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Eliminating infectious diseases of livestock: A metapopulation model of infection control

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ABSTRACT

When novel disease outbreaks occur in livestock, policy makers must respond promptly to eliminate disease, and are typically called on to make control decisions before detailed analysis of disease parameters can be undertaken. We present a flexible metapopulation model of disease spread that incorporates variation in livestock density and includes occasional high-mixing locations or events, such as markets or race meetings. Using probability generating functions derived from this branching process model, we compare the likely success of reactive control strategies in eliminating disease spread. We find that the optimal vaccine strategy varies according to the disease transmission rate, with homogeneous vaccination most effective for low transmission rates, and heterogeneous vaccination preferable for high levels of transmission. Quarantine combines well with vaccination, with the chance of disease elimination enhanced even for vaccines with low efficacy. Control decisions surrounding horse race meetings were of particular concern during the 2007 outbreak of equine influenza in Australia. We show that this type of high-mixing event is a powerful spread mechanism, even when the proportion of time spent at such events is low. If such locations remain open, elimination will require a highly effective vaccine with high coverage. However, a policy of banning animals from quarantined regions from attending such events can provide an effective alternative if full closure of events is economically or politically untenable.

1. Introduction

When a novel infection enters livestock populations, control measures are largely reactive, and directed towards elimination of disease (Capua and Marangon, 2006; Edwards et al., 2000; Firestone et al., 2011). That is, although the disease in question may be endemic in other regions or countries, elimination of disease in a country, state, or other pre-determined area, is the aim. In this paper, we compare reactive control measures for diseases of livestock where it is possible to enforce local quarantine, and a vaccine is available. Our focus is on elimination rather than endemic control. As such, the methodology we develop is appropriate for diseases such as avian influenza in domestic poultry (Capua and Marangon, 2006; Marangon et al., 2008), classical swine fever in regions free of the disease (Edwards et al., 2000; Moennig, 2000), and equine influenza in Australia (Baguelin et al., 2010; Perkins et al., 2011).

The key control measures we consider are vaccination, quarantine and culling. For infections that are not endemic, prophylactic vaccination often presents a considerable disadvantage when aiming for elimination, as it can be difficult to distinguish vaccinated and recently infected animals (Capua and Marangon, 2006; Edwards et al., 2000; Firestone et al., 2011). However, reactive or emergency vaccination is sometimes used as a control measure during widespread outbreaks. While reactive quarantine measures are typically applied as part of disease control, the level of quarantine will depend on the disease in question. For some diseases, widespread quarantine is combined with local culling in infected regions, while for others – such as equine influenza – there is often economic pressure to relax quarantine measures sufficiently to enable race meetings to occur.

This provides a further complication for control; that is, disease is often spread by means of high-mixing locations or events. In the case of equine influenza, horses from a large number of regions mix together at race meetings (Firestone et al., 2011). In the case of avian influenza, live bird markets (Webster, 2004) and long range transmission of infection via wild birds (Ellis et al., 2004) provide these high-mixing opportunities. For swine fever, the high-mixing locations represent markets or other venues (such as artificial insemination centres Elbers et al., 1999) where large numbers of animals from many regions can come into contact with one another.

We approach the problem of elimination by means of a non-spatial metapopulation model that includes high- and low-density regions. These regions represent intensive versus smaller-scale

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farming in the case of avian influenza or swine fever, and rural horses versus racehorse yards in the case of equine influenza. We also allow for high-mixing events as described above. Although large-scale simulation models are very valuable for providing disease and location-specific advice (Baguelin et al., 2010), our aim here is to develop a flexible model that is applicable to a range of infections and could be used in the event of a novel disease outbreak. We use a branching process model (Grimmett and Stirzaker, 1992) of disease spread within and between regions, and use probability generating functions (Becker, 1974; Miller, 2007; Trapman et al., 2004) to calculate the probability that disease is eliminated under control strategies. Although branching processes are often used to model the early stages of a disease outbreak (Colizza and Vespignani, 2007), the use of probability generating functions is less common. The technique is ideal for analysing the probability that disease outbreaks occur (Miller, 2007; Nishiura et al., 2011; Trapman et al., 2004; Vergu et al., 2010), the probability of disease emergence (Reluga et al., 2007), and the characteristics of outbreaks that do (Miller et al., 2010) or do not take off (Farrington and Grant, 1999). Here, we use probability generating functions to analyse the impact of control measures on the probability of disease elimination.

The paper is presented as follows: In Section 2, we outline the structure of the model without control measures. In Section 3, we consider the impact of vaccination. Section 4 considers reactive quarantine of regions, Section 5 discusses culling, while Section 6 considers the impact of restricting high-mixing events or locations. We report the numerical results in Section 7, and discuss the implications of our findings in Section 8.

