The UK foot-and-mouth disease outbreak — the aftermath

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The 2001 epidemic of foot-and-mouth disease in the United Kingdom triggered a livestock culling campaign that involved the slaughter of more than 6.5 million animals. Three years later, management of the epidemic remains controversial. Some believe that untried control methods based on unvalidated models replaced well-established policy, motivating an unnecessary slaughter. Others hold that rigorous quantitative approaches provided the basis for new incisive policies that significantly curtailed the epidemic. Now, new and more flexible control policies have been adopted throughout Europe. For these policies to receive the full confidence of scientists, veterinarians and the general public, it is necessary that we improve both our understanding of where, how and why control measures initially failed in 2001 and how new policies should be implemented.

Foot-and-mouth disease (FMD) is a highly infectious viral disease of cloven-hoofed animals. Its main epidemiological features are described in box 1. The Office Internationale des Epizooties (OIE) recognizes countries (or regulated regions within countries) to be in one of three disease states: FMD free without vaccination; FMD free with vaccination; and FMD present with or without vaccination. Countries move through these stages, typically accessing wider and more profitable livestock commodities should be strongly discouraged. Most of which was that in the early stages of the epidemic the authorities were unable to apply traditional control methods to a high standard in all areas. For the first time mathematically based computer models were used in the management of an outbreak. In contrast to empirically derived ‘tried and tested’ FMD control policies that have been in use over the past several decades, the results of this modelling indicated that the epidemic would be controlled more effectively if widespread culling of apparently unaffected herds, and, in particular, culling based purely on geographical proximity was adopted. These observations beg two questions. First, why did the models produce such a contrasting FMD control
Foot-and-mouth disease (FMD) is a disease of cloven-hoofed animals such as cattle, pigs, sheep and goats. The pathology of FMD includes fever, vesicles in the mouth, feet and udders, loss of milk production in adult animals and death in young animals. Infected cattle, sheep and goats can become carriers of FMD that are persistently infected (and occasionally infectious) for up to 3.5 years depending on the host species.

FMD virus is an RNA virus of the family Picornaviridae (genus Aphthoviridae). It has seven distinct serotypes, between which there is no immunological cross-reactivity. The FMD virus genome contains 8,400 nucleotides and 12 genes, four of which encode capsid proteins. FMD virus genomes are diverse: capsid genes of the same serotype can differ by more than 30% of nucleotides and distant subtypes within the same serotype may only elicit weak cross-reactivity, so the choice of (inactivated) vaccine strains must be carefully matched to outbreak strains against which protection is sought. The virus can evolve rapidly (for example, 1.5% of capsid gene nucleotides can change per year, or at an estimated fixation rate of one nucleotide in these genes over the course of an individual infection

One of the most intriguing aspects of the epidemiology of FMD is the seemingly high variability in the transmissibility of the virus. It is thought to have one of the lowest infectious doses of any virus has enormous potential for infectiousness within herds and, under the right conditions, a remarkable capacity to spread by aerosol over considerable distances. Oddly however, under other conditions, FMD virus seems to be less infectious — for example, there is some evidence that FMD virus cannot be maintained over long time periods in sheep populations and when the Pan-Asia virus spread to the Netherlands, studies showed that it failed to spread between calves that were in direct contact with each other. More than half (98) of the 180 primary cases reported in the United Kingdom between 1954 and 1967 failed to infect any other premises and in the 2001 epidemic the first case — a large pig farm left infectious for at least 2 weeks during meteorological conditions favourable to transmission — is thought only to have infected 1–10 neighbouring farms before it was finally culled.

