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Modeling the impact of vaccination control strategies on a foot and mouth disease outbreak in the Central United States.

Sara W. McReynolds[1], Michael W. Sanderson[1], Aaron Reeves[2], Ashley E. Hill[3].

[1] Diagnostic Medicine and Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS 66502

[2]Epidemiology Research Unit, Scotland's Rural College (SRUC), Inverness, UK (Reeves);

[3]California Animal Health and Food Safety Laboratory, University of California, Davis CA (Hill).

corresponding author: Mike Sanderson, 785-532-4264, fax 785-532-4851, sandersn@vet.k-state.edu

Abstract

The central United States (U.S.) has a large livestock population including cattle, swine, sheep and goats. Simulation models were developed to assess the impact of livestock herd types and vaccination on Foot and Mouth Disease (FMD) outbreaks using the North American Animal Disease Spread Model. In this study, potential FMD virus outbreaks in the central region of the U.S. were simulated to compare different vaccination strategies to a depopulation only scenario. Based on data from the U.S. Department of Agriculture National Agricultural Statistics Service, a simulated population of 151,620 livestock operations characterized by latitude and longitude, production type, and herd size was generated. For the simulations, a single 17,000 head feedlot was selected as the initial latently infected herd in an otherwise susceptible population. Direct and indirect contact rates between herds were based on survey data of livestock producers in Kansas and Colorado. Control methods included ring vaccination around infected herds. Feedlots ≥3,000 head were either the only production type that was vaccinated or were assigned the highest vaccination priority. Simulated vaccination scenarios included low and high vaccine capacity, vaccination zones of 10 km or 50 km around detected infected premises, and vaccination trigger of 10 or 100 detected infected herds. Probability of transmission following indirect contact, movement controls and contact rate parameters were considered uncertain and so were the subjects of sensitivity analysis. All vaccination scenarios decreased number of herds depopulated but not all decreased outbreak duration. Increased size of the vaccination zone during an outbreak decreased the length of the outbreak and number of herds destroyed. Increased size of the vaccination zone primarily resulted in vaccinating feedlots ≥3000 head across a larger area. Increasing the vaccination capacity had a smaller impact on the outbreak and may not be feasible if vaccine production and delivery is limited. The ability to vaccinate all the production types surrounding an infected herd did not appear as beneficial as priority vaccination of feedlot production types that have high numbers of indirect contacts. Outbreak duration, number of herds depopulated and the effectiveness of vaccination were sensitive to indirect contact transmission probability and movement

restrictions. The results of this study will provide information about the impacts of disease control protocols which may be useful in choosing the optimal control methods to meet the goals of rapid effective control and eradication.

Introduction

Foot and Mouth Disease (FMD) is a highly contagious disease that affects all cloven-hooved animals and is endemic in parts of Asia, Africa and South America. The FMD virus can spread rapidly through susceptible livestock populations prior to the recognition of clinical signs (Burrows, 1968;Burrows et al., 1981); consequently, early detection prior to the spread of the disease is difficult. FMD is a major constraint to international trade because countries currently free of FMD, like the United States (U.S.), take every precaution to prevent the entry of the disease. The U.S. livestock population is naïve to FMD with the last outbreak occurring in 1929 (Graves, 1979).

The potential impact of an outbreak in the U.S. would likely be devastating. A secure food supply is vital to the economy with U.S. farms selling $297 billion in agriculture products through market outlets in 2007 (USDA-NASS 2007). In the U.S. the concern for FMD virus re-introduction and the potential economic impacts have risen with the increase of international travel and trade of animals and animal products. At the same time agriculture has become more concentrated with larger capital investments (Hueston, 1993) resulting in increased risk to agricultural production and business continuity.

Because FMD is a foreign animal disease in the U.S., there are few avenues available for the study of potential impacts of and effective control strategies for the disease in the event of an introduction. Epidemiological disease modeling is one such avenue. In such models, various control measures, such as movement restrictions, increased biosecurity, depopulation, pre-emptive culling, and vaccination have been implemented in various combinations to evaluate the spread of simulated outbreaks (Ferguson et al., 2001; Gibbens et al., 2001; Bouma et al., 2003; Sutmoller et al., 2003; Perez et al., 2004; Pluimers, 2004; Yoon et al., 2006; Volkova et al., 2011). Depending on the size of the outbreak, timeliness of control implementation, the workforce capacity, and the available resources, the optimal control strategy may vary. The efficacies of different control measures under different conditions can be readily compared using epidemiological modeling.

In the U.S., epidemiological disease models have been used to estimate the potential economic impacts of an outbreak. Pendell et al. (2007) estimated economic losses of an outbreak confined to Kansas ranged from $43 to $706 million depending on the type of livestock herd that was initially infected. In an economic model of the impact to the entire U.S., Paarlberg et al. (2002) estimated that a FMD outbreak could decrease U.S. farm income by approximately $14 billion and in 2012 it was estimated that an outbreak originating from the proposed National Bio- and Agri-Defense Facility in Kansas could exceed $100 billion in costs (NBAF, 2012).

Epidemiological disease models are dependent on accurate estimates of the frequency and distance distribution of contacts between livestock operations to estimate disease spread and impact, and to guide control measures (Gibbens et al., 2001; Woolhouse and Donaldson, 2001; Dickey et al., 2008; Premashthira et al., 2011). Previous studies that have modeled FMD outbreaks in the central U.S. have relied on expert opinion or contact rates adapted from other regions (Pendell et al., 2007; Greathouse, 2010; Premashthira, 2012). In order to improve the validity of models of this region of the U.S., we used the results of a recent survey of livestock producers (McReynolds et al., 2014a) to inform model parameters used in the current study.

The primary objective of this study was to model FMD outbreaks in the Central U.S., using the best available information to establish rates of contact among herds in this region, to identify optimal vaccination control strategies based on their effectiveness in minimizing simulated outbreak durations and numbers of herds depopulated. A secondary objective was to analyze the sensitivity of the model to specific input parameters,including movement controls, direct contact rate, indirect contact rate, and probability of indirect transmission.

Materials and Methods

Study Population

The number of herds, type of herds and herd sizes at the county level were generated from the U.S. agricultural census 2007 NASS data (NASS, 2007) and adjusted according to criteria by Melius et al. (2006). The study area included Wyoming, South Dakota, Colorado, Nebraska, Kansas, the northern region of New Mexico and Oklahoma, and the Texas Panhandle (Fig. 1). There were 151,620 livestock herds in the study area in 2007 (USDA, 2007) including 86,655 cow/calf, 3,232 dairy, 979 large feedlots (≥3,000 head), 25,096 small feedlots (<3,000 head), 1,071 large swine (≥1,000 head), 6,463 small swine (<1,000 head), 5,159 beef and swine, and 22,965 small ruminant herds (Table 1). NASS data do not account for mixed production types such as beef-swine yet data suggest approximately 7% of Kansas and Colorado herds report having both beef cattle and swine (McReynolds et al., 2014a) To account for this production type seven percent of beef and swine operations were randomly re-designated in the NASS data set from the population of cow/calf operations and small swine in Kansas, Nebraska, Eastern Colorado, and Oklahoma (McReynolds et al., 2014a). The total population was 39,413,228 animals in all production types (Table 1). Heterogeneous random locations within counties were generated for herds using a weighting scheme based on altitude, flatness, and human population developed by Lawrence Livermore National Laboratory for USDA (Hullinger et al., 2009). This method assures that number of herds, number of animals in each herd and production types match at the county level (herds are always allocated to the county they reside in based on NASS data). The geo-located population data set was provided to the authors by USDA.

Simulation model

The North American Animal Disease Spread Model (NAADSM), an open source) herd-based spatial stochastic epidemic simulation model (Harvey and Reeves, 2010; Harvey et al., 2007) was used to model FMD eradication strategies. Scenarios were simulated for various FMD vaccination protocols, and were compared to a scenario that made use of only depopulation of detected infected herds and traced forward direct contacts of infected herds (Scenario 1). Modeled scenarios are listed in Table 2 and include variations in vaccine capacity, vaccination zone diameter, and the number of infected herds before a vaccination program is initiated. Simulated vaccination protocols included low and high vaccine capacity, which were defined based on results from a Kansas and Colorado livestock producer survey (McReynolds et al., 2014a). The livestock survey asked producers to report the time it would take to vaccinate, tag, and keep records for their entire herd. Vaccination was carried out either for large feedlots only (low vaccine capacity 1 herd per day by day 22 and 3 herds per day by day 40 and high vaccine capacity 8 herds per day by day 22 and 15 herds per day by day 40) or for all herd types (low vaccine capacity 5 herds per day by day 22 and 10 herds per day by day 40 and high vaccine capacity 50 herds per day by day 22 and 80 herds per day by day 40). When vaccination capacity was limiting, herds were vaccinated according to a priority scheme based on production type. Vaccination priority from highest to lowest for scenarios where all herd types could be vaccinated was: large feedlot (≥3,000 head), small feedlot (<3,000 head), large swine (≥1,000 head), small swine (<1,000 head), beef-swine, dairy, cow-calf, and small ruminant. Feedlots are prioritized for vaccination because the large number of cattle on a premises makes it difficult to depopulate all of the cattle in a timely fashion and because they are terminal animals that fit a vaccinate to slaughter strategy thus conserving destruction capacity and production value. The low vaccine capacity was to simulate administration by USDA personnel and the high capacity producer administration of vaccine. The vaccinated animals remain in the population unless infected after their immune period ends.

