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Preventive Veterinary Medicine 82 (2007) 176–197
PREVENTIVE VETERINARY MEDICINE
www.elsevier.com/locate/prevetmed

The *North American Animal Disease Spread Model*: A simulation model to assist decision making in evaluating animal disease incursions

Neil Harvey [a], Aaron Reeves [b], Mark A. Schoenbaum [c], Francisco J. Zagmutt-Vergara [b,1], Caroline Dubé [d], Ashley E. Hill [b], Barbara A. Corso [e,*], W. Bruce McNab [f], Claudia I. Cartwright [g,2], Mo D. Salman [b]

[a] *Department of Computing and Information Science, University of Guelph, Guelph, Ontario N1G 2W1, Canada*
[b] *Animal Population Health Institute, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523-1681, USA*
[c] *United States Department of Agriculture, Animal Plant Health Inspection Service, Veterinary Services, Western Regional Office, Mail Stop 3E13, 2150 Centre Avenue, Building B, Fort Collins, CO 80526-8117, USA*
[d] *Canadian Food Inspection Agency, 59 Camelot, Ottawa, Ontario K1A 0Y9, Canada*
[e] *United States Department of Agriculture, Animal Plant Health Inspection Service, Veterinary Services, Centers for Epidemiology and Animal Health, Mail Stop 2W4, 2150 Centre Avenue, Building B, Fort Collins, CO 80526-8117, USA*
[f] *Ontario Ministry of Agriculture Food & Rural Affairs, 1 Stone Road, Guelph, Ontario N1G 4Y2, Canada*
[g] *United States Department of Agriculture, Animal Plant Health Inspection Service, International Services, 4700 River Road, Unit 65, Riverdale, MD 20740, USA*

Received 22 February 2007; received in revised form 2 May 2007; accepted 18 May 2007

Abstract

The *North American Animal Disease Spread Model* is a stochastic, spatial, state-transition simulation model for the spread of highly contagious diseases of animals. It was developed with broad international support to assist policy development and decision making involving disease incursions. User-established parameters define model behavior in terms of disease progression; disease spread by animal-to-animal contact, contact with contaminated personnel or equipment, and airborne dissemination; and the implementation of control measures such as destruction and vaccination. Resources available to implement

* Corresponding author. Tel.: +1 970 494 7312; fax: +1 970 494 7269.
E-mail address: Barbara.A.Corso@aphis.usda.gov (B.A. Corso).
[1] Present address: Vose Consulting, 2891 20th Street, Boulder, CO 80304, USA.
[2] Present address: Food and Agriculture Organization of the United Nations, Emergency Center for Transboundary Animal Diseases, Crisis Management Centre, Viale delle Terme di Caracalla, 00153 Rome, Italy.

0167-5877/$ – see front matter
doi:10.1016/j.prevetmed.2007.05.019

disease control strategies, as well as the direct costs associated with these strategies, are taken into consideration. The model records a wide variety of measures of the extent of simulated outbreaks and other characteristics. The graphical interface and output visualization features also make it a useful tool for training and preparedness exercises. This model is now being used to evaluate outbreak scenarios and potential control strategies for several economically important exotic animal diseases in the United States, Canada, and elsewhere. *NAADSM* is freely available via the Internet at http://www.naadsm.org.

Keywords: Computer simulation; Herd-level; Foot-and-mouth disease (FMD); Stochastic; Spatial; State-transition model; Animal disease model

1. Introduction

The use of simulation modeling for estimating the spread of highly contagious animal diseases and for conducting risk assessments for various control measures has become common (Morris et al., 2002; Risk Solutions, 2005; Keeling, 2005; Guitian and Pfeiffer, 2006). During the last few decades, several models have been developed to mimic outbreaks of diseases such as foot-and-mouth disease (FMD) and classical swine fever (CSF) in specific regions or countries (*e.g.*, Jalvingh et al., 1999; Durand and Mahul, 2000; Bates et al., 2003a; Karsten et al., 2005; Garner and Beckett, 2005; Stevenson et al., submitted for publication). Some of these models were used in retrospective analyses of outbreaks to study aspects of disease transmission or evaluation of "what if?" questions (Yoon et al., 2006; Nielen et al., 1999), while others were developed to support policy decisions during actual outbreaks (Ferguson et al., 2001a,b; Keeling et al., 2001). Models have been used in preparedness planning as policy formulation tools, to aid in decision making and to assess economic impacts (Tomassen et al., 2002; Bates et al., 2003a,b; Schoenbaum and Disney, 2003; Keeling et al., 2003; Garner and Beckett, 2005; Stevenson et al., submitted for publication). The use of models as a support to decision making prior to and during disease outbreaks is the subject of several recent reviews (Woolhouse, 2003; Taylor, 2003; Kitching et al., 2006). Careful evaluation of available models is a prerequisite for their effective use in these roles, as subtle differences in model design may affect projected outcomes (Dubé et al., 2007).

As a result of the 2001 FMD outbreak in the UK and the use of models in decision making, the North American Foot-and-Mouth Disease Vaccine Bank (NAFMDVB) organized a workshop in Fort Collins, Colorado in July 2002. The purpose of the meeting was to identify a suitable model for use in policy formulation in North America. Various models from the United States and other countries were presented, including the model developed by Schoenbaum and Disney (2003). Because this model was considered user-friendly and flexible in the sense of allowing the simulation of an FMD outbreak anywhere in the world, it was selected by NAFMDVB as a planning tool for North America. Several scientific and professional national and international meetings were conducted subsequently to enhance and further refine the model. For example, a review of the conceptual model and its assumptions was carried out by experts in the field of FMD and modeling through a subject matter expert meeting held in Fort Collins, Colorado in 2004. Among the suggested improvements were inclusion of various livestock species, production systems, and a variety of mitigation strategies, as well as extension of the utility of the model to diseases other than FMD.

The purpose of this manuscript is to present a description of this modified model, the *North American Animal Disease Spread Model* (*NAADSM*), which is now being used to simulate

disease control strategies and estimate the epidemiological and economic impacts of these strategies in the United States and Canada should a highly contagious disease such as FMD occur.

2. Materials and methods

Like several similar models (Bates et al., 2003a; Garner and Beckett, 2005; Stevenson et al., submitted for publication), *NAADSM* is a spatially explicit, stochastic, state-transition model. In this model, disease spread occurs between animal units (described in more detail in Section 2.1) at precisely specified locations, and is influenced by the relative locations and distances between these units. When a disease occurs within a unit, it follows a natural, predictable cycle over time, moving from one disease state to the next. This cycle may be interrupted by intervention of disease control mechanisms. Stochastic processes drive virtually all operations within the model and are based on distributions and relational functions specified by the user. Probability density functions are used to represent parameters such as disease state durations and distances of animal movements between units. Relational functions represent variation of a particular parameter as a function of time: such functions might be used, for example, to simulate a decline in the rate of animal movements or an increase in the capacity to carry out disease control measures as an outbreak progresses.

The components and input parameters of the model are described in the following sections: (Section 2.1) units and time-steps, (Section 2.2) disease, (Section 2.3) spread, (Section 2.4) disease detection, (Section 2.5) tracing out, (Section 2.6) control measures, (Section 2.7) priorities of actions and (Section 2.8) costs.

2.1. Units and time-steps

In this model, a cluster of animals called a ‘‘unit’’ is the basis of simulation. A unit has a production type, number of animals, point location (expressed in terms of longitude and latitude), and a transition state. Production types, which are defined by the user, typically encompass a group of units that have similar within-herd disease transmission and similar rates of animal shipments, indirect contacts, and airborne dissemination. The production type may be a single kind of livestock (*e.g.*, ‘‘dairy cattle’’) or a mixed type (*e.g.*, ‘‘sheep and goats’’).

