Epidemiol. Infect. (2004), **132**, 495–505. © 2004 Cambridge University Press
DOI: 10.1017/S0950268803001729 Printed in the United Kingdom

GIS-supported investigation of human EHEC and cattle VTEC O157 infections in Sweden: Geographical distribution, spatial variation and possible risk factors

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(*Accepted 23 October 2003*)

SUMMARY

This article describes the spatial and temporal distribution of verotoxin-producing *Escherichia coli* among humans (EHEC) and cattle (VTEC) in Sweden, in order to evaluate relationships between the incidence of EHEC in humans, prevalence of VTEC O157 in livestock and agricultural structure by an ecological study. The spatial patterns of the distribution of human infections were described and compared with spatial patterns of occurrence in cattle, using a Geographic Information System (GIS). The findings implicate a concentration of human infection and cattle prevalence in the southwest of Sweden. The use of probability mapping confirmed unusual patterns of infection rates. The comparison of human and cattle infection indicated a spatial and statistical association. The correlation between variables of the agricultural structure and human EHEC incidence was high, indicating a significant statistical association of cattle and farm density with human infection. The explained variation of a multiple linear regression model was 0·56.

INTRODUCTION

Since their emergence and the first described foodborne outbreak of human illness caused by enterohaemorrhagic *Escherichia coli* (EHEC) in the United States in 1982 [1], which was traced to hamburgers from a fast-food chain, several outbreaks and numerous sporadic EHEC infections have occurred worldwide [2]. EHEC became one of the major foodborne pathogens, especially in industrialized countries with a highly developed food industry like the United States, Japan, Germany, United Kingdom and Sweden. Several large outbreaks, high infectivity and severity of the disease, especially in children under 5 years and elderly people, contribute to the high impact on public health. EHEC are seen as the most important group of emerging foodborne pathogens [3].

EHEC are toxin-producing [Shiga-like toxins (STEC) also referred to as verotoxin (VTEC)] serotypes of *Escherichia coli* bacteria known to be associated with a wide spectrum of clinical human illnesses, from asymptotic shedding, watery or bloody diarrhoea, haemorrhagic colitis to the haemolytic–uraemic syndrome (HUS) [2]. EHEC are the major cause of HUS, the most common cause of acute renal failure in children [4]. The serotype most frequently associated with human infection is EHEC O157. Nevertheless, there have also been outbreaks and sporadic cases associated with other serotypes [5–7].

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Administration of antibiotics may precipitate HUS [2], so that treatment of infected people remains supportive. Currently, there is no vaccination available against the infection [8]. Under these circumstances, the understanding of the epidemiology and factors that may influence the emergence of the disease, and prevention of infection, is important for the public health authorities [9].

E. coli O157 are regularly isolated from their main reservoir, clinically healthy cattle and other ruminants. The World Health Organization (WHO) emphasized that in view of the high prevalence (up to 28%) in cattle [10] the eradication in livestock does not appear to be feasible [11]. They are transmitted to humans via the faecal–oral route through an increasing variety of foods, predominantly from bovine products like undercooked meat or unpasteurized milk to contaminated vegetables or apple cider [9, 12]. Contaminated drinking water or recreational water can also serve as a vehicle for transmitting infections [13, 14]. Even the swallowing of small amounts of contaminated water may cause illness, since the infectious dose has been reported to be as low as approximately 10 bacteria [7, 13]. Additionally, direct contact with infected cattle as the source of infection, and secondary infections from person to person, are frequently recorded. *E. coli* O157 can survive for a long time in food or in the environment. It has been found to survive for up to 70 days in bovine faeces [15, 16] and water [17]. Cooking or pasteurization, however, will inactivate it. *E. coli* O157 tolerates acid environments well, with survival down to pH 2 being reported [18, 19], which could explain the bacteria's ability to survive in the stomach environment and to infect people if a low dose is ingested.

The geographic variations in the frequency of the disease, in Great Britain, Canada [20–23], or Sweden [24], are not well understood. Areas of higher risk have been associated with the agricultural structure [21]. *E. coli* O157 represent a great challenge for the epidemiology and surveillance of food safety, particularly with regard to the low infectious dose and the ability to survive in the environment. The most important strategy in preventing the foodborne disease risk is to understand the modes of contamination and disease transmission well enough to interrupt them [15].

This paper presents an ecological study concerning the frequency and spatial patterns of human EHEC infections in Sweden and the relation to agricultural structure and VTEC O157 prevalence in livestock. The comparison between human and cattle infection patterns with respect to agricultural structure could give insight into the causes of transmission and possible risk factors. The study is designed to investigate regional conditions (i.e. agriculture, water, local food) potentially contributing to the distribution of EHEC cases in Sweden in opposition to industrially processed and widely distributed food which has frequently been addressed as a EHEC risk factor before.

METHODS

Within this study all available data concerning reported human EHEC infections and proven bovine VTEC O157 occurrences in Sweden up to April 1999 were combined and evaluated concomitantly.