The distributions for within herd prevalence of FMDV for NAADSM were produced using a within herd prevalence model (WH) (Reeves, 2012a) based on estimates for the latent, subclinical infectious, and clinical infectious stages. The WH model operates at the level of the individual animal, and incorporates sources of individual-level variation such as variability in the durations of incubating and infectious periods, the stochastic nature of the disease spread among individuals, the effects of vaccination, and disease mortality (Reeves, 2012b). Distributions of the clinical stages of FMD in individual animals were based on a meta-analysis of the duration of the disease states where the infectious period was reported including the subclinical and clinical periods (Mardones et al., 2010). The reported clinical period in Mardones et al., (2010) is the time when clinical signs are apparent which includes a period when the animal is no longer infectious. The WH model requires durations for the latent, subclinical infectious and clinical infectious stages. Distributions for the latent and subclinical states were used directly as they are reported in Mardones et al. (2010) but the reported distributions were not suitable for the clinical infectious period in WH and required adjustment for the period when the animal is not infectious. As reported in figure 1of Mardones et al. (2010) the

Subclinical period + Clinical period = Infectious period

therefore

Infectious period - Subclinical period = Clinical period

The clinical infectious period distribution for cattle, swine and small ruminants was calculated for *WH* by using monte-carlo simulation (@Risk 5.01, Palisade Corp., Ithaca, NY, USA) to sample 10,000 values from the subclinical infectious period and the infectious period reported in Mardones et al. (2010). When the sampled value from the infectious period was greater than the sampled value for the subclinical period, the value for the subclinical period was subtracted from the sampled values for the infectious period. The resulting distribution of values was fit to a theoretical distribution (@Risk 5.0.1) to estimate the clinical infectious period for use in WH to estimate the within herd prevalence over time for each production type. The probability of infection following a direct contact in NAADSM was based on within-herd prevalence of the infected herd as a function of time since infection. Model parameters were set to allow virus to spread by direct contact, indirect contact, and airborne/local spread. In NAADSM a direct contact represents the movement of infected livestock between premises. An indirect contact represents the movement of a fomite such as contaminated vehicle, equipment, clothing, or a person between premises. Direct and indirect contacts between livestock production types were based on a livestock contact survey in the central U.S. (McReynolds et al., 2014a) (Appendix Tables A1 and A2). The direct contact rate was calculated from the reported count of contacts between specific production types to provide an overall production type specific number of contacts per day. Destination to source combinations for indirect contact were calculated based on the total number of indirect contacts reported for each production type, multiplied by the proportion of all indirect contact made to the respective production type to produce the number of daily indirect contacts between each destination to source combination. For example if cow-calf operations received 0.7 total visits from potential indirect contacts per day, and 18.8% of all potential indirect contacts (across all production types) were to Cow-Calf operations then in 0.133 visits per day the previous production type exposure of the indirect contact was a Cow-Calf operation resulting in an indirect contact between two Cow-Calf operations (0.7*18.8% = 0.133 contacts per day as shown in Table 2A). The daily indirect contact rate between each production type was adjusted based on the assumption that not all production types are equally connected (e.g. beef operations are more connected with each other than with swine operations). The daily mean number of direct and indirect contacts between production types were used to parameterize the model. Generation of actual direct and indirect contacts between production types in the NAADSM model were stochastically generated for each infected herd each day from a Poisson distribution with lambda equal to the calculated mean contact rate (direct and indirect) for that production type combination (Tables A1 and A2). Specific susceptible recipient herds of direct or indirect contacts were selected based on a random draw from the respective distance distribution for contacts between specific production types (Tables A1 and A3). The probability of airborne/local spread at 1 km was 0.5% per day and declined linearly to 0% at the maximum distance of spread of 3 km. The probability of local/airborne transmission was calculated based on distance between the infected and susceptible herd, herd size and within herd prevalence. Actual transmission between the infectious and susceptible herd was generated based on generation of a random number *r* between 0 and 1 where infection is transmitted when *r* is less than the calculated probability of transmission.

Days to first disease detection was a generated output by the NAADSM model based on the probability of disease recognition within infected herds as a function of the amount of time the herd has been clinical infectious. Actual detection of a clinical herd (both the initial and subsequent herds) was based on generation of a random number *r* between 0 and 1 where the infected herd is detected when when *r* is less than the calculated probability of recognition. The probability of recognition increased over time within a herd peaking at 100% by day 10 in all herd types except small ruminants where recognition probability did not reach 100% until day 14 following introduction of disease to that herd. For all scenarios,

a) All herds detected positive and the forward traced direct contacts of detected herds were depopulated.
b) The probability of indirect disease transmission following indirect contact between an infected and susceptible herd was held fixed at 20% for all production types except swine which was set at 30% to account for increased FMD virus shedding by swine based on subject matter expert opinion solicited by USDA.
c) Direct contact through animal movement was linearly reduced to 10% of pre-outbreak levels and indirect contacts were linearly reduced to 30% of pre-outbreak levels by day 7 after the first disease detection to allow for time delays in implementation and enforcement of movement controls based on subject matter expert opinion solicited by USDA.
d) Depopulation capacity was linearly increased from 0 to 8 herds/day by day 10 and 16 herds/day by day 30 after first disease detection.

e) A 100% effective quarantine of infected premises and a ban on livestock movement from known infected premises was assumed.

Depopulation was set to begin on day 2 after first disease detection of the outbreak. All scenarios were run for 200 iterations. The mean, 5th and 95th percentiles of outbreak duration, number of destroyed herds and number of animals vaccinated were monitored for convergence. The end of the active disease phase (i.e., the point in time at which no infected herds remained in the population) was the endpoint for all scenarios. Conditions of the NAADSM model used in this study of a hypothetical outbreak in the central U.S.were:

a) There are eight defined livestock operation production types in the study region (Table 1) and wildlife are not included.
b) All herds in the same production type have the same disease parameters. Probability density functions characterize the length of the disease periods and this length is determined stochastically by a random draw from the distributions for each new infected herd.
c) The population is closed and constant. Herds only exit the population by depopulation.
d) There is no mortality from FMD during the simulated outbreak.
e) There are no virus carrier states for recovered animals.
f) Vaccine is 100% effective following a 7 day delay after vaccination.
g) Quarantine of infected herds is 100% effective for all contacts and implemented until the herd is depopulated.
h) Detection of positive herds was based on the probability of visual, clinical disease recognition within infected herds as a function of time the herd has been clinical infectious.

Experimental design

In all scenarios, a single 17,000 head feedlot in Northeast Colorado was latently infected and served as the index herd for the outbreak. Seventeen different disease mitigation scenarios were simulated as described in Table 2.

Sensitivity Analysis

Values of selected uncertain parameters were varied from baseline values in a sensitivity analysis to assess their independent influence on the disease modeling results. The 17 scenarios were simulated for each variable change. The baseline probability of transmission given indirect contact was 20% and the sensitivity analysis assessed it at 15% and 25%. Sensitivity analysis of the contact rates were also completed with the direct contact rates adjusted to +/- 20% and +/-50% of the baseline rate parameter. Sensitivity of the indirect contact rates for each production type combination was assessed by changing all production type combination rates by +/- 20% from the calculated parameter for all scenarios. Lastly the influence of indirect movement controls was assessed by changing the baseline indirect movement control of 30% of pre-outbreak levels to 20% and 40% of pre-outbreak movement levels to represent a relatively wide range of indirect movement control.

Data analysis

The NAADSM model produced results for each day of the outbreak for each iteration. The results from each scenario were aggregated into weekly outcome counts for each iteration of each scenario. Summary statistics were generated for each of the scenarios. Outbreak duration was calculated from the first day of the simulation to the end of the active disease phase of the outbreak. Analysis was performed in commercially available software (Stata12.1, (StataCorp., 2011) and in open source 64 bit *R* 2.15.2 (R development core team, 2011). To test the statistical differences between scenarios, a Kruskal-Wallis one-way analysis of variance was used to identify significant differences in outbreak duration and number of herds depopulated controlling for multiple comparisons at $p<0.05$ according to the method of Holm (1979) implemented in *R*.

Results

The mean, 5th and 95th percentiles of outbreak duration, number of destroyed herds and number of animals showed less than 4% change at 200 iterations for all scenarios. Most scenarios converged at approximately 100 iterations and all scenarios converged before 200 iterations. In all scenarios the main source of new infections was indirect contacts; approximately 95% of infected herds resulted from an indirect contact and the remaining 5% were infected from direct contact or airborne/local-area spread. In all scenarios the median first day of detection was at 10 or 11 days. The median day of first vaccination was 17-22 days following first detection for scenarios where vaccination was initiated after 10 herds were detected positive. For scenarios where vaccination was initiated after 100 herds were detected the median day of first vaccination was 57-65 days after the first detection.

For scenario 1 with no vaccination, there was a sharp peak in the weekly number of detected herds compared to the scenarios with vaccination (Figure 2). In scenario 1 there were 104 new herds detected during week 18 and during week 28, 342 herds were detected. By comparison, in scenario 2, which used a small vaccine capacity and small vaccination zone, 74 new herds were detected during week 18 and 60 herds were newly detected during week 28. The total median number of herds detected as clinically infected per outbreak in scenario 1 was 10,139, which represented approximately 6.5% of the herds in the region. All vaccination scenarios had fewer detected clinical herds: for example, scenario 2 had a median of 2,183 clinically infected herds per outbreak, and scenario 4 had a median of 419 clinically infected herds per outbreak.

Outbreak Duration

The model outcomes are reported in Table 3. The scenarios with vaccination zones of 50 km (scenarios 4, 5, 8, 9, 12, 13, 16, and 17), had a shorter median and 90th percentile durations compared to the scenarios with 10 km vaccination zones (scenarios 2, 3, 6, 7, 10, 11, 14, and 15): the best eight ranked scenarios for shortest median duration all had 50 km vaccination zones (Table 3). Scenario 16 had the shortest median outbreak duration, followed by scenarios 4, 8, 12, and 17. The vaccination capacity and the number of herds infected prior to starting vaccination had less impact on median outbreak duration than the size of the vaccination zones: scenarios with both high and low vaccination capacity and number of herds infected to initiate vaccination were among the top ranked scenarios. Scenario 1 ranked 10th in median outbreak duration. Scenarios 7, 10, and 2 had the three longest median outbreak durations and all had vaccination zones of 10 km. Additionally, scenarios 7 and 10 had a late vaccination trigger of 100 herds infected prior to the initiation of vaccination.

Depopulation

All vaccination scenarios decreased the median number of herds depopulated compared to scenario 1. The 7 scenarios with the lowest median number of depopulated herds all had a vaccination zone radius of 50 km, ranging from median numbers of depopulated herds from 252 to 1,735. Scenario 1 had a median of 6,890 herds depopulated per simulated outbreak. The distribution was heavily skewed toward larger numbers depopulated (Table 3). In scenario 1, the median number of herds depopulated included all large feedlot and dairy herds in the population. Also, scenario 1 was the only scenario with herds waiting to be depopulated at the end of the active disease phase (median 2,830 herds waiting per simulated outbreak, data not shown). Scenario 16 depopulated the fewest number of herds followed by scenarios 4, 8, and 17 which did not significantly differ from one another.

Vaccination

In the best 8 scenarios in terms of vaccinating the smallest median number of herds, only large feedlots were vaccinated. None of these scenarios were among the best scenarios in terms of median outbreak duration or median number of herds depopulated. Scenario 11 vaccinated the fewest number of herds followed by scenarios 3 and 7, which did not differ significantly from each other (Table 3). The only scenarios in which all production types were vaccinated were scenarios 6 and 14, which had a high vaccine capacity and a small zone size. Due to vaccine capacity in the remaining scenarios, only large and small feedlots were vaccinated. The number of herds vaccinated differed greatly between the scenarios. Scenarios 16 and 8 had a high vaccine capacity with large feedlots having first priority and vaccinated approximately 10,000 herds, compared to scenarios 4 and 12, which had a low vaccine capacity and vaccinated approximately 1,800 herds. However, in scenario 17 only large feedlots were vaccinated resulting in 1,329 herds vaccinated and the number of herds depopulated was similar to scenarios 4, 8 and 12.

