Chapter 11

Quantitative evaluation of AI vaccination efficacy for the control of Low Pathogenic Avian Influenza in north-eastern Italy from 2000 to 2006

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Abstract

Avian Influenza (AI) has an increased importance in the fields of animal and human health. The main goal to achieve in order to protect animal and human health from the direct consequences of AI still remains the eradication of the disease in birds, but limited epidemiological data are available on the efficacy of the control measures and on the results of the different vaccination strategies applied in case of AI. Some field evidence supports the efficacy of vaccination coupled with enhanced biosecurity and monitoring measures for AI control. In Italy, emergency vaccination programs for the control of LPAI started in November 2000, and in July 2004 the EU Commission authorised Italy to implement a prophylactic vaccination programme in the high risk areas of Veneto and Lombardy, based on the application of a bivalent (H5/H7) inactivated vaccine.

This paper analyses the effect of emergency and preventive vaccination for LPAI control in Italy and appraises the effect of some risk factors for AI infection at the farm level. To our knowledge, this is the first attempt to quantitatively analyse the effect of emergency and preventive vaccination to control LPAI infections in densely populated poultry areas in the EU.

1. Introduction

The increased importance that avian influenza (AI) has gained in the fields of animal and human health, related mainly to the worldwide spread of the H5N1 highly pathogenic (HP) AI virus, has highlighted the lack of information on many aspects of the disease.

To date, the main goal to achieve in order to protect animal and human health from the direct consequences of AI still remains the eradication of the disease in birds (Alexander, 2007), but limited epidemiological data are available on the efficacy of the control measures and on the results of the different vaccination strategies applied in case of AI.

Although AI vaccines have been available for several years, many countries are still reluctant to use vaccination to support AI eradication because of the fear of trade restrictions on vaccinated poultry and poultry products and the risk of endemicity of the circulating field virus as a consequence of its inappropriate use. However, field evidence has shown that vaccination coupled with enhanced biosecurity and monitoring measures could contribute to AI control (Capua and Marangon, 2006).

In particular, the use of vaccination to complement LPAI control or eradication measures in industrial meat turkeys and layers has been described in the US since 1995 (Halvorson et al., 1997, Halvorson, 2002, Swayne and Akey, 2005). Vaccination had also been successfully implemented in Mexico, Pakistan and Hong Kong for the control of HPAI H5 and H7 epidemics (Villarreal-Chavez and Rivera-Cruz, 2003; Naeem and Siddique, 2006; Ellis et al., 2006).

Since 1999, the emergence and re-emergence of LPAI viruses of the H5 and H7 subtypes in a densely populated poultry area (DPPA) of Italy, located in the north-eastern part of the

country, has provided circumstantial evidence of the high risk of their introduction from the wild bird reservoir. In addition, the risk of mutation into the HPAI form posed by the H5 and H7 LPAI viruses in the event of uncontrolled circulation in domestic poultry, has emphasized the need to implement emergency control and vaccination strategies, aimed primarily at eradicating the disease.
Emergency vaccination programs for the control of LPAI started in Italy in November 2000 (CEC, 2000) and in July 2004 the EU Commission authorised Italy to implement a prophylactic vaccination programme in the high risk areas of Veneto and Lombardy based on the application of a bivalent (H5/H7) inactivated vaccine (Marangon and Capua, 2006). Vaccination mainly targeted meat turkeys, which have been shown to be highly susceptible to AI infections (Mutinelli et al., 2003; Tumpey et al., 2003, Busani et al., 2008), and other poultry production types with a long life span, such as layers. In addition, to monitor the possible evolution of the infection in the vaccinated population and to identify field-exposed vaccinated flocks, a serological monitoring programme and a 'DIVA' vaccination strategy (Differentiating Infected from Vaccinated Animals) were enforced (Capua et al., 2003b).
This paper describes the strategies implemented for the control and eradication of LPAI infections affecting the Italian poultry producing sector from 2000 to 2005, and analyses the effect of vaccination on the risk of AI infection for poultry farms in the DPPA. In addition, a quantitative analysis of the main risk factors for AI infection at the farm level is presented for industrial meat turkeys involved in the 2002-2003 H7N3 LPAI.

2. Materials and methods

2.1. Study area and reference population

For the purpose of the analysis, a study area was defined as "the geographical area composed by the municipalities in which at least one outbreak occurred and by the neighbouring communities". This area was different for each epidemic. According to this definition, the reference population for each epidemic was defined as "all industrial poultry farms located in the study area with an ongoing production cycle during the study period".
The beginning and end of the different LPAI epidemics included in the study were defined respectively by the date of detection of the first and the last infected premise (IP). This period was arbitrarily extended up to 60 days before the first outbreak detection and 15 days after the last outbreak in order to take into account any change in the poultry population before and after the epidemic. This time period was selected for descriptive purposes only and was not considered in the analyses.

2.2. Data sources

Spatial coordinates, farm size (number of birds per production cycle), bird species and type of production were obtained for each poultry farm included in the study from the regional databases of the industrial poultry holdings of Veneto and Lombardy. These databases were regularly updated for each registered farm with: i) dates of stocking and slaughter of the birds; ii) vaccination dates; iii) number of vaccine doses delivered in the different vaccination campaigns. The cost of vaccination was estimated considering that the cost of a single vaccine administration, including manpower and vaccine price, was equal to 0.174 Euros. Costs were charged in full to the poultry producers (Busani and Marangon, 2006).
Backyard flocks have never been vaccinated for AI and were not therefore included in the study.