Between 1988 and 1994 only a few (0–3) human EHEC infections have been reported in Sweden each year. In 1995, the number rose to 127 [25] and thereafter between 100 and 200 cases were reported annually. Since 1996, all human cases of enterohaemorrhagic disease associated with *E. coli* O157 are notifiable in Sweden. All reported cases are recorded at the Swedish Center for Infectious Disease Control (SMI). A total of 525 human cases of infection with EHEC (>90% O157) have been reported in Sweden between July 1995 and April 1999 and were included in this study.

In 1996 *E. coli* O157 were first found within Swedish livestock and the first association between a human EHEC O157 infection and the occurrence of VT-producing *E. coli* O157 in cattle herds was also established [26]. By that time, surveillance of VTEC O157 in Swedish livestock was initiated. Several investigations within Swedish cattle herds have been carried out. The results have been collected and analysed by the National Veterinary Institute (SVA) and the Swedish Board of Agriculture (SJV).

From 1996 to 1998, 5602 samples were taken in an abattoir monitoring programme from 17 large-scale abattoirs in which 90% of Swedish cattle are slaughtered [27]. A positive finding was a sample from which VTEC O157 could be isolated. A second study including 17 farms was carried out by the SVA in order to follow-up farms where infections with EHEC O157 were identified during different investigations. Eight of these farms were connected with a human case. Regular testing of animals and the environment (barns, water, etc.) were carried out. The third study was initiated by the SVA together with the Swedish Dairy Association (Svensk Mjölk) and was intent on detecting the prevalence in Swedish dairy farms. A

Table 1. *Dependent and explanatory variables*

Abbreviation	Explanation
INC	Mean annual incidence 1995–1998
FD	Farm density (farms/km²) 1996
FDAL	Farm density (farm/ha agricultural land) 1996
PFC	Percentage of farms with cattle 1996
CD	Cattle density (cattle/km²) 1996
NFC	Number of farms with cattle 1996
PAP	Percentage of agricultural population 1997
PAL	Population per agricultural land 1997
ALA	Agricultural land per area
ASF	Abattoir Study: prevalence of positive samples farms
ASA	Abattoir Study: prevalence of positive samples abattoirs
ASHS	Abattoir Study: positive houses and samples
SVA	SVA Study: positive farms
PSD	Prevalence Study Dairy Farms: positive farms
FAS	Positive farms of all studies
HSAS	Positive houses and samples of all studies

Sources: Swedish Institute for Infectious Disease Control 1999; National Veterinary Institute 1999; Yearbook of Agricultural Statistics 1999.

total of 249 dairy farms were investigated in this study, 125 during autumn 1998 and 124 during spring 1999.

Additionally, several independent variables were sampled to represent agricultural dimensions suspected of being associated with *E. coli* O157 (Table 1). Data for these variables were derived from the Swedish Yearbook of Agricultural Statistics [28].

A multistep ecological analysis was carried out in the 21 counties of Sweden. All data was geo-referenced and transferred to a Geographical Information System (GIS, ArcView© 3.2, ESRI, Redlands, CA, USA) for spatial display and analysis. Statistical analysis was performed by means of standard statistical software (SPSS 10.0.7, SPSS Inc., Chicago, IL, USA).

A spatial analysis of all reported findings of EHEC in humans and VTEC O157 in cattle in Sweden was carried out for the entire investigation period (1995–1999). All human cases have been geo-referenced with respect to the place of residence. Mean annual incidence rates were calculated per county. To obtain larger case numbers, annual data of the investigation period was pooled. This was seen to be justifiable since the basic conditions were consistent throughout the period. A χ^2 test was used to test for spatial heterogeneity of incidence beyond random [29]. Moran's I test [30] and joint count statistics [31] were used to test for spatial autocorrelation. Seasonality was considered by time-series to detect the predominant occurrence of human infections in certain time periods.

The incidence variation of disease associated with EHEC among Swedish counties was visualized and examined to exhibit spatial patterns by using different disease-mapping techniques (dot maps, choropleth maps, probability mapping).

Probability mapping was based on the calculation of the probability of the counties' incidence rates [32]. Counties with significantly higher incidence of EHEC infections ($P<0{\cdot}001$ and $P<0{\cdot}0001$ respectively) were identified by comparing the observed case frequency distribution with that expected under the assumption of a Poisson probability distribution [31]. The expected number of cases in each area is derived, under the null model of spatial homogeneity of risk, by multiplying the countrywide average rate by each county's population.

Sites from which positive bovine VTEC O157 samples were found, were digitized at the place of occurrence for the farm studies and at both the place of occurrence and the place of finding (i.e. abattoir) for the abattoir study. For the Abattoir Prevalence Study the county prevalence of positive samples was calculated until October 1997. The spatial patterns of human cases and cattle findings were displayed simultaneously by combined dot and choropleth maps to visualize and uncover coincidences.

Correlations were examined by the use of Pearson's coefficients of correlation not only between explanatory and dependent variables, but also between the explanatory variables to uncover multi-collinearity.