In scenarios with large feedlot vaccination priority, a large vaccination zone and high vaccine capacity (scenarios 8 and 16) there was a sharp peak at the beginning of the outbreak in the number of animals vaccinated but it dropped off sooner than the scenarios with a small zone and high capacity (scenarios 6 and 14) (Figure 3). The median of the maximum number of animals vaccinated in a 1 week period ranged from 163,124 to 963,427, and the maximum 90th percentile ranged from 251,883 to 2.5 million animals in one week depending on vaccine capacity and zone size.

Sensitivity analysis

When the probability of transmission following indirect contact was increased to 25% and decreased to 15%, it was influential in determining the duration of the outbreak, the number of herds depopulated, and the numbers of herds and animals vaccinated. Vaccination was less beneficial in mitigating the effects of an outbreak when probability of transmission following indirect contact was decreased to 15%. In all such scenarios, the median duration of the outbreak was approximately 100 days (range 93-150) (Figure 4) and the median number of herds depopulated was approximately 50 (range 36-83) (Figure 5). The number of herds depopulated decreased by over 90% in most scenarios (range 82-99%) when the probability of indirect transmission was 15%, and increased by over 200% in all but scenario 1 when the probability of indirect transmission was 25% (range 218-1381%). When the probability of indirect transmission was 25% the median duration of the outbreak was over 500 days for most scenarios (range 418-792) (Figure 4), and the median number of herds depopulated was over 5000 for all scenarios except 8, 16 and 17 (Figure 5). In scenarios with vaccination zones of 50 km, when the probability of indirect transmission was increased to 25%, the median duration of the outbreak increased by over 100% compared to an increase of less than 5% in the scenarios with vaccination zones of 10 km. All scenarios with a vaccination zone of 50 km except scenario 12 still had shorter duration and fewer herds depopulated compared to scenarios with a 10 km vaccination zone.

Changes in the effectiveness of indirect contact movement controls were also influential within the range examined in determining the outbreak duration, the number of herds depopulated and vaccinated (Figures 7, 8, 9). When indirect movement controls were increased to achieve 20% of pre-outbreak levels (as opposed to 30% in the baseline scenarios), the median duration of all scenarios was approximately 100 days (range 85-120) (Figure 7). The median numbers of herds depopulated decreased 65-95% to approximately 50 herds (range 39-66) in all scenarios (Figure 8). When indirect movement controls were set at 40% of pre-outbreak levels, median duration of the outbreak was approximately 500 days for all scenarios (range 481-726) (Figure 7), and the median number of herds depopulated increased over 200% for all but scenario 1 to over 5000 for all scenarios except 8 and 16 (Figure 8).

Changes in the indirect contact rates between herds were influential in the number of herds depopulated, but less so on outbreak duration. When indirect contact rates were decreased by 20% the

10th percentile of outbreak duration was decreased approximately 25-72% and the median by 33-72% (Figure 10). Median number of herds depopulated decreased 65-97% to 58 to 584 herds (Figure 11). When indirect contact rates were increased by 20% the median number of herds depopulated increased 60-89% to greater than 5,000 herds for all scenarios except 4, 8, 16 and 17.

Sensitivity analysis scenarios ranked similarly to the baseline with scenario 16 or 17 always having the fewest median number of herds depopulated for all sensitivity scenarios. Scenarios 8 and 4 were also among the best ranking scenarios for the lowest median number of herds depopulated. Scenario 1 was ranked in the best 5 scenarios for number of herds depopulated when movement controls were either 20% or 40% of pre-outbreak indirect contact levels or when the indirect contact rate was increased by 20% (Table 4). The sensitivity analysis scenario rankings for outbreak duration showed more variation from the baseline and among the sensitivity scenarios. Scenario 4 was always among the best five scenarios for outbreak duration and scenario 16 was among the best five in all sensitivity scenarios except when indirect movement control was 40% of pre-outbreak indirect contact levels. Scenario 1 was ranked best for outbreak duration when indirect movement control was 40% of pre-outbreak indirect contact levels and among the best five scenarios for outbreak duration when indirect transmission probability was 25% and when the indirect contact rate was increased by 20% (Table 4).

Increasing direct contact rate by 20% or 50% had little impact of the outcome of the results (data not shown).

Discussion

General discussion

Modeling is a widely used method for assessing the impact of an FMDV introduction in the U.S. and the effectiveness of control because of its nature as a highly infective foreign animal disease. Control methods in the face of an outbreak of FMD include movement controls on livestock and support industries, increased biosecurity such as disinfection of traffic on and off the farm, slaughter of affected and in contact or high risk animals, and vaccination. In this study probability of indirect transmission, movement controls, and vaccination protocols were analyzed to determine the impact of the different control methods. We interpret probability of indirect transmission as a surrogate for disinfectant or biosecurity practices on farm in the sensitivity analysis.

The number of herds depopulated was greatest for scenario 1 and the least for scenario 16 (Table 3). In scenario 1, the number of herds depopulated was much higher than the scenarios that included vaccination. The outbreak in scenario 1 spread rapidly and it was the only scenario with herds waiting to be depopulated at the end of the active disease phase, having exceeded the depopulation capacity. Scenario 16, which had a large vaccination capacity as well as a large vaccination zone, was able to contain the spread. Due to workforce and vaccine capacity, the high capacity vaccination in a large zone might not be feasible during an outbreak. In the scenarios with a larger vaccination zone, vaccination was advantageous in controlling depopulation and duration suggesting a threshold level of vaccination necessary to bring the outbreak under rapid control. The results reported here represent onset of immunity at 7 days after vaccination and a predominantly indirect contact infection challenge. These results support the value of vaccination strategies, particularly those with large vaccination zones, to control disease impact. The model assumed 100% vaccine efficacy so this is clearly an upper bound of the potential vaccine effect. NAADSM does not currently allow for variation in vaccine efficacy and further studies examining the effect of vaccine are warranted. High potency vaccines formulated for emergency vaccination have shown 100% efficacy by 2-4 days after vaccination in small studies of cattle and pigs challenged by indirect aerosols (Cox and Burnett, 2009). Efficacy was only 70-75% at 10 days after vaccination when a direct exposure to shedding animals was used as the challenge (Cox and Burnett, 2009).

Scenarios 7, 10, and 2 (each of which had small vaccination zone and low vaccination capacity) had a longer duration of outbreak when compared to scenario 1 (only depopulation). The duration of the outbreak may potentially be shorter in scenario 1 due to rapid expansion and burnout without vaccination to slow the spread of the virus. Limited vaccination programs may reduce the number of infections without effectively bringing the outbreak to an end. Perez et al. (2004) concluded from the Argentina outbreak in 2001 that mass vaccination can be useful in controlling a large epidemic but that it could take a long time to bring the outbreak under control (Perez et al., 2004). The number of herds depopulated in the results reported here however, was decreased in all vaccination scenarios including scenarios 2, 7 and 10. Based on number of herds depopulated, scenario 2, 7, and 10 control methods are advantageous compared to scenario 1 despite the longer duration of outbreak. An economic analysis of a subset of these scenarios however indicated that outbreak duration was a major determinant in increasing outbreak cost (Schroeder et al. accepted).

Despite the large region represented in the model, in reality not all movements would be confined to the modeled area as in this hypothetical FMD outbreak, so a real outbreak could spread further. The duration of a hypothetical epidemic modeled in the Texas Panhandle region had a median of 25-52 days (Ward et al., 2009) which was much shorter than the results in the study reported here where median duration ranged from 181-608 days. Ward et al. (2009) was confined to an eight county region and the outbreak could easily be larger following spread to other regions. We chose an initially latent herd in the central location of our population to allow the most geographic freedom of disease spread and minimize any geographic boundary effect in the results.

The median number of herds detected as clinically infected for scenario 1 represented approximately 6.5% (10,139 /151,620) of the herds in the study population and scenario 2 represented 1.4% (2,183/151,620) of the herds. The results of scenario 2 are comparable to the 2001 U.K. FMD outbreak where 1.4% of herds (2030/146,000) were reported as infected (Anderson, 2002) and an FMD model of 3 counties in California where 2% of herds were infected (Bates et al., 2003b). In the study reported here, scenario 16 had the lowest number of infected herds detected at 0.16% followed by scenario 4 at 0.3% of the herds detected as clinically infected.

Our data is consistent with a large vaccination zone having the biggest impact on the duration of the outbreak. Bates et al. (2003b) found that vaccinating all herds within 50 km of an infected herd was an effective strategy to reduce duration of the outbreak when modeling an FMD outbreak in a 3-county region of California. In that regional study the outbreaks in scenarios with the large vaccination zone lasted the shortest number of days despite not all the herds in the zone getting vaccinated due to capacity limitations.

Our low vaccination capacity scenarios were meant to represent vaccine administration by USDA personnel only. Livestock production type had priority over days waiting in queue for vaccination so the only scenarios where any production type besides feedlots were vaccinated were scenarios that had a high vaccination capacity and a small vaccination zone. However, these small zone and high capacity scenarios had outbreaks that lasted longer, leading to more herds being vaccinated compared to high capacity and large zone scenarios. The two scenarios that had the highest number of herds vaccinated (scenarios 14 and 6) had high vaccination capacity, a small zone, vaccinated all herd types and exceeded 30,000 herds vaccinated. However, they were never among the top ranked scenarios for outbreak duration or number of herds depopulated. Because of the high percent of infections resulting from indirect contacts in these models, the ability to vaccinate all the production types surrounding an infected herd did not appear as beneficial as priority vaccination of feedlot production type that have high numbers of indirect contacts.

The high vaccine capacity scenarios were meant to represent vaccination being carried out by the farmers and ranchers as was done in the 2001 Uruguay outbreak. Data from the Uruguay outbreak indicates an average vaccination rate of 350,000 cattle per day in each round of vaccination (Sutmoller et al., 2003) which is a higher rate than the requirement in our high vaccine capacity scenarios where the median of the maximum animals vaccinated in a 1 week period was 963,427, and similar to the 90th percentile (2.5 million animals in one week). In the U.S., animal health officials could have some concerns regarding producers administering FMD vaccine themselves, as it is a restricted and controlled vaccine. While reliable procedures for administering vaccine and identifying vaccinates would be necessary, allowing producers and private veterinarians to perform vaccination would increase the capacity dramatically.

Minimizing the number of herds vaccinated is not the most appropriate measure of the best vaccination strategy, but is useful for identifying the most efficient use of vaccination. The scenarios with the shortest duration of outbreak and the lowest number of herds depopulated varied in the number of herds vaccinated, but were consistently scenarios with large vaccination zones.

