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Estimating the between-farm transmission rates for highly pathogenic avian influenza subtype H5N1 epidemics in Bangladesh between 2007 and 2013

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Summary

Highly Pathogenic Avian Influenza (HPAI) is classified by the World Organization for Animal Health as one of the notifiable diseases. Its occurrence is associated with severe socio-economic impacts and is also zoonotic. Bangladesh HPAI epidemic data for the period between 2007 and 2013 were obtained and split into epidemic waves based on the time lag between outbreaks. By assuming the number of newly infected farms to be binomially distributed, we fit a Generalized Linear Model to the data to estimate between-farm transmission rates (β). These parameters are then used together with the calculated infectious periods to estimate the respective basic reproduction numbers (R_0). The change in β and R_0 with time during the course of each epidemic wave was explored. Finally, sensitivity analyses of the effects of reducing the delay in detecting infection on a farm as well as extended infectiousness of a farm beyond the day of culling were assessed. The point estimates obtained for β ranged from 0.08 (95% CI: 0.06–0.10) to 0.11 (95% CI: 0.08–0.20) per infectious farm per day while R_0 ranged from 0.85 (95% CI: 0.77–1.02) to 0.96 (95% CI: 0.72–1.20). Sensitivity analyses reveal that the estimates are quite robust to changes in the assumptions about the day in reporting infection and extended infectiousness. In the analysis allowing for time-varying transmission parameters, the rising and declining phases observed in the epidemic data were synchronized with the moments when R_0 was greater and less than one, respectively. From an epidemiological perspective, the consistency of these estimates and their magnitude ($R_0 \approx 1$) indicate that the effectiveness of the deployed control measures was largely invariant between epidemic waves and the trend of the time-varying R_0 supports the hypothesis of sustained farm-to-farm transmission that is possibly initiated by a few unique introductions.

KEYWORDS
disease control, transmission, veterinary epidemiology, zoonosis/zoonotics

1 | BACKGROUND

The poultry industry is an economically and socially important sector to Bangladesh as a source of income (for more than 70% of rural households) and animal proteins (Islam, Uddin, & Alam, 2014). This industry has been affected by, amongst other things, high feed prices and periodic epidemics of Highly Pathogenic Avian Influenza (HPAI) subtype H5N1 (Islam et al., 2014) and other poultry diseases such as

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Newcastle disease. This effect is reflected in the declining number of poultry farms that has dropped from more than 114,000 farms in 2008–2009 to 64,000 farms in 2010–2011 (Islam et al., 2014).

Given the importance of poultry production in the livelihoods of the rural households in developing countries, epidemics involving HPAI, an OIE (World Organization for Animal Health)-listed disease, raise concern for socio-economic reasons and the zoonotic aspect of the disease, although the number of cases recorded in humans has remained low.

Five hundred and six HPAI outbreaks involving the H5N1 subtype have been officially reported in Bangladesh during the study period (i.e., 2007–2013). These outbreaks were found to be clustered in time and most of them are preceded by the bird migratory period in early winter, thus supporting the hypothesis that migratory birds may be playing a role in the initial introduction of the virus (Ahmed, Ersbøll, Biswas, & Christensen, 2010). Additionally, the possibility of under-reporting of cases in backyard flocks together with the existence of asymptomatic cases and silent reservoirs such as ducks playing a part in virus propagation is hypothesized (Ahmed et al., 2010). Yet, HPAI virus detection relies mainly on the observation of clinical signs of the disease and the increased mortality in the flock (Ahmed et al., 2010). Moreover, some Asian countries are believed to be especially vulnerable to virus perpetuation because of low-level biosecurity, rearing of chickens and ducks together, selling of live birds and deficient disease surveillance (Biswas et al., 2008; Fournié et al., 2013).

In the course of most epidemics especially those involving OIE-listed diseases, outbreak data are collected. These data can among other things be used in studies geared towards improving disease management during future epidemics. Mathematical modelling provides a means to draw inferences based on the collected data. For example, models that are informed by the data collected can be used to estimate pathogen transmission rates between epidemiological units which can range from the individual host to different geographical locations of farms.

Examples on the use of outbreak data to infer about HPAI epidemics include the estimation of per contact transmission probabilities of the virus between farms (Ssematimba, Elbers, Hagenaars, & de Jong, 2012), the assessment of the impact of intervention strategies in controlling outbreaks (Bett et al., 2014; Stegeman, Bouma, & de Jong, 2010; Stegeman et al., 2004; Walker et al., 2015) and general inference about epidemic-specific characteristics (Bavinck et al., 2009; Bos et al., 2009; Stegeman et al., 2004).

One of the epidemiologically important parameters in studying disease dynamics is the basic reproduction number (R_0). It is defined as the average number of secondary infections caused by a typically infectious individual throughout its infectious period when introduced into a naïve population (Diekmann, Heesterbeek, & Metz, 1990). In deterministic models, if $R_0 < 1$ the infection dies out while if $R_0 > 1$ an epidemic occurs. Therefore, as the transmissibility of an infection can be quantified by its R_0, its magnitude provides clues on the efforts required to control the disease. Note that R_0 is influenced by the transmission probability per contact, the mean contact rate and the length of infectious period. These factors vary between pathogen subtypes, geographical regions and husbandry practices. This renders extrapolation of R_0 estimates from epidemics in different geographical regions and those involving different pathogen subtypes less reliable. Thus, in an ideal situation where field outbreak data are available, an epidemic-specific R_0 should be estimated to ensure reliability of the recommendations for control strategies it informs.

