Available online at www.sciencedirect.com
SCIENCE DIRECT
ELSEVIER
Preventive Veterinary Medicine 71 (2005) 209–223
PREVENTIVE VETERINARY MEDICINE
www.elsevier.com/locate/prevetmed

Temporal and spatial analysis of the 1999 outbreak of acute clinical infectious bursal disease in broiler flocks in Denmark

J. Sanchez [a,*], H. Stryhn [a], M. Flensburg [b], A.K. Ersbøll [c], I. Dohoo [a]

[a] *Department of Health Management, Atlantic Veterinary College, UPEI, 550 University Avenue, Charlottetown, PEI, Canada C1A 4P3*
[b] *EpiConsult ApS, Hørkær 14, DK-2730 Herlev, Denmark*
[c] *The Royal Veterinary and Agricultural University, Department of Large Animal Sciences, Grønnegårdsvej 8, DK-1870, Frederiksberg C, Denmark*

Abstract

The objective of this study was to describe the spatial and temporal dynamics of the 1999 outbreak of acute clinical infectious bursal disease (IBD) in broiler chicken farms in Denmark. The analysis was performed using data from all broiler farms located in the Jutland peninsula and the island of Funen (168 municipalities). The Moran's index *I*, *K*-functions and scan statistics were used to describe the dynamics of the epidemic. In addition, spatially correlated survival analyses were performed and the posterior frailties were mapped to identify areas with high or low survival times. From January to October 1999, a total of 43 farms (81 flocks) out of a total of 299 farms (2970 flocks) in 110 municipalities were infected with IBD. The outbreak developed more or less simultaneously in two regions, one in the north and the other in the center of the study area. The space–time descriptive methods suggested that the cases were more likely to occur during a short period of time and over relatively short distances, indicating that local factors facilitated the spread of the virus. For instance, the highest risk, as estimated by the *K*-function, was within 20 km and 20 days. The risk of transmission peaked in July and remained high until the end of the study. The spatially correlated survival analysis identified municipalities with low survival times that roughly corresponded to the

* Corresponding author. Tel.: +1 902 566 0803; fax: +1 902 566 0823.
E-mail address: jsanchez@upei.ca (J. Sanchez).

0167-5877/$ – see front matter
doi:10.1016/j.prevetmed.2005.07.006

clusters found using scan statistics. The analysis for the full hierarchical structure of the dataset identified variation (i.e. clustering) at the farm and municipality levels.

Keywords: IBD; Gumboro; *K*-function; Scan statistic; Moran's *I*; Frailty; Survival analysis

1. Introduction

Infectious bursal disease (IBD), a highly contagious viral poultry disease (also known as Gumboro disease), is a major global concern to the poultry industry. The economic impact of this disease is related to losses due to mortality, growth retardation or rejection of carcasses (van den Berg, 2000). A 10-year simulation study of broiler chicken farms in New Zealand suggested that the introduction of classical IBD might cause a loss of US$ 10 million per year (Christensen, 1985). Approximately 3 days after infection with the virus, the acute clinical form of IBD causes mortalities of up to 25% in broiler chickens and 60% in layers. Only the horizontal transmission of this disease has been described (van den Berg, 2000). The virus is excreted in the feces 48 h post-infection and it may be transmitted for a period of 16 days after that. Although contact with feces from infected birds is the main factor involved in the transmission of IBD, other factors such as wild birds (Ogawa et al., 1998) or rodents might also play a role in spreading the disease (Edgar and Cho, 1976). IBD was first reported in broiler chickens in Denmark in 1992, affecting 11 farms but was subsequently eliminated by a vaccination strategy. In 1998 and 1999, IBD was reintroduced in two apparently unrelated outbreaks affecting a larger number of broiler chicken farms (Flensburg, 2001). The 1998 data have been analyzed using logistic regression (Flensburg et al., 2002). Also, a risk factor analysis in a nested case-control design for the 1999 data investigated the effects of covariates related to hatchery of origin, feed mills, and slaughterhouse system while accounting for local infection spread (Flensburg et al., 2000); however, this study did not involve spatial or spatio-temporal statistics.

The study of the distribution of disease occurrence in space and time is one of the bases of epidemiology, with two of the major approaches being disease mapping and investigation of disease clustering (Lawson et al., 2003). Descriptive statistics and tests can be used to quantify clustering in space, time and space–time as well as to assess the statistical significance of clustering and of specific clusters detected. These methods apply to area (count) data (e.g. Moran's *I*) or to point data (e.g. scan statistics and the *K*-function) or to both data types; see Ward and Carpenter (2000) and Carpenter (2001) for reviews in the context of veterinary epidemiology.

Disease mapping produces maps of the estimated risk of a disease across a geographical area, and generally aims at elucidating the spatial distribution of disease and identifying areas with low or high rates. The maps are usually drawn using regional administrative units such as provinces, counties or municipalities. The underlying data often, in particular in human health studies, consist of the number of events and the population at risk within these areas. Such data lead to Poisson distribution models with the extra-Poisson variation represented by random effects of spatial or non-spatial character. In veterinary

epidemiology, point data are common and when the outcome of interest is the time-to-event, these may be analyzed by survival models incorporating random effects to account for unobserved heterogeneity in survival time or hazard rates. In both situations, the preferred statistical approach is Bayesian with Markov chain Monte Carlo (MCMC) estimation, due to the complexity of the spatial models involved. A popular spatial, lattice model based on a given neighborhood relationship is the conditional autoregressive (CAR) model (Besag et al., 1991; Mollié, 1996). In this model, the conditional mean of the relative risk (or hazard), in a given area, is a weighted average of the neighboring relative risks, while the conditional variance is inversely proportional to the sum of neighbor weights. Temporal trends and spatio-temporal interactions have been incorporated into this framework (Waller et al., 1997; MacNab and Dean, 2002). Several recent studies have used similar parametric and semi-parametric survival models (Henderson et al., 2002; Banerjee et al., 2003; Banerjee and Carlin, 2003), where the resulting posterior frailties are plotted and compared among different areas to identify spatial, temporal and spatio-temporal trends. In addition, the effect of different covariates in explaining the observed frailty patterns can be assessed in these models.

