Emergency vaccination use in a modelled foot and mouth disease outbreak in Minnesota

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Summary

Epidemiological modelling is an important approach used by the Veterinary Services of the United States Department of Agriculture Animal and Plant Health Inspection Service to evaluate the potential effectiveness of different strategies for handling foot and mouth disease (FMD). Identifying the potential spread of FMD by modelling an outbreak, and then considering the impacts of FMD vaccination, is important in helping to inform decision makers about the potential outcomes of vaccination programmes. The objective of this study was to evaluate emergency vaccination control strategies used in a simulated FMD outbreak in Minnesota. The North American Animal Disease Spread Model (NAADSM Version 3.2.18) was used to simulate the outbreak. Large-scale (1,500 herds per day) emergency vaccination reduced the size of the modelled outbreak in both swine and dairy production types, but the effect was larger when the outbreak began in a dairy herd. Large-scale vaccination also overcame limitations caused by delays in vaccine delivery. Thus, even if vaccination did not begin until 21 days into the outbreak, large-scale vaccination still reduced the size and duration of the outbreak. The quantity of vaccine used was markedly higher when large-scale vaccination was used, compared with small-scale (50 herds per day) vaccine administration. In addition, the number of animals and herds vaccinated in an outbreak originating in a herd of swine was substantially lower than in an outbreak beginning in a herd of dairy cattle.

Keywords

Epidemiology – FMD – Foot and Mouth Disease – Modelling – Vaccination.

Introduction

In the United States (USA), the approach for handling an outbreak of foot and mouth disease (FMD) is outlined in ‘Foot and Mouth Disease Response Plan: the Red Book’ (1), which can be viewed as a living document that can be revised and updated as more is learnt about this disease from scientific research and experiences in handling outbreaks worldwide. The Red Book outlines many aspects of how the USA will respond in the event of an outbreak, among which are four strategies that are not mutually exclusive: stamping out; stamping out modified with emergency vaccination-to-slaughter; stamping out modified with emergency vaccination-to-live; and emergency vaccination-to-live without stamping out. Thus, three of the four strategies require vaccination as a component of the response. These strategies parallel the development and use of vaccination that has been incorporated into policy guidance by the World Organisation for Animal Health

(OIE), and are consistent with response strategies used by many countries working to control and eventually eradicate FMD from within their borders (2, 3, 4, 5, 6, 7).

The USA is currently FMD-free and has been so since 1929 (1). Consequently, direct experience with the disease is limited to a tiny fraction of the veterinarians, scientists and producers who would be heavily engaged during an outbreak. Incident Commanders of potential FMD outbreaks have expressed considerable support for early vaccination as a response component (8). Indeed, 'intensive, large-scale food production systems are at risk of destruction and bankruptcy if traditional massive depopulation is pursued in a foreign animal disease response' (9).

The risk of FMD introduction through live animal imports is low (10); nonetheless, the disease could be introduced into the USA by many different means. Understanding the potential spread of FMD through outbreak modelling, together with considering the impacts of different responses, are important in informing decision makers about the potential consequences of alternative approaches.

Epidemiological modelling is one approach used by the United States Department of Agriculture (USDA) Veterinary Services (VS) to evaluate the potential effectiveness of different strategies for handling FMD and other foreign animal diseases. Modelling is particularly useful for diseases, such as FMD, of which there is little direct recent experience in the USA. Previous modelling of FMD in Minnesota (MN) found, in some instances, that an outbreak could result in large numbers of animals and farms becoming infected (11). In that study, more traditional approaches of FMD containment were considered, including quarantining infected farms, stopping movement orders in the entire livestock population of MN, and depopulation of infected herds. The objective of the present study was to evaluate emergency vaccination control strategies used in a simulated FMD outbreak in MN.

Materials and methods

The North American Animal Disease Spread Model (NAADSM Version 3.2.18) (12) was used to simulate an FMD outbreak in MN. Important vaccine explanatory variables included:

– vaccine delivery times ('shipment delay') (7, 14 or 21 days)

– the capacity to administer the vaccine (no vaccination, 50 herds per day or 1,500 herds per day)

– the time lapse (four or seven days) between vaccine administration and the development of effective vaccine immunity (hereafter referred to as 'immunity delay'.

These three vaccination-related parameters were compared for their impact on the following outcome variables:

– numbers of infected farms

– numbers of infected animals

– duration of active disease

– duration of outbreak.

Disease duration refers to the number of days of active spread of FMD; outbreak duration refers to the number of days from the beginning of the outbreak until completion of all disease control measures, even after disease spread has ceased. In the model used here, vaccination may continue after disease spread has ceased. Details of the model are explained in a companion paper (11) that describes the development of the epidemiological model and the outcomes associated with disease spread. In brief, MN subject-matter experts provided MN-specific data used to parameterise the NAADSM in order to model a MN outbreak and the associated use of vaccine. In that paper (11), the type of production system (dairy or large-scale swine production) in which the outbreak began was found to be important. The type of herd in which the outbreak started was therefore included as an explanatory variable.