Dates and results of serological and virological tests performed as part of monitoring activities in vaccinated and unvaccinated poultry farms, were collected from the laboratory database at the Italian Reference Laboratory for AI and linked with the record of the corresponding production cycle by the farm ID code and the date of the test.
In all the IPs, epidemiological investigations were conducted by official veterinarians who interviewed the farmers using a standardised questionnaire (Busani et al., 2008).

2.3. Vaccination

Meat turkeys were vaccinated according to the scheme reported by Capua and Marangon (2007) that had proved to be effective in an experimental challenge (Capua et al, 2004):
First administration: 20-30 days of age (15-25 for females).
Second administration: 45-55 days of age (35-45 for females).
Third administration: 70-80 days of age (60-70 for females).
During the 2002-2003 epidemic, a fourth administration was scheduled, but this protocol was discontinued and the three-administration protocol re-established in July 2003 due to field evidence of a lower immune response provided by turkeys submitted to four vaccinations compared to those with three vaccinations only.
Laying hens received the first vaccination at about 45 days of age and the second before the beginning of the laying period (about 120 days of age).
Vaccination coverage was calculated for meat turkeys and laying hens. For calculation purposes, poultry farms vaccinated according to the above mentioned vaccination scheme were counted as “properly vaccinated”; this number was divided by the total number of farms of the same species and production type present in the study area and included in the vaccination program.
Suspected and confirmed LPAI outbreaks were defined according to EU legislation (CEC, 2005). The incidence of newly infected poultry farms was calculated on a weekly basis.

2.4. Statistical analyses

The risk factors considered were poultry species and production type, farm size and the distance of the IP from the nearest infected or potentially infectious farm.
The definition of potentially infectious farms was based on the definition of a temporal risk window (TRW) (Taylor et al., 2004). An IP’s TRW is the time interval during which clinical signs of disease can be detected in another flock following transmission from the IP.
The date of virus introduction in a poultry flock was estimated by taking into account the date of sampling and the type of test resulting positive (detection of virus antigen or antibodies or both). In the case of AI virus detection by PCR or virus isolation, a random number between two and six days before the sampling date was assumed. In the case of detection of antibodies to the AI virus, a random number between 10 and 15 days before the sampling date was assumed (estimates from experimental data, Capua et al., 2004). The interval was arbitrarily extended to 14-21 days for layers in order to consider the delay of the virus spread within the flock as a consequence of the cage system of farming.
The end of the TRW was considered to be the date of outbreak extinction.

2.5. Survival analysis

The evolution of the epidemics was described by estimating the probability of virus introduction over time.
The survival function S(t), estimated using the Kaplan-Meier formula, describes in this case the probability of a flock surviving uninfected for longer than a specified time "t". The probability of flocks escaping infection was displayed graphically as a survival curve. The log-rank test was used to compare infectious history among different groups as defined by each risk factor for non time-dependent variables, while the Mantel-Byar test was used for the time-dependent risk factor (distance from the nearest IP) (Marubini and Valsecchi, 1995).
Distance from the nearest IP was categorized as: <1.5, 1.5-3, 3-4.5 and ≥4.5 Kilometres (Km), whilst farm size was categorized as: up to 10,000, between 10,000 and 30,000, between 30,000 and 50,000, and more than 50,000 birds (Busani et al., 2008).
The survival analysis was performed on the 2000-2001 and 2002-2003 LPAI epidemics since it was not possible to compare the risk of infection between vaccinated and unvaccinated poultry holdings in the 2004 and the 2005 LPAI epidemics, due to their occurrence in an already vaccinated population (Table 1).
All the analyses were performed considering the farm as the statistical unit.
Descriptive analyses were carried out by Stata ver. 9 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA), while the survival analyses were performed by R package (version 2.6.0) (R Development Core Team, 2007).

3. Results

3.1. Description of the epidemics

From 2000 to 2005, the four LPAI epidemics which occurred in North-eastern Italy showed different outcomes, in terms of number of outbreaks and duration of the epidemic (Table 1).

2000-2001 H7N1 LPAI epidemic - From August to November 2000, four months after the eradication of the H7N1 HPAI virus which affected the Italian poultry production sector in 1999-2000, an H7N1 LPAI strain re-emerged and infected 55 poultry farms, mainly located in the southern part of the province of Verona (Veneto region). A targeted emergency vaccination program was implemented in the southern part of the province of Verona in November 15, 2000. Vaccination was carried out only on meat turkey and layer farms. Three hundred meat turkey farms and six layer operations, accounting for a total of 20.4 million vaccine doses, were vaccinated up to March 31, 2002 (Table 2).
Between August 14, 2000 and March 20, 2001 the LPAI H7N1 subtype virus infected 73 meat turkey farms, one layer farm and four quail farms in the provinces of Verona, Padua and Vicenza. The epidemic evolved in two distinct waves: the first in the province of Verona, which lasted until November 2000 and corresponds to the first peak in Figure 1 (A), while the second, occurring in the provinces of Padua and Vicenza, started in January 2001 and ended in March 2001 (Figure 1). Vaccination coverage of meat turkey farms in the province of Verona reached 95% at the end of the epidemic, while coverage was about 42% in laying hens (Figure 1).

2002-2003 H7N3 LPAI epidemic - The 2002-2003 H7N3 LPAI epidemic started in July 29, 2002, on detection of four infected meat turkey flocks located in the province of Brescia (Lombardy region). Restriction and monitoring measures were immediately implemented, and up to October 10, 2002, no other infected poultry flocks were found. On October 10, 2002, the same virus re-emerged in meat turkey flocks in the provinces of Brescia and Verona and rapidly spread in the DPPA, despite the strict control and eradication measures immediately put into force.