The top five ranking scenarios for outbreak duration and number of depopulated herds contained scenarios with both 10 and 100 herds infected prior to the initiation of vaccination suggesting the decision to vaccinate may not need to be made at the very beginning of the outbreak allowing additional time to produce adequate vaccine supplies to meet demand and to evaluate the need for vaccination. These results also suggest that a proper vaccination plan could decrease the number of personnel needed for depopulation to partly make up the likely increased personnel requirements to implement vaccination. Vaccination zone size was the most important factor determining the outbreak duration and the number of herds depopulated. All five top ranked scenarios for the duration of the outbreak and number of herds depopulated had large vaccination zones. Vaccination does not require the time or the quantity of labor that are needed for depopulation and disposal of carcasses. The disadvantages of vaccination are imperfect efficacy, the delay before protection of almost a week (Salt et al., 1998), the challenge of producing sufficient quantities of strain specific vaccine, the lack of cross immunity between strains, and the trade implications of vaccinating and recovering disease free status (Office International des Epizooties/World Organisation for Animal Health, 2013).

Some previous research has found that vaccination protocols in the control of a FMD outbreak were not economically beneficial (Schoenbaum and Disney, 2003; Elbakidze et al., 2009). Bates et al. (2003) in a benefit-cost analysis model of a FMD outbreak in 3 counties in California, found vaccination would be a cost-effective strategy if vaccinated animals were not subsequently depopulated (Bates et al., 2003a). Vaccinated herds in the scenarios reported here were not depopulated and all vaccination scenarios in this study did decrease the number of herds depopulated compared to depopulation only. Further, an economic analysis of these results found that vaccination was also advantageous to decreasing the median economic impact of the outbreak (Schroeder et al., accepted).

FMD simulation models have found that targeting high-risk production types can increase the efficiency of vaccination (Keeling et al., 2003). In the current study large feedlots were prioritized for vaccination due to their high contact rate and the large number of feedlots in the central region of the U.S. Large feedlots have a high number of indirect contacts (McReynolds et al., 2014a) potentially increasing their risk of becoming infected and spreading infection during an outbreak. In this study, the scenarios with large vaccine zones and feedlot vaccination priority, predominantly vaccinated large and small feedlots but had a similar impact on the outbreak as scenarios where only large feedlots were vaccinated. Scenario 17 is of note as a top ranking large feedlot only vaccination scenario with high capacity (8 herds by 22 days and 15 herds by 40 days) and large vaccination zone. This suggests there may be methods to efficiently apply vaccination to high risk groups and efficiently use resources (Keeling et al., 2003; Keeling and Shattock, 2012). Animals in large feedlots are also a natural vaccinate to die (slaughter) population perhaps facilitating restoration of FMD free without vaccination status, without the cost of depopulation or the loss of valuable protein for human nutrition. However, vaccinating to live versus to die has different implications from an international trade perspective. In vaccinate to live scenarios, export market access would likely be delayed at least 3 additional months relative to a depopulating all vaccinated animals.

Sensitivity of input values

The operational validity of the model was assessed using a sensitivity analysis to determine the impact of uncertainty in contact and control methodologies (Frey and Patil, 2002; Garner and Hamilton, 2011). Indirect contacts are a potential risk for disease spread particularly for a highly contagious disease such as FMD (Cottral, 1969; Ellis-Iversen et al., 2011) and in our scenarios approximately 95% of the infections were transmitted through indirect contacts. The sensitivity analysis was used to determine the impact of changes in the disease control methods and the contact rates on the model results. The sensitivity analysis of the direct contact rate demonstrated that the model was not sensitive to changes in the direct contact rate, which may be due in part to the 100% quarantine of infected herds within the model. The model was sensitive to changes in the indirect contact rate. This highlights the need for accurate data regarding indirect contacts between livestock producers. Indirect contact rates used here are based on a survey of producers in Kansas and Colorado (McReynolds et al., 2014a) representing all modeled production types and provide the best available estimates of direct and indirect contacts between production types for the region being simulated. When the indirect contact rates for all production types were decreased by 20%, the median duration of the outbreak and number of herds depopulated decreased substantially. The ranking of the best scenarios by number of herds depopulated remained similar (Table 8) but the impact of vaccination was substantially decreased.

When the indirect contact rates increased 20%, scenarios with a small vaccination zone had larger outbreaks than scenario 1. Again scenario 1 did appear to spread quickly with the number of herds exposed to the virus and waiting for depopulation being the largest of all the scenarios. When the indirect contact rate was increased the number of infected herds increased rapidly and the vaccination capacities modeled were not sufficient to control the outbreak. In the face of an outbreak that is spreading rapidly vaccine capacity appears to be important. In the Taiwan outbreak inadequate vaccine supply was one of the potential factors in the large epidemic (Yang et al., 1999). This may also be a factor in our scenarios where the vaccination zone was small and the outbreak lasted longer than the depopulation alone scenario.

Due to the impact of movement controls on an agriculture community and on animal welfare, a sensitivity analysis on the impact of movement controls within the model was simulated. Feed delivery, supplies, and labor are indirect movements that must be maintained for business continuity and for animal welfare reasons in the face of a FMD outbreak. The minimum amount of movements that will be necessary will vary for different production types. Decreasing indirect movement from 30% to 20% of pre-outbreak levels substantially decreased the number of herds depopulated and the duration of the outbreaks to similar levels in all scenarios. None of the vaccination scenarios were different from scenario 1 for number of herds depopulated and duration of outbreak. While decreasing movement was effective in decreasing the number of herds depopulated, the ability to achieve a decrease in indirect movement to 20% of the pre-outbreak level without animal welfare issues is not clear. The animal welfare consequence of these movement controls on un-infected or infected herds awaiting depopulation has been found to be significant (Laurence, 2002). If this level of movement control is achievable in the face of an outbreak consistent with acceptable animal welfare, it may be sufficient and vaccination may have little additional benefit. When indirect movement control was set at 40% of pre-outbreak levels, the duration of the outbreaks were all similar to scenario 1, lasting 500 to 700 days and scenario 1 had the third lowest number of herds depopulated. This demonstrates that if strict indirect movement controls are not possible, vaccination might not be effective in disease outbreak control. Because the range of estimates of indirect movement control (20% to 40% of pre-outbreak levels) used in the sensitivity analysis identified substantial variation in the outcomes, additional estimates outside that range were not evaluated. Achievable movement controls consistent with acceptable animal welfare require additional investigation to support more refined modeling.

Probability of transmission given an indirect contact showed a similar effect in the sensitivity analysis. When the probability of indirect transmission was decreased from 20% to 15% the number of herds depopulated and the outbreak duration decreased substantially in all scenarios. The probability of transmission following indirect contact between an infected and susceptible herd could represent a measure of the biosecurity practices applied to traffic and people on and off the farm. Important aspects include truck washing, boot washing and control of visitor contact with animals. With increased biosecurity, vaccination did not offer any benefit over the depopulation alone control strategy but again the impact and ability to achieve this level of biosecurity is unknown. Increased biosecurity would be an important aspect of control efforts and could be a welfare friendly option to control spread compared to increased movement controls. Alternately, decreased probability of transmission following indirect contact may be representative of FMD strains with lower transmissibility. When the probability of transmission given an indirect contact was increased from 20% to 25% the number of herds depopulated was substantially increased and the impact of vaccination decreased. Biosecurity and movement controls are known to be important aspects of a control strategy during a FMD outbreak due to the potential risk of disease spread (Anderson, 2002; Cottral, 1969; Ellis-Iversen et al., 2011). Additionally, identifying the personnel requirements to achieve sufficient levels of biosecurity and movement controls is needed, as well as the impact on animal welfare.

The estimates of the probability of indirect transmission and achievable movement controls are uncertain parameters, based solely on USDA subject matter expert opinion. Model outputs are quite sensitive to these parameters and an improved knowledge of the efficacy of biosecurity practices and the ability to achieve movement controls to limit direct and indirect transmission are necessary for more focused planning of optimal control efforts.

The validity of results reported here are dependent on application of sufficient resources required to implement the controls. Depopulation has been a mainstay of FMDV control plans however the ability to depopulate large feedlots may be questionable (McReynolds et al 2014b), and further modeling may be necessary to assess alternatives.

Finally, the results reported here do not account for the potential of a reservoir of FMDV infection in the wildlife population. FMDV can infect deer and feral swine and establishment in these populations could substantially complicate eradication efforts (Ward et al., 2007).

Conclusion

In this simulation study of an FMD outbreak in the central U.S., scenarios with large vaccination zones had shorter median outbreak durations and fewer numbers of herds destroyed. Increasing the vaccination capacity had a small impact on the outbreak and may not be feasible if vaccine production and delivery is limited. In these scenarios, feedlots ≥3,000 head had the highest vaccination priority and even with larger vaccine capacity few other production types were vaccinated in some scenarios. Outbreak size and number of herds depopulated were sensitive to biosecurity practices and movement controls and to a lesser extent indirect contact rates. The level of biosecurity required to achieve a given probability of indirect transmission and the ability to restrict indirect movement consistent with acceptable animal welfare is uncertain. Vaccination was not beneficial compared to depopulation alone to control the outbreak when biosecurity and movement controls were increased. A better understanding of the biosecurity changes necessary during an outbreak to attain these levels is needed. The results of this study will provide information about the impacts of disease control protocols which may be useful in choosing the optimal control methods to meet the goal of rapid effective control and eradication. The results and impact of the control methods however may not be applicable to other regions due to the variability of livestock production systems that are found in different regions in the U.S.

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Table 1. Simulation population of the 8-state region in the central U.S. that was used in NAADSM with the number of animals and herds by production type.

Production Type	Animals	Herds
Cow-calf	9,698,630	86,655
Feedlot-Large (≥3,000 head)	9,147,279	979
Feedlot-Small (<3,000 head)	7,377,698	25,096
Dairy	1,062,276	3,232
Swine-Large (≥1,000 head)	9,227,569	1,071
Swine-Small (<1,000 head)	663,465	6,463
Beef-swine mix	520,283	5,159
Sheep	1,716,028	22,965
Total	39,413,228	151,620

Table 2. Description of vaccination strategy for 17 simulated scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.

Scenario	Large Feedlots Vaccination [b]	Vaccination Capacity [c]	Vaccination Trigger (herds)	Size of Vaccination Zone (km)
1[a]	-	-	-	-
2	Priority	5,10	10	10
3	Only	1,3	10	10
4	Priority	5,10	10	50
5	Only	1,3	10	50
6	Priority	50,80	100	10
7	Only	8,15	100	10
8	Priority	50,80	100	50
9	Only	8,15	100	50
10	Priority	5,10	100	10
11	Only	1,3	100	10
12	Priority	5,10	100	50
13	Only	1,3	100	50
14	Priority	50,80	10	10
15	Only	8,15	10	10
16	Priority	50,80	10	50
17	Only	8,15	10	50

[a] Scenario 1 baseline depopulation without vaccination

[b] Priority – from highest to lowest: large feedlot (≥3,000 head), small feedlot (<3,000 head), large swine (≥1,000 head), small swine (<1,000 head), beef-swine, dairy, cow-calf, and small ruminant.

Only – Large feedlots only vaccinated.

