

# Quantitative effects of a declaration of a state of emergency on foot-and-mouth disease

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## Abstract

**Objectives** The law in Japan requires the declaration of a state of emergency and implementation of countermeasures for an epidemic of a new infectious disease. However, because a state of emergency has never been declared in Japan, its effects remain unknown. The required countermeasures are similar to those implemented in the foot-and-mouth disease epidemic in Miyazaki in 2010. This study aimed to quantitatively estimate the effect of the declaration in 2010 and investigate the nature of the epidemic based on the day on which the declaration took effect.

**Methods** Only publicly available data were used. Data for farms in the most affected town were analyzed. A modified susceptible–infected–recovered model was used to estimate the effect and for the simulation. Another model was used to estimate the effective reproduction number.

**Results** After the declaration, the intra-bovine transmission rate decreased by 18.1 %, and there were few days when the effective reproduction number was  $>1.0$ . A few weeks delay in the declaration significantly increased the possibility of epidemic, number of farms at peak, and final infection scale.

**Conclusions** Based on the substantial decrease in the transmission rate after the declaration of a state of emergency in 2010, a future declaration will have a similar effect for a new infectious disease even though a direct extrapolation is not valid. Although a declaration should be carefully considered owing to the potential socioeconomic effects, it is essential to prepare for the implementation given that a delay of only a few weeks should be acceptable.

**Keywords** New infectious disease · Foot-and-mouth disease · Effective reproduction number · Mathematical model · Declaration of a state of emergency

## Introduction

Emerging diseases remain serious public health issues, such as with the outbreak of Ebola virus disease in West Africa in 2014 [1] and the Middle East Respiratory Syndrome epidemic in the Republic of Korea in 2015 [2]. Neither a therapeutic method nor an effective vaccine has been established for the majority of emerging diseases. Thus, interventions addressing the route of transmission remain the main control measure to prevent the spread of emerging diseases.

In Japan, the Enactment of the Act on Special Measures for Pandemic Influenza and New Infectious Diseases Preparedness and Response was established in 2012 and is intended to strengthen the countermeasures against infectious diseases. Based on this act, the National Action Plan for Pandemic Influenza and New Infectious Diseases was also drafted [3, 4]. According to article 32 of the law, a nationwide declaration of a state of emergency regarding a new infectious disease with high pathogenicity and

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infectivity that has a potentially serious impact on the nation's health can be imposed. In this situation, the population is asked to refrain from going out unless it is urgent or unavoidable and to restrict the use of public facilities. Furthermore, public vaccination and healthcare delivery through temporary medical facilities are implemented [5]. Although an emergency situation has not yet been declared in Japan, emergency situations have been declared in the USA for the 2009 H1N1 influenza pandemic [6] and in Sierra Leone, Liberia, Nigeria, and Guinea for the Ebola virus disease pandemic; in addition, the World Health Organization declared the Ebola outbreak an international public health emergency in 2014 [7–10].

In the Miyazaki prefecture of Japan in 2010, there was an outbreak of foot-and-mouth disease (FMD), which is a viral disease specific to both domestic and wild cloven-hoofed animals such as cows, pigs, goats, sheep, buffalo, camels, and deer. Clinical symptoms generally begin with a fever accompanied by depression and inappetence, and FMD is characterized by vesicles on the tongue, lips, gums, dental pads, nares, interdigital skin of the feet, coronary bands, and bulbs of the heels and teats [11, 12]. Although FMD-related mortality is not high, FMD has extremely high infectivity [13, 14]. The basic reproduction number ( $R_0$ ), which is defined as the average number of cases that a case generates over the course of an infectious period, for FMD is 21 or 38.4 [15, 16]; comparatively, that of high pathogenic avian influenza is estimated at  $<5.0$  [17–20]. On May 18 (Day 40), the local government of Miyazaki prefecture declared a state of emergency because of the significant increase in infected farms since early May [21]. Different control measures were implemented on a regional basis. In regions with suspected animals with FMD (i.e., a local town with a confirmed case and its peripheral areas), livestock farmers had to refrain from going out unless it was urgent or unavoidable, thoroughly implement infection prevention measures, and refrain from going to the livestock barns. In other regions, livestock farmers were requested not to enter hot regions. Regardless of the area, non-livestock farmers were also asked to refrain from going out unless it was urgent or unavoidable, disinfect vehicles thoroughly, and postpone events that could attract a lot of people. Furthermore, everyone was expected to thoroughly disinfect public facilities in which people could gather and to undertake primary infection prevention measures such as hand-washing and gargling at home [22].

The control measures based on the declaration of a state of emergency in the 2010 FMD epidemic in Miyazaki and those enacted by the Act on Special Measures for Pandemic Influenza and New Infectious Diseases Preparedness and Response share two common characteristics. The first is to refrain from going out unless it is urgent or unavoidable, and the second is to postpone events that could attract a lot

of people. Incidentally, the transmission route is different for pandemic influenza and FMD. The former transmits via infected droplets or an intermediary medium. In contrast, the latter is predominantly transmitted by means of an intermediate medium; because movement of livestock is restricted, vehicles and human beings moving between livestock farms usually transmit the disease [23–25]. Because person-to-person contact is essential for both diseases to spread widely, countermeasures that reduce contact frequency are expected to affect the transmission route.

As mentioned, the main control measures against pandemic influenza and new infectious diseases are primarily focused on the transmission pathway owing to difficulties implementing measures for susceptibility such as vaccinations, particularly with new infectious diseases. Because an emergency situation based on the Act on Special Measures for Pandemic Influenza and New Infectious Diseases Preparedness and Response has not yet been declared in Japan, its effectiveness has not been quantitatively evaluated. Hence, the first aim of this study was to estimate the effect of the declaration of a state of emergency in Miyazaki in 2010 using a mathematical model. The next aim was to determine when to declare an emergency situation for an epidemic based on a simulation analysis.

