MODELING MANAGEMENT OF FOOT AND MOUTH DISEASE IN THE CENTRAL UNITED STATES

by

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B.A., Dordt College, 2004
D.V.M., Kansas State University, 2008
M.P.H., Kansas State University, 2008

AN ABSTRACT OF A DISSERTATION

submitted in partial fulfillment of the requirements for the degree

DOCTOR OF PHILOSOPHY

Department of Diagnostic Medicine and Pathobiology
College of Veterinary Medicine

KANSAS STATE UNIVERSITY
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Abstract

The last outbreak for Foot and Mouth Disease (FMD) in the United States (U.S.) was in 1929. Since that time the U.S. has not had any exposure to the disease or vaccination, creating a very susceptible livestock population. The central U.S. has a large susceptible livestock population including cattle, swine, sheep, and goats. The impact of FMD in the U.S. would be devastating. Simulation modeling is the only avenue available to study the potential impacts of an introduction in the U.S.

Simulation models are dependent on accurate estimates of the frequency and distance distribution of contacts between livestock operations to provide valid model results for planning and decision making including the relative importance of different control strategies. Due to limited data on livestock movement rates and distance distribution for contacts a survey was conducted of livestock producers in Colorado and Kansas. These data fill a need for region specific contact rates to provide parameters for modeling a foreign animal disease.

FMD outbreaks often require quarantine, depopulation and disposal of whole herds in order to prevent the continued spread of the disease. Experts were included in a Delphi survey and round table discussion to critically evaluate the feasibility of depopulating a large feedlot. No clearly acceptable method of rapidly depopulating a large feedlot was identified. Participants agreed that regardless of the method used for depopulation of cattle in a large feedlot, it would be very difficult to complete the task quickly, humanely, and be able to dispose of the carcasses in a timely fashion.

Simulation models were developed to assess the impact of livestock herd types and vaccination on FMD outbreaks in the central U.S. using the North American Animal Disease Spread Model (NAADSM), a spatially explicit, stochastic state-transition simulation model.

Simulation scenarios with large vaccination zones had decreased outbreak length and number of herds destroyed. Vaccination did not provide additional benefit to control compared to depopulation alone when biosecurity and movement controls were high, however the ability to achieve high levels of biosecurity and movement control may be limited by labor and animal welfare concerns.

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Table of Contents

List of Figures

List of Tables

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Chapter 1 - Literature Review – Epidemiology, control methods, and predictive modeling of Foot and Mouth Disease

Introduction

The Foot and Mouth Disease (FMD) virus is a highly contagious RNA virus that has seven serotypes and over 60 subtypes. It primarily affects cloven-hoofed animals, such as cattle, pigs, sheep, and goats. Despite the low mortality, the economic impact of the disease is severe due to the decrease in production and more importantly the loss of international trade. FMD is among the most significant diseases and can damage not only a national economy but also has significant global implications (Forman et al., 2009; Knight-Jones and Rushton, 2013). It is endemic in much of Africa and Asia, and sporadic in South America. Countries currently free of FMD, like the United States (U.S.), take every precaution to prevent entry of the disease so it is a major constraint to international trade. The U.S. has a livestock population that is naïve to FMD with the last outbreak occurring in 1929 (Graves, 1979). In the U.S. the concern of FMD virus re-introduction and the potential economic impacts have risen with the increase of international travel of individuals, and trade of animals and animal products and the emergence of domestic and international terrorists groups that may desire to harm U.S. agriculture (Neher, 1999; Knowles, 2011; Yeh et al., 2013). Additional concern with FMD is that the virus can spread rapidly through susceptible livestock populations prior to the appearance of clinical signs (Burrows, 1968b; Burrows et al., 1981) causing early detection prior to the spread of the disease difficult.

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, 2007b). Since FMD is a foreign animal disease in North America, simulation modeling is the only avenue available to study the potential impacts of an introduction and is an essential tool to evaluate control methods (Bates et al., 2001; 2003b; c; Schoenbaum and Disney, 2003; Harvey et al., 2007). Many disease modeling programs have been developed to simulate the spread of disease in populations. 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; Dickey et al., 2008; Premashthira et al., 2011).

Control measures, such as, movement restrictions, increased biosecurity, depopulation, pre-emptive culling, and vaccination have been implemented to decrease the spread of the outbreak in various combinations (Ferguson et al., 2001a; 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 the implementation, the workforce capacity, and the available resources, the control strategies will vary. In the face of a FMD outbreak, well- informed decisions on the best control strategy will need to be made.

Foot and Mouth Disease

Etiology

FMD virus is a member of the genus Aphthovirus in the Picornaviridae family. There are seven immunologically distinct serotypes of FMD virus: O, A, C, South African Territories (SAT) 1, 2, 3, and Asia 1, and over 60 strains. The serotypes are not cross-protective so the location of each is important however new strains occasionally develop spontaneously.

Additionally cross-protection between strains varies by antigenic similarity. FMD virus serotypes and strains vary within each geographic region.

Distribution

Type O, A, and Asia 1 are common throughout Asia and O, A, C have been found in Europe and South America. SAT strains 1, 2, and 3 have been identified in Africa and the Middle East has had A, O, Asia 1, and SAT 1. South America is a meat exporting continent that has worked hard to eliminate the disease but it is still found sporadically throughout the continent. FMD is endemic in much of Africa and Asia. Australia, North America, and Europe have been free for a number of years and New Zealand has never had FMD.

Pathogenesis

All cloven-hoofed animals are susceptible to FMD virus. The virus gains entrance though the respiratory tract or through abrasions in epithelium of, for example, the oral cavity, feet or teats (Sutmoller et al., 1968; Sellers and Parker, 1969; McVicar and Sutmoller, 1976). The clinical signs of the disease are vesicular lesions around the coronary band of the foot, mucosa of the mouth, and on the teats and udder. Occasionally, the vesicles may occur on the vulva, prepuce, or pressure points on the legs. Other clinical signs include salivation, lameness, fever, lethargy, weight loss, and anorexia. The clinical signs can vary in severity based on species and strain of FMD. Sheep do not develop as severe of clinical signs and often the disease can be misdiagnosed, for example, as ulcerations on gums due to grazing, orf, facial eczema, trauma, or foot rot (Ayers et al., 2001; Black et al., 2004). Pigs typically have the most severe lesions on their feet with the first symptom being lameness progressing to ataxia and the shedding of claws (Yoon et al., 2012). Cattle usually become febrile and develop lesions in the oral cavity and muzzle. Frequent clinical signs in cattle are excessive salivation, nasal discharge, mastitis and loss of milk production subsequent to teat lesions. There are also reported differences in the strains. For example in the 1997 Taiwan outbreak serotype O caused severe lesions in pigs but no clinical signs were seen in small ruminants or cattle (Dunn and Donaldson, 1997; Yang et al., 1999) while in the U.K. 2001 outbreak serotype O caused clinical signs in ruminants (Sutmoller et al., 2003).

FMD has high morbidity and low mortality in adults but in young animals a high mortality can be seen due to multifocal necrosis of the myocardium (Alexandersen et al., 2003). In countries with a naïve livestock population the virus can spread rapidly and be associated with high morbidity rates. The incubation period of FMD is 2-14 days but is dependent on the strain of the virus, virus dose, route of transmission, animal species, and environmental conditions (Garland and Donaldson, 1990; Alexandersen et al., 2003). The virus initially infects and grows in the pharyngeal area (McVicar and Sutmoller, 1976; Burrows et al., 1981) and has been isolated from secretions and excretions for 1-5 days prior to clinical signs and after the appearance of clinical signs (Burrows, 1968a; Sellers and Parker, 1969; Burrows et al., 1981; Donaldson, 1997). In a more recent study, Charleston et al. (2011) found that cattle infected with FMD virus are substantially less likely to be infectious before showing clinical signs than previous studies had found, thus the likelihood of transmission may be dramatically decreased if control can be implemented just 24 hours earlier. This would greatly increase the effectiveness of early response to control an outbreak; however, the estimates are contrary to previous research and should be cautiously applied. Charleston et al. (2011) included only 8 pairs of cows to measure the transmission of a single strain of FMD virus so their limited observations need additional confirmation and may be consistent with the previous estimates. Additionally the results of transmission of one strain of FMD virus cannot be inferred to all strains of the virus

(Kitching, 2005). Inappropriate application of the results from this study in modeling may substantially underestimate the transmission of FMD and subsequently outbreak size and resource needs if they are not representative.

Epidemiology

Transmission

The virus is spread commonly to susceptible animals by the movement of infected animals. The susceptible animals are infected via inhalation of infectious droplets coming from the breath of infected animals (Sellers, 1971; Sellers et al., 1971b). The FMD virus can also be transmitted through abrasions in the skin or mucosa. Cattle and pigs may become infected with as little as 1 International Unit of the virus by injection (Burrows, 1966; Sellers, 1971). The virus can be shed by nasal discharge, exhaled air, saliva, lesion tissue, urine, feces, semen, and milk and tends to drop quickly by day 5-7 after the development of clinical signs. This coincides with the drop in virus titers and the first development of antibodies (Graves et al., 1971). Cattle excrete the virus in milk for several days before the clinical signs of the disease become apparent but with the proper control methods such as pasteurization the spread of FMD in the milk can be prevented (Donaldson, 1997).

Airborne transmission between farms without the movement of animals is not as common but can occur under certain climatic conditions. Favorable conditions for airborne spread are a relative humidity of at least 55% and minimal mixing of the air by turbulence and convection (Alexandersen et al., 2003). It is believed that large amounts of excreted infectious particles behave like a fine dust that spreads over premises and stick to fomites (Sutmoller et al., 2003). Plumes of the virus have been determined to disperse by wind over long distances (up to 60 km over land and 250 km over water) (Hugh-Jones and Wright, 1970; Donaldson et al., 1982;

Gloster et al., 2011). Airborne spread between farms is not as common as direct contact or feeding of contaminated products but in ideal environmental conditions it is uncontrollable (Donaldson et al., 1982). The airborne spread of the virus can vary due to susceptibility of animals, level of virus excreted by infected animals, and species (Sutmoller et al., 2003).

FMD virus does differ significantly in transmission between infected animals due to difference in shedding of virus among species, serotype/strain virulence, and the timing of appearance of clinical signs (Kitching, 2005; Honhold et al., 2011). Pigs exhale the largest amount of virus and are especially a concern for airborne transmission of the virus (Sellers and Parker, 1969; Sellers et al., 1971b; Alexandersen et al., 2003). However, pigs require as much as 6,000 Tissue Culture Infective Doses 50 (TCID50) for aerosolized infection (Alexandersen et al., 2002a; Kitching et al., 2005). Cattle as well as sheep are highly susceptible to infection by the aerosol route requiring only 10 TCID50 (McVicar and Sutmoller, 1968; Kitching, 2005). Cattle on the other hand are the most likely species to become infected with the virus and are generally the first species to show clinical signs in an outbreak. Cattle appear to be at a higher risk of infection because they have a higher respiratory volume than sheep (Kitching et al., 2005). In comparison to swine, ruminants produce at least 3,000 times less aerosolized virus a day during the early clinical phase of the virus (Kitching et al., 2005). The threat of aerosol transmission was demonstrated in 1981 when aerosol virus spread from infected pigs in France, across the Island of Jersey where cattle were infected, and then to an island off the coast of England (Donaldson et al., 1982).

FMD virus also differs in transmission between strains (Kitching, 2005). A study comparing three strains of FMDV in pigs, using controlled direct contact found that transmission took 14 hours longer for serotypes Asia 1 and O compared to A. Additionally with Asia 1 serotype not all the contact pigs were infected after an 18 hour direct contact, exposure between infected pigs and naïve pigs (Pacheco et al., 2012). In the field, a serotype O strain isolated from Kinmen Island in the Republic of China did not cause disease in cattle, a species that usually is very susceptible (Knowles et al., 2001a). The difference among serotypes could have implications for control methods, vaccine testing, and disease modeling.

Dissemination

The FMD virus can be spread between herds directly by movement of infected livestock, and through indirect contacts through people, or contaminated material such as equipment, vehicles, or clothing and by animal products (milk, meat, semen) (Cottral, 1969; Sellers, 1971; Gibbens et al., 2001; Fevre et al., 2006; Ellis-Iversen et al., 2011). The movement of livestock has long been recognized as an important route of the spread of disease (Woolhouse et al., 2001; Ortiz-Pelaez et al., 2006; Velthuis and Mourits, 2007; Dube et al., 2009). In 2001 a shipment of calves from Ireland led to a FMD outbreak in the West of France and the Netherlands (Sutmoller et al., 2003) and the 2001 U.K. outbreak spread throughout the country through the long-distance movement of infected sheep (Gibbens et al., 2001). Indirect contacts have played a role in outbreaks as well, during the U.K. 1967-1968 outbreak, the movement of milk was found to be a major hazard in the spread of the disease (Dawson, 1970; Hedger and Dawson, 1970). The movement of milk could cause further spread either through feeding infected milk to animals on another farm or through indirect contact of the milk tanker during connection to the bulk tank, dip stick measurement, displacement of air during tank filling, or vacuum-operated bulk tanker discharge systems (Dawson, 1970). FMD has also been spread by the ingestion of contaminated fodder (Kitching et al., 2005), unheated waste food (Knowles et al., 2001b), and imported straw was implicated as the source of the 2000 outbreak in Korea (Sugiura et al., 2001).

The dissemination of FMD can vary by region or country due to differences in agriculture production systems. Within the U.S. there are regional differences in production types, management systems, operation size distributions, distance distributions that make comparison between regions difficult. Unfortunately due to the variation in both the number and frequency the contacts of similar farms, it is difficult to capture the livestock contact. Some farms are highly connected with frequent direct and indirect contacts while others have very few contacts (Brennan et al., 2008). In order to understand the possible spread of a highly infectious disease such as FMD, understanding the contact structure among animals and/or farms in a population is important including regional differences. Often there is little knowledge of what contacts (direct and indirect) exist between farms.

Some research has been done to better understand the contacts between farms but as expected results vary by region and by production type (Dickey et al., 2008; Ribbens et al., 2009; Tildesley et al., 2011). The livestock industry is heterogeneous requiring livestock movement to be studied at the country or regional level. Several countries such as the United Kingdom, Canada, Japan, Australia, and Brazil have implemented an electronic identification system to track the movement of livestock in order to have traceability within the food system. These databases also enable researchers to study animal movements. Other countries that do not have access to such a database must rely on questionnaires and surveys to livestock owners in order to understand the movements that occur in the industry.

Countries with electronic livestock movement databases have data to develop networks of livestock movements and the connections between premises. In the contact networks the unit of interest is the holding premises, and the relationship is the movement which produces paths on which infectious diseases can spread (Dubé et al., 2011a). By determining the network structure of a population you can determine a number of individual measures that may correlate with the risk of infection which is valuable in disease surveillance and control methods (Christley et al., 2005). This is important because a contact network with a short average path length will exhibit fast disease spread (Shirley and Rushton, 2005). In a contact network a path length is the minimal number of steps that are needed to connect two farms. The shorter the path length between two farms, the more likely one farm will become infected, should the other one already be infected (Kiss et al., 2006). Additionally, the more movements between farms, the more opportunities there are to transmit disease. Contact network analysis can be a useful tool for epidemiologists to gain a better understanding of livestock movements and the information also can be used to help parameterize disease spread models to produce more valid results.

Countries that do not have access to livestock movement databases must rely on periodic survey information obtained from producers on the frequency of movements on and off farms to gain an understanding of the possible spread of FMD. Studies conducted in New Zealand, the Netherlands, California, and Texas have identified and quantified these contacts with surveys. Due to the diversity of in the agriculture systems there are differences among the study regions. A study in the Netherlands found that on average 91 direct and indirect contacts occurred per farm for all types during a 2 week period with large numbers of individual pigs being moved (Nielen et al., 1996) compared to New Zealand where 50 contacts of people, animals, and materials were reported during a 2 week period (Sanson et al., 1993). In two U.S. surveys the contacts were broken down by herd type to capture the variation in production systems in the regions. In the Panhandle of Texas the average number of direct contacts was less than 2 direct contacts in a 2 week period for large cow/calf operations and large dairies. The operation with the highest number of direct contacts was small feedlots (<1,000 head) with 14 direct contacts in

2 weeks (Ward et al., 2009; Hagerman et al., 2013). A survey of producers in 3 counties in central California reported large dairies averaged approximately 9 direct contacts in a 2 week period. Large swine operations in the same 3 counties in California had 9 direct contacts in a 2 week period (Bates et al., 2001). The indirect contacts also varied by production type and region in the U.S. In the Texas Panhandle large feedlots with ≥50,000 head had the highest number at 630 indirect contacts in 2 weeks (Ward et al., 2009; Hagerman et al., 2013). In California, Bates et al. (2001) found that dairy calf and heifer ranches with ≥250 calves had the greatest number of indirect contacts at 284 in 2 weeks. Dairy calf ranches in the Texas Panhandle study reported 70 indirect contacts in a 2 week period. Other differences in the indirect contacts by region existed among cow/calf, small ruminant, and backyard herds with the operations in the Texas Panhandle having a higher number of indirect contacts compared to the herds in the California survey. The variability illustrates the complexity of understanding the possible spread of a FMD outbreak but also stresses the need for further region specific data collection. Due to the regional differences among livestock operations and management practices in the U.S. predicting disease dissemination will require ongoing local data collection of contact relationships and premises type (Dickey et al., 2008).

There can be seasonality in livestock movement patterns as well. In Great Britain, September and August are intense trading months and if an epidemic would begin during this time it has the potential to be widespread and reach many different parts of the livestock network (Kiss et al., 2006). In Scotland, spread of an infectious disease through livestock movements is low, but distinct cyclical patterns are present with peaks in May and August (Tildesley et al., 2011). With the seasonality of livestock movements there is also seasonality of indirect contacts. Survey results of California beef producers found a pattern of cattle movements from primary premises to other locations at the time of cattle going to pastures for grazing. This movement of cattle coincided with an increase in numbers of seasonal employees reported by some respondents. An increase in movement of animals as well as an increase in indirect contacts could lead to an increased disease risk (Marshall et al., 2009).

Furthermore, hubs, such as auction markets, within a network can play a key role in maintaining the connectivity of farms (Shirley and Rushton, 2005) and result in wide spread dissemination of infectious agents (Fevre et al., 2006). McLaws and Ribble (2007) identified movements through auction markets as the most critical factor that contributed to the unusual magnitude of very large epidemics when studying 24 epidemics, between 1992 and 2003, in countries that had previously been free of FMD. These results agree with a simulation study which demonstrated that only small outbreaks are possible in Great Britain without the amplification of an auction market (Green et al., 2006).

In a survey of California beef producers, more than 40% of livestock movements were to an auction market (Marshall et al., 2009) and another study in 3 counties of California found that 32% of the livestock sold at the auction markets were destined for a location ≥ 60 km away (Bates et al., 2001). In the U.K., farms are also highly interconnected with very active auction markets that have large numbers of animals passing through (Kao et al., 2006; Volkova et al., 2011). In a contact network analysis of cattle movements in Great Britain from January 2002 and December 31, 2004, Robinson and Christley (2007) found that 41% of cattle movements from single operation through an auction market were dispersed to between 2 and 4 different livestock operations. Additionally it was found that cattle moved from a single operation as a group could be dispersed to up to 62 holdings on a single day. The same study reported that movements through markets covered longer distances than movements that were farm-to-farm.

This would allow wide distribution of highly contagious disease such as FMD. Auction markets are not the only hubs that can be within a contact network though. Individual farms with frequent movements can also play a key role in the dissemination of an infection in livestock populations (Ortiz-Pelaez et al., 2006).

The distance of movements also varies by region which can likewise lead to wider dissemination of a disease outbreak. Surveys in both the Netherlands and New Zealand reported >50% of direct contacts were within 10 km (Sanson et al., 1993; Nielen et al., 1996). The distance of movements though is more of concern in North America. In Ontario, Canada dairy movements covered a maximum distance of 1417 km (Dube et al., 2008). In a region of California it was found that dairies, dairy calf and heifer ranches, and large swine producers had frequent indirect contact with animals on other livestock facilities located at a distance of up to 105 km (Bates et al., 2001). A third of respondents to a beef producer survey in California reported that cattle were shipped to or received from other states, and a median value of these interstate movements was twice per year (Marshall et al., 2009). Lastly in the U.S. it was found that cattle tend to be moved towards the center of the country (Forde et al., 1998) demonstrating the movement of cattle to the Midwestern states with a high density of feedlots. With more than 50% of the total U.S. sales of cattle and calves coming from Texas, Kansas, Nebraska, Iowa, and Colorado (USDA-NASS, 2007a), an introduction of a disease to this region would be devastating to producers as well as the local, state, and national economy.

Finally, indirect contact spread may also occur through people. Sellers et al. (Sellers et al., 1971a) found that after inhalation of virus-rich aerosols, FMD virus can survive in the human respiratory tract and be transmitted. Later studies contradicted those results and found the transmission can be prevented if farm workers or investigators change into clean outerwear and wash their hands, and no virus was found in the human respiratory tract (Amass et al., 2003; Amass et al., 2004). Good biosecurity of workers and other people handling the livestock is extremely important in the prevention of the spread of FMD.

Persistence of FMD

A further concern of FMD is the persistence of the virus. The FMD virus can survive in milk and milk products, meat, frozen bone marrow or lymph nodes, and it can remain active in rich organic materials under moist cool temperatures. However no outbreak has been attributed to heat treated milk products (De Leeuw et al., 1978). Relative humidity levels of about 55%, cool temperatures, and pH range of 7.0 - 8.5 support prolonged survival in infected aerosols and on fomites (Sellers et al., 1971b; Donaldson, 1986). The virus has been found to survive in straw up to 15 weeks (Cottral et al., 1960).

Persistent or carrier cases of FMD have been observed where the virus was isolated from the pharynx at least 28 days after being infected (Alexandersen et al., 2002b). Experimentally ruminants have been found to be carriers (Gaggero and Sutmoller, 1965; Burrows, 1966; 1968b; Sutmoller et al., 1968) with the African buffalo found to be a carrier of FMD for at least 5 years (Hedger, 1972; Condy et al., 1985; Hedger and Condy, 1985). The only reports of transmission from carrier animals were to cattle in Zimbabwe (Thomson et al., 1984; Hedger and Condy, 1985). The reasons for lack of transmission are uncertain (Thomson, 1996). The carrier period varies in length by species; cattle may be carriers for up to 12 months, and sheep and goats up to 9 months (Condy et al., 1985). Lastly the concern of spread due to a carrier animal has decreased after experimental data demonstrated that transmission occurs from carrier animals to susceptible animals at very low frequencies and currently in unidentified circumstances (Davies, 2002).

Outbreaks

Outbreaks of FMD have occurred in every region of the world containing livestock with the exception of New Zealand (Grubman and Baxt, 2004). In endemic countries, the disease has a low mortality rate but the frequency of outbreaks and the large numbers of livestock affected results in an ongoing high economic impact (Knight-Jones and Rushton, 2013). In free countries the impact of a FMD outbreak would be devastating as well and is a constant threat. Taiwan, after being free of the disease for over 68 years, had a FMD outbreak in 1997 that was estimated to cost $378.6 million (Yang et al., 1999). In 2001 the U.K. had an outbreak after being free for 34 years and the estimated number of productive animal lives lost was 8 million due to the number of pregnant animals that were culled (Sutmoller et al., 2003). The total estimated cost of the 2001 U.K. outbreak was $6 to $10 billion (Anderson, 2002). Shortly after the outbreak started in the U.K. it spread through the shipment of animals to the Netherlands. The outbreak was much smaller compared to the U.K. outbreak but it caused infection in 26 herds and resulted in the depopulation and disposal of 267,992 animals on 2,763 farms (Bouma et al., 2003). South American countries have had a continuous battle with FMD, and in 2000, Brazil had an outbreak resulting in approximately 11,000 head of livestock being depopulated followed by an outbreak in Uruguay in 2001 that cost $13.6 million to eradicate (Sutmoller et al., 2003). Despite measures and controls in place many countries have been devastated by FMD leading to much research on control and eradication of the disease.

Control and eradication methods

Surveillance and Detection

Surveillance programs are essential in early detection of a FMD outbreak. The large magnitude of the 2001 U.K. outbreak has been attributed to having an estimated 57 herds infected prior to the first case being reported (Ferguson et al., 2001b; Gibbens and Wilesmith, 2002; Thompson et al., 2002; Haydon et al., 2003). A similar delay in detection was seen in the large 1997 outbreak in Taiwan (Carpenter et al., 2011) and the 1951-1952 outbreak in Canada (Sellers and Daggupaty, 1990).

In simulation models of FMD outbreaks in the U.S., surveillance leading to early detection has been found to be important to reducing the impact of an outbreak (Bates et al., 2003c; Ward et al., 2009) and risk-based surveillance systems offers a more efficient approach to early disease detection and management of outbreaks (Kao et al., 2006; Stark et al., 2006). The current program in the U.S. relies on recognition and reporting of clinical signs by producers, caretakers, meat inspectors, or veterinarians (Bates et al., 2003d) which is a passive surveillance program. Countries with recent outbreaks such as the U.K., Taiwan, and Argentina at the time relied on the same method of surveillance (Bates et al., 2003d). The concern with this method of surveillance is that the first observers of the animals must be able to recognize the clinical signs and the importance of reporting the disease. This concern was demonstrated in a study of a possible FMD introduction at a state fair in California that found the disease would likely go undetected until after the animals had left the fair allowing for possible wide dissemination of the virus (Carpenter et al., 2007). An alternative to the passive surveillance method would be to include testing for FMD in current active surveillance systems that collect and screen samples for various other diseases that affect livestock such as brucellosis and pseudorabies (Bates et al., 2003d). Due to the cost of an active surveillance program an approach is needed to determine disease priorities for surveillance based on risk.

Tracing also plays a critical role in controlling an outbreak. After an outbreak has been detected, tracing of all animals in contact with the infected herd is needed to prevent further dissemination. In a simulation model of an outbreak in the Texas High Plains, rapid and effective tracing accomplished in 2 days led to a reduction in the number of animals depopulated, animals under movement restrictions, and government control cost compared to scenarios with tracing accomplished in 10 days (Hagerman et al., 2013). The relative benefit of a livestock movement tracing system was dependent on herd type in model results based on California. There was little benefit in early tracing from beef premises and swine premises, but substantial benefits with calf and heifer raising, goat, and sheep herds if the movements in the previous 10 days could be identified in a single day of tracing (Mardones et al., 2012). The same study found that electronic records were more effective for tracing than paper-based records. A concern is that without an electronic animal identification system in place, accomplishing rapid tracing during an outbreak may be difficult in less than 10 days. Furthermore in a California model a coordinated electronic national animal identification system program and a 48-hour traceability of all herds infected through animal shipments decreased the severity of a FMD outbreak (Mardones et al., 2012). In addition to the constraints of not having electronic records, manpower constraints are a concern in the ability to have an effective and efficient tracing and surveillance program and delays could lead to increased infections (Mardones et al., 2012). Manpower constraints will increase if paper records are used to trace animal movements compared to electronic records due to the need for more people and additional time to accomplish the physical task. In the U.K. 2001 outbreak, the lack of accurate movement data was one of the main obstacles to disease control in the initial stages (Gibbens et al., 2001). This led to the establishment of an animal movement licensing system to record livestock movements for the movements of sheep, pig, and goats in addition to the existing cattle tracing system

(Ortiz-Pelaez et al., 2006). Tracing is a possible critical area of control but in order to effectively utilize it organized and clear records will be needed.

Control methods

Successful disease control requires good disease surveillance, rapid diagnosis, and quick intervention (Keeling et al., 2001). Quick intervention with control methods, such as, movement restrictions, increased biosecurity, depopulation, pre-emptive culling, and vaccination have been implemented in various combinations to decrease the spread of the outbreak (Ferguson et al., 2001a; 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).

Identified risk factors of an introduction of infectious diseases to farms by direct contact with livestock, include the contact with stray, purchased or brought-in-animals, and boarding or co-mingling with other herds (Sanderson et al., 2000; Van Schaik et al., 2002; Bates et al., 2003b). Consequently working to control the spread of infectious diseases with animal movement restrictions and strict biosecurity has been critical. Studies have found that farmers will apply biosecurity measures if they consider them important/useful for their farms (Casal et al., 2007; Toma et al., 2013). After the 2000 FMD outbreak in Korea, farmers were educated on the importance of good biosecurity in the hope of preventing further outbreaks (Wee et al., 2004) and despite an outbreak in 2002 improvements were evident. Education is also needed in the U.S. Despite high direct and indirect contacts feedlots have been found to have poor implementation of biosecurity and bio-containment (Brandt et al., 2008). The effectiveness of biosecurity practiced on livestock facilities contribute to the size of a FMD epidemic both for livestock new to the herd prior to an outbreak being detected and after an outbreak to prevent further spread.

Movement restriction is also a critical control method in a FMD outbreak. During an infectious disease outbreak like FMD the first goal would be to stop the movement of livestock in order to prevent widespread dissemination of the virus (Giles, 2001). A simulation study of movement restrictions as a control method in outbreaks in the Netherlands found that the prevention of infectious contacts to other livestock areas by the implementation of movement restrictions resulted in a concentration of the epidemics in a particular area and in a reduction of the size of the epidemics (Velthuis and Mourits, 2007). With movement restrictions however animal welfare has to be considered (Laurence, 2002). During the 2001 FMD outbreak in the U.K. more than 6 million animals were culled for disease control or welfare problems resulting from animal movement restrictions (National Audit Office, 2005). All herds under a movement restriction are potentially at risk for welfare concerns due to stopping direct and indirect movements. Direct movement controls would certainly be a concern for swine operations that frequently are moving animals out of a barn to make room for the next group on a strict time schedule. Indirect contact movement controls would also be a concern for swine operations as well as dairy and feedlots that frequently have feed delivered. Due to the impact of movement restrictions on the agriculture industry, control methods must include multiple strategies and cannot rely on a complete stop of direct and indirect movements.

In areas with high density of cattle and pigs farms, the disease might spread regardless of movement restrictions through the virus being aerosolized, so control measures against sources of infection, such as immediate depopulation of infected farms are also essential (Howard and Donnelly, 2000; Muroga et al., 2013). Depopulation of herds reduces transmission by removing diagnosed and undiagnosed but infected animals while reducing the susceptible population (Ferguson et al., 2001a). Additionally, pre-emptive culling of herds that have had direct contact with a positive herd is generally considered a beneficial control method in the face of a FMD outbreak (Howard and Donnelly, 2000; Ferguson et al., 2001a; Morris et al., 2001). The depopulation of infected herds and pre-emptive culling of all herds that had direct contact with the infected herds or 'stamping out' was the first FMD control program which was established in 1892 in Britain (Sutmoller et al., 2003). In addition to its successful implementation in Europe it was also used in 1929 in the U.S. and in 1951-1952 outbreak in Canada (Sutmoller et al., 2003). The strategy of 'stamping-out' was not successful however in controlling the 1946 outbreak in Mexico. Despite assistance from the U.S., after 500,000 cattle and 380,000 sheep, goats, and pigs were depopulated there was out-cry from farmers (Machado Jr, 1969) halting the depopulation program. Vaccination was initiated to control the outbreak and the last animal was vaccinated in 1950.

Control of a FMD outbreak in a country that has been free of the disease is initially implemented by depopulation of infected herds and all in-contact animals, movement restrictions, disinfection of infected premises, and intense surveillance (Kitching et al., 2005). However as was necessary in the 1946 outbreak in Mexico, vaccination is another control method. During the 2001 Netherlands outbreak vaccination was also implemented to suppress the spread by vaccinating in-contact herds to gain time for pre-emptive culling (Velthuis and Mourits, 2007). Vaccination can be used in an emergency and also prophylactically to protect a population against a future outbreak. Vaccination without depopulation has been successfully used to eliminate an outbreak as was the case in the 2001 Uruguay outbreak (Sutmoller et al., 2003), but it is more widely used in conjunction with depopulation of infected and in-contact herds (Davies, 2002). The disadvantage of vaccination is the delay before protection of almost a week (Salt et al., 1998) and the potential increased length on time to return to free of FMD international trade status due to the difficulty of distinguishing vaccinated animals from natural infected animals. Due to international trade regulations countries that have World Health Organization (OIE) free of FMD status consider eradication methods such as depopulation only prior to initiating vaccination in the face of an outbreak. To recover FMD free status after an outbreak has occurred one of the following waiting periods is required to regain the status or where vaccination is not practiced:

1) Three months after the last case where a stamping-out policy and serological surveillance are applied
2) Three months after depopulation of all vaccinated animals where a stamping-out policy, emergency vaccination and serological surveillance are applied

Or,

3) Six months after the last case or last vaccination, where a stamping-out policy, emergency vaccination not followed by the depopulation of all vaccinated animals, and serological surveillance are applied, provided that surveillance survey based on detection of antibodies to nonstructural proteins of FMD virus demonstrates the absence of infection in the remaining vaccinated population (Office International des Epizooties/World Organization for Animal Health, 2012).

Despite some previous research finding vaccination protocols in the control of a FMD outbreak were not economically beneficial (Garner and Lack, 1995; Schoenbaum and Disney, 2003; Elbakidze et al., 2009) it has been used to control outbreaks. The 2010 outbreak in Japan resulted in 293 infected farms and nearly 300,000 infected animals, including vaccinated animals, being depopulated. To control further spread, emergency vaccination was done in a 10 km zone around infected cattle and pigs farms. After vaccination had begun, the number of detected herds detected per day decreased (Hayama et al., 2012). In the 2002 outbreak, Korea also quickly implemented vaccination as one of the control methods and contained the outbreak in 30 days (Wee et al., 2004). The Netherlands vaccinated animals in the face of the 2001 outbreak also to slow the spread of the disease and followed with depopulation of all vaccinated animals to regain FMD free trade status (Pluimers et al., 2002). In the U.S. the goal of the outbreak response will be to regain the FMD-free status but vaccination is included in guidelines to a FMD outbreak response for extensive outbreak. The highest priority will be ensuring a safe food supply and business continuity for livestock producers (USDA-APHIS, 2012).

Workforce capacity can limit the method and scale of disease control strategies (Morris et al., 2002). Vaccination requires less time and labor than are needed for depopulation and disposal of the carcasses. In the 2001 outbreak in the Netherlands the available workforce was not sufficient to provide adequate depopulation capacity (Bouma et al., 2003). In the 1997 Taiwan outbreak four major factors were reported as responsible for the rapid spread of FMD: inability to shut down livestock auction markets; long delays in depopulating the livestock on infected farms; high density of pig farms; and inadequate vaccine supply (Yang et al., 1999). The workforce needed for depopulation in a high density region such as the central U.S. is especially a concern. In a Texas Panhandle FMD exercise it was found that completing depopulation and disposal on premises within 72 hours and 96 hours, respectively, was not feasible due to the high livestock density (Texas Animal Health Commission, 2007). The number of individuals available during an outbreak and the type of herds infected may play a role in determining the appropriate control methods implemented.

Targeting high risk farms in control strategies could be beneficial in controlling the dissemination of FMD. The heterogeneities in the contact patterns on farms and their effect on the magnitude of R_o, imply that targeting interventions at farms contributing the most to R_o could be efficient (Volkova et al., 2010). Mass vaccination targeting high risk herds or herds with a higher number of direct and indirect contacts could greatly reduce the potential for a large epidemic (Keeling et al., 2003). Previous studies have found that large farms tend to have an increased risk of infection in the early stages of the epidemic. In the later stages of the epidemic the number of large susceptible farms decreases faster than the number of small susceptible farms. The large farms usually are located in areas with greater contacts and road density increasing their risk of infection as was seen in the 2001 UK outbreak (Ferguson et al., 2001b; Keeling et al., 2001). Similar results were found in the 2000 Japanese FMD outbreak where medium and larger cattle farms were found to have a greater risk of infection by local spread than did small cattle farms (Hayama et al., 2012). The proximity to infected herds also put farms at increased risk. In a New Zealand simulation model of a FMD outbreak the probability of farms within 10 km of an infected premise becoming infected was higher than those outside 10 km, suggesting increased monitoring for that distance would be beneficial in the face of an outbreak (Sanson et al., 1993). In the same study, in order to stop 95% of the direct movements a movement control radius of 100 km would be needed around the infected premise (Sanson et al., 1993). Control methods that target the high risk neighbors of an infected herd are critical despite variability among similar production systems (Keeling et al., 2001).

In the U.S. there is a need for clarification of the role of vaccination during a possible FMD outbreak. In a survey of experienced likely decision-makers in the event of an U.S. outbreak there was a lack of clarity regarding factors to consider before implementing a FMD vaccination campaign (Parent et al., 2011). Some respondents in the study favored initiating vaccination early in the outbreak, others late in the outbreak, and one did not want vaccination used as a control method. This lack of consensus on the situations where vaccine would be considered useful and the criteria for a decision to implement it is concerning. The criteria for a decision to implement vaccination is necessary in order to have a decision made in a timely manner, not delayed because of indecision or disagreement that could have been avoided. A study modeling the impact of FMD vaccination as a control method in a region of California found that vaccination must be implemented quickly in order to have maximum effectiveness (Bates et al., 2003c).

In the past the trade restrictions were in place due to the difficulty of distinguishing vaccinates and natural infected animals, and the concern of carrier animals. This made re-establishing freedom from FMD difficult. Recently, the U.S has developed a vaccine that enables vaccinated cattle to be distinguished from those that were naturally infected with the disease (Anonymous, October, 2012). Though not currently the case, such a vaccine could in the future make the depopulation of vaccinated animals unnecessary to regain trade status. Recent research and outbreak experience highlight the need for re-evaluation of the pre-planning strategies for a FMD outbreak in order to optimize the response.