[c] The capacity for vaccination protocols in number of herds per day by 22 days after disease detection and by 40 days after disease detection

Table 3. Median duration of outbreak, number of herds depopulated, number of animals depopulated, number of herds vaccinated, and number of animals vaccinated for each scenario (10^{th} - 90^{th} percentiles) [rank most to least optimal] of a potential foot and mouth disease virus outbreak in a central region of the U.S.

Scenario	Outbreak Duration (days)	Number of Herds Depopulated	Number of Animals Depopulated (1000)	Number of Herds Vaccinated	Number of Animals Vaccinated (1000)
1	527^{f} (87-621)	6,890^{h} (32-8,101) [17]	13,663 (196-17,611)		
2	608^{i} (102-767)	2,227^{g} (42-2,449) [13]	9,921 (222-10,600)	5,709^{i} (657-7304)	7,644 (0-8,500)
3	530^{fg} (48-687)	2,248^{g} (10-3,156) [11]	9,939 (72-11,500)	472^{b} (0-514) [3]	4,319 (0-4,764)
4	223^{b} (86-310)	416^{b} (31-879) [2]	1,736 (238-3,214)	1,876^{g} (494-2,736)	16,400 (1,490-
5	389^{e} (286-559)	1,735^{e} (1,326-2,063)	7,508 (5,774-8,591)	1,043^{e} (725-1,460) [6]	10,300 (7,000-
6	459^{fg} (45-721)	1,991^{f} (9-2,301) [9]	9,098 (65-10,000)	30,594^{k} (0-51,136) [15]	19,600 (0-23,832)
7	550^{ghi} (64-753)	2,249^{g} (15-5,133) [15]	10,000 (81-12,500)	458^{b} (0-488) [2]	4,183 (0-4,600)
8	202^{ab} (131-390)	440^{b} (233-616) [3]	1,863 (1,071-2,395)	10,000^{j} (6,400-24,560)	14,900 (10,000-
9	342^{d} (256-528)	1,605^{d} (1,242-3,712)	6,950 (5,600-10,400)	1,044^{e} (784-1,398) [7]	10,400 (7,400-
10	596^{hi} (154-800)	2,203^{g} (49-3,270) [12]	9,968 (341-11,121)	5,165^{h} (0-7,030) [11]	7,132 (0-8,330)

11	540^{fgh} (90-709)	$2{,}276^{g}$ (32-7,318) [16]	10,000 (268-15,000)	425^{a} (0-463) [1]	3,851 (0-4,263)
12	250^{c} (146-318)	855^{c} (234-1,150) [5]	3,702 (968-4,727)	$1{,}800^{g}$ (635-2,420) [9]	17,200 (6,250-
13	369^{de} (244-579)	$1{,}848^{f}$ (1,320-7,904)	8,008 (6,275-16,360)	859^{d} (528-1,098) [5]	8,461 (4,833-11,000)
14	527^{fghi} (77-791)	$1{,}925^{f}$ (22-2,174) [8]	9,098 (141-10,000)	$37{,}928^{l}$ (746-59,380)	21,600 (205-25,800)
15	545^{fgh} (363-706)	$2{,}238^{g}$ (1,681-2,648)	9,922 (8,017-10,675)	499^{c} (432-525) [4]	4,561 (3,850-4,860)
16	181^{a} (123-366)	252^{a} (107-427) [1]	1,028 (515-1,644)	$11{,}902^{j}$ (6,923-26,654)	15,500 (10,000-
17	241^{bc} (133-568)	440^{b} (87-850) [4]	1,754 (521-3,373)	$1{,}329^{f}$ (528-2,718) [8]	13,100 (5,000-

Values within columns with different superscripts are different $p<0.05$ (adjusted p-value accounting for multiple comparisons)

Table 4. The top 5 rankings of the scenarios with the lowest number of herds depopulated and shortest outbreak duration of a potential foot and mouth disease virus outbreak in a central region of the U.S. Rankings based on a Kruskal-Wallis one-way analysis of variance.

Sensitivity Analysis Parameter	Lowest number of herds depopulated					Shortest outbreak duration				
Rank	1	2	3	4	5	1	2	3	4	5
Baseline Scenarios	16	4	8	17	12	16	4	8	12	17
Indirect Transmission 15%	17	16	4	10	6	17	16	4	8	10
Indirect Transmission 25%	16	8	4	17	1	4	1	11	16	3
Indirect Movement Control 40% of baseline	16	8	1	4	17	1	17	11	4	3
Indirect Movement Control 20% of baseline	16	4	17	8	1	16	4	17	8	7
Indirect Contact Rate -20%	16	4	17	8	12	16	4	17	8	12
Indirect Contact Rate +20%	16	8	4	17	1	4	16	7	1	11

Appendix 1. Disease state and spread parameters

Table A1. Calculated mean daily direct contact rates per herd used to parameterize the NAADSM model based on livestock contact survey results in Colorado and Kansas.

Source Production Type	Destination Production Type	Mean Number of Contacts per Day per Herd	Movement distance in km
Cow/Calf	Cow/Calf	0.027	Exponential (116.88)
Cow/Calf	Large Feedlot	0.002	Weibull (1.35,344.40)
Cow/Calf	Small Feedlot	0.002	Weibull (1.35,344.40)
Cow/Calf	Beef/Swine	0.027	BetaPERT (1.60,80.50,241.40)
Dairy	Dairy	0.065	Pearson 5 (1.01,7.73)
Large Feedlot	Large Feedlot	0.005	Gamma (6.87,71.25)
Large Swine	Large Swine	0.186	LogLogistic (1.10,66.10,1.24)
Small Feedlot	Large Feedlot	0.019	Weibull (1.46,547.06)
Small Feedlot	Small Feedlot	0.017	Beta (8.04,33.76,0.00,2643.80)
Small Swine	Small Swine	0.013	BetaPERT (0,20,181)
Small Swine	Beef/Swine	0.013	Lognormal (166.74,748.64)
Beef/Swine	Cow/Calf	0.027	Exponential (116.68)
Beef/Swine	Large Feedlot	0.003	Weibull (1.35,344.40)
Beef/Swine	Small Feedlot	0.003	Weibull (1.35,344.40)
Beef/Swine	Beef/Swine	0.026	Lognormal (166.74,748.64)
Beef/Swine	Small Swine	0.013	Lognormal (166.74,748.64)
Small Ruminant	Small Ruminant	0.024	Exponential (116.88)

[a] All combinations that are not listed above had a mean daily contact rate of 0.

[b] Beta distribution is a continuous distribution defined by four parameters: α1, α2, a minimum value, and a maximum value.

Table A2. Calculated mean daily indirect contact rate (per herd per day) by production type used to parameterize the NAADSM model based on livestock contact survey results in Colorado and Kansas.

	FROM							
TO	Cow/Calf	Small Feedlot	Large Feedlot	Dairy	Small Swine	Large Swine	Small Ruminant	Beef/Swine
Cow/Calf	0.133	0.090	0.123	0.181	0.005	0.026	0.018	0.009
Small Feedlot	0.141	0.095	0.131	0.191	0.005	0.028	0.019	0.009
Large Feedlot	1.711	1.155	1.589	2.326	0.063	0.337	0.229	0.114
Dairy	0.623	0.420	0.578	1.045	0.026	0.136	0.093	0.041
Small Swine	0.020	0.014	0.019	0.030	0.003	0.014	0.003	0.003
Large Swine	0.044	0.030	0.041	0.066	0.015	0.086	0.015	0.013
Small Ruminant	0.052	0.035	0.048	0.078	0.002	0.008	0.070	0.001
Beef/Swine	0.092	0.062	0.086	0.125	0.007	0.033	0.012	0.006

Table A3. Distance distributions of indirect contacts

Production type of movement source	**Movement distance in km for indirect contacts**
Cow/calf	Beta (8.39,18.78,0.00,887.39)
Dairy	Beta (7.41,8.86,0.00,1580.40)
Large feedlots	Gamma (6.87,71.25)
Small feedlots	Beta (8.04,13.76,0.00,2463.80)
Large swine	Beta (4.55,4.35,0.00,1143.80)
Small swine	Beta (4.42,4.19,0.00,1167.00)
Beef/swine	Beta (5.48,14.55,0.00,791.36)
Small ruminants	Beta (5.21,4.26,0.00,332.66)

[a] Beta distribution is a continuous distribution defined by four parameters: α1, α2, a minimum value, and a maximum value.

Table A4. Defining the duration of the *disease state* periods in days by production type[a]

Production type	**Duration of the *latent period***	**Duration of the *subclinical, infectious period***	**Duration of the *clinical, infectious period***	**Duration of the *immune period***
Cow/calf	Neg. binomial (12,0.77)	Poisson (1.77)	Gamma (35.94,0.65)	Gaussian (1095, 180)
Dairy	Neg. binomial (20,0.85)	Poisson (1.74)	Gamma (26.72,1.03)	Gaussian (1095, 180)
Large feedlots	Neg. binomial (26,0.87)	Binomial (9,0.19)	Gamma (170.51,0.23)	Gaussian (1095, 180)
Small feedlots	Neg. binomial (16,0.82)	Poisson (1.70)	Gamma (48.01,0.58)	Gaussian (1095, 180)
Large swine	Neg. biniomial (4, 0.58)	Poisson (2.05)	Gamma (81.90,0.49)	Weibull (5, 985)
Small swine and beef/swine	Neg. biniomial (4, 0.56)	Poisson (2.10)	Gamma (12.78,1.66)	Weibull (5, 985)
Small ruminants	Neg. biniomial (14, 0.74)	Neg. binomial (14,0.85)	Gamma (15.78,1.22)	Gaussian (930, 90)

[a] from Mardones et. al., 2010 see text for details.

Figure 1. An 8-state outlined region of central U.S. selected for modeling the potential of a foot and mouth disease outbreak initiated in a large feedlot in Northeast Colorado.

Figure 2. Median number of new herds detected as clinically infected by week of a potential foot and mouth disease virus outbreak in a central region of the U.S.

