

Developing stochastic epidemiological models to quantify the dynamics of infectious diseases in domestic livestock¹

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ABSTRACT: A stochastic model describing disease transmission dynamics for a microparasitic infection in a structured domestic animal population is developed and applied to hypothetical epidemics on a pig farm. Rational decision making regarding appropriate control strategies for infectious diseases in domestic livestock requires an understanding of the disease dynamics and risk profiles for different groups of animals. This is best achieved by means of stochastic epidemic models. Methodologies are presented for 1) estimating the probability of an epidemic, given the presence of an infected animal, whether this epidemic is major (requires inter-

vention) or minor (dies out without intervention), and how the location of the infected animal on the farm influences the epidemic probabilities; 2) estimating the basic reproductive ratio, R_0 (i.e., the expected number of secondary cases on the introduction of a single infected animal) and the variability of the estimate of this parameter; and 3) estimating the total proportion of animals infected during an epidemic and the total proportion infected at any point in time. The model can be used for assessing impact of altering farm structure on disease dynamics, as well as disease control strategies, including altering farm structure, vaccination, culling, and genetic selection.

Key Words: Disease Resistance, Epidemiology, Pigs, Stochastic Models

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Introduction

Animal health issues in livestock populations are a major concern to animal scientists who seek to ameliorate the consequences of disease in terms of cost, animal welfare, and food safety. With infectious diseases, rational disease control decisions (e.g., vaccination or genetic selection) require an understanding of the disease dynamics and risk profiles for different groups of animals. Only after these are quantified, by means of epidemic models, can the costs and benefits of alternative control strategies be calculated.

When modeling infectious diseases, it is important to distinguish between macroparasitic (e.g., nematode parasites) and microparasitic (e.g., viruses) infections. Macroparasitic infections require the extent of infection of each animal to be modeled, whereas microparasitic infections may be modeled with compartmental models, such as “infected or not” (Anderson and May, 1992). Macroparasitic infections in domestic livestock have been extensively modeled (Bishop and Gettinby, 2000),

but there are fewer models of microparasitic infections. In microparasitic infections, farm structure imposes both spatial and interanimal heterogeneity that affects the dynamics of disease invasion and spread (Dushoff and Levin, 1995). In such situations, disease spread is best studied in a stochastic rather than a deterministic framework (Dushoff, 1999), allowing incorporation of chance effects into the model as well as complexity due to the heterogeneity.

The objective of this work was to address microparasitic infections, developing a stochastic epidemic model using the methodology of Renshaw (1991), extending deterministic concepts developed by MacKenzie and Bishop (1999). We demonstrate the use of stochastic models to investigate the outcome of an epidemic (i.e., the basic reproductive ratio, the probability of an epidemic, and the number of animals infected). Further, we provide the framework for investigating control strategies such as altering farm structure.

Materials and Methods

General Methodology

A stochastic model is a mathematical model that takes into consideration the effects of random variation in one or more parameters or variables. The predictions of these models are therefore probability distributions

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rather than single points. A stochastic epidemic model, applicable to a microparasitic infection, simulates the epidemic process as a series of random events in space and time with the probability of specific events defined by the model parameters. The parameters in the simplest stochastic epidemic model are the transmission coefficient (β) and the recovery rate (γ). The transmission coefficient denotes the rate at which susceptible animals become infected and is the expected number of new infections per infectious animal per susceptible animal per day. The recovery rate is the reciprocal of the infectious period and is the expected number of recoveries per infected animal per day. More complex models describing specific diseases may have additional parameters (e.g., the length of a latency period or disease-dependent mortality).

There are two components to a simple stochastic epidemiological model: the time until the next event and the event type. The mean time until the next event is a function of the total number of infected individuals on the farm (Y), the total number of susceptible individuals in contact with infected animals (X), β , and γ , and is given by $1/(Y(\gamma + \beta X))$. The inter-event time is thus drawn from an exponential distribution as $-\ln(r)/(Y(\gamma + \beta X))$, where r is a random number in $[0, 1]$.

For a simple stochastic model, the next event could be either that the infected animal infects another animal or that it recovers. The event type is determined using the number of event possibilities. In the model used in this paper it comprises 1) the product of the number of infectious animals \times the number of susceptible animals in contact with infectious animals \times the transmission coefficient \times the contact rate and 2) the number of infected animals \times the recovery rate. Thus, if there are X susceptible animals and Y infectious animals, with a contact rate c_{xy} , then the total number of possible events is $Y(\beta X c_{xy} + \gamma)$. The probability that the event is an infection is $\beta Y X c_{xy} / Y(\beta X c_{xy} + \gamma)$ and a recovery is $\gamma / Y(\beta X c_{xy} + \gamma)$.

We now wish to apply this simple framework to a structured pig farm. The description given above can be extended to allow heterogeneity between pigs as follows. Assume there are n types (classes) of animals. An animal of type i has contact with animals of type i and type j given by a matrix with elements c_{ji} . The inter-event time is now

$$-\ln(r) / \left(\gamma \sum_{i=1}^n Y_i + \beta \sum_{i=1}^n \sum_{j=1}^n c_{ji} Y_i X_j \right) \quad [1]$$

where r is again a random number in $[0, 1]$ and c_{ji} is the contact rate between type j and type i pigs. The recovery rate is γ and β is the transmission coefficient, both of which are constant for all types in this example; therefore, no opportunities for genetic selection or density-dependent effects on disease incidence are considered at this stage.