## Materials and methods

### Data

All study data for the epidemic originated from reports released by the Ministry of Agriculture, Forestry and Fisheries (MAFF) and were available on the MAFF website [26]. The original data included location, species of livestock, number of livestock, diagnostic examination, date of confirmed diagnosis, and date of the implementation of biosecurity measures on each infected farm. Only the date of occurrence was confirmed by either the report that was presented to The World Organization for Animal Health (OIE) by MAFF or the report presented after the epidemic ended [27]. Days were counted from April 8, 2010, which was confirmed as the date of the primary case and set at Day 0. Although all of the infected farms were distributed in 11 towns or cities, 67.5 % (197 out of 292) were located in one town. We focused on this town owing to the extremely high density of livestock farmers.

### Management of data and farms

The infected livestock species were dairy cows, beef cattle, pigs, and goats. Dairy cows and beef cattle were classified together as the “bovine” group because few reports have addressed the difference in transmission dynamics between

dairy cows and beef cattle. Similarly, pigs were classified as the “swine” group. Goats were not included because there were too few goat farms to examine the transmission dynamics. Two infected farms kept both bovine and swine; these were counted separately, accounting for two bovine farms and two swine farms in the analysis. Each farm was regarded as an individual unit (i.e., the infectious premise [IP]) for two reasons [28, 29]. First, no information regarding intra-farm transmission was available, such as the number of infected and uninfected livestock on each farm. Second, FMD is likely to spread rapidly within a farm because it is highly contagious. Modified data were used to estimate parameters of the mathematical model.

**Mathematical model**

The effective reproduction number, which is defined as the actual average number of secondary cases per primary case at the calendar time [30], was estimated as the scaling factor of the next-generation matrix including both bovine and swine IPs as a function of calendar time [21]. As the basis for modeling the transmission of FMD, a susceptible–infected–recovered (SIR) model was used [31, 32]. In this model, transmission was described by the fluctuations in the susceptible (S), infectious (I), removed (R), and total (N) numbers of farms. To consider the spread of infection from a bovine farm to a swine farm and vice versa, the system of differential equations was modified as follows:

$$\begin{aligned}
 \frac{dS_1(t)}{dt} &= -S_1(t)(\beta_{11}I_1(t) + \beta_{12}I_2(t)), \\
 \frac{dS_2(t)}{dt} &= -S_2(t)(\beta_{21}I_1(t) + \beta_{22}I_2(t)), \\
 \frac{dI_1(t)}{dt} &= S_1(t)(\beta_{11}I_1(t) + \beta_{12}I_2(t)) - \gamma_1I_1(t), \\
 \frac{dI_2(t)}{dt} &= S_2(t)(\beta_{21}I_1(t) + \beta_{22}I_2(t)) - \gamma_2I_2(t), \\
 \frac{dR_1(t)}{dt} &= \gamma_1I_1(t), \\
 \frac{dR_2(t)}{dt} &= \gamma_2I_2(t), \\
 N_1(t) &= S_1(t) + I_1(t) + R_1(t) = \text{constant}, \\
 N_2(t) &= S_2(t) + I_2(t) + R_2(t) = \text{constant},
 \end{aligned}
 \tag{1}$$

in which 1 and 2 represent bovine and swine, respectively. An infected farm was defined as an IP during the period from occurrence to the implementation of biosecurity measures because it was considered a potential FMD infection source. In this model,  $\beta$  is the transmission rate, defined as the average number of newly infected farms among the susceptible farms per unit time. The infectious period ( $1/\gamma$ ) was defined as the period during which a farm was considered an IP. Thus,  $1/\gamma$  was calculated as

$13.6 \pm 5.6$  (mean  $\pm$  standard deviation [sd]) and  $12.6 \pm 1.5$  (mean  $\pm$  SD) for bovine and swine IPs, respectively, from epidemiological data for the FMD infection in 2010. The distributions of bovine and swine  $1/\gamma$  were almost normal [33] and logarithmic normal, respectively. In this study, unit time was set as a day, and only this model was used in the estimation and simulation.