Potential options for vaccination administration in the model included *i)* the use of official veterinary vaccinators or *ii)* the use of producers under the guidance of accredited veterinarians. Meetings held with the MN Board of Animal Health authorities found that local officials had a strong commitment to limit vaccine administration to official veterinary personnel only (Meeting with MN Incident Command Team, 9 August 2011). The maximum number of MN official teams available for emergency disease response was stated to be about 50 (on average, one herd vaccinated by each team per day). However, MN industry experts found that the livestock producers and their associated accredited veterinarians wanted direct involvement in vaccine administration in order to limit the number of individuals who would enter their farm premises, a particularly important consideration during the time of an outbreak (Production livestock industry expert meetings, 25 July [Cattle] and 26 July [Swine], 2011). If producers were to carry out vaccination themselves, vaccination of 80% of the MN susceptible animal population could be achieved within one week by setting dairy herds and large herds of swine (total number approximately 10,500) as the highest priority. Thus, the capacity for vaccination in the model was set at either 50 herds or 1,500 herds per day.

Shipment delay was estimated to be in the range of 7–21 days once an FMD outbreak had been identified. A member of the modelling team (Miller) worked with USDA personnel to determine realistic shipment delays. The minimum period of seven days is optimistic and would require an almost immediate decision to activate the North American FMD Vaccine Bank, where frozen FMD antigen is stored. Previous research has outlined the importance of rapid vaccination (13) in response to an FMD outbreak, with vaccine being most effective if administered by day 12 post-outbreak. However, it is possible that it could take as many as three weeks for the circumstances to have reached a point where it becomes clear to decision makers in the Incident Command that vaccination is appropriate.

Rodriguez and Gay (14) state that vaccines containing a minimum of six times the PD_{50} (protective dose that protects 50% of challenged animals) provide protection from challenge within four to seven days post-vaccination. Thus, the parameter for immunity delay was set at either four or seven days.

No definitive policy exists for determining when to implement FMD vaccination in the USA (1). Certainly, the size and speed of spread of an outbreak would influence the triggering of vaccine use (1, 8). Based on discussions held with USDA personnel and MN subject-matter experts, the vaccination trigger parameter was set at a detection threshold of five herds with FMD. This parameter prevented the use of vaccination in modelled outbreaks that were small enough to be contained by depopulation alone. This parameter works in conjunction with shipment delay. The time interval between the beginning of the outbreak and the beginning of vaccination is either the same as the shipment delay or the time it takes for 5 herds to become infected, whichever is longer. For example, if the shipment delay is 7 days and the fifth herd becomes infected on day 13, then vaccination commences on day 14. If the shipment delay is 7 days, and the fifth herd becomes infected on day 3, then vaccination commences on day 8.

When vaccination capacity was set at 50 herds per day, each detected herd triggered a 10-km vaccination ring. However, when capacity was set at 1,500 herds per day, the vaccination ring was set at 240 km. In both vaccination applications, overlapping vaccination rings did not result in repeated vaccination of already vaccinated herds. Herds were not vaccinated primarily on the basis of proximity to a detected herd but in accordance with the vaccination order parameter, which was a model parameter that set which production type would be vaccinated first, second and so on. Once vaccination was implemented within a given radius around the detected farm, the first farms vaccinated were dairy, followed by large swine, then beef, then small swine, and then small ruminants.

Statistical differences between means were evaluated using SAS version 9.2. Multivariate analysis of variance was used to assess mean differences associated with the following explanatory variables: type of production system in which the outbreak began (starting herd), vaccination scale (capacity), differences in immunity delay, and differences in shipment delay. Data associated with outbreak duration, number of farms infected, number of animals infected and disease duration were used as outcome variables. Interaction effects were also evaluated but are not included for discussion, because the overall complexity of interactions was beyond the scope and capability of the simulation. A *p* value of 0.05 was considered statistically significant.

Results

Large-scale (1,500 herds per day) emergency vaccination reduced the size of the modelled FMD outbreak for both production types (Figs 1 and 2), and the effect was larger when the outbreak began in a dairy herd than when it began in a swine herd (Figs 1 and 2). This was evident when outbreak size was measured as the number of farms infected (Fig. 1) or as the number of animals infected (Fig. 2). When the outbreak began in a dairy herd, the number of infected farms typically decreased by about half when large numbers of herds (1,500) were vaccinated per day, compared with small numbers of herds (50) (Fig. 1); the number of infected animals decreased by about 75% when compared with no vaccination (Fig. 2). In contrast, when the outbreak began in swine, large-scale vaccination decreased the number of infected farms by about 10% (Fig. 1) and the number of infected animals by about 25% (Fig. 2), compared with no vaccination. When large-scale vaccination was compared with baseline or small-scale vaccination, differences in all mean values were significant.

Regarding duration, when the modelled FMD outbreak began in a dairy herd, large-scale emergency vaccination was more effective than small-scale vaccination in reducing both outbreak duration and disease duration (Figs 3 and 4). Disease duration decreased by approximately 10–20 days, but showed little change for outbreaks that began in a swine herd (Fig. 3); outbreak duration decreased by about half in outbreaks that began in a dairy herd, but showed little change for outbreaks that began in a swine herd (Fig. 4).

