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## Key Findings

- Despite control efforts, HPAI transmission is being sustained ( $R > 1$ ) in areas close to the Red River delta and in the Mekong area.
- There is strong evidence of an increase in the infectious period post-vaccination in both the North and the South.
- There was a significant reduction in the infectivity of communes post vaccination in the North; this was not observed in the South.
- Following vaccination there remained a substantial number of communes with  $R > 1$  allowing less intense but longer outbreak waves, both in the North and the South.

## Controlling Avian Flu and Protecting People's Livelihoods in the Mekong Region

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## Modelling the Temporal and Spatial Dynamics of the Spread of HPAI H5N1 in Viet Nam

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Highly pathogenic avian influenza threatens the health, livelihoods and income of those reliant on poultry production whilst simultaneously posing serious public health risks, both in terms of the current human mortality and the spectre of a global pandemic. Thus, effective control measures are required to reduce the scope of HPAI outbreaks in poultry, but interventions, which have serious implications for those whom outbreaks already affect the most may result in an unwillingness to report cases, providing the disease with more time and opportunity to spread.

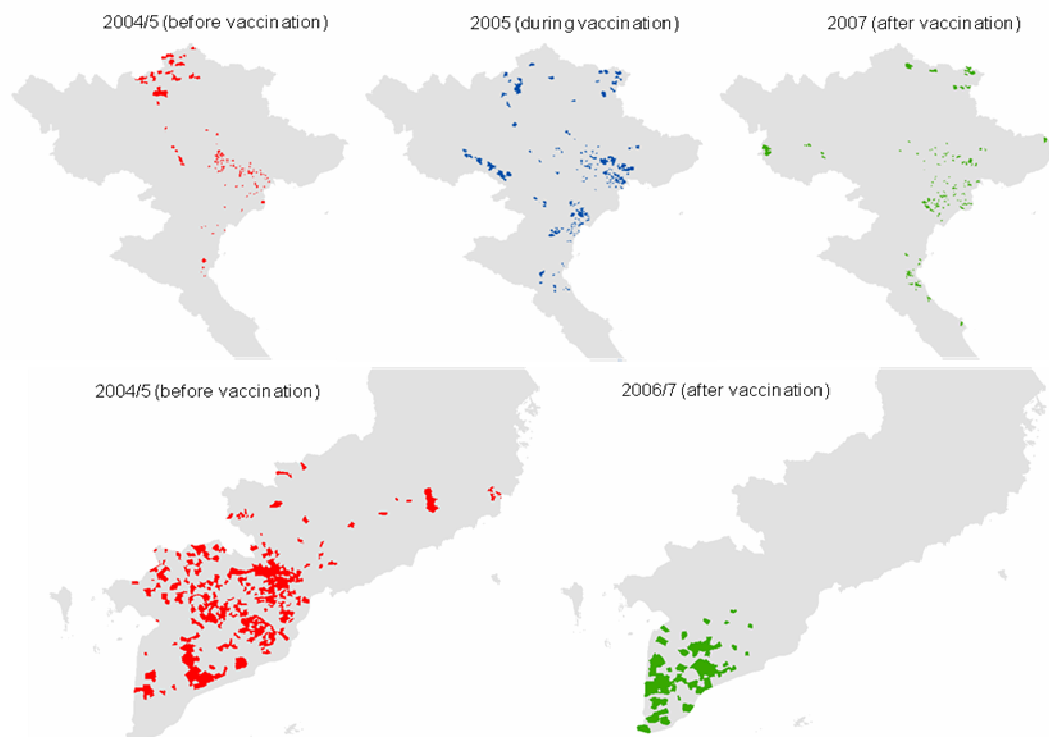
Outbreaks of H5N1 in poultry in Viet Nam continue to threaten the livelihoods of those reliant on poultry production whilst simultaneously posing a severe public health risk given the high mortality associated with human infection. Authorities have invested significant resources in order to control these outbreaks. Of particular interest is the decision, following a second wave of outbreaks, to move from a "stamping out" approach to the implementation of nationwide, mass vaccination campaigns. Quantifying the changes in the dynamics of transmission around this shift in policy provides an indication of how effective vaccination has been in preventing infection and what further needs to be achieved in order to control the disease.