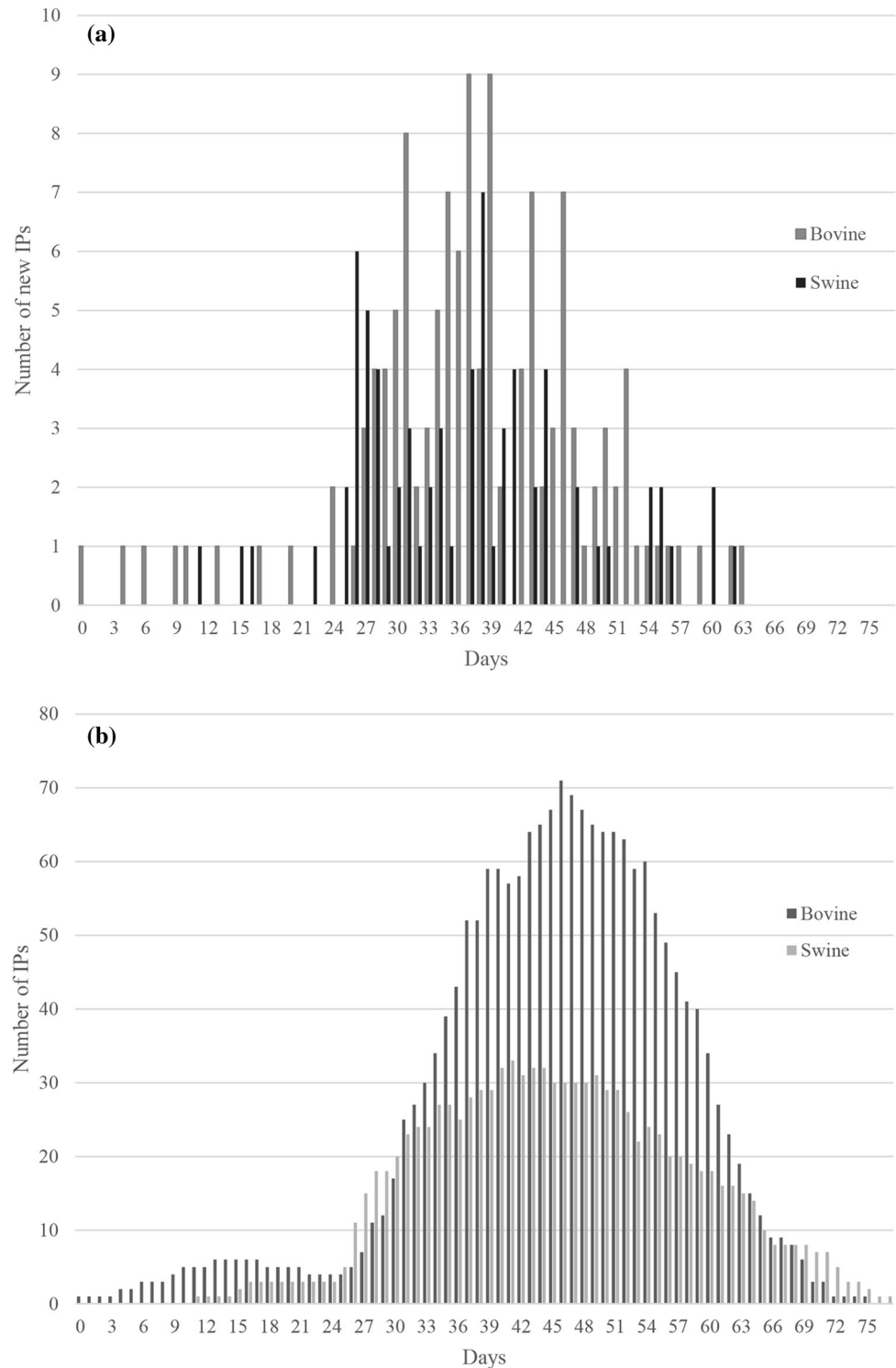
**Parameter estimation**

It was assumed that control measures (i.e., the declaration of a state of emergency) decreased the transmission rate by a constant rate. The initial effect of a vaccination reportedly requires 4 days post-vaccination (dpv) for bovine and 7 dpv for swine, and the full effect requires 11 dpv for bovine and 14 dpv for swine [34]. Therefore, the vaccine was assumed to begin taking effect on May 28 (Day 50) because the vaccine inoculation began on May 24 (Day 46). eDAY was defined as the day on which a declaration of a state of emergency had an effect and was assumed to occur during Days 40–49. Thus, we estimated  $\beta_{ij}$  using the least-squares method for the period from Day 0 to the day before eDAY and estimated the effect of control measures on  $\beta_{ij}$  using the least-squares method for the period from eDAY to Day 49. Putting them together, eDAY,  $\beta_{ij}$ , and the effect of a declaration were determined. The distribution of each  $\beta_{ij}$  was estimated using Markov chain Monte Carlo methods. It was also assumed that initial bovine and swine IPs emerged on Days 0 and 11, respectively, as is the case with the epidemic.

**Simulation**

Simulations were conducted using eight scenarios to investigate the change in the epidemic nature depending on eDAY. In scenarios 1–7, eDAY was set at Day 1, 8, 15, 22, 29, 36, or 43, respectively. In scenario 8, no declaration of a state of emergency was assumed. Each scenario included 10,000 trials, and the trials were adopted only when the maximum number of either bovine or swine IPs was  $>1$ . The maximum number of both bovine and swine IPs  $\leq 1$  was defined as the baseline. To analyze the epidemic, four outcomes were introduced: the period to the peak of the IPs, rate of trials beyond the baseline, number of IPs at the peak, and final infection scale. The final infection scale was defined as the sum of  $I_i$  and  $R_i$  on Day 77. Even during the simulation, it was assumed that initial bovine and swine IPs emerged on Days 0 and 11, respectively. To compare scenarios, Wilcoxon tests or Chi-square goodness-of-fit tests were conducted with Holm correction. All estimations and simulations were conducted using R, version 3.2.2. A violin plot was used to graphically show the data; this is a combination of a box plot and kernel density plot [35]. Goodness of fit was calculated based on previous reports [36, 37].

**Fig. 1** Epidemiology of foot-and-mouth disease in the focus town in the Miyazaki prefecture of Japan in 2010. **a** Distribution of new infectious premises (IPs) along the time axis. **b** Number of IPs before biosecurity measures were implemented. Days are counted from April 8, 2010 onwards

