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Review

Models of foot-and-mouth disease

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During the 2001 foot-and-mouth disease outbreak in the UK, three very different models were used in an attempt to predict the disease dynamics and inform control measures. This was one of the first times that models had been used during an epidemic to support the decision-making process. It is probable that models will play a pivotal role in any future livestock epidemics, and it is therefore important that decision makers, veterinarians and farmers understand the uses and limitations of models. This review describes the utility of models in general before focusing on the three foot-and-mouth disease models used in 2001. Finally, the future of modelling is discussed, analysing the advances needed if models are to be successfully applied during any subsequent epidemics.

Keywords: livestock disease; mathematical models; control

1. INTRODUCTION

Livestock diseases are becoming increasingly important owing to their welfare and economic consequences. Notable examples of livestock diseases include classical-swine-fever and swine vesicular disease in pigs, bovine spongiform encephalopathy (BSE), lumpy skin disease and tuberculosis in cattle, and scrapie, sheep pox and peste des petits ruminants in sheep. Additionally, some diseases such as avian influenza and brucellosis have the potential to cause infection in humans, increasing concern about their prevalence. However, foot-and-mouth disease (FMD) is considered by far the most serious of all these infections owing to its rapid transmission between a wide range of livestock species. In general, FMD is rarely fatal to adult livestock, but causes blisters on the mouth and feet (hence the name) and a deterioration of condition, often leading to a dramatic decline in milk production in dairy cattle and very slow weight gain in other livestock (Alexandersen *et al.* 2003*b*). In addition, the economic consequences of infection within a country are severe, preventing the export of meat and milk to many regions of the world, thus eliminating a vital source of revenue. Therefore, following detection, the main aim of any control policy is to achieve disease-free status as quickly as possible (allowing exports to resume), with the minimum of impact on the livestock community. Unfortunately, these two motivating ideals of minimizing the time and minimizing the disturbance are often in conflict. Determining what is the correct balance between these two elements is a critical decision that must be taken by the appropriate stakeholders and government agencies. Without such guidance, it is meaningless to talk about optimal control strategies, or even whether one policy is 'better' than another.

In principle, given a clear definition of what is considered to be optimal, models should be able to resolve the conflict between disturbance and duration, providing the best trade-off between the differing elements and predicting the optimal use of limited resources. However, models are neither infallible nor a panacea. Therefore, in common with models for other diseases (Ferguson *et al.* 2003), it is important that decision makers who use the results of model prediction, and those individuals on the ground who are affected by these decisions, understand both the uses and limitations of the particular model. Here, the three models that were used during the 2001 UK epidemic are reviewed, and their strengths and weaknesses are discussed.

2. WHAT ARE MODELS?

Models provide frameworks that allow us accurately to conceptualize and communicate our ideas about the behaviour of a particular system. In general, such models are often mathematical, as this provides the most rigorous language with which to define our ideas. Additionally, these mathematical models can be readily simulated by computer, and hence our basic ideas at one scale can be integrated to provide predictions of the dynamics at a larger scale. However, it should also be realized that many verbal models exist, and that these are often used by experts to express their understanding, which is built upon experience and intuitive knowledge. Models *per se* are not new to epidemiology (Hamer 1906; Kermack & McKendrick 1927; Soper 1929). It is simply that, in recent years, the computational power has become available to solve models and provide detailed predictions (Levin *et al.* 1997). One of the greatest challenges for modellers is to take the verbal models of experts and translate them into the types of mathematical models that computers can process. Ideally, this should be a two-way process, with the experts who formulated the verbal model checking that the mathematical model and computer predictions agree with their understanding.

3. WHY MODEL?

The question of whether models should be used as a tool for understanding and optimizing disease control is explicitly

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linked to the questions of what models can and cannot do. We will begin with what models cannot do, as this is far simpler to define. Models are necessarily abstractions and simplifications of the real world and, as such, the results they generate will always be approximations. For the spread of FMD, existing biological and veterinary knowledge is still not sufficiently quantified to enable the creation of a complex model that can accurately encompass all the mechanisms of disease transmission both within and between farms, and more basic research is needed (Keeling *et al.* 2001; Moutou 2002; Woolhouse 2003).

However, even if all the mechanisms were understood and encoded, models would still be limited by the available data. Although the amount of data available on the location and movement of livestock is vast in comparison with our knowledge of human movements and interactions, it is still far too imprecise to allow a definite prediction of disease spread. In addition, features such as the level of biosecurity on a farm are difficult to quantify, and although they are not recorded, they have a profound impact on the spread of infection.

