Mathematical modelling of zoonotic influenza A applied to Bangladesh

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1. The Problem

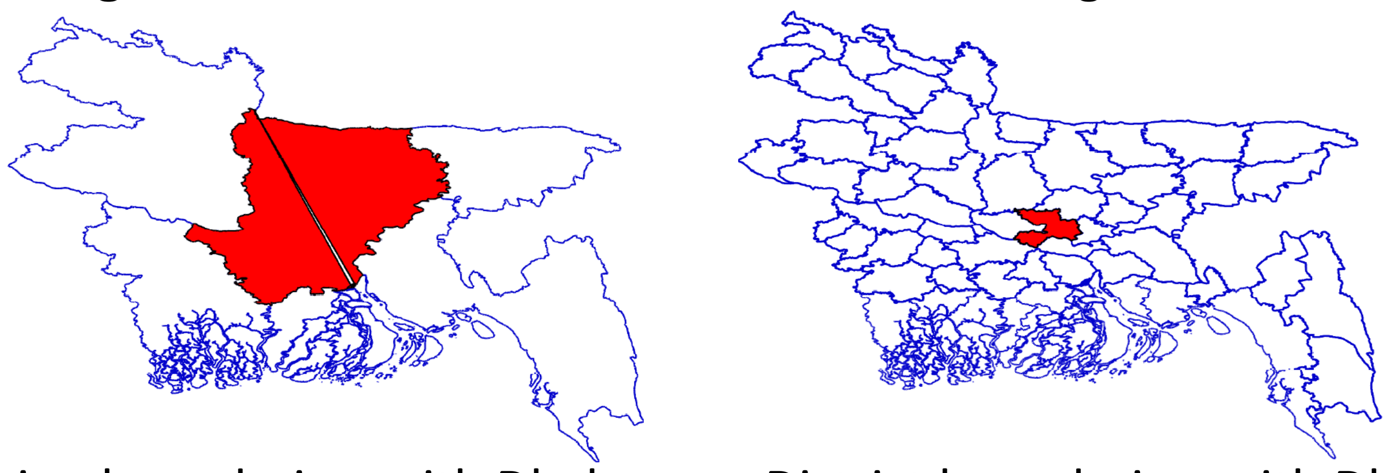
Influenza A has **many strains** and inhabits **many hosts**. It is critically important to understand how likely it is that more **lethal strains** will cause a **pandemic** in the human population. One such example is **H5N1 avian influenza**, which has had a devastating impact in South-east Asia. In particular, since 2007, **Bangladesh** has had at least 550 commercial poultry premises infected and **7 human cases**.

2. Objectives

i. Develop a model framework incorporating **zoonotic transmission**.

ii. Fit a set of models to **three H5N1 avian influenza epidemic waves** in Bangladesh, focussing on the **Dhaka region** (Fig. 1), to determine the key factors that best capture the observed cases. We used **waves 2,5 & 6** (from 2008, 2011 and 2012 respectively).

Fig. 1: Division and district boundaries of Bangladesh



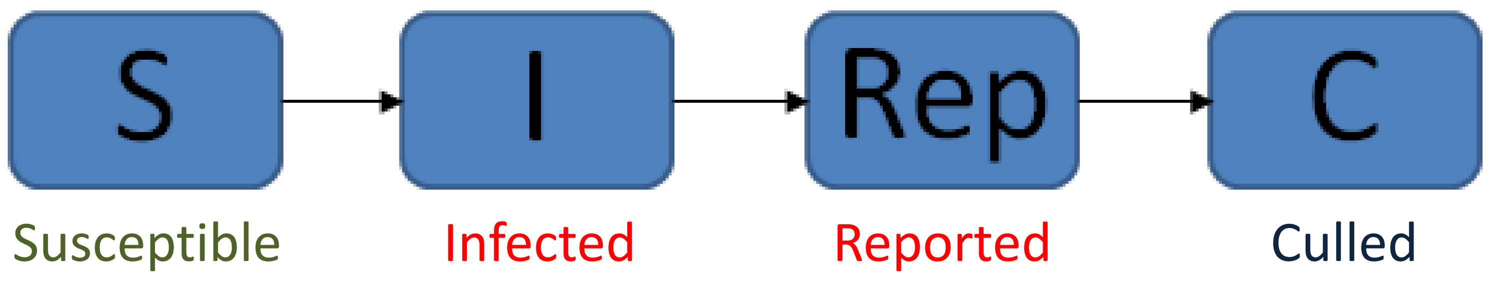
Division boundaries, with Dhaka division in red. District boundaries, with Dhaka district in red.

