Q fever transmission to humans and local environmental conditions

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Summary

The size of the Q fever outbreaks in 2007, 2008 and 2009 in the Netherlands suggests that transmission to humans took place through environmental contamination or multiple point-source contamination sites, rather than from direct contact with animals. Conclusive evidence on environmental factors is still lacking and a number of dairy goat farms outside the high incidence areas had major Q fever problems without any human cases in the surroundings. This study assessed whether these discrepancies in transmission to humans of Q fever between the different infected farms can be explained by environmental local conditions. Environmental datasets were gathered on soil texture, land use, soil moisture and climate. The strongest correlation was found with vegetation density (NDVI) and average groundwater conditions which are strongly related to the soil moisture regime. The results confirm that it is very likely that these two environmental factors determine the transmission of Q fever from an infected source to humans. Further investigation is recommended to assess how the spatial distribution around the point source of these factors controls the transmission to humans of Q fever.

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1 Introduction

1.1 Background

Coxiella burnetii is a bacterium with a worldwide reservoir in many different animal species. In some animals, especially small ruminants (sheep and goats), but also domestic cats, extremely large numbers of Coxiella can be excreted with birth products like placenta and amniotic fluids. Although direct exposure to parturient animals or their birthing products poses a high risk for infection with C. burnetii (Q fever), the organism's ability to persist in the environment may result in a continued risk for infection weeks to months after the birthing event (Yanase et al. 1998). The potential for transmission is greatly enhanced by the extremely low infectious dose for C. burnetii, which is reported to be as small as a single organism (Tigertt et al. 1961). Q fever is a zoonotic disease with no evidence for human-to-human transmission.

Infection with *C. burnetii* (Q fever) is likely to occur when a number of environmental conditions are met, such as warm weather with dry soil conditions and with wind speed and wind direction that allows airborne contaminated dust particles to be inhaled by people and animals that are at close distance to the contaminated soil. It has been suggested that under dry, dusty conditions infective aerosols can travel several km's down wind and large human outbreaks have been linked to wind dispersion from sites where infected animals are kept (Hawker et al. 1998, Tissot-Dupont et al. 1999).

Outbreaks of human Q fever of unprecedented size occurred in the Netherlands in 2007, 2008, and 2009 (Schimmer et al. 2008, 2009). The size of the community outbreak in The Netherlands suggests that transmission takes place through wide-scale environmental contamination or multiple point-source contamination sites, rather than from direct (occupational) contact with animals, consumption of contaminated unpasteurised milk, or from parturient pet animals. Ongoing studies in the south of the Netherlands suggest that infected animals in large-scale dairy goat farms are the major source of environmental contamination. The affected area has a very high density of dairy goat farms and dairy sheep farms and several farms experienced clinical signs with abortion waves that were confirmed as Q fever with immunohistochemistry.

However, conclusive evidence on environmental factors is still lacking and a number of dairy goat farms outside the high incidence area had major Q fever problems without any human cases in the surroundings. This raises the question whether environmental conditions in the high incidence area were more conducive for transmission than elsewhere. In the present study the importance of these factors will be assessed, with a focus on soil composition, land use and soil moisture, while accounting for other possible explanations for small area variations such as differences in human population density and weather conditions.

1.2 The aerosol route

Aerosol transmission of Q fever occurs through the inhalation of contaminated dust. The origin of potentially contaminated dust can be either the infected farm itself or soil dust coming from sparsely vegetated or bare areas around the farm. The transport and sedimentation of both dust sources are mainly a function of wind velocity and the near-surface turbulence. These factors are related to the surface roughness, vegetation and land use characteristics. The impact of soil dust from natural and anthropogenic sources on climate and air-quality has been recognized at the global scale [Sokolik and Toon, 1996; Tegen and Fung, 1994]. However, the regional characteristics of soil dust production, transport and removal processes are poorly understood.

The mobilization of fine particles requires the knowledge of the surface wind and the threshold velocity of wind erosion. The threshold velocity depends on the particle size and soil moisture. The mass flux of wind-transported dust particles depends on the excess of the wind friction speed over the threshold wind friction velocity for erosion.

Soil moisture increases the threshold friction velocity. Chepil (1956) considered that the influence of soil moisture on wind erosion rates depends on soil texture and can be explained by interparticle cohesion forces due to soil water retention processes. The soil clay content was found to be the main parameter that controls the minimal soil moisture required to induce an increase in the threshold friction velocity (Fécan et al, 1998).

Vegetation has a sheltering effect on erodible land surfaces (e.g. Lancaster and Baas [1988] and Stockton and Gillette [1990]) and thus reduces dust emissions. Vegetation traps particles and extracts momentum from the air flow depending on the roughness structure of the vegetated area. A high density of roughness elements (as for example trees) increases the threshold friction velocity and reduces wind speed. This removes particles from the air flow and reduces dust concentrations (deposition). The degree to which dust emissions are controlled by vegetation cover and geomorphic setting was investigated using dust storm frequency data. Engelstaedter [2003] showed that dust storm frequency is inversely correlated with leaf area index (an index of vegetation density) and net primary productivity.

1.3 Objectives

The overall objective of this study is to assess whether and how local environmental conditions influence the likelihood of transmission to humans of Q fever. This will be done using data on the Q fever outbreaks of 2008 and 2009 from the high incidence areas in the Netherlands. The study focuses on soil cover, composition, moisture and meteorological conditions, while at the same time accounting for other possible explanations that can lead to small area variations such as differences in population density, farm sizes, production methods and weather conditions. Results of this assessment can be used to carry out more detailed studies on the aerosol transmission route in order to mitigate the risk of Q fever for humans.

2 Environmental datasets

The following datasets were selected for analyzing the possible causal relationship between environmental factors and the transmission to humans of Q fever from infected farms:

- Vegetation index
- Land cover
- Soil characteristics
- Soil humidity
- Past weather conditions

Each of the datasets, its source, characteristics and limitations are discussed in the following paragraphs.

2.1 Vegetation index

2.1.1 Background

Vegetation is part of the friction surface which determines the wind velocities and erosion and deposition of particles near the ground. Forests and other vegetated areas are characteristically rough surfaces and thus contribute to air turbulence. Especially leaf canopies are very effective in slowing down wind movements because of its large friction area and they enhance the deposition of wind-transported dust particles.

To which degree the wind speed is reduced inside a vegetation patch depends on its internal structure, density and height and on the wind speed above the vegetation. The density of vegetation is strongly related to the total leaf area, a variable that differs strongly during the year. For this reason, it is likely that the effect of vegetation on the transport of contaminated dust particles has a strong seasonality.

2.1.2 Vegetation and remote sensing

To obtain data on historical vegetation densities, the most appropriate source of information is satellite images (remote sensing). To determine the density of green on a patch of land, one measures the intensity of the distinct colors (wavelengths) of visible and near-infrared sunlight reflected by the plants. When sunlight strikes the plants, certain wavelengths of the sunlight spectrum are absorbed and other wavelengths are reflected. The pigment in plant leaves, chlorophyll, strongly absorbs visible light (from 0.4 to 0.7 µm) for use in photosynthesis. The cell structure of the leaves, on the other hand, strongly reflects near-infrared light (from 0.7 to 1.1 µm). The more leaves a plant has, the more these wavelengths of light are affected.

In general, if there is much more reflected radiation in near-infrared wavelengths than in visible wavelengths, then the vegetation in that pixel is likely to be dense and may contain some type of forest. If there is very little difference in the intensity of visible and near-infrared wavelengths reflected, then the vegetation is probably sparse and may consist of grassland, heath or bare covers. To quantify this difference, different spectral vegetation indices are in use.

Spectral vegetation indices have been found to be related to a number of biophysical parameters (variables) of interest, including Leaf Area Index (LAI), percent vegetation cover, green leaf biomass, fraction of absorbed photosynthetically active radiation (fAPAR), photosynthetic capacity, and carbon dioxide fluxes.

Nearly all satellite vegetation indices compare the differences between the red and near-infrared reflectances to quantify the greenness of land in a certain area. The most commonly used index is called the Normalized Difference Vegetation Index (NDVI). Written mathematically, the formula is:

NDVI = (NIR — VIS)/(NIR + VIS)

where NIR and VIS are the response in the near-infrared and visible bands respectively. Calculations of NDVI for a given pixel always result in a number that ranges from minus one (-1) to plus one (+1); however, no green leaves gives a value close to zero. A zero means no vegetation and close to +1 (0.8 - 0.9) indicates the highest possible density of green leaves.

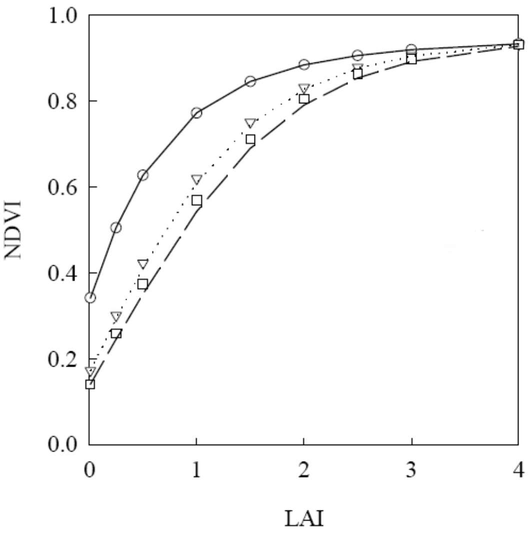

Figure 1. Example of a typical relationship between NDVI and LAI for different soil reflectances.

Before an NDVI image can be used for analysis, some preprocessing steps have to be performed to reduce the effects of clouds, sensor degradation, sensor viewing angle, sun angle, and atmospheric effects. After preprocessing, however, the NDVI still is sensitive to external factors such as soil background that are most obvious in areas with sparse vegetation.

Despite these limitations, the NDVI can be considered the most accepted indicator of the differences in vegetation density within the exposure radius of the infected farms and to analyze the differences among the affected areas. Higher NDVI values around an infected farm correspond to a higher vegetation density and thus reduced local wind velocities. On the other hand, low NDVI values indicate sparsely vegetated areas where wind stress can be higher and more dust can be transported over larger distances.

2.1.3 Data source

The project preceding this research was focused on method development and the identification of potential environmental datasets (Hunink and Droogers, 2009). Decadal NDVI data with a resolution of 1 x 1 km, covering the entire Netherlands, were obtained from the SPOT VEGETATION distributor (VITO, 2005). The analysis confirmed that NDVI values around the infected farms are of influence on the transmission to humans of Q fever. The present study uses a higher quality product with a more detailed spatial resolution of 250 meters (compared to 1 km) from the MODIS sensor on board of NASA satellites.