Immunity delay did not have a noticeable effect on outcomes; the differences in outcome variables were not statistically significant (Figs 1, 2, 3, and 4).

The quantity of vaccine used was markedly higher when large-scale vaccination was compared with small-scale vaccination (Table I). The numbers of animals and herds vaccinated were substantially higher for outbreaks that began in a dairy herd than in a swine herd.

Discussion

All outcomes support vaccination on a large scale

The value of large-scale vaccination was confirmed in the present study, as in others (4, 6, 7). Use of large-scale vaccination overcame the limitations of shipment delay: thus, even when vaccination did not begin until 14 or 21 days into the outbreak, large-scale vaccination still reduced the size and duration of the outbreak, regardless of whether it began in a dairy or a swine herd, although the effect was substantially larger when the outbreak began in a dairy herd (Figs 3 and 4 respectively).

When the outbreak began in a dairy herd, large-scale vaccination came close to being equivalent to mass (blanket) vaccination (1) of all animals. The requirement of a detection threshold of five infected herds caused vaccination to be used in approximately 99% of outbreaks that began in a dairy herd. Mean numbers of animals vaccinated in those circumstances represented approximately 95% of the total population, which is almost the equivalent of mass vaccination. In contrast, outbreaks that began in a swine herd resulted in approximately 50% of outbreaks being controlled by vaccination.

In emergency response, considerable time and complexity could be saved with mass vaccination rather than ring vaccination. These findings suggest that mass vaccination should be considered in FMD outbreaks, particularly for outbreaks that begin in a dairy herd. Furthermore, mass vaccination has been used in other countries to control FMD outbreaks (6).

Large-scale vaccination was associated with decreased duration of active FMD spread (reduced by 15–21 days), with approximately 160 fewer farms and approximately 45,000 fewer animals infected on average when an outbreak began in a dairy farm. This reduction in infected farms and animals is important, because it decreases the numbers of premises and animals depopulated as part of FMD control/eradication efforts. This outcome was consistent across the variables of shipment delay and immunity delay.

Large-scale vaccination is achievable only with use of industry vaccinators

Large-scale vaccination could only be achieved in MN (and probably many other states) by using industry (farm-specific) vaccinators. Many models do not account for the spread of disease by control personnel, and implicitly assume such individuals cannot spread the disease. But each person entering a farm has a risk of transmitting the infection. By using farm personnel, instead of personnel moving between farms, the risk of transmission will be reduced. This is not possible in countries where 'official veterinarians' are required to administer the vaccines and conduct physical checks on each farm within some specified radius of infected or vaccinated farms.

Immunity delay has little influence on outcomes

Immunity delay (four or seven days) had little impact when large-scale emergency vaccination was implemented. Thus, large-scale vaccination can overcome some problems that are likely to occur in an emergency response, such as delays in vaccine distribution and the inherent delays in development of immunity after vaccination. More notably, large-scale vaccination, even when started 21 days into the outbreak, was effective at reducing the duration and size of the outbreak.

Model validity, other studies and important vaccination considerations

In any modelling study, the question of model validity is always an important consideration, and the only means of reasonable assessment is by comparison with other studies. The present results are in basic agreement with the findings of Backer *et al.* (4, 5) in a model of regaining FMD-free status. In their assessment of whether vaccination-to-live poses a higher risk of undetected infected animals than non-vaccination strategies, vaccination-to-live was shown to be as effective as pre-emptive slaughter, which is in agreement with the results of other studies (4, 5, 15).

An FMD-free status is desired by all countries where exports of animals or animal products are important. To prevent transmission of FMD between countries, the OIE has developed standards and guidelines for affected countries to regain FMD-free status; these allow a more rapid return to FMD-free status when an outbreak is controlled by depopulation and/or slaughter, or when emergency vaccination is implemented and all vaccinated animals are promptly slaughtered, compared with a scenario where control is achieved through vaccination without slaughter of vaccinated animals (16). In the latter case, a waiting period of six months following the last case or last vaccination is required before a country can regain FMD-free status. However, De Vos *et al.* (17) question the value of this guidance by demonstrating that resuming swine exports after a six-month waiting period did not reduce the probability of exporting an infected carcass any more than one-month or three-month waiting periods.

Many countries around the world incorporate vaccination into their emergency response plans, including vaccination-to-live strategies. Stamping out can be successful if the disease has not spread too widely and if the density of livestock in the area is relatively low (2, 4). Brito *et al.* (6) reported on within-herd transmission of FMD and the protective effect of vaccination in the 2001 Argentina outbreak, which was one of the largest ever to be controlled through a systematic mass-vaccination campaign. The protective effect of vaccination was evident in the lower rate of within-herd transmission among vaccinated herds, and this impact extended even to herds where vaccine was given shortly before or after initial infection.