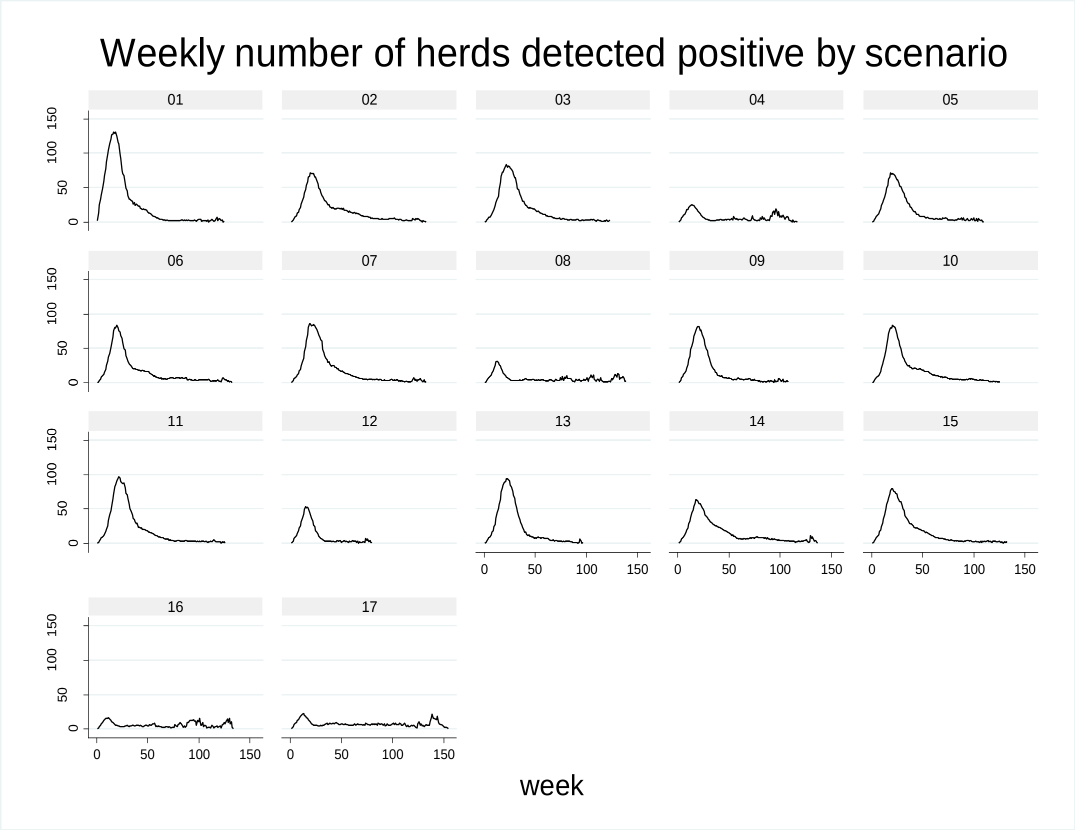


Figure 3. The total number of animals vaccinated each week by scenario number of a potential foot and mouth disease virus outbreak in a central region of the U.S.

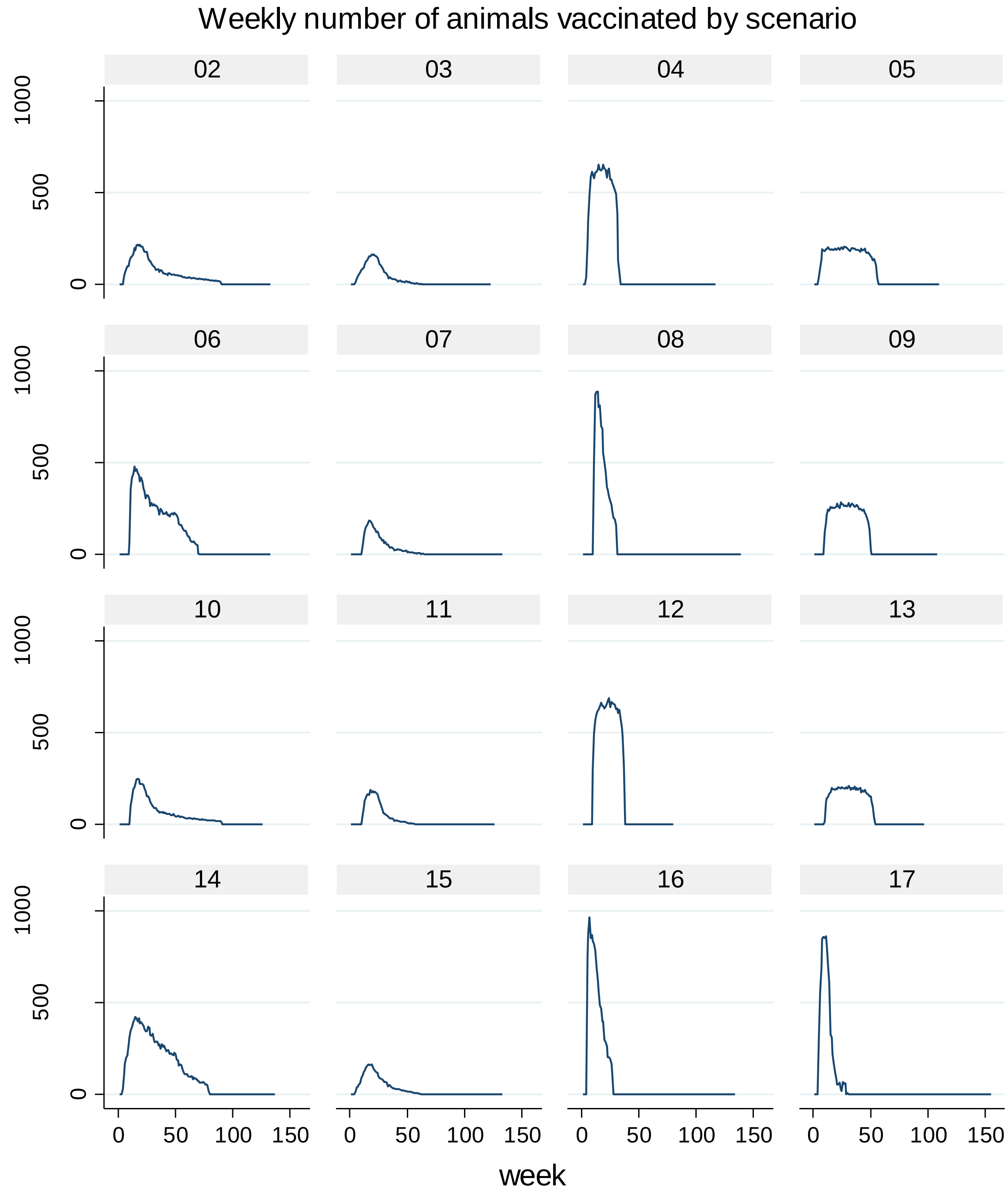
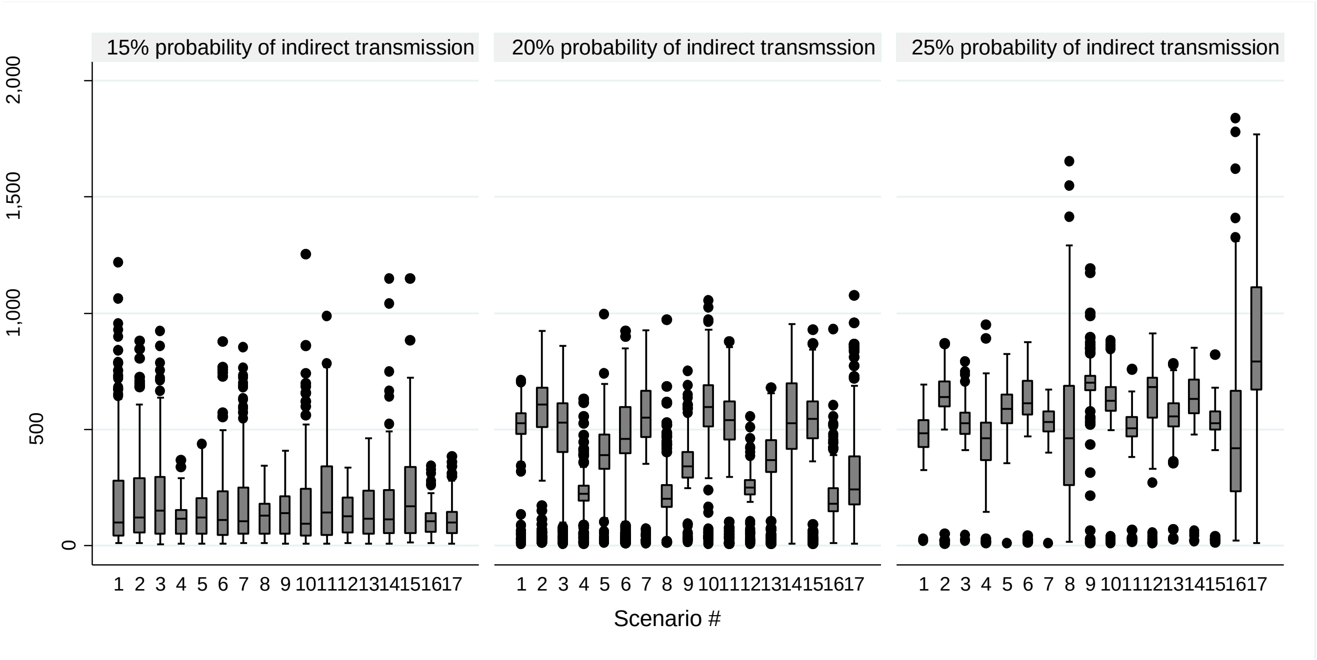
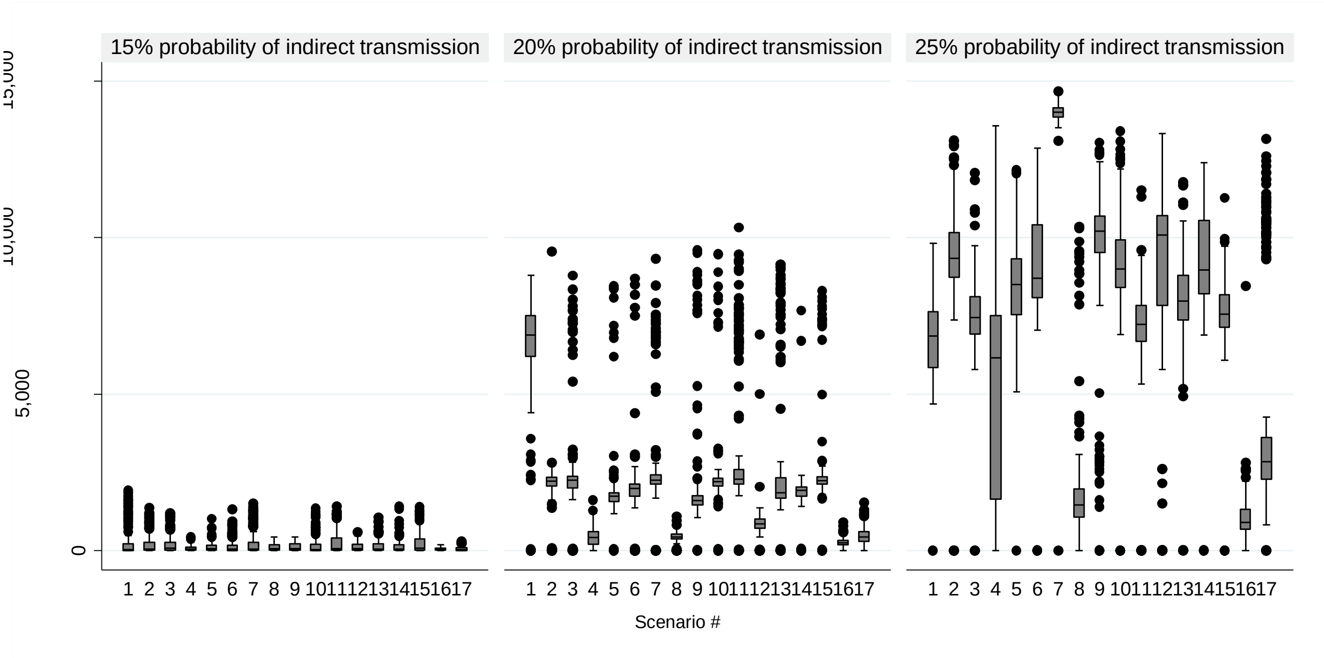