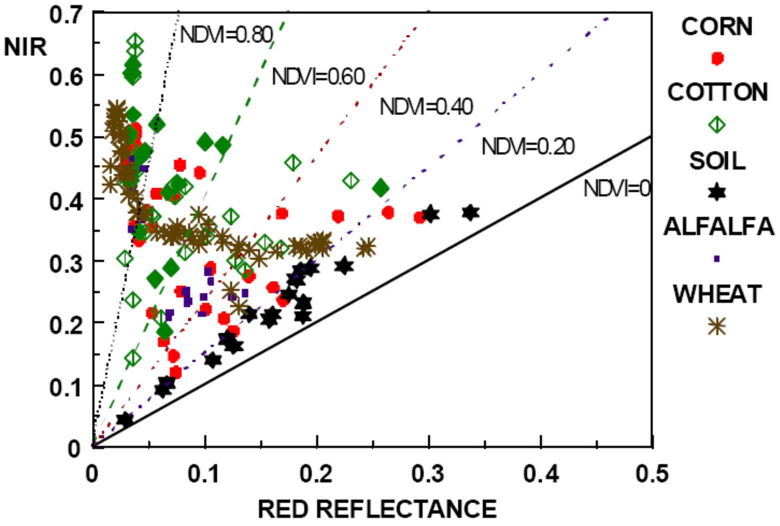

Figure 2. Cloud of reflectance points in NIR-red waveband space and different NDVI values for agricultural crops observed throughout the growing season (Huete et al, 1999).

MODIS (Moderate Resolution Imaging Spectroradiometer) is an instrument on board of the Terra and Aqua satellites designed to provide information on global dynamics and processes occurring on the land, in the oceans, and in the lower atmosphere. The instruments were launched in 1999 and 2002 respectively. Terra's orbit around the Earth is timed so that it passes from north to south across the equator in the morning, while Aqua passes south to north over the equator in the afternoon.

Terra MODIS and Aqua MODIS are viewing the entire Earth's surface every 1 to 2 days, acquiring data in 36 spectral bands, or groups of wavelengths. Blue, red, and near-infrared reflectances, centered at 469-nanometers, 645-nanometers, and 858-nanometers, respectively, are used to determine the MODIS daily vegetation indices.

The MODIS repeat cycle is sixteen days, during which each point on the earth is viewed with a range of view angles. Using a compositing period equal to the repeat cycle it is possible to obtain reliable gridded products with a spatial resolution of 250 meters. One of the products delivered is a global NDVI coverage with these characteristics. The MODIS NDVI products are computed from atmospherically corrected bi-directional surface reflectances that have been masked for water, clouds, heavy aerosols, and cloud shadows.

2.1.4 Image quality and selection

Version-5 MODIS/Aqua Vegetation Indices products have been extensively validated, meaning that accuracy has been assessed over a widely distributed set of locations and time periods via several ground-truth and validation efforts. However, individual images can be of poorer quality due to unfavorable atmospheric conditions (clouds, aerosols, haze)

Separate image stacks were developed for the NDVI data and the Quality Assessment dataset that provides pixel-wise data quality ratings. For the selected months, the quality ratings were within the acceptable levels. Visual judgment of each of the separate images showed that the quality of some of the images was affected probably due to hazy atmospheric conditions (Table 1). These images were left out from the analysis.

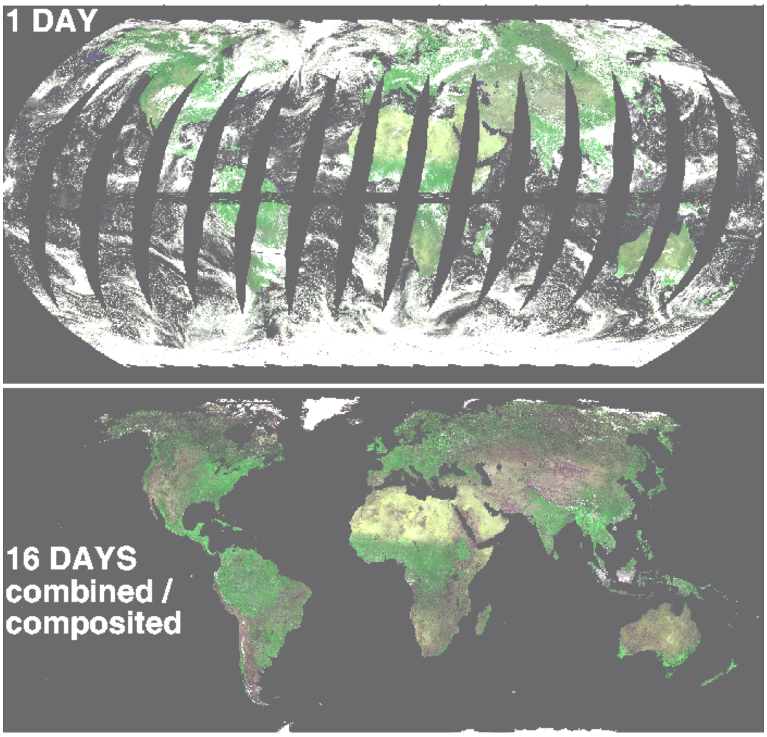

Figure 3. Illustration of the combination of 1 day images to obtain global coverage

The original image stacks were rescaled to obtain the correct NDVI values. As can be seen in Table 1, the composite range of the NDVI images does not coincide with the start and end of the months. Therefore, it was decided to use only one single image for each month, of which the 16 day range falls entirely within the corresponding month. For April 2009 and June 2009 the adjacent image in time was used due to quality restrictions.

Table 1. MODIS images used for analysis

	Start composite date	End composite date	Quality	Month
1	06/04/2008	21/04/2008	haze	
2	22/04/2008	07/05/2008	ok	Apr-08
3	08/05/2008	23/05/2008	ok	May-08
4	24/05/2008	08/06/2008	ok	
5	09/06/2008	24/06/2008	ok	Jun-08
6	25/06/2008	10/07/2008	ok	
7	06/04/2009	21/04/2009	ok	Apr-09
8	22/04/2009	07/05/2009	ok	
9	08/05/2009	23/05/2009	ok	May-09
10	24/05/2009	08/06/2009	ok	Jun-09
11	09/06/2009	24/06/2009	haze	
12	25/06/2009	10/07/2009	haze	

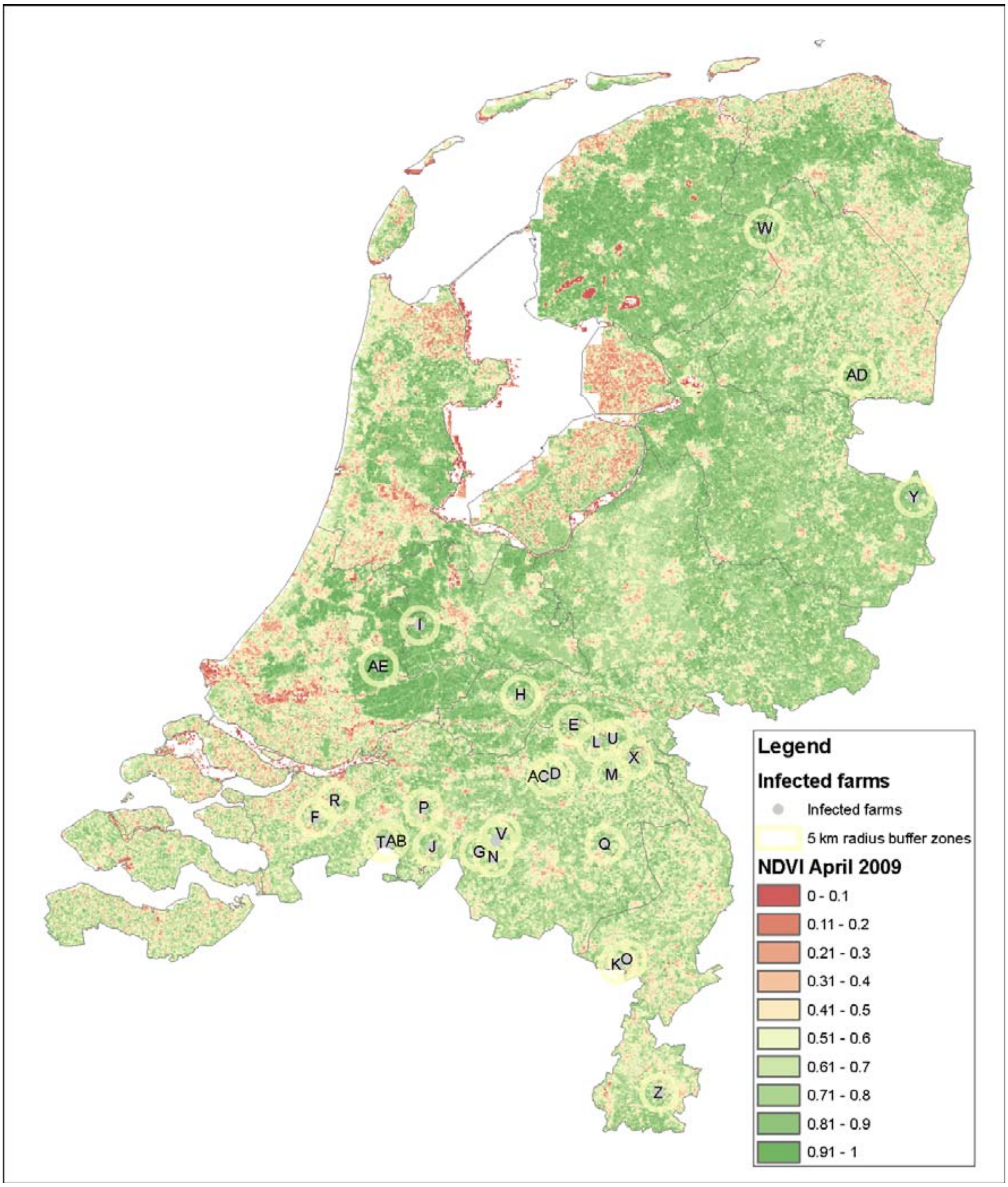

Figure 4. Vegetation index of the Netherlands for April 2009. Letters indicate infected farms.

