Spatial, temporal, and spatio-temporal epidemiology of foot-and-mouth disease in Cumbria, February to September 2001

Mark Stevenson[1], John Wilesmith[2] Clifton King[3] & Roger Morris[1]

[1]EpiCentre, Institute of Veterinary, Animal and Biomedical Sciences
Massey University, Palmerston North, New Zealand
Phone: +64 6 350-5915 Fax: +64 6 350-5716
Email: M.Stevenson@massey.ac.nz

[2]Epidemiology Department, Veterinary Laboratories Agency
New Haw, Addlestone, Surrey KT15 3NB, England

[3]National Centre for Disease Investigation
PO Box 40742 Upper Hutt, New Zealand

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ABSTRACT

We describe the spatial, temporal, and spatio-temporal features of the 2001 British foot-and-mouth disease epidemic in the county of Cumbria using hazard functions, extraction mapping and the space-time K-function.

Foot-and-mouth disease was first diagnosed in Cumbria in early March 2001 and eradication of the disease in this area of Great Britain was not achieved until September 2001. Delays to eradication were consistent with a large number of cattle holdings infected early in the epidemic creating a high environmental viral load and a relatively large amount of medium to long distance spread of the virus associated with seasonal farming activities such as shearing and contract hay and silage making, compounded to some extent by the movement of people and vehicles between disaggregated farm land parcels. Analysis of the spatio-temporal interaction of disease risk in Cumbria showed that premises remained infectious for a longer period of time throughout May, June and July consistent with delays in disease detection during this period.

Assessment of the adequacy of response efforts to large-scale infectious disease epidemics in animal populations is based on a synthesis of information accumulated from a variety of sources. We conclude that descriptive analyses of the spatial, temporal and spatio-temporal features of foot-and-mouth disease epidemic data provide valuable evidence to support field observations and opinions concerning factors that may be influencing disease control. With these factors known and understood emerging changes in epidemic behaviour can be identified promptly and appropriate action taken, as individual circumstances dictate.

Keywords and phrases**:** foot-and-mouth disease, spatial epidemiology, survival analysis, extraction mapping, space-time K-function

1.0 INTRODUCTION

The 2001 foot-and-mouth disease (FMD) epidemic in Great Britain has been a timely reminder of the value of geo-referenced farm data in the management animal disease outbreaks. Where large numbers of personnel are deployed to carry out control activities accurate and up-to-date maps showing farm locations and herd disease status have proven essential for this work to be carried out quickly and efficiently (Morris *et al.* 2002). For those involved in setting policies related to disease eradication geo-referenced data is essential - firstly for monitoring progress (Sanson *et al.* 1991) and secondly for predictive modelling of alternative control strategies (Howard and Donnelly 2000; Ferguson *et al.* 2001; Kao 2001; Keeling *et al.* 2001; Morris *et al.* 2001).

In the absence of vaccination, strategies for dealing with a foot-and-mouth disease epidemic involve four main elements: (1) the rapid slaughter of all stock on premises known to be infected, (2) pre-emptive slaughtering of stock on premises within a prescribed distance of those infected, (3) the imposition of bans on the movement of stock and/or people within defined infected areas, and (4) surveillance to detect infected premises (Sanson 1993; Blood *et al.* 1994). The removal of stock on infected premises and those in the immediate vicinity attempts to limit local spread of the disease and restrictions on animal and animal product movement attempts to reduce the spread of disease across larger spatial scales.

Foot-and-mouth disease outbreaks are characterised by spatio-temporal clustering of infection among susceptible farm holdings, the magnitude of which varies in response to the scale of the original infection challenge, the geographical distribution of the animal population at risk and the effectiveness of control efforts applied during eradication. As a result of the dynamic nature of outbreak situations where the animal population at risk is constantly changing and control measures vary in their effectiveness and intensity of application, it is important that response managers are aware of changes in the relative importance of the spatial and temporal components of infection risk that occur over time.

With this background, the aim of this study was to describe the spatial, temporal and spatio-temporal features of the incidence of foot-and-mouth disease among holdings in the county of Cumbria from 20 February 2001 to 12 September 2001. Appreciation of each of these aspects of foot-and-mouth disease epidemiology means that decisions concerning practical issues such as defining the size of pre-emptive culling radii, the length of surveillance periods, the resources required, and the appropriate effort to trace the spread of infection from infected premises can be made with greater objectivity and modified appropriately.