Finally, even if both the mechanisms and the data were known in detail, models would still be unable to predict which farms would be infected and when. Infection is a stochastic process, so each realization of the model will lead to a different epidemic with different farms being infected on different days, just as any two real epidemics will be different (Medley 2001). At best, model results are therefore probabilistic, with the certainty of any prediction decaying as we attempt to predict further into the future. In summary, given our lack of knowledge and understanding, and the simplified nature of models themselves, the predictive accuracy at the farm level is likely to be low.

Given their inherent uncertainties, it is reasonable to question whether models have any predictive power. The three predictive models used during 2001 can each capture the temporal number of cases, the approximate spatial concentration of cases and the overall magnitude and duration of the epidemic. It is these large-scale aggregate quantities that are of primary concern to policy makers, and therefore models can play an important role in aiding national-level decisions.

Models can play three main roles in informing policy. First, they can be used predicatively, taking the current situation together with the known behaviour and attempting to determine the future. For disease models, we would ideally be able to predict the size and location of an epidemic, so that adequate logistics can be made available. Second, models can be used to extrapolate, using the known dynamics with one set of parameters to construct the probable dynamics for another. In a disease scenario, we may be interested in the epidemic behaviour if control measures are relaxed or enhanced. Finally, models can be used experimentally to test rapidly a wide range of control strategies and outbreak scenarios without any of the risks associated with testing during a real epidemic. Hence, given an accurate model of FMD, it should be possible to test a range of control measures, from reactive vaccination to ring culling, to determine which strategies produce the 'best' results for a variety of initial seeds of infection. It remains an open question whether the local-scale inaccuracies present in the models are sufficient to invalidate any of the national-scale predictions.

4. CONFLICTS OF SCALE

During the 2001 epidemic, there was considerable tension between some members of the veterinary profession (who implemented the control strategies) and the modelling community (Anon 2001; Eddy 2001; Anderson *et al.* 2001; Green & Medley 2002; Taylor *et al.* 2004). This can be partially attributed to issues of scale and emphasis. Even the most ardent modeller would agree that, on a farm-by-farm basis, veterinary judgement was (and still is) the best available. Veterinary opinion will use a host of subtle details and local information that models could not hope to replicate. At the most local of scales, veterinary judgement is always more accurate than even the most sophisticated model. However, the power of models comes from their ability to compound the approximate behaviour of thousands, if not millions, of individual elements. As a simplistic analogy, a sportsperson using their skill and experience can anticipate (predict) the trajectory of a ball, accounting for the effects of gravity, drag, spin and so on. However, if we want to understand the dynamics of several colliding balls (or the detailed trajectory of spacecraft and satellites), then human intuition no longer suffices and computer models become necessary. The same is true for the spread of FMD, where the stochastic transmission of infection between farms and the compounding of many rare events mean that human intuition is not a good predictor of national-scale dynamics. Therefore, while veterinary judgement is far more accurate at the farm level, mathematical models become necessary for larger spatial scales.

This same conflict between spatial scales operates when we consider what control policies are optimal. Consider the fate of a farm that is suspected of coming into contact with the virus. Such farms are often referred to as 'dangerous contacts' (DCs; defined as farms that are probably infected owing to the movement of livestock, vehicles or personnel). It is worth noting that the culling of DCs plays a similar role to the quarantine of traced contacts during human epidemics (Riley *et al.* 2003). For the farmer who owns the DC, the optimal strategy is to resist any form of preventive cull of their animals as there is always a chance that their animals have not contracted the disease and may survive the epidemic. At the community scale, the culling of DCs is optimal as it prevents the probable spread of infection from these DCs to other susceptible farms. Hence, at this local scale, the culling of DCs results in the loss of fewer animals, despite the fact that some susceptible animals, which have the potential to escape infection, have been destroyed. If we now consider the dynamics at a national or regional scale, more dramatic culling may be necessary. It may be optimal to cull more animals within a region to prevent spread into new areas. Thus, as we move from the farm to the community to the national scale, the optimal strategy is to reduce the threshold probability of infection above which farms are culled (Matthews *et al.* 2003). As such, at the national level, the optimal strategy is very risk averse, where livestock on farms with even a small chance of being infected should be culled to prevent further spread. It is interesting to speculate that if we move from a national to European perspective, then the culling strategy should become even more stringent.