A multiple linear regression model of the human incidence of EHEC infections was calculated over the 4-year study period (1995–1998) applying the ordinary least squares procedure. Normal distribution of the dependent variable was proved by use of a Kolmogoroff–Smirnoff test ($P<0{\cdot}01$). Correlation coefficients $>0{\cdot}6$ between explanatory variables were noted in regard of their possible importance for biasing parameter estimates of the model. As most of the correlations between different cattle VTEC O157 infection measures [Abattoir Study: prevalence of positive samples farms (ASF), Abattoir Study: prevalence of positive samples abattoirs (ASA), Abattoir Study: positive houses and samples (ASHS), SVA Study: positive farms (SVA), Prevalence Study Dairy Farms: positive farms (PSD), positive farms of all studies (FAS), positive houses and samples of all studies (HSAS)] were strong, these variables were

Table 2. *Human EHEC cases 1995 (April)–1999*

Year	EHEC infections	Male	Female	<5 years
1995	126	54	71	41
1996	118	52	66	44
1997	162	65	97	76
1998	108	51	57	27
1999 (1–4)	11	6	5	4
1995 (Apr.)–1999	525	228	296	192

Source: Swedish Institute for Infectious Disease Control 1999.

not entered into the same model. Instead, a separate regression was performed with each of these variables and the best-fitting model (which was the 'ASA model') was chosen. Instability of the regression model was assumed if t values changed rapidly and regression coefficients changed their sign [33].

Explanatory variables were selected by backward selection. They were removed stepwise from the regression model in the order of their contribution to reduction of scaled deviance. Variables were left included, if they significantly contributed to the explanatory power of the model ($\alpha = 0{\cdot}05$). The tolerance and condition indexes were examined for every variable to uncover collinearity. The model was rechecked by forward selection of the variables and stepwise removal of the included variables to ensure that this process resulted in a significant reduction in the model's explanatory power.

Due to high incidence of human disease and the high prevalence of VTEC O157 in cattle, the county of Halland (Southeast Sweden) was selected for a more detailed consideration. For this county, incidence rates have been calculated for each municipality.

RESULTS

During the period 1995–1998, the number of human EHEC infections in Sweden fluctuated at a level of more than 100 cases per year with a peak of 162 cases in 1997 (Table 2). Between 1995 and April 1999, a total of 525 human EHEC infections were reported. The sex ratio was 43% male to 57% female cases, and 36% of the infections occurred in children less than 5 years old. The incidence decreased with increasing age. In 68 cases (13%) HUS was reported. Presumptive information about a possible source of infection was only given in 23% of the cases. There was only one domestic case where the source of infection could be verified as foodborne (privately

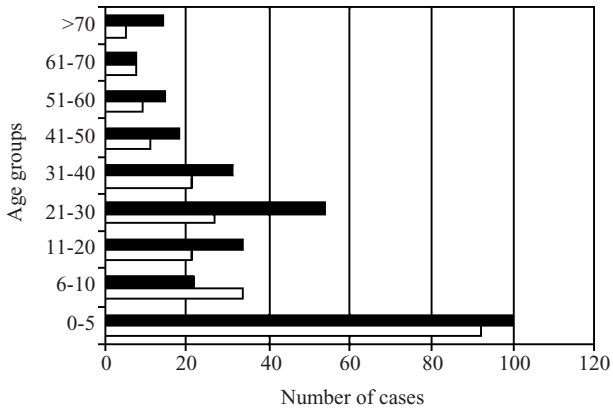

Fig. 1. Age groups and sex proportion of human EHEC infections. ■, Female; □, male.

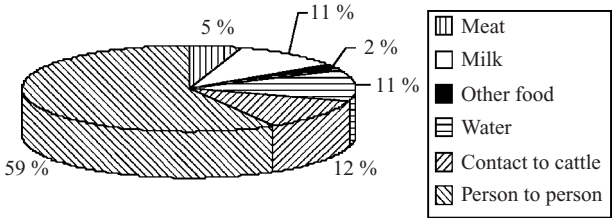

Fig. 2. Presumed sources of human EHEC infections for 23% (122) of all cases 1995–1999 (525).

imported sausage) [34]. However, presumed sources of infections, which have been suspected epidemiologically, were person-to-person transmission, food (meat, unpasteurized milk), contact with agricultural cattle, or water.

Concerning the spatial distribution of human cases (Fig. 1) an accumulation of cases in the west coast counties (Skåne, 123 cases; Halland, 76; Västra Götaland, 129) was obvious. High numbers of cases were also recorded in central Sweden and in the Stockholm capital region. In all other counties small numbers of cases (0–10 cases) occurred. Most cases were concentrated along the coastline, near lakes or along rivers. Figure 1 displays the counties' mean annual incidence (1995–1998). The overall annual incidence rate (1995–1998) for Sweden was 1·45/100 000 of population. The incidence rate was highest in Halland (7·0), followed by Skåne (2·8), Örebrö (2·4) and Västra Götaland (2·1).

The χ^2 test indicated a significant heterogeneity ($P = 0{\cdot}025$). However, neither Moran's I test ($r = 0{\cdot}13$) nor joint count statistics [$z = 0{\cdot}111$, $\phi(z) = 0{\cdot}456$] did indicate a significant spatial autocorrelation.