The primary objective of the present study was to describe the temporal and spatial distribution of the outbreak of IBD in broiler chicken farms in Denmark during 1999. As the broiler chicken production is highly hierarchically structured, with flocks housed in separate production houses at each broiler chicken farm, a secondary objective was to review how spatial statistical methods should properly be applied to the hierarchically structured data. Particular consideration was given to whether analyses should be performed at the farm, house or flock level.

2. Materials and methods

2.1. Study population

The study area consisted of all municipalities located in the Jutland peninsula and the island of Funen in Denmark. The geographical coordinates of all broiler chicken farms in the study region were obtained from the Danish Central Husbandry Registry (CHR). In addition to the location of the farms, the hatchery date and slaughter date were retrieved from the Danish antemortem and postmortem databases, as described previously (Flensburg et al., 2002). The date of disease outbreak was defined as the first day with elevated mortality in the daily record of deaths in each broiler chicken house. The study population included all flocks in the study area slaughtered between 1 January and 30 October 1999. Houses and farms were considered continuously at risk until the first outbreak of IBD (at the house or farm) or the slaughter date of the last flock slaughtered within the study period.

2.2. Analytical methods

Temporal, spatial and spatio-temporal descriptive analyses as well as different types of survival analyses were performed to investigate the dynamics of the outbreak.

2.3. Descriptive analysis

Cluster detection was carried out using scan statistics based on Poisson models for farm outcomes that were either dichotomous (farm model) or counts of the number of houses infected and at risk (house model), respectively (Kulldorff, 1997). Time and space scan windows were set at 10% of the study period (303 days) and 10% of the population at risk, as described in Hjalmars et al. (1996). These analyses used the SaTScan software, version 4.0 (Kulldorff, 2003).

Spatial correlation between municipalities was assessed by Moran's I in a version adjusted for population density (Empirical Bayes Index; Assuncao and Reis, 1999), because of the small and variable number of farms in a municipality. The index may be thought of as a correlation between the prevalence of IBD-infected farms in neighboring municipalities. The neighbor relationships were represented by a binary adjacency weight matrix. In addition, spatial correlation between farms was estimated by a point-data version of Moran's I, using the proportion of infected houses at each farm. The neighbor weights were inverse distances between farms within 13 km—the minimal distance for every farm to have at least one neighbor. Statistical significance of the attained value of I was assessed by a permutation (Monte Carlo) test using 999 simulations in which the P-value equaled the proportion of times the actual value was exceeded in the simulations. The null hypothesis of the test was that the prevalences are either constant or heterogeneous but spatially uncorrelated. These analyses used the SPDEP library (Bivand, 2002) within the R statistical package (Ihaka and Gentleman, 1996).

Space–time interaction was assessed using the K-function (Diggle et al., 1995). This was implemented in the SPLANCS library (Rowlingson and Diggle, 1993; Bivand and Gebhardt, 2000) within the R package, based on the cumulative numbers of IBD-outbreak farms within a given distance and time interval. Specifically, the relative increase in cases attributable to space–time interaction, D_0, was computed as a ratio between the observed cumulative number of cases minus the expected number of cases (if no space–time interaction was present), divided by the latter quantity. Values of $D_0 > 0$ indicated the presence of a space–time interaction, and values of $D_0 \geq 1$ indicated at least a doubling of the observed number relative to the expected number of cases. The calculations were carried out using an equidistant 20×8 grid of space and time values ranging from zero up to 40 km and 80 days, respectively. A similar house-level analysis was enabled by artificially declustering the house locations by small distances (as the houses were not geo-referenced separately). The statistical significance for the presence of space–time interaction was assessed by a permutation test using 999 simulations, as described above. Although the K-function derives from the theory of stationary point processes, the permutation test is valid for a nonstationary underlying process (Diggle et al., 1995).

2.4. Survival analysis

Initially, a Kaplan–Meier product limit estimate of the daily farm level hazard, since the beginning of the study period, was plotted to visualize the presence of any pattern over time. Parametric survival models were fit to the farm level survival times, and a log-normal distribution of survival times was chosen for further modelling because of its slightly better

fit than the more commonly used Weibull distribution and its ability to adapt to a non-monotonic hazard function.

The farm level models included the number of houses (categorized as 1, 2 and $\geq$3 houses) as a predictor, whereas the house level models had no predictors. Random effects (frailties) were incorporated for the municipalities, and in the house level analysis for the farms, corresponding to the hierarchical data structure. The municipality random effects could either be unstructured (i.e. independent) or spatially structured (i.e. spatially correlated) in a conditional autoregressive (CAR) model.

Specifically, in the unstructured model the mean survival time (μ_i) of farm i was expressed as $\ln(\mu_i) = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \theta_{\mathrm{mun}(j)}$, where x_1 and x_2 were indicator variables representing the fixed effects of the number of houses, the β's were regression coefficients, and the θ_j's were municipality random effects assumed to follow an $N(0, \sigma_u^2)$ distribution. In the spatially structured model, the set of municipality random effects term (θ_j) was specified by the conditional distributions: $\theta_J|\theta_{k\neq j} \sim N(a_j, \sigma_j^2)$ with the conditional mean and variance given as $\alpha_j = \sum w_{jk}\theta_k / \sum w_{jk}$ and $\sigma_j^2 = \sigma_s^2 / \sum w_{jk}$. The neighborhood weights (w_{jk}) were binary, so that $w_{jk} = 1$ for municipalities with a common boundary, and $w_{jk} = 0$ otherwise. House level models were similar but could have additional farm level random effects.