Disease simulation modeling

Simulation models

Simulation models are valuable tools for evaluating potential disease spread, and the impact of control and eradication strategies (Garner and Hamilton, 2011; Mardones et al., 2012). Simple simulation models are easy to understand but are misleading if they do not appropriately represent the system. For this reason, complex models have been produced to try and better represent the spread of infectious diseases. Complex models also can be misleading though if they do not appropriately represent the system. Deterministic models are used where input parameters are specified by a single, fixed value. For example, deterministic models may be useful for finding equilibrium points and predicted outcomes. Stochastic models were later developed which led to a more accurate approximation of the epidemic wave (Bartlett, 1953; Bartlett, 1956). Stochastic models allow for variation by using a distribution for the input parameter instead of a single value in the deterministic models. Stochastic models may be used when parameter inputs are uncertain or variable so a range of possible values are included in the model as a probability distribution. The probability distributions allow for a more realistic way of describing variability and uncertainty in variables. Therefore, stochastic models generate a range of possible outcomes. Due to this, the stochastic models also allow estimation of the distribution of the total epidemic size and duration, and provide the best guidance for decision making (Carpenter, 2011; Miller and Parent, 2012).

Additionally, a simple model is non-spatial which assumes a random or homogenous contact relationship of individuals or herds without specifying any spatial location or relationship thus all units in the population are equally likely to interact. For relationships that are geographically non-random or heterogeneous a spatial model is necessary to simulate more accurate results. Modeling the spread of disease among herds located at fixed premises is an example of the need for increased spatial complexity to provide more realistic results because the probability of contact is related to the distance between farms (Carpenter, 2011). Models that presume homogeneity among livestock contacts may underrepresent actual movement patterns (Bigras-Poulin et al., 2006) and underestimate the initial rate of transmission (Christley et al., 2005). Even small levels of spatial heterogeneity can have large effects on epidemic behavior of diseases (Andersson, 1997). Spatial models reflect local spread of the epidemic better than non-spatial ones, even early in the epidemic, most likely due to contact probability related to interfarm distance and control methods coverage such as vaccination (Chowell et al., 2006). For spatial models to produce the most accurate results, spatial locations must be known or accurately estimated in aggregate for use in the model (Tildesley et al., 2010). For highly infectious diseases like FMD, transmission often occurs over relatively short distances so spatial structure of farm locations can play three roles: susceptible farms that are far from infected animals are at very little risk, local transmission and depletion of susceptible hosts can dramatically reduce the speed of the epidemic, and local control methods can be applied using proximity to infected animals (Tildesley et al., 2010).

During the 2001 U.K. FMD outbreak three main disease spread models were used to support the response efforts (Ferguson et al., 2001b; Kao, 2001; Keeling et al., 2001; Morris et al., 2001; Kao, 2002). Ferguson et al. (2001b) used an ordinary differential equation model that considers the number of farms in each disease state and the number of locally connected farms. The model assumes that all farms can weakly transmit the disease at random over long distances (Keeling, 2005). Both Keeling et al. (2001) and Morris et al. (2001) models are stochastic and all farms were uniquely identified. The Keeling model is simpler than the Morris model, using an approach that is relatively robust and facilitates better communication and understanding of transmission principles (Kao, 2002). The Morris model which is the base of the InterSpreadPlus model (Stevenson et al., 2013) is a large, complex and flexible model that is capable of estimating the influence of many factors on spread of infection influenced by many factors (Keeling, 2005). The Keeling model, which is based on transmission kernels, was modified to support modeling and planning for future outbreaks. The model concentrates on the spatial structure of the population considering farm size and livestock species as parameters affecting farm to farm susceptibility and transmission. The transmission kernel accounts for all transmission mechanisms simultaneously and provides a function of risk of transmission versus distance to an infected farm. The transmission kernel is determined empirically by epidemic data (Kao, 2002; Haydon et al., 2003; Rorres et al., 2010). It has been argued that once movement restrictions are in place the ‘proximity to the disease is the greatest risk factor for its secondary spread’ (Gibbens and Wilesmith, 2002; Bessell et al., 2008; Tildesley et al., 2012). Additionally it has been shown that when local spread predominates, the qualitative ranking of the control methods is not sensitive to the quantitative details of transmission (Keeling et al., 2001). The model can be used to rapidly evaluate control methods when contact rates among livestock premises are not known.

Additional disease spread models have been developed, Bates et al. (2003b; Carpenter et al., 2004) constructed a simulation model to predict the spread and control methods using spatio-temoporal simulations involving the random sampling of each probability distribution within the model. The results are output distributions from which statistics such as minimums, medians, and maximums can be obtained. For each time step in the simulation, the model calculates the risk of exposure for susceptible herds and the number of contacts originating from infected herds by considering the location, size, and species of each herd (Bates et al., 2003b). The North American Animal Disease Spread Model (NAADSM) (Schoenbaum and Disney, 2003; Harvey et al., 2007), AusSpread (Garner and Beckett, 2005), and the previously mentioned InterSpreadPlus (Stevenson et al., 2013) are stochastic, state-transition simulation models also developed to study the spread of highly contagious diseases such as FMD. The models require fixed locations, and contact rates, and contact distance distributions for herds that are dependent on the defined production type. The model user establishes the parameters for transition between disease states (e.g. susceptible, latent, subclinical, clinical immune), direct contacts, indirect contact, and airborne spread. The control methods are user defined as well and can include quarantine, movement restriction, depopulation, forward tracing, backward tracing, pre-emptive culling, vaccination, and surveillance. This requires substantial data to parameterize the model but allows for heterogeneous contact rates between herds and the results of the model can also be used to evaluate potential control strategies (Premashthira et al., 2011). In comparison to models that use a transmission kernel the parameter set is more extensive but easier to understand, while the transmission kernel is less intuitively understandable.

All models must be verified to ensure that the description of how a disease is spread in the study population has been translated correctly in the computer code (Reeves et al., 2011). Models that are used for decision making or scientific research should be expected to meet a high standard. Once a model is verified, validation is necessary to determine if the model portrays the process that it has been designed to represent. A model can be validated internally by making sure the outputs for the study population make epidemiological sense based on the parameters of the simulation. External validity however requires real world epidemic data to determine that the model results are comparable to the outcome. When epidemic data is not available for a country, it is necessary to determine how representative the simulation outputs are (Kelton and Law, 2000; Dube et al., 2007).

In order to validate and increase user-confidence in NAADSM, AusSpread, and InterSpreadPlus, relative validation exercises were done to compare the results and differences among the models (Dube et al., 2007; Sanson et al., 2011). For example, the AusSpread and InterSpreadPlus models allow for active and passive disease surveillance where the NAADSM model does not allow for active disease detection, only passive surveillance. Additionally NAADSM has no explicit way of including auction markets in the population however

InterSpreadPlus and AusSpread include the possibility of disease spread through the movement of animals through an auction for the purposes of non-slaughter sale.

The first ‘relative’ validation exercise was to compare the outputs of the models produced by simulation of a series of relatively simple scenarios within a hypothetical study population. The models were found to have agreement in terms of the number of premises predicted to become infected, the temporal onset of the infection, and the spatial distribution of infected premises despite there being statistical differences among model outputs (Dube et al., 2007). The second ‘relative’ validation exercise was to compare the models using more complex scenarios based on real farm data and actual livestock movement data (Sanson et al., 2011). There was consistency in the models’ outputs in the between scenario comparisons. In all the models the early use of ring vaccination resulted in the largest drop in number of infected premises compared to depopulation only scenarios. There were differences though in size of the outbreaks. The NAADSM model tended to have the larger outbreaks. One possible reason for this is in the AusSpread and the InterSpreadPlus models, infected but not yet detected herds could still send animals to detected premises, although they had no effect on the recipient herd’s status. In contrast, the NAADSM model always selects non-detected herds to receive movements, this could lead to an increase in disease transmission which produces larger outbreaks (Sanson et al., 2011). The exercises did demonstrated consistency among the models which increases user-confidence in them.

Models have been used to predict the spread and control of disease as well as aid decision makers in evaluating control strategies of a FMD outbreak if it were introduced to a naïve population (Howard and Donnelly, 2000; Ferguson et al., 2001a; Gibbens et al., 2001; Keeling et al., 2001; Bates et al., 2003c; Garner and Beckett, 2005; Ward et al., 2009; Tildesley et al., 2012). However the first use of models to make farm-by-farm real time decisions during an outbreak was in the 2001 U.K. FMD epidemic and the use of models has been criticized due to out-of-date parameters, poor quality data, and poor epidemic knowledge (Eddy, 2001; Green and Medley, 2002; Taylor et al., 2004; Kitching et al., 2006; Mansley et al., 2011). Despite the concerns of the use of disease spread simulation models and the recognized deficiencies of them there is value in studying the results in order to gain a perspective on disease control and prevention options but not for tactical decision making (Keeling, 2005; Miller and Parent, 2012).

A hindrance in modeling is the lack of parameters for the model including good demographic data, patterns and rates of animal, vehicle, and personnel movement (Woolhouse and Donaldson, 2001; Taylor, 2003; Miller and Parent, 2012). Despite the increased user-confidence in the models in order to have output that will be realistic for a region, reliable input parameters that are representative for the study population are necessary (Dubé et al., 2011b). Precise farm locations are not available in the U.S. but aggregate farm statistics are and models with aggregated data can play a role in informing policy decisions (Tildesley et al., 2010). Quantitative simulation models are also dependent on accurate estimates of the frequency and distance distribution of contacts between livestock operations to estimate disease spread and impact and to guide intervention plans (Spedding, 1988; Gibbens et al., 2001; Taylor, 2003; Harvey et al., 2007). Models based on expert opinion have inherent limitations (Ward et al., 2009) and responses from experts are highly variable leading to wide and flat probability distributions (Bates et al., 2003b). Modeling contacts between premises for the different regions will require ongoing local data collection of contact relationships and the type of premise (Dickey et al., 2008). A lack of data on the contact network when modeling an infectious disease like FMD leads to simplification of local and long-distance spread (Gerbier et al., 2002).

Epidemiological models can also be parameterized with historical data or data from past outbreaks to be used as a tutoring tool and for solving problems (Kitching et al., 2005). Again a model's results will depend largely on the parameters within it.

Models are important for policy decisions prior to an epidemic (Keeling, 2005). After the development of a model, validation is necessary to ensure that the model provides an adequate illustration of the process it is designed to represent by making biological sense, mimicking real life, not being overly sensitive to the influence of uncertain parameters as well as fitting the use for which it was designed (Taylor, 2003). A validated model can play an important role in defining policy in disease control strategies but collaboration with veterinarians, disease modelers, and epidemiologists is necessary to continue to the improve the models' accuracy.

Foot and Mouth Disease predictive modeling

Several models have been used to evaluate the spread of FMD (Keeling et al., 2001; Schoenbaum and Disney, 2003; Garner and Beckett, 2005; Beckett and Garner, 2007; Harvey et al., 2007; Kobayashi et al., 2007; Sanson et al., 2011; Stevenson et al., 2013). The aim of modeling FMD is to gain a better understanding of the behavior of an epidemic and to evaluate the effectiveness of control methods (Gerbier et al., 2002; Bates et al., 2003c; Carpenter, 2011).

In order to improve the contact parameters for epidemiological models of FMD, which frequently has been based on expert opinions and questionnaires (Schoenbaum and Disney, 2003; Dickey et al., 2008; Ribbens et al., 2009; Ward et al., 2009), The Bates et al. (2001) contact rates where used in later studies modeling the spread of FMD and impact of control methods (Bates et al., 2003b; c). In the 3 county region of California, results demonstrated that pre-emptive culling of herds with highest risk for exposure and vaccination of all animals in a specified radius from an infected herd decreased the size and duration of the outbreak compared with a no vaccination strategy (Bates et al., 2003c). An economic analysis of the same region found that the cost of a FMD epidemic could range from $4.3 million to $3.5 billion (Bates et al., 2003a) highlighting the need for further research on surveillance and control methods.

Following the 2001 FMD outbreak in the U.K., a model was developed to predict the impact of an outbreak in France (Le Menach et al., 2005). The model indicated a FMD epidemic in France may be largely dependent on the location, size, and species type of the initially infected farms (Le Menach et al., 2005). When there were high density cattle or sheep farms, the disease was transmitted quickly which highlighted the need for accurate farm location data. The study also found that pre-emptive culling and ring vaccination had the greatest impact on the reducing the disease duration (Le Menach et al., 2005).

When modeling alternative control methods in three regions in the U.S. in the face of a FMD outbreak, Schoenbaum and Disney (2003) compared the epidemiological and economic impact of 72 different scenarios. The three regions in the study population were a county in south-central U.S., a county in north-central U.S., and a county in the western U.S. The three counties were chosen due to the demographic diversity of the U.S. in hopes of representing the U.S. agriculture systems. They found that the appropriate control strategy depended on the county due to herd demographics and the contact rate between herds. Pre-emptive culling and ring vaccination decreased the duration of the outbreak, consistent with other research (Bates et al., 2003c; Le Menach et al., 2005). Schoenbaum and Disney (2003) also found that even with the increased expense of higher capacity vaccination and depopulation the decrease in the duration of the outbreak decreased the overall cost of the outbreak. Similar results from a model based on an intensive livestock region of Australia found that when FMD spreads rapidly vaccination may be cost effective due to the available resources being insufficient for depopulation alone (Abdalla et al., 2005).

Epidemiological modeling has also been used to assess legislative decisions on FMD control methods in Spain. A simulation model of the spread of an FMD epidemic in the Castile and Leon region of Spain found depopulation in conjunction with vaccination to be beneficial but in smaller zones than those legislated. Depopulation and vaccination of premises within a radius of < 1 km and <3 km, respectively, around infected herds significantly decreased the number of infected herds compared to the legislated radius of <3 km and <5 km (Martínez López et al., 2010). Vaccination was further studied in Europe by Backer et al. (2012) and the model suggested that vaccination may effectively control an epidemic as quickly as pre-emptive ring culling in a densely populated livestock area in the Netherlands.

Differences in model output are expected due to the regional differences in the agricultural industry and the associated differences in contact parameters, limited geographic model regions/populations and the subsequent limited opportunity for spread in models. A study of the spread of FMD in the livestock dense region on the Texas Panhandle did not find vaccination advantageous in controlling the outbreak (Ward et al., 2009). The study control strategies included an emergency 5 km ring vaccination and a targeted vaccination of high risk herds. The results of the model indicated that even with adequate vaccine supply, it did not offer any advantage as a control method. Ward et al. (2009) also found that the number of herds depopulated was associated with the production type of the initially infected herd. More herds were depopulated when the initial herd infected was a large feedlot compared to the initial herd being a herd with ≥100 adult beef cows. In another study in California looking at the impact of the initially infected herd the mean duration of outbreaks beginning in dairy herds was significantly longer than for outbreaks beginning in beef herds (Pineda-Krch et al., 2010). This indicates that initial herd could have great impact on the outbreak size but it would vary by regional agricultural systems. Regional differences do occur in the results but limited geographic model populations are important to consider. Both Ward et al., (2009) and Pineda-Krch et al., (2010) assume that all movements would be contained to the study region during an outbreak. In reality direct and indirect contact movements outside the study region could lead to additional outbreaks outside the model population leading to an extended outbreak and potentially different outcomes.

Due to the limited number of validated simulation models, the ability to use them in countries they were not developed for is advantageous; however country specific data is needed to appropriately parameterize the models. Tildesley and Keeling (2008) evaluated the use of the kernel transmission model in Denmark and found that the transmission kernel used in the U.K. was not applicable to Denmark. The difference in types and density of livestock was found to greatly influence the control methods recommended by the model. The model was also used to evaluate control methods in Pennsylvania (Tildesley et al., 2012). The study was conducted to determine if the kernel transmission model could be useful in the U.S. where there is a lack of direct and indirect contact data available. The transmission kernel used in the study was derived from a U.K. FMD outbreak where the farm density was high so it was necessary to apply it to a region of the U.S. that had a similar farm density. In addition to having a similar density of farms, Pennsylvania also had similar farm sizes to the U.K. The model demonstrated that the transmission kernel that was sufficient to cause an extensive outbreak in the U.K. was not sufficient in Pennsylvania. A possible reason for this is that the density of the farming areas between the two regions is similar however there are more farms in the U.K. and approximately twice the land area.

Due to the structural complexity and heterogeneity of contacts, models that include regional contact rates may be more effectively adapted. Both NAADSM (U.S.) and InterSpreadPlus (New Zealand) have been successfully modified to regions other than the ones for which they were developed. InterSpreadPlus was used to re-create the 2002 FMD epidemic in Korea and the model demonstrated its ability to represent a real epidemic (Yoon et al., 2006). NAADSM has been used in South America to evaluate outbreaks and improve the model (Rivera et al., 2009) but further validation is needed.

Predictive epidemiological disease models have been used to estimate the potential economic impacts of an outbreak as well. 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). In all scenarios an outbreak of FMD would have a drastic effect on the agriculture industry and the U.S. economy.

Conclusion

FMD is an infectious disease found in cloven-hooved animals in many parts of the world. The disease is highly contagious and can spread through the movement of animals, equipment, people, waste, and through the air in certain conditions. The ability of FMD to spread prior to clinical signs makes rapid intervention critical but difficult.

With the devastating economic impact of FMD, control and eradication are important aspects and need to remain a focus of research. Even with many outbreaks every year throughout the world, published research on the outbreaks and the control methods that were used is limited. Additionally with the advances in the development of a FMD vaccine which allows for differentiation of vaccinated animals from infected animals highlights the need for re-evaluation of OIE trade regulations. Currently the data is lacking on the impact of vaccination as a control strategy in all regions of the U.S. Further the workforce and vaccine dose requirements necessary to carry out vaccination as a control method are uncertain.

Epidemiological simulation modeling has been used to assess control methods in countries that are currently free of the disease. As with all models there are limitations to the results based on the quality of the data that is used to parameterize them. The regional differences in livestock contact and the movement through auction markets require continued research to generate region and production type specific rates. Currently there is a gap in livestock contact data for the U.S. with the exception of limited data available for California and the Panhandle region of Texas. Any model will depend for its legitimacy on the accuracy on the data supporting it. The limited livestock contact data leads to uncertainty in outcomes and identification of control policies in the U.S. as well as the inability to assess resource needs of possible control strategies in the face of an FMD outbreak. Additionally, in order to increase the user-confidence of the results of the model, further research is needed on model validation. Validation exercises comparing the NAADSM, InterSpreadPlus, and AusSpread have demonstrated the value of the models and have been beneficial in validating the models however further validation using outbreak data is needed. Every opportunity should be taken to parameterize these models for countries that have suffered recent outbreaks and compare the model output to the actual outbreak.

In the U.S., models have been used to predict the impact of a FMD outbreak and guide control plans. The models are regional due to the differences in livestock production throughout the country. Further research and model development is needed to expand simulation model results to the entire U.S. while allowing for the regional differences of animal movements. The economic impact of FMD is too great to not continue to improve simulation models and the data used to parameterize them.

References

Abdalla, A., S. Beare, L. Cao, G. Garner and A. Heaney, A. e. 06.6, 2005. Foot and Mouth Disease: Evaluating Alternatives for Controlling a Possible Outbreak in Australia. http://143.188.17.20/data/warehouse/pe_abarebrs99001177/PC13123.pdf (accessed September 26, 2013).

Alexandersen, S., I. Brotherhood and A. I. Donaldson, 2002a. Natural aerosol transmission of foot-and-mouth disease virus to pigs: minimal infectious dose for strain O1 Lausanne. Epidemiol. Infect. 128: 301-312.

Alexandersen, S., Z. Zhang, A. Donaldson and A. Garland, 2003. The pathogenesis and diagnosis of foot-and-mouth disease. Journal of comparative pathology 129: 1-36.

Alexandersen, S., Z. Zhang and A. I. Donaldson, 2002b. Aspects of the persistence of foot-and-mouth disease virus in animals--the carrier problem. Microbes Infect 4: 1099-1110.

Amass, S., J. Pacheco, P. Mason, J. Schneider, R. Alvarez, L. Clark and D. Ragland, 2003. Procedures for preventing the transmission of foot-and-mouth disease virus to pigs and sheep by personnel in contact with infected pigs. Vet. Rec. 153: 137-140.

Amass, S. F., P. W. Mason, J. M. Pacheco, C. A. Miller, A. Ramirez, L. K. Clark, D. Ragland, J. L. Schneider and S. J. Kenyon, 2004. Procedures for preventing transmission of foot-and-mouth disease virus (O/TAW/97) by people. Vet. Microbiol. 103: 143-149.

Anderson, I., 2002. Foot & mouth disease 2001: lessons to be learned inquiry report. The Stationary Office.

Andersson, H., 1997. Epidemics in a population with social structures. Math. Biosci. 140: 79-84.

Anonymous, October, 2012. New Foot-and-Mouth Disease Vaccine Gets Licensed for Use on Cattle. http://www.dhs.gov/publication/st-piadc-press-release-oct-2012 (accessed April 30, 2013).

Ayers, E., E. Cameron, R. Kemp, H. Leitch, A. Mollison, I. Muir, H. Reid, D. Smith and J. Sproat, 2001. Oral lesions in sheep and cattle in Dumfries and Galloway. Vet. Rec. 148: 720.

Backer, J. A., T. J. Hagenaars, G. Nodelijk and H. J. van Roermund, 2012. Vaccination against foot-and-mouth disease I: epidemiological consequences. Prev. Vet. Med. 107: 27-40.

Bartlett, M., 1956. Deterministic and stochastic models for recurrent epidemics. Proceedings of the third Berkeley symposium on mathematical statistics and probability, University of California Press Berkeley.

Bartlett, M. S., 1953. Stochastic processes or the statistics of change. Applied Statistics: 44-64.

Bates, T. W., T. E. Carpenter and M. C. Thurmond, 2003a. Benefit-cost analysis of vaccination and preemptive slaughter as a means of eradicating foot-and-mouth disease. Am. J. Vet. Res. 64: 805-812.

Bates, T. W., M. C. Thurmond and T. E. Carpenter, 2001. Direct and indirect contact rates among beef, dairy, goat, sheep, and swine herds in three California counties, with reference to control of potential foot-and-mouth disease transmission. Am. J. Vet. Res. 62: 1121-1129.

Bates, T. W., M. C. Thurmond and T. E. Carpenter, 2003b. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. Am. J. Vet. Res. 64: 195-204.

Bates, T. W., M. C. Thurmond and T. E. Carpenter, 2003c. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. Am. J. Vet. Res. 64: 205-210.

Bates, T. W., M. C. Thurmond, S. K. Hietala, K. S. Venkateswaran, T. M. Wilson, B. W. Colston, Jr., J. E. Trebes and F. P. Milanovich, 2003d. Surveillance for detection of foot-and-mouth disease. J. Am. Vet. Med. Assoc. 223: 609-614.

Beckett, S. and M. G. Garner, 2007. Simulating disease spread within a geographic information system environment. Vet. Ital. 43: 595-604.

Bessell, P. R., D. J. Shaw, N. J. Savill and M. E. Woolhouse, 2008. Geographic and topographic determinants of local FMD transmission applied to the 2001 UK FMD epidemic. BMC Vet. Res. 4: 40.

Bigras-Poulin, M., R. A. Thompson, M. Chriel, S. Mortensen and M. Greiner, 2006. Network analysis of Danish cattle industry trade patterns as an evaluation of risk potential for disease spread. Prev. Vet. Med. 76: 11-39.

Black, H., M. Evans, M. Stone and A. Julian, 2004. Lip and gum lesions in sheep at two abattoirs in New Zealand. N. Z. Vet. J. 52: 95-98.

Bouma, A., A. R. Elbers, A. Dekker, A. de Koeijer, C. Bartels, P. Vellema, P. van der Wal, E. M. van Rooij, F. H. Pluimers and M. C. de Jong, 2003. The foot-and-mouth disease epidemic in The Netherlands in 2001. Prev. Vet. Med. 57: 155-166.

Brandt, A. W., M. W. Sanderson, B. D. DeGroot, D. U. Thomson and L. C. Hollis, 2008. Biocontainment, biosecurity, and security practices in beef feedyards. J. Am. Vet. Med. Assoc. 232: 262-269.

Brennan, M. L., R. Kemp and R. M. Christley, 2008. Direct and indirect contacts between cattle farms in north-west England. Prev. Vet. Med. 84: 242-260.

Burrows, R., 1966. Studies on the carrier state of cattle exposed to foot-and-mouth disease virus. J. Hyg. (Lond). 64: 81-90.

Burrows, R., 1968a. Excretion of foot-and-mouth disease virus prior to the development of lesions. Vet. Rec. 82: 387-388.

Burrows, R., 1968b. The persistence of foot-and mouth disease virus in sheep. J. Hyg. (Lond). 66: 633-640.

Burrows, R., J. A. Mann, A. J. Garland, A. Greig and D. Goodridge, 1981. The pathogenesis of natural and simulated natural foot-and-mouth disease infection in cattle. J. Comp. Pathol. 91: 599-609.

Carpenter, T. E., 2011. Stochastic, spatially-explicit epidemic models. Rev. Sci. Tech. 30: 417-424.

Carpenter, T. E., L. E. Christiansen, B. F. Dickey, C. Thunes and P. J. Hullinger, 2007. Potential impact of an introduction of foot-and-mouth disease into the California State Fair. J. Am. Vet. Med. Assoc. 231: 1231-1235.

Carpenter, T. E., J. M. O'Brien, A. D. Hagerman and B. A. McCarl, 2011. Epidemic and economic impacts of delayed detection of foot-and-mouth disease: a case study of a simulated outbreak in California. J. Vet. Diagn. Invest. 23: 26-33.

Carpenter, T. E., M. C. Thurmond and T. W. Bates, 2004. A Simulation Model of Intraherd Transmission of Foot and Mouth Disease with Reference to Disease Spread before and after Clinical Diagnosis. J. Vet. Diagn. Invest. 16: 11-16.

Casal, J., A. De Manuel, E. Mateu and M. Martin, 2007. Biosecurity measures on swine farms in Spain: perceptions by farmers and their relationship to current on-farm measures. Prev. Vet. Med. 82: 138-150.

Charleston, B., B. M. Bankowski, S. Gubbins, M. E. Chase-Topping, D. Schley, R. Howey, P. V. Barnett, D. Gibson, N. D. Juleff and M. E. Woolhouse, 2011. Relationship between clinical signs and transmission of an infectious disease and the implications for control. Science 332: 726-729.

Chowell, G., A. L. Rivas, N. W. Hengartner, J. M. Hyman and C. Castillo-Chavez, 2006. The role of spatial mixing in the spread of foot-and-mouth disease. Prev. Vet. Med. 73: 297-314.

Christley, R. M., G. L. Pinchbeck, R. G. Bowers, D. Clancy, N. P. French, R. Bennett and J. Turner, 2005. Infection in social networks: using network analysis to identify high-risk individuals. Am. J. Epidemiol. 162: 1024-1031.

Condy, J. B., R. S. Hedger, C. Hamblin and I. T. Barnett, 1985. The duration of the foot-and-mouth disease virus carrier state in African buffalo (i) in the individual animal and (ii) in a free-living herd. Comp. Immunol. Microbiol. Infect. Dis. 8: 259-265.

Cottral, G., B. Cox and D. Baldwin, 1960. The survival of foot-and-mouth disease virus in cured and uncured meat. Am. J. Vet. Res. 21: 288-297.

Cottral, G. E., 1969. Persistence of foot-and-mouth disease virus in animals, their products and the environment. Bulletin - Off. Int. Epizoot. 71: 549-568.

Davies, G., 2002. Foot and mouth disease. Res. Vet. Sci. 73: 195-199.

Dawson, P., 1970. The involvement of milk in the spread of foot-and-mouth disease: an epidemiological study. Vet. Rec. 87: 543-548.

De Leeuw, P., J. Van Bekkum and J. Tiessink, 1978. Excretion of foot-and-mouth disease virus in oesophageal-pharyngeal fluid and milk of cattle after intranasal infection. J. Hyg. (Lond). 81: 415-426.

Dickey, B. F., T. E. Carpenter and S. M. Bartell, 2008. Use of heterogeneous operation-specific contact parameters changes predictions for foot-and-mouth disease outbreaks in complex simulation models. Prev. Vet. Med. 87: 272-287.

Donaldson, A., 1986. Aerobiology of foot-and-mouth disease (FMD): an outline and recent advances. Rev. Sci. Tech. 5: 315-321.

Donaldson, A. I., 1997. Risks of spreading foot and mouth disease through milk and dairy products. Rev. Sci. Tech. 16: 117-124.

Donaldson, A. I., J. Gloster, L. D. Harvey and D. H. Deans, 1982. Use of prediction models to forecast and analyse airborne spread during the foot-and-mouth disease outbreaks in Brittany, Jersey and the Isle of Wight in 1981. Vet. Rec. 110: 53-57.

Dube, C., C. Ribble, D. Kelton and B. McNab, 2008. Comparing network analysis measures to determine potential epidemic size of highly contagious exotic diseases in fragmented monthly networks of dairy cattle movements in Ontario, Canada. Transbound Emerg Dis 55: 382-392.

Dube, C., C. Ribble, D. Kelton and B. McNab, 2009. A review of network analysis terminology and its application to foot-and-mouth disease modelling and policy development. Transbound Emerg Dis 56: 73-85.

Dubé, C., C. Ribble, D. Kelton and B. McNab, 2011a. Introduction to network analysis and its implications for animal disease modelling. Rev. Sci. Tech. 30: 425.

Dubé, C., J. Sanchez and A. Reeves, 2011b. Adapting existing models of highly contagious diseases to countries other than their country of origin. Rev. Sci. Tech. 30: 581.

Dube, C., M. A. Stevenson, M. G. Garner, R. L. Sanson, B. A. Corso, N. Harvey, J. Griffin, J. W. Wilesmith and C. Estrada, 2007. A comparison of predictions made by three simulation models of foot-and-mouth disease. N. Z. Vet. J. 55: 280-288.

Dunn, C. S. and A. I. Donaldson, 1997. Natural adaption to pigs of a Taiwanese isolate of foot-and-mouth disease virus. Vet. Rec. 141: 174-175.

Eddy, R. G., 2001. Vets asked valuable questions about foot-and-mouth measures. Nature 412: 477.

Elbakidze, L., L. Highfield, M. Ward, B. A. McCarl and B. Norby, 2009. Economics Analysis of Mitigation Strategies for FMD Introduction in Highly Concentrated Animal Feeding Regions. Applied Economic Perspectives and Policy 31: 931-950.

Ellis-Iversen, J., R. Smith, J. Gibbens, C. Sharpe, M. Dominguez and A. Cook, 2011. Risk factors for transmission of foot-and-mouth disease during an outbreak in southern England in 2007. Vet. Rec. 168: 128-128.

Ferguson, N. M., C. A. Donnelly and R. M. Anderson, 2001a. The Foot-and-Mouth Epidemic in Great Britain: Pattern of Spread and Impact of Interventions. Science 292: 1155.

Ferguson, N. M., C. A. Donnelly and R. M. Anderson, 2001b. Transmission intensity and impact of control policies on the foot and mouth epidemic in Great Britain. Nature 413: 542-548.

Fevre, E. M., B. M. Bronsvoort, K. A. Hamilton and S. Cleaveland, 2006. Animal movements and the spread of infectious diseases. Trends Microbiol. 14: 125-131.

Forde, K., A. Hillberg-Seitzinger, D. Dargatz and N. Wineland, 1998. The availability of state-level data on interstate cattle movements in the United States. Prev. Vet. Med. 37: 209-217.

Forman, S., F. Le Gall, D. Belton, B. Evans, J. François, G. Murray, D. Sheesley, A. Vandersmissen and S. Yoshimura, 2009. Moving towards the global control of foot and mouth disease: an opportunity for donors. Rev. Sci. Tech. 28: 883-896.

Gaggero, A. and P. Sutmoller, 1965. The use of serum and blood dried on blotting paper in the detection of foot-and-mouth disease antibody. Br. Vet. J. 121: 509-514.

Garland, A. and A. Donaldson, 1990. Foot-and-mouth disease. Surveillance 17: 6-8.

Garner, M. and S. Hamilton, 2011. Principles of epidemiological modelling. Rev. Sci. Tech. 30: 407.

Garner, M. G. and S. Beckett, 2005. Modelling the spread of foot-and-mouth disease in Australia. Aust. Vet. J. 83: 758-766.

Garner, M. G. and M. Lack, 1995. An evaluation of alternate control strategies for foot-and-mouth disease in Australia: a regional approach. Prev. Vet. Med. 23: 9-32.

Gerbier, G., J. Bacro, R. Pouillot, B. Durand, F. Moutou and J. Chadoeuf, 2002. A point pattern model of the spread of foot-and-mouth disease. Prev. Vet. Med. 56: 33-49.

Gibbens, J., J. Wilesmith, C. Sharpe, L. Mansley, E. Michalopoulou, J. Ryan and M. Hudson, 2001. Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months. Vet. Rec. 149: 729-743.

Gibbens, J. C. and J. W. Wilesmith, 2002. Temporal and geographical distribution of cases of foot-and-mouth disease during the early weeks of the 2001 epidemic in Great Britain. Vet. Rec. 151: 407-412.

Giles, J., 2001. UK foot-and-mouth epidemic slows. Nature 410: 727-727.

Gloster, J., L. Burgin, A. Jones and R. Sanson, 2011. Atmospheric dispersion models and their use in the assessment of disease transmission. Rev. Sci. Tech. 30: 457.

Graves, J., 1979. Foot-and mouth disease: a constant threat to US livestock. J. Am. Vet. Med. Assoc. 174: 174.

Graves, J. H., J. W. McVicar, P. Sutmoller and R. Trautman, 1971. Contact transmission of foot-and-mouth disease from infected to susceptible cattle. The Journal of infectious diseases 123: 386-391.

Green, D. M., I. Z. Kiss and R. R. Kao, 2006. Modelling the initial spread of foot-and-mouth disease through animal movements. Proc Biol Sci 273: 2729-2735.

Green, L. E. and G. F. Medley, 2002. Mathematical modelling of the foot and mouth disease epidemic of 2001: strengths and weaknesses. Res. Vet. Sci. 73: 201-205.

Grubman, M. J. and B. Baxt, 2004. Foot-and-mouth disease. Clin. Microbiol. Rev. 17: 465-493.

Hagerman, A. D., M. P. Ward, D. P. Anderson, J. C. Looney and B. A. McCarl, 2013. Rapid effective trace-back capability value: A case study of foot-and-mouth in the Texas High Plains. Prev. Vet. Med. 110: 323-328.

Harvey, N., A. Reeves, M. A. Schoenbaum, F. J. Zagmutt-Vergara, C. Dube, A. E. Hill, B. A. Corso, W. B. McNab, C. I. Cartwright and M. D. Salman, 2007. The North American Animal Disease Spread Model: a simulation model to assist decision making in evaluating animal disease incursions. Prev. Vet. Med. 82: 176-197.

Hayama, Y., N. Muroga, T. Nishida, S. Kobayashi and T. Tsutsui, 2012. Risk factors for local spread of foot-and-mouth disease, 2010 epidemic in Japan. Res. Vet. Sci. 93: 631-635.

Haydon, D. T., M. Chase-Topping, D. J. Shaw, L. Matthews, J. K. Friar, J. Wilesmith and M. E. Woolhouse, 2003. The construction and analysis of epidemic trees with reference to the 2001 UK foot-and-mouth outbreak. Proc Biol Sci 270: 121-127.

Hedger, R. S., 1972. Foot-and-mouth disease and the African buffalo (Syncerus caffer). J. Comp. Pathol. 82: 19-28.

Hedger, R. S. and J. B. Condy, 1985. Transmission of foot-and-mouth disease from African buffalo virus carriers to bovines. Vet. Rec. 117: 205.

Hedger, R. S. and P. S. Dawson, 1970. Foot-and-mouth disease virus in milk: an epidemiological study. Vet. Rec. 87: 186-188 passim.

Honhold, N., N. Taylor, S. Mansley, P. Kitching, A. Wingfield, P. Hullinger and M. Thrusfield, 2011. Control of foot-and-mouth disease. Vet. Rec. 168: 541-542.

Howard, S. and C. Donnelly, 2000. The importance of immediate destruction in epidemics of foot and mouth disease. Res. Vet. Sci. 69: 189-196.

Hugh-Jones, M. E. and P. B. Wright, 1970. Studies on the 1967-8 foot-and-mouth disease epidemic. The relation of weather to the spread of disease. J. Hyg. (Lond). 68: 253-271.

Kao, R. R., 2001. Landscape fragmentation and foot-and-mouth disease transmission. Vet. Rec. 148: 746-747.

Kao, R. R., 2002. The role of mathematical modelling in the control of the 2001 FMD epidemic in the UK. Trends Microbiol. 10: 279-286.

Kao, R. R., L. Danon, D. M. Green and I. Z. Kiss, 2006. Demographic structure and pathogen dynamics on the network of livestock movements in Great Britain. Proc Biol Sci 273: 1999-2007.

Keeling, M. J., 2005. Models of foot-and-mouth disease. Proc Biol Sci 272: 1195-1202.

Keeling, M. J., M. E. Woolhouse, R. M. May, G. Davies and B. T. Grenfell, 2003. Modelling vaccination strategies against foot-and-mouth disease. Nature 421: 136-142.