An emergency vaccination program was implemented in an area that included part of the Lombardy and Veneto regions (4760sq. Km), with a total of 1,550 poultry farms and more than 45 million bird places (Figure 1). DIVA strategy was based on the AI inactivated heterologous vaccine (strain A/ck/IT/1999-H7N1), but due to its unavailability at the beginning of the epidemic, the DIVA vaccination campaign was delayed to December 31, 2002. In the meantime, the homologous vaccine A/ck/PK/1995-H7N3 was used to immunize 62 layer operations (10,163,000 doses) and 54 turkey flocks (1,284,000 doses). At the end of the epidemic 838 flocks had been vaccinated (81.3% meat turkey flocks) and over 61 million vaccine doses delivered (Table 2).

From October 10, 2002 to September 30, 2003, a total of 380 poultry holdings (329 meat turkey farms) of Veneto and Lombardy were infected, involving 7,660,005 birds. Of the affected farms, 88 were vaccinated flocks with a total of 1,523,320 birds. All the infected vaccinated flocks were meat turkeys, mainly located in a limited area of the southern part of the province of Verona. The first outbreak in a vaccinated flock occurred on April 18, 2003. The incidence curve of this epidemic (Figure 1 (B)) shows two distinct peaks; the first was observed about twenty days after the beginning of the vaccination campaign and could be due to the low proportion of vaccinated and fully immunized flocks at that time (44% and 29% of turkey and layer flocks, respectively). The second peak came later (June 2003) in relation to the outbreaks in the 88 vaccinated meat turkey flocks. Vaccination coverage of turkey flocks steeply increased, reaching about 90% in March 2003 and remaining high until the end of the epidemic. In laying hens, coverage had reached 78% at the end of the epidemic.

2004 H7N3 LPAI epidemic - Between September 16, 2004 and December 10, 2004, the LPAI H7N3 subtype re-emerged in the southern part of the province of Verona and infected a quail holding and 27 turkey flocks (Table 1).

Vaccination coverage of meat type turkey flocks ranged between 53.2% and 88.1%, with the highest coverage during the last phase of the epidemic; laying-hen coverage was 80% at the beginning and 100% at the end of the study period (Figure 1).

2005 H7N1 LPAI epidemic - On April 15, 2005 an LPAI virus of the H5N2 subtype was detected in four turkey farms in the vaccination area of the Lombardy region (Table 1). From May 15, 2005, 15 meat turkey farms were found positive: 13 were preventively vaccinated with an H5/H7 bivalent vaccine, while the other two farms were outside the vaccination area. The only measure in place at the beginning of the epidemic was vaccination and coverage was over 79% in meat turkey flocks and 98% in laying hens flocks (Figure 1).

The prophylactic vaccination program was discontinued on December 31, 2006, due to the difficulties encountered by farmers in sustaining the costs of this program. Between 2000 and 2006, a total of 202,140,000 vaccine doses were administered in the implemented emergency and preventive vaccination programs, and 69% of them were used to immunize the turkey flocks (Table 2). Total direct vaccination-related costs amounted to about 35 million euros (Table 2).

3.2. Survival analysis

Cumulative survival probability at the end of the study period for non vaccinated flocks was 47.5% and 40.3% for the 2000-2001 and 2002-2003 epidemics, respectively (Figure 2.1). In 2000-2001, this probability decreased slowly from 100% to 77% between day 78 (September 2000) and day 210 (January 2001), which coincided with circulation of the H7N1 LPAI virus in the province of Verona (Fig. 2.1A). After day 220, the probability of infection decreased steeply to 47.5% and represented the spread of the infection in the provinces of Padua and Vicenza, where vaccination was not implemented. In 2000-2001 only one vaccinated flock was infected by the H7N1 LPAI virus.

In the 2002-2003 epidemic (2.1B), cumulative survival probability for non vaccinated flocks decreased steeply from day 200 (vaccination starting) to day 280 (January 2003, peak of incidence) and reached a plateau after day 345 (April 1, 2003). Cumulative probability of survival of vaccinated flocks was 100% until day 368 (April 18, 2003), which was the date LPAI infection was first observed in vaccinated meat turkey flocks. At the end of the epidemic, the survival probability of vaccinated flocks was 77% compared to 40% in non vaccinated ones.

For the 2002-2003 epidemic, cumulative survival probability by risk factor is shown in Fig. 2.2 (A-D). At the beginning of the epidemic, cumulative survival probability in Lombardy was lower than in Veneto (Fig. 2.2A), but after day 265 (January 11, 2003), the risk of infection (1-cumulative survival probability) was higher in Veneto than in Lombardy; at the end of the epidemic, cumulative survival probability was 76% and 65.5% for Lombardy and Veneto, respectively.

As regards poultry species and type of production, survival probability was low for meat turkeys (42.3%) and quails (49.8%), but was higher than 80% for all the other poultry species and production types (Fig. 2.2B).

For meat turkey flocks only, cumulative survival probability was also calculated considering the number of vaccine administrations (from 0=not vaccinated to 4 vaccine administrations, according to the protocol reported in Materials and Methods), the number of birds raised per production cycle, and the distance from an IP in TRW.

In vaccinated meat turkeys, the lowest probability of survival was observed for farms vaccinated two and four times (68.3%), while it was 88.6% for flocks vaccinated three times (Figure 2.2C). Only 22 flocks were vaccinated once.

Regarding farm size, cumulative survival probability decreased progressively with increase in size, ranging from 48.4% for farms with up to 10,000 birds to 9.4% for farms with more than 50,000 birds (Figure 2.2D).

