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Operational Research in Indonesia for More Effective Control of Highly Pathogenic Avian Influenza

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1. Executive Summary

The Operational Research in Indonesia for More Effective Control of Highly Pathogenic Avian Influenza (ORIHPIA) Project was undertaken to provide an evidence base to inform decision-making on highly pathogenic avian influenza (HPAI) control. Adaptive management strategies integrate the need for timely action through decision-making based on best available information with the need to continuously improve information and knowledge to enhance future decision-making. Operational research is the embedding of research and learning activities within ongoing program activities. It uses information derived from actual program activities as an opportunity to enhance the information base for future decision-making.

The objectives of ORIHPAI were:

1. To evaluate the feasibility and impact of the implementation of control strategies for HPAI in Indonesia.
2. To assess risk factors for HPAI outbreaks and collect information on transmission dynamics.

The ORIHPAI Project met the first objective through the implementation of a longitudinal study to measure the impact of HPAI control interventions on the incidence of HPAI-compatible disease over the course of one year. The second objective was met through a series of targeted studies designed to answer specific research questions. These studies measured the association between potential HPAI risk factors and indicators of disease occurrence, the sensitivity and specificity of clinical case definitions, as well as disease transmission rate parameters. The ORIHPAI Project made use of multiple methods to address each research objective and utilized existing data, as well as new primary data collected by the Project and its partners. The research activities were integrated with the overall goal to better inform control strategies. To this end, the analysis of results seeks to synthesize the findings of the suite of research activities with information available in the HPAI literature.

Longitudinal Study

At the request of stakeholders, the longitudinal study evaluated two mass vaccination control interventions within the context of the ongoing participatory disease surveillance and response (PDSR) program. A third control intervention – culling with immediate compensation – was proposed but not tested due to institutional constraints related to policies on financial control. Sixteen districts participated in the longitudinal study and each control intervention was implemented in a randomly selected block estimated to contain 100,000 smallholder poultry in each of the 16 districts. This size of treatment block was sufficiently large to capture population ("herd") effects of the control interventions.

Considerable investments were made in strengthening vaccination campaign management, cold chain infrastructure, and the capacity of personnel to deliver effective vaccine and vaccination sero-monitoring. The results of sero-monitoring indicated that the vaccination program achieved moderate level of flock antibody (33.8% and 27.4% had titres $\geq \log_2 4$ to H5 in the two vaccination treatment groups). For comparison, in the targeted studies, only about 70-80% of Kampong chickens vaccinated at 14 days or older at the laboratory developed significant antibody responses (titres $\geq \log_2 4$ to H5). Although vaccination was carefully applied in these studies, the Kampong birds were kept in open-air enclosures and were exposed to inter-current infections. This value can be taken as the upper limit of flock antibody achievable in Kampong chickens kept in traditional settings if vaccine application was rigorously monitored in individually identified birds. Three factors probably contributed to the lower result in the mass vaccination studies: high population turnover rates, incomplete participation or coverage, and gaps in logistic and technical practice associated with the rapid scale-up to population level control programs. Part of the strength of the operational research

approach is that it evaluates the impact of variables associated with the scale-up of activities to real time applications of control measures.

The three principal indicators used to judge the impact of vaccination were changes in the incidence of HPAI-compatible events as measured by participatory impact assessment (PIA) teams, changes in the effective reproductive number (R_e), and trends in disease surveillance data as collected by the PDSR teams. The level of flock immunity induced by the program was found to cause a reduction in:

- HPAI-compatible events as measured by PIA of 46%
- Within flock transmission rates (R_e reduced from 2.76 to 2.21)
- Between flock transmission rates (R_e reduced from 2.07 to 1.9)
- The number of outbreaks detected by PDSR (12 to 24%)

The reduction in HPAI-compatible events and transmission rates was statistically significant. It should be noted that these result relate directly to severe HPAI and the methodology may have missed mild HPAI infections, to the extent there were any. The sensitivity analysis of the case definitions, baseline sero-surveys in the OR districts and serology in the vaccine trials that indicated recovery is very rare, all suggest the sudden death and HPAI compatible case definitions were useful indicators of disease incidence. Thus, the moderate level of flock immunity achieved was shown to suppress HPAI-compatible events in the treatment blocks.

The participatory impact assessment system utilized semi-structured interview techniques combined with mapping, scoring and timeline exercises to detect HPAI compatible events. The diagnostic process was a two-stage process in which PIA teams first used a sudden death clinical case definition. Events that met the criteria of the sudden death case definition were then evaluated using a HPAI clinical case definition and classified as HPAI-compatible, ND-compatible or other. Analysis was conducted on both sudden death events and HPAI-compatible events. The purpose of the ND and other category was to assist the PIA teams to exclude events that were not compatible with HPAI from the HPAI category. These methodologies are reported in detail in the methodology sections of the Longitudinal Study (Section 3.1.2) and the Sensitivity and Specificity of Clinical Diagnosis (Section 4.8.2).

An unanticipated outcome of the research was that a greater reduction in the incidence of HPAI-compatible events was observed in the combined HPAI and ND vaccination group than in the HPAI-only vaccination group (70% and 23%, respectively). The study was not designed to measure the impact of ND vaccination at the biological level and no ND-only vaccination group was included. The combined vaccination group was only included to determine if the availability of ND vaccination would act as an incentive to increase participant uptake of vaccination. The serological survey did not indicate greater participation in the combined vaccination group than in the HPAI only group. Two probable explanations can be given for the greater impact of the combined (HPAI + ND) vaccination compared to the HPAI vaccination alone on the incidence of HPAI compatible disease in the results.

One potential explanation is that there was a differential misclassification bias of the outcome between the different treatment groups. Differential misclassification relates to an assumption that combined HPAI and ND vaccination was able to suppress both HPAI and VVND cases. The number of negative diagnoses was large (for example, 2847 negative diagnoses for VVND-compatible disease) in comparison to the number of positive diagnoses for HPAI-compatible disease (91) and VVND-compatible disease (26). This suggests that the negative predictive values for each of the different treatment groups would be the critical parameters for assessing the impact of differential misclassification because of the large number of negative diagnoses. A small difference in the negative predictive values could result in large numbers of differentially misclassified cases. Since HB1 ND vaccine was used, suppression of ND in adults cannot be merely assumed. In fact, vaccination with HB1 is not generally recommended in adult chickens, as it is considered insufficiently immunogenic, and it did not in fact protect against the natural challenge that resulted from exposure to ND field viruses circulating in the communities during the vaccine trials (Section 4.1). However, if a change in ND prevalence between the groups did occur, it would have led to differences in the predictive value of diagnostic procedures in the different groups, which could have lead to bias. Given that no VVND-specific laboratory test was available, the sensitivity and specificity of the VVND-compatible disease diagnosis is not known and this does not allow us to determine if these considerations affected the outcome.

A second explanation is based on the consideration that the practice of simultaneous vaccination has been observed to give rise to interactions that can either potentiate or interfere with immune responses. For example, it has been observed that a simultaneous administration of live and inactivated oil-based ND vaccines can yield a substantially greater immune response relative to live vaccine alone. There is, however, no evidence to suggest that the same effect can be obtained by using HPAI and ND vaccines concurrently.

Overall, there is no evidence to choose between the two possible explanations for the larger reduction in incidence observed in the combined vaccination group as the study was not designed to test the biological impact of ND vaccination. Given the potential significance of either positive or negative immunological impact of simultaneous vaccination with live HPAI and ND vaccines for control programs, these interactions should be explored in laboratory challenge trials.

The transmissibility study found a significant reduction in the transmissibility of HPAI in vaccinated populations. This study used infection tree reconstruction techniques starting from index cases confirmed by biological tests and utilized a separate data set form the PIA system. The transmissibility results fully support and cross-validate the finding of the PIA system that HPAI vaccination suppressed the incidence of HPAI compatible disease.

Economic analysis of the vaccination program showed that each injection cost US$ 0.12 and a complete vaccination (primary and booster injections) US$ 0.24. Cost-effectiveness analysis found that the cost of avoiding one poultry death (US$ 8-22) was far greater than the value of a bird. Willingness-to-pay studies indicated that poultry owners did see value in vaccination and were willing to pay a percentage of the cost. Taken together, the economic analysis suggests that sustaining mass vaccination programs is difficult from an economic perspective, if public health risks are not considered.

The feasibility analysis considered technical, logistical, economic and institutional dimensions of disease control. The social science concept of institutions was applied to animal health delivery institutions and refers to all the organizations and stakeholder groups and the rules (laws, regulations, customs, expectations, etc.) that govern their interaction in the delivery of disease control services. One conclusion of the feasibility analysis was that the operational research showed that mass vaccination is a technically feasible, but logistically challenging, tool for suppressing HPAI. In terms of resources as logistics and management capacity, the program was very demanding, yet covered only about 1% of the backyard poultry population of Java. These models were expensive to implement and would likely not be sustainable as largely public sector-funded programs supported by donors. At US$ 0.12 per injection, it would cost US$ 288 million to mass vaccinate (using primary and booster injections) Indonesia's 300 million backyard poultry four times per year, with an outcome of moderate and transient suppression of disease. Greater empowerment and participation of local stakeholders in the management and implementation of vaccination activities would enhance sustainability. Moreover, continued support to institutional capacity building for vaccine delivery (including management, social and technical issues) would likely be a beneficial use of public sector resources.

Despite these concerns, our research has shown that vaccination can reduce the incidence of HPAI-compatible events and, when human health impacts are considered, may be justified. We suggest that further research is required to identify incentives for participation by stakeholders and methods to target vaccination to critical control points as a means of leveraging investment in vaccination, as well as other control measures.

Targeted Research

The targeted studies identified a number of research questions designed to complement the longitudinal study, enrich the overall analysis of the operational research, and enhance the database available for disease control decision-making.

- The profiling and livelihoods studies provided baseline data and contextual information for the overall operational research program;
- The vaccine trials provided information on specific vaccination protocols (age of vaccination, number of injections, dosage) and the levels of sero-conversion achievable in Kampong poultry in the face of inter-current disease challenges typical of the local environment;
- The three analytical studies conducted on the original PDSR data (spatial and temporal patterns, content analysis of clinical course and risk factors associated with infection, and multivariable analysis of risk factors associated with detection of disease by the surveillance system) provide information that contributes to the characterization of the disease challenge; and
- The assessment of the sensitivity and specificity of clinical case definitions in the diagnosis of sudden death and HPAI-compatible disease added to the evidence base on the use of clinical diagnostic methods in surveillance.

Profiling of ORIHPAI Districts

Three distinct profiling activities were carried out as part of the ORIHPAI project to better understand the environment in which HPAI is circulating and control measures are implemented. No comparable previous studies were found in the literature. Concurrent projects also provided some insight to poultry rearing in the region, however with a focus on commercial poultry operations. The results demonstrated the diversity in poultry husbandry and management across Java, indicating that it is difficult to generalize on the poultry situation. The risks associated with these realities should be fully characterized in order to identify the most feasible and effective mitigation measures.

Prior to the mass vaccination implemented during the OR, there was no consistent HPAI vaccination policy across the 16 districts. Some districts implemented a considerable amount of vaccination, others hardly any. Some vaccinated both chickens and ducks, others only chickens. Because HPAI is an infectious disease that does not respect borders, disease control practices in one district will impact HPAI incidence in nearby districts, or even in remote districts that are linked by trade. Therefore it is important that bio-security and vaccination practices are improved across all areas.

The profiles highlighted some characteristics of the poultry industry that likely contribute to the spread of HPAI in Indonesia. For example, all types of premises (farms, markets, shops, etc.) reported that they engage in at least some inter-provincial poultry trade, particularly poultry shops and layer farms. Because the movement of poultry and poultry products is an important contributor to the spread of diseases, including HPAI, it is important to understand the nature of the movement and consider ways to minimize the associated risk, while also considering the impact on the livelihoods of the people involved.

Other practices that likely contribute to the spread of HPAI (and other infectious diseases) include the common practice of off-site waste disposal for abattoirs, mixing of different species at markets, apparent poor bio-security standards on commercial farms, and the ubiquitous importance of traders. The risks associated with these realities should be fully characterized in order to identify the most feasible and effective mitigation measures. Furthermore, the profiling highlighted the power of the district government to determine disease-control policies, as well as the considerable variation in the practical execution of HPAI-control measures across different districts. This can dilute the ability of a central disease control directive to effectively control disease.

Livelihoods study
Qualitative information regarding livelihood impacts, as well as the incentives and disincentives to participation in control programs was obtained across three districts in Java: Cirebon, Semerang and Kulon Progo. Strategies for promoting HPAI-control programs among smallholder farmers were also identified. Poor households were clearly the most vulnerable and were disproportionately affected by the sudden death of poultry due to disease. They rely on poultry rearing for additional income, for savings, and/or for emergency cash to cover a range of costs, such as buying food and paying school fees and electricity bills. Moreover, income from poultry often fills the income gaps that arise due to the seasonality of crop production. Poultry is also inextricably linked to other socioeconomic realities, such as the independence of women and household equity, as well as the need to participate in significant community events, such as weddings and other social ceremonies. The spread of HPAI can be very disruptive, especially for poor households, and produce negative impacts that may require considerable time and resources from which to recover.

The spread of HPAI, because of its negative effects on poultry prices, affects household consumption of all food commodities, especially among poor households. Women are often responsible for rearing poultry and managing the income generated from the enterprise, and may therefore be more heavily affected by poultry losses than other household members. Despite the frequency of past HPAI outbreaks, farmer knowledge about the disease and its control remains limited.

Vaccine trials
A series of experiments were undertaken in collaboration with the Wates Laboratory, both on the laboratory compound and at the community level, to answer specific questions on the best way to apply in-activated vaccines based on the Legok 2003 strain of H5N1 virus. The specific research questions were: what is the optimal age of first vaccination, comparison of boostered vs. single dose vaccination regimens, and the effect of double the antigen content in the vaccine on vaccination response and the need for a booster. It was clearly demonstrated that vaccination was not effective below 2 weeks of age and that the booster regimen was required when using vaccines with normal antigen levels. Doubling the antigen content enhanced the response to vaccination and is strongly recommended. Doubling antigen content showed promise as a potential approach to eliminating the need for a booster by achieving high initial titres, but more work is required to demonstrate equivalent duration of immunity. Demographic results of the community trials indicate that 39-45% of Kampong chickens were consistently under 2 months of age, which is a clear indication that vaccination must be carried out at least quarterly to maintain meaningful levels of flock immunity. The prevalence of antibody in the community trials was generally below the threshold for eradication predicted by the transmissibility studies (65% within flock).

Transmissibility of HPAI
The results of the transmissibility study using infection tree reconstruction methods indicated that the moderate levels of vaccination sustained by the operation research resulted in a statistically significant reduction of the transmission of HPAI both within and between flocks. Due to the clinical method tree reconstruction, the study may have missed some mild cases in partially protected vaccinates, if any did occur. However, the programs objective was to measure the impact of vaccination on both infection and disease. The result was fully consistent with the results of the longitudinal follow-up using participatory impact assessment methods to measure changes in incidence and the reduction in reports of outbreaks observed in the PDSR surveillance system. The level of population immunity necessary to fully interrupt transmission between birds within a household flock was found to be between 43.5% and 63.8%, depending on the calculation method used. To interrupt transmission between household flocks in a neighborhood (RT), the thresholds ranged between 34.1% and 51.7%, depending on the method. The transmissibility study was

efficient in terms of the use of resources and provided information on both within and between flock transmission, risk factors associated with transmission, and immunity thresholds required to interrupt transmission. The approach provides essential guidance for vaccination strategy and is important in decision-making. The results suggest that vaccination campaigns should have a goal of achieving approximately 65% immunity within about 50% of flocks. It should be noted that the only the vaccine trials at the laboratory achieved these levels, where vaccine was carefully applied in wing tagged Kampong chickens exposed to inter-current infectious disease burdens typical for the region. Neither the treatment groups in the operational research nor the communities vaccinated in the small community trial led by the laboratory were able to achieve antibody levels consistent with disease eradication.

Analyzing patterns of HPAI in the PDSR data

The PDSR data were analyzed to describe the temporal and spatial distribution of highly pathogenic avian influenza (HPAI) cases detected by the program from January 2006 to May 2008, and secondly to characterize the 16 districts that participated in the ORIHPAI project with respect to the density of backyard poultry and the response to HPAI outbreaks. The key results of our study include: 1) evidence to support that HPAI has seasonal fluctuations; 2) considerable regional variability in the patterns of case detection suggesting that data aggregated nationally should be interpreted with caution; and 3) considerable variation between and within districts in the implementation of HPAI control measures. However, most districts have recorded only limited vaccination and/or culling activities. This last point indicates that, on average, the control blocks in the operational research received very little in the way of vaccination or culling interventions.

The reason for the variation is not fully understood. It may due to different husbandry practices, poultry population densities, environmental factors such as temperature and rainfall, and/or surveillance practices. On the other hand, the diversity of patterns may be the result of chance in nature (stochastic or chaotic) and reflect the absence of dominant drivers of disease transmission patterns. Aggregation of data, nationally or by larger administrative units, may obscure important local patterns. Further studies to better characterize the nature and causes of the variation should be conducted to provide insight to measures that would effectively control HPAI.

Content analysis of the original PDSR data

A wealth of information about the clinical presentation and risk factors associated with HPAI in Indonesia is contained within free text fields of the PDSR database. The operational research developed text-mining analytical approaches for the PDSR data using WordStat 5.1 (Provalis Research) text-mining software. The PDSR officers most frequently attributed the source of HPAI and its spread to inappropriate carcass disposal, the presence of free-ranging poultry, and to poultry trading practices. These factors would cause the spread of HPAI both within and between communities. Sudden death and cyanosis were the most commonly reported clinical signs and, along with respiratory signs, inflammation, haemorrhage, and high population mortality rates, they were significantly associated with positive rapid-test diagnoses. While these results must be interpreted in the context of the surveillance program in which they were collected, they clearly demonstrate the utility of text-mining programs and content analysis, and add value to information collected through the semi-structured survey methods used in participatory epidemiology.

Multivariable analysis of the original PDSR data

The multivariable analysis was performed to identify factors associated with the incidence of HPAI detection by PDSR officers in selected districts on the island of Java. A causal web diagram was developed to guide the modeling process, and demonstrated that the available data allows us to model the incidence of HPAI detection, rather than the true incidence of HPAI. In this analysis, the detection of HPAI was consistently associated high human population density, and low NVDI. These findings are broadly consistent with many other studies. Duck density, which has been found as a risk factor in models from other countries, was not found to be a risk factor in ORIHPAI work.

These analyses demonstrate that quantitative statistics must be interpreted carefully, and specifically how important it is to have a good understanding of how the data were collected and analyzed. The explicit construction of causal diagrams is an important step in documenting the decision-making process in the construction of statistical models. In the case of PDSR data, the data is appropriate to assess risk factors for HPAI detection by the PDSR surveillance system. This analysis is a valuable contribution to the global study of HPAI risk factors because it illustrates the biases that may be present within surveillance data and that should be explicitly considered in the analysis. These issues are common to many published risk-factor studies, but rarely addressed. With the current trend towards risk-based surveillance systems that are designed to enhance disease detection rates, understanding data relationships will become key to reliable analysis.

Ideally, to verify both these results and those from other studies, an important next step in the understanding of HPAI epidemiology should be carefully designed risk-factor studies involving primary data collection, in which the biases associated with surveillance data are avoided. The challenge will be to develop a sampling procedure that can cost-effectively generate a sufficiently large data set for this acute, highly fatal viral infection without using risk-based sampling approaches.

Sensitivity and specificity of clinical diagnoses for HPAI

Quantifying the incidence of HPAI is challenging due to the lack of indicators of infection that are easily measured. Chickens rarely survive infection and as a result serology is not very a very useful tool for estimating the prevalence of infection. Diagnostic tools that rely on agent detection are only useful for actively infected cases. Acute viral infections are of short duration and prevalence studies based on agent detection require prohibitively large sample sizes to find sufficient cases in the narrow window of infection. Diagnostic procedures that rely on clinical indicators can be evaluated quantitatively using the same methods applied to laboratory testing procedures (sensitivity and specificity). It is important to remember that each diagnostic decision-tree (combinations of sampling procedures, and clinical and biological tests) has unique a unique set of sensitivity and specificity parameters. Thus, values for different applications of PE and PDS are specific to the detailed system in place at the time. If the diagnostic protocol is changed, the sensitivity and specificity of the system also change.

The sensitivity and specificity study showed that clinical diagnostic procedures based on clinical case definitions have reliable levels of sensitivity and specificity for use in research. The clinical diagnosis of HPAI-compatible disease was found to have a sensitivity and specificity of 54.4$\pm$8.1% and 78.0$\pm$6.6% respectively. As a laboratory approach was not available that could differentiate VVND form other forms on ND, it was not possible to estimate the sensitivity and specificity of VVND-compatible disease. However, as comparison of clinical diagnostics to laboratory gold standard tests required that the research be carried out during active outbreaks, the results are not directly transferable to the participatory impact assessment system where case definitions were applied to historical events. This study supported the strategic value of participatory approaches as important tools to answer epidemiological questions.

Recommendations from the Closing Workshop of the HPAI Operational Research Program

Appended below are the verbatim recommendations of the Closing Workshop of the HPAI Operational Research Program held in Bandung, 1-2 December 2009, followed by discussion and/or principal conclusions relative to the specific recommendations of the meeting.

"The Operational Research was an implementation of research to assess vaccination conducted in 16 Districts, 3 Provinces (West Java, Central Java, and D.I Yogyakarta). From the results of the Operational Research, the following points are recommended:

1) The success of the Operational Research is evident because the disease was controlled through vaccination, and at the same time it also improved the human resources of the officers and the community.
2) The Operational Research showed increasing community participation and contribution, and their support in controlling HPAI.
3) The Operational Research was a fruitful and important example of how an evidence-based approach may be used in policy-making. In the future, control programs should implement monitoring activities capable of measuring the impact of each.
4) The results of the Operational Research show significant success in HPAI disease control, and it should be followed up with:
    a. Targeted and structured vaccination implementation.
    b. Empowerment of the trained officers and communities so that their competencies are integrated into the animal health service system.
    c. Dissemination of cold chain information and capacity.
    d. Reinforcement and empowerment specifically of animal health posts to lead HPAI control efforts, and animal health services in general.
5) Partnership and collaboration amongst government, the private sector, and the farmer community in controlling HPAI is important.
6) An HPAI research strategic plan is being prepared by the MoA, and it will be used to identify research priorities and to assess future research proposals.
7) To support HPAI control, the improvement in numbers and capacity of animal health officers, along with financial support, are very much needed at central, provincial and district/city levels."

Jakarta, 2 December 2009[1]

Discussion and Principal Conclusions

Adaptive management assumes that the effectiveness of programs can be improved as more information and knowledge becomes available. This approach advocates for the incorporation of learning elements within operating programs. Operational research is an evidence-based approach to learning from experience where formal sampling and study designs are incorporated into on-going operations.

The ORIHPAI Project utilized multiple methods to address several key questions. This was in part because HPAI is especially challenging to study given the high mortality and short duration of the infection. Cases are over quickly and the disease does not leave many survivors to tell the immunological tale. Traditional diagnostic methods based on detection of infectious material from active cases or serology on survivors is not practically applicable for the measurement of disease incidence given the characteristics of HPAI. Comparison of results from multiple methods, given that all methods found the same trends, served to cross-validate our results. Recommendation 3 of the Closing Workshop recognizes the success of the Operational Research Project with respect to

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evidence-based approaches and advocates for continuation of evidence-based approaches to program monitoring and evaluation.

In retrospect, the most valuable, cost effective and simple method for assessing the epidemiological impact of control measures was the estimation of transmission parameters (R_0 and R_e). This involved using the infection tree reconstruction method, focused on rapid test-confirmed outbreaks. As such, the data set upon which the transmission analysis was based was fully independent of the participatory impact assessment. The advantage of the transmissibility approach is that the data collection measuring R_0 and R_e is inherently easier than that for estimating disease incidence. The results of the transmission study fully agree with the results of the participatory impact assessment based on disease incidence and thus validate the method.

The ORIHPIA project has documented a successful, sustained clinical suppression of HPAI-compatible disease in large populations of backyard and small-scale commercial poultry (Recommendation 1). Our research found that mass vaccination could achieve moderate levels of flock immunity leading to a statistically significant reduction in the incidence of HPAI-compatible disease. However, despite focused efforts, flock immunities did not approach the 50% to 65% thresholds predicted by the transmissibility study as being required to fully interrupt transmission. The small community vaccination trial conducted as part of the targeted studies found that even when birds were marked and vaccination was closely supervised, population antibody prevalence levels were for the most part below 50%. This combination of studies implies that, regardless of the care taken, vaccination with available vaccines against Indonesian strains was not sufficient to eradicate HPAI. Thus, the mass vaccination of smallholder poultry is an open-ended commitment that can suppress disease, but not eradicate it.

When information from the technical, logistical, economic and institutional levels was synthesized in the feasibility study, the mass vaccination approach was not found to be a practical intervention that could be scaled out or sustained. The potential situations where vaccination is appropriate are:

- As a short term intervention to reduce human exposure and risk of infection;
- As one tool in a multi-component strategy (e.g., vaccination, elimination of infectious birds through culling, bio-security measures, and industry restructuring to eliminate transmission pathways); and
- As a tool targeted on critical control points at the producer level in specific disease transmission pathways.

This conclusion on the role of vaccination is supported by Recommendation 4a.

The control of endemic HPAI in Indonesia is an especially challenging undertaken given the institutional complexity of animal health, poultry production and marketing systems. The district profiling has documented the local bio-security challenges associated with traditional poultry keeping while at the same time highlighting the interconnectedness of all levels of production. Superimposed on this is the decentralized nature of the control infrastructure and the power of local authorities in terms selecting policies and control strategies. We wish we could prescribe simple technical remedies, but the solution will ultimately come through institutional change and capacity building.

For the future, our research suggests that the best way forward for planning disease control strategy is to institutional a risk-based approach to the targeting of control interventions that integrates risk analysis techniques with value chain analysis. The objective of this approach is to identify: critical control points; technically effective control interventions; and actors with the capacity and incentive to act. We make these suggestions as input to Recommendation 6 on the development of research plans.

The information presented in this report is a rich source of data and new knowledge to inform risk analysis to determine critical control points and risk-mitigation strategies. The district profiles, livelihoods study, and analyses of the original PDSR data bring forward important data for constructing risk-pathway diagrams and value chain maps. In terms of assessing interventions in a risk-based framework, the progression of vaccine studies from small, contained studies through to community trials, and finally the longitudinal study, highlights the importance of scale of implementation as a determinant of the quality of implementation and ultimately impact.

In the end, integrated control programs that target specific points and implementers in poultry value chains will require strong public-private-community partnerships based on realistic policies and positive incentive systems (Recommendation 5). Strong veterinary infrastructure staffed by well trained and empowered personnel (Recommendations 4b, 4d and 7) will be essential to establishing credible partnerships with industry and the communities.

To implement risk-based approaches, new skills will be needed at the managerial and coordination levels in terms of the capacity to conduct risk analysis as well as value chain analysis. The ORIHPAI project has contributed to capacity development in terms of participatory and epidemiological skills at the local level, and these skills will add value to future control efforts (Recommendation 2).

We would like to suggest that one of the main reasons for the success of the vaccination evaluated by the ORIHPAI project was that the interventions were carried out in a focused and intensively managed manner. National, local and international stakeholders worked closely together to insure that the intervention was implemented to the best of their ability. We would like to congratulate and thank all project participants.

This should be contrasted with the findings of the district profiling activity, which revealed that intervention measures (vaccination, culling, containment, bio-security, etc.) were being implemented in a highly variable manner across 16 districts. This was the background activity present throughout the districts and included the control treatment blocks monitored in the operational research. This suggests that one of the important institutional lessons from the operational research is the value of program focus, clear achievable goals and strong management and coordination that extends to include local authorities and stakeholders.

The principal technical recommendation is that vaccination and other control options should be used as tools targeted to narrowly defined poultry populations at key risk points in the disease transmission cycle. Definition of targets should be based on evidence-based studies that integrate risk analysis, value chain analysis, epidemiological modeling and a realistic appreciation for the incentive for key actors to participate in control programs combined with an understanding of how policies and institutions shape incentives. As noted by the participants of the Closing Workshop, all control interventions should be monitored and assessed for impact based on an appropriate set of indicators as part of an adaptive management strategy. This approach will provide an evidence base for risk-based decision-making leading to programs that are more effective in both epidemiological and economic terms.

2. Introduction

Type A H5N1 HPAI emerged in the Guangdong Province of China, was first detected and reported in Hong Kong in 1997, and subsequently spread throughout Asia, Europe, the Middle East and Africa (Sims, 2007; Morris and Jackson, 2006). In Indonesia, the first human case of H5N1 infection was detected in mid-2005 (WHO, 2009). However, the first poultry epidemic of H5N1 HPAI occurred in late 2003 on the Island of Java, with a second epidemic in 2004 affecting Java, Sumatra, Kalimantan, Bali and West Timor (OIE, 2009). By 1 December 2009, 141 cases of human H5N1 were detected in Indonesia, with the highest case fatality rate in the world at 81.6% (WHO, 2009). In the poultry sector the disease is considered endemic on Java, and the island is considered the epicenter for expansion of the virus in Indonesia (OIE 2009; Takano et al. 2009).

According to the FAO, Indonesia is the seventh largest poultry producer in the world, where 50% of the country's total livestock units are poultry, 75.2% of poultry systems are small-scale commercial and backyard, and meat from backyard chickens (Kampong) and eggs are the third and eight most important commodities, respectively (FAO, 2005a; FAO, 2005b). Backyard poultry keeping in Indonesia is a cultural tradition thousands of years old – a home is complete when the family possesses a few Kampong chickens. In a country where 45% of the population is engaged in agriculture and 52.4% of the population earns less than US$ 2/day, backyard poultry are important livelihood assets and small-scale commercial poultry production is an important pathway out of poverty. Thus, in addition to the human health threat posed by HPAI in Indonesia, the endemic and frequent nature of the disease seriously impacts diverse livelihoods and economies (McLeod et al., 2005).

In January 2006, working with the FAO, the GoI Ministry of Agriculture began a program in Participatory Disease Surveillance and Response (PDSR) for HPAI in poultry. However, as of 2007 efforts to control the disease in small-scale commercial and backyard flocks had not proven effective. Multiple factors contributed to this difficult disease control situation, including ineffective policies, cumbersome decision-making processes, limited disease control resources, the sheer size and complexity of the poultry industry (including an estimated 300 million chickens in the backyard sector alone), and the ineffective implementation of vaccination programs.

The ORIHPAI program was developed to evaluate intervention strategies against HPAI in backyard and small-scale commercial farms by assessing the feasibility of implementing the interventions, and the impact of the interventions on the incidence of HPAI-compatible outbreak events. Operational research (OR) in disease control means learning from the ongoing implementation of disease control strategies that have the potential to decrease the incidence of the target disease (Zachariah et al., 2009). The program consisted of two main components: a longitudinal study combined with ancillary data collection activities (Section 3 of this report) and a series of targeted studies to address specific epidemiological questions (Section 4). In the longitudinal study, the outcome of interest is disease incidence, and the hypothesis to be tested is that the control measure will lead to a decrease in disease incidence. However, many other factors contribute to whether a strategy can feasibly contribute to controlling a target disease, including cost, capacity, simplicity and acceptability. Therefore, ORIHPAI evaluated the feasibility of HPAI control options in addition to measuring the impact of disease control on the incidence of HPAI-compatible events.

The ORIHPAI program was designed in 2006 through a consultative process involving FAO, the GoI MoA, USAID, and the World Bank. As a research partner, ILRI became involved later at the request of the partners. This led to a commitment of funds to the research by the World Bank and MoA through the Avian and Human Influenza Facility (AHIF) grant in 2006, and USAID in 2007.Although these two funding streams were designed to commence together and support multiple partners involved in the research, the reality is that USAID co-funding commenced in the second half of 2007, while AHIF funding through the MoA did not become available until the end of 2008.The ORIHPAI program was completed in December 2009.Throughout the implementation of the program, quarterly progress reports were submitted to USAID, and semi-annual reports to the GoI MoA AHIF office. At each stage, a preliminary analysis of data was conducted and reported. This final report to USAID and the GoI MoA AHIF program covers all components and findings of the ORIHPAI.

The control options to be tested and geographic areas to be involved in ORIHPAI were identified through a series of formal and informal stakeholder meetings and workshops. The original proposal was to test the following HPAI control options:

- Control (normal PDSR activities);
- PDSR immediate response with ring vaccination fully supported;
- PDSR immediate response with ring vaccination and culling fully supported;
- Socially marketed preventative vaccination; and
- Preventive mass vaccination against HPAI.

These control options were presented to program partners and donors during a pre-planning meeting held 17-18 September 2007, and a group of program partners, donors and other stakeholders at an inception workshop held in Jakarta on 28 September 2007.The objective of ring vaccination was described as an approach to focus vaccination to high-risk areas, rather than the traditional containment activity. During these meetings a diversity of views were expressed regarding disease control measures that had the greatest potential for the control of HPAI in Indonesia, and it became clear that the partners wanted to change the disease control options to be tested. Therefore, a survey was implemented in the inception workshop in which stakeholders prioritized four control options favored by the majority of participants: 1) blanket vaccination against HPAI; 2) blanket vaccination against both HPAI and ND; 3) culling with immediate compensation; and 4) fully implemented PDSR with all the necessary compensation funds and vaccine to implement their standard operating procedures (SOP) every time active HPAI was diagnosed. Taking advantage of the expertise available in these meetings, the size of treatment areas and number of treatment group replicates was also discussed.

These workshops were followed by further research design meetings with program partners and donors to finalize control options to be tested, geographic areas to be covered, and sample framework issues such as treatment group replicates. The geographic areas of Java selected for ORIHPAI were the parts of West Java Province not engaged in large-scale commercial production (the eastern half of the Province), Central Java Province, and Yogyakarta Province. These areas were selected because they experienced frequent outbreaks of HPAI according to the PDSR surveillance system, and because they contain high populations of backyard and small-scale commercial poultry. The following control options were those finally selected by project partners and donors, and studied in the ORIHPAI:

- Control (normal PDSR activities);
- Preventative mass vaccination against HPAI with Legok 2003 H5N1 vaccine;
- Preventative mass vaccination against HPAI and ND with Legok 2003 H5N1 and Hb 1 ND; and
- Culling and immediate compensation.

Although the culling and immediate compensation control option was the most interesting to the GoI MoA, it later had to be dropped because no institutional mechanism for immediate compensation could be identified that complied with GoI financial directives.

In January 2009, a project meeting for local government partners was held and decision-makers from 16 candidate districts attended. The objectives, design and potential benefits of ORIHPAI were presented, and districts invited to participate in the program. All 16 districts chose to participate (Figure 2.1).

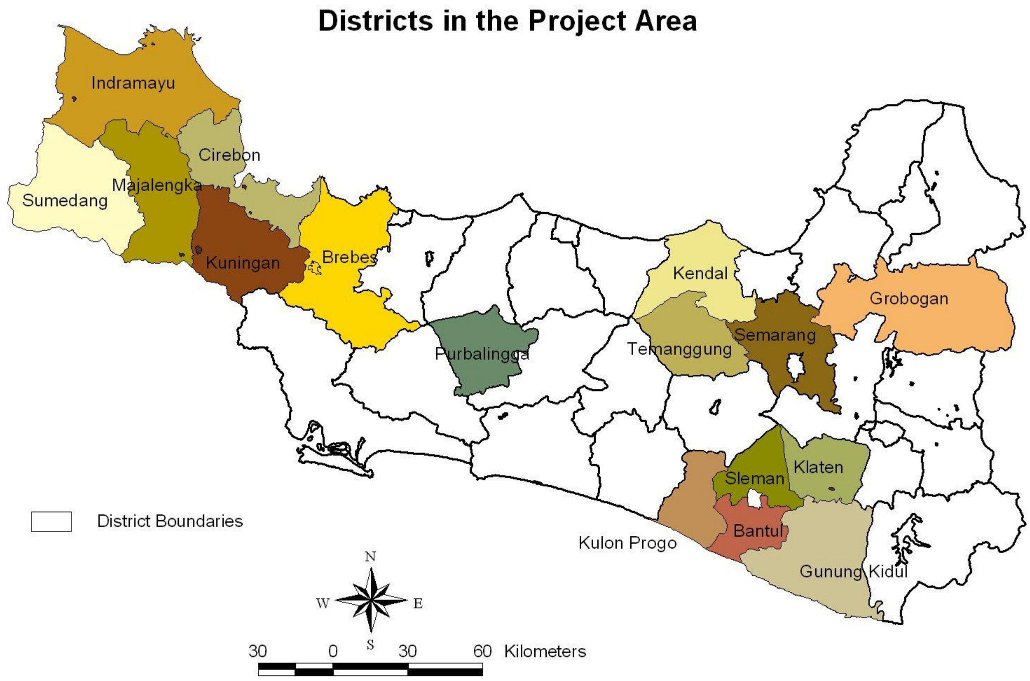

Figure 2.1: A map of the 16 operational research districts

During the implementation phase of the program, two workshops to communicate interim findings were held in 2008 and 2009.The objective of these workshops was to review progress and preliminary findings, and solve problems in implementation.

In December 2009, a closing workshop was held for partners, as well as district and national government stakeholders who participated in ORIHPAI. The results of the research were presented, and the stakeholders formulated recommendations to the GoI MoA based on the findings. This was followed by a closing technical workshop of national and international HPAI experts, in which results were discussed, and recommendations made regarding interpretation and further analysis.

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3.0 Longitudinal Study to Assess the Impact of Control Interventions

A longitudinal study is a research activity in which sites or participants are repeatedly sampled over time. In the case of our operational research, selected treatments were applied to specific locations over the course of a year and these locations were assessed quarterly to determine the amount of HPAI-compatible disease that occurred within the treatment area. The impact of the treatments was then determined by comparing the level of disease in the treated areas with disease from areas where treatments were not applied. A participatory impact assessment system was used to complete the repeated assessments.

A number of activities were carried out that collected data or analyzed data directly derived from the longitudinal study. These were:

- An assessment of the impact of the control interventions on disease incidence;
- Sero-monitoring for HPAI and ND antibody in three of the operational research districts to assess the prevalence of antibodies and coverage of the vaccination programs;
- A cost-effectiveness study of the vaccination interventions;
- An adoption and willingness-to-pay study of the vaccination interventions; and
- A comprehensive feasibility study that assessed the technical, logistical, economic and institutional feasibility of the control interventions.

In addition, the impact of the vaccinations carried out in the longitudinal study on the transmission of HPAI was assessed using infection tree reconstruction techniques to estimate the basic reproductive number for HPAI. This assessment technique did not make use of the longitudinal study sampling methods and is reported as a targeted study in Section 4.4 of the report.

3.1 The effectiveness of preventative mass vaccination regimes against the incidence of highly pathogenic avian influenza in the Java Island, Indonesia

Abstract

We conducted an operational research study involving backyard and semi-commercial farms on Java Island, Indonesia between April 2008 and September 2009 to evaluate the effectiveness of two preventive mass vaccination strategies against highly pathogenic avian influenza (HPAI). One regimen used Legok 2003 H5N1 vaccine; the other used both Legok 2003 H5N1 and HB1 Newcastle disease (ND) vaccine. A total of 16 districts were involved in the study. The sample size was estimated using a formal power calculation technique that assumed a detectable effect of treatment as a 50% reduction in the baseline number of HPAI-compatible outbreaks. Within each district, candidate treatment blocks with village poultry populations ranging from 80,000 to 120,000 were created along sub-district boundary lines. Four of these blocks were then randomly selected and assigned one treatment from a list that comprised control, vaccination against HPAI, vaccination against HPAI and ND, and culling with immediate compensation. However, culling with immediate compensation was later dropped because no institutional mechanism for immediate compensation could be developed that complied with the government of Indonesia's system for dispersing funds. Four rounds of vaccination were administered at quarterly intervals beginning in July 2008. Data on disease incidence and vaccination coverage were also collected at quarterly intervals using a participatory impact assessment system. The analysis suggests that HPAI vaccination reduced the number of HPAI-compatible outbreaks by 23% (p = 0.46), while the combined HPAI and ND vaccination regimen reduced the number of HPAI-compatible events by 70% (p = 0.01). The effect of treatment did not vary with time or district. These results were validated by comparing them with those obtained by serology, measuring the impact of vaccination on transmission rate parameters, and analyzing secondary data from the participatory disease and response (PDSR) database. All methods showed an equivalent level of impact. We therefore conclude that moderate levels of HPAI vaccination are sufficient to reduce the incidence of HPAI-compatible events.

1 Introduction

Indonesia officially reported confirmed outbreaks of highly pathogenic avian influenza (HPAI) caused by Type A H5N1 virus to the World Organization for Animal Health (OIE) in January 2004 (OIE, 2004; Simmons, 2006). By February 2007, the disease had spread across 31 of 33 provinces and led to the death of about 11.3 million chickens (Sumiarto and Arifin, 2008). The government, with strong international support, developed a national strategy and work plan that proposed institutional changes and technical interventions to contain the spread of the disease. A participatory disease surveillance and response (PDSR) program, which applies rural appraisal methods to disease surveillance, was one of the technical interventions implemented. The pilot phase of the program was implemented in 12 districts on Java Island from January to May 2006, and by May 2007 parts of Sumatra and Bali had been covered. Although the program was very successful in identifying outbreaks in backyard and small-scale commercial poultry systems, knowledge on the epidemiology of the disease and ways in which the existing control measures could be used was lacking – particularly for the backyard poultry system.

This operational research project was therefore implemented to evaluate the impact of two preventive mass vaccination strategies against HPAI incidence in backyard and small-scale commercial farms on Java Island, Indonesia. These interventions were used together with other measures that the PDSR program was using at the time, such as improved bio-security, rapid response, and community education.

2 Materials and Methods

2.1. Study design

Treatments – Several meetings were held with various stakeholders to develop the design of the study and to select treatments. The treatments selected initially were:

- Control (baseline PDSR activities);
- Preventative mass vaccination against AI with Legok 2003 H5N1 vaccine;
- Preventative mass vaccination against AI and Newcastle disease (ND) with Legok 2003 H5N1 and Hb 1 ND vaccines; and
- Culling with immediate compensation.

Culling with immediate compensation was later dropped because no institutional mechanism for immediate compensation could be developed that complied with the Government of Indonesia's system for dispersing funds to local governments.

Sample size estimation – We used a longitudinal study design that indicated at least 14 replications (participating districts) of each intervention were required in order to detect a 50% reduction in the baseline number of HPAI outbreaks while allowing for type I and type II error margins of 5% and 20%, respectively. *A priori* estimates of the mean number and standard deviation of HPAI outbreaks by sub-district per quarter were 10 and 6.8, respectively. These estimates were derived from data collected by the PDSR officers over a period of 2 years, mostly on Java Island. The sample size estimation procedure incorporated an intra-class correlation coefficient (ICC) of 0.4 to account for clustering of observations over time. A high internal correlation coefficient was used because it was assumed that using defined geographical blocks as treatment units would increase the baseline ICC. A study conducted by Otte (1997) indicated that ICCs for most infectious diseases range between 0.04 and 0.42.

Study districts, treatment and assessment units – After the sample size had been determined, district selection criteria were developed with the Campaign Management Unit for Avian Influenza Control (CMU). A district was legible for inclusion if it (i) was not participating in any other research activity, (ii) had frequent outbreaks of HPAI based on the observations made by PDSR teams, (iii) had high populations of backyard and small-scale commercial poultry, and (iv) had a strong team of PDSR officers. Figure 3.1.1 shows districts that satisfied these four criteria and were selected for the study; all of them accepted to participate.

Within each district, candidate treatment blocks with village (Kampong) poultry populations ranging from 80,000 to 120,000 were created along sub-district boundary lines. Alternatively, village boundary lines were used to create treatment blocks in densely populated sub-districts that had more than 120,000 poultry. Poultry population statistics were obtained from district government livestock production offices. Four treatment blocks were then randomly selected from each district and allocated one of the four treatments in a sequential version, starting with the control, HPAI vaccination, HPAI + ND vaccination, and culling with immediate compensation. Within each treatment block, 10 RTs were randomly chosen to serve as fixed assessment units for measuring treatment coverage and the number of outbreaks. A formal sample size estimation procedure was used to determine the number of RTs required, assuming a mean number and standard deviation of HPAI outbreaks in a sub-district of 10 and 6.8, respectively.

Assessment units were selected using a random coordinate point system in ArcMap 3.0. Up to 11 random points were generated and uploaded into hand-held GPS units using OZIExplorer 3.95.4q; the additional point served as a back-up that could be used whenever any one of the primary ones could not be accessed (for example, if it fell in forests, lakes or volcanoes). Hand-held GPS units were used to trace individual RTs using GOTO function. Figure 3.1.2 shows the hierarchical relationships of the study units described in this section using one of the study districts as an example.

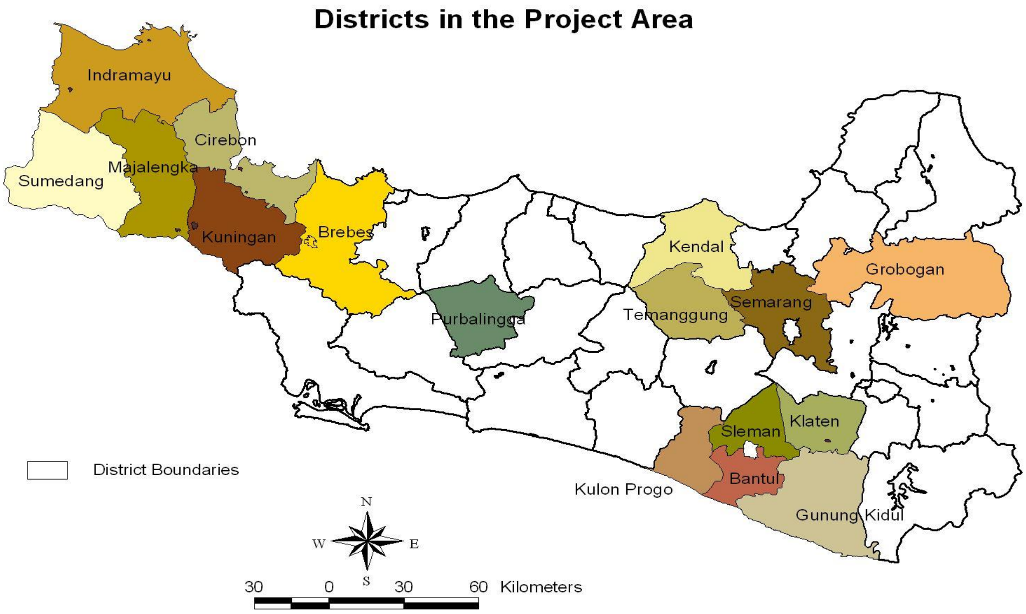

Figure 3.1.1: Relative locations of the 16 districts used for the operational research project on Java Island, Indonesia (January 2008 – July 2009)

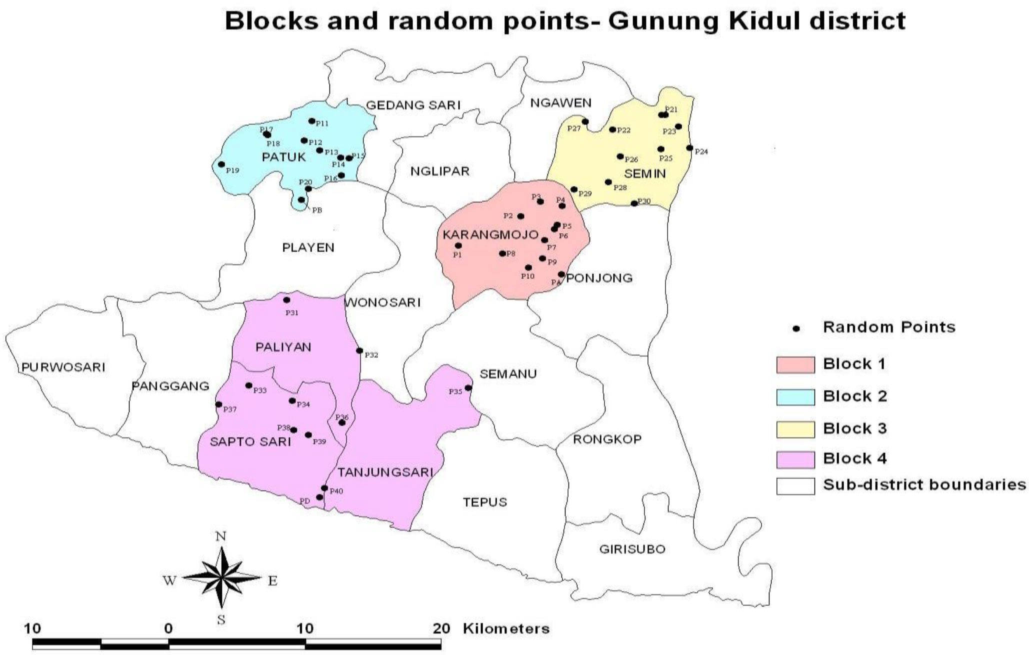

Figure 3.1.2: A map of Gunung Kidul district – one of the study districts – illustrating the hierarchical relationship between the district, treatment blocks and assessment units

Causal web model – A causal web model was developed for identifying causal relationships in the system being studied. This helped to identify confounding, intervening and other variables, as well as methods that could be used for analyzing data. These relationships were derived from expert opinion and published information, such as Joffe and Mindell (2006) and Vineis and Kriebel (2006). The model is presented in Figure 3.1.3.

The causal-web model shows:

- The exposure (vaccination) and outcome (HPAI disease incidence) variables in yellow boxes;
- Variables that have direct influence on either the exposure or the outcome variables in blue boxes;
- Potential confounding factors that influence exposure-outcome relationship in green boxes; and
- Intervening variables for the exposure - outcome relationship in white boxes.