Keeling, M. J., M. E. Woolhouse, D. J. Shaw, L. Matthews, M. Chase-Topping, D. T. Haydon, S. J. Cornell, J. Kappey, J. Wilesmith and B. T. Grenfell, 2001. Dynamics of the 2001 UK foot and mouth epidemic: stochastic dispersal in a heterogeneous landscape. Science 294: 813-817.

Kelton, W. D. and A. M. Law, 2000. Simulation modeling and analysis, McGraw Hill Boston, MA.

Kiss, I. Z., D. M. Green and R. R. Kao, 2006. The network of sheep movements within Great Britain: Network properties and their implications for infectious disease spread. J R Soc Interface 3: 669-677.

Kitching, R. P., 2005. Global epidemiology and prospects for control of foot-and-mouth disease. Curr. Top. Microbiol. Immunol. 288: 133-148.

Kitching, R. P., A. M. Hutber and M. V. Thrusfield, 2005. A review of foot-and-mouth disease with special consideration for the clinical and epidemiological factors relevant to predictive modelling of the disease. Vet. J. 169: 197-209.

Kitching, R. P., M. V. Thrusfield and N. M. Taylor, 2006. Use and abuse of mathematical models: an illustration from the 2001 foot and mouth disease epidemic in the United Kingdom. Rev. Sci. Tech. 25: 293-311.

Knight-Jones, T. and J. Rushton, 2013. The economic impacts of foot and mouth disease–What are they, how big are they and where do they occur? Prev. Vet. Med.

Knowles, N. J., P. R. Davies, T. Henry, V. O'Donnell, J. M. Pacheco and P. W. Mason, 2001a. Emergence in Asia of foot-and-mouth disease viruses with altered host range: characterization of alterations in the 3A protein. J. Virol. 75: 1551-1556.

Knowles, N. J., A. R. Samuel, P. R. Davies, R. P. Kitching and A. I. Donaldson, 2001b. Outbreak of foot-and-mouth disease virus serotype O in the UK caused by a pandemic strain. Vet. Rec. 148: 258-259.

Knowles, T., 2011. Defining Law Enforcement's Role in Protecting American Agriculture from Agro-Terrorism, DIANE Publishing.

Kobayashi, M., T. E. Carpenter, B. F. Dickey and R. E. Howitt, 2007. A dynamic, optimal disease control model for foot-and-mouth disease: I. Model description. Prev. Vet. Med. 79: 257-273.

Laurence, C., 2002. Animal welfare consequences in England and Wales of the 2001 epidemic of foot and mouth disease. Rev. Sci. Tech. 21: 863.

Le Menach, A., J. Legrand, R. F. Grais, C. Viboud, A. J. Valleron and A. Flahault, 2005. Modeling spatial and temporal transmission of foot-and-mouth disease in France: identification of high-risk areas. Vet. Res. 36: 699-712.

Machado Jr, M. A., 1969. Aftosa. A historical Survey of foot-and-mouth disease and inter-American relations. Aftosa. A historical Survey of foot-and-mouth disease and inter-American relations.

Mansley, L., A. Donaldson, M. Thrusfield and N. Honhold, 2011. Destructive tension: Mathematics versus experience—The progress and control of the 2001 foot and mouth disease epidemic in Great Britain. Rev. Sci. Tech. 30: 483.

Mardones, F. O., H. Zu Donha, C. Thunes, V. Velez and T. E. Carpenter, 2012. The value of animal movement tracing: A case study simulating the spread and control of foot-and-mouth disease in California. Prev. Vet. Med.

Marshall, E. S., T. E. Carpenter and C. Thunes, 2009. Results of a survey to estimate cattle movements and contact rates among beef herds in California, with reference to the potential spread and control of foot-and-mouth disease. J. Am. Vet. Med. Assoc. 235: 573-579.

Martínez López, B., A. M. Martínez López, J. M. Perez and V. Sánchez, 2010. A simulation model for the potential spread of foot-and-mouth disease in the Castile and Leon region of Spain. Prev. Vet. Med. 96: 19-29.

McLaws, M. and C. Ribble, 2007. Description of recent foot and mouth disease outbreaks in nonendemic areas: Exploring the relationship between early detection and epidemic size. The Canadian Veterinary Journal 48: 1051.

McVicar, J. W. and P. Sutmoller, 1968. Sheep and goats as foot-and-mouth disease carriers. Proc. Annu. Meet. U. S. Anim. Health Assoc. 72: 400-406.

McVicar, J. W. and P. Sutmoller, 1976. Growth of foot-and-mouth disease virus in the upper respiratory tract of non-immunized, vaccinated, and recovered cattle after intranasal inoculation. J. Hyg. (Lond). 76: 467-481.

Miller, G. Y. and K. Parent, 2012. The Economic Impact of High Consequence Zoonotic Pathogens: Why Preparing for these is a Wicked Problem. J. Rev. Global Econ. 1: 47-61.

Morris, R. S., R. L. Sanson, M. W. Stern, M. Stevenson and J. W. Wilesmith, 2002. Decision-support tools for foot and mouth disease control. Rev. Sci. Tech. 21: 557-567.

Morris, R. S., J. W. Wilesmith, M. W. Stern, R. L. Sanson and M. A. Stevenson, 2001. Predictive spatial modelling of alternative control strategies for the foot-and-mouth disease epidemic in Great Britain, 2001. Vet. Rec. 149: 137-144.

Muroga, N., S. Kobayashi, T. Nishida, Y. Hayama, T. Kawano, T. Yamamoto and T. Tsutsui, 2013. Risk factors for the transmission of foot-and-mouth disease during the 2010 outbreak in Japan: a case--control study. BMC Vet. Res. 9: 150.

National Audit Office, Department of Environment, Food and Rural Affairs, 2005. Foot and Mouth Disease: Applying the Lessons. www.nao.org.uk (accessed October 23, 2012).

NBAF, (National Bio and Agro-Defense Facility), 2012. Updated Site-Specific Biosafety and Biosecurity Mitigation Risk Assessment, United Stated Department of Homeland Security.

Neher, N. J., 1999. The need for a coordinated response to food terrorism: The Wisconsin experience. Ann. N. Y. Acad. Sci. 894: 181-183.

Nielen, M., A. Jalvingh, H. Horst, A. Dijkhuizen, H. Maurice, B. Schut, L. Van Wuijckhuise and M. De Jong, 1996. Quantification of contacts between Dutch farms to assess the potential risk of foot-and-mouth disease spread. Prev. Vet. Med. 28: 143-158.

Office International des Epizooties/World Organisation for Animal Health, 2013 "Foot and mouth disease." Terrestrial animal health code Chapter 8.6 http://www.oie.int/en/international-standard-setting/terrestrial-code/ (accessed August 28, 2013)

Ortiz-Pelaez, A., D. Pfeiffer, R. Soares-Magalh es and F. Guitian, 2006. Use of social network analysis to characterize the pattern of animal movements in the initial phases of the 2001 foot and mouth disease (FMD) epidemic in the UK. Prev. Vet. Med. 76: 40-55.

Paarlberg, P. L., J. G. Lee and A. H. Seitzinger, 2002. Potential revenue impact of an outbreak of foot-and-mouth disease in the United States. J. Am. Vet. Med. Assoc. 220: 988-992.

Pacheco, J. M., M. Tucker, E. Hartwig, E. Bishop, J. Arzt and L. L. Rodriguez, 2012. Direct contact transmission of three different foot-and-mouth disease virus strains in swine demonstrates important strain-specific differences. Vet. J. 193: 456-463.

Parent, K. B., G. Y. Miller and P. J. Hullinger, 2011. Triggers for foot and mouth disease vaccination in the United States. Rev. Sci. Tech. 30: 789.

Pendell, D. L., J. C. Leatherman, T. C. Schroeder and G. S. Alward, 2007. The Economic Impacts of a Foot-And-Mouth Disease Outbreak: A Regional Analysis. J. Agr. Appl. Econ. 39: 19-33.

Perez, A. M., M. P. Ward and T. E. Carpenter, 2004. Control of a foot-and-mouth disease epidemic in Argentina. Prev. Vet. Med. 65: 217-226.

Pineda-Krch, M., J. M. O'Brien, C. Thunes and T. E. Carpenter, 2010. Potential impact of introduction of foot-and-mouth disease from wild pigs into commercial livestock premises in California. Am. J. Vet. Res. 71: 82-88.

Pluimers, F. H., 2004. Foot-and-Mouth disease control using vaccination: the Dutch experience in 2001. Dev Biol (Basel) 119: 41-49.

Pluimers, F. H., A. M. Akkerman, P. van der Wal, A. Dekker and A. Bianchi, 2002. Lessons from the foot and mouth disease outbreak in The Netherlands in 2001. Rev. Sci. Tech. 21: 711-721.

Premashthira, S., M. D. Salman, A. E. Hill, R. M. Reich and B. A. Wagner, 2011. Epidemiological simulation modeling and spatial analysis for foot-and-mouth disease control strategies: a comprehensive review. Anim. Health Res. Rev. 12: 225.

Reeves, A., M. Salman and A. Hill, 2011. Approaches for evaluating veterinary epidemiological models: verification, validation and limitations. Models in the management of animal diseases (P. Willeberg, ed.) Rev. sci. tech. Off. int. Epiz 30: 499-512.

Ribbens, S., J. Dewulf, F. Koenen, K. Mintiens, A. de Kruif and D. Maes, 2009. Type and frequency of contacts between Belgian pig herds. Prev. Vet. Med. 88: 57-66.

Rivera, A., E. G., C. Dube and J. Sanchez, 2009. Strategies for control of FMD outbreak in Chile using the North American Animal Disease Spread Model. International Society for Veterinary Epidemiology and Economics, Durban, South Africa, Proc. 12th International Symposium on Veterinary Epidemiology and Economics.

Robinson, S. E. and R. M. Christley, 2007. Exploring the role of auction markets in cattle movements within Great Britain. Prev. Vet. Med. 81: 21-37.

Rorres, C., S. T. Pelletier, M. J. Keeling and G. Smith, 2010. Estimating the kernel parameters of premises-based stochastic models of farmed animal infectious disease epidemics using limited, incomplete, or ongoing data. Theor. Popul. Biol. 78: 46-53.

Salt, J., P. Barnett, P. Dani and L. Williams, 1998. Emergency vaccination of pigs against foot-and-mouth disease: protection against disease and reduction in contact transmission. Vaccine 16: 746-754.

Sanderson, M. W., D. A. Dargatz and F. B. Garry, 2000. Biosecurity practices of beef cow-calf producers. J. Am. Vet. Med. Assoc. 217: 185-189.

Sanson, R. L., N. Harvey, M. G. Garner, M. A. Stevenson, T. M. Davies, M. L. Hazelton, J. O'Connor, C. DubÃƒ, K. N. Forde Folle and K. Owen, 2011. Foot and mouth disease model verification and 'relative validation' through a formal model comparison. Rev. Sci. Tech. 30: 527-540.

Sanson, R. L., G. Struthers, P. King, J. F. Weston and R. S. Morris, 1993. The potential extent of transmission of foot-and-mouth disease: a study of the movement of animals and materials in Southland, New Zealand. N. Z. Vet. J. 41: 21-28.

Schoenbaum, M. A. and W. T. Disney, 2003. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. Prev. Vet. Med. 58: 25-52.

Sellers, R., 1971. Quantitative aspects of the spread of foot and mouth disease. Vet. Bull 41: 431-439.

Sellers, R. and J. Parker, 1969. Airborne excretion of foot-and-mouth disease virus. J. Hyg. (Lond). 67: 671-677.

Sellers, R. F. and S. M. Daggupaty, 1990. The epidemic of foot-and-mouth disease in Saskatchewan, Canada, 1951-1952. Can. J. Vet. Res. 54: 457-464.

Sellers, R. F., K. A. Herniman and A. I. Donaldson, 1971a. The effects of killing or removal of animals affected with foot-and-mouth disease on the amounts of airborne virus present in looseboxes. Br. Vet. J. 127: 358-365.

Sellers, R. F., K. A. Herniman and J. A. Mann, 1971b. Transfer of foot-and-mouth disease virus in the nose of man from infected to non-infected animals. Vet. Rec. 89: 447-449.

Shirley, M. D. F. and S. P. Rushton, 2005. The impacts of network topology on disease spread. Ecol. Complex. 2: 287-299.

Spedding, C. R. W., 1988. An introduction to agricultural systems.. ed. 2.

Stark, K. D., G. Regula, J. Hernandez, L. Knopf, K. Fuchs, R. S. Morris and P. Davies, 2006. Concepts for risk-based surveillance in the field of veterinary medicine and veterinary public health: review of current approaches. BMC Health Serv Res 6: 20.

Stevenson, M. A., R. L. Sanson, M. W. Stern, B. D. O'Leary, M. Sujau, N. Moles-Benfell and R. S. Morris, 2013. InterSpread Plus: a spatial and stochastic simulation model of disease in animal populations. Prev. Vet. Med. 109: 10-24.

Sugiura, K., H. Ogura, K. Ito, K. Ishikawa, K. Hoshino and K. Sakamoto, 2001. Eradication of foot and mouth disease in Japan. Rev. Sci. Tech. 20: 701-713.

Sutmoller, P., S. S. Barteling, R. C. Olascoaga and K. J. Sumption, 2003. Control and eradication of foot-and-mouth disease. Virus Res. 91: 101-144.

Sutmoller, P., J. W. McVicar and G. E. Cottral, 1968. The epizootiological importance of foot-and-mouth disease carriers. I. Experimentally produced foot-and-mouth disease carriers in susceptible and immune cattle. Arch. Virol. 23: 227-235.

Taylor, N., 2003. Review of the use of models in informing disease control policy development and adjustment. A report for Defra. Defra, London 94.

Taylor, N. M., N. Honhold, A. D. Paterson and L. M. Mansley, 2004. Risk of foot-and-mouth disease associated with proximity in space and time to infected premises and the implications for control policy during the 2001 epidemic in Cumbria. Vet. Rec. 154: 617-626.

Texas Animal Health Commission, 2007. Operation Palo Duro February 21-23. http://www.tahc.state.tx.us/emergency/May2007_OperationPaloDuro.pdf (accessed April 01, 2013).

Thompson, D., P. Muriel, D. Russell, P. Osborne, A. Bromley, M. Rowland, S. Creigh-Tyte and C. Brown, 2002. Economic costs of the foot and mouth disease outbreak in the United Kingdom in 2001. Rev. Sci. Tech. 21: 675-685.

Thomson, G., R. Bengis, J. Esterhuysen and A. Pini, 1984. Maintenance mechanisms for foot-and-mouth disease virus in the Kruger National Park and potential avenues for its escape into domestic animal populations. Proceedings of the XIIIth World Congress on Diseases of Cattle.

Thomson, G. R., 1996. The Role of Carriers in the Transmission of Foot and Mouth Disease. 64th General Session of the Office Internationale des Epizooties, Paris.

Tildesley, M. J., T. A. House, M. C. Bruhn, R. J. Curry, M. O'Neil, J. L. Allpress, G. Smith and M. J. Keeling, 2010. Impact of spatial clustering on disease transmission and optimal control. Proc. Natl. Acad. Sci. U. S. A. 107: 1041-1046.

Tildesley, M. J. and M. J. Keeling, 2008. Modelling foot-and-mouth disease: a comparison between the UK and Denmark. Prev. Vet. Med. 85: 107-124.

Tildesley, M. J., G. Smith and M. J. Keeling, 2012. Modeling the spread and control of foot-and-mouth disease in Pennsylvania following its discovery and options for control. Prev. Vet. Med. 104: 224-239.

Tildesley, M. J., V. V. Volkova and M. E. Woolhouse, 2011. Potential for epidemic take-off from the primary outbreak farm via livestock movements. BMC Vet. Res. 7: 76.

Toma, L., A. W. Stott, C. Heffernan, S. Ringrose and G. J. Gunn, 2013. Determinants of biosecurity behaviour of British cattle and sheep farmers—A behavioural economics analysis. Prev. Vet. Med. 108: 321-333.

USDA-APHIS, 2012. Classification of phases and types of a foot and mouth disease outbreak and response. http://www.cfsph.iastate.edu/pdf/phases-and-types-of-an-fmd-outbreak (accessed Oct. 22, 2013).

USDA-NASS, United States Department of Agriculture, National Agriculture Statistics Service., 2007a. Census of Agriculture United States Cattle Production. http://www.agcensus.usda.gov/Publications/2007/Online_Highlights/Fact_Sheets/Production/beef_cattle.pdf (accessed December 6, 2012).

USDA-NASS, United States Department of Agriculture, 2007b. National Agriculture Statistics Service. http://www.agcensus.usda.gov/Publications/2007/index.asp (accessed November 10, 2012).

Van Schaik, G., Y. Schukken, M. Nielen, A. Dijkhuizen, H. Barkema and G. Benedictus, 2002. Probability of and risk factors for introduction of infectious diseases into Dutch SPF dairy farms: a cohort study. Prev. Vet. Med. 54: 279-289.

Velthuis, A. G. J. and Mourits, 2007. Effectiveness of movement-prevention regulations to reduce the spread of foot-and-mouth disease in The Netherlands. Prev. Vet. Med. 82: 262-281.

Volkova, V. V., P. R. Bessell, M. E. Woolhouse and N. J. Savill, 2011. Evaluation of risks of foot-and-mouth disease in Scotland to assist with decision making during the 2007 outbreak in the UK. Vet. Rec. 169: 124.

Volkova, V. V., R. Howey, N. J. Savill and M. E. Woolhouse, 2010. Potential for transmission of infections in networks of cattle farms. Epidemics 2: 116-122.

Ward, M. P., L. D. Highfield, P. Vongseng and M. Graeme Garner, 2009. Simulation of foot-and-mouth disease spread within an integrated livestock system in Texas, USA. Prev. Vet. Med. 88: 286-297.

Wee, S. H., J. Y. Park, Y. S. Joo, J. H. Lee and S. H. An, 2004. Control measures implemented during the 2002 foot-and-mouth disease outbreak in the Republic of Korea. Vet. Rec. 154: 598-600.

Woolhouse, M. and A. Donaldson, 2001. Managing foot-and-mouth. Nature 410: 515-516.

Woolhouse, M. E., P. Coen, L. Matthews, J. D. Foster, J. M. Elsen, R. M. Lewis, D. T. Haydon and N. Hunter, 2001. A centuries-long epidemic of scrapie in British sheep? Trends Microbiol. 9: 67-70.

Yang, P. C., R. M. Chu, W. B. Chung and H. T. Sung, 1999. Epidemiological characteristics and financial costs of the 1997 foot-and-mouth disease epidemic in Taiwan. Vet. Rec. 145: 731-734.

Yeh, J. Y., J. H. Lee, J. Y. Park, Y. S. Cho and I. S. Cho, 2013. Countering the Livestock-Targeted Bioterrorism Threat and Responding with an Animal Health Safeguarding System. Transbound Emerg Dis 60: 289-297.

Yoon, H., S. H. Wee, M. A. Stevenson, B. D. O'Leary, R. S. Morris, I. J. Hwang, C. K. Park and M. W. Stern, 2006. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth disease outbreak in the Republic of Korea. Prev. Vet. Med. 74: 212-225.

Yoon, H., S. Yoon, S. Wee, Y. Kim and B. Kim, 2012. Clinical Manifestations of Foot-and-Mouth Disease During the 2010/2011 Epidemic in the Republic of Korea. Transbound Emerg Dis 59: 517-525.

Chapter 2 - Direct and Indirect Contact Rates among livestock operations in Colorado and Kansas

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Abstract

Objective — To characterize direct and indirect contacts among livestock operations in Colorado and Kansas.

Design — Quarterly questionnaire.

Sample Population — 532 livestock producers in Colorado and Kansas.

Procedures — A quarterly questionnaire distributed to livestock producers in Colorado and Kansas from January 2011 through December 2011. Data from completed questionnaires were entered manually into an electronic format and statistically summarized

Results — Direct outgoing contacts were highest among large swine operations for all quarters. Dairy operations moving cattle to auction and other dairy operations had the next highest number of direct outgoing contacts. Mean daily incoming direct contact rates were highest for large feedlots and dairies. The yearly indirect contact for large feedlots exceeded 750 per year each from feed trucks, livestock haulers, and manure haulers. Dairy operations averaged over 400 indirect contacts per year primarily from milk trucks, 283 from manure haulers, and 150 from feed trucks.

Conclusions and Clinical Relevance — High rates of direct contact among large swine operations may represent risk for direct transmission of disease predominantly within the integrated swine system. The high number of indirect contacts in a year as well as high rate of incoming direct contacts from auctions and small feedlots put large feedlots at substantial risk for introduction of disease.

These direct and indirect contact rates of producers in Colorado and Kansas will be useful for establishing and evaluating policy and biosecurity guidelines for producers and for sources of indirect contact among livestock producers. They also can be used to inform efforts to model transmission and control of infectious diseases such as Foot and Mouth Disease.

Introduction

The central United States (U.S.) has a relatively high concentration and a diverse range of livestock operations. These herds are susceptible to a broad range of diseases transmitted by both direct and indirect contact between herds. Foot and Mouth Disease (FMD) is a highly contagious infectious disease that affects cloven-hoofed 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 appearance of clinical signs[1-2] causing early detection, prior to the spread of the disease, to be difficult. FMD has not occurred in the U.S. since 1929 and no vaccination has been practiced, resulting in a fully susceptible livestock population. Due to the susceptibility, diversity and the large scale operations in this region an introduction of FMD would be economically devastating. Recent estimates place the cost of an FMD introduction into the United States at $14 billion, causing a 9.5% decrease in farm income[3]. An epidemiological disease spread model to determine the economic impact of FMD in southwest Kansas found that the economic loss on the local economy would be about $35 million[4]. With more than 50% of total U.S. sales of cattle and calves coming from five states in the central US,[5] the introduction of a highly infectious disease, like FMD, would be damaging to the entire region.

The FMD virus can be spread between herds by movement of infected animals (direct contact), and through indirect contacts such as vehicles, people, or contaminated material[6-7]. In outbreaks of FMD in the United Kingdom in 2001 and 2007, transmission was attributed to both direct and indirect contacts[8-9].

Since FMD is a foreign animal disease in North America, simulation modeling is the only avenue available to study the potential impacts of a potential introduction in the U.S.[10-14]. Quantitative simulation models like these 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 intervention plans[15-16,8,14]. Limited data exist in the U.S. regarding livestock movement rates and distance distributions for both direct and indirect contacts. Bates et al.[10] reported contact rates among livestock operations within a three-county region of California and Marshall et al.[17] reported contact rates among beef producers in California, however no data exists for livestock in the central U.S.

The direct contacts of livestock operations are important in predicting the spread of FMD because the virus can be transmitted prior to the development of clinical signs[1-2]. The direct contacts between farms were the major route of the initial spread of the FMD outbreak in the U.K. in 2001. After livestock movement restrictions around infected premises and closure of markets were in place the virus was spread mainly through the indirect contacts[8] indicating that livestock movement controls were not sufficient to control disease spread.

With the increased concern of foreign animal disease introduction as well as the changing dynamics of the livestock industry further research is needed to estimate the contact rates[18,19] and possible spread of diseases among livestock operations. The objective of this paper is to report the findings from a study conducted to estimate contact rates and contact distance distributions in the central U.S. and to improve the accuracy of contact parameters used in disease spread modeling using a survey among livestock operations.

Materials and Methods

Study region

Colorado and Kansas were selected as the region to collect survey data. These states were selected because they represent livestock operations and management in the central region of the U.S.

Sampling frame and selection of participants

To develop the livestock contact survey mailing list, producer lists were generated for beef cattle, dairy cattle, swine, and small ruminant through communication with livestock producer groups in Colorado and Kansas. Groups included the Kansas Livestock Association (KLA), Colorado Livestock Association (CLA), Colorado Cattlemen's Association (CCA), Kansas Pork Association (KPA), Kansas Sheep Association (KSA), Colorado Wool Growers Association (CWGA), Kansas Meat Goat Association (KMGA), and Kansas Farm Bureau (KFB). All members of the KLA, CCA, KPA, KSA, CWGA and the KMGA were sent letters of invitation to participate in the survey on their respective association letterhead except for KPA and CLA which elected to use Kansas State University and Colorado State University letterhead respectively. The KFB included a column about the survey in their electronic newsletter and provided information on their website. Additionally an article was published in the Western Dairy Newsletter[20], focusing on FMD and introducing the study. Further publicity was generated through web site announcements, and extension e-mails. A Livestock Contact Survey website was developed and publicized providing more information for producers about the survey as well as an electronic sign-up form. In order to reach as many producers as possible, in Colorado, flyers were distributed at two large auction markets, the National Western Stock

Show, Dairy Day, and through 4-H extension agents throughout the state; personal visits to sheep, goat, and cattle producers in Northern Colorado were made accompanied by a private veterinarian. In Kansas, invitation letters to participate in the survey were mailed to operations in Kansas with a Confined Animal Feeding Permit, operations that received a commodity milk payment, and members of the Local Harvest organization, an organization of farmers selling their products directly to the public. The KLA sent out 3,650 letters, the KPA 460, the CCA and CWGA 1,615, and an additional 2,000 were sent out from the remaining lists. Duplication of invitation letters was highly likely due to sending out through multiple organizations and mailings. Producers were asked to volunteer to participate in the survey by returning a postcard with their name and preferred communication information. To ensure that information collected during the study remained anonymous, communication information and survey responses were kept separate throughout the study.

Survey questionnaire

A six page questionnaire[a] was developed to collect contact data from producers. The questionnaire was mailed to six producers in Colorado and Kansas to pre-test it for clarity. After the suggested revisions were made, the questionnaire was sent electronically or by surface mail, based on cooperator preference, to all enrolled participants. The mailings included a cover letter, the 6-page questionnaire, and a postage paid return envelope. For the participants that requested to receive the questionnaire via email a cover letter was attached to the email along with the questionnaire. Four quarterly surveys were sent to all participants in March, June, September and December to capture variation in movement throughout the year. A reminder email or postcard was sent to non-responders approximately four weeks after the survey was sent.

Approval for this survey was obtained from the Kansas State and Colorado State University Review Boards for Research Involving Human Subjects.

Classification of type of operation

Participants in the survey were asked the current number and type of livestock at the operation as well as the primary type of operation. Participants who returned a survey but did not own any cattle, pigs, or small ruminants were not used in the survey analysis. Some participants selected more than one type of operation, so a classification system was used to assign a production type to all participants. Survey participants were placed into 9 operation types based on the description of operation chosen on the survey and type and number of livestock in the operation. Operation types were classified based on types of contacts with in the livestock production system. So for example large and small feedlots were separated to represent backgrounders and finish feedlots which fit into a different place in the production chain so types of contacts may be different; large swine are likely part of an integrated swine business so behavior is different than small swine operations. Cow/Calf operations included all operations that described their operation as commercial cow-calf or beef seed stock. Small cow/calf operations had ≤100 head and large cow/calf operations had >100 head. Small feedlot included all operations that selected stocker grazer, beef backgrounder, and/or cattle finish feedlot that had <3,000 head. Large feedlot included all cattle finish feeders that had ≥3,000 head. If a participant selected more than one type of operation, the type with the greater number of livestock was selected as the assigned operation type. Operations with a majority of beef cattle that selected commercial cow-calf operation along with another type were placed in a cow-calf operation type. Dairy operations included seed stock producers, commercial dairy operations, and calf raisers. Sheep, dairy goat and meat goat operations were combined into a small ruminant operation type. Swine operations with <1000 head were assigned as small swine herds and those with ≥ 1000 were assigned as large swine herds Because seven percent of participants reported having swine and beef cattle we added a mixed beef and swine operation type in our analysis. Operations reporting both beef and swine with >40% of either beef or swine and at least 11% of the other type were classified as mixed beef-swine.

Estimation of direct contact rates and distance of contacts

Participants were asked to record all shipments of livestock, both incoming and outgoing, for seven days. The survey included two pages for recording direct contacts including date of movement, species moved, number of animals, source of livestock, destination of livestock and the distance traveled. For the source and destination a brief description of the type of location was requested, for example auction or feedlot. An additional page was provided for cow-calf and sheep producers to record movements for the previous three months, to more accurately portray the movements in those operations since these producers have fewer movements in general. The record included month of movement, species of livestock, number of shipments, the approximate distance the livestock were moved, and the destination or source. For all operation types, movements to pasture, pen, grazing, headquarters, stock fields, crop fields, and calving pen that were <11 km were classified as movement within the operation. Those that were ≥ 11 km were included in contact movements due to the distance traveled and the increased concerns of contact with other livestock. Other reported movements could not be clearly classified for contact with a particular operation type. These reported movements of livestock to a veterinary clinic, for semen testing, or for embryo transfer were classified as veterinary visits and movement to rodeos, petting zoos, fairs, and shows were classified as show. All contacts were dropped if the destination or source listed only a city or state because the type of contact was unknown. The contact rate was calculated by producing a count of contacts of each participant for each destination-source combination. The total number of the contacts was divided by the duration of the time frame from the survey to get daily rate. The daily rate for seven day movements and three month movements were combined to generate a mean quarterly number of contacts for each livestock type combination.

Estimation of indirect contact and distance of contacts

Indirect contacts were defined as contact between livestock indirectly through an intermediary such as a person, vehicle, or feed. Survey participants were asked to record the frequency of visits by potential indirect contacts to their operation and the approximate distance that was traveled by the indirect contact to reach the operation. As with the direct contacts, all participants were asked to complete a record for the seven days after survey arrival, and cow-calf and sheep producers were also asked to record the number of visitors and approximate distances for the previous 3-months. The survey listed 28 categories of visitors (Table 7). A free form entry of other visitors that were not included in the list was also provided. The indirect contract rate was calculated by converting the seven day and three month records into daily rates and combining the rates to produce the number of quarterly mean indirect contacts for each contact-livestock type combination.

Statistical Analysis

Descriptive statistics were calculated for survey response and percentiles were calculated for contact rates utilizing commercially available statistical software.[b]

Results

Response to survey

A total of 1136 surveys were returned from a total of 532 unique participating operations. A total of 182 equine movements were reported with 88% of them from cow/calf operations and remaining 12% were from small feedlot and mixed beef and swine operations. Six returned surveys were dropped from analysis because no livestock were on the premise. In addition, 38 outgoing movements and 483 incoming movements were dropped from the data that was analyzed due to type of contact being left blank or not recording a specific operation type for source or destination. These movements accounted for 6.5% of the total direct movements reported. Of the movements that were dropped due to unknown type of contact, 320 came from the small swine production type due to no response given for source for incoming livestock and 103 were due to a small ruminant producer bringing livestock in from "out of state". These reported contacts could not be categorized as to source and so could not be accurately included in contact calculations. Of the returned surveys 66% were from Kansas. In Colorado, 791 surveys were sent out and 388 responses were received from 141 unique participants. In Kansas, 1609 surveys were sent out and 742 responses were received from 391 unique participants. The first quarterly survey (Dec-Feb) had the highest response rate with 354 (56.4%) surveys returned of the 628 sent out. Kansas had surveys returned from 93 of the 105 counties in the state and Colorado had 42 out of the 64 counties represented. The overall response rate of the survey was 47.3% of all surveys returned from participants and the first quarter of the survey was the highest response rate for both Colorado and Kansas (Table 1). Cow/calf producers made up 60.5% of the operations that participated in the survey (Table 2). Number of unique participants for each operation type for Colorado and Kansas are reported in Table 2. The survey was completed by the owner of the operation 89% percent of the time, 7% of the time by the manager, 3.5% selected other as role in operation, and the remaining 0.5% did not give a response. Herd size distribution of livestock types is reported in Table 3.

Direct animal contact

The average number of outgoing contacts during each quarter varied for each operation type (Table 4). Large swine to other large swine operations had the highest number of outgoing direct contacts for all quarters (median 5.9-24.53). Dairy operations moving cattle to auction and other dairy operations had the next highest number of contacts in a quarter (median 2.6-10.34). The mean number of contacts for large cow/calf operations were highest to auctions (median 1.28-2.88-2.55). Mixed beef-swine, small swine and small ruminant operations reported similar contact rates and were higher than small cow/calf movements.

For some reported outgoing movements (e.g. those to a veterinarian, a show, or to another site within an operation), the type(s) of operations (if any) in contact with the shipped animals was not clear (Table 5). Large cow/calf, small cow/calf, beef/swine, and small feedlot operations were the only operations to report movements of < 11 km to home grazing. No operation type reported more than two visits to a show in a quarter (Table 5).

The incoming number of contacts also fluctuated by quarter. Incoming contacts from auctions to dairies were only reported during June through August (Table 6). Large feedlots reported the highest number of incoming direct contacts from auctions, peaking in the March to May quarter, with a mean of almost 12 contacts for the quarter.

Indirect animal contact

The indirect contacts included in the analysis are reported in Table 7. The yearly number of indirect contacts varied substantially by operation type and visitor type. The highest reported estimated mean daily incoming contact rates were for large feedlots and dairies. The yearly contact for large feedlots exceeded 725 contacts per year (181 contacts per quarter) each from feed trucks, livestock haulers, and manure haulers. Dairy operations averaged over 400 contacts per year (100 contacts per quarter) from milk trucks, 282 contacts (70 contacts per quarter) from manure haulers, and 146 contacts (36 contacts per quarter) from feed trucks (Table 7).

Distance traveled by indirect contacts to each operation type was similar across the quarters of the year for reported indirect contacts except for livestock haulers. Livestock haulers traveled a median of 113 km for each contact in the months of September to November compared to approximately 64 km for the rest of the year (data not shown). Distances traveled by all indirect contacts to each production type are reported in Table 8. The longest median distance traveled by indirect contacts was to large feedlot operations (Table 8).

Discussion

The purpose of this survey was to characterize the movements of livestock and the types of contacts that occur among livestock operations in Colorado and Kansas. The region for this study represented the west central region of the U.S. with a wide variety of livestock operations types. Previous studies have been conducted to evaluate the contact rates in the state of California[10,17], the Netherlands[21], and New Zealand[22] but due to the difference in operation types, sizes and regionally specific management practices this study provides a more specific description of contacts in the west central U.S. Due to the practical limitations of enrollment of participants in this study, true random sampling of livestock operations was not possible.

Participation in the survey was by self-selected volunteers. As such our survey is subject to volunteer bias in the response. Reasons for declining to participate may have included perceived time requirement, concerns with privacy issues and confidentiality of information. Previous studies of livestock operation contact rates[10, 21,22] faced similar limitations, but concluded that results were still broadly representative of their respective surveyed populations.

In order to reach as many producers as possible invitation letters and flyers were distributed through a wide variety of organizations and methods. Our intention was to invite as broad a range of participants as possible. One result of this was a high probability of duplicate invitations and an inability to enumerate the number of unique invitations made or calculate the initial survey invitation response rate. During the survey the response rate of the self-selected volunteers decreased from 56% for the first survey of the year to 41% for the fourth and final survey. The decrease in the response rate throughout the survey may have been due to participants becoming uninterested or perceiving little direct benefit from taking the time to complete the survey. Kansas had a greater number of participants, which was expected due to the larger number of livestock operations compared to Colorado. The responses to the survey did include all livestock production types and a range of herd sizes within each type. The numbers of participants for the dairy and large feedlot operation types were lowest. Since approximately seven percent of participants reported owning both swine and beef cattle, we considered this a potentially important conduit for spread of disease from a swine operation to a beef cattle operation and a mixed beef and swine production type was included. The inclusion of mixed livestock production systems could increase contact rates between species leading to larger outbreaks of infectious diseases that infect both species such as FMD. An additional consideration is the removal of all movements with undetermined source or destination. The majority of movements removed were incoming contacts for small swine and small ruminant operations so their contacts may be underestimated. The equine movements were not included in the analysis because the survey did not ask for equine movements so the reported numbers are likely not reliable estimates of overall equine movement.

The average cattle on feed per feedlot in Colorado is 1,665 head and in Kansas it is 2,022[23] which does represent the relatively large number of small feedlots compared to large feedlots as was also reflected in the survey response. Both large and small feedlots in this survey had substantial numbers of direct and indirect contacts. Previously reported data from California included only a few small feedlots [10,17].

The average beef cow herd in Colorado and Kansas is approximately 60 head[23] and the average beef cow herd size was 369 in this survey. Our average herd size will be somewhat inflated as the participants in our quarterly survey were asked to record the current number of livestock including calves and bulls, while the 2007 USDA: NASS census results include only the number of cows in the herd. Due to the reporting of total number of livestock we did have a decrease in the number of cattle reported in later quarters of the year as calves were mostly likely weaned and removed from the operation. Still this survey population appears to represent larger cow-calf herds within Colorado and Kansas.

In previously reported data from California, approximately 30% of beef cattle herds were kept at multiple locations[17]. The number of movements recorded in this survey to other locations that were part of the same operation suggests that Kansas and Colorado beef herds are similarly managed on multiple sites. Multiple locations that were part of the same operation could be located some distance apart from one another. For purposes of this report, we included direct contacts between two locations that were part of the same operation when these locations were more than 11 km apart. Due to the likelihood of fence line contact with other operations; transmission to other locations is still a concern even for movement within an operation. This may over-represent contact rates if those are quarterly herd movements and the herd remains isolated with no contact with other livestock. The movements of < 11 km were included in the outgoing contact rate within an operation. Eleven kilometers was chosen due to a natural break in the data from the survey (data not shown).

The average herd size of dairy herds is 283 cows in Colorado and 150 cows in Kansas[23]. The median herd size in this survey for dairy operations was 138 head for the 33 dairy herds who participated in the survey. Dairy operations in this survey had over 3 indirect contacts a day or 280 contacts a quarter, a much lower indirect contact rate than found in small dairies (< 1,000 cattle) in California[10]. The lower indirect rate among dairies in this study is most likely due to the smaller size of herds in Colorado and Kansas relative to those in California. The number of dairies responding to the survey was low however and caution should be exercised in over interpreting the reported contact rates.