The temporal distribution (Fig. 2) showed a seasonal peak of human cases in late summer and

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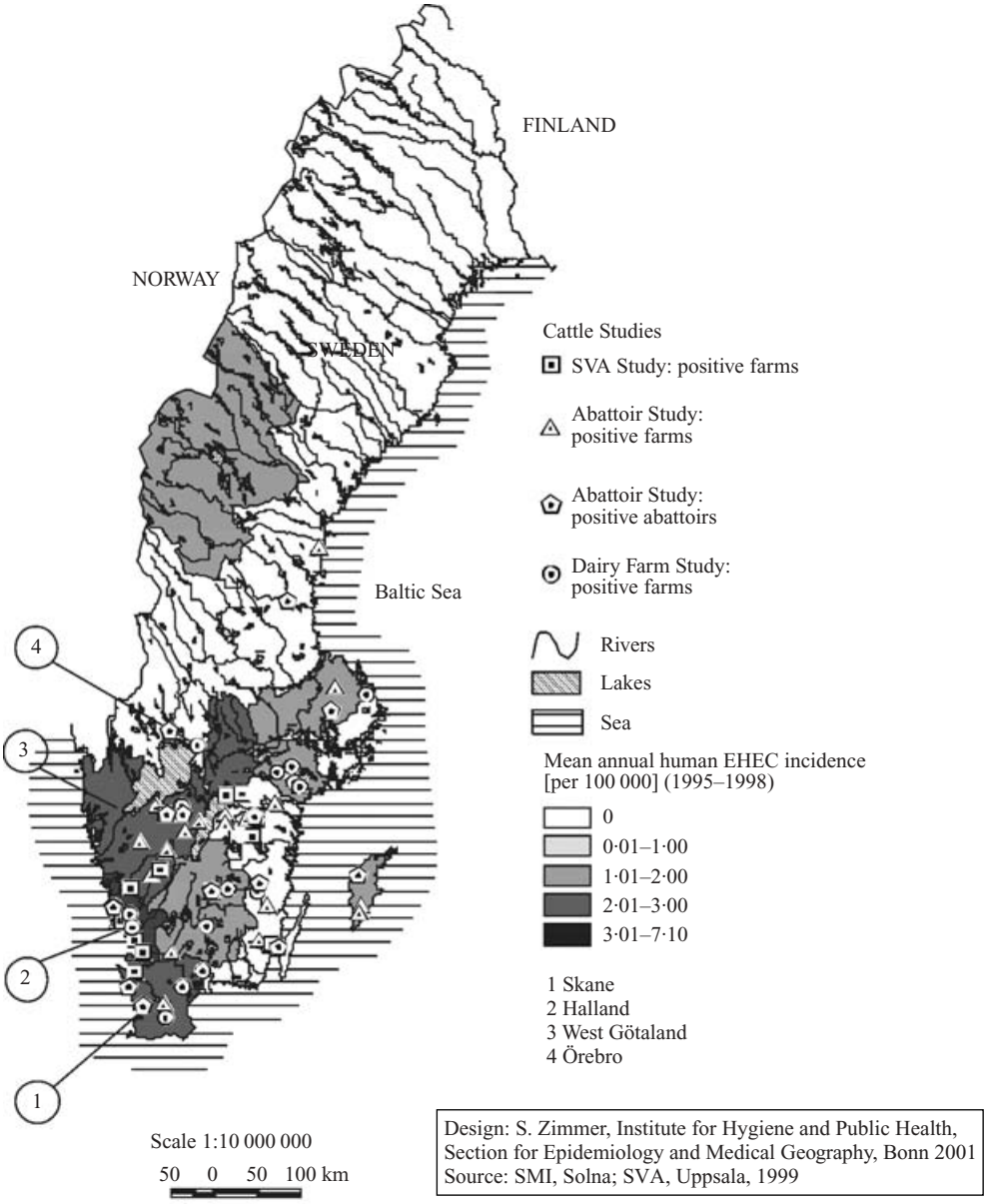

Fig. 3. Mean annual incidence 1995–1998 of human EHEC infections and positive VTEC samples of cattle studies.

autumn. Most of the cases occurred in the second half of the year and most of them in September, where the prevalence of VTEC O157 in the Abattoir Study was also highest.

Assuming a Poisson distribution for the incidences, the observed incidences in Halland, Västra Götaland and Skåne were significantly higher than expected ($P < 0{\cdot}0001$) (Fig. 5), while in Stockholm, for example, a significantly lower incidence was observed ($P < 0{\cdot}0001$).