In an extensive review of the eradication of FMD, Sutmoller *et al.* (2) state that vaccination drastically reduces rates of incidence and morbidity, as well as the amount of virus circulating during outbreaks. However, there is some concern about diagnostic complications and carrier issues associated with FMD vaccination. Nonetheless, the real epidemiological risk of a link between vaccination and associated spread of FMD from carrier animals appears markedly less than is often feared. Thus, Tenzin *et al.* quantified the transmission risk from carriers to susceptible animals at 0.0256 infections per carrier per month (18). Moreover, the development and use of genetically altered vaccines that permit differentiation of infected from vaccinated animals will alleviate some of these fears.

The question of controlling FMD through vaccination during an epidemic has been addressed in a review by Hutber *et al.* (19), who report that vaccination may reduce the amount of excreted and circulating virus, and that the virulence of the epidemic strain will influence the value of vaccination. It is suggested that, with effective management, slaughter/depopulation of infected animals can be achieved within 48 hours, an assumption that is not valid for the USA. The size of the large intensive animal operations in the USA makes depopulation of these facilities impossible within that time, unless depopulation strategies that are not normally considered are used. Well over half of all swine are in herds of more than 5,000 animals, and over 85% are in herds of more than 2,000 animals (20). Almost half of all dairy cows in the USA are in herds of over 500 animals, and 21.6% are in herds of more than 2,000 animals (21). These numbers have steadily changed in the USA as herd numbers have declined and herd sizes have increased.

Many factors influence the use of vaccination, but one factor that is particularly important to consider is whether the outbreak appears to be uncontrolled by depopulation. For example, in the 2010 FMD outbreak in Japan (7), emergency vaccination of all cattle and swine was implemented when the number of farms awaiting livestock destruction exceeded 100 during a two-week period at the peak of the epidemic. By comparison, vaccination was implemented in the MN model when the number of infected farms reached a threshold of five.

Differences between swine and dairy herds

Another important finding in the present study was the difference between dairy herds and swine herds. Outbreaks that began in swine were consistently smaller in size (fewer infected farms/animals) and shorter in duration of both disease and outbreak. There is consensus among industry experts that many risk parameters for disease transmission are lower in swine than in dairy herds (11), which is the probable explanation for these findings. Although swine have long been thought to be virus amplifiers, results from the present modelling study suggest that airborne transmission from swine operations is not a major influence on FMD spread.

Vaccination capacity

The available capacity for vaccination is crucial when considering vaccine use for reducing the scale of an FMD outbreak (22). Without sufficient quantities of vaccine and adequate resources for its administration, the effectiveness of a vaccination response is hampered. Among some of the more important considerations are that sufficient numbers of teams are trained to administer vaccines in ways that do not compromise appropriate vaccine handling, maintenance of premises biosecurity, and safety of personnel and animals. Analysis of the MN model suggests that it is advantageous to vaccinate large numbers of herds rapidly. Such an approach entails providing accredited veterinarians with vaccine and, under their oversight and especially in larger herds, using vaccination teams made up of farm employees. This ensures that larger numbers of animals can be vaccinated in a shorter period of time.

Economic and other considerations in foot and mouth disease vaccination

Backer *et al.* (15) modelled an FMD outbreak in the Netherlands, where approximately 17 million animals (cattle, hogs, sheep) were at risk for the disease. They showed that 2-km or 5-km ring vaccination is the economically preferred strategy, rather than a 1-km pre-emptive culling strategy, for control of FMD in areas densely populated by livestock. Culling may be the preferred strategy in areas sparsely populated by livestock. The Netherlands has a higher animal density than MN, where total farm numbers were 46,650 and total animal numbers were 11.2 million head in 2007 (11). Consideration of the economics of FMD management in MN was beyond the scope the present study.

Differences in management in different geographical areas of MN, based on animal density, were not considered. Some areas of MN have a very high density of animals, such as the approximately seven million swine in the southern third of the state, which might be considered similar to the animal density in the Netherlands. This aspect of the structure of animal industries in MN may have partly contributed to the impacts observed in the present study.

The economic impact of the disease is substantial: in FMD-endemic countries the total global visible production losses and vaccination costs are US$6.5–21 billion/year; in FMD-free countries >US$1.4 billion/year (23). The complications involved in responding to FMD and the high economic consequences when an outbreak does occur are part of what makes FMD a so-called ‘wicked’ problem (24). Knight-Jones and Rushton estimated the worldwide annual number of vaccine doses at 2.35 billion, with China administering 68% of all doses (23). Nevertheless, one economic study examining the use of emergency FMD vaccine in the USA did not find vaccination to be economically advantageous (25). However, the assumptions were conservative, directly determining the economic implications. It was assumed that all vaccinated animals would be depopulated, all infected and direct-contact animals would be depopulated, and all export markets would be lost. Estimation of the economic impact in the modelled MN outbreak was beyond the scope of the present study.

The number of infected herds is an important consideration (Fig. 1), because every additional herd (regardless of size) requires attention, and certain response activities complicate the response efforts. For example, emergency personnel that visit an infected farm could subsequently have their own movements controlled until a certain period of time has elapsed.

