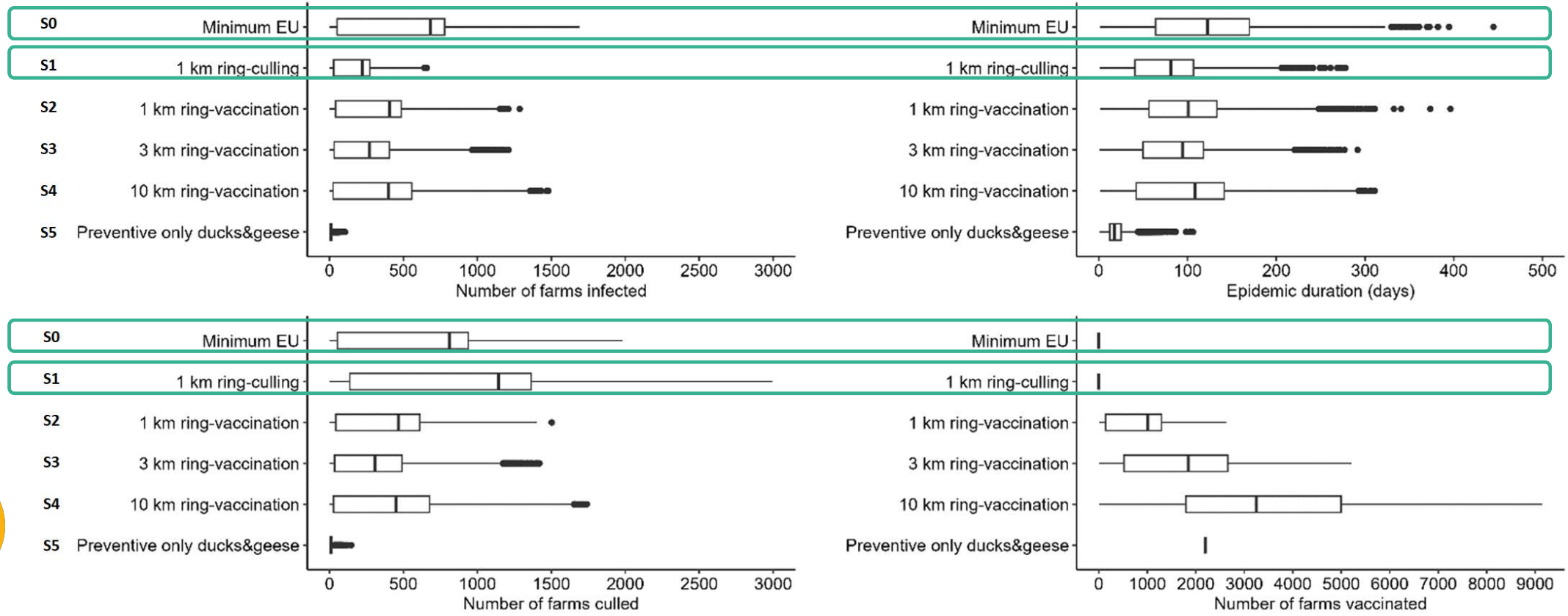


Rh=1.05

(farm density > 0.84 farm/km2)