In this study, we quantify the between-farm transmission rates or adequate contact rates (β) which are defined as the average number of farms infected per infectious farm per day and their corresponding R_0 for H5N1 HPAI virus for the epidemic waves that hit Bangladesh between 2007 and 2013. We also explore the change in β and R_0 with time during the course of each of the epidemic waves.

2 | MATERIALS AND METHODS

2.1 | Data

We used the HPAI-H5N1 outbreak data that were compiled by the Department of Livestock Services, Dhaka, in collaboration with Emergency Centre for Transboundary Animal Diseases, Food and Agriculture Organization of the United Nations (FAO), Bangladesh. Although the first outbreak is believed to have occurred around January 2007, the country was officially declared to be HPAI-H5N1-virus positive in March 2007 (OIE, 2015). Therefore, the data that were used for this study included outbreaks from March 2007 up to March 2013. That dataset contained details on the dates of clinical suspicion and culling of all infected and detected farms. It also contained information on the location of the farm, the number of birds on the farm and eggs destroyed (where applicable) as well as details about the owner and source of chicks, among others.

In this study, an epidemic wave was defined as a continuous chain of outbreaks. The chain was assumed to break if the time between the infection of a new farm and the culling of its immediate predecessor was more than 21 days, in line with earlier analyses (Henning et al., 2009). Day records in which the number of infectious farms was zero were deleted.

2.2 | Model assumptions

Let $S(t)$, $I(t)$ and $R(t)$ be, respectively, the number of susceptible, infectious and removed farms and $C(t)$ and $N(t)$ be the number of newly infected and total number of farms on a given day of the epidemic wave, respectively. The disease dynamics were modelled with farms as individual units and in accordance with the standard SIR epidemic model formulation with a frequency-dependent transmission term and a homogeneous-mixing approximation. The homogeneous-mixing approximation is motivated by the observed transmission patterns in which long-distance jumps were common [with almost every new outbreak occurring in a different subdistrict (Loth, Gilbert, Osmani, Kalam, & Xiao, 2010)], the formation of secondary (global) clusters within ranges of 150–300 km being indicative of long-distance virus spread (Ahmed et al., 2010), and the wide live bird market network in Asia in general (Fournié et al., 2013). The probable day of virus introduction onto a farm was assumed to be 7 days prior to the day of reporting based on the findings from a study based on data from the 2003 HPAI epidemic in the Netherlands (Stegeman et al., 2004). This caters for the silent virus circulation within the flock preceding detection through passive surveillance [which is common in Bangladesh (Ahmed et al., 2010)] that requires a recognizable increase in mortality and morbidity in the flock.

2.3 | Data analysis

Assuming a stochastic SIR epidemic model, we derive the probability of infection and use it to estimate the transmission rate parameter β from longitudinal data of an epidemic as follows: Let $p_{esc}(t)$ be the probability that a certain susceptible farm remains uninfected up to a time t, then,

$$\frac{dp_{\mathrm{esc}}(t)}{dt} = -\lambda(t)p_{\mathrm{esc}}(t), \tag{1}$$

where $\lambda(t)$ is the force of infection given by $\lambda(t) = \beta\,(I(t)/N(t))$ and β is the desired transmission rate parameter or adequate contact rate. Integrating Equation 1 gives the probability of escaping infection during the time interval $(t, t + \Delta t)$ as $p_{esc}\,(t, t + \Delta t) = \exp\,(-\beta\,(I(t)/N(t))\,\Delta t)$ and the complement gives the probability of infection.

With the assumptions listed and using the methods described by (Becker, 1989; Mollison, 1995), the number of newly infected farms is approximately binomially distributed: $C(t, \Delta t) \sim \mathrm{Bin}\,(S(t), p_{\mathrm{inf}}\,(t, \Delta t))$ with,

$$p_{\mathrm{inf}}(t,\Delta t) = 1 - \exp\left(-\beta\frac{I(t)}{N(t)}\Delta t\right), \tag{2}$$

as the probability of infection per time step $\Delta t = 1$ day in this case.

Re-arranging Equation 2 gives,

$$\log(-\log(1 - p_{\mathrm{inf}})) = \log(\beta) + \log\left(\frac{I(t)}{N(t)}\right), \tag{3}$$

Technically from Equation 3, to estimate β, we fit a Generalized Linear Model (GLM) with a complementary log–log link function and $\log(I(t)/N(t))$ as the offset variable to the data (see (Bos et al., 2009) for an application example). The optimization procedure is implicitly based on the maximum likelihood estimation approach and similar results can be obtained by maximizing the corresponding likelihood function given by,

$$L_\beta = \prod_{t=1}^{t_{\max}}\left(1 - \exp\left[-\beta\frac{I(t)}{N(t)}\right]\right)^{C(t)}\left(\exp\left[-\beta\frac{I(t)}{N(t)}\right]\right)^{S(t)-c(t)}, \tag{4}$$

as done by (Bavinck et al., 2009).