Figure 4. Box plots of the duration of the active disease phase for the sensitivity analysis of the probability of transmission given indirect contact is at 15%, 20%, and 25% for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



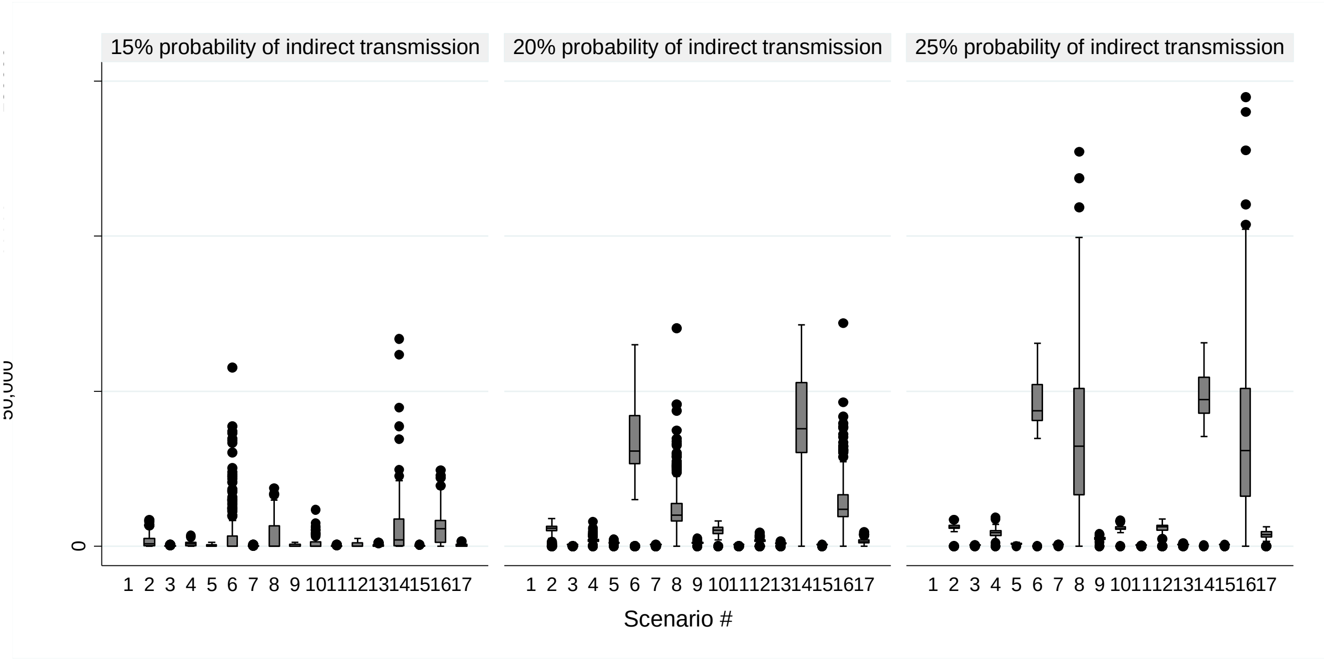
[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 5. Box plots of the number of herds depopulated for the sensitivity analysis of the probability of transmission given indirect contact at 15%, 20%, and 25% for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



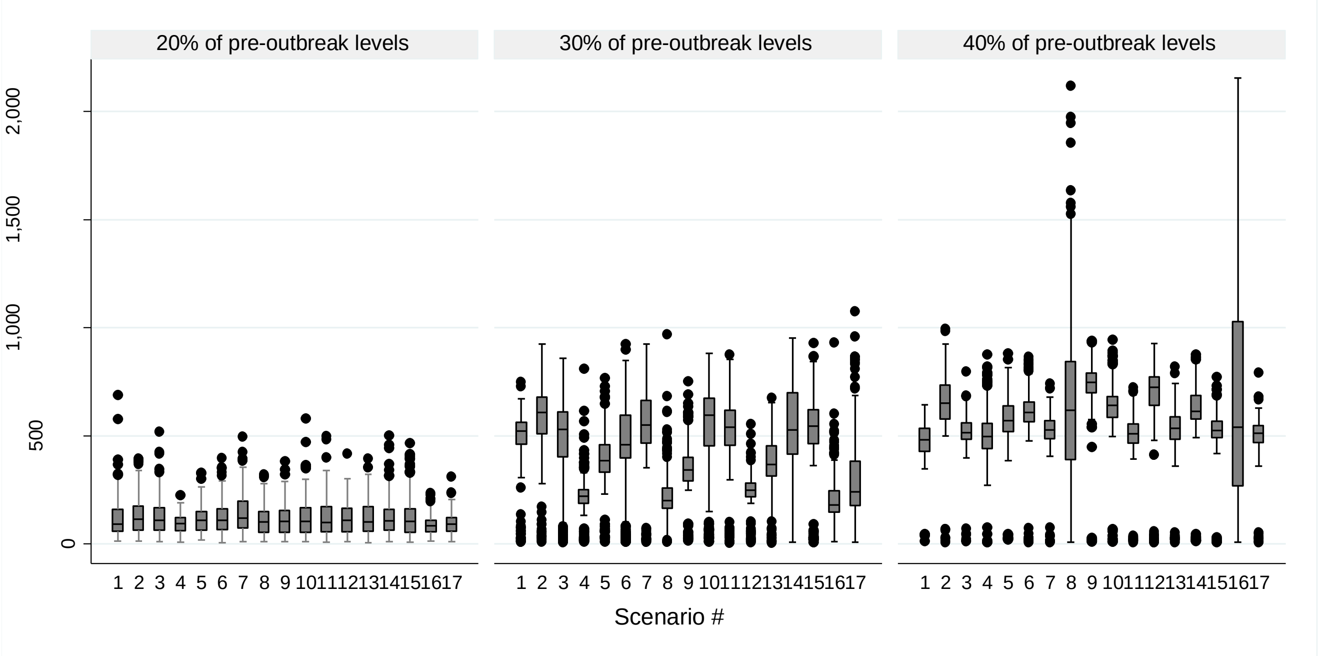
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 6. Box plots of the number of vaccinated herds for the sensitivity analysis of the probability of transmission given indirect contact is at 15%, 20%, and 25% for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



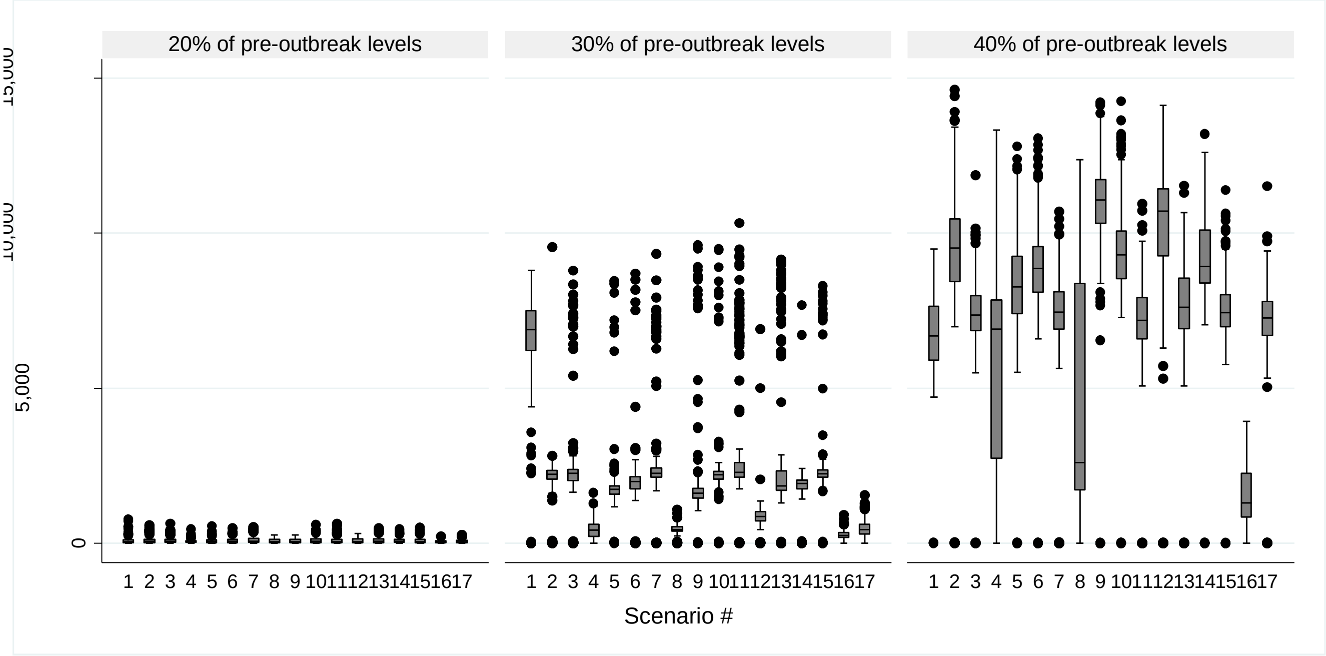
[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 7. Box plots of the duration of the active disease phase for the sensitivity analysis of the movement controls at 20%, 30%, and 40% of pre-outbreak levels for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