These different optimal strategies at different scales led to a secondary tension between modellers, who were asked

to consider the dynamics at a national level, and control centres or veterinarians, who were dealing with infection at a far more local level. Therefore, it is not surprising that what the models predicted to be optimal was viewed as too intensive by some in the farming and veterinary community. This problem is exacerbated by the fact that when faced with uncertainties about the precise level of optimal control, it is always better to apply the measures too strongly because if the measures are applied too weakly, then the epidemic will run out of control (Matthews *et al.* 2003). These two factors mean that optimal national decisions will be viewed as too intensive by individuals considering the epidemic at a local scale.

5. MODELS USED IN 2001

Three different models were used in 2001, which we will refer to as the imperial model (Ferguson *et al.* 2001*a*,*b*) the Cambridge–Edinburgh model (Keeling *et al.* 2001, 2003) and InterSpread (Morris *et al.* 2001). These range from a set of deterministic differential equations to a complex simulation model, reflecting the elements that the groups felt were most important and those that could be neglected. However, despite these huge differences in methodology, all three models made similar predictions about the types of controls that were needed to prevent the epidemic from spreading. Before we contrast the approaches adopted by these models, we briefly review the literature on FMD modelling, to place these models in their historical context.

Epidemiological models have a very long and rich history (Kermack & McKendrick 1927). However, their primary focus has been on understanding human diseases (Anderson & May 1991) and, until recently, detailed predictive models were computationally infeasible (Levin *et al.* 1997). Despite the potential to gather far more data, models for livestock diseases have been comparatively limited. Before 2001, the majority of FMD models were based upon the traditional SIR model for disease transmission (Kermack & McKendrick 1927), treating the farm as a single unit that could be either susceptible, infectious or removed (Miller 1976; Hutber & Kitching 1996; Haydon *et al.* 1997; Durand & Mahul 2000; Howard & Donnelly 2000). Many researchers added an economic element to this simple framework, so that the cost of the epidemic and controls to the farming industry or country can be calculated (Garner & Lack 1995*a*,*b*; Mahul & Durand 2000). Such simplistic models ignore the spatial clustering of infection that is a key feature of FMD epidemiology (Wilesmith *et al.* 2003) and assume that any farm can infect any other farm, irrespective of their separation. However, this simplification allows for rapid simulation, easy parameterization and results that are readily interpreted. In general, all of these previous models emphasize the importance of rapid culling of animals on infected farms (stamping out) and, in some cases, more extensive culls or vaccination campaigns are justified on epidemiological or economic grounds.

Spatial models are able to capture the clustering of cases, but are obviously more complex to formulate and more computationally intensive, limiting the number of scenarios that can be studied. Prior to the 2001 epidemic, there were relatively few attempts to model the spatial spread of FMD (or any other livestock disease). Most notably, Morris and coworkers developed a variety of spatial simulation models (Morris & Anderson 1976; Sanson *et al.* 1991, 1993, 1999). These models were the forerunners of the InterSpread simulation used by DEFRA (Department for Environment, Food and Rural Affairs) in 2001, and have been used by other researchers as a modelling framework (Nielen *et al.* 1996; Jalvingh *et al.* 1999). In addition, Muller *et al.* (2000) proposed a rather theoretical, network-based spatial model, where transmission is either strongly local (between farms that are directly connected in the network) or weakly at random in relation to any other farm. All of these models consider the farm as the basic unit, emphasize the importance of local clustering of cases for the dynamics of the disease, and predict that intensive control of high-risk farms near to the infected premises will be optimal.

The final type of model that was developed before 2001 used detailed knowledge of physical processes and meteorological conditions to predict the airborne spread of viral plumes (Moutou & Durand 1994; Casal *et al.* 1997; Sorensen *et al.* 2000). However, there is limited evidence for wind-borne spread during the UK epidemic in 2001 (Alexandersen *et al.* 2003*a*; Mikkelsen *et al.* 2003), and thus, for the purposes of this review, such models will be ignored.