To determine the next event type, the sum

$$\sum_{i=1}^n \sum_{j=1}^n Y_j \left(\beta X_i c_{ji} + \gamma \right)$$

is calculated. If we denote this sum by RATE then the probability that the next event is infection of a pig of type i by a pig of type j is given by

$$\beta X_i Y_j c_{ji} / \text{RATE} \quad [2]$$

for all i, j and the probability that the next event is recovery of a type j animal

$$Y_j \gamma / \text{RATE} \quad [3]$$

for all j .

The full stochastic model is illustrated by modeling infection on a 500-sow farrow-to-finish pig farm, as described by MacKenzie and Bishop (1999). There are 54 types of pig, the type describing the physiological status of an animal on a weekly basis, which determines how susceptible or infectious it is, the disease-independent mortality and contact between pigs of different types. Pigs also have a "type-age," which records how long they have been in their current type. It takes 50 wk from the time of insemination until the resulting gilts are used as breeding stock. During four of those weeks, piglets are housed with their mothers, hence the need for 54 types of pig. Specifying all 54 types as distinct categories allows different ages of animals to have different levels of susceptibility, for subsequent developments that may include host genotype for susceptibility. For the purposes of the model, a 55th type is generated that has one pig, the index case (the initial infected animal). This type is created to enable the index case to be monitored, allowing determination of infections caused by, and recovery of, the index case. It has the correct contact rate with animals of the actual type of the index case. For example, if the index case belongs to a type with 25 animals, say a mating sow, then the contact rate between the type 55 animal and the other mating sows is 1.0 (i.e., it only has contact with mating sows), the contact rate between the mating sows and the index case is 0.04 (i.e., $1/n$ where n is the number of mating sows), and the contact rate between mating sows is 0.96 (i.e., $1 - (1/n)$).

The farm structure used is illustrated in Figure 1. Each week 25 sows are inseminated. A proportion of these sows, selected at random, become pregnant and enter the gestating sheds. There are four gestating sheds on the farm, each containing 84 sows. Gestation lasts 16 wk and then the sows move to the farrowing shed, where they spend the next 4 wk with their piglets. They then return to the insemination stage. Sows are replaced at a rate of 45% per annum. The piglets are modeled as having 10% preweaning mortality and deaths are assumed to occur randomly among the piglets. After weaning at 4 wk of age, the piglets are moved to the nursery for 6 wk and then on to the finishing shed for 16 wk. A proportion of the finishing pigs are

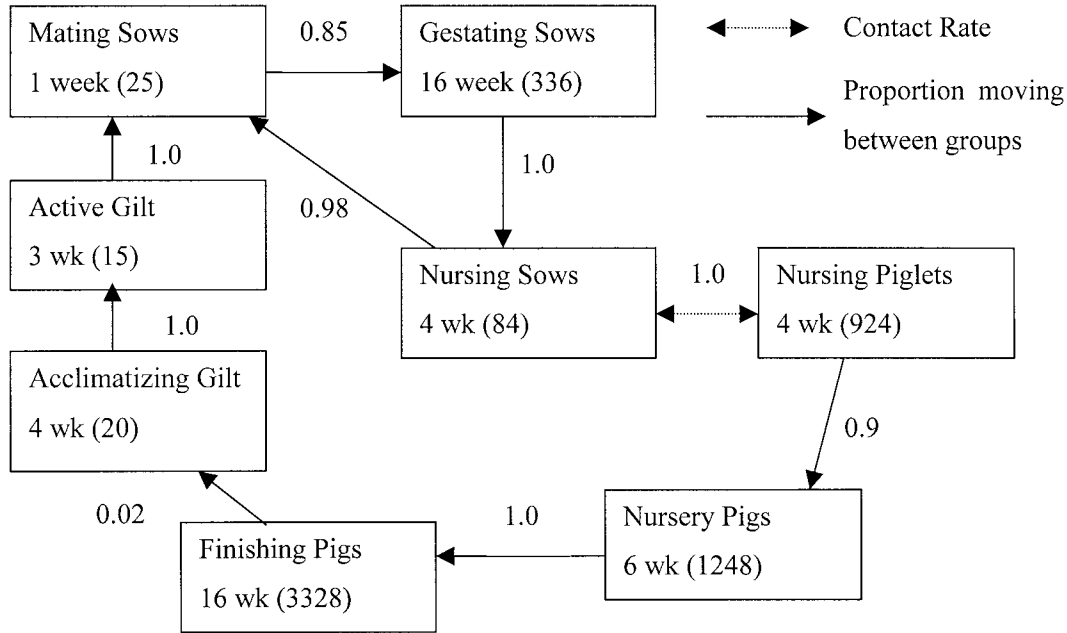


Figure 1. Pig farm structure.

retained on the farm to replace sows as they are removed. These gilts, selected at random from the finishing pigs, spend 4 wk acclimatizing to the microflora on the farm (denoted “Acclimatizing Gilt”) followed by 3 wk during which they come into estrus (denoted “Active Gilt”). The farm is thus a closed system. The contact rate between animals in the same shed is 1.0 and, apart from the nursing sows and nursing piglets, the contact rate between animals in different sheds is 0. Nursing sows are assumed to be in contact only with nursing piglets, and these piglets have contact with other piglets and their mother. It is assumed in this model that within sheds animals are able to make contact with all other animals with equal probability. This might be modified according to different housing systems.

The model is implemented by introducing a single infected pig of type i , the index case. The inter-event time is calculated, the type of the first event is determined, and the epidemic commences. The inter-event time is based on the farm structure at the time of calculation. During the course of long inter-event times (> 1 wk), the culling or relocation of infected animals may cause slight alterations in the RATE parameter before the event occurs. This potential bias is small and not included in this model. However, changing farm structure is accounted for insofar as the next event can only occur to animals present on the farm at the time of the next event. The epidemic runs until either there are no more infected animals on the farm or the epidemic has lasted for 1 yr. This is done for all possible index case types. All output data are stored for future use, as described below.