TOR 2 – VACCINATION SCENARIOS

Results from the model simulation for each scenario in **France**



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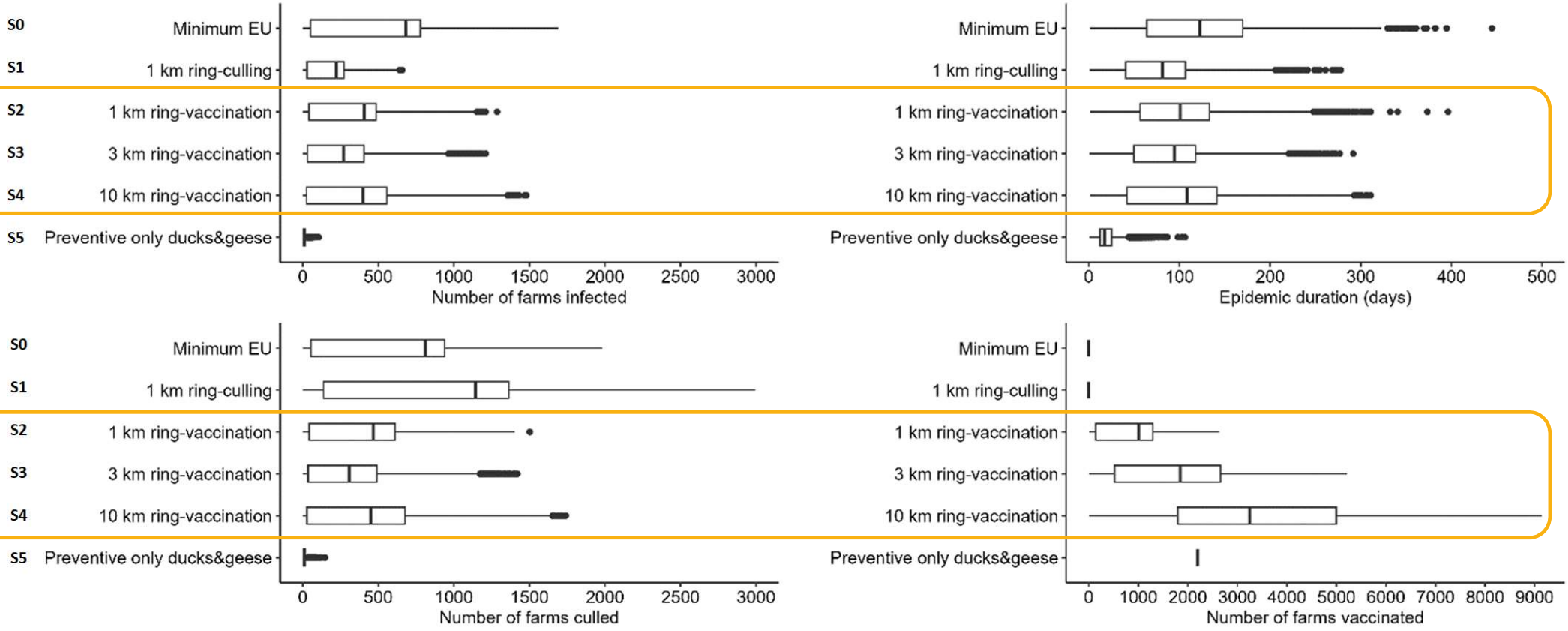

TOR 2 – VACCINATION SCENARIOS

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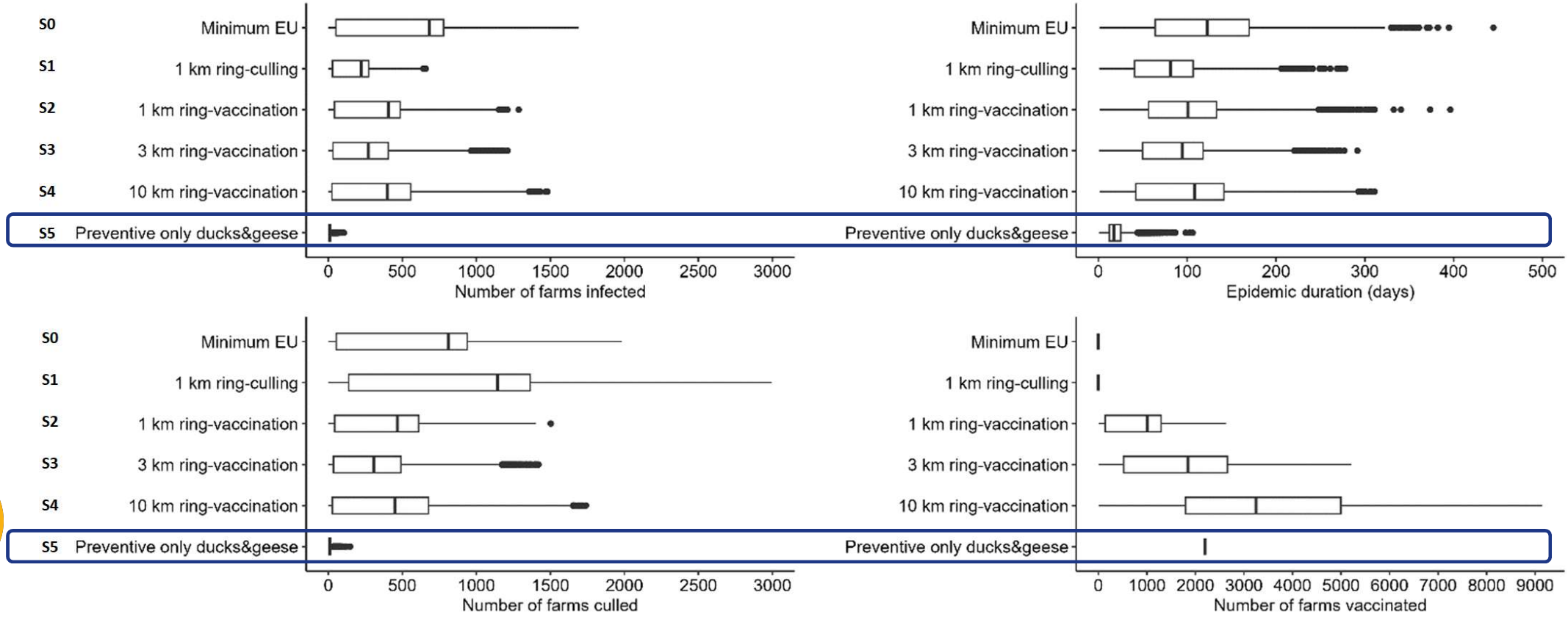