The number of animals in each unit is assumed to be static: unit populations are not altered by the movement of animals or disease mortality (*i.e.*, the modeled disease is never fatal). Only when a unit is destroyed (see Section 2.6 below) will the number of animals be affected.

The simulation proceeds in time-steps of 1 day. On each simulation day, several types of processes may affect individual units: processes contributing to disease spread (*e.g.*, contact or airborne spread), the natural progression of disease of infected units, and/or disease control actions (*e.g.*, detection, vaccination, and destruction). The ‘‘model’’ is the sum of these processes and actions.

2.2. Disease

When a susceptible unit is infected, it begins to make a transition from one disease state to the next, as shown in Fig. 1. The user specifies the durations of each disease state as separate distributions for each production type (Table 1). Upon infection, a unit becomes latent. Unless intervening disease control action is taken (see Section 2.6 below), an infected unit will proceed naturally from its latent state to a subclinically infectious state (shedding agent without visible signs of disease), followed by a clinically infectious state (shedding agent with visible signs of

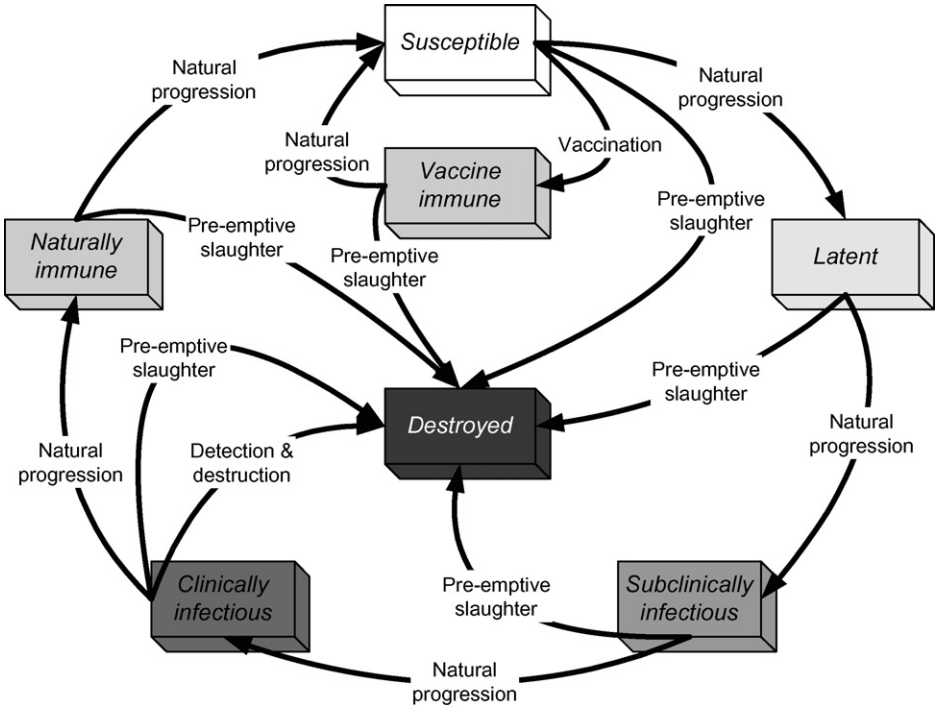

Fig. 1. States and transitions simulated by *NAADSM*. Without intervention, units will follow the state progression indicated in the outer loop. Upon the implementation of disease control measures, intervening actions may alter the normal disease cycle, as shown inside the loop.

disease). The unit will then progress to the natural immune state, and after a period of time, will transition back to the susceptible state. The duration of each of these states for each particular unit is selected stochastically from the distributions entered by the user.

All infected units will eventually return to the susceptible state unless they are destroyed. As a result, if time frames for simulations are extended, a particular unit may progress through the infected states more than once. A state may also be bypassed by setting its duration to 0 day. For example, a unit may undergo a transition from latent directly to infectious clinical without being subclinical. A unit undergoes its first transition state change on the day immediately following its infection. Attempting to infect a unit that is not susceptible has no effect: the course of disease in a unit that is already infected will be unaltered, and naturally immune units cannot be infected. Finally, if two units are at the same location, infecting one does not automatically infect the other.

2.3. Spread

2.3.1. Direct contact spread

The simulation of direct contacts – movement or shipment of animals among units – occurs as illustrated in Fig. 2. Parameters used for direct contact spread are listed in Table 1. A baseline rate of contact from one production type to another is independently specified for movement in each direction between each pair of production types. For example, the contact rate from beef to dairy units can be different than from dairy to beef units, and the contact rate from beef to beef units can be different again.

Table 1
Input parameters used in *NAADSM* for disease and disease spread

Parameter description	Parameter type	Level of application
Disease parameters		
Latent period	Probability density function (days)	Production type
Subclinically infectious period	Probability density function (days)	Production type
Clinically infectious period	Probability density function (days)	Production type
Naturally immune period	Probability density function (days)	Production type
Direct contact spread parameters		
Mean rate of animal shipments	Rate (number of recipient units per source unit per day)	Combination of source and recipient production types
Movement distance	Probability density function (km)	Combination of source and recipient production types
Shipping delay	Probability density function (days)	Combination of source and recipient production types
Probability of infection of the recipient unit, given exposure to an infected unit	Probability, 0 to 1	Combination of source and recipient production types
Movement rate multiplier	Relational function: scalar value as a function of the number of days since first detection of the outbreak	Combination of source and recipient production types
Can latent units spread disease by direct contact?	Yes/no	Combination of source and recipient production types
Can subclinically infectious units spread disease by direct contact?	Yes/no	Combination of source and recipient production types
Indirect contact spread parameters		
Mean rate of animal shipments	Rate (number of units receiving shipments form the source unit per day)	Combination of source and recipient production types
Movement distance	Probability density function (km)	Combination of source and recipient production types
Shipping delay	Probability density function (days)	Combination of source and recipient production types
Probability of infection of the recipient unit, given exposure (receipt of animals) from an infected unit	Probability, 0 to 1	Combination of source and recipient production types
Movement rate multiplier	Relational function: scalar value as a function of the number of days since first detection of the outbreak	Combination of source and recipient production types
Can subclinically infectious units spread disease by indirect contact?	Yes/no	Combination of source and recipient production types
Airborne transmission parameters		
Probability of infection at 1 km from source	Probability, 0 to 1	Combination of source and recipient production types
Wind direction, given as a range (start and end)	Degrees, 0–360, where 0 indicates north	Combination of source and recipient production types
Maximum distance of spread	Scalar value (km)	Combination of source and recipient production types
Airborne transport delay	Probability density function (days)	Combination of source and recipient production types

Baseline contact rates may be altered over time in a fashion specified by the user. This adjustment is based on the number of days since the initial case of disease was detected. In this way, the model can be used to mimic the implementation of movement controls over the course of an outbreak response. It can also accelerate movement before controls are implemented. As with baseline contact rates, movement control functions are specified for each pair of source and recipient production types.

Any unit that is infected and not quarantined (see Section 2.6 below) may be capable of spreading disease. Clinically infectious units are always capable of spreading disease, while the user may specify whether latent and subclinical units can spread disease by direct contact.

On each simulation day, the model determines the number of contacts that will occur from each infectious unit, based on the baseline contact rate, adjusted by a movement control function if necessary. For each infectious unit, the number of contacts is determined by sampling from a Poisson distribution whose mean is the adjusted contact rate.

For each contact from an infected unit, a distance D is stochastically selected from a movement distance distribution. Then, from all eligible recipient units (*i.e.*, those that have not been destroyed, are not quarantined, and are not the source of the contact), the program chooses the recipient unit whose distance from the source is closest to distance D selected from the distribution. The distance between two units is calculated according to Formula (1):

$$d = \frac{c}{360}\sqrt{x^2 + y^2} \tag{1}$$

where d is the distance between two units, y = (unit 1 latitude) − (unit 2 latitude), x = [(unit 1 longitude) − (unit 2 longitude)] × cos(unit 2 latitude), and c is the circumference of the earth.