Probability of Epidemic

By recording the number of simulations that result in an epidemic, the probability that an epidemic will

occur can be determined. The model was implemented such that the number of animals infected (n) during the simulation was counted. If $n = 1$ at the end of the simulation there was no epidemic, if $n > 1$ but the epidemic dies out within 1 yr without intervention then we have a minor epidemic, otherwise the epidemic is classed as major. The limit of 1 yr is somewhat arbitrary and was selected on the grounds that the endemic stage of the epidemic, should it occur, will be well established by this time. Figure 2 illustrates the difference between minor and major epidemics. For this figure, the total number of pigs infected at a particular time during an epidemic is shown.

It has been shown previously (Renshaw, 1991) that the probability of an epidemic in a homogeneous mixed population depends on whether or not the number of susceptible animals (X) in the population, given one

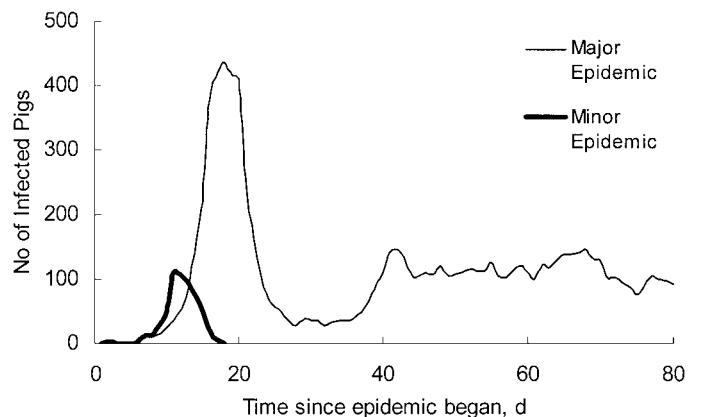


Figure 2. Example of a minor and a major epidemic ($\beta = 0.0005, \gamma = 0.05$).

infected individual, a recovery rate γ , and the transmission coefficient β , is less or greater than the relative removal rate, γ/β . If $X < \gamma/\beta$ the expectation is that there will not be an epidemic, if $X \geq \gamma/\beta$ the expectation is that there will be a minor epidemic with probability $(\gamma/\beta)/X$ and a major epidemic with probability $1 - (\gamma/\beta)/X$. These equations can be used to describe an epidemic process involving a homogeneous population in which all animals are in direct contact (i.e., contact rate = 1.0). The solutions to these equations are not directly applicable to the current situation, in which we are dealing with a heterogeneous population and the number of susceptible animals with which the single infected animal (the index case) is in contact changes with time. Therefore, differences between the simulated values and the theoretical expectations of Renshaw (1991) quantify the degree to which the dynamic heterogeneity of the population influences the disease transmission, and thus they highlight the differences between homogeneous and heterogeneous populations.

Consideration should be given to the number of occurrences of a no/minor/major epidemic for each of the different index case types. The results of simulations by index case type demonstrate the dependence of the probability of no epidemic or minor or major epidemic on population size and farm structure. In other words, the results quantify the risk profiles associated with each type of pig.

Basic Reproductive Ratio (R_0)

Fundamental to describing the transmission of disease through a population is R_0 , the basic reproductive ratio. The basic reproductive ratio was defined by Diekmann et al. (1990) as the expected number of secondary infections produced by the introduction of an infected individual, during the course of its infectious period, into an otherwise completely susceptible population. To condense the results of a particular parameter set into a single value (i.e., R_0), the output from the model was used to construct a next-generation matrix \mathbf{M} describing the disease transmission probabilities (De Jong et al., 1994). An epidemic was simulated with each animal in turn being the index case. The number of secondary infections caused in type j pigs when the index case was initially type i was stored. Thus, the element m_{ij} of \mathbf{M} is the number of secondary infections in type j animals caused by the index case of type i . The m_{ij}^{th} element of the matrix obtained is divided by the number of simulations performed for each index case i . The basic reproductive ratio was then estimated as the dominant eigenvalue of this matrix (Diekmann et al., 1990).

Precision and Distribution of the Estimate of R_0

The basic reproductive rate is generally presented as a single point estimate, with no indication of the variability inherent in the estimation of biological parameters. The stochastic model allows this variability

to be quantified. To estimate the SE of the estimate of R_0 from a complete set of simulations, bootstrapping was applied to the disease transition matrix, \mathbf{M} . Thus, the SE of the estimate of R_0 was obtained by repeated sampling, with replacement, of the number of secondary infections caused by each type of animal. One sample was drawn for each animal on the farm. The samples were used to construct a new disease transition matrix from which R_0 was estimated. This process was repeated 1,000 times. The distribution of the 1,000 bootstraps gives an estimate of the distribution of estimated values of R_0 , the mean of the distribution being the mean estimate of R_0 and the SD being the SE of the estimate of R_0 .

To investigate the distribution of estimates of R_0 obtainable from this stochastic model, as opposed to the precision of the estimate of the mean R_0 , a different approach was used. A simulation was performed in which the next-generation matrix was constructed using a single simulation for each type of pig, as defined in Figure 1. Again, 1,000 simulations were performed to provide the estimate for the distribution of the estimate of R_0 . This process gives an indication of the possible range of estimated values of R_0 given a particular set of parameters. The two techniques together allow determination of the precision of the estimate of R_0 as well as the distribution of estimated values of R_0 .