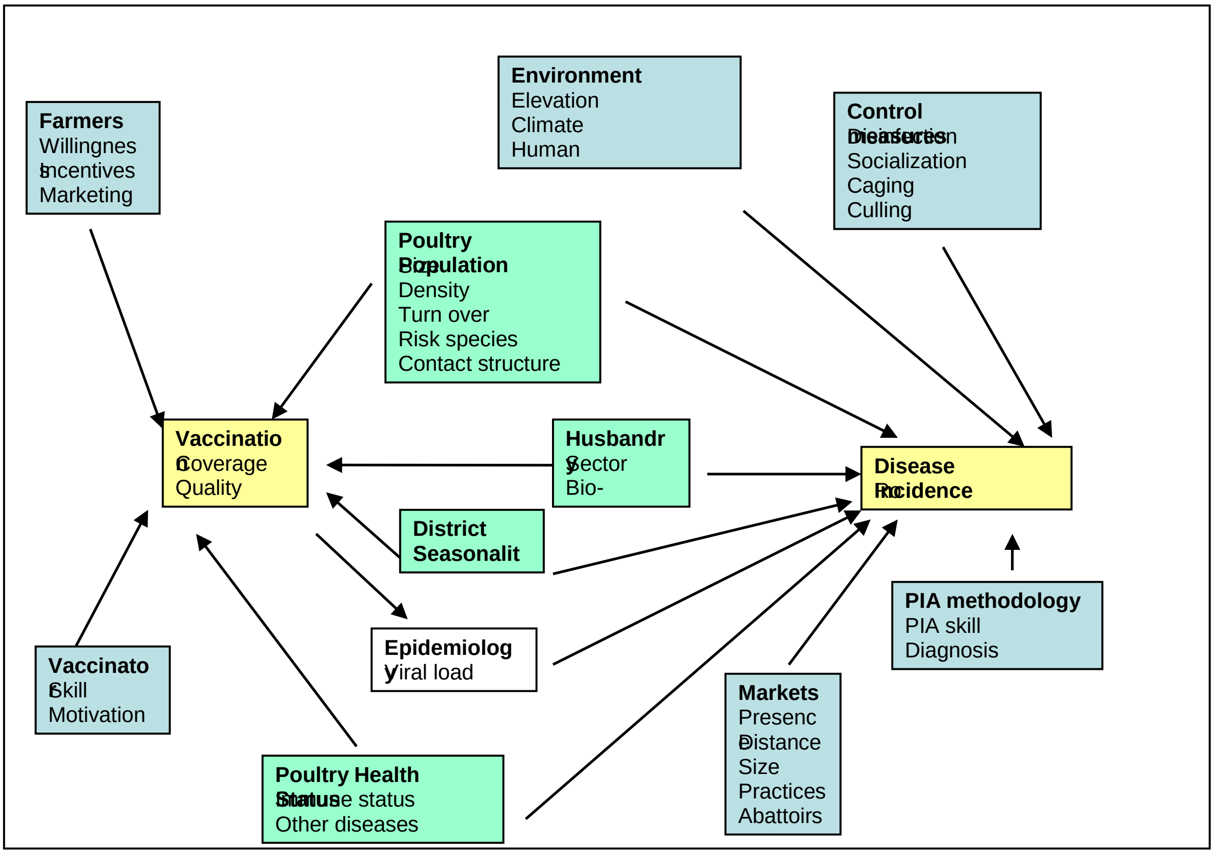

Figure 3.1.3: A diagram showing a causal relationship between vaccination and HPAI incidence in mixed small-scale commercial and backyard poultry populations in West and Central Java (potential confounders, or factors related to both the variable of interest and the outcome, are represented in the green boxes)

2.2. Data collection

Data on the number of outbreaks observed and the level of vaccination coverage achieved after each vaccination were collected on quarterly basis. A participatory impact assessment (PIA) system was applied that uses participatory rural appraisal methods to collect epidemiological information from livestock farmers (Mariner and Paskin, 2000; Catley et al., 2004). Participatory epidemiology tools used included semi-structured interviews (Catley et al., 2001), proportional piling (Mariner and Paskin, 2000), relative incidence scoring (Bett, et al., 2009; Bedelian et al., 2007), timelines (Mariner and Paskin, 2000), matrix scoring (Catley et al., 2004; Catley et al., 2001), mapping (Mariner and Paskin, 2000) and transect walk (Mariner and Paskin, 2000). Each district nominated two PDSR officers who were trained in PIA techniques at the beginning of the study. They also received refresher training at 6-month intervals.

During each visit to an RT, the PIA teams conducted at least three group interviews involving at least five people in each group. Participants were purposefully selected to represent different gender, age, ethnic, wealth, and religious groups.

The type of data collected in these interviews included:

i. Types of poultry species kept and their relative proportions

Semi-structured interviews and proportional piling were used to collect these data. Participants were first asked to give a list of the poultry species they kept; circles representing each species mentioned were then marked on a flip chart. Subsequently, participants were given 100 beans and asked to distribute them into the circles marked based on relative populations of the poultry species identified.

ii. Dates (timeline) of outbreaks during the previous quarter

Timelines were used to determine the dates when sudden death outbreaks occurred during each quarter. These outbreaks were classified into HPAI-compatible events, ND-related, or unknown using a clinical case definition for HPAI. It was assumed that outbreaks occurring 14 days apart were independent from one another. The clinical case definition used was as follows:

Step 1: PIA teams first determined whether an outbreak could be classified as being a "sudden death" event based on the level of mortality. An outbreak that had a high mortality rate (≥80%), with poultry dying within 12 hours of the onset of clinical signs, was classified as being a sudden death event.

Step 2: Sudden death events were then subjected to a second screening to determine whether they could be classified as being HPAI-compatible events, ND-related (based on the PIAs' clinical knowledge), or unknown (if the PIA could not diagnose it as HPAI-compatible or due to ND). An HPAI-compatible outbreak was characterized by a high mortality rate (≥80%) at the household level, per acute death or death within 4 hours from the recognition of clinical symptoms, and involvement of more than one household in a given period. Blue discoloration of the head and body was included as an optional clinical sign.

iii. Relative incidence of each outbreak identified in the timeline

Relative incidence scoring was then used to determine mortality rates for each sudden death event identified in the timeline. Like the proportional piling technique, a total of 100 beans representing the population of poultry in the RT were used. Participants were asked to divide the beans into two, a pile representing a proportion of poultry that became ill in the outbreak verses a proportion that remained healthy. The participants were further asked to split the pile of beans representing the number of poultry that became ill into those that died verses those that recovered. The proportion that remained healthy was split into poultry that were kept verses those that were sold in the course of the outbreak.

iv. The number and distribution of households affected by each outbreak using a participatory map

Participants from RTs that reported sudden death outbreaks were asked to draw a map of their neighborhood indicating the distribution of households, road network and other physical features such as rice paddies, etc. Following this, they were asked to indicate on the map patterns of the disease spread by marking index and other households that were affected and dates when each household was affected.

v. Veterinary interventions implemented and the coverage achieved

A time line and proportional piling were again used to identify the timing of vaccination campaigns and perceived coverage of each campaign reported. Participants were asked to split 100 beans into two groups representing the proportion of poultry that was vaccinated verses the proportion that was not.

2.3. Vaccination

Four quarterly vaccination campaigns were conducted under the project. The first vaccination was done in July 2008. For each campaign, primary and booster vaccinations were given at an interval of 21 days. A single vaccination might not have sustained the required levels of flock immunity given the short life span of poultry.

A total of 1088 community vaccinators and 64 vaccination coordinators from all the districts were identified and trained on vaccine delivery, storage and administration. A cold chain storage system was also set up at each district headquarters comprising refrigerators, cool boxes and incinerators. Vaccines were delivered by the manufacturer to each district headquarter after ascertaining the functionality of the cold chain system established. Poultry population statistics obtained from the government were used to determine the number of doses that each district received at any one time. Vaccination coordinators supplied the vaccines to the community vaccinators on daily basis. Farmers participated in the exercise voluntarily and were not expected to pay for the service.

Legok 2003 H5N1 vaccine was administered intramuscularly while Hb 1 ND vaccine was given as an eye drop.

2.4. Data analysis

RTs were used as the unit of analysis, though treatments were allocated at the sub-district level in order to increase the statistical power of the study. Data were stored in a relational database constructed using Microsoft Access and analyzed in STATA version 10. Data collected from the culling and compensation treatment block, which was never implemented, were combined with those from the control group.

Descriptive analyses were done to demonstrate trends of HPAI-compatible events and sudden death events in all the treatment groups over the study period, including the baseline phase of the project. A Generalized Linear and Latent Mixed Model (GLLAMM) with Poisson link function was used to conduct both unconditional relationships between the outcome and treatment. Multivariable analyses were also done. The number of HPAI-compatible events was used as the outcome, and the number of visits was used as an exposure (offset) variable. Independent factors considered for multivariable analysis included treatments and quarters. The district was used as a random-effect variable. A first-order interaction term between quarter and treatment was created and its significance was determined using a likelihood ratio test – however, this was found to be insignificant. The goodness of fit of the model was assessed using residual plots.

2.5. Comparison of PIA and PDSR data

The results from the data collected by the PIA teams regarding the impact of the vaccinations were compared with trends in the number of Anigen® rapid-tested confirmed outbreaks that were diagnosed by the PDSR teams using data from May 2008 – Sept 2009 in the PDSR database. The data included: date and location of surveillance visits; date and location of confirmed outbreaks; and the number of *desas* (villages) in each sub-district. Outbreaks are at the *desa* level in this database. Bar charts were used to examine the pattern of outbreak detection by treatment over time. To ensure that the observed trends were not biased by the number of villages per sub-district or by the number of PDSR visits per sub-district, alternate y variables were used in the graphs: the number of HPAI outbreaks; the number of HPAI outbreaks per PDSR visit; and the number of HPAI outbreaks per *desa* were each plotted. A multivariable model (mixed effects Poisson regression) using the PDSR data was constructed to assess the impact of vaccination. Data from May and June 2008 were excluded from the multivariable analysis because vaccination did not start until July 2008. The outcome variable was the number of observed outbreaks per sub-district per quarter, and the exposure variable was the number of *desas* in the sub-district. District and time were controlled for as possible confounders; district by the addition of a random effect and time as a fixed effect representing the quarter. The number of PDSR visits per quarter was also included in the model to control for confounding.

3. Results

The commonly kept poultry species, in decreasing order of abundance, were chickens, Muscovy ducks, songbirds, pigeons and ducks. The proportion of households that kept poultry ranged between 70.7-78.2%.

3.1. Distribution of sudden death events over time

A total of 4,007 visits were made during the study; these included 1,139 visits made in the baseline period (quarters 1 and 2). From these visits, 241 HPAI-compatible cases and 330 sudden death events were identified. The distribution of the number of HPAI-compatible events and sudden death events by treatment group and quarter are shown in Figures 3.1.4 and 3.1.5. These graphs show that the number of cases declined over time in all the treatment groups and that the number of cases observed in the vaccinated groups was consistently lower than in the control group.

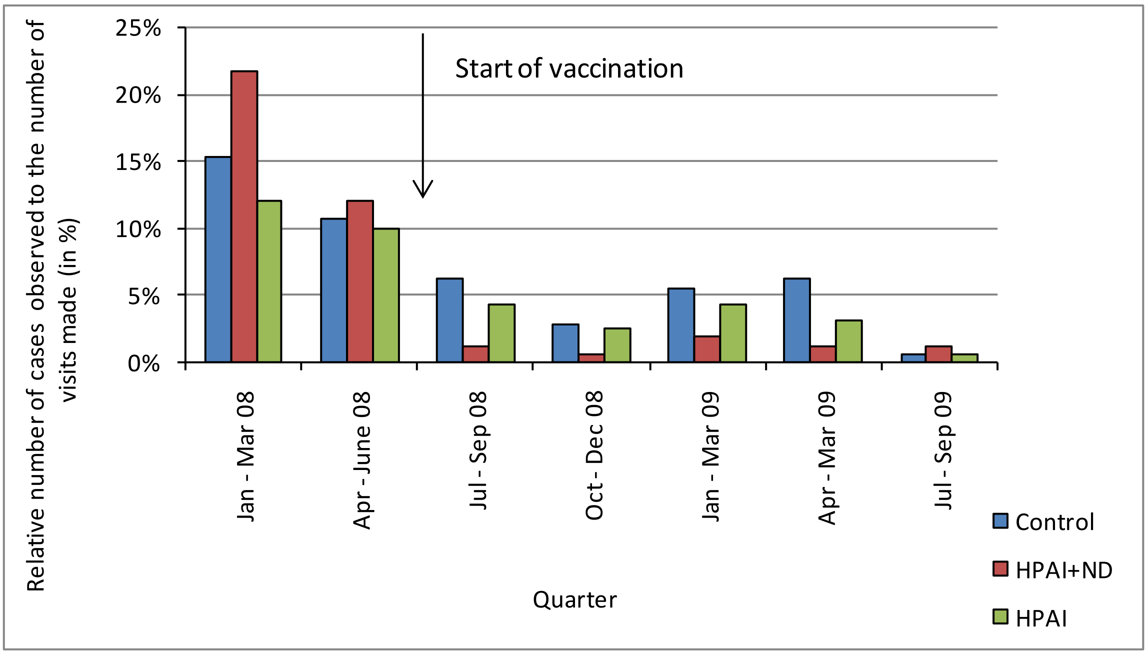

Figure 3.1.4: Distribution of HPAI-compatible events over study period (January 2008 – September 2009)

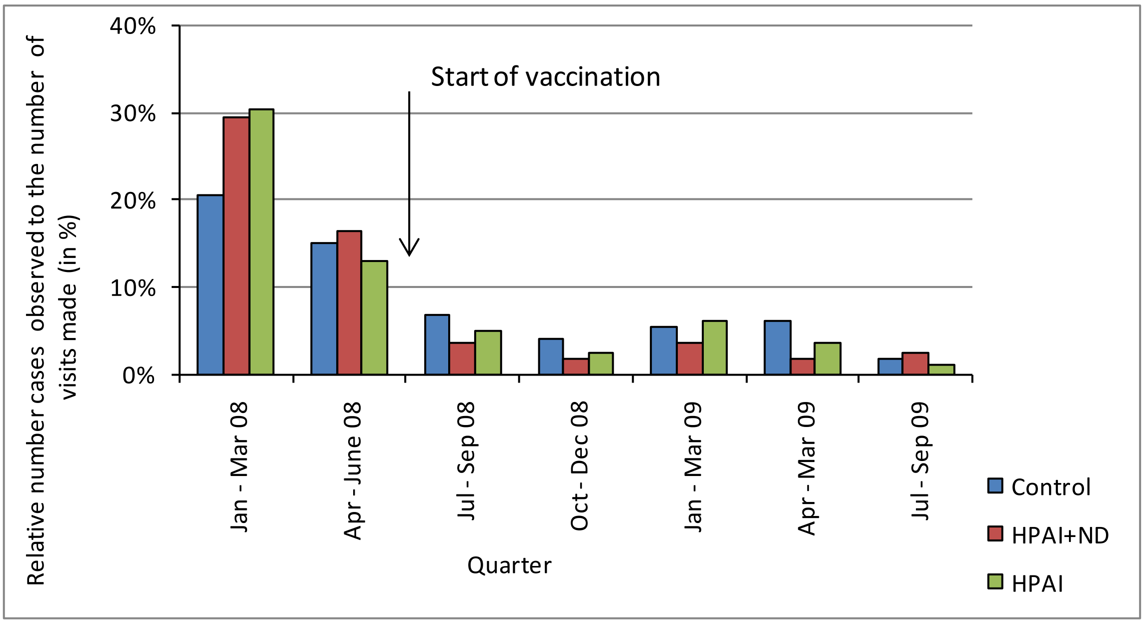

Figure 3.1.5: Distribution of sudden death events over study period (January 2008 – September 2009).

Table 3.1.1 gives mortality rates estimated for each of the three clinical outcomes (HPAI-compatible events, ND-related events, and unknown sudden death events) using relative incidence scoring. These estimates were not stratified by species.

Table 3.1.1: Mortality rate by clinical diagnosis estimated from relative incidence scoring (n = 279)

Clinical diagnosis	Mortality rate (%)
HPAI-compatible disease	53.8±25.9%
ND-compatible disease	31.42±25.3%
Unknown	56.7±29.3%

3.2. Crude incidence rate ratio

Table 3.1.2 shows crude incidence rate ratios for each treatment generated using GLAMM. This analysis excludes records from the baseline phase of the study.

Table 3.1.2: Unadjusted effect of the preventive mass vaccination programs against HPAI and both HPAI and Newcastle Disease in backyard and semi-commercial poultry farms on Java Island, Indonesia (July 2008 – September 2009)

Treatment	No. of records	No. of cases	IRR[a] (95% CI)	P value
HPAI	800	24	0.69 (0.19, 2.51)	0.57
HPAI + ND	800	10	0.30 (0.06, 1.40)	0.13
Control [b]	1268	57	1.00	

[a] **Incidence Rate Ratio;**
[b] **Control group combines both control and culling and compensation treatments**

3.3. Multivariable analysis

Table 3.1.3 gives adjusted incidence rate ratios estimated using a multivariable GLLAMM. This model identified quarter (used as a proxy for seasonal effects) and district (random effect) as being significant. The analysis suggests that vaccinating poultry against only HPAI would reduce the number of HPAI-compatible outbreaks by 23%, while vaccinating them against both HPAI and Newcastle Disease would reduce the number of HPAI-compatible events by 70%. There was no significant interaction between treatment and quarter (LR χ^2 test = 1.97, P = 0.78).

Table 3.1.3: Outputs from a Generalized Linear and Latent Mixed Model showing the effect of preventive mass vaccination programs against HPAI and both HPAI and Newcastle Disease in backyard and small-scale commercial farms in selected sites on Java Island, Indonesia (July 2008 – September 2009)

Log likelihood = -185.76

hpai	IRR	SE	z	P>|z|	[95% Conf. Interval]	
HPAI vac	0.77	0.27	-0.73	0.46	0.39	1.52
HPAI_ND vac	0.30	0.13	-2.79	0.01	0.13	0.70
Control	1.00					
Quarter_4	0.48	0.18	-2.24	0.03	0.26	0.91
Quarter_5	0.93	0.25	-0.27	0.79	0.55	1.57
Quarter_6	0.82	0.25	-0.65	0.52	0.44	1.51
Quarter_7	0.19	0.10	-3.07	0.00	0.07	0.55
Quarter_3	1.00					

Variances and covariances of random effects

***level 2 (assessment unit)
    var(1): 0.38 (0.29)
***level 3 (district)
    var(1): 0.71 (0.41)

Results of the residual analyses conducted to check the goodness of fit of the model are shown in Figure 3.1.6. Deviance residuals did not have any recognizable pattern and very few observations had extreme values (> 2). An assessment of Cooks distance residuals, however, showed that data collected from two districts (Kendal and Cirebon) had high leverage values. To assess whether these data might have influenced the magnitude of the estimates given in Table 3.1.3, the analysis was repeated with data from these districts excluded from the dataset. There was not any change in the parameter estimates, therefore the second model was not considered further.

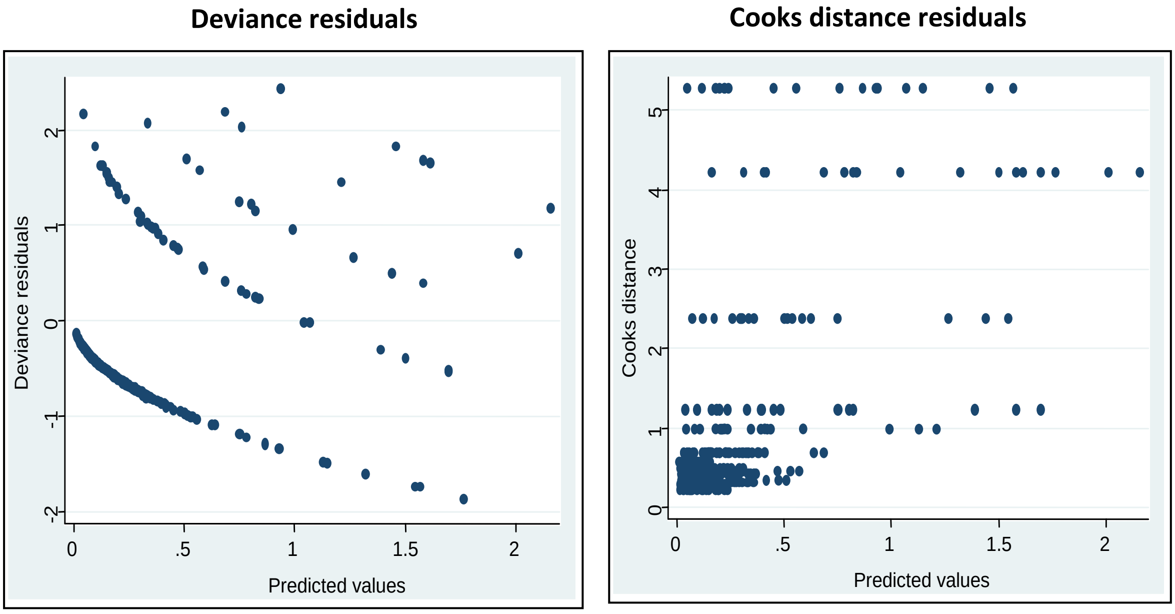

Figure 3.1.6: Deviance and Cooks distance residuals obtained from the GLLAMM plotted against predicted values

3.4. Triangulation with PDSR records

Distribution of PDSR cases by treatment group – During the time that vaccination was implemented, 246 outbreaks were detected by PDSR in the sub-districts included in the study; 121 of these were in the control areas, 69 (57% of control level) in the areas vaccinated against only HPAI and 56 (46% of control level) in areas with vaccination against both HPAI and ND. The overall patterns observed with respect to outbreaks detected over space and time did not change with alternate y-axis variables [number of outbreaks; number of outbreaks per visit; number of outbreaks per *desa* (data not shown)]. The number of outbreaks detected per visit varied over time, and was consistent with previous years in that the most outbreaks were observed between January and March (Figure 3.1.7).

As we have found with previous analyses using both PDSR and PIA data, the number and temporal pattern of HPAI outbreaks varied greatly between districts (Figure 3.1.8).

Multivariable analysis – The Poisson regression model showed that the incidence rate of HPAI detection by PDSR in the HPAI vaccination areas was 12% lower and in the HPAI plus ND vaccination area 24% lower than in the control areas. Because time (quarter), the number of PDSR visits and district were controlled for in the model, the difference between the vaccination and control groups is not due to these external (confounding) influences (Table 3.1.4). The observed differences were not statistically significant, however the probability that the lower incidence observed in the HPAI & ND vaccinated area was due to chance alone is only 9%.

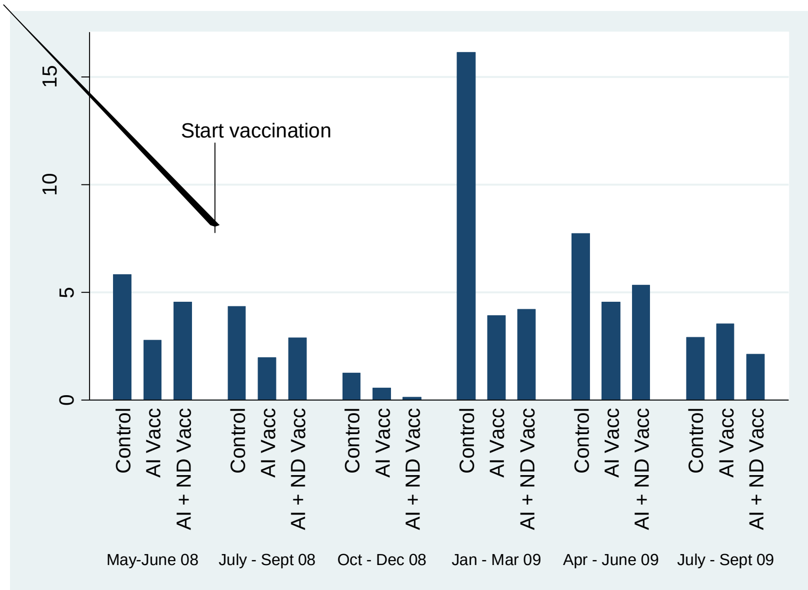

Figure 3.1.7: The number of outbreaks per visit detected by PDSR system in ORIHPAI vaccination and control areas

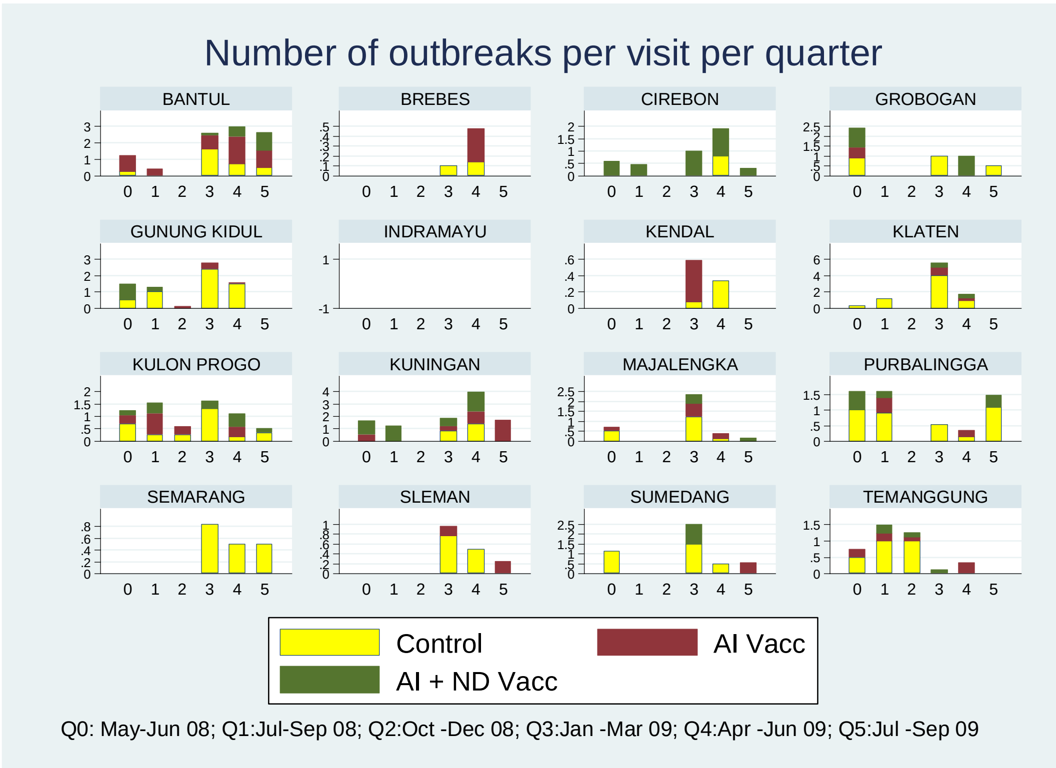

Figure 3.1.8: The number of outbreaks detected per visit in ORIHPAI vaccination and control areas, stratified by quarter (y-axis) and district (note that the y-axis is different in each graph)

Table 3.1.4: Regression model for the number of outbreaks per sub-district

Variable	IRR (95% CI)	SE	p
HPAI Vaccination	0.88[a] (0.64-1.22)	0.14	0.45
HPAI and ND Vaccination	0.76 (0.54-1.06)	0.13	0.11
Quarter 2[b] (Oct – Dec 08)	0.23 (0.11-0.51)	0.09	<0.001
Quarter 3 [b] (Jan – Mar 09)	2.26 (1.5-3.38)	0.47	<0.001
Quarter 4 [b] (Apr – June 09)	1.52 (1-2.33)	0.33	0.05
Quarter 5 [b] (July – Sept 09)	1.39 (0.86-2.24)	0.34	0.18
PDSR visit	1.21 (1.16-1.26)	0.02	<0.001

[a] Sub-districts with HPAI vaccination detected 0.88 times as many cases of HPAI compared to areas without any vaccination, controlling for district, time and number of PDSR visits.
[b] Quarter 1 (July – Sept 08) is the reference group
Model log likelihood = -374.8, n = 413. Random effect District was significant (sd = 0.78 (95% CI 0.50 – 1.24), SE = 0.18).

3.5. Number of birds vaccinated

On average, 2.9 million birds were vaccinated in each vaccination campaign. By the end of the study, more than 23 million doses of HPAI Legok vaccine had been administered.

Discussion

This study combined participatory epidemiological methods with a longitudinal study design and standard statistical modeling to evaluate the effectiveness of two vaccination regimes against HPAI. Participatory epidemiological methods were used to determine the incidence of HPAI-compatible events because it could have been difficult or expensive (e.g., PCR technique) to use standard screening tests for routine analysis of samples. Serology, for example, cannot be used for most cases of HPAI because a majority of exposed birds die quickly before they mount an antibody response. Diagnostic tests based on antigen or RNA detection can only be carried out on active outbreaks, and such tests would have required weekly visits to sampling sites. These tests should however be used for spot checks. We compared our results with data collected by PDSR teams that used the rapid Anigen® test for HPAI diagnosis (Azhar et al., 2010). These teams also submitted some of the samples for real-time PCR analyses based on type A matrix assay (Azhar et al., 2010). Treatments were not blinded from the researchers, surveillance teams, and poultry owners because this would have required significant additional operational costs to support the deployment of vaccination teams in all the treatment blocks, including the control units. Serology to monitor population antibody prevalence was carried out in three operational research districts and the results were in agreement with moderate vaccination success in terms of antibody production (Section 3.2). Overall, the analysis therefore followed the principle of "intention-to-treat" by which subjects are analyzed according to their initial treatment assignment (Dohoo et al., 2003; Peduzzi et al., 2002).

Baseline comparison of the treatment blocks (data not shown) indicated that treatment groups were appropriately matched. This suggests that the blocking and randomization design used was effective in controlling for confounding. Nevertheless, a multivariable GLLAMM was applied to investigate whether the effect of treatment varied with season. The adjusted effect of the combined AI and ND vaccination was significant (a decrease of 70%) but the effect of AI only vaccination was not. Combining the two vaccination treatments as one still produced a significant effect of 46% (P = 0.05). Similar results were obtained from a parallel study that evaluated the effective reproductive number of the disease (R_e). That study determined that the R_e between chickens in vaccinated areas was significantly lower than the reproductive number (R_o) in unvaccinated areas (see Section 4.4). The level of population immunity necessary to interrupt transmission between birds within a household flock is 63.8% according to the GSE, and 43.5% using the final fraction size calculation. To interrupt transmission between household flocks in an RT, population immunity of 51.7% is needed according to the GSE and 34.1% by the final fraction size method. A sero-monitoring survey performed in this project to determine the prevalence of antibodies to H5 and ND antigens in control and vaccinated treatment areas suggests that the vaccination coverage attained was moderate, with only 20-45% of poultry in vaccinated areas having titres $\geq \log_2 4$ to H5 after each round of vaccination, compared to only 2-3% in the control group (described in Section 3.2). The moderate levels of vaccination achieved, and the within-and between-flock basic reproductive numbers measured in the transmissibility study are consistent with the degree of the suppression of HPAI incidence measured by the PIA system.

The study was not designed to measure the impact of ND vaccination at the biological level and no ND-only vaccination group was included. The combined vaccination group was only included to see if the availability of ND vaccination would act as an incentive to increase participant uptake of vaccination. The serological survey did not indicate greater participation in the combined vaccination group than in the HPAI only group. Two probable explanations can be given for the greater impact of the combined (HPAI + ND) vaccination compared to the HPAI vaccination alone on the incidence of HPAI-compatible disease in the GLAMM results.

One is that there is a differential misclassification bias between the different treatment groups and potential biological interactions between the combined vaccines. Differential misclassification relates to an assumption that HPAI + ND vaccination was able to suppress both HPAI and VVND cases, as described by Nayak et al., (2009) and Veits et al. (2006). The number of VVND-compatible negative diagnoses was large (2847) in comparison to the number of positive diagnoses for HPAI-compatible disease (91) and VVND-compatible disease (26). This suggests that a negative VVND predictive value in the different treatment groups would be the critical parameter for assessing the impact of differential misclassification. Since HB1 ND vaccine was used, suppression of ND in adults cannot be merely assumed. In fact, vaccination with HB1 did not protect against the natural challenge that resulted from exposure to ND field viruses circulating in the communities during the vaccine trials (Section 4.3). However, if a change in ND prevalence between the groups did occur, it would have led to differences in the predictive value of diagnostic procedures in the different groups, which could have lead to bias. The unknown sensitivity and specificity of the process does not allow us to determine if these considerations affected the outcome.

A second explanation is based on the consideration that the practice of simultaneous vaccination has been observed to give rise to interactions that can either potentiate or interfere with immune responses. For example, Pollard (1982) has observed that a simultaneous administration of live and inactivated oil-based ND vaccines can yield a substantially greater immune response relative to live vaccine alone. There is, however, no evidence to suggest that the same effect can be obtained by using HPAI and ND vaccines concurrently. Overall, there is no evidence to choose between the two possible explanations for the larger reduction in incidence observed in the combined vaccination group as the study was not designed to test the biological impact of ND vaccination. Given the potential significance of either positive or negative immunological impact of simultaneous vaccination with live HPAI and ND vaccines for control programs, these interactions should be explored in laboratory challenge trials.

PDSR data obtained from the study areas indicated a similar distribution of HPAI cases to that indicated by the PIA data. The systems had different objectives and close congruence in terms of the magnitude of effects was not expected. The PIA system was intended to measure the incidence of sudden death events in poultry, and thus designed such that a constant proportion of all HPAI-compatible events that occurred in the participating RTs (assessment units) over time should be captured in the data. These RTs were randomly selected and visited at regular intervals, so results from them can be reliably extrapolated to measure the incidence of HPAI-compatible events in the treatment areas. In contrast to PIA, the PDSR system was not intended to measure incidence, but rather is designed as a case-detection system using a purposive or risk-based sampling approach. Data collection visits were not regularly timed. The PDSR system balanced available resources between the needs of disease monitoring and outbreak response. Therefore, it did not systematically capture HPAI events within a defined area, but instead employed a risk-based approach to surveillance in which PDSR officers visited areas they believed they would most likely find HPAI, often because they have received a farmer report of an outbreak. They then focused on active, rapid test-confirmed cases where a response could be mounted subject to available resources. As such, the measurement of HPAI incidence using PDSR data was biased because the system was not designed to make representative estimates.

The results from this study support previous findings that show that H5 vaccine can interrupt H5N1 transmission in the field, especially if other measures such as enhanced bio-security are used at the same time (Ellis et al., 2004). AI vaccines will continue to play an important role in H5N1 control, although vaccination against H5N1 virus in the face of an outbreak can promote asymptomatic circulation of the virus if not administered properly.

Conclusions

The PIA impact assessment results indicate that the amount of HPAI vaccination carried out was sufficient to significantly reduce the incidence of HPAI-compatible events in mixed populations of small-scale commercial and backyard poultry. The results of the transmissibility study, the analysis of the PDSR data, and the serological results are all consistent with this finding and validate the PIA methodology.

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3.2. Serological monitoring of the mass vaccination campaigns

Abstract

Sero-monitoring was conducted to assess the proportion of the poultry population that had sero-converted following vaccination under the ORI HPAI project. Sampling was between 3 weeks and 2 months after each round of vaccination conducted in 3 randomly selected districts (out of 16 districts that participated in the project). The target population included both vaccinated and unvaccinated birds. Four rounds of sample collection were completed (one after each round of vaccination) with more than 6400 samples collected during each round. The proportion of the population with a positive titre to HPAI and ND over the entire study was significantly higher in the areas that received mass vaccinations compared to the control areas. In the mass vaccination areas, 20-45% of poultry sampled had titres $\geq \log_2 4$ to H5 after each round of vaccination, compared to only 2-3% in the control group. In the HPAI + ND vaccination group, the proportion of the population over the entire study period with ND titres $\geq \log_2 4$ ranged from 12-25%. Several factors likely impeded the achievement of a higher level of sero-conversion, including 1) poultry population factors (turnover rate, reduced immune-competence, waning antibody levels prior to sampling); 2) vaccine factors (low potency, including because of breaks in the cold chain); and 3) factors related to application (proportion of population vaccinated and the use of poor techniques). In the case of ND, additional factors to consider are that 1) the ND vaccine used was a modified live vaccine, which is more sensitive to breaks in the cold chain than the inactivated vaccine used for HPAI vaccination, and 2) the HB1 vaccine strain is generally not recommended as an effective immunogen for the vaccination of poultry older than two weeks. Assuming the levels of antibody thresholds used were consistent with protection, the serology results were consistent with the suppression of disease observed in the longitudinal study to measure the impact of vaccination on disease.

1. Introduction

It is critical to monitor the coverage obtained by vaccination in order to assess its efficacy and guide policy (Alders, Bagnol and Young et al., 2007). To some extent, this may be done using records (the number of birds vaccinated divided by the census numbers of poultry), however the usefulness of this method is limited because of the inaccuracy associated with census data and also because not all birds vaccinated will mount a serological response. Therefore, sero-monitoring was performed to determine the prevalence of antibodies to H5 and ND virus in control and vaccinated treatment areas. By comparing the response to vaccination (the sero-conversion level) with the incidence of HPAI in an area, it is possible to assess the level of protection that the level of sero-conversion provides.

2. Methods

This activity was undertaken in collaboration with FAO, the MoA CMU and Wates DIC, and the Indonesia-Dutch Partnership program on HPAI Control (Wageningen University). Additionally, the Australian Animal Health Laboratory had laboratory-strengthening missions to Wates DIC laboratory while our project was operating to ensure that the results obtained were reliable.

In order to maximize financial efficiency, sero-monitoring was done in 3 of the 16 districts, which were selected randomly on the basis of one per province. Sampling protocols were developed to obtain a representative sample under field conditions. Poultry were sampled randomly *irrespective of vaccination status*, such that the population levels of sero-conversion following vaccination could be determined. These protocols should be useful for future post-vaccination sero-monitoring campaigns in Indonesia.

Four rounds of sample collection were completed (one after each round of vaccination) with more than 6400 samples collected during each round. In each round, 6 villages per district were randomly selected, and 130 samples collected from each village. In each village, approximately 100 chickens and 30 ducks were sampled, which reflects the average ratio of the chicken:duck population. As villages can be very large in Indonesia, at least three sub-villages were visited in each village to ensure wide geographical representation of samples. Villages were randomly selected from a list of all villages in the treatment areas. Because no sampling frame of poultry-owning households was available, a transect walk was conducted within each sub-village, and a maximum of 5 poultry were sampled from every third household. Sampling continued until 20-25 samples were collected from each sub-village.

To ensure a high level of quality and consistency between districts, refresher training courses reviewing the sampling protocol were held before the second and fourth rounds of sample collection, and field-monitoring visits were undertaken in each district during the third round of sample collection. The trainings were organized by ILRI and FAO, and FAO staff performed field visits.

Following collection, all samples were processed by the relevant provincial laboratory and then sent to Wates DIC for analysis. Haemagglutination inhibition (HI) tests were used to measure antibody titres for H5 and ND. Antigens used in the HI tests were produced by Pusvetma, Surabaya. An antigen from a virus isolate from Kediri district, East Java was used to perform the H5 HI test. Antigen from the ICHII ND strain was used in the ND test. Both HI tests were performed as outlined by the OIE (Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2010 World Organisation for Animal Health: 2009). Results were entered into a Microsoft Access database that was specially created for this activity. Two Wates DIC staff members received training in the use of Access for data input and basic analyses.

Log_2 4 was considered the cut-off for a positive titre for H5 and ND, both in our analysis and by the OIE. The level of protection associated with a particular titre depends on the nature of the circulating field strain(s) and how well it "matches" the vaccine strain. A "positive" titre, therefore, does not imply that vaccinated birds with that titre will always be protected, or that birds with lower titres will always be susceptible.

Most results were analyzed at the individual bird level. However, In order to assess the efficacy of the vaccine to reduce transmission of HPAI, the H5 sero-conversion results were also analyzed at the household and neighborhood (RT) levels. Results from the transmissibility study GSE SIR model suggest that 63.8% of birds in household flocks need to be immune to H5N1 to interrupt transmission, and 49.7% of household flocks in a neighborhood, in areas where no vaccination has taken place in the past year. These values were used to set the cut-offs in the analysis (65% of birds "immune" for within-flock transmission and 50% of households "immune" for between-flock transmission).

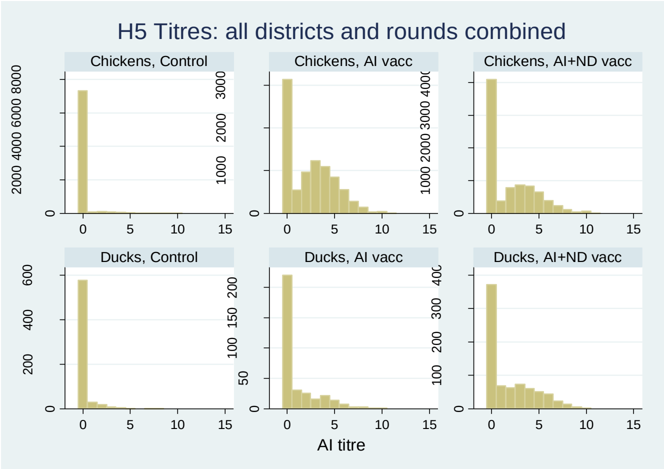
3. Results

The timing of sample collection following vaccination was variable due to logistical issues. Serum samples were collected two months following the first round of mass vaccination, three weeks following the second and third rounds and one month after the fourth round.

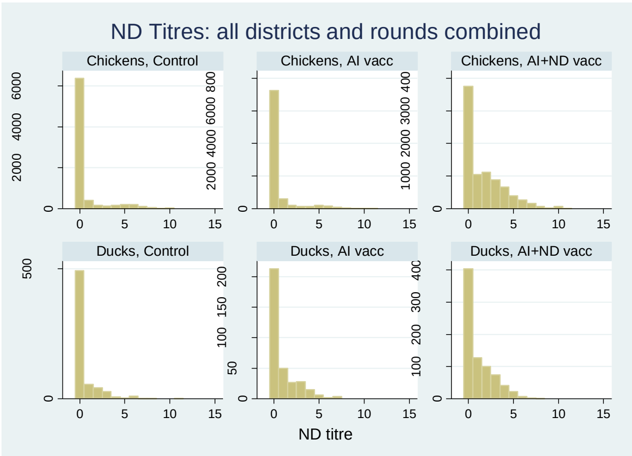
H5 and ND Titres – The proportion of the population with a positive titre to HPAI and ND over the entire study was significantly higher in the areas that received mass vaccination compared to the control areas. In the mass vaccination areas, 20-45% of poultry sampled had titres $\geq \log_2 4$ to H5 after each round of vaccination, compared to only 2-3% in the control group (Table 3.2.1).

Overall, fewer birds had positive titres to ND compared to H5. In the HPAI + ND vaccination group, the proportion of the population over the entire study period with ND titres $\geq \log_2 4$ was quite low (12-25 %) (Table 3.2.1). More birds had ND titres in the HPAI and ND vaccination group compared to the other groups (Figure 3.2.1). However, substantial numbers of birds in the areas not receiving any

ND vaccination (control and HPAI vaccination groups) also had ND titres. Of the poultry that had a titre > 0, the mean titre for both H5 and ND was between 2-3 in all groups (Figure 3.2.1).



(a)



(b)

Figure 3.2.1: Histogram of $\log_2 X$ (a) H5 titres and (b) ND titres in each treatment group over the entire study period (Note that the y-axis is different in each graph)

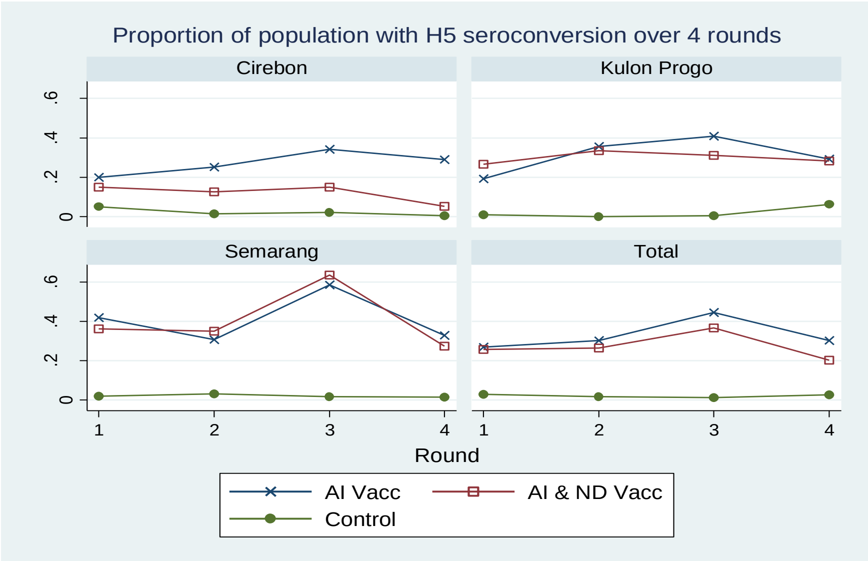
Table 3.2.1: The percentages of chickens and ducks with titres above $\log_2 4$ against H5 and ND following each round of mass vaccination

		Number sampled		Percent with HPAI titre $\geq \log_2 4$ (95% CI)			Percent with ND titre $\geq \log_2 4$ (95% CI)		
Treatment	**Round**	**Chicken**	**Duck**	**Chicken**	**Duck**	**Overall**	**Chicken**	**Duck**	**Overall**
Control	1	1753 (1747 for ND)	161	2.9 (2.2 - 3.8)	4.3 (1.7 - 8.6)	3 (2.3 - 3.9)	10.5 (9.1 - 12)	11 (6.6 - 16.8)	10.5 (9.2 - 12)
	2	1903	69	2 (1.5 - 2.8)	0 (0 - 5.2)	2 (1.4 - 2.7)	13.4 (11.9 - 15)	7.2 (2.4 - 16.1)	13.2 (11.7 - 14.7)
	3	2096	110	1.3 (0.9 – 1.9)	1.8 (0.2 – 6.4)	1.4 (0.9 – 1.9)	5.3 (4.4 – 6.3)	0.1 (0.0 – 5.0)	5.1 (4.2 – 6.1)
	4	2043	304	3.0 (2.3 – 3.9)	0.3 (0.01 – 1.8)	2.7 (2.1 – 3.4)	9.9 (8.6 - 11.2)	1.3 (0.3 - 3.3)	8.7 (7.7 - 10.0)
	Overall	**7795 (7789 for ND)**	**644**	**2.2 (1.9 - 2.6)**	**1.2 (0.5 - 2.4)**	**2.1 (1.8 – 2.5)**	**9.5 (8.9 – 10.2)**	**4.0 (2.7 – 5.9)**	**9.1 (8.5 – 9.7)**
AI vaccination	1	2026	164	28.1 (26.1 - 30.1)	13.3 (8.5 - 19.5)	27 (25.1 - 28.9)	8.5 (7.3 - 9.8)	7.3 (3.8 - 12.4)	8.4 (7.3 - 9.6)
	2	2169	139	31.4 (29.5 - 33.4)	14.4 (9 - 21.3)	30.4 (28.5 - 32.3)	7.2 (6.2 - 8.4)	7.9 (4 - 13.7)	7.3 (6.2 - 8.4)
	3	2323	35	44.9 (42.8 – 46.9)	22.9 (10.4 – 40.1)	44.5 (42.5 – 46.6)	6.5 (5.5 – 7.6)	11.4 (3.2 – 26.7)	6.6 (5.6 – 7.6)
	4	2364	7	30.2 (28.4 – 32.1)	28.6 (3.7 – 71.0)	30.2 (28.4 – 32.1)	7.7 (6.7 - 8.9)	0.0 (0.0 - 41.0)	7.7 (6.7 - 8.8)
	Overall	**8882**	**345**	**33.8 (32.8 - 34.8)**	**15.1 (11.5 - 19.3)**	**33.1 (32.2 – 34.1)**	**7.4 (6.9 – 8.0)**	**7.8 (5.2 – 11.2)**	**7.4 (6.9 – 8.0)**

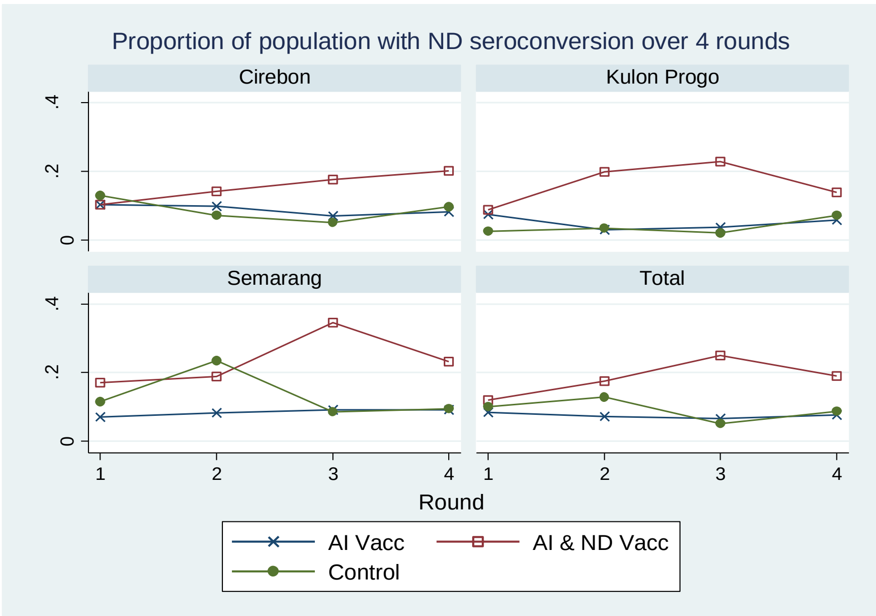
Table 3.2.1 (continued)

		Number sampled		Percent with HPAI titre $\geq \log_2 4$ (95% CI)			Percent with ND titre $\geq \log_2 4$ (95% CI)		
Treatment	Round	Chicken	Duck	Chicken	Duck	Overall	Chicken	Duck	Overall
AI and ND vaccination	1	1998 (1997 for ND)	301	26.2 (24.3 - 28.2)	22.9 (18.3 - 28.1)	25.8 (24 - 27.6)	12.7 (11.2 - 14.2)	8.6 (5.7 - 12.4)	12.1 (10.8 - 13.5)
	2	2011	221	25.6 (23.7 - 27.6)	36.9 (30.6 - 43.7)	26.7 (24.9 - 28.6)	18.3 (16.6 - 20)	12.6 (8.5 - 17.7)	17.7 (16.1 - 19.3)
	3	2204	150	36.9 (34.9 – 39.0)	32.0 (24.6 – 40.1)	36.6 (34.7 – 38.6)	26.0 (24.1 – 27.8)	12.0 (7.3 – 18.3)	25.1 (23.3 – 26.9)
	4	2233	109	21.0 (19.3 – 22.8)	4.6 (1.5 – 10.4)	20.2 (18.6 – 21.9)	19.9 (18.2 - 21.6)	2.7 (0.6 - 7.8)	19.1 (17.5 - 20.7)
	Overall	**8846 (8845 for ND)**	**781**	**27.4 (26.5 - 28.4)**	**26 (22.9 - 29.2)**	**27.3 (26.4 – 28.2)**	**19.3 (18.5 – 20.2)**	**9.5 (7.5 – 11.7)**	**18.5 (17.7 – 19.3)**

Figure 3.2.2 shows the proportion of the population with positive H5 and ND antibody titres in each district over time. It is evident that there are differences between the districts, which probably reflect variable implementation of the vaccination program in each district. The accuracy of the initial population estimates would also impact the vaccination coverage attained. In areas where the target population was underestimated, the vaccination coverage will be low because insufficient resources (vaccine and vaccinators) would have been allocated to that area.



(a)



(b)

Figure 3.2.2: Percentage of poultry with positive (a) H5 and (b) ND titres (> $\log_2$ 4) by district and overall, over the four rounds of sero-monitoring

Table 3.2.2 shows that a greater proportion of the adult bird population had positive H5 and ND titres compared to the proportion of the population with positive titres in young birds. This is probably because many of the young birds sampled were not vaccinated, as they were too small or not even born yet. Because the population turnover rate is very high, the young bird population represents approximately 50% of village chickens at any one time (see Community Trial results).

Table 3.2.2: Percentage of poultry in each treatment group with positive H5 and ND titres (> $\log_2$ 4), stratified by adult and young birds over the entire study period

	Percent of population with positive titre (95% CI)			
Treatment group	**H5**		**ND**	
	Young	**Adult**	**Young**	**Adult**
Control	1.02 (0.64-1.4)	2.41 (1.95-2.87)	5.48 (4.61-6.35)	10.18 (9.28-11.08)
AI Vaccine	22.97 (21.36-24.58)	39.17 (37.83-40.51)	2.98 (2.33-3.63)	9.35 (8.55-10.15)
AI & ND Vaccine	19.5 (17.93-21.06)	31.6 (30.34-32.86)	12.48 (11.18-13.79)	22.74 (21.6-23.88)

Table 3.2.3 shows results of the analysis at the household and neighborhood (RT) levels. Using the estimates of coverage needed to block transmission from the transmissibility study (see Section 4.4), in areas with HPAI vaccination, 8-30% of household flocks had sufficient levels of sero-conversion in individual chickens to interrupt *within-flock* viral transmission. Considering viral transmission *between* flocks, 4-25% of neighborhoods had a sufficient number of successfully immunized flocks to block viral transmission in each round.