If several possible targets are the same distance from the source, then the model selects one at random, giving preference to larger units (a unit with twice as many animals is twice as likely to be selected). If the recipient unit is not susceptible, the contact has no effect on its disease state but is recorded as an exposure. If there are no units of the desired recipient production type, or if all units of the desired recipient production type are destroyed or quarantined, the contact does not occur. For susceptible recipients, a random number r is generated from 0, up to but not including 1. If r is less than the specified probability of infection given exposure (see Table 1), then the recipient's state is changed to latent after a user-specified shipping delay.

The disease state is an attribute of the unit as a whole rather than a direct reflection of the state of a particular animal in the unit. Newly infected units always start their disease cycle in the latent state, regardless of whether the shipping unit was latent, subclinically infectious, or clinically infectious. Technically, a unit that receives clinically infectious animals could be regarded as immediately clinically infectious. Treating the receiving unit as latent, however, reflects the fact that most of the animals in this unit still need to progress through the earlier disease states.

Direct contacts, including those that do not result in a new infection, are recorded and can be identified later during trace-out (trace-forward) investigations (see Section 2.5 below). The number of animals in a shipment is not considered.

2.3.2. *Indirect contact spread*

Indirect contacts, such as movement of people, materials, vehicles, equipment, animal products, *etc.*, among units, are simulated in the same manner as direct contact, except that only subclinically infectious and clinically infectious units, not latent units, can act as the source of infection. Quarantined units may also act as sources of indirect contact. The parameters for indirect contact (Table 1) are similar to but independent of those for direct contacts. Indirect

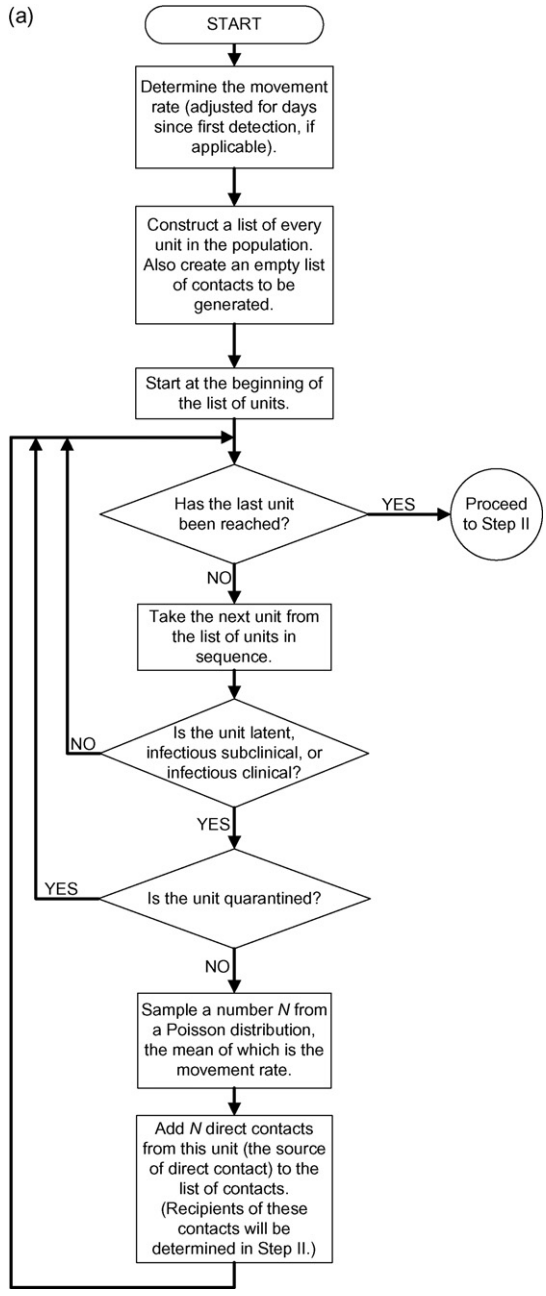

Fig. 2. (a) A flow chart demonstrating the generation of direct contacts (Step I). On each day of a simulated outbreak, every infectious unit will have direct contact with some number of other units in the population. Only movements from infectious (latent, infectious subclinical, or infectious clinical) units that have not been quarantined are recorded. The number of direct contacts from each infectious unit is drawn from a Poisson distribution as shown. Once the total number of contacts that will occur is established as shown here, the model then determines which units will receive those contacts, as well the effects of each contact (b). (b) A flow chart demonstrating the generation of direct contacts (Step II). After the source units for each direct contact are established (a), recipient units for each contact are determined, based on the

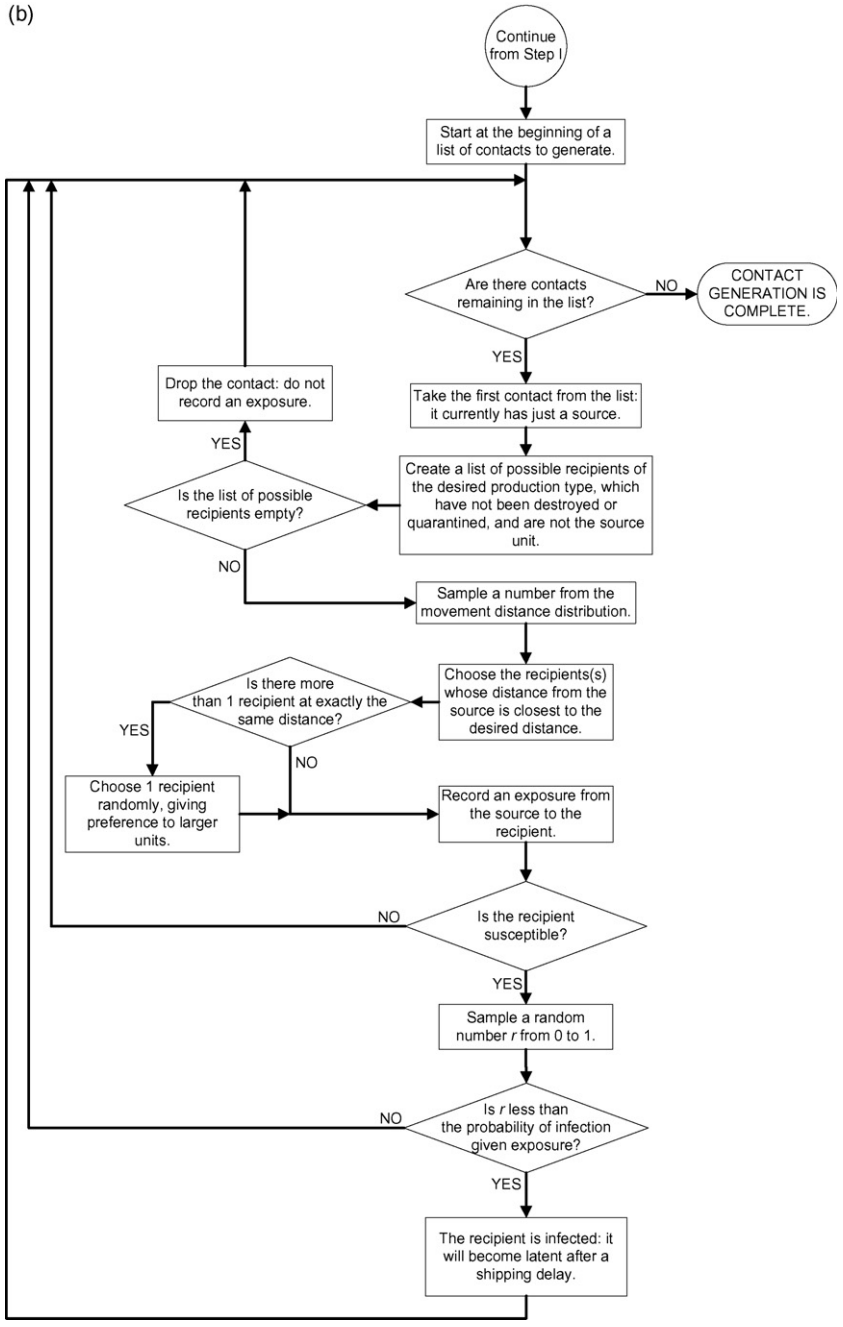

Fig. 2. (*Continued*).

distance of potential recipients from a source. If a susceptible recipient unit is selected for a contact, a stochastic process determines whether that source unit will become infected.

contacts are recorded and can be identified during trace-out (trace-forward) investigations (Section 2.5).