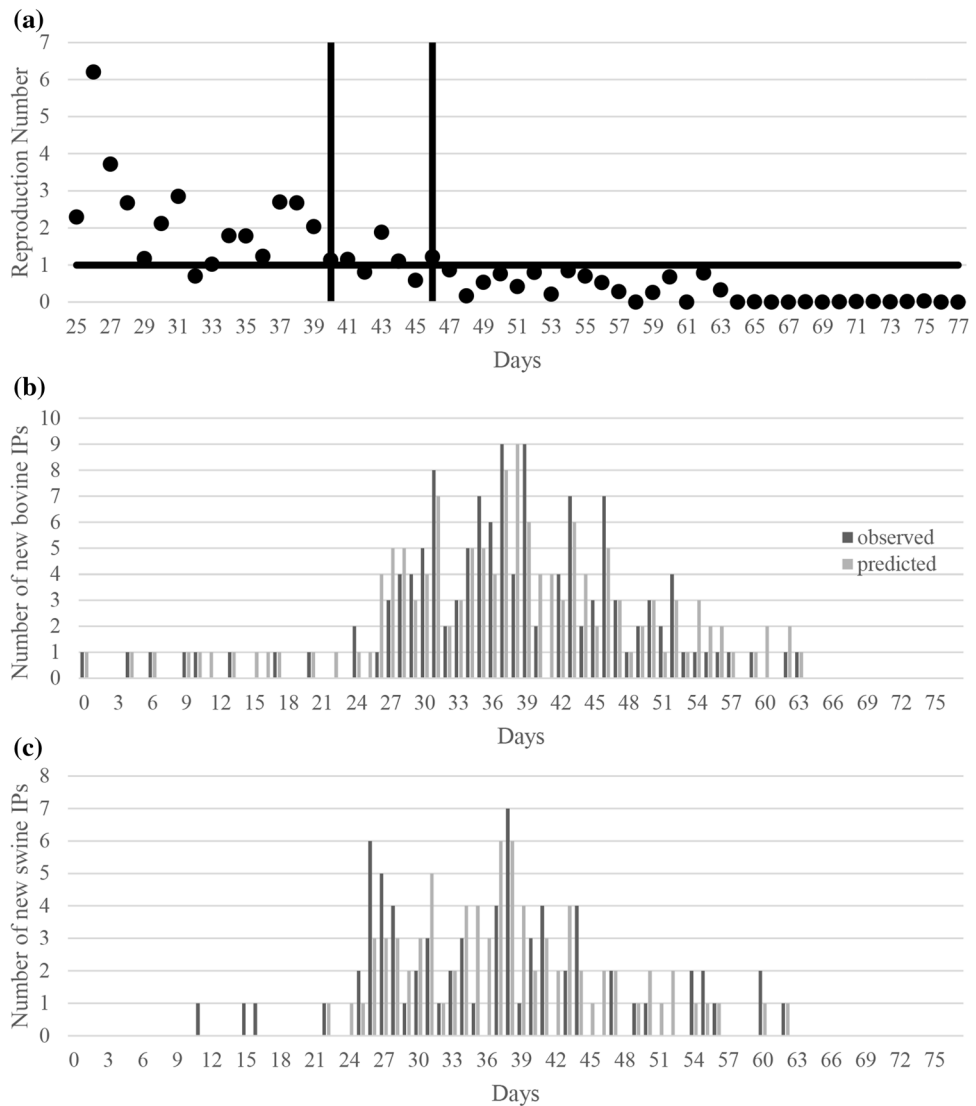


## Results

According to the report submitted to the OIE from the MAFF, the primary case was confirmed on April 8, and the last case was confirmed on July 10 in the focus town. While 129 bovine farms and 70 swine farms were infected, 297

bovine farms and 83 swine farms were susceptible. The epidemic curve in the focus town is shown in Fig. 1a. The maximum number of new bovine IPs was nine on Days 37 and 39 and that of new swine IPs was seven on Day 38. Figure 1b shows the number of IPs, based on the assumption that a farm was infectious from the onset of the confirmed

**Fig. 2** The estimated effective reproduction number and estimated epidemic curve of foot-and-mouth disease in the focus town. **a** Effective reproduction number ( $R_t$ ) along the time axis. The dots represent the maximum likelihood estimates, and the horizontal line is the threshold value,  $R_t = 1$ . The vertical lines at Days 40 and 46 represent the implementation of control measures (i.e., declaration of a state of emergency and vaccination, respectively). Comparison between the observed (black bars) and predicted (gray bars) number of new IPs for bovine (b) and swine (c)

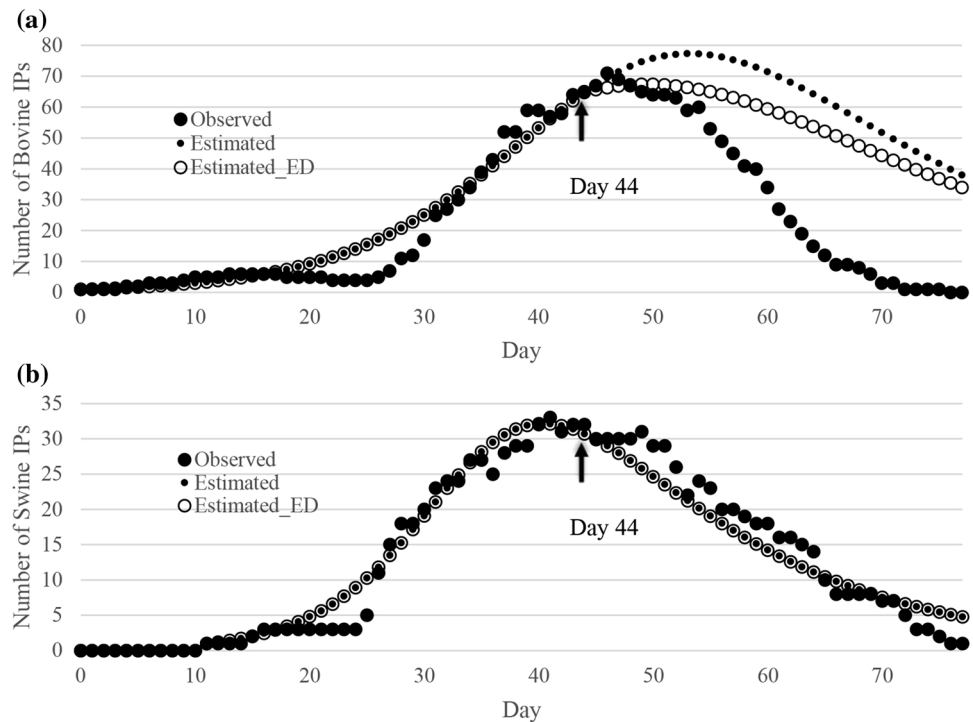


diagnosis to the implementation of control measures. The maximum numbers of bovine and swine IPs were 71 on Day 46 and 33 on Day 41, respectively. The number of bovine IPs decreased from six on Days 13–17 to five on Day 18 and to four on Day 22; however, it increased from Days 26 to 46.

The estimated effective reproduction number is shown in Fig. 2a. It decreased between Day 40, when the state of emergency was declared, and Day 46, when the vaccination program began. Furthermore, it never increased beyond 1.0 after the beginning of the vaccination program. The actual number and estimated number of new IPs are shown in Fig. 2b, c; the estimated data fitted the epidemic data well (goodness of fit =  $1.6 \times 10^{-7}$  for bovine and  $1.9 \times 10^{-4}$  for swine). The relative susceptibility of a typical bovine IP was estimated to be 18.6 times greater than that of a typical swine IP. However, a swine IP was estimated to be 4.1 times more infectious than a bovine IP.