Table 3.2.3: Percentage of sampled households and neighborhoods where the sero-conversion level is sufficient to interrupt HPAI transmission, by treatment group

		"Immune" Households (where >=65% poultry have H5 titre>$\log_2$ 4)			"Immune" Neighborhoods (where >=50% households "immune")		
Treatment group	**Round**	**No. Sampled**	**No.**	**% (95% CI)**	**No. Sampled**	**No.**	**% (95% CI)**
Control	1	338	1	0.30 (0.01-1.64)	59	0	0.00 (0-6.06)
	2	418	1	0.24 (0.01-1.32)	60	0	0.00 (0-5.96)
	3	501	1	0.20 (0.01 – 1.11)	91	0	0.00 (0-3.97)
	4	557	10	1.80 (0.86- 3.28)	78	3	3.85 (0.80-10.83)
HPAI	1	329	25	7.60 (4.98-11.01)	73	3	4.11 (0.86-11.54)
	2	473	85	17.97 (14.61-21.73)	105	22	20.95 (13.62-29.99)
	3	502	148	29.48 (25.52-33.68)	99	24	24.24 (16.19-33.89)
	4	562	97	17.26 (14.25-20.64)	110	15	13.64 (7.84-21.49)
HPAI & ND	1	356	44	12.36 (9.12-16.24)	65	11	16.92 (8.76-28.27)
	2	429	68	15.85 (12.52-19.66)	79	12	15.19 (8.10-25.03)
	3	531	142	26.74 (23.02-30.72)	102	26	25.49 (17.38-35.08)
	4	497	41	8.25 (5.98-11.02)	86	6	6.98 (2.60-14.57)

Discussion

It is extremely rare for chickens to survive natural infection with H5N1, therefore the low level of sero-conversion that was observed in the control group was likely due to vaccination – by owners, birds vaccinated under the OR project and then moved into the control area, or birds vaccinated by *Dinas* but not as part of ORIHPAI) – rare birds that survived naturally, or false positive laboratory results. Substantial numbers of birds in the areas not receiving any ND vaccination (control and HPAI vaccination groups) also had ND titres. This reflects the fact that ND is often not fatal and so birds will recover from natural infection. As with H5, some of these titres might also be due to vaccination outside of the OR project, movement of birds from areas with vaccination, or represent false positive results.

Although the proportion of the population with antibodies was higher in vaccination areas than in control areas, sero-prevalence rates in vaccinated areas were moderate (25-45% of the sampled population for H5, 12-25% for ND). Probable contributing factors were:

- A low proportion of the population was vaccinated, in part due to underestimation of the population size in treatment blocks;
- Improper vaccine storage and transport and/or poor vaccination technique;
- Poor response to vaccination due to reduced immune-competence of backyard poultry;
- A high population turnover rate, resulting in a high proportion of the population at the time of sero-monitoring being sero-negative; and
- Waning antibody levels in the interval between vaccination and sample collection for serology. This would be particularly important if the birds did not receive a booster vaccine.

In the case of ND, additional factors to consider are:

- The ND vaccine used was a modified live vaccine, which is more sensitive to breaks in the cold chain than the inactivated vaccine used for HPAI vaccination; and
- The vaccine strain selected by stakeholders (HB1) is generally not recommended as an effective immunogen for the vaccination of poultry older than two weeks.

The vaccination coverage is comparable to that reported for HPAI in Vietnam in 2006 (Taylor and Dung, 2007), in which it was estimated that 44% of the chicken population was immunized. Because the sampling strategy was different in Vietnam (only vaccinated poultry were sampled for sero-monitoring, rather than random sampling of the entire population), this coverage was based on the census data and may be an overestimation.

The proportion of the population with antibody levels $\geq \log_2 4$ varies significantly between the sampled districts for both H5 and ND. This suggests varying levels of implementation quality were achieved in the vaccination campaign in different districts. Cirebon district consistently had lower antibody levels compared to Semarang and Kulon Progo districts. Alternately, it is possible that the target population was underestimated more in Cirebon than in the other districts.

Comparison of results from different rounds must be done with care because the samples were collected at different times following each round of vaccination and therefore the effects of population turnover and waning immunity was not constant between rounds. We cannot conclude that immunity to HPAI or ND increased over successive rounds of vaccination. This was probably primarily because of the high population turnover rates, but could also reflect the fact that immunity in individual birds wanes over time. These two factors dictate the need for frequent revaccination to maintain high population immunity. However, a recent modeling study demonstrated that vaccination of 100% of the population every 4 months was insufficient to achieve immunity levels greater than 30% due to natural flock population turnover rates (Lesnoff et al., 2009).

The relatively consistent vaccination coverage obtained over time indicates that the communities continued to participate and present their birds for vaccination over the year that the project was operational.

Levels of sero-conversion were consistently higher in adults than young birds (Table 3.2.3). This is to be expected, because many of the young birds sampled would not have been present at the time of vaccination. It is also possible that adult birds had a better response to vaccination compared to younger birds.

No consistent difference was observed between chickens and ducks in the percentage of the population with H5 positive titres (Table 3.2.1). For ND, however, the proportion of the population with positive titres was consistently higher in the chicken compared to the duck population. This difference was often, but not always, statistically significant. Because the owners of ducks were generally less willing to allow samples to be collected, field teams were often unable to collect sufficient samples to allow for an accurate estimation of the sero-conversion level.

There is no evidence that H5 titres were higher in areas receiving both HPAI and ND vaccination. In fact, the percentage of birds with a positive titre is consistently lower in the group vaccinated against both HPAI and ND compared to that vaccinated only against HPAI. This suggests that offering ND vaccination may not improve community participation in an HPAI vaccination campaign.

Based on results from the transmissibility study (see Section 4.4) we estimated that with this level of sero-conversion, within-flock transmission would be interrupted in up to 30% of flocks, and between-flock transmission in up to 25% of neighborhoods (Table 3.2.3), with variation between rounds. This result depends on the assumption that poultry with a titre greater than $\log_2 4$ can neither be infected nor transmit HPAI. Due to a “herd immunity” effect, it is reasonable to assume that the actual decrease in incidence could be greater than the proportion of “immune” flocks because of decreased exposure or challenge in the area. These findings are broadly consistent with the decrease in incidence observed by the PIA observed in the vaccination treatment groups.

Conclusion

Sero-monitoring demonstrated that the extensive vaccination campaigns yielded moderate levels of sero-conversion (25-45% of the sampled population for H5, 12-25% for ND). The level of H5 sero-conversion varied by district and the age of the bird that was sampled, but not by species (i.e., ducks versus chickens). Assuming that a positive titre equates with protection against HPAI infection, the sero-conversion rate was such that HPAI transmission 25% of neighborhoods would be immune to outbreaks.

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3.3. An evaluation of cost-effectiveness of HPAI mass vaccination in Indonesia

Abstract

At the request of program stakeholders, two publically funded mass vaccination programs were evaluated by our operational research (OR) for more effective HPAI control measures. The activity was implemented under the overall leadership of the Ministry of Agriculture, with the Food and Agriculture Organization (FAO) principally responsible for the design and implementation of the vaccination activities and ILRI focused on measuring the impact and economic effectiveness of mitigation options. Poultry raisers in 16 OR districts participated in the study. Based on one year of program implementation, the vaccine delivery models were estimated to cost about US$ 2.9 million, or about US$ 0.12 per shot per bird based on the estimated number of birds vaccinated during four campaign periods. The international cost of managing the vaccination treatment groups tested was estimated at US$ 0.5 million in one year, representing some 17% of the total cost of the program.

The mass vaccination models evaluated will not be sustainable as largely publicly supported programs using donor funds. In terms of cost effectiveness, a 1% reduction in HPAI-compatible outbreaks within the study area was achieved at a cost of about US$ 59,000 under the AI-only vaccination option; this cost is reduced to about US$ 22,000 under the AI + ND vaccination option. The AI + ND option was more effective because it appears to have lowered the incidence of HPAI-compatible events, considerably more so than HPAI-only vaccination (see Section 3.1). Alternatively, the cost per bird saved in HPAI-compatible events through AI-only vaccination is US$ 22.00, while only costing US$ 8.00 per bird using the AI + ND vaccination option.

The results therefore indicate that, under the OR vaccination program, the cost of saving one bird is much higher than its average (potential) market value. Although vaccination was moderately successful at suppressing disease incidence, the cost relative to market value of the birds suggests that it will be difficult to establish incentive systems to drive mass vaccination on a wide scale. Since the vaccination models tested in the OR were a 100% publicly provided program, it would make sense to explore possible cost-sharing scenarios with poultry owners to enhance the sustainability of programs. Based on the estimated cost of US$ 0.12 per shot and a primary and booster dose vaccination regimen, an annual program of quarterly mass vaccination that covers all of Indonesia's 300 million backyard poultry would cost US$ 288 million. Clearly, strategies for targeting vaccination to high impact control points are needed. Continued support in the institutional capacity building aspects of vaccine delivery will likely be an optimal use of public funds.

1. Introduction

Bird flu caused by HPAI (Highly Pathogenic Avian Influenza) virus was first reported in Indonesia in 2004, and is currently endemic in several provinces. The persistence of the disease presents a risk for both the poultry sector and local communities where poultry raising has always been part of the way of life of Indonesians. As a zoonotic disease, not only does it pose a threat to poultry as a source of livelihoods, but more importantly to public health as it occasionally causes human deaths and has the potential to evolve into a pandemic agent. Recognizing this, significant investments both by the international donor community and the Government of Indonesia have been made to suppress the disease through various control options.

One of the initiatives implemented to improve HPAI control in Indonesia is the ORI-HPAI Project that is the focus of this report. Supported by USAID and the World Bank, the Project was led by the Government of Indonesia and implemented with assistance from FAO and John Snow International (JSI), a consultant, in the implementation of the cold chain component of the program. The Project assessed the impact, feasibility and sustainability of HPAI control strategies that were nominated by the Government of Indonesia and the UN/FAO, and which made use of a longitudinal study design.

The main objective of the ORI-HPAI Project was to evaluate the feasibility and impact of the implementation of alternative control strategies for HPAI in Indonesia. It included a retrospective analysis of PDSR data, evaluation of HPAI mitigation measures, and targeted studies to answer specific epidemiological questions about HPAI. The key features of the longitudinal study to evaluate control options under the Project included: the participation of 16 districts as implementation sites; target populations of 1.6 million poultry for quarterly AI vaccinations and another 1.6 million poultry for quarterly vaccinations using AI + ND vaccines; and significant management inputs from international and national technical experts to design and implement the Project, as well as develop institutional capacity for vaccine delivery.

A cost-effectiveness evaluation of the Project is important for providing guidance in identifying appropriate and cost-effective interventions to policymakers, guidance on how existing resources could be reallocated to support these, and identifying the need for new resources.

This study focuses on the cost-effectiveness analysis (CEA) of vaccination to control HPAI as added treatment options to ongoing PDSR activities in the OR project districts. The main objective of the cost-effectiveness analysis was to evaluate cost-effective AI control strategies that can be implemented in Indonesia. The main hypothesis being tested is that AI vaccination is a cost-effective control strategy in reducing the incidence of HPAI-compatible events or outbreaks. In this case, vaccination as a treatment option is evaluated for cost effectiveness vis-à-vis the baseline control option, which in this case is PDSR (Participatory Disease Surveillance Research) only, i.e., no vaccination. Given the public health threat associated with HPAI, it was not considered ethical to have a control population where no action was taken. CEA estimates the cost to generate an expected result or outcome. Since CEA is based on estimating the impact of an intervention in relation to its objective, e.g., reduced outbreaks or averted mortalities, it provides easily understood findings that can inform the development of an effective HPAI control program.

2. Materials and Methods

2.1. Study design

The CEA is based on the analysis of the cost of vaccine delivery in the OR treatment groups relative to the outcomes achieved from the treatments used. Our study involved collection of cost data pertaining to the vaccination campaigns being implemented under the OR-HPAI project. Such costs include: the cost of the vaccine; the infrastructure and logistics required for its delivery to the intended treatment groups; and the cost of manpower required to deliver the vaccine, including costs associated with building the manpower capacity to implement these tasks. Costs of participation or compliance were not considered. Two types of outcomes were considered at the start of the study: 1) reduced incidence of reported outbreaks, and 2) reduced mortality of birds. These outcomes were based on information obtained from the monitoring reports of PIA field officers at the OR project sites.

2.2. Data and methodology

Cost of vaccination – Data on the cost of vaccine delivery were provided by FAO; the information available pertains to three vaccination campaigns only, and information pertaining to a fourth vaccination campaign was not available. Hence, to arrive at the cost of the program for four campaign periods, the costs of the fourth campaign were projected based on the average number of birds vaccinated during the third period. The cost items collected and analyzed to date were classified into the following categories: vaccine cost (the direct cost of the vaccine); vaccinator cost (the incentive payments to the vaccinators based on the actual number of birds vaccinated, covering the first and second vaccination periods); variable costs (recurrent costs for vaccine delivery including supplies and transportation); fixed investment cost (the cost of cold chain equipment and infrastructure put in place to support the effective delivery of the vaccine to the target project sites); training costs (the cost of training of vaccinators and other manpower required to build local capacity for vaccine delivery); and sero-monitoring costs (costs of serum sample collection and analysis for assessment of the response to the vaccine of the bird population in each treatment group relative to the control). Using the available cost information and the reported number of birds vaccinated per district, the average cost of injection per bird was computed (i.e., the cost per shot).

Cost-effectiveness analysis – Cost effectiveness analysis is an economic analysis tool that compares relative costs and effects of two or more treatments. In its most common form, CEA compares the outcomes of new treatment groups with a control group, producing a cost-effectiveness indicator (CEI). This is typically defined as the ratio of the change in costs to the change in effect associated with a treatment. That is:

$$CEI = \frac{\text{Cost}_{\text{new treatment}} - \text{Cost}_{\text{current treatment}}}{\text{Effect}_{\text{new treatment}} - \text{Effect}_{\text{current treatment}}}$$

A detailed discussion of cost-effectiveness analysis is given in Gold et al. (1996).

The method has been extensively used in various fields to measure the impacts of an intervention with respect to its cost [see Tiongco (2008) and Civic Consulting-Agra CEAS Consulting (2007) for a review of methodologies to evaluate costs and benefits of HPAI control measures]. In veterinary research, the method is widely applied to measuring the impacts of treatments to prevent or control diseases, including that of vaccination and other preventive actions. This is of paramount importance to highlight whether a treatment is worth implementing, i.e., whether its benefits outweigh its costs. For example, Hannon et al. (2009) compared the cost effectiveness of a new combination product against two commercially available products for the treatment of undifferentiated fever in beef calves that received long-acting oxytetracycline when arriving at the feedlot. They showed that it was more effective to use the new product. Similarly, Martinez-Lopez et al. (2009) examined the cost effectiveness of measures to prevent Aujeszky disease virus (ADV) through breeding and fattening pigs in Spain. They indicated that testing pigs on fattening farms 15 days prior to shipment could reduce the probability of introducing ADV-infected animals by 91%, with no additional cost. Nahamya et al. (2006) investigated the cost effectiveness of vaccination against Newcastle Disease in free-range poultry in Uganda and found marked benefits from the vaccination program.

Given the recent outbreaks and damage caused by HPAI, some studies have focused on exploring cost-effective detection and control measures. Knight-Jones et al. (2010) assessed the cost effectiveness of various methods of wild bird surveillance for detecting HPAI. They used the ratio of mean monthly cost to the mean monthly probability of detection as the CEI, and showed that if HPAI-H5N1 was present at 1% prevalence and assuming HPAI resulted in bird mortality, sampling dead birds found by the public and sentinel surveillance were the most sensitive approaches. Sampling birds found dead was the most cost-effective strategy, but this depends strongly on bird mortality and awareness of the public. On the other hand, using traps was the least cost-effective approach. Specifically, it costs, on average, 603 Euros per month for HPAI detection using birds found dead, 9,786 Euros using sentinel surveillance, and 194,285 Euros, using traps. Thus, prioritizing sentinel surveillance was recommended and, if high mortality is expected, testing the birds that are found dead.

Vaccination is the most common preventive measure and has been tested in HPAI control. Fasina et al. (2007) provided a cost-benefit analysis of AI vaccination in Nigeria, using a projection scenario in 2006-2009, and found that applying a combination of vaccination and testing/eradication practices is 52 times better than taking no action. To our knowledge, no other cost-effectiveness analyses of HPAI vaccination targeted to the backyard poultry sector are available in the current literature.

Previous experience on ND vaccination delivery to backyard poultry suggested positive economic returns at minimal costs. For example, Tomo (2009) and Woolcock et al. (2004) estimated that the cost per bird of ND vaccination is US$ 0.02 based on data from village poultry in Mozambique, and vaccination would remain a profitable option up to a maximum per bird cost of vaccination of US$ 0.22. Johnston et al. (1992) estimated that it would require about US$ 0.04 per bird (at current prices) to implement an ND vaccination program for backyard poultry in the Philippines and estimated returns from the program would be about 14 times higher than the costs. On the other hand, Sen et al. (1998) found that expected profit was maximized when a combination of enhanced bio-security and ND vaccination was implemented, based on data from cooperative and individual commercial broiler farms in Cambodia and Southeast Asia.

In our study, the CEIs are derived using information on outbreaks from the PIA database to evaluate treatment effects and the associated costs of the treatment. The cost of treatment is the cost of vaccination and the effect of the new treatment is the outcome of vaccination. We assume that there is no other treatment currently in place, so the CEI is simply the ratio of the cost of vaccination to the effect of vaccination. Note that vaccination costs are actually incremental to the cost of PDSR activities being implemented across the two treatment groups and the control group. Since information on costs of the PDSR program was not available at the time of the study, we assumed that PDSR costs were constant across the vaccination treatment groups, so that in the control group, the cost of treatment is taken as zero and the costs of AI vaccination are seen as incremental costs.

The outcome being measured is the reduction in incidence of outbreaks under the vaccination treatment options relative to the control; this is viewed as the treatment effect or the outcome from the treatment. The case definition used for the quantification of outbreaks is defined in Section 3.1 on the longitudinal study design. The other outcome that can be used in the CEA is the reduction in mortality (or reduction in number of poultry deaths).

3. Results

Cost of vaccination – The cost of the vaccine comprised the largest share, i.e., about one-third, of total cost of vaccination, as shown in Table 3.3.1, based on actual costs for three campaign periods. Fixed costs consisting of cold chain infrastructure and equipment accounted for 14% of total cost, while vaccinator costs, including incentives paid to vaccinators, accounted for 21% of total costs. Training costs accounted for 5% and sero-monitoring costs for 3% of the total. The cost of managing the program accounted for about 17% of total costs, i.e., the management costs for salaries and cost-of-living expenses for international and national technical experts who were providing inputs on a full- or part-time basis to the program. Based on consultations with the key persons involved in the management of the vaccination program, a ballpark figure of about US$ 0.5 million per year was considered appropriate.

Total cost of the vaccination program implemented over four campaign periods amounted to about US$ 2.9 million, resulting in some 23 million birds vaccinated in the 16 OR districts covered by the Project. Thus, it costs about US$ 0.12 per shot to vaccinate one bird with AI vaccine using the delivery options used in this program. The relative share of each cost item is shown in Figure 3.3.1.

One feature of the OR model is the cold chain infrastructure put in place aimed at improving the effectiveness of vaccine delivery by reducing spoilage. The cost of vaccination that has been estimated and presented here is computed based on a zero spoilage assumption, i.e., no vaccines were wasted or spoiled during the vaccination period. However, this may not necessarily be true in the actual implementation of such programs, and additional costs are likely to be incurred from vaccine spoilage.

To investigate the cost of spoilage that can be avoided and the corresponding investment justified to avoid those costs, several cost scenarios were explored using different rates of vaccine spoilage, as shown in Figure 3.3.2. Costs due to vaccination failure as a result of spoilage justify at least US$

9,000 up to some US$ 87,000 of investment in alternative cold chain facilities to avoid losses from vaccine spoilage rates of 1-10%. This analysis does not take into account the increased costs incurred due to increased disease burden resulting from vaccination failures, which is often assumed to be the most significant impact of spoilage. The corresponding marginal increase in cost per unit of vaccination under the various spoilage rate scenarios is shown in Figure 3.3.3. The marginal rate of increase in cost per unit cost ranges from less than 1% for a 1% reduction in the cost of spoilage to as much as 3.6% to avoid the added cost from a vaccine spoilage rate of 10%. In order to ascertain the feasibility and effectiveness of any future proposed cold-chain investments, these estimated costs will need to be compared with the actual costs associated with setting up alternative cold chain facilities.

Cost sharing scenarios – Alternative cost-sharing scenarios between the public and the private sector were explored to show how much the publicly funded cost of vaccination might change based on the relative share of costs that are shifted to poultry growers and private sector stakeholders, including industry, input suppliers and commercial poultry operators. The estimated cost of vaccination under the different cost-sharing scenarios is presented in Table 3.3.2. The scenarios are based on the relative share of the cost that the private sector pays, e.g., the column showing "50%" indicates the cost of vaccination per shot paid by the public sector when the private sector pays 50% of the cost.

The cost of vaccination in each of the three scenarios is compared with the cost of vaccination in the vaccination models we tested (assuming zero vaccine spoilage). Among the three proposed cost-sharing arrangements, the highest reduction in publicly funded cost of vaccination will be achieved when the cost of the vaccine, its delivery, and the fixed-cost investments in cold chain infrastructure are paid by the target beneficiaries in the private sector. In this case, the public sector share of the cost per shot will be US$ 0.04 (or about 400 IDR) on average, when all costs are taken into account. When management costs are not accounted for, the cost per unit is slightly lower at US$ 0.02 (or approximately 200 IDR). At the levels of coverage tested in the OR (i.e., 23 million birds vaccinated over four campaigns), it would cost the government about US$ 0.5 million to implement a mass vaccination program under this cost-sharing arrangement in the study area.

Cost-effectiveness indicators – We estimate the CEIs using cost data projected for four vaccination campaign periods (based on actual data from three campaign periods), and the outbreak data for four campaign periods beginning with the study period in July-September 2008 (the first campaign), October-December 2008 (the second campaign), January-March 2009 (the third campaign), and April-June 2009 (the fourth campaign). The treatment effect was computed as the relative change in HPAI-compatible outcomes between the control and the treatment group as obtained from epidemiological analyses using GLLAMM to estimate incidence rate ratios (IRRs), as shown in Table 3.3.3. Two models were estimated to derive incidence rate ratios. Model 1 compared all samples from AI-vaccinated treatment groups to the control group; Model 2 estimated coefficients for two treatment groups, i.e., AI only and AI + ND, relative to the control group. The results from Model 1 show that reduction in the incidence of HPAI-compatible events in all AI-vaccinated treatment groups relative to the control group is 0.46.The results from Model 2 show that incidence rate reduction in the AI-only treatment group relative to the control group is 0.23, and the AI + ND treatment group relative to the control group is 0.70. These estimates are used to generate the CEIs.

Table 3.3.1: Cost of vaccination (per shot, per bird) based on data from three campaign periods, projected to four campaign periods

Cost Items	AI only	%	AI + ND	%	Total	%
Vaccine cost	389,573	28	484,647	32	874,220	30
Vaccinator cost	296,842	22	299,810	20	596,652	21
Recurrent equipment cost	103,926	8	155,981	10	259,907	9
Other recurrent cost	3,941	0	7,882	1	11,823	0
Fixed Investment Cost	209,025	15	209,025	14	418,049	14
Training cost	71,689	5	71,689	5	143,378	5
Sero-monitoring	43,897	3	43,897	3	87,793	3
Management cost	250,000	18	250,000	16	500,000	17
Total cost	**1,368,892**	**100**	**1,522,931**	**100**	**2,891,823**	**100**
Number of birds vaccinated	**11,594,432**		**11,594,432**		**23,188,864**	
Average cost per shot per bird	**0.12**		**0.13**		**0.12**	
Average cost per shot per bird without management cost	**0.10**		**0.11**		**0.10**	

Notes:

1. The number of bird vaccinated in the 4th quarter is equal to the average of the first three quarters

2. Vaccine cost is based on the assumption of 1 dose per bird vaccinated

3. DCVC and CV (cost items in FAO data) are combined into vaccinator cost

4. Vaccinator cost is assumed to be 1% higher for AIND group

5. Other recurrent costs include cold storage/cold chain cost and recurrent transportation cost

6. Details on the allocation of recurrent costs for AI and AIND groups are available upon request. In general, recurrent costs that include cost of non-disposable items stop watches, safety boxes, etc. were allocated between AI-only and AI-ND groups based on the 50-50 assumption. For disposable items such as plastic gloves, etc., we allocated twice as much for the AI-ND groups to account for the disposable items used in the separate applications of the AI and ND vaccines per bird. Other recurrent costs include cost of cooling and storage and transportation cost. We allocated twice as higher for AI-ND assuming that these costs for AI and for ND are the same (that means AI plus ND is twice as higher than AI only).

7. Vaccine cost, vaccinator cost, sero-monitoring cost are projected from data for 3 campaign periods

Source of data: FAO-CMU and ILRI

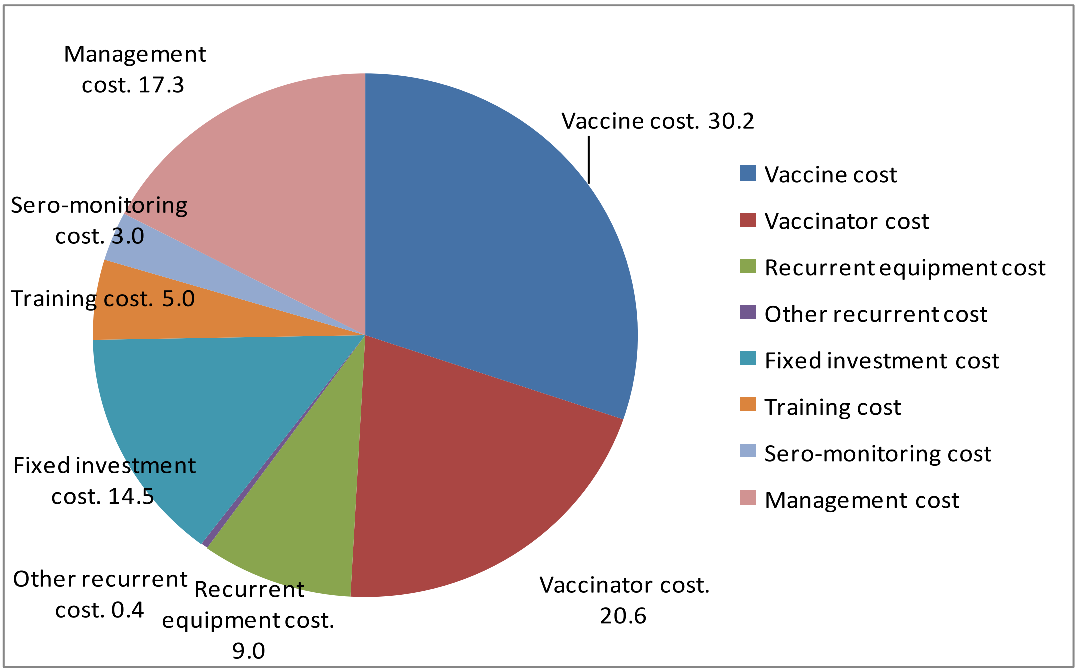

Figure 3.3.1: Vaccination cost composition including management cost in OR program

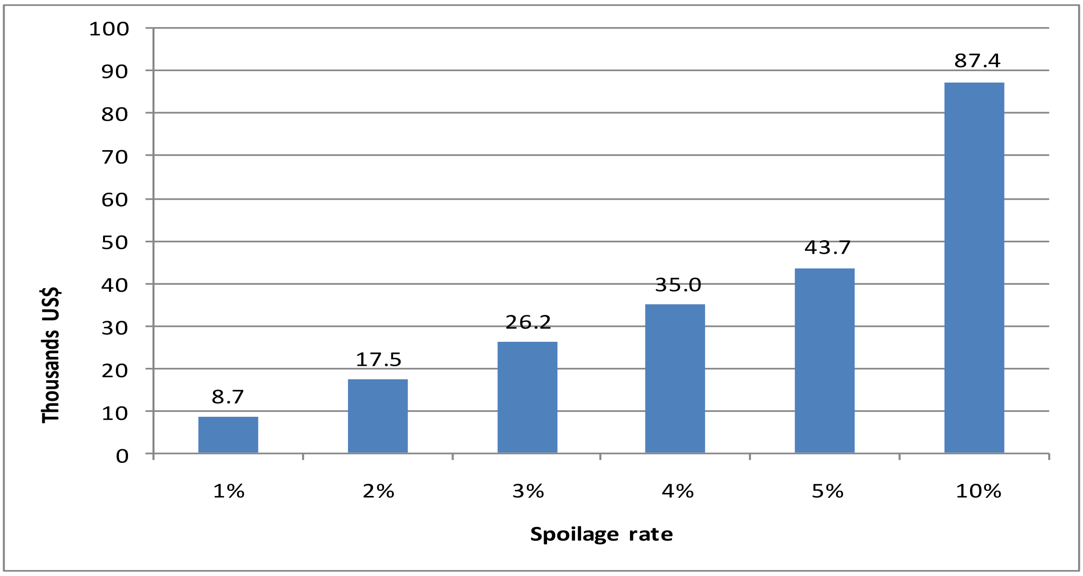

Figure 3.3.2: Additional costs associated with different vaccine spoilage scenarios

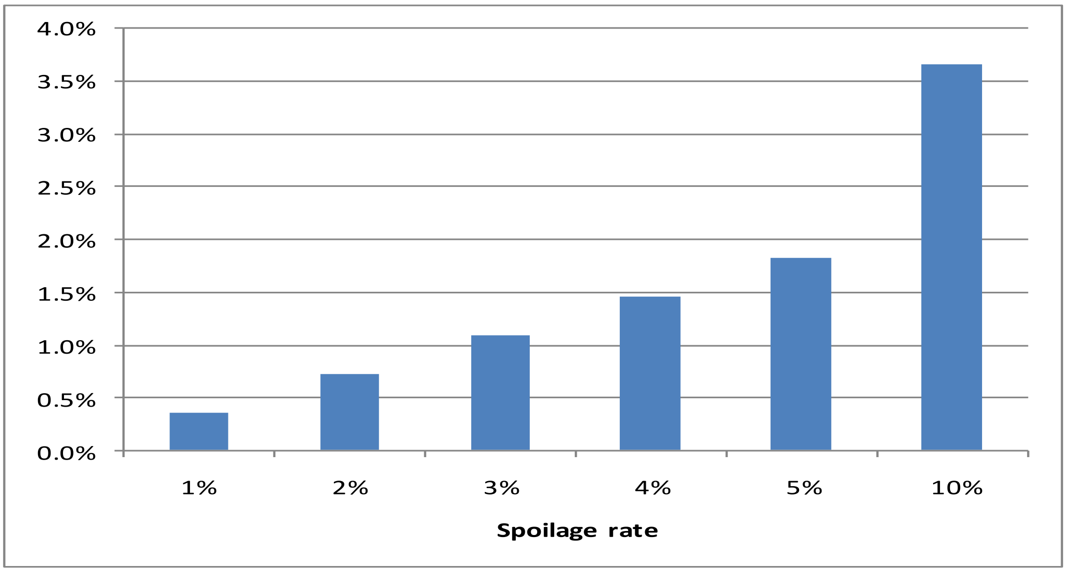

Figure 3.3.3: Marginal increase in vaccination unit cost associated with different spoilage scenarios

Table 3.3.2: Cost of vaccination under different cost-sharing scenarios between the public and private sector (in US$ per shot of vaccination)

Scenarios	**Including management costs**			**Excluding management costs**		
	50%	**75%**	**100%**	**50%**	**75%**	**100%**
OR model			0.12			0.10
1. Vaccine cost by private sector	0.10	0.09	0.08	0.08	0.07	0.06
2. Vaccine cost + delivery cost by private sector	0.09	0.07	0.06	0.07	0.06	0.04
3. Vaccine cost + delivery cost + fixed investment cost by private sector	0.08	0.06	0.04	0.06	0.04	0.02

Notes:

1. Vaccine cost is paid by target beneficiaries (private sector); the rest of the cost is paid by the public sector.

2. Vaccine cost and delivery cost (e.g., vaccinator incentive payments) paid by target beneficiaries; the rest of the cost is paid by the public sector.

3. Vaccine cost, delivery cost, and fixed investment cost of the cold chain are paid by the private sector (e.g., private sector provides the cold chain infrastructure and maintenance support and target beneficiaries and/or the public sector pay a service fee to the provider).

Source of data: FAO-CMU and ILRI

Table 3.3.3: Incidence rate ratios (IRRs) based on estimates from GLLAMM model of HPAI-compatible events as outcome

Model	Incidence Rate Ratio
Model 1:	
Combined AI and AI-ND treatment groups	0.46
Model 2:	
AI only treatment group	0.23
AI-ND treatment group	0.70

Source of data: ILRI-PIA database

Two types of CEIs were computed, as shown in Table 3.3.4. CEI 1 represents the cost per 1% incidence reduction in HPAI-compatible events. CEI 2 represents the cost per bird saved in HPAI-compatible events. The impact of vaccination on ND-compatible events (i.e., ND-compatible losses averted) is not considered in the analysis. The results show that it costs about US$ 60,000 to obtain a 1% reduction in outbreak from AI-only vaccination in the 16 OR districts. This cost is reduced to about US$ 22,000 per 1% reduction in HPAI-compatible outbreaks using the AI + ND vaccination option. Using the combined sample from all AI treatment groups in the 16 OR districts, the estimated cost per 1 % reduction in HPAI-compatible outbreaks rises to about US$ 63,000.

In terms of bird mortalities averted in HPAI-compatible events, the cost per bird saved (CEI 2) in AI-only vaccination is US$ 22.00; this is about three times higher than the combination of AI + ND vaccination. When all AI treatment groups are considered, the cost per bird saved in HPAI-compatible events is US$ 24.00 under the OR model. This cost is considerably higher than the estimated market value of one Kampong chicken (i.e., 31,000 IDR or about US$ 3.00).

Table 3.3.4: Cost-effectiveness indicators (CEIs)

	AI-only	AI + ND	Combined
CEI 1 (Cost per incidence of HPAI-compatible event averted, US$)	59,517	21,756	62,866
CEI 2 (Cost per bird saved, US$)	22	8	24
Number of bird deaths prevented	61,123	186,026	122,246

Notes:

1. Reduction in outbreak is computed from estimated coefficient of treatment effects (e.g., AI vaccination or AI-ND vaccination) controlling for time in a GLLAMM regression.

2. Number of bird deaths prevented is computed by applying the estimated IRRs to the total number of bird deaths in the control group (i.e., no AI vaccination, only PDSR activities).

3. Cost of vaccination assumes zero spoilage and represents four campaign periods.

Source of data: ILRI-PIA database

Benefits from vaccination – The direct losses avoided from poultry deaths as previously shown in Table 3.3.4 are valued and the results are shown in Table 3.3.5, specifically the computed values of direct losses avoided under three cases, e.g., AI-only, AI + ND-only, and combined (all samples).

Table 3.3.5: Estimated value of direct losses avoided from AI vaccination under the OR program (US$)

	AI-only	AI + ND	Combined
Estimated value of direct losses avoided (benefits)	221,265	673,416	442,530
Cost of OR vaccination program (1 year)	1,368,892	1,522,931	2,891,823
Difference between direct benefits and cost	-1,147,627	-849,515	-2,449,293
Ratio of benefits to cost	0.16	0.44	0.19

Notes:

1. Reduction in outbreak is computed from estimated coefficient of treatment effects (e.g., AI vaccination or AI-ND vaccination) controlling for time in a GLLAMM regression.

2. Number of bird deaths prevented is computed by applying the estimated IRRs to the total number of bird deaths in the control group (i.e., no AI vaccination, only PDSR activities).

3. Cost of vaccination assumes zero spoilage and represents four campaign periods.

Source of data: ILRI-PIA database and FAO-CMU

For example, a 23% reduction in outbreaks under AI vaccination can be translated into about 61,000 avoided bird deaths in HPAI-compatible events, based on actual vaccination coverage and documented outbreak mortalities as reported by respondents interviewed in the 16 OR districts. By applying the weighted average prices of birds (based on distribution of type of poultry, e.g., Kampong chicken, fancy chicken, Muscovy ducks, etc., in the OR districts) the value of bird deaths prevented is computed at about US$ 221,000. This amount represents the value of birds saved in terms of potential market value of birds sold or consumed. As indicated above, this estimate does not include the value of other economic activities, such as feed production and trade and support services, including employment that generate livelihoods for households engaged in poultry production. Due to a lack of information, it was not possible to estimate these other potential economic and social benefits. Comparing the value of direct benefits with the cost of vaccination under the AI-only vaccination option, it is shown that the estimated value of direct benefits represents only about 16% of the cost of treatment. The AI + ND vaccination option produces the highest benefit:cost ratio (0.44) in the context of the OR. Based on the combined sample, the benefit:cost ratio is 0.19, suggesting that US$ 1.00 invested in the OR program generates about US$ 0.20 in return.

Discussion

The mass vaccination targeted on the backyard poultry sector is challenging and expensive to implement, based on the cost information and vaccination coverage obtained from our study. The cost per shot of AI vaccination is US$ 0.12; this is higher than the estimate of US$ 0.05 by Rafani (2009), although this cost estimate was based on a vaccination program for the commercial poultry sector in Indonesia, and about US$ 0.06 per shot per bird based on the Vietnam experience (Hinrichs et al., Undated). At US$ 0.12 per injection, it would cost US$ 288 million to mass vaccinate (primary and booster injections) the 300 million backyard poultry four times per year with an outcome of moderate, transient suppression of disease. Cost of vaccine delivery to backyard poultry in Africa is estimated at US$ 0.38 per dose (McLeod and Rushton 2007), and this is much higher than the estimate obtained in the present study. On the other hand, estimates by Vandendriessche et al.

(2009) from the AI vaccination program implemented in the Belgian poultry sector showed that it cost 0.11 Euros per bird (or approximately US$ 0.15 @ Euro 1.00 = US$ 1.35).

Management costs account for about 17% of the total costs of the vaccination programs and are slightly higher than the fixed investment costs for the cold chain infrastructure. These costs can be justified as critical to the successful implementation of the program, particularly in providing significant technical inputs in planning and design, in monitoring implementation, and ensuring quality control in the implementation of activities and delivery of outputs. Even when management costs are included in the total cost of the vaccination program, the cost of the vaccine and the vaccinators still account for at least half the total.

At the estimated cost of US$ 2.9 million per year to run the program in an area that covered about 1% of the target population of Java, it is unlikely to be sustainable as a largely publicly funded program using donor funds. On the other hand, a vaccination program implemented in Vietnam over a two-year period and designed to cover 160 million birds was allocated a budget of US$ 17.3 million (Hinrichs et al., 2006). It is important to bear in mind that the politico-economic context in which the two countries are implementing epizootic disease control are very different, and that transaction costs for the management, implementation and coordination of vaccination programs in a decentralized system such as Indonesia are much higher than in Vietnam. Areas where possible cost savings might be realized may include: 1) the direct cost of the vaccine, by identifying low-cost vaccine options at the same level of efficacy; 2) fixed investment costs, by identifying low-cost options for cold chain infrastructure and/or equipment that can deliver the vaccine at the same level of efficiency and effectiveness; 3) and variable costs associated with vaccine delivery, e.g., identifying potential savings in utilities, transportation, and eliminating wastage in the use of supplies. While incentive payments to vaccinators also account for a significant share of total costs, it should be noted that these costs are directly correlated with the rate of vaccine coverage, i.e., reducing the incentive payments may negatively affect coverage rate. In the Indonesia experience, field personnel were paid on the basis of quotas based on poultry population estimates that turned out to be under-estimated. Reports from the field indicated that this functioned as a disincentive and actually limited coverage in some areas in that, once the quota was reached, the vaccinator stopped working. Exploration of areas where vaccinator efficiency may be improved through the right incentives is worth pursuing as alternative options for improving cost efficiency in this particular cost item.

Cost-sharing arrangements with civil society will likely reduce the total financial burden of vaccination programs to the public sector. The largest reduction of the public sector burden for implementing a vaccination campaign similar to the mass vaccination models evaluated here will likely be achieved when beneficiaries take on the costs of the vaccine, its delivery, and the fixed investments, particularly in establishing and managing the cold chain infrastructure. The latter can be organized under a service contract arrangement in which the private sector, for example the animal health industry, provides and manages the cold chain for a fee. These various cost-sharing arrangements will need to be assessed in terms of the overall technical and economic feasibility of the program, as well as their acceptability to the various stakeholders.

Economic losses from bird deaths that are equivalent to the potential market value of bird sales or home consumption can be avoided through AI vaccination. While the direct benefits from avoiding such losses is only about 20% of the total cost of the vaccination program, it is likely that other significant direct and indirect benefits accruing to various actors in the poultry value chain can potentially be generated from investments in AI vaccination. These potential benefits will need proper documentation to be useful in making future decisions about AI vaccination investments [see Tiongco (2008) for a review of approaches to evaluate benefits from HPAI control measures]. For example, the direct benefits from vaccination include the value of losses from bird deaths that could be prevented, as well as the value of human life that could be saved from succumbing to avian influenza through exposure or direct contact with infected poultry. Indonesia experienced a significant number of human casualties from AI during the first wave of outbreaks in 2004, and the prevailing global perception that every human infection increases the risk that the virus will evolve into a pandemic strain capable of transmitting between people underpins the significant resources mobilized for HPAI control initiatives.

There are also significant indirect benefits that accrue from losses avoided along the poultry value chain, e.g., lost earnings from employment in the poultry sector, lost earnings from inputs and services linked with poultry production and marketing, and others that are not easily quantified due to lack of appropriate and reliable information. However, AI vaccination targeted to the backyard poultry sector will need to be viewed in the broader context of public health risk of a zoonotic disease such as avian influenza, given the significant cost it entails to deliver a vaccination program as a control strategy to this sector. Noting the high cost of widespread application of mass vaccination, it is probably not possible to mobilize sufficient investment, even in light of the public health significance of the disease. An assessment of the risks that AI outbreaks in backyard poultry present to the health and livelihoods of the community would be useful in guiding investment decision-making.

The computed CEIs suggest that AI vaccination in combination with ND vaccination was more cost-effective when compared with the AI-only vaccination option. The dual vaccination appeared to be more effective at lowering the incidence of HPAI-compatible events (see Section 3.1). However, the longitudinal study was designed only to determine the impact of the addition of ND vaccination as an incentive for participation in the vaccination programs, and not to evaluate any potential vaccine interactions at the biological level. Thus, the cost-effectiveness result for the combined vaccination group must be interpreted with caution. The cost of ND vaccine was much lower than that of the AI vaccine, and even if ND vaccine delivery entails additional costs, these costs do not significantly inflate the total costs in the AI + ND group relative to the AI-only group – the increase in costs is worth the relatively higher reduction in incidence of HPAI-compatible events observed in the AI + ND group. In terms of per unit cost, the combination of AI + ND vaccines will add US$ 0.01 to the cost per shot compared to the AI-only option. Our results also suggest that the cost of saving one bird under the OR program is significantly higher than the potential market value of the bird. This suggests that, while vaccination is a tool that can be used effectively, more research is needed on how to target vaccination programs on critical control points in order to maximize impact, design the appropriate incentives for effective participation, and generate optimal returns on investment.

Conclusions

The vaccination strategies evaluated by the Project resulted in a statistically significant, but moderate, reduction in the incidence of HPAI-compatible events in the treatment areas. In terms of such resources as logistics and management capacity, the program was very demanding, yet covered only about 1% of the backyard poultry population of Java. These models were expensive to implement and would likely not be sustainable as largely public sector funded programs supported by donor funds. At US$ 0.12 per injection, it would cost US$ 288 million to mass vaccinate (primary and booster injections) Indonesia's 300 million backyard poultry four times per year with an outcome of moderate, transient suppression of disease. Greater empowerment and participation of local stakeholders in the management and implementation of vaccination activities would enhance sustainability. Moreover, continued support to institutional capacity building for vaccine delivery (including management, social and technical issues) would likely be a beneficial use of public sector resources.

Despite these concerns, our research has shown that vaccination can reduce the incidence of HPAI-compatible events and, when human health impacts are considered, may be justified. We suggest that further research is required to identify incentives for participation by stakeholders and methods to target vaccination to critical control points as a means of leveraging investment in vaccination, as well as other control measures.

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3.4. Adoption of and willingness-to-pay for animal disease control measure: The case of vaccination for avian influenza control in Indonesia

Abstract

A household survey to elicit information about decision-making on adoption of HPAI control strategies was implemented as a complement to the cost-effectiveness analysis of the mass vaccination activities that were evaluated as part of the operational research to identify more effective HPAI control strategies for poultry in Indonesia. The empirical estimates of adoption and willingness-to-pay for vaccination can provide guidance in designing appropriate mechanisms to enhance the acceptability and uptake of a mass-vaccination program for the backyard poultry sector. Specifically, our results suggest that the cost of the mass vaccination was much higher than what its target beneficiaries – the backyard poultry sector – are willing to pay. While there are economic incentives arising from market opportunities presented by poultry sales, particularly in native chicken markets, these appeared to be reduced by scale effects, i.e., smaller flock sizes inhibit backyard poultry raisers from adopting and willingly pay for vaccination, as compared to households that are more commercially oriented and have larger flock sizes. Also, given that household adoption decisions are influenced to a great extent by their subjective perception of uncertainty – in this case, the risk of disease outbreak from AI virus infection – more exposure by households to appropriate information that will reduce their subjective uncertainty would go a long way towards eliciting appropriate behavior.

1. Introduction

The Operational Research (OR) Project was implemented with support from international donors and in collaboration with the Government of Indonesia to evaluate technical control options applied in the context of a strong bottom-up approach, e.g., participatory disease surveillance (PDSR), to address the public health and economic issues presented by Avian influenza. The Project was implemented in June 2008 in 16 districts in 3 provinces of West Java, Central Java and Yogyakarta. A longitudinal study was designed to collect information for assessing the feasibility and effectiveness of possible control options. One of many desirable outcomes of such a program is to promote appropriate behavior in response to disease outbreaks, i.e., higher uptake of risk-reducing and/or risk-mitigating interventions. Our study seeks to investigate what determines adoption of one AI control measure, specifically, vaccination, among households engaged in raising backyard poultry. In addition, our study also elicits empirical evidence to understand what drives the willingness of backyard poultry raisers to pay for vaccinations. We envision that results from our study will be useful in designing effective policy actions and programs for enhancing the social acceptability and wider uptake of appropriate measures for avian influenza control.

2. Materials and Methods

2.1. Study design

The Project was implemented in 16 districts in Indonesia and was initially designed to include four treatment groups: 1) control (to include only PDSR activities); 2) PDSR with AI vaccination; 3) PDSR with AI and Newcastle Disease (ND) vaccination; and 4) PDSR with culling and an improved compensation process. The culling and improved compensation option was not implemented due to policy constraints, leaving only three treatment groups as basis for designing the household surveys in this study. The surveys were targeted to cover 300 households from the three treatment groups (control, AI and AI + ND) in three selected districts among the 16 in which the Project was carried out. The surveys were implemented in a single round of face-to-face interviews using a survey instrument. Information collected from the household surveys was analyzed to assess factors motivating household decisions to participate in vaccination programs, and evaluate their willingness-to-pay for vaccinations.

2.2. Data and methodology

Survey sites and sample selection – Three districts were identified as survey sites: Cirebon, Semarang, and Kulon Progo, which were the same areas in which the sero-monitoring surveys were being undertaken. Since the target sample size of 300 households with 100 households per district is less than the total number of households in the survey sites, random points for identifying sample households were selected in each district, as shown in Table 3.4.1. The target sample respondents of 100 per district were planned to be equally distributed across the three treatment groups (control, AI and AI + ND).

Table 3.4.1: Distribution of target and actual sample respondents, by treatment group, by location

Treatment group	Cirebon			Semarang			Kulon Progo		
	Assessment RT	Target sample size	Actual sample size	Assessment RT	Target sample size	Actual sample size	Assessment RT	Target sample size	Actual sample size
Control	H6	16-17	51	F9	16-17	33	Q6	16-17	35
	HA	16-17		F5	16-17		Q10	16-17	
		33			*33*			*33*	
AI only	H19	16-17	16	F20	16-17	31	Q13	16-17	29
	H11	16-17		F14	16-17		Q18	16-17	
		33-34			*33-34*			*33-34*	
AI + ND	H22	16-17	33	F24	16-17	36	Q26	16-17	36
	H28	16-17		F27	16-17		Q30	16-17	
		33-34			*33-34*			*33-34*	
Total samples/ district		**100**	**100**		**100**	**100**		**100**	**100**

An Indonesian research organization (InterCAFE) was identified and contracted to implement the household surveys in collaboration with ILRI. Three enumerator teams were organized, each team consisting of three persons, one of who was designated as team supervisor, and assigned to one district. The enumerator teams implemented the surveys during the period 25 May to 1 June 2009, with prior authorization from and coordination with the local authorities in each district, sub-district and RT. The household surveys were completed during the first week of June 2009. The households surveyed were randomly chosen from each treatment groups: AI only, AI + ND only, and control groups in each of the survey sites according to the target sample allocation shown in Table 3.4.1. The actual number of households surveyed is also shown in Table 3.4.1. Processing of the information from the surveys, including cleaning and editing, was undertaken immediately after the completion of the field surveys.

Survey instruments – Survey instruments were developed and pre-tested on 27 and 29 April 2009 in two villages in Bogor, areas similar to the survey sites in Cirebon, Semarang, and Kulon Progo. The pre-tests revealed information about possible local conditions in poultry production and management that guided the further revision of the survey instruments. Training of enumerators was implemented on 5 and 22 May in Bogor. The training included detailed discussions about household poultry production, management and sales, and identification of AI outbreaks given specific indicators or clinical symptoms that may accompany observed sudden death incidence. Enumerators were also trained to use a GPS instrument to document the coordinates of each household selected as a respondent. A copy of the survey instruments used is available on request.

Econometric analysis of adoption and willingness-to-pay – To explore the drivers behind households' decisions to participate or not in a vaccination campaign, a discrete choice-modeling framework was employed. A discrete choice model is an appropriate framework to examine adoption decisions (see, for example, Feder et al., 1981 for a review of empirical approaches in adoption studies). A general discussion of discrete choice modeling principles and methods is presented in, for example, Greene (1997); Ben-Akiva and Lerman (1985); and Horowitz, Koppelman, and Lerman (1986). The adoption decision can be conceptualized as a binary choice to adopt or not to adopt a treatment and modeled as a dummy variable. A dummy variable is essentially a binary variable that is commonly used in regression analysis to build discrete shifts of the function being estimated into a regression model (Greene, 2003), such as for example, in evaluating treatment effects where a binary variable is defined as equal to one if the decision to adopt an intervention is made and zero if it is not. This decision is assumed to be influenced by a number of factors given the context within which the analysis is framed (Feder et al., 1981). If we further assume that the relationship between the underlying drivers and the probability that a decision is made follows a logistic distribution, using a binary logit model is in order.

Logit models have been widely used in practice to model binary choice problems (Greene, 1997; McFadden, 1976). For example, Sheikh et al. (2003) use a logit model to identify factors that influence the uptake of new "no-tillage" technologies by farmers in rice-wheat and cotton-wheat farming systems in Punjab, Pakistan. Ward et al. (2008) examine the adoption of cow-calf production practices in Oklahoma. We used the same approach to model household decisions to adopt vaccination control measures and their willingness-to-pay for them. The assumption of this model was that households are essentially rational decision-makers seeking to maximize their total utility or satisfaction. Gramig (2008) used a logit model to analyze the determinants of bio-security adoption behavior in the management of livestock diseases. In the context of our study on avian influenza control, with specific focus on adoption of vaccination as a control strategy, we hypothesize that a household's decision to vaccinate poultry and their willingness-to-pay depend on demographic characteristics, poultry raising practices, awareness of disease threats, and the potential benefit of vaccination and the adoption of alternative control strategies. A Tobit model was used to estimate the actual amount that households are likely to be willing to pay for vaccinations and identify relevant drivers of this decision, using the same set of covariates as the logit model for willingness-to-pay. The choice of covariates to include in the logit and Tobit models was guided by the descriptive analysis details that are discussed in the following sections.