Here, Mathematica 10.3 (Wolfram Research, Inc.) linked to the statistical package R (R Development Core Team, 2005) was used to estimate β and its 95% Confidence Interval (CI). The basic reproduction numbers (R_0) were then calculated as the product of the estimated transmission rate parameter β and the mean infectious period T calculated for that particular epidemic wave based on the set assumptions.

2.4 | Estimation of time-varying β and R_0 during each epidemic wave

By definition, R_0 is an average quantity. Consequently, when a transmission parameter is estimated from the entire epidemic data, the resulting value is an averaged-out estimate of the different values that the parameter attains at the different stages of the epidemic. However, there is more information that can be derived from the distributions, over time, of the transmission parameters. For example, the distribution may provide a way to assess the effectiveness of control strategies that were implemented at the different stages of the epidemic (Ferguson, Donnelly, & Anderson, 2001; Wallinga & Lipsitch, 2007). Here, this approach is used to provide support for the study assumption that, during the different epidemic waves, farm-to-farm disease spread was the main transmission route and not multiple introductions alone.

We obtain the time distribution of the transmission parameters over the course of the different epidemic waves by splitting the epidemic wave durations into 21-day-long episodes and estimating their corresponding R_0. For example, an epidemic wave that lasted 107 days is split into five subwaves with the first subwave starting at epidemic day 1 and lasting until epidemic day 21 and the last subwave starting at epidemic day 86 and lasting until epidemic day 107. The estimated time-varying R_0 values were then compared with the epidemic temporal pattern observed during those periods in the overall epidemic curve.

2.5 | Sensitivity analyses

Sensitivity analysis was performed to assess the effect of reducing the farm detection delay from 7 to 2 days which could occur in an ideal situation. Additionally, it is noted that virus persistence in the environment may play a role during disease outbreaks (Sooryanarain & Elankumaran, 2015) as a culled farm may not be immediately and completely cleared of infectious material (Bett et al., 2014; Ssematimba et al., 2012; Ypma et al., 2012). The potential effect of a possibly prolonged infectivity on the estimates was assessed through extending farm infectiousness by 3 days post-culling in the baseline scenario.

3 | RESULTS

Figure 1 presents a summary of the epidemic waves extracted from the data in which six major epidemic waves are identified. The first wave started in March 2007 and lasted until July 2007 affecting 55 farms while the second wave started in October 2007 and went on until April 2008 affecting 231 farms. The third and fourth waves, respectively, occurred from December 2008 to April 2009 and

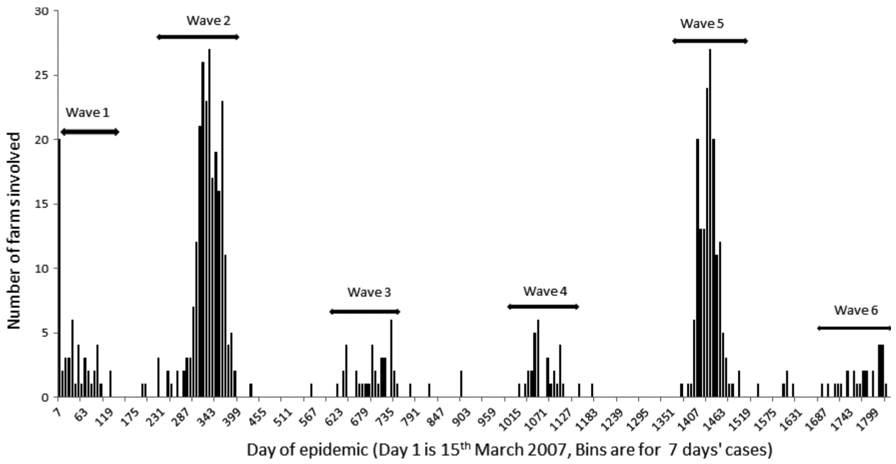

FIGURE 1 The weekly epidemic curve of HPAI-H5N1 outbreaks in Bangladesh from March 2007 through March 2013 with 15th March 2007 as Day 0. The bars represent outbreaks over 7 days. Epidemic wave 1 was from March to July 2007; Wave 2 was from October 2007 to April 2008; Wave 3 was from December 2008 to April 2009; Wave 4 was from January to April 2010; Wave 5 was from January to May 2011; and Wave 6 was from November 2011 to April 2012

January to April 2010, affecting 36 and 28 farms. Finally, the fifth wave started in January to May 2011 affecting 161 farms and that sixth wave was from November 2011 to April 2012 affecting 26 farms. Only five more sporadic outbreaks were reported between April 2012 and March 2013 namely; one each in October and December 2012 and two in February 2013 and one in March 2013.

For each of those six waves identified, we present the boxplots summarizing the distribution of "reaction" time (i.e., the number of days between outbreak reporting and culling of that farm) in Figure 2 and the time-varying R_0 during the 21-day periods of the different waves is presented in Figure 3. The estimates for the transmission rate parameter, infectious period and basic reproduction number for the default scenario are presented in Table 1 and in Table 2 for the sensitivity analyses.