2.2 Land use

Similar to the vegetation index, the type of land cover within the buffer zones is likely to affect the airborne transport of contaminated dust. In fact, depending on its characteristics, land cover can be either a limiting or an enhancing factor. For example, the neighborhood of arable lands could augment the available dust coming from bare areas under dry conditions. On the other hand, forest is likely to reduce wind velocities and thus form a sink of airborne dust.

The most detailed available information on land cover in the Netherlands is the Dutch land use database (LGN) which is a raster database with 25*25m resolution covering the entire Dutch territory and presenting the land use in 39 classes (Thunnissen and De Wit, 2000). From 1986 onwards the database is frequently updated with a 3-5 years interval. It is based on a combination of geodata and satellite images. The LGN database is a product of the Centre for Geo-Information which is part of the Wageningen University and Research Centre.

LGN is based on multitemporal classification of satellite imagery and integration with ancillary data. Currently 5 versions exist (LGN1 – LGN5), which span a time period of 1986 to 2004. The latest two versions are connected with the Dutch topographical database (TOP10vector) for agricultural crops.

The LGN classes were converted into 4 main land cover classes found relevant for this study, being:

- Arable and cultivated land
- Pastures
- Open spaces with little or no vegetation (including heathland)
- Forest

Also the surface of residence areas was extracted to calculate the incidence rates of human infection around each farm. The area of each of the separate classes was also used as input data for the statistical analysis, to check whether the existence of a certain specific land type enhances or inhibits the transmission to humans.

Figure 5. Map showing land use cover used to obtain the total surface of the 4 aggregated classes within each buffer zone (south of the Netherlands)

2.3 Soil texture

The soil map of the Netherlands 1:50 000 provides information on important characteristics of the soil profile up to a depth of 1.20 m (Van Kuilenburg, 1981). A countrywide soil map of the Netherlands is available since 1986 and the digital version is available since 1999. Data have been collected between 1958 and 1999. For this study only the soil texture at the surface is a variable of interest as it controls the wind erosion threshold velocity. Therefore it was necessary to reduce the large number of classes in order to extract the dominant surface texture. This allows quantifying the relative presence of clay, sand and peat around the surrounding farm areas.

The Ministry of Transport and Public Works (Rijkswaterstaat) in cooperation with a number of research institutes carried out a policy analysis called PAWN (Policy Analysis for the national Water management of the Netherlands in which they reduced the high number of classes in the soil map (Wösten et al. 1988). This classification was used to determine the dominant surface texture. In this way, a nationwide database of the surface texture could be obtained, using 6 classes, as can be seen in Figure 6.

To quantify the relative proportion of clay, sand or peat around the infected farms, these classes were used to obtain the following three variables, used for the statistical analysis:

- Sand covered soils (% of total area)
- Clay covered soils(% of total area)
- Peat covered soils (% of total area)

For soils covered with loamy material it was assumed that the ratio clay to silt is 1:1.

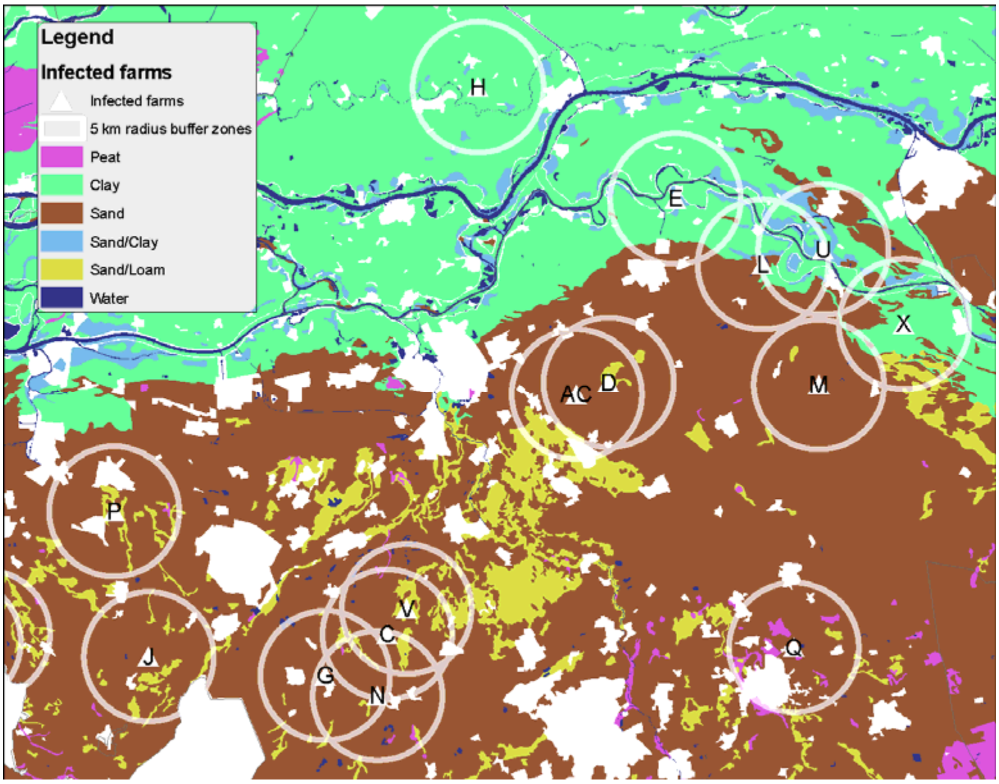

Figure 6. Map showing surface texture classes used for the analysis (south of the Netherlands)

2.4 Soil moisture

2.4.1 Groundwater depth

Groundwater tables in the Netherlands are relatively shallow due to the low elevations of the ground surfaces. The conventional way to express groundwater depths is in terms of groundwater depth classes (‘grondwatertrap’, abbreviation Gt in Dutch). These classes use a combination of average highest groundwater depth (‘GHG’) and average lowest depth (‘GLG’) throughout the year (Table 2) . The entire Netherlands have been mapped using this classification (Figure 7). Lower Gt numbers correspond to shallow groundwater tables, while higher Gt numbers indicate average deeper groundwater levels. The major part of the Netherlands has groundwater tables between 1 and 3 meters depth.

Table 2. Groundwater depth classes with corresponding groundwater levels

Code GWT	GHG (cm depth)	GLG (cm depth)
I	-	< 50
II	-	50 - 80
II*	25 – 40	50 - 80
III	< 40	80 - 120
III*	25 – 40	80 - 120
IV	> 40	80 - 120
V	< 40	> 120
V*	25 - 40	> 120
VI	40 - 80	> 120
VII	80 - 140	> 120
VIII	> 140	> 120

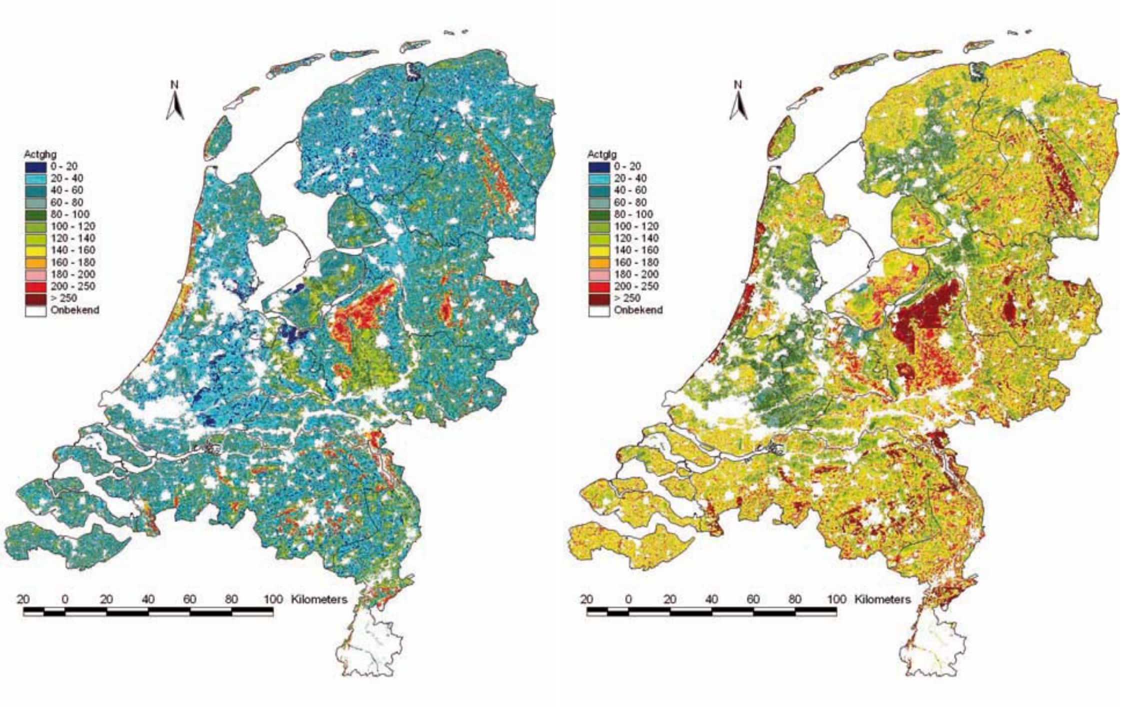

Figure 7. Average shallowest (left) and deepest (right) groundwater depth of the Netherlands (source: Gaast et al. 2007)

The upward movement of water through capillary rise from the groundwater table can cause wetting of the soil if groundwater tables are shallow enough. Generally speaking, soils with shallow groundwater tables are wetter, while soils with average deep groundwater conditions are drier. The Gt number can therefore be used as an indicator of average soil moisture conditions. Higher numbers indicate potentially dry soils, while low numbers correspond to average wetter soil conditions. The mean, minimum and maximum Gt numbers were calculated around each of the infected farms and used for the statistical analysis.

2.4.2 Relative soil humidity

Historical data on soil moisture on a national scale is not available. Soil moisture obtained from remote sensing satellite sources has a spatial resolution which is too course to be applicable for this study. The spatial heterogeneity and temporal variability of soil moisture still poses one of the biggest challenges within hydrology. For this study, it was crucial to have an indicator of the relative temporal differences in soil humidity among the infected farms. The relative differences in time are mainly controlled by the water balance, i.e. daily precipitation and evapotranspiration.

A straightforward model was set up to quantify temporal variation of the relative soil humidity using the information on precipitation and evapotranspiration from the KNMI weather stations. The obtained daily timeseries were aggregated to 10 days and spatially interpolated using kriging. The resulting decadal maps gives insight in the relative temporal differences in humidity, assuming a uniform soil profile.