Total and Maximum Proportions of Infected Pigs

Two methods for determining the total proportions of pigs infected during the epidemic (I) and the maximum proportion at any one time (y_{max}) were examined. The first was based on the theoretical relationships among I , y_{max} , and R_0 assuming a homogeneous, unstructured population (Anderson and May, 1992):

$$I = 1 - \exp(-R_0 I) \quad [4]$$

$$y_{max} = 1 - (1 + \ln(R_0))/R_0 \quad [5]$$

The second used the output of the simulation directly. The total proportion is calculated by counting the total number of pigs of all types infected and dividing that total by the total number of susceptible pigs on the farm during the simulation. The maximum proportion infected at any one time is obtained by calculating the proportion of animals infected at each stage of the epidemic.

In order to compare the estimates for the proportions of pigs infected using the stochastic epidemic model with those predicted by Eq. [4] and [5], based on the value of R_0 , a simulation was performed wherein the animals on the farm were all in direct contact.

Effect of Farm Structure on the Stochastic Epidemiological Model

To illustrate the effect of altering the farm structure on R_0 , two strategies were adopted. The first involved

Table 1. Probability^a of no epidemic or a minor or major epidemic for varying transmission coefficients (β) and recovery rates (γ)

β	γ	Probability of		
		No epidemic	Minor epidemic	Major epidemic
0.0001	0.01	0.51	0.13	0.35
0.0001	0.05	0.88	0.12	0.00
0.0001	0.10	0.95	0.05	0.00
0.0005	0.01	0.15	0.01	0.85
0.0005	0.05	0.44	0.10	0.46
0.0005	0.10	0.64	0.29	0.07
0.001	0.01	0.08	0.00	0.92
0.001	0.05	0.27	0.02	0.71
0.001	0.10	0.44	0.08	0.48

^aThe failure of a given row of probabilities to sum to 1.0 is attributable to rounding error.

altering piglet retention time and the second changed the housing policy for sows. These were seen as realistic alterations; different farms remove piglets at different ages and many farms house sows together rather than in multiple sheds. The models allow the effect of changing the number of pigs on the farm and the contact between pigs to be investigated. Again, epidemics were simulated with each animal in turn being the index case.

The implementations investigated included removing piglets at 3 wk of age (Model 1), removing piglets at 12 wk of age (Model 2), keeping finishing pigs for 16 wk (Model 3), and housing all gestating sows in a single shed rather than in four sheds (Model 4).

Parameter Space Investigated

Three transmission coefficients ($\beta = 0.0001, 0.0005,$ and 0.001) and three recovery rates, representing diseases with infectious periods of 100, 20, and 10 d, were investigated. Results are presented both as the average for the whole population and broken down according to index case type. Unless otherwise stated, results are based on a total of 5,400 simulations for each set of parameters, allowing 100 simulations per index case type.

Results

Probability of an Epidemic

The probabilities that an animal infected with a given pathogen will cause no epidemic or a minor or a major epidemic are presented in Table 1. These results are for the farm as a whole, averaged across all types of pig. The results show that for a fixed transmission coefficient (β) the probability of a major epidemic increases as the infectious period ($1/\gamma$) increases. Likewise, for a fixed recovery rate (γ) the probability of a major epidemic increases as the transmission rate increases.

It is difficult to compare the results in Table 1 with actual pathogens because we are not aware of published data regarding the probability of an epidemic for any

pathogens. Such probabilities are very hard to estimate because if the introduction of infectious material on a farm results in no epidemic (or even a minor epidemic), it is likely that this will go unrecorded. Generally, the infectious period for a pathogen is known, but because the transmission coefficient is extremely hard to estimate, it is difficult to allocate the rows of Table 1 to particular infections. However, the parameters are known for transmissible gastroenteritis. Hone (1994) estimated the transmission coefficient to be 0.0007 and the recovery rate to be 0.057. The simple stochastic model described above estimates the probability of no epidemic for these parameters to be 0.53 with minor or major epidemics occurring with probability 0.14 and 0.33, respectively.

Table 2 shows the probability of each situation (no epidemic or minor or major epidemic) according to index case type for disease with an infectious period of 100 d ($\gamma = 0.01$) or 20 d ($\gamma = 0.05$). To obtain the results for these tables, the relative contribution of each type of pig to the total farm population was used to derive the probability that an epidemic starts given that the index case was of that type.

The probability that an index case causes a major epidemic depends on whether that index case is in a position to infect a group which is made up of a large number of animals, which in turn depends on the infectious period. When the index case is, say, a mating sow, and the infectious period is short, any infectious animals will have recovered before the infection reaches the nursery pigs. This may not apply for the sows in wk 9 to 12 of gestation. Some of these sows will give birth within the next 5 wk. Their piglets will be exposed to the infectious agent and still be infectious when they come into contact with the nursery pigs, some of which will still be infectious when they move to the finishing sheds. The results show that when the index case belongs to a class of animal with few members, then there is no epidemic. Conversely, if the index case can infect, directly or otherwise, piglets or growing pigs (nursery or finishing pigs), then the probability of an epidemic increases dramatically. For the farm structure used in

Table 2. Probability of no/minor/major epidemic by index case type for transmission coefficient (β) of 0.0001 and recovery rates (γ) of 0.01 or 0.05