From Figure 2, we observe that the median reaction time reduced from 4 and 3 days in epidemic waves 1 and 2, respectively, to a mere 1 day in all other waves. A similar decreasing trend is observed for the maximum reaction time with 16 and 21 days in waves 1 and 2, respectively, and between 3 and 5 days in all other waves.

Our findings (Table 1) indicate that the transmission rate parameters for the different epidemic waves in Bangladesh ranged from 0.08 to 0.11 per infectious farm per day with the lowest and highest 95% confidence limits being 0.06 and 0.20 per infectious farm per day, respectively. The average infectious period ranged from 7.9 days (for wave 3) to 12 days (for wave 1). The estimated basic reproduction numbers (R_0) were consistently very close to one (i.e., the threshold value for disease persistence) with the lowest and highest 95% confidence limits of 0.57 and 1.58, respectively, and all confidence intervals contained the threshold value for disease persistence namely, $R_0 = 1$.

On the distribution of R_0 over time, as hypothesized, we observe (Figure 3) that considering only the overall average value that is obtained from analysing a full epidemic masks the otherwise informative time-varying dynamics. Figure 3 elucidates this and we observe, for example, that the estimated (split) R_0 values are above one around the sixth 21-day period of wave 2 and around the second such period for wave 5. More importantly, the depicted trend is in synchrony with that observed in the epidemic curve in Figure 1, that is the periods when $R_0 > 1$ coincide with the observed rise in

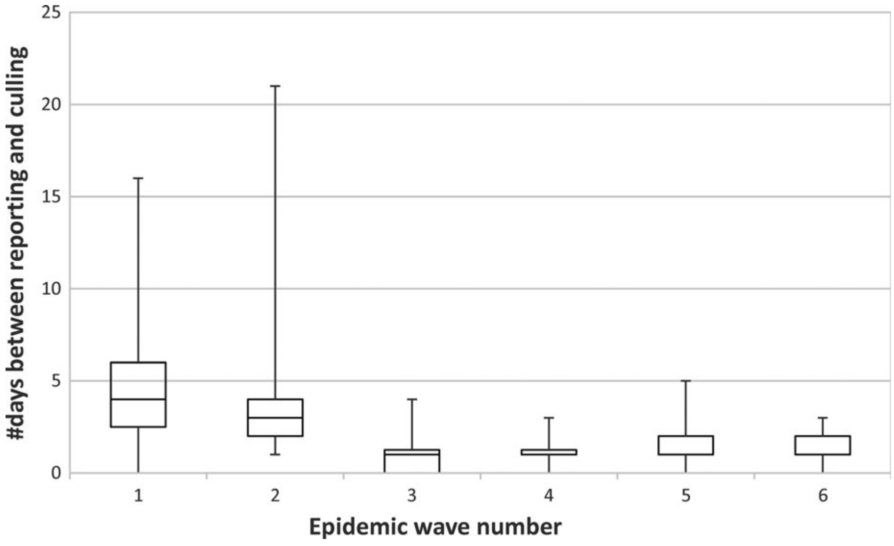

FIGURE 2 Boxplots depicting the minimum, 25th percentile, median, 75th percentile and the maximum number of days between disease reporting and culling of the affected farm that is reaction time distribution. For example, in the plot for wave 2, the lower caped end is the minimum value, followed, respectively, by the horizontal bars for the 25th percentile, median and 75th percentile and the top-most caped bar is the maximum value. The median value coincides with the 25th percentile at a value of one in the last three epidemic waves