(a) *InterSpread*

When the FMD epidemic was first detected in the UK in February 2001, the InterSpread model used by DEFRA was the only viable means to predict the spread of this infection. InterSpread was founded upon the research by R. S. Morris and coworkers in the early 1990s and, in particular, on the Ph.D. work of Sanson (1993). InterSpread is a large, complex and very flexible stochastic simulation model capable of predicting the spread of infection influenced by many different factors. InterSpread is initially seeded with the known location of all farms within the UK populated with the number and type of livestock recorded in the latest census. Transmission of FMD from an infectious to a susceptible farm is modelled stochastically, with the probability depending on the number and type of livestock on each farm, as well as the distance between farms and the route of transmission. InterSpread is therefore more of a framework within which a model can be specified, rather than actually being a model itself. It is capable of simulating a variety of models and model assumptions, from very simple spatial models to very complex ones. However, given the ability to include more detail it is natural to try to use this facility and create models that attempt to reflect reality in every way.

The vast number of mechanisms through which infection can be spread is both a strength and a weakness of InterSpread. Complex models have an intuitive appeal and are frequently considered better and more accurate. However, a model is only as good as the data that are used to parameterize it, and complex models require more parameters. Let us consider one example in detail. InterSpread can model transmission from the routes taken by dairy tankers visiting farms. Clearly, this level of detail is needed if models are to inform about limiting milk tanker visits as a means of controlling the epidemic. However, for such models to be useful, milk tanker routes need to be known (or plausible routes simulated),

and we require a quantitative understanding of the risks posed by milk tanker visits relative to other transmission mechanisms. Therefore, a fine balance exists between incorporating sufficient mechanisms to reflect the real epidemic processes, but not so many that it is impossible to find all the necessary parameters. InterSpread clearly favours the use of more mechanisms and therefore relies heavily on expert opinion to obtain the 50 or so parameters that are needed. Indeed, during the 2001 epidemic, some of the mechanisms in InterSpread were ignored in favour of simpler parameterization. However, many of the parameters used are still subject to some uncertainty, and are difficult to fine-tune to match the given epidemic situation and particular strain characteristics. An exception occurred early in the 2001 outbreak, when the reduced level of aerosol transmission from pigs (compared with the parameterization from the 1967 to 1968 outbreak) was incorporated into InterSpread, dramatically reducing the predicted epidemic size.

One of the primary uses of InterSpread during the 2001 epidemic was to compare short-term model predictions with the observed number of cases. In this way, areas with many unexpected cases could be discovered and targeted for further investigation. This novel use of predictive models essentially identifies regions whose parameters do not agree with the national average. In this way, the problems in south Penrith were detected, where a longer time to detection and greater movement of equipment were causing many new cases. This localized epidemic was then controlled by the imposition of tighter control measures in the local region.

In summary, InterSpread is a very flexible spatial modelling tool. However, owing to its flexibility, it is slower than the other two models used during 2001. It includes the effects of a vast number of details that the other models used during 2001 ignored; however, these extra details must be weighed against difficulties in parameterization (which quantifies the effects of observable characteristics on the epidemic process), with expert opinion being required to estimate many important quantities. Unfortunately, the complexity of the model and the number of possible parameters mean that replication of the InterSpread methodology by independent research groups is infeasible. Predictions from this model are in qualitative agreement with the spatial and temporal pattern of cases observed in 2001 (Stevenson 2003), and suggest that the level of culling performed during 2001 was necessary (Morris *et al.* 2001). However, given the large number of mechanisms and parameters present in the InterSpread model, it is a daunting task to assess how robust such conclusions are to the model assumptions.

(b) *Cambridge–Edinburgh model*

The Cambridge–Edinburgh model is an explicit spatial model, which is initialized with the location of all farms in the UK and their livestock, as recorded at the last census. As such, the starting conditions are the same as those of InterSpread, but this model has a more simple and transparent transmission mechanism, leading to fewer parameters and easier parameterization. Transmission is modelled as a simple function of disease between infectious and susceptible farm, compounded by the number and species of animals on each. Hence, the transmission rate to farm j (which is assumed to be susceptible) is given by:

$$\text{Infection rate for farm } j = \text{Susceptibility}^j \times \sum_{\text{infectious farms } i} \text{Infectivity}^i \times K(d_{ij}),$$

where

$$\text{Susceptibility}^j = \sum_{\text{s}} N_{\text{s}}^j S_{\text{s}} \quad \text{Infectivity}^i = \sum_{\text{s}} N_{\text{s}}^i T_{\text{s}}.$$

Here, N_{s}^i gives the number of livestock of species s on farm i as recorded in the census, S and T are species-specific susceptibility and transmission rates, and K is the transmission kernel, which defines how infectivity decreases with distance, d_{ij}, between farms i and j. Hence, K has to subsume all of the different transmission mechanisms that exist in reality, although this has the distinct advantage that the kernel can be readily parameterized from contact tracing work undertaken during the epidemic.