3. Results

3.1. Descriptive analysis of survey data

Profile of household respondents – Raising poultry is generally considered a secondary occupation by the household heads among those interviewed; only about 17% of the household heads interviewed consider raising poultry as their main occupation (Table 3.4.2). A higher proportion of households in the control group indicated raising poultry as the main occupation of the household head compared to those in the AI and AI + ND treatment groups; average annual income from poultry among households within the control group was relatively lower than those of households in the AI vaccination groups. Among households having poultry as the main occupation of the household head, income from poultry accounts for around 20% of total household income. For the whole sample, income from poultry is just under 10% of total income. Experience with poultry raising was much the same across the three groups, on average. On the other hand, more households in the control group indicated having experienced poultry deaths compared with those in the AI vaccination groups.

Table 3.4.2: Profile of survey respondents by treatment group (combined sample from 3 districts)

	Control	AI	AI – ND
Number of households	119	76	105
% HH with poultry raising as main occupation of HH head	26	16	7
% HH with poultry raising as secondary occupation of HH head	57	59	56
% Islam	76	89	94
Maximum no. of years HH had been raising poultry (mean)	20	22	19
Crop income (mean, '000 IDR)	940	615	519
Livestock income (non-poultry) (mean, '000 IDR)	378	480	151
Poultry income (mean, '000 IDR)	781	865	808
Total HH income (mean, '000 IDR)	11,976	9,974	19,588
% HH having non-poultry livestock	42	57	36
% HH with experience of poultry deaths	69	63	54

Source of data: ILRI-InterCAFE survey, 2009

Characteristics of households having experienced poultry deaths –Among households with poultry raising as the main occupation of household heads, more had experienced poultry deaths than not (Table 3.4.3). These households also had relatively higher annual income from poultry raising, on average. Among households where poultry raising was a secondary occupation of the household head, a lower proportion had experienced poultry deaths than those who had not.

The incidence of use of vaccination was slightly higher among households without poultry death experience, but the difference was not statistically significant. However, among households that kept poultry in cages or fenced in all day, the number of those that reported poultry deaths was half the number of those that reported no deaths. Cleaning cages also appeared to have been effective as a deterrent to infection, i.e., a higher proportion of households that reported not having experienced poultry deaths also reported that they clean the cages where their poultry was kept. Relatively more households that have experienced poultry deaths also indicated buying live poultry for their own consumption. In both groups, about one-third each do nothing to prevent AI.

Risk of disease from markets –There were three main sources from which farmers obtain poultry: their own production, live bird markets, and neighbors (Table 3.4.4). The majority of farmers in the districts produced their own chicks. About 10% of them purchased stock from village live bird markets, and a few farmers purchased from their neighbors. A fifth of farmers surveyed bought stock from other sources; the same proportion did not state the sources of their stock. There appears to be no statistically significant difference in the incidence of poultry deaths among households engaged in different types of input stock procurement.

There were also three main outlets that farmers used to sell their poultry: live bird markets, hawkers and neighbors. Among households that sell poultry to hawkers, a higher number had experienced poultry deaths than those that reported no poultry death experience.

Table 3.4.3: Profile of households having/not having experienced sudden deaths in their poultry flock (combined sample from 3 districts)

	Experienced death in poultry	Not experienced death in poultry
% Poultry raising as main occupation***	22	8
% Poultry as secondary occupation***	51	67
% Islam	85	88
Max no. years of raising poultry*	21 (16)	18 (15)
Crop income,'000 IDR	787 (2,671)	640 (1,424)
Poultry income, '000 IDR***	1,074 (1,663)	377 (707)
Other livestock income, '000 IDR	412 (3,062)	179 (1,040)
Total income, '000 IDR	13,465 (15,220)	15,238 (33,864)
% HH having non-poultry livestock	45	42
% HH having experience with vaccination	30	38
% HH used AI vaccination	20	25
% HH used multiple disease vaccination	5	10
% HH keep poultry in fence or cage all day**	6	12
% HH buy live poultry for consumption (%)***	39	11
% HH use disinfectant in farm**	22	15
% HH do nothing to prevent AI	37	33
% HH clean cages to prevent AI**	21	35
% HH Had recent AI outbreak (%)***	67	19

Note: The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level. Figures in parentheses are standard deviation.**

Source of data: ILRI-InterCAFE survey, 2009

Use of vaccinations and the willingness-to-pay –The most widely used vaccine reported by survey respondents was AI (66%), followed by multiple types of vaccines. The application of ND and Gumboro vaccines alone was rare among the survey respondents. However, we do not have information from survey data to confirm if these vaccines were easily available and accessible to the respondents. Only a third of households surveyed had their poultry vaccinated in the past. Almost half of the households had used vaccinations because they thought that it might help to prevent diseases or make their poultry become healthy (Table 3.4.5). The other half did not seem to recognize any potential benefit from vaccination, i.e., about a third opted for vaccination because it was a program being promoted by the government, and the rest indicated they opted for the use of vaccination because it was provided free of charge.

Table 3.4.4: Access to input and output markets.

	Experienced poultry death (%)	Not experienced poultry death (%)	Total (%)
Input stock from:			
Own production	75	72	74
Live bird market	10	7	9
Neighbor	3	5	4
Other or no answer	19	18	19
Market outlets:			
Live bird market	11	15	13
Hawker***	19	4	13
Neighbor**	23	35	28
Other or no answer	47	46	46

Note: The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level.**

Source of data: ILRI-InterCAFE survey, 2009

Table 3.4.5: Reasons for vaccination

Reason for Vaccination	Number of households	%
Prevent AI	19	19
Immune from disease	7	7
Make poultry healthy	21	21
Following government programs	30	30
Free of charge	15	15
Don't know	1	1
Others	6	6
Total	**99**	**100**

Source of data: ILRI-InterCAFE survey, 2009.

Among 300 households surveyed, only 5 had ever paid for poultry vaccinations, with a maximum price paid of less than 13,000 IDR (about US$ 1.30) per treatment, on average. Among 52 households that responded to the question about the cost of vaccination, 92% thought that it was expensive. On the other hand, 86% of households indicated they were willing to pay for AI and AI + ND vaccination (Table 3.4.6), although the amount they indicated they were willing to pay was much lower than the average cost of vaccinating their poultry flock, i.e., about 130 IDR per shot based on estimates from available information on the cost of vaccination. It is understandable that low-income households would tend to be willing to pay less for vaccinations (Table 4.3.7). Interestingly, perceptions of willingness-to-pay were highest in the middle-income group. Another paradoxical finding was that those households that considered raising poultry as the main occupation of the household head would want to pay less than those households where poultry raising was a secondary occupation undertaking.

Table 3.4.6: Percentage of households with different levels of willingness-to-pay for vaccination

	AI vaccination		AI-ND vaccination	
	Min payment	Max payment	Min payment	Max payment
Not willing to pay	20	14	20	14
Less than 100 IDR	32	16	23	5
From 100 IDR to less than 1000 IDR	44	60	52	63
1000 IDR and above	4	10	5	18
Total	**100**	**100**	**100**	**100**

Source of data: ILRI-InterCAFE survey 2009

Table 3.4.7: Willingness to pay across income terciles and poultry raising groups (in IDR)

	AI vaccination		AI-ND vaccination	
	Min payment	Max payment	Min payment	Max payment
Low income group	89	191	136	255
Middle income group	197	539	319	685
High Income group	168	395	313	652
Poultry raising is main occupation of HH head	93	230	180	392
Poultry raising is not main occupation of HH head	164	406	272	561

Source of data: ILRI-InterCAFE survey, 2009

On the other hand, more households that have experienced poultry deaths indicated willingness-to-pay for vaccinations than those not having experienced poultry deaths (Table 3.4.8).

For those who opted to not adopt vaccinations, several reasons were cited for their decision (Table 3.4.9). For some, vaccinations were not necessary; for others, the number of poultry they had was not significant ("large enough") to justify vaccinations. About half of the households surveyed did not have access to information about vaccination and its benefits. Some households refused to vaccinate their poultry because they did not want to pay. A few were afraid of the negative effects of vaccinations.

Table 3.4.8: Incidence of poultry deaths and willingness-to-pay for vaccination

	Experienced poultry death	Not experienced poultry death
Willing to pay for AI vaccination (%)**	89	80
Max WTP for AI (mean, in IDR)	417	454
Min WTP for AI (mean, in IDR)	141	134
Willing to pay for AIND vaccination (%)**	89	80
Max WTP for AIND (mean, in IDR)	597	632
Min WTP for AIND (mean, in IDR)	240	394

Note: The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level.**

Source of data: ILRI-InterCAFE survey, 2009

Table 3.4.9: Reasons for not having vaccination

Reason	Number of Households	%
Afraid of negative effects	9	4
Lack of information	40	20
Do not want to pay	23	11
Not necessary	12	6
Number of chickens is not significant	10	5
Don’t know or understand	68	34
No idea	14	7
Others	25	12
Total	**201**	**100**

Source of data: ILRI-InterCAFE survey, 2009

Bio-security and other practices to control AI infection and spread – Besides vaccination, a number of other options have been used by households to prevent or reduce the incidence of AI. Table 3.4.10 summarizes these options. The most common practice adopted by 35% of households surveyed was cleaning of poultry cages and the ground. About one-fifth of households used medical treatment or special feed for poultry to avoid AI infection. This was observed to be widely practiced in Cirebon. Other households (about 1 in 10) immediately sold their poultry once there was an outbreak in the community or when they suspected that their flock may be infected. About one-third of households surveyed considered various other alternatives for AI prevention.

Table 3.4.10: Bio-security measures to prevent AI infection

		Clean cage and ground	Medical/feed treatment	Immediately sold	Others
Cirebon	HH	24	45	0	31
	%	24	45	0	31
Semarang	HH	43	8	23	26
	%	43	8	23	26
Kulon Progo	HH	38	14	7	41
	%	38	14	7	41
Total sample	**HH**	**105**	**67**	**30**	**98**
	%	**35**	**22**	**10**	**33**

Note: Medical/feed treatment includes giving human medicine, traditional medicine and special feed to poultry

Source of data: ILRI-InterCAFE survey, 2009

Treatment of dead poultry was also a critical risk factor in the spread of diseases. Four options being practiced by households were reported in the survey: 1) dispose of dead poultry in rivers, 2) bury them, 3) burn and bury them, and 4) other actions (Table 3.4.11). More than half of households (57%) chose to throw dead poultry into rivers. About one-third of respondents buried dead poultry without burning. Only a fraction of respondents burned dead poultry before burying them, while a few respondents choose other alternatives.

Table 3.4.11: Actions taken to dispose of dead poultry within 12 hours of death

		Dispose in river	Bury	Burn & bury	Others
Cirebon	HH	14	42	2	3
	%	23	69	3	5
Semarang	HH	134	13	4	0
	%	89	9	2	0
Kulon Progo	HH	7	50	0	1
	%	12	86	0	2
Total sample	**HH**	**155**	**105**	**6**	**4**
	%	**57**	**39**	**2**	**2**

Source of data: ILRI-InterCAFE survey, 2009

Areas that need supportive measures as identified by respondents –Information dissemination was the most frequently cited issue in the effective control of HPAI (Table 3.4.12). Nearly 50% of households surveyed would like to see improvements in information dissemination, to allow better access to information about diseases and appropriate preventive measures. Specifically, households would like to receive information about technical assistance in disease prevention and control, information on preventive measures, handling techniques of sick birds, and good poultry management practices (Table 3.4.13). Households also indicated the need for the government and the community to take actions in controlling diseases. However, a significant proportion of households surveyed still indicated no specific ideas to support AI control initiatives.

Table 3.4.12: Support needed in AI prevention

		Information dissemination	Government action	Society empowerment	No idea	Others
Cirebon	Times	56	23	1	11	9
	%	56	23	1	11	9
Semarang	Times	27	4	6	58	5
	%	27	4	6	58	5
Kulon Progo	Times	56	21	11	3	9
	%	56	21	11	3	9
Total sample	**Times**	**139**	**48**	**18**	**72**	**23**
	%	**46**	**16**	**6**	**24**	**8**

Source of data: ILRI-InterCAFE survey, 2009

Table 3.4.13: Information to improve knowledge about AI

		Technical assistance	Good management practice	Preventive action	Handling techniques	No idea	Other s
Cirebon	Times	12	8	55	18	4	3
	%	12	8	55	18	4	3
Semarang	Times	27	1	5	17	30	20
	%	27	1	5	17	30	20
Kulon Progo	Times	22	5	16	15	38	4
	%	22	5	16	15	38	4
Total sample	**Times**	**61**	**14**	**76**	**50**	**72**	**27**
	%	**20**	**5**	**25**	**17**	**24**	**9**

Source of data: ILRI-InterCAFE survey, 2009

3.2. Empirical analysis of adoption and willingness-to-pay

Adoption of vaccination for HPAI control –Table 3.4.14 presents descriptive statistics showing significant differences between adopters and non-adopters of vaccination, in terms of ethnicity, access to vaccination (as captured by being located in RTs identified as AI treatment assessment units), experience in recent AI outbreaks, differences in market prices received for sick and healthy poultry, use of control options such as spraying disinfectant or selling poultry immediately upon learning of an outbreak, or some risky practices, such as disposing dead poultry in rivers, and some indicator of exposure to risk from markets, such as buying live poultry from live bird markets for consumption. These are hypothesized as possible drivers of the decision to adopt vaccination.

Results of the logit model estimation are reported in Table 3.4.15, showing only the estimated coefficients of the significant covariates and their corresponding marginal effects (or the marginal change in the probability of adoption of vaccination given a change in a particular covariate in the model). The results suggest that the decision to adopt AI vaccination is influenced by exposure to the program or having access to it (as proxied by the location dummy of RT with AI vaccination), market forces (as captured by the price difference between sick and healthy poultry), use of other bio-security measures such as disinfection, and marketing behavior (where poultry is sold, for example). Interestingly, selling poultry to a neighbor reduces the probability of adopting vaccination. This result appears to be plausible in the context of backyard poultry in Indonesia, where many market transactions occur between neighbors that reduces transaction costs, particularly search costs for information, and where economic incentives to adopt vaccination are weak among backyard growers.

Willingness-to-pay for AI vaccination –The descriptive statistics of the covariates used in the logit model for willingness-to-pay for AI vaccination are summarized in Table 3.4.16. Based on the descriptive statistics, a number of variables are hypothesized to potentially influence households' willingness-to-pay for AI vaccination, including: proxy variables for income (i.e., variables that could be used to capture the effect of income in the absence of observable counterparts and reliable indicators for this covariate, such as for example, high- or low-income group, occupation, etc.); past adoption of vaccination; difference in price between sick and healthy poultry; attitude towards vaccination; access to input and output markets as a buyer or seller of live birds or stock; and practices used to dispose of dead poultry.

The estimated coefficients and corresponding marginal effects of significant covariates from the logit model results are reported in Table 3.4.17. The results suggest that a household's willingness-to-pay for vaccination is influenced by household characteristics, specifically household size, previous experience with AI outbreaks, previous experience in the use of vaccination, and perceptions about vaccination as a control measure. The estimated marginal effects suggest that the likelihood of willingness-to-pay for vaccination increases by 4% for every sudden death experience (i.e., poultry death within 12 hours) that a similar household has. Previous experience with vaccination also increases the probability by 6% that a similar household would be willing to pay for vaccination. Having a positive attitude towards vaccination as a control measure for AI likewise increases the likelihood by 5% that a similar household would be willing to pay for vaccination.

The estimated Tobit model results of the extent of willingness-to-pay for AI vaccination showing only the coefficients of significant covariates and their corresponding marginal effects are in Table 3.4.18. Here, significant drivers of the extent of the willingness-to-pay for vaccination among surveyed households include ethnicity, access to an AI vaccination program, attitude towards vaccination as a control measure for AI, and practices that proxy for risk factors in disease spread.

Table 3.4.14: Profile of households that have/have not used vaccination (combined sample from 3 districts)

Variables	Have used vaccination	Have not used vaccination
Household size	4	4.3
Poultry raising as main occupation of HH head (%)	12	19
Religion dummy = 1 for Islam (%)	90*	84*
Ethnicity dummy = 1 for Javanese (%)	82	75
Households belonging to high-income group (%)	38	31
Households belonging to low-income group (%)	30	35
Share of poultry income in total income (mean %)	7.6	8.2
Having non-poultry livestock (%)	40	45
Had experienced AI outbreak in community (%)	40**	53**
Located in RT for AI vaccination treatment group (%)	34**	21**
Located in RT AI & ND vaccination group (%)	40	32
Willing to pay for vaccination (%)	88	85
Difference in market price between sick and healthy bird (%)	79***	61***
Sell poultry immediately to avoid AI disease (%)	5**	12**
Clean poultry cage and ground to avoid AI disease (%)	41	32
Consider vaccination as a measure to prevent AI (%)	33**	46**
Keep poultry in cages or fenced area (%)	9	8
Use of disinfectant in farm (%)	23**	12**
Throw away inedible parts of poultry (%)	5	8
Dispose dead poultry in river (%)	16*	26*
Produce own chicks for stock replacement (%)	73	76
Buying live poultry for consumption (%)	15***	29***
Sell poultry in live bird market (%)	16	11
Sell poultry to neighbor (%)	25	29
Having problem in accessing information about AI (%)	43	48

Note: The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level.**

Source of data: ILRI-InterCAFE survey, 2009

Table 3.4.15: Factors affecting household decision to adopt vaccination (based on data from combined sample from 3 districts)

Variables	Estimated coefficient	Marginal effect
Located in RT for AI vaccination treatment group (dummy)	1.33 (0.38)***	0.30 (0.09)***
Located in RT for AI & ND vaccination treatment group (dummy)	0.68 (0.38)*	0.15 (0.08)*
Willing to pay for vaccination (dummy)	1.13 (0.49)**	0.19 (0.06)***
Difference in market price between sick and healthy poultry (%)	0.87 (0.41)**	0.17 (0.07)**
Consider vaccination as a measure to prevent AI (dummy)	-0.58 (0.33)*	-0.12 (0.06)*
Use of disinfectant in farm (dummy)	1.22 (0.4)***	0.28 (0.1)***
Buying live poultry for consumption (dummy)	-1.01 (0.70)	-0.19 (0.11)*
Sell poultry to neighbor (dummy)	-0.61 (0.37)	-0.12 (0.07)*
Log likelihood	**-162.56**	
LR Chi^2 (25)	**54.59**	
Prob>Chi^2	**0.0006**	
Pseudo R^2	**0.1438**	

Notes: The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level. Figures in parentheses are standard errors.**

Source of data: ILRI-InterCAFE survey, 2009

Three types of marginal effects were obtained from the Tobit model as shown in Table 3.4.18: 1) the change in probability that a household is willing to pay for vaccination; 2) the additional amount that that a household is willing to pay given that it is willing to pay for vaccination (or has actually paid for vaccination); and 3) the additional amount that an average household is willing pay for vaccination. Also of interest are the estimated amounts that households indicated they were willing to pay for vaccination evaluated at the mean values of the covariates. That is, in the case of a household that is willing to pay for vaccination (or actually paid for vaccination), the estimated amount that a similar household is likely to be willing to pay is about IDR 347 or US$ 0.03 per treatment (at IDR 10,000 = US$ 1.00). An average household, on the other hand, is likely to be willing to pay about IDR 203 or US$ 0.02 per treatment.

Table 3.4.16: Profile of household respondents according to their willingness-to-pay for vaccination (combined sample from 3 districts)

Variables	Willing to pay for vaccination	Not willing to pay for vaccination
Household size	4.2***	3.4***
Poultry raising as main occupation of household (%)	18	8
Religion dummy =1 for Islam (%)	86	87
Ethnicity dummy =1 for Javanese (%)	77	74
Households belonging to high-income group (%)	36**	16**
Households belonging to low-income group (%)	31**	50**
Share of poultry income in total income (mean %)	8.5*	4.4*
Having non-poultry livestock (%)	44	42
Having experienced recent AI outbreak in community (%)	49	47
Number of times experienced poultry death within 12 hrs	0.96***	0.45***
Located in an RT for AI vaccination group (%)	25	29
Located in an RT for AI + ND vaccination group (%)	35	37
Having used vaccination in the past (%)	35**	18**
Difference in market price between sick and healthy poultry (%)	65**	82**
Sell poultry immediately to avoid AI disease (%)	10	8
Clean poultry cage and ground to avoid AI disease (%)	37	24
Consider vaccination as a measure to prevent AI (%)	45***	18***
Keep poultry in cages or fenced area (%)	8	11
Use of disinfectant in farm (%)	17	11
Buying live poultry for consumption (%)	26*	13*
Throw away inedible parts of bought poultry (%)	7	8
Dispose dead poultry in river (%)	25***	5***
Produce own chicks for stock replacement (%)	76**	61**
Sell poultry in live bird market (%)	13	11
Sell poultry to neighbor (%)	26*	39*
Having problem in accessing information about AI (%)	48*	32*

Note: The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level.**
Source of data: ILRI-InterCAFE survey, 2009

Table 3.4.17: Factors affecting household's willingness-to-pay for vaccination (combined sample from three districts)

Variables	Estimated coefficient	Marginal effect
Household size	0.39 (0.15)***	0.02 (0.009)**
Number of times experienced deaths in poultry within 12 hours	0.81 (0.45)*	0.04 (0.02)*
Consider vaccination as a measure to prevent AI (dummy)	0.86 (0.51)*	0.05 (0.03)*
Had used vaccination in the past (dummy)	1.23 (0.53)**	0.06 (0.02)**
Number of observations	**300**	
Log likelihood	**-86.64**	
LR chi2 (25)	**54.45**	
Probability > Chi2	**0.0009**	
Pseudo R2	**0.2391**	

Notes: The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level. Figures in parentheses are standard errors.**

Source of data: ILRI-InterCAFE survey, 2009

Discussion

Evidence from descriptive analysis of survey data suggests a number of interesting risk factors for AI infection. For example, access to input and output markets may expose households to disease risk from contact with market actors and their flock. The source of input stock can affect a farmer's susceptibility to disease since purchased stock is a potential carrier of diseases that can introduce infection to the farmer's flock of birds, although this may not hold true for all inputs, e.g., empirical results suggest that the source of input stock such as chicks does not seem to matter as a risk factor for disease transmission in this particular study.

Outlets to which farmers sell their poultry may have different quality and safety requirements, and depending on the stringency of the quarantine and disease monitoring systems that are in place, a farmer engaging in markets to sell their birds also exposes himself and his flock to risk of disease infection. It is shown that in the context of Indonesia, backyard poultry raisers generally sell their birds or procure their stock from outlets that have less stringent safety requirements, in the absence of strict quarantine inspection and control in the country. For example, higher incidence of poultry deaths was observed among households selling poultry to hawkers (informal poultry traders). This is consistent with findings from other studies, e.g., Chi et al. (2002) where "open" farms having free entry and exit of animals into/out of the herd have a higher incidence of virus infection. It is possible that hawkers and their poultry are potential carriers of infection and the pathway of transmission can be through exposure of the farmer to these, or through direct contact of the farmer's flock if the hawkers pick up the birds on farm.

Table 3.4.18: Significant coefficients and marginal effects of Tobit regression of household's indications of willingness-to-pay for AI vaccination (combined sample from 3 districts).

	Estimated coefficient	Marginal effects		
		(1) Change in probability of willingness-to-pay	(2) Additional amount a household will pay given it is willing to pay	(3) Additional amount an average household will pay
Ethnicity (dummy=1 for Javanese)	-162 (75)**	-0.15 (0.07)**	-71.3 (35.4)**	-101.4 (50.2)**
Low income group (dummy)	-147 (65)**	-0.15 (0.07)**	-58.8 (25.3)**	-82.6 (35.2)**
Located in AI treatment RT (dummy)	-172 (69)**	-0.17 (0.07)**	-66.8 (25.4)**	-93.3 (34.7)**
Consider vaccination as a measure to prevent AI (dummy)	142 (58)**	0.14 (0.06)**	59.9 (25)**	84.8 (35.3)**
Dispose dead poultry in river (dummy)	159 (88)*	0.15 (0.08)*	70.1 (41.4)*	99.6 (58.7)*
Sell poultry in live bird market (dummy)	176 (86)**	0.16 (0.07)**	80 (42.9)**	113.7 (60.6)**
Expected value of dependent variable at the mean values of independent variables			**346.7**	**202.9**
Number of observations	**299**			
Log likelihood	**-1,796.85**			
LR Chi^2 (26)	**42.31**			
Prob>Chi^2	**0.0228**			
Pseudo R^2	**0.00116**			

Notes: Three types of marginal effects were estimated based on the following, as follows:

1. **Probability of being uncensored – refers to the change in probability that a household will pay for vaccination, given that this household is willing to pay for vaccination.**
2. **Expected value for uncensored y – refers to the additional amount a household is willing to pay for vaccination given that this household is willing to pay for vaccination.**
3. **Expected value for y – refers to the additional amount an average household is willing to pay for vaccination.**

The asterisk (*) denotes the level of significance in the difference of the mean between the variables: * - significant at 1% level; ** - significant at 5% level; * - significant at 10% level. Figures in parentheses are standard errors.**

Source of data: ILRI-InterCAFE survey, 2009

Hawkers and traders in live animal markets are also likely to be handling larger numbers of birds from other farms and hence are likely to have greater contact with birds from multiple sources with higher likelihood of exposure to various diseases (Chi et al., 2002). On the other hand, among those households that sell poultry to neighbors, the number of those without poultry death experience is higher than those with poultry death experience. Information about diseases usually spreads easily among neighbors so that farmers and their neighbors are likely to be aware of the disease status of birds for any market transaction that takes place between them. Hence, the likelihood of spread of an infected bird through an exchange between neighbors is usually prevented by not encouraging the practice of selling infected birds to neighbors. Nearly half of farmers surveyed did not state their market outlets.

The observation that more households that experienced poultry deaths were also buying live poultry for their home consumption may also suggest this market-related practice as a potential entry point for infection of their poultry flock. More detailed studies now available do suggest that markets and market-related movements are clearly being implicated in the spread of the virus (Forster, 2009; Chi et al., 2002).

Some household practices, such as keeping poultry in cages, were also associated with low incidence of poultry deaths, suggesting that this practice may be effective in keeping the flock relatively "clean" by lessening exposure to and contact with birds from other flocks. Interestingly, among households that use disinfectants, there appeared to be a relatively higher incidence of poultry deaths. This may suggest that disinfection was not effective as applied and acted as a marker for disease presence, or that disinfection as practiced was a risk factor for disease spread. On the other hand, these households may also have started using disinfectants as a preventive measure for future outbreaks after experiencing poultry deaths.

The empirical results from this study suggest that having access to a vaccination program, such as being located in an RT for AI vaccination treatment, increases the likelihood that a household will adopt vaccination for AI control. Households that have indicated a willingness-to-pay for vaccination are also likely to adopt vaccination. Market incentives are also likely to drive adoption decisions, i.e., households that are aware of (or have received) different market prices for sick and healthy poultry are also more likely to adopt vaccination. The use of bio-security measures, such as use of disinfectant or use of cages and fences, were considered to be complementary control measures, as these interventions were associated with adoption of vaccination. Between the two, the use of disinfectant was shown to be positively associated with the likelihood of vaccination adoption. That is, households that use disinfectant on their farms are also likely to adopt AI vaccination relative to those households that do not use disinfectant. However, it was also observed from descriptive data that households using disinfectants also experienced more HPAI-compatible outbreaks. This poses some confounding issues in causality, and may need to be further explored empirically.

Paradoxically, we find that households that consider vaccination as a measure to prevent AI are less likely to adopt vaccination. This result could possibly be an outcome of previous AI-related poultry deaths that motivated these households to consider vaccination as an option to control future AI-related poultry deaths. This is consistent with observations from survey data wherein among households that consider vaccination as a preventive measure, the proportion of those that have experienced death in poultry was higher than the proportion of those that have not experienced poultry death.

Empirical evidence from this study also suggests that backyard poultry households are generally willing to pay for vaccination but only at levels that are relatively lower than the estimated cost per unit of vaccination of $0.12 for AI and $0.13 for AI + ND in the operational research model. Interestingly, households that sell poultry in live bird markets are likely to be willing to pay a higher amount, e.g., by IDR 80 by a similar household that already pays for vaccination, or IDR 114 by a similar average household. This may capture market incentives that drive willingness-to-pay for vaccination, being currently engaged in poultry sales and therefore the need to protect poultry assets. The estimated WTP rates in this study are, however, within the range of the cost estimate reported in an FAO study (Rafani, 2009), i.e., it was cited that "the average cost of AI including price of vaccine and labor cost of vaccination in sector-3 poultry is about IDR 400 (US$ 0.04) per bird per treatment" (p. 23). It should be noted however, that the target recipients referred to in the FAO study is sector-3 (small-scale commercial poultry), whereas the target recipients in the mass vaccination campaigns evaluated in the OR is sector 4 (backyard and semi-commercial poultry). Moreover, it has been noted that the delivery mechanisms evaluated in the HPAI-OR were high-cost options. Omission of the community-based approaches proposed in the design of the OR was a missed opportunity and this approach has a clear potential to reduce costs and close the gap between community perceptions of the value of vaccination and the cost of vaccination.

In addition, household size, previous experience with AI outbreak, previous experience with use of vaccination, and attitude about vaccination as a control option were also found to be significant drivers of the willingness-to-pay. Thus, willingness-to-pay for vaccination appears to be strongly driven by previous experience with AI outbreaks and use of AI vaccination. Such experiences may have positively influenced attitudes toward AI as an effective control measure, thereby motivating higher likelihood of willingness-to-pay for it. This suggests the importance of the demonstration effect as an incentive to encourage potential adopters to pay for vaccination and is consistent with results from previous studies on the role of demonstration effect in engendering adoption of agricultural innovations (Feder et al., 1981). Further work to understand private incentives to engender appropriate "bio-securing" behavior in response to AI outbreaks would be worth exploring (see, for example, Hennessy, 2005).

An interesting result that is useful to highlight for its policy implications is that the extent of the willingness-to-pay will likely decline among households that are currently located in areas with ongoing AI vaccination programs. This result possibly captures household response to free vaccinations being promoted by these programs, so that a similar household is likely to reduce the amount it is willing to pay when there is an ongoing program that is perceived to be providing AI vaccination for free. The income effect is also shown as a significant driver in the extent of the willingness-to-pay. Lower income households, for example, are less likely to pay for vaccination in general, as indicated by the negative coefficients in Table 3.4.18. If they arewilling to pay, however, they are likely to be willing to pay less than average households in the same income group (IDR 59 compared to IDR 83). Our research also indicates that a positive attitude towards or experience with AI vaccination will likely increase the amount that a household will be willing to pay by about IDR 60.

Conclusions

This study has provided empirical evidence showing that the adoption of vaccination is influenced by access to a vaccination campaign; thus, the implementation of the vaccine delivery models evaluated in the operational research may have facilitated access to vaccination. Market incentives stimulate vaccination adoption; this result is useful for informing the development of strategies for targeting higher uptake of vaccination. Households' willingness-to-pay for vaccination is influenced by their attitude towards vaccination, specifically whether or not it helps in preventing disease. This is also shaped by their past experience with the use of vaccination. Hence, households that have previously used vaccination and derived positive benefits from it are more likely to pay for vaccination, highlighting the role of demonstration effects in engendering adoption.

The cost of vaccination in the models evaluated by the OR was much higher than what an average household was likely to be willing to pay and will likely be a barrier to uptake among backyard poultry owners. There appears to be a valid economic rationale for investing in vaccination, i.e., the cost of vaccination to protect a bird (about $0.24 for two shots including the AI vaccine and a booster) was still less than the value of this bird when sold (at about US$ 3.00 per bird or 31,000 IDR based on current average market prices). However, this aspect is more complex among backyard poultry owners with very small flocks, e.g., 1-2 hens, where the costs of participation (such as the value of owners' time) are very high per bird, than it is for households that are more commercially oriented and raise poultry as a business enterprise and hence have relatively bigger flocks.

Other potentially cost-effective options that households with backyard poultry can use (or are using) include bio-security measures like cleaning poultry cages, or using alternative treatment options such as application of herbal or traditional medicine or special feeds for poultry; these are well worth investigating in more detail to assess impacts on suppression of AI relative to vaccination as a control option.

There were clear indications that some households respond to an AI outbreak in ways that will probably contribute to the continued spread of the disease. For example, many households simply resort to risky behavior to cut losses when there are disease outbreaks by selling poultry immediately; this will provide an entry point for disease transmission not just between birds, but possibly between birds and humans. It is also noted that risky behavior in the disposal of dead poultry was a common practice among households surveyed, e.g., disposal of dead poultry or inedible poultry parts in rivers, both of which are likely factors in disease transmission or spread. It is important that farmers are made aware of the proper way of handling dead poultry and that accessible and appropriate disposal mechanisms and facilities are put in place to make safe disposal possible. Support is also necessary in terms of information dissemination, especially information on handling techniques, preventive actions, technical assistance, and good management practices, so that farmers are well informed about this disease and effective ways to deal with it. Respondents highlighted government programs and actions as important for establishing and maintaining an effective AI control strategy.

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3.5. Assessing the feasibility of the OR interventions

Abstract

As part of the operational research to develop more effective control interventions for highly pathogenic avian influenza in Indonesia, the feasibility of control interventions was assessed from a logistic, economic and institutional perspective. The operational research set out to evaluate three intervention approaches implemented in the context of the ongoing participatory disease surveillance and response program. These interventions were two approaches to mass vaccination and an enhancement to the outbreak response culling and compensation program to provide on-the-spot compensation rather than the time-consuming reimbursement procedure in place. The research showed that was logistically and technically feasible to mount a mass vaccination program in smallholder poultry that suppressed the incidence of HPAI outbreaks, but that the approach was costly to implement effectively and faced many hurdles in terms of economic incentives for participation and institutional capacity to support implementation. The overall recommendation was that vaccination can be used effectively, but should be implemented in a targeted manner that focuses on critical control points and is integrated within a range of bio-security and containment interventions.

1. Introduction

Operational research is scientific investigation embedded in the ongoing field programs that the research is intended to benefit. Operational research seeks to enhance interventions, strategies, or tools used in the programs. It is designed to assess effectiveness or test the feasibility of interventions in routine practice settings (Zachariah et al., 2009). In addition to assessing the impact of interventions selected by stakeholders, ORIHPAI assessed the feasibility of implementation of control interventions over both the short and the long term in the context of real control programs. Feasibility studies have been defined in a number of ways, but generally take into account the context, resources and probability of success of an undertaking in a specific setting (Justis and Kreigsmann, 1979).

In assessing the feasibility of ORIHPAI control options in Indonesian poultry, three aspects of feasibility were considered:

Is it technically and logistically feasible?

> Given the available managerial, human and physical resources, is it possible to implement the intervention? This is the straightforward nuts and bolts operational question that asks if all the equipment, trained personnel and capacity to manage the resources to deploy the intervention are available. Although straightforward, this is a critical area that is often neglected in selecting and planning interventions.

Is the proposed intervention economically viable in terms cost-effectiveness, sources of funding, and incentives for stakeholders to sustain the intervention?

> This question asks if interventions make economic and livelihoods sense at a number of levels of scale. At the coarsest level, an intervention will need to have an attractive cost-effectiveness or benefit-cost ratio. However, this by itself does not mean an intervention is feasible. Consideration must also be given to how the benefits and costs are distributed across the various stakeholders involved in production and control processes and what the incentives (or disincentives) are for key actors to participate in the proposed intervention.

Is the proposed intervention feasible in within the animal health institutional context of Indonesia?

The term “animal health institution” is being used in the social science sense. In this case, it refers to all the organizations and stakeholders that come together to effect delivery of animal health services and the “rules” that govern their interactions (Aligica, 2006; Hogdson, 2006; IFAD 2011). Examples of key animal health organizations and stakeholders that make up the animal health institution are the producers, market actors, public veterinary services (national and local), private veterinarians, veterinary and producer associations, input suppliers, etc. Examples of rules that shape the relationships between the actors in the arena of animal health service delivery are policies, laws, regulations, customs, values, expectations and ethics. So, this question asks If the set of organizations active in animal health service delivery and the rules that govern their interaction are conducive to successful delivery of a proposed control intervention over the short and long term.

The three questions are areas of focus that help clarify the analysis that are all interlinked. For example, the institutional environment shapes the stakeholder incentives for implementation, and policies often shape incentive systems. In addition, the availability of physical resources is in part determined by funding options and perceived return on investment.

This feasibility analysis synthesizes information from a number of components of the operational research with data on the extent of intervention implementation.

2. Methods

In ORIHPAI, the feasibility of three control interventions was assessed by test implementation of the interventions in representative poultry populations and contexts. Populations of sufficient size (100,000 chickens) in 16 districts were selected so that both population level immunity effects and realistic elements of logistical and institutional complexity were part of the analysis. The three control interventions tested were: 1) focal culling, with immediate cash compensation; 2) mass vaccination of backyard and small-scale commercial poultry for AI using an inactivated vaccine based on the Legok 2003 strain of H5N1 AI virus; and 3) mass vaccination of backyard and small-scale commercial poultry against AI and ND using an inactivated vaccine based on the Legok 2003 strain of H5N1 AI virus and a live ND vaccine containing the HB1 stain of ND virus.

The culling and immediate compensation strategy involves disbursement of small sums of money to large numbers of people. The system in place prior to the operational research required poultry owners to apply for compensation through the local government to a national compensation fund. The procedure required several months to effect payment and this was believed to be a major disincentive to poultry owner participation in culling programs. As part of the operational research, the MoA proposed that funds be advanced from the national fund to districts so that they could effect immediate payment at the time of culling.

The ORIHPAI vaccination campaigns were donor funded with a publically managed cold chain and vaccination delivery system. Vaccination was offered free of charge to poultry owners. The mass vaccination was carried out to see if it could be used as routine program to reduce the number of outbreaks and disease transmission.

Data on the extent of the implementation was synthesized with the results of the participatory impact assessment and targeted studies (i.e., economics, impact, livelihoods, and district profiling). Observations by stakeholders and the sharing of lessons learned by key participants enriched the process. Thus, the feasibility study drew on all aspects of the research and included assessment of epidemiological, economic and livelihoods indicators, such as sero-prevalence rates, the cost per vaccination, and the impacts of HPAI. The analysis took place during partner meetings that brought together the GoI, ILRI, FAO and JSI.

In order for an effective vaccination campaign to be logistically feasible, a checklist of criteria was assessed. This checklist consisted of:

- A safe and effective vaccine that stimulates immunity against circulating field strains was available;
- An effective system of management and coordination was in place;
- A well-functioning cold chain was in place at all levels of the distribution system;
- Skilled vaccinators who are accepted by the community were available;
- Appropriate vaccination materials were available where needed in sufficient quantities; and
- The program was designed and delivered in a manner that meet farmer's needs.

The methods used in the economic (cost-effectiveness and willingness-to-pay) and livelihoods assessments are presented in their respective sections (Sections 3.3, 3.4 and 4.3). For economic feasibility and sustainability, the following criteria were considered:

- The intervention was cost effective;
- Sustainable sources of funding were available; and
- Incentives for participation (not necessarily monetary) were present for key actors (service providers and poultry owners).

In order to determine if the interventions were feasible from an institutional perspective, five key questions were asked:

1) Was the intervention suited to achieve institutional objectives?
2) Were government policies and regulations on disease control, service delivery and financial control compatible with the proposed intervention?
3) Were there incentives or motivations for stakeholders at all levels (farmers, vaccinators, *Dinas* (local and central government), and international organizations to participate?
4) Was it possible to implement in a coherent manner within the governance environment?
5) Did animal health institutions (public, private and civil components) have the capacity to carry out the intervention?

3. Results

The culling and immediate compensation treatment group was found not to be feasible early in the life of the project and was abandoned for institutional reasons. No mechanism could be identified to advance funds for compensation from central to local governments that met national standards for financial control.

The two vaccination interventions (AI only, and AI+ND) were fully implemented and pursued through to the completion of the project. On average, 2.9 million birds were vaccinated (received primary and booster injections) in each round of vaccination. Vaccination campaigns were implemented in 16 districts within three provinces. In these districts, 73 sub-districts out of a total of 360 sub-districts were selected to be included in the vaccination campaign. A total of 722 villages were covered. During the four vaccination campaigns, more than 23 million doses of vaccine were administered. A total of 1,088 vaccinators (VMs) and 64 vaccination coordinators (KVMs) were involved per campaign and vaccinated on average 182 birds/vaccinator/day.

Community vaccinators, working under the supervision of KVMs, performed the vaccinations. The total number of poultry vaccinated per district is shown in Table 3.5.1. There is considerable variation in the number of birds vaccinated from district to district and from campaign to campaign. However, in each round of vaccination, most districts came very close to (or in some cases exceeded) the target of vaccinating 200,000 poultry.

After the initial round of the first vaccination campaign, vaccination-induced poultry mortality was reported from some villages in the districts of Gunung Kidul, Klaten and Sleman. This may have caused lower participation in the second round, particularly in Klaten. Mortality was not reported in subsequent campaigns.

Table 3.5.1: Total Number of poultry vaccinated during the first, the second, third and fourth vaccination campaigns

District	Campaign 1		Campaign 2		Campaign 3		Campaign 4	
	Initial	Booster	Initial	Booster	Initial	Booster	Initial	Booster
Yogyakarta								
Sleman	108,038	106,085	116,333	119,277	100,537	82,730	99,928	99,928
Kulon Progo	169,809	179,948	175,453	188,998	199,045	181,286	199,076	198,559
Gunung Kidul	176,492	194,618	203,834	205,825	199,108	205,334	202,527	207,036
Bantul	166,757	185,641	191,862	192,457	191,484	192,864	192,434	194,524
Central Java								
Brebes	196,897	196,942	189,687	192,811	193,498	192,661	193,350	195,843
Grobogan	210,982	213,257	209,731	206,456	207,104	207,251	208,242	203,549
Kendal	206,616	205,867	207,457	207,354	205,727	207,378	208,178	206,825
Klaten	205,537	176,022	215,670	214,962	214,946	214,738	212,166	213,367
Purbalingga	116,311	124,669	147,269	138,996	142,048	140787	167,199	149,891
Semarang	203,768	208,997	201,067	204,927	211,231	205,303	218,138	205,535
Temanggung	199,585	192,428	192,428	178,622	182,667	178,733	184,996	187,008
West Java								
Kuningan	206,991	206,168	203,401	199,025	204,079	197,514	201,197	203,229
Cirebon	143,493	143,265	167,881	172,667	166,773	119,799	173,631	171,066
Sumedang	212,783	216,132	215,732	215,192	217,664	207,149	213,339	209,279
Majalengka	130,020	165,287	177,307	188,446	190,147	156,589	196,586	198,428
Indramayu	208,540	212,917	211,610	170,948	210,900	207,706	225,171	233,858
Total	**2,862,619**	**2,928,243**	**3,026,722**	**2,996,963**	**3,036,958**	**2,897,822**	**3,096,158**	**3,077,925**

Source: ORIHPAI, 2009

The logistics criteria checklist was generally met in the course of implementation, although a number of areas required reinforcement:

- Evidence was available at the outset to demonstrate that vaccines based on the Legok 2003 strain were safe and provided effective immunity in the face of circulating field strains (60, 90 and 100% protection against three Indonesian field strains)(Swayne, 2007).
- The operational research (especially FAO and GoI) established a strong management and coordination team to oversee logistic assessments, timely procurement and disbursement of vaccines and materials, and design of capacity building activities to fill skills gaps. The complexity of this task was daunting given the quarterly vaccination schedule where each round of vaccination consisted of a primary inoculation, followed by a booster after three weeks.

- An assessment of the cold chain found that facilities and quality control procedures needed significant strengthening, and action was taken to establish cold chain facilities and training in all 16 operational research districts. This was a major area of investment. All OR districts were provided with equipment, and extensive monitoring of cold chain implementation was done. Project staff performed monitoring visits after each vaccination campaign, and it was found that overall the cold chain performed adequately, particularly at the district level. Improvements were needed in some districts to maintain the cold chain for the vaccine from the district office to the birds; these improvements were mostly a question of improved cold boxes for transport and better refrigerators at the sub-district level.
- Community vaccinators and vaccination coordinators were selected from local communities and trained in all OR districts.
- Vaccination materials were purchased by the implementing projects and distributed to vaccination teams.
- A significant percentage of the community presented poultry for vaccination over the course of a one-year long campaign, suggesting that this criterion was marginally met.

Therefore, the implementation of the mass vaccination campaign in backyard poultry was logistically feasible in the 16 ORIHPAI districts, given that major investments were made to strengthen management, cold chain facilities and staff capacity.

The serology results indicate that the vaccination campaign achieved moderate coverage and the results of the PIA system, analysis of transmissibility, and PDSR database indicate a moderate suppression of the incidence HPAI-compatible outbreaks.

The economic feasibility criteria were only partially met:

- The cost of vaccination per bird saved was higher than the market value of poultry (Section 3.3).
- The measure was found to be relatively costly (US$ 0.12/injection or US$ 0.24/vaccination) especially when appropriate management and logistical investments were made to assure effective vaccination.
- The annual cost estimates for generalization of the mass vaccination to the national backyard poultry population was US$ 288 million, far exceeding available funding.
- The willingness-to-pay assessment suggests that poultry owners would contribute to the cost of vaccination if requested.
- No evidence was obtained during the operational research that HPAI vaccination increased the market value of poultry

In terms of institutional feasibility:

- Vaccination programs, if applied with concerted effort, are capable of suppressing disease, reducing the risk of human exposure, and are suited to national control objectives.
- Government policies and regulations are partially suited to successful application of the intervention. The high level of decentralization requires considerable input into coordination, management and training of a large number of implementing partners. One of the principal findings of the profiling studies of the 16 districts was the power of the district government to determine disease-control policies, as well as the considerable variation in the practical execution of HPAI-control measures across different districts.
- The incentives used to drive the vaccination program were largely externally derived (donor driven) and lacked sustainability. The vaccination activity was essentially approached as an emergency intervention, and little effort was made to structure the program in a manner that would capture stakeholder needs as drivers.
- It is possible to implement the interventions in a coherent manner, given the governance of the backyard and small-scale commercial sector.

- The program created the necessary technical capacity through tailored training programs, and it supplemented management capacity with contracted coordinators and logistics staff. It is not clear that the authorities would have been able to maintain the quality of implementation in the absence of continued assistance.

Discussion

Technical and Logistical feasibility – The ORIHPAI has shown that it is logistically feasible to mount a mass vaccination campaign in backyard poultry in Indonesia. A cold chain was put into place in 16 districts and more than 23 million doses of vaccine were administered by 1088 community vaccinators over four vaccination campaigns in 73 sub-districts, comprising about 20% of all sub-districts in the 16 ORIHPAI districts, or a total of 722 villages. The level of implementation led to a statistically significant reduction in outbreaks compatible with HPAI.

Vaccination coverage and impact – The prevalence of chickens with titres $\geq \log_2 4$ at the time of the sero-monitoring visits was approximately 30% for H5, although it ranged from 20-45% in the different districts over the different rounds. These levels were attained by supplying a booster to all poultry presented for vaccination three weeks after an initial vaccination. Laboratory trials showed that a booster is needed to develop a high titre especially for young birds vaccinated for the first time. However the booster round in every campaign doubles the total rounds per year.

No cumulative effect in the proportion of the population with H5 titres was shown over the consecutive campaigns. The proportion of chickens younger than two months of age is 40% in backyard poultry flocks, indicating that the population turnover rate is high. The high level of poultry population turnover is one of the main constraints to achieving a high level of population protection and, because of this, vaccination needs to be repeated at least every three months in mass vaccination programs.

PIA data showed that the moderate levels of HPAI vaccination achieved in the treatment groups suppressed HPAI-compatible events in vaccinated areas by 46% compared with control areas. Suppression of HPAI outbreaks was also shown in PDSR data from the same areas. The PIA measured clinical disease and it can be speculated that vaccination caused some cases to be less severe, or sub-clinical, rather than fully prevented. If this was the case, the results would still be consistent with an overall reduction in the amount of circulating virus, and thereby lower risk of transmission.

The impact of the mass vaccination was achieved by using the Legok 2003 H5N1 vaccine, the vaccine strain best matched to field strains circulating in Indonesia at the time of the research. A greater impact might have been achieved by using a vaccine containing a more recent strain or a multivalent vaccine containing multiple strains, if such a vaccine had been available.

The ORIHPAI results demonstrate that with the relatively low level of vaccination coverage achieved and by using the Legok 2003 H5N1 strain, the incidence of HPAI-compatible events in backyard poultry was reduced but not eliminated. Therefore, to further control the spread of HPAI, vaccination coverage should be intensified (perhaps by targeting critical points or populations) and/or vaccination should be used in combination with other control measures, such as increased bio-security.

Economic feasibility – Major cost components were the cost of the HPAI vaccine (35%) and vaccinator cost (27%). Therefore the total cost would have been much higher if more sub-districts had been included in the campaign. The vaccination campaigns were publicly funded and vaccination was provided free of charge. A willingness-to-pay survey indicated that households are prepared to pay an amount between US$ 0.02-0.03/vaccination. This is a positive finding but lower than the estimated cost of HPAI vaccination of US$ 0.10/treatment under vaccine delivery systems studied in the ORIHPAI project. Even if cost sharing was applied at the level of these estimates, 70-

80% of the cost of a mass vaccination campaign in small-scale commercial and backyard poultry would still not be covered.

In ORIHPAI, it was shown that poultry will be presented when vaccine is offered free of charge. Cost sharing can have complex effects on the level of vaccination coverage. In public sector-dominated campaigns, it can reduce the level of participation. Cost sharing combined with public/private partnerships to deliver services can enhance community ownership and increase participation, as well as the quality of implementation.An interesting area for further action research would be to test different cost-sharing strategies to more fully develop the knowledge base in this area for decision-making. For example, the commercial farms may be interested to contribute to community programs in their immediate area to reduce risk to the commercial farms.

Whereas cost-sharing might lower the share of the cost of the vaccination campaign borne by the government, public/private partnerships to provide cold chain management and vaccine delivery could be explored as options for reducing total costs and enhancing incentives, leading to more efficient campaigns both in economic and epidemiological terms.

Institutional feasibility – Assessing the feasibility of a proposed intervention includes assessing its appropriateness in the broader institutional context.

Is mass vaccination consistent with the Indonesian HPAI control policy?

HPAI is an endemic disease in many areas in Indonesia. Indonesian policy has embraced vaccination, including mass vaccination, as a control measure. Current policy is shifting, but is leaning toward targeted vaccination. However, guidelines for targeting need to be clearly defined, particularly in terms of risk targets, poultry population targets, public resource utilization and private sector engagement. It is doubtful that geographically wide-scale, publicly funded mass vaccination should be part of a government program. The resource demands far exceed both human and financial resource availability, and the cost/benefit ratio as identified in the OR (cost per value of bird life saved) is less than one. It would be more appropriate to target vaccination on clearly defined risk points in value chains or very specific high-risk locations. Another option is to ensure the availability of vaccine to farmers in a private capacity as insurance against disease outbreaks. Mass vaccination could be justified if evidence indicated that it would lead to a significant reduction of outbreaks and that it could eventually be replaced by other control measures as an exit strategy. A holistic analysis of national policy objectives will inform the decision as to the best use of vaccination in the overall national strategy. Enough resources have to be made available to implement this policy successfully. As the willingness-to-pay study indicated that cost sharing would cover only a part of the cost in the backyard sector, the policy will have to include some public sector support. The public health impacts of HPAI justify that the public sector remain engaged in the control effort.

Is mass vaccination of backyard poultry likely to assist disease control?

With the sheer numbers of poultry and their high population turnover, it will not be possible to control HPAI solely through vaccination in vast areas in Indonesia. The OR demonstrated that mass vaccination could reduce the incidence of HPAI-compatible events. However, unless vaccination continues, population immunity will disappear within six months due to the short duration of immunity and high population turnover resulting in a resurgence of HPAI. In addition, public fatigue would lead to declining vaccination rates as mass-vaccination campaigns continued over time. If mass vaccination is applied it should be have clear achievable objectives and be time-limited in line with program objectives, and a vaccine strain should be used that gives the solid protection against infection and virus shedding. As reported by OFFLU in November 2009, new vaccines are becoming available and the Legok 2003 H5N1 strain will eventually become obsolete.

What are the incentives for the different stakeholders?