Numbers of animals in infected herds is also an important consideration, because indemnity payments in the USA have historically been based on numbers of animals depopulated (5). The number of infected animals typically decreased by 60–75% with large-scale vaccination when the outbreak began in a dairy herd (Fig. 2). In the present analyses, all the animals in an infected herd were assumed to be depopulated. In the event of an outbreak, producers would receive indemnity payments for each of these animals; they could also be entitled to additional payments if animals in at-risk, but non-infected farms, were also depopulated; however, this circumstance was not considered in the present study.

The overall risk of introduction of FMD into the USA is unknown. The risk through importation of live animals has been estimated as extremely small, equivalent to one introduction every 241 years (10). It may be difficult to justify governmental spending on vaccination for events of such low probability (10). However, although risks from other sources are unknown, they are certainly not zero. These sources include import of animal products, accidental introduction by US citizens who travel abroad or by visitors from abroad travelling to the USA, or from intentional introduction in a bioterrorist event. Thus, studies such as the present modelling of the use of FMD vaccine and its impact on outbreak outcomes remain valuable for response and policy decisions.

Perhaps some of the most compelling reasons for considering FMD vaccination as a component of FMD response are not about the direct implications in terms of decreased size or economic impact of FMD outbreaks but rather that 'for obvious ethical reasons, there is a strong desire to reduce reliance on large-scale culling of animals to control future outbreaks of FMD' (26).

In the USA, the approach to an FMD outbreak would be 'a science- and risk-based approach that protects public and animal health and stabilizes animal agriculture, the food supply, and the economy … at all times' (1). This approach includes many factors influencing the use of FMD vaccination: resources for vaccination, speed and degree of spread of the outbreak, public acceptance of stamping out, and assessments and economic analyses of competing control strategies (1).

Conclusions

Vaccination is a powerful tool in the control of FMD outbreaks as it reduces transmission and may be the major contributor to mitigation of risk. All outcomes show that vaccination on a large scale is more effective than that on a small scale. The present study supports these statements, especially in the dense populations of production animals found in MN, where average herd sizes are generally larger than in many countries around the world. Specifically, large-scale emergency vaccination reduced the size of the modelled FMD outbreak in MN for both dairy and swine production. In addition, the effectiveness of large-scale vaccination is supported by its use in the Netherlands (2001) (3), Japan (2010) (7), and many other countries (2, 6, 23). Large-scale vaccination could overcome impacts from delays in beginning vaccination or immunity delay. A full risk assessment was beyond the scope of this study.

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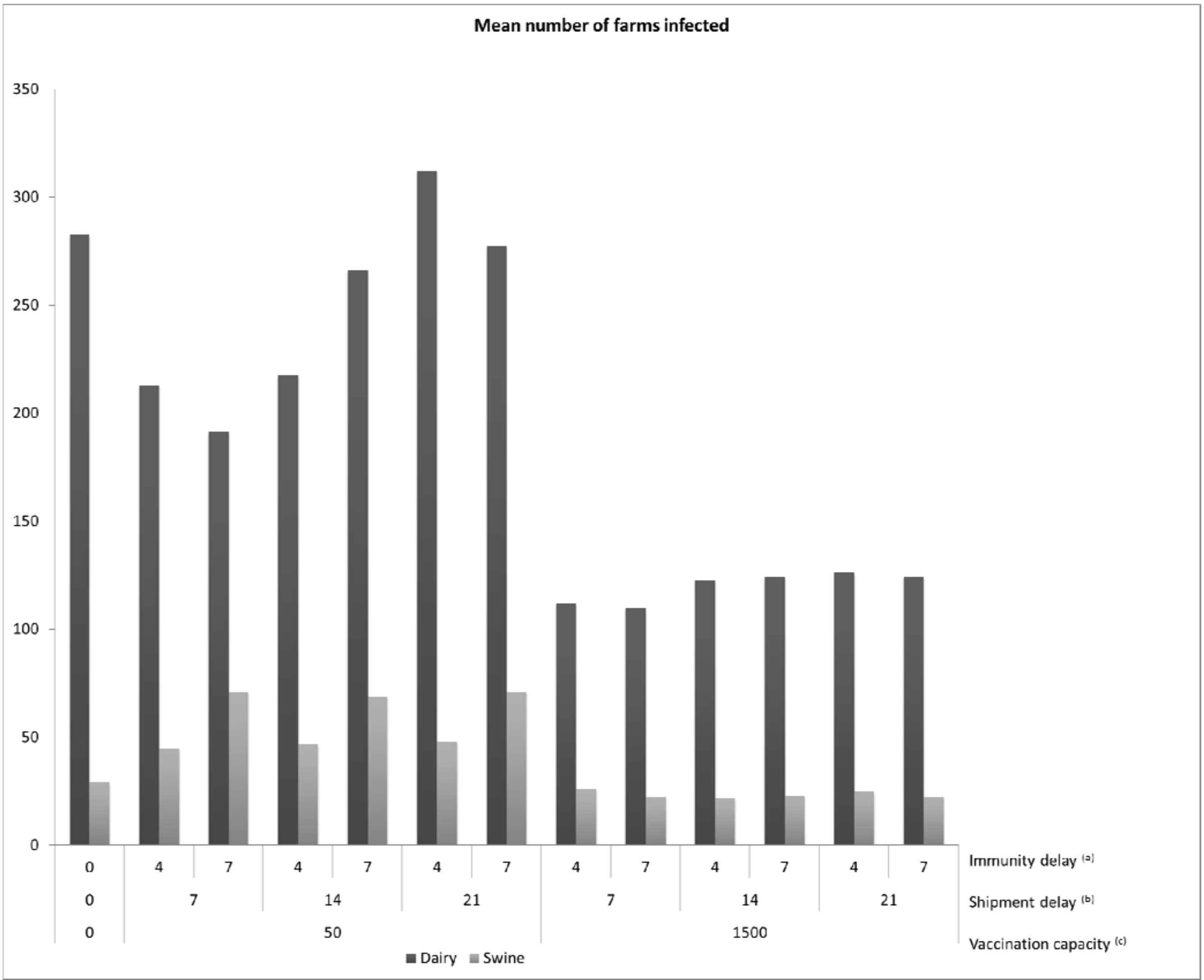
Table I