The positive cattle samples of the different studies appeared to be concentrated in the southern and central parts of Sweden (Fig. 1). A concentration of cases along the southwest coast (Skåne, Halland, Västra Götaland), extending to central Sweden and up to the east coast near Stockholm could be detected. Few positive samples were found north of Stockholm. The Abattoir Study identified 44 positive samples with an overall prevalence of 0·8% until 1998. During 1996/1997 the prevalence amounted to 1·2% (37 out of 3072 samples were positive). Prevalence was highest in Halland (6·0%). During the Prevalence Study Dairy Farms, 21 out of 249 farms were tested positive (8·4%), seven in 1998 (5·6%), 14 in 1999

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Table 3. *Correlation matrix of dependent and explanatory variables* (*for abbreviations see Table 1*)

	INC	FD	FDAL	PFC	CD	NFC	PAP	ALA	ASF	ASA	ASHS	SVA	PSD	FAS
FD	**0·62**													
FDAL	−0·16	−0·47												
PFC	0·22	0·39	0·09											
CD	0·55	**0·93**	−0·48	**0·77**										
NFC	0·31	**0·64**	−0·07	0·26	0·53									
PAP	0·31	0·45	−0·29	**0·68**	**0·68**	0·12								
ALA	0·47	**0·89**	**−0·76**	0·43	**0·86**	0·45	0·47							
ASF	0·33	0·20	0·26	0·38	0·21	0·09	0·19	−0·01						
ASA	**0·71**	0·49	−0·12	0·43	0·54	0·21	0·56	0·31	0·27					
ASHS	0·59	**0·63**	−0·24	0·42	**0·61**	**0·68**	0·38	0·47	0·21	**0·72**				
SVA	**0·70**	0·56	−0·18	0·37	0·53	**0·57**	0·21	0·38	0·21	**0·70**	**0·94**			
PSD	**0·61**	0·55	−0·28	0·36	0·54	0·32	0·16	0·48	0·23	0·48	0·54	**0·70**		
FAS	**0·65**	**0·65**	−0·28	0·44	**0·63**	**0·65**	0·30	0·51	0·23	**0·69**	**0·96**	**0·97**	**0·75**	
HSAS	**0·64**	**0·64**	−0·25	0·43	**0·62**	**0·66**	0·35	0·48	0·22	**0·73**	**0·99**	**0·97**	**0·64**	**0·98**

Dependent variables shaded.
Correlation coefficients >0·6 shown in bold.

(up to April) (11·2%). All the cattle studies identified Halland as the county with highest prevalence of VTEC O157.

The spatial comparison of human and cattle infection patterns showed that in areas with more human EHEC infections a higher prevalence of VTEC O157 was detected in cattle also. The locations of human and cattle infections were often close to each other, indicating a spatial association between cattle and human cases. Simultaneous mapping of human and cattle cases uncovered some interesting features concerning the distribution (Figs 1 and 3). We found both higher human incidence and cattle prevalence (Halland, Skåne and Västra Götaland) and counties which had neither high human incidence nor many positive cattle samples (northern counties), indicating a correlation between cattle prevalence and human incidence. In some counties (southeast coast), however, plenty of positive cattle findings occurred, but human incidence was below average. Another county (northern central Sweden), yielded approximately average human incidence but not one cattle infection was found.

Table 3 shows the correlation matrix of the incidence of EHEC infections between 1995 and 1999 and the independent variables monitoring agricultural conditions as well as bovine VTEC O157 infections. Several coefficients of correlation between the incidence of human EHEC infections per county and variables of agricultural structure, respectively cattle prevalence being high and statistically significant ($P<0{\cdot}001$). Farm density ($r=0{\cdot}62$), cattle density (0·55), Abattoir Study prevalence (0·71) and positive farms out of all cattle studies (0·65) were significantly correlated with the mean annual human incidence. Those cattle infections which have been associated with a human case (8) did not have a significantly increasing effect on the coefficients.

Table 4. *Stepwise regression, reduction in scaled deviance*

Dependent variable ($n=21$)	Null model scaled deviance	Variable 1 deviance reduction	Variable 2 deviance reduction
Human EHEC incidence rate	228·93	ASA −109·06	FD −18·86

Variables included if r^2_{adj} changes significantly ($P<0{\cdot}05$); only included variables shown.

Regarding univariate regression results, most of the variables according to cattle infection rates (ASA, ASHS, SVA, PSD, FAS, HSAS) showed strong associations. However, some variables depicting the agricultural structure [farm density (FD), cattle density (CD)] provided a large reduction in scaled deviance. Farm density per agricultural land (FDAL), percentage of farms with cattle (PFC) and population per agricultural land (PAL) provided no explanation of variation. Table 4 displays the reduction in deviance caused by the introduction of explanatory variables into the multiple regression model. ASA appeared to be the most important variable. FD contributed a great deal less to the further reduction of deviance. Table 5 shows the results of the linear