Here we describe results obtained from fitting a spatial transmission dynamics model to the spatially-stratified outbreak data from both North and South Viet Nam between 2004 and 2007. The purpose of this model fitting is to enable assessment of the impact of the implemented HPAI control policies, including the widespread vaccination campaign, on the incidence of disease, and by extension, the likely impact of such policies in other countries in the Mekong region.

## Theoretical Background and Data

The likelihood of onwards disease transmission from infected to non-infected communes is determined by two factors: (i) the duration of time an infected commune remains infectious, the infectious period, and (ii) the transmissibility of infection during this period. The reproductive number, i.e. the average number of susceptible communes infected by each infected commune combines these factors to provide an indication of the likelihood that the disease will spread. In the case of Viet Nam, only the dates at which an outbreak within a commune was reported are available. As a consequence, we have attempted to simultaneously estimate the infectious period and the reproductive number for each infected commune. To do this we used Bayesian Monte Carlo techniques to fit a spatio-temporal transmission model to the outbreak report data. In northern Viet Nam, three waves of infection were defined occurring before (late 2004-early 2005), during (mid 2005) and after (mid 2007) the initial implementation of the vaccination campaign. In southern Viet Nam during this period there were only two waves, the first occurring concurrently with the 2004/5 wave in northern Viet Nam and the second occurring, post-vaccination, in late 2006-early 2007 (Figure 1).

**Figure 1: Spatial distribution of waves of outbreaks in the North and South of Viet Nam from late 2004 to 2007.**

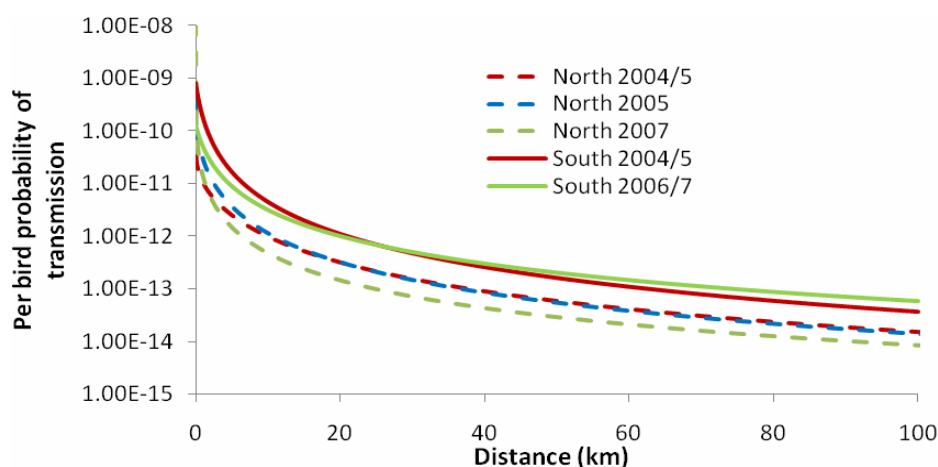


## Vaccination and Spatial Transmissibility between Communes

In the absence of any specific data, we assumed that following a report of an outbreak, the poultry within a commune was removed from the outbreak by the end of the following day. We then estimated the infectious period for each infected commune as the time between infection (which is estimated in the model) and the time the outbreak is reported. At the same time, we estimated the average onward infectiousness of each commune for each outbreak wave.

To capture the spatial spread of the disease a transmission kernel describing how the probability of transmission is related to the distance from a potential source of infection was fitted.

**Figure 2: Daily probability of transmission by distance.**



In the North, the estimated onward infectivity of each commune varied little between 04-05 (pre-vaccination) and 05 (during vaccination). However, there was a significant decrease in infectivity in 07 (after vaccination). We thus obtained an estimate of a 55% reduction in infectivity after vaccination, consistent with an effective vaccination coverage of 45%. This is consistent with a post-campaign sero-surveillance study in which it was estimated that 60% protection had been achieved.