2. General model formulation without control

For any disease there are likely to be distinct mechanisms of spread. Here we consider two levels—local, or within-region, spread (stock in sheds, or on neighbouring properties, or in specified spatial locations, for example) and global, or between-region, spread (between sheds, etc.), where transmission in each case is modelled by means of a branching process. Further, transmission rates within regions may be distinct. Here we consider two types of living conditions that lead to high and low density regions, depending whether individuals live in close proximity (such as in sheds or yards), or not. And we include a further mechanism of spread through occasional high-density 'meetings' (sale yards or race meetings, for example). Fig. 1 provides a diagram of our approach. We note that although we have considered two types of regions (based on stock density) and two levels of spread (local and global), our model serves as an illustration of how processes with any number of identified spread mechanisms, or region types, can be modelled. We now develop our model in detail.

We model transmission of infection using a non-spatial metapopulation model consisting of two types of regions (high-density and low-density) and two levels of transmission (within region and between regions). High-density regions are intended to represent intensive farms or studs and have sufficiently high levels of mixing that large outbreaks can occur locally—that is, within the region. Low-density regions represent rural settings and have insufficient mixing to sustain a large local outbreak (Boender et al., 2007; Moennig, 2000; Perkins et al., 2011). We assume both types of region contain n animals, and a proportion π of all regions are high-density. Transmission is modelled by means of branching processes, with one process representing within-region spread, and another (metapopulation-level) process representing spread between regions. Fig. 1 shows a diagram of the model, and Table 1 provides a listing of parameters used in the model. We consider plausible ranges for all key parameters in order to provide a general understanding for a very broad range of possible disease characteristics, and discuss the sensitivity of the model to the fixed parameters in the supplementary online material.

Table 1
Description of parameters used in the model.

Symbol	Definition
λ_H	Mean local cases infected by a case in a high-density region.
λ_L	Mean local cases infected by a case in a low-density region.
μ	Mean regions infected by a single case (in either region).
π	Proportion of regions that are high-density.
n	Number of animals in a region.
q_H	Probability that an outbreak in a high-density region dies out.
q_L	Probability that an outbreak in a low-density region dies out.
s_H	Probability of elimination if the first case is in a high-density region.
s_L	Probability of elimination if the first case is in a low-density region.
α_I	Vaccine impact on infectivity, where $\alpha_I = 1$ indicates no impact.
α_S	Vaccine impact on susceptibility, where $\alpha_S = 1$ indicates no impact.
v	Proportion of animals vaccinated under homogeneous vaccination.
V	Proportion of regions vaccinated under heterogeneous vaccination.
p_1	Proportion of infectivity of primary case before quarantine in place.
p_2	Proportion of infectivity of secondary cases before quarantine in place.
f	Proportion of time animals spend at high-mixing events.

We do not attempt to forecast the long-term progress of an outbreak, but focus on strategies that can eliminate disease spread entirely. As a result, we can adopt a branching process model (Grimmett and Stirzaker, 1992) for transmission, and we use probability generating functions (Becker, 1974; Miller, 2007; Trapman et al., 2004) to calculate the probability of disease extinction. Further details on the use of probability generating functions in this context are provided in the supplementary online material.

We assume that the infection is spread by animal-to-animal transmission, that the population is homogeneous and that the distribution for the number of local cases infected by one animal is Poisson, with mean λ_H in high-density regions and λ_L in low-density regions. We model between-region transmission by assuming all regions are equally likely to become infected, and that the distribution for the number of regions infected by a single infected animal is Poisson with mean μ. While this assumption may over-estimate spread for high values of μ, we confine our attention to values of μ where disease elimination is possible. An implication of the single value of μ for both region types is that animals in either region type are equally likely to infect other regions. We add further mechanisms by which high-density regions contribute more inter-region transmission in Section 6. Note that as we are only interested in the early stages of the outbreak, we do not need to specify the number of regions in the metapopulation. We assume that transmission between regions occurs according to the proportion of high-density (proportion π) and low-density (proportion $1-\pi$) regions in the population, so that the mean between-region transmission matrix, which provides average predictions of infection spread over successive generations, has the form:

$$M = \begin{pmatrix} m_{HH}(x_H) & m_{HL}(x_H) \\ m_{LH}(x_L) & m_{LL}(x_L) \end{pmatrix} = \begin{pmatrix} x_H\mu\pi & x_H\mu(1-\pi) \\ x_L\mu\pi & x_L\mu(1-\pi) \end{pmatrix}, \qquad (1)$$

where x_H and x_L are the mean outbreak sizes in high and low-density regions, respectively, and we interpret m_{ij} as the mean number of regions of type j infected by an infected region of type i. For clarity, if $\mathbf{w}$ is a vector of the number of infected high-density and low-density regions, then $M\mathbf{w}^T$ (where T represents transpose) is the number of high-density and low-density regions that are infected in the following generation.

Throughout the paper, we consider two distinct measures to compare intervention strategies: the probability of elimination, and regions of parameter space for which elimination occurs with certainty. For the latter, we calculate the effective reproduction