3. Model Formulation

Our modelling framework consists of two components:

i. Poultry component

Individual compartment based spatial model at the **premises level.**



- Compared a set of nested models, of varying complexity, for the force of infection (see Model boxes below).
- Various fixed values for infected to reporting time: 2,4,7 days.
- Reporting to culling times known from data.

ii. Zoonotic transmission component

Currently assume human case occurrence is a Poisson process:

Daily Infection Rate: $\lambda(t) = \beta I_b(t) + \epsilon_h$

Daily Event Probability: $1 - \exp(-\lambda(t))$

where I_b - number of infected poultry, ϵ_h - human case spark term.

Parameter inference was performed using MCMC methods and plotting likelihood surfaces. **Stochastic simulations** were used to verify our model fitting procedure.

Model A

Farms only, fit the following:
- Individual transmissibility
- Transmission kernel
- Spark term

Model B
- Add population size exponents

Model C

Incorporate more complex spark terms:
- Live bird markets
- Presence of rice
- Presence of water bodies
- Presence of ducks

4. Results: Poultry Model

Competing models were compared using **deviance information criterion (DIC)**. Preferred models are summarised below:

District
- Infected to Reported time: **2 days** (Wave 2), **7 days** (Wave 5).
- **Model A, no exponents** on premises populations.

Division
- Infected to Reported time: **7 days** preferred.
- **Model B, including exponents** on premises populations.

- District level simulations obtained **good correspondence** with **case size data** (Fig. 2).
- Division level simulations found the areas infected most often lay north of the main band of observed infected premises (Fig. 3).

Fig. 2: Simulated epidemic size distribution versus observed wave 2 data at the district level.

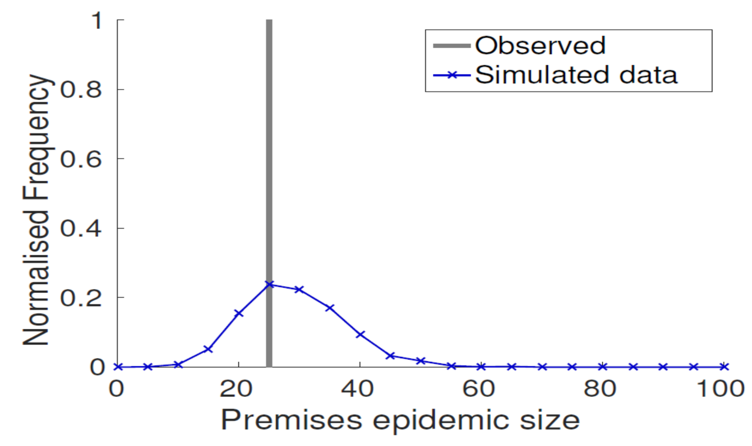
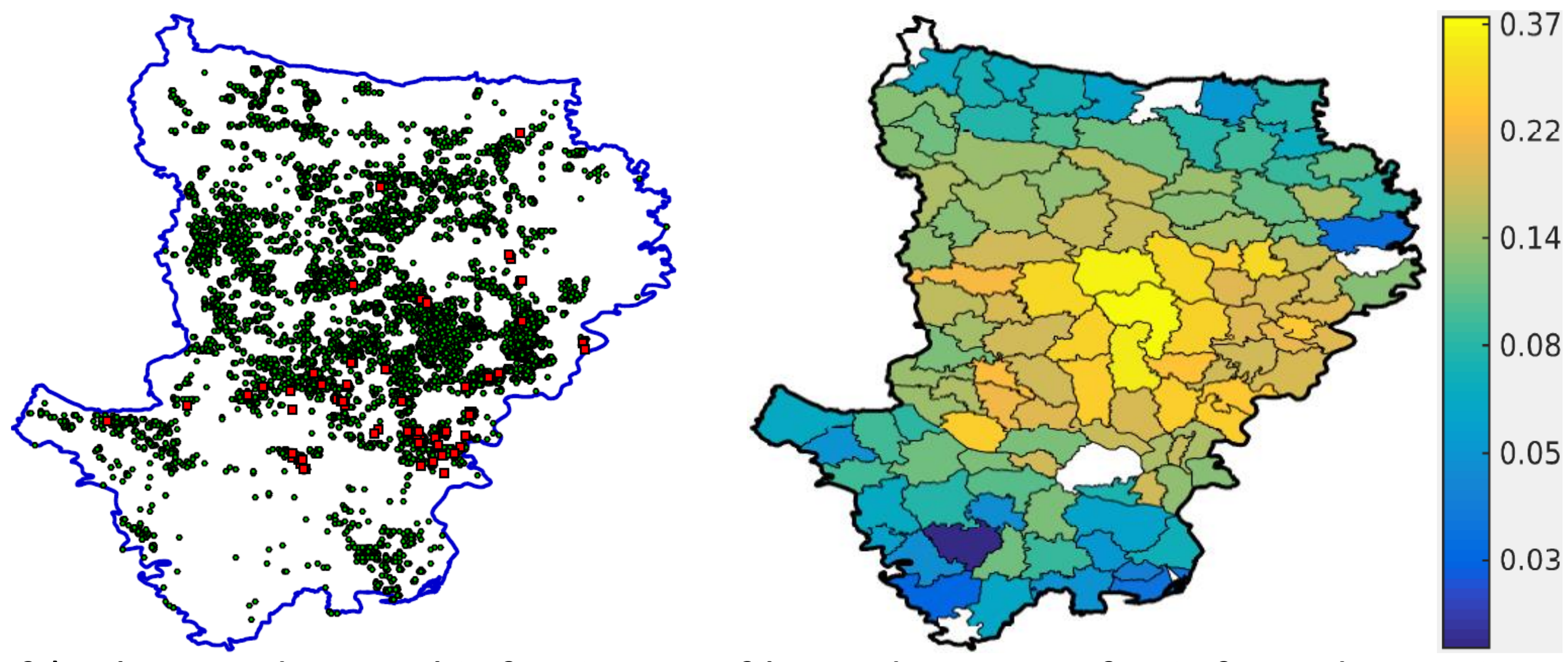