Cost/benefit analysis of the ORIHPAI vaccination campaigns indicates that the value of the estimated loss due to poultry deaths averted by vaccination was lower than the total cost of the vaccination campaigns. However, other indirect economic losses caused by HPAI are not included in this estimate, for instance the loss of market value. For HPAI, a zoonosis, loss of human life that can be prevented by reducing HPAI incidence in poultry should also be considered. Thus, it has been argued that overall economic and public health incentives justify control. Unfortunately, even if justification exists, national and even international public resources are insufficient to sustain an open-ended commitment to vaccination on a meaningful scale.

Incentives for individual poultry owners to vaccinate their poultry are related to their assessment of the risk of losing poultry in relation to the cost of vaccination. This becomes even more important if cost sharing is introduced in mass vaccination. Further consideration of incentives is needed for both the backyard and commercial sector. Large commercial farms might find it worthwhile to vaccinate surrounding smallholder farms to reduce the risk of HPAI on their premises. This is already being done in some ORIHPAI areas.

Does mass vaccination fit in a decentralized environment?

Mass vaccination campaigns are more difficult to implement in countries with a decentralized veterinary service. If bordering districts are not all involved in the same level of HPAI control and vaccination, the impact of mass vaccination will be reduced because HPAI is an infectious disease that does not respect borders.

Conclusions

The ORIHPAI has shown that it is logistically feasible to mount a mass vaccination campaign against HPAI in backyard poultry. Vaccination was shown to suppress HPAI-compatible events and this was consistent with the objective of the program. As was expected, it did not stop outbreaks from occurring. To maintain mass vaccination campaigns for indefinite periods, or to expand them to more areas, involves large recurrent costs. Ultimately, vaccination is just one tool to achieve a specific time-bound objective within a broader program. It needs to be combined with other control measures. An institutional strategy that devolves costs to beneficiaries or discontinues the vaccination activity in a responsible manner needs to be a part of disease control planning.

For vaccination (or any control measure) to be implemented successfully, it is extremely important that all stakeholders have incentives and motives to participate. As well as the local and central levels of government, key stakeholders are the implementers of the vaccination campaign (vaccinators) and the recipients (poultry owners and commercial producers). For vaccination strategies to be feasible and sustainable over the long term, the financial and non-financial incentives for participation must also be sustainable. If a public/private partnership approach were adopted, incentives for private veterinarians and commercial suppliers would also have to be an integral part of the program's structure. Partnerships and cost sharing are important areas for further innovation and action research.

The ORIHPAI has provided valuable information about the implementation of mass vaccination campaigns against HPAI and shown that it is an effective tool for specific purposes. In formulating a control program, it is essential to set epidemiological and economic objectives that guide the selection of appropriate tools. At what scale and in which areas vaccination will be used as a HPAI control strategy in Indonesia will ultimately depend on the GoI's policy and the technical information on the performance of vaccination as a tool for the control of HPAI. The confirmation that mass vaccination suppressed but did not fully interrupt transmission within vaccination zones indicates that mass vaccination is an open-ended commitment. The high cost and level of impact of publically executed mass vaccination in backyard poultry suggests that public sector-driven mass vaccination would not be a sustainable HPAI control intervention in backyard poultry. Targeting vaccination to high-risk populations/areas should be considered as an alternative to mass vaccination and applied in conjunction with other control measures such as improved bio-security, and models should be developed for public/private partnerships that link government, private sector suppliers and service delivery agents with communities. This would allow available resources to maximize the impact on HPAI incidence.

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4.0 Targeted Studies

The targeted studies are specific research activities that were not directly dependent on the longitudinal study, but that complimented it. These studies identified a number of research questions that add value to the longitudinal study, enrich the overall analysis of the operational research, and enhance the database available for disease control decision-making. Our targeted studies include:

- A district profiling study to collect baseline information on the poultry production and marketing systems, as well as animal health institutions at the district level. These were carried out in all 16 operational research districts.
- A livelihoods study to provided baseline data and contextual information on the role of poultry in households and local communities. This information is useful for understanding the impact of disease and control interventions and sheds light on incentives for participation in control programs. This study was carried out in three operational research districts.
- Small-scale vaccine trials were completed at the Wates Laboratory to provide information on specific vaccination protocols (age of vaccination, number of injections, dosage) and the levels of sero-conversion achievable in Kampong poultry in the face of inter-current disease challenges typical of the local environment. In addition, a small-scale community trial was completed where poultry were marked and poultry movement and off-take was not controlled. The purpose of the community trial was to document the levels of antibody prevalence that could be achieved under natural conditions when inoculations are carefully supervised and documented.
- Three analytical studies on the original PDSR data to provide background information on the epidemiology of the HPAI disease challenge in the study area, and more generally on the risk factors associated with disease detections.
    - Spatial and temporal patterns of HPAI outbreaks;
    - Content analysis of clinical course and risk factors associated with infection using text-mining software: and
    - Multivariable analysis of risk factors associated with detection of disease by the surveillance system.
- An assessment of the sensitivity and specificity of clinical case definitions in the diagnosis of sudden death and HPAI-compatible disease added to the evidence base on the use of clinical diagnostic methods in surveillance.

4.1 Profiling the ORIHPAI districts

Abstract

Three distinct profiling activities were carried out as part of the ORIHPAI project to better understand the environment in which HPAI is circulating and control measures are implemented. The results demonstrated the diversity in poultry husbandry and management across Java, indicating that it is difficult to generalize on the poultry situation. Some characteristics of the poultry industry that likely contribute to the spread of HPAI in Indonesia were identified, such as regular long-distance movements of poultry, the common practice of off-site waste disposal for abattoirs, mixing of different species at markets, apparent poor bio-security standards on commercial farms, and the ubiquitous importance of traders. The risk associated with these realities should be fully characterized in order to identify the most feasible and effective mitigation measures.

1. Introduction

The dynamics of HPAI infection in a population will depend on many different factors, including the bird species present, densities of the respective bird populations, poultry husbandry practices, marketing practices, human population density, the community and veterinary response to the detection of clinical disease, etc. Profiling activities were carried out as part of the ORIHPAI project to better understand the environment in which HPAI is circulating and control measures implemented. A rapid assessment was undertaken in all 16 districts participating in the project, providing an overview of the role of agriculture in the district with emphasis on poultry enterprises. The Participatory Impact Assessment (PIA) teams conducted short surveys in each of the neighborhoods that they visited to characterize the randomly selected sites used to assess the impact of the longitudinal study (Section 3.1). Finally, a detailed survey focusing on bio-security and marketing practices was done in 3 districts.

2. Methods

Three profiling activities were carried out as part of the collection of background information on the districts:

1) A questionnaire implemented in each OR district by the PIA teams.
2) A rapid appraisal carried out in each of the 16 districts by a member of the OR technical assistance team.
3) In-depth survey implemented in three districts by the non-governmental organization (NGO) Crescent.

The district profiles provide an overview of the poultry industry in the districts participating in the OR and provide background information on risk factors of interest to HPAI epidemiology.A rapid rural appraisal approach was used. Rapid rural appraisal is a set of techniques that can be applied at a preliminary stage when embarking on new study. The technique involves an informal, rapid, exploratory study of a specified geographical area designed to establish an “understanding” of local agricultural conditions, problems and characteristics (Crawford, 1997). These appraisals can provide basic information on the feasibility of beginning a survey project in an area, particularly when one is intending to survey an area about which little is known. The advantage of this technique is that it allows for cost-effective data collection that can yield very accurate and unbiased results when performed by skilled practitioners (Chambers, 1994).

In this case, a checklist was prepared outlining the general objectives and information sought. The rapid appraisals involved participatory data collection using semi-structured interviews with *Dinas* staff, poultry keepers, commercial poultry farms, traders and slaughterhouse managers to determine the characteristics of each district with respect to poultry management, movement, markets and other risk factors. Key poultry sites by sub-district and movement of poultry and poultry products were recorded and mapped for each district.

The district profiles were complemented by an in-depth survey in selected districts. This survey provided a snapshot of the poultry industry with respect to factors that might be important in the transmission of HPAI. The survey was designed by ILRI and implemented by the NGO Crescent in three districts on Java (Kuningan, Semarang and Kulon Progo). From 25-31 August 2008, enumerators visited commercial poultry farms, collection points, live birds markets, poultry shops and poultry abattoirs in each of these districts, geo-referenced the premises and administered a short questionnaire.

Reports from all 16 districts and the questionnaire survey from the 3 districts were translated into Bahasa Indonesia and shared with the Campaign Management Unit (CMU), and the relevant the provincial and district *Dinas,* together with a district-specific analysis of data from the original PDSR database showing the cases detected over time and the application of control measures.

3. Results

The district profiles demonstrated the diversity in poultry husbandry and management across Java, indicating that it is difficult to generalize on the poultry situation. However, some common themes were found:

- Scavenging ducks were very mobile and moved in and out of districts according to the rice harvest, making estimates of duck numbers in districts with scavenging ducks unreliable.
- There was generally poor understanding of HPAI among the people interviewed, but especially the market traders and slaughterhouse managers.
- Despite the effort made in community awareness on HPAI through multiple media, most people interviewed received their information from the television.
- Understanding of bio-security was poor and usually only a few of the recommended practices were used. Some examples:
  - Poultry carcasses (including deaths due to HPAI-compatible disease) were commonly dumped in the local drainage systems and rivers, hence enhancing the spread of the disease.
  - Some of the commercial farms allowed their workers to move in and out of the premises with limited precautions, e.g., changing street clothes.
  - Transport vans were frequently permitted to bypass the disinfection troughs, complaining that the disinfectant corroded the vehicles' tires.
  - Some of the farmers living around the commercial farms were allowed to purchase carcasses from the farms for feeding catfish.
  - Clinically sick chickens were occasionally found being sold in the market.
  - The hygienic standards in most of the slaughterhouses were low and workers did not have protective clothing.
  - Effluent from most of the slaughterhouses was allowed to seep out to the neighboring farms.
  - Most slaughterhouses did not have good dumping sites.
  - There was trade in sick and dead birds; poultry owners and traders tended to slaughter birds immediately when they appeared sick and the carcasses were sold to restaurants, fed to catfish or thrown in the river.

Key findings from each questionnaire are summarized below:

Poultry shops:

- The enumerators visited 32 shops.
- The majority of poultry shops (78%) acted as brokers for live poultry (i.e., they sold birds not kept on the shop premises), but only 19% reported that they sold live poultry on-site.
- DOCs were the most common type of bird sold (59% of shops), followed by broilers and songbirds.
- Most shops sold poultry that originated from traders and farms within the same district and even the same sub-district where the poultry shop was located. However, 50% of shops also sold poultry that came from other provinces.
- All shops reported that at least some of the poultry they sold remained within the sub-district and only two shops reported that the poultry they sold left the province. However, many shops did not respond to this question, which probably indicates that the shop personnel often do not know the destination of the poultry they sell.
- Buyers of poultry included small-scale farms, traders and commercial farms.

Collection points:

- The enumerators visited 30 collecting points (CPs).
- Up to four different poultry types were traded within each CP, with an average of two to three types traded at each point. The most commonly traded poultry were broilers and Kampong chickens. Seven CPs indicated that they dealt with ducks, and a further seven with Muscovy ducks.
- Excluding the CPs that trade duck eggs, the median number of poultry traded on a daily basis was only 75 birds (range = 5-4000).
- Poultry were supplied to collection points by farms and traders from all over the province, and were primarily purchased by traders and consumers from within the district.
- In our survey, 23 of 30 (77%) of CPs indicated that they sold poultry to "non-dead-end" purchasers (e.g., traders, farms) who might maintain the birds alive and thus allow any infected birds to potentially spread disease such as HPAI to other poultry.

Live bird markets:

- Enumerators visited 35 markets.
- Each of the surveyed districts had several small markets (>10 traders, <500 birds/day) and 1-2 large markets (trading >1000 birds/day).
- Markets without formal stalls are probably less likely to maintain infection with HPAI than markets with formal stalls because:
  - They are not usually open every day; and
  - They do not usually keep poultry overnight.
- Markets hosted up to eight different poultry species, with an average of three to four species being traded at each market. Kampong chickens were the most common poultry in markets, followed by Muscovy ducks and ducks.
- In most of the visited markets, fewer than 500 birds are traded on a daily basis.
- The vast majority of markets reported that the poultry traded originated primarily from within the same district and often the same sub-district as the location of the market. Most markets also reported that the poultry traded usually remained within the district after being sold.

- Overall**,** owners of backyard poultry (household farmers with ≤ 20 poultry) and traders were the main vendors in all markets, and individual consumers were the most important buyers. In this survey, 89% of markets indicated that some poultry were sold to non-dead-end purchasers, and the poultry purchased were likely to contact other live poultry.

***Abattoirs*:**

- Enumerators visited 44 abattoirs.
- The majority of the abattoirs slaughtered broiler chickens exclusively. Most slaughtered only one species, although two killed up to four different species.
- The median of poultry "usually" slaughtered per day was 90 (range 20-1500).
- Most abattoirs receive poultry from traders and commercial farms within the relevant district. However, several abattoirs (57%) reported that some poultry originated from outside the district and/or outside the province (19% of abattoirs).
- The most common clients were individuals (presumably buying for personal consumption) and the abattoir owners themselves, who would then sell the carcasses directly to market or else to a trader.
- Feeding fish was a common form of disposal for all types of abattoir waste, except feathers, which were usually thrown away or used as compost/fertilizer.
- Waste disposal was usually *off* the abattoir premises, which represents a possible method of spreading disease, including HPAI, should live poultry come into contact with the waste.

***Commercial farms*:**

- Enumerators visited 152 farms: 57 layer farms, 79 broiler farms and 16 other types of farms that included hatcheries, duck and quail farms.
- The median population on layer farms was 10,000 birds (range: 200-100,000) and 5,000 birds for broiler farms (range: 0-43,000).
- Almost all of the broiler farms (95%) were contract farms; this was consistent for both large and small farms.
- 63% of the layer farms reported being contract farms. Stratified by poultry population, 81% of small farms were contractors, whereas only 36% of the large layer farms were contractors.
- Most farms reported that barns were empty between production cycles, however less than half of the farms visited reported that the entire farm was empty between production cycles.
- Small layer farms mainly sourced new birds from poultry shops and traders, while big layer farms sourced from commercial farms and partnership companies. Poultry on all layer farms most often originated from other provinces, especially for small layer farms.
- Most poultry raised on commercial broiler farms came either from within the district (particularly for small farms) or within the province (for large farms). Most broiler farms sourced their new birds/eggs from poultry shops and partnership companies.
- Some layer and broiler farms reported that the poultry/eggs they produced would be transported outside of the province when sold; this was more common in layer farms (35-39%) than broiler farms (10-19%).
- Overall, traders and individual buyers formed the largest bulk of buyers from commercial layer farms. Poultry shops were the most common buyers from small commercial broiler farms while both poultry shops and partnership companies were the main buyers from large commercial broiler farms.
- Enumerators' observations suggest that there is plenty of room for improvement in some important bio-security practices: only 14% of farms were observed to have footbaths, and

enumerators were queried about previous poultry contact on only 4% of farms. Practices were slightly better on layer than broiler farms.

Discussion

These studies were specifically designed to characterize the districts participating in the ORIHPAI project. No comparable previous studies were found in the literature. Concurrent projects also provided some insight to poultry raising in the region, however with a focus on commercial poultry operations (FAO, 2008).

Prior to the mass vaccination implemented during the OR, there was no consistent HPAI vaccination policy across the 16 districts. Some districts implemented a considerable amount of vaccination, others hardly any. Some vaccinated both chickens and ducks, others only chickens. Because HPAI is an infectious disease that does not respect borders, disease control practices in one district will impact HPAI incidence in nearby districts, or even in remote districts that are linked by trade. Therefore it is important that bio-security and vaccination practices are improved across all areas.

The profiles highlighted some characteristics of the poultry industry that likely contribute to the spread of HPAI in Indonesia. For example, all types of premises (farms, markets, shops, etc.) reported that they engage in at least some inter-provincial poultry trade, particularly poultry shops and layer farms. Because the movement of poultry and poultry products is an important contributor to the spread of diseases, including HPAI, it is important to understand the nature of the movement and consider ways to minimize the associated risk, while also considering the impact on the livelihoods of the people involved.

Other practices that likely contribute to the spread of HPAI (and other infectious diseases) include the common practice of off-site waste disposal for abattoirs, mixing of different species at markets, apparent poor bio-security standards on commercial farms, and the ubiquitous importance of traders. The risk associated with these realities should be fully characterized in order to identify the most feasible and effective mitigation measures. Furthermore, the profiling highlighted the power of the district government to determine disease-control policies, as well as the considerable variation in the practical execution of HPAI-control measures across different districts. This can dilute the ability of a central disease control directive to effectively control disease (Sims, 2007).

Conclusion

The findings contained with the district profiles and the survey conducted by Crescent demonstrate the diversity in poultry husbandry, management and trading practices across the districts that participated in the OR project. We found that there is considerable room for improvement in bio-security practices at all levels of the poultry industry, from backyard birds to commercial birds to the marketing and slaughtering systems.

References

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4.2 Study of poultry livelihoods

Abstract

The effects of sudden poultry deaths were evaluated in this study across three districts in Java: Cirebon, Semerang and Kuon Progo. Qualitative information regarding livelihood impacts, as well as the incentives and disincentives to participation in control programs was obtained. Strategies for promoting HPAI-control programs among small-scale farmers were also identified. Poor households were clearly the most vulnerable and were disproportionately affected by the sudden death of poultry due to disease because they rely on poultry rearing for additional income (additional to crop production income), for savings, or for emergency cash to cover a range of costs, such as buying food and paying school fees and electricity bills. Moreover, income from poultry often fills the income gaps that arise due to the seasonality of crop production.

The spread of HPAI, because of its negative effects on poultry prices, affects household consumption of all food commodities, especially among poor households. Women are often responsible for rearing poultry and managing the income generated from the enterprise, and may therefore be more heavily affected by poultry losses than other household members. Despite the frequency of past HPAI outbreaks, farmer knowledge about the disease and its control remains limited. Special efforts are underway to provide information, educate farmers, and promote their understanding of and participation in various control programs.

1. Introduction

While remarkable strides have been made in global and national assessments of the impact of HPAI on smallholder poultry keepers, less concerted effort has been made towards understanding the effects of mitigation strategies on people's livelihoods in affected countries. Indonesia is of particular interest because of the many cases of HPAI-related deaths, both in domestic and wild birds. A systematic program of control measures was sanctioned in three Indonesian districts. We present here findings about the implementation of these measures, focusing on community perceptions of the performance of the control measures and the factors that influence community participation in various intervention programs. It is envisioned that this information will form a basis for a better understanding of effective and socially equitable control measures and implementation strategies appropriate for different sectors and household producer types.

Our study was carried out in Cirebon, Semerang and Kuon Progo districts. The objectives of the survey were to: obtain comprehensive qualitative information on the impacts on local livelihoods in relation to the control measures of HPAI; understand the incentives and disincentives to participation in HPAI vaccination programs from livelihoods perspectives; and identify strategies to enhance the relevance, acceptability and ownership of HPAI vaccination programs by small-scale farmers. The study was led by a livelihoods' specialist from ILRI and the survey was team drawn from the University of Bogor, International Center for Applied Finance and Economy. Our study was carried out from 14 June 2009 to 7 July 2009.

2. Methods

PRA tools, such as community mapping, proportional piling, ranking, matrix scoring/ranking, in-depth interviews and focus group discussions were used to collect data on district and village resource profiles, wealth ranking, and the role of poultry in community livelihoods. Information was also obtained on the constraints to and opportunities for poultry production, the impacts of HPAI and ND on livelihoods, and the institutional dynamics for managing HPAI. Insights into gender and other crosscutting issues were also obtained. With regard to interventions, information was collected on their history and effectiveness, incentives and disincentives for community participation, livelihood impacts, and strategies and institutional linkages in implementation.

To enable comparison with results from a previous household survey by ILRI on cost-effectiveness of HPAI control in Indonesia, the villages in the first survey were selected for the current one, but emphasis was given to those where vaccinations were used as a control measure. In a specific district, villages were selected where different HPAI control programs had been introduced, specifically HPAI vaccination and HPAI + ND vaccinations.

3. Results

3.1. Community livelihood analysis

Livelihood strategies can be categorized as on-farm, off-farm or non-farm. On-farm refers to agricultural activities that are based on natural resources, such as crop farming, livestock rearing and fisheries. Off-farm refers to the processing of the products yielded by on-farm activities, while non-farm refers to activities outside and unrelated to farming.

The livelihood strategies of the people in the survey locations include crop farming, livestock rearing, regular employment, artisanry, business, unskilled employment, and fish farming. Crop farming is the most important livelihood activity in all survey locations because of their favorable agro-ecological conditions. However, in Plumbon village the most important livelihood activity was regular employment in industry or government offices, due to small farm sizes and the existence of many textile and rattan furniture industries. Livestock rearing is dominant in Bergas Kidul village because of the availability of large areas of land.

Livestock rearing was the second most important livelihood activity in all survey villages (except Bergas Kidul) and yet was conducted mostly as a side activity. While considered a side activity, raising livestock has important cash- and non-cash-related benefits for farmers. Other livelihood activities vary from village to village depending on demand and include artisanry, rattan furniture making, bamboo basket weaving, unskilled employment at construction sites and trade in cash crops.

Crop farming and regular employment, respectively, are the top two sources of cash income. The relative importance of a livelihood activity as a source of cash income differs from one village to another. For example, artisanry is a main source of cash income in Plumbon and Bergas Kidul, but is conducted only as a side activity in Truko, Krembangan and Jatimulyo. Likewise, business is a main source of cash income in Plumbon and Krembangan, but is conducted only as a side activity in other villages. Unskilled employment is a main source of cash income in Ciawiasih, Bergas Kidul and Krembangan, but is considered only a side activity in Truko and Jatimulyo.

With regard to trends over the past 10 years, livestock rearing has become more important because it provides additional income to pay for various needs otherwise uncovered by the main source of income. In addition, raising livestock is considered easy to do during the farmers' spare time. Livestock sales have also increased, thus making livestock the most preferred side activity. However, in Krembangan Village, this trend only applies to large livestock, such as cows, goats and sheep, because they have higher selling price than poultry. Poultry have also become less important over the past 10 years because there are many poultry diseases that still cannot be managed by farmers.

Differences related to gender can be observed from the types of livelihood strategies. Both men and women perform several livelihood activities, but there are those that are only performed by men. When the activities are performed by both sexes, there are task divisions between men and women. Differences related to gender can also be observed from the physical labor and time needed by a certain task. Men usually perform tasks that are more labor demanding and time consuming, while women perform those that require less physical labor. The types of activity can also indicate gender-related differences. For example, if the activity is the main livelihood activity, men usually perform it, but if it is a side activity then women usually perform it because it will not interrupt their domestic activities. Lastly, differences can be observed from the skills needed for the livelihood strategies, e.g., tasks that need to be done delicately and neatly, such as in garment industries, require female workers.

Men usually engage in unskilled employment because of the physical labor involved. They also engage in fish farming because of specific skills required that are usually mastered by men. Both men and women can and do engage in crop farming, livestock rearing, regular employment, and artisanry. However, a division of labor is observed when the activities are performed by both sexes. A case in point is crop farming in Truko Village, which is conducted by both sexes but women are tasked only with planting the seeds. Meanwhile, in Bergas Kidul, men usually perform crop farming. Poultry rearing is another example. Despite the fact that women perform it as a side activity, men usually clean the poultry house, especially if the poultry are kept together with other livestock. Differences in the types of livestock reared are also sometimes found between men and women. For example, Bangkok chickens are reared by men and Kampong chickens by women. Regular employment and artisanry can involved both men and women. While men usually engage in artisanry as a main activity, women conduct it only as a side activity. Another example is poultry rearing, which is carried out by men only if it is the main source of income.

As already mentioned, differences related to gender are determined by the labor needed to perform a certain activity. For example, men usually rear large livestock (goats, sheep, and cows) whereas women usually rear poultry – with the exception of Bangkok chickens, which are usually reared by men. Children may rear certain types of livestock, such as rabbits. Regarding business activities, men or women, depending on the commodities traded, may be involved. Men usually engage in trading large livestock species while women trade in vegetables or household commodities. In all survey locations, men generally perform unskilled employment.

3.2. Role of poultry in livelihoods

In general, the types of poultry reared in all survey villages are Kampong chicken, Bangkok chicken, broiler chicken, layer chicken, duck, Muscovy duck, quail, geese and fancy birds. The average number of reared poultry is determined by the mode of ownership, whether owned independently or in partnership (Table 4.2.1).

Table 4.2.1: Average number of poultry reared and mode of poultry ownership

Type of poultry	Mode of ownership	Average number per household
Kampong chicken	Independent	5-100
Bangkok chicken	Independent	2-40
Duck	Independent	2-50
Muscovy duck	Independent	2-100
Broiler/layer	Independent	100-500
Broiler/layer	Partnership	5000

Quail enterprises are only found in Krembangan village, with a range of 1000-5000 birds kept per household. Geese are reared only in Krembangan and Jatimulyo, and fancy birds in Truko and Jatimulyo, on average two birds per household in both cases. Households in Truko and Krembangan keep between 500-5000 birds on average. Women traditionally rear Kampong chickens, ducks and Muscovy ducks, whereas men rear Bangkok chickens and broilers.

In general, 80% of poultry farmers come from lower socioeconomic classes and consider poultry rearing as an important source of income. Farmers keep poultry for several reasons. One is that poultry, particularly Kampong chickens, can be sold quickly to obtain cash to pay for daily or routine needs that cannot be covered by the main source of income. Kampong chickens can also be used as assets to cover daily needs while waiting for the output of crop farming, a practice that has been adopted in Truko village. Farmers in the survey villages ranked the different roles of poultry in livelihoods on a scale of 1 (most important) to 10 (least important). The results are summarized in Table 4.2.2. In addition to contributing to household cash income (either as the main source or a supplementary one), poultry also play certain socio-religious roles. None of the surveyed villages had poultry farmers' groups, mainly because poultry were reared only on a small scale under the independent ownership mode. Sharing of information about poultry keeping was mainly done at meeting held by goat or cow farmers' groups.

Table 4.2.2: Ranking of the different contributions of poultry to farmers' livelihoods

Role of poultry	Cirebon district		Semarang district		Kulon Progo district	
	Plumbon	Ciawiasih	Bergas Kidul	Truko	Krembangan	Jatimulyo
Additional income	1	1	1	1	1	1
Hobby	3	5	5	4	6	3
Eggs and meat consumption on religious holidays	2	4	2	2	3	2
Religious/traditional ceremonies	4	3	4	3	5	5
Main source of cash		2	8	5	4	4
For needy neighbors/families		6				
Saving			3		2	
Manure			6			
Gifts			7			

3.3. Constraints and opportunities in poultry production

Table 4.2.3 summarizes the main constraints faced by poultry farmers. They generally perceived lack of knowledge as the most important constraint because they could not access information on good poultry rearing practices due to limited education. Poultry are usually reared modestly, without farmers having the knowledge on what kinds of feed should be given and how to control and treat diseases; thus chickens become more susceptible to diseases and farmers face high risk of poultry mortality. In Plumbon, sanitation was the most important constraint, followed by lack of knowledge, diseases and insecurity/theft.

Poultry diseases – Poultry farmers ranked HPAI as the most important disease (Table 4.2.4). It occurs in all survey villages and was considered important because it causes widespread poultry deaths and is transmissible between poultry species and to humans. Other important poultry diseases are ND, nasal discharge and pullorum.

Diseases that rank 1 to 4 are those that often strike poultry in the village. CRD only occurs in Plumbon and is considered the third most important disease in the village. However, it results in a fairly high mortality rate and thus should be a candidate for immediate eradication.

Table 4.2.3: Ranking of the most important constraints to poultry keeping

Constraint	D1		D2		D3		Number of villages
	V1	V2	V3	V4	V5	V6	
Diseases	2	1	2	2	3	5	All
Feed	6		2	5	5	4	5
Space and housing system	5	4	5	4		3	5
Insecurity/theft	2	4	6				3
Sanitation	1	3					2
Capital					2	2	2
Lack of knowledge	2	1	1	1	1	1	All
Predators			2	3	5	6	4
Adaptation to climate					3		1

Ranking scale: 1 (most important) to 10 (least important)

Meanwhile, coccidiosis (found in Plumbon, Ciawiasih, Krembangan and Jatimulyo), fowl pox (in Ciawiasih, Krembangan, and Jatimulyo), warts on legs (in Bergas Kidul and Truko) and scabies (in Bergas Kidul and Truko) are considered only somewhat important because farmers can easily control and treat these diseases and they do not cause a high mortality rate.

Coping strategies – Poultry farmers use various coping strategies to minimize the risksassociated with constraints to poultry production. The constraints and the corresponding strategies are described below.

Diseases: Treatment with traditional or human medicine, vaccination, selling of poultry, spraying of housing with detergent/disinfectant, maintaining housing cleanliness, and vitamins are generally used to prevent and cope with diseases. These strategies are employed so that diseases do not spread widely.

Feed: Use of alternative feeds, such as rice bran mixed with leftover rice, chopped vegetables, rice husks, and broken rice, is the main strategy used to overcome feed-related constraints. However, this strategy is not used in Ciawiasih and Jatimulyo, where feed is not considered a constraint. Other strategies include the sale of the chickens/poultry (used in Bergas Kidul) or production of rice bran during harvest time (in Truko). In addition, poultry may be simply left to scavenge for food, as is practiced in almost all survey villages.

Housing and sanitation: Poultry housing is commonly built adjacent to the farmers' houses. To maintain a clean environment, farmers routinely clean the housing and backyard. Farmers with limited space and poultry housing sell their chickens whenever the chicken population increases in order to earn income. This is the most common strategy and is adopted in Plumbon, Ciawiasih, Truko and Jatimulyo villages. In Bergas Kidul, poultry housing is modified to provide perches. In Plumbon, housings are sprayed with leftover disinfectant from crop farming activities or detergent water (laundry wastewater).

Table 4.2.4: Ranking of the most important poultry diseases

Disease	D1		D2		D3		Rank	Remarks
	V1	V2	V3	V4	V5	V6		
ND	1	2	2	4	2	2	2	Strikes in all villages and *important*
HPAI	2	1	1	1	1	1	1	Strikes in all villages and the *most important*
CRD	3							Only strikes in Plumbon Village but quite lethal
Gumboro	6	6	4	2		5		Strikes in 5 villages, but not lethal, with the exception of Truko Village
Nasal discharge	4	3	3	5		3	3	Strikes in 5 villages and quite lethal
Coccidiosis	5	5			5	6		Strikes in 4 villages but not lethal and not important
Pullorum		3	5	3	3		4	Strikes in 4 villages but quite lethal
Fowl pox		7			4	4		Only strikes in 3 villages and not important
Warts on legs			7	7				Only strikes in 2 villages and not lethal
Scabies			6	6				Strikes in 2 villages and not lethal

Ranking scale: 1 (most important) to 10 (least important)

Security: Enhancing the community watch program has been adopted in Plumbon, Ciawiasih and Bergas Kidul villages to deal with insecurity. Other strategies include increasing vigilance at night time (adopted in Ciawiasih), building fences around the poultry housing or keeping poultry together with other types of livestock in one housing unit built inside the kitchen (adopted in Bergas Kidul).

Capital: Although farmers did not explicitly state capital as a constraint, problems in building housing and providing feed are caused by lack in capital. Only farmers in Krembangan explicitly stated capital as a constraint. One of the strategies adopted to minimize feed cost is to release poultry in the morning to scavenge for food and drink. Other strategies include taking loans and setting aside a part of the income for chickens or poultry rearing costs.

Knowledge about poultry rearing: Awareness and active participation are needed to obtain comprehensive information from animal health officers and VMs in order to improve farmers' knowledge on poultry rearing. Farmers in Jatimulyo have tried to broaden their knowledge by reading books on animal husbandry. Meanwhile, farmers in Krembangan still rear poultry based on their own perceptions, particularly with regard to preventing and treating poultry diseases.

Predators: Poison is considered the most effective strategy in coping with the problem of predators. This strategy is used in Bergas Kidul, Truko and Jatimulyo. Alternatives include the use of trained dogs to locate the predators and killing them with an air rifle. In Jatimulyo, chickens are caged, while in Krembangan, farmers sprinkle salt, tobacco or kerosene around the fence to keep predators away from the poultry house.

Adaptation to climate: To deal with poultry disease during change of seasons, farmers in all the surveyed villages sell the birds in order to minimize losses. In addition, farmers share information on diseases that occur in other areas.

Discussion

Poor households are most vulnerable to the impacts of HPAI and ND. Poultry deaths are the direct impacts experienced by farmers. Mortality from HPAI brings multiple impacts related to the roles of poultry in farming households. Poultry deaths identified as HPAI-positive were diagnosed by PDSR in three of the communities studied: Plumbon, Bergas Kidul and Krembangan. A farmer in Ciawiasih mentioned that towards the end of 2005, 150 of his chickens died suddenly, but because the deaths were not reported, the *Dinas* did not conduct HPAI tests and the cause of death could not be determined. When enquiries were made, the *Dinas* stated that Ciawiasih village was not affected by HPAI. However, villagers in Ciawiasih claimed that the clinical symptoms they saw in their poultry were HPAI-compatible.

The other important poultry disease is ND. The villagers of Ciawiasih, Bergas Kidul and Truko claimed that they were able to differentiate the symptoms of poultry deaths caused by ND and HPAI. They reported that when HPAI-compatible disease strikes, poultry in one block might all die within a short time. On the other hand, ND strikes gradually, i.e., within a day several birds may die and several others die over the next few days, such that eventually most of the chickens in one block die within a week. Thus, the mortality rate of ND is also relatively high. While poultry suffering from ND can potentially recover, lack of farmers' knowledge about the disease makes it hard to control.

Different vaccination programs, i.e., HPAI vaccination and HPAI + ND vaccinations, resulted in different responses toward the programs. In the villages of Ciawiasih, Truko and Jatimulyo (which received only HPAI vaccinations) farmers stated that ND, which strikes at least twice a year during the change of season, is still a major constraint as it causes a high death rate (> 50%). In villages that received HPAI + ND vaccinations, such as Plumbon, Bergas Kidul and Krembangan, poultry death rates reported by farmers decreased, including deaths caused by ND. However, not all villagers were aware that the vaccinations administered by way of injections and drops have different functions. Most of them thought that the vaccinations were given only to prevent or control HPAI.

The spread of HPAI results in widespread poultry deaths and loss of assets after burning of poultry houses in a bid to prevent transmission of the disease. Large capital outlays are needed to restart poultry enterprises, build new houses and buy chicken feed, as experienced by farmers in Ciawiasih. This caused farmers to reduce the number of birds they reared.

Following sudden poultry deaths, farmers empty the poultry houses for 1-3 months, interrupting the poultry production cycle. Quail are reared for eggs in Krembangan Village. However, as the result of HPAI, only two farmers are still rearing quail on a scale of 1000 birds per farmer. Most farmers no longer rear quail because they are hampered by limited capital and a fear of incurring heavy losses. Because poultry rearing still carries high risks related to diseases that are difficult to handle, farmers have had to depend on other activities, such as crop farming, for their livelihoods.

Although crop farming is the main livelihood activity in the villages we surveyed, poultry are reared as a source of additional income, savings, or emergency cash. Various household needs are met through small-scale poultry production, such as buying food, paying monthly school fees, paying electricity bills, and giving gifts to families or neighbors who hold ceremonies, such as weddings. Thus the sudden losses caused by HPAI disproportionally affect poor farmer households.

In all surveyed villages, the selling price of poultry dropped significantly – by as much as 50% – during HPAI outbreaks. This reduction in price is experienced even in those villages where HPAI outbreaks have not occurred because news about an HPAI outbreak in one area creates panic among villages that the disease will spread and affect their flocks. To avoid incurring heavy losses, some farmers will immediately sell their poultry even at a lower price than usual. A decrease in poultry prices can also be due to reduced consumer demand resulting from fear of consuming poultry products.

Lower selling prices for poultry and the loss of cash income for poultry farmers affects household income and thus food consumption. The seasonal nature of income from crop farming requires additional sources of income to smooth consumption between harvests; poultry farming can play this role. The selling price of Kampong chickens (IDR 30,000-40,000 per chicken) is higher than that of broiler chickens (IDR 20,000 per kilogram). Therefore income from the sale of one Kampong chicken can be used to buy broiler chicken meat, tofu, fermented soybean cake and other food that is not produced in the household. Thus, the spread of HPAI affects household consumption of all food commodities, especially among poor households.

One of the objectives of poultry rearing is for consumption on special occasions. This is particularly so for Kampong chickens, which are cooked and served whole during various traditional, spiritual or religious ceremonies. This cooked, whole Kampong chicken is called *bakakak* in West Java or *ingkung* in Yogyakarta and Central Java. The spread of HPAI prevents villagers from undertaking these social practices, as other types of poultry or livestock cannot be substituted for Kampong chicken during the ceremonies.

The spread of HPAI affects the existence of waterfowl because they are considered to be carriers. Such a case was found in Ciawiasih, where villagers were reluctant to rear Muscovy ducks, because were perceived to be carriers of HPAI, able to transmit it to other types of poultry, particularly Kampong chickens.

Poultry are mostly reared by women. Likewise, women manage the income earned from the sale of the chickens. This suggests that by rearing poultry, women become more empowered, independent and able to manage their income. Therefore, HPAI can decrease or diminish women's independence.

Considering the frequent occurrence of HPAI over the past five years, villagers' knowledge about and awareness of HPAI was still relatively low. As a result, traditional poultry rearing systems were still often being used, contributing to subsequent disease outbreaks. In addition, several villagers objected to vaccinating their poultry, and sanitation of poultry housing was poor.

In order to control the spread of HPAI, several prevention measures have become more common: 1) vaccination; 2) bio-security by cleaning and disinfecting the housing of HPAI-infected birds; 3) focal depopulation by culling of sick poultry, followed with compensation; and 4) improved communication, information and education (*komunikasi, informasi dan edukasi*, KIE).

KIE programs are conducted by the Livestock Services and the Health Service, which train community vaccinators and organize public awareness outreach campaigns to prevent panic and misinformation regarding consumption of poultry products, particularly chicken meat and eggs. The office of Public Veterinary Health has distributed leaflets, posters and video compact disks (VCD) on the safety of poultry products to local Livestock Services offices in the districts of Sukabumi, Cirebon, Subang, Pandeglang, Wajo, Maros, Sopeng, Sidrap, Kupang, as well as the cities of Sukabumi and Kupang. KIE programs also give information regarding prevention of human and poultry HPAI.

Conclusions

Poultry rearing is a very important activity for small-scale farmers in Indonesia, providing a critical source of additional income, savings and emergency cash. It is also inextricably linked to other socioeconomic realities, such as the independence of women and household equity, as well as the need to participate in significant community events, such as weddings and other social ceremonies. The spread of HPAI can be very disruptive, especially for poor households, and produce negative impacts that may require considerable time and resources to recover from. Despite the increasing implementation of selected control measures, more must be done to educate farmers about poultry diseases, especially HPAI, and to encourage their participation in available control programs.

4.3 Vaccine trials

Abstract

Vaccination trials (H5N1 HPAI) were carried out to evaluate the effect: 1) of the age of chicks at first vaccination (day 1, 14, 21 and 28), 2) of a booster regime vs. a non-booster regime, and 3) of a vaccine with increased (doubled) antigen content on antibody profiles in Kampong chickens. In addition, field (community) trials measured the role of continuous off-take and replacement – naturally occurring in Kampong chicken populations – on antibody profiles. All trials took place in the Yogyakarta Province, Java, Indonesia. Results show that it is, in general, possible to achieve high levels of sero-conversion in Kampong chickens when using quarterly re-vaccinations and, in particular, if a 21-day booster regimen or double dose vaccine is used. Findings suggest that chicks from 14 days of age onwards should be vaccinated, with a booster 21 days later. Earlier vaccination (e.g., day 1) is not recommended. A booster regime is required, as it resulted in significantly higher overall individual HI (H5) titres in all trials. A double-dose vaccine using a non-booster regime provided nearly the same results as a standard dose booster regime immediately post vaccination. However, we observed lower flock protection levels being achieved at days 60 and 90 post-vaccination compared to a standard dose booster regime. Further research is required to consolidate these results, particularly regarding the duration of immunity, before concluding that vaccines with increased antigen content can replace use of a booster. Demographic results of the community trials indicate that 39-45% of Kampong chickens were consistently under 2 months of age, which is a clear indication that vaccination must be carried out at least quarterly to maintain meaningful levels of flock immunity.

1. Introduction

Highly pathogenic avian influenza (HPAI) of the subtype H5N1 was officially declared present in Indonesia in February 2004, and is now considered to be endemic in many parts of the country (OIE, 2004; Sawitri, 2007). The persistence of the disease despite the application of various control measures indicated the need for an assessment of existing interventions, including vaccination. To meet this need, the ORI-HPAI program was designed to evaluate intervention strategies against HPAI in backyard and small-scale commercial poultry operations; the feasibility of implementing selected interventions was evaluated, and their impact on the incidence of HPAI-compatible outbreak events was gauged. The intervention strategies chosen consisted of HPAI or HPAI/ND mass vaccination regimes. Targeted vaccination trials were designed to support the mass vaccination program by providing additional information through the evaluation of various vaccination regimes.

Kampong chicken populations are likely to have a high proportion of chicks that are less than two months old (CMU, 2008; Priyono, 2008). However, no recent studies were available. Determining the optimal age of first vaccination was therefore key to developing an effective vaccination strategy. At the onset of the study, anecdotal evidence existed that locally produced HPAI vaccines with increased antigen content were used on some commercial farms. However, these vaccines were never approved by the Ministry of Agriculture (MoA) of Indonesia, nor were results of test trials available. Moreover, the use of vaccines with greater antigen content was strongly recommended by Swayne (Swayne, 2008), who tested locally produced vaccines for their antigen content.

Several vaccination trials were designed to evaluate efficacy relative to the age at first vaccination, the effect of a booster regime, and of a vaccine with increased (doubled) antigen content on antibody profiles in Kampong chickens using laboratory trials. In addition, the effects of a continuous off-take and replacement – naturally occurring in Kampong chicken populations – on antibody profiles were evaluated in field (community) trials.

2. Methods

The study presented here consists of three sub-activities:

- The age of first vaccination trial;
- The booster and antigen content trial in adult chickens; and
- The field (community) trials.

All studies were carried out in collaboration with the Wates DIC laboratory, Yogyakarta. We used Legok 2003 H5N1 vaccine (H5N1 strain A/Chicken/Legok/2003) with a standard antigen vaccine concentration (PD50) that was supplied by Medion®, a local vaccine producer (Medion, 2011). The chosen AI vaccine represented the recommended vaccine by the CMU/MoA at the onset of the study (CMU, 2008) and was recommended by Swayne (2008).

Age of first vaccination trial – The ages of the first vaccination we tested were 1, 14, 21 and 28 days (Treatment groups 1 to 4, respectively). A total of 180 chicks were used in the study, 40 of which were randomly assigned to each group. Half of each group (n=20) received a booster vaccination 21 days after the first vaccination. In addition there was a control group (n=20). Twenty additional chicks were randomly selected for euthanasia at one day of age, and blood was collected to evaluate the level of material antibodies to HPAI.

Serum was collected from all groups at 30-day intervals until 270 days of age. Individual antibody profiles for HPAI and ND were determined by haemagglutination inhibition (HI) tests; HI titres of $\log_2$ 4 were considered to be positive for HPAI (Kumar et al., 2007; OIE, 2009) and ND (EEC, 1992). For the HPAI HI tests, we used a virus isolate from Java [A/ck/pare-kediri/2003, produced by Pusvetma (Pusvetma, 2011)]. According to Claasen (2011a), Morrissy (2011) and Priyono (2011), this isolate is antigenically and genetically related to the Legok 2003 isolate and therefore suitable for post-vaccination surveillance in populations where Legok 2003 vaccine was used. The used HI strain for the ND diagnostic was Hitcher B1 (HB1), ISHII originated from Japan (Morrissy, 2011; Priyono, 2011).

As a protective measure, we planned to vaccinate all chicks quarterly using Hitcher B1 (HB1) ND vaccine, and the chicks were vaccinated at four days of age accordingly. However, because of ND outbreaks in the lab, the chicks were re-vaccinated at days 89 and 143 instead. To understand the extent that infectious bursal disease (IBD, Gumboro) may have influenced immune responses to vaccination, all chickens were tested for IBD antibodies using an Enzyme-Linked Immunosorbent Assay (ELISA) (BioCheck IBDV ELISA kit) at the end of the trial (day 270).

Booster and antigen content trials in adult chickens –These laboratory trials compared the effects of single versus booster vaccination regimens, as well as the effects of a vaccine with increased (doubled) antigen content, on the antibody profiles in adult Kampong chickens. Two protocols were tested in two separate populations. One protocol involved a single vaccination. The other involved a primary vaccination followed by a booster vaccination after 21 days. Re-vaccination in both protocols occurred at 90 and 180 days. Two additional groups received a vaccine formulation with double the normally used antigen content, in similar single and booster regimens. The double antigen content vaccine was exclusively produced for this trial and supplied by Medion® (Medion, 2011). The specific group composition is presented in Table 4.3.1.

Table 4.3.1: Treatment group composition

Group	Description	N
Treatment 1	No booster standard antigen content	20
Treatment 2	21-day booster standard antigen content	20
Treatment 3	No booster double antigen content	20
Treatment 4	21-day booster double antigen content	20
Control	Control	20

All chicks were vaccinated quarterly against ND using Lasota vaccine, as HB1 vaccine was found not to protect against natural ND challenge in the age of first vaccination trial (see above). Serological samples were collected monthly until day 270 of the trial.

All chicks were tested for IBD at the end of the trial (day 270). Serological tests for AI, ND and IBD followed the same protocols as described above.

In the first week of May 2008, an outbreak of ND occurred in chickens received at the laboratory for this trial. Control measures were immediately implemented (culling, cleaning, disinfection and emergency vaccination of other chickens). The trial was restarted at end of June 2008 with a new batch of chickens. However, a disease event occurred between day 53 and 66 of the trial, which caused a mean loss of 19% of the study population. Results of post-mortem and patho-histological investigations were inconclusive and this second disease event was not diagnosed.

Community trials –The purpose of these trials was to compare flock antibody profiles resulting from quarterly vaccination programs that employed either a single dose regimen or a primary vaccination followed in 21 days by a booster shot in naturally occurring Kampong chicken populations with typical age profiles and continuous off-take and replacement. Twelve communities with estimated chicken populations of 300-500 each were enrolled in the study: six in Sleman District and six in Kulon Progo District. Four communities were assigned to a booster vaccination regime, four to a single vaccination regime, and four remained as un-vaccinated control communities. Between February and June 2008, sampling details were finalized, data on poultry populations in the enrolled districts were obtained, questionnaires were prepared, equipment was ordered, and randomly selected communities were sensitized for the upcoming field trials. The start of the trials was delayed in some of the selected communities because HPAI outbreaks occurred when vaccinations were planned to start.

Vaccinations were carried out quarterly (Table 4.3.2). In each of the 12 communities, one person received training on vaccination and data collection. Serological samples were collected in six-week intervals, 60 per community and up to five per selected household from randomly selected chickens, and subjected to HI (H5) testing. Sera obtained from the first sampling (day 1) were also tested for ND. A subset of samples was subjected to IBD ELISA testing. All test were applied as described above. Households were visited at weekly intervals to collect data on the exit/entries of birds. All birds vaccinated or serologically sampled received an ear or wing tag. To simplify data entry and to reduce data entry failures an Access database was developed.

Table 4.3.2: Selected activities implemented in the community vaccination trial

Day	Activities and Location (July 2008 - May 2009)
1	Vaccination (8 communities) and blood sampling* (12 communities)
21	Booster vaccination (4 communities)
45	Blood sampling* (12 communities)
90	Vaccination (8 communities) and blood sampling* (12 communities)
111	Booster vaccination (4 communities)
135	Blood sampling* (12 communities)
180	Vaccination (8 communities) and blood sampling* (12 communities)
225	Blood sampling* (12 communities)
270	Blood sampling* (12 communities)

***60 serum samples per community and up to five samples per household. All households are also visited weekly to collect data on exits and entries, including clinical reports of suspected diseases of chickens**

3. Results

Age at first vaccination trial –No maternal-derived antibodies (MDA) were detected in the randomly selected euthanized day-old chicks (DOCs). Without a booster, the proportion of the chick flocks vaccinated at 1, 14, 21 and 28 days of age that had titres of $\log_2$ 4 or higher peaked at 50-70% by 60 days of age (earlier for DOCs) and then dropped to 15-32% or 0% (for DOCs) by 90 days of age (Figure 4.3.1).

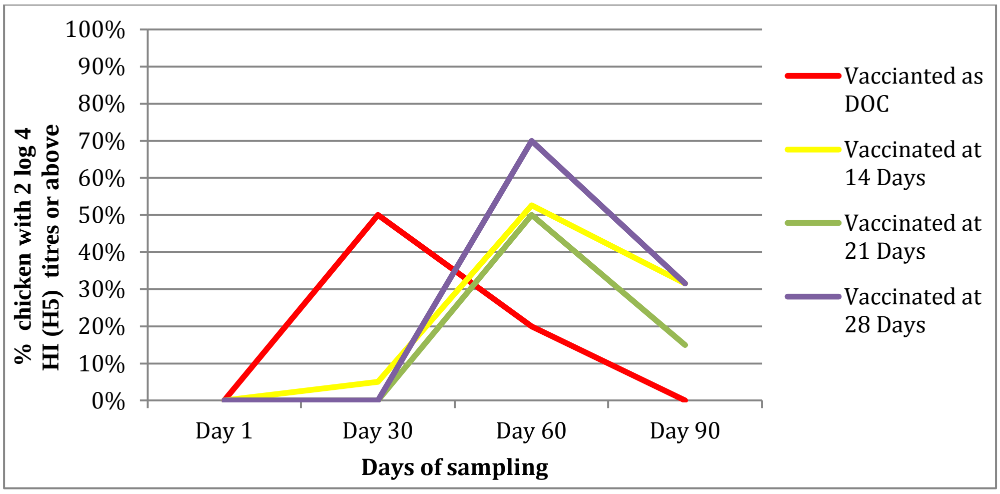


Figure 4.3.1: HI (H5) results for the age of first vaccination trial treatment groups without booster

Booster vaccinations resulted in a higher proportion of the flock in all age groups achieving and maintaining titres of $\log_2$ 4 or higher up to day 90 (Figure 4.3.2). These results are significant when comparing HI (H5) titres over the entire first quarter (Kruskal Wallis, $p<0.01$), as well as when comparing titres at day 90 after vaccination within groups first vaccinated at day 14, 21 and 28 compared to a non-booster regime (Kruskal Wallis, $p<0.05$).

Even with a booster, the proportion of chicks vaccinated as DOCs that developed titres of $\log_2$ 4 or higher was significantly lower than in the other age groups. These results were significant when comparing HI (H5) titres at day 90 after vaccination (Kruskal Wallis, $p<0.05$).