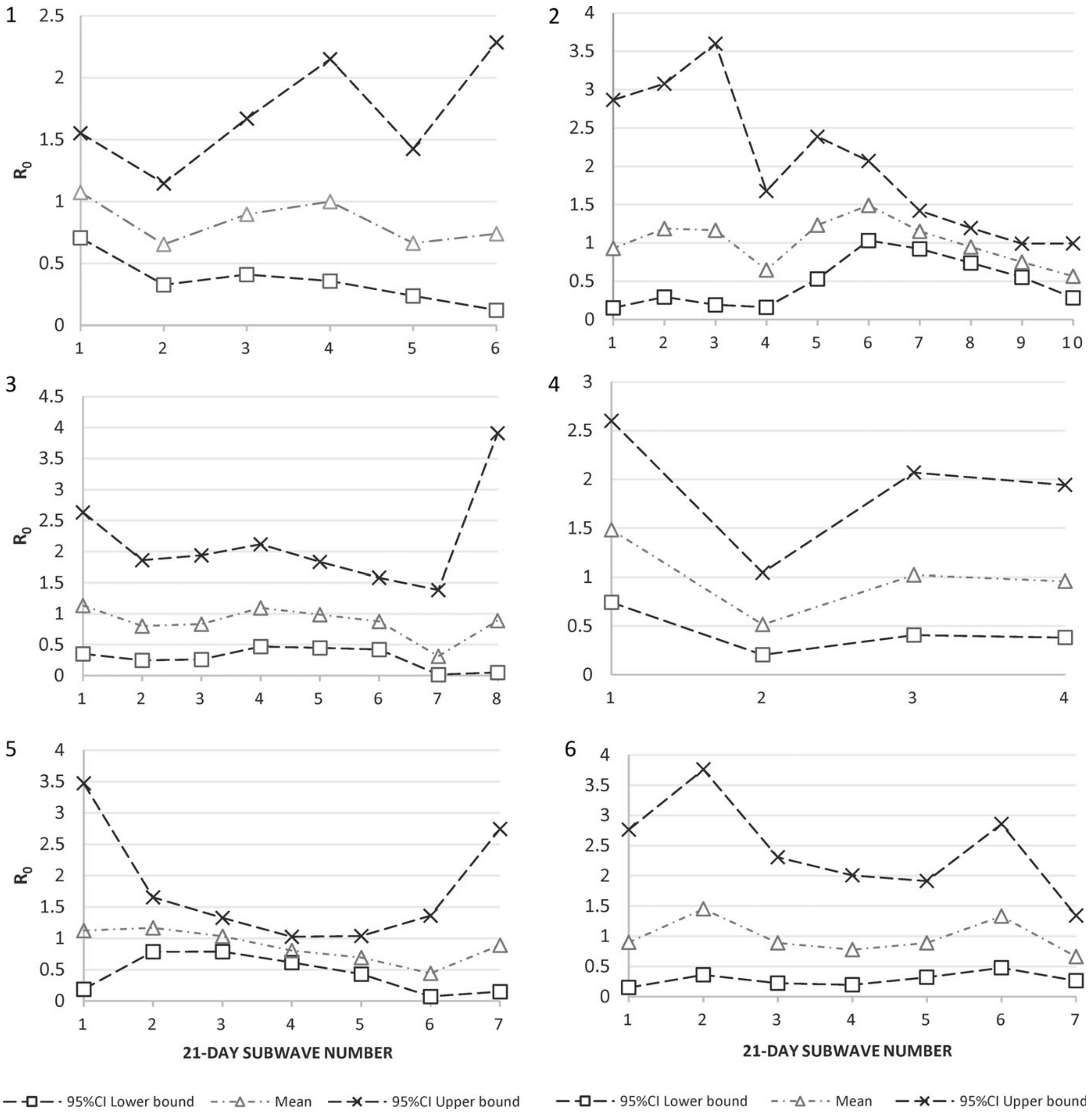

FIGURE 3 Time-varying basic reproduction number during the different epidemic waves. Panel numbers represents the epidemic wave number and the horizontal axis captures the 21-day subwave number during that epidemic wave

the number of newly infected farms and vice versa for $R_0 < 1$. The rise and fall in the incidence rate is, among other factors, driven by the depletion of susceptible farms through infection and culling as well as the possibility of improved awareness (and consequently improved biosecurity) as the epidemic unfolds.

In the sensitivity analysis, compared to the default scenario, reducing the detection delay to 2 days or extending the infectious period by 3 days post-culling did not have a statistically significant effect (at a *p*-value of .05) on the estimated parameters.

4 | DISCUSSION

Whenever appropriate data is available, as was the case in this study, the estimation of transmission rate parameters provides a means to better understand the dynamics of the outbreak. Such a quantification provides the most informative and reliable basis for assessments of disease management strategies.

In this study, the point estimates for the transmission rate parameter β ranged from 0.08 to 0.11 per infectious farm per day

TABLE 1 Summary of the parameter estimates obtained for each of the six epidemic waves using the default scenario in which 7 days delay in detection is assumed with no extended infectiousness post-culling

Epidemic wave number and period	Total number of farms[a]	Total number of Infected farms	Infectious period, T (days)[b]	Transmission rate β (95% CI)	Basic reproduction number $R_0 = \beta T$ (95% CI)
I: Mar 2007–Jul 2007	55,000	55	12	0.08 (0.06–0.10)	0.96 (0.72–1.20)
II: Oct 2007–Apr 2008	55,000	231	10.7	0.09 (0.08–0.10)	0.96 (0.86–1.07)
III: Dec 2008–Apr 2009	114,763	36	7.9	0.11 (0.08–0.20)	0.87 (0.63–1.58)
IV: Jan 2010–Apr 2010	74,000	28	8.1	0.11 (0.07–0.12)	0.89 (0.57–0.97)
V: Jan 2011–May 2011	64,000	161	8.5	0.10 (0.09–0.12)	0.85 (0.77–1.02)
VI: Nov 2011–Apr 2012	64,000[c]	26	8.5	0.11 (0.07–0.15)	0.94 (0.60–1.28)

[a] Obtained from (Islam et al., 2014).

[b] Calculated from the data by increasing the calculated mean infectious period by the assumed delay in detection of 7 days.

[c] Extrapolated from the number of farms during the previous period.