Pig type	Probability of epidemic for given γ values					
	$\gamma = 0.01$			$\gamma = 0.05$		
	No epidemic	Minor epidemic	Major epidemic	No epidemic	Minor epidemic	Major epidemic
Mating sow	0.92	0.04	0.04	1.00	0.00	0.00
Gestating sow 1 ^a	0.93	0.04	0.03	1.00	0.00	0.00
Gestating sow 2 ^a	0.88	0.05	0.07	1.00	0.00	0.00
Gestating sow 3 ^a	0.79	0.07	0.15	0.99	0.01	0.00
Gestating sow 4 ^a	0.76	0.08	0.16	0.96	0.04	0.00
Nursing sow	0.79	0.08	0.13	0.87	0.13	0.00
Nursing piglet	0.40	0.11	0.50	0.86	0.14	0.00
Nursery pig	0.41	0.13	0.47	0.87	0.13	0.00
Finishing pig	0.54	0.15	0.31	0.87	0.13	0.00
Acclimatizing gilt	0.98	0.02	0.01	1.00	0.00	0.00
Active gilt	0.94	0.05	0.01	1.00	0.00	0.00

^aThe four entries for gestating sows are needed because there are four different sheds containing gestating sows. The final number denotes the current stage of gestation (i.e., “Gestating sow 1” is a shed containing sows in the first 4 wk of gestation).

these models, the high-risk classes are sows in the second half of gestation, nursing sows, piglets, and growing pigs. For an infection with an infectious period of 20 d and a relatively low transmission coefficient, the probability of a major epidemic is zero and only classes of animal with, or in contact with, large numbers of animals suffer from minor epidemics.

For comparison purposes the results based on the expected probabilities (Renshaw, 1991) for the homogeneous population in a single contact group are provided in Table 3. The differences between the results in Table 2 and 3 are presumed to be due to the farm structure. It is informative, however, to note that the group with the highest risk category predicted by both methods is the nursing piglets, and that the groups with large numbers of animals pose more of a risk than small

groups. Additionally, disease transmission dynamics within groups with large numbers of animals are closer to that expected in homogeneous populations.

Properties of the Basic Reproductive Ratio

The mean values of the estimator of R_0 for each parameter combination and the bootstrap SE are presented in Table 4. As the recovery rate increases, for a given transmission coefficient, R_0 decreases. Conversely, for a fixed recovery rate, the more infectious the pathogen (i.e., as the transmission coefficient increases), the higher the value of R_0 predicted. For a given recovery rate or transmission coefficient, the increase in R_0 as the transmission coefficient or recovery rate increases is very close to linear. The bootstrapped

Table 3. Expected probability of no/minor/major epidemic by index case type in an unstructured homogeneous population (transmission coefficient, $\beta = 0.0001$; recovery rate, $\gamma = 0.01$)

Pig type	Probability		
	No epidemic	Minor epidemic	Major epidemic
Mating sow	1	0	0
Gestating sow 1 ^a	1	0	0
Gestating sow 2 ^a	1	0	0
Gestating sow 3 ^a	1	0	0
Gestating sow 4 ^a	1	0	0
Nursing sow	1	0	0
Nursing piglet	0	0.43	0.57
Nursery pig	0	0.47	0.52
Finishing pig	0	0.47	0.52
Acclimatizing gilt	1	0	0
Active gilt	1	0	0

^aThe four entries for gestating sows are needed because there are four different sheds containing gestating sows. The final number denotes the current stage of gestation (i.e., “Gestating sow 1” is a shed containing sows in the first 4 wk of gestation).

Table 4. The mean and variability of the estimator of the basic reproductive ratio (R_0) based on 1,000 bootstraps on the disease transition matrix for different parameter values

β^a	γ^b	Mean R_0	SE(R_0)
0.0001	0.01	1.45	0.034
0.0001	0.05	0.39	0.012
0.0001	0.10	0.19	0.009
0.0005	0.01	5.89	0.073
0.0005	0.05	2.01	0.040
0.0005	0.10	1.02	0.032
0.001	0.01	7.38	0.066
0.001	0.05	3.81	0.063
0.001	0.10	2.11	0.046

^a β = transmission coefficient.

^b γ = recovery rate.

SE shown in Table 4 are small for all the parameter combinations, suggesting that the mean value for R_0 is precisely estimated. However, there is an indication that as R_0 increases the SE of the estimate of R_0 increases. The estimated correlation between R_0 and SE(R_0) is 0.9.

Figure 3 shows a histogram of the results obtained when $\beta = 0.0005$ and $\gamma = 0.01$. The Kolmogorov-Smirnov goodness-of-fit test for these data give a P -value of > 0.15 , demonstrating that the normal distribution gives an adequate description of the data. This is as would be expected under the Central Limit Theorem because each point in the histogram is based on the average of 5,980 individual epidemics.

The results for the distribution of R_0 based on 1,000 disease transition matrices obtained from a single sim-

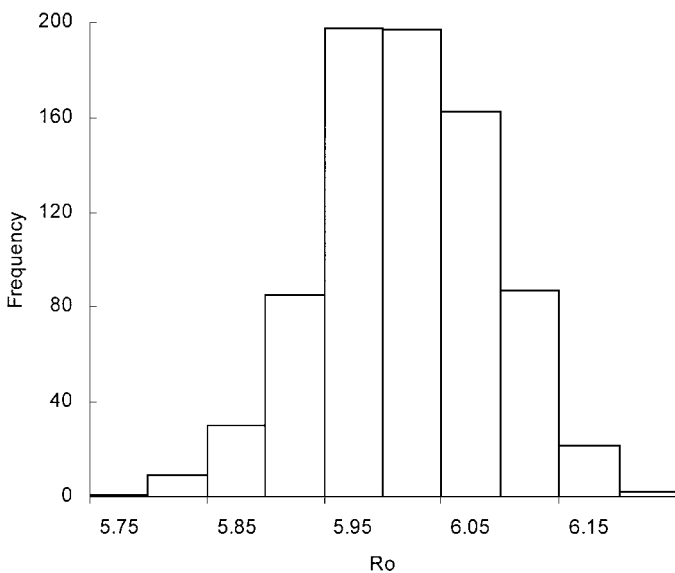


Figure 3. Histogram of the mean value of the estimator of R_0 , obtained from 1,000 bootstraps on the next-generation matrix (M) for $\beta = 0.0005$ and $\gamma = 0.01$.

ulation per index case type are presented in Table 5. The maximum values of R_0 obtained from the simulations are included. The SD is again correlated with R_0 ($r = 0.82$). Mean R_0 values differ slightly between Tables 4 and 5 due to the slightly different simulation procedures.