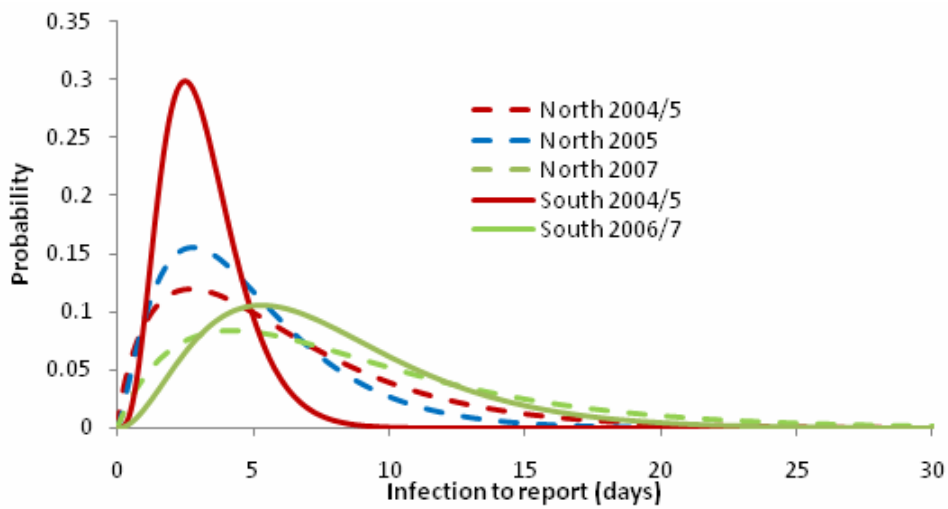
In the South, our estimates did not suggest any decrease in the per-capita poultry infectivity between the 04-05 wave and the 06-07 wave. This may be a consequence of the model being unable to fit to the spatial distribution of outbreaks which occurred in 2006/7 based upon poultry densities alone, as demonstrated by the disparity between the location of outbreaks and areas the model suggests were at high risk of infection (see below).

## Interval between Infection and Reporting

The reduction in infectivity observed in the North was, to some extent, offset by an increasing time from infection to report, resulting in an extended infectious period. This was consistently observed in the post-vaccination waves in both the North and the South and resulted in outbreaks which were overall lower in intensity but of a longer duration. This may in part be due to the direct effect of vaccination reducing the visibility of disease. However, there was also a shift in the poultry population during this period with a larger proportion of ducks in the later periods.

The model also estimated that, relative to the preceding wave, the mean infection to report interval was approximately a day shorter during the 2005 wave in the North, coinciding with an increase in the level compensation awarded to farmers with infected flocks.

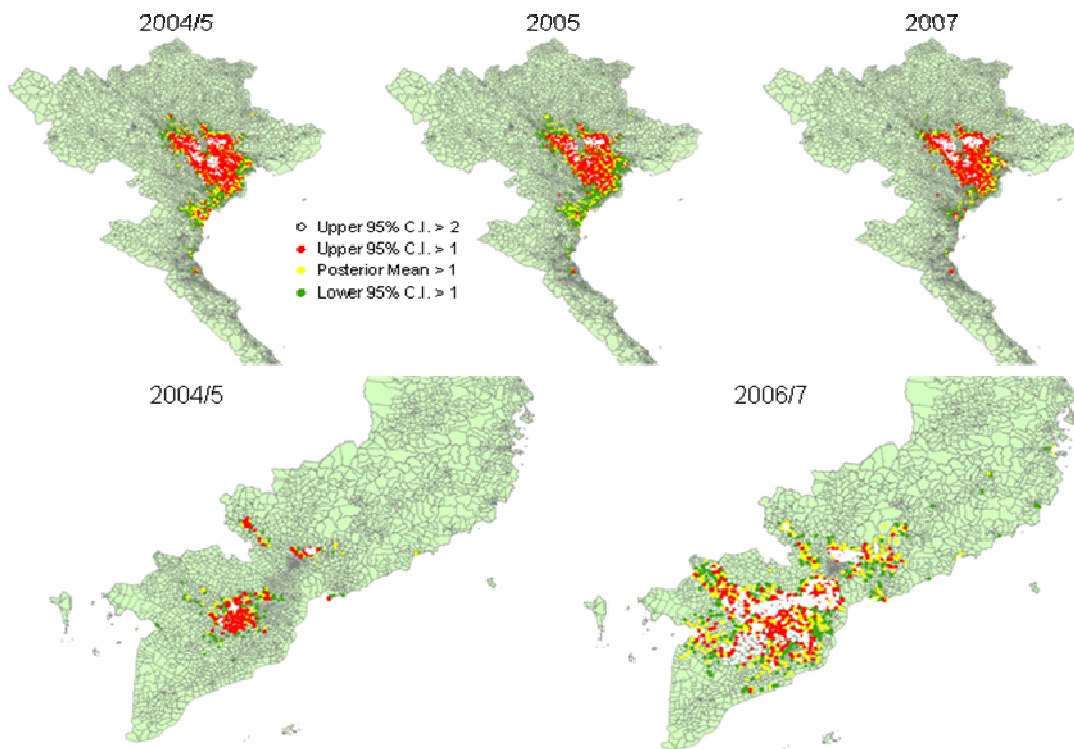
**Figure 3: Estimated distribution of the infectious period over the complete outbreak for each of the three outbreak waves in the North (04-05, 05, 07) and the two waves in the South (04-05, 06-07)**