TABLE 2 Summary of the parameter estimates obtained for each of the six epidemic waves in the sensitivity analyses. The two scenarios assessed are; assuming 2 days delay in detection and, assuming a 3 day extended infectiousness

	2 days delay and no extended infectiousness			7 days delay and 3 days extended infectiousness		
Epi No.[a]	β (95% CI)	T^b	$R_0 = \beta T$ (95% CI)	β (95% CI)	T^b	$R_0 = \beta T$ (95% CI)
Epi 1	0.13 (0.10–0.16)	7	0.91 (0.70–1.12)	0.06 (0.05– 0.08)	15	0.90 (0.75–1.20)
Epi 2	0.15 (0.13–0.17)	5.7	0.86 (0.74–0.97)	0.07 (0.06–0.08)	13.7	0.96 (0.82–1.10)
Epi 3	0.26 (0.18–0.35)	2.9	0.75 (0.52–1.02)	0.08 (0.06–0.11)	10.9	0.87 (0.65–1.20)
Epi 4	0.24 (0.16–0.34)	3.1	0.74 (0.50–1.05)	0.08 (0.06–0.12)	11.1	0.89 (0.67–1.33)
Epi 5	0.22 (0.19–0.25)	3.5	0.77 (0.67–0.88)	0.08 (0.07–0.09)	11.5	0.92 (0.81–1.04)
Epi 6	0.22 (0.15–0.32)	3.5	0.77 (0.53–1.12)	0.08 (0.05–0.11)	11.5	0.92 (0.56–1.27)

[a] Epi No. stands for epidemic wave number.

[b] Reported in days and it is calculated from data by adjusting the mean infectious period based on the scenario assumptions.

and the estimated R_0 values over the full epidemics were consistently close to one (Table 1). Yet, due to a possibility of under-reporting of outbreaks to OIE, we argue that these estimates could even be conservative. Nonetheless, the finding that $R_0 \approx 1$ indicates that the impact of the deployed control strategies did not significantly change between epidemic waves.

Additionally, we gain insight about the unravelling of the various epidemic waves from the time-varying R_0 estimates in Figure 3. For example, we observe that R_0 was above one for some subwaves and not for others. A comparison of the epidemic curve (Figure 1) and the time-varying R_0 estimates (Figure 3) reveals that the epidemic temporal patterns are in synchrony with the estimated time-varying transmission parameters. The pattern of R_0 estimates being above one in the beginning of a wave and dropping below one in the final part of the wave is characteristic of epidemic spread and thus supports the hypothesis that the epidemics are more likely to be due to between-farm transmission rather than to multiple introductions alone.

Although the basic reproduction number is both pathogen- and population- specific, we note that closely related studies involving a similar pathogen subtype albeit in different geographical locations and involving different epidemiological units (e.g., villages instead of farms) give estimates within the same range. For example, Ward, Maftei, Apostu, and Suru (2009) estimated a between-village R_0 ranging from 1.68 to 2.95 in an HPAI-H5N1 outbreak that occurred in Romania where 110 outbreaks occurred over 25 days. Marquetoux et al. (2012) estimated a between- subdistrict R_0 varying between 1.27 and 1.60 in Thailand using 1208 outbreaks that occurred between July 2004 and April 2005. In a study based on 33 outbreaks in West Bengal, India during the period between 2008 and 2010, Pandit, Bunn, Pande, and Aly (2013) estimated R_0 that ranged from 0.859 to 1.069 and Bett et al. (2014) found a between-village R_0 ranging from 0.7 to 1.1 for an epidemic that occurred in Nigeria.

Regarding the model assumptions on the length of the infectious period, sensitivity analyses revealed that introducing a post-culling farm infectiousness of 3 days or reducing the detection delay to 2 days would not significantly affect the estimated R_0 for any of the epidemic waves. This was because the change in the assumed infectious period was in both cases accompanied by an opposite effect on the estimated transmission rate parameter.

In Table 1, we present the total number of poultry farms in Bangladesh from 2007 onwards and earlier data can be found in (Islam et al., 2014). Prior to 2007–2008, Islam et al. (2014) show that there were only 43,589 farms in 1993–1994, which increased substantially to reach 150,000 by the year 2006–2007 and declined afterwards. This fluctuating trend is a manifestation of the challenges faced by the Bangladesh poultry industry in general. For example, Raha (2014) reported that the major challenges to the poultry sector were limited access to credit, competition from imports and outbreak of diseases like avian influenza. Other authors have also mentioned fluctuations in feed prices (Islam et al., 2014) as an influencing factor.

On the variation of reaction time to suspected outbreaks between waves (Figure 2), the trend reflects one of the adopted changes by the Government after the first epidemic wave through improving surveillance and conducting immediate culling, on the farm or within 24 hr at a local laboratory, of avian influenza A-positive test farms (Loth et al., 2010). Quick culling of suspected cases is important as it ensures that a farm is removed when the number of infectious birds, and consequently the infection pressure it exerts on other susceptible farms, is still low. This may partly explain the lower number of cases in the third and fourth epidemic waves at $C = 36$ and 28, respectively. However, the change in trend in epidemic wave 5 that involved 161 cases remains a mystery based on the currently available epidemiological information. Note that, after that big wave, the next one only involved 26 reported cases (Table 1).

In that wave, much as the reaction time was similar to that of the preceding two epidemic waves, the number of outbreaks was higher. It can be hypothesized that this may have been amplified due to the introduction of clade 2.3.2 and 2.3.4 viruses into Bangladesh in 2011 in addition to clade 2.2 that has been circulating since (Haque, Giasuddin, Chowdhury, & Islam, 2014; Islam et al., 2012). Generally, cautious interpretation of the observed trend in number of reported cases is advised as the numbers could be influenced by the surveillance system implemented, which is predominantly passive, yet, factors such as the government's ability to pay indemnity to affected farmers are known to affect reporting.