The average herd size of swine in Colorado is approximately 750 and in Kansas it is 1,300 head[23]. The large swine production type had a high number of contacts which included any movements reported to another location even if part of the same operation. Most large swine production is part of an integrated industry with livestock shipped within operations and then directly to slaughter, making it unique compared to the other operations in our study population[24]. The high number of direct contacts for large swine facility to large swine facility most likely represents this vertical integration in the swine industry, and may represent risk for direct transmission of disease predominantly within the integrated system and not to other types of livestock operations.

Multiple production types reported high outgoing and incoming contact with auction markets, suggesting markets are an important potential distribution and surveillance point for infectious disease spread. Bates et al.[10] also found that large numbers of livestock were purchased from livestock auctions in herds in a three county region in California. The results of our study also demonstrate all cattle operations reporting livestock incoming from auctions. Multiple herds and livestock types mix at auction markets before dispersal to individual herds providing substantial opportunity for disease transmission and dispersal. Continued education to producers on the risks of bringing outside livestock onto the premise and the importance of quarantine, and open vs. closed herds to prevent the possible spread of diseases such as infectious bovine rhinotracheitis virus, bovine viral diarrhea virus, *Tritririchomonas foetus*, porcine epidemic diarrhea virus, and porcine reproductive and respiratory virus remains important. Separation of sick animals from healthy animals to prevent direct exposure is the basis for control of spread of endemic pathogens[25,26]. Additionally biosecurity of cleaning and disinfecting livestock trailers may also help control disease spread. This survey provides data to quantitate the magnitude of the risk from contact between herds through auction markets.

Indirect contacts are a potential risk for disease spread particularly for a highly contagious disease such as FMD[27, 9]. Indirect contact could allow disease spread after livestock movement controls have been in place, resulting in a longer outbreak[8]. Some indirect contacts must be maintained for animal welfare reasons and for continuity of business and long term survival of livestock production even in the face of an outbreak. Delivery of feed, supplies, and labor will be necessary and will require increased efforts in biosecurity and disinfection to control risk. Large feedlots had the highest number of indirect contacts in a year as well as high incoming direct contacts from auctions and small feedlots putting them at substantial risk for introduction and spread of disease. These contacts occur over a potentially long distance as well, increasing the risk of relatively long distance transmission of disease in an outbreak. This data provides an estimate of the number of contacts for planning the resources that will be required to institute biosecurity and disinfection procedures to control indirect transmission risk in the face of an FMD outbreak in the central U.S.

These direct and indirect contact rates of producers in Colorado and Kansas will be useful for establishing and evaluating policy and biosecurity guidelines for producers and for sources of indirect contact among livestock producers. With the high indirect contact rates found in this study, cleaning and disinfection is imperative to prevent the transmission and persistence of diseases such as porcine reproductive and respiratory syndrome (PRRSV), Salmonella spp, bovine viral diarrhea virus, and *Escherichia coli* O157. Both *Salmonella dublin* and *Escherichia coli* O157 have been shown to persist in cattle manure[28,29] and indirect transmission of bovine viral diarrhea virus and porcine reproductive and respiratory syndrome has been reported[30,31,32]. Furthermore the contact rates will be useful to planners to estimate the number of contacts and identify the resource requirements to control them in the face of a disease outbreak. For example the large number of feed truck visits and need to deliver feed daily has huge welfare impact and magnifies the need for accurate estimates of contacts and well planned biosecurity and disinfection while still allowing contact consistent with good animal welfare.

The direct and indirect contact rates also can be used to inform efforts to model transmission and control of infectious diseases such as FMD which infects multiple species. The results can lead to biosecurity improvements for emergency planning during an infectious disease outbreak among livestock as well as provide data to parameterize simulation models to evaluate control methods during a possible outbreak. Contacts from this study are specific to the central US, allowing modeling with region specific parameters for increasing validity of results[19]. Prior to this data no direct and indirect contact rates were available for the central U.S. and simulation models of livestock disease outbreaks lacked an essential element to provide valid model results and evaluate alternate control methods in this important agriculture region. This data fills a need for region specific contact rates to provide parameters for modeling a foreign animal disease and producing valid results helpful for planning and decision making including the relative importance of different control strategies such as biosecurity and movement control.

[a]The questionnaire is available from the senior author upon request.

[b]StataCorp. 2011. Stata: Release 12. Statistical Software. College Station, TX: StataCorp LP.

References

1. Burrows, R. Excretion of foot and mouth disease virus prior to development of lesions. Vet Rec 1968; 82:387-388.
2. Burrows, R, Mann, JA, Garland, AJM, et al. The pathogenesis of natural and simulated natural foot-and-mouth disease infection in cattle. J Comp Path 1981; 91:599-609.
3. Paarlberg, PL, Lee, JG, & Seitzinger, AH. Potential revenue impact of an outbreak of foot-and-mouth disease in the United States. J Am Vet Med Assoc 2002; 220:988-992.
4. Pendell, DL, Leatherman, J, Schroeder, TC, et al. The economic impacts of a foot-and-mouth disease outbreak: a regional analysis. J Agric Appl Econ 2007; 39:19-33.
5. United States Department of Agriculture National Agriculture Statistics Service website. 2007 Census of Agriculture United States Cattle Production. Available at: http://www.agcensus.usda.gov/Publications/2007/Online_Highlights/Fact_Sheets/Production/beef_cattle.pdf. Accessed December 6, 2012.
6. Sellers, RF. Quantitative aspects of the spread of foot and mouth disease. The Veterinary Bulletin 1971; 41:431–439.
7. Fèvre, EM, Bronsvoort, BMDC, Hamilton, KA, et al. Animal movements and the spread of infectious diseases. Trends Microbiol 2006; 14:125-131.
8. Gibbens, JC, Wilesmith, JW, Sharpe, CE, et al. Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months. Vet Rec 2001; 149: 729-743.
9. Ellis-Iversen, J, Smith, RP, Gibbens, JC., et al. Risk factors for transmission of foot-and-mouth disease during an outbreak in southern England in 2007. Vet Rec 2011; 168:128-128.

10. Bates, TW, Thurmond, MC, & Carpenter, TE. (2001). Direct and indirect contact rates among beef, dairy, goat, sheep, and swine herds in three California counties, with reference to control of potential foot-and-mouth disease transmission. Am J Vet Res 2001; 62:1121-1129.

11. Bates, TW, Thurmond, MC, & Carpenter, TE. Description of an epidemic simulation model for use in evaluating strategies to control an outbreak of foot-and-mouth disease. Am J Vet Res 2003; 64:195-204.

12. Bates, TW, Thurmond, MC, & Carpenter, TE. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. Am J Vet Res 2003; 64:205-210.

13. Schoenbaum, MA, & Disney, WT. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. Prev Vet Med 2003; 58:25-52.

14. Harvey, N, Reeves, A, Schoenbaum, MA, et al. The North American Animal Disease Spread Model: A simulation model to assist decision making in evaluating animal disease incursions. Prev Vet Med 2007; 82:176-197.

15. Spedding CRW. An introduction to agricultural systems. Elsevier Applied Science 1988; London.

16. Taylor, N. (2003). Review of the use of models in informing disease control policy development and adjustment: A report for DEFRA 2003; School of Agriculture, Policy and Development, University of Reading, Earley Gate, Reading UK.

17. Marshall, ES, Carpenter, TE, & Thunes, C. Results of a survey to estimate cattle movements and contact rates among beef herds in California, with reference to the

potential spread and control of foot-and-mouth disease. J Am Vet Med Assoc 2009; 235:573-579.

18. Woolhouse M, Donaldson A. Managing foot-and-mouth. Nature. 2001; 410:515-516.
19. Dickey BF, Carpenter TE, Bartell SM. Use of heterogeneous operation-specific contact parameters changes predictions for foot-and-mouth disease outbreaks in complex simulation models. Prev Vet Med. 2008; 87(3-4):272-287.
20. Sinclair, M, and Reeves, A. Foot-and-mouth disease threat to U.S. livestock production is real and growing. Western Dairy News 2011; 11:47-48. Available at: http://www.cvmbs.colostate.edu/ilm/proinfo/wdn/2011/March%20WDN%5B1%5D.pdf.
21. Nielen, M, Jalvingh, AW, Horst, HS, et al. Quantification of contacts between Dutch farms to assess the potential risk of foot-and-mouth disease spread. Prev Vet Med 1996; 28:143-158.
22. Sanson, RL. A survey to investigate movements off sheep and cattle farms in New Zealand, with reference to the potential transmission of foot-and-mouth disease. N Z Vet J 2005; 53:223-233.
23. United States Department of Agriculture National Agriculture Statistics Service. 2007 Census of Agriculture - Summary and State Data Vol 1. Available at: http://www.agcensus.usda.gov/Publications/2007/index.asp. Accessed December 6, 2012.
24. Reimer, JJ. Contract and Exit Decisions in Finisher Hog Production Am J Agr Econ 2010; 92:667-684.
25. Marshall B, Petrowski D, Levy SB. Inter- and intraspecies spread of Escherichia coli in a farm environment in the absence of antibiotic usage. Proc Natl Acad Sci U S A. 1990; 87:6609-6613.

26. Talafha AQ, Hirche S, Ababneh MM, et al. Prevalence and risk factors associated with bovine viral diarrhea virus infection in dairy herds in Jordan. Tropical Anim Health Prod. 2009; 41:499-506.

27. Cottral, GE. Persistence of foot-and-mouth disease virus in animals, their products and the environment. Bull Off Int Epizoot 1969; 71:549.

28. Himathongkham S, Bahari S, Riemann H, et al. Survival of Escherichia coli O157:H7 and Salmonella typhimurium in cow manure and cow manure slurry. FEMS Microbiol Lett. 1999; 178:251-257.

29. Plym-Forshell L, Ekesbo I. Survival of salmonellas in urine and dry faeces from cattle--an experimental study. Acta Vet Scand. 1996;37(2):127-131.

30. Wills RW, Zimmerman JJ, Swenson SL, et al. Transmission of PRRSV by direct, close, or indirect contact. Swine Health Prod. 1997; 5:213-218.

31. Otake S, Dee SA, Rossow KD, et al. Transmission of porcine reproductive and respiratory syndrome virus by fomites (boots and coveralls). Journal of Swine Health and Production. 2002; 10:59-66.

32. Niskanen R, Lindberg A. Transmission of bovine viral diarrhoea virus by unhygienic vaccination procedures, ambient air, and from contaminated pens. Vet J. 2003; 165:125-130.

Table 2.1 - Distribution of 2,400 livestock operation contact surveys sent by method and total returned by state and quarter. Percent responded is unique responses for each quarter and total responses for each state and overall.

State	Quarter	Surface Mail	E-Mail	Total Sent	Total Responses	Percentage Responded
CO	Dec-Feb	126	75	201	115	57.2%
CO	Mar-May	118	75	193	98	50.8%
CO	June-Aug	124	75	199	90	45.2%
CO	Sept-Nov	123	75	198	89	44.9%
Total CO		491	300	791	392	49.6%
KS	Dec-Feb	245	182	427	239	56.0%
KS	Mar-May	244	152	396	195	49.2%
KS	June-Aug	242	151	393	155	39.4%
KS	Sept-Nov	242	151	393	155	39.4%
Total KS		973	636	1609	744	46.2%
Overall Total		1464	936	2400	1136	47.3%

Table 2.2. - Distribution of 1130 livestock operation contact surveys returned by 532 unique participants by operation type.

	Surveys Returned		Unique Participants	
Assigned Operation Type	Colorado	Kansas	Colorado	Kansas
Large Cow/Calf	150	275	51	143
Small Cow/Calf	103	147	39	72
Dairy	13	21	6	13
Large Feedlot	6	23	2	11
Small Feedlot	41	104	14	65
Large Swine	0	53	0	25
Small Swine	2	33	1	16
Beef and Swine	10	55	5	29
Small Ruminant	63	31	23	17
Total	388	742	141	391

Table 2.3 - Distribution of 1130 livestock operation contact surveys returned by 532 unique participants by operation type.

Operation Type	Mean	10th Percentile	Median	90th Percentile	Type of Livestock Counted
Large Cow/Calf	499	120	318	926	Beef Cattle
Small Cow/Calf	47	10	50	80	Beef Cattle
Dairy	1,274	40	138	4,000	Dairy Cattle
Large Feedlot	17,615	3,326	10,974	50,000	Beef Cattle
Small Feedlot	615	125	500	1,208	Beef Cattle
Large Swine	5,280	1,326	2,675	12,000	Swine
Small Swine	271	36	250	670	Swine
Beef/Swine	178	8	70	650	Beef Cattle*
Beef/Swine	353	4	125	756	Swine*
Small Ruminant	258	15	65	215	Sheep and Goats

Table 2.4 - Mean (10th percentile, 90th percentile) total number of outgoing direct contacts by quarter reported by 1130 quarterly surveys from 532 livestock operations in Colorado and Kansas.

Source - Operation Type	Destination- Operation Type	Dec-Feb contacts	Mar-May contacts	June-Aug contacts	Sep-Nov contacts
Large Cow/Calf	Auction	2.88 (1.0,5.0)	1.42 (0,4.0)	1.35 (0,5.0)	1.28 (0,4.0)
Large Cow/Calf	Large Cow/Calf	1.43 (0,1.98)	2.0 (0,8.0)	1.35 (0,4.0)	0.92 (0,3.0)
Large Cow/Calf	Feedlot	2.87 (1.0,5.1)	0.17 (0,0)	0.13 (0,0)	0.09 (0,0)
Small Cow/Calf	Auction	0.74 (0,2.0)	0.81 (0,3.0)	0.36 (0,2.0)	0.86 (0,2.0)
Small Cow/Calf	Small Cow/Calf	0.49 (0,1.0)	1.51 (0,5.0)	0.70 (0,3.0)	0.52 (0,2.0)
Small Cow/Calf	Feedlot	0.05 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Dairy	Auction	4.37 (0,13.0)	5.19 (0,13.0)	10.34 (0,26.0)	5.2 (0,13.0)
Dairy	Dairy	5.80 (0,19.5)	3.90 (0,13.0)	7.28 (0,26.9)	2.6 (0,13.0)
Small Feedlot	Auction	0.65 (0,1.0)	0.34 (0,0)	0.69 (0,0)	4.34 (0,13.0)

Small Feedlot	Large Feedlot	0.88 (0,1.0)	3.08 (0,13.0)	1.07 (0,3.0)	1.58 (0,2.8)
Small Feedlot	Small Feedlot	2.92 (0,13.0)	0.56 (0,1.9)	0 (0,0)	1.00 (0,0)
Large Swine	Large Swine	24.53 (0,78.0)	15.56 (0,65.0)	16.81 (0,65.0)	5.9 (0, 13.0)
Small Swine	Auction	0 (0,0)	0 (0,0)	3.33 (0,13.0)	1.85 (0, 13.0)
Small Swine	Small Swine	1.27 (0,1.0)	1.86 (0,13.0)	0 (0,0)	1.63 (0,13.0)
Beef/Swine	Auction	1.63 (0,3.0)	1.29 (0,2.0)	1.15 (0,1.0)	2.13 (0, 13.0)
Beef/Swine	Beef/Swine	1.06 (4.0)	4.73 (0,7.4)	0.69 (0,3.0)	1.05 (0,3.7)
Small Ruminant	Auction	1.06 (0,3.0)	2.29 (0,4.0)	2.24 (0, 10.0)	1.69 (0,7.0)
Small Ruminant	Small Ruminant	1.68 (0,3.0)	1.84 (0,6.0)	1.43 (0,5.0)	2.44 (0,13.0)

Table 2.5 - Mean (10th percentile, 90th percentile) total number of outgoing direct contacts by quarter for producers with likely livestock contact but where the specific operation type(s) contacted is not clear, reported by 1130 quarterly surveys from 532 livestock operations in Colorado and Kansas.

Source - Operation Type	Destination- Operation Type	Dec-Feb contacts	Mar-May contacts	June-Aug contacts	Sep-Nov contacts
Large Cow/Calf	Within Operation <11 km	0.52 (0,1.0)	0.56 (0,2.0)	0.07 (0,0)	0.34 (0,1.0)
Large Cow/Calf	Show	0.04 (0,0)	0.02 (0,0)	0.11 (0,0)	0 (0,0)
Large Cow/Calf	Veterinarian	0.07 (0,0)	0.10 (0,0)	0.07 (0,0)	0.08 (0,0)
Small Cow/Calf	Within Operation <11 km	0.11 (0,0)	1.07 (0,2.0)	0.31 (0,0)	0.69 (0,0)
Small Cow/Calf	Show	0.02 (0,0)	0.04 (0,0)	0.22 (0,0)	0.05 (0,0)
Small Cow/Calf	Veterinarian	0.12 (0,1.0)	0.15 (0,1.0)	0.14 (0,0)	0.13 (0,1.0)
Dairy	Within Operation	0 (0,0)	1.30 (0, 6.5)	0 (0,0)	0 (0,0)

	<11 km				
Dairy	Veterinarian	1.30 (0,6.5)	1.30 (0, 6.5)	1.45 (0,13.0)	0 (0,0)
Small Feedlot	Within Operation <11 km	1.66 (0,0)	3.13 (0,13.0)	0.42 (0,0)	0.82 (0,0)
Small Feedlot	Show	1.33 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Small Feedlot	Veterinarian	0.26 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Small Swine	Show	1.18 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Beef/Swine	Within Operation <11 km	4.1 (0,13.0)	0.94 (0, 3.0)	1.31 (0,3.0)	0.13 (0,0)
Beef/Swine	Show	0.68 (0,0)	0 (0,0)	0.85 (0,4.0)	0 (0,0)
Beef/Swine	Veterinarian	1.37 (0,13.0)	0.88 (0, 1.0)	0 (0,0)	0.18 (0,1.0)
Small Ruminant	Within Operation <11 km	0.10 (0,0)	8.68 (0,5.0)	0.04 (0,0)	0 (0,0)
Small Ruminant	Show	0.48 (0,0)	1.20 (0,2.8)	1.0 (0,3.0)	0.73 (0,0)
Small Ruminant	Veterinarian	0 (0,0)	1.64 (0,0)	0.13 (0,0)	0.11 (0,0)

Table 2.6 - Mean (10th percentile, 90th percentile) total number of incoming direct contacts by quarter and by each reported source and destination combination reported by 1130 quarterly surveys from 532 livestock operations in Colorado and Kansas.

Source - Operation Type	Destination- Operation Type	Dec-Feb contacts	Mar-May contacts	June-Aug contacts	Sep-Nov contacts
Auction	Large Cow/Calf	0.88 (0,2.0)	0.54 (0,1.0)	0.08 (0,0)	0.47 (0,1.0)
Auction	Small Cow/Calf	0.03 (0,0)	0.41 (0,0)	0 (0,0)	0.04 (0,0)
Auction	Dairy	0 (0,0)	0 (0,0)	1.45 (0,13.0)	0 (0,0)
Auction	Large Feedlot	7.55 (0,26.0)	11.56 (0,65.0)	0 (0,0)	6.50 (0,39.0)
Auction	Small Feedlot	2.82 (0,13.0)	0.34 (0,0)	2.10 (0,0)	3.85 (0,13.0)
Auction	Small Swine	1.18 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)
Auction	Beef/Swine	1.37 (0,13.0)	0.06 (0,0)	0 (0,0)	0.06 (0,0)
Auction	Small Ruminant	0.04 (0,0)	0.08 (0,0)	0.55 (0,0)	0 (0,0)
Large Cow/Calf	Large Cow/Calf	1.09 (0,3.0)	1.40 (0,3.0)	1.43 (0,3.0)	3.06 (0,10.0)

Large Cow/Calf	Feedlot	0.3 (0,0)	0 (0,0)	0 (0,0)	0.06 (0, 0)
Small Cow/Calf	Small Cow/Calf	0.69 (0,2.0)	0.93 (0,2.0)	0.59 (0,3.0)	0.66 (0,3.0)
Small Cow/Calf	Feedlot	0 (0,0)	0 (0,0)	0 (0,0)	0.07 (0,0)
Dairy	Dairy	3.9 (0,19.47)	3.90 (0,19.5)	5.78 (0,26.0)	4.27 (0,13.0)
Large Swine	Large Swine	3.19 (0,13.0)	2.64 (0,13.0)	1.50 (0,7.5)	1.64 (0,5.0)
Small Feedlot	Large Feedlot	8.65 (0,13.0)	7.19 (0,65.0)	0 (0,0)	0 (0,0)
Small Feedlot	Small Feedlot	0.64 (0,1.0)	1.46 (0,1.0)	1.32 (0,0)	0.88 (0,3.0)
Small Swine	Small Swine	1.18 (0,0)	0 (0,0)	0 (0,0)	1.63 (0,13.0)
Beef/Swine	Beef/Swine	2.00 (0,13.0)	0.59 (0,2.0)	1.37 (0,3.0)	1.58 (0,6.5)
Small Ruminant	Small Ruminant	0.55 (0,1.0)	1.16 (0,5.0)	0.42 (0,1.0)	0.22 (0,1.0)

Table 2.7 - Mean (10th percentile, 90th percentile) total number of indirect contacts per year by operation type and by indirect contact source reported by 1130 quarterly surveys from 532 livestock operations in Colorado and Kansas.

Indirect Contact	Large Cow-Calf	Small Cow-Calf	Small Feedlot	Large Feedlot	Dairy	Small Swine	Large Swine	Small Ruminant	Beef/ Swine
AI technician	0.21 (0,0)	0.08 (0,0)	0.00	0.00	16.90 (0,52.2)	0.00	0.00	0.00	0.00
Ag-tours	0.05 (0,0)	0.05 (0,0)	10.15 (0,0)	1.94 (0,0)	0.00	3.26 (0,0)	0.88 (0,0)	59.13 (0,4.0)	0.21 (0,0)
Colostrum delivery	0.00	0.00	0.78 (0,0)	0.00	4.59 (0,0)	0.00	0.00	0.00	0.0
Extension agent	0.4 (0,0)	0.01 (0,0)	0.50 (0,0)	0.00	0.00	0.00	0.00	0.55 (0,0)	0.91 (0,0)
Feed truck	1.84 (0,5.0)	0.27 (0,1.0)	19.11 (0,52.2)	899.65 (0,4,223)	146.65 (0,208.1)	23.40 (0,52.2)	232.17 (0,312.8)	16.86 (0,11.0)	7.67 (0,24.1)
Hoof trimmer	0.20 (0,1.0)	0.27 (0,0.1)	2.74 (0,0)	7.72 (0,52.2)	27.72 (0,52.2)	0.00	0.00	0.55 (0,0)	0.00
Livestock hauler	1.74 (0,4.0)	0.78 (0,1.0)	38.22 (0,104.3)	725.99 (0,1,825)	19.93 (0,52.2)	0.00	52.41 (0,156.4)	13.3 (0,12.0)	3.65 (0,24.1)

Manure hauler	0.11 (0,0)	0.03 (0,0)	10.18 (0,0)	822.10 (0,2,085)	282.25 (0,52.2)	0.00	0.88 (0,0)	2.77 (0,0)	0.00
Milk truck	0.00	0.00	0.00	0.00	434.25 (0,1,303)	0.00	0.00	2.77 (0,0)	0.00
Neighbor	6.99 (0,17)	5.13 (0,13.5)	48.18 (0,149.0)	60.46 (0,156.4)	33.22 (0,104.4)	34.24 (0,104.3)	1.67 (0,0)	50.00 (0,156.4)	14.60 (0,56.1)
Nutritionist	0.02 (0,0)	0.02 (0,0)	4.38 (0,0)	23.18 (0,52.1)	24.46 (0,52.2)	1.63 (0,0)	2.56 (0,0)	1.66 (0,0)	(0,0)
Processing crew	0.70 (0,2.0)	0.44 (0,0)	0.54 (0,0)	1.94 (0,0)	0.00	0.00	1.20 (0,0)	2.22 (0,0)	1.03 (0,0)
Renderer	0.03 (0,0)	0.02 (0,0)	8.63 (0,0)	143.36 (0,312.8)	30.66 (0,156.2)	0.00	26.61 (0,52.2)	0.00	0.00
Sales rep	0.57 (0,2.0)	0.17 (0,0)	8.50 (0,52.2)	69.67 (0,260.7)	30.67 (0.52.2)	0.00	9.70 (0,26.1)	4.53 (0,0)	1.24 (0,0)
Semen delivery	0.15 (0,0)	0.10 (0,0)	0.00	0.00	28.37 (0,52.2)	0.00	35.76 (0,104.3)	0.80 (0,0)	0.55 (0,0)

Shearer	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.70 (0,4.0)	0.00
Veterinarian	1.18(0,3.0)	1.08 (0,2.5)	5.99 (0,18.6)	29.41 (0,104.3)	44.17 (0,104.3)	0.00	20.81 (0,52.2)	7.77 (0,33.5)	1.21 (0,8.0)

Table 2.8 - Distance traveled in kilometers by all indirect contacts (10th, 50th and 90th percentiles) to each operation type reported by 1130 quarterly surveys from 532 livestock operations in Colorado and Kansas.

Operation Type	Mean	10th percentile	Median	90th percentile
Large Cow/Calf	66	3	16	145
Small Cow/Calf	37	2	16	90
Dairy	101	5	16	145
Large Feedlot	221	8	109	322
Small Feedlot	108	8	52	217
Large Swine	84	8	40	306
Small Swine	39	3	20	97
Beef and Swine	52	3	24	97
Small Ruminant	101	8	32	161
Total	81	3	24	161

Chapter 3 - The feasibility of depopulating a large feedlot during a possible Foot and Mouth Disease outbreak

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Abstract

Objective - To examine the ability to depopulate a large feedlot during a possible Foot and Mouth disease outbreak in the Central United States.

Design – Delphi survey followed by face-to-face facilitated discussion.

Sample – Experts in the related fields which included academic toxicologists, pharmacologists and animal behaviorists as well as feedlot managers and consulting veterinarians.

Procedures – A total of 4 large animal veterinary pharmacologists, 5 veterinary toxicologists, 4 animal welfare experts, 26 veterinary consultants, and 8 feedlot managers were invited to participate.

Results – 27 of the 47 invited experts participated in the survey. The consensus of the survey was that several toxicological agents were deemed highly effective; however, all of these agents also had high animal welfare concerns. The only pharmacologic agent that was considered highly effective for euthanasia was pentobarbital sodium IV and the only agent highly effective for sedation was xylazine. All the clinical signs of toxic agents were deemed high or moderate welfare concerns; yet there were minimal concerns with penetrating captive bolt and intravenous injection. However, both veterinarians and managers identified penetrating captive bolt as a minimally effective method of mass euthanasia. Veterinarians had high concerns for public perception, human safety during euthanasia, and completing the mass euthanasia in a timely manner.

Conclusions and Clinical Relevance - Regardless of the method used for depopulation of cattle in a large feedlot, it would be very difficult to complete the task humanely, and in a timely fashion.

Introduction

During the Foot and Mouth Disease (FMD) outbreak in the United Kingdom (UK), more than 6 million animals were culled for disease control or welfare problems resulting from animal movement restrictions[1]. The United States (US) has a large, highly productive and efficient agriculture industry that is increasingly concentrated compared to the agriculture production in the UK. With the last FMD outbreak in the US occurring in 1929, the increased movement of livestock and agriculture products, and the lack of any vaccination program, the US cloven-hoofed domestic and wild animals are fully susceptible to FMD.

The central US has a large number of large feedlot operations and an economy that is largely linked to the agriculture industry. A published model of an FMD outbreak beginning in a south-west Kansas large feedlot (> 40,000 head) predicted that over 1.2 million of 2 million animals in the study population would be destroyed[2]. Another study limited to eight counties in the Panhandle region of Texas, a high-density livestock area with an estimated 1.8 million cattle on feed, found that outbreaks initiated in >50,000 head feedlots required that as many as 230 of these feedlots be depopulated[3]. The United States Department of Agriculture National Agricultural Statistics Service reported 330 operations with cattle on feed in the US that had ≥ 8,000 head of cattle[4]. The introduction of FMD in the US would be devastating to producers as well as the local, state and national economy.

Highly infectious diseases such as FMD, often require quarantine, depopulation and disposal of whole herds in order to prevent the continued spread of the disease. Depopulation refers to the killing of animals efficiently and quickly under extenuating circumstances, such as animals with a zoonotic disease, during rapidly spreading outbreaks, or when animals are isolated by natural disaster[5]. The immediate depopulation of animals on farms where FMD clinical cases have occurred has been considered a mainstay of foreign animal disease eradication[6]. An emergency response to a FMD outbreak would require an extensive understanding of the scientific, technical, and social aspects to depopulation to effectively control spread of disease and minimize economic impact, while considering human and animal health and welfare concerns. Early in the 2001 UK outbreak it became clear that the logistics of killing large numbers of animals had received little consideration[7]. Numerous public complaints were reported to the Royal Society for the Prevention of Cruelty to Animals[8].

Substances used for euthanasia should minimize environmental contamination or exposure of other animals or humans to agents or toxins. The Texas Panhandle region Palo Duro Exercise in 2007 determined the goals of depopulation and disposal of the carcasses was not feasible in a timely manner[9]. It is critical to determine if it is possible to humanely depopulate the animals in a large feedlot. The effect of culling on veterinarians and the farming community during an outbreak can be traumatic[10]. The lesson to be learned from the 2001 UK FMD outbreak is that ‘a balance must be struck between disease control and welfare, but welfare must not be set aside, even in an emergency’[11]. The AVMA guidelines for humane euthanasia states that under unusual situations such as disease eradication, euthanasia options may be limited so the most appropriate technique that minimizes human and animal health concerns must be used[12]. Depopulation is defined as the killing of animals in large numbers in response to an animal health emergency where all due consideration is given to the terminal experience of the animal, but the circumstances surrounding the event are understood to be exigent and extenuating[13]. The objective of this study was to research possible methods to depopulate a large feedlot in a timely and efficient manner that minimizes the human and animal health concerns.

Methods

An online Delphi survey was conducted utilizing experts within the cattle feedlot industry to explore potential methods of euthanasia in a large commercial feedlot. Experts in food animal pharmacology, food animal toxicology, food animal welfare, as well as feedlot veterinary consultants and feedlot managers were asked questions to identify possible methods and time requirements for depopulation of large cattle feedlots. Experts identified the parameters for the discussion in an exploratory phase followed by an online iterative Delphi approach to generate expert consensus in each area of expertise. The Delphi method involved repeated polling of the experts using anonymous questionnaires to structure group communication[14]. It is based on the assumption that group judgments are more valid than individual judgments, while avoiding the potential bias of face to face discussion. The responses of each round are used in the subsequent round as controlled feedback, and the final round, where the response of the participants did not change from one iteration to another, was used to produce a group judgment. Briefly, participants in each group answer the same survey questions in each iteration of the survey. Following the first iteration question-specific median responses from all participants from the previous round are provided for participant consideration during the next round of the survey. This allows participants to reconsider their responses in light of their peers' responses to the same questions from the previous round. Following the online Delphi survey, a facilitated round table discussion was held with an expert from each area to allow group learning of the technical and practical aspects of the problem[15]. Approval for this survey was obtained from the Kansas State University Institutional Review Board committee for Research Involving Human Subjects.

Study participants

Large animal veterinary pharmacologists, veterinary toxicologists, animal welfare experts, veterinary consultants, and feedlot managers were invited to participate. Pharmacology, toxicology and welfare experts were invited to participate based on literature review for authors of publications and on expert opinion. Veterinary consultants were recruited from the membership of the Academy of Veterinary Consultants. The feedlot managers were recommended for the survey by the participating veterinary consultants based on experience and knowledge of the industry.

Survey Design

The initial exploratory round of the survey was designed to allow each group of experts to identify the important issues and methods related to depopulation of a large number of cattle in a feedlot. Veterinary toxicologists and pharmacologists were asked to identify potential agents and methods for use in timely mass cattle euthanasia. Timely mass cattle euthanasia was defined as large numbers of cattle in a short period of time. Pharmacologists were also asked to list agents that could be used for mass sedation. Both toxicologists and pharmacologists were also asked to list animal welfare considerations and human safety concerns and environmental disposal considerations for each of the agents they listed. In the initial exploratory round, consulting veterinarians and feedlot managers were asked to list possible methods to kill a large number of cattle in a short period of time in large feedlots and list possible concerns relative to mass euthanasia.

The following rounds used the depopulation methods and issues generated in the first round in a Delphi survey with the responses from the exploratory phase being listed as potential methods and agents. For the iterative phase of the Delphi survey effective depopulation was defined as the ability to quickly and efficiently depopulate the cattle in the feedlot. Pharmacology and toxicology experts were asked to rate effectiveness of the agents identified in the exploratory phase. The consulting veterinarians and feedlot managers were asked to rate the effectiveness and their concerns with methods identified by all experts in the exploratory Delphi phase. Participants were asked to rate their level of concern or rate the effectiveness of the agent for depopulation on a Likert scale of 1-5 (1 = "highly effective" or "high concerns", 2 = "moderately effective" or "moderate concerns, 3 = "minimally effective" or minimal concerns", 4 = "not effective" or "no concerns" and 5="do not know"). An effective agent was defined as an agent that would successfully and reliably depopulate a large number of confined cattle in a short period of time.

From the euthanasia and depopulation methods identified by the exploratory round of the survey, and using toxicology textbooks for reference[16-19], a list of likely clinical signs was developed for presentation to animal welfare experts. Welfare experts were asked to rate the likely clinical signs for animal welfare concerns and for public perception concerns. The Delphi survey portion for each group varied in the number of rounds, based on how quickly consensus was reached. The median result for each questions was monitored and the survey was stopped when there was no or minimal change in the median value of the responses from one iteration to the next. Animal welfare experts received two rounds, pharmacologists and veterinary consultants received three rounds and toxicologists received four rounds of the Delphi survey.

Round Table

After the completion of the Delphi survey one pharmacologist, toxicologist, animal welfare expert, and two veterinary consultants and feedlot managers were invited to a face to face round-table discussion on the methods of depopulation as well as the time and labor requirements. Prior to the face to face discussion each participant was emailed an outline of the facilitated discussion itinerary and the results from the Delphi survey. The discussion began with a brief overview of the results of the Delphi survey and statement of the goal of the discussion to reach consensus regarding optimal methods and time requirements for mass cattle euthanasia in large feedlots. The discussion was structured to sequentially address the survey categories of methods including pharmacologic, toxicologic, and physical methods of euthanasia. In each category the Delphi results were summarized and the floor was opened for discussion to identify and clarify key points, and identify potentially acceptable methods, limitations and unacceptable methods. A final summary discussion was used to compare potentially acceptable methods and assess time and labor requirements. The discussion was completed in approximately 2 hours. It was taped and a transcript was produced to aid in summarizing the comments. Comments were assessed to identify consensus opinion of the group as well as areas of disagreement.

Results

Delphi survey

A total of 47 experts were asked to participate in the online Delphi survey. Four pharmacologists were invited, three pharmacologists completed the survey and one selected to drop out after the initial round. Three out of the four food animal welfare experts invited agreed to participate in the survey. All five veterinary toxicologists who were invited agreed to participate. Twenty-six feedlot veterinary consultants were invited via email to participate and 12 agreed. The feedlot managers were recommended for the survey by the participating veterinary consultants; eight invitations based on recommendations of three veterinary consultants were sent out via email and four accepted and participated.

In the first round of the survey, toxicologists identified 13 potential agents and pharmacologists identified four potential agents for use in depopulation. Pharmacologists also identified six potential agents for sedation prior to euthanasia. In subsequent rounds of the survey each group evaluated the respective agents according to the effectiveness for euthanasia, human health risk, animal welfare concerns, carcass disposal concerns, and availability of sufficient supply (Table 1). Several toxicological agents were deemed highly effective however all of these agents also had high animal welfare concerns.

The only pharmacologic agent that was considered highly effective for euthanasia was pentobarbital sodium IV and the only agent highly effective for sedation was xylazine (Table 2).

Animal welfare and behavior experts were asked to evaluate the animal welfare impacts of expected clinical signs of toxic agents for the animals experiencing the signs and for pen mates and cattle in the vicinity. All the clinical signs of toxic agents were deemed high or moderate welfare concerns; however there were minimal concerns with penetrating captive bolt and intravenous injection (Table 3). There were also moderate concerns for the welfare of other cattle in the vicinity of animals being euthanized by sharpshooters in a lane or small pen.

The only method of depopulation identified as highly effective by veterinary consultants and feedlot managers was feeding a toxic agent to cattle while in pens (Table 4). Both veterinarians and managers identified penetrating captive bolt as a minimally effective method of mass euthanasia. Veterinarians identified sharpshooters shooting cattle as moderately effective however managers rated it not effective. Veterinarians had high concerns for public perception, human safety during euthanasia, and completing the mass euthanasia in a timely manner. They had moderate concerns for mental trauma to the workforce doing the euthanasia, animal welfare and carcass disposal.

Round table discussion results

Present for the discussion was a veterinary pharmacologist, veterinary toxicologist, veterinary animal welfare expert, two veterinary consultants, and one feedlot manager. The discussion was moderated by a one of the authors (Sanderson).