2.0 MATERIALS AND METHODS

The study area comprised a 50 kilometre square grid in the county of Cumbria with its northern border situated just to the south of the city of Carlisle and including the towns of Penrith, Brough, and Windermere, as shown in Figure 1. This area was selected for analysis because it was a region where control and eradication of the disease, in comparison with other regions of Great Britain, proved to be difficult (Gibbens *et al.* 2001). The period of interest was from 20 February 2001 to 12 September 2001.

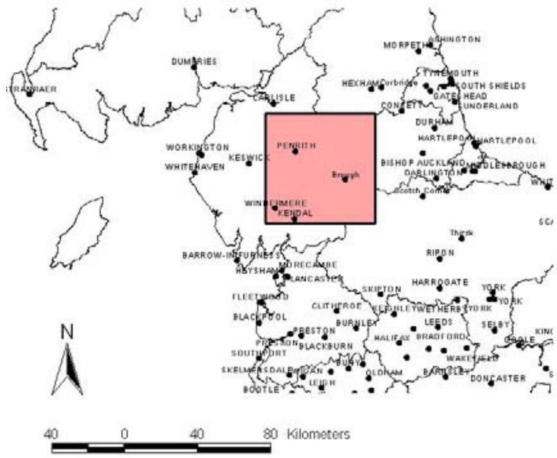


Figure 1. Map of the north of England showing the boundaries of the area described in this study.

The population of interest included all farm holdings containing at least one of the five FMD-susceptible domestic species (cattle, sheep, goats, deer or pigs) that were located within the boundaries of the defined study area. Holding-associated data was retrieved from the agricultural census data collected by the Ministry of Agriculture, Fisheries and Food (MAFF 2000) for the twelve months to June 2000 and subsequently revised throughout the course of the 2001 FMD epidemic. Data recorded for each holding included the county-parish-holding identifier, easting and northing coordinates of the main farm building and counts of the number of adults present of each of the FMD-susceptible species.

Cases were holdings located within the defined study area that were declared as FMD-infected premises under the Foot-and-Mouth Disease Order 1983 (HMSO 1983). These were holdings where the clinical signs of FMD were observed by a Department for Environment, Food and Rural Affairs (DEFRA) investigating officer or holdings where there was laboratory confirmation of infection within the herd or flock (typically the case for holdings depopulated as direct contacts or holdings that were slaughtered on suspicion of infection). Details of case holdings (county-parish-holding identifier, estimated infection date, confirmation date and slaughter date) were retrieved from the FMD case database (DEFRA 2001) and merged with the agricultural census database.

To describe the temporal pattern of infection among holdings in each area a survival analysis approach was used in which the outcome of interest was each holding's estimated FMD infection date. Estimated infection date was recorded at the time of diagnosis and was determined on the basis of the history provided by the holding manager or on the basis of lesions observed at the time of examination. For the later case estimated infection date was the date of examination minus the age (in days) of the oldest lesions identified minus an additional four days to represent an incubation period for the disease. Holdings that were pre-emptively slaughtered or slaughtered on suspicion of infection were right-censored on the date of slaughter. Holdings that remained free of disease throughout the period of interest were right-censored on 12 September 2001. The weekly hazard of FMD infection, representing the instantaneous risk of infection given that a holding remained disease-free to at least the specified point in time was computed using the LOCFIT library (Loader 1999) implemented in the R statistical package (Ihaka and Gentleman 1996). We compared the hazard of FMD infection for two groups: cattle holding types and sheep, goat, deer, pig and mixed holding types considered as a single group under the title of 'other'.