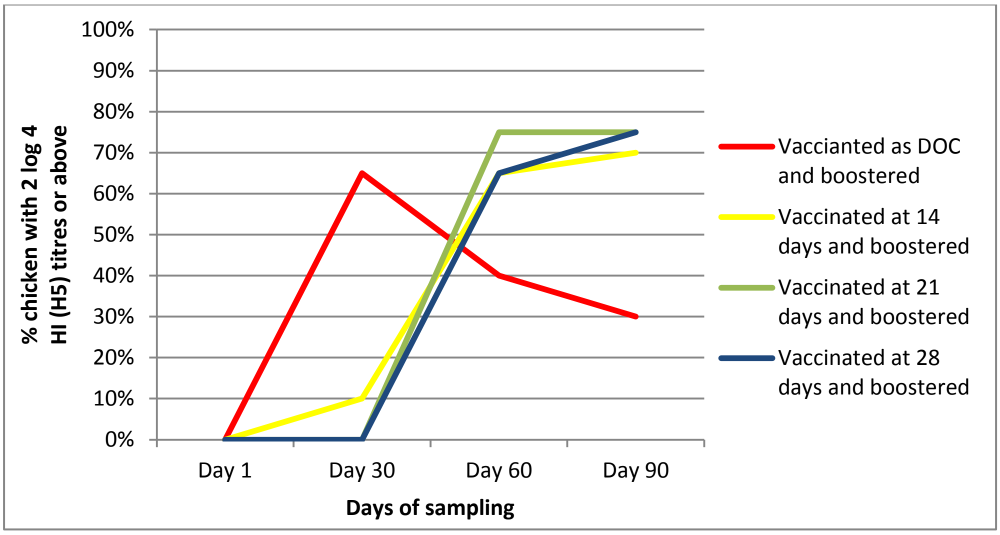


Figure 4.3.2: HI (H5) results for the age of first vaccination trial using a regime that includes a booster 21 days following initial vaccination

A revaccination (with or without booster) was provided to all groups at days 90 and 180 of life. Different levels of response to re-vaccination were observed in the different groups. Figure 4.3.3 below shows the results of the groups that received a booster.

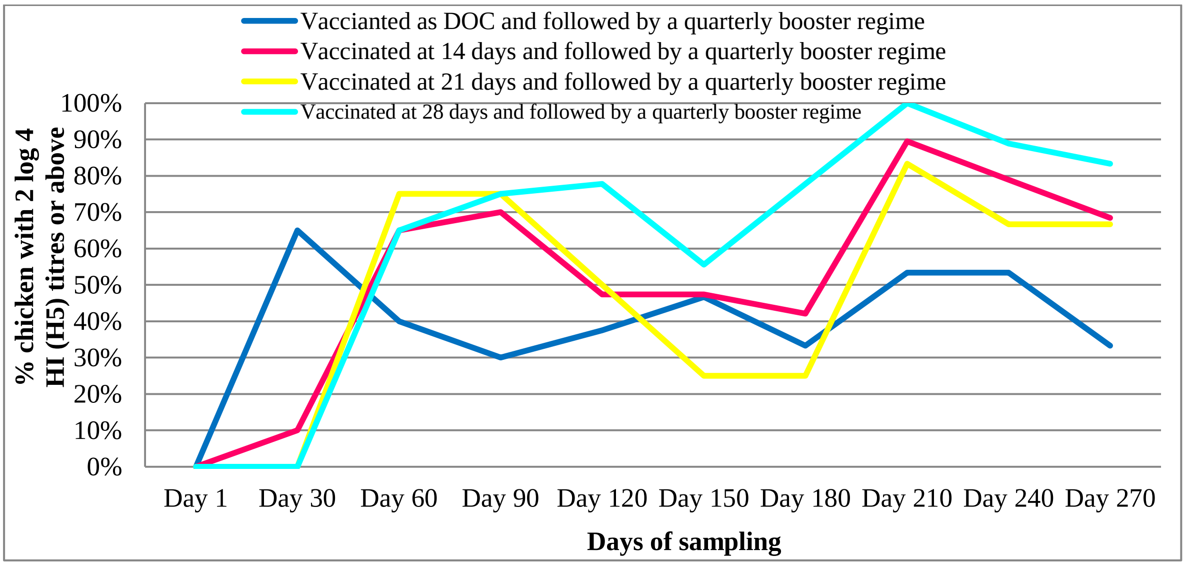


Figure 4.3.3: HI (H5) results for the age of first vaccination trial using a booster quarterly regime

None of the randomly selected and euthanized chicks had MDA. ND vaccination using HB1 vaccine at day 4 of life resulted in a very low proportion of chicks with HI titres of log_2 4 or above at day 30 of life (Figure 4.3.4). At day 90 of life, none of the chickens had titres of log_2 4 or above. An outbreak of ND occurred between day 96 and 117 of life, which caused an average mortality of 21% (5-47%) in the different treatments groups.

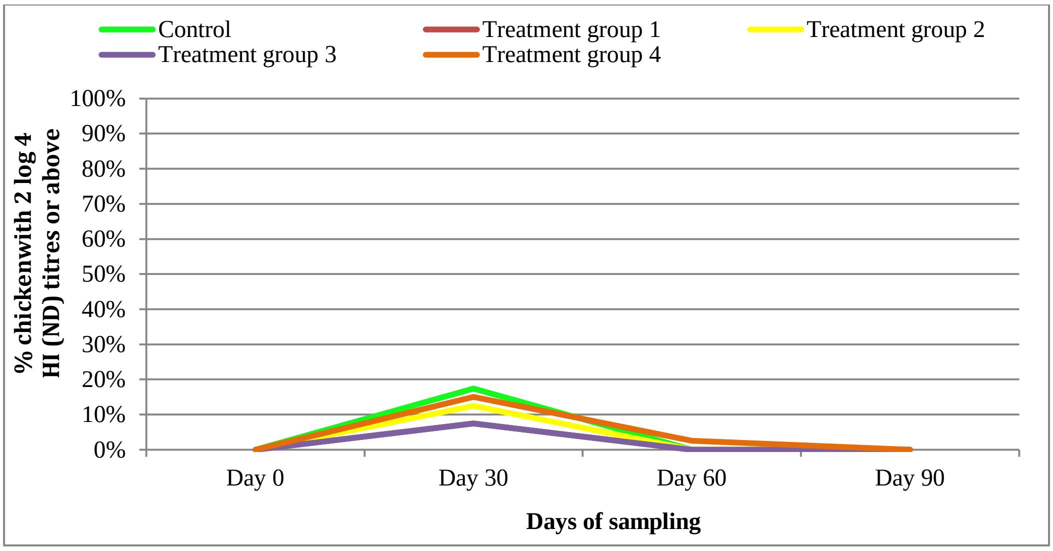


Figure 4.3.4: HI (ND) results for the age of first vaccination trial presented for the first quarter

Ninety-seven percent of chickens tested at day 270 of life were positive for IBD. However, clinical symptoms were not observed during the trial.

Booster and antigen content trials in adult chickens –Using a standard antigen vaccine concentration (PD 50), a booster regime that was repeated at three-month intervals resulted in higher proportions of the flock with HI (H5) titres of $\log_2$ 4 or above, compared to a non-booster regime (Figure 4.3.5). When comparing the HI (H5) titres by quarter, the results are significant for each quarter (days 1-90, days 91-180 and days 181-270) (Kruskal Wallis comparison of median, $p \leq 0.05$).

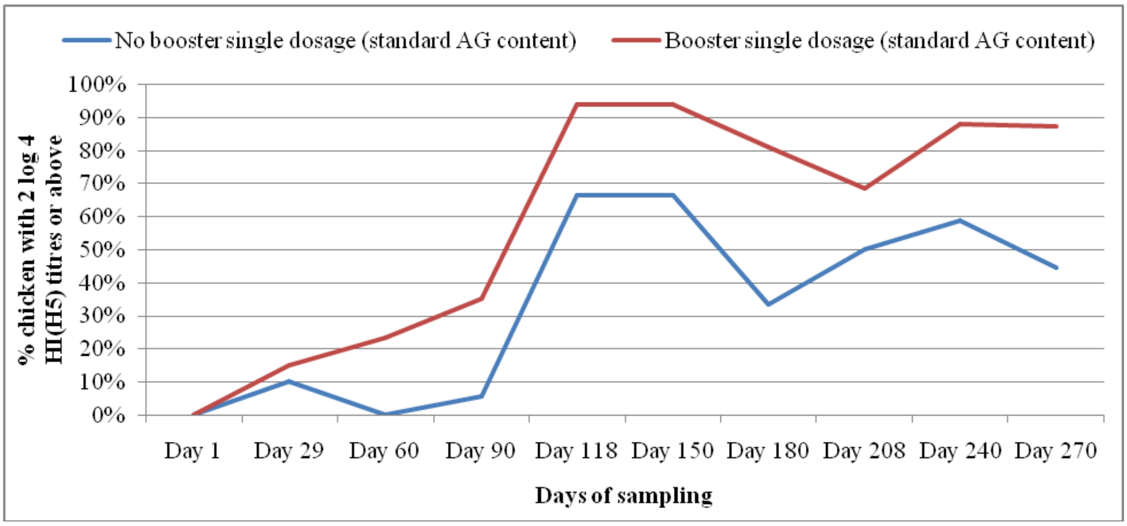


Figure 4.3.5: Results of the adult Kampong chicken trial comparing quarterly vaccination using a single dosage (standard antigen content) of HPAI vaccine without and with booster

A double-antigen content vaccine repeated quarterly resulted in higher proportions of the flock with HI (H5) titres of $\log_2$ 4 or above, compared to a standard dose non-booster regime (Figure 4.3.6). More importantly, it provided results similar to a standard antigen vaccine followed by a booster in quarters 2 (days 91-180) and 3 (days 181-270) (Figure 4.3.6). In quarter 1 (days 1-90), however, the proportion of the flocks with HI (H5) titres of $\log_2$ 4 or higher fell below the level of standard dose with booster group between days 60 and 90. In general, only low proportions of chickens developed HI (H5) titres of $\log_2$ 4 or above during the first quarter. However, after quarterly re-vaccination (day

90 and 180) high levels of sero-conversion were achieved, particularly in groups with a booster or double-dosage regime (Figures 4.3.5 and 4.3.6).

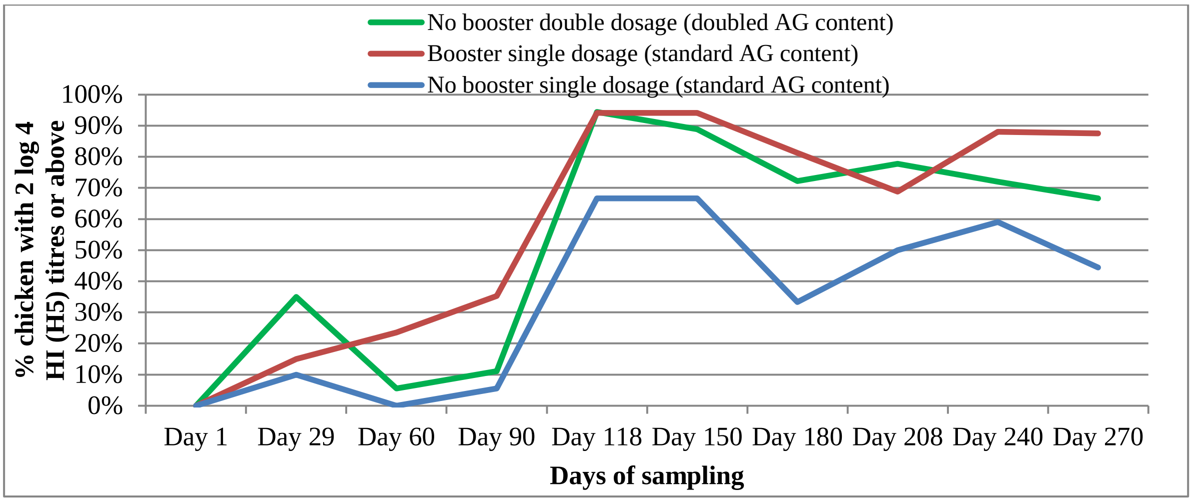


Figure 4.3.6: Results of the adult Kampong chicken trial comparing quarterly vaccination using a double dosage without a booster compared to a standard dosage with booster and without a booster

HI H5 antibody titre results were compared for populations receiving a single dose non-booster (SDNB), a single-dose booster (SDB), and a double-dose (double antigen content) without a booster (DDNB) vaccination. The SDB and DDNB provided significantly higher HI (H5) titres (Kruskal Wallis, $p \leq 0.05$) compared to the SDNB in all three quarters. There was no significant difference between SDB and DDNB in any of the three quarters.

At the start of the trials, a proportion of chickens (15-30%) had HI (ND) titres of $\log_2$ 4 or above. These results may indicate previous ND vaccinations applied in the flocks of origin and/or natural infections. A single ND vaccination (Lasota strain) applied at day 3 of the trials did not result in an increase of flock immunity at day 30. At day 90, none of the chickens had HI (ND) titres of $\log_2$ 4 or above. Quarterly applied re-vaccinations resulted in flock immunity 22% or more after day 90 re-vaccination and 67% or more after day 180.

Ninety-eight percent of chickens were positive for IBD at day 270. However, clinical symptoms were not observed during the trial. As almost all the chickens were IBD positive, it was not possible to test for an association between the presence of IBD antibodies and response to vaccination.

Field (community) trials –The actual size of the chicken populations in the enrolled communities at the start of the field trials varied from the expected population (217-530 actual, 300-500 expected). Between 24 to 32, and 24 to 52, households were visited throughout the field trials in communities located in Kulon Progo and Sleman Districts, respectively (Yogyakarta Province). On average, households were visited 40 times in Kulon Progo and 44 times in Sleman. The vaccination coverage (i.e., the number of vaccinated chickens versus the total number present in the community) varied between communities and over the period of the trial (Table 4.3.3).

Farmers' compliance with vaccination and weekly population data recording was generally high. However, in one community (Balong) farmers' compliance declined over time due to mortality not related to AI. As a result, HPAI vaccinations were not applied as planned. Balong was therefore excluded from the overall serology analysis.

Results of HPAI serology – Booster vaccinations resulted in significantly higher overall individual HI (H5) titres over the field trials at all sampling dates (Kruskal Wallis, $p < 0.01$). In communities with quarterly booster vaccination, flock sero-prevalence (the proportion of chickens with H5 titres of

$\log_2$ 4 or above was between 15% and 40% higher than in communities that followed a quarterly regime without a booster) (Figure 4.3.7). The observed differences are significant for each day of sampling (Chi square, Yates corrected, $p < 0.01$).

Poultry population results – The overall number of chickens over time in the 12 participating communities changed only marginally (21-37 chickens) when comparing means, but varied widely between communities (see further below). A proportion of 39-44% of chickens were younger than two months of age over time (Figure 4.3.8). More than two-thirds of the chickens were younger than four months. Male and female adults represented 10% and 20% of the total population, respectively.

Table 4.3.3: Proportion of chicken received vaccination presented by communities with applied vaccination for Kulon Progo (KP) and Sleman (SL)

Community	Vaccination regime	Proportion vaccinated	Comments
Sindutan A (KP)	Booster quarterly applied	64 – 99%	During booster vaccination lower coverage (fewer chickens presented)
Cepit (SL)	Booster quarterly applied	68 -88%	During booster vaccination lower coverage (fewer chickens presented)
Balong (SL)	Booster quarterly applied	≥89% (1st & 2nd) & 22% (3rd round)	Low farmer compliance with vaccination during last vaccination round due to non-AI related mortality
Senden (KP)	Booster quarterly applied	60-80%	During booster vaccination lower coverage (fewer chickens presented)
Purwobinangun (SL)	Quarterly vaccination regime	≥89%	
Kalimanjung (SL)	Quarterly vaccination regime	67 – 80%	
Wates (KP)	Quarterly vaccination regime	≥68%	
Bulak (KP)	Quarterly vaccination regime	45 -74%	

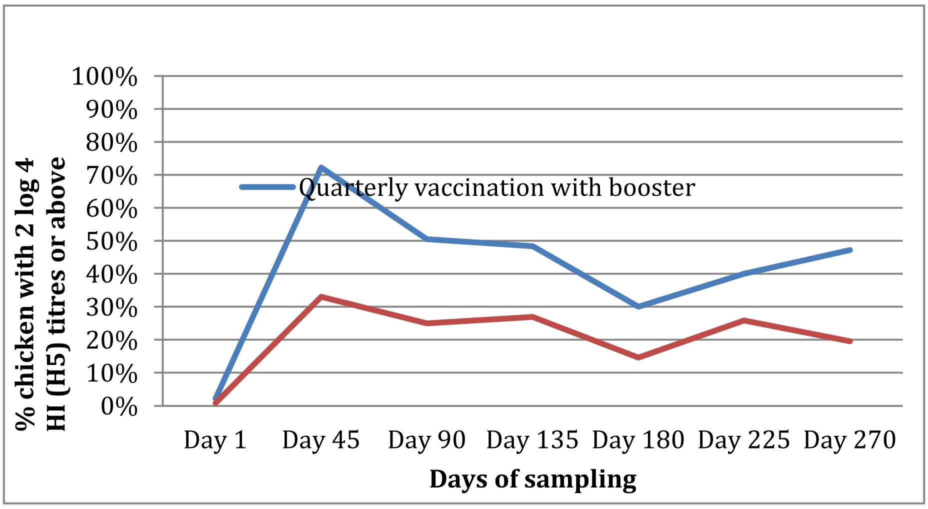


Figure 4.3.7: Results for the community trial comparing quarterly HPAI vaccination with and without a booster. Graph includes analysis for 4 communities with quarterly vaccination and 3 communities with a quarterly booster regime. One community was excluded due to low compliance with vaccination

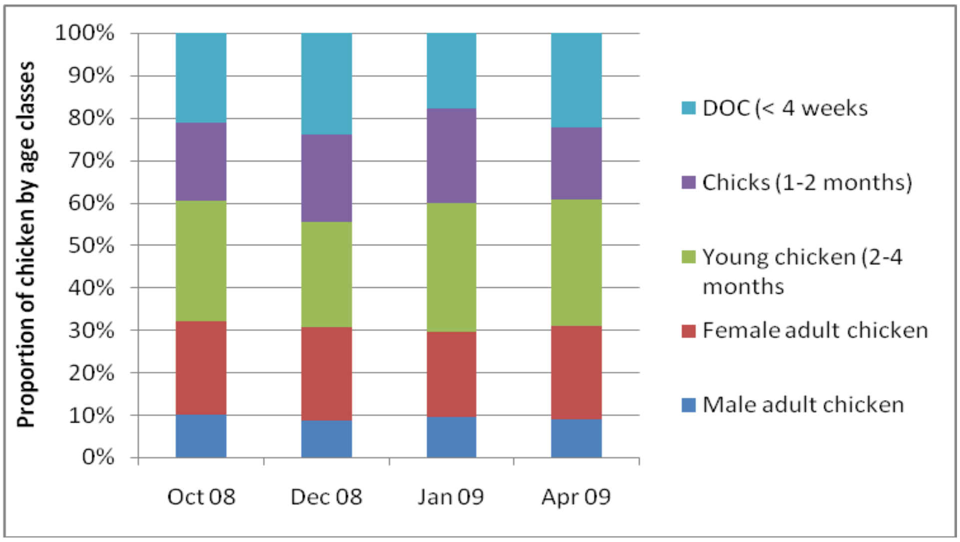


Figure 4.3.8: Average proportion of the total chicken population by age class in enrolled communities over time

Chicken population dynamics varied between communities and over time as shown in Figure 4.3.9 for communities located in Kulon Progo.

Poultry population dynamics are presented below for two communities, Kalimanjung (a community with quarterly vaccinations) and Sindutan A (a community with quarterly booster vaccinations).

The overall population size remained almost unchanged in Kalimanjung over the trials (Table 4.3.4). Though overall population size was stable, the number of chickens changed widely within age classes. In the month of October, there was an increase in the number of DOCs (due to re-stocking after sales) and a decrease in the number of chicks (which were sold for ceremonies related to Muslim holidays in mid-October 2008. Each quarter, there was a 50% or higher turnover of the population (Table 4.3.5).

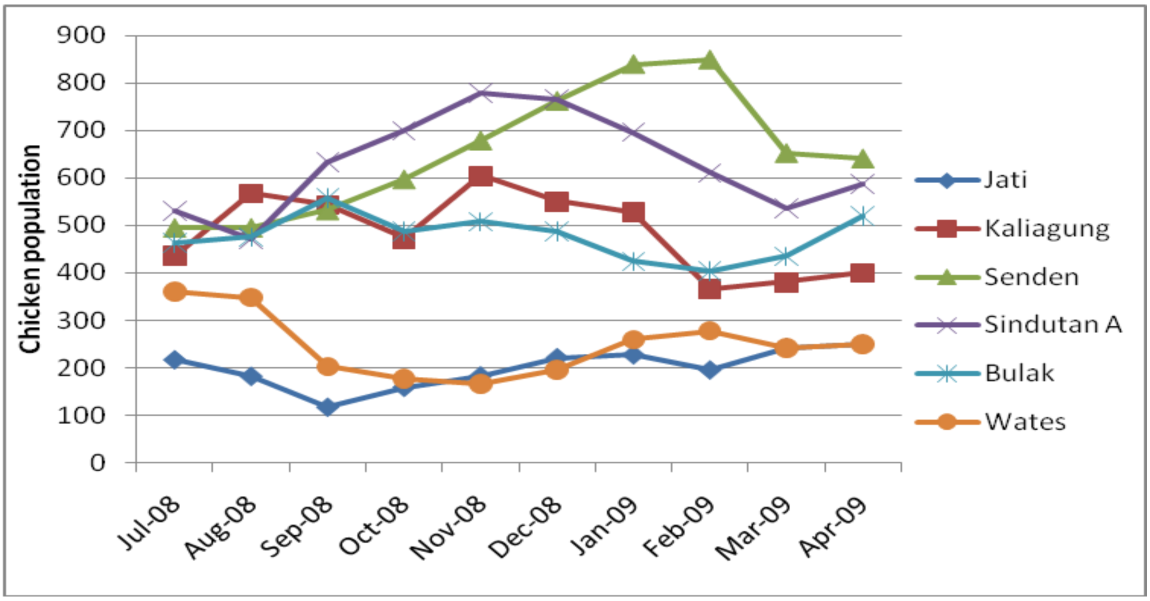


Figure 4.3.9: Total chicken population in communities located in Kulon Progo over time

In Sindutan A, the overall population size change was as high as 31% over the length of the trials. Between quarters there was a renewal (entries into the populations) of 43-56% (Table 4.3.5).

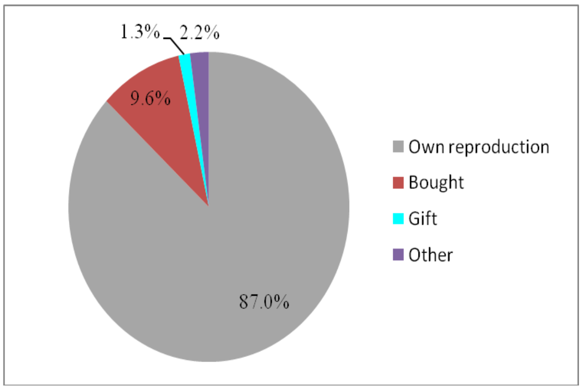
Table 4.3.4: Poultry population statistics for two communities (Kalimanjung and Sindutan A)

	Total chickens	Male adult chickens (> 4 months)	Female adult chickens (> 4 months)	Young chickens (2-4 months	Chicks (1-2 months)	DOC (< 4 weeks)
Kalimanjung						
Jul 2008	356.0	29.0	70.0	44.0	115.5	97.5
Oct 2008	368.5	22.0	77.8	45.5	52.0	171.3
Jan 2009	378.0	18.8	62.8	92.5	103.8	100.3
Apr 2009	371.5	20.0	73.3	98.5	97.0	82.8
Sindutan A						
Jul 2008	531.3	26.7	79.0	173.3	135.3	117.0
Oct 2008	700.0	25.0	98.4	220.0	180.0	175.8
Jan 2009	697.4	36.0	102.0	257.4	162.8	139.2
Apr 2009	588.0	24.0	108.0	183.8	168.5	103.8

Table 4.3.5: Change of poulation over time for Sindutan A and Kalimanjung over time

		Jul-Oct 2008	Oct 2008 – Jan 2009	Jan – Apr 2009
Kalimanjung				
	Total entries	72%	58%	49%
	Total Exits	69%	56%	51%
Sindutan A				
	Total entries	56%	43%	49%
	Total Exits	19%	44%	68%

Figure 4.3.10 shows sources of entries into the overall chicken population during the study period. Most chickens in a population result from reproduction within a household flock (87%), followed by purchases (9.6%). Reasons reported for off-take varied and were categorized into six classes (sold, died, consumed, predator, gift, and others). Figure 4.3.11 shows the proportion of each category. The majority of exits were related to sales (67%) followed by death (10.7%). Another 10.7% of exits were for a variety of reasons and classified as other.



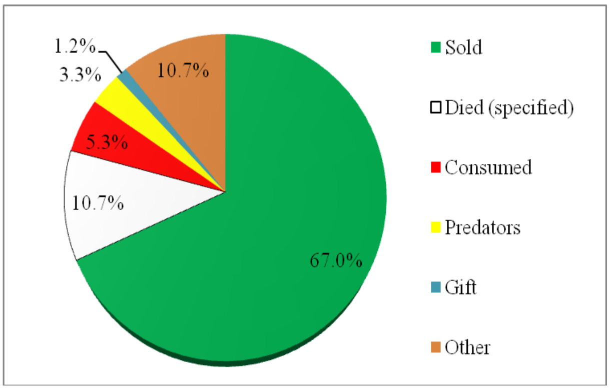


Figure 4.3.10: Chicken population entries by origin from community trials

Figure 4.3.11: Categories of chicken off take from community trials

Antibodies against ND and IBD –A subset of chickens (60 in each community) were tested for ND at the start of the trials. Three to seven percent had HI (ND) titres of log_2 4 or above (Table 4.3.6).

The majority of chickens (81%) were positive for IBD. However, specific clinical symptoms were not observed during the trials.

Farmer compliance with vaccination and population data collection was generally high, with the exception of one community. Post-vaccine complications were very rarely observed. Owners or household members were often not aware of the exact number and current location of their chickens. This created a challenge for population data recording.

Table 4.3.6: Results of ND antibody testing in community trials

	N	Chicken with log_2 4 HI (ND) titre or above	%
Control group	241	16	6.6
Treatment group 1 (primary vaccination)	240	15	6.3
Treatment group 2 (booster vaccination)	240	6	2.5
Total	**721**	**37**	**5.1**

Discussion

The age of first vaccination study showed that booster vaccinations for HPAI result in a greater proportion of Kampong chicks with HI (H5) titres of log_2 4 or above. Results of the booster trials in adult chickens and the community trials confirm findings that a booster regime is more effective in Kampong flocks. Only very low flock immunity levels were achieved in the community trials when no booster regime was applied.

As vaccination of DOCs (day 1) did not result in a high proportion of the flock with HI (H5) titres of log_2 4 or above in the first 90 days of life, it is not recommended. The observed poor duration of antibodies in DOCs might be related to partial immune-competence in very young individuals. Since there is no difference in response to vaccinations between the groups vaccinated at 14, 21 and 28 days, it is recommended from our findings to vaccinate chicks from 14 days of age onwards, with a booster 21 days later. Our results differ from recent findings presented by Claasen (2011b), in which no differences in HI responses were found for broiler chicks vaccinated at day 1 or day 10, respectively. However, the studies are difficult to compare due to dissimilar study design and population. In the latter trials, only a single vaccination was applied. The generally low or missing responses were explained by the possible influence of maternal-derived antibodies (Claasen, 2011b). In our trial, no indications of maternal-derived antibodies were found. Currently, one of the main Indonesian AI vaccine suppliers recommends 10 days for the age of first vaccination (Medion, 2011).

Quarterly HPAI re-vaccinations (at days 90 and 180) resulted in the age of first vaccination trials producing different levels of response in the various groups. This may have been influenced by inter-current disease. However, as shown for chickens older than 180 days, our Kampong chickens were able to develop high levels of responses if quarterly vaccination schemes were applied. This observation is similar to results from Claasen (2011a) for vaccinated Kampong chicken populations.

A single ND vaccination using the HB1 strain at day 4 of life resulted in only a very low flock sero-prevalence by day 30, and no detectable antibodies by day 90 in the age of first vaccination trials. Moreover, the birds were not protected against a natural ND outbreak in the study population. In the adult trial, at least two quarterly applied Lasota ND vaccinations were needed to provide moderate flock immunity levels. A booster after the initial vaccination appears warranted, as flock immunity was very low or undetectable in the first quarter after a single vaccination. The selection of the HB1 vaccine strain should be reconsidered in any future ND vaccination programs and our results suggest that the HB1 ND vaccination in the longitudinal study (Section 3.1) probably did not result in any appreciable protection or change in ND prevalence**.**

In the booster and antigen content trials in adult Kampong chickens, results for the second and third quarter indicate that it is possible to achieve high levels of sero-conversion, using quarterly re-vaccinations and, in particular, if a 21-day booster regimen or double-antigen dosage vaccine is used. As mentioned above, our observations are similar to results from Claasen (2011a) for vaccinated Kampong chicken populations. Medion-Indonesia recommends 3-4 monthly re-vaccination intervals for its H5N1 vaccine for layer flocks, depending on serological post-vaccination monitoring (Medion, 2011).

The low proportions of the flocks in all groups with HI H5 titres of $\log_2 4$ or higher in the first quarter may have been influenced by a disease outbreak of unknown etiology in the first quarter, which killed 19% of the chickens. This is perhaps representative of the real situation for Kampong chickens in the field where inter-current disease may result in a poor response to vaccination. On the other hand, it may indicate that Kampong chickens do not develop high titres until re-vaccination after 90 days. However, taking into account the results of the age of first vaccination trials and the community trials, this seems very unlikely.

As noted by Claasen (2011a), for Kampong chicken IBD was highly endemic in all our study populations. However, due to the very high sero-prevalence of IBD, it was not possible to test whether there was any association between IBD serological status and HPAI vaccination response.

A double strength vaccine produced good results in quarters two and three, where the re-vaccinations at day 90 have acted as a booster, despite decreased titres but previous presentation of the AG and sensitization of the immune system. In the first 90 days, however, the titres did not appear to last, resulting in a lower level of flock protection at days 60 and 90, compared to a booster regimen. This observation is of particular concern, as vaccination during the first 90 days is critical to reaching moderate flock immunity levels due to high population turnover rates in backyard poultry. One local vaccine supplier produces an AI H5N1 vaccine (different from Legok) with higher antigen content for its own research purposes. However, this vaccine is not yet registered (Vaksindo, 2010), and further details about it were not provided. As mentioned above, there is anecdotal information that local vaccine suppliers in Indonesia provide higher antigen-content vaccines to the commercial sector as a special request. Our results indicate an advantage for a double strength vaccine, especially in the second and third quarter, which supports prior recommendations given by Swayne (2008) and recently presented by OFFLU, Indonesia (2009). Both of these authors emphasize the use of higher antigen-content vaccines in the future. However, further field research is required to consolidate these laboratory trial-based results and before concluding that vaccines with increased antigen content can eliminate the need for a booster. Such an enhancement would greatly reduce the logistical complexity and cost of vaccination programs. In the meantime, use of higher antigen-content vaccines should be adopted in existing booster regimens, as it enhances flock immunity at modest additional cost.

More than two-thirds of the backyard chicken populations are younger than four months. Moreover, 39-45% of chickens are younger than 2 months, which means that approximately 40% of a natural backyard population will be un-vaccinated by 60 days after the vaccination campaign. Because such a high percentage of the population is new each quarter, the booster round of vaccination is required in every quarter. This leads to high costs and is a significant logistical challenge. According to the results of the transmissibility study (Section 4.4), 63.8% of birds in household flocks need to be immune to H5N1 to interrupt transmission, and 51.7% of household flocks in a neighborhood. The studies conducted at the laboratory with small numbers of confined, marked Kampong chickens exposed to inter-current disease challenges typical of the region had difficultly sustaining levels of antibody consistent with the eradication threshold. The community study where birds were marked and vaccination was conducted on a small and carefully monitored scale only achieved antibody levels consistent with the eradication threshold on one occasion. These combined results suggest that it is not possible to eradicate HPAI in backyard poultry using mass vaccination approaches alone. It is possible to suppress disease and mitigate the risk of human exposure using mass vaccination, but only with a continuous and significant input of effort and investment.

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4.4 Study of the transmissibility of H5N1 in Indonesia

Abstract

The basic reproduction number (R_0) of an infection is an indicator of the number new individuals that will become infected from a single infected individual in a completely susceptible population, while the effective reproduction number (R_e) is an indicator of the number that will become infected in an incompletely susceptible population where some control measures have been implemented. Our study was designed to measure R_0 and R_e in mixed populations of backyard and small-scale commercial chickens in West and Central Java, where other domestic fowl such as ducks are in direct contact with chickens. A participatory approach adapted from infection tree reconstruction was used to trace affected chickens and households in RTs (neighborhoods) in which PDSR practitioners diagnosed HPAI. Final fraction size equation calculations showed that, for the overall operational research study area, R_e between chickens within household flocks was 1.72 and between households it was 1.48; R_e between chickens within household flocks in vaccinated areas was 1.66; R_o in un-vaccinated areas was 1.77; R_e between households in vaccinated areas was 1.42; and R_o in un-vaccinated areas 1.52. A GSE SIR model showed slightly higher reproduction numbers, with an R_e between household flocks for the overall operational research study area of 2.01 and within flocks it was 2.54; within-flock R_e in vaccinated areas was 2.21; R_o in un-vaccinated areas was 2.76; between flock R_e in vaccinated areas was 1.9; and R_o in un-vaccinated areas was 2.07. Based on the GSE estimates for un-vaccinated areas, these results indicate that 63.8% of birds in a household flock need to be immune to H5N1 to interrupt transmission within the flock, and that 51.7% of household flocks in a neighborhood need to be immune in order to interrupt transmission between the flocks. A significant risk was found for HPAI outbreaks to occur in households raising Muscovy ducks, non-commercial (backyard) chickens, broilers and geese, with Muscovy duck presence in a household showing the highest risk. Duck and pigeon presence were not associated with households being affected during outbreaks.

1. Introduction

The basic reproduction number (R_0) is a measure of the transmissibility of an infectious agent in a specific population and is defined as the number of new individuals that will become infected from a single infected individual in a completely susceptible population. If R_0 is greater than 1 the infection is capable of spreading in that population, but if it is less than one it will eventually die out on its own with no further intervention. The larger the R_0, the more difficult an outbreak will be to control. For example R_0 for airborne measles is between 12 and 18, indicating how difficult it is to control this disease. For human influenzas spread by airborne droplets, R_0 is between 2 and 3, making them easier to control. Ferguson et al. (2001) estimated the R_0 of the 2001 foot and mouth disease outbreak in Great Britain to be 4.5 (Ferguson, Donnelly, and Anderson, 2001), while Stegeman et al. (1999) estimated the R_0 of the 1997-1988 classic swine fever outbreak in the Netherlands to be 2.9 (Stegeman, Elbers and Bouma et al., 1999). Lineage-1 rinderpest was estimated to have an R_0 of 4.4 and lineage-2 between 1.2 and 1.9 (Mariner et al., 2005).

In any given population, R_0 is affected by the structure of the population, particularly the number of new, susceptible individuals an infected individual comes in contact with, how long infected individuals remain infective, and the infectiousness of the pathogen. In other words, one can expect differences in R_0 for the same disease in different types of populations. Knowing the R_0 is important for designing a successful disease control program and gives an indication of how effective control interventions need to be to interrupt transmission. In vaccination programs, R_0 is a useful indicator of the proportion of a population that needs to be rendered immune in order to stop the spread of the disease. As has been said, $R_o$applies to completely susceptible populations and is a benchmark value for an agent in a specific population. Control interventions reduce the value of the reproductive number and the term "effective reproductive number (R_e)" is used to describe the value of the reproductive number in situations where control actions are being implemented. If the value of $R_e$is reduced to and maintained below 1, the infection will fade out from the population.

The goal of any control program is to decrease the number of new individuals a single infected individual can infect, thereby limiting the spread of an infection. When R_e is <1 for a sufficient period of time chains of infection will die out and the infection will be eradicated. Often a single control measure succeeds in reducing $R_{e,}$ but not below 1, and it is a combination of control measures that succeeds in eradicating an infection by pushing R_e below 1 (Heffernan, Smith and Wahl, 2005; Ferguson, Donnelly and Anderson, 2001; Stegeman, Elbers and Smak et al., 1999).

R_0 for HPAI has been measured in a variety of situations. It is important to remember that R_0 is specific to the situation for which it is reported, and will not be exactly the same in other populations. In a laboratory transmission experiment, it was found that R_0 for H7N7 in un-vaccinated chickens was infinite (van der Goot et al., 2005). However, R_0 measured within a commercial chicken flock infected with H7N7 in the 2003 Netherlands outbreak was measured to be as high as 6.5, while between commercial farms it was measured to be 3.1 (Stegeman et al., 2004). The mean commercial chicken farm-to-farm R_0 for H5N1 in affected industrialized countries was found to be 1.1 to 2.4 (Garske, Clarke and Ghani, 2007). R_0 for H5N1 spread between villages with backyard chickens in the 2006 outbreak in Romania was estimated to be between 1.95 and 2.68 (Ward et al., 2009). In the 2004 H5N1 outbreak in Thailand involving flocks of backyard and commercial chickens, within-flock R_0 was estimated to be between 2.26 and 2.64 (Tiensin et al., 2007). From laboratory transmission experiments, it was found that R_0 for H5N1 in un-vaccinated chickens was 1.6 (Bouma et al., 2009). The literature on the transmissibility of HPAI in poultry species other than chickens is relatively limited. Three papers were found covering experimental infections in pheasants, teal and Pekin ducks designed to evaluate vaccine impact on transmission (van der Goot et al., 2007; van der Goot et al., 2008; van der Goot et al., 2003). All of these studies found estimates of R_0 that were at least 1.5 using the final fraction size method. Upper bounds to the estimates could not be established because 100% infection was experienced in some experimental groups. R_0 of the cluster of H5N1 cases in humans in North Sumatra in May 2006 was 1.14 (Yang et al., 2007). These results indicate that the R_0 for H5N1 infection between chickens and between chicken flocks is relatively low, and that control of the disease in Indonesia may be a reasonable goal from the perspective of the transmissibility of the agent.

The objective of our study was to provide decision makers with information to help them understand what level of chicken population immunity must be achieved in order to interrupt HPAI transmission and decrease the incidence of disease using vaccination (Halloran, 1998; De Jong and Bouma, 2001). We designed our study to measure the reproduction number of H5N1 in mixed populations of backyard and small-scale commercial chickens in West and Central Java, where other domestic fowl such as ducks are in direct contact with chickens. We applied an adapted participatory infection tree methodology used to trace outbreaks in village settings, which also allowed for understanding the relative risk of different poultry species being involved in outbreaks, and documentation of parameters that provide a previously unavailable descriptive context to village HPAI outbreaks in Indonesia.

2. Methods

The study was carried out between 26 February and 20 November 2009. One to four outbreaks of Anigen® rapid test-confirmed HPAI were investigated in each of the 16 operational research districts. Each district *Dinas* generated a list of all outbreaks diagnosed by PDSR teams that occurred during the six months prior to the investigation. The outbreaks were divided into vaccinated and non-vaccinated areas, and those included in the study were chosen at random from the stratified list. The Rukun Tetangga (RTs) where the PDSR teams obtained positive Anigen® rapid tests, identified by GPS point, were considered the outbreak's study-RT. Contiguous RTs within the same Rukun Warga

(RW) – defined as housing not separated by major roads, rivers, forests, rice fields or other agricultural or natural features – were considered RT-clusters. Each investigation took a minimum of one day to complete, and consisted of a group interview of residents from the study-RT that was guided by a checklist (see Box), followed by a transect walk with interviews of groups and individuals throughout the study-RT and two other RTs in the RT-cluster.

Checklist of subjects covered in each transmissibility study outbreak investigation

- √ General description of outbreak (start and stop, diagnosis, intervention, vaccination status);
- √ Species present in RT and observed to be affected;
- √ Household flocks of up to 6 farmers (chicken morbidity, mortality, slaughter and sales, timeline, husbandry, free range distance);
- √ RT flock (map of all houses, affected houses and species kept in each, order and dates of household involvement, neighbouring RTs and their involvement, order and dates of neighbouring RT involvement);
- √ Epidemiological relationships between birds, households and RTs;
- √ GPS – index house, second affected house, closest affected house, closest unaffected house; and
- √ Housing density, house separation, topography, and commercial farms.

Using an approach adapted from infection tree reconstruction (Ferguson, 2008; Ferguson, Donnelly and Anderson, 2001) and intending to feed a stochastic susceptible-infected-removed (SIR) model (Ball and Neal, 2002), the study-RT was fully mapped, including all households, the types of poultry kept in each household, and all households affected (clinically sick or dead poultry) in the outbreak. As such, individual cases of sick or dead chickens that occurred in the study RT during the outbreak and that were determined to fit the PIA HPAI-compatible disease case definition were considered to be infected by HPAI. The vaccination status of the study-RT was determined, and any veterinary interventions as a result of the outbreak were documented. The timeline of the outbreak in selected individual households, the study-RT and the RT-cluster was obtained, including start and end dates, time from when the index case (symptomatic or dead) was noted (chickens at the household level, households at the RT level) to the second case, and the time between up to four subsequent cases. Household morbidity, mortality, sales and slaughter rates were obtained, as were poultry housing practices, and the number of households visited for free range birds. Households were marked using GPS so as to calculate the distance between the index and second affected household, index and closest affected household, and index and closest unaffected household. Factors directly related to the introduction and spread of HPAI in the RT were probed and documented, as were behaviors that may have led to limiting the outbreak. The density of housing patterns in the RT was noted (high density being <10m apart, medium being separation of between 10 to 50m, and low density being >50m apart), as was the type of separation between houses (none, gardens/trees, or rice fields), the topography (hilly/mountainous or low/flat) and nearest commercial farm (in the RT, RW, sub-village, village or none).

Data was entered into a Microsoft Access database and exported into Excel for analysis. It was assumed that data distribution was normal. The Z-test was used to determine statistical significance of relative risk ratios. The two-tailed McNemar's test was used to determine if any risk factors for HPAI introduction or spread occurred in a significantly higher proportion of outbreaks than other factors. The student's t-test was used to determine the statistical difference between the means of two independent datasets. Confidence intervals were used to determine the statistical difference between R, R_0 and R_e within flocks and between flocks calculated using the final fraction size equation for epidemic outbreaks (Diekmann and Heesterbeek ,2000; Heffernan, Smith and Wahl, 2005):

R_0 = -Ln(1-f)/f, where f is the final fraction size (f = number infected/total)

However, final fraction size calculations are generally more applicable to larger outbreaks where n>50, which was not always true for outbreaks included in our study. A collaborating team from the Imperial College, London, modeled both within-flock and between-flock transmission as separate generalized stochastic epidemic (GSE) SIR models, treating birds within a flock and the households within RTs as the respective epidemiological units of interest.

The GSE is a standard SIR model in a closed population of □ individuals, with □ initially infectious individuals and □ initially susceptible. Once infected, individuals remain infectious for a period of time according to a given distribution □, which can take any form. These individuals then transmit infection according to the points of a homogeneous Poisson process with intensity□/□. Once an individual reaches the end of its infectious period, it is removed and plays no further role in the epidemic. This is then a mass-action transmission model whereby the rate of transmission is independent of population size and, therefore, an infectious individual infects a susceptible individual at a rate inversely proportional to the size of the population. The assumption also results in an □$_0$ that is independent of population size, which provides an easy to interpret measure of the spread of infection when analyzing flocks of different sizes. Under this mass-action assumption the basic reproduction number is then:

$$R_0 = \beta E[I].$$

Using this construction, Ball (1986) derived the following relation between the final size outbreak probabilities $p^n_{y,s}(k)$, the transmission parameter β and the infectious period distribution I:

$$\sum_{k=0}^{l} \frac{\binom{s-k}{l-k} p^n_{y,s}(k)}{\left[\phi\left(\frac{\beta(s-l)}{n}\right)\right]^{k+y}} = \binom{s}{l}, \quad 0 \le l \le k \le n.$$

Here, $\phi(x) = E[\exp(-xI)]$, is the Laplace transformation of the assumed probability distribution of the infectious period I and $p^n_{y,s}(x) = P(Z = x | s, y, n, \beta, I)$ is the probability that $Z = x$ initially uninfected individuals are infected during the course of the outbreak given an initial susceptible population s, infectious population y, population size n, transmission parameter β and infectious period distribution I. These probabilities can then be rewritten as a triangular set of equations that can be solved recursively:

$$p^n_{y,s}(k) = \frac{1 - s_k}{a_{kk}}, \quad s_k = \sum_{l=0}^{k-1} a_{kl} p^n_{y,s}(l), \quad k = 0, \dots, N,$$

where

$$a_{lk} = \frac{\binom{s-k}{l-k}}{\binom{s}{l}\left[\phi\left(\frac{\beta(s-l)}{n}\right)\right]^{k+y}}.$$

Given the probability distribution of I, the infectious period distribution, it is possible to obtain the likelihood of any set of N final outbreak sizes, number of initial infectives and population sizes $(\underline{x}, \underline{y}, \underline{n}) = \{(x_0, y_0, n_0), \dots, (x_N, y_N, n_N)\}$ for any chosen value of β in an unvaccinated population:

$$\pi\left(\beta \middle| \left(\underline{x}, \underline{y}, \underline{n}\right), I\right) \propto \pi\left(\left(\underline{x}, \underline{y}, \underline{n}\right) \middle| \beta, I\right) \pi(\beta)$$

$$\text{with } \pi\left((\underline{x},\underline{y},\underline{n})\middle|\beta,I\right)=\prod_{i=0}^{N} p_{y_i,n_i-y_i}^{n_i}(x_i)$$

This likelihood can then be explored using a standard random-walk Metropolis-Hastings algorithm to reach and draw from the posterior distribution of β and thus R_0. 100,000 iterations of the algorithm following a "burn-in" of 2000 iterations was assessed to be sufficient. This analysis was repeated at the between- and within-flock level, and we assessed the extent to which the estimates of β varied when calculated for outbreaks occurring in RTs designated un-vaccinated or vaccinated. The extent to which the obtained posterior distributions supported a reduction in transmissibility in vaccinated RTs relative to that in un-vaccinated RTs was then assessed by calculating the posterior odds that □was lower which, as no prior information about □was assumed, then provides a Bayes Factor (BF) for this hypothesis. The evidence in favor of lower transmissibility in outbreaks occurring in vaccinated areas was then judged by the Jeffreys scale, namely, if BF varies between 1 and 3, the evidence for a given hypothesis is poor; if it is between 3 and 10, this evidence is substantial; if it is between 10 and 30, it is strong; if it is between 30 and 100, it is very strong; and if it is above 100 it is decisive.

R_0 calculated in this manner allows for the calculation of the fraction of the population that needs to be immune (ƒ) in order to interrupt transmission according to the equation (Halloran 1998):

$ƒ > 1-(1/R_0)$

The relative risk of a species to be present in a household that experienced an outbreak was calculated using the following equation (Sheskin, 2004):

Relative risk = (A/(A+B)) / (C/(C+D)), where:

- A = number of affected households with the species present;
- B = number of unaffected households with the species present;
- C = number of affected households without the species present; and
- D = number of unaffected households without the species present.

3. Results

Of the 41 outbreaks studied, fifteen were in vaccinated areas of the operational research and 26 in non-vaccinated areas (Table 4.4.1). Of the outbreaks from vaccinated areas, four RTs (26.7%) had received vaccination in the six months prior to the outbreak. At the time they were investigated, 17 of the outbreak sites were considered by PDSR to be apparently free of HPAI, 15 were considered controlled, two were suspect and seven were infected. Eight of the outbreaks had received no veterinary interventions in response to the outbreak. Of the 33 that did receive veterinary interventions, all were sprayed, and in one outbreak culling was also carried out.

Most backyard poultry in the study area were free range (90.7% of responding households), with the majority caged at night and allowed to roam during the day (64%), and a minority fully free range (26.7%) (Table 4.4.2). The mean number of households visited by all types of free-range chickens was 4.2 (±4.2).

Outbreaks in this study tended to occur in areas with medium to high-density housing (houses separated by <10-50m), and where small agricultural plots separated houses. Commercial poultry were present within the village in 47-50% of the outbreaks (Table 4.4.3).

The length of outbreaks in vaccinated areas (4.0±5.2; 31.4±27.1; and 43.9±32.8 days, respectively for household flocks, RTs and neighborhoods) tended to be shorter than in non-vaccinated areas (6.8±15.3; 34.0±29.2; and 46.5±36.4 days, respectively), and the proportion of susceptible units affected lower (67.4±27.2%; 53.7±36.4%; and 83.9±24.9%, respectively for household, RT and neighborhood flocks in vaccinated areas, and 71.2±31.9%; 58.8±30.2%; and 84.3±23.2%, respectively for non-vaccinated areas) (Tables 4.4.4 and 4.4.5). However, these results are not significant according to the student's t-test for independent samples. The mean number of hours between the first and second chickens infected in a household flock was 27.4±30.1, while the mean number of hours between the first and second infected households in an RT was 41.7±40.9 hours (Table 4.4.6).

Table 4.4.1: Number and types of transmissibility studies per district

District	Study Month	Total Outbreaks Studied	Outbreaks in Vaccinated Groups Studied	Outbreaks in non-Vaccinated Groups Studied	Affected households in Vaccinated Groups Studied	Affected households in non-Vaccinated Groups Studied
Bantul	May	3	2	1	7	5
Brebes	July	3	0	3	0	9
Cirebon	September	3	2	1	4	3
Grobogan	October	2	0	2	0	2
Gunung Kidul	November	1	0	1	0	3
Indramayu	March	2	1	1	3	6
Kendal	July	2	0	2	0	6
Klaten	October	2	1	1	2	2
Kulon Progo	August	3	2	1	6	2
Kuningan	September	2	2	0	7	0
Madjelengka	February	3	1	2	2	7
Purbalingga	September	4	2	2	3	4
Semerang	November	4	0	4	0	8
Sleman	May	3	0	3	0	8
Sumedang	April	2	1	1	3	2
Temangung	November	2	1	1	3	3
Totals		**41**	**15**	**26**	**40**	**70**

Table 4.4.2: Types of poultry housing, and the number of other houses visited by household chickens

	Free Range	Night Caging	Permanent Caging
Number of Households (n=75)	20 (26.7%)	48 (64.0%)	7 (9.3%)
Mean Number of Other Houses Visited (in contact) by Household Chickens (±SD) (n=68)	3.6±2.8	4.5±4.7	N/A

Table 4.4.3: Geographic and settlement patterns and their association with outbreaks in vaccinated and non-vaccinated areas

	Housing Density			Housing Separation			Topography		Commercial Poultry Presence					
	L	M	H	Gardens	Rice fields	None	Flat	Hilly/ mountains	RT	RW	Sub-village	Village	None	Presence Total
Vaccinated (n=15)	2	9	4	13	0	2	9	6	2	1	1	3	8	7 (47%)
Non-vaccinated (n=26)	3	11	12	15	0	11	19	7	3	3	0	7	13	13 (50%)

L: low; M: medium; H: high

Table 4.4.4: Mean length of outbreak at different population levels in days

	Household Flock (+SD)	**RT(+SD)**	**Neighborhood* (+SD)**
Vaccinated	4.0±5.2 (n=27)	31.4±27.1 (n=15)	43.9±32.8 (n=14)
Non-vaccinated	6.8±15.3 (n=48)	34.0±29.2 (n=25)	46.5±36.4 (n=22)
One-tailed P**	0.18	0.39	0.41

*** Defined as a group of contiguous RTs within an RW**
**** Student's t-test for independent samples**

Table 4.4.5: Proportion of susceptible units affected at different population levels

	% Chickens in Household Flock (+SD)	% Households in RT (+SD)	% RTs in Neighborhood* (+SD)
Vaccinated	67.4+27.2 % (n=41)	53.7+36.4 % (n=15)	83.9+24.9 % (n=15)
Non-vaccinated	71.2+31.9 % (n=68)	58.8+30.2 % (n=25)	84.3+23.2 % (n=26)
One-tailed P**	0.23	0.32	0.48

*** Defined as a group of contiguous RTs within an RW**
**** Student's t-test for independent samples**

Table 4.4.6: Mean number of hours between the index case and second case at different population levels

	Hours	SD	n
Between house 1 and house 2	41.7	40.9	25
Between chicken 1 and chicken 2	27.4	30.1	47

Although there was no significant difference (p=0.16) using the student's one-tailed t-test for independent samples in the distance from the index household to the closest affected household (35.5+27.8) and from the index household to the second affected household (44.5+36.2), the distance from the index to the closest unaffected household (92.2+70.3) was significantly greater than that from the index to the closest affected (p=0.0003) (Table 4.4.7).