Despite these similarities, some important differences must be recognized when comparing the two epidemics. In 1967 slaughter was mostly confined to animals from IPs, whereas in 2001 animals were culled on a further 8,131 premises that were close to, or in some other way associated with, IPs. In 1967, approximately 442,000 animals were slaughtered to control the epidemic, whereas in 2001 at least 4 million animals were slaughtered for the purposes of disease control, with at least a further 2.5 million animals destroyed in 'welfare culls'. Nationally, prior to the 2001 epidemic, total numbers of the two most important host species for the FMD virus (cattle and pigs) were 8% less than 1967 figures. The average dairy herd size had doubled since 1967, but the effects of fewer larger herds on disease control are unclear (although obviously the number of individuals culled per IP must increase). In addition, sheep numbers had increased by 46% and the physical movement of infected sheep was responsible for much of the early dissemination of infection in 2001. Sheep were present on 80% of all IPs, including 15% that were solely sheep farms. By contrast, the 1967 epidemic was mostly restricted to cattle. Diagnosis in sheep is much more difficult, which probably led to delays in the identification of IPs in 2001. However, sheep are less infectious than both pigs and cattle. The modern livestock industry involves the movement of many more animals than in 1967, but the epidemiological significance of this diminishes after the imposition of movement bans. The effects of these changes on the efficacy of traditional measures in controlling FMD outbreaks remain largely unexplored.

The extent to which pathogens are infectious prior to the onset of discernable pathology is obviously an important determinant of the extent to which epidemics can be efficiently controlled. The FMD virus is genetically diverse and it is plausible that differences in both the transmissibility and the route of transmission might exist between strains, which could alter the effectiveness of...
Although successful control can be considered to be the prevention of endemic disease, the aims of a successful control strategy may have changed since traditional methods were last tested. Control strategies might seek to minimize various quantities, such as total animal loss, duration of the epidemic (which is currently the main objective in England and Wales), regional spread, financial loss (to several economic sectors) or animal suffering. Moreover, a small outbreak that is under control, and therefore in decline, is likely to be viewed as acceptable, but when the number of extant IPs is high, a substantial and potentially unacceptable number of new cases can still arise from an epidemic that is — technically — considered to be under control and might therefore necessitate further control measures. Historically, traditional methods that have been viewed as successful because FMD has not become endemic in the UK might now be rejected on the grounds that they might be unable to contain FMD outbreaks under climatic conditions that are favourable to viral transmission and in areas of high livestock density. However, controversy persists because assembling evidence that alternative methods of control might work any better is not straightforward.

**The models — strengths, weaknesses**

There is one other difference between the management of the control strategy in 2001 to that of previous outbreaks. Soon after the discovery of the first case of FMD in 2001, members of the 'FMD Science Group' oversaw the construction and analysis of three independently developed epidemiological models of FMD spread. These models, which were based on computer simulation and mathematical techniques, were fitted to data as they were collated over the course of the epidemic and used to predict the future course of the epidemic under several control scenarios. Although some very good quantitative epidemiologists were present in the United Kingdom in 1967, there is no record of any of them advising the FMD control policy at that time. The new and important role for quantitative modelling in real-time disease-control management reflects technological developments (such as powerful computers and spatial data), the maturing of quantitative epidemiology as an academic discipline and unusually direct communication between leading epidemiologists and senior government scientific advisors. More importantly, it reflects a growing awareness of the need for rigorous data analysis, which was highlighted by the experience with BSE in the United Kingdom.

Despite the many differences between the two epidemics, it is reassuring to find that the traditional methods directed at culling animals from IPs and DCs within 24 hours of reporting disease, were attempted up to 23 March, after which additional measures were introduced that included: slaughter on suspicion of infection; culling of pigs, sheep and goats on premises within 3 km of an IP in both Dumfries and Galloway and in Cumbria; and culling all premises contiguous to an IP within 48 hours. This last measure became known as the ‘24/48’ IP/CP cull policy and would prove highly controversial. There are instructive regional variations in the extent to which this policy was implemented; it seemed to be somewhat discretionary in Scotland, and may not have been “more than 50% implemented” elsewhere. Indeed, although the CP cull is in principle easy to define, what is truly ‘contiguous’ is subject to interpretation, and the most appropriate definition is contingent on the assumed mode of disease transmission.