Numbers of herds and animals vaccinated against foot and mouth disease

	Vaccination capacity: 50 herds per day				Vaccination capacity: 1,500 herds per day			
	Shipment delay	Immunity delay	Mean no. of herds vaccinated	Mean no. of animals vaccinated	Shipment delay	Immunity delay	Mean no. of herds vaccinated	Mean no. of animals vaccinated
Dairy	7	4	4,265	317,924	7	4	44,524	10,718,776
	7	7	4,062	588,519	7	7	44,536	10,743,929
	14	4	4,148	661,423	14	4	44,316	10,662,883
	14	7	4,255	788,644	14	7	44,653	10,785,577
	21	4	4,169	926,603	21	4	44,455	10,677,123
	21	7	4,400	827,727	21	7	44,447	10,693,196
Swine	7	4	856	510,193	7	4	24,534	6,063,964
	7	7	964	303,656	7	7	24,394	6,054,455
	14	4	914	232,694	14	4	23,231	5,731,652
	14	7	1,018	308,214	14	7	24,061	5,939,555
	21	4	977	243,539	21	4	24,187	5,962,989
	21	7	1,110	361,650	21	7	23,030	5,677,338



a) number of days between vaccine administration and the development of effective vaccine immunity

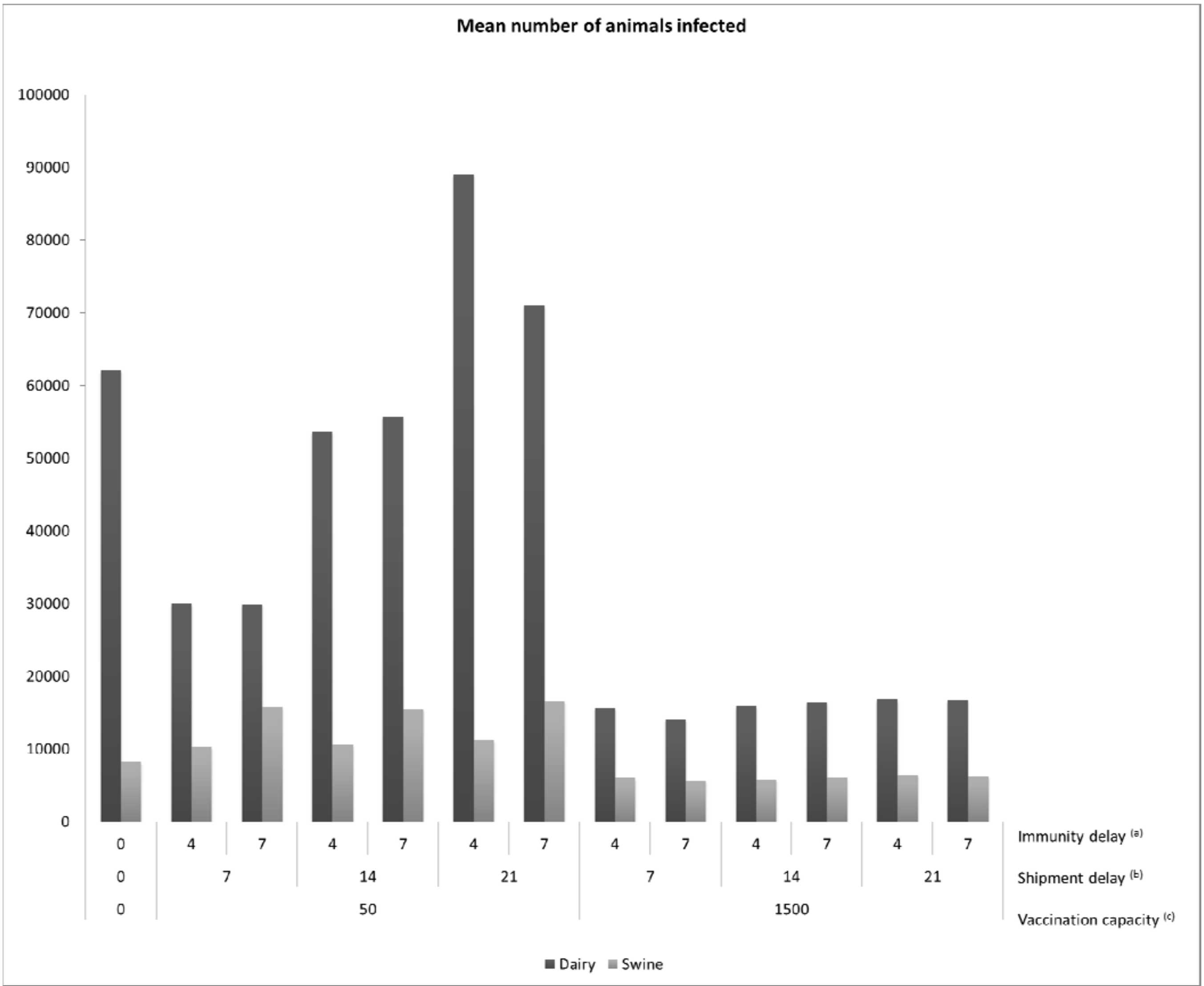
b) number of days between the identification of an outbreak and the delivery of vaccine