2.3.3. Airborne spread

The parameters for airborne spread are given separately for spread in each direction between each pair of production types (Table 1). This serves to account for potential differences in the amount of virus produced and/or different minimum infective doses for animals in different production types. Airborne spread can occur from and to quarantined units. Infections caused by airborne spread cannot be identified by tracing, but the overall contribution of airborne spread is still recorded.

Subclinically and clinically infectious units may act as sources of airborne spread. A unit is an eligible recipient for airborne spread if it is in the susceptible state, if it is within the maximum distance of spread from a source unit, and if the direction to the source is consistent with the specified prevailing wind direction.

For each combination of source and destination production type, a value is specified that represents the baseline probability of disease spread from an infectious unit of average size (based on the number of animals) to a susceptible unit, also of average size, located 1 km away. This baseline probability is adjusted in the model for both source and recipient units that have either more or fewer animals than the average unit in the population included in the simulation: the probability of spread at 1 km between the largest units in a population will be almost twice the specified average probability, and the probability of spread at 1 km between the smallest units will be almost 0. The baseline probability is further adjusted based on the distance between a source and potential recipient units. The user specifies a maximum distance of disease spread by airborne transmission, and the probability of spread decreases linearly from the baseline probability, dropping to 0 at this maximum distance. The final probability of disease spread by airborne transmission between a particular source and a particular recipient is calculated as shown in Formula (2):

$$P = p_{1\,\mathrm{km}} \times \text{distanceFactor} \times (\text{adjustment for size of source unit, as described above}) \times (\text{adjustment for size of recipient unit, as described above}) \quad (2)$$

where P is the probability of disease spread by airborne transmission between two units; $p_{1\ \mathrm{km}}$ the baseline probability of spread between units of average size 1 km apart; distanceFactor = (maximum distance of spread − distance between units)/(maximum distance of spread − 1).

For each potential airborne exposure, a random number r, from 0 up to but not including 1, is generated. If r is less than the calculated probability, the recipient unit's state is changed to latent after the airborne transport delay has elapsed.

2.4. Disease detection

Two probabilities contribute to the overall probability of disease detection, as demonstrated in Table 2 and Fig. 3: these are the probability that clinical signs of disease will be observed, and the probability that a unit with observed clinical signs will be reported to authorities. These two probabilities may be specified separately for each production type. On each day, for each production type, the model determines the probability of observing signs, which is a

Table 2
Input parameters used in *NAADSM* for disease detection and control

Parameter description	Parameter type	Level of application
Detection parameters		
Probability of observing clinical signs in an infected unit	Relational function: probability (0 to 1) as a function of the number of days a unit has been in an infectious clinical state	Production type
Probability of reporting units with observed clinical signs	Relational function: probability (0 to 1) as a function of the number of days since the first detection of an outbreak	Production type
Parameters for tracing out		
Probability of a trace-out investigation succeeding when direct contact has occurred	Probability, 0 to 1	Production type
Period of interest for trace-out investigations of direct contacts	Fixed integer value (days)	Production type
Probability of a trace-out investigation succeeding when indirect contact has occurred	Probability, 0 to 1	Production type
Period of interest for trace-out investigations of indirect contacts	Fixed integer value (days)	Production type
Destruction parameters		
Delay to begin a destruction program	Fixed integer value (days)	Entire scenario
Destruction capacity	Relational function: number of units that can be destroyed as a function of the number of days since the first detection of an outbreak	Entire scenario
Destruction priorities	Rank order of reasons for unit destruction, as described in the text	Entire scenario
Does detection of an infected unit trigger a destruction ring?	Yes/no	Production type
Radius of destruction ring, if a ring is triggered	Fixed value (km)	Production type
Will units be destroyed in a ring destruction program?	Yes/no	Production type
Will units identified by trace-out after direct contact be destroyed?	Yes/no	Production type
Will units identified by trace-out after indirect contact be destroyed?	Yes/no	Production type
Vaccination parameters		
Number of units that must be detected before vaccination begins	Fixed integer value (number of detected units)	Entire scenario
Vaccination capacity	Relational function: number of units that can be vaccinated as a function of the number of days since the first detection of an outbreak	Entire scenario
Vaccination priorities	Rank order of reasons for unit vaccination, as described in the text	Entire scenario
Does detection of an infected unit trigger a vaccination ring?	Yes/no	Production type
Radius of vaccination ring, if a ring is triggered	Fixed value (km)	Production type
Will units be vaccinated in a ring vaccination program?	Yes/no	Production type
Minimum time between vaccinations	Fixed integer value (days)	Production type

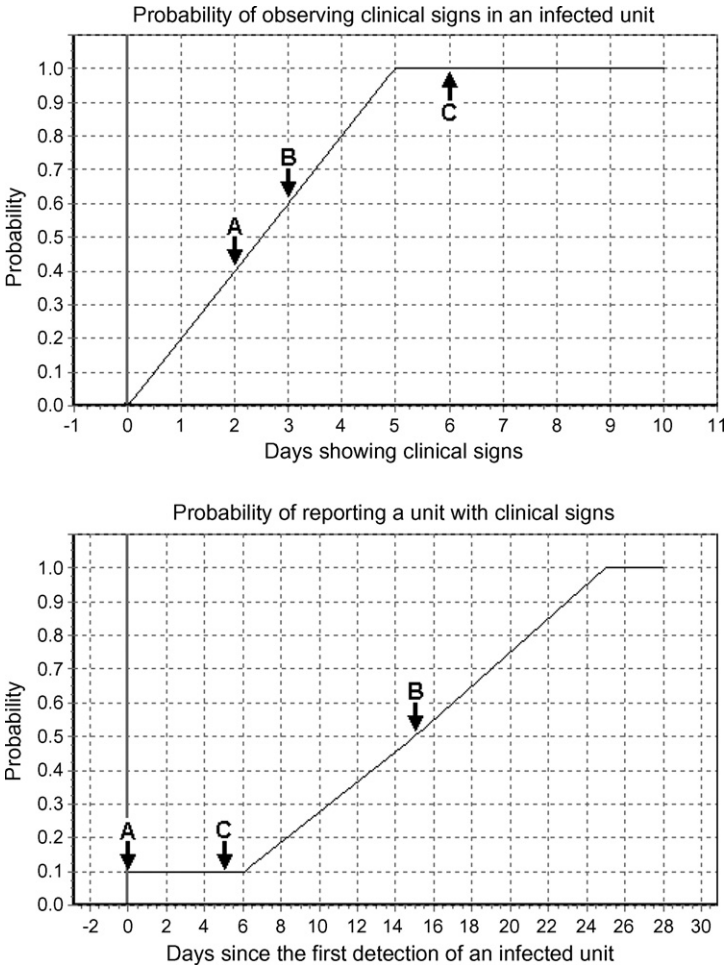

Fig. 3. Calculating the overall probability of disease detection. Two relational functions, established by the user, are used to determine the probability of disease detection of each particular infected unit on each simulation day. The probability of observing clinical signs is a function of the length of time that a unit has been showing clinical signs. The probability of reporting units with observed clinical signs is a function of the length of time since the first detection of any infected unit in the outbreak. Examples of two possible detection functions are shown here. The overall probability of detection of an infected unit on a particular day is the product of these two component probabilities. Three hypothetical situations (designated A, B, and C) are used to illustrate this calculation—Situation A: a unit has shown clinical signs for 2 days, and no unit has previously been detected. Probability of detection = $0.4 \times 0.1 = 0.04$. Situation B: a unit has shown clinical signs for 3 days, and initial detection occurred 15 days ago. Probability of detection = $0.6 \times 0.5 = 0.3$. Situation C: a unit has shown clinical signs for 6 days, and initial detection occurred 5 days ago. Probability of detection = $1.0 \times 0.1 = 0.1$.