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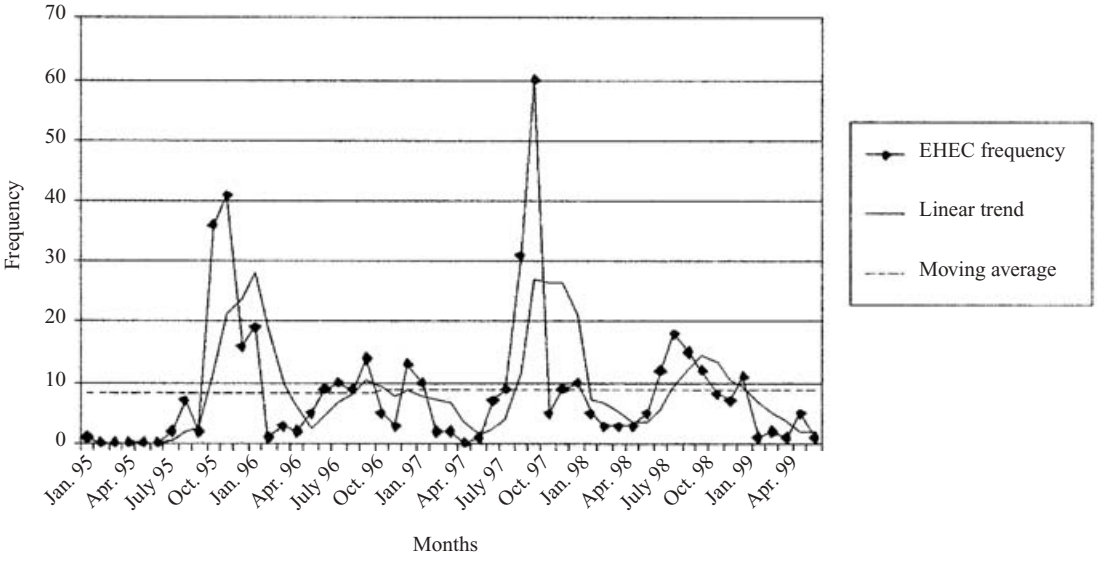

Fig. 4. EHEC time series, linear trend and moving average, 1995–1999.

Table 5. *Results of stepwise multiple regression analysis*

Dependent variable: human EHEC incidence rate (per 1 000 000 of population)					
$n=21$	B	S.E. of B	β	t_0	P
Intercept	0·496	3·943		0·126	0·901
ASA	5·602	1·775	0·535	3·156	0·005
FD	20·556	9·609	0·362	2·139	0·046

$r=0{\cdot}779$, $r^2_{\text{adj}}=0{\cdot}562$, $P<0{\cdot}000$, $F_{(3,19)}=13{\cdot}847$, S.E. of estimate is 100·21, Durbin–Watson $d=2{\cdot}237$.

multiple regression. The explained variation of the multiple linear regression model (r^2_{adj}) was 0·56. (F test for explanatory contribution of included variables, standard error of estimate and Durbin–Watson test are given in the notes to Table 5.) Values of Durbin–Watson test statistics near to 2 indicate that there was no autocorrelation of residuals in the model.

The county of Halland was identified having significantly higher cattle prevalence and higher human incidence. The positive cattle samples originated from a few sites where frequently more than one infection was recorded. The reported human infections were often located in the same settlements (Fig. 6), even clusters of human cases were seen to occur in sites where cattle were tested positive. The display of incidences per municipality underscored this tendency: incidence was higher in municipalities where more animals tested positive.

DISCUSSION

The observed pattern of human EHEC infection incidence in Swedish counties was rather heterogeneous. However, spatial statistical methods failed to prove that this was unlikely to occur by chance. This result is probably due to the relatively low number of spatial units (21 counties) and their specific spatial arrangement. Some factors, which were spatially differentiated, were assumed to influence the obvious spatial variation.

The consideration of existing data sets concerning human EHEC infections and cattle VTEC O157 prevalence in Sweden between 1995 and 1999 resulted in spatial similarities. The vicinity of cases indicated a positive association between human and cattle infection. The correlation coefficients confirmed this relationship between infections in cattle populations and disease in humans and also indicated a significant association between cattle density, farm density and human infections.

Two independent variables could be included into the regression model. Cattle VTEC O157 prevalence and farm density, which could represent the probability of human contacts with agriculture, contributed to further insight in the disease ecology of human EHEC infections in Sweden.

Concerning the temporal changes, human infections increased since 1995. Despite improved surveillance and increased public concern since 1996, the increase in recorded human cases might reflect a true increase to some degree, whereas no conclusions on