To describe the spatial evolution of infection among holdings in each area four time periods were defined starting from 20 February 2001. These periods were thought to broadly represent the natural phases of the epidemic: the first (20 February to 28 March 2001) being the period of uncontrolled spread of the disease, the second (29 March to 23 May 2001) a period where there was a sharp reduction in incidence, the third (24 May to 18 July 2001) a period of relatively constant incidence, and the fourth period (19 July to 12 September 2001) being a period where incidence decreased to negligible levels. For each period two kernel density surfaces were constructed: the first comprising the density of all holdings identified as FMD-positive during the period and the second comprised of the density of holdings present at the start of the period. The ratio of the kernel density surface of the FMD-positive holdings to that of the population of holdings at risk at the start of each period provided a relief map of the distribution of the proportion of FMD-affected holdings per square kilometre (Bithell 1990; Lawson and Williams 1994; Bowman and Azzalini 1997). These plots, termed extraction maps by Lawson and Williams (1993) provided a spatial description of the proportion of holdings that were FMD-positive per square kilometre. Smoothing parameters for the kernel density surfaces were determined on the basis of holdings at risk at the start of each time interval and were calculated by cross validation (Bowman 1994).

The presence of space-time interaction was assessed using the space-time K-function (Diggle *et al.* 1995) implemented in the SPLANCS library (Rowlingson and Diggle 1993; Bivand and Gebhardt 2000) in R. The respective data sets were restricted to include cases only and the space-time K-function $K(h,t)$ was calculated as the cumulative number of cases that were expected within distance h and time interval t of an arbitrarily-selected case. Letting $K_S(h)$ define the K-function in space and $K_T(t)$ define the K-function in time, the K-function difference $D(h,t)$ was computed as:

$$D(h,t) = K(h,t) - K_S(h)K_T(t)$$

which estimates the cumulative number of cases expected within distance h and time interval t of an arbitrarily-selected case that were attributable to the interaction between space and time. To facilitate comparison among time periods we computed $D_0(h,t)$ as:

$$D_0(h,t) = \frac{D(h,t)}{K_S(h)K_T(t)}$$

which estimates, for any given distance and time separation, the ratio of the observed number of cases attributable to space-time interaction to the expected number, under the assumption that space-time interaction did not exist (Diggle *et al.* 1995). Separate space-time K-function analyses were conducted for each of the time periods described.

3.0 RESULTS

Table 1 provides counts of holdings present at the start of the study period stratified by holding type and FMD status on 12 September 2001. On 20 February 2001 there were 1555 farm holdings each containing at least one or more adults of the five FMD-susceptible domestic species. A total of 346 holdings (22%) were confirmed FMD-positive with an additional 329 holdings (21%) pre-emptively slaughtered up to 12 September 2001.

Table 1. Counts of holdings present in the Cumbria study area on 1 February 2001 stratified by holding type and FMD status on 30 September 2001.

Holding type	FMD-positive	Pre-emptively slaughtered	Slaughtered on suspicion	FMD-negative	Total
Cattle	76	36	0	148	260
Deer	0	1	0	0	1
Goat	0	1	0	11	12
Mixed	11	1	0	2	14
Pig	3	2	0	6	11
Sheep	256	288	5	708	1257
Total	346	329	5	875	1555

Figure 2 shows the weekly hazard of FMD infection for cattle and other holding types as a function of calendar time. Infection hazard peaked in the week commencing 8 March 2001 then rapidly declined from 28 March as effective control measures were applied. At this time the weekly hazard of infection was greater for cattle holdings (6.0%) than for other enterprise types (2.5%). From April through to August the weekly infection hazard for cattle holdings remained relatively static at 0.8% whereas for other holding types there was a steady increase in hazard, reaching 1.4% by the end of July.