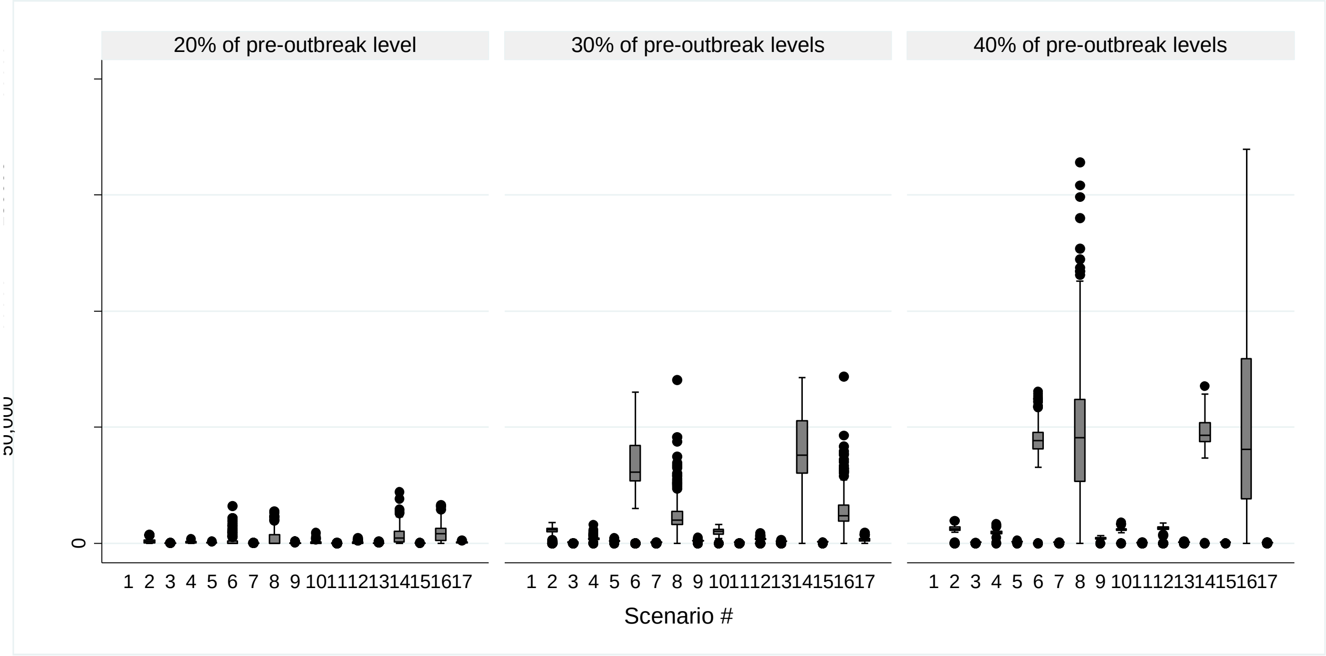
[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 8. Box plots of number of herds depopulated for the sensitivity analysis of the movement controls at 20%, 30%, and 40% of pre-outbreak levels for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



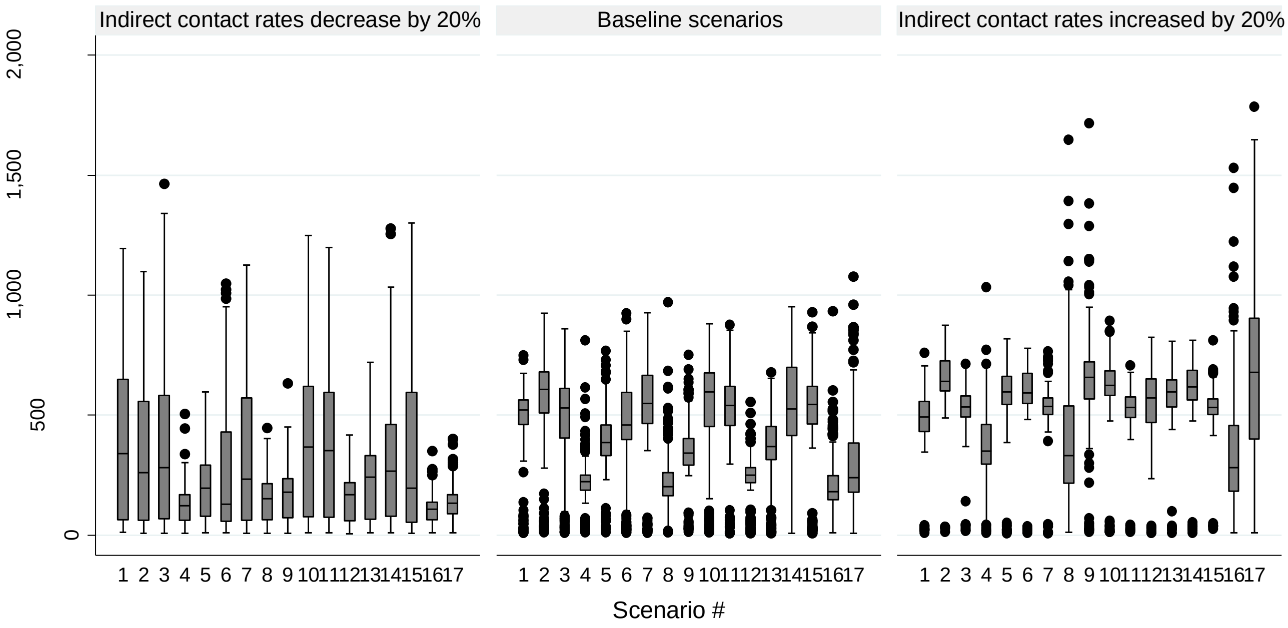
[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 9. Box plots of number of herds vaccinated for the sensitivity analysis of the indirect movement controls at 20%, 30%, and 40% of pre-outbreak levels for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



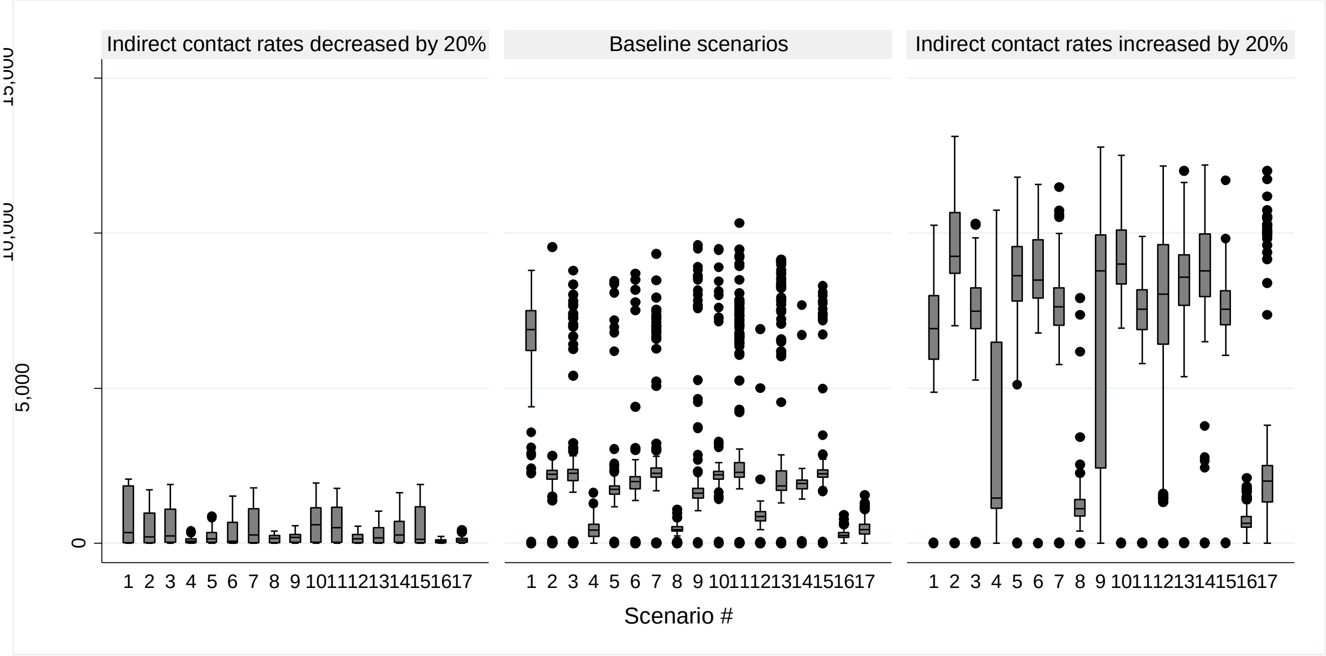
[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 10. Box plots of the duration of the active disease phase for the sensitivity analysis of the indirect contact rate and the baseline indirect contact rate for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



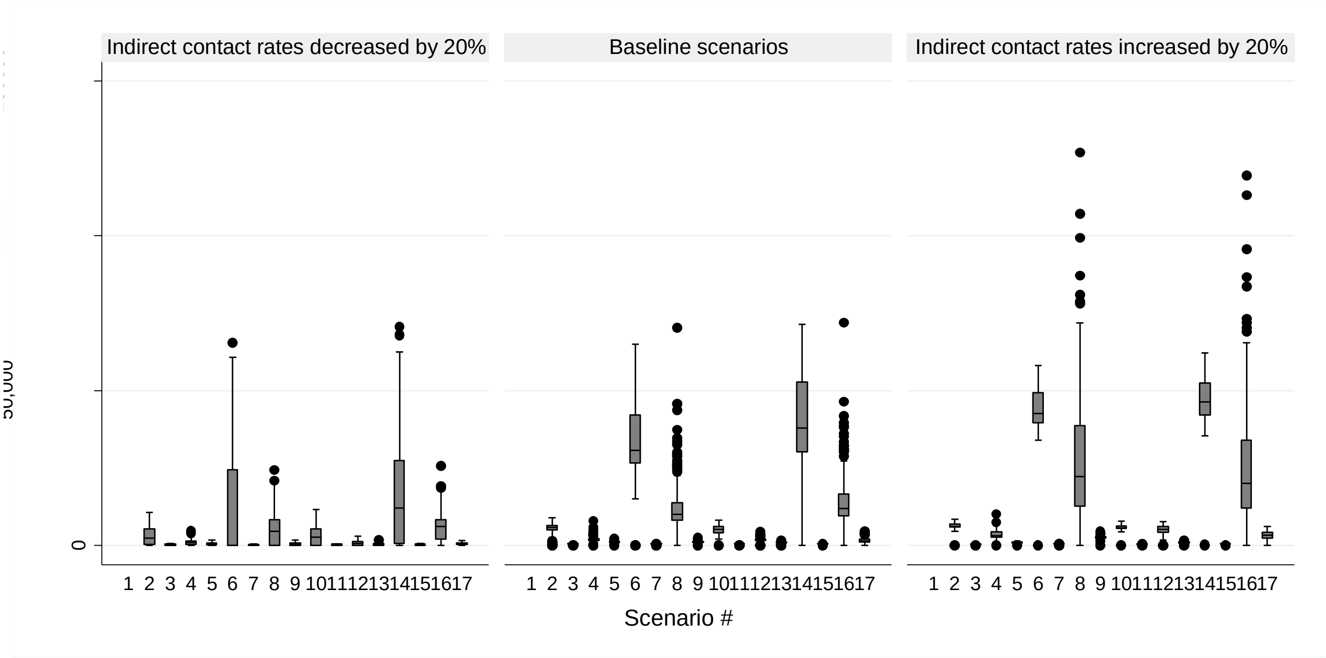
[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 11. Box plots of the number of herds depopulated for the sensitivity analysis of the indirect contact rate and the baseline indirect contact rate for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 12. Box plots of the number of herds vaccinated for the sensitivity analysis of the indirect contact rate and the baseline indirect contact rate for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



[a]The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.