### Local Reproductive Numbers and Risk Maps

Based on the obtained distribution of the infectious periods and the spatial transmission kernel, the local reproductive number for each commune was calculated. This provides the expected number of secondary outbreaks which would have occurred had the first outbreak occurred in a given commune. Commune reproductive numbers were then used to produce risk maps to highlight areas most likely to propagate outbreaks.

**Figure 5: Risk maps and local reproductive numbers**



We found that for all three waves in the North of Viet Nam, the fitted model was able to highlight the areas close to the Red River Delta as being at high risk of infection (Figure 5) but could not explain the transmission which occurred in more remote border areas based upon poultry numbers alone. Combining the estimated reduction in infectivity (potentially due to vaccination) with the increased time taken to report an outbreak following initial infection resulted in only a minor reduction in overall risk. Thus sustained transmission in the Red River Delta reoccurred, producing a less intense but more prolonged wave of outbreaks.

The model was able to highlight some areas in the South of Viet Nam which were at high risk of infection during the 2004/5 wave but, based upon poultry numbers alone, was unable to replicate the level of transmission which occurred around sections of the Cambodian border and the southernmost tip of the country. The latter area experienced a large number of outbreaks despite having relatively low poultry density.

## Conclusions

We found a large reduction in between-commune infectivity in northern Viet Nam. Assuming this is a result of the vaccination campaign, the size of the reduction provides an estimate of a 45% effective vaccination coverage achieved by mass vaccination campaigns. However, in both northern and southern Viet Nam we found an increase in the commune-level infectious period due to outbreaks remaining unreported for a longer duration. This could be the result of the “silent spread of disease” where outbreaks in vaccinated flocks are more difficult to detect, a consequence of less rigorous surveillance or a reduction in the willingness to report disease. As the proportion of outbreaks occurring in ducks has increased it may also be partly attributable to differential pathogenicity in chickens and ducks.

We conducted an analysis of the reconstructed epidemic tree and estimated that, had detection levels been maintained at the levels estimated pre-vaccination, around two-thirds of outbreaks which occurred in the 2007 wave in northern Viet Nam would have been prevented. This highlights the fact that, regardless of the underlying reasons for less rapid reporting of outbreaks, in order to translate the reductions in commune-level transmissibility following vaccination into greater gains in disease control, more effective reporting and surveillance strategies are required.

The inability of the model to predict the areas at high-risk of infection in the 2006/7 wave in southern Viet Nam, with the majority of outbreaks concentrated near the south coast, an area where human and poultry populations are not particularly dense, may suggest that there may be other factors not captured in the model such as heterogeneity in host species, regional variation in vaccine coverage, poultry movements or possibly even the movement of vaccinators playing a more prominent role in transmission.

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