According to the parameter estimation using the modified SIR model, the estimated values of  $\beta_{11}$ ,  $\beta_{22}$ ,  $\beta_{12}$ , and  $\beta_{21}$  were  $6.51 \times 10^{-04} \pm 1.57 \times 10^{-05}$  (mean  $\pm$  SD; normal distribution),  $3.20 \times 10^{-03} \pm 1.31 \times 10^{-04}$  (mean  $\pm$  SD; normal distribution),  $5.41 \times 10^{-07} \pm 8.46 \times 10^{-08}$  (mean  $\pm$  SD; normal distribution) and  $5.19 \times 10^{-07} \pm 1.55 \times 10^{-07}$  (mean  $\pm$  SD; normal distribution), respectively. Furthermore,  $\beta_{11}$ ,  $\beta_{22}$ ,  $\beta_{12}$ , and  $\beta_{21}$  decreased by 18.1 % (95 % CI 10.3–29.0 %), 0.1 % (95 % CI 0–19.5 %), 36.4 % (95 % CI 30.5–49.4 %), and 11.1 % (95 % CI 10.5–29.4 %) after eDAY; all of these were uniformly distributed. When conducting the simulation, the daily determined random digits were introduced as parameters (i.e.,  $1/\gamma_i$ ,  $\beta_{ij}$ , and decreasing ratios of  $\beta_{ij}$ ), depending on the distribution: normal random number with sd, logarithmic normal number with sd or uniform random number with 95 % CI. Furthermore,  $\beta_{ii}S_i(t)I_i(t)$ ,  $\beta_{ij}S_i(t)I_j(t)$ , and  $\gamma_i I_i(t)$  were

**Fig. 3** Observed and estimated epidemic of foot-and-mouth disease in the focus town. Comparison among the observed (*black circles*), estimated (*little black circles*), and estimated considering the emergency declaration (*white circles*) daily number of IPs along the time axis for bovine (a) and swine (b)



assumed to follow the binomial random number, which was determined using success probabilities (i.e.,  $\beta_{ii}I_i$ ,  $\beta_{ij}I_j$  and  $\gamma_i$ , respectively) in one trial per day. At the same time, eDAY was estimated as Day 44; the estimated epidemic curve is shown in Fig. 3a, b. The epidemic among bovine farms ended much earlier than the estimated epidemic. However, the epidemic among swine farms ended around the same time as the estimated epidemic.

Regarding the period to the peak of the IPs (i.e., the first outcome), the median (90 % CI) periods for bovine in scenarios 1–8 were 12 (0–76), 19 (0–76), 21 (0–75), 23 (0–75), 28 (0–75), 32 (0–74), 34 (0–74), and 36 (0–75) days, respectively. Those of swine were 30 (0–72), 28 (0–72), 33 (11–72), 32 (11–68), 31 (11–63), 34 (11–57), 35 (11–52), and 36 (11–58) days, respectively. The violin plot and results of the multiple comparisons are shown in Fig. 4. The period for the number of IPs to peak took longer with later eDAYs (Fig. 4), although this was not statistically significant. Particularly for swine farms, later eDAYs resulted in a unimodal density plot (Fig. 4b).

The numbers of trials beyond the baseline in each scenario (i.e., the second outcome) were 8587, 8794, 9082, 9169, 9196, 9137, 9242, and 9191/10,000, respectively (Table 1). The number of trials beyond the baseline significantly decreased only for scenarios 1 and 2.

The median (90 % CI) numbers of IPs at the peak (i.e., the third outcome) for bovine were 4 (1–56), 6 (1–57), 8

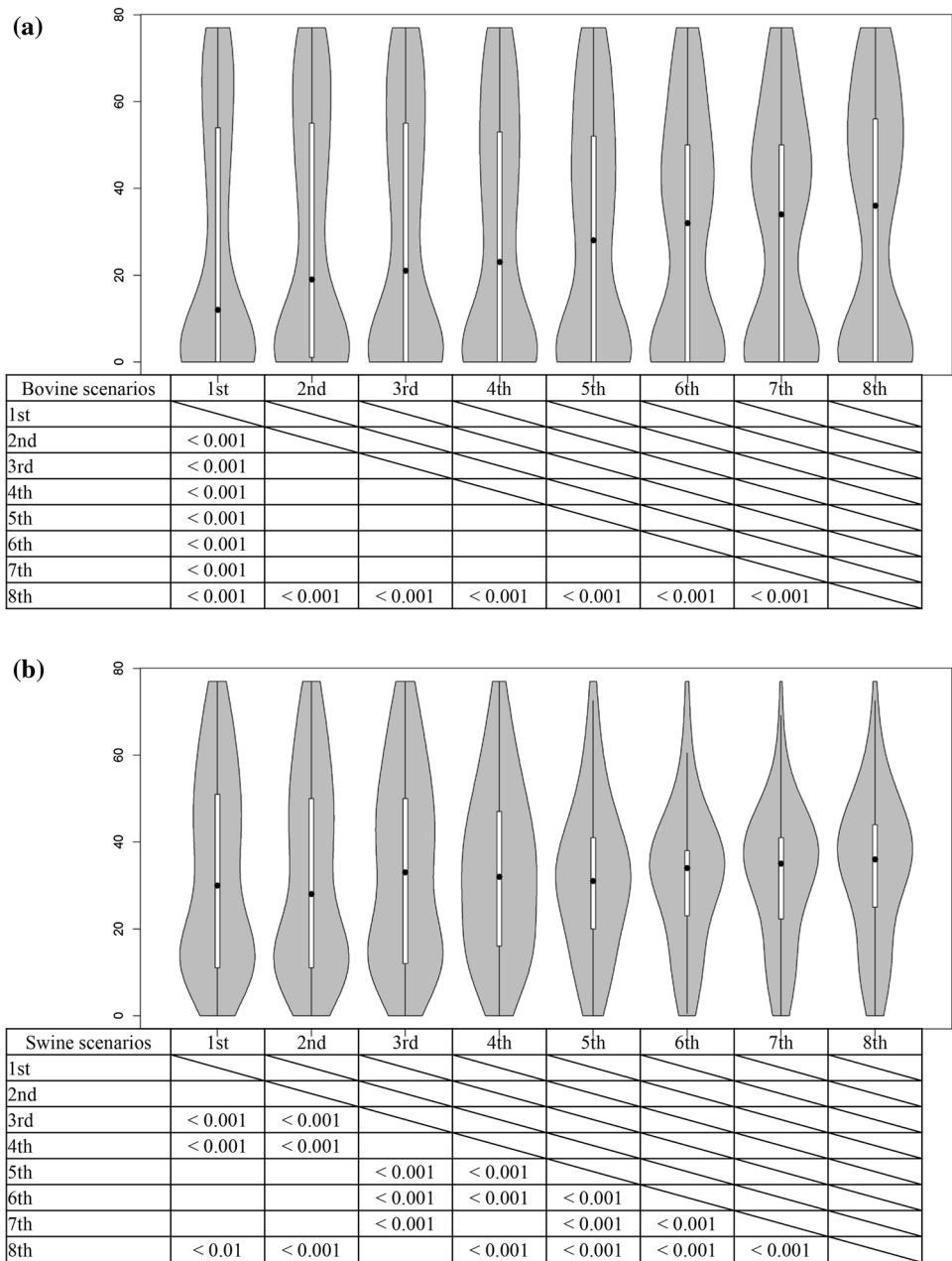
(1–58), 9 (1–62), 12 (1–65), 15 (1–72), 19 (1–77) and 27 (1–84) in scenarios 1–8, respectively. Those of swine were 6 (0–24), 5 (0–24), 10 (1–25), 14 (1–27), 17 (1–34), 22 (1–38), 25 (1–40) and 27 (1–40), respectively. The violin plot and results of the multiple comparisons are shown in Fig. 5. Later eDAYs resulted in significantly larger numbers of IPs at the peak for both bovine and swine.