**Controlling transmission**

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**Figure 1 | Past performance and implementation of traditional methods.**

**a** | Primary outbreaks of FMD from 1954 to 1967, together with the number of associated secondary outbreaks. Primary outbreaks are those that cannot be linked with any known source in Great Britain and are therefore attributed to FMD introduction from abroad. Secondary outbreaks are all those that arose by the spread of infection from primary outbreaks. Numbers in brackets refer to the actual number of outbreaks for those epidemics with more than 50 secondary cases. **b** | Comparison of the time between reporting or confirmation of FMD and slaughter of animals, for the epidemics in 1967 and 2001. Time intervals refer to the difference between the dates of reporting/confirmation and slaughter from 25 October onward for 1967 (REF. 4) and IPs with confirmation dates on or after 24 February for 2001. This figure was constructed using the most recent DEFRA data. IP, infected premises.
The models are compared in detail elsewhere. As they adopted different approaches yet still obtained similar important results, it has been argued that the conclusions derived from them are likely to be robust. However, this confidence should not be exaggerated because all the models share certain fundamental similarities. One is that they assumed that the location of the farming premises as recorded in the agricultural census of 2000 was an appropriate surrogate for the location of livestock. Discrepancies between the location of livestock and the location according to the census were well known, and would limit the spatial resolution at which these models could determine local culling strategies. For example, the value of quantitative comparisons amongst a 3 km, 2 km, 1.5 km or CP cull would have been unclear. Another similarity is that they were all parameterized using the same epidemiological data (provided by DEFRA), and it was assumed that these data were sufficiently accurate to allow detailed, predictive mathematical modelling at a level adequate to advise policy. Although models are valuable because they allow the objective exploration of data, all models must inevitably make assumptions and it is part of the modelling process to explore, question and review the consequences of these assumptions in an attempt to improve understanding of model behaviour and acquire greater and more widespread confidence in their predictions. We believe there are a number of points arising from the use of the outbreak data that require further examination in the published literature.

First, contact-tracing data indicated that premises were infectious as early as 3.5 days after the estimated date of infection, with a constant probability of transmission until all the animals were slaughtered. Unless transmission to an IP has occurred by animal movement, IPs would not always be expected to be infectious so quickly, and infectiousness might be expected to increase over time as the number of infected animals in the herd increases. The high estimated levels of infectiousness soon after the date of infection could be due to consistent error in identification of the source IP or in estimation of the date of contact with the infection. The date of contact is estimated by the date of the earliest known contact with an IP or by the age of lesions; however, in pigs and cattle older lesions have an error estimate of ± 3 days. Although other factors, such as increased biosecurity on uninfected farms close to IPs might reduce the effects of rising infectivity over time, the models could be sensitive to changes in the infectiousness profile, and overestimation of the early infectiousness of IPs would lead to models exaggerating the importance of CP culling. The sensitivity of the models to this assumption remains unclear.

Second, the relationship between the probability of transmission and the distance to an IP (known as the ‘transmission kernel’) is based directly on the contact-tracing data. Although the data represents the best estimate of ‘who infected whom’, underlying biases in these estimates are mostly unexplored in the literature. Simulations of the epidemic in Cumbria overestimate the number of IPs close to locations at which the epidemic originated. This might have been the result of excessive wave-like progression of the simulated epidemics, caused by an overestimation of the importance of local spread, and could lead to an exaggerated estimate of the value of CP culling.

Third, it is assumed that identification of the disease on farms was accurate. Detailed analysis of the proportion of IPs that were confirmed as infected by laboratory tests is yet to be published, but given the difficulty of diagnosing disease in sheep, it is anticipated to be substantially less than 100% — for example, in 1967, fewer than 20% of doubtful cases were subsequently found to be infected. Subsequent analysis has revealed that the role of animal movement in the early spread of infection might have been underestimated, leading to a potential overestimation of the number of premises that were infected after the movement ban was imposed. Both sources of error could cause the models to overestimate the control effort that was required.