Figure 4 shows a histogram of R_0 obtained from the next-generation matrices when $\beta = 0.0005$ and $\gamma = 0.01$. The normality tests for these data reject the hypothesis that these data come from a normal distribution ($P < 0.01$). The distribution is skewed with a higher than expected number of large estimates for R_0 .

Total and Maximum Proportion of Pigs Infected

To obtain estimates of the total proportion of animals likely to be infected (I) during the course of an epidemic, the simulated epidemic has to last for a very long time. Figure 5 shows how I and the current proportion of animals infected change as a typical epidemic proceeds. The parameters used to generate Figure 5 were $\beta = 0.0005$ and $\gamma = 0.01$. Although the maximum proportion of pigs infected during the course of an epidemic (y_{max}) occurs early in the epidemic, it takes many years for the total proportion of pigs infected (I) during an epidemic to reach a plateau. After 30 yr $I = 0.89$ and $y_{max} = 0.51$. Nevertheless, I has reached 90% of its final value after 15 mo and 95% within 3 yr. The corresponding value for the basic reproductive rate given in Table 4 is 5.89. The theoretical expectation of the total proportion of pigs infected during the course of such a major epidemic is 0.997 and for the maximum proportion is 0.53, using Eq. [4] and [5], which assume homogeneous unstructured populations. The theoretical expectation overestimates the total proportion of pigs infected by 11% and the maximum proportion infected at one time by 4% for these parameter values and farm structure.

Figure 6 shows the estimates for I and y_{max} predicted by the stochastic model for different values of R_0 . Each point represents the mean of five simulations, each of which was stopped when the increase in the total proportion of pigs infected was less than 0.1% over a period of 1 yr. Only simulations that resulted in major epidemics were used. For comparison, the theoretical values based on R_0 are shown. The difference between the two sets of curves is due, in part, to the fact that the expectations based on R_0 assume a homogeneous population of pigs in direct contact, but also that these expectations assume that there is no migration or immigration in the population. Thus, it is apparent that the farm structure plays a major role in the spread of infection. To verify this, a model was implemented in which the pigs were all in direct contact. The results of this implementation are presented in Figure 7. It can be seen in Figure 7 that the proportions of pigs infected as predicted by the stochastic model is in close agreement with the theoretical expectation. Comparing Figures 6 and 7 demonstrates that dividing the population into discrete groups reduces the proportion of pigs

Table 5. Estimates of mean, variability, and maximum of the estimator of the basic reproductive ratio (R_0), obtained from 1,000 transition matrices based on one simulation per pig type

β^a	γ^b	Mean R_0	SD(R_0)	Max(R_0)
0.0001	0.01	1.65	0.59	4.56
0.0001	0.05	0.90	0.48	2.45
0.0001	0.10	0.66	0.53	2.00
0.0005	0.01	6.23	0.96	9.63
0.0005	0.05	2.60	0.79	6.38
0.0005	0.10	1.66	0.68	4.00
0.001	0.01	7.73	0.92	10.68
0.001	0.05	4.57	1.02	8.49
0.001	0.10	2.97	0.89	6.22

^a β = transmission coefficient.
^b γ = recovery rate.

infected during an epidemic, for highly infectious diseases.

Effect of Farm Structure on the Stochastic Epidemiological Model

The effect of farm structure on the results of the stochastic epidemiological model was illustrated by fitting four alternative models: piglets removed at 3 wk (Model 1), piglets removed at 12 wk of age (Model 2), finishing pigs kept for 16 wk, as in the main model (Model 3), and housing gestating sows in a single shed rather than in four sheds (Model 4). Results are the mean of 20 estimates for R_0 . Table 6 gives the mean and SE for the estimate of R_0 for the four models described.

The results demonstrate the effect of farm structure on the outcome of the introduction of infectious material

on a farm. The difference between Models 2 and 3 is not very large, demonstrating that removing the finishing pigs early does not have a great influence on R_0 . This result is in agreement with Hone (1994), who estimated that R_0 would be approximately 2.0 on a breeding farm but 4.0 on a finishing farm.

When all the gestating sows were housed in a single shed, the value obtained for R_0 of 2.74 (SE = 0.04) was directly comparable to that of Model 3. This suggests that increasing the number of sows in direct contact from 84 to 336 does not significantly increase R_0 .