Toxicological agents

Organophosphates were identified as potential toxic agents for use in depopulation, and that depending on the compound a very small amount would be effective. Panelists agreed that with the most potent compounds of organophosphates, animals would die acutely with few clinical signs. Supply of organophosphates was not a concern but achieving consumption of a homogenous and adequate dose when feeding in the bunk was a concern. Panelists agreed that while an adequate toxic dose can be calculated not all the cattle in the pen will eat immediately, some being more aggressive than others. To encourage all animals to eat immediately, feeding 3 hours later than the regular schedule was recommended. The panel toxicologist indicated that power washing and detergent would be sufficient to clean the equipment used to deliver toxic feed. Additional issues that were brought up included manpower to dispose of the carcasses, environmental residue, and predator concerns due to secondary poisonings. The panelists indicated that carcass removal and disposal would be a major problem. Panelists agreed that with any toxicological agent a secondary method would be necessary to humanely euthanize cattle that did not receive an adequate dose in feed. The panel toxicologist indicated 95% would likely die acutely from the feed toxin and some other method would be necessary to euthanize the remaining 5% of cattle. Panelists agreed that feeding a toxic agent to cattle would not fit the definition of euthanasia but would be considered depopulation.

Pharmacological methods

Due to availability and disposal concerns, panelists agreed intravenous phenobarbital sodium would not be effective for mass euthanasia in this type of situation. Panelists also expressed concern regarding the cost of intravenous pentobarbital. For intravenous injection euthanasia, each animal would be run through the chute, and removed after euthanasia in order to get the next animal in. While panelists indicated that a large feedlot could process approximately 1,000 head of cattle per day for vaccination, the need to manually remove each animal from the chute would slow this process down dramatically. Sedative agents, xylazine and ketamine mixed together were considered very effective even in fractious cattle for sedation and release from the chute prior to euthanasia following recumbency in the pen. Panelists had concerns regarding availability of xylazine and a much smaller dose of xylazine was considered effective if used in conjunction with ketamine. Xylazine and ketamine sedation was not believed to provide sufficient sedation to use potassium chloride for euthanasia. Acepromazine was another sedative agent discussed that could be top dressed on feed but availability was a concern. Any method of sedation would require follow-up euthanasia with captive bolt or firearm after they are released, become recumbent and are restrained with a halter. This method would be timelier than euthanasia in the chute but panelists had some concerns on human safety with the use of captive bolt or firearms on recumbent cattle in the pen.

Physical methods

Captive bolt and gunshot were both identified as effective methods to euthanize individual cattle but neither was considered an effective way to depopulate a large number of cattle in a timely manner. For captive bolt euthanasia, like IV euthanasia, each animal would be run through the chute, and removed after euthanasia in order to get the next animal in slowing this process down dramatically. The timeliness would be improved if cattle were sedated in the chute and then released in an alleyway or pen for euthanasia, by captive bolt or gunshot, once they were recumbent. Due to safety concerns of euthanizing sedated unrestrained cattle in an alleyway, personnel with trained sharp-shooting experience were considered to be a better option than captive bolt euthanasia of unrestrained sedated cattle. Panelists agreed the most convenient, lowest cost option appeared to be the intramuscular injection of a combination of xylazine and ketamine for immobilization of animals while the animals are in the working alley followed by euthanasia with captive bolt or firearm after they are released. An additional method that was discussed was sharpshooters depopulating unrestrained and unsedated cattle in an alleyway. The panelists agreed that this method had high animal welfare, human safety, and public perception concerns.

Though carbon monoxide gas was not considered effective by the Delphi survey participants, the panelists did discuss whether it could be a timely method of depopulation. Panelists did not agree whether it was a timely, practical method.

Discussion

One method to combine expert opinion in an unbiased way is a Delphi process[20]. A properly conducted Delphi survey greatly improves the chances of obtaining unbiased estimates that account for the knowledge and judgment of experts compared to traditional discussions and meetings[21]. To control investigator bias the exploratory round of the Delphi survey was used to allow the participants to identify the methods to be further investigated. In the exploratory round of questions for the Delphi survey each group of experts generated the list of possible agents or methods that would be considered within their area of expertise. Experts were asked to provide any agent or method that might be used to kill large numbers of cattle in a short period of time. These results were used to generate the subsequent iterative Delphi survey. The Delphi process allows participants to provide feedback on questions without the bias associated with group pressure or dominant individual pressure as individuals can reassess their expert opinions based on anonymous information from previous iterations[14]. Following the Delphi survey, the face to face discussion allowed the subject matter experts from each area to review and discuss the results. The value of the face to face discussion is to allow group learning of the technical and practical aspects of the problem across disciplines[15] and to arrive at a consensus of the "best" approach to a problem. To control for bias in the round table discussion the moderator was present to allow the expert in the field being discussed to have the table at the start of each discussion. The discussion was then allowed to flow with the moderator working to engage all experts in each field for each method. The moderator also made sure that all Delphi identified effective methods were deliberated.

Despite the number of possible agents and methods included in the Delphi survey there were no agents or methods that were agreed upon as a safe, humane, and able to quickly kill large numbers of cattle (timeliness). Veterinary consultants and feedlot managers indicated the most effective method for timely and humane depopulation in a large feedlot would be feeding a toxic agent. The toxicologists agreed that several toxic agents would be effective but there was also agreement that animal welfare and safe disposal of carcasses was a high concern with the use of the toxicological agents for depopulation. The addition of expertise from environmental toxicologists would strengthen the data reported here in terms of disposal concerns for toxic agents. Veterinary toxicologists are sufficiently trained and have experience to identify agents of concerns but they lack the training in environmental disposal that an environmental toxicologist would have been able to add to the discussion. In the survey of pharmacological agents, pentobarbital was considered effective for euthanasia but there was concern over timeliness of euthanasia, disposal of carcasses and whether there would be sufficient drug supply available. Xylazine was agreed upon as an effective option for sedation followed by another method of euthanasia but again timeliness and supply were concerns.

AVMA's guidelines distinguish depopulation activities, recognizing depopulation in some cases may not fit the definition for euthanasia. While desiring to induce as little distress as possible, the goal of rapid depopulation may not be compatible with elimination of distress and euthanasia. In the face to face discussion it was believed that a high dose of organophosphate could be used that would cause an acute death and minimize the animal welfare concerns for most cattle in a pen. The human safety concern to the personnel was considered minimal due to the ability to effectively clean the equipment that would dispense the toxin in the feed. The clinical signs that are present with organophosphate toxins are salivation, lacrimation, and diarrhea. Though the organophosphates were deemed to be the best option for toxicological depopulation of a large feedlot there were substantial concerns over animal welfare and ability to dispose of the carcasses. In the face to face discussion it was clear that using organophosphates in the feed would be considered a method of depopulation and not humane euthanasia leading to concerns over animal welfare and public perception. Organophosphate compounds have been reported as highly toxic but the reports are from accidental exposures where the dose is often unknown. This lack of knowledge related to dose complicates calculation of the needed dose in feed for reliable and quick death. Due to the lack of data on appropriate dose for any toxic agent, use of a toxicological agent in feed would require a secondary option be immediately available to humanely euthanize calves that did not die quickly. Both firearms and captive bolt were regarded as options to humanely euthanize the cattle with concern for the safety and mental state of the personnel carrying out the process. Furthermore, depopulation of cattle using intoxicants such as organophosphates would likely require burial of carcasses in landfills designated for hazardous waste depending on the lethal dose of the agent[22] and would require additional manpower for transport. A large number of cattle would likely strain or exceed the capacity of available nearby landfills designated for hazardous waste.

Carbon monoxide was discussed during the face to face discussion as being potentially timely but Delphi survey participants did not consider it effective. Participants expressed concern over the concentration of carbon monoxide necessary for humane euthanasia and the welfare of personnel and animals. Previous research found that guinea pigs collapsed in 40 seconds to 2 minutes at 8% carbon monoxide concentration[23]. Carbon monoxide does induce loss of consciousness with minimal discomfort and often rapid death, but significant care must be taken due to possible exposure to personnel with this technically complex method. Participants were concerned with providing an adequate carbon monoxide source and environment that would minimize the stress to the animals while allowing rapid rise in carbon monoxide levels and other noxious gases that are present in exhaust. The AVMA euthanasia guidelines report that the carbon monoxide flow rate must be adequate to rapidly achieve a uniform concentration of at least 6%[13]. Whether this concentration could be achieved utilizing an ad hoc system in a large feedlot is unknown but due to human health and animal welfare concerns a consensus was not reached on its effectiveness.

Pharmacological methods for depopulation were also contemplated and there was agreement with the results of the Delphi survey and the face to face discussion. Sedation of cattle with xylazine or a xylazine/ketamine combination followed by the use of a captive bolt or firearm for euthanasia was considered an acceptable and humane method for depopulation. This would require working all cattle through an alley and chute to administer the sedative followed by release and then euthanasia of recumbent individuals in pens or alleyways. A portion of cattle would likely not become recumbent and would require an alternate method for euthanasia such as gunshot by sharpshooters. Braun, et al., demonstrated that xylazine at 0.5 mg/kg IM resulted in 52 out of 90 healthy cows lying down within 20.7 ± 8.4 minutes[24]. Due to the uncertainty surrounding recumbency and concerns regarding xylazine supply, there was concern about the feasibility of this method. Any method involving moving cattle through an alley and chute would require proper handling to minimize pain and distress in animals, to ensure safety of the person performing the euthanasia, and, often to protect other people and animals[13]. This method would require the cattle to be handled twice (once through the chute and once while recumbent in the pen) but it would not require the cattle to be removed from the chute manually. Additionally as with the use of any chemicals for depopulation, disposal could potentially be complicated. Panelists indicated in a large feedlot approximately 1,000 head could be worked through the chute for vaccination in a day. Depending on the methods used for depopulation the daily number of head worked could be much lower. If the feedlot had 50,000-100,000 head of cattle it would be very difficult to euthanize the animals in a timely manner and properly dispose of the carcasses.

The final methods of depopulation that were studied were physical methods. With physical methods of euthanasia, welfare concerns included correct placement of the captive bolt or gun shot as well as having enough personnel that understand and are experienced in animal handling. Lack of trained personnel was a reported welfare problem during the depopulation of animals during the 2001 UK outbreak[8] and a concern of the panelists. The captive bolt would be a humane euthanasia method and it is currently 90% effective without a secondary step. New research for an air-injection system for captive bolt could render it a one-step process. With gun-shot and current captive bolt technology, the acceptable secondary methods are pithing, shooting a second time, and using potassium chloride intravenously. The panelists agreed that euthanasia with a captive bolt in restrained cattle in the chute is humane and preferred method but it would be difficult to depopulate a feedlot in a timely manner. If animals are restrained in a chute for captive bolt, removal of the down cattle from the chute would dramatically slow the process. Participants agreed that utilizing sharpshooters and gunshot, while potentially faster, has concerns regarding animal welfare and the safety of personnel. There were additional concerns over having enough qualified personnel and the public perception of this method of depopulation.

For intoxicants, organophosphates were deemed the best option due to minimal operator or human safety concerns and the high toxicity of the agent. Animal welfare concerns were high due to inconsistent consumption and a secondary option for euthanasia would be required. Due to concerns with environmental residue issues and welfare concerns the use of intoxicants for depopulation was not considered an acceptable method. Physical methods of euthanasia and depopulation such as captive bolt of cattle restrained in a chute were agreed upon to be an effective and safe method, for personnel and the animals, but it would not be a timely method to euthanatize a large feedlot because of delays in removing euthanized cattle from the chute. Due to additional environmental residue concerns of intravenous pentobarbital sodium euthanasia as well as concerns of this method not being timely, captive bolt in the chute was considered the better of the two options and is often considered the method of choice in emergency euthanasia.

With prior sedation, firearm or captive bolt euthanasia was considered timely but the concern for personnel and animal welfare was high due to animals not being fully restrained in a chute for euthanasia. The panelists agreed that the use of sharpshooters to euthanize the cattle had very high human safety, animal welfare, and public perception concerns.

While not the focus of the survey, for all methods, the removal and disposal of the carcasses was a frequent topic of concern during the round table discussion. Panelists agreed a tremendous about of labor would be required for all methods including veterinarians and equipment operators. Almost all of the experts at the discussion had experience with small numbers of animal carcasses due to disasters and related the difficult experience with animal removal and disposal. Animals cannot be left in the environment for extended periods of time so the rate of depopulation should not exceed the rate of disposal. Managing traffic of equipment to pull cattle away rapidly was considered a major issue. Any method such as an IV injectable euthanasia or captive bolt in the chute that resulted in cattle dying in or near the chute was particularly concerning. Moving a large number of carcasses in a feedlot in general was regarded as a very difficult task even with trained and experienced personnel on site. Participants agreed that during a FMD outbreak having enough trained and experienced personnel could also be an issue as well as proper burial of the large number of carcasses. Burial of carcasses is considered the most cost efficient method of disposal of occasional livestock losses but it could pose serious pollution risk to local groundwater and surface water resources if thousands of tons of carcasses needed to be disposed of quickly[25]. An additional concern if burial of a carcass with an intoxicant was allowed was the possibility of organophosphates, pentobarbital sodium, xylazine, or other agents leaching into the soil, groundwater contamination, and secondary poisoning (eagles, hawks, coyotes, foxes domestic dogs and cats).

The rate of disposal of the carcasses would be important to prevent secondary poisonings. While not the focus of this project, the participants expressed concern that despite the difficulties of timely depopulation, timely and appropriate disposal may be an even bigger problem.

The panel participants suggested that an alternative to mass depopulation would be to humanely euthanize animals as needed based on clinical signs in the face of a FMD outbreak in a large feedlot while allowing the disease to run its course. The size of FMD epidemics have been attributed to factors such as livestock density, effectiveness of control methods, late detection, and animal movement[26-28]. If FMD was allowed to run its course in a feedlot, biosecurity would be a major concern to prevent the direct or indirect spread of the virus to other livestock operations as well welfare aspects of providing the animals with feed under quarantine. Since FMD does not affect humans, the animals could still be salvaged and slaughtered once the feedlot was no longer having new cases of disease.

Vaccination may be effective in decreasing transmission between and even within feedlots, decreasing the need for depopulation. Perez et. al, found that vaccination of cattle and movement restrictions significantly decreased the transmission of the virus in the 2001 FMD epidemic in Argentina[29]. Vaccination is more widely used in conjunction with depopulation to control the spread of the highly infectious FMD virus[30]. In the 2001 FMD outbreak in the Netherlands and the 2001 outbreak in Uruguay; after depopulating infected herds for a period of time, vaccination was initiated and was successful in stopping the outbreak[11]. In the U.S, a vaccine has been developed that enables vaccinated cattle to be distinguished from those that were naturally infected with the disease[31]. Such a vaccine could make the slaughter of vaccinated animals unnecessary to regain trade status.

The goal of every response effort will be to stop the spread of the FMD but the best strategy will depend on many factors. The United States Department of Agriculture states in their FMD Response Plan that emergency vaccination may be considered and the strategy decision will be influenced by many factors including the location of the outbreak, FMD vaccine availability, and the resources available to implement response strategies[32].

Conclusion

No clearly acceptable method of rapidly depopulating a large feedlot was identified from this survey and discussion. All methods identified had serious drawbacks. Participants agreed that regardless of the method used for depopulation of cattle in a large feedlot, it would be very difficult to complete the task quickly, humanely, and be able to dispose of the carcasses. These results suggest that control of FMD in large feedlots will require other methods than depopulation and available alternatives should be researched.

References

1. National Audit Office Department of Environment, Food and Rural Affairs. Foot and Mouth Disease: Applying the Lessons. 2005, Available at: www.nao.org.uk. Accessed Oct 23, 2012.
2. Pendell DL, Leatherman JC, Schroeder TC, et al. The Economic Impacts of a Foot-And-Mouth Disease Outbreak: A Regional Analysis. J Agric Appl Econ. 2007 October 15;39:19-33.
3. Ward MP, Highfield LD, Vongseng P, et al. Simulation of foot-and-mouth disease spread within an integrated livestock system in Texas, USA. Prev Vet Med. 2009;88(4):286-297.
4. United States Department of Agriculture, National Agriculture Statistics Service. National Statisitics for Cattle. Available at: http://quickstats.nass.usda.gov/results/0C9713F1-79E1-3B6E-B286-92370887B62E?pivot=short_desc. Accessed Jul 11, 2013.
5. Burns K, Kahler SC. More news from the boardroom: poultry depopulation. J Am Vet Med Assoc. 2007;230(5):657-658.
6. Howard S, Donnelly C. The importance of immediate destruction in epidemics of foot and mouth disease. Res Vet Sci. 2000;69(2):189-196.
7. Crispin SM, Roger PA, O'Hare H, et al. The 2001 foot and mouth disease epidemic in the United Kingdom: animal welfare perspectives. Rev Sci Tech. 2002;21(3):877-883.
8. Laurence C. Animal welfare consequences in England and Wales of the 2001 epidemic of foot and mouth disease. Rev Sci Tech. 2002;21(3):863.

9. Texas Animal Health Commission. Operation Palo Duro February 21-23. 2007, Available at: http://www.tahc.state.tx.us/emergency/May2007_OperationPaloDuro.pdf. Accessed Apr 01, 2013
10. Sutmoller P, Barteling SS, Olascoaga RC, et al. Control and eradication of foot-and-mouth disease. Virus Res. 2003;91(1):101-144.
11. Farm Animal Welfare Council. Department for Environment, Food and Rural Affairs Publications/Division; Foot and mouth disease 2001 and animal welfare: lessons for the future. 2002, p. 21.
12. AVMA Guidelines for Euthanasia. 2007, Available at: www.avma.org/KB/Policies/Documents/euthanasia.pdf Accessed Oct 23, 2012.
13. Nusbaum KE, Wenzel GW, Everly Jr. GS. Psychologic first aid and veterinarians in rural communities undergoing livestock depopulation. J Am Vet Med Assoc. 2007;231(5):692-694.
14. Hsu, C.-C. and B. A. Sandford (2007). "The Delphi technique: making sense of consensus." Practical Assessment, Research & Evaluation **12**(10): 1-8.
15. Stalker SA, Weir E, Vessel SL, et al. Planning a coordinated local health care system response to a pandemic using an accelerated Delphi technique: phase 1. Can J Public Health. 2009 Jan-Feb;100(1):65-69.
16. Buck WB, Osweiler GD, VAn Gelder GA. Clinical and diagnostic veterinary toxicology. Hunt, Dubuque, Iowa: Kendall; 1976. p. 326.
17. Lorgue G, Lechenet J, Rivière A, et al. Clinical veterinary toxicology: Blackwell Science; 1996.
18. Plumlee K. Clinical veterinary toxicology: Mosby; 2003.

19. Cynthia M, Kahn M. The merck veterinary manual. Philadelphia. 2005;131:425.
20. Jones J, Hunter D. 1995 Qualitative research: consensus methods for medical and health services research. Brit. Med. J. 311:376-380.
21. Green KC, Armstrong JS, Graefe A. Methods to elicit forecasts from groups: Delphi and prediction markets compared. Int J Forecast. 2007;8:17-20.
22. U.S. National Archives and Records Administration. Code of Federal Regulations. Title 40. Definition of hazardous waste. Available at http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&SID=c3e2fa9b9bcc7198976902819e7953e3&tpl=/ecfrbrowse/Title40/40cfr261_main_02.tpl. Accessed Aug 14, 2013.
23. Ramsey TL, Eilmann HJ. Carbon monoxide acute and chronic poisoning and experimental studies. J Lab Clin Med. 1932;17:415-427.
24. Braun U, Abgottspon S, Gubler E, et al. Decreased sedation by xylazine and high blood pressure in cows with BSE. Vet Rec. 1999;144(26):715-717.
25. Glanville TD, Richard TL, Harmon JD, et al. Environmental impacts and biosecurity of composting for emergency disposal of livestock mortalities. 2006.
26. Yang PC, Chu RM, Chung WB, et al. Epidemiological characteristics and financial costs of the 1997 foot-and-mouth disease epidemic in Taiwan. Vet Rec. 1999 Dec 18-25;145(25):731-734.
27. Gibbens J, Wilesmith J, Sharpe C, et al. Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months. Vet Rec. 2001;149(24):729-743.
28. Ferguson NM, Donnelly CA, Anderson RM. The Foot-and-Mouth Epidemic in Great Britain: Pattern of Spread and Impact of Interventions. Science. 2001;292(5519):1155.

29. Perez AM, Ward MP, Carpenter TE. Control of a foot-and-mouth disease epidemic in Argentina. Preventive Veterinary Medicine. 2004 Oct 14;65(3-4):217-226.

30. Davies G. Foot and mouth disease. Res Vet Sci. 2002;73(3):195-199.

31. New Foot-and-Mouth Disease Vaccine Gets Licensed for Use on Cattle. October, 2012, Available at: http://www.dhs.gov/publication/st-piadc-press-release-oct-2012. Accessed Apr 30, 2013.

32. United States Department of Agriculture Animal and Plant Health Inspection Service Veterinary Services. National Center for Animal Health and Emergency Management. FAD PReP Foreign Animal Disease Response Plan. May 2012, Accessed Dec 28, 2012.

Table 3.1 – Agents identified by veterinary toxicologists in the exploratory phase of the survey and attributes for mass euthanasia/depopulation of cattle in a large feedlot in the United States from the Delphi survey.

Agent	Effectiveness	Human Health Risk	Animal Welfare Concerns	Carcass Disposal Concerns	Availability of Sufficient Supply
Arsenic	Not effective	Minimal concerns	High concerns	High concerns	Minimal concerns
Cyanide	Highly effective	High concerns	High concerns	No concerns	Moderate concerns
Nitrates	Moderately effective	No concerns	High concerns	No concerns	Minimal concerns
Nitrite	Moderately effective	No concerns	High concerns	No concerns	Minimal concerns
Urea	Moderately effective	No concerns	High concerns	No concerns	Minimal concerns
Aluminum phosphide	Highly effective	High concerns	High concerns	Moderate concerns	Moderate concerns
Strychnine coated milo	Highly effective	Moderate concerns	High concerns	Moderate concerns	Moderate concerns
Organophos-phates	Highly effective	High concerns	High concerns	Moderate concerns	No concerns
Taxus sp.	Moderately	Minimal	High	Minimal	Moderate

	effective	concerns	concerns	concerns	concerns
Bluegreen algae	Moderately effective	No concerns	High concerns	Minimal concerns	High concerns
Oleander	Moderately effective	No concerns	High concerns	Minimal concerns	High concerns
Carbon monoxide	Minimally effective	High concerns	Moderate concerns	No concerns	Minimal concerns
Carbamates	Highly effective	Moderate concerns	High concerns	Moderate concerns	No concerns

Table 3.2 - Agents identified by veterinary pharmacologists in the exploratory phase of the survey and attributes for mass euthanasia/depopulation of cattle in a large feedlot in the United States from the Delphi survey.

Agent	Effectiveness	Human Health Risk	Animal Welfare Concerns	Carcass Disposal Concerns	Availability of Sufficient Supply
Pentobarbital sodium IV	Highly effective	Minimal concerns	Minimal concerns	High concerns	High concerns
T61 euthanasia solution	Minimally effective	Moderate concerns	High concerns	High concerns	High concerns
Potassium chloride	Minimally effective	Moderate concerns	High concerns	No concerns	Minimal concerns
Magnesium chloride	Minimally effective	Moderate concerns	High concerns	No concerns	Moderate concerns
Pentobarbital IM*	Minimally effective	Moderate concerns	Moderate concerns	High concerns	High concerns
Xylazine*	Highly effective	Moderate concerns	Minimal concerns	Moderate concerns	Moderate concerns
Xylazine/ Ketamine*	Moderately effective	Moderate concerns	Minimal concerns	Moderate concerns	Moderate concerns
Acepromazine injection*	Moderately effective	Moderate concerns	Minimal concerns	Minimal concerns	Moderate concerns
Potent opiates	Moderately	High	Moderate	Moderate	Moderate

via darting*	effective	concerns	concerns	concerns	concerns
Acepromazine granulates*	Moderately effective	Minimal concerns	Minimal concerns	Minimal concerns	Moderate concerns

*agent identified for sedation prior to euthanasia/depopulation

Table 3.3 - Animal behaviorists evaluation of animal welfare and public perception concerns associated with specific methods of mass euthanasia/depopulation of cattle in a large feedlot in the United States and the Delphi survey results.

Methods of Depopulation	Animal Welfare Concerns	Public Perception Concerns
Penetrating captive bolt while in a chute	Minimal concerns	No concerns
Penetrating captive bolt in a lane or pen after cattle have been sedated in a chute and released	Minimal concerns	Minimal concerns
Intravenous injection while in a chute	Minimal concerns	Minimal concerns
Feeding a toxic agent to cattle while in pens	High concerns	High concerns
Sharpshooters shooting cattle while grouped in a lane or pen	Moderate concerns	Moderate concerns
Carbon monoxide, cattle would be herded in a silage pit with a tarp over the top	Moderate concerns	Moderate concerns

Table 3.4 - Veterinary consultant and feedlot manager list of possible methods and the evaluation of their effectiveness to mass euthanasia/depopulation of cattle in a large feedlot in the United States and the Delphi survey results.

Methods of Depopulation	Effectiveness	
	Veterinarians	Managers
Penetrating captive bolt while in a chute	Minimally effective	Minimally effective
Penetrating captive bolt in a lane or pen after cattle have been sedated in a chute	Moderately effective	Minimally effective
Intravenous injection while in a chute	Minimally effective	Minimally effective
Feeding a toxic agent to cattle while in pens	Highly effective	Highly effective
Gunshot by sharpshooters shooting cattle while grouped in a pen or lane	Moderately effective	Not effective
Carbon monoxide, cattle would be herded into a silage pit with a tarp over the top	Moderately effective	Minimally effective

Chapter 4 - Modeling the impact of vaccination control strategies of a foot and mouth disease outbreak in the Central United States

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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 (NAADSM), a spatially explicit, stochastic infectious disease model. In this study, a potential FMD virus outbreak in the central region of the U.S. was simulated comparing different vaccination strategies to a depopulation only scenario. Based on data from the U.S. Department of Agriculture National Agricultural Statistic Service, a simulated population of livestock operations was generated. The population included 151,620 herds

defined by latitude and longitude, production type, and herd size. 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. The control methods included ring vaccination around infected herds. Feedlots ≥3,000 head were either the only production type that was vaccinated or had the highest vaccination priority. Simulated vaccination protocols included low and high vaccine capacity based on results from a livestock producer survey, vaccination zones of 10 km or 50 km, and vaccination trigger of 10 herds or 100 herds. A sensitivity analysis of the biosecurity, movement control and contact rate parameters was done. All vaccination scenarios decreased number of herds depopulated but not all decreased outbreak duration. When feedlots ≥3,000 head had the highest vaccination priority few other production types were vaccinated in most scenarios. Increased size of the vaccination zone during an outbreak decreased the length of the outbreak and number of herds destroyed. Increasing the vaccination capacity had a smaller impact on the outbreak and may not be feasible if vaccine production and delivery is limited. Outbreak duration and number of herds depopulated were sensitive to biosecurity practices and movement restrictions. Vaccination was not beneficial compared to depopulation alone to control the outbreak when biosecurity and movement restrictions were increased. 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.

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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 appearance of clinical signs (Burrows, 1968; Burrows et al., 1981) subsequently 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). 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.

During a 2001 FMD outbreak in the United Kingdom (U.K.) more than 6 million animals were culled for disease control or welfare problems resulting from animal movement restrictions (National Audit Office, 2005). The total estimated cost was $6 to $10 billion (Anderson, 2002). 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). The potential impact of an outbreak in the U.S. would be devastating. Because FMD is a foreign animal disease, epidemiological disease modeling is the only avenue available to study the potential impacts of and effective control strategies for an introduction. 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).

Previous studies that have modeled FMD outbreak 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). 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). Control measures, such as, movement restrictions, increased biosecurity, depopulation, pre-emptive culling, and vaccination have been implemented in various combinations to decrease the spread of the outbreak (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 control strategy will also vary. In the face of a FMD outbreak, well-informed decisions on the best control strategy will need to be made. Within the U.S. there are regional differences in production types, management systems, operation size distributions, distance distributions that make comparison between regions difficult. In order to produce the most accurate results for the region producer-reported contact data was used to parameterize the model. The objective of this study was to model FMD outbreaks to identify vaccination control measures based on their effectiveness in controlling the outbreak duration and number of herds depopulated. A secondary objective was to analyze the sensitivity of the model to specific input parameters.

Materials and Methods

Study Population

The simulated population was based on the 2007 NASS data and production types 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 simulated 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. Seven percent of beef and swine operations were randomly re-designated from the population of cow/calf operations and small swine based on a livestock survey of the same region in which approximately 7% of herds reported having beef cattle and swine (McReynolds et al., in press). The total population was 39,413,228 animals in all production types (Table 1).

Simulation model

The North American Animal Disease Spread Model (NAADSM), an open source (Harvey and Reeves, 2010) herd-based spatial stochastic epidemic simulation model (Schoenbaum and Disney, 2003; Harvey et al., 2007) was used to model FMD eradication strategies. Scenarios were simulated for various FMD vaccination protocols compared to a depopulation only scenario. Modeled scenarios are reported in Table 2 and include variations in vaccine capacity, vaccination zone diameter, and the number of infected herds required to initiate a vaccination program. Simulated vaccination protocols included low and high vaccine capacity based on results from a Kansas and Colorado livestock producer survey. The livestock survey asked producers to report the time it would take to vaccinate their entire herd including tagging and keeping records. Vaccination priority was either large feedlot 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 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). 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. 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.

Distributions of the clinical stages of FMD 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 clinical infectious period distribution for cattle, swine and small ruminants was calculated 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. Values were discarded when the sampled subclinical value was greater than the infectious value. The resulting distribution of values was fit to a theoretical distribution (@Risk 5.0.1) to estimate the clinical infectious period for use in NAADSM. The probability of infection following a direct contact was based on within-herd prevalence as a function of time since infection. The distributions for within herd prevalence for NAADSM were produced using a within herd prevalence model (WH) (Reeves, 2012) 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 et al., in preparation). Direct and indirect contacts between livestock production types were based on a livestock contact survey in the central U.S. (McReynolds et al., in press) (Table 3 and 4). The direct contact rate was calculated from the reported count of contacts between specific production types to provide an overall production type specific daily contact rate (McReynolds et al., in press). Destination-source combinations for indirect contact were calculated based on the total number of support industry contacts with each production type, multiplied by the proportion of all support industry visits made to the respective production type to produce the number of daily contacts between each destination source combination. The daily indirect contact rate between each production type was adjusted based on the assumption that not all production types are equally connected (beef operations are more connected with each other than with swine operations). The daily mean direct (Table 3) and indirect contact rate (Table 4) between production types were used to parameterize the model. Actual contacts between production types in the NAADSM model were generated from a Poisson distribution with lambda equal to the mean contact rate for that production type combination.

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 is a fomite such as contaminated vehicle, equipment, clothing, or a person. The probability of airborne spread at 1 km was 0.5% and the maximum distance of spread was 3 km. For all scenarios, 1) the days to first disease detection was generated by the NAADSM model; 2) 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; 3) direct contact through animal movement was reduced to 10% of pre-outbreak levels by day 7 and indirect contacts were reduced to 30% of pre-outbreak levels by day 7 after disease detection; and 4) depopulation capacity was set at 8 herds/day by day 10 and 16 herds/day by day 30 after disease detection. In all simulations, quarantine of infected premises and a ban on livestock movement from infected premises was assumed. Depopulation was set to begin on day 2 after first disease detection of the outbreak. For all herds that were detected as positive, direct contacts were identified, traced forward, and depopulated. All scenarios were run for 200 iterations. The end of the active disease phase was the endpoint for all scenarios.

Experimental design

In all scenarios a single 17,000 head feedlot in Northeast Colorado was latently infected. Seventeen different disease mitigation strategies were simulated (Table 4).

Sensitivity Analysis

Values of selected 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 increasing all production type combination rates by 20% from the calculated parameter, and decreasing all production type combinations 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.

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 and daily outcome counts for each iteration of each scenario. Summary statistics were generated for each of the scenarios. Outbreak duration was calculated 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

In all scenarios the main source of new infections was indirect contacts with approximately 95% of infected herds resulting from an indirect contact and the remaining 5% infected from direct contact or airborne spread. In all scenarios the median first day of detection was at 10 or 11 days. For scenario 1, depopulation without 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. In scenario 2, with 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 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 while scenario 4 had 419 clinically infected herds.

Outbreak Duration

The model outcomes are reported in Table 5. The scenarios with a vaccination zone of 50 km (scenarios 4, 5, 8, 9, 12, 13, 16, and 17), had a shorter median and 90th percentile duration compared to the scenarios with a 10 km vaccination zone (scenarios 2, 3, 6, 7, 10, 11, 14, and 15); the best eight ranked scenarios for shortest duration all had a 50 km vaccination zone (Table 5). Scenario 16 had the shortest outbreak duration followed by scenario 4, 8, 12, and 17. The vaccination capacity and the number of herds infected prior to starting vaccination had less impact with both high and low vaccination capacity and number of herds infected to initiate vaccination represented in the top ranked scenarios. Scenario 1 ranked 10th in outbreak duration despite being a depopulation only scenario with no vaccination. Scenarios 7, 10, and 2 had the three longest outbreak durations and all had a vaccination zone of 10 km. Additionally, scenarios 7 and 10 had a late vaccination trigger of 100 herds infected prior to the initiation of vaccination.

Number of herds depopulated

Scenario 1 had a median of 6,890 herds depopulated and the distribution was heavily skewed toward higher numbers depopulated (Table 5). In scenario 1, the median number of herds depopulated included all large feedlot and dairy herds in the population. All vaccination scenarios decreased the number of herds depopulated compared to scenario 1 and scenario 1 was the only scenario with herds waiting to be depopulated at the end of the active disease phase (2,830 herds waiting, data not shown). Scenario 16 depopulated the lowest number of herds followed by scenarios 4, 8, and 17 which did not significantly differ. The best 7 scenarios with the lowest number of depopulated herds all had a vaccination zone radius of 50 km.

Herds vaccinated

Scenario 11 vaccinated the fewest number of herds followed by scenarios 3 and 7 which did not differ from each other (Table 5). The best 8 scenarios that vaccinated the fewest number of herds only vaccinated large feedlots. None of these scenarios were among the best scenarios for outbreak duration or number of herds depopulated. 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. 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

The probability of transmission of FMD virus following indirect contact was 20% in the baseline scenarios and in the sensitivity analysis it was increased to 25% and decreased to 15%. Probability of indirect transmission was influential within the range examined in determining the duration of the outbreak, the number of herds depopulated and vaccinated. Vaccination was less influential in mitigating the effects of an outbreak when probability of transmission following indirect contact was decreased to 15%. In all scenarios when the probability of indirect transmission was 15% 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%) (Table 6) 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 a vaccination zone 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 a vaccination zone of 10 km (Table 7).

Changes in the indirect contact movement controls were 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 the median duration of all scenarios was approximately 100 days (range 85-120) (Figure 7) and median herds depopulated decreased 65-95% (Table 6) to approximately 50 herds (range 39-66) (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 (Table 6) 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% (Table 7 and Figure 10). Median number of herds depopulated ranged decreased 65-97% (Table 6) to 58 to 584 herds (Figure 11). When indirect contact rates were increased by 20% the median number of herds depopulated increased 60-89% (Table 6) 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 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 but scenario 12 only ranked among the best five scenarios when the indirect contact rate was decreased by 20%. 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 8). 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 in the sensitivity analysis scenario where 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 8).

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

Discussion

General discussion

Because of the nature of FMD as a highly infective foreign animal disease, the only method to assess the impact in the U.S. of an introduction and effectiveness and effect of control is through modeling. 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 biosecurity, movement controls, and vaccination protocols were analyzed to determine the impact of the different control methods.

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 the 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 reported 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 2001

U.K. FMD outbreak where 1.4% of herds were reported as infected (Keeling et al., 2001) 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 based on visual inspection only.

In scenarios 4, 8, 12, and 16 where all production types were eligible for vaccination with large feedlots as the first priority, outbreak duration was significantly shorter than the same scenario with vaccination only in large feedlots (scenarios 5, 9, 13 and 17). However scenario 17, the same as 16 but with vaccination in large feedlots only, was ranked fifth shortest in duration of outbreak. Scenarios 4, 8, 12, 16, and 17 all had a large vaccine zone but varied in vaccine capacity and vaccine trigger. Our data is consistent with a large vaccination zone having the biggest impact on the duration of 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 outbreak when modeling a FMD outbreak in 3-county region of California. In this 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.

Scenarios 7, 10, and 2 had a longer duration of outbreak when compared to scenario 1 (only depopulation). Each of these scenarios had a small vaccination zone and low vaccination capacity. 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. The number of detected herds in scenario 1 had a steeper peak compared to scenarios with a longer duration of outbreak (Figure 2). Scenario 1 had median peak of 458 new clinically detected herds on week 32 and then fell rapidly. Scenarios 2, 7 and 10 had a peak of approximately 80 new clinically detected herds at week 22 but the outbreak persisted longer. There are likely a lower number of susceptible herds in scenario 2 due to the vaccination but the vaccination control is not able to stop the outbreak resulting in extended outbreak duration. Limited vaccination programs may limit 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 reported here however, was decreased in all vaccination scenarios including 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 determinate of outbreak cost (Schroeder et al. in review).

In the baseline scenarios number of herds depopulated was the greatest for scenario 1 and the least for scenario 16 (Table 5). 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 and not caught up with the depopulation backlog. Scenario 16, which had a large vaccination capacity as well as a large vaccination zone, was able to contain the spread by decreasing the number of susceptible herds. Due to workforce and vaccine capacity, the high capacity vaccination in a large zone might not be feasible during an outbreak. After scenario 16, scenarios 4, 8, and 17 depopulated the least number of herds and all had a large vaccination zone, though vaccination capacity varied. These results support the value of vaccination strategies, particularly those with large vaccination zones, to control disease impact.