Fourth, although it is well known that after movement restrictions were imposed in late February the transmission kernel changed to reflect much higher levels of local transmission, a constant transmission kernel was assumed in all models thereafter. The transmission kernel only describes the effect of distance on infectious contact without distinguishing amongst airborne, animal contact or mechanical transmission. Early on in the course of the epidemic, aerosol transmission may have been important, but environmental conditions and the lack of transmission to pigs reduced its later impact. Anecdotally, the proportion of infectious contacts that were assigned to animal movements or human activity increased over the time course of the epidemic. Transmission is assumed to be independent of the control policy but changing the control policy might affect logistics, farmer compliance or the implementation of biosecurity. Ferguson et al. have suggested that significant increases in the transmission rate might have occurred towards the end of the epidemic. Although difficult to prove, the extensive movements of people, animals and vehicles owing to the intensive slaughter policy could have exacerbated transmission.

Finally, the models assume that the linear distance between farms was the main determinant of transmission risk. If two farms have the same composition and are equidistant from an IP, then the models assume that they are equally likely to become infected, and so a purely spatially motivated policy like the CP cull is favoured. However, if one is more likely to become infected than the other (for example, if two farms are connected by a well-used road), then identifying the high-risk property becomes more worthwhile. This is the question that lies at the core of the controversy over the control policy — what is the effectiveness of a DC cull compared with a CP cull? Although the models predict that, as implemented, the cull was superior to the other options considered, a comparison with a well-managed traditional policy is yet to be published. More recent analyses indicate that even very precise DC culling would only have been valuable if the time between disease diagnosis and slaughter could have been reduced, and that the overall number of premises subject to culling may be fairly insensitive to overculling at the local level. This indicates that the superior performance of the CP cull in reducing the epidemic duration might be more important than any apparent over-culling. However, a better understanding of the risk factors that are associated with transmission of infection is critical for a comprehensive evaluation of the benefits of DC culling.

The main factor responsible for the end of the epidemic probably varied regionally, but there is evidence that factors other than the change in control policy could have been the most important. Whatever future analyses may tell us, unprecedented numbers of animals were slaughtered in a new and untested control procedure, largely formulated and justified with the use of necessarily hastily developed computer models. Given uncertainties in the data and the reliance of these models on assumptions that are necessarily crude and also difficult to verify, it is difficult to make the argument that mathematical models showed that implementation of widespread and intensive culling was the only tenable option. Models did show clearly, and at a relatively early stage, that a traditional policy, as previously implemented, was not sufficient to prevent the development of a very large epidemic. However, the main arguments in favour of a CP cull are simpler decision-making and ease...
of management, together with the benefit that, in a time of great chaos and uncertainty, a clearly defined policy with simple goals can be of both logistical and political value.

**Looking to the future**
The direct and indirect economic tolls of the 2001 epidemic are estimated to have been at least UK £3 billion and UK £5 billion, respectively\(^{31,32}\). This, together with widespread public disquiet at the visible slaughter of at least 6.5 million animals, has prompted a major revision of outbreak contingency planning. Many excellent recommendations have been made by commissioned reports\(^{5,6,33}\) and have been incorporated into future contingency plans\(^2,7\). An obvious recommendation is the imposition of an automatic nationwide movement ban on all livestock immediately after confirmation of the first case. In 2001, such action could have halved the size of the epidemic\(^1\). More radical is the recommendation that emergency vaccination “should now be considered as part of the control strategy from the start of any outbreak”\(^4\). This recommendation arises partly from the positive outcomes of vaccination campaigns.
carried out in Uruguay\textsuperscript{24} and experience in the Netherlands\textsuperscript{25} in 2001.