The model assumes an average root depth of 50 cm, with porosity of 1/3 of the total soil volume. The incoming flux is the daily precipitation, assumed to fully infiltrate if storage is not full. Water is lost from storage either when storage is full or by evapotranspiration. The actual evapotranspiration is calculated from the Makkink daily reference evapotranspiration, one of the variables in the meteorological dataset. It was assumed that the evapotranspiration diminishes linearly when the soil is at 2/3 of its total water capacity. The schematization is resumed in the following model equation:

$$RSH_t = \min(1; RSH_{t-1} + \frac{P - ET_{ref} \cdot \min(1; {}^{3}\!/_{2} \cdot RSH_{t-1})}{150}$$

with RSH = Relative Soil Humidity (%), P = Precipitation (mm/day) and ET_{ref} = Reference evapotranspiration (mm/day). It has to be noted that the model does not include any information on soil characteristics and is purely based on the water balance terms. However, soil characteristics are taken into account separately in the statistical analysis.

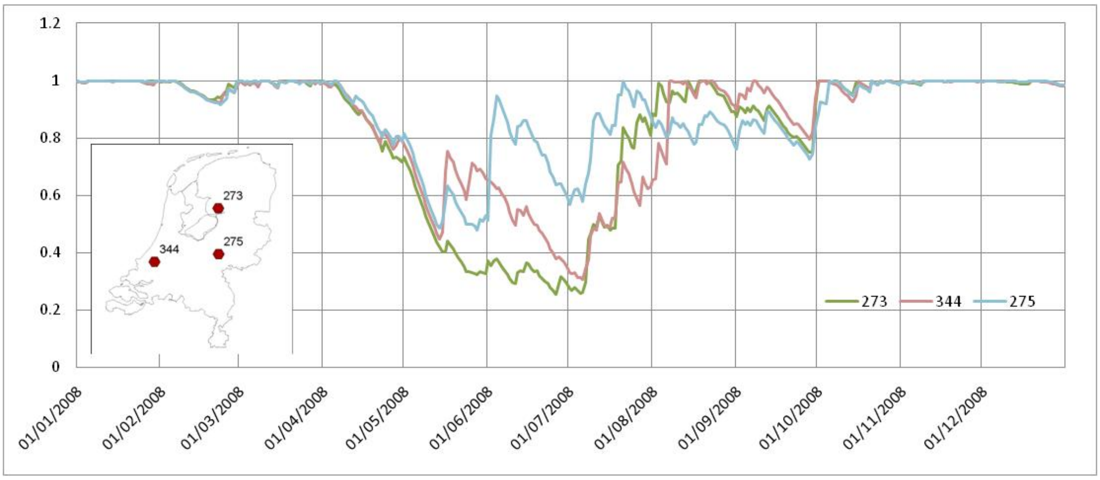

Figure 8. Relative soil humidity for 3 points in the Netherlands during 2008.

2.5 Climate

The meteorological conditions that are likely to promote the production and dispersion of dust are dry and windy weather as they induce the production and dispersion of dust. Therefore, weather conditions at the time of human infection are expected to be related with the incidence rates of Q fever within the area. The following variables were found relevant for this study
:

- Average wind velocity
- Maximum hourly wind velocity
- Temperature
- Global radiation

Wind velocity triggers the dust production, depending on the wind erosion threshold. Temperature and global radiation may influence the persistence of the Q fever bacterium in the environment, so they were taken into account as well for the statistical analysis.

The daily timeseries of the following 18 KNMI weather stations were used for the analysis: Schiphol, De Bilt, Leeuwarden, Marknesse, Deelen, Lauwersoog, Hoogeveen, Eelde, Woensdrecht, Rotterdam, Cabauw, Gilze-Rijen, Herwijnen, Eindhoven, Volkel, Ell, Maastricht and Arcen. To obtain information on these variables at the surroundings of the infected farms, the daily timeseries were first aggregated to 10-day averages. These averages were spatially interpolated (kriging). For two farms that are located outside of the weather stations' extent data of the nearest station were used.

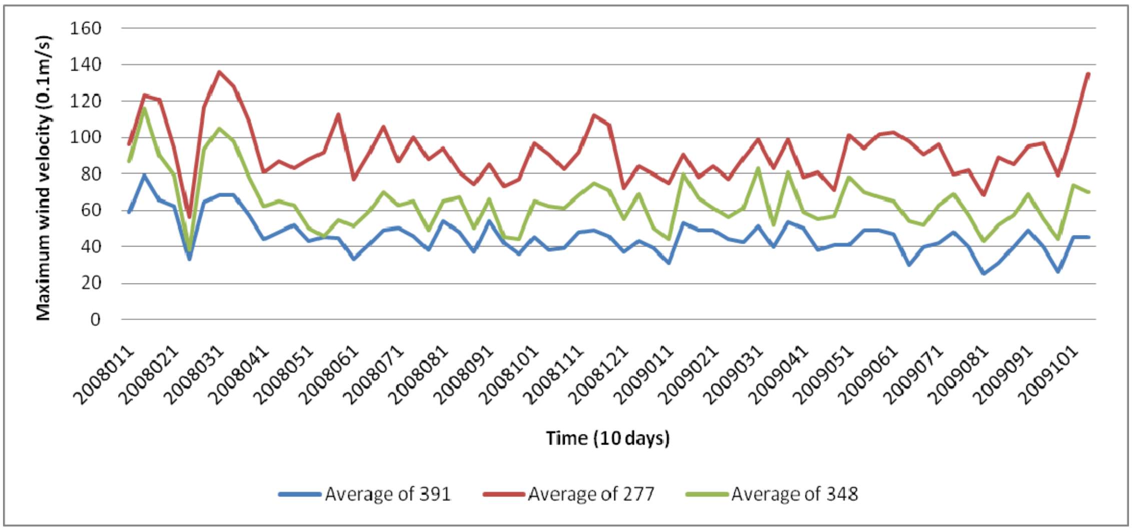

Figure 9. Hourly maximum of wind velocity for 3 different weather stations in the Netherlands during 2008 and 2009.

3 Methods

3.1 Study area

The total number of registered small ruminant farms in the Netherlands is 52,000, of which 350 are professional dairy goat farms with more than 200 adult goats and 40 are professional dairy sheep farms. The animals on these farms remain in the stable year-round and all practices are carried out indoors. Dairy goat farmers generally do not have land and manure is often transported to other parts of the country.

Following the 2007 outbreak, an informal agreement was made that the veterinary and the public health sectors would exchange information on farms with newly diagnosed animal cases of Q fever to allow for an adequate response and control. In June 2008, notification of Q fever in small ruminants became mandatory: farmers and veterinarians have to report symptoms compatible with Q fever, usually abortion waves. In addition, it was imposed on all farms that manure could only be spread or transported after 90 days of storage on the farm.

3.2 Data on outbreaks

Information on human Q fever cases was obtained from the electronic notification system Osiris for the years 2008 and 2009. Data on the location and the first day of Q fever symptoms were used to quantify the number of infected people around the infected farms.

Information on the location of the infected dairy goat and dairy sheep farms was obtained from the Animal Health Service. They provided the exact location of the farms where abortion waves took place from the year 2005. Also information on the number of animals on the farms, the type of farm (goat or sheep), and the total number of goats, sheep and cattle in the 5 km zone around infected farms was provided.

It was assumed that infected farms are a source of infection during the consecutive years of detection. Q fever among animals is known to be persistent and it is likely that infected farms maintain their potential as a source of contamination. Farms infected from 2006 and later were taken into account for analysis of the outbreaks of 2008 and 2009. The following table shows the number of farms for which data were available on the location for each year.

Table 3. Number of farms where Q fever was detected from 2006

Year	Number of farms	Total farms infected
2006	7	7
2007	7	14
2008	9	23
2009	4	27

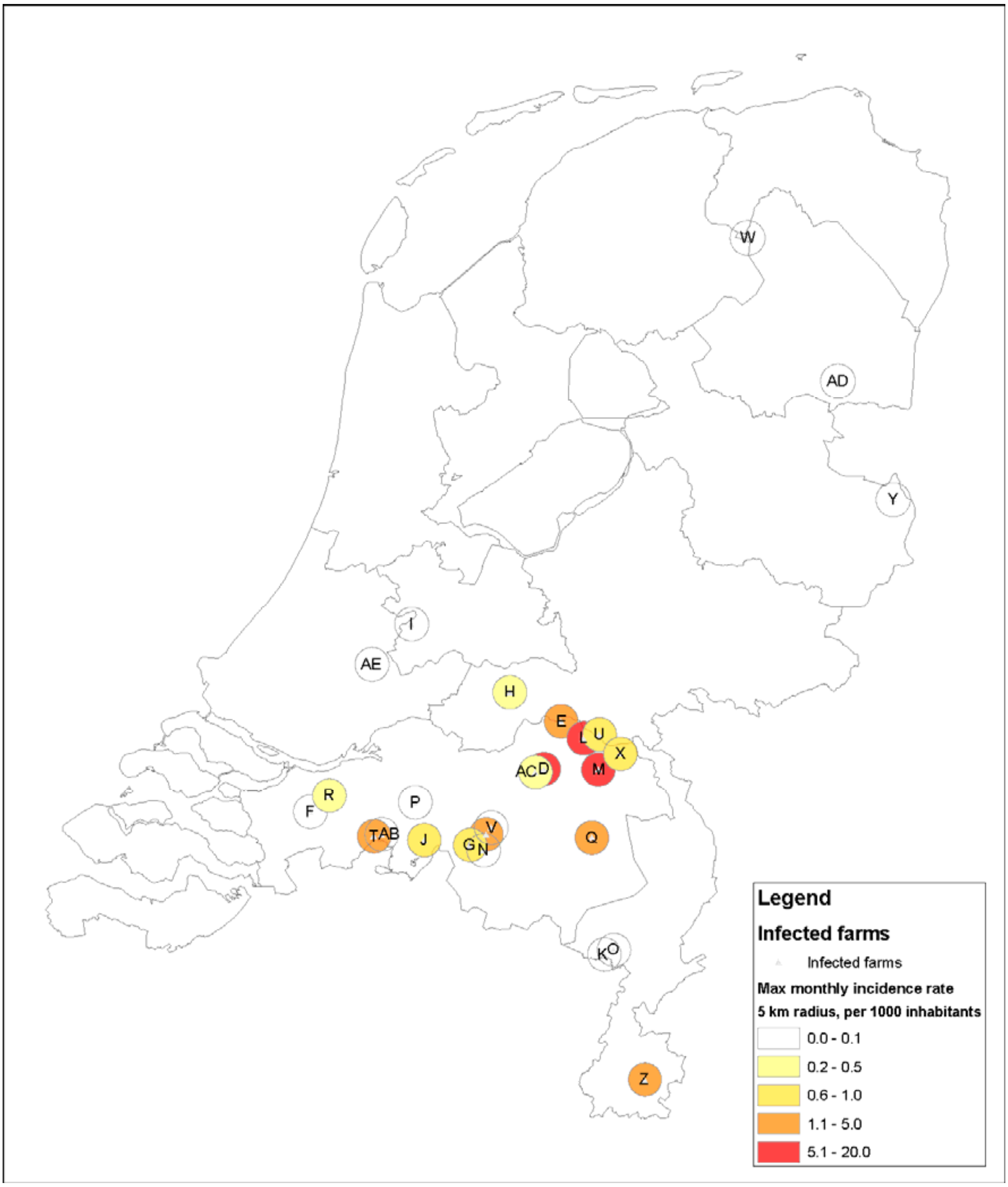

Figure 10. Location and 5 km exposure radius of the farms where Q fever was detected. Colors indicate the maximum incidence rate observed of the 6 analyzed months.