The use of this model has tended to be confined to the spatial aspects of disease spread, ignoring some of the temporal aspects of infectivity at the farm level. This means that while livestock number and species contribute towards the rate of transmission, the latent and infectious periods were modelled as a fixed number of days without any variability or differences between farms. Owing to the complexity of modelling spatial systems, simulation times are slow (although faster than InterSpread because fewer mechanisms are included). This means that detailed parameterization through repeated epidemic simulation is a time-consuming process. Although this model was fine-tuning during the epidemic to match the available data, repeated re-parameterizations were computationally infeasible. For a similar reason, one set of best-fit parameters was used throughout 2001. Ideally, the robustness of conclusions to parameter estimates should have been considered but this was impractical given the time constraints. Therefore, while later research has shown the invariance of these results (Keeling *et al.* 2003), at the time, small changes in the parameter estimates could have potentially led to very different policies being considered optimal.

This model has been shown to be in close agreement with the spatio-temporal pattern of the 2001 outbreak, identifying Cumbria, Devon and the Welsh boarders as the main focuses of disease, and even being able to capture the long tail of the epidemic (Keeling *et al.* 2001). Both culling and vaccination strategies have been examined with this model (Keeling *et al.* 2001, 2003). These results generally supported the policy decisions made during the 2001 epidemic, showing that the culling of contiguous premises (CPs) was beneficial in reducing the numbers of animals and farms lost. However, CP culling can never be precisely modelled as only the point location of the farm house is recorded and information on the boundaries of farms is not available. The Cambridge–Edinburgh model was unique in that it mimicked CP culling by tessellating around each infected farm and removing a proportion of its connected neighbours. While vaccination during the latter part of the epidemic was shown to be ineffective (Keeling *et al.* 2001), well-targeted large-scale vaccination applied early in the epidemic was predicted to be

beneficial. Finally, in agreement with the other models, it was shown that much earlier implementation of stringent control measures could have reduced the number of farms lost to just 50%, and that much earlier detection of the first cases could have reduced the impact even further (Keeling *et al*. 2001).

Clearly, this model is much simpler than InterSpread and, in theory, could be simulated within the InterSpread framework. This simplification has meant that the formulation and assumptions are far more transparent and open to scientific scrutiny. In addition, the few necessary parameters can (with some difficulty) be estimated from the early behaviour of the 2001 epidemic. Hence, if faced with another outbreak, this model could be re-parameterized to reflect the epidemiological characteristics of the invading FMD strain.

(c) *Imperial model*

The imperial model is strongly based on the traditional SIR-type differential equations of Kermack & McKendrick (1927), again treating the farm as the individual unit and classifying each farm by its infectious status. The initial model (Ferguson *et al*. 2001*a*,*b*) was formulated during the first few weeks of the epidemic and was necessarily a crude approximation, ignoring farm differences and only differentiating between local and long-range transmission. This model also sacrifices many of the details present in InterSpread for the ability rapidly and robustly to parameterize the equations from the epidemic data. However, whereas standard SIR models ignore all spatial structure, the imperial model attempts to capture the clustering of infection (and hence the increased competition for susceptible farms) by assuming that all farms can weakly transmit infection at random over long distances but can only strongly have a limited number of local connections (estimated between 5.5 and 8.3). Therefore, this model not only considers the number of farms in each state, but also the number of pairs of locally connected farms through which the effects of clustering can be captured (Keeling 1999). The rate at which new cases are produced is therefore given by

$$\text{Infection rate} = \tau[SI] - p\beta SI/N,$$

where $[SI]$ gives the number of locally connected, susceptible and infectious farms and τ is the transmission rate across such local contacts; p is the proportion of contacts that are long range, and $\beta SI/N$ is the familiar mass-action, (random-mixing) transmission of infection, where β is the transmission rate and S, I and N are the number of susceptible farms, infectious farms and total number of farms, respectively.

A later model (Ferguson *et al*. 2001*b*) additionally structured farms by their livestock, classifying each farm as either cattle, sheep, pig or small (fewer than 100 animals), and defining a transmission rate and susceptibility risk for each of these four categories. Thus, although the absolute number of animals on a farm is not accounted for, some adjustments are made depending on the dominant species. The parameterization for this later model was based on results from a spatially explicit statistical model, which highlights the need to consider the full spatial structure associated with epidemic spread of foot-and-mouth disease. This refined model also subdivided the country into regions (such as Cumbria and Devon) and so added an extra layer of metapopulation-type spatial structure.