user-specified function of the number of days that the unit has been in the infectious clinical state. Similarly, the model determines the probability of reporting, which is a function of the number of days since the first detection in the population. This allows the user to simulate the impact of improved awareness of a disease situation as an outbreak progresses. A non-zero baseline value represents the probability of reporting before the first detection occurs in a simulation. The overall probability of detection of a clinical unit is the product of these two component

probabilities. The model then generates a random number r as above. If r is less than the overall probability of detection, the unit is designated as detected. Subsequent control measures that are dependent on detection may then be initiated.

Only units in the clinical infectious state can be detected, and there are no false-positive detections.

2.5. Tracing out

When an infected unit is detected, other units to which it initiated contact within a certain number of days prior to its detection may be identified by tracing out (tracing forward). The model simulates tracing out of direct and indirect contacts one level forward, as summarized schematically in Fig. 4. The parameters specified by the user for tracing out for each production type are listed in Table 2.

Trace investigations are instantaneous, and only consider immediate contacts from detected units (*i.e.*, tracing occurs only one step forward, as shown in Fig. 4). Imperfect tracing may be simulated, by specifying a probability of conducting a successful trace of less than 100%. Units identified by tracing out are quarantined (Section 2.6.1), and may be designated for pre-emptive

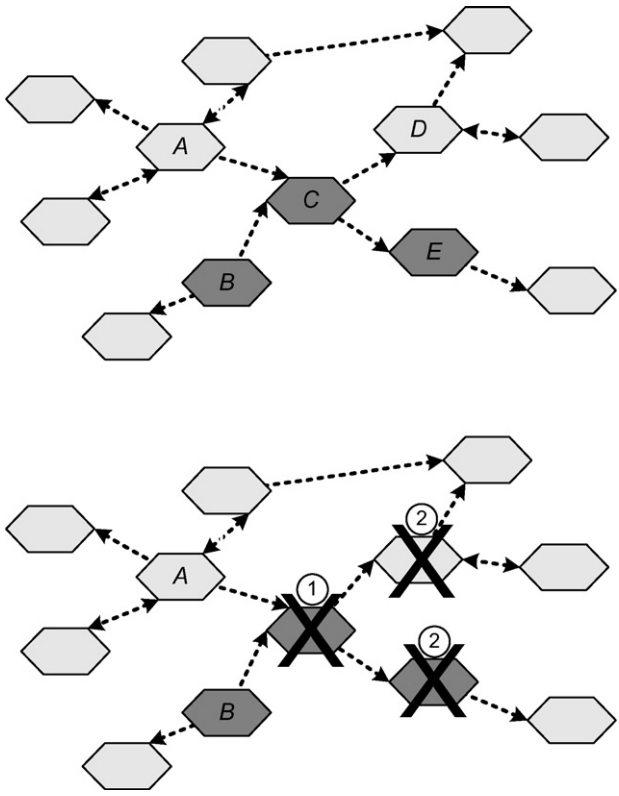

Fig. 4. Trace out investigations, as simulated by *NAADSM*. Arrows show contacts that occurred among units. When unit *C* is detected (1), units to which *C* has shipped animals or sent people or equipment can be traced (2) and are quarantined and may be designated for destruction. The trace does not extend further, *e.g.*, to units that shipped animals to *C* (*A* or *B*), or units that received animals from *D* or *E*.

destruction (Section 2.6.2). The model does not simulate tracing back to units that were potential sources of infection for detected units.

2.6. Control measures

Disease control measures simulated by *NAADSM* are quarantine, destruction, and vaccination.

2.6.1. Quarantine

Units are quarantined in the model for one or more of the following reasons. A diseased unit is quarantined on the day immediately following its detection. Units identified by trace-out investigations of direct or indirect contact recipients are also quarantined. Finally, units are quarantined when they are placed on the prioritized waiting list for destruction (Section 2.6.2).

Quarantined units can neither receive nor generate direct contacts, but indirect contacts and airborne spread may still occur to or from a quarantined unit. Quarantine does not affect the probability of detection: units that become infected while quarantined are no more likely to be detected than any other infected unit of the same production type.

2.6.2. Destruction

Table 2 summarizes global and production type-specific parameters that may be entered into the model for destruction of units. When the first detection is noted, the model can simulate a destruction program. The user defines the number of days from initial detection until the destruction program begins. All detected units may be designated for destruction. Units identified through trace-out investigations (dangerous contact destruction) and units within a given distance of detected units (ring destruction) may also be designated for pre-emptive destruction.

A production type-specific parameter determines whether detection of an infected unit of that type will trigger the formation of a destruction ring. For example, detection of an infected swine unit might lead to the destruction of surrounding units of various production types, while detection of an infected sheep unit might not. A production type-specific parameter also governs whether units of a particular type will be included in a destruction ring. For example, dairy cattle units might be destroyed in response to the detection of a diseased unit nearby, while sheep units might not be destroyed.

There is a limit to the number of units that can be destroyed per day. This is referred to as the destruction capacity. Destruction capacity does not consider the number of animals in units to be destroyed. Destruction capacity is specified as a function of the number of days since the first detection of disease. A single destruction capacity applies to units of all production types: for example, if the destruction capacity on a given day is 10 units, then 10 beef units may be destroyed on that day, or 10 swine units, or six units of one and four of the other, depending on the assigned destruction priorities.

If a unit is designated for destruction but cannot be destroyed immediately (*i.e.*, because maximum capacity has been reached), the unit is quarantined and placed on a prioritized waiting list (queue) for destruction. Three criteria are used to prioritize destruction, which the user must rank in order or importance: the production type of the unit, the reason for destruction of the unit, and the number of days a unit has been waiting in the destruction queue. Further details for these criteria must also be specified. Within the production type criterion, production types present in a scenario are further prioritized (*e.g.*, cattle may have a higher destruction priority than swine or *vice versa*). Similarly the reasons for destruction are further prioritized according to the criteria specified above. For example, cattle herds that are designated for destruction because they were

detected as diseased may have a higher priority than cattle herds that are designated for destruction because they are located within a destruction ring.

On each day, the authorities destroy as many units as possible (up to the destruction capacity for that day) from the waiting list, beginning with the highest priority. Criteria with the highest priority are applied first. In the event that two units are encountered that have the same priority based on the top criterion, subsequent criteria are applied. No two production type/reason-for-destruction combinations can have the same priority. No distinction in destruction priority is made based on source of exposure.

2.6.3. Vaccination

Ring vaccination may be used as part of a disease control program. Table 2 summarizes parameters used by the model's vaccination component.

A vaccination program is initiated when the user-specified number of infected units has been detected. Once this critical number has been reached, vaccination rings may be created around any unit that is detected on that simulation day and on subsequent simulation days. Units located within such rings may be designated for vaccination. It is possible to simulate a strategy in which ring vaccination is implemented only around certain production types, or in which only units of selected production types within such rings are vaccinated.