The statistical modelling and analysis was carried out in a Bayesian framework using non-informative prior distributions for all parameters. The priors were as follows: a gamma(0.01, 0.01) distribution for $1/\sigma_s^2$, gamma(0.001, 0.001) distributions for all other inverse variance parameters (the variance parameter of the log-normal survival distribution, and shared frailty variance parameters), and an N(0, 1/10,000) distribution for the regression coefficients in the farm level model. (According to recent recommendations (Lawson et al., 2003), we used an improper flat prior for the intercept β_0; however, the results were unaffected by shifting to a N(0, 1/10,000) distribution).

The statistical inference was based on Markov chain Monte Carlo simulations as implemented in the WinBUGS software, version 1.4 (Gilks et al., 1994). The posterior median frailties were monitored and used for mapping the results by municipalities. For all the models three chains were run with different starting values; the burn-in period was 10,000 iterations and the estimation sample comprised 10,000 values after a thinning of the chains by a factor 10. Convergence was assessed using correlation plots, sample trace plots, and the Gelman–Rubin statistic modified by Brooks and Gelman (1998). The deviance information criterion (DIC; Spiegelhalter et al., 2002) was used to compare the fit of models for the same dataset in a similar fashion as in Henderson et al. (2002) and Banerjee and Carlin (2003).

3. Results

The data comprised a total of 2970 flocks reared in 673 houses on 299 farms (1–16 houses per farm) in 110 municipalities. A total of 81 flocks/houses on 43 farms in 22 municipalities were diagnosed with IBD during the study period (Fig. 1). Fig. 2 depicts the case farms with the size of the pie proportional to the total number of positive houses. The first reported case was on 28 February and the last on 19 October. Twelve farms experienced more than one outbreak; the median time between outbreaks in those farms was 3 days (range: 1–7 days). The median age of the broiler chickens at the onset of the

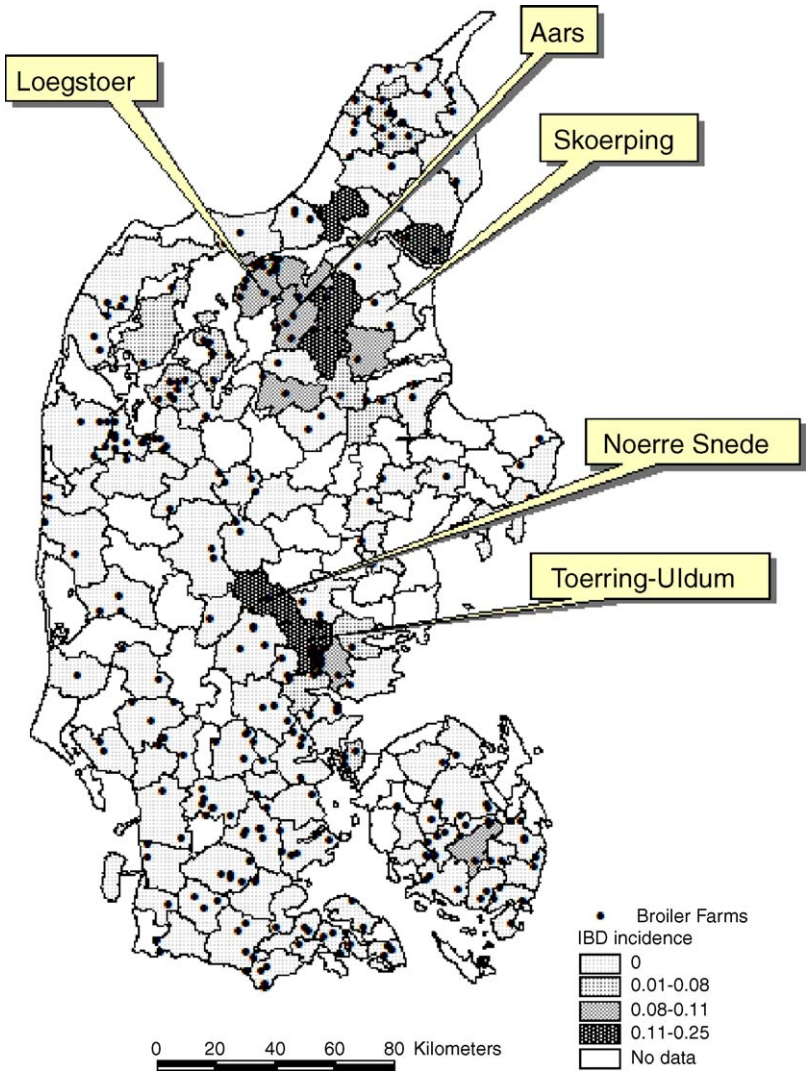

Fig. 1. Incidence and distribution of the 299 broiler chicken farms in Jutland and Funen during the 1999 IBD outbreak in Denmark. Municipality names show cluster centers identified by the scan statistic.

outbreak was 35 days and ranged from 17 to 54 days. The production time from hatchery to slaughter was, on average, 39 days and ranged from 31 to 59 days, while the average empty period between flocks was 14 days and ranged from 2 to 80 days.