Cumulative survival probability related to proximity to an IP (Figure 3E) differed between farms at more than 4.5 Km from an IP (survival probability 80%) and farms within 4.5 Km of an IP (survival probability from 17.4% to 20.8%). For those within 4.5 Km of an IP, no significant difference was observed in survival probability among the three categories considered in the analysis (≤1.5 Km, 1.5-3 Km and 3-4.5 Km).

4. Discussion

The four LPAI epidemics which occurred in the DPPA in North-East Italy from 2000 to 2006 were analysed and compared in order to evaluate the outcome of the implemented vaccination policies. This study is, to our knowledge, the first attempt to quantitatively analyse the effect of emergency and preventive vaccination to control LPAI infections. Although vaccination in poultry production is a well-established practice for the control of a number of diseases, it has only recently been applied to AI control, and evidence is needed to support its application.

Emergency vaccination:
Emergency vaccination was implemented to control and eradicate the 2000-2001 and 2002-2003 LPAI infections, with different outcomes. Marangon et al. (2004) suggested different conditions within the poultry production system in the two periods that could have affected these results. In particular, in 2000 there was a reduced number of operating poultry farms and a homogenous poultry population, while the opposite was the case in 2002.
In both the epidemics, vaccination coverage of meat turkey flocks reached 95% at the end of the epidemic period. In 2000-2001, the start of the vaccination campaign coincided with the end of the epidemic in the vaccination area and the spread of the virus to unvaccinated neighbouring areas (provinces of Padua and Vicenza). Nevertheless, the epidemic was eradicated and only 20 flocks were infected outside the vaccination area. In 2002-2003, the start of vaccination was delayed and the incidence peak occurred when coverage was still low (44%), involving at that time only unvaccinated poultry farms. The incidence of AI infection started decreasing when about 65% of meat turkey flocks had been vaccinated and, apart from the late outbreaks occurring in vaccinated turkey flocks (April-June, 2003), it remained low until the end of the epidemic.
The observed survival probability of vaccinated and unvaccinated flocks in the two epidemics was different. In particular, it was about 100% in 2000-2001 for vaccinated flocks (only one vaccinated flock was infected) but decreased to 77% in 2002-2003 (Figure 3.1). This difference is probably related to the following factors that could have influenced the outcome of the two vaccination campaigns. In 2000, vaccination of replacements was carried out after complete depopulation of poultry farms due to the 1999-2000 H7N1 HPAI epidemic, the start of the vaccination program was correctly planned and farm restocking was carried out accordingly. This induced a homogeneous immunological status in the population. Conversely, in 2002-2003, vaccination of replacements was applied in the presence of active virus circulation, and the start of the vaccination campaign was delayed due to the unavailability of vaccine, inducing a heterogeneous immunological status in the population. Furthermore, in 2000 poultry density in the area was lower, less infected birds were marketed, and a smaller area was involved than in 2003. Motivation in the industry and among farmers was high in 2000 but only limited in 2003, probably influencing the application of biosecurity and vaccination measures (Marangon et al., 2004).
Some risk factors related to the LPAI infection at farm level were investigated in meat turkeys using the data collected in the 2002-2003 epidemic. The difference between Lombardy and Veneto in the risk of infection changed over time. One possible explanation is that the epidemic began in the Lombardy region, and spread only after a few weeks to Veneto, particularly to the province of Verona, where there was the highest concentration of meat turkey farms in Italy. In general turkeys are highly susceptible to AI infections, and taking into account all the LPAI epidemics analysed in this study, meat turkeys accounted for 87.5% of the outbreaks (447 out of 511 infected flocks). In 2002-2003 meat turkey farms had the lowest survival probability (42.3%) of the various poultry species and production types in the study area. This finding is consistent with previous reports of differences in susceptibility among species to both low and high pathogenic AI viruses (Perkins and Swayne, 2003; Tumpey et al., 2003) and of turkeys' higher susceptibility to AI infections compared to chickens (Mutinelli et al., 2003; Tumpey et al., 2003, Busani et al., 2008).
An interesting observation with regard to the poultry species involved in LPAI outbreaks in Italy was the low survival probability of quails. Capua and Marangon (2007) maintained that the quail farming system was critical for LPAI virus maintenance, but did not stress the high risk of AI infection among this type of poultry production. Compared to meat turkeys and quails, the other species and types of production showed an almost double survival probability (from 83.8% in turkey breeders to 96% in the other species). In the case of turkey breeders,

this finding could be related to both a higher biosecurity level compared to the measures applied in meat turkeys, and their location outside the affected DPPA in areas with a low AI risk. During the 2002-2003 epidemic, different vaccination protocols were applied to immunize meat turkeys and the outcome in terms of increased survival probability differed significantly. Interestingly, better results were obtained with three vaccine administrations instead of four. The difficulty of protecting turkeys from AI infection by vaccination has already been described by Tumpey et al. (2004), who vaccinated one-day-old and four-week-old turkeys either once or twice under experimental conditions, leading to the prevention of clinical disease but not of infection.