Owing to the model speed and ease of parameterization, the imperial group concentrated on a detailed description of the delays (such as infection-to-reporting and report-to-slaughter), and how these distributions varied over the course of the epidemic. This type of attention to detail at the farm level highlighted the intuitive need to cull animals on infected premises and DCs as soon as possible, thereby limiting the spread of infection. In fact, it was shown that prompt IP, DC and CP culling from the start of the epidemic could have reduced the number of farms lost by 45%. The imperial model was also used to investigate ring culling and ring vaccination, and concluded that both could be used to control the epidemic if applied sufficiently rigorously, with vaccination requiring comparatively larger rings (Ferguson *et al*. 2001*a*).

Although it was able to capture accurately the temporal dynamics of the 2001 foot-and-mouth disease epidemic, the imperial model suffers from being deterministic and non-spatial. Being deterministic, questions such as the duration of the epidemic, which have a strong stochastic element, cannot be accurately judged. In addition, the model always predicts an average epidemic, so that extreme situations and unlikely scenarios are never encountered. As such, the model cannot inform about strategies that are risk adverse; only ones which perform well on average. However, this lack of variability between simulations is offset by the ability to include the variability in parameter estimates (Ferguson *et al*. 2001*a*). The lack of true spatial structure is of more concern. The spatial clustering of cases is mimicked by a few aggregate parameters, and so fails to capture the heterogeneous density of farms with tight aggregations separated by less dense regions. Also, without an explicit spatial location for each farm, the localized effects of CP and DC culling have to be defined externally to the main model, and act to modify the structure of locally connected farms. However, despite these complications, the approximations used within the model perform well and provide a reasonably accurate description of the dynamics of foot-and-mouth disease in 2001, presumably owing to the occasional longer-range transmission event, which broke up much of the spatial structure (Wilesmith *et al*. 2003). Hence, the most significant problem with the lack of explicit space is the inability to predict where the infection is probably most prevalent.

In summary, the lack of explicit spatial structure and the deterministic nature of the equations places many constraints on the way in which this model can be used. However, these limitations are offset by the speed with which simulations can be run, and the flexibility with which parameters and their distributions can be estimated.

(d) *Post-2001*

Since the UK FMD epidemic in 2001 raised the profile of this disease and highlighted the potential for modelling such infections, a range of new models and formulations has been postulated. As before, many of these are based upon the SIR paradigm, although greater detail is now being included, and models are generally being used to determine optimal response to an outbreak

(Tomassen *et al.* 2002; Schoenbaum & Disney 2003). However, there has been an increasing trend for developing spatio-temporal simulations (Gerbier *et al.* 2002; Kao 2003; Bates *et al.* 2003*a*,*b*,*c*), or models that make some allowance for spatial structure (Matthews *et al.* 2003). In addition, all three models used during 2001 have continued to be substantially refined. Any future epidemics of foot-and-mouth disease (or other livestock diseases) in the UK or elsewhere will probably witness the use of a variety of models to help better inform policy decisions.

6. THE FUTURE

It is vitally important that we learn from the mistakes made during the 2001 FMD epidemic (Woolhouse 2003; Salman 2004). Although many new measures have been implemented to prevent foot-and-mouth disease from arriving in the UK, we are still at risk from this and other infections (Yu *et al.* 1997). It is also important that the lessons learnt are flexible; it is unlikely that the next outbreak will have the same epidemiological characteristics or affect the same livestock to the same degree. It is therefore important to model a wide variety of scenarios, to calculate the optimal strategy for each, and to find methods of readily identifying the scenario that is occurring from the earliest epidemic data. It is also important that modelling approaches take into account logistical constraints and the trade-offs between strategies that may be caused by limited resources. Current work by all three modelling groups is attempting to formulate such models and characterize a range of plausible epidemiological scenarios and responses.