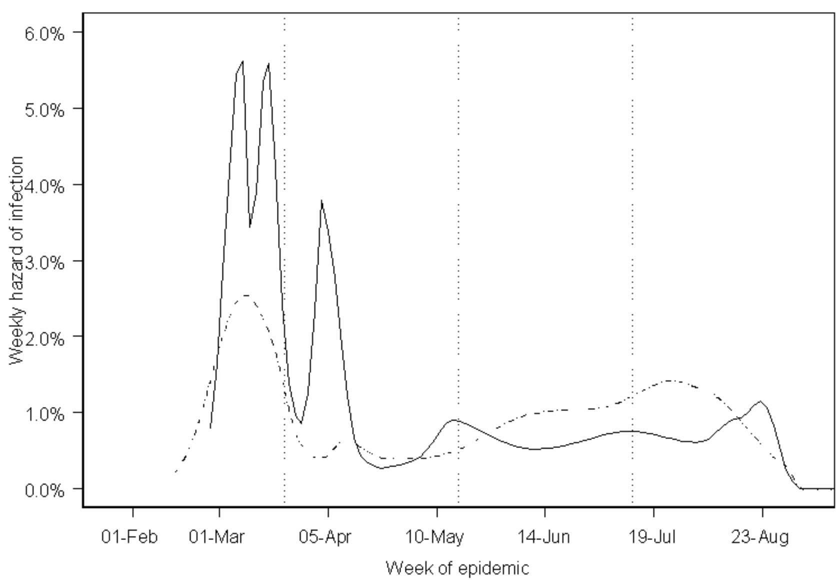
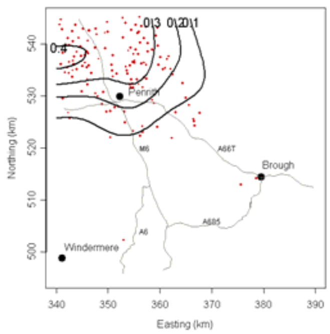
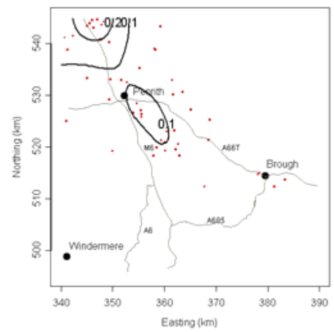


Figure 2. Weekly hazard of foot-and-mouth disease for cattle holding types (solid lines) and 'other' holding types (dashed lines) in the Cumbria study area. The hazard at week t represents the probability of a holding becoming infected given that it has remained free of disease up to week t. Vertical lines mark the four time intervals described (20 February – 28 March, 29 March – 23 May, 24 May – 18 July, 19 July – 12 September).

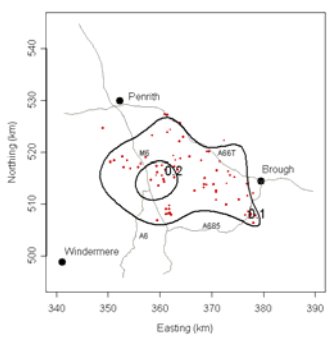
Figures 3(a) to 3(d) show the spatial evolution of FMD infection among holdings in the study area. In this map series contour lines show areas where there were greater than 10, 20, 30 and 40% of incident holdings per square kilometre.