The median (90 % CI) final infection scales (i.e., the fourth outcome) for bovine were 6 (1–189), 15 (1–193), 19 (1–198), 25 (1–205), 37 (1–213), 53 (1–223), 64 (1–230) and 94 (1–249) in scenarios 1–8, respectively. Those of swine were 18 (1–67), 13 (1–66), 32 (1–68), 46 (1–71), 55 (1–74), 63 (1–78), 68 (1–80) and 76 (1–82), respectively. The violin plot and results of the multiple comparisons are shown in Fig. 6. Later eDAYs resulted in significantly larger final infection scales for both bovine and swine.

## Discussion

Based on the quantitative estimate of the effect of the declaration of a state of emergency for the FMD epidemic in Miyazaki 2010 using a mathematical model, the declaration decreased the transmission rate. In particular, the intra-bovine transmission rate decreased by 18.1 %. The simulation analysis resulted in the following: a later dec-

**Fig. 4** Violin plot and statistical analysis of the period to the peak of the infectious premises (IPs). **a** Bovine IPs and **b** swine IPs. *P* values were determined using pairwise Wilcoxon tests. “<0.001”, “<0.01” and “<0.05” are represented when *P* value was <0.001, <0.01 and <0.05, respectively



laration resulted in a higher rate of trials beyond the baseline only when the effect of a declaration emerged on Day 1 or 8; higher number of IPs at the peak; and larger final infection scale.

The  $\beta$  value is time dependent and is estimated to be higher in the early stage of an epidemic. Therefore, the effect of the declaration might be overestimated when  $\beta$  is estimated from Day 0 to eDAY and from eDAY to Day 50. However, the nature of the time dependency of  $\beta$  is probably not considerable in this study. The peak IPs were reached on Days 46 and 41 for bovine and swine, respectively. The period for estimation of  $\beta$  is from Day 0 to Days

39–49, which is not the early stage of the epidemic; therefore, it is reasonable that the estimated  $\beta$  is not much affected by time dependency. Actually,  $\beta_{11}$  was estimated as  $6.5 \times 10^{-4}$  and  $\beta_{22}$  as  $3.2 \times 10^{-3}$  even when the period for estimation varied from Days 39–45. In this study, the effect of the emergency declaration was estimated from eDAY to Day 50, and it increased from 3 to 22 % for  $\beta_{11}$ , via a time step. However, that was not observed in other  $\beta_{ij}$ . Thus, the validity of the estimates for bovine is considered high, but that of swine is not necessarily high.

The estimates of the effective reproduction number on each day, relative susceptibility, and infectiousness in the

**Table 1** Comparison of the rate of trials beyond the baseline in scenarios 1–8

| Scenarios | 1st    | 2nd    | 3rd    | 4th | 5th | 6th | 7th | 8th |
|-----------|--------|--------|--------|-----|-----|-----|-----|-----|
| 1st       |        |        |        |     |     |     |     |     |
| 2nd       | <0.001 |        |        |     |     |     |     |     |
| 3rd       | <0.001 | <0.001 |        |     |     |     |     |     |
| 4th       | <0.001 | <0.001 |        |     |     |     |     |     |
| 5th       | <0.001 | <0.001 |        |     |     |     |     |     |
| 6th       | <0.001 | <0.001 |        |     |     |     |     |     |
| 7th       | <0.001 | <0.001 | <0.001 |     |     |     |     |     |
| 8th       | <0.001 | <0.001 |        |     |     |     |     |     |

*P* values were determined using pairwise Chi-square goodness-of-fit tests. “<0.001”, “<0.01” and “<0.05” are represented when *P* value was <0.001, <0.01 and <0.05, respectively

present study were consistent with previous reports; the relative susceptibility of a typical bovine farm was greater than that of a typical swine farm, and the relative infectiousness of a swine farm was greater than that of a bovine farm [21]. Swine are considered an amplifier host of FMD because they are less susceptible to FMD [21, 28] but excrete 1000-fold more viruses than bovine [38, 39], resulting in greater infectiousness [21, 40–43]. Infected swine excrete more than 106 tissue culture infective dose (TCID<sub>50</sub>) FMD viruses via aerosol per day [38, 44, 45].

Except for Day 32, the estimated effective reproduction number was greater than 1.0 from Day 24 to Day 40. However, after Day 40, it was greater than 1.0 only on Days 41, 43, 44, and 46. A state of emergency was declared on Day 40, the vaccination program began on Day 46, and we estimated that the effect of the declaration appeared on Day 44. Therefore, it is highly likely that the declaration was a particularly effective measure against FMD; a previous study estimated the effect of vaccination to appear after Day 50. Because of the declaration of a state of emergency for the Ebola outbreak in Sierra Leone, Liberia, and Guinea in August and in Nigeria in October of 2014, schools and markets were closed. The effective reproduction number in Sierra Leone decreased from August to December [46]; basic interventions in public health were expected to control this Ebola outbreak in 2014 [47], and early isolation was considered effective in Nigeria [48].