Regarding AI vaccination of laying hens, no cases were observed in vaccinated flocks irrespective of the number of vaccine administrations, confirming that chickens are less susceptible to AI viruses than are turkeys and that AI vaccines provide better protection in this species compared to turkeys. As observed in the previous study on the H7N1 HPAI epidemic in Italy (Busani et al., 2008), farm size was confirmed to influence the risk of LPAI infection at farm level. In the 2002-2003 epidemic, a progressive decrease in survival probability was observed in meat turkeys with increase in farm size. As previously suggested (Busani et al., 2008), this might be due to the higher number of at-risk contacts in larger farms, because of the more frequent movement of feed trucks and the presence of additional temporary staff, especially during specific phases of the production cycle (e.g., debeaking, vaccine administration, individual drug treatment, and loading for slaughter). Our findings on the effect of proximity to an IP during its infectious period (TRW) on the risk of infection were consistent with observations on the H7N1 HPAI epidemic in Italy (Mannelli et al., 2006, Mulatti et al., 2006, Busani et al., 2008). In the 2002-2003 LPAI epidemic too, having an IP within 4.5 Km was a risk factor for AI infection at farm level. Nevertheless, the effect of proximity provided slightly different results compared to our observations during the 1999-2000 HPAI epidemic. In the HPAI epidemic there was a progressive increase in risk with decrease in distance from an IP. Conversely, during the LPAI epidemic survival probability was almost the same for farms within 4.5 Km of an IP but then increased dramatically for more distant farms. The difference observed in the HPAI and LPAI epidemics could be due to differences in spread capability from an IP to the contiguous farms of HP compared to LPAI viruses. It has been demonstrated that HP viruses have higher infectivity than do LP ones, on the basis of transmission parameters calculated in experimental infections (Van der Goot et al., 2005), and this evidence could highlight the importance of radial dispersion for HPAI viruses. A more detailed analysis on the effect of proximity and spatial aggregation of cases in the LPAI epidemics would help explain the differences observed in local dispersion patterns of HPAI and LPAI viruses.

Prophylactic vaccination

In 2004 and 2005 we observed the re-emergence of the H7N3 LPAI virus and the introduction from the wild reservoir of an LPAI virus of the H5N2 subtype in vaccinated poultry populations. The increased resistance to the field virus challenge of vaccinated birds and the reduction of virus shedding, combined with restrictions, biosecurity and appropriate surveillance, resulted in a rapid eradication of the two outbreaks. Considering the number of affected farms and the duration of the 2004 and 2005 epidemics (Table 1), we observed that although it was not possible to avoid the introduction of AI viruses in vaccinated meat turkey flocks, the spread of the infection was limited, with a marked reduction in the economic impact of the epidemics.

The overall cost of the vaccination campaigns borne by poultry producers between 2000 and 2006 amounted to about 35 million euros, and the direct costs charged to the health authorities for reimbursement of the farmers involved in the LPAI epidemics, reached about 55 million euros, which was less than the estimated 110 million Euros paid in farmer compensation after the 1999-2000 HPAI epidemic.

The analysis of the four LPAI epidemics which occurred in Italy between 2000 and 2005 and are presented in this study, provides a better understanding of the Italian experience in controlling this disease in a DPPA. The applied control policies were based on a combination of vaccination and other disease control options (restrictions, stamping out or controlled marketing of slaughterbirds in IPs, biosecurity, etc.) and were implemented on the basis of a learning-by-doing process. We also provided some insights on the risk factors for LPAI virus infection at farm level, compared to what we observed in the HPAI epidemic occurring in 1999-2000 in the same area. This paper is also the first example of a comparison of the outcomes of two vaccination strategies against LPAI: emergency and prophylactic vaccination. Both emergency and preventive vaccination, associated with restrictions, bio-security and active surveillance for the prompt identification and the appropriate management of any AI outbreaks in vaccinated flocks, could support the control and eradication of LPAI infections in DPPAs. Preventive vaccination provided better results in terms of reduction of the number of outbreaks and duration of the epidemic.
These findings could help in the setting up of contingency plans for AI that include decision-making patterns under different scenarios and also take into account vaccination.

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Table 1. Low pathogenic avian influenza epidemics in Italy (2000-2005), virus subtype involved, vaccine and vaccination strategy implemented, duration of the epidemic and number of outbreaks by species and production (modified from Busani et al., 2007).

Epidemic	**Vaccine and vaccination strategy**	**Duration of the epidemic (weeks)**	**No. of outbreaks by species**	**Estimate of direct costs for farmers' compensation (Euros)**
2000-2001 LPAI **H7N1**	Monovalent A/ck/PK/95-**H7N3** Emergency DIVA	31.3	73 meat turkeys 4 quails 1 laying hen 2 other species	About 10 million
2002-2003 LPAI **H7N3**	Monovalent A/ck/IT/1999-**H7N1** Emergency DIVA	50.6	329 meat turkeys 12 laying hens 16 breeders 4 broilers 19 other species	About 40 million
2004 LPAI **H7N3**	Bivalent A/ck/Italy/22A/98-**H5N9** A/ck/Italy/1067/99-**H7N1** Preventive DIVA	12.3	27 meat turkeys 1 quail	About 600,000
2005 LPAI **H5N2**	Bivalent A/ck/Italy/22A/98-**H5N9** A/ck/Italy/1067/99-**H7N1** Preventive DIVA	4.6	15 meat turkeys	About 4 million

n.d. not determined

Table 2. number of AI vaccine doses delivered for the control of low pathogenicity avian influenza virus epidemics from 2000 to 2006 in Italy, by species and production type.

Species	**2000-2002***	**2002^**	**2003**	**2004**	**2005**	**2006**
Meat type turkeys	14,285,000	2,018,000	47,242,000	36,171,000	28,318,000	10,908,000
Laying hens	703,000	5,831,000	26,830,000	13,263,000	7,577,000	5,459,000
Cockerels	n.i.	n.i.	1,061,000	1,261,000	n.i.	n.i.
Capons	41,000	n.i.	301,000	268,000	192,000	211,000
Guinea fowls	n.i.	n.i.	n.i.	84,000	75,000	41,000
Total doses	*15,029,000*	*7,849,000*	*75,434,000*	*51,047,000*	*36,162,000*	*16,619,000*
Cost in €	*2,615,046*	*1,365,726*	*13,125,516*	*8,882,178*	*6,292,188*	*2,891,706*

*From November 15, 2000 to May 15, 2002
^December 2002
n.i. = not included in the vaccination program

Figure 1. Weekly incidence in meat turkey flocks and laying hens flocks during the 2000-2001 (A), 2002-2003 (B), 2004 (C) and 2005 (D) Low Pathogenic Avian Influenza epidemics and proportion of meat turkeys and laying hens vaccinated flocks (vaccination coverage) during the emergency (A and B) and preventive (C and D) vaccination programs.