Discussion

Our aim has been to develop a simple stochastic epidemic model, applicable to a structured farm, and to investigate the properties of this model and the information it provides. The model used is flexible and allows many aspects of the spread of disease to be examined

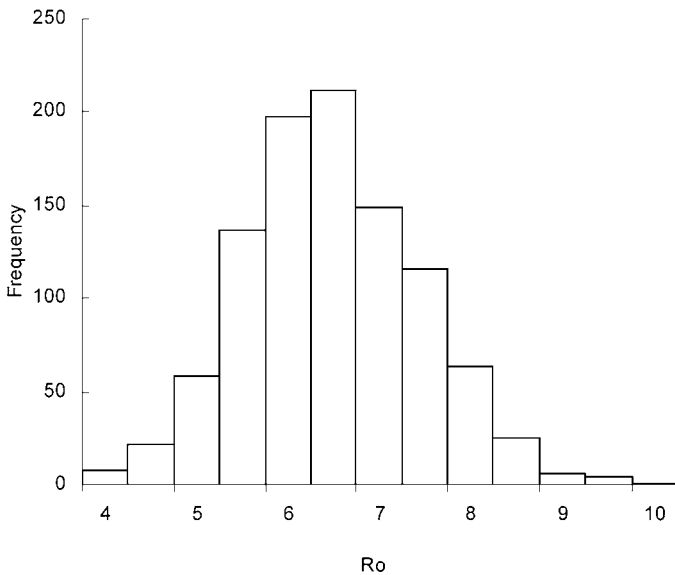


Figure 4. Histogram of distribution of the estimator of R_0 , obtained from 1,000 simulated next generation matrices (M), based on one simulation per type when $\beta = 0.0005$ and $\gamma = 0.01$.

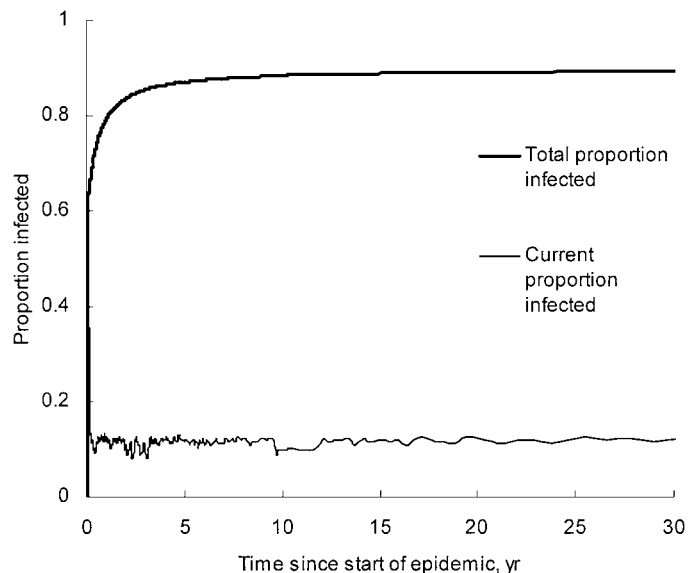


Figure 5. Proportions of infected pigs estimated from a simulated, long-term major epidemic ($\beta = 0.0005$, $\gamma = 0.01$).

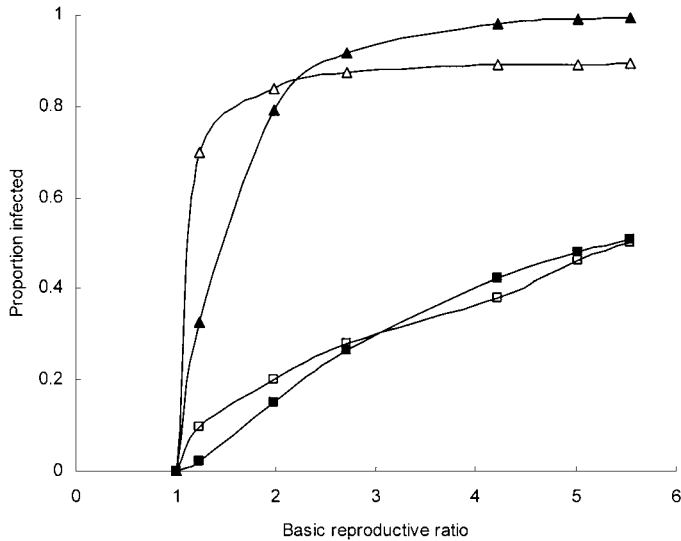


Figure 6. Comparison of the total proportion of pigs infected during an epidemic (■) and the maximum proportion at any one time (▲) obtained from simulation (open symbols) and from expectation based on R_0 (filled symbols).

in detail. The models used are simple insofar as the only epidemiological parameters included are transmission coefficient and recovery rate. However, other parameters can easily be incorporated, as demonstrated by MacKenzie and Bishop (2001). Similarly, the farm parameters, such as contact rate, can be modified to inves-

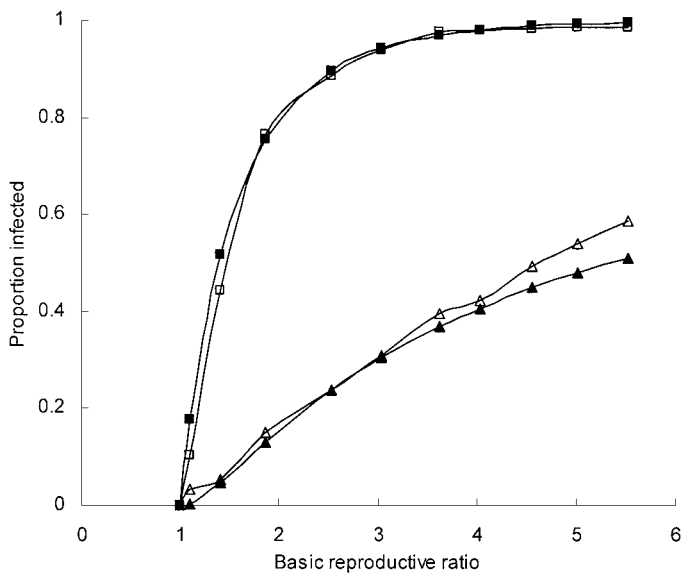


Figure 7. Comparison of the total proportion of pigs infected during an epidemic (■) and the maximum proportion at any one time (▲) obtained from simulation (open symbols) and from expectation based on R_0 in a homogeneous population when all pigs are in direct contact with each other (filled symbols).