In this study, the modified SIR model for each IP was adopted for several reasons. First, there was little information that was publicly available. For instance, although the number of livestock fed on each infected farm was reported, the number was not reported for farms that were not infected. Furthermore, likely because of the protection of personal information, the correct addresses were not available for infected or non-infected farms. Second, the

farms located in the focus town were assumed to be within a closed population with little turnover because most of the focus town was designated as an area with restricted movement. Furthermore, all of the farms were susceptible to FMD because prophylactic vaccination against FMD was not conducted in Japan. An experimental infection with the FMD virus strain (O/JPN/2010) that was isolated from the 2010 epidemic in Miyazaki showed that the latency and incubation periods were 2–3 and 2–4 days, respectively, for bovine and 1–4 days (for both periods) for swine [49]. However, livestock in different stages of the infection were comingled within the same farm. Therefore, a model that did not consider the latency or incubation period was preferred. If the number of livestock fed on all of the farms located in the focus town had been officially reported, an intra-farm SIR model could have been used. In addition, information about the number of external people visiting each farm would have enabled us to establish another model, such as a network model.

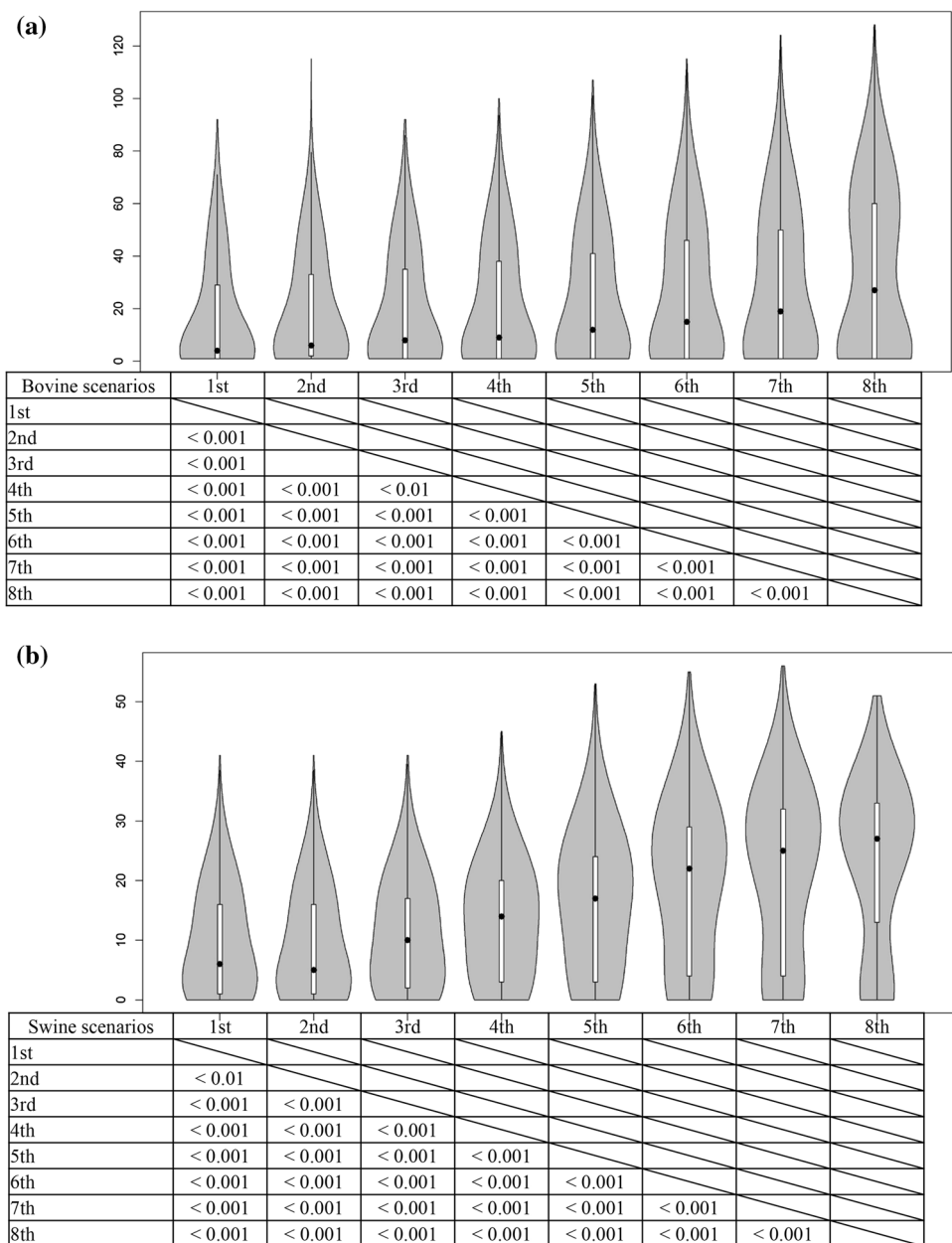
Regardless of an emergency declaration, the end of the estimated epidemic was later than that of the actual epidemic in 2010. The effectiveness of specific countermeasures such as initiating vaccination on Day 46 and increasing the number of self-defense forces on Days 68 and 70 likely resulted in an earlier termination of the epidemic. However, the actual number of IPs was higher than that acquired by estimated parameters from Days 43 to 64 for swine farms. A similar situation was also observed in the early stage of the epidemic in bovine farms. Therefore, FMD was likely to be transmitted from local towns neighboring the focus town.

Although the rate of transmission from bovine to bovine decreased by 18.1 %, the transmission rate for swine barely decreased with an emergency declaration. The first potential explanation is that the sequence of measures was not effective for the prevention of transmission among swine farms. The effect of both the declaration and vaccination likely appeared after the number of IPs had peaked. Second, FMD infection was also observed in farms in a neighboring town. Thus, the high frequency of FMD transmission from sites external to the focus town resulted in underestimation of the effect.