The number of units that can be vaccinated per day, referred to as the vaccination capacity, is handled in the same way as destruction capacity. The daily limits for destruction and vaccination operate independently of one another: the model does not dynamically shift resources from one task to the other.

If a unit is designated for vaccination but cannot be vaccinated immediately, it is placed on a prioritized waiting list. Vaccination priorities are set similarly to destruction priorities. Two criteria may be used to prioritize vaccination: (i) the production type of the unit waiting to be vaccinated and (ii) the number of days that a unit has been in the vaccination queue.

When a susceptible unit is vaccinated, it remains susceptible for a specified time until immunity develops, and then becomes vaccine-immune. Vaccine immunity is assumed to be 100% effective: while a unit is vaccine immune, it cannot become infected. The duration of the immune period is determined stochastically for each newly vaccinated unit. If a unit is infected after being vaccinated but before becoming vaccine immune, then the vaccination is assumed to have no effect, and the unit will enter the normal disease cycle. Vaccinating a unit that is not susceptible has no effect on its disease state.

Units may be vaccinated multiple times over the course of a simulation. A specified minimum number of days, determined by the user, must pass before a unit can be revaccinated. Once this number of days has elapsed, a unit may be revaccinated if it is targeted within a vaccination ring. Fig. 5 illustrates this approach.

2.7. Priorities of actions

Because the events in a given day happen simultaneously within the model, it is necessary to order and prioritize the processes run in the model to prevent the application of conflicting changes to a unit. If a unit is to be both infected and vaccinated, or infected and destroyed on the same day, then the order in which these are applied is chosen randomly. However, if a unit is to be vaccinated and destroyed on the same day, destruction will always have precedence. If all three actions (infection, destruction, and vaccination) are scheduled to occur on the same day, a unit may or may not be classified as infected before it is destroyed, but it will never be

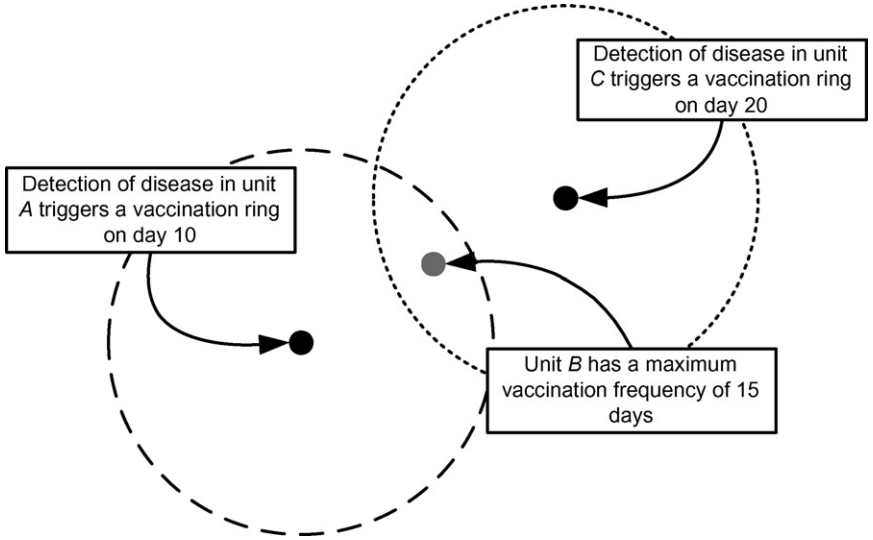

Fig. 5. An example of a unit that might receive multiple vaccinations. Disease is detected in unit *A* 10 days before disease is detected in unit *C*. Both detections trigger vaccination circles as shown. Unit *B* is within vaccination circles triggered by detection of units *A* and *C*, and will be added twice to the queue of units to be vaccinated. If there is no waiting period for vaccination (*i.e.*, vaccination capacity is not reached), unit *B* will receive only one vaccination. If vaccination capacity has been reached, unit *B* will receive two vaccinations if the elapsed time between the first and second scheduled vaccinations exceeds the unit's minimum time between vaccinations, 15 days.

vaccinated. If two or more processes infect the same unit on the same day (*e.g.*, direct contact from one unit and indirect contact from another unit), one process is chosen randomly and is reported as the cause of the infection. Similarly, if there are two or more reasons for vaccinating or destroying a unit, one reason is chosen randomly for the purpose of reporting. Infection, destruction, and vaccination are all considered to occur before natural state transitions on the same day: if a unit is due to change from vaccine immune to susceptible on a particular day, and also receives adequate contact from an infectious unit on the same day, the unit in question will not become infected, since contact is considered to have occurred while the unit was still immune.

2.8. Costs

Estimates of the direct costs associated with destruction and vaccination may be calculated in the model to compare the costs of different control measures. Table 3 lists the required cost parameters for destruction and vaccination.

2.8.1. Costs associated with destruction

In this model, there is a fixed cost associated with appraisal of each destroyed unit, regardless of the number of animals in the unit. The cost associated with cleaning and disinfecting each unit is also fixed regardless of the number of animals in each unit. In addition to these fixed per-unit costs, per-animal costs for euthanasia, carcass disposal, and indemnification are also applied. The total cost of destruction for each unit of a particular production type is calculated as shown in Formula (3). The total cost of destruction for each production type is calculated as shown in

Table 3
Input parameters used in *NAADSM* for determining direct costs associated with disease control

Parameter description	Parameter type	Level of application
Parameters associated with destruction		
Appraisal	Dollar amount per unit	Production type
Cleaning and disinfection	Dollar amount per unit	Production type
Euthanasia	Dollar amount per animal	Production type
Indemnification	Dollar amount per animal	Production type
Carcass disposal	Dollar amount per animal	Production type
Parameters associated with vaccination		
Number of animals that can be vaccinated at the baseline cost	Fixed integer value	Production type
Baseline cost of vaccination	Dollar amount per animal	Production type
Additional cost incurred when the number of animals vaccinated exceeds the threshold set above	Dollar amount per animal	Production type
Cost of vaccination site set-up	Dollar amount per unit	Production type

Formula (4):

$$\begin{aligned}\text{total unit costs} = {} & (\text{appraisal cost} + \text{cleaning and disinfection cost}) \\ & + [(\text{number of animals in the unit}) \times (\text{cost of euthanasia} \\ & + \text{cost of indemnification} + \text{cost of disposal})] \end{aligned} \tag{3}$$

$$\begin{aligned}\text{total production type costs} = {} & (\text{number of units destroyed}) \times (\text{appraisal cost} \\ & + \text{cleaning and disinfection cost}) \\ & + [(\text{Total number of animals destroyed}) \\ & \times (\text{cost of euthanasia} + \text{cost of indemnification} \\ & + \text{cost of disposal})] \end{aligned} \tag{4}$$

2.8.2. Costs associated with vaccination

There is a fixed cost associated with vaccination set-up for each vaccinated unit, regardless of the number of animals in the unit. The cost of vaccination of each animal in the unit is added to this fixed unit cost. The cost of vaccination of each animal will depend on the total number of animals vaccinated. For each animal up to a specified threshold, only a baseline vaccination cost applies. For each animal over this threshold, an additional cost applies. If this threshold is not reached, the total cost of vaccination for each production type is calculated as shown in Formula (5). If this threshold is surpassed, the total cost of vaccination for each production type is calculated as described in Formula (6):

$$\begin{aligned}&\text{total vaccination costs (when vaccination threshold is not exceeded)} \\ &= [(\text{number of units vaccinated}) \times (\text{cost of site set-up})] \\ &\quad + [(\text{total number of animals vaccinated}) \times (\text{baseline cost per animal})] \end{aligned} \tag{5}$$

$$\begin{aligned}&\text{total vaccination costs (when vaccination threshold is exceeded)}\\&= [(\text{number of units vaccinated}) \times (\text{cost of site set-up})]\\&\quad + [(\text{threshold level}) \times (\text{baseline cost per animal})]\\&\quad + [(\text{total number of animals vaccinated} - \text{threshold level})\\&\quad \times (\text{baseline cost per animal} + \text{additional cost per animal})] \qquad (6)\end{aligned}$$

3. Results

As a result of the wide range of values and combinations of parameters that can be entered, the user can create models for a broad array of specific scenarios and approaches to disease control. Each specific model can be run once to provide point estimates of various outcomes of interest such as the ''actual'' (modeled) and the ''apparent'' (modeled detected) epidemic curves, the duration of the outbreak, the total number of units and animals destroyed and vaccinated, and the total direct costs associated with disease control measures. More typically, a specific model can be run many times to generate distributions of outcomes of interest and descriptive statistics such as the mean, range, standard deviation, and selected percentiles for these outcomes. A record of all events (infections and control measures) that occurred on each day of a simulation is available to recreate the simulated outbreak.