The number of herds vaccinated was lowest in scenarios 11, 3 and 7 which all had a low vaccine capacity and vaccinated only large feedlots. Our low vaccination capacity for the scenarios where only large feedlots were vaccinated and where all herds were eligible but large feedlots were the first priority 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 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 with a small zone, vaccinated all herd types and exceeded 30,000 herds vaccinated. 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 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 of producers administering FMD vaccine since it is a restricted and controlled vaccine.

Minimizing the number of herds vaccinated is not the appropriate measure of the best vaccination strategy but rather identifying the most efficient use of vaccination. Scenarios 16, 4, 8, 12 and 17 had the shortest duration of outbreak and the lowest number of herds depopulated. The number of herds vaccinated differed greatly between the scenarios. Scenarios16 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. There may be efficiencies associated with concentrating vaccination to fewer herds such as large feedlots only in scenario 17. Animals in large feedlots are also a natural vaccinate to die (slaughter) population perhaps facilitating restoration of FMD free without vaccination status. Depopulating vaccinated animals would be a massive waste of human protein nutrition.

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. Vaccination zone size was most important. All five top ranked scenarios for the duration of the outbreak and number of herds depopulated had large vaccination zones. None of the top ranked scenarios had the low large feedlot only vaccination capacity. In the scenarios where all herds were eligible for vaccination but large feedlots had first priority followed by small feedlots, the only scenarios where any production type besides large and small feedlots were vaccinated were scenarios that had a large vaccination capacity and small vaccination zone (scenarios 6 and 14). The scenarios with the large feedlots having first priority had a higher vaccine capacity compared to matched scenarios with large feedlot only vaccination (i.e. scenarios 4 and 5, 8 and 9, 12 and 13, and 16 and 17) which allowed more large feedlots as well as small feedlots to get vaccinated. The increased vaccine capacity did improve the impact of the control methods although scenario 17 did rank in the top five scenarios for depopulation and outbreak duration. Vaccination does not require the time or the quantity of labor that are needed for depopulation and disposal of carcasses. The disadvantages of vaccination is 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 (OIE/World Organization 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).

All vaccination scenarios did improve the number of herds depopulated compared to depopulation only and an economic analysis found that vaccination was also advantageous to decreasing the median economic impact of the outbreak (Schroeder et al., in review). 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. 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. However, vaccinating to live versus to die has different implications from an international trade perspective. In that under vaccinate to live scenarios, export market access would likely be delayed at least one additional 3 months relative to a depopulating all vaccinated animals. Vaccinating to live would be advantageous in saving valuable genetics and food produced.

FMD simulation models have found that targeting high-risk production types can increase the efficiency of vaccination (Keeling et al., 2003). In this 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. Vaccination of large feedlots, which are intended for slaughter, were the focus of the vaccination protocols in these scenarios. Large feedlots have a high number of indirect contacts (McReynolds et al., in press) potentially increasing their risk of receiving and spreading infection during an outbreak. In this study the scenarios with large vaccine zones where vaccination was predominantly feedlots had a similar impact on the outbreak as scenarios where only feedlots were vaccinated in large vaccine zones. 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).

Discussion of 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 likely due to the 100% quarantine of infected herds within the model. The model was sensitive to changes in the indirect contact rate. Indirect contact rates used here are based on a survey of producers in Kansas and Colorado (McReynolds et al., in press) representing all modeled production types and provide the best available estimates of direct and indirect contacts between production types. 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, the depopulation only scenario. Again scenario 1 did appear to spread quickly with the number 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. Model results were sensitive to the indirect contact rate which was based on a survey of 532 producers in Colorado and Kansas. This highlights the need for accurate data regarding direct and indirect contacts between livestock producers.

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 due to 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 to 20% of pre-outbreak levels (baseline 30%) 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 "business as usual" 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, 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. Achievable movement controls consistent with acceptable animal welfare require additional investigation.

Probability of transmission given an indirect contact showed a similar effect in the sensitivity analysis. When the probability of indirect transmission was decreased to 15% (baseline 20%) 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 is 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 to the depopulation alone control strategy but again the 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 to 25% the number of herds depopulated was substantially increased and the impact of vaccination decreased.

The scenarios with a large vaccination zone had the greatest percentage of increase in the duration of the disease when movement controls or biosecurity was decreased. This may indicate that without sufficient movement and biosecurity controls even extensive vaccination programs may not be effective. When strict biosecurity and movement was in place in scenarios with a vaccination trigger at 100 herds, the median number of herds vaccinated was 0, likely representing the ability to effectively manage the outbreak with movement controls, biosecurity, and depopulation of infected herds.

Conclusion

In this simulation study of a FMD outbreak in the central U.S., scenarios with increased size of the vaccination zone had decreased length of the outbreak and number of herds destroyed. Increasing the vaccination capacity had a smaller 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 was 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 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. 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 (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 their impact on animal welfare. An improved knowledge of the biosecurity practices and the ability to achieve strict movement controls to limit direct and indirect transmission would allow more focused planning of optimal control efforts. 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.

References

Anderson, I., 2002. Foot & mouth disease 2001: lessons to be learned inquiry report. The Stationary Office.

Bates, T. W., T. E. Carpenter and M. C. Thurmond, 2003a. Benefit-cost analysis of vaccination and preemptive slaughter as a means of eradicating foot-and-mouth disease. Am. J. Vet. Res. 64: 805-812.

Bates, T. W., M. C. Thurmond and T. E. Carpenter, 2003b. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. Am. J. Vet. Res. 64: 205-210.

Bouma, A., A. R. Elbers, A. Dekker, A. de Koeijer, C. Bartels, P. Vellema, P. van der Wal, E. M. van Rooij, F. H. Pluimers and M. C. de Jong, 2003. The foot-and-mouth disease epidemic in The Netherlands in 2001. Prev. Vet. Med. 57: 155-166.

Burrows, R., 1968. The persistence of foot-and mouth disease virus in sheep. J. Hyg. (Lond). 66: 633-640.

Burrows, R., J. A. Mann, A. J. Garland, A. Greig and D. Goodridge, 1981. The pathogenesis of natural and simulated natural foot-and-mouth disease infection in cattle. J. Comp. Pathol. 91: 599-609.

Cottral, G. E., 1969. Persistence of foot-and-mouth disease virus in animals, their products and the environment. Bulletin - Off. Int. Epizoot. 71: 549-568.

Dickey, B. F., T. E. Carpenter and S. M. Bartell, 2008. Use of heterogeneous operation-specific contact parameters changes predictions for foot-and-mouth disease outbreaks in complex simulation models. Prev. Vet. Med. 87: 272-287.

Elbakidze, L., L. Highfield, M. Ward, B. A. McCarl and B. Norby, 2009. Economics Analysis of Mitigation Strategies for FMD Introduction in Highly Concentrated Animal Feeding Regions. Applied Economic Perspectives and Policy 31: 931-950.

Ellis-Iversen, J., R. Smith, J. Gibbens, C. Sharpe, M. Dominguez and A. Cook, 2011. Risk factors for transmission of foot-and-mouth disease during an outbreak in southern England in 2007. Vet. Rec. 168: 128-128.

Ferguson, N. M., C. A. Donnelly and R. M. Anderson, 2001. The Foot-and-Mouth Epidemic in Great Britain: Pattern of Spread and Impact of Interventions. Science 292: 1155.

Frey, H. C. and S. R. Patil, 2002. Identification and review of sensitivity analysis methods. Risk Anal. 22: 553-578.

Garner, M. and S. Hamilton, 2011. Principles of epidemiological modelling. Rev. Sci. Tech. 30: 407.

Gibbens, J., J. Wilesmith, C. Sharpe, L. Mansley, E. Michalopoulou, J. Ryan and M. Hudson, 2001. Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months. Vet. Rec. 149: 729-743.

Graves, J., 1979. Foot-and mouth disease: a constant threat to US livestock. J. Am. Vet. Med. Assoc. 174: 174.

Greathouse, B. D., 2010. Vaccination Strategies for a Foot-and-Mouth Disease Outbreak in Southwest Kansas, Colorado State University.

Harvey, N. and A. Reeves. 2010. Model description: North American Animal Disease Spread Model 3.2.

Harvey, N., A. Reeves, M. A. Schoenbaum, F. J. Zagmutt-Vergara, C. Dube, A. E. Hill, B. A. Corso, W. B. McNab, C. I. Cartwright and M. D. Salman, 2007. The North American Animal Disease Spread Model: a simulation model to assist decision making in evaluating animal disease incursions. Prev. Vet. Med. 82: 176-197.

Holm, S., 1979. A simple sequentially rejective multiple test procedure. Scandinavian journal of statistics: 65-70.

Hueston, W., 1993. Assessment of national systems for the surveillance and monitoring of animal health. Rev. Sci. Tech. 12: 1187-1187.

Keeling, M. J. and A. Shattock, 2012. Optimal but unequitable prophylactic distribution of vaccine. Epidemics 4: 78-85.

Keeling, M. J., M. E. Woolhouse, R. M. May, G. Davies and B. T. Grenfell, 2003. Modelling vaccination strategies against foot-and-mouth disease. Nature 421: 136-142.

Keeling, M. J., M. E. Woolhouse, D. J. Shaw, L. Matthews, M. Chase-Topping, D. T. Haydon, S. J. Cornell, J. Kappey, J. Wilesmith and B. T. Grenfell, 2001 "Supplementary material for dynamics of the 2001 UK foot and mouth epidemic-dispersal in a heterogeneous landscape." Science 294 http://www.sciencemag.org/content/294/5543/813.full.pdf (accessed July 24, 2013)

Laurence, C., 2002. Animal welfare consequences in England and Wales of the 2001 epidemic of foot and mouth disease. Rev. Sci. Tech. 21: 863.

Mardones, F., A. Perez, J. Sanchez, M. Alkhamis and T. Carpenter, 2010. Parameterization of the duration of infection stages of serotype O foot-and-mouth disease virus: an analytical review and meta-analysis with application to simulation models. Vet. Rec. 41: 45.

McReynolds, S. W., M. W. Sanderson, A. Reeves, A. E. Hill, M. Sinclair and M. D. Salman, 2013. Direct and Indirect contact rates among livestock operations in Colorado and Kansas. J. Am. Ved. Med. Assoc. in press.

Melius, C., A. Robertson and P. Hullinger, 2006. Developing livestock facility type information from USDA agricultural census data for use in epidemiological and economic models. Department of Homeland Security, Lawrence Livermore National Laboratory, UCRL-TR 226008.

National Audit Office, Department of Environment, Food and Rural Affairs, 2005. Foot and Mouth Disease: Applying the Lessons. www.nao.org.uk (accessed October 23, 2012).

NBAF, (National Bio and Agro-Defense Facility), 2012. Updated Site-Specific Biosafety and Biosecurity Mitigation Risk Assessment, United Stated Department of Homeland Security.

Office International des Epizooties/World Organisation for Animal Health, 2013 "Foot and mouth disease." Terrestrial animal health code Chapter 8.6 http://www.oie.int/en/international-standard-setting/terrestrial-code/ (accessed August 28, 2013)

Paarlberg, P. L., J. G. Lee and A. H. Seitzinger, 2002. Potential revenue impact of an outbreak of foot-and-mouth disease in the United States. J. Am. Vet. Med. Assoc. 220: 988-992.

Pendell, D. L., J. C. Leatherman, T. C. Schroeder and G. S. Alward, 2007. The Economic Impacts of a Foot-And-Mouth Disease Outbreak: A Regional Analysis. J. Agr. Appl. Econ. 39: 19-33.

Perez, A. M., M. P. Ward and T. E. Carpenter, 2004. Control of a foot-and-mouth disease epidemic in Argentina. Prev. Vet. Med. 65: 217-226.

Pluimers, F. H., 2004. Foot-and-Mouth disease control using vaccination: the Dutch experience in 2001. Dev Biol (Basel) 119: 41-49.

Premashthira, S., 2012. Uses of quantitative spatial analysis and epidemiological simulation modeling for assessing control strategies for foot-and-mouth disease, Colorado State University.

Premashthira, S., M. D. Salman, A. E. Hill, R. M. Reich and B. A. Wagner, 2011. Epidemiological simulation modeling and spatial analysis for foot-and-mouth disease control strategies: a comprehensive review. Anim. Health Res. Rev. 12: 225.

Reeves, A., 2012 "User's guide for WH: A simulation model of within-unit disease dynamics." Colorado State University http://www.naadsm.org/wh (accessed June 17, 2013)

Reeves, A., M. Talbert, M. D. Salman and A. E. Hill, in preparation "Development of a stochastic, individual-based modeling framework for within-unit transmission of highly infectious animal diseases. ." in preparation Draft available at: http://www.naadsm.org/wh (accessed July 17, 2013)

Salt, J., P. Barnett, P. Dani and L. Williams, 1998. Emergency vaccination of pigs against foot-and-mouth disease: protection against disease and reduction in contact transmission. Vaccine 16: 746-754.

Schoenbaum, M. A. and W. T. Disney, 2003. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. Prev. Vet. Med. 58: 25-52.

StataCorp. 2011. Stata: Release 12. Statistical Software College Station, TX, StataCorp LP.

Sutmoller, P., S. S. Barteling, R. C. Olascoaga and K. J. Sumption, 2003. Control and eradication of foot-and-mouth disease. Virus Res. 91: 101-144.

Volkova, V. V., P. R. Bessell, M. E. Woolhouse and N. J. Savill, 2011. Evaluation of risks of foot-and-mouth disease in Scotland to assist with decision making during the 2007 outbreak in the UK. Vet. Rec. 169: 124.

Ward, M. P., L. D. Highfield, P. Vongseng and M. Graeme Garner, 2009. Simulation of foot-and-mouth disease spread within an integrated livestock system in Texas, USA. Prev. Vet. Med. 88: 286-297.

Woolhouse, M. and A. Donaldson, 2001. Managing foot-and-mouth. Nature 410: 515-516.

Yang, P. C., R. M. Chu, W. B. Chung and H. T. Sung, 1999. Epidemiological characteristics and financial costs of the 1997 foot-and-mouth disease epidemic in Taiwan. Vet. Rec. 145: 731-734.

Yoon, H., S. H. Wee, M. A. Stevenson, B. D. O'Leary, R. S. Morris, I. J. Hwang, C. K. Park and M. W. Stern, 2006. Simulation analyses to evaluate alternative control strategies for the 2002 foot-and-mouth disease outbreak in the Republic of Korea. Prev. Vet. Med. 74: 212-225.

Figure 4-1 - 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 4-2 - 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.

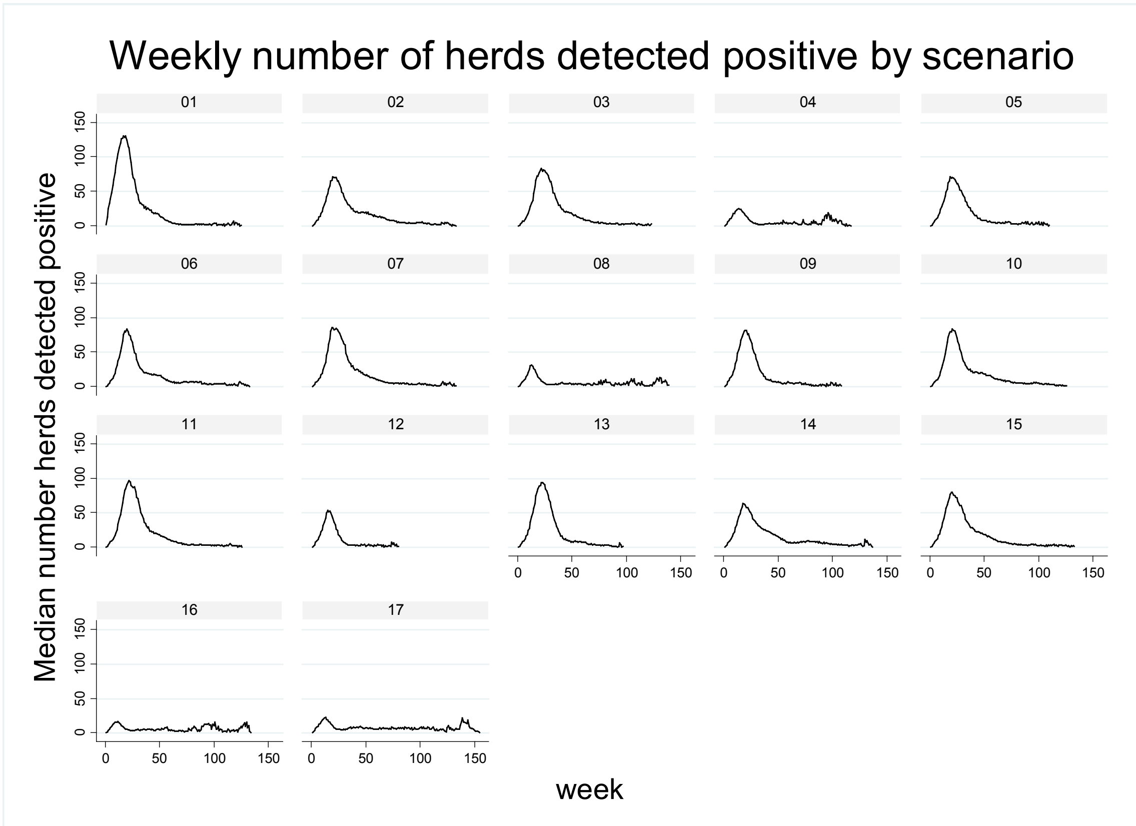


Figure 4-3 - The total number of animals vaccinated each week by scenario number of a potential foot and mouth disease virus outbreak in a central region of the U.S.

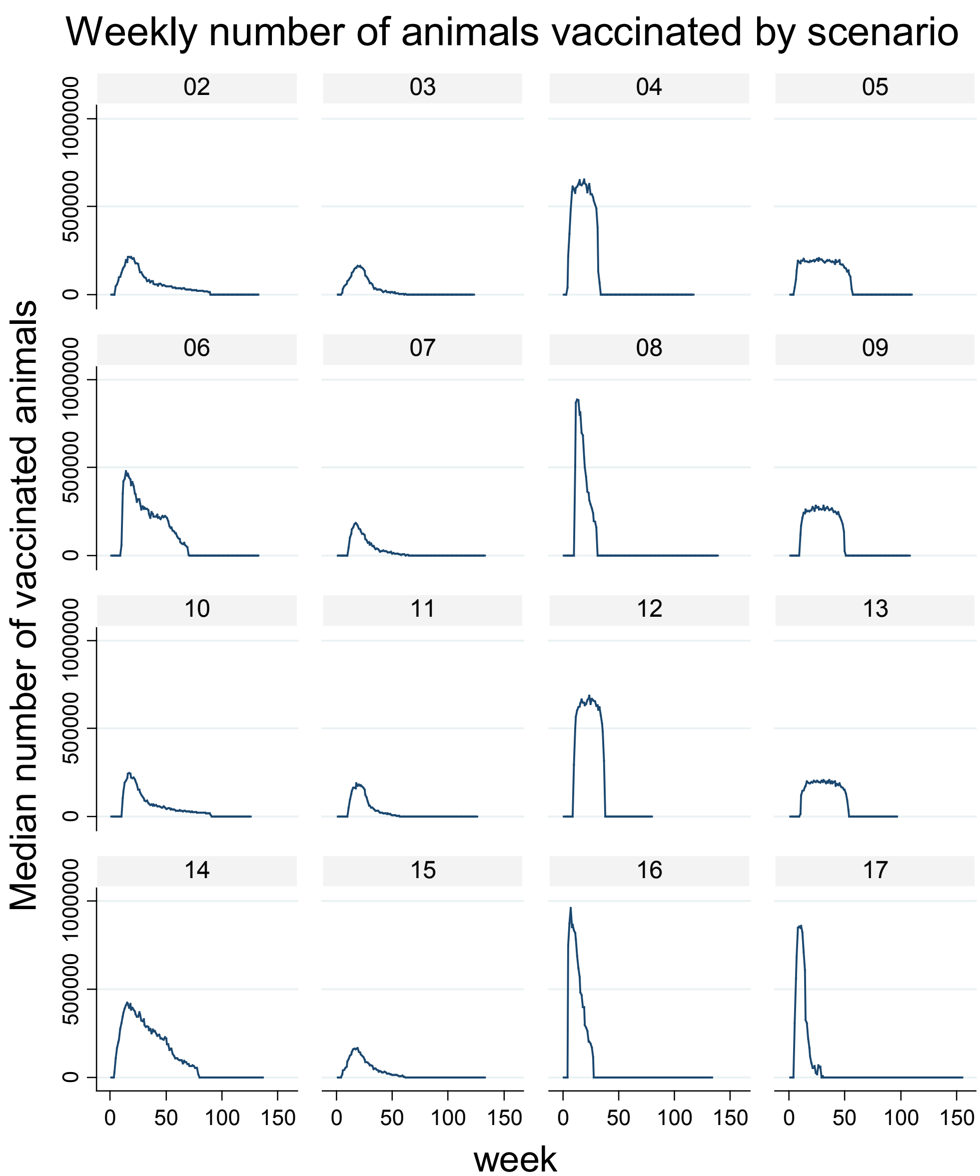
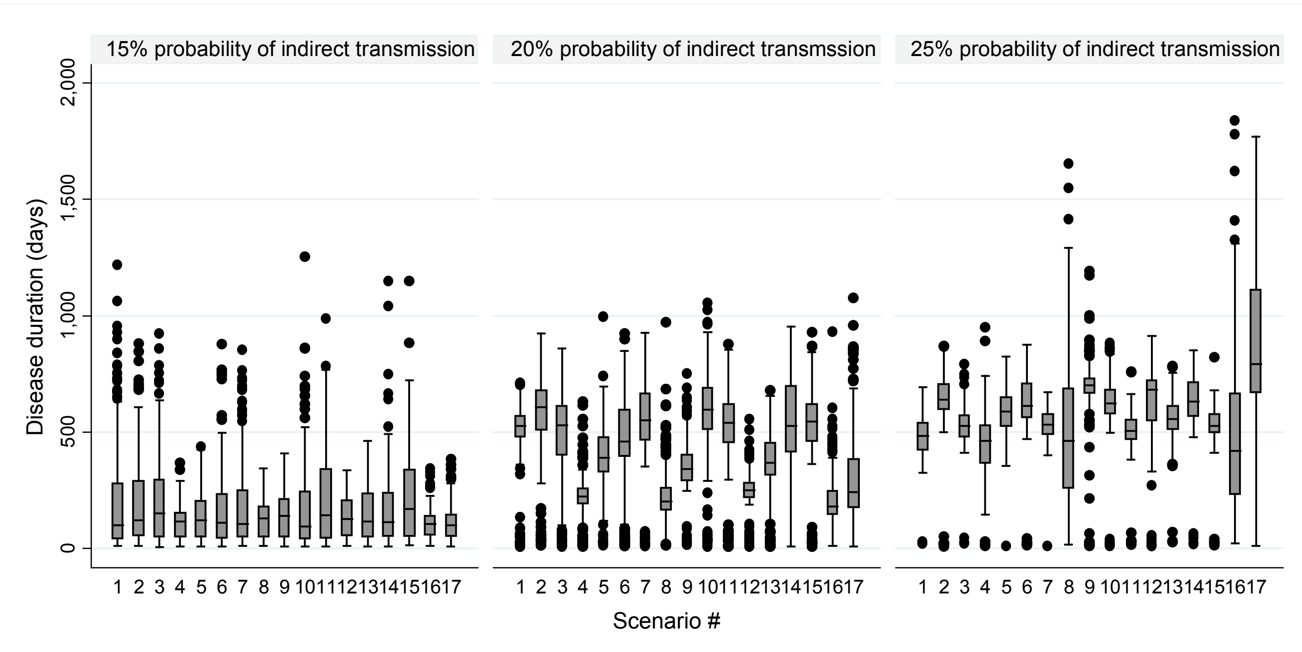
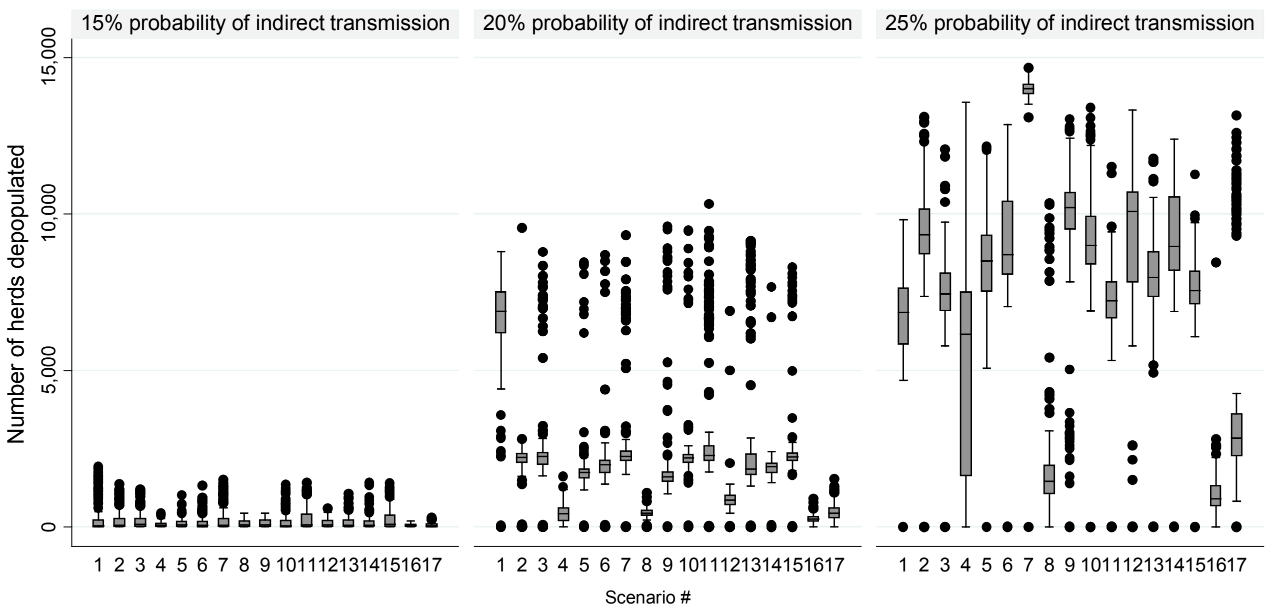


Figure 4-4 - Box plots of the duration of the active disease phase for the sensitivity analysis of the probability of transmission given indirect contact is at 15%, 20%, and 25% for all scenarios of a potential foot and mouth disease virus outbreak in a central region of the U.S.



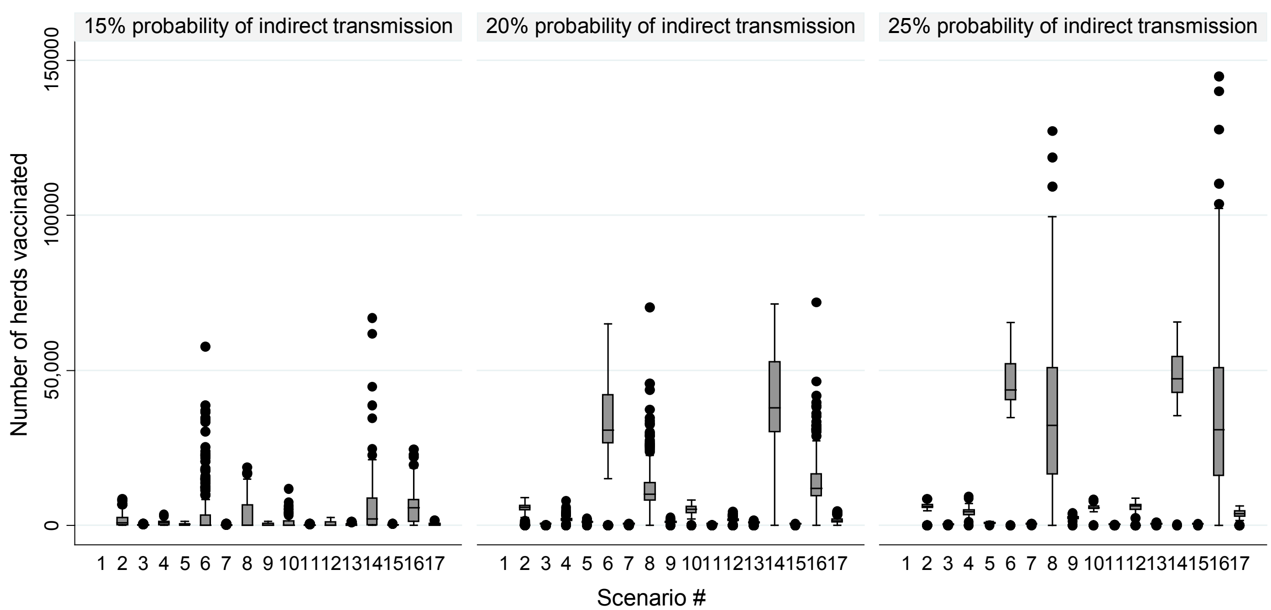
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 4-5 - 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.



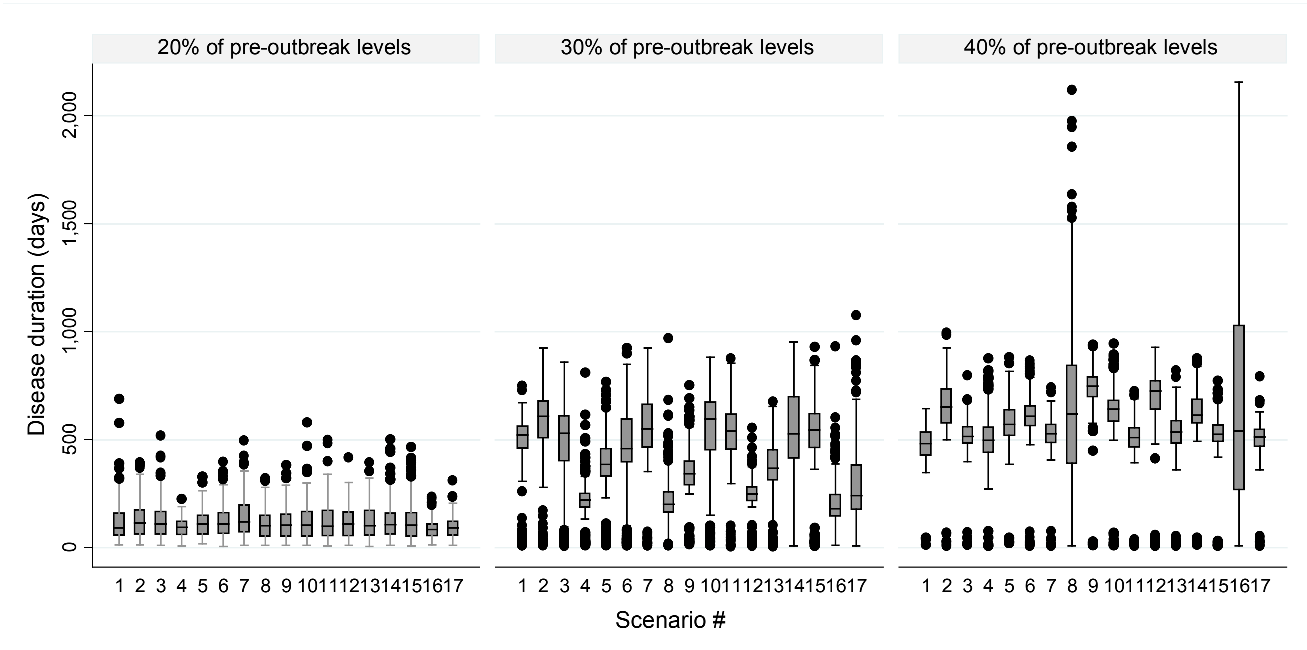
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 4-6 - 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.



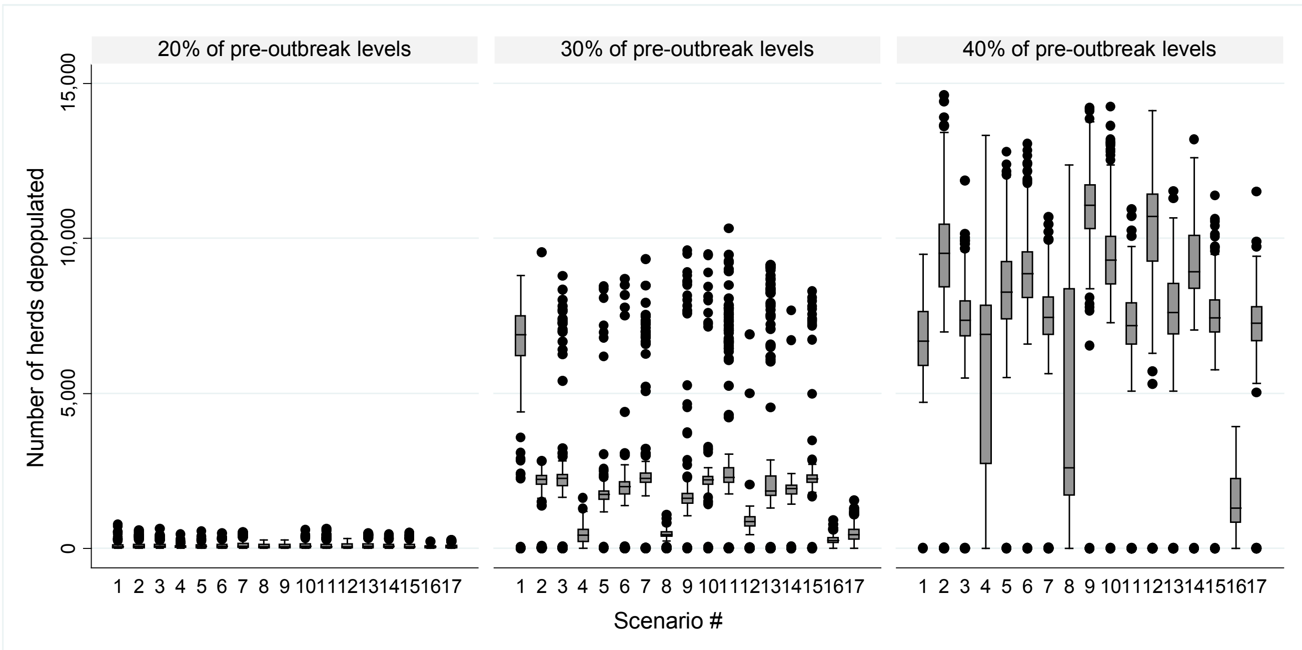
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 4-7 - 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.



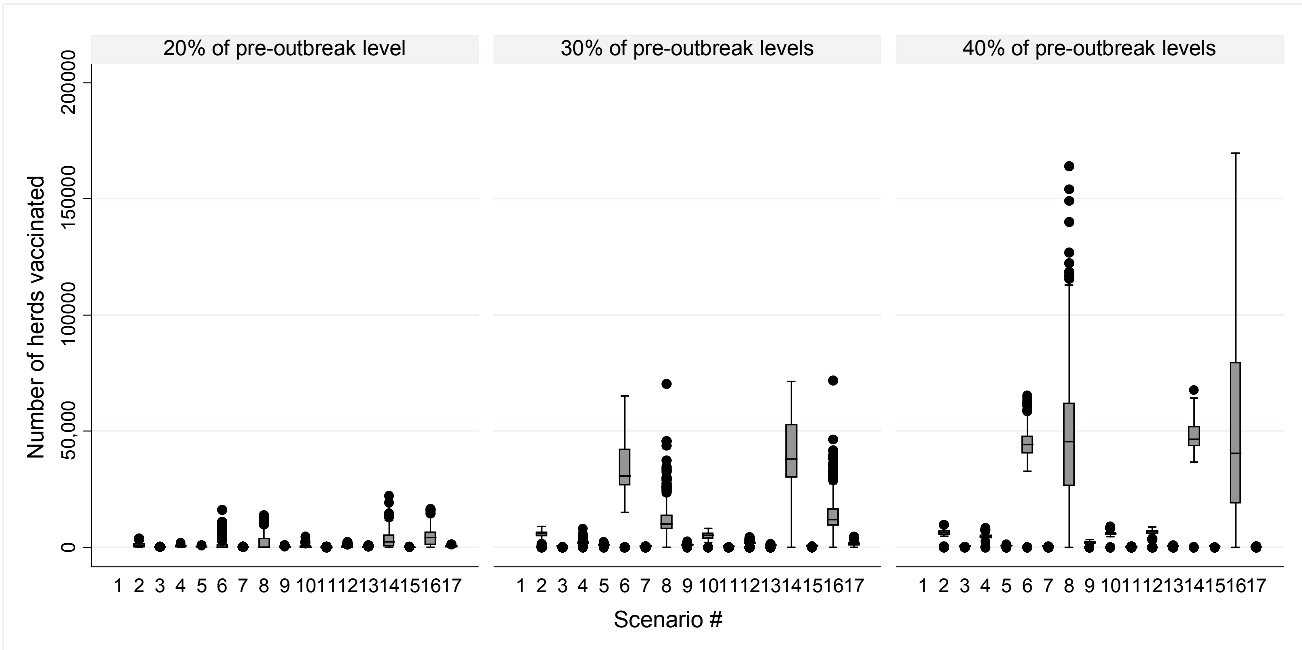
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 4-8 - 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.