3.3 Exposure

From a study around the town of Helmond there is evidence that the risk for Q fever infection shows a monotonous decline with distance, with no increased risk for people living >5km from the infection source. For this reason, the analysis was done using 5 km buffers around the infected farms as the radius of exposure. When these 5 km buffer zones overlapped, it was assumed that the human cases located in the overlapping area could be attributed to the closest farm.

The time span analyzed with the different variables is one month. The time period during the year in which most transmission to humans takes place is from April to June (Figure 11).

Therefore, for this study it was decided to focus on the human cases infected only during these months. The number of infected cases around the infected farms in 2007 was so low that no useful statistical analysis could be performed. Data were available on the day of the first Q fever symptoms of each individual and an average incubation period was assumed of 15 days.

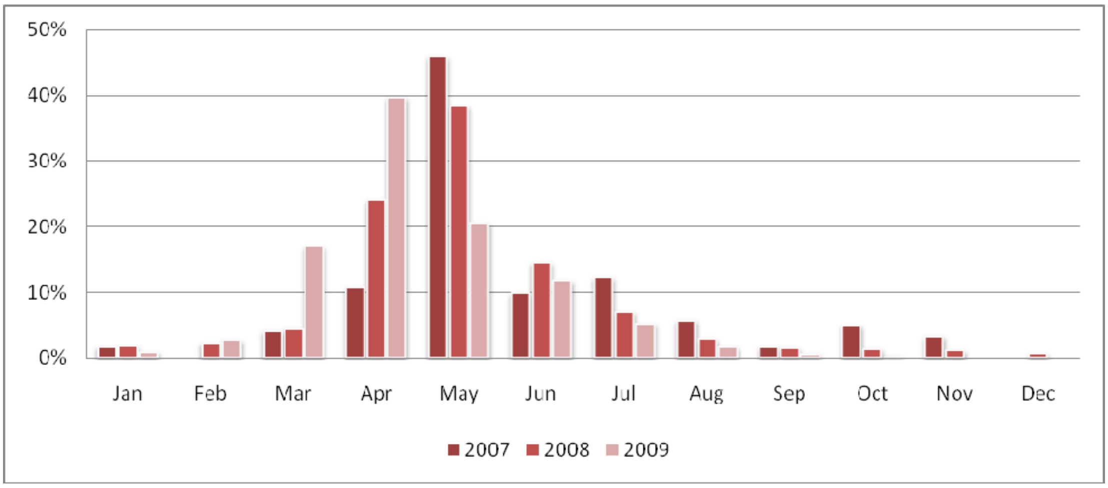

Figure 11. Relative number of infected people per year

The number of human Q fever cases within the 5 km buffer zone was calculated around each infected farm. In case the buffer zones overlapped, the Q fever case was assigned to the closest infected farm.

The spatial distribution of human cases in 2008 and 2009 shows outbreaks around farms where Q fever was detected during previous years. Besides, the Q fever bacteria are known to persist for a long time in the environment. For this reason, it was assumed that a farm remained infected during the years following the first detection of Q fever. The information available confirms that at a few locations Q fever was detected twice, 1 to 3 years after the first detection.

3.4 Statistical analysis

The environmental datasets were used to extract different potential explanatory variables from the buffer zones around the infected farms. The total area was calculated of each of the classes within each buffer zone and the spatial average, median, minimum and maximum was extracted. This resulted in one dataset for each of the 6 analyzed months (April, May, June for 2008 and 2009) with the values for each of the variables that correspond to each infected farm.

Of the spatial datasets that were variable in time (NDVI, meteorological variables and soil humidity) the temporal analysis base was 10 days (decadal). To obtain monthly values, the three corresponding subsequent decadal values were used. The soil and land use information was assumed to be invariable over the analyzed time period.

The incidence rates (number of human cases divided by population) within the 5 km radius buffer zone around the infected farms were used to determine whether Q fever transmission through the environment to humans took place or not. The threshold value was set at an incidence rate of 1:10.000, with more than 1 person infected.

Accordingly, the continuous dependent variable of the number of human cases was transformed to a yes/no variable indicating whether transmission to humans took place or not (dichotomous transformation). The dichotomous variable on transmission to humans divides each dataset in two exclusive groups: those where it is assumed that transmission to humans took place and those where no or very few human cases were observed. These groups were then used to analyze for each month whether statistically significant differences could be found in the identified explanatory variables. This was done using the Student t-test to examine whether the means of the analyzed variable are likely to be equal (null hypothesis) or not. Additional bivariate logistic regression was performed after dichotomizing the relevant explanatory variables to obtain an indication of the risk factors. Multivariate logistic regression was used to check for potential confounding factors.

4 Discussion

4.1 Results

The incidence rates within the 5 km radius buffer zone were calculated for the months April, May and June of the years 2008 and 2009. For each of these months, the various possible explanatory variables were extracted for each of the buffer zones and the time-dependent variables were aggregated to one month.

The complete dataset joins all the cases for each farm and for each analyzed month with the corresponding values of the local and environmental variables. This dataset was used to assess which of the variables may condition the transmission to humans of Q fever by comparing the cases where transmission to humans took place and those where no transmission took place. This was done by assessing the significance of the differences of means between both groups of all the analyzed variables. The entire dataset has 150 cases: 2008 23 infected farms * 3 months and 2009 27 infected farms * 3 months. The following table shows the results:

Table 4. Means and p-value (t-test) for the complete dataset (150 cases).

		Transmission			
		No	**Yes**	**p**	
Vegetation	Median vegetation index	0.70	0.67	0.00	**
	Min vegetation index	0.27	0.24	0.14	
	Max vegetation index	0.89	0.89	0.26	
Land use	Arable lands (km²)	22.5	27.4	0.00	**
	Pasture lands (km²)	33.2	29.2	0.01	**
	Forest cover (km²)	7.8	8.0	0.77	
	Bare cover and heath (km²)	0.3	0.2	0.10	
	Residential area (km²)	7.1	8.6	0.02	**
Soil texture	Peat covered soils (%)	7.3	0.8	0.00	**
	Clay covered soils (%)	24.2	26.4	0.67	
	Sand covered soils (%)	59.5	62.6	0.58	
Soil moisture	Mean groundwater table class	4.96	5.24	0.00	**
	Min groundwater table class	2.11	2.36	0.00	**
	Max groundwater table class	6.94	6.95	0.87	
	Relative soil humidity (%)	0.621	0.657	0.19	
Climate	Mean wind velocity (0.1 m/s)	34.8	32.9	0.00	**
	Max wind velocity (0.1 m/s)	57.8	55.1	0.00	**
	Temperature (0.1°C)	137	137	0.99	
	Global radiation (J/cm²)	1797	1765	0.39	
	N	95	55		

*p-value < 0.1; **p-value < 0.05

Table 5 shows the monthly means of the variables and the corresponding significance for level 0.1 and 0.05. The results will be discussed for each of the environmental datasets in the following sections.

Table 5. Differences of means for all selected datasets and significances.

		April 2008			May 2008			June 2008			April 2009			May 2009			June 2009		
		No	Yes		No	Yes		No	Yes		No	Yes		No	Yes		No	Yes	
Vegetation	Median vegetation index	0.69	0.65		0.7	0.66	*	0.73	0.72		0.72	0.68	*	0.67	0.64	**	0.7	0.67	**
	Min vegetation index	0.26	0.22		0.27	0.2		0.33	0.3		0.26	0.19		0.28	0.27		0.24	0.27	
	Max vegetation index	0.9	0.9		0.9	0.9		0.89	0.86	**	0.92	0.92		0.86	0.86		0.89	0.9	
Land use	Arable lands (km^2)	21.6	28.8	*	24.0	25.1		23.6	25.4		21.8	27.6	*	22.2	28.9	**	22.2	28.9	**
	Pasture lands (km^2)	34.3	27.9		33.7	28.8		32.9	30.4		33.3	29.2		32.7	29.2		32.7	29.2	
	Forest cover (km^2)	7.7	7.9		7.4	8.3		7.0	8.9		8.1	7.9		8.2	7.5		8.2	7.5	
	Bare cover and heath (km^2)	0.3	0.3		0.3	0.3		0.4	0.3		0.3	0.2		0.3	0.1		0.3	0.1	
	Residential area (km^2)	7.1	8.7		7.3	8.4		7.2	8.5		6.8	8.5		7.1	8.6		7.1	8.6	
Soil texture	Peat covered soils (%)	8.2	0.8		8.1	0.9		8.8	0.7		7.3	0.6		6.1	0.9		6.1	0.9	
	Clay covered soils (%)	24.6	26.6		24.9	26.0		19.5	33.0		23.8	26.0		25.6	22.6		25.6	22.6	
	Sand covered soils (%)	58.3	64.3		57.7	65.2		62.5	58.3		59.9	61.5		59.3	63.5		59.3	63.5	
Soil moisture	Mean groundwater table class	4.93	5.26		4.84	5.40	**	4.82	5.37	**	4.94	5.24		5.07	5.05		5.07	5.05	
	Min groundwater table class	2.07	2.33		2.07	2.33		2.00	2.40	*	2.13	2.36		2.16	2.38		2.16	2.38	
	Max groundwater table class	6.93	7.00		6.93	7.00		6.92	7.00		6.94	6.91		6.95	6.88		6.95	6.88	
	Relative soil humidity (%)	0.88	0.87		0.56	0.59	**	0.48	0.59	**	0.8	0.83	**	0.57	0.56		0.47	0.44	**
Climate	Mean wind velocity (0.1 m/s)	36.8	35.4	*	34.0	33.0		33.6	31.6	**	31.4	29.9	*	39.3	37.7	*	33.3	31.0	**
	Max wind velocity (0.1 m/s)	59.6	57.8		54.4	53.2		57.0	53.5	**	54.2	53.3		64.9	61.9	**	55.3	51.8	**
	Temperature (0.1°C)	87	86		156	155		162	163		120	123	**	138	141	*	156	158	
	Global radiation (J/cm^2)	1430	1420		1963	1938	**	1938	1950		1550	1559		1822	1802		2034	1977	**
	N	14	9		14	9		13	10		16	11		19	8		19	8	

*p-value < 0.1; **p-value < 0.05

Many of the selected environmental variables are highly correlated with each other (Table 6). For example, the differences in the vegetation distribution among the buffer zones is strongly correlated with land use. The vegetation index distribution is negatively correlated with the total area of arable lands within the buffer zones. This is due to the fact that arable lands tend to have bare surfaces (among the crops). Moreover, in the start of the growing season these areas are fully bare or sparsely vegetated. This explains that buffer zones with more arable lands tend to have lower vegetation indices. On the other hand, pasture lands are normally fully covered with vegetation with a low seasonal variation, resulting in a positive correlation with the vegetation index.