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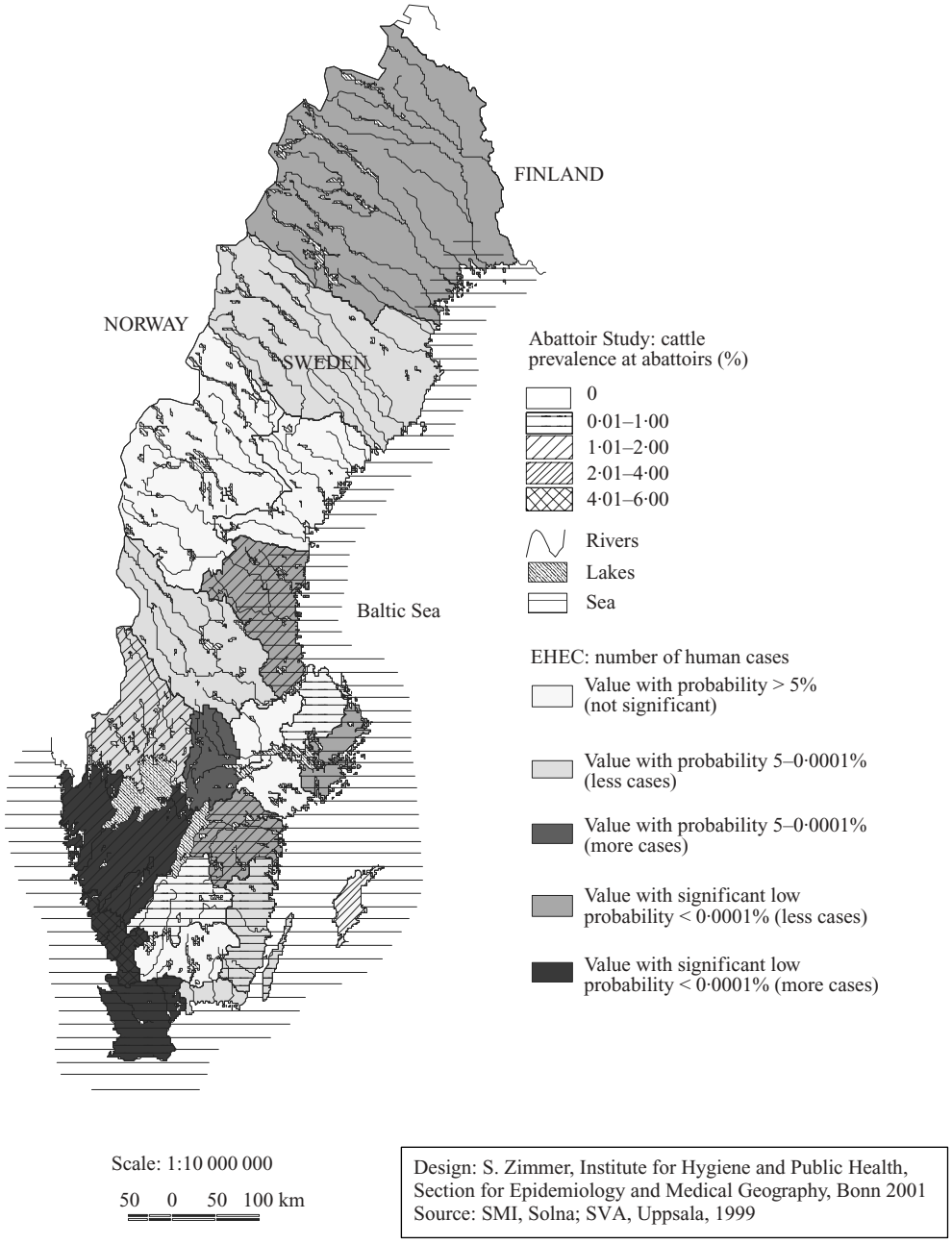

Fig. 5. Probability of incidence rates assuming a Poisson distribution and prevalence of positive abattoir samples per county.

the changes of cattle prevalence can be drawn since no surveillance was carried out prior to 1996.

Taking into account the agricultural structure and characteristics in leisure-time activities (bathing in potentially contaminated water-courses), there seemed to be reasonable causes for a concentration of human and cattle infections in the southwest of Sweden. In Sweden cattle are kept on pasture during summer. The density of cattle and farms is highest in the southwest of Sweden. The mean annual incidence of human EHEC incidence infection in Halland (1995–1998, range 1·9–16·9) was at 7·0, a value which is extremely high even in an international context of high-prevalence regions (e.g. Alberta/Canada 1987–1991, 12·1 [20]; 1991, 8·4 [20]; Grampian/Scotland 1988–1990, 6·0 [23]; Scotland 1996, 9·9 [35]). The practice of cattle pasturing next to lakes and rivers which are also used for bathing was not restricted in any way during the study period until 1998. Due to superficial water run-off this practice could