c) number of herds vaccinated per day

Fig. 1

The effect of different model parameters on the mean number of infected farms

Minnesota livestock population was 11,228,000 animals in 46,650 herds (11)



a) number of days between vaccine administration and the development of effective vaccine immunity

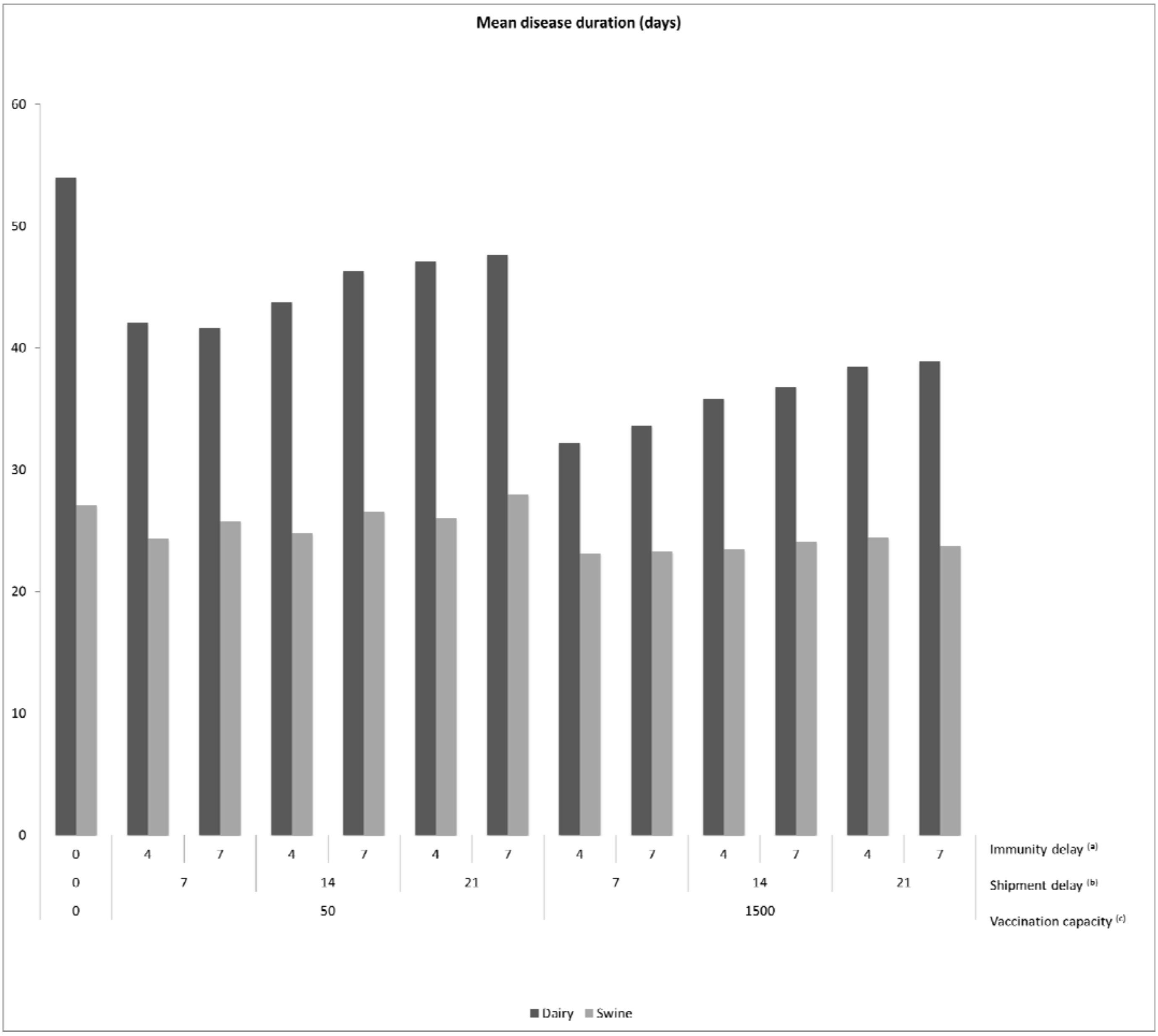
b) number of days between the identification of an outbreak and the delivery of vaccine

c) number of herds vaccinated per day

Fig. 2

The effect of different model parameters on the mean number of infected animals

Minnesota livestock population was 11,228,000 animals in 46,650 herds (11)



a) number of days between vaccine administration and the development of effective vaccine immunity