Table 4.4.7: Distances between the index household and other households in RTs affected by HPAI outbreaks

	Meters+SD
Index household to second affected household (n=28)	44.5 + 36.2
Index household to closest affected household (n=26)	35.5 + 27.8
Index household to closest unaffected household (n=19)	92.2 + 70.3

For the outbreaks in this study, the mean morbidity was 80.9+28.8%, mortality 77.6+27.7%, and case fatality 97.3+12.3%. This provides a recovery rate of 2.7+12.3%. When outbreaks occurred, 9.3+20.7% of chickens in an RT were sold and 5.0+14.0% were slaughtered and consumed by individual households (Table 4.4.8).

Table 4.4.8: Mean morbidity, mortality, case fatality, sales and slaughter rates

n=103	Morbidity %	Mortality %	Case Fatality %	Sales Rate %	Slaughter Rate %
Mean	80.9	77.6	97.3	9.3	5.0
SD	28.8	27.7	12.3	20.7	14.0

There was significant risk for HPAI outbreaks to occur in households where Muscovy ducks (*Cairina moschata*) ($p<0.0001$), non-commercial chickens ($p=0.0001$), broilers ($p=0.003$) and geese ($p=0.005$) were kept, but there was not a significant risk associated with keeping pigeons ($p=0.20$) or ducks (Anatidae family not including *Cairina moschata*) ($p=0.95$) (Table 4.4.9).

Table 4.4.9: Relative risk of different species being present in households affected by HPAI

Species (n present, n absent)	Relative Risk Ratio	95% CI	Z statistic	P value
Muscovy Ducks (194, 756)	1.38	1.24-1.53	6.00	<0.0001
Non-commercial chickens (901, 49)	2.96	1.70-5.16	3.83	0.0001
Broilers (24, 926)	0.14	0.04-0.51	2.95	0.003
Geese (22, 928)	1.34	1.09-1.64	2.80	0.005
Pigeons (57, 839)	0.84	0.64-1.10	1.29	0.20
Ducks (62, 888)	1.00	0.80-1.24	0.06	0.95

Four risk factors were documented to have played a role in the spread of outbreaks in an RT: bird contact between households, such as in gardens or at water points (73.2% of outbreaks); carcass disposal in rivers (29.3%); local chicken traders (19.5%); and people visiting other households during outbreaks (9.8%). The proportion of outbreaks associated with bird contact between households was significantly higher than the other three risk factors for outbreak spread ($p<0.0003$ or less). There was no significant difference between the proportion of outbreaks associated with carcass disposal in rivers and local chicken traders ($p=0.42$) or with people visiting other households during outbreaks ($p=0.08$), nor was there a significant difference between the proportion of outbreaks associated with local chicken traders and people visiting households during outbreaks ($p=0.34$).

Four risk factors were documented to have played a role in the introduction of HPAI to an RT: new bird entry into household flocks (24.4%); outbreaks in local markets (19.5%); local chicken traders (19.5%); and outbreaks in commercial poultry farms (7.3%). There was no significant difference in the proportion of outbreaks associated with these four risk factors (Figure 4.4.1).

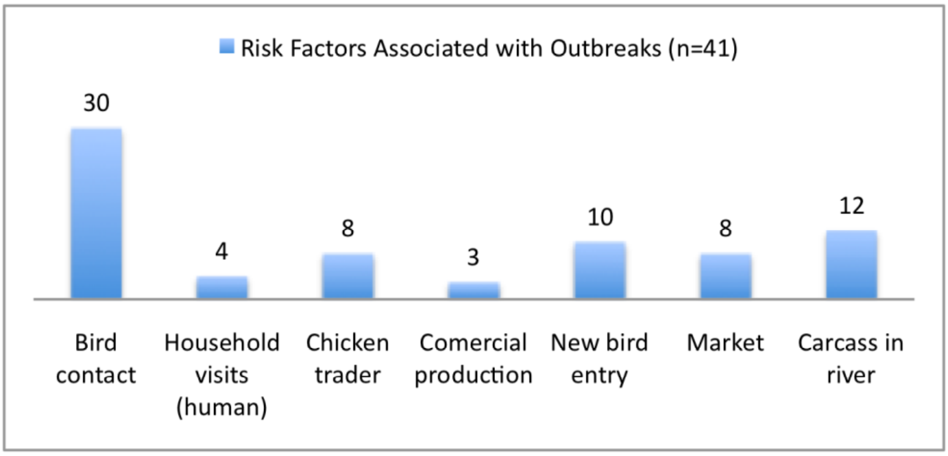

Figure 4.4.1: Risk factors identified to have been associated with an outbreak during the course of the investigation

Using the final fraction size equation, for the overall operational research study area R_e between birds within flocks was 1.72 (1.60-1.87, 95% CI), and between flocks 1.48 (1.34-1.66).There is little overlap between these 95% confidence intervals, indicating that $R_e$between chickens was significantly higher than $R_e$between flocks in the study area. R_e between chickens in vaccinated areas (1.66, 1.50-1.88) was lower than R_o in unvaccinated areas (1.77, 1.60-2.01), as was R_e between flocks in vaccinated areas and R_o in unvaccinated areas (1.42, 1.22-1.78; and 1.52, 1.34-1.79, respectively), but not significantly so.

Similarly, the GSE SIR model showed that for the overall operational research study area R_e within flocks (posterior mean 2.54, 95% CIs 2.35-2.74) was higher than between flocks (posterior mean 2.01, 95% CIs 1.81-2.23) and this difference was decisive according to the Jeffreys scale. It also found that within-flock R_e in vaccinated areas (posterior mean 2.23, 95% CIs 1.96-2.51) was decisively lower than R_o in non-vaccinated areas (posterior mean 2.79, 95% CIs 2.52-3.1). Between-flock R_e and R_o werevery similar in non-vaccinated areas (posterior mean 2.07, 95% CIs 1.82-2.35) and vaccinated (posterior mean 1.9, 95% CIs 1.59-2.26), respectively, although, with a BF=7.69, there was substantial evidence of a lower R_e according to the Jeffreys scale.

The level of population immunity necessary to interrupt transmission between birds within a household flock is 63.8% (95% CIs 59.8-67.2) according to the GSE and 43.5% (95% CIs 37.5-50.2) according to the final fraction size calculation, and to interrupt transmission between household flocks in an RT, 51.7% (95% CIs 43.5-55.4) according to the GSE and 34.1% (95% CIs 25.5-44.0) according to the final fraction size calculation (Table 4.4.10).

Discussion

Vaccinations for the operational research took place between July 2008 and July 2009. Thus, the second half of this study (which ended in November 2009) may have been biased towards more major and fewer minor outbreaks in the vaccinated areas as population protection levels waned, thereby decreasing the difference between R_e in vaccinated areas and R_o in unvaccinated areas. Of the 41 H5N1 outbreaks studied, nine (22% of the total) were considered by the PDSR system to be currently infected with H5N1, and therefore may have benefited from more accurate farmer recall than the other 32.

Table 4.4.10: Levels of population immunity necessary to interrupt transmission within a household and between households according to R_o obtained from the GSE model and final fraction size equation

	GSE			Final Fraction Size		
	% Flock protection	Lower 95% CI	Upper 95% CI	% Flock protection	Lower 95% CI	Upper 95% CI
Between household flocks	49.7%	43.5%	55.4%	34.1%	25.5%	44.0%
Between birds in a household	63.8%	59.8%	67.2%	43.5%	37.5%	50.2%

The number of outbreaks studied in non-vaccinated areas was 26, while the number of outbreaks studied in vaccinated areas was 15 (63% and 37% of the total, respectively). The predominance of outbreaks from non-vaccinated areas is likely a reflection of HPAI being somewhat controlled in vaccinated areas. Of the 15 outbreaks that occurred in vaccinated areas, vaccinations had actually been given in only four of the areas (26.7%) during the last six months. This level of coverage is consistent with the proportion of birds at the flock level having antibodies against H5N1 in vaccinated areas (~30%) from the serological monitoring (Section x) and vaccination program coverage levels reported by PIA practitioners (section y).

This is the first study to report R_o at both the within-flock and between-flock levels for mixed populations of small-scale commercial and backyard chickens in Indonesia. Using both final fraction size and a GSE SIR model, it was found that R_o between chickens within a flock was significantly higher than the R_o between flocks. This finding is consistent with other studies reported in the literature (Tiensin et al., 2007; Bouma et al., 2009; Ward et al., 2009), although the magnitude of difference is smaller in our study. Our results indicate that 63.8% of birds in household flocks need to be immune to H5N1 to interrupt transmission in a flock, and that 49.7% of household flocks need to be immune (meaning 63.8% of the flock members are immune) in a neighborhood to interrupt transmission within a neighborhood, according to the GSE SIR model results. These preliminary findings provide an important guide for vaccination program policy and deserve validation through further research.

The GSE SIR model showed that within-flock R_e in vaccinated areas was significantly lower than R_o in non-vaccinated areas (Stegeman, Elbers and Smak et al., 1999; (Ball and Neal, 2002; Bos et al., 2009; de Jong and Hagenaars, 2009). This is consistent with the findings of the longitudinal study, in which the incidence of HPAI-compatible events in vaccinated areas was found to be significantly lower than in control areas, even though only modest levels of vaccination coverage were achieved. Although between-flock R_e and R_o were significant different, the differences were not large. This suggests that households' flocks mix frequently and would be better described as meta-populations. For the future, our findings indicate that meta-population models may be a more appropriate way to describe neighborhood poultry populations.

It is probable, since the majority of outbreaks included in this study (92.7%) were diagnosed only by the PDSR case definition and rapid test, that a small percentage of the sample set were outbreaks of other diseases misclassified as HPAI. The PDSR diagnosis involves application of a very broad clinical case definition (mortality in one or more birds) in response to farmer reports of suspect HPAI outbreaks. When the case definition is met, it is followed by testing of up to three birds in the affected flock with the Anigen® rapid test for Type A influenza antigen. Thus the PDSR diagnosis is at the flock level, where the threshold for calling the flock positive is at least one positive test. It is also a series of three tests: the farmer's recognition and report, the subsequent application of the PDSR case definition, and the subsequent testing of three chickens with the Anigen® rapid test. As there are no published reports on the accuracy of the PDSR case definition, it is assumed here, given the broad nature of the definition, that its sensitivity is high but that its specificity is low. The sensitivity and specificity of the Anigen® test was determined by Boland et al. (2006) for a mixed population of small-scale commercial and backyard chickens in Indonesia to be 76% and 97%, respectively (Boland et al., 2006). Thus the sensitivity and specificity of the Anigen® rapid test to positively identify at least one infected bird out of three tested is 77.9% and 91.3%, respectively. As the PDSR responds mainly to farmer reports, one may assume a relatively high HPAI prevalence among the sample population being tested in the PDSR diagnostic scheme. Thus using the accuracy of the Anigen® rapid test as determined by Boland and applied to three animals in a flock – assuming high sensitivity (90%) and low specificity (40%) of the PDSR case definition, and an HPAI prevalence of 50% – one can expect that the serial sensitivity, specificity and positive predictive value of the PDSR diagnostic procedure to be in the range of 70%, 95% and 93%, respectively. Thus, three (7%) of the outbreaks in this study may have been caused by ND or other agents. No figures for ND R_o could be found in the literature. Given the probability that only a small number of diagnosed outbreaks that were false positives were included in our study, it is not likely that they had an appreciable impact on the reproduction numbers we determined.

Mortality rates from our study (77.6$\pm$27.7%) are consistent with the PIA case definitions for sudden death and HPAI-compatible disease (over 80% in a household flock). Recovery rates in our study were unusually high (2.7$\pm$12.3%), and may indicate an attenuation of virus pathogenicity. However, given that 7% of the outbreaks studied may have been due to diseases other than HPAI, and higher recovery rates are more commonly associated with these diseases, it is likely that the recovery rate we observed is due to inclusion of some non-HPAI outbreaks.

In our study a significant risk was found for antigen test-confirmed HPAI outbreaks to occur in households raising Muscovy ducks, non-commercial (backyard) chickens, broiler chickens, and geese; households with Muscovy ducks present showed the highest risk. The presence of ducks and pigeons was not associated with households being affected during outbreaks. This finding may indicate that the presence of ducks and pigeons does not place households at higher risk for HPAI outbreaks than other households. However, it is also possible that the majority of households that keep ducks or pigeons do not keep other types of poultry, and therefore did not notice that their poultry were affected during the outbreaks. Contact between birds from different household flocks was the risk factor most frequently documented to have contributed to the spread an outbreak (70.7% of outbreaks), while the introduction of new birds to a household flock was most frequently documented to have led to the introduction of the disease (22.0%). Carcass disposal in rivers (29.3%) was also an important risk factor documented to have contributed to the spread of outbreaks.

The majority of farmers in our study raise their poultry in free-range systems (90.7%), and the average number of households contacted by a single free-range chicken was 4.2. This finding was consistent with the similarity of within flock and between flock R_0 estimates. These findings indicate that backyard poultry populations as they occur on Java provide the necessary environment for indefinite HPAI transmission, and suggest that the backyard sector may be capable of maintaining HPAI endemically independent of other populations. However, it must be kept in mind that, although evidence directly linking an outbreak to commercial poultry production could only be documented in 7% of the outbreaks in our study; 49% of the outbreaks were detected in villages where commercial farms were present. Population and disease modeling using these parameters and the R_o from our study would provide further insight into the capacity of backyard flocks on Java to maintain HPAI endemically without introduction from commercial and/or market flocks (Lesnoff et al., 2009).

Conclusion

The results of the transmissibility study indicate that the moderate levels of vaccination sustained by the operation research resulted in a statistically significant reduction of the transmission of HPAI both within and between flocks. This is fully consistent with the results of the longitudinal follow-up using participatory impact assessment methods and the reduction in reports of outbreaks observed in the PDSR surveillance system.

The level of population immunity necessary to interrupt transmission between birds within a household flock is 63.8% (95% CIs 59.8-67.2) according to the GSE and 43.5% (95% CIs 37.5-50.2) according to the final fraction size calculation, and to interrupt transmission between household flocks in an RT, 51.7% (95% CIs 43.5-55.4) according to the GSE and 34.1% (95% CIs 25.5-44.0) according to the final fraction size calculation.

The transmissibility study utilized far fewer resources than the PIA approach and provided information on both within and between flock transmission rates as well as information on risk factors associated with transmission. In addition, analysis of the population immunity thresholds required to interrupt transmission provides essential guidance for vaccination strategy and is an important in decision-making.

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4.5. Analyzing patterns of HPAI outbreaks diagnosed by PDSR

Abstract

The objectives of this study were to describe the temporal and spatial distribution of highly pathogenic avian influenza (HPAI) cases detected by the Participatory Disease Surveillance and Response (PDSR) program in Indonesia from January 2006 to May 2008, and secondly to characterize the 16 districts that participated in the ORIHPAI project with respect to the density of backyard poultry and the response to HPAI outbreaks. The key results of our study include: 1) evidence to support that HPAI has seasonal fluctuations; 2) we found considerable regional variability in the patterns of case detection suggesting that data aggregated nationally should be interpreted with caution; and 3) there is considerable variation between and within districts in the implementation of HPAI control measures; however, most districts have recorded very little vaccination and/or culling activities.

1. Introduction

The PDSR program began in 12 districts of Indonesia and, upon finding a considerable burden of HPAI, the program rapidly expanded (Jost et al. 2007) and by May 2008 covered 212 districts. PDSR officers are local government officers who work actively with communities to detect, control and prevent HPAI. They are primarily concerned with village (backyard) poultry, but also have some involvement with small-scale commercial producers. Part of their work entails searching for and responding to reports of suspect HPAI cases. Whenever suitable specimens are available, a rapid antigen test is done to test for HPAI. Data from all visits is recorded in an MS Access database.

The objectives of our study were to:

- Explore HPAI case detection by participatory disease surveillance (PDS) over time, nationally; and
- Characterize the 16 districts involved in the ORIHPAI project with respect to PDS case detection over time, density of backyard poultry, and the use of vaccination and culling by participatory disease response (PDR) teams.

2. Methods

All analyses were done using the original PDSR database, which contains data on PDS and PDR visits from January 2006-May 2008. It is an MS Access relational database composed of many tables. All data are entered at the respective local disease control center (LDCC) and forwarded to the FAO epidemiology team in Jakarta on a weekly basis.

Data in the “PDS Interview” table reflect the results of interviews performed by PDS officers searching for HPAI cases. Each interview was recorded as a separate “visit”. In some instances, a team might have conducted several interviews in one village over a short period of time (i.e., on the same day); each of these interviews was entered as a different visit. If an HPAI-compatible event was detected during the visit, a rapid antigen test was usually performed to confirm the presence of HPAI, depending on the possibility of collecting suitable samples.

The “PDR data” table contains the results of visits by PDR officers to communities. These visits might or might not occur in response to an active HPAI outbreak.

The number of positive rapid test cases, the number of PDS visits, and the number of HPAI outbreaks were extracted, by date and location, from the “PDS Interview” table. PDS interview data contained within the PDR data table were also included if the PDR visit was not in response to a PDS visit. The numbers of vaccinations and culls, and the numbers of animals involved in each, were extracted from the PDR data table for the 16 districts involved in the OR. All analyses were done using Stata SE 10.1 (StataCorp, College Station, Texas).

The results from the analysis using national data were presented to stakeholders (CMU, DGLS, FAO and USAID) in Jakarta in oral and written presentations. The results specific to the 16 districts were combined with the district profiles and presented to the districts in individual "district information packages".

3. Results

The key results of our study include:

1) There is evidence to support that HPAI has seasonal fluctuations, with peaks between February and April and a trough in November to December (Figure 4.5.1).
2) There is considerable regional variability in the patterns of case detection. Therefore, data aggregated nationally could be misleading and should be interpreted with caution. Further research is required to understand the variations between regions (Figure 4.5.2).
3) There is considerable variation between and within districts in the implementation of HPAI control measures. Generally, more culling and vaccination has occurred in areas reporting higher numbers of HPAI cases, as in Yogyakarta province. Exceptions to this occur, however. For example, large numbers of birds were vaccinated in Indramayu, but no cases were reported. Perhaps the vaccination protected the poultry in this area from HPAI infection. Also, there are areas where a large number of cases have been found, but no response recorded, such as in selected sub-districts in Kulon Progo.

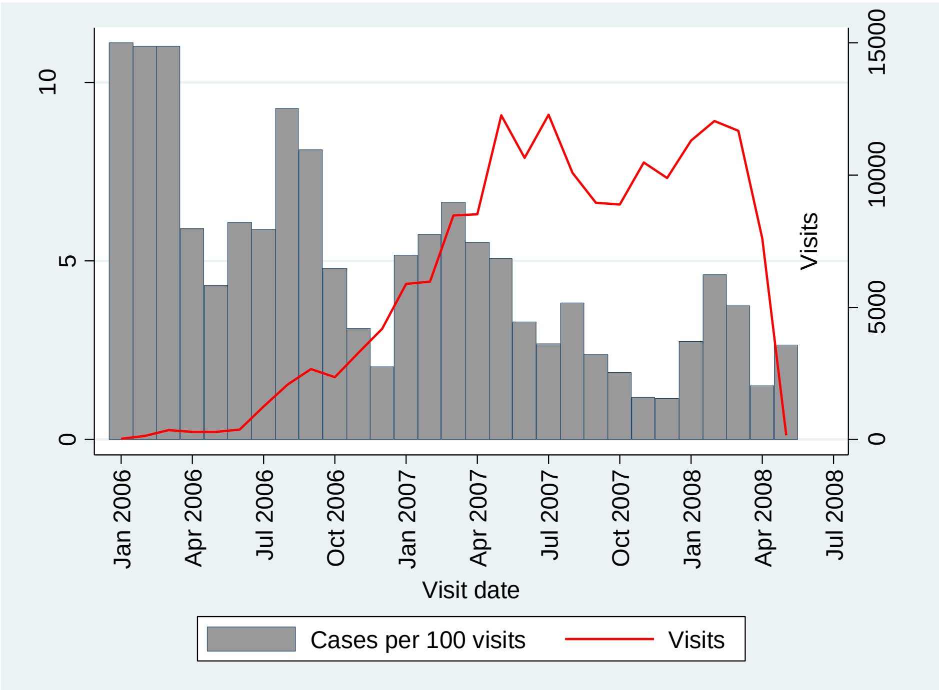

Figure 4.5.1: Number of positive rapid test HPAI cases found per 100 PDS visits, and the total number of PDS visits, over time

Descriptive maps were produced to examine the distribution of cases, PDSR visits, and the implementation of control measures (Figures 4.5.3-5). These maps reinforce the large variation between the districts in the distribution of cases, PDSR visits, the reported poultry populations, and the application of control measures. In these maps, it is evident that variation occurs both between and within districts (i.e., between sub-districts). This variation in case distribution is not clearly related to the size of poultry populations nor the number of PDSR visits carried out. This suggests foci of heightened transmission that warrant further study. There appears to be a tendency to have higher duck populations along the north coast, and native chicken populations are larger in Brebes than any other district. However, the poultry population data is of questionable accuracy.

Discussion

Over the life of the original PDSR database, the total number of PDSR visits gradually increased between January 2006 and May 2007, and then reached a plateau. This reflects the growth of the PDSR program. Looking at nationally aggregated data, there were peaks in the number of cases per visit from January-March in both 2007 and 2008, and troughs in December in both 2006 and 2007, suggesting a seasonal pattern to HPAI incidence. The change in the case-detection rate over time could also reflect changes or events in the PDSR system (e.g., trainings) that temporarily improved detection efficiency.

When the plots were stratified by local disease control center and district, it became apparent that there is considerable regional variability in the patterns of case detection. There is a consistent peak in the case detection rate between March and May in 7 out of 14, or 50%, of LDCCs (Lampung, Bandung, Malang, Semarang, Yogyakarta, Kalimantan and Tuban). As with the nationally aggregated data, these observed fluctuations could result from differences in LDCC and district practices, and/or seasonality in the level of HPAI in different regions. Because the seasonal pattern observed when the data are aggregated nationally is not always consistent, the aggregated data should be interpreted with caution.

In the vast majority of PDR visits in the 16 OR districts, neither culling nor vaccination was performed, regardless if they were responding to a case of active HPAI or not. This indicates that the PDR immediate response policy was not implemented. In order to learn lessons from this experience, a detailed social analysis is warranted to examine the needs, roles and attitudes of stakeholders at all levels of the response system.

Conclusions

This analysis demonstrated that there is considerable variation over time and space in the detection of HPAI cases by the PDSR teams. The reason for this variation is not fully understood, but is assumed to be due to different husbandry practices, poultry population densities, and environmental factors such as temperature and rainfall and/or surveillance practices. Some of these potential risk factors were investigated in Section 4.5 of this report. Further studies to better characterize the nature and causes of the variation should be conducted to provide insight to measures that would effectively control HPAI.

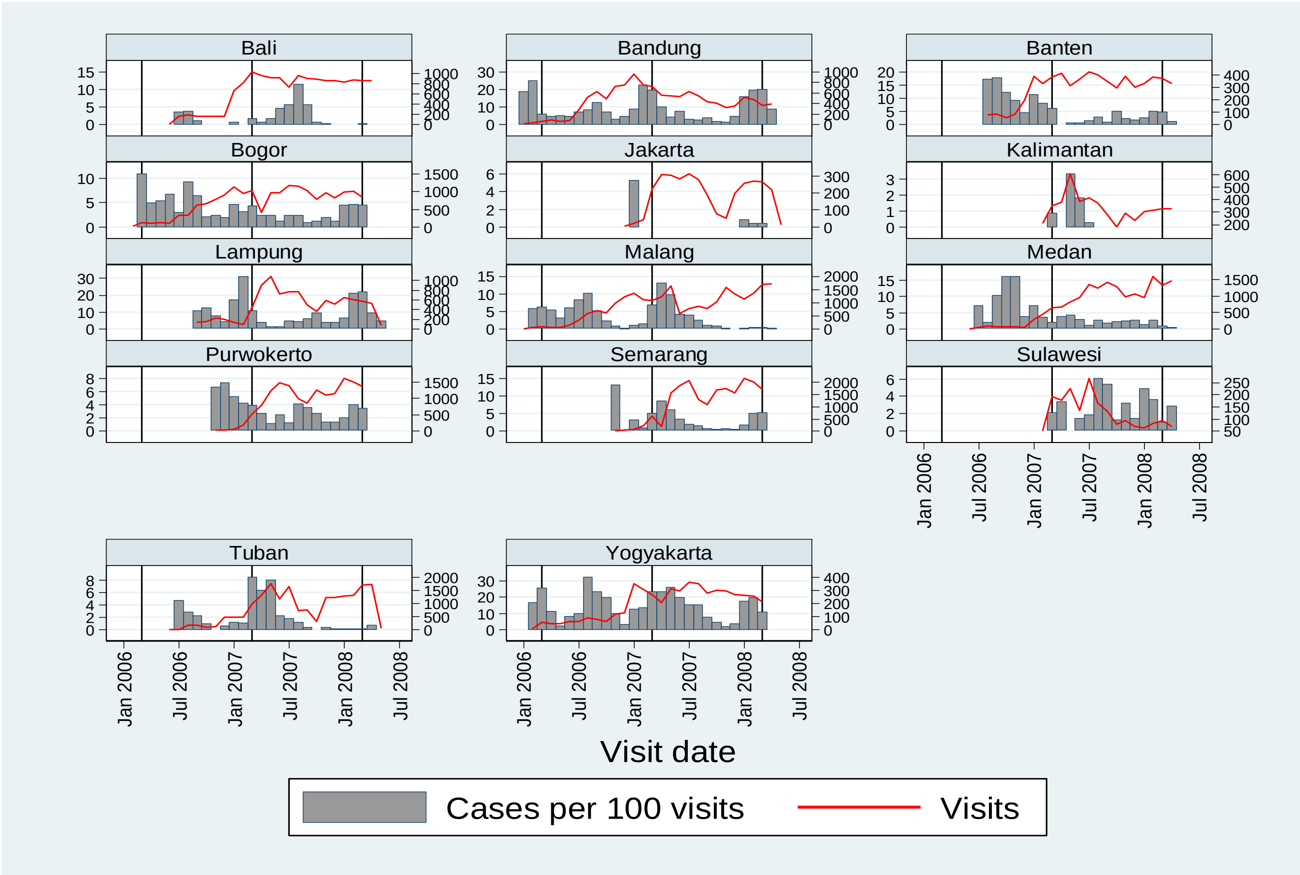

Figure 4.5.2: Number of rapid test positive HPAI cases found per 100 PDS visits (bars), and the total number of PDS visits (line), over time for different LDCCs (note that the axis' scale changes for each LDCC and that March of each year is indicated with a vertical line)

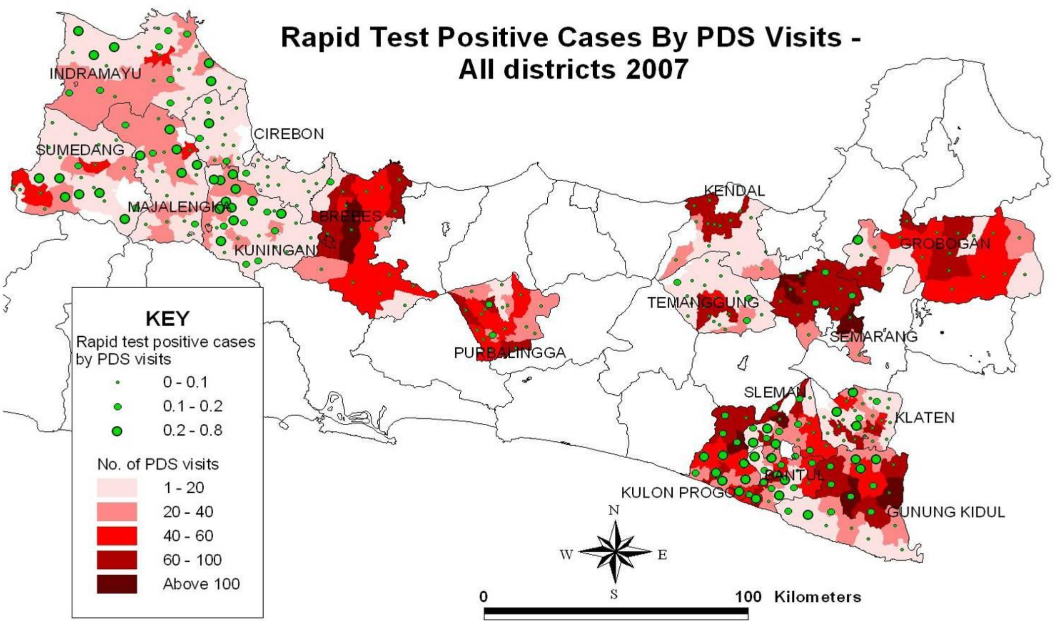

Figure 4.5.3: Map showing the ratio of rapid test positive cases to the number of PDSR visits (circles) and the total number of PDSR visits (shading) in districts participating in the OR

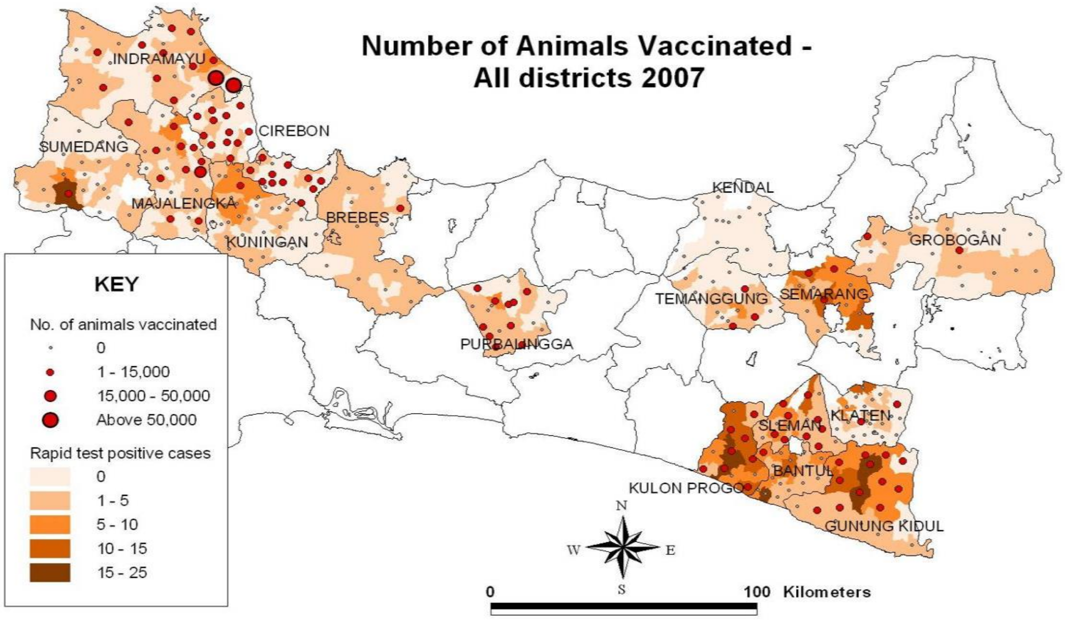

Figure 4.5.4: Map showing the number of animals vaccinated against HPAI (circles) and the number of positive HPAI rapid test cases by sub-district (shading) in districts participating in the OR

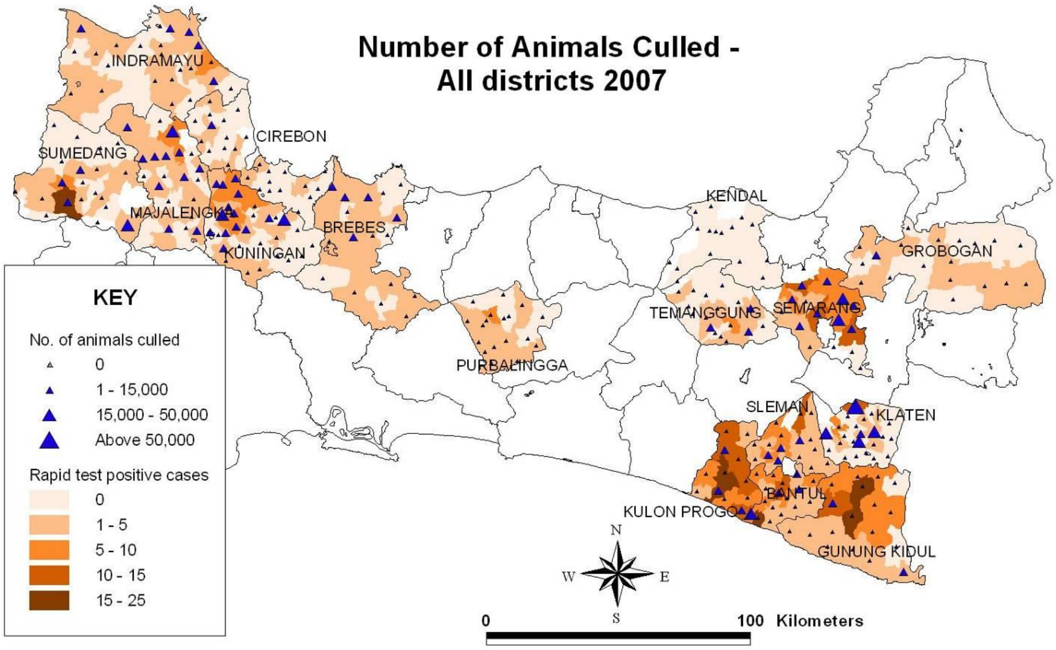

Figure 4.5.5: Map showing the number of poultry culled (triangles) and the number of positive HPAI rapid test cases by sub-district (shading) in districts participating in the OR

References

Jost C.C., Mariner, J.C., Roeder, P.L., Sawitri, E. and Macgregor-Skinner, G.J. 2007. "Participatory epidemiology in disease surveillance and research." *Rev Sci Tech*, 26:537-549.

4.6 Content analysis of the original PDSR database

Abstract

A wealth of information about the clinical presentation of HPAI in Indonesia is contained within free text fields in the Indonesian Ministry of Agriculture's Participatory Disease Surveillance and Response (PDSR) database. This surveillance system uses semi-structured interviews and open-ended questions that enhance the system's ability to discover unanticipated information and knowledge. However the resulting open-ended responses create special challenges for analysis in standardized databases. A text-mining program was used to describe the clinical signs and perceived risk factors observed by field veterinarians and recorded in the database. Two bilingual categorization dictionaries were manually constructed, one for risk factors and another for the clinical signs, using WordStat 5.1 (Provalis Research). The dictionary was structured as a hierarchical tree, with categories selected by the investigators and structured to provide information useful to the disease control program. From January 2006-May 2008, 12,348 PDSR visits resulted had a free text entry in at least one of the database fields of interest and were included in this analysis. The PDSR officers most frequently attributed the source of HPAI and its spread to inappropriate carcass disposal, the presence of free-ranging poultry, and to poultry trading practices. These factors would cause the spread of HPAI both within and between communities. Sudden death and cyanosis were the most commonly reported clinical signs and, along with respiratory signs, inflammation, haemorrhage, and high population mortality rates, they were significantly associated with positive rapid-test diagnoses. Gastrointestinal signs, neurological signs, anorexia, and depression were significantly associated with a negative rapid-test result. While these results must be interpreted in the context of the surveillance program in which they were collected, they clearly demonstrate the utility of text-mining programs and content analysis, and add value to information collected through semi-structured survey methods.

1. Introduction

Text mining is broadly defined as an analytical process that adds value to information provided in text form. It can categorize information and search for links between terms and/or documents. It has been extensively applied in the biomedical sciences (Zweigenbaum et al., 2007) and has also been used to derive information from dictated or electronic medical records (Heinze et al., 2001; Muscatello, Churches and Kaldor et al., 2005). Content analysis is a kind of text mining commonly used in the social sciences to classify the content of open questions, but to date it has rarely been used in veterinary medicine. Because veterinary medicine uses its own, very colloquial, terminology, tools developed for human medicine cannot be easily applied. A web and literature search turned up only two examples of text mining or content analysis in the veterinary sciences (Berezowski, Snyder and McLarty, 2007; Lam et al., 2007).

From January 2006-May 2008, information about each PDSR visit (N=172,458) was recorded in an MS Access database. When suspect cases were identified, information about the clinical signs that were observed, the most likely source of infection, and the possible factors contributing to disease spread were recorded in free text form, either in English or Indonesian (along with other data). The data in these free text fields cannot be analyzed using traditional quantitative techniques. Therefore, the objective of our study was to derive further information from the data stored in these fields.

2. Methods

Two categorization dictionaries – one for the "source field" (*sf*) and "risk factor field" (*rff*), and another for the "clinical signs field" (*csf*) – were manually constructed using WordStat 5.1 (Provalis Research). The content of the relevant database field(s) determined the terms (the words or phrases) included in each dictionary.

The dictionaries were structured as hierarchical trees. At the bottom of each tree, synonyms were grouped together to form a single category. Related categories were then grouped under progressively broader categories. The investigators selected the categories, and the hierarchical trees were structured to provide information useful to the disease control program (Table 4.6.1).

The "clinical signs", "risk factor" and "source" fields were analyzed separately. Frequencies of each category were determined. For the source and clinical signs fields, the category frequencies were cross-tabulated against the results of the rapid test, and the equality of the proportions testing positive and negative were assessed using a Chi square test to determine if there was any association between the category and the rapid test status of the outbreak. Records with missing rapid test results were excluded from this part of the analysis.

Table 4.6.1: The broad categories in the categorization dictionary developed for analysis of the risk factor and source fields in the PDSR database, and the key subcategories contained within each

Broad category	Factors that:	Key sub-categories:
Spread *within* community	Increase the risk of local (within community) spread	Inappropriate carcass disposal; Bird species raised in community; Nearby HPAI infection
Spread both between *and* within communities	Increase the probability of infection from either an internal or external source	Free range poultry; Unclean housing; Lack of vaccination
Spread *between* communities	Increase the risk of introduction from a source outside of the community	Poultry trade; Movement people/animals
Climate	Are related to season or weather	Change of season
Human infection	Increase the risk of human exposure to the HPAI virus	Consuming sick poultry; Handling poultry

3. Results

From January 2006-May 2008, there were 172,459 PDSR visits, of which 12,348 had a free text entry in at least one of the fields of interest. Within these, there were 11,995 HPAI-compatible events recorded and 8,737 rapid tests performed, of which 6,221 (71%) were positive.

Risk factors –There were 10,175 records with entries in the *rff and*, 4,716 with text in the *sf.* In both the *sf* and *rff*, factors that would cause "*spread within community"* (26.1% *sf* and 43.1% *rff*) and "*spread both between and within communities"* (25.7% *sf* and 41.1% *rff*) were most commonly cited. Within the "*spread within community*" category, the subcategory *inappropriate carcass disposal* (particularly into rivers) accounted for more than half of the entries in both fields. *Free-range poultry* was the most common category within the "*spread both between and within communities*" category (41% *sf* and 64% *rff*), followed by other *poultry management practices* (49% *sf* and 26% *rff),* which included *unclean housing* and *no vaccination*.

Factors that would cause "*spread between communities*" were mentioned in 15.6% of *sf* and 35.7% of *rff* visits. *Poultry trade* was the largest subcategory, and is more frequently mentioned in the *sf* (85%) than the *rff* (69%).

When the source of infection was attributed to "*spread within community*" or "*spread between communities*", the suspect cases were more often rapid-test positive than negative ($p< 0.001$). However, when the source was attributed to unclean housing, poor hygiene or climatic factors, suspect cases were more often rapid-test negative ($p < 0.001$) than positive.

Clinical signs – There were 12,028 entries describing clinical signs. Twenty different broad categories were used to describe the clinical signs, of which 10 were mentioned > 200 times. Sudden death and cyanosis were most commonly reported and, along with respiratory signs, inflammation, haemorrhage, and high population mortality rates, they were significantly associated with a positive rapid-test diagnosis. Gastrointestinal signs, depression, anorexia and neurological signs were significantly associated with a negative rapid-test result (Table 4.6.2).

Table 4.6.2: The frequency and number of visits where clinical signs described in the PDSR database were categorized, by broad category and rapid test result

Broad category	Frequency of rapid test result			Number of visits	% rapid-test positive (of those tested)	P (2-tails)
	Missing	*Negative*	*Positive*			
Sudden death	2854	2099	5624	10577	72.8%	<0.001
Cyanosis	1599	1178	4084	6861	77.6%	<0.001
Respiratory	779	660	1997	3436	75.2%	<0.001
Inflammation	680	632	1946	3258	75.5%	<0.001
Haemorrhage	88	75	616	779	89.1%	<0.001
Gastrointestinal	155	260	190	605	42.2%	<0.001
Depression	166	244	132	542	35.1%	<0.001
Anorexia	204	84	27	315	24.3%	<0.001
High Mortality	46	44	202	292	82.1%	0.001
Neurological	123	84	54	261	39.1%	<0.001

Discussion

In this study, richly descriptive but cumbersome text fields were analyzed to yield useful information about risk factors and clinical signs of HPAI reported by teams in the field. These field teams have a wealth of experience in dealing with this zoonosis, and it is important that the findings of their case investigations are examined. The results are of interest on several fronts. For example, the finding that officers working in the field attributed the source and spread of HPAI in backyard poultry to factors related to "*spread within the community*" (primarily because of inappropriate carcass disposal practices), "*spread both within and between the community*", and poultry trade, suggests that both introduction from external sources and internal spread must be addressed for control efforts to be successful in Indonesia.

Our study is different from most other HPAI risk factor studies (e.g. Loth et al., 2010; Pfeiffer et al., 2007; Gilbet, Xiao and Pfeiffer et al., 2008) because it focuses on farm (village)-level factors rather than area-level factors such as population density, road density, climate etc. A study of farm-level risk factors was done using data from Vietnam (Henning, Henning and Morton et al., 2009), however, our study had a very different design (case control) and we examined different risk factors, so the results cannot be compared with the Vietnam study. However, the use of a similar case control design would be an appropriate follow-up to further examine the factors identified in our study, such as the role of inappropriate carcass disposal in the spread of HPAI.

In the literature, the clinical signs associated with HPAI in gallinaceous domestic poultry are severe depression, anorexia, high morbidity and high mortality rates; and nervous signs are occasionally observed if affected individuals survive beyond the peracute stage (Swayne, 2007). In chickens, common lesions include edema to necrosis of the comb and wattle, edema of the head and legs, subcutaneous hemorrhage of legs, and lungs that fill with fluid and blood (Swayne, 2007), which in our study would account for the recorded observations of cyanosis, respiratory difficulty, inflammation and hemorrhage. Although anorexia is a common symptom of HPAI, it was not significantly associated with a positive laboratory diagnosis in our study. This is probably because it is a non-specific symptom, observed with HPAI but also with many other poultry diseases. Our results suggest that anorexia alone should not warrant a clinical diagnosis of HPAI.

The tools we used in our analysis could contribute to the monitoring and evaluation of the PDSR program. Using these tools, it would be possible to examine how different teams completed their field investigations. Furthermore, our results could be used to provide valuable feedback to the field officers about their work. For example, it could be emphasized to teams that they make sure they use a rapid test when they encounter poultry with haemorrhage, as opposed to relying on clinical signs alone, because these cases often test negative.

Our results provide a good example of the utility of text mining in veterinary science. Text mining has been used previously in veterinary science to categorize the reasons for retirement of race horses (Lam et al., 2007) and to describe clinical signs observed in suspect cases of bovine spongiform encephalopathy (Berezowski, Snyder and McLarty, 2007). As in the other studies, performing this analysis would be prohibitively laborious without the use of the tools contained within the text-mining software. Moreover, our analysis was complicated by the bilingual nature of the data. Creating the dictionaries was the most challenging task in the analysis. It was necessary to strike a balance between simplicity and comprehensiveness, and was intentionally structured to inform the disease control program. The design of the dictionaries was necessarily subjective and influenced the outcome of our study, and the users of the output should take this into account.

Our results must be interpreted in the context of the surveillance program in which they were collected. If HPAI was detected on a visit, the PDSR officers recorded much more data than if HPAI was not found, – and thus the “source” and “risk” factors that were found to associated with HPAI occurrence must be studied further to validate these findings, perhaps with a case control design as was found useful in other studies (Henning, Henning and Morton et al., 2009). Furthermore, the content and quality of both the outbreak investigation and recording of results varies with the individual officers collecting the data (>2,100 individuals trained) (Azher, Lubis and Siregar et al., 2010). However, it is an extremely large sample and the trends and factors identified are worthy of further investigation.

Conclusions

Considerable data about highly pathogenic avian influenza (HPAI) in poultry in Indonesia have been collected by the Participatory Disease Surveillance and Response (PDSR) program, which is a component of the Indonesian Ministry of Agriculture’s HPAI Control Program. When suspect cases were identified, information about clinical signs, the probable source of infection and risk factors was recorded in a database in free text form, which until now, has been not analyzed.

The PDSR officers most frequently attributed the source of HPAI and its spread to inappropriate carcass disposal, the presence of free-ranging poultry, and to poultry-trading practices. These factors would cause the spread of HPAI both within and between communities. Sudden death and cyanosis were the most commonly reported clinical signs and, along with respiratory signs, inflammation, haemorrhage, and high population mortality rates, they were significantly associated with a positive rapid-test diagnosis. Gastrointestinal signs, neurological signs, anorexia and depression were significantly associated with a negative rapid-test result. While these results must be interpreted in the context of the surveillance program in which they were collected, they clearly demonstrate the utility of text mining to add value to information from free text fields. This analytical technique enhances participatory epidemiology studies or participatory disease surveillance systems, and should be applied in other programs, such as those in Egypt (see http://www.saidr.org/index.php) and Pakistan (Jost et al., 2007). It would be particularly powerful in a situation where the unstructured and rich information captured through open-ended questions is collected by highly trained teams to minimize potential biases.

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4.7 Multivariable analysis of the original PDSR database

Abstract

A multivariable analysis was performed to identify factors associated with the incidence of HPAI detection by Participatory Disease Surveillance and Response (PDSR) officers in selected districts on the island of Java, in Indonesia. A causal web diagram was developed to guide the modeling process, and clearly demonstrated that the available data allows us to model the incidence of HPAI detection*, rather than the true incidence of* HPAI*. We found that high native chicken density, high human population density, and the presence of broilers were positively associated with the incidence rate of HPAI detection. A high NVDI during the dry season was protective for HPAI detection incidence. District, included as a random effect, was statistically significant, which indicates that there is significant variation in counts of HPAI detection incidence between districts that is not accounted for by the identified risk factors. These results are generally similar to those that have been published from similar studies using data from other countries, but they are quite different from another study using Indonesian data. We suggest that the reason for this hinges on different analytical decisions, and underlines the need for a thorough understanding of the data throughout the modeling process, which will also inform the interpretation and communication of the results.*

1. Introduction

The identification of risk factors for HPAI infection can be used to guide policy makers in targeting the limited resources available for disease surveillance and control to where they will have the most impact. Studies in other countries have found that medium to high poultry density, duck density, and high human population density are consistently associated with an increased risk of outbreaks. Geographical and climatic factors have also been implicated, including average NVDI and elevation (Pfeiffer et al., 2007; Henning, Pfeiffer and Vu, 2009; Gilbert, Xiao and Pfeiffer et al., 2008; Loth et al., 2010). However, a recent study in Indonesia yielded somewhat different results, concluding that high poultry density was negatively associated with HPAI outbreaks in poultry, and finding no association between the occurrence of HPAI and human density, paddy fields, or water sources (Yupiana et al., 2010). The objective of our analysis was to use the data from the districts that participated in the ORIHPAI study to further investigate risk factors for HPAI outbreaks in poultry. Particular attention was given to the nature of the available data and the ability to extrapolate from these data to the true incidence of HPAI.

2. Methods

Our analysis was done using data from districts that were participating in ORIHPAI, reported outbreaks of HPAI, and had high-quality PDSR teams. The PDSR surveillance system has been described thoroughly elsewhere (Jost et al., 2007; Azhar, Lubis and Siregar et al., 2010).

A Poisson regression model was used to study factors associated with the incidence rate of HPAI detection (the Incidence Rate Model, where incidence rate = the number of cases detected per “unit of village-time at risk”). The outcome of interest was the number of HPAI outbreaks detected by PDSR within a sub-district over the study time period. The exposure was village-time at risk (the number of surveillance months that the sub-district had participated in the PDSR program, multiplied by the number of villages within the sub-district). The number of surveillance months was calculated as the number of months from the first surveillance visit to May 2008. This was calculated on a district basis; because the PDSR program is administered at the district level, the entire district was considered under surveillance from the time of the first visit.

Information about PDSR visits and HPAI outbreaks was extracted from the “original” PDSR database. Data were available on all PDSR visits that occurred from January 2006 to May 2008. It was common practice to conduct several PDS interviews in a single village over a short period of time, even on the same day. If HPAI was confirmed more than once during such interviews, it probably reflected disease spread between households and as such is most appropriately considered a single outbreak for the purposes of our analysis. Therefore, to avoid over-reporting of cases, an "outbreak" was defined as a positive rapid antigen test case that occurred in a village at least 21 days after the most recent previous positive rapid test case in the same village. Similarly, a "visit" was defined as a PDSR report filed in the database at least 21 days after the most recent previous report.

Risk factors included in our analysis were determined by a causal diagram, taking into account findings from previous research papers and the epidemiology of HPAI (Figure 4.7.1). These risk factors included geographic data (NDVI, elevation, rainfall), agricultural data (poultry populations), and demographic information (human population density). Risk factor data were obtained from district statistical records (poultry populations), the United States Department of Agriculture (USDA) (ports, roads, rivers), WorldClim (precipitation, length of growing period and temperature), Nelson (2007) (travel time to the nearest large population center), Center for International Earth Science Information Network (CIESIN) 2005 Grump (human population density), Shuttle Radar Topography Mission (SRTM) digital elevation model (DEM) (elevation, available from: http://srtm.csi.cgiar.org/), and an unconfirmed source for NVDI.

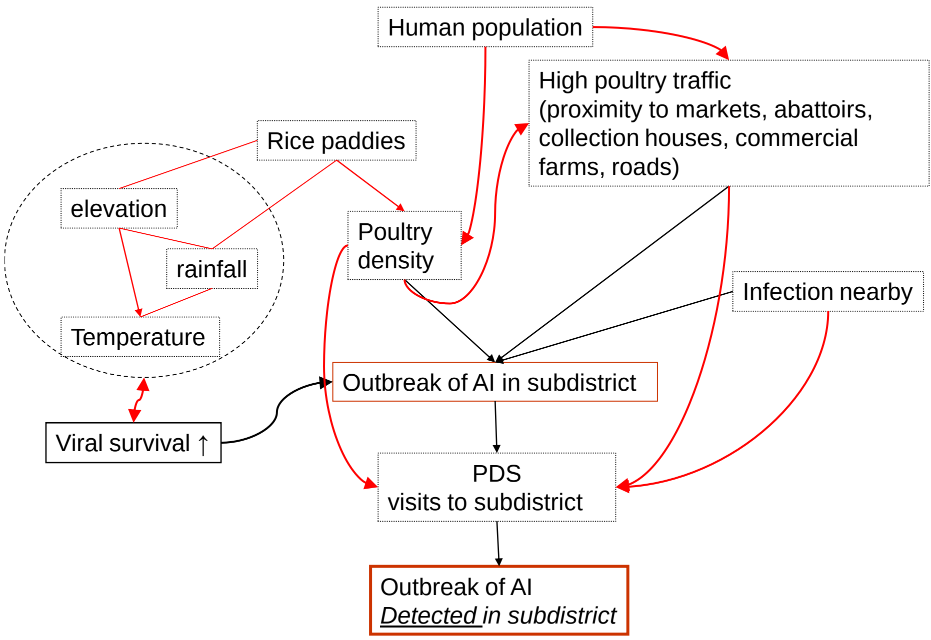


Figure 4.7.1: Causal diagram – the black arrows indicate the relationship with HPAI outbreaks, and the red ones indicate inter-factor relationships

All analyses were done using Stata 10.1 (Statacorp, College Station, Texas USA). Unconditional associations were determined using simple Poisson regressions. District was included as a random effect to control for clustering. The data were likely clustered at the district level because of spatial influences (observations close in space are more likely to be similar) and also because disease control policies are highly variable between districts.