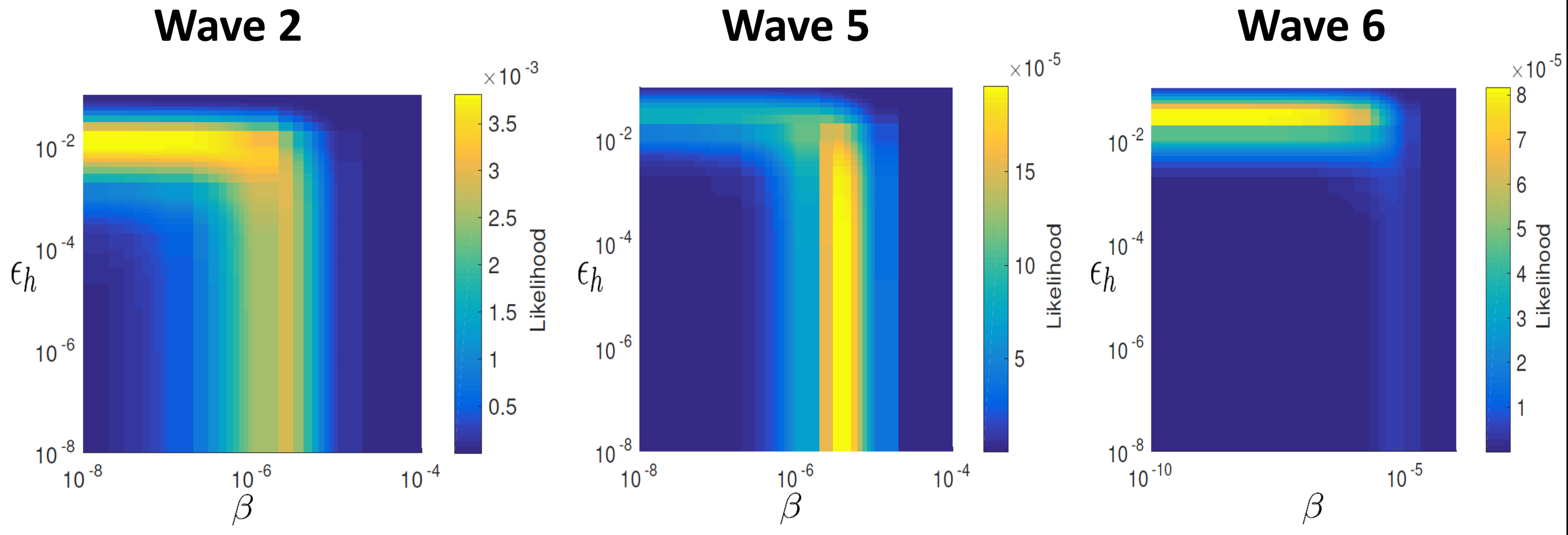
Fig. 3: Model verification for Dhaka division wave 5 data.



(left) Observed spatial infection profile; red squares for infected premises, green circles for uninfected premises. (right) Simulated risk of infection, aggregated at a subdistrict level.

5. Results: Zoonotic Transmission

Fig. 4: Likelihood surfaces for the zoonotic transmission model.



Suggestion of **differing causal mechanisms** for human cases (Fig. 4).
- Wave 5 suggests strong dependence on infected poultry.
- In contrast, waves 2 and 6 gave little support to that factor.

6. Future work

Investigate the impact of **control strategies** applied across both humans (quarantine, anti-viral medication, vaccination) and animals (culling, vaccination, movement bans).

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