Figs. 6 through 8 illustrate a small sample of the outputs of one model using a fictitious population database. For Figs. 6 and 7, this simulation was run 100 times, and these figures show summary outputs based on all 100 replications. Fig. 8 shows output based on only a single run of the model.

The actual epidemic curve (based on the number of units infected during each 2-week time period) and apparent epidemic curve (based on units detected during each 2-week time period) are shown in Fig. 6. For the actual outbreak, the 95th percentile for all replications reached a peak of 85 units at just over 120 days and an outbreak length of about 350 days. By contrast, because imperfect detection was modeled, the apparent epidemic curve shows a peak at 140 days and of only 53 units.

Fig. 7 shows summary results—mean, standard deviation, low, high, 5th, 25th, 50th, 75th, and 95th percentiles for an output recording the total number of cattle units vaccinated in rings around detected–infected units (*vaccURing*) over the course of 100 iterations. Histograms also illustrate this output's values and indicate mean convergence across iterations. As illustrated in the figure, results for numerous model outputs can be shown in this manner.

Fig. 8 reveals the cumulative direct costs for a single model run, broken down by type of cost. By day 160, total costs, dominated by indemnity expenses in this illustration, reach over $35 million. *NAADSM* has built-in support for a wide range of epidemiological and cost accounting outputs that might be of interest, as well as the capacity for users to define additional outputs of their own.

4. Discussion

We have observed in recent years several examples of costly livestock epidemics (Elbers et al., 1999; Meuwissen et al., 1999; Yang et al., 1999; Thompson et al., 2002; Bouma et al., 2003;

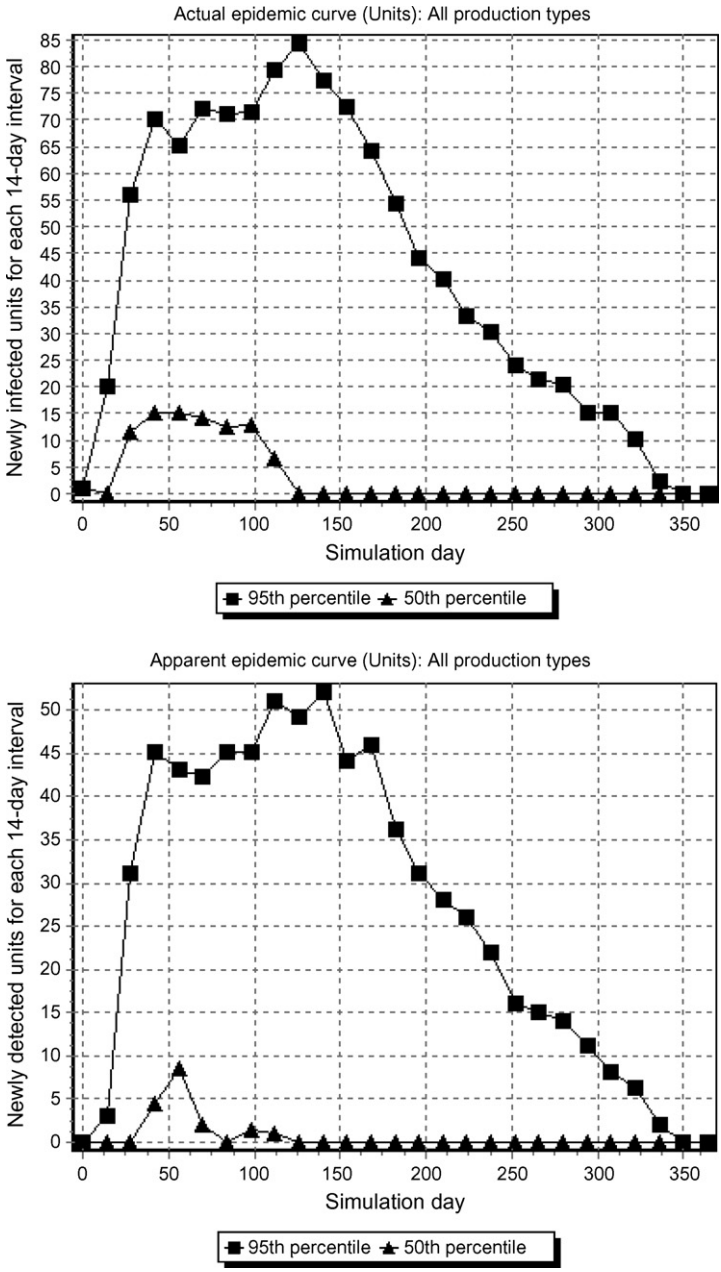

Fig. 6. Epidemic curves summarizing 100 replications of a scenario. Each point represents the number of newly infected or detected units over a 14-day interval. In the actual epidemic curve (top panel), the upper line indicates the 95th percentile values for the number of newly infected units: this curve can be interpreted as an upper extreme outcome of this particular scenario. Similarly, the lower line indicates the 50th percentile values, and can be interpreted as a ''typical'' or ''average'' outcome. The lower panel shows an apparent epidemic curve: since detection was imperfect, disease was detected in fewer units than were actually infected.