Table 6. Pearson correlation indices for some of the environmental variables

	Relative soil humidity	Mean wind velocity	Median vegetation index	Groundwater table class	Arable lands	Pasture lands	Peat covered soils
Relative soil humidity	1	-.066	-.072	.045	.051	-.087	-.061
Mean wind velocity	-.066	1	.180*	-.333**	-.248**	.433**	.272**
Median vegetation index	-.072	.180*	1	-.502**	-.599**	.712**	.497**
Mean groundwater table class	.045	-.333**	-.502**	1	.453**	-.752**	-.738**
Arable lands	.051	-.248**	-.599**	.453**	1	-.747**	-.476**
Pasture lands	-.087	.433**	.712**	-.752**	-.747**	1	.709**
Peat covered soils	-.061	.272**	.497**	-.738**	-.476**	.709**	1

*p-value < 0.05; **p-value < 0.01

4.2 Environmental datasets

4.2.1 Vegetation

Considerable temporal variation was found for the NDVI distribution within the buffer zones during the 6 analyzed months in 2008 and 2009 (Figure 12). These temporal differences can be attributed to crop growth cycles and seasonal variations of the natural vegetation. Figure 12 shows also that the variation range among the infected farms differs substantially. The analysis showed that a relation exists between these temporal and spatial differences of the NDVI distribution with the transmission of Q fever.

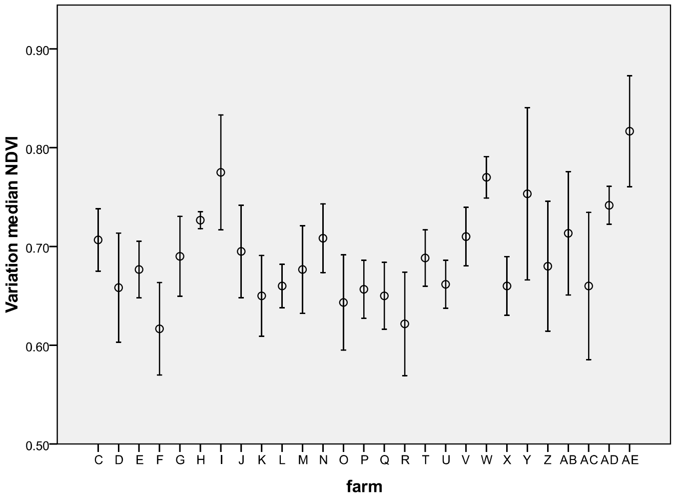

Figure 12. Temporal variation of the median NDVI value at the buffer zones around the infected farms and for the 6 analyzed months in 2008 and 2009

The areas where no transmission to humans took place from the infected farms are generally more densely vegetated than the non-transmitted farms (Table 5). The distribution of NDVI values within the buffer zones tends to have a lower middle value (median) at the farms where Q fever was transmitted to humans. A high significance was found for the difference of means between the yes/no groups using the complete dataset.

Also the analysis of the monthly datasets shows a significant difference for half of the 6 analyzed months (Table 5). Moreover, for all the months the average vegetation index is smaller for the farms where transmission to humans took place than the average of the non-transmitted farms.

A causal link seems plausible as vegetation is known to reduce the production of dust from erodible surfaces and to remove dust from the air flow. To which degree dust concentrations are reduced inside and above a vegetation patch depends on its internal structure, density and height. The results confirm that the risk for transmission to humans is reduced when higher vegetation densities occur in the direct surrounding of the infected farms.

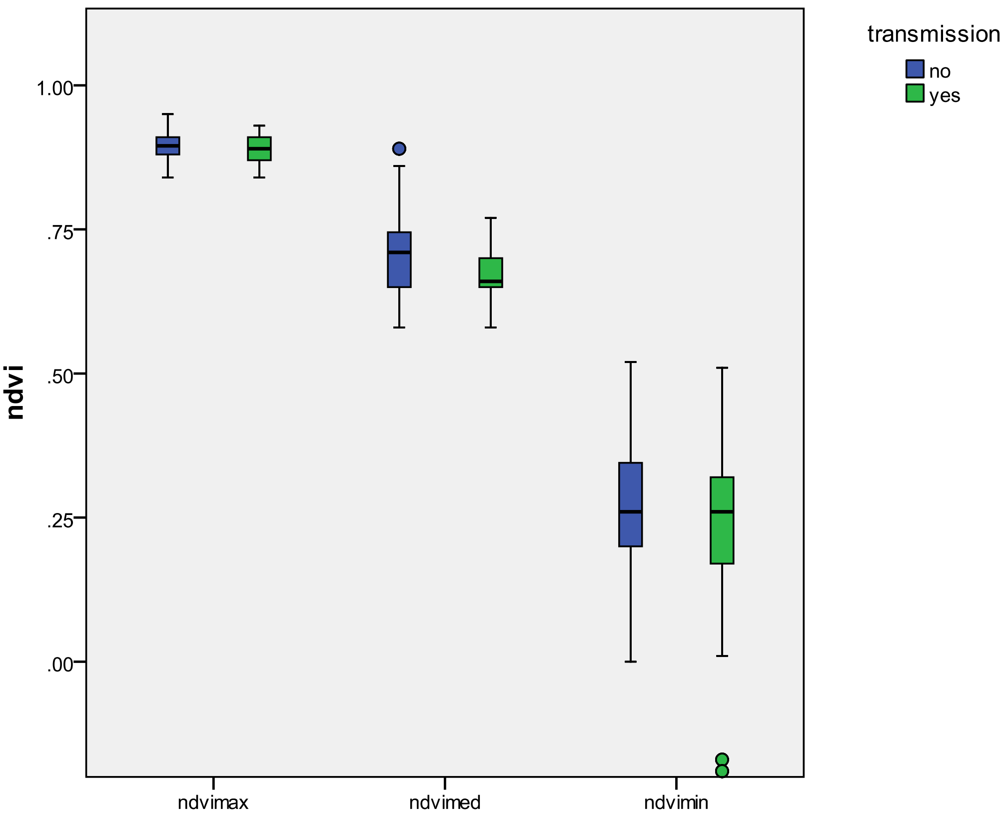

Figure 13. Boxplot of the maximum, median and minimum (resp.) vegetation index around the infected farms

4.2.2 Land use

A clear relation was found between land use and the risk for human transmission of Q fever. Infected farms surrounded by relatively more arable fields co-occur with higher Q fever human incidence rates. On the other hand, lower incidence rates have been observed within buffer zones with relatively more pasture fields. The analysis of the complete dataset and the monthly datasets confirms this relationship.

The analyzed land use classes were generalized classifications from the original land use dataset. Most of the arable lands class consists of maize fields. A considerable part of the soil surface of maize fields is bare which enhances the production of dust. Especially at the start of the growing season (April) it can be expected that these surfaces are prone to wind erosion. Besides, this crop demands relatively much water and for that reason the soil surface is drier and dust production higher. Pasture fields are less seasonal variable and are generally covered entirely with vegetation, limiting the production of dust.

The other three land use classes do not show significant difference between the two groups. The share of bare and open surfaces ('bare' class) within the buffer zones is probably too small to make it an explanatory variable in the analysis. Also forest and residential areas were not found to be indicative for human transmission risk of Q fever. The lack of a relation with forest area is somewhat surprisingly as leaf canopies are known to be very effective in slowing down wind movements and enhancing the deposition of wind-transported dust particles. Most likely possible effects of forest patches between the infected source and residential areas should be studied with a more detailed and location-specific analysis taking into account the patchy spatial distribution of the forest areas and their spatial location compared to the farms and urban settlements.

It has to be noted that the land use dataset is not time variable which means that temporal differences related to the crop season during the year are not taken into account in this study. Also, the used dataset was based on information from a few years before the outbreaks so some agricultural lands might have altered since then.