3.1. Descriptive analyses

Overall, the hazard was approximately constant until the beginning of June, and from then on it increased (Fig. 3). The fact that the epidemic declined towards the end of the

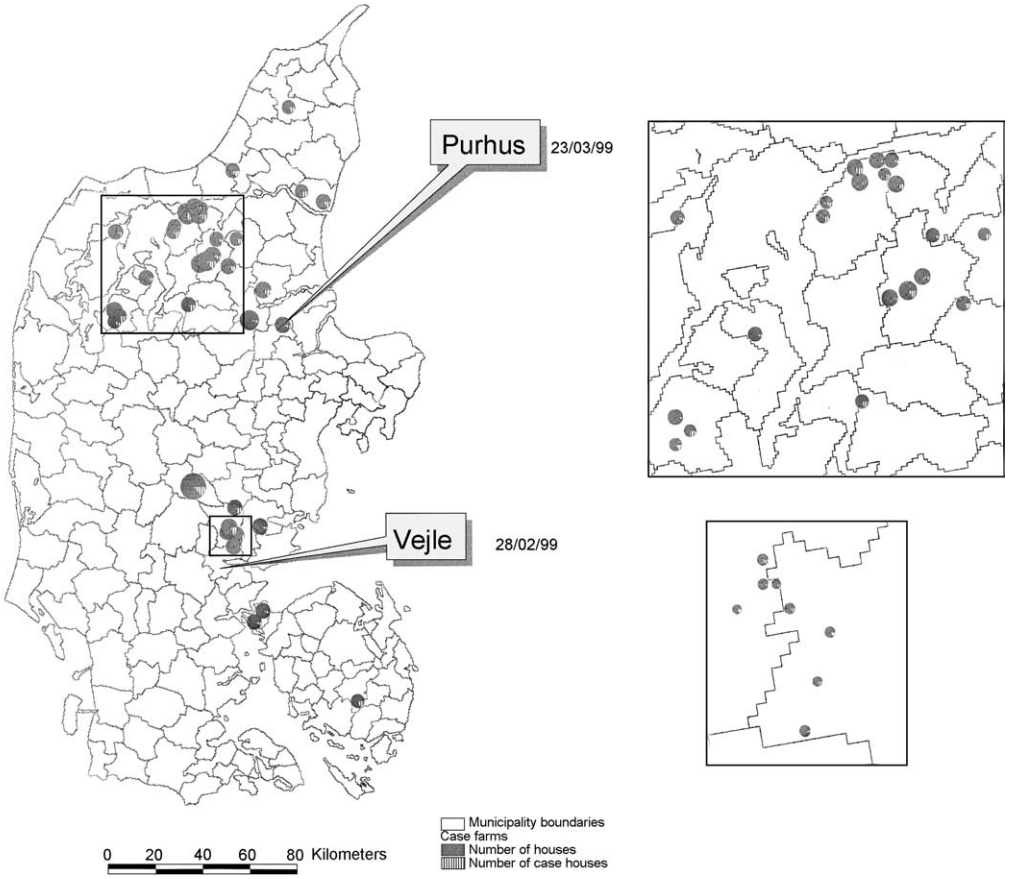

Fig. 2. Location of IBD case-farms in Denmark during the 1999 outbreak. The pies are sized proportional to the number of flock-houses in each farm and the slices represent the number of infected houses. Municipality names and dates represent the first IBD farm-cases for the south and north regions.

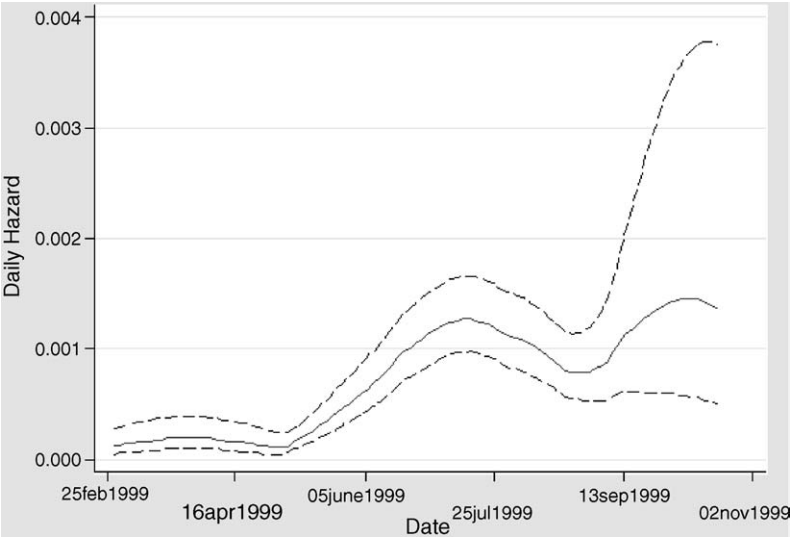

Fig. 3. Estimated daily farm-level hazard (with 95% CI) of IBD infection during the 1999 IBD outbreak in Denmark.

study period was to some extent masked by the censoring of farms at the end of the study period. Both versions of the temporal scan statistic reported a highly significant temporal cluster of length about 1 month, starting at 10 July.

Moran's *I*, adjusted for the population at risk, was 0.34 ($P = 0.001$) and 0.15 ($P = 0.001$) for the area and point analyses, indicating a moderate and significant spatial dependence between municipalities and farms, respectively. The space–time scan statistic detected two or four clusters depending on the model used (Table 1; Fig. 1). The farm level version of the space–time scan statistic identified the municipalities of Aars and Toerring-Uldum (Fig. 1) as centers of the two most likely clusters ($P < 0.001$ and <0.01), with radii of 21.8 and 1.7 km and including 25 and 6 case farms, respectively. Three additional clusters were identified when accounting for number of houses in the space–time scan statistic. The most likely cluster was one farm reporting 13 cases in the municipality of Noerre Snede (Fig. 1; Table 1). The first secondary cluster (Loegstoer) was close in time and space to the most

Table 1
Statistically significant clusters ($P < 0.01$) detected by the space–time scan statistic for the 1999 IBD outbreak in Denmark

Model (see text)	Cluster center	Radius (km)	Cluster period (day/month)	Number of farms	Number of cases		*P*
					Observed	Expected	
Farm	Aars	21.81	28/June–25/July	25	10	0.33	0.001
	Toerring-Uldum	1.67	12/July–1/August	6	5	0.06	0.003
House	Noerre Snede	0.0	12/June–18/June	1	13	0.04	0.001
	Loegster	15.74	3/July–23/July	16	14	0.28	0.001
	Skoerping	30.53	31/July–3/September	11	14	0.42	0.001
	Toerring-Uldum	2.18	10/July–6/August	6	8	0.11	0.001