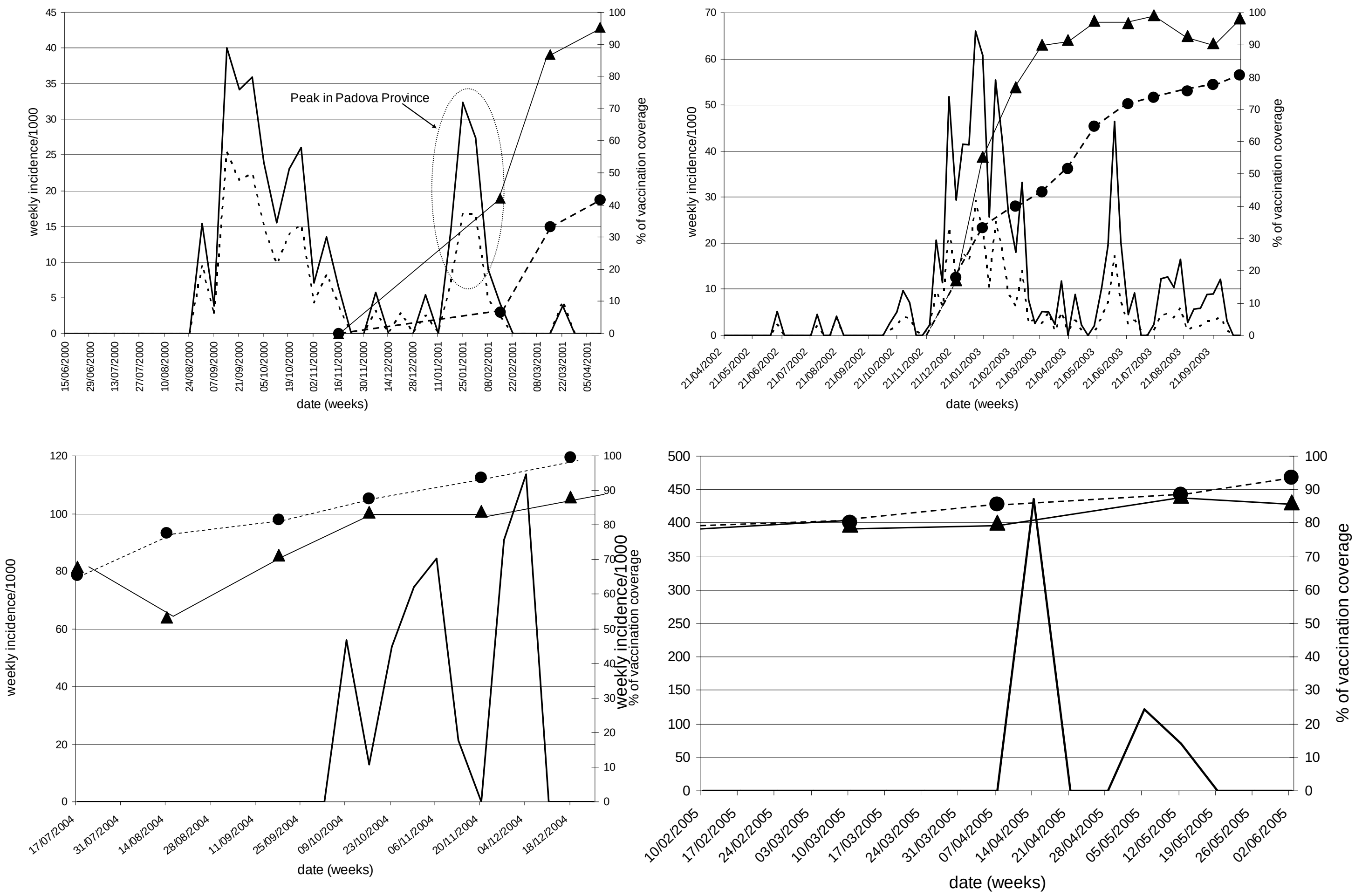


Figure 2.1. Low pathogenic avian influenza: Kaplan-Meier plot of the cumulative survival probability at farm level in vaccinated and unvaccinated meat turkeys and laying hens flocks. A: 2000-2001 epidemic, B: 2002-2003 epidemic