On another note, it is not clear how these seasonal epidemic patterns are sustained but, what is apparent is fact that there is good disease management especially in between the waves when no outbreaks are reported. It is hypothesized that migratory birds may be playing a role in the initial introduction of the virus in the different waves. It could also be that, between epidemic waves, the virus remains endemic in some subpopulations of poultry, for example ducks and epidemics subsequently occurred when: (i) optimal environmental conditions are attained, and (ii) poultry populations would have recovered to levels that are critical for transmission events to occur.

On the consistency of the estimated parameters between the successive epidemic waves, we hypothesize that this indicates that the impact of the deployed intervention strategies did not change over the period of study. This could echo the existence of; untraced transmission routes that may not be targeted by the current protocols (Nickbakhsh et al., 2013; Ssematimba et al., 2013), indirect transmission mechanisms in general (van Bunnik et al., 2014), and/or the existence and contribution of other untraceable mechanisms such as the windborne route.

In conclusion, the findings of this study can facilitate the visualization of the required efforts to reduce the disease's basic reproduction number to below unity, which is an epidemiologically derived requirement for the prevention of further spread of the virus. This knowledge is important in informing the development of pro-poor intervention strategies that can easily be adopted in resource-constrained countries. With the current Bangladesh passive surveillance system in which HPAI virus detection relies mainly on recognition of the disease's clinical signs and an increased mortality (Ahmed et al., 2010), reducing between-farm contacts and improving biosecurity during the necessary ones can play an important role in controlling future epidemics.

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REFERENCES

Ahmed, S. S. U., Ersbøll, A. K., Biswas, P. K., & Christensen, J. P. (2010). The space–time clustering of highly pathogenic avian influenza (HPAI) H5N1 outbreaks in Bangladesh. *Epidemiology and Infection*, *138*(06), 843–852.

Bavinck, V., Bouma, A., Van Boven, M., Bos, M., Stassen, E., & Stegeman, J. (2009). The role of backyard poultry flocks in the epidemic of highly pathogenic avian influenza virus (H7N7) in the Netherlands in 2003. *Preventive Veterinary Medicine*, *88*(4), 247–254.

Becker, N. G. (1989). *Analysis of infectious disease data*. London: Chapman and Hall.

Bett, B., Henning, J., Abdu, P., Okike, I., Poole, J., Young, J., . . . Perry, B. (2014). Transmission rate and reproductive number of the H5N1 highly pathogenic avian influenza virus during the December 2005–July 2008 epidemic in Nigeria. *Transboundary and Emerging Diseases*, *61*(1), 60–68.

Biswas, P. K., Christensen, J. P., Ahmed, S. S. U., Barua, H., Das, A., Rahman, M. H., . . . Debnath, N. C. (2008). Avian influenza outbreaks in chickens, Bangladesh. *Emerging Infectious Diseases*, *14*(12), 1909–1912. https://doi.org/10.3201/eid1412.071567

Bos, M. E. H., Nielen, M., Koch, G., Bouma, A., de Jong, M. C. M., & Stegeman, A. (2009). Back-calculation method shows that within-flock transmission of highly pathogenic avian influenza (H7N7) virus in the Netherlands is not influenced by housing risk factors. *Preventive Veterinary Medicine*, *88*(4), 278–285. https://doi.org/10.1016/j.prevetmed.2008.12.003

van Bunnik, B. A. D., Ssematimba, A., Hagenaars, T. J., Nodelijk, G., Haverkate, M. R., Bonten, M. J. M., . . . De Jong, M. C. M. (2014). Small distances can keep bacteria at bay for days. *Proceedings of the National Academy of Sciences*, *111*(9), 3556–3560. https://doi.org/10.1073/pnas.1310043111

Diekmann, O., Heesterbeek, J. A. P., & Metz, J. A. J. (1990). On the definition and the computation of the basic reproduction ratio R_0 in models for infectious-diseases in heterogeneous populations. *Journal of Mathematical Biology*, *28*(4), 365–382.

Ferguson, N. M., Donnelly, C. A., & Anderson, R. M. (2001). Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. *Nature*, *413*(6855), 542–548. Retrieved from http://www.nature.com/nature/journal/v413/n6855/suppinfo/413542a0_S1.html

Fournié, G., Guitian, J., Desvaux, S., Cuong, V. C., Dung, D. H., Pfeiffer, D. U., . . . Ghani, A. C. (2013). Interventions for avian influenza A (H5N1) risk management in live bird market networks. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(22), 9177–9182. https://doi.org/10.1073/pnas.1220815110

Haque, M., Giasuddin, M., Chowdhury, E., & Islam, M. (2014). Molecular evolution of H5N1 highly pathogenic avian influenza viruses in Bangladesh between 2007 and 2012. *Avian Pathology*, *43*(2), 183–194.