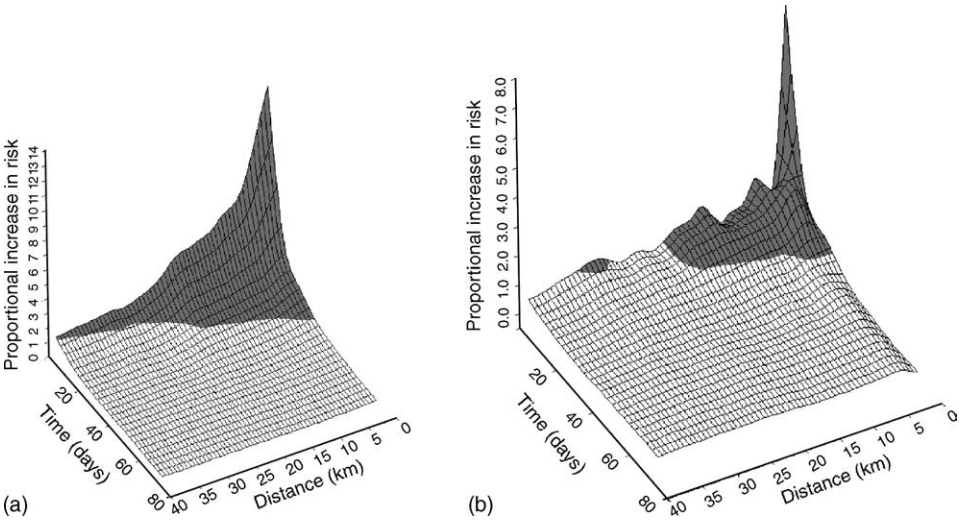

Fig. 4. Spatio-temporal interaction plots of IBD risk among infected houses/farms during the 1999 IBD outbreak in Denmark. The dark-shaded area shows the distance–time separations where the observed number of cases exceeded at least twice the number expected. (a) House level and (b) farm level.

likely cluster identified for the farm model (Fig. 1). Both models identified one small cluster in the municipality of Toerring-Uldum. The municipality of Skoerping was only identified for the house level model at the end of the study period.

The space–time K-function showed different patterns according to level of analysis (Fig. 4), the D_0's ranged from 0.1 to 13.6 and from −0.1 to 7.6 for the house and farm level analyses, respectively. The highest risks were observed within a distance of 20 km and during the first 20 days for the house and farm analyses. The permutation tests for space–time interaction had corresponding one-sided P-values of <0.001 and <0.002, respectively.

Table 2
Deviance, effective number of parameters (pD) and deviance information criterion (DIC) values of survival models (see text) at the farm and house levels for the 1999 IBD outbreak in Denmark

Model (level and description)	Deviance	pD	DIC
Farm			
No random effects	686.34	3.91	690.25
Structured heterogeneity (municipality)	586.54	34.68	621.22
Unstructured heterogeneity (municipality)	580.25	40.73	620.98
Structured and unstructured heterogeneity (municipality)	582.80	35.59	618.39
House			
No random effects	1326.90	1.94	1328.84
Structured heterogeneity (municipality)	1103.74	36.87	1140.62
Unstructured heterogeneity (farm)	1060.79	80.77	1141.56
Unstructured heterogeneity (municipality)	1101.33	38.63	1139.97
Unstructured heterogeneity (farm) + structured heterogeneity (municipality)	1058.25	60.27	1118.52

Table 3
Summary statistics of posterior distributions from Bayesian analysis of survival models at the farm level for the 1999 IBD outbreak in Denmark

	Model					
	Structured heterogeneity			Unstructured heterogeneity		
	2.5%	50%	97.5%	2.5%	50%	97.5%
Parameter						
β_0 (intercept)	6.50	6.94	7.61	6.42	6.83	7.45
β_1 (2 vs. 1 house)	−0.46	−0.09	0.29	−0.44	−0.11	0.20
β_2 ($\geq$3 vs. 1 house)	−0.83	−0.46	−0.12	−0.85	−0.51	−0.22
σ^a	0.39	0.52	0.71	0.37	0.48	0.66
σ_s	0.70	1.23	2.05	–	–	–
σ_u	–	–	–	0.48	0.76	1.22

σ_s = standard deviation of the structured municipality random effects, σ_u = standard deviation of the unstructured municipality random effects.

3.2. Spatially correlated survival analysis

The median observed days at risk was 258 days (range: 58–300 days) for the farm level analysis and 257 days (range: 54–300 days) for the house level analysis. The fit of the models is presented in Table 2. The DIC is defined similarly to the AIC as the expected deviance plus the expected number of effective parameters (pD). Small values of the deviance indicate a good fit, and small values of pD indicate a parsimonious model. The