The British government is now committed to considering vaccination as a viable defence in the face of an outbreak because vaccination is used to combat a wide variety of human and animal diseases, although not always without controversy (Jefferson *et al.* 2003). Certainly, it would seem intuitive to use vaccination in this context. However, several difficulties exist. Most importantly, vaccination against human infections is a continual on-going process used prophylactically to combat an endemic infection. In contrast, reactive vaccination against FMD would need to be implemented in the face of an epidemic and would thus require prohibitively large amounts of trained labour to vaccinate all susceptible livestock rapidly (Keeling *et al.* 2003). This is where modelling can play an important role, informing the optimal use of limited resources. As vaccination has not been used in this context before, modelling is necessary to extrapolate from the detailed knowledge of the efficacy of the vaccine on different species, which can be gained from individual-level experiments (Barnett *et al.* 2003) to a national picture of the epidemic behaviour. Finally, if the vaccine is not specific for the invading strain of disease (Barnett *et al.* 2001), then modelling can also be used to test the effects of diminished efficacy.

A second issue that will need further consideration in the future is how the development of more sensitive and reliable molecular diagnostic tests can be used. A test that could readily identify whether an animal was infected, even before it was infectious, would have a variety of powerful uses. It could be used to screen DCs, so that fewer fully susceptible farms are culled, although the issue of false negatives could cause a problem. The test could also be used proactively, searching among low-risk farms for early signs of infection. This could dramatically reduce the reproductive ratio for the disease, by culling the animals before they even begin to shed virus. Obviously, as such new tools have not been used before, modelling will play a vital role in developing an understanding of their use and limitations.

It is probable that as our understanding of spatio-temporal disease dynamics increases and our quantitative knowledge of foot-and-mouth disease epidemiology grows, so, too, will models become more complex and include even more factors that may influence the disease dynamics. Two advancements will need to be made if such models are to be of use. The first is a requirement for far more data on a range of facets that may modify the susceptibility to infection or the risk of transmission. Factors such as topography, farm management and biosecurity are all important elements in the spread of infection that could be included in future models if the data were available. In conjunction with the acquisition of more data, we also need more sophisticated means of parameterization to determine the impact associated with each of these elements.

Two features were absent from the three models used during 2001, despite their inclusion in other research; namely, within-farm dynamics (Woolhouse *et al.* 1996) and economics (Garner & Lack 1995*a*; Mahul & Durand 2000). All three models treated the farm as a single unit, such that all the animals became infected *en masse*. In reality, the infection will initially spread through the farm before spreading between farms. However, predicting such dynamics is complicated by our lack of knowledge of the infection at this level of detail. While, in principle, it is simple to simulate a within-farm epidemic using standard SIR-type models, it is not clear how the initial number of infected animals should be determined, or how the reproductive ratio of the disease on a farm should scale with the number and density of livestock. Until such questions can be answered, treating the farm as a single infectious unit is as reliable as attempting to simulate within-farm epidemics. Given that the control of foot-and-mouth disease is ultimately driven by economic considerations, it seems imperative that an economic component should be incorporated into future models (Bates *et al.* 2003*c*). However, while costs to the farming industry owing to loss of livestock are easy to ascertain, the consequences of export bans and reduced tourism during an epidemic are more difficult to calculate. Clearly, the economic costs of an epidemic are multi-faceted (Thompson *et al.* 2002; Paarlberg *et al.* 2002); and more research is required before all the elements are well understood.

Finally, probably one of the most important advancements for the future would be to combine the expertise of modellers, veterinarians and those responsible for implementing policy (Eddy 2001). Veterinary judgement, experience and local knowledge can provide the most accurate assessment of infection risk for particular farms, while modelling techniques can be used to integrate this knowledge to a more global scale and to advise on the most optimal national strategy. However, this sort of collaborative interaction requires strong communication and trust on the behalves of both parties. Those implementing

policy at a local level need to trust the model predictions and understand that it may be necessary to cull extensively in a limited area to reduce the risk of a larger-scale outbreak. Modellers need to trust that vets and other workers on the ground will make informed decisions. Modellers also need to obtain sufficient feedback to enable the actual levels of control being implemented to be incorporated into real-time simulations to access their impact.

Therefore, in conclusion, the variety of foot-and-mouth disease models currently available are useful tools for (and in fact the only means of) predicting epidemic dynamics at the national scale. Models have an important role to play in defining policy before any cases occur, as once an epidemic starts there is insufficient time to experiment with control measures given the rapid spread of FMD between farms. Thus, mathematical and computer models are therefore likely to play an increasing role in the future, but improvements in their accuracy and in the control of foot-and-mouth disease (and other livestock diseases) will only arise from an interdisciplinary collaboration between modellers, veterinarians and epidemiologists working in this area.

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