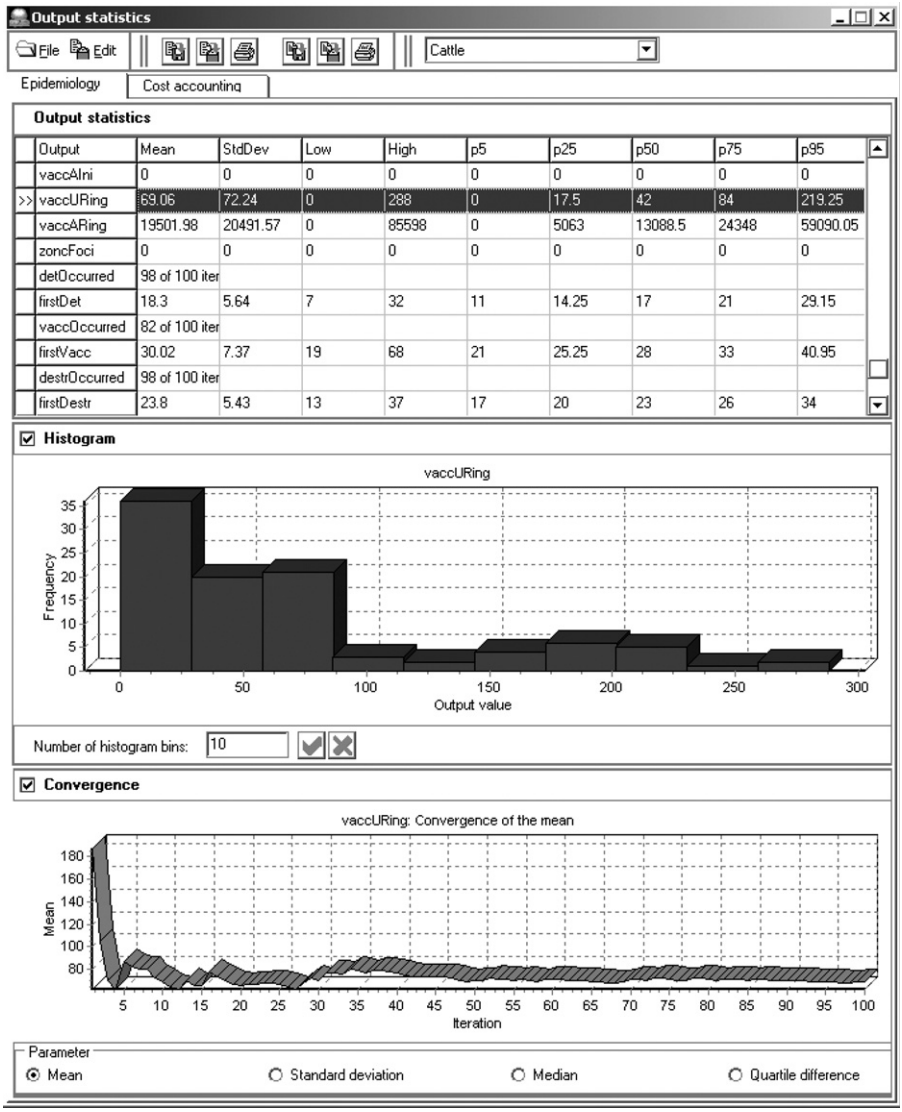

Fig. 7. Summary statistics calculated for 100 replications of a scenario. The upper panel shows summary statistics (mean, standard deviation, low, high, and selected percentile values) for representative outputs (*e.g.*, *vaccURing*—the number of units included in simulated ring vaccination programs, and *firstDet*—the day on which detection first occurred across all replications). The center panel shows the distribution of values for the selected output (*vaccURing*) across all replications. The lower panel shows the affect of each subsequent replication on the mean value of *VaccURing*.

Haydon et al., 2004), which highlight the importance of and need for coordinated disease response plans. Simulation models now play a significant role in the development and testing of such plans (Morris et al., 2002; Risk Solutions, 2005; Keeling, 2005; Guitian and Pfeiffer, 2006). If the models used are well characterized and understood, they can potentially provide significant insight to those responsible for animal health and outbreak response decisions. Just as importantly, having a thorough understanding of the mechanisms and limitations of simulation

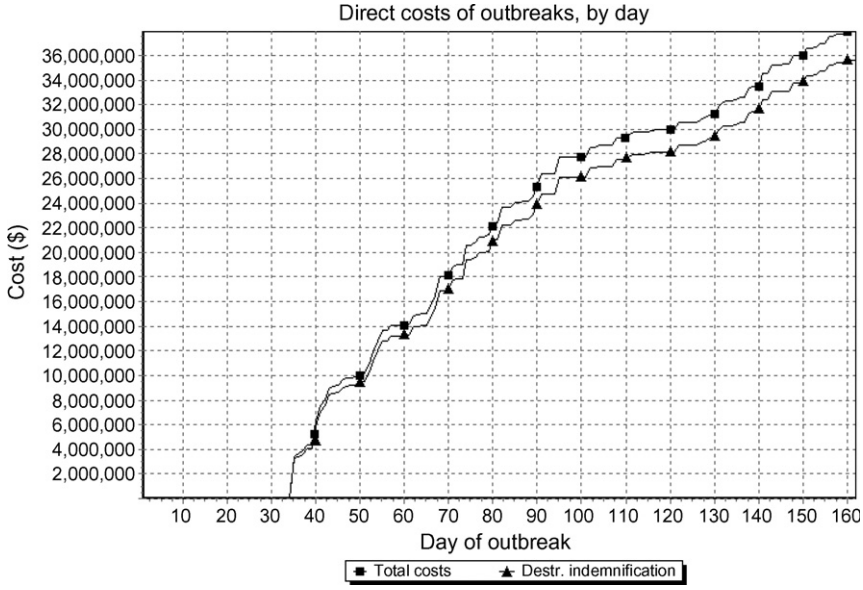

Fig. 8. Cumulative government accounting costs for a single iteration. The upper line shows the total cumulative costs on each day of the simulated outbreak. The lower line indicates the contribution of indemnification costs alone.

models will aid in preventing the misapplication of model results. Here we have presented a comprehensive description of the *North American Animal Disease Spread Model*, which is now being used in a variety of analyses intended to aid regulatory and policy decisions.

We are currently pursuing several lines of continuing investigation, involving the application of *NAADSM* as well as its continued development. The model is included in the first formal international comparison and validation of models intended to support decision making by animal health authorities (Dubé et al., 2007). *NAADSM* is being applied to questions related to FMD (Pendell, 2006), pseudorabies, highly pathogenic avian influenza (HPAI), CSF, and exotic Newcastle disease. Furthermore, an ongoing study being conducted for the North American Foot-and-Mouth Disease Vaccine Bank involves the estimation of the number of doses of vaccine that would be required in North America should there be outbreaks in one or more countries. Canada and the United States are currently developing collections of simulated outbreak scenarios using *NAADSM* and other models to represent various strains of FMD, methods of introduction, climatic conditions, and control options that will be used for policy formulation and for decision making.

The economic component of *NAADSM* itself is limited to providing estimates of direct costs. *NAADSM* has been designed, however, to produce output suitable for incorporation into more detailed economic models (*e.g.*, Pendell, 2006; Paarlberg et al., 2007). This modular, multidisciplinary approach allows users to address questions of broader economic concern, such as the possible impact of a disease outbreak on producers, consumers, international trade, *etc*.

While *NAADSM* is designed to model a variety of contagious diseases, it is not suitable for simulating chronic, vertically transmitted, sexually transmitted, or vector-borne diseases. Likewise, *NAADSM* does not consider climatic or environmental factors that might influence disease spread. These limitations should be considered before attempts are made to apply *NAADSM* to new situations or other diseases.

The development of several key extensions to *NAADSM*, which will implement recommendations made by subject matter experts, is well underway. New capabilities to simulate enhanced surveillance, disease control zones, and variability of within-herd disease prevalence are now being tested by the development team. The simulation of disease control and surveillance zones will improve our ability to fine-tune the application of control measures. Implementation of a model of disease mortality, enhanced tracing capabilities, modeling of diagnostic testing for disease detection, and refining the simulated effects of vaccination are planned for subsequent versions.

The *North American Animal Disease Spread Model* has been and continues to be developed with support, involvement, and advice from a broad, international pool of livestock health experts, disease modelers, and other specialists. While a major emphasis of the *NAADSM* project is the development of a model suitable for use in North America, it has been used in several training courses offered to largely international audiences. The model has also been used for several domestic training exercises, intended to test and inform emergency response plans, most recently to simulate an outbreak of HPAI in North Carolina and Georgia in the United States. The *NAADSM* application itself is published under an open source software license (Free Software Foundation, 1991), and is freely available via the Internet at http://www.naadsm.org. It is hoped that this will foster the development of a community of users that will continue to be actively involved in the improvement of the model as it is applied to various situations.

Acknowledgments

The authors gratefully acknowledge the contributions of Anne Berry and Ann Hillberg Seitzinger, who were instrumental in the preparation of this manuscript, as well as Kim Forde-Folle and Renée Dewell for their helpful suggestions. We also wish to thank the Chemical, Biological, Radiological and Nuclear Research and Technology Initiative (CRTI) in Canada for funding a portion of this project.

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