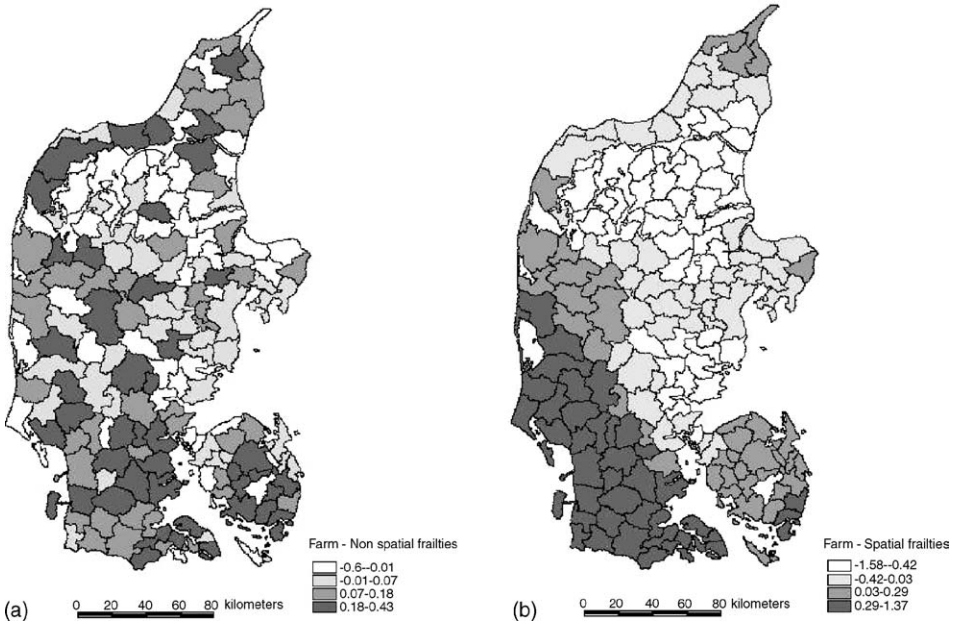

Fig. 5. Posterior median frailties of the IBD survival models at the farm level model with (a) unstructured and (b) structured heterogeneity for the 1999 IBD outbreak in Denmark.

Table 4
Summary statistics of posterior distributions from Bayesian analysis of survival models at the house level, including unstructured farm and structured municipality heterogeneities, for the 1999 IBD outbreak in Denmark

	2.5%	50%	97.5%
Parameter			
β_0 (intercept)	6.54	6.91	7.54
σ^a	0.34	0.41	0.52
σ_{farm}	0.15	0.33	0.53
σ_s	0.70	1.21	2.03

σ_{farm} = standard deviation of the unstructured farm random effects, σ_s = standard deviation of the structured municipality random effects.
[a] σ = standard deviation of the natural log of survival times.

models that included random effects gave a much better fit than the non-random effects models. In the farm level analysis, the model including two random effects had essentially the same DIC as both of the models including a single random effect (unstructured or structured). The parameter estimates from the models with structured and unstructured heterogeneity are shown in Table 3. Predicted median survival times for different farm types ranged from 135 to 4038 days and from 121 to 1317 days from the structured and unstructured random effects models, respectively. These large values reflect the small number of failures (cases) in the dataset, and the fact that the spatial smoothing of the structured random effect leads to low predicted frailties far away from the outbreak centers. Farms with three or more houses had a markedly shorter survival time compared with farms with only one house; the difference between one and two houses was less clear. The posterior median frailties for the models at the farm level with unstructured and structured heterogeneity are depicted in Fig. 5. The house level models with a single random effect either at municipality or farm level presented similar fit. However, the model including unstructured farm and structured municipality heterogeneities had the lowest DIC (Table 2). Table 4 gives the estimates from this model. When combining two frailties at the municipality level in a model, the Markov chains behaved less well, possibly an indication of identifiability problems (Eberly and Carlin, 2000).

4. Discussion and conclusion

4.1. Outbreak of IBD

The most striking overall feature of the IBD outbreak was that it involved two separate clusters, one in the north and one in the center of the study area (Fig. 1). The outbreaks developed more or less simultaneously in these two regions (Table 1). The first two observed cases were in the central region, but the third case was in the northern region, 1 month later (Fig. 2). In total, more farms were affected in the northern region.

The space–time descriptive methods suggested that the cases were more likely to occur during a short period of time and distance, indicating that local factors probably facilitated the spread of the virus. The transmission risk, as estimated by the *K*-function (Fig. 4), was highest within 20 km and 20 days. Such local factors could be traffic, wilds birds or

airborne transmission (Edgar and Cho, 1976). It has been suggested that the transport of feed from infectious farms to susceptible flocks may play an important role in the disease transmission. Flensburg et al. (2002) showed a significant association between IBD and feed mills, possibly reflecting that geographically close farms are visited by the same feed trucks during a short time interval. Flensburg et al. (2000) also found an increased risk of IBD associated with slaughter and partial slaughter at some abattoirs.

The risk of transmission peaked in July. This seasonal pattern of the disease may be the result of environmental factors that increase the probability of infection during the summer months. The presence of wild birds during these months might also contribute to the occurrence of IBD, as serological surveys suggest a possible role of feral birds as a reservoir for IBD (Ogawa et al., 1998).

The data also showed a strong within-farm clustering (in the survival analysis; Table 4). In total, 62% of the cases occurred in 12 out of the 43 farm-cases. The short time (1–7 days) observed between outbreaks at the same farm agrees with incubation times described for IBD (van den Berg, 2000). Such short incubation periods, in combination with the observed outbreak patterns, made it unlikely that the outbreak developed from a single source.

4.2. Spatial statistical methods

Both the descriptive spatial statistics and the survival models involved some assumptions whose impacts on the results were difficult to assess. The houses were assumed to be continuously at risk even if the study period included empty periods. Aged chickens could be important as they were more likely to show clinical signs between 3 and 6 weeks of age (van den Berg, 2000). Also, edge effects in the map and the neighbor relations (mainly due to locations bordering on the sea) conflict with assumptions of stationarity (e.g. for the *K*-function) and may cause problems in the interpretation of CAR model parameters (Wall, 2004). However, the different statistical approaches gave a consistent picture of the outbreak. For example, the relatively low values of Moran's *I* seem to agree well with the relatively localized transmission risks of the *K*-function and the moderate spatial dependence in the survival models. Also, the municipalities with shorter predicted survival times corresponded closely with the clusters identified by the scan statistic (Figs. 1, 5 and 6).