There is some delay between the time of the declaration and its effect. For example, in the FMD epidemic of 2010, materials (e.g., disinfectant) and human resources had to be secured and transported. The permissible delay for the eDAY was estimated considering the four outcomes. Significant differences in the outcomes were observed with the eDAY set to Day 15, 22, or 29 compared with the eDAY set to Days 1 and 8. Therefore, it is essential to prepare for the implementation until Day 15 given that a delay of only



**Fig. 5** Violin plot and statistical analysis of the number of infectious premises (IPs) at the peak. **a** Bovine IPs and **b** swine IPs. *P* values were determined using pairwise Wilcoxon tests. “<0.001”, “<0.01” and “<0.05” are represented when *P* value was <0.001, <0.01 and <0.05, respectively

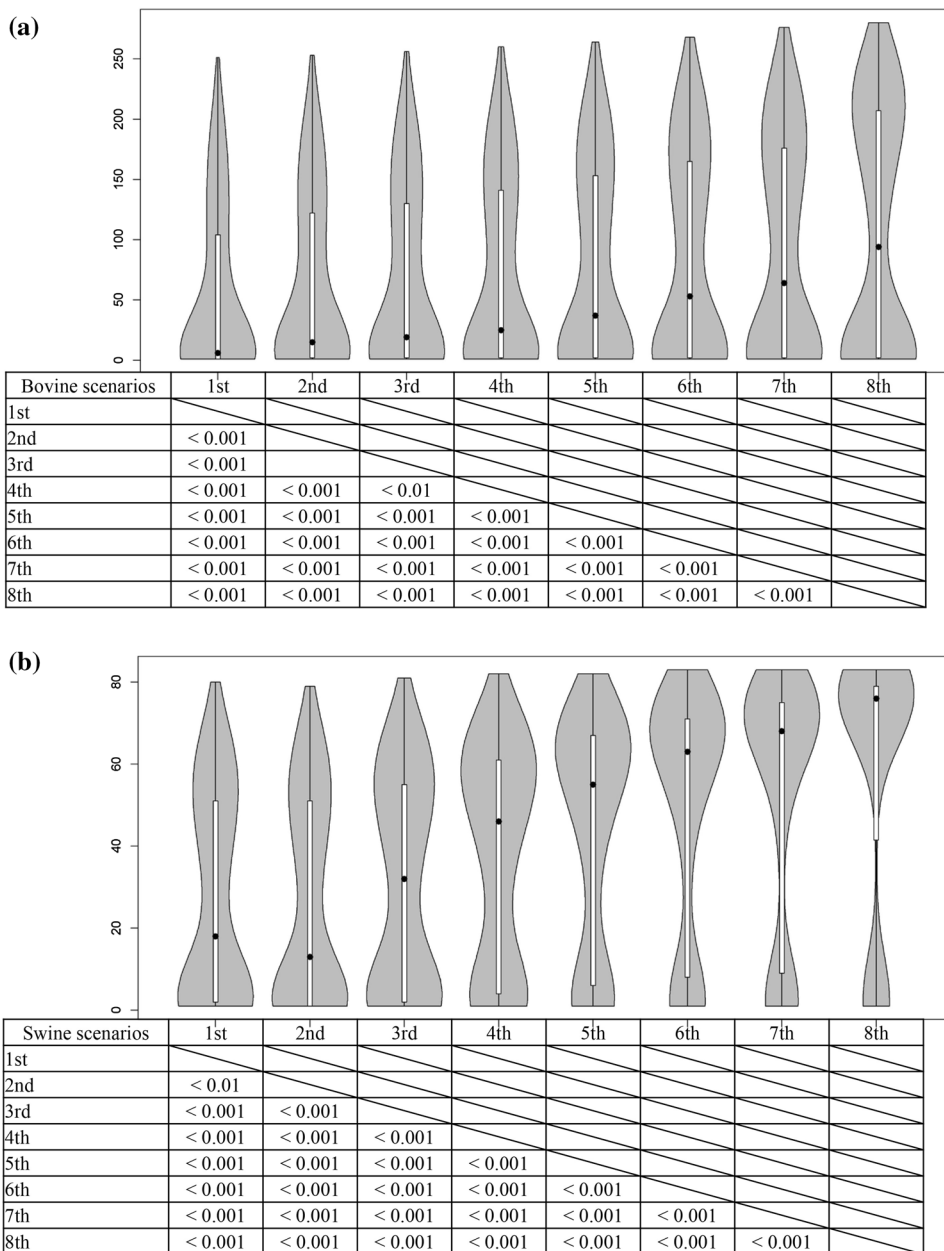


a few weeks should be acceptable. However, because preventive measures related to the transmission pathway, such as refraining from going out unless necessary and postponing events, have a considerable socioeconomic impact, it is essential to conduct a cost–benefit analysis before implementation.

Based on the quantitative analysis in the present study, the state of emergency declared for the FMD epidemic in Miyazaki in 2010 efficiently inhibited transmission of FMD because of the countermeasures such as refraining

from going out. Countermeasures based on the Enactment of the Act on Special Measures for Pandemic Influenza and New Infectious Diseases Preparedness and Response are similar to those that were implemented in 2010. Therefore, they are expected at least to decrease the number of the infected at the peak and to decrease the final infection scale. Only a few weeks would remain for careful consideration of the negative socioeconomic effect of these measures, and it is essential to prepare resources in advance to implement measures as soon as possible. It

**Fig. 6** Violin plot and statistical analysis of the final infection scale. **a** Bovine IPs and **b** swine IPs. *P* values were determined using pairwise Wilcoxon tests. “<0.001”, “<0.01” and “<0.05” are represented when *P* value was <0.001, <0.01 and <0.05, respectively



would not be considered valid to extrapolate all of the present results to new infectious diseases in humans because the analyses were conducted with FMD, which is an infectious disease in animals. However, these results are useful for future prediction.

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**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** For this type of study, formal consent is not required.

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