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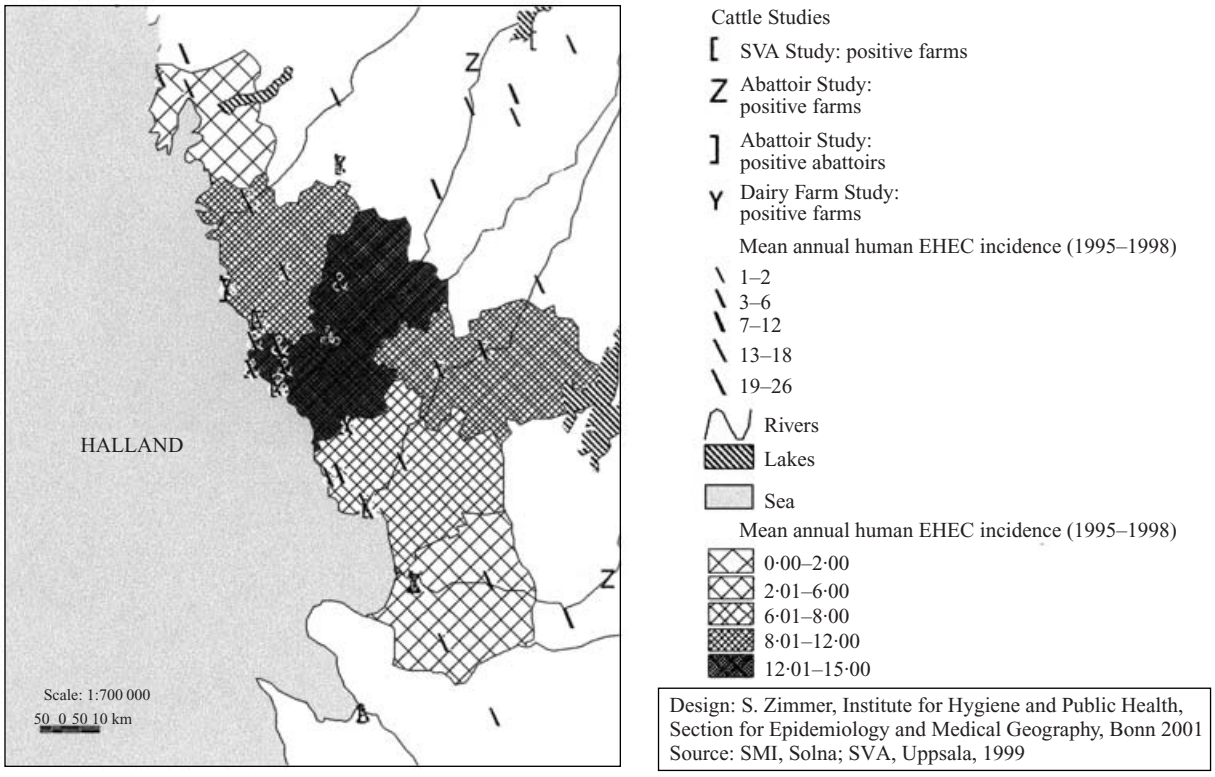

Fig. 6. Halland: location of human EHEC infections, human incidences per municipality and positive VTEC samples of cattle studies.

cause invisible faecal contamination of the lakes, rivers and seaside. The high incidence at the south-west coast occurred especially during warm and sunny weather periods (late summer 1995, summer 1997), when air temperatures were high and outdoor recreational water was used most intensively. In August 1995, just before the first large Swedish EHEC outbreak, air temperatures in Halland were the highest for decades.

A case-control study, initiated after the increase of EHEC cases in 1997 at the west coast, did not identify a common source of infection, but some putative risk factors were noted: farm visits, contact to cattle manure, drinking unpasteurized milk and swimming in lakes [34]. Eleven children contracted *E. coli* O157 after swimming in a small lake. A similar EHEC outbreak associated with bathing in a lake was observed in Finland [13]. Since 1998 it has been recommended to keep grazing cattle separate from human bathing areas and to inform people about the possible hazards. These actions seem to be promising, since the number of infections decreased in 1999.

From our results it appeared that local conditions seem to have a high impact on the routes of EHEC transmission in Sweden. This putative hypothesis includes close contact to (infected) cattle, due to an agricultural environment, including picnicking next to grazing cattle, pasturing cattle or disposal of manure close to where people swim and possibly the consumption of local food (meat, milk or manured vegetables), as has been reported in other studies [9, 21, 36]. This may explain the observed spatial coincidence of human EHEC and livestock VTEC infection patterns and agricultural structure.

It is not the nationwide distribution of industrially processed food, as reported for many outbreaks worldwide, e.g. the United States [37], but predominantly the spatial contiguousness to farms and cattle and different opportunities for contact with faecal contamination that seem to be important for EHEC transmission in Sweden.

In North America the highest incidences throughout the 1980s and early 1990s were recorded in Alberta/Canada [21] and highest rates in Great Britain in Scotland [20]. Different surveillance strategies may have had an influence, but could not be responsible for the whole divergence [20]. Michel et al. [21] identified areas of obviously higher risk for humans in Ontario/Canada and was able to state a positive and significant spatial association between cattle density

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and human EHEC incidence. They discussed the importance of living in rural areas or working in an agricultural environment as a risk factor for contracting the disease due to cattle and manure contact or the consumption of unpasteurized milk, or other locally produced and processed food. The possible contamination of water and the exposure to cattle could also be risk factors.

EHEC infections have emerged as a zoonotic disease during the last 20 years, and it is possible that the number of outbreaks and sporadic cases will increase further. During the last few years effective measures for the prevention of EHEC infections in humans were supposed to be located in the food production and processing chain [38]. The spatial distribution of enterohaemorrhagic disease and the possible causes for EHEC infections in Sweden were characterized by obvious spatial patterns. There is evidence that the observed pattern of human EHEC infections in Sweden could be associated to local agricultural structures. The results of this study, as with the practical experience gained from the control measures implemented, indicated, as has been stated for Ontario previously [21], that direct or indirect contact to cattle rather than the consumption of industrial processed and distributed food was a major risk factor in Sweden during the study period 1995–1999. Although ecological study conclusions may be subject to ecological fallacy [39–41], their value can be substantiated by understanding the factors determining health outcomes [42]. Spatial comparison and mapping of disease data by use of GIS was helpful to organize the available data, to communicate results and to generate appropriate hypotheses on disease causation and spreading.

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