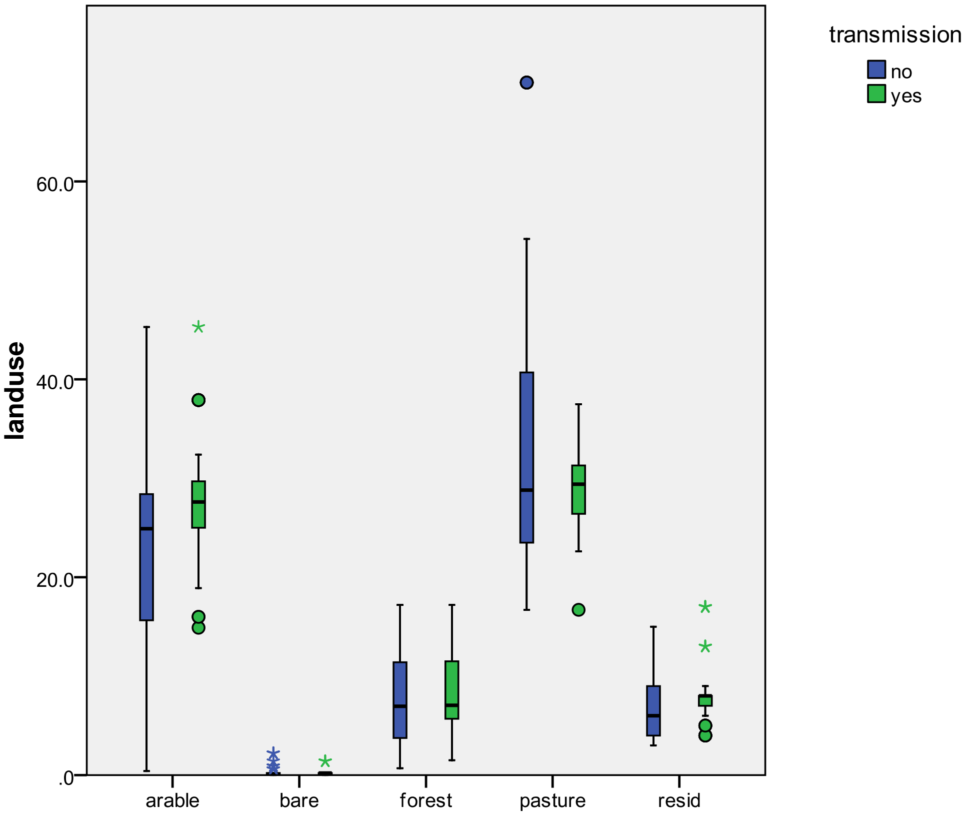

Figure 14. Boxplots of arable lands, bare areas, forests, pasture and residential areas (km2) around the infected farms

4.2.3 Soil texture

A weak relationship was found between the texture of the soil surface and the incidence rate of Q fever around infected farms. One variable shows a significant difference being the area percentage of peat covered soils within the 5 km buffer zones. Sand and clayey soils do not show any relationship based on the analyzed datasets.

In areas with a relatively large share of peat covered soils transmission of Q fever to humans is less likely than areas without any peat soils. This result can be explained by the fact that peat areas tend to be relatively wet (shallow groundwater tables, as confirmed by correlation matrix in Table 6) with low dust production rates.

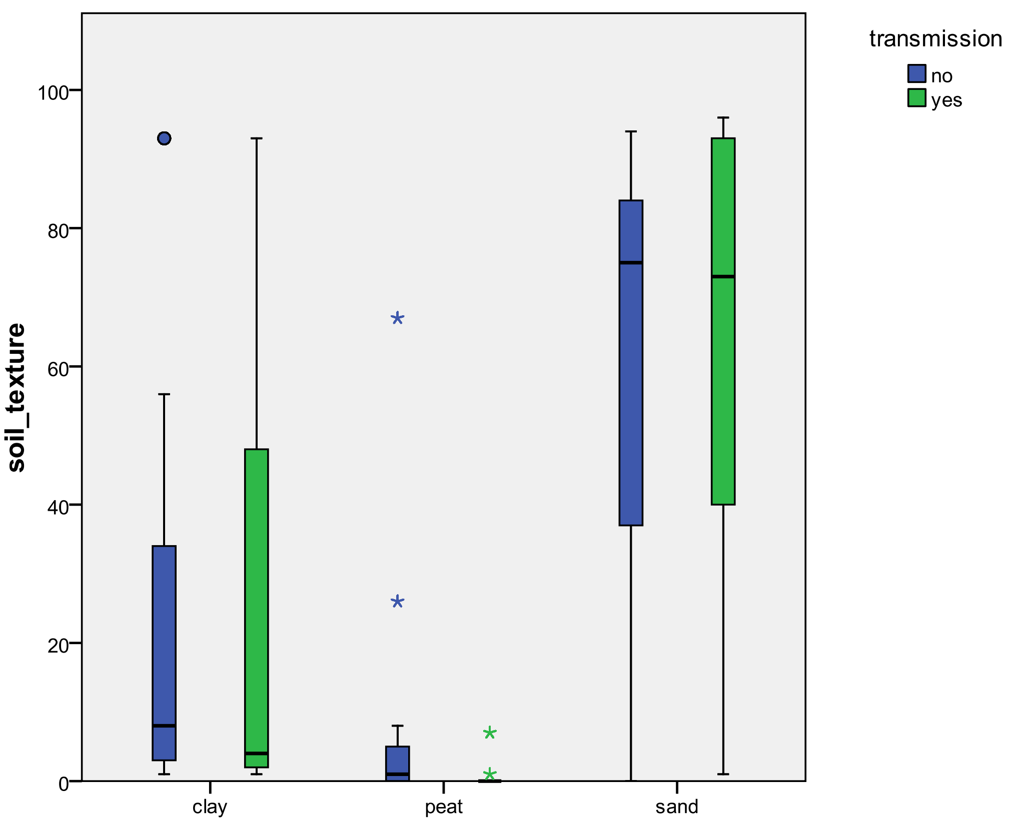

Figure 15. Boxplots of peat, clay, sand (in % area of buffer zone) covered soils around the infected farms

It can be expected that soil surface texture is only of influence when bare surfaces are present. This is why the interactions between soil surface and land use are of crucial importance when studying these relationships.

4.2.4 Soil moisture

Groundwater tables

Groundwater tables are deeper around the farms where transmission to humans took place, compared to the non-transmitted farms (Table 4 + 5 and Figure 16). The average value of the groundwater table class is lower (i.e. groundwater table is shallower) for the buffer zones where Q fever incidence rates were low or zero. Also the minimum groundwater class value found within the 5 km radius buffer zones is generally lower for the non-transmitted cases.

The results show clearly that farms where no transmission to humans took place are related to shallower groundwater tables. Shallow groundwater tables generally lead to wetter soil moisture conditions through capillary rise, especially in fine textured soils. Wet soil inhibits the production of dust and might as well increase the deposition of dust. Besides, it has to be noted that groundwater tables are correlated with soil texture and vegetation characteristics (Table 6).

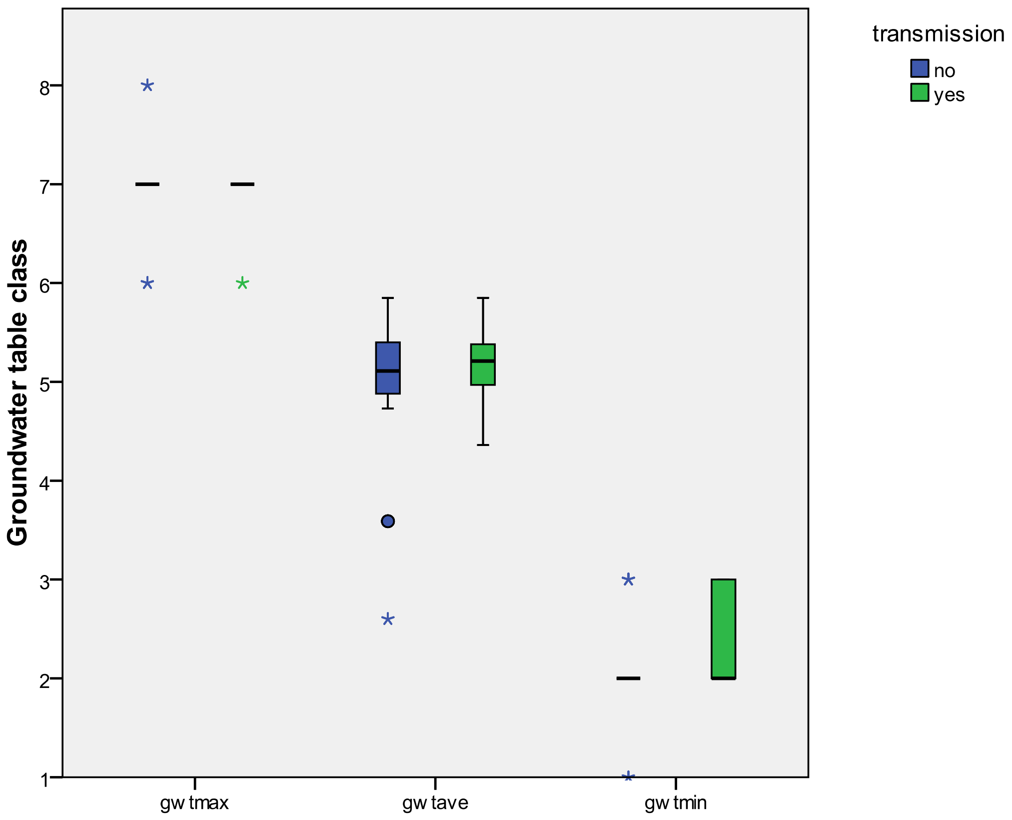

Figure 16. Boxplots of the minimum, maximum and average groundwater table class within the 5 km buffer zone

Relative soil humidity

The differences in average relative soil humidity do not show a consistent tendency: during some months average values are higher while during other months lower for the human transmitted compared to the non-transmitted farms (Figure 17). The weather-based indicator of soil humidity does not seem to have any relation with the transmission of Q fever.

The indicator for the relative soil humidity was based on a simplified spatially homogeneous schematization of soil water storage. The simplified model set up for this study did not incorporate spatially variable information on soil characteristics, irrigation practices, plant transpiration, etc. To assess the influence of past weather conditions (precipitation and evapotranspiration) on the Q fever transmission to humans a more detailed physically-based approach is recommended in order to obtain reliable estimates of soil moisture variable in time and space.