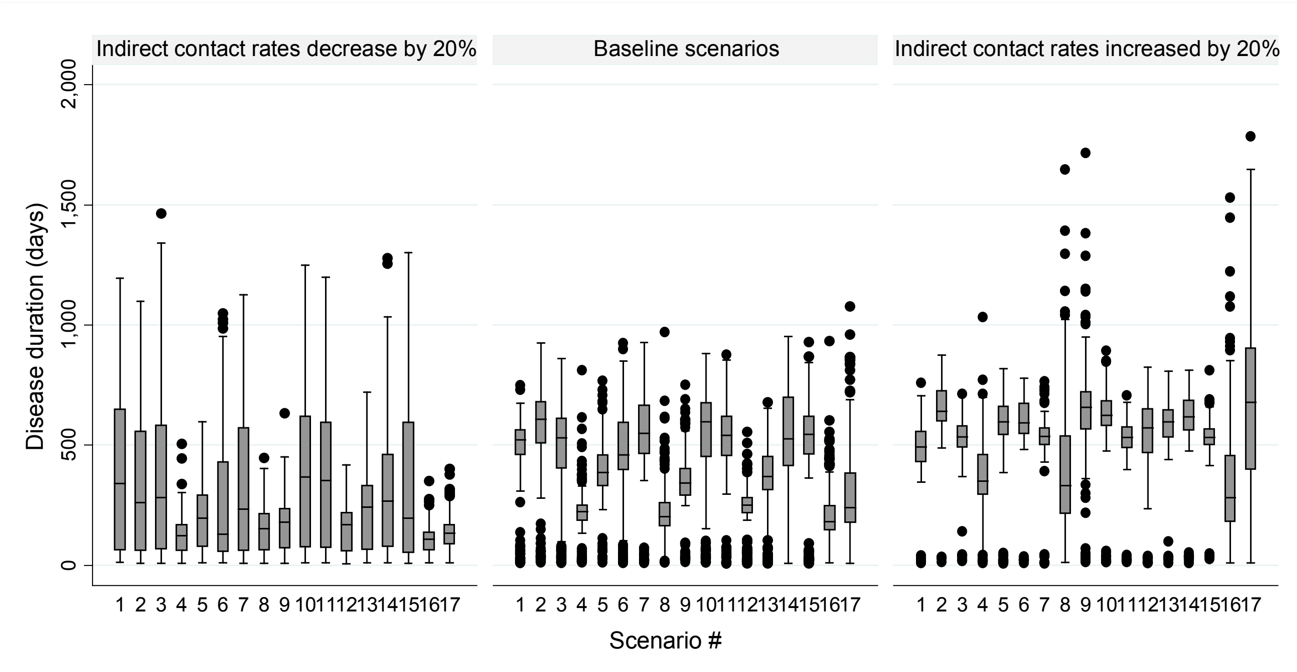
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 4-9 - 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.



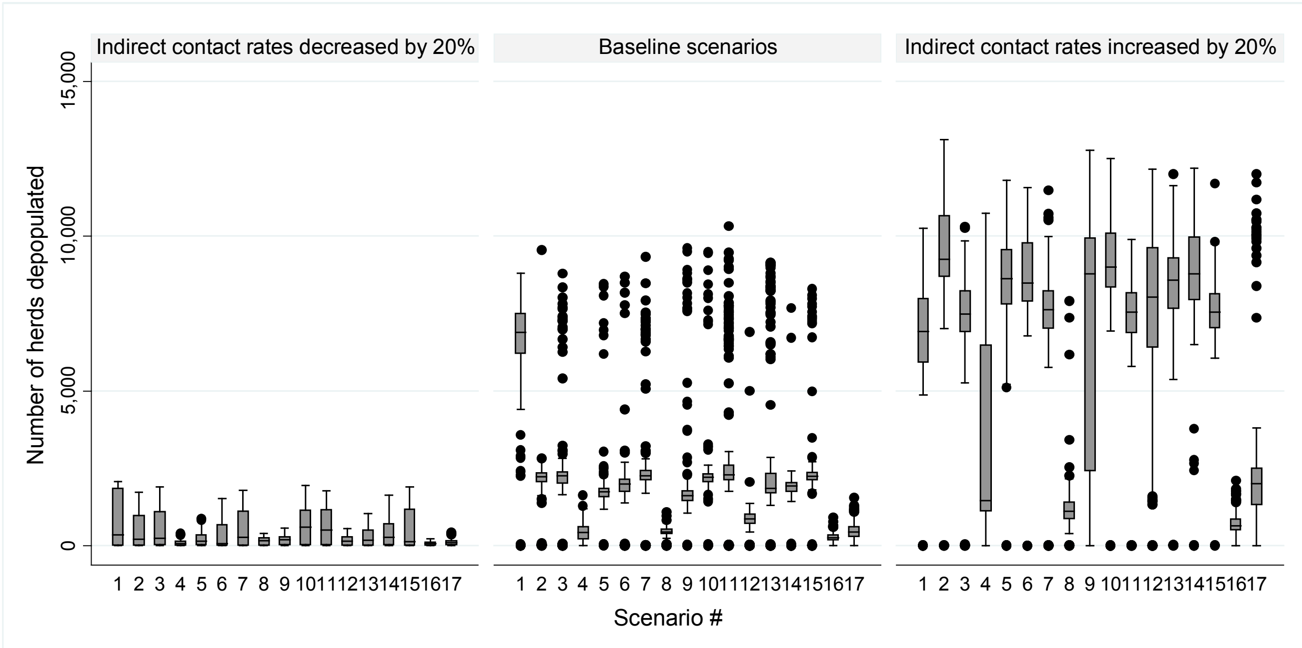
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 4-10 - 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.



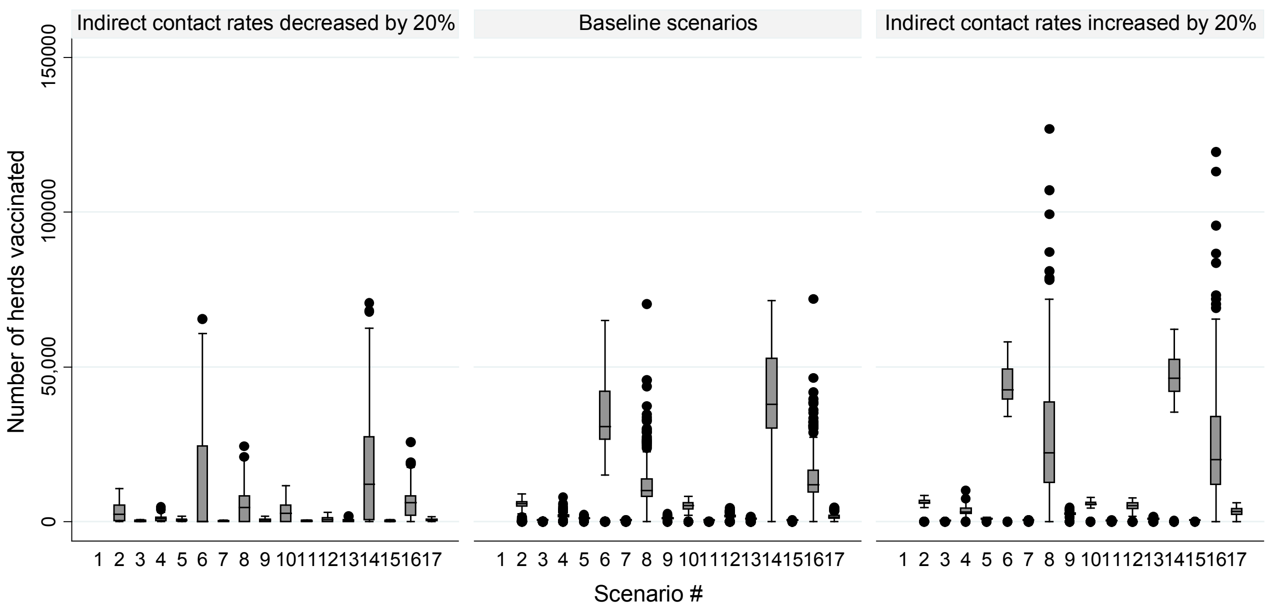
[a] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 4-11 - 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 4-12 - 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.

Table 4.1 - 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 4.2- 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 [a]	Vaccination Capacity [b]	Vaccination Trigger (herds)	Size of Vaccination Zone (km)
1	-	-	-	-
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] 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.

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

Table 4.3 - Calculated mean daily direct contact rates 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
Cow/Calf	Cow/Calf	0.027
Cow/Calf	Large Feedlot	0.002
Cow/Calf	Small Feedlot	0.002
Cow/Calf	Beef/Swine	0.027
Dairy	Dairy	0.065
Large Feedlot	Large Feedlot	0.005
Large Swine	Large Swine	0.186
Small Feedlot	Large Feedlot	0.019
Small Feedlot	Small Feedlot	0.017
Small Swine	Small Swine	0.013
Small Swine	Beef/Swine	0.013
Beef/Swine	Cow/Calf	0.027
Beef/Swine	Large Feedlot	0.003
Beef/Swine	Small Feedlot	0.003
Beef/Swine	Beef/Swine	0.026
Beef/Swine	Small Swine	0.013
Small Ruminant	Small Ruminant	0.024

[a]All combinations that are not listed above had a mean daily contact rate of 0.0.

Table 4.4 - Calculated mean daily indirect contact rate 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 4.5 - 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) of a potential foot and mouth disease virus outbreak in a central region of the U.S.

Scenario Name	Outbreak Duration	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)	13,663 (196-17,611)		
2	608 [i] (102-767)	2,227 [g] (42-2,449)	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)	9,939 (72-11,500)	472 [b] (0-514)	4,319 (0-4,764)
4	223 [b] (86-310)	416 [b] (31-879)	1,736 (238-3,214)	1,876 [g] (494-2,736)	16,400 (1,490-23,640)
5	389 [e] (286-559)	1,735 [e] (1,326-2,063)	7,508 (5,774-8,591)	1,043 [e] (725-1,460)	10,300 (7,000-14,800)
6	459 [fg] (45-721)	1,991 [f] (9-2,301)	9,098 (65-10,000)	30,594 [k] (0-51,136)	19,600 (0-23,832)
7	550 [ghi] (64-753)	2,249 [g] (15-5,133)	10,000 (81-12,500)	458 [b] (0-488)	4,183 (0-4,600)
8	202 [ab] (131-390)	440 [b] (233-616)	1,863 (1,071-2,395)	10,000 [j] (6,400-24,560)	14,900 (10,000-25,800)
9	342 [d] (256-528)	1,605 [d] (1,242-3,712)	6,950 (5,600-10,400)	1,044 [e] (784-1,398)	10,400 (7,400-14,200)
10	596 [hi] (154-800)	2,203 [g] (49-3,270)	9,968 (341-11,121)	5,165 [h] (0-7,030)	7,132 (0-8,330)
11	540 [fgh] (90-709)	2,276 [g] (32-7,318)	10,000 (268-15,000)	425 [a] (0-463)	3,851 (0-4,263)

12	250 ^{c} (146-318)	855 ^{c} (234-1,150)	3,702 (968-4,727)	1,800 ^{g} (635-2,420)	17,200 (6,250-22,600)
13	369 ^{de} (244-579)	1,848 ^{f} (1,320-7,904)	8,008 (6,275-16,360)	859 ^{d} (528-1,098)	8,461 (4,833-11,000)
14	527 ^{fghi} (77-791)	1,925 ^{f} (22-2,174)	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)	4,561 (3,850-4,860)
16	181 ^{a} (123-366)	252 ^{a} (107-427)	1,028 (515-1,644)	11,902 ^{j} (6,923-26,654)	15,500 (10,000-23,200)
17	241 ^{bc} (133-568)	440 ^{b} (87-850)	1,754 (521-3,373)	1,329 ^{f} (528-2,718)	13,100 (5,000-26,310)

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

Table 4.6 - Percent difference of median number of herds depopulated for sensitivity analysis scenarios compared to original comparable baseline scenario of a potential foot and mouth disease virus outbreak in a central region of the U.S.

Scenario	Baseline Herds Depopulated (Median)	Probability of Indirect Transmission		Indirect Movement Control (Percent of Pre-outbreak)		Indirect Contact Rate	
		15%	25%	20%	40%	-20%	+20%
1	6,890	-99.5%	-0.4%	-99.4%	-2.9%	-95.0%	-1.1%
2	2,227	-97.6%	319.2%	-97.2%	327.6%	-91.1%	75.9%
3	2,248	-96.5%	231.1%	-97.6%	227.1%	-89.5%	70.0%
4	416	-88.0%	1381.0%	-89.3%	1562.5%	-84.0%	70.7%
5	1,735	-96.3%	390.1%	-96.9%	376.6%	-92.1%	80.5%
6	1,991	-97.8%	337.1%	-97.4%	345.3%	-97.1%	76.5%
7	2,249	-98.1%	523.2%	-97.1%	231.6%	-88.6%	70.5%
8	440	-87.0%	232.0%	-89.3%	490.8%	-64.8%	60.4%
9	1,605	-96.2%	536.5%	-97.0%	590.3%	-88.3%	81.7%
10	2,203	-98.4%	308.4%	-97.5%	321.8%	-73.5%	75.1%
11	2,276	-97.0%	218.0%	-98.0%	215.5%	-78.0%	69.8%
12	855	-92.9%	1080.2%	-94.1%	1152.8%	-83.4%	89.4%
13	1,848	-97.3%	331.3%	-96.9%	312.0%	-90.6%	78.5%
14	1,925	-97.3%	366.1%	-96.9%	363.9%	-86.4%	78.1%
15	2,238	-96.3%	237.9%	-97.8%	232.1%	-94.7%	70.3%
16	252	-82.3%	259.3%	-84.7%	413.7%	-77.0%	60.4%
17	440	-90.9%	545.7%	-89.3%	1550.2%	-81.0%	78.0%

Table 4.7 - Percent difference of median outbreak duration for sensitivity analysis scenarios compared to original comparable baseline scenario of a potential foot and mouth disease virus outbreak in a central region of the U.S.

Scenario	Baseline Outbreak Duration (Median)	Probability of Indirect Transmission		Indirect Movement Control (Percent of Pre-outbreak)		Indirect Contact Rate	
		15%	25%	20%	40%	-20%	+20%
1	527	-80.8%	-7.3%	-82.2%	-7.9%	-34.9%	-5.7%
2	608	-80.0%	5.1%	-81.2%	7.3%	-57.2%	5.4%
3	530	-71.8%	-0.5%	-79.1%	-2.7%	-47.0%	0.9%
4	223	-47.7%	108.1%	-57.9%	124.1%	-44.8%	57.9%
5	389	-68.7%	52.7%	-71.2%	48.1%	-49.0%	54.9%
6	459	-75.9%	33.1%	-76.4%	32.5%	-72.0%	29.0%
7	550	-80.8%	-3.1%	-78.2%	-3.9%	-57.5%	-2.5%
8	202	-35.5%	129.5%	-48.9%	207.4%	-24.8%	64.0%
9	342	-59.4%	105.0%	-69.3%	118.7%	-48.0%	92.1%
10	596	-84.4%	4.5%	-82.4%	7.5%	-38.6%	4.4%
11	540	-73.4%	-6.4%	-81.7%	-5.6%	-34.9%	-1.7%
12	250	-49.7%	172.9%	-55.9%	190.8%	-32.7%	129.5%
13	369	-68.7%	50.7%	-72.6%	45.1%	-34.3%	61.7%
14	527	-78.7%	19.8%	-79.5%	16.7%	-49.5%	17.4%
15	545	-68.8%	-3.2%	-80.8%	-3.9%	-64.1%	-2.4%
16	181	-42.5%	130.9%	-53.0%	197.8%	-40.1%	55.0%
17	241	-58.8%	229.1%	-61.5%	112.7%	-44.3%	181.9%

Table 4.8 - 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	Number of Herds Depopulated					Outbreak Duration				
Rank	1	2	3	4	5	1	2	3	4	5
Baseline	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%	16	8	1	4	17	1	17	11	4	3
Indirect Movement Control 20%	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

Chapter 5 - The effect of multiple initially latent herds on a foot and mouth disease outbreak in the Central United States

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Abstract

The central United States (U.S.) has a large livestock population including cattle, swine, sheep and goats that are fully susceptible to Foot and Mouth Disease (FMD). Introduction of FMD to the U.S. would have potentially devastating consequences to the livestock industry. Auction markets could play a critical role in increasing initial spread of an FMD incursion prior to detection. We simulated the impact of an FMD outbreak beginning in multiple herds using the North American Animal Disease Spread Model (NAADSM), a spatially explicit, stochastic infectious disease model.

Using USDA, National Agricultural Statistic Service data, a simulated population of 151,620 livestock operations in the central U.S. was defined by latitude and longitude, production type, and herd size. To simulate auction market dispersal, two different starting

conditions of12 initially latently herds in eastern Colorado and western Nebraska were modeled. One starting condition included 1 cow/calf herd, 2 large feedlots, 5 small feedlots, 1 dairy, 2 small ruminants, and 1 small swine herd. A second starting condition included only beef operations, 2 cow/calf, 3 large feedlots, and 7 small feedlots. Results from the multiple initial latently infected herds were compared to identical scenarios with a single 17,000 head feedlot in northeast Colorado as the initial latently infected herd.

Direct and indirect contact rates between herds were based on survey data of livestock producers in Kansas and Colorado. Scenarios were simulated with either no vaccination or with vaccination zone radius 10 km or 50 km and vaccination capacity high or low. Scenarios were compared to assess the effect of multiple herds initially infected representing an outbreak spreading from an auction market.

The initial incidence of newly detected herds was greater in the scenarios with multiple initially latent herds. The weekly number of new herds detected at week 8 of the outbreak was approximately 35 herds for scenarios with multiple initially latent herds compared to approximately 7 new herds in scenarios with a single initial latent herd. Multiple initial latently infected herds had minimal impact on the median outbreak duration, and the total number of herds depopulated and vaccinated when compared to single latent herd scenarios. Outbreaks dispersed from auction markets may have initially increased incidence and resource needs but may have little influence on final outcome.

Introduction

The United States (U.S) has a livestock population fully susceptible to foot and mouth disease (FMD) due to the last outbreak having occurred in 1929. The economic costs of FMD are increased in countries where export markets are large such as the U.S. Taiwan had a FMD outbreak in 1997, after being free of the disease for over 68 years, that was estimated to cost $378.6 million (Yang et al., 1999). Following the 2001 FMD outbreak in the United Kingdom (U.K.) economic losses to agriculture and the food chain were estimated to be approximately $5 billion (Thompson et al., 2002). The more recent FMD outbreaks in countries that had previously been free of the disease demonstrate the need for research and extensive planning on the possible control strategies that could be utilized during an FMD outbreak in the U.S.

Auction markets have been reported as being the most critical factor contributing to large FMD epidemics in countries which have previously been free of the disease (McLaws and Ribble, 2007). This is likely due to the auction markets leading to wider dissemination of the virus. For example in the 2001 U.K. outbreak the FMD virus was widely disseminated throughout the country prior to the first diagnosis being made (Gibbens et al., 2001). The ability of the virus to spread prior to detection is a concern in the U.S. as well, due to the frequency at which animals are moved and the movements through auction markets. Recent analysis of interstate certificate of veterinary inspection data for livestock found that the entire U.S. is closely connected with the central plains states having the most livestock connections (Buhnerkempe et al., 2013).

As of May 2012, there were 1,229 auction markets in the U.S. registered with the Grain Inspection, Packers, and Stockyards Administration (USDA-GIPSA, May 2012). In a government survey of cow-calf producers in the U.S., 61% reported using auction markets as the primary method of sale and over 50% of operations used an auction market as their primary method of sale of weaned or older heifers not intended for breeding (USDA-APHIS, 2010). Research in California found that among beef producers, movements to auction markets accounted for 41.3% of the three most recent movements (Marshall et al., 2009). Considering the large number of cattle sold and fed in the central U.S., auction markets would likely play an important role in disease spread.

Previous research utilizing the North American Animal Disease Spread Model (NAADSM) for modeling of FMD, suggests that vaccination, strict movement controls, and increased biosecurity can decrease the duration of the outbreak and the number of animals depopulated (McReynolds et al., in preparation). The research also suggests that the size of the vaccination zone has more of an impact on the outbreak duration and number of animals depopulated than the control method of early vs. late vaccination trigger. NAADSM currently has no explicit way of including auction markets in the population. With the number of auction markets in the U.S. and the high utilization of auction markets by livestock producers (USDA:APHIS 2010, Marshall et al., 2009), markets could potentially result in widespread initial disease dispersal. One way to represent the wide dispersal of FMD that originates in an auction market is to include multiple initially latent herds at the beginning of the outbreak. Once FMD is detected in the U.S. it is assumed that auction markets will be closed to prevent further dissemination of the disease so they would no longer play a role in the spread. Previous research modeling an FMD outbreak in the central U.S. has been done with one initially latent large feedlot (McReynolds et al., in preparation) but due to the exclusion of auction markets in the population, uncertainty remains especially with the potential impact of the initial spread of FMD virus. With the closure of auction markets after detection of FMD, it was assumed that their role in dissemination would occur at the beginning and could be captured by including multiple initially latent herds. The objective of this study was to assess the impact of wider dissemination of the FMD virus on a potential FMD outbreak in the central plains region of the U.S.

Materials and Methods

Study Population

The simulated study population was based on the 2007 NASS livestock herd data and production types adjusted according to criteria by Melius et al. (2006). The 8-state study area included Wyoming, South Dakota, Colorado, Nebraska, Kansas, the northern region of New Mexico and Oklahoma, and the Texas Panhandle (Fig. 1). The number of herds in the simulated study population was 151,620 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. The total population was 39,413,228 animals in all production types (Table 1). Seven percent of beef and swine operations were randomly re-designated from the population of cow/calf operations and small swine based on a livestock contact survey where approximately 7% of herds in Kansas and Colorado reported having beef cattle and swine (McReynolds et al., in press).

Simulation model

NAADSM was used to model FMD eradication strategies. NAADSM is an open source (Harvey and Reeves, 2010) herd-based spatial stochastic epidemic simulation model (Schoenbaum and Disney, 2003; Harvey et al., 2007). Nine scenarios were simulated for various FMD vaccination protocols compared to the depopulation only baseline scenario. Each of the nine scenarios was simulated with 3 different starting conditions for the number and type of initially latent herds. Modeled scenarios included variations in vaccine capacity (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), vaccination zone diameter (10 km or 50 km), and the number of infected herds required to initiate a vaccination program (10 or 100 herds). The simulated vaccination strategies included low and high vaccine capacity to represent USDA administration of vaccine (low capacity) or producer administration of vaccine (high capacity). Vaccination strategies included all herd types with 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.

The clinical stages of disease distributions are based on a meta-analysis of the duration of the disease states (Mardones et al., 2010). The clinical infectious period distribution for cattle, swine and small ruminants was calculated as reported previously (McReynolds et al., in preparation). Briefly monte-carlo simulation (@Risk 5.01, Palisade Corp., Ithaca, NY, USA) was used to sample values from the subclinical infectious period and the infectious period reported in Mardones et al. (2010). The value for the subclinical period was subtracted from the sampled values for the infectious period to generate a distribution for the clinical period which was fit to a theoretical distribution (@Risk 5.0.1) to estimate the clinical infectious period for use in NAADSM. The within-herd prevalence as a function of time since infection was used to determine the probability of infection following a direct contact. The within herd prevalence model (WH) (Reeves, 2012) based on estimates for the latent, subclinical infectious, and clinical infectious stages was used to produce the distributions for within herd prevalence for NAADSM. 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 et al., in preparation). The results of a livestock contact survey in the central U.S. (McReynolds et al., in press) were used to calculate direct and indirect contacts between livestock production types. Actual contacts between production types in the NAADSM model were generated from a Poisson distribution with lambda equal to the mean contact rate for that production type combination.

The assumptions in the model were that the virus could 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 is a fomite such as a contaminated vehicle, equipment, clothing, or a person. The probability of airborne spread at 1 km was 0.5% and the maximum distance of spread was 3 km. For all scenarios, 1) the days to first disease detection was generated by the NAADSM model; 2) direct contact through animal movement was reduced to 10% of pre-outbreak levels by day 7 and indirect contacts were reduced to 30% of pre-outbreak levels by day 7 after disease detection; 3) 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 shedding; and 4) depopulation capacity was set at 8 herds/day by day 10 and 16 herds/day by day 30 after disease detection. For all herds that were detected as positive, direct contacts were identified, traced forward, and depopulated. Depopulation did not begin until day 2 after first disease detection of the outbreak. In all simulations a 100% quarantine of infected premises and a ban on livestock movement from infected premises was assumed. The endpoint for all the scenarios was the end of the active disease phase.

Model Scenarios

All 9 of the scenarios were simulated in the population each with three different starting conditions for the number and type of initially latent herds (Table 2). In the first condition, the initial latently infected herd was a single 17,000 head feedlot in Northeast Colorado. In order to simulate FMD dissemination to multiple premises from an auction market, two additional starting conditions were modeled each with 12 initially latent herds. The second starting condition had 12 initial herds that were latently infected in eastern Colorado and western Nebraska including 1 cow/calf herd, 2 large feedlots, 5 small feedlots, 1 dairy, 2 small ruminant herds, and 1 small swine herd. The third starting condition also had 12 initial latently infected herds that were all beef production types in western Nebraska. The latent herds were 2 cow/calf, 3 large feedlots, and 7 small feedlots. The choice of initially latent herds was based on data collected from auction markets in northwest Colorado and western Nebraska on the percentage of production types sold and distance shipped. For each scenario 200 iterations were simulated.

Data analysis

The NAADSM model produced outputs for each day of the outbreak for each iteration. The outputs from each scenario were aggregated into weekly and daily outcome counts for each iteration of each scenario. Disease duration was calculated to the end of the active disease phase of the outbreak. Summary statistics were generated for each of the scenarios. Analysis was performed in commercially available software Stata12.1, (StataCorp., 2011) and in open source 64 bit R 3.0.1 (R development core team, 2013). A Kruskal-Wallis one-way analysis of variance was used to test the statistical differences between scenarios and within initially latent populations. The test was used to identify significant differences in disease 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 outbreak duration, number of herds depopulated, and weekly number of new infections were not normally distributed. The weekly analysis of results only included the iterations that still had an active outbreak. For example the number of iterations with an active outbreak by week 50 was less than 5% of the total iterations for scenario 4 (Figure 2). Tails of the scenario distribution medians were impacted by this as long outbreak durations were highly influential in the upper tails of the median outcome curves (Figure 3).

Detected herds

The median first day of detection was at day 10 or 11 (5th percentile day 5 and 95th percentile day 16) for the nine scenarios with a single large feedlot initial latently infected. However for scenarios with 12 herds initially latent, the median first day of detection was at day 5 or 6 (5th percentile day 3 and 95th percentile day 8) and the initial incidence of newly detected herds was greater compared with the scenarios with single initially latent large feedlot in the population (Figure 3). At the time of first detection the median total number of herds that were infected was 3 or 4 for scenarios with one initially latent feedlot and 15 or 17 for scenarios with multiple initially latent herds. At week 2 of the simulations, a total of 1 herd had been detected in the scenarios with a single large latent feedlot initially latent compared to 14 to 16 herds for the scenarios with multiple initially latent herds. The initial incidence was higher for all scenarios with multiple initially latent herds. The weekly median number of new herds detected at week five was 7 or 8 for all scenarios with the starting condition of a single latent large feedlot compared to 33-35 herds for scenarios with multiple initial latent mixed production types and 41-

44 herds for scenarios with the multiple initial latent beef production types. At week 8 the weekly number of new herds detected was 12-16 for scenarios with a single large latent feedlot compared to 33-62 herds for multiple mixed production type latent scenarios and 35-75 herds for multiple beef production latent scenarios.

Based on the Kruskal-Wallis test, scenario 16 had the lowest final number of herds detected under all three initial latent herd conditions (medians, 248-380 herds) and scenario 1, the baseline scenario, had the highest for all initial conditions (medians, 10,087-10,300 herds). In the scenarios with a large vaccination zone of 50 km the number of herds detected at the end of the outbreak was increased when there were multiple initially latent herds, for example, in scenario 4 the median increased from 407 when a single large feedlot was initially latent to 913 when multiple mixed production types were initially latent and 988 when multiple beef production types were initially latent. However in the baseline scenario the number of herds detected at the end of the outbreak was comparable for the three initially latent conditions (median, 10,087-10,334). The scenarios with a small vaccination zone of 10 km also had comparable results, for example in scenario 2 the median ranged from 2,183 to 2,262 herds detected with clinical infections among the three initially latent conditions.

Outbreak duration

Box plots of disease duration in days, categorized by initially latent condition, are shown in Figure 4. The median outbreak duration of the baseline scenario, 1, was approximately 500 days for all initially latent herd conditions (median range 480-522). Despite the scenarios having comparable medians among all three initially latent herd conditions, the lower end of the distribution is cut off when multiple herds were initially latent compared to single initially latent herd.

Within each initially latent herd condition, the outbreak duration was longer in the vaccination scenarios with a vaccination zone of 10 km (medians, 455-608 days) compared to the scenarios with a vaccination zone of 50 km (medians, 142-250 days). Outbreak duration was similar for like scenarios between the two multiple initially latent herd conditions. Like scenarios were significantly shorter for scenarios with the multiple initially latent herds compared to the scenarios with a population with a single initially latently herd for all scenarios except scenario 14. Outbreak duration of scenario 14 was similar among all initial latent conditions. The Kruskal-Wallis ranking of scenarios within initial latent conditions were similar with scenarios 16, 8, 12 and 4 having the shortest durations and scenarios 10 and 2 the two longest durations in all three initially latent conditions.

Herds depopulated

Box plots of the number of herds depopulated by initially latent condition are shown in Figure 5. In the baseline scenario, the median number of herds depopulated was approximately 7,000 for all initially latent conditions (range 6,890-7,080) and it had the largest number of herds depopulated for each initially latent condition. The median result for like scenarios was similar for each of the initially latent conditions, however comparing like scenarios between initially latent conditions, the scenarios with a single initially latent feedlot were always ranked first in depopulating the lowest number of herds. Scenarios 16, 8 4, and 12, all with 50 km vaccination zones, depopulated the lowest number of herds in each initially latent population based on the Kruskal-Wallis test. The scenarios with a small vaccination zone and late vaccination trigger (scenarios 6 and 10) however had wider distribution with a long upper tail when multiple beef herds were initially latently infected.

Herds vaccinated

The day of first vaccination for the scenarios with an early (10 herds infected) trigger was later in scenarios with a single latently infected feedlot at the beginning of the outbreak (medians, day 27-29) compared to the scenarios with multiple herds initially latently infected (median, day 13). Similar results were found when the vaccination trigger was late (100 herds infected) the median day of first vaccination ranged from day 70 to 74 for a single initially latent herd compared to day 33 to 37 for scenarios for multiple initially latent herds. The median number of animals vaccinated at the end of the outbreak was comparable across the different initial latent conditions (Figure 6). In scenarios 2 and 10 with small vaccine capacity and vaccination zone, the fewest number of animals were vaccinated in all initially latent conditions, these two scenarios however were not among the best for number depopulated or duration of the outbreak.

Discussion

Auction markets have been found to play a critical role in causing wide dissemination of disease and in increasing the magnitude of FMD outbreaks (Bates et al., 2001; Shirley and Rushton, 2005; Fevre et al., 2006; McLaws and Ribble, 2007). One impact of auction markets in disease dissemination is to widely disperse disease to multiple operations following common exposure at the market and subsequent animal dispersal to multiple farms. Other research has found that the larger the number of detected herds within the first 14 days of an outbreak, the higher the risk of a large subsequent spread of FMD (Hutber et al., 2006; Halasa et al., 2013). In the Taiwan FMD outbreak four major factors were reported as responsible for the rapid spread of FMD in the 1997 outbreak: inability to shut down auction markets; the long delays in depopulating the livestock on infected farms; the high density of pig farms; and inadequate vaccine supply (Yang et al., 1999). The NAADSM model used in this study does not explicitly include auction markets. However one potential way to assess the possible impact of an outbreak spreading through an auction market prior to detection is to simulate scenarios initiated with multiple initially latent herds. The results were then compared between like scenarios for the different initial latently infected conditions.

The number of herds detected increased when multiple herds were initially infected. However the outbreak duration was statistically shorter compared to the single initially infected feedlot for all scenarios except 14. Despite the shorter outbreak duration when multiple herds were initially latent, the lower outliers that were present when a single feedlot was initially latently infected disappeared. This implies that the chance of having a small outbreak duration when multiple herds are initially latently infected is very small. The control methods were robust enough though that the same control method that would be the most effective to decrease outbreak duration when a single herd is initially latent are the same when multiple herds are initially latent. Scenarios with a large vaccination zone had the shortest outbreak duration for all initially latent conditions. Interestingly figure 3 illustrates late peaks in number of new infections for scenarios with a large vaccine zone, such as scenario 4, 8, 12, and 16. Due to the effect of outlying large outbreaks increasingly influencing the median as time passes and most outbreaks are brought under control. The peaks represent the larger outbreaks.

The number of herds depopulated was fewer when a single herd was initially latent compared to scenarios with multiple initially latent herds. The scenarios with a large vaccination zone were again the most effective across all three initially latent conditions. In the each of the different initially latent conditions, scenario 16, which had a high vaccine capacity, early vaccine trigger, and large vaccination zone, always depopulated the lowest number of herds. Scenario 4, with a small vaccine capacity, early trigger, and large vaccination zone depopulated ranked second for the lowest median number of herds and did not differ from scenario 8 when the initially latent condition was a single large feedlot but when multiple herds were latently infected, scenario 8 depopulated fewer herds. Scenario 8 also had a large vaccination zone but it also had a high vaccine capacity of 50 herds by day 22 of the outbreak. This effectiveness of large vaccination radius and capacity implies that when multiple herds are infected early in an outbreak the more aggressive vaccination strategies are the most beneficial.

The initial incidence density was higher in the scenarios with multiple initially latent herds and by week 2 approximately 15 herds had been detected. The increased incidence would require a large number of personnel and resources for tracing, depopulation, disposal, disinfecting premises, and vaccination at the beginning of the outbreak. By week 5 the number of newly detected herds ranged from 33 to 44 per week for the populations with multiple initial latently infected herds compared to 7 to 8 herds for the scenarios with a single initial latently infected herd. While this study suggests the final distribution of outbreak size may be comparable between the initial starting herd populations, the front loaded resource needs of multiple initially latent herds may be substantial and could complicate timely control. Workforce capacity can limit the method and scale of disease control strategies (Morris et al., 2002). The workforce needed for a rapid response in a high density region such as the central U.S. is especially a concern. Additionally, the NAADSM model was constrained by not accounting for transmission to livestock beyond the defined 8-state region, and transmission of FMD virus that might have originated outside the study population and been re-introduced. The rapid expansion of the outbreak might continue for longer if there were more herds available over a wider area.

Though the median number of animals vaccinated did not change substantially among the three initial latent conditions, multiple latent herds would require an increased supply of vaccine and personnel to be available earlier in the outbreak. If vaccine availability and resources were limited early in a FMD outbreak it could negatively impact control. A study modeling the impact of FMD vaccination as a control method in a region of California found that vaccination must be implemented quickly in order to have maximum effectiveness (Bates et al., 2003). Scenarios 16, 8, 4, and 12 ranked as the best scenarios in terms of outbreak duration and number of herds depopulated for all initially latent conditions and all had a large vaccination zone of 50 km. A large number of resources and personnel would be needed to set up a large vaccination zone around each detected herd. If this could not be achieved effective control might be hampered. If aggressive vaccination strategies are most beneficial, careful planning to assess the resource requirements and ability to provide sufficient resources is necessary.

While vaccination has been used to successfully stop outbreaks when used in combination with depopulation (Leforban and Gerbier, 2002), Ward et al. (2009) found that vaccination was not significantly beneficial even with an adequate supply in a high density livestock region of Texas. In the study the ring vaccination was within a radius of 5 km of a newly identified infected herd. In our study, the ring vaccination zone of 10 km found similar results. The baseline scenario which was depopulation without vaccination had an outbreak duration as short as or shorter than scenarios with a 10 km vaccination zone. However, when the vaccination zone was 50 km vaccination decreased both the number of herds depopulated and the outbreak duration for all initially latent herd populations.

Previous FMD simulation model studies had found that when an auction market was the index herd the median size of the outbreak increased by 837% compared to randomly selected initial infected herds in a 3-county region in California (Bates et al., 2003). However in the Bates et al. (2003) study there was a 21 day delay in diagnosis compared to this study which found that detection occurred earlier when multiple herds were initially latently infected. In Ward et al. (2009) simulation model early detection in the initially infected herd had the largest effect on reducing the outbreak duration and the number of herds depopulated to control outbreaks. Based on Ward et al. (2009) results a possible explanation of the shorter outbreak duration in this study when multiple herds were initially latent compared to scenarios with a single initially latent herd is the earlier detection time.