Among the descriptive statistics, analyses at the house and farm levels gave similar results, although the farm-level clustering inherent in the house-level data was not directly accounted for. This applied to the *K*-function estimated from house-level data where the extreme peak at close distance was an artifact generated by the multiple houses at the same farm (Fig. 4). Another example of within-farm correlation was the spatio-temporal cluster detected by the scan statistic that involved multiple outbreaks at a single farm (Table 1). In this case, the inherent stationary Poisson distribution is clearly invalidated. This example also illustrates the more general problem of applying spatial methods to a highly contagious disease, as opposed to their applications in human health for non-infectious diseases. The only statistical procedure applied to both point and area data was Moran's *I* with a higher value obtained from the latter showing how the magnitude of clustering depends on the level of aggregation.

The survival models clearly indicated the need for random effects but were less clear as to which form was preferable. The farm-level models suggested the presence of regional

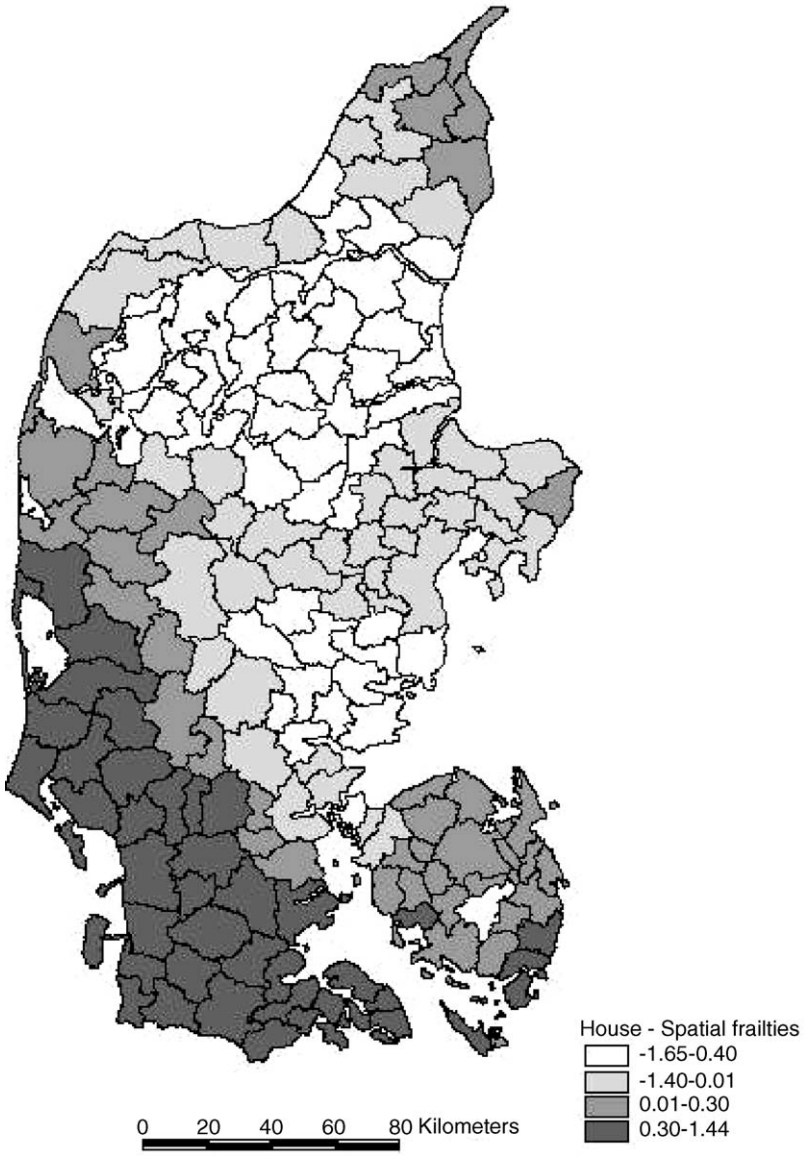

Fig. 6. Posterior median spatial frailties of the IBD survival model at the house level with structured municipality heterogeneity and unstructured farm heterogeneity for the 1999 outbreak in Denmark.

areas with low survival times in agreement with localized patterns in the *K*-function. Generally, studies reported in the literature showed better fits by the CAR model (Waller et al., 1997; Banerjee et al., 2003; Banerjee and Carlin, 2003). One possible explanation is the sparseness of the present data, in contrast to the large-scale human health observational studies. As expected, a somewhat higher degree of smoothing was seen in the CAR model,

especially for municipalities with an outbreak surrounded by non-case municipalities (Fig. 5, south-eastern municipalities). The estimated frailty standard deviation was smaller when adjusting for an average of five neighbors in the CAR model; the median adjusted standard deviation would be $1.23/\sqrt{5} = 0.55$ versus 0.76 for the unstructured heterogeneity. The house-level model allowed us to take into account the full hierarchical structure, and the best model fit was obtained with random effects for both farm and municipality (CAR model). The plotted frailties of this model showed a very similar pattern (Fig. 6) compared with the farm-level model with structured heterogeneity. The structured municipality standard deviation was roughly twice the unstructured farm standard deviation indicating that the between-farm variation was smaller than the variation between municipalities. The municipality random effects were of the same magnitude as in the farm-level model. The number of houses was a significant predictor but it was not able to explain the spatial distribution of the outbreak.

A potential drawback reported with a district level modelling approach, as it was used in the present survival analysis, is the possibility of ecological bias, whereby the same municipality effect is assumed to apply to all the farms (Henderson et al., 2002). An alternative approach has been suggested by Henderson et al. (2002), where correlations are modeled as a function of distance between point locations rather than by a lattice neighborhood structure. The authors compared a district-level analysis with a point-level approach to investigate the spatial variation in survival of leukemia patients. Although, the latter produced more dispersed parameter estimates, the two models predicted a very similar frailty surface. The sparse data renders estimation of a semi-variogram and distance-based correlations difficult, so this approach was not pursued here.