Correlation between continuous variables was assessed with Pearson's correlation coefficient. Scatter plots, stratified box plots and the lincheck[2] command in Stata 10.1 were used to assess the nature of relationships between outcomes and predictors, and predictor variables without linear relationships with outcomes were both categorized and log (ln) transformed, with the former (categorized) generally fitting the data better.

Multivariable models were built manually using a backwards elimination procedure. Statistically significant factors (with a liberal p value of < 0.2) were included in the initial model. For highly correlated continuous variable pairs, only one was included in the multivariable analysis (the most statistically significant or the one with most complete data). We assessed confounding by monitoring changes in the coefficients as variables were removed from the model. Covariates not included in the model that resulted from the backwards elimination procedure were evaluated again, and any that were statistically significant were retained in our final model.

The number of PDSR visits to an area could act as a confounding variable, associated both with the outcome (the more visits, the more cases detected) and the risk factor of interest (PDSR officers actively search for HPAI, and therefore preferentially visit areas with possible risk factors). To explore the impact of the number of PDS visits to each sub-district, it was included as a covariate in the final model. Once the final model was determined, the fit was assessed using residual plots.

3. Results

Descriptive – One of the 16 OR districts did not report any HPAI cases during the study period, and therefore was not included in our analysis. Of the 319 sub-districts we included, 257 (80.3%) had at least one confirmed outbreak. The number of outbreaks detected per sub-district ranged from 0-20, with the mean number of outbreaks equal to 3.6 (SD = 4.2). There was no obvious geographical pattern to these outbreaks (Figure 4.7.2).

The number of months that the district had had PDSR surveillance ranged from 13.1 to 26.6 (mean = 19.9, SD = 4.9). The number of villages per sub-district ranged from 2 to 33 (mean = 12, SD = 5).

The following covariate pairs were highly correlated (Pearson's correlation coefficient >0.7): temperature and elevation, temperature and travel time, elevation and travel time, NVDI in the rainy season, NVDI in the dry season, length of growing period, and rainfall.

Incidence rate model – Poultry density (all types), length of growing period, NVDI, the presence of a market and abattoir in the sub-district, distance to nearest port, road length in the sub-district, and the travel time to large urban centers were associated with the number of outbreaks detected per sub-district in the univariable analysis, and subject to inclusion in the backwards elimination model building procedure (Table 4.7.1). Because NVDI in the dry season and the rainy season were highly correlated, only the NVDI in the dry season was considered in the multivariable model. Human population density was statistically significant when presented back into the model that resulted from the backwards elimination procedure, and so we included it in the final model.

The final regression models (with and without the number of surveillance visits) are presented in Tables 4.7.2 and 4.7.3. In the model excluding surveillance visits, a high density of native chickens, high human population density, and the presence of broilers were positively associated with the incidence rate of HPAI detection. A high NVDI during the dry season was found to be protective for HPAI detection incidence. District as the random effect was statistically significant, which indicates that there is significant variation in counts of HPAI detection incidence between districts that is not

[2] Lincheck makes a new categorical variable that breaks the continuous covariate into quartiles. It then re-estimates the generalized linear model using dummy variables for the quartiles, and provides a graph of estimated coefficients plotted against the medians of the quartiles. A linear graph supports the assumption of linearity of the continuous covariate.

accounted for by the identified risk factors. When we added the number of surveillance visits to the sub-district as a variable in the model, it was significant (IRR = 1.02, $p < 0.001$), however, both native chicken density and the presence of broilers lost statistical significance.

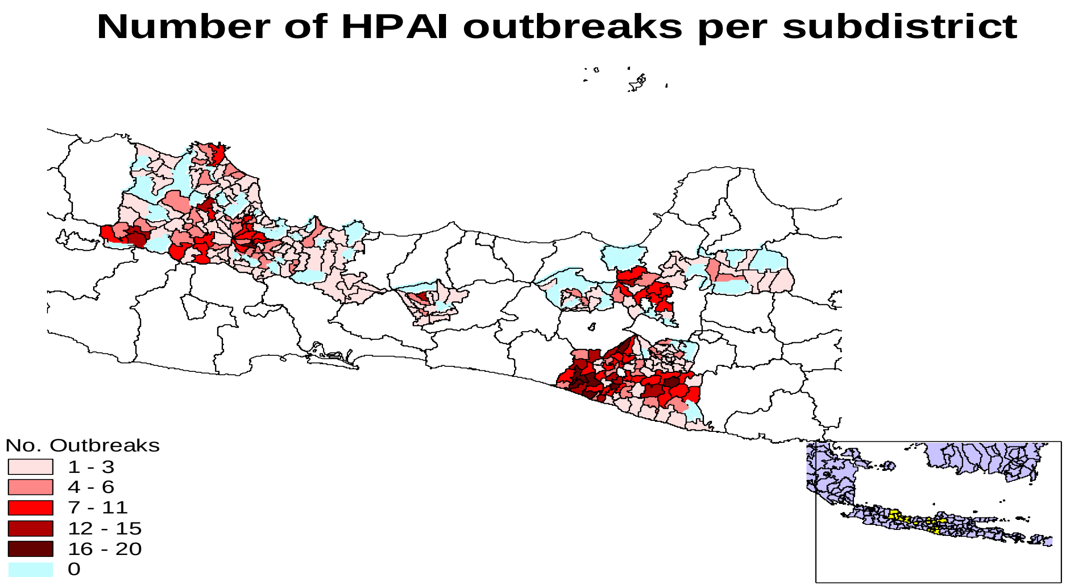


Figure 4.7.2: Number of HPAI outbreaks per sub-district in the study area from January 2006-May 2008

Residual plots were generated and did not indicate any problems with the models (Figure 4.7.3). However, tools for model checking are not well developed for generalized linear mixed models (GLLAMMs).

Discussion

We found that a high density of native chicken, high human population density, and the presence of broilers were positively associated with the incidence rate of HPAI detection in 15 districts on the island of Java, Indonesia. A high NVDI during the dry season was found to be protective for HPAI detection incidence in these districts. HPAI detection is a necessary surrogate for the real outcome of interest – HPAI incidence – because of the nature of the surveillance data on which this analysis was based.

From 2006-2008, the PDSR system used primarily risk-based surveillance, which means that PDSR officers visited areas where they believed they were most likely to find HPAI more often than areas where they did not think they would find it. This is appropriate because the PDSR system was not intended to measure incidence, but rather was designed as a case-detection and response system. It balanced its available resources between the needs of disease monitoring and outbreak response, and focused on active, rapid test-confirmed cases where a response could be mounted subject to available resources. Because the sites visited were not random, this limits the use of the data to identify risk factors definitively associated with *true HPAI incidence,* because the difference in "PDSR visit risk" between high-risk and low-risk populations is unknown (Stark, Regula and Hernanadez et al., 2006). Rather, the data gives insight into the *incidence of HPAI detection.* For example, suppose that PDSR officers visited villages close to broiler farms more often than villages far away from such farms because they believed they would be more likely to find HPAI in these areas. Regardless of if there were a true association between HPAI incidence and broiler farms, more HPAI might be detected around these farms simply because veterinary officers visited those areas more often (Figure 4.7.1). Therefore, it is not possible to definitively conclude from this analysis that the identified risk factors for detection of outbreaks are risk factors for *HPAI incidence,* or if they are associated with the outcome purely because sub-districts with these characteristics are more likely to receive more surveillance visits. Despite this, the results of our study still contribute to the growing body of literature on HPAI risk factors, provided we assume with caution that there is a relationship between the true incidence of HPAI and HPAI detection. This association could be quantified in further studies specifically designed to measure HPAI incidence.

Table 4.7.1: Candidate risk factors for multivariable model and results of univariable analysis, based on Poisson model (outcome = number of outbreaks/sub-district, offset = number of villages* surveillance time)

Variable			IRR	p
Poultry Densities	Native chicken	*Medium** *High**	1.64[a] 1.31	<0.001
	Layers	*Medium** *High**	1.44 1.91	<0.001
	Broilers present		2.03	<0.001
	Duck	*Medium** *High**	1.06 .801	0.0003
Climate/Geography	Mean rainfall		1.00	0.54
	Length of growing period		1.00	0.174
	River length		0.99	0.003
	Mean temperature		0.98	0.22
	Mean NVDI (dry season)		0.26	<0.001
	Mean NVDI (wet season)		0.44	0.03
	Mean elevation		1.00	0.22
Human Activity	Market in sub-district		1.85	<0.001
	Abattoir in sub-district		1.46	0.0003
	Human population density	*Medium** *High**	0.95 0.92	0.54
	Distance to port		1.01	<0.001
	Travel time to urban centre		1.00	<0.001
	Road length		1.00	0.01
	Number of PDSR visits		1.05	<0.001

*** Compared to low**

[a] Sub-districts with medium native chicken density have 1.37 times more cases of HPAI per surveillance month compared to areas with low native chicken density

Table 4.7.2: Results of Poisson regression model of the counts of outbreaks per sub-district (n= 299 sub-districts, number of surveillance visits excluded). Model log likelihood = -731.9. District was included as a random effect (SD = 0.95, SE = 0.18)

Risk Factor		IRR	CI	SE	p
Native chicken density	Medium*	1.21[a]	1.01-1.46	0.11	0.04
	High*	1.38	1.11-1.72	0.15	<0.001
Human population density	Medium*	1.45	1.23-1.71	0.12	<0.001
	High*	1.64	1.33-2.03	0.18	<0.001
Broilers in sub-district	Yes	1.19	0.99-1.44	0.11	0.06
Mean NVDI – dry season		0.36	0.23-0.57	0.08	<0.001

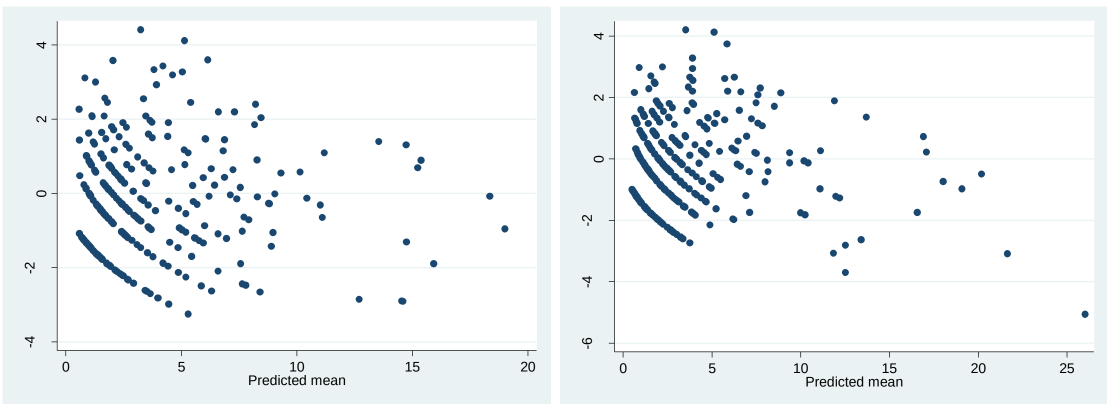
*** Compared to low**

[a] Sub-districts with medium native chicken density have 1.21 times more cases of HPAI per village-month compared to areas with low broiler density, when all other factors are equal

Table 4.7.3: Results of the Poisson regression model of the number of outbreaks per sub-district (n = 319 sub-districts, number of surveillance visits included). Model log likelihood = -750.43. District was included as a random effect (SD = 0.79, SE = 0.15)

Risk Factor		IRR	CI	SE	p
Human population density	Medium*	1.30	1.11 – 1.51	0.10	0.001
	High*	1.45	1.17 – 1.72	0.14	<0.001
Mean NVDI – dry season		0.42	0.27 – 0.67	0.10	<0.001
Number of PDSR visits		1.02	1.02 – 1.03	0.002	<0.001

*** Compared to low**



(a) (b)

Figure 4.7.3: Scatter plot of deviance residuals versus predicted means for (a) the model excluding surveillance visits and (b) the model including surveillance visits

Our analysis highlights an important methodological issue for the analysis of risk-based surveillance data in research to understand risk factors for *HPAI incidence*. The central question is whether the number of visits should be treated as a confounder or a necessary intervening variable. If it is a confounder, then it should be included in the model to control for the confounding. On the other hand, if it is a necessary intervening variable, then it should not be included in the model. In the PDSR system, the density of visits will influence the number of disease detections, but a visit is necessary for a disease detection to take place. Thus, the number of visits has characteristics of both a confounder and an intervening variable and it is not possible to quantify these relative roles. Our analytical strategy was to compare the results of models that treated the number of visits either as a confounder or an intervening variable. The robust results are those that are consistent between both models (risk factors or non-risk factors).

Bias due to the misclassification of disease status is another potential concern when interpreting the results from our study. The outcome of interest was outbreaks detected by PDSR. To confirm an HPAI outbreak, PDSR applied a rapid antigen test (Anigen® Rapid AIV) on samples from poultry with clinical signs compatible with HPAI. In individual birds, this test has a high specificity (98%, 95% CI: 0.93-0.99) but only moderate relative sensitivity (69%, 95% CI: 0.56-0.80) (Loth et al., 2008) compared to a real-time reverse transcription polymerase chain reaction (RT-PCR). Therefore, some cases might be false negatives and thus misclassified in our analysis. It is reasonable to assume that misclassification of disease status is not related to any of the exposure variables (i.e., on differential misclassification), which normally biases estimates of association towards the null.

The issue of whether the presence of broiler chickens is a risk factor for HPAI detection is important. Because the PDSR data contains mostly outbreak data about native chickens, the finding of broiler chickens as a possible risk factor provides may provide some evidence supporting spill-over of infection between the commercial and backyard poultry sectors. On the other hand, the fact that controlling for the number of visits causes this exposure to drop out of the model may indicate that surveillance in back yard poultry was biased towards areas of broiler production. At present, it is largely unknown how different sectors in the poultry industry contribute to the maintenance of HPAI in Indonesia. This is an important area where further research is needed because it has implications regarding the most effective targeting of control measures.

Our results indicate that higher human population density is associated with a higher incidence rate of HPAI detection; and that the HPAI detection rate decreases with increasing NVDI. The finding of high human population density as a risk factor supports the hypothesis that human activity contributes to the spread of HPAI. It is important to note that the significance of high human population density was a robust finding that was present in both the models regardless of whether the number of visits was treated as a confounder or intervening variable. This has been found in other studies concerning HPAI in Thailand and Vietnam (Pfeiffer et al., 2007; Gilbert, Xiao and Chaitaweesub et al., 2007). Higher outbreak risk associated with low NVDI was also found in Vietnam in an analysis considering outbreaks from 2004-2006 (Pfeiffer et al., 2007).

An area of particular interest has been the role of ducks in the epidemiology of HPAI in Indonesia. Ducks can be sub-clinically infected and so may act as silent carriers of HPAI, spreading the virus when in contact with chickens. It has been speculated, however, that ducks have a different role in the epidemiology of HPAI in Indonesia because rice production is less seasonal and ducks are not grazed in the same manner as in other Asian countries (Gilbert, Xiao and Pfeiffer et al., 2008). Duck density was not statistically significant in the final multivariable model and actually had a protective effect in the univariable analysis. This is different from other studies in Thailand and Vietnam, where ducks are consistently positively associated with HPAI incidence. Rice paddy density was not included in our model because we were not confident about the quality of available datasets – two alternate data sources were analyzed and found to be uncorrelated and yielded opposite results. Therefore, at present, the role of ducks and rice in the epidemiology of HPAI in Indonesia is inconclusive and needs further research.

These findings are generally consistent with most studies from other countries. Pfeiffer et al. (2007) and Henning et al. (2009) did not distinguish between backyard and commercial poultry in their analyses, but broadly concluded that there is a positive association with high- to medium-high poultry density and HPAI incidence. In the study by Loth et al. (2010) using data from Bangladesh, commercial poultry density was found to be a risk factor for HPAI incidence, but high backyard density was not. However, a study using data from Thailand found the reverse – an association with HPAI outbreaks and native chicken numbers, but not HPAI incidence and numbers of commercial poultry (Gilbert, Chaitaweesub and Parakamawongsa et al., 2006). These contrasting findings suggest that different risk factors might be at play in different countries, which is very likely given the different farming and cultural practices. However, potential problems with data quality should also be considered, as "HPAI incidence" is usually based on surveillance data in which the presence of disease is often ascertained, but the absence of disease is normally less certain. The accuracy of data on poultry populations should also be further investigated, particularly for native chickens, which have an extremely high population turnover rate.

Although our findings are consistent with many other studies, they are rather different from those from another study considering HPAI outbreaks in West Java (Yupiana et al., 2010). In that study, poultry density actually had a negative association with the incidence of HPAI, and there was no association between the number of HPAI outbreaks and human population density. These contrasting findings are most likely due to the use of different data subsets and/or different analytical approaches. In the study by Yupiana et al. (2010), the study area consisted of 25 districts from West Java province, and so was similar but not identical to our study. Poultry density was calculated by grouping broilers, layers and backyard chicken numbers and the human population data was from a different source. We chose to disaggregate the poultry density data by poultry type because the husbandry systems are very different and so they likely have different associations with HPAI incidence. Importantly, in the other study, data were analyzed at the district rather than sub-district level. It is quite likely that district-level risk factors might be different from those operating at a smaller scale. Within a district, poultry density is likely to be extremely variable and districts with an overall low poultry density might well have high-density pockets (e.g., where commercial farms are located). In calculating the average poultry density per district, this potentially important information is lost. These contrasting findings highlight that different approaches to the same question can yield different results, and therefore a thorough understanding of the data by the modelers, and careful interpretation is critical.

Conclusion

These analyses demonstrate that quantitative statistics must be interpreted carefully, and specifically how important it is to have a good understanding of how the data were collected and analyzed. The explicit construction of causal diagrams is an important step in documenting the decision-making process in the construction of statistical models. In the case of PDSR data, the data is appropriate to assess risk factors for HPAI *detection* by the PDSR surveillance system. This analysis is a valuable contribution to the global study of HPAI risk factors because it illustrates the biases that may be present within surveillance data and that should be explicitly considered in the analysis. These issues are common to many published risk-factor studies, but rarely addressed. With the current trend towards risk-based surveillance systems that are designed to enhance disease detection rates, understanding data relationships will become key to reliable analysis.

In this analysis, the detection of HPAI was consistently associated high human population density, and low NVDI. These findings are broadly consistent with many other studies. Duck density, which has been found as a risk factor in other models, was not found to be a risk factor in our work. We suggest that to verify both these results and those from other studies, an important next step in the understanding of HPAI epidemiology should be carefully designed risk-factor studies involving primary data collection, in which the biases associated with surveillance data are avoided.

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4.8 Sensitivity and specificity of clinical diagnoses for HPAI and ND in chickens in West and Central Java

Abstract

Clinical case definitions are an important tool for the detection of disease, particularly in resource-limited settings. This study used virus isolation and typing to measure the accuracy of clinical diagnoses for sudden death, HPAI-compatible disease and VVND-compatible disease in chickens in West and Central Java, Indonesia. Using frequentist calculations, the diagnosis of sudden death was found to have a sensitivity of 76.4±5.9%, specificity of 41.8±9.8%, and positive predictive value of 72.7±6.0%. The diagnosis of HPAI-compatible disease was found to have a sensitivity of 71.2±7.3%, specificity of 62.3±7.7%, and positive predictive value of 64.6±7.4%. When considering the sensitivity and specificity of the diagnosis of HPAI-compatible disease as series diagnoses, the sensitivity and specificity was found to be 54.4±8.1% and 78.0±6.6%, respectively. Determining the accuracy of the VVND-compatible disease diagnosis was not possible in that an appropriate 'gold standard' test that differentiated VVND from other forms of ND was not available. Various elements of study design and laboratory analysis could have influenced the sensitivities and specificities of the clinical diagnoses used in this study. Further analysis is warranted, including Bayesian approaches that do not assume a gold standard.

1. Introduction

Clinical case definitions are an important tool for the detection of diseased individuals or populations, particularly in resource-limited settings (Meintjes et al., 2008; Périssé and Strickland, 2008) In the public health field, clinical case definitions have been described for a wide variety of diseases, including dengue fever (sensitivity 74%, specificity 79%) (Chadwick et al., 2006), mumps (sensitivity 96.9-97.5%) (Dominguez et al., 2009), malaria (sensitivity 27-53%, specificity 79-88%) (Périssé and Strickland, 2008), pertussis (sensitivity 84-92%, specificity 63-90%) (Patriarca et al., 1988), paediatric HIV (sensitivity 16.7-66.7%, specificity 74.0-96.0%) (Abbas et al., 2010), and influenza-like illness (sensitivity 43.5-75.1%, specificity 46.6-80.3%) (Thursky et al., 2003). In veterinary epidemiology, Elbers et al. found that increased mortality or swollen head were the most sensitive clinical indicators for H7N7 HPAI in backyard chickens in the Netherlands (sensitivity 100%, specificity 20-32%), while the addition of cyanosis to the case definition increased the specificity of a diagnosis (sensitivity 65-100%, specificity 68-80%) (Elbers, Koch and Bouma, 2005).

Our operational research in Indonesia represents the first known attempt to use a clinical case definition as the diagnostic method in a study of disease incidence in livestock; it was, in fact, the only diagnostic method available because our research required the diagnosis of historical outbreaks. Our study was designed to measure the accuracy of this approach to diagnosing HPAI-compatible and VVND-compatible disease sudden deaths in chickens. Clinical information was used to retrospectively diagnose outbreaks involving high poultry mortality. The population of interest in our research was all poultry in the RT during the study period. However, active HPAI and ND infections are rare events. For our study, the same diagnostic procedure was used but applied to active outbreaks from which biological samples could be collected. The likelihood of inclusion of diseased poultry in our study was increased by defining the reference population as all sick chickens in the RT during the study period (Greiner and Gardner, 2000; Ngaira, 2003).

2. Methods

Our study was carried out between 17 March and 30 September 2009. When practitioners began a normal quarterly RT assessment, they asked residents if there were active cases of illness in small-scale commercial or backyard chickens in the RT. If the residents reported that there were sick chickens, the practitioners carried out the sensitivity and specificity protocol before returning to their normal activities. They also investigated other reports of poultry illness received by the district veterinary office, even if the reports were from RTs not included in the operational research program. If, using the case definition, practitioners determined losses could be characterized as sudden death (level 1), they further diagnosed the problem as HPAI-compatible, VVND-compatible or "unknown" (level 2) (Figure 4.8.1). Therefore, strains of avian influenza and pathotypes of ND that were not highly pathogenic would not have fit the clinical case definitions used in this study, and would have been diagnosed as "not sudden death".

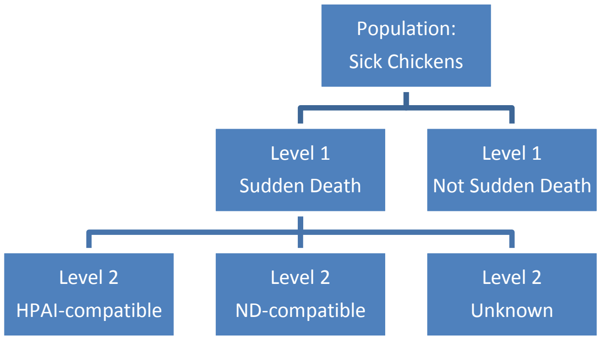

Figure 4.8.1: Clinical case definition diagnostic tree

After interviewing farmers to make their diagnoses, the practitioners examined any affected chickens and, based on the additional information that a physical exam provided, they determined if they wanted to change their diagnosis. They then followed standard World Health Organization (WHO) H5N1 sampling protocols to collect tracheal samples from up to 25 affected chickens. They used sterile cotton swabs, placing five swabs in each universal transport medium (UTM) tube containing antibiotics (WHO, 2006).

Samples were maintained in the field (and subsequently shipped to the laboratory) at 4°C in 1-litre Rubbermaid® coolers with icepacks lining the four walls and top of the cooler so that the samples sat in a central cooled pocket. Transport cold chain temperatures were pre-tested by data loggers with repeated the measurements every 15 minutes; the coolers were found to maintain a temperature of 4°C or less for up to 16 hours. The time between sampling and arrival at the laboratory was limited to 48 hours, with a change of ice packs if necessary every 12 hours.

Samples were received at Wates DIC, split into two aliquots in Eppendorf tubes, and immediately stored at -80°C. For virus isolation, amplification and typing, one aliquot from each sample was thawed and inoculated into three 10-12 day old specific pathogen free (SPF) embryonated eggs. Allantoic fluid from eggs in which the embryo had died was harvested and subjected to haemagglutination. Those samples that haemagglutinated at concentrations above 2° were subjected to inhibition using H5N1 (A/chicken/Pare/East Java/2004) and ND (is:ichii) specific antibodies produced by Pusvetma in Surabaya, Indonesia. After first passage, any samples that were negative or haemagglutinated at 2° were subjected to up to three more passages (for a maximum of four) before being diagnosed as haemagglutination negative. For any sample, if no chicks died they were blocked at five days by cooling and the allantoic fluid re-inoculated into three new eggs for up to four passages. For outbreaks in which more than one sample tube was received, the outbreak was considered positive for H5N1 or ND if one or more tubes were positive on inhibition for one of the diseases. The outbreak was considered positive for both diseases if at least one tube from an outbreak was positive on inhibition for each disease.

Win Episcope 2.0 was used to calculate minimum sample size and the power of the study. Assuming a sensitivity of 80%, a 95% confidence interval, a population level HPAI prevalence of 20%, and a sample HPAI prevalence of 60%, the estimated necessary sample size to determine the sensitivity and specificity of the HPAI-compatible disease diagnosis was determined to be 410 investigations with 25 birds sampled (Jones, Carley and Harrison, 2003; Carley et al., 2005). Given that ND was diagnosed less frequently by the PIA, we concluded that a larger sample size would be necessary to determine the sensitivity and specificity of the clinical diagnosis of VVND-compatible disease. A database containing sample information, outbreak diagnoses, and laboratory results was created in Microsoft Excel.

Using virus isolation and typing as the gold standard (test Y) for H5N1 HPAI, the sensitivity, specificity, positive and negative predictive values of the clinical diagnosis of HPAI-compatible disease (test Z) were determined according to the following equations (Table 4.8.1):

- Sensitivity = Z+Y+/Y+; where Z+Y+ includes all samples diagnosed as H5N1 HPAI both by practitioners and the lab; and Y+ includes all laboratory H5N1 diagnoses;
- Specificity = Z-Y-/Y-; where Z-Y- includes all samples diagnosed by practitioners as not sudden death, VVND or unknown, and also diagnosed as negative or ND by the lab; and Y- includes all laboratory samples diagnosed as negative or ND;
- Positive predictive value = Z+Y+/Z+; where Z+Y+ includes all samples diagnosed as H5N1 HPAI both by practitioners and the lab; and Z+ includes all samples diagnosed by practitioners as H5N1 HPAI;
- Negative predictive value = Z-Y-/Z-; where Z-Y- includes all samples diagnosed by practitioners as not sudden death, VVND, or unknown, and diagnosed by the lab as negative or ND; and Z- includes all samples diagnosed by practitioners as not sudden death, VVND, or unknown.

Table 4.8.1: Two-by-two table used to compare clinical diagnostic results with laboratory diagnostic results

	Test Y: Virus isolation and typing			
Test Z: Clinical Diagnosis		**+**	**–**	
	+	**Z+Y+**	**Z+Y-**	**All Z+**
	–	**Z-Y+**	**Z-Y-**	**All Z-**
		All Y+	**All Y-**	**All Outbreaks**

The accuracy of the clinical diagnosis of VVND-compatible was similarly determined. In the field, the clinical diagnoses of HPAI-compatible and VVND-compatible disease occurred in a two-step series, in which only those outbreaks that the practitioners found to be sudden death positive were further assessed as either HPAI-compatible or VVND-compatible. The overall accuracy of a diagnosis made in a two-step series can be calculated as:

- Combined Sensitivity = Sensitivity 1st test x Sensitivity 2nd test; and
- Combined Specificity = 1 – (1 – Specificity 1st test) x (1 – Specificity 2nd test)

3. Results

The total number of outbreaks investigated was 375. Of these, practitioners incorrectly used the case definition in 37 (9.9%) of outbreaks by diagnosing an outbreak as not sudden death, but then continuing on to diagnose the outbreak as either HPAI-compatible, VVND-compatible or unknown. Of the samples received, the laboratory failed to analyze 41 (10.9%) prior to the end of the project. Incorrectly diagnosed outbreaks and those with un-analyzed samples were eliminated from further analysis, leaving 297 outbreaks included in this study.

The average number of outbreaks investigated per district was 18.6 (SD$\pm$7.8). Brebes submitted the least number of samples (4), while Bantul submitted the most (29). Sudden death was diagnosed in 70.4% of the outbreaks (Table 4.8.2).

Table 4.8.2: Outbreaks investigated, according to the level 1 (sudden death or not-sudden death) diagnosis

District	Not Sudden Death	Sudden Death	Total Outbreak Investigated	Percent of Outbreaks Diagnosed as Sudden Death
Bantul	5	24	29	82.8
Brebes	1	3	4	75.0
Cirebon	2	11	13	84.6
Grobogan	2	5	7	71.4
Gunung Kidul	8	16	24	66.7
Indramayu	2	4	6	66.7
Kendal	7	14	21	66.7
Klaten	8	11	19	57.9
Kulon Progo	8	19	27	70.4
Kuningan	9	17	26	65.4
Majalengka	6	14	20	70.0
Purbalingga	9	15	24	62.5
Semarang	6	13	19	68.4
Sleman	6	19	25	76.0
Sumedang	2	11	13	84.6
Temanggung	7	13	20	65.0
Grand Total	**88**	**209**	**297**	**70.4**

Of the 209 sudden death outbreaks diagnosed by the practitioners, 77.0% were further diagnosed as HPAI-compatible, 14.8% as VVND-compatible, and 8.1% as unknown (Table 4.8.3). Brebes and Grobogan had the highest rate of HPAI-compatible disease diagnoses (100%), while Sumedang had the lowest rate (45.5%). Cirebon and Sumedang had the highest rate of VVND-compatible disease diagnoses (36.4%), while seven districts never diagnosed VVND-compatible disease. Kuningan had the highest rate of unknown diagnoses (29.4%), while nine districts never diagnosed an outbreak as unknown.

On five occasions (1.7%), the practitioners chose to change their diagnosis of an outbreak after physically examining sick birds (Table 4.8.4).

The majority of outbreaks investigated occurred in areas outside the geographic area of the operational research (229 or 77.1%). From within ORI-HPA areas, 34 outbreaks (50.0%) came from vaccinated areas. A total of 263 (88.6%) outbreaks investigated occurred in non-vaccinated areas (Table 4.8.5). The most common diagnosis by practitioners in all areas, regardless of vaccination status of the area, was HPAI-compatible, with 100% of outbreaks in HPAI-vaccinated areas diagnosed as HPAI-compatible, 72.7% in AI-ND vaccinated areas, 79.2% in the operational research control areas, and 76.4% in non-operational research areas.

Table 4.8.3: Outbreaks investigated, according to the level 2 (HPAI-compatible, ND-compatible or unknown) diagnoses

Row Labels	HPAI-compatible	VVND-compatible	Unknown	% HPAI-compatible	% VVND-compatible	% Unknown
Bantul	19	5		79.2	20.8	0.0
Brebes	3			100.0	0.0	0.0
Cirebon	7	4		63.6	36.4	0.0
Grobogan	5			100.0	0.0	0.0
Gunung Kidul	13		3	81.3	0.0	18.8
Indramayu	4			100.0	0.0	0.0
Kendal	11	1	2	78.6	7.1	14.3
Klaten	7	1	3	63.6	9.1	27.3
Kulon Progo	15	4		78.9	21.1	0.0
Kuningan	12		5	70.6	0.0	29.4
Majalengka	13		1	92.9	0.0	7.1
Purbalingga	11	4		73.3	26.7	0.0
Semarang	12		1	92.3	0.0	7.7
Sleman	15	4		78.9	21.1	0.0
Sumedang	5	4	2	45.5	36.4	18.2
Temanggung	9	4		69.2	30.8	0.0
Grand Total	**161**	**31**	**17**	**77.0**	**14.8**	**8.1**

Table 4.8.4: Diagnosis change based on physical examination of sick birds

Change	Number
HPAI-compatible to VVND-compatible	1
HPAI-compatible to Unknown	2
VVND-compatible to HPAI-compatible	1
Unknown to HPAI-compatible	1

Of the 297 outbreaks, 138 (46.5%) were found to be H5N1 positive on virus typing, 53 (17.8%) were found to be ND positive, eight (2.7%) were found to be both H5N1 and ND positive, and 98 (33.0%) were found to be negative. The percentage of outbreaks found to be H5N1 positive was highest in the AI-ND vaccinated group (58.3%) and lowest in the non-vaccinated groups (45.0% and 47.1% in the non-OR and control groups, respectively).

The clinical diagnosis of sudden death was found to have a sensitivity of 76.4±5.9%, specificity of 41.8±9.8%, and positive predictive value of 72.7±6.0% (Table 4.8.7). The clinical diagnosis of HPAI-compatible disease was found to have a sensitivity of 71.2±7.3%, specificity of 62.3±7.7%, and positive predictive value of 64.6±7.4%. The clinical diagnosis of VVND-compatible disease was found to have a sensitivity of 13.1±8.5%, specificity of 90.3±3.8%, and positive predictive value of 25.8±15.4%.

When considering the sensitivity and specificity of the clinical diagnoses of HPAI-compatible and VVND-compatible disease as series diagnoses, the sensitivity and specificity of the HPAI-compatible diagnosis was found to be 54.4±8.1% and 78.0±6.6%, respectively, and of the VVND-compatible diagnosis 10.0±7.5% and 94.3±3.0%, respectively.

Discussion

The calculated sample size for this study was 410, based on an anticipated sensitivity of 80%, but the number of outbreaks analyzed was 297. As a result, wide confidence intervals are observed for some values calculated from small numbers of samples. Diagnostic sensitivities of 76.4 (±5.9%) and 71.2 (±7.3%) for a clinical case definition (sudden death and HPAI-compatible diagnoses, respectively) are within acceptable ranges reported in the literature for clinical case definitions developed for other diseases. However for a study of the impact of control measures on disease incidence, higher sensitivities would have been more desirable.

Determination of diagnostic accuracy using a frequentist approach, without taking into account the effects of testing in series, may be misleading. Testing in series with a more specific second test tends to increase specificity and decrease sensitivity of the overall diagnosis. Therefore, the serial results of HPAI-compatible sensitivity and specificity, at 54.4±8.1% and 78.0±6.6%, respectively, may be considered more accurate than the simple frequentist results.

The very low sensitivity obtained for the VVND-compatible disease diagnosis, 13.1+8.5% frequentist and 10.0+7.5% serial sensitivity, is not surprising given the nature of the laboratory diagnostic method used. The laboratory test detected all three pathotypes of ND, while the clinical case definition was specific for VVND. Thus, the laboratory method used as a gold standard in our study was inappropriate for evaluating the accuracy of the clinical diagnosis of VVND-compatible disease, and the sensitivity of the clinical diagnosis of VVND-compatible disease was probably higher than reflected in our study.

The population considered in our study did not correspond to that of that of the operational research, as only RT flocks with sick chickens were considered. The operational research considered all flocks regardless of health status. The methodology chosen to identify populations for our study increased the chance of including flocks affected by HPAI and ND, outbreaks of which are rare at any given moment in time. However, the difference in populations studied means that diagnostic accuracy as determined in our study cannot be directly applied to the actual PIA diagnostic accuracy in the operational research.

It is possible that in the operational research some VVND-compatible disease was misclassified as HPAI-compatible in the control and HPAI vaccinated groups, while better control of VVND in the HPAI/ND vaccinated group meant that there were fewer opportunities for similar misclassifications in that group. This is because any difference in VVND prevalence between the different treatment groups would lead to differences in the predictive value of the diagnostic process when applied in the different treatment groups. The number of negative diagnoses was large (for example, 2847 negative diagnoses for VVND-compatible disease) in comparison to the number of positive diagnoses for HPAI-compatible disease (91) and VVND-compatible disease (26). This suggests that the negative predictive values for each of the different treatment groups would be the critical parameters for assessing the impact of differential misclassification because of the large number of negative diagnoses. A small difference in the negative predictive values could result in large numbers of differentially misclassified cases. The impact of this misclassification bias could be to inflate the IRR of HPAI-compatible events between the HPAI vaccinated groups. The unknown sensitivity and specificity of the process does not allow us to determine if these considerations affected the outcome of the operational research. It should also be noted that HB1 vaccine was used and there was no evidence that this vaccination had any impact on the incidence of VVND in the treatment groups or in the vaccination trials (Section 4.3).

Table 4.8.5: Number of outbreaks investigated according to operational research treatment group

OR Treatment Group	Total Outbreaks Investigated	Not Sudden Death	Sudden Death	% Diagnosed as Sudden Death	HPAI-compatible	% Diagnosed as HPAI-compatible	VVND-compatible	% Diagnosed as VVND-compatible	Unknow n	% Unknow n
AI vaccinated	10	4	6	60.0	6	100.0	0	0.0	0	0.0
AI-ND vaccinated	24	2	22	91.7	16	72.7	6	27.3	0	0.0
Control	34	10	24	70.6	19	79.2	4	16.7	1	4.2
Non-OR	229	72	157	68.6	120	76.4	21	13.4	16	10.2
Grand Total	**297**	**88**	**209**	**70.4**	**161**	**77.0**	**31**	**14.8**	**17**	**8.1**

Table 4.8.6: Virus typing results for outbreaks by operational research treatment group

OR Treatment Group	H5N1	H5N1/ND	ND	Negative	% H5N1	% H5N1 /ND	% ND	% Negative
AI vaccinated	5	1	1	3	50.0	10.0	10.0	30.0
AI-ND vaccinated	14	0	4	6	58.3	0.0	16.7	25.0
Control	16	1	5	12	47.1	2.9	14.7	35.3
Non-OR	103	6	43	77	45.0	2.6	18.8	33.6
Grand Total	**138**	**8**	**53**	**98**	**46.5**	**2.7**	**17.8**	**33.0**

Table 4.8.7: Sensitivity and specificity of level 1 and level 2 clinical diagnoses using the frequentist approach

	Sudden Death			HPAI-compatible			VVND-compatible		
	%	SE	95% CI	%	SE	95% CI	%	SE	95% CI
Sensitivity	76.4	3.0%	5.9	71.2	3.7%	7.3	13.1	4.3%	8.5
Specificity	41.8	5.0%	9.8	62.3	3.9%	7.7	90.3	1.9%	3.8
Predictive Value +	72.7	3.1%	6.0	64.6	3.8%	7.4	25.8	7.9%	15.4
Predictive Value –	46.6	5.3%	10.4	69.1	4.0%	7.8	80.1	2.4%	4.8

The sensitivity of the Wates virus isolation and typing for H5N1 and ND may have been reduced by freezing of samples at -80°C prior to isolation and concentration. However, amplifying through four passages should have reduced this bias. The selection of only clinically ill chickens to include in our study may have increased sensitivity of all diagnostic methods, with the level of bias per diagnostic method difficult to estimate. The majority of outbreaks included in this study were from non-vaccinated areas, so the study did not exactly simulate the 50/50 split in the longitudinal study between vaccinated and non-vaccinated areas. Outbreaks of HPAI can occur in vaccinated flocks, such that the key indicators used by the practitioners to make their diagnoses (80% flock mortality, death in <4 hours, cyanosis) are less apparent. Thus, the emphasis on non-vaccinated areas in this study may have increased the specificity of the HPAI-compatible diagnosis. However, the objective of vaccination as an HPAI control tool in an endemic situation such as that found on Java is to reduce the amount of virus in the environment, not to eradicate the disease. Vaccinated flocks shed less virus particles than unvaccinated flocks; therefore, the higher specificity reported in this study for the HPAI-compatible diagnosis does not indicate that there is potentially more H5N1 virus in the environment.

Virus isolation and typing are the accepted gold standard for H5N1 and ND diagnosis (OIE, 2009). However, the accuracy of the method varies by laboratory. The sensitivity of virus isolation and typing conducted in this study may not have the same high level expected for the methods, and may have contributed to the lower sensitivities for the HPAI-compatible and VVND-compatible diagnoses found in this study (Greiner and Gardner 2000). These concerns warrant retesting of the unused aliquots from each sample in a reference laboratory to confirm diagnoses.

In only five cases (1.7%) the practitioners diagnosed an outbreak using their case definition, and then elected to change their diagnosis once they physically examined sick chickens. This indicates that the practitioners had a high degree of confidence in their ability to diagnose historic outbreaks, and that applying the diagnostic method to active rather than historic disease was not a major source of bias in our study.

Brebes and Indramayu districts may be under-represented in our study. The Brebes practitioners diagnosed four outbreaks, three of which they called HPAI-compatible and one they called not-sudden death. All four outbreaks were H5N1 positive on virus isolation (75% overall accuracy). The Indramayu practitioners diagnosed six outbreaks. They diagnosed four as HPAI-compatible, but only two of these were H5N1 positive on virus isolation. They diagnosed two as not-sudden death, however one of these proved to be ND positive on virus isolation (50% overall accuracy). The Brebes practitioners reported few sudden death outbreaks in the operational research. This may be because there are few outbreaks of HPAI or VVND in Brebes, and the sensitivity and specificity study results do not indicate that the Brebes practitioners missed a large number of outbreaks. Indramayu reported an average number of outbreaks for the longitudinal study, and may be under-represented in our study because they did not actively search for opportunities to diagnose outbreaks.

Bantul district, with 29 outbreaks diagnosed, may be over-represented here. The Bantul practitioners diagnosed five outbreaks as not-sudden death, of which three were negative on virus isolation, one was ND and one was both H5N1 and ND. They diagnosed 19 as HPAI-compatible, of which 11 were H5N1 positive on virus isolation, six were negative, and two were ND. And they diagnosed five as VVND-compatible, of which three were H5N1 positive on virus isolation, one was negative and one was ND. This provides an overall accuracy of 50.0%, HPAI-compatible accuracy of 57.9%, and may indicate some over-reporting of HPAI-compatible events by the Bantul practitioners in the operational research.

Our study assumes that the sensitivity and specificity of the clinical diagnoses of HPAI-compatible and VVND-compatible disease are the same for each of the treatment groups. This may not be true, as our study was not blinded and the practitioners may have been biased in their diagnoses in vaccinated areas, i.e., they may have under-diagnosed the diseases they thought were being controlled through vaccination. However, given that 82.6% of outbreaks in vaccinated areas were diagnosed as sudden death, versus 68.8% in unvaccinated areas, the results indicate that this bias was not strong, if it existed at all.

Further analysis of samples and data could help to clarify questions regarding the accuracy of the laboratory methods used in our study, including comparing the diagnostic results obtained with RRT-PCR analysis of the same samples. However, given questions regarding the accuracy of laboratory results compared to internationally established standards for the techniques used, a Bayesian approach that does not assume a gold standard and combines results from field diagnoses, virus typing and RRT-PCR, would be more helpful in elucidating the sensitivity and specificity of field and laboratory diagnostic methods (Branscum, Gardner, and Johnson 2005).

Conclusion

Quantifying the incidence of HPAI is challenging due to the lack of indicators of infection that are easily measured. Chickens rarely survive infection and as a result serology is not very a very useful tool for estimating prevalence of infection. Diagnostic tools that rely on agent detection are only useful for in active cases. In the case of acute viral infections of short duration, prevalence studies based on agent detection require prohibitively large sample sizes.

In this paper we have shown that clinical diagnostic procedures based on clinical case definitions have reliable levels of sensitivity and specificity for use in research. The clinical diagnosis of HPAI-compatible disease was found to have a sensitivity and specificity of $54.4 \pm 8.1\%$ and $78.0 \pm 6.6\%$ respectively. As a laboratory approach was not available that could differentiate VVND from other forms on ND, it was not possible to estimate the sensitivity and specificity of VVND-compatible disease. However, as comparison of clinical diagnostics to laboratory gold standard tests required that the research be carried out in active outbreaks, the results are not directly transferable to the participatory impact assessment system, which applied case definitions to historical events. It is important to remember that each diagnostic decision-tree (combinations of sampling procedures, and clinical and biological tests) has unique a unique set of sensitivity and specificity parameters. Thus, values for different applications of PE and PDS are specific to the detailed system in place at the time. Thus, if the diagnostic protocol is changed, the sensitivity and specificity of the system change. This study supports the strategic value of participatory approaches as important tools to answer epidemiological questions.

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5. Glossary

Aliquots – A portion of a sample.

Allantoic fluid – The clear fluid in an egg (not the yolk).

Aujeszky disease virus (ADV) – The virus that causes pseudo-rabies in swine.

Basic Reproductive Number (R_0) – An indicator of the number new individuals that will become infected from a single infected individual in a completely susceptible population.

Bayes Factor –This is the dominant method of Bayesian model testing. A Bayes Factor is the Bayesian analogue of a likelihood ratio test. The basic intuition is that prior and posterior information are combined in a ratio that provides evidence in favor of one model specification verses another.

Blind study – A study design where the treatment group assignments are concealed from the participants (single blind) or both the participants and the scientists administering the study (double blind). In a vaccination study in poultry for example, treatment groups would be designated by codes (Group A, Group B, etc.) and all groups would receive injections. One group would be a control group and the injections they received would not contain any active ingredient. The purpose of blinding is to reduce bias resulting from participant expectations regarding outcomes of the treatment.

Clinical case definitions – A standard definition to diagnose a disease case using clinical and epidemiological information.

Confounding variable – An extraneous variable (confounder) that is correlated either positively or negatively with both the outcome (in this case the incidence of HPAI-compatible events) and the independent factor being studied (i.e., treatment). If the effects of a confounder are not accounted for, the relationship between the factor and the outcome will be inaccurate.

Cost effectiveness – A form of economic analysis that compares the relative expenditure (costs) and outcomes (effects) of two or more actions, e.g., medical treatments or governmental interventions. Cost-effectiveness is typically expressed as an incremental cost-effectiveness ratio (ICER). ICER is the ratio between the difference in costs and the difference in benefits of two treatments or interventions. By using the results of a cost-effectiveness analysis, a decision maker can better judge whether a particular cost per effect represents good value for the money.

Differential (non-random) misclassification bias – This is a type of misclassification of either the exposure factor or outcome variable that occurs in different proportions in each treatment group. For example, we might have a misclassification ratio of 10% (for instance, proportion of HPAI cases wrongly classified as ND) in treatment 1 and 20% in treatment 2.

Effective Reproductive Number (R_e) – An indicator of the number new individuals that will become infected from a single infected individual in an incompletely susceptible population where some control measures have been implemented.

Epizootic – An increase in the occurrence of an animal disease above normal levels.

Eppendorf tubes – A type of tube used in the laboratory for storing samples.

Fixed effects – Explanatory variables whose quantities are treated as being non-random; this arises when the levels of a factor being studied (for example treatment) constitute the entire population; the results of a statistical model will therefore be applicable only to the levels considered.

Frequentist calculations – These are based on a "frequentist approach" to statistical analysis, where the interpretation of an event's probability is the limit of its relative frequency in a large number of trials. This is different from Bayesian calculations/approach where evidence or observations are used to calculate (or update) the probability of an event.

Gold standard test – The best diagnostic test available.

Haemagglutination – Agglutination of virus particles in suspension using red blood cells.

HPAI-compatible disease diagnosis – A disease outbreak in poultry that has been diagnosed as being compatible with HPAI according to the case definition used in this study.

Incidence rate ratio (IRR) – The relative magnitude of the incidence rate of an outcome variable in one level of a factor compared to the one used as the reference.

Intervening variable – In causal or temporal terms, an intervening variable comes between exposure and disease; such variables should be excluded from analysis when assessing the relationship between the exposure and disease because they cause similar changes in the measure of association as explanatory variables.

Intra-class correlation – Refers to the correlation between two observations within a cluster; for example, RTs within the same village might share several characteristics, and hence be correlated; a correlation coefficient is often calculated for use in epidemiological studies, such as when calculating the sample size.

Immunogen – A protein or infectious agent that is capable of provoking an immune response. The term is often used to indicate the active ingredient in a vaccine that is responsible for inducing a protective response in the individual who is injected.

ISHII – Part of the designation for the strain of ND used in the immunological tests for ND virus.

Jeffreys Scale – A statistical scale for judging significance used in Baysian analysis.

Leverage points – Refers to influential data points that, if altered, will have a large effect on the outcome of the analysis; uncovering leverage points involves understanding interrelationships that define the model.

Longitudinal study design – An analytical study design where subjects are selected based on their exposure status and followed up over a specified period of time after which incidence rates of the outcome are compared between the different groups defined by the exposure status to identify the consequences of the exposure factor.

ORIHPAI – "Operational Research in Indonesia for More Effective Control of HPAI"

Oxytetracycline – An antibiotic common in veterinary applications.

Participatory epidemiology – The use of participatory methods (a toolkit of flexible, qualitative and semi-quantitative techniques designed to learn from community knowledge systems) to study patterns of occurrence of a disease in a population.

Participatory impact assessment (PIA) – The use of participatory epidemiological techniques to assess the impact of diseases on farmers' livelihoods as well as the impact of disease control measures on the epidemiology of the disease.

Pathogenic – Capable of causing disease.

Pathotypes – Strains of an infection agent with differing capabilities to cause disease.

PDSR – Participatory Disease Surveillance and Response.

Posterior distribution – is the distribution of the random event/variable being estimated after taking into account the relevant evidence (i.e. conditional on the evidence).

Power of a study – The probability of rejecting a false null hypothesis. The studies power can be understood as its ability to detect an effect, if it is present.

Predictive Value Negative – The proportion of individuals diagnosed as negative that is truly negative.

Predictive Value Positive – The proportion of individuals diagnosed as positive that is truly positive.

Random effects – Explanatory variables whose quantities are treated as random; this applies to situations when an investigator wants to make inferences about the whole population and the levels of a factor used in the analysis only represent a sample from that population (for example districts).

RT – *Rukun Tetangga*, the smallest administrative unit in Indonesia. It is sometimes translated as a neighborhood and can vary in size from 10 up to 100 households.

Sensitivity – The proportion of actual positive individuals that are identified as such by a diagnostic method.

Sero-conversion – A type of immune response to an exposure to a protein or infectious agent that causes the individual to produce antibodies specific to the exposure.

Sero-monitoring – The survey of a population after vaccination to detect the level of specific antibodies resulting from the vaccination. It is used as a tool to measure the effectiveness of vaccination programs.

Specificity – The proportion of actual negative cases that is identified as negative by a diagnostic method.

Sudden death event – For the purposes of the OR, a sudden death event was a case that met the sudden death case definition. The sudden death case definition was a syndromic description designed to use sudden death as simple indicator to detect HPAI cases for further consideration.

Titre – A procedure for quantify antibodies or virus in a sample where the material is diluted in a series of steps and the most dilute step that still has some detectable material is the titre of the sample.

Type I error – This is the probability of rejecting a null hypothesis of a statistical test when in fact it is true. A null hypothesis would be framed as: vaccination does not reduce the incidence of HPAI. In this example, a Type I error would consist of concluding that vaccination reduces the incidence of HPAI when in reality it did not.

Type II error – This is the probability of failing to reject a null hypothesis when in fact it is false. A null hypothesis would be framed as: vaccination does not reduce the incidence of HPAI. In this example, a Type II error would consist of concluding that vaccination does not reduce the incidence of HPAI when in reality it did.

VVND-compatible disease diagnosis – A disease outbreak in poultry that has been diagnosed s being compatible with VVND according to the case definition used in this study.

Wates DIC – The diagnostic laboratory in Wates, Yogyakarta Province.

Win Episcope 2.0 – An epidemiology software package capable of calculating sample sizes.

Zoonosis – A disease that is transmissible from animals to man.

4.