TOR 2 – RECOMMENDATIONS

- To minimise the number of infected and culled farms and epidemic duration, **preventive vaccination of the most susceptible and/or infectious poultry species is recommended** in high-risk transmission areas. Depending on the region, these species are ducks, geese, turkeys and layers chickens
- In case of an outbreak in a high-risk transmission area, **emergency protective vaccination in a 3-km radius is recommended**, as it showed to be the most effective strategy among the three emergency vaccination scenarios tested
- **Monitoring of vaccine efficacy over time** should be planned under the implementation of every vaccination strategy, due to possible changes in the antigenicity of circulating HPAI viruses, changes that can also be accelerated by the selection pressure exerted by vaccine-induced immunity

TOR 3 – SURVEILLANCE

SURVEILLANCE ACCORDING TO DELEGATED REGULATION (EU) 2023/361

Type of vaccination	Surveillance				
	Surveillance category	Testing procedure	Frequency	Minimum detectable prevalence/type of information collected	Duration
Emergency protective	Reinforced laboratory	Virological	2 weeks	5% prevalence with 95% confidence level	According to the duration of the recovery period
	Reinforced				-
Preventive	Er				ong as there e vaccinated birds in the stablishment
		virological		(representative sample)	

According to **WOAH**:
→ where vaccination is carried out, surveillance for **demonstration of freedom** from HPAI requires that **all vaccinated flocks** are tested to prove absence of viral circulation, with a frequency that is proportional to the risk in that zone

SURV: DIAGNOSTIC METHODS

DIAGNOSTIC METHODS: RECOMMENDATIONS

- The vaccination plan should already **pre-select the most appropriate diagnostic** assays
- Members States are encouraged to conduct **additional studies to collect field experience** and validation data on alternative diagnostic methods in vaccinated establishments
- The use of **diagnostic methods with high sensitivity** is recommended → **molecular methods (PCR)**
- Serological results when aiming at demonstrating **disease freedom** must be confirmed with molecular virological investigations

Seropositive results in **DIVA-vaccinated** flocks require **confirmation by molecular** assays on swab samples

SURV: EMERGENCY VACCINATION

EMERGENCY VACCINATION

Surveillance strategy	Emergency protective vaccination scenario – Surveillance within the vaccination zone			
	Strategy E1	**Strategy E2**	**Strategy E3**	**Strategy E4**
Objective of surveillance	HPAIV early detection (to be implemented also in the peri-vaccination zone)	Assessment of vaccination effectiveness	Demonstrating freedom from HPAIV in the vaccinated establishment (to authorise the movement of birds from that establishment)	Demonstrating freedom from HPAIV in the vaccinated zone

identification of HPAIV to remove the establishment before it transmits the infection to other establishments
→ **Rh** as a measure of transmission
→ **surveillance is effective** if contributes to **Rs < 1**