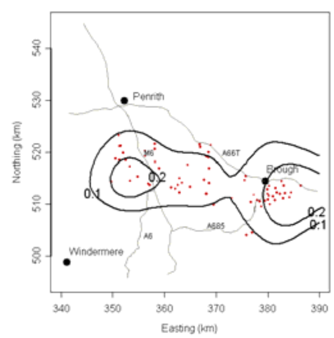
(a) 20 Feb – 28 Mar



(b) 29 Mar – 23 May



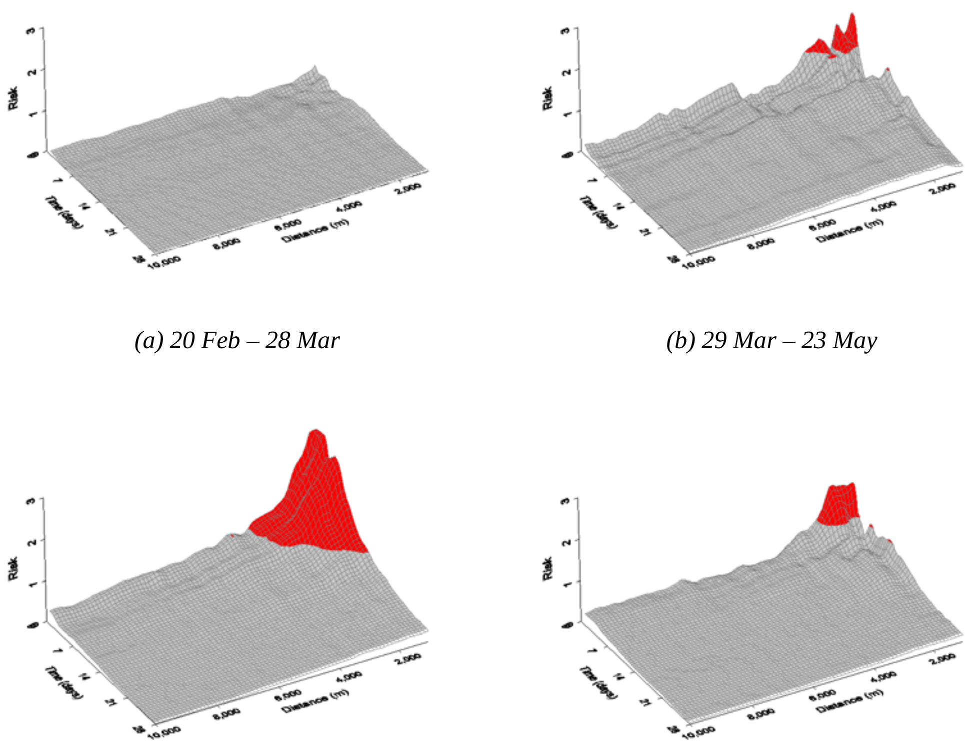
(c) 24 May – 18 Jul



(d) 19 Jul – 12 Sep

Figure 3. Dot maps showing the location of incident foot-and-mouth disease affected holdings in the Cumbria study area for the four time intervals described. Contour lines show the proportion of holdings that were FMD-positive per square kilometre.

Surface plots showing $D_0(h,t)$ as a function of distance and time from an arbitrarily-selected case for each time period are shown in Figures 4(a) to 4(d). In each plot surface values where $D_0(h,t)$ exceeds one are marked showing the distance and time separation where the observed number of cases exceeded that which was expected, under the assumption that space-time interaction did not exist.



(a) 20 Feb – 28 Mar

(b) 29 Mar – 23 May

(c) 24 May – 18 Jul

(d) 19 Jul – 12 Sep

Figure 4. Surface plots showing $D_0(h,t)$ as a function of distance and time from an arbitrarily-selected case holding for each time period. Surface values where $D_0(h,t)$ exceeds one are shown as dark shading and identify the distance and time separations where the observed number of cases exceeded that expected, under the assumption that space-time interaction did not exist.

4.0 DISCUSSION

The observed start of the 2001 foot-and-mouth disease epidemic in Great Britain was 20 February when the disease was identified in 308 pigs sent for slaughter to an Essex abattoir. By the end of epidemic on 30 September 2001 2026 holdings throughout Great Britain had been confirmed with the disease and had been slaughtered and an additional 8481 holdings had been pre-emptively slaughtered as part of the control measures introduced after 24 February 2001 making this epidemic the largest and most expensive in a temperate country in recent years. The analyses presented in this study relate to an area of Great Britain where there was a relatively high incidence of the disease.

There were marked changes in the spatial pattern of incident holdings for the four time periods described. From 20 February to 28 March the highest density of incident holdings was in an area of approximately 570 square kilometres north west of, and including, the town of Penrith, Figure 3(a). The period 29 March to 23 May was characterised by incident holdings appearing further to the north west and south east of this primary focus, indicative of the disease moving into a population of susceptible holdings, Figure 3(b). From 24 May to 18 July a secondary focus of incident holdings approximately 500 square kilometres in size developed within the triangular area bounded by the M6, A685 and A66 arterial routes, Figure 3(c). Similar to the behaviour noted in the first two periods the distribution of incident holdings in the period 19 July to 12 September shows the disease moving into a population of susceptible holdings which, in this case, were further to the east and west, as shown in Figure 3(d).

Eradication of foot-and-mouth disease in Cumbria proved to be difficult as a result of a number of factors. From 20 February to 28 March large numbers of cattle holdings were infected resulting in a large environmental viral load (Sellers 1971). Although control activities resulted in a rapid drop in infection hazard after 28 March the epidemic remained incompletely controlled. Incomplete control, accompanied by the onset of seasonal farming activities such as shearing and contract hay and silage making facilitated medium to long distance spread of virus and is thought to be at least partly responsible for the steady increase in infection hazard that occurred from 19 April to 15 August. Although not evident from these analyses, where farm holdings have been represented by a single point in space, holdings made up of disaggregated land parcels and the unavoidable movement of animals and animal product between these parcels would have further complicated control efforts in this area (Ferguson *et al.* 2001; Kao 2001).