Table 6. Effect of altering farm structure on the estimator of the reproductive ratio (R_0) and its SE based on 20 estimates of R_0 (transmission coefficient, $\beta = 0.001$; recovery rate, $\gamma = 0.07$)

Model	R_0	SE(R_0)
1 ^a	1.00	0.008
2 ^b	2.59	0.014
3 ^c	2.72	0.019
4 ^d	2.74	0.040

^aPiglets removed at 3 wk of age.

^bPiglets removed at 12 wk of age.

^cFinishing pigs kept for 16 wk.

^dAll gestating sows housed in a single shed.

tigate the effect of farm structure on disease epidemiology.

Specific diseases, or aspects of disease spread, have previously been investigated using stochastic epidemic models. As an example of their utility, Bouma et al. (1995) used a stochastic susceptible-infectious-recovered (SIR) model to estimate the transmission of pseudorabies virus from the number of contact-infections in an experiment aimed at demonstrating the importance of population size in disease transmission. Innocent et al. (1997) used a stochastic model to simulate the spread of bovine viral diarrhoea virus through a closed dairy herd and to investigate the effect of different management practices on disease status. Likewise, Stärk et al. (2000), modeling classic swine fever, used a stochastic model to demonstrate inter-farm spread of disease and to estimate the probability that an infected pig is included in a shipment spreading infection from one farm to another. Although these published models fulfilled the aims of the experimenters, the descriptions often do not fully demonstrate the methodology or the information available from such models.

In this paper, we more fully demonstrate the use of stochastic epidemic models, including the influence of disease transmission and recovery rate on the probability of epidemics, numbers of pigs infected, and the basic reproductive rate have all been investigated.

The probability that an epidemic occurs and whether that epidemic is likely to be major or minor provides a useful tool for quantifying the risks associated with particular farm structures, subsets of animals within this structure, and particular pathogens. This result cannot be obtained from deterministic models, which allow either that an epidemic will not occur, with probability 1.0, or that it will occur and will either be minor or major. The investigation highlighted the areas of high risk on the farm: sheds containing large numbers of pigs. In the absence of disease-dependent mortality, if a substantial number of the nursery pigs become infected, it is unlikely that an epidemic will die out without intervention, making the probability of a major epidemic high and creating an endemic residing in the nursery and finishing pigs. The major hurdle to accu-

rate estimation of the probability of a major epidemic for a particular pathogen is the lack of epidemiological parameter estimates.

The model provides estimates of the basic reproductive ratio based on a disease transition matrix as described by De Jong et al. (1994). The precision of the estimate of R_0 is highly dependent on the number of simulations performed, but when a large number is used the results are very precise. The distribution of R_0 based on one epidemic per index case type demonstrates the variability in R_0 , as may be obtained when estimating R_0 from field data.

The outputs of this model illustrate the impact of population heterogeneity on the spread of disease, derived in a deterministic framework by Dushoff and Levin (1995). These authors found that with equal mixing among animals in different groups, disease invasion dynamics may be obtained by averaging the properties of the individual groups. However, with differential mixing among groups of animals (i.e., the farm structure in this paper) the expected disease dynamics alter and outcomes depend on variability of mixing (or contact) rates. In this paper this phenomenon is illustrated in both the different epidemic probabilities for different animal types. Furthermore, we have demonstrated that the relationship within homogeneous populations between R_0 and the proportions of animals infected does not hold for heterogeneous populations.

The model developed potentially has several uses and applications. The model would be useful in assessing possible disease eradication strategies. Management strategies would include altering the farm structure and changing the contact between pigs. The effect of allowing pigs to be introduced from outside the farm, vaccination, or culling of infected animals could all be investigated, in addition to selection strategies. Damrongwatanapokin (1993) used a stochastic model as a guide to different strategies for the control of pseudorabies. The results of Damrongwatanapokin's model suggest that population size is an important factor in determining whether or not an infectious agent will become endemic in a herd. Although this was not directly tested in this paper, endemics only occurred if the infection reached large groups of pigs.

In the farm situation there are many factors (e.g., weather, hygiene, disease-dependent mortality) that affect the spread of infectious material that are not included in the model. Hence, the estimate of R_0 obtained by modeling, no matter how accurate, can only be used as a guideline. The model provides insight into the epidemic process that is more informative than a single statistic such as the basic reproductive rate, especially when R_0 may be considered to be only a sample from a hypothetical distribution of R_0 values.

In summary, we have developed a simple but flexible stochastic model that is generally applicable to micro-parasitic infectious diseases in structured domestic animal populations. The model can be used to quantify

risk profiles associated with various groups of animals and investigate disease control strategies.

Implications

A model has been developed that allows the consequences of the spread of viral or bacterial infection on a pig farm to be quantified. The model demonstrates the relative risk of different parts of the farm in terms of the probability of an epidemic and, if one occurs, the probability of its being minor or major. The total number of animals infected and the maximum infected at one time can be estimated. The model can be used to investigate the effects of different strategies for controlling the spread of infectious disease (e.g., vaccination, genetic selection, culling infected animals, or segregation of infected animals). It provides a powerful tool for investigating the costs, benefits, and risks associated with control strategies for specific diseases.

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