E1, LAYERS

Efficacy of surveillance options for early detection of vaccinated-infected flocks

In flocks **>3000**

Results are reported only for effective surveillance strategies

Turkeys: similar results

Sample type (diagnostic test)	Sample size	Sampling interval (days)	Percentage of outbreak simulations with the probabilities of escaping detection below 1%[b]	Detection time as days post introduction (median (2.5–97.5 CI))	Prevalence (%) infectious birds (median (2.5–97.5 CI))	Prevalence (%) recovered birds (median (2.5–97.5 CI))	R_h/R_s (reproduction number) (median (2.5–97.5 CI))
Passive reporting (reference)				31 (25–43)	3.93 (3.44–4.5)	2.16 (1.86–2.46)	1.4
Mortality threshold (0.13%)				28 (22–39)	2.35 (2.01–2.75)	1.26 (1.06–1.49)	1.09 (1.04–1.1)
Dead birds (qPCR)	≤5	7	99%	20 (14–31)	0.34 (0.25–0.43)	0.18 (0.11–0.24)	0.13 (0.1–0.16)
		14	90%				
		21	51%				
		30	0%				
	≤10	7	99%	18 (13–30)	0.26 (0.19–0.34)	0.14 (0.08–0.19)	0.1 (0.08–0.13)
		14	98%	21 (15–33)	0.44 (0.35–0.56)	0.23 (0.15–0.31)	0.17 (0.15–0.2)
		21	94%				
		30	84%				
	≤15	7	99%	18 (13–30)	0.26 (0.19–0.33)	0.13 (0.08–0.19)	0.1 (0.08–0.13)
		14	99%	20 (15–32)	0.41 (0.32–0.52)	0.21 (0.15–0.29)	0.16 (0.14–0.19)
		21	97%	22 (16–34)	0.56 (0.45–0.71)	0.3 (0.21–0.39)	0.22 (0.19–0.26)
		30	92%				
Live birds (qPCR)	60	14	72%				
		30	30%				
	120	14	89%				
		30	69%				
Live birds (serology)	60	14	47%				
		30	9%				

E1, DUCKS

Efficacy of different surveillance options for early detection of vaccinated-infected flocks

In flock **≥6000**

Results are reported only for effective surveillance strategies

Sample type (diagnostic test)	Sample size	Sampling interval (days)	Percentage of outbreak simulations with the probabilities of escaping detection below 1%[b]	Detection time as days post-introduction (median (2.5–97.5 CI%))	Prevalence (%) infectious birds (median (2.5–97.5 CI))	Prevalence (%) recovered birds (median (2.5–97.5 CI))	R_h/R_s (reproduction number) (median (2.5–97.5 CI))
Passive reporting (reference)				23 (19–32)	20.5 (18.9–22.3)	33.31 (29.26–37.26)	1.8
Mortality threshold (0.17%)				17 (13–26)	5.84 (4.83–7.22)	6.13 (4.9–7.28)	0.62 (0.49–0.63)
Dead birds (qPCR)	≤5	7	98%	15 (11–24)	3.09 (2.51–3.86)	3.09 (2.33–3.88)	0.21 (0.18–0.26)
		14	70%				
		21	0[b]				
		30	0%				
	≤10	7	99%	14 (11–23)	2.35 (1.87–3.02)	2.35 (1.74–3)	0.17 (0.14–0.19)
		14	97%	16 (12–25)	4.29 (3.48–5.19)	4.37 (3.34–5.38)	0.3 (0.26–0.34)
		21	89%				
		30	36%				
	≤15	7	99%	14 (10–23)	2.33 (1.86–2.96)	2.3 (1.72–2.99)	0.16 (0.14–0.19)
		14	98%	16 (12–24)	3.93 (3.18–4.8)	3.99 (2.97–4.94)	0.28 (0.24–0.32)
		21	96%	17 (13–26)	5.5 (4.54–6.68)	5.75 (4.43–6.97)	0.39 (0.35–0.44)
		30	89%				
Live birds (qPCR)	60	14	97%	17 (13–25)	4.95 (4.03–5.98)	5.05 (3.9–6.34)	0.35 (0.32–0.39)
		30	44%				
	90	14	98%	15 (12–24)	3.34 (2.64–4.11)	3.33 (2.49–4.17)	0.23 (0.21–0.26)
		30	93%				
Live birds (serology)	60	14	97%	17 (13–25)	5.16 (4.25–6.28)	5.34 (4.17–6.62)	0.36 (0.29–0.44)
		30	93%				

