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Q fever in The Netherlands: the role of local environmental conditions

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The Netherlands is facing a Q fever epidemic in which dairy goats are implicated. People living close to an affected farm have an increased risk. However, no human cases were reported around a number of farms with serious Q fever problems. To assess the role of local environmental conditions which may add to the transmission or risk of Q fever, we gathered datasets on vegetation, land use, soil characteristics, and weather conditions in 5 km areas around infected farms. Areas without transmission had a higher vegetation density and relatively shallow groundwater conditions. Vegetation and soil moisture are relevant factors in the transmission of *Coxiella burnetii* from infected farms to humans, by reducing the amount of dust available for dispersion of the bacteria. The findings suggest that intensive goat and sheep husbandry should be avoided in areas that are characterized by a combination of arable land with deep groundwater and little vegetation.

Keywords: Q fever; *Coxiella burnetii*; environment; goats; The Netherlands

Introduction

In 2007 Q fever emerged in The Netherlands as an infectious disease of great public health importance. The extent of the seasonal outbreaks in 2008 and 2009 with more than 3,300 human cases was unprecedented in the world (Figure 1). The causative bacterium, *Coxiella burnetii* has a worldwide reservoir in many different animal species but in The Netherlands dairy goats and to a lesser extent dairy sheep were implicated (van der Hoek et al. 2010a). The most affected area in the south of the country had a high density of dairy goat farms and several farms experienced clinical signs with abortion waves that were confirmed as Q fever with immunohistochemistry on placental tissue (van den Brom and Vellema 2009). Infection of humans is caused by inhalation of contaminated aerosols. Especially when infected pregnant small ruminants abort, billions of *C. burnetii* end up in the environment while fewer than 10 organisms are sufficient to seed an infection (Benenson and Tigertt 1956). The organism's ability to persist in the environment may result in a continued risk for infection weeks to months after the birthing event. Q fever is a zoonotic disease with no convincing evidence for human-to-human transmission. The size of the community outbreak in The Netherlands suggests that transmission

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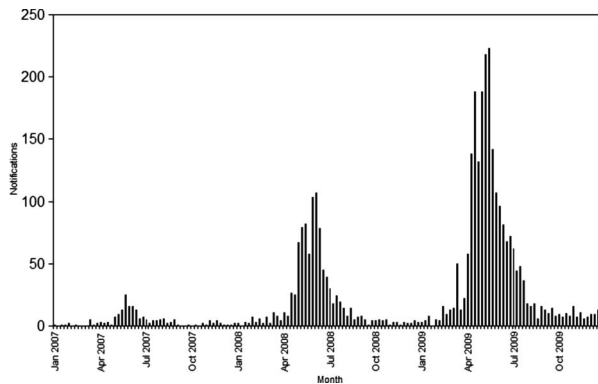*Corresponding author. Email: wim.van.der.hoek@rivm.nl

Figure 1.   Q fever notifications in The Netherlands by date of onset of illness. Bars represent notifications per week. Information on onset of illness was available for 194 patients in 2007, 982 in 2008, and 2,313 in 2009.

predominantly takes place through wide-scale environmental contamination or multiple point-source contamination sites. To a lesser extent direct recreational and occupational contact with animals plays a role (van der Hoek et al. 2010a).

Individual-level risk factors for Q fever include male gender, older age, smoking, contact with hay, straw and manure, and living close to an infected dairy goat farm (Karagiannis et al. 2009). It has been established that people living within 5 km of an affected farm have a much higher risk for Q fever than those living more than 5 km away (Schimmer et al. 2010). Under dry, dusty conditions infective aerosols can travel several km 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. 2004).

A number of dairy goat farms outside the high incidence area in The Netherlands had major Q fever problems without any human cases in the surrounding population. 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 was assessed, with a focus on vegetation, land use, soil characteristics, and weather conditions, while accounting for other possible explanations for small area variations such as differences in human and animal population density.

Materials and methods

Human cases

Q fever is a notifiable disease in The Netherlands and information on human cases is available in the national electronic infectious diseases surveillance database. Full (six-digit) postal codes are not available in this database but were provided separately by the Municipal Health Services to allow georeferencing of residential addresses. The time period during the year in which most transmission to humans takes place was from April to June, assuming a median incubation period of 21 days (Porten et al. 2006; Figure 1). It was decided to focus on the human cases infected during these months only.

Veterinary data

The Animal Health Service provided information on the locations of the 25 dairy goat farms and two dairy sheep farms that had experienced abortion waves from 2006–2009, with 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 (Figure 2).

Q fever among animals is known to be persistent and it was assumed that infected farms maintain their potential as a source of contamination at least a year after the abortion wave (Berri et al. 2007). Therefore, farms infected from 2006 and later were taken into account for analysis of the outbreaks of 2008 and 2009. The locations of