Culling of animals on IPs will continue to remain part of any control programme, and therefore any outbreak will always involve slaughter regardless of whether emergency vaccination is implemented. Nevertheless, the recommendation to vaccinate is welcome provided several important difficulties are overcome. Vaccinated animals will always require time to acquire protective immunity, although this time can be substantially reduced by the use of high-potency vaccines\textsuperscript{26}. Furthermore, vaccination might not always prevent infection or the establishment of a long-term asymptomatic but potentially infectious carrier state in cattle and sheep\textsuperscript{37} (although recent results seem to also confirm the effectiveness of high-potency vaccines in inhibiting the carrier state\textsuperscript{38}). For this reason, OIE regulations had required a delay of 1–2 years before countries that had an FMD outbreak, and which had used emergency vaccination, could reapply for full disease-free status (in contrast to just 3 months if culling alone was used). This delay has recently been reduced to 6 months provided adequate numbers of vaccinated animals are subject to a test for antibodies to viral non-structural proteins (NSPs) that can, in principle, distinguish between animals that have been vaccinated and those that are, or have been, infected. However, there are some problems with this approach— for example, it is doubtful that putative carrier animals always produce detectable quantities of antibody to NSPs\textsuperscript{39} and the development of more sensitive tests will require the use of more highly purified and expensive vaccines. Policy on emergency 'vaccination-to-live' is now included in the EU directive 2003/85/EC (Article 61)\textsuperscript{40}, which also requires member states to "make all arrangements necessary for emergency vaccination" on confirmation of the first identified case of disease (Article 14.3). Article 64.1 of this directive prohibits the movement of vaccinated animals between member states and, in all likelihood, the movement of such animals would also be restricted nationally, anticipating the difficulty that authorities would have in identifying virus carriers using existing NSP tests. In the UK, a further consequence has been the extension of the legal authority to cull, which now includes "any animal the Secretary of State thinks should be slaughtered with a view to preventing the spread of foot-and-mouth disease," as outlined in the Animal Health Act of 2002.

The UK authorities were poorly prepared for the 2001 outbreak, and the subsequent renewal of investment in attempts to develop better vaccines and diagnostic methods, and to improve contingency planning is both welcome and long overdue. The addition of epidemiological models to the range of techniques used in the formulation of FMD control policy is a significant advance. However, we must learn how information from quantitative models should be incorporated into policy formulation in a balanced way, mindful of its persuasive but often illusory level of numerical precision. It is essential that models are developed and used in a manner that allows both their strengths and inevitable short-comings to be recognized and widely understood\textsuperscript{13,44}. The implications of limited logistical and human resources need to be integrated into modelling of control scenarios and we need to understand how such limitations influence the choice of policy options. The aims of a successful control policy need to be defined more precisely and the ability to coordinate policy centrally, without losing capability to tailor control tactics locally needs to be developed. We need to understand more about the precise mechanisms that allow the local spread of disease. We need to develop rigorous protocols for exploring phenotypic variability which might characterise different viral strains, and not simply track, but react to, the locations of strains worldwide. In addition, although traditional methods have worked for most occasions when infection has been introduced into the United Kingdom, we need to learn why and when these measures fail.

The current DEFRA FMD contingency plan recognizes the need for a flexible set of control procedures, but the timing of the decisions regarding control options is crucial, and criteria are required with which the serious of outbreaks can be evaluated early so that an appropriately measured response is selected. On the basis of analyses of published data from the 2001 epidemic, we cannot conclude that traditional methods of control no longer work, only that, as implemented in 2001, they did not work to an acceptable standard. What is now required is a marriage of the value of the expert advice so staunchly defended by the veterinary practice, with the benefits of modern surveillance, diagnostic and data management technologies and the analytical capabilities of theoretical modelling at the strategic level. This will require drive, focus and coordinated cross-disciplinary communication, and patience, good listeners, and open minds. Properly resourced, FMD contingency planning should provide a model for twenty-first century disease control.
Foot-and-mouth disease in the UK: what should we do next time?


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Competing interests statement

The authors declare that they have no competing financial interests.

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Daniel T. Haydon’s laboratory:

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