We have presented a temporo-spatial analysis of the 1999 IBD outbreak in Denmark and an attempt to model the spatial variation in time to outbreak of IBD in broiler farms. All the methods indicated that this outbreak was spatially focal and seasonal. The survival analysis indicated the relative importance of sources of variation (i.e. municipality and farm) and the geographical location of the highest risk areas after accounting for the complete hierarchical structure of the dataset. The results showed overall trends in the dynamics of this outbreak and identified geographical regions in which to target further investigation.

References

Assuncao, R.M., Reis, E.A., 1999. A new proposal to adjust Moran's *I* for population density. Statist. Med. 18, 2147–2162.

Banerjee, S., Carlin, B.P., 2003. Semiparametric spatio-temporal frailty modeling. Environmetrics 14, 523–535.

Banerjee, S., Wall, M.M., Carlin, B.P., 2003. Frailty modeling for spatially correlated survival data, with application to infant mortality in Minnesota. Biostatistics 4, 123–142.

Besag, J., York, J., Mollié, A., 1991. Bayesian image restoration, with two applications in spatial statistics. Ann. Inst. Statist. Math. 43, 1–59.

Bivand, R., 2002. Spatial econometrics functions in *R*: classes and methods. J. Geograph. Syst. 4, 405–421.

Bivand, R., Gebhardt, A., 2000. Implementing functions for spatial statistical analysis using the *R* language. J. Geograph. Syst. 2, 307–317.

Brooks, S., Gelman, A., 1998. General methods for monitoring convergence of iterative simulations. J. Comput. Graph. Statist. 7, 434–455.

Carpenter, T.E., 2001. Methods to investigate spatial and temporal clustering in veterinary epidemiology. Prev. Vet. Med. 48, 303–320.

Christensen, N.H., 1985. The cost to the meat chicken industry of the introduction of infectious bursal disease to New Zealand. NZ Vet. J. 33, 191–193.

Diggle, P.J., Chetwynd, A.G., Haggkvist, R., Morris, S.E., 1995. Second-order analysis of space–time clustering. Statist. Meth. Med. Res. 4, 124–136.

Eberly, L.E., Carlin, B.P., 2000. Identifiability and convergence issues for Markov chain Monte Carlo fitting of spatial models. Statist. Med. 19, 2279–2294.

Edgar, S.A., Cho, Y., 1976. The epizootiology of infectious bursal disease and prevention of it by immunization. Dev. Biol. Stand. 33, 349–356.

Flensburg, M.F., 2001. Epidemiological evaluation of the viral diseases in the Danish broiler chicken production using the example of infectious bursal disease and newcasttle disease. PhD Thesis. The Royal Veterinary and Agricultural University.

Flensburg, M.F., Ersbøll, A.K., Jørgensen, P.H., 2002. Risk factors associated with the introduction of acute clinical infectious bursal disease among Danish broiler chickens in 1998. Avian Pathol. 31, 23–29.

Flensburg, M.F., Stryhn, H., Jørgensen, P.H., 2000. Epidemiological risk factor analysis for outbreak of acute, clinical IBD among Danish broiler chickens in Denmark in 1999. Report. Danish Poultry Meat Association (in Danish).

Gilks, W.R., Thomas, A., Spiegelhalter, D.J., 1994. A language and program for complex Bayesian modelling. The Statistician 43, 169–177.

Henderson, R., Shimakura, S., Gorst, D., 2002. Modeling spatial variation in leukemia survival data. J. Am. Statist. Assoc. 97, 965–972.

Hjalmars, U., Kulldorff, M., Gustafsson, G., Nagarwalla, N., 1996. Childhood leukaemia in Sweden: using GIS and a spatial scan statistic for cluster detection. Statist. Med. 15, 707–715.

Ihaka, R., Gentleman, R., 1996. *R*: a language for data analysis and graphics. J. Comput. Graph. Statist. 5, 299–314.

Kulldorff, M., 1997. A spatial scan statistics. Commun. Statist.: Theory Meth. 26, 1481–1496.

Kulldorff, M., 2003. SaTScan v4. 0: Software for the Space and Space–Time Scan Statistics Information Management Services, Inc., http://www.satscan.org.

Lawson, A.B., Browne, W.J., Vidal Rodeiro, C.L., 2003. Disease Mapping with WinBUGS and MLwiN. John Wiley & Sons, Chichester, UK.

MacNab, Y.C., Dean, C.B., 2002. Spatio-temporal modelling of rates for the construction of disease maps. Statist. Med. 21, 347–358.

Mollié, A., 1996. Bayesian mapping of disease. In: Gilks, W.R., Richardson, S., Spiegelhalter, D.J. (Eds.), Markov Chain Monte Carlo in Practice. Chapman & Hall/CRC Press, London, pp. 359–376.

Ogawa, M., Wakuda, T., Yamaguchi, T., Murata, K., Setiyono, A., Fukushi, H., Hirai, K., 1998. Seroprevalence of infectious bursal disease virus in free-living wild birds in Japan. J. Vet. Med. Sci. 60, 1277–1279.

Rowlingson, B.S., Diggle, P.J., 1993. SPLANCS: spatial point pattern analysis code in S-PLUS. Comput. Geosci. 19, 627–655.

Spiegelhalter, D.J., Best, N.G., Carlin, B.P., 2002. Bayesian measures of model complexity and fit. J. R. Statist. Soc. B 64, 583–639 (with discussions).

van den Berg, T., 2000. Acute infectious Bursal disease in poultry, A review. Avian Pathol. 29, 175–194.

Wall, M.M., 2004. A close look at the spatial structures framework for ecological and aggregate studies. J. Statist. Plan. Infer. 311–324.

Waller, L.A., Carlin, B.P., Xia, H., Gelfand, A.E., 1997. Hierarchical spatio-temporal mapping of disease rates. J. Am. Statist. Assoc. 92, 607–617.

Ward, M.P., Carpenter, T.E., 2000. Techniques for analysis of disease clustering in space and in time in veterinary epidemiology. Prev. Vet. Med. 45, 257–284.