Henning, K. A., Henning, J., Morton, J., Long, N. T., Ha, N. T., & Meers, J. (2009). Farm- and flock-level risk factors associated with Highly Pathogenic Avian Influenza outbreaks on small holder duck and chicken farms in the Mekong Delta of Viet Nam. *Preventive Veterinary Medicine*, *91*(2–4), 179–188. Retrieved from http://www.sciencedirect.com/science/article/pii/S0167587709001688

Islam, M. R., Haque, M. E., Giasuddin, M., Chowdhury, E. H., Samad, M. A., Parvin, R., … Monoura, P. (2012). New introduction of clade 2.3.2.1 avian influenza virus (H5N1) into Bangladesh. *Transboundary and Emerging Diseases*, *59*(5), 460–463. https://doi.org/10.1111/j.1865-1682.2011.01297.x

Islam, M. K., Uddin, M. F., & Alam, M. H. (2014). Challenges and prospects of poultry industry in Bangladesh. *European Journal of Business and Management*, *6*(7), 116–127.

Loth, L., Gilbert, M., Osmani, M. G., Kalam, A. M., & Xiao, X. (2010). Risk factors and clusters of highly pathogenic avian influenza H5N1 outbreaks in Bangladesh. *Preventive Veterinary Medicine*, *96*(1), 104–113.

Marquetoux, N., Paul, M., Wongnarkpet, S., Poolkhet, C., Thanapongtharm, W., Roger, F., … Chalvet-Monfray, K. (2012). Estimating spatial and temporal variations of the reproduction number for highly pathogenic avian influenza H5N1 epidemic in Thailand. *Preventive Veterinary Medicine*, *106*(2), 143–151.

Mollison, D. (1995). *Epidemic models and their relation to data*. Cambridge: Cambridge University Press.

Nickbakhsh, S., Matthews, L., Dent, J. E., Innocent, G. T., Arnold, M. E., Reid, S. W. J., & Kao, R. R. (2013). Implications of within-farm transmission for network dynamics: Consequences for the spread of avian influenza. *Epidemics*, *5*(2), 67–76. https://doi.org/doi: 10.1016/j.epidem.2013.03.001

OIE (2015). *WAHID Interface Animal Health Information: Update On Highly Pathogenic Avian Influenza In Animals (Type H5 and H7)*. Retrieved from http://www.oie.int/en/animal-health-in-the-world/update-on-avian-influenza/2007/. 18th February 2015.

Pandit, P. S., Bunn, D. A., Pande, S. A., & Aly, S. S. (2013). Modeling highly pathogenic avian influenza transmission in wild birds and poultry in West Bengal, India. *Scientific Reports*, *3*, 2175. https://doi.org/10.1038/srep02175 http://www.nature.com/articles/srep02175#supplementary-information

R Core Team (2005). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. https://www.R-project.org/.

Raha, S. K. (2014). *Poultry Industry in Bangladesh: Present status and future potential*. Retrieved from http://www.bea-bd.org/site/images/pdf/084.pdf. 23rd June 2017.

Sooryanarain, H., & Elankumaran, S. (2015). Environmental role in influenza virus outbreaks. *Annual Review of Animal Biosciences*, *3*(1), 347–373.

Ssematimba, A., Elbers, A. R. W., Hagenaars, T. J., & de Jong, M. C. M. (2012). Estimating the per-contact probability of infection by highly pathogenic avian influenza (H7N7) virus during the 2003 epidemic in The Netherlands. *PLoS One*, *7*(7), e40929. Retrieved from https://doi.org/10.1371%2fjournal.pone.0040929

Ssematimba, A., Hagenaars, T., de Wit, J., Ruiterkamp, F., Fabri, T., Stegeman, J., & de Jong, M. (2013). Avian influenza transmission risks: Analysis of biosecurity measures and contact structure in Dutch poultry farming. *Preventive Veterinary Medicine*, *109*(1), 106–115.

Stegeman, A., Bouma, A., & de Jong, M. C. M. (2010). Use of epidemiologic models in the control of highly pathogenic avian influenza. *Avian Diseases*, *54*(s1), 707–712. https://doi.org/10.1637/8821-040209-Review. 1

Stegeman, A., Bouma, A., Elbers, A. R. W., de Jong, M. C. M., Nodelijk, G., de Klerk, F., … van Boven, M. (2004). Avian influenza A virus (H7N7) epidemic in the Netherlands in 2003: Course of the epidemic and effectiveness of control measures. *Journal of Infectious Diseases*, *190*(12), 2088–2095.

Walker, P., Jost, C., Ghani, A., Cauchemez, S., Bett, B., Azhar, M., … Mariner, J. (2015). Estimating the transmissibility of H5N1 and the effect of vaccination in Indonesia. *Transboundary and Emerging Diseases*, *62*(2), 200–208.

Wallinga, J., & Lipsitch, M. (2007). How generation intervals shape the relationship between growth rates and reproductive numbers. *Proceedings of the Royal Society B: Biological Sciences*, *274*(1609), 599–604. https://doi.org/10.1098/rspb.2006.3754

Ward, M., Maftei, D., Apostu, C., & Suru, A. (2009). Estimation of the basic reproductive number (R0) for epidemic, highly pathogenic avian influenza subtype H5N1 spread. *Epidemiology and Infection*, *137*(02), 219–226.

Ypma, R. J. F., Bataille, A. M. A., Stegeman, A., Koch, G., Wallinga, J., & van Ballegooijen, W. M. (2012). Unravelling transmission trees of infectious diseases by combining genetic and epidemiological data. *Proceedings of the Royal Society B: Biological Sciences*, *279*(1728), 444–450. https://doi.org/10.1098/rspb.2011.0913

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