EMERGENCY VACCINATION: RECOMMENDATIONS

- **Molecular testing of dead** birds is recommended for early detection surveillance
- The effectiveness of surveillance is increased by the **repeated sampling** in time
- **Chicken layers**, **ducks** and **turkeys**: a number of effective options testing **dead birds** have been identified
- **Ducks**: alternatives can be carried out testing **live** ducks or based on **mortality threshold but not recommended**
- **Effective options** should be selected according to **country's specific circumstances** and resources

SURV: PREVENTIVE VACCINATION$_{22}$

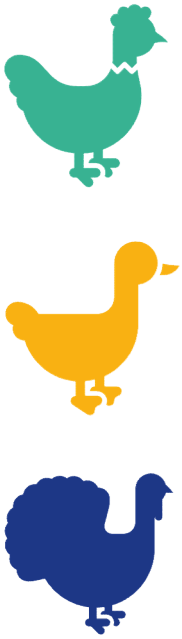
PREVENTIVE VACCINATION

Surveillance strategy	Preventive vaccination scenario – Surveillance within vaccination zone			
	Strategy P1	**Strategy P2**	**Strategy P3**	**Strategy P4**
Objective of surveillance	Early detection in case of HPAIV introduction	Assessment of level of immune response induced by vaccination	Demonstrating freedom from HPAIV in the vaccinated establishment (to authorise the movement of birds from that establishment)	Demonstrating freedom from HPAIV in the vaccinated area (considering that also non-vaccinated establishments might be present)

the probability that at least one infected establishment is detected by the surveillance

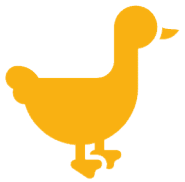
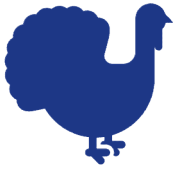
probability that the population is free from HPAI, given that surveillance did not detect any infected establishment and assuming perfect specificity

PREVENTIVE VACCINATION: ASSESSMENT



Sampling scheme	% farms under surveillance	EDSe	Pfree
molecular testing up to 15 dead birds monthly	100%	92%	>99%
		74%	>99%
		93%	>99%

PREVENTIVE VACCINATION: ASSESSMENT

	% farms under surveillance				
	100%	50%	25%	EDSe	Pfree
	monthly	-	weekly	>92%	>99%
	monthly	every 2 weeks	-	>74%	>98%
	monthly	-	weekly	>93%	>98%

PREVENTIVE VACCINATION: RECOMMENDATIONS

- **Many options available**
  - **Molecular** virological testing of up to **15 dead birds every 30** days in vaccinated flocks is recommended to effectively **demonstrate disease freedom with > 99% confidence** within high-risk zones for HPAIV infection
  - If the aim is to **increase the early detection** surveillance sensitivities, then it is recommended to **reduce the sampling intervals**
- Maintaining **passive surveillance efforts in unvaccinated** establishments in vaccinated zones is recommended to enhance the overall sensitivity of the surveillance system
- **MSs** will need to make a dedicated **plan according to their situation**

TOR 4 – RISK MITIGATION MEASURES

TOR 4 – RISK MITIGATION STRATEGIES

To enable safe movement of vaccinated birds EFSA recommends:

Emergency vaccination

- existing rules set out in Reg 2023/361 and Reg 2020/687 are valid and **molecular testing is recommended:** all up to a number of 15 dead birds no earlier than 72 h before movement
- testing could coincide with the sampling session of the surveillance in place

Preventive vaccination

- existing rules set out in Reg 2023/361 are valid
- if the vaccinated establishment is **not under surveillance**, **molecular testing is recommended**: all up to 15 dead birds should be tested no earlier than 72 h before movement

THANKS TO ALL THE EXPERTS INVOLVED

Working group experts

- BASTINO Eleonora (EMA)
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