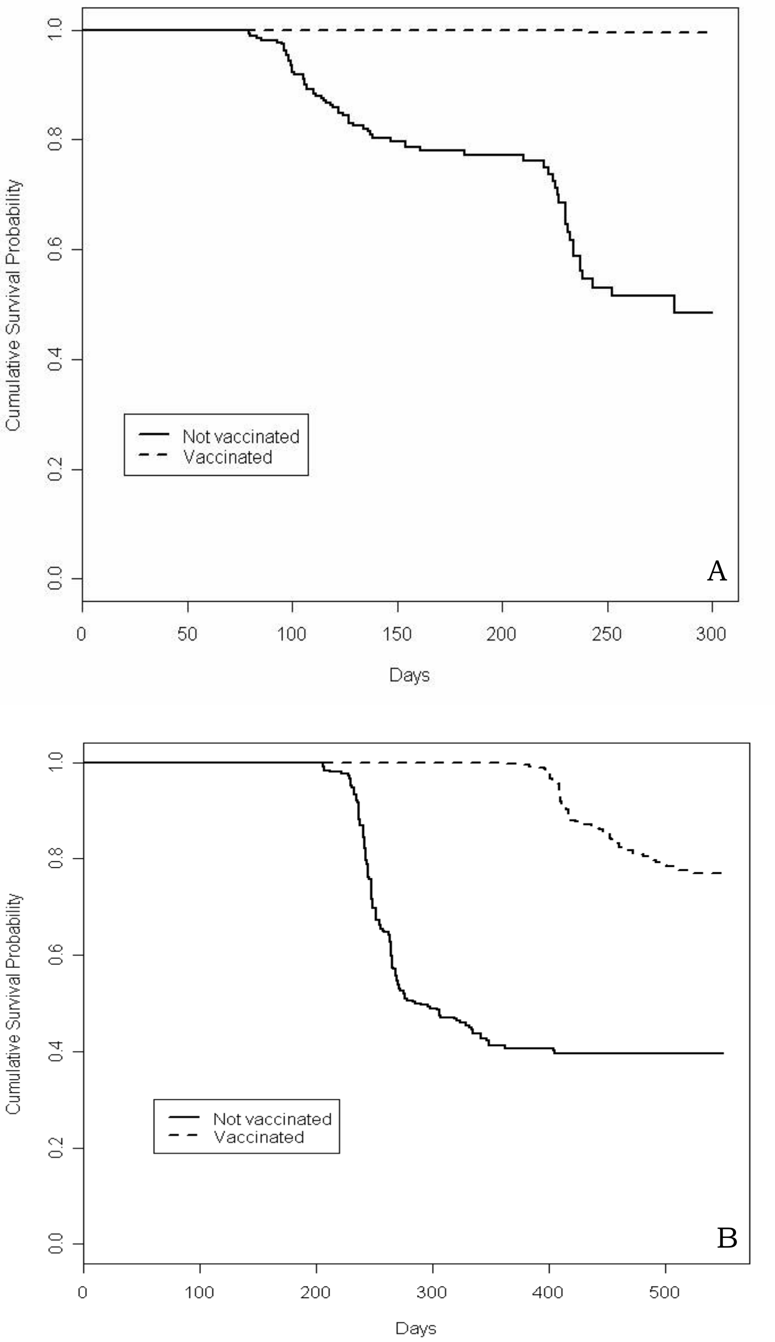
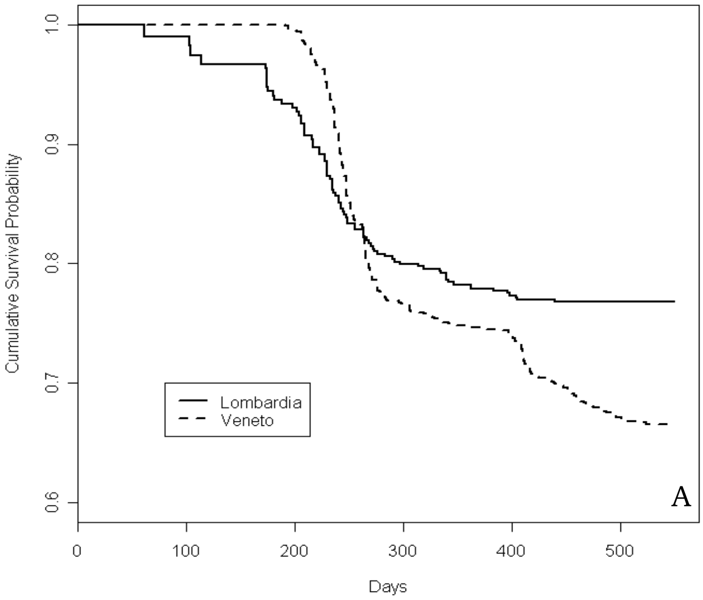
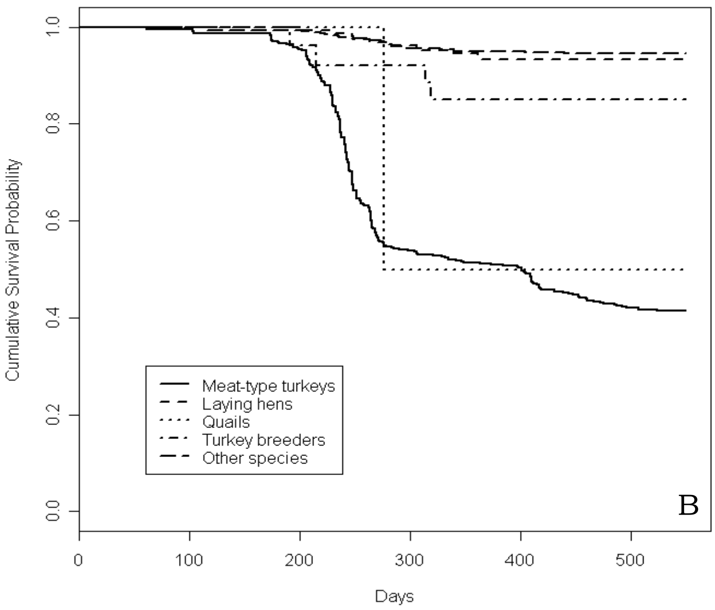
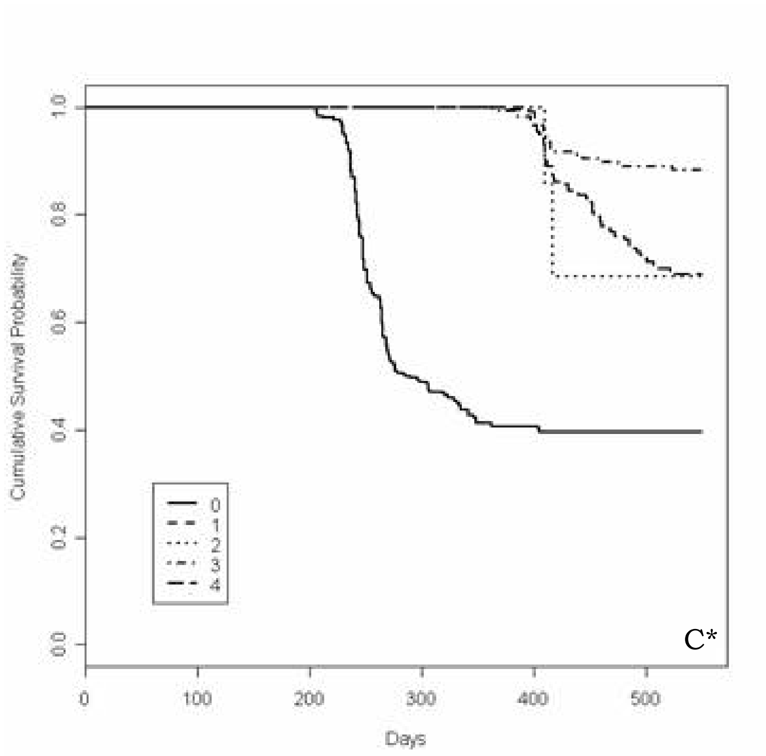
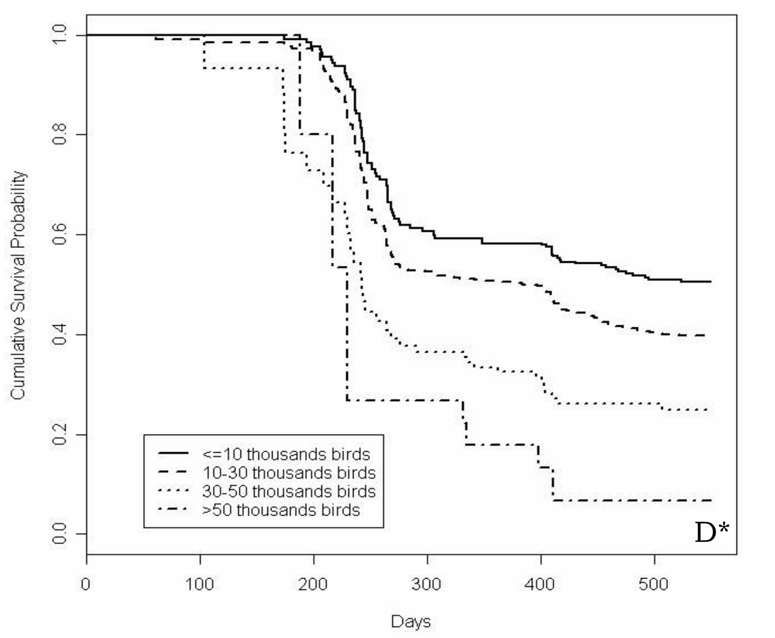