FMD simulation models suggest the day of detection is one of the most influential parameters (Ward et al., 2009; Boklund et al., 2013). The NAADSM simulation model generates the day of detection for each herd. The probability of detecting the disease is based on the probability of detecting clinical signs in a herd based on the number of days the herd has been clinically infected. Over time the probability of observing clinical signs increases as more animals are likely becoming infected in the herd and signs become more obvious. The NAADSM criterion for detection is independent for each herd but based on how long the herd has been clinical. The first day of detection was at approximately day 11 for the scenarios with a single large feedlot initial latently infected. The NAADSM simulation study of an outbreak originating from the National Bio and Agro-Defense Facility in Kansas had similar day of detection at day 15 of the outbreak (NBAF, 2012). However in this study when 12 herds were initially latent, the first day of detection was approximately day 6. In this study using NAADSM with 12 initially latent herds with an independent probability of detection there is a higher probability on each day that one of the herds will be detected. The scenarios with 12 initially latent herds have an earlier first day of detection due to the probability of detecting one of 12 herds being greater than when only one herd is initially latent. Still, the number of herds infected at first detection is increased for multiple initially latent starting herds. The U.K. 2001, the Netherlands 2001, and the Japan 2010 FMD outbreaks all took 20 to 21 days to detect the disease (Gibbens et al., 2001; Pluimers et al., 2002; Nishiura and Omori, 2010). The ability to rapidly detect a FMD outbreak in the central plains is unknown but in production types that are monitored daily for illness such as feedlots the probability of detecting the clinical signs is likely higher than cow/calf herds or small ruminants that are out to pasture.

This study raises a number of questions for future research. Further research on the day to detection, wide spread dissemination of the disease, as well as different vaccination strategies could be evaluated. With early detection, outbreaks dispersed from auction markets may have initially increased incidence and resource needs but may have little influence on final outcome; however the effect of an unconstrained population geography and potential delayed detection may substantively alter this conclusion.

References

Bates, T. W., M. C. Thurmond and T. E. Carpenter, 2001. Direct and indirect contact rates among beef, dairy, goat, sheep, and swine herds in three California counties, with reference to control of potential foot-and-mouth disease transmission. Am. J. Vet. Res. 62: 1121-1129.

Bates, T. W., M. C. Thurmond and T. E. Carpenter, 2003. Results of epidemic simulation modeling to evaluate strategies to control an outbreak of foot-and-mouth disease. Am. J. Vet. Res. 64: 205-210.

Boklund, A., T. Halasa, L. E. Christiansen and C. Enoe, 2013. Comparing control strategies against foot-and-mouth disease: Will vaccination be cost-effective in Denmark? Prev. Vet. Med. 111: 206-219.

Buhnerkempe, M. G., D. A. Grear, K. Portacci, R. S. Miller, J. E. Lombard and C. T. Webb, 2013. A national-scale picture of U.S. cattle movements obtained from Interstate Certificate of Veterinary Inspection data. Prev. Vet. Med.

Fevre, E. M., B. M. Bronsvoort, K. A. Hamilton and S. Cleaveland, 2006. Animal movements and the spread of infectious diseases. Trends Microbiol. 14: 125-131.

Gibbens, J., J. Wilesmith, C. Sharpe, L. Mansley, E. Michalopoulou, J. Ryan and M. Hudson, 2001. Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months. Vet. Rec. 149: 729-743.

Halasa, T., P. Willeberg, L. E. Christiansen, A. Boklund, M. AlKhamis, A. Perez and C. Enøe, 2013. Decisions on control of foot-and-mouth disease informed using model predictions. Prev. Vet. Med. 112: 194-202.

Harvey, N. and A. Reeves. 2010. Model description: North American Animal Disease Spread Model 3.2.

Harvey, N., A. Reeves, M. A. Schoenbaum, F. J. Zagmutt-Vergara, C. Dube, A. E. Hill, B. A. Corso, W. B. McNab, C. I. Cartwright and M. D. Salman, 2007. The North American Animal Disease Spread Model: a simulation model to assist decision making in evaluating animal disease incursions. Prev. Vet. Med. 82: 176-197.

Holm, S., 1979. A simple sequentially rejective multiple test procedure. Scandinavian journal of statistics: 65-70.

Hutber, A. M., R. P. Kitching and E. Pilipcinec, 2006. Predictions for the timing and use of culling or vaccination during a foot-and-mouth disease epidemic. Res. Vet. Sci. 81: 31-36.

Leforban, Y. and G. Gerbier, 2002. Review of the status of foot and mouth disease and approach to control/eradication in Europe and Central Asia. Rev. Sci. Tech. 21: 477-492.

Mardones, F., A. Perez, J. Sanchez, M. Alkhamis and T. Carpenter, 2010. Parameterization of the duration of infection stages of serotype O foot-and-mouth disease virus: an analytical review and meta-analysis with application to simulation models. Vet. Rec. 41: 45.

Marshall, E. S., T. E. Carpenter and C. Thunes, 2009. Results of a survey to estimate cattle movements and contact rates among beef herds in California, with reference to the potential spread and control of foot-and-mouth disease. J. Am. Vet. Med. Assoc. 235: 573-579.

McLaws, M. and C. Ribble, 2007. Description of recent foot and mouth disease outbreaks in nonendemic areas: Exploring the relationship between early detection and epidemic size. The Canadian Veterinary Journal 48: 1051.

McReynolds, S. W., M. W. Sanderson, A. Reeves and A.E. Hill. Modeling the impact of vaccination control strategies of a foot and mouth disease outbreak in the Central United States. in preparation.

McReynolds, S. W., M. W. Sanderson, A. Reeves, A. E. Hill, M. Sinclair and M. D. Salman, 2013. Direct and Indirect contact rates among livestock operations in Colorado and Kansas. J. Am. Ved. Med. Assoc. in press.

Melius, C., A. Robertson and P. Hullinger, 2006. Developing livestock facility type information from USDA agricultural census data for use in epidemiological and economic models.

Department of Homeland Security, Lawrence Livermore National Laboratory, UCRL-TR 226008.

Morris, R. S., R. L. Sanson, M. W. Stern, M. Stevenson and J. W. Wilesmith, 2002. Decision-support tools for foot and mouth disease control. Rev. Sci. Tech. 21: 557-567.

Nishiura, H. and R. Omori, 2010. An epidemiological analysis of the foot-and-mouth disease epidemic in Miyazaki, Japan, 2010. Transbound Emerg Dis 57: 396-403.

Pluimers, F. H., A. M. Akkerman, P. van der Wal, A. Dekker and A. Bianchi, 2002. Lessons from the foot and mouth disease outbreak in The Netherlands in 2001. Rev. Sci. Tech. 21: 711-721.

Reeves, A., 2012 "User's guide for WH: A simulation model of within-unit disease dynamics." Colorado State University http://www.naadsm.org/wh (accessed June 17, 2013)

Reeves, A., M. Talbert, M. D. Salman and A. E. Hill, in preparation "Development of a stochastic, individual-based modeling framework for within-unit transmission of highly infectious animal diseases. ." in preparation Draft available at: http://www.naadsm.org/wh (accessed July 17, 2013)

Schoenbaum, M. A. and W. T. Disney, 2003. Modeling alternative mitigation strategies for a hypothetical outbreak of foot-and-mouth disease in the United States. Prev. Vet. Med. 58: 25-52.

Shirley, M. D. F. and S. P. Rushton, 2005. The impacts of network topology on disease spread. Ecol. Complex. 2: 287-299.

StataCorp. 2011. Stata: Release 12. Statistical Software College Station, TX, StataCorp LP.

Thompson, D., P. Muriel, D. Russell, P. Osborne, A. Bromley, M. Rowland, S. Creigh-Tyte and C. Brown, 2002. Economic costs of the foot and mouth disease outbreak in the United Kingdom in 2001. Rev. Sci. Tech. 21: 675-685.

USDA-APHIS, A. a. P. H. I. S. United States Department of Agriculture, 2010. Reference of Beef Cow-calf Management Practices in the United States. http://www.aphis.usda.gov/animal_health/nahms/beefcowcalf/ (accessed Nov. 14, 2012).

USDA-GIPSA, United States Department of Agriculture, May 2012. Grain Inspection, Packers & Stockyards Administration. http://www.aphis.usda.gov/animal_health/livestock_markets/ (accessed Nov 21, 2012).

Ward, M. P., L. D. Highfield, P. Vongseng and M. Graeme Garner, 2009. Simulation of foot-and-mouth disease spread within an integrated livestock system in Texas, USA. Prev. Vet. Med. 88: 286-297.

Yang, P. C., R. M. Chu, W. B. Chung and H. T. Sung, 1999. Epidemiological characteristics and financial costs of the 1997 foot-and-mouth disease epidemic in Taiwan. Vet. Rec. 145: 731-734.

Figure 5-1 - 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 5-2 - The number of iterations included in the analysis by week for scenario 4 during the Foot and Mouth disease outbreak in the central U.S.

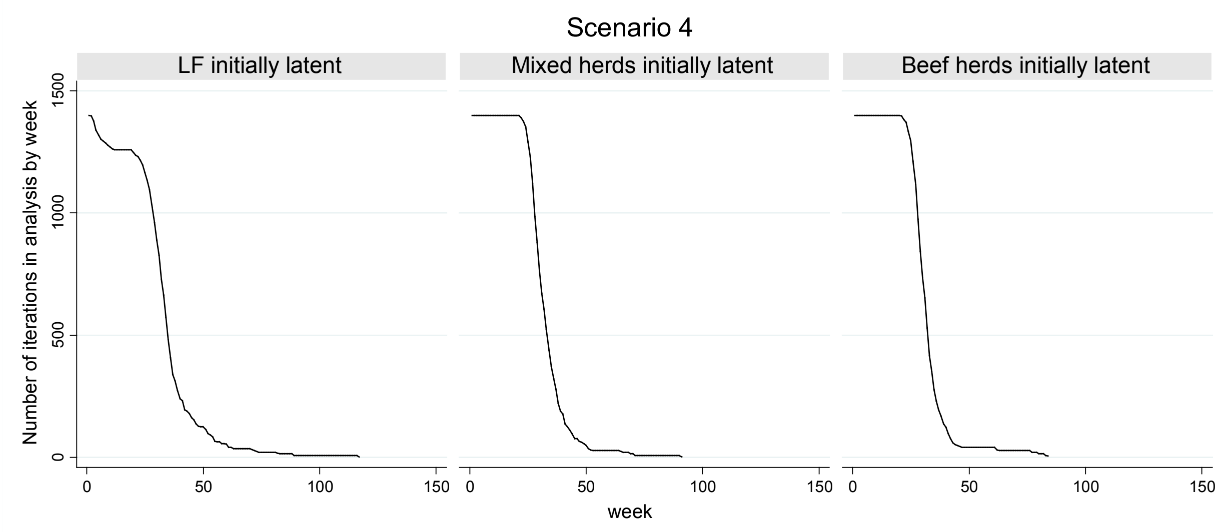
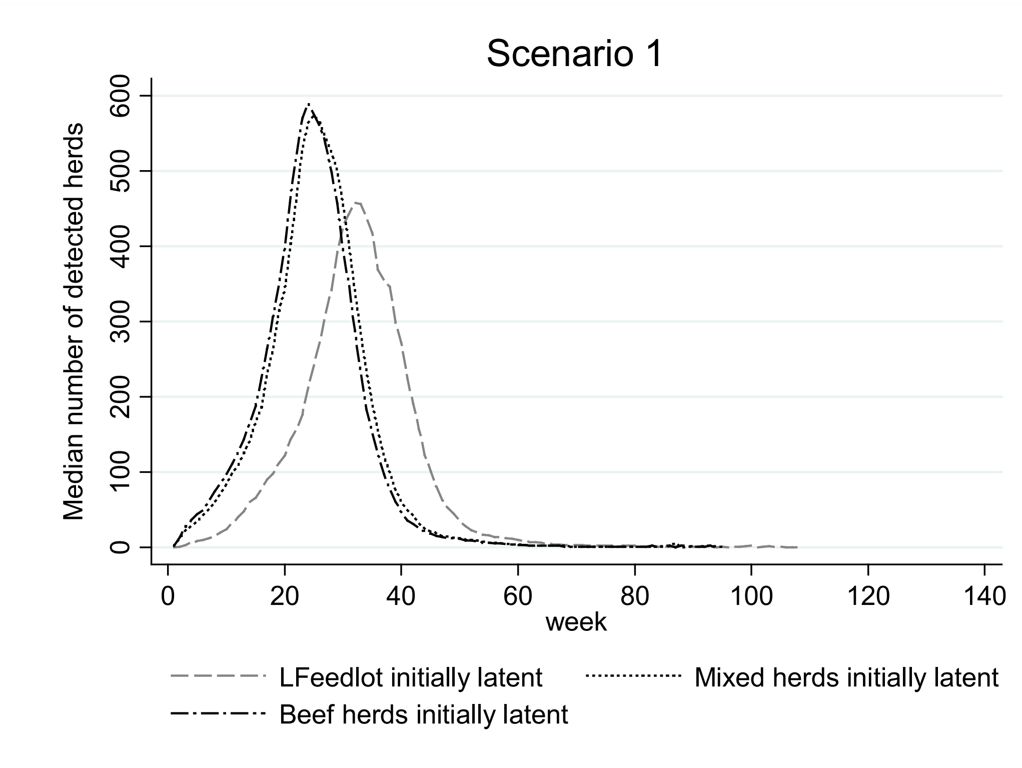
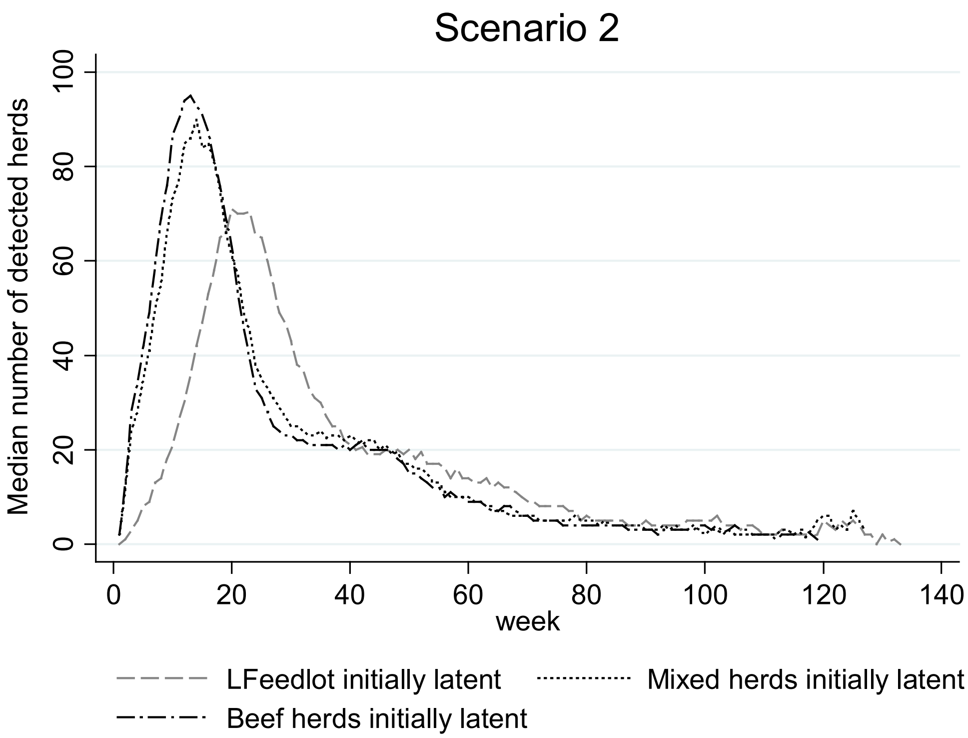


Figure 5-3 - Median number of new herds detected as clinically infected by week categorized by initially latent condition for a potential foot and mouth disease outbreak in the central region of the U.S. for each scenario.



[a] Baseline scenario with depopulation and no vaccination

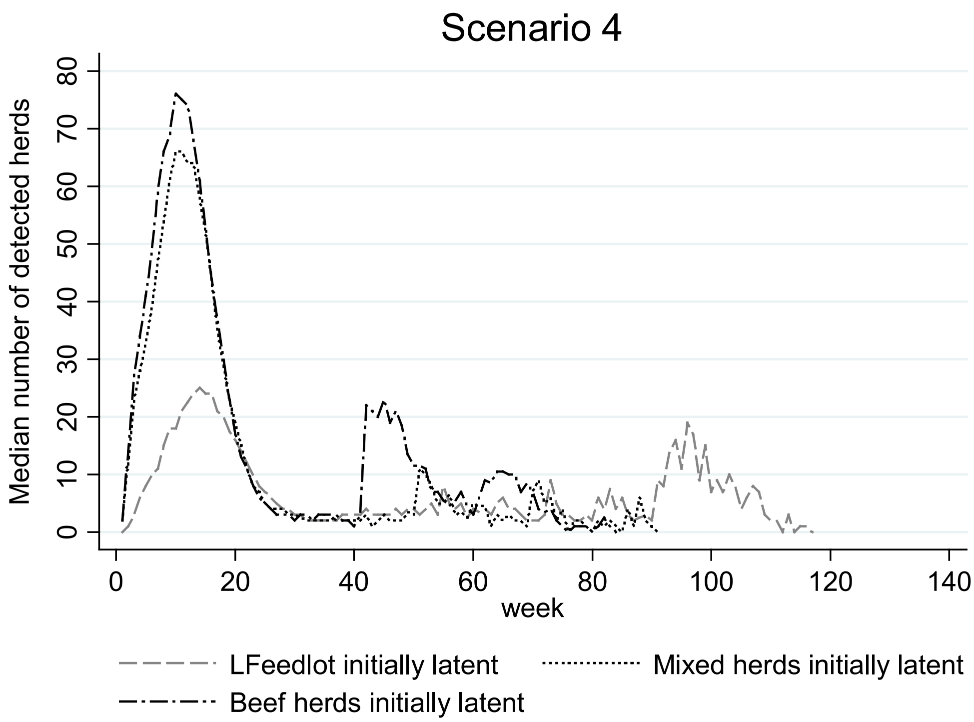


[a] The capacity of 5 in herds per day by 22 days after disease detection and 10 herds by 40 days after disease detection

[b] Vaccination trigger of 10 herds

[c] Vaccination zone of 10 km.

[d] Results of scenarios 6, 10, and 14 were similar to scenario 2

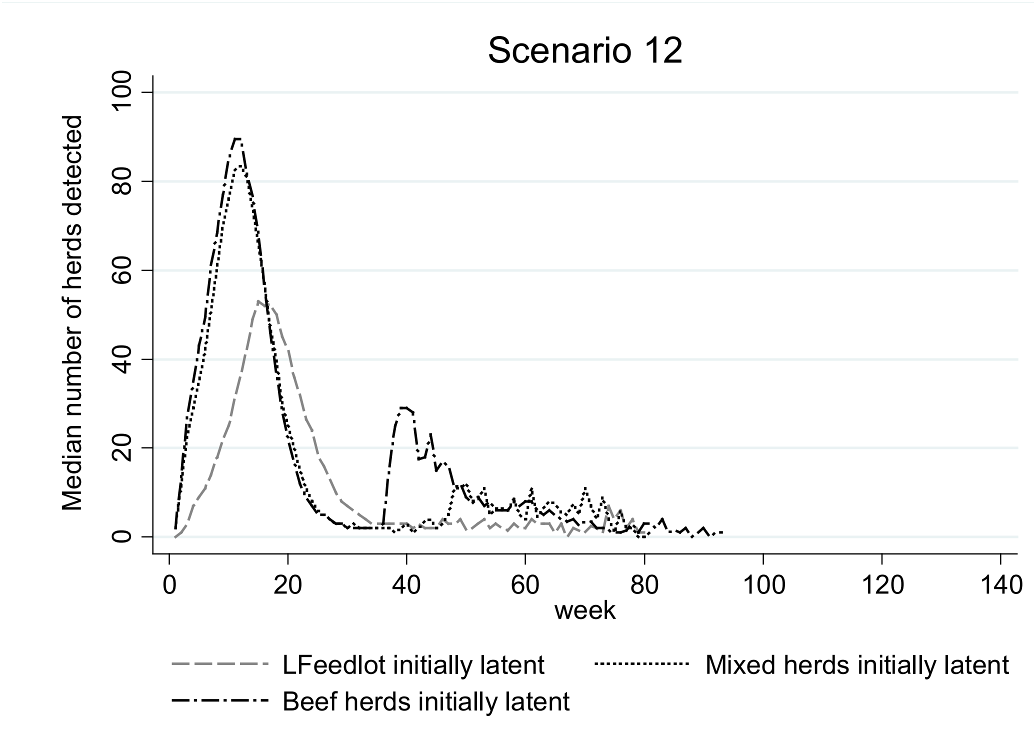


[a] The capacity of 5 in herds per day by 22 days after disease detection and 10 herds by 40 days after disease detection

[b] Vaccination trigger of 10 herds

[c] Vaccination zone of 50 km.

[d] Results of scenarios 8 and 16 were similar to scenario 4

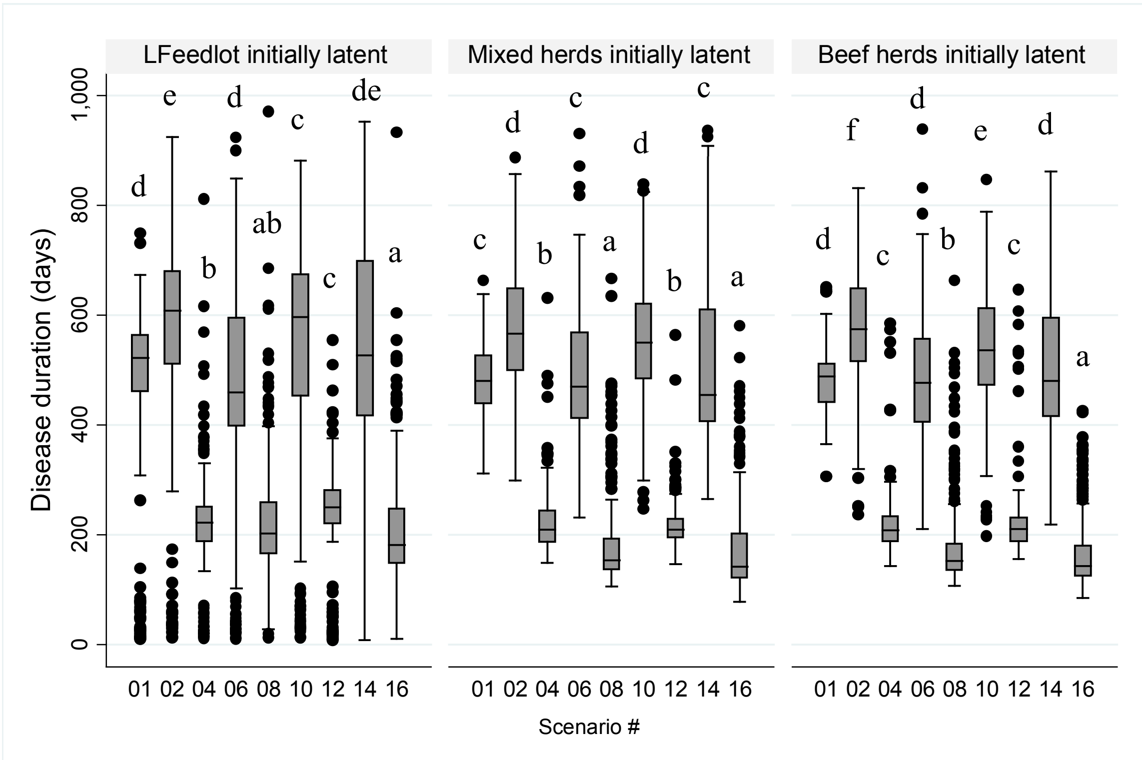


[a] The capacity of 5 in herds per day by 22 days after disease detection and 10 herds by 40 days after disease detection

[b] Vaccination trigger of 100 herds

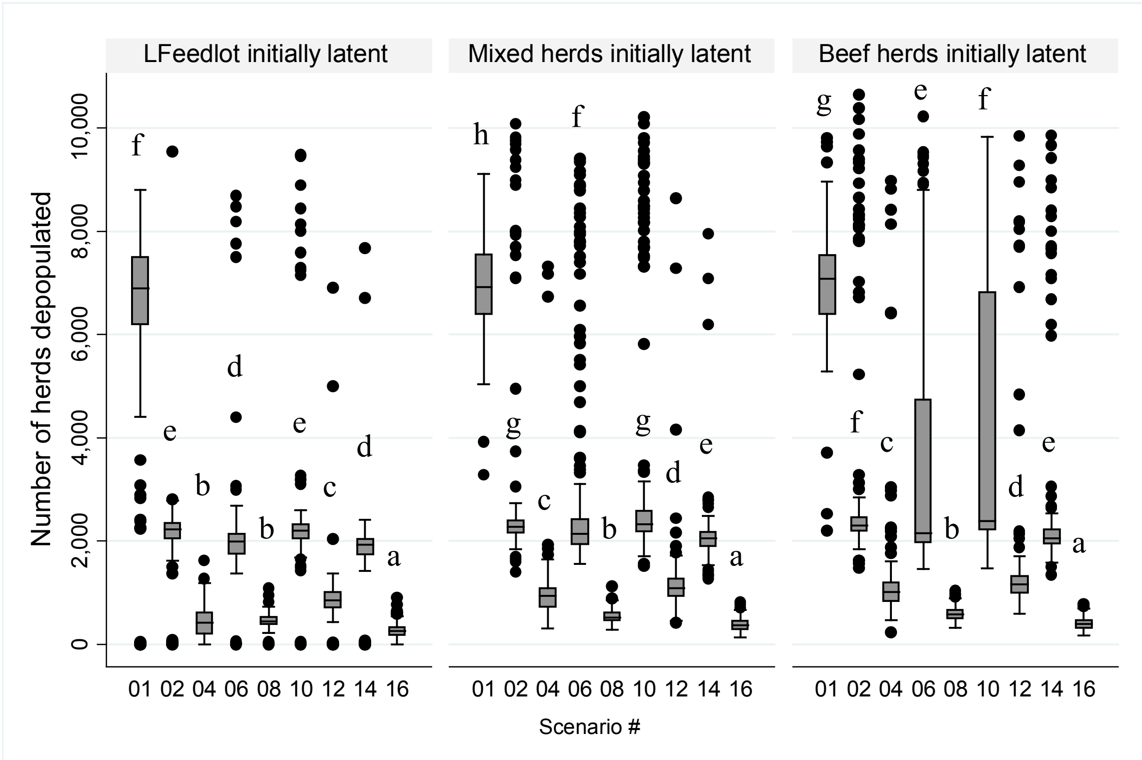
[c] Vaccination zone of 50 km

Figure 5-4 - Box plots of outbreak duration in days by initially latent condition of the 9 simulated scenarios for a potential foot and mouth disease virus outbreak in the central region of the U.S.



[a] Values within initially latent condition with different superscripts are different p<0.05 (adjusted p-value accounting for multiple comparisons) for each population of initially latent herds.

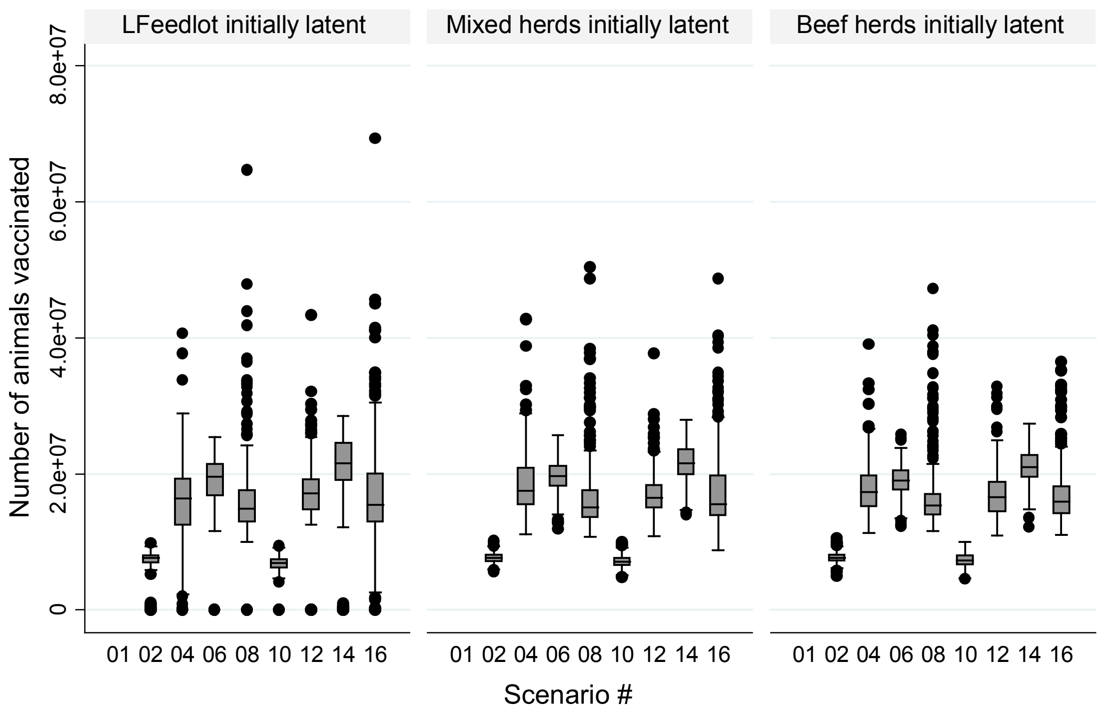
Figure 5-5 - Box plots of number of herds depopulated by initially latent condition of 9 simulated scenarios for a potential foot and mouth disease virus outbreak in the central region of the U.S.



[a] Values within initially latent condition with different superscripts are different p<0.05 (adjusted p-value accounting for multiple comparisons) for each population of initially latent herds.

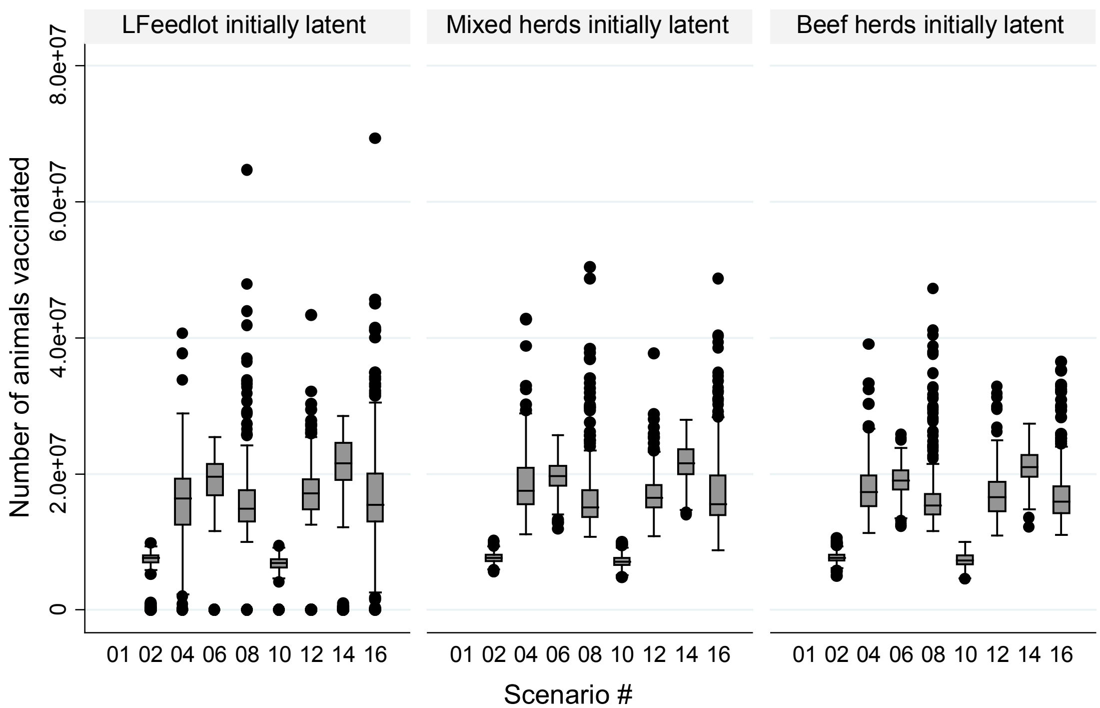
[b] The box plot parameters are boxes at 25th and 75th percentiles, the line in the box is the median, whiskers are 5th and 95th percentiles and dots are outliers.

Figure 5-6 - Box plots of the number of animals vaccinated for each initially latent condition 9 simulated scenarios for a potential foot and mouth disease virus outbreak in the 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 5-7 - Box plots of the number of animals vaccinated for each initially latent condition 9 simulated scenarios for a potential foot and mouth disease virus outbreak in the 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.

Table 5.1 - 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 5.2 - Description of vaccination strategy for 9 simulated scenarios that were simulated for each of the initially latent populations of a potential foot and mouth disease virus outbreak in a central region of the U.S.

Scenario	Vaccination Capacity [a]	Vaccination Trigger (herds)	Size of Vaccination Zone (km)
1	-	-	-
2	5,10	10	10
4	5,10	10	50
6	50,80	100	10
8	50,80	100	50
10	5,10	100	10
12	5,10	100	50
14	50,80	10	10
16	50,80	10	50

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

Chapter 6 - Conclusion

The objective of this comprehensive review and research was to determine the impact of a possible Foot and Mouth Disease (FMD) outbreak and impact of control methods in the central United States (U.S.). The economic impact of a FMD outbreak in the U.S. would be devastating due to the decrease in production and more importantly the loss of international trade. In the face of a FMD outbreak, well- informed decisions on the best control strategy will need to be made.

Simulation modeling is the only avenue available to study the potential impacts of a foreign animal disease introduction and is an essential tool to evaluate control methods. One limitation of epidemiological disease models is that they dependent on accurate estimates of the frequency and distance distribution of contacts between livestock operations to estimate disease spread. Prior to the livestock survey of Kansas and Colorado producers, few direct and indirect contact rates were available for the central U.S. and simulation models of livestock disease outbreaks lacked an essential element to provide valid model results and evaluate alternate control methods in this important agriculture region. The results of the livestock survey reported here help to fill that knowledge gap and provide baseline data to guide biosecurity improvements for emergency planning during an infectious disease outbreak among livestock as well as provide data to parameterize simulation models to evaluate control methods during a possible outbreak. This data fills a need for region specific contact rates to provide parameters for modeling a foreign animal disease and producing valid results helpful for planning and decision making including the relative importance of different control strategies such as biosecurity and movement control.

The next phase of the research was to use the region specific contact data to parameterize the North American Animal Disease Spread Model (NAADSM). In this simulation study of a FMD outbreak in the central U.S., scenarios with increased size of the vaccination zone had decreased length of the outbreak and number of herds destroyed. Vaccination trigger and vaccination capacity had less of an impact on the outbreak. A concern with the large vaccination zone and the large vaccination capacity are workforce constraints and the feasibility if vaccine production and delivery is limited. Increased vaccine capacity and large vaccination zones both will require a large workforce. However, vaccination requires less time and labor than are needed for depopulation and disposal of the carcasses. In the face of workforce limitations one solution is to prioritize the high risk herds for vaccination. The high contact rates of large feedlots and the high density of them in the central U.S. led to them having the highest vaccination priority when all production types were vaccinated.

Further analysis of the scenarios demonstrated that outbreak size and number of herds depopulated was 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 transmission and the ability to restrict indirect movement consistent with acceptable animal welfare is uncertain. When biosecurity and movement controls were increased, vaccination was not beneficial compared to depopulation alone to control the outbreak. 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.

Auction markets could play a critical role in increasing initial spread of a FMD incursion prior to detection. Since NAADSM currently does not have an explicit way of including auction markets, a simulation study on the impact of a FMD outbreak beginning in multiple herds and production types was evaluated. The day of detection was approximately 5 days earlier when multiple herds were initially latent compared to scenarios where a single herd was initially latent. The initial incidence of newly detected herds was greater in the scenarios with multiple initially latent herds. However, multiple initial latently infected herds had minimal impact on the median outbreak duration, and the total number of herds depopulated and vaccinated when compared to scenario results with a single herd initially latently infected. Due to the greater initial incidence of detected herds, the impact on resource needs may be substantial and could complicate timely control when there are multiple initially latent herds. Overall, outbreaks dispersed from auction markets may have initially increased incidence and resource needs but may have little influence on final outcome.

Depending on the location of the outbreak, size of the outbreak, timeliness of the implementation, the workforce capacity, and the available resources the control strategies will vary. The central U.S. has a high density of livestock with a large number of large feedlots. Depopulation of infected herds and herds that have been in contact with infected animals has been an essential component of outbreak control methods to reduce transmission of FMDV. The feasibility of depopulating a large feedlot in a timely and efficient manner that minimizes the human and animal health concerns is a key question to be answered in considering a depopulation program. An expert Delphi survey and roundtable discussion did not identify a clearly acceptable method of rapidly depopulating a large feedlot. All methods for euthanasia or depopulation identified had serious drawbacks. Participants in the study agreed that regardless of the method used for depopulation of cattle in a large feedlot, it would be very difficult to complete the task quickly, humanely, and be able to dispose of the carcasses.

These studies raise a number of questions for future research. Further research on the control methods, days to detection, and wide spread dissemination of the FMD virus could be evaluated. A better understanding of the biosecurity changes necessary during an outbreak to attain these levels is needed. Additionally, identifying the personnel requirements to achieve sufficient levels of biosecurity and movement controls is needed, as well as their impact on animal welfare. An improved knowledge of the biosecurity practices and the ability to achieve strict movement controls to limit direct and indirect transmission would allow more focused planning of optimal control efforts. With early detection, outbreaks dispersed from auction markets may have initially increased incidence and resource needs but may have little influence on final outcome; however the effect of an unconstrained population geography and potential delayed detection may substantively alter this conclusion. Lastly, due to the infeasibility of timely depopulating a large feedlot in the face of an outbreak, further research on available alternatives for control of FMD in large feedlots is also needed.