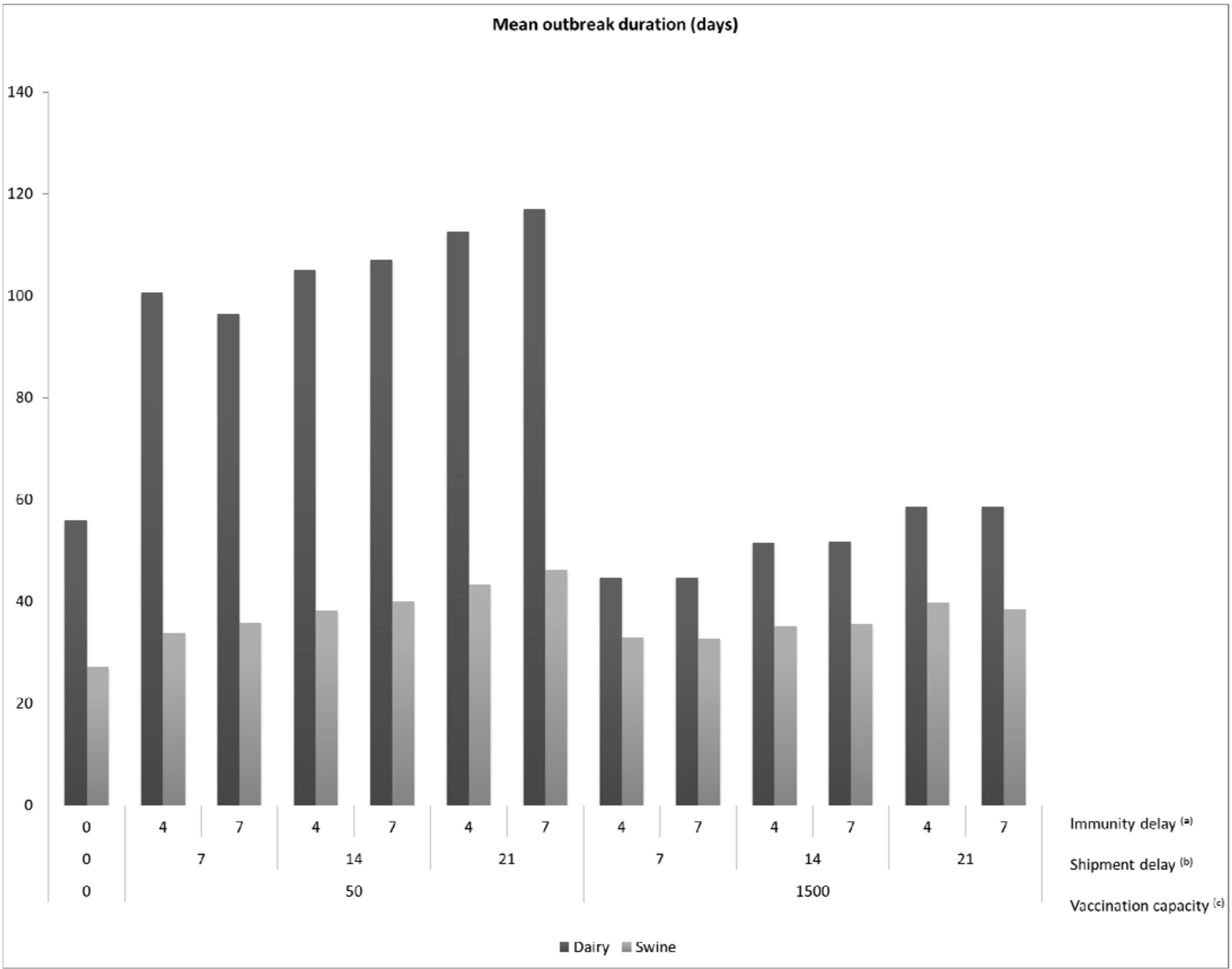
b) number of days between the identification of an outbreak and the delivery of vaccine

c) number of herds vaccinated per day

Fig. 3

The effect of different model parameters on disease duration

Minnesota livestock population was 11,228,000 animals in 46,650 herds (11)



a) number of days between vaccine administration and the development of effective vaccine immunity

b) number of days between the identification of an outbreak and the delivery of vaccine

c) number of herds vaccinated per day

Fig. 4

The effect of different model parameters on outbreak duration

Minnesota livestock population was 11,228,000 animals in 46,650 herds (11)