Figure 2.2. 2002-2003 H7N3 low pathogenic avian influenza epidemic in Italy: Kaplan-Meier plot of the cumulative survival probability at farm level by region (A), species and type of production (B), number of vaccine administrations (C), number of birds raised per production cycle (D) and distance from an infected premise (IP) (E).

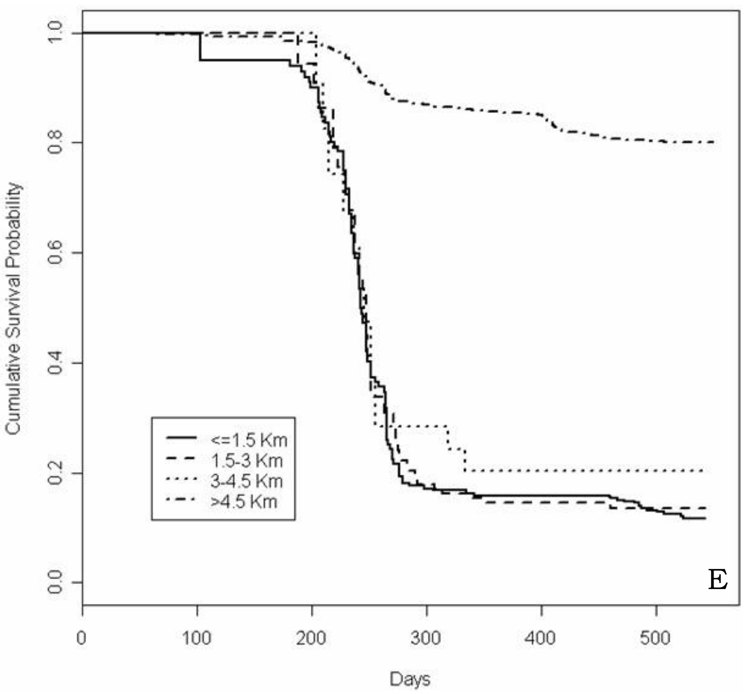








*C= the survival probability is estimated for meat type turkey farms only



1.0
0.8
0.6
0.4
0.2
0.0
Cumulative Survival Probability
<=1.5 Km
1.5-3 Km
3-4.5 Km
>4.5 Km
E
0
100
200
300
400
500
Days