A critical element in managing a foot-and-mouth disease outbreak is defining the size of pre-emptive culling radii and defining how long surveillance activities should go on for within surveillance zones. If pre-emptive culling radii are large and surveillance periods long control of an epidemic will be theoretically rapid but at the expense of unnecessary use of resources and unnecessary slaughter of stock. Conversely, if pre-emptive culling radii are small and surveillance periods short there is a risk of ongoing local spread and ultimately, a greater number of holdings affected.

Changes in the position of the $D_0(h,t) = 1$ risk contour over evaluated time periods provided insight into the changes in the spatio-temporal interaction of infection that occurred throughout the epidemic. In the context of foot-and-mouth disease epidemiology, increases in the distance of the $D_0(h,t) = 1$ risk contour at $t = 0$ days over successive time periods implies a need to re-assess the effectiveness of control measures aimed at reducing local spread of the disease. Conversely, increases in the temporal position of the $D_0(h,t) = 1$ risk contour at $d = 0$ kilometres suggests that infected holdings are remaining infectious for a longer time interval implying a need to enhance detection, the speed of depopulation and/or cleaning and disinfection procedures. Figures 4(b) shows that for holdings infected between 29 March and 23 May 2001 the $D_0(h,t) = 1$ risk contour extended as far a 3 kilometres from any arbitrarily-selected case at $t = 0$ and this distance steadily declined over a period of approximately three to five days. For holdings infected between 24 May and 18 July the shape of the contour differed somewhat: the $D_0(h,t) = 1$ risk contour persisted at 4 kilometres for seven days, then declined to 0 kilometres by day 15, Figure 4(c). For the period 19 July to 12 September 2001 the $D_0(h,t) = 1$ risk contour took on a similar pattern to that described for 29 March to 23 May 2001, declining from just under 2 kilometres at $t = 0$ days to 0 kilometres at five days.

This said, it appears that whereas the spatial component of spatio-temporal disease risk in Cumbria was never greater than 5 kilometres, the temporal component varied. Given that the process of slaughtering, disposal and disinfection of infected premises was well-established in the Cumbria area early in the epidemic (by 29 March 2001, greater than 50% of infected premises were slaughtered within one day of confirmation) we conclude that the major reason for the increased amount of time infected premises posed a risk to others throughout the May to July period was delays in detection of disease. The movement of the disease into ‘other’ (predominantly sheep) holding types from May to July, where the identification of clinical signs was known to be more difficult (Kitching and Mackay 1995) would have no doubt been influential in accounting for this pattern. In addition, the diagnostic ‘fatigue’ exhibited by many stock owners, and observed by the local veterinary staff at this later stage of the epidemic would have affected the rapidity of reporting of suspicious clinical signs of FMD in all species. This appears to be important, as the epidemic in Cumbria was predominantly a cattle-based outbreak with infection spilling over into sheep flocks in the area.

5.0 CONCLUSIONS

Assessment of the adequacy of response efforts to large-scale infectious disease epidemics in animal populations is based on a synthesis of information accumulated from a variety of sources. Information includes observations made by field staff, details provided by those with local knowledge of the area of investigation and data collected throughout the course of an outbreak (location of holdings infected at a given point in time, number of animals present on infected premises and so on). This paper provides a systematic approach to describing the spatial, temporal and spatio-temporal features of an infectious disease epidemic. Survival analyses allow the temporal evolution of the epidemic to be described, accounting for a population at risk that is under constant change. Extraction maps describe the spatial distribution of disease, accounting for the heterogenous geographical distribution of the population at risk, and the space-time K-function provides insight into the components of spatio-temporal disease risk, removing the confounding influence of disease spread attributable to the separate influences of space and time. We conclude that 'suites of analyses' of this type provide valuable supportive evidence to field observations and opinions concerning factors that may be influencing the spread of disease. With these factors known and understood, emerging changes in epidemic behaviour can be identified promptly and appropriate action taken, as individual circumstances dictate.

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