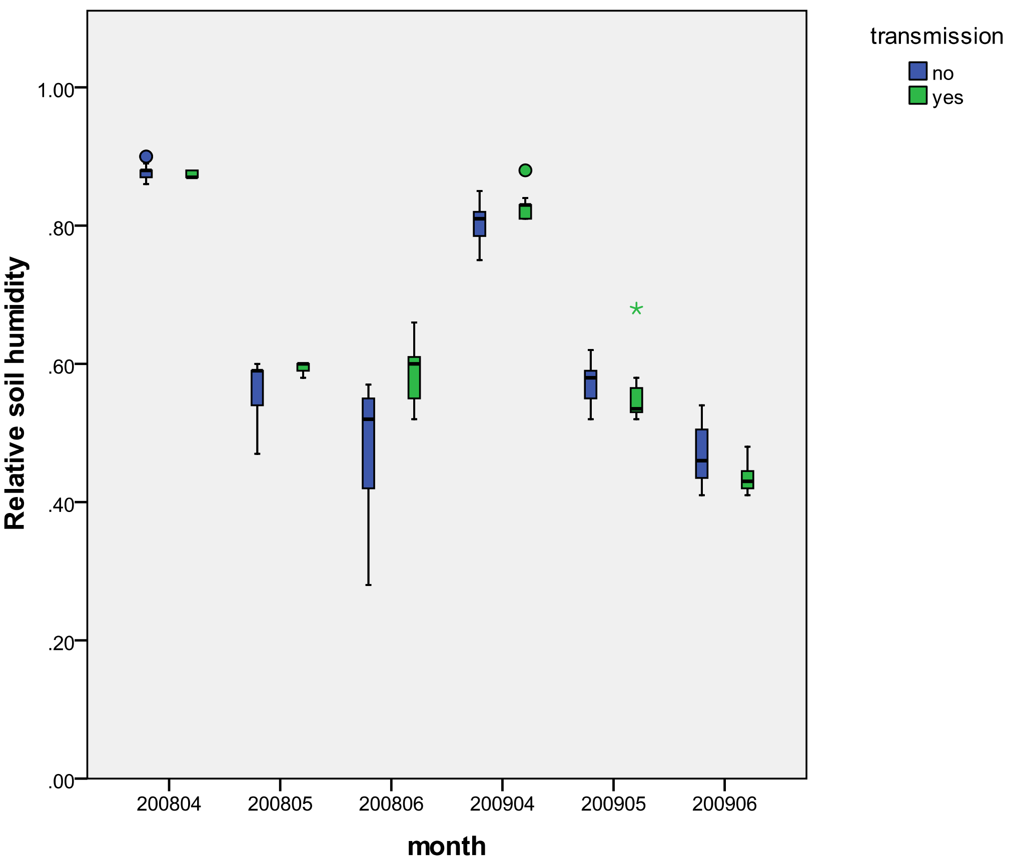

Figure 17. Monthly boxplots of the relative soil humidity

No historic soil moisture data were available for this study with sufficient detail. Ground measurements do hardly exist and remotely sensed soil moisture does not have sufficient spatial resolution. The most reliable indicator of the soil moisture conditions around the infected farms is the groundwater table class which has a strong influence on soil moisture in the low-lying Netherlands.

In summary, it can be concluded that average groundwater conditions are highly related to the transmission to humans of Q fever. Wetter soils tend to have lower human incidence rates because of the reducing effect on air-transported contaminated dust. To obtain better insight in the temporal interaction between soil moisture and transmission risk it is recommended to simulate historical soil moisture conditions through detailed spatially distributed hydrologic modeling.

4.2.5 Climate

In contrast to what one expects, the average wind velocity seems to be generally slightly lower around farms where transmission to humans took place compared to the non-transmitted farms. Also the hourly maximum wind velocity is lower around the farms where high human Q fever incidence rates were observed. The average temperature and global radiation around the farms do not show a tendency from which any conclusions can be drawn.

Most likely the monthly time scale used for the analysis is too long. Moreover, wind direction was not considered in this study, but is known to be an important factor. Another factor is the influence of vegetation on the wind speeds. The roughness structure of vegetation and residential areas are very likely to alter the wind speeds locally. A more detailed location-specific assessment is necessary to study the influence of wind velocity.

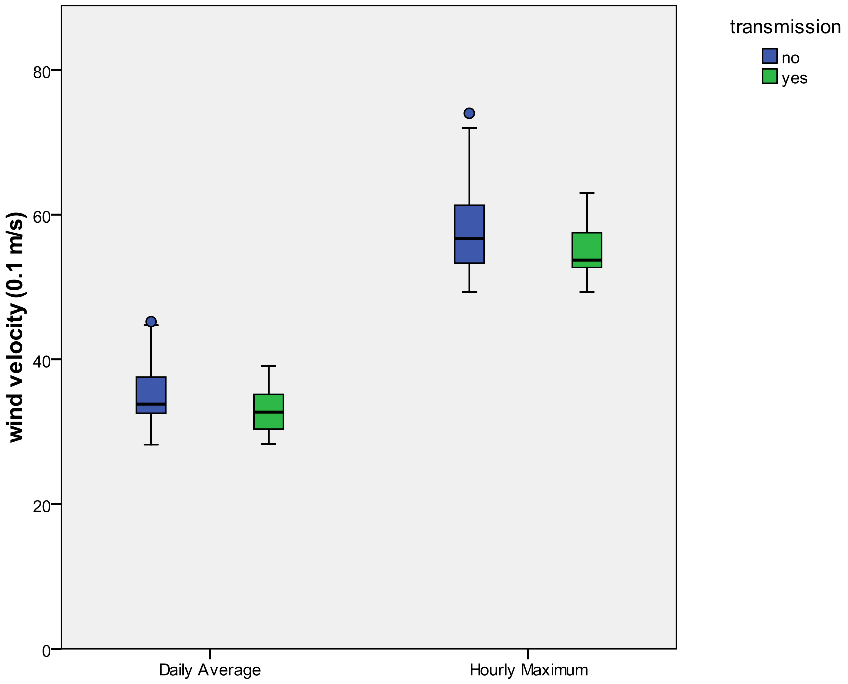

Figure 18. Boxplots of the wind velocity (average and maximum, in 0.1 m/s) within the buffer zone

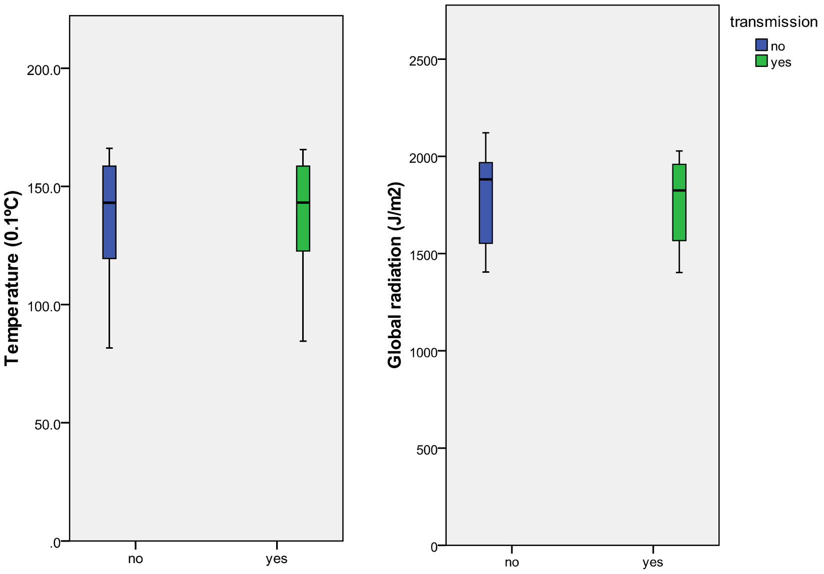

Figure 19. Boxplots of the temperature (in 0.1°C) and global radiation (J/cm^2) within the buffer zone.

4.3 Risk factors

To allow for a multivariate analysis with transmission to humans yes/no as the dependent variable, relevant explanatory variables were dichotomized, based on the distribution of the variables and using the median as cutoff point. Table 7 shows the results of the bivariate logistic regression analysis, listing the odds ratios for the most relevant variables. The odds ratio and the corresponding confidence intervals give an indication of the likelihood of Q fever transmission to humans if a certain environmental factor is present. As described before, high vegetation index and shallow groundwater levels (i.e. low groundwater table classes) were protective for transmission. Greater goat and cow densities in the 5 km buffer zone were a risk factor for transmission to humans.

Table 7. Odds ratios for relevant variables.

Variable	Cutoff	Odds ratio	95% CI**
NDVI (median)	>0.69	0.24	0.11-0.49
	<=0.69	1[*]	
Average groundwater table class	<5.21	0.73	0.38-1.43
	>=5.21	1	
Minimum groundwater table class	<3	0.35	0.16-0.76
	3	1	
Goats	>3200	2.36	1.19-4.68
	<=3200	1	
Cows	>11,000	2.10	1.04-4.27
	<=11,000	1	

[*] Reference category, ** CI: Confidence interval

In multivariate logistic regression models the NDVI and minimum groundwater level remained independent explanatory variables, when controlling for different sets of potentially confounding variables. It was verified that the proximity of the populated areas to the infected source is not a confounder of the variables being studied. This was analyzed using the population fraction within a 2 km radius compared to the 5 km radius buffer zone.

5 Conclusions and recommendations

The objective of this explorative study was to investigate whether relationships could be found between the risk for Q fever transmission to humans and environmental local conditions. Of all the environmental datasets being studied, the strongest relation was found with the vegetation density (NDVI) and average groundwater conditions as an indicator for soil moisture.

Farms with a surrounding low vegetation density have a higher probability of transmitting Q fever to humans. This can be concluded from the analysis of the distribution of vegetation index values within the 5 km buffer zones around the infected farms. It confirms the hypothesis that vegetation reduces the amount of dust available for dispersion of the Q fever bacterium.

More confidence on the causality of this relationship could be obtained by studying the spatial distribution of vegetated patches around and between the source and residential areas. The results indicate that vegetation density is a promising estimator of the friction of the landscape for Q fever bacteria to travel from the infected farm to urban settlements. Therefore, a thorough analysis of the relative distribution and distances from the different vegetation patches compared to the infection source and surrounding residential areas is required. This would lead to a better understanding of the influence of vegetation on the risk of Q fever transmission to humans.

Farms with shallow groundwater tables, i.e. with wetter average soil moisture conditions, have lower human Q fever risk within the direct surrounding of the infected source. Significantly more human Q fever cases were observed around farms where groundwater tables are lower compared to the farms where no or very few cases were recorded. It is likely that this relation is caused by the influence of soil moisture on dust production and deposition. Drier soils are more prone to wind erosion and are also correlated with lower vegetation densities.

A few recommendations can be made for further studies:

- Further investigate the relationship with vegetation density and vegetation patches and distribution using geospatial statistical methods to obtain better insight in the enhancing and reducing effects of vegetation around infected sources. This could be used for risk assessments and maps and could lead to guidelines for decision making on the location of future dairy goat farms.
- Obtain and analyze more detailed estimates of soil moisture conditions through detailed spatially distributed modeling of soil moisture to obtain insight in the temporal dynamics of Q fever transmission. Further knowledge on these relationships could help to establish risk warnings for public health as a function of previous and forecasted weather conditions.

This study confirms that environmental factors play a significant role in the transmission to humans of the Q fever bacterium. The magnitude of the Q fever outbreaks in the Netherlands during the last 3 years is unprecedented and requires more investigation on the influence of the particular Dutch environmental conditions. Further findings could play a role in the ongoing discussions on mitigation of health risks of (large-scale) farming, for example through location, determining minimal distances between farms and human habitation. Further investigation could also lead to better preparedness through the development of risk maps for Q fever transmission and public warnings to reduce the exposure during certain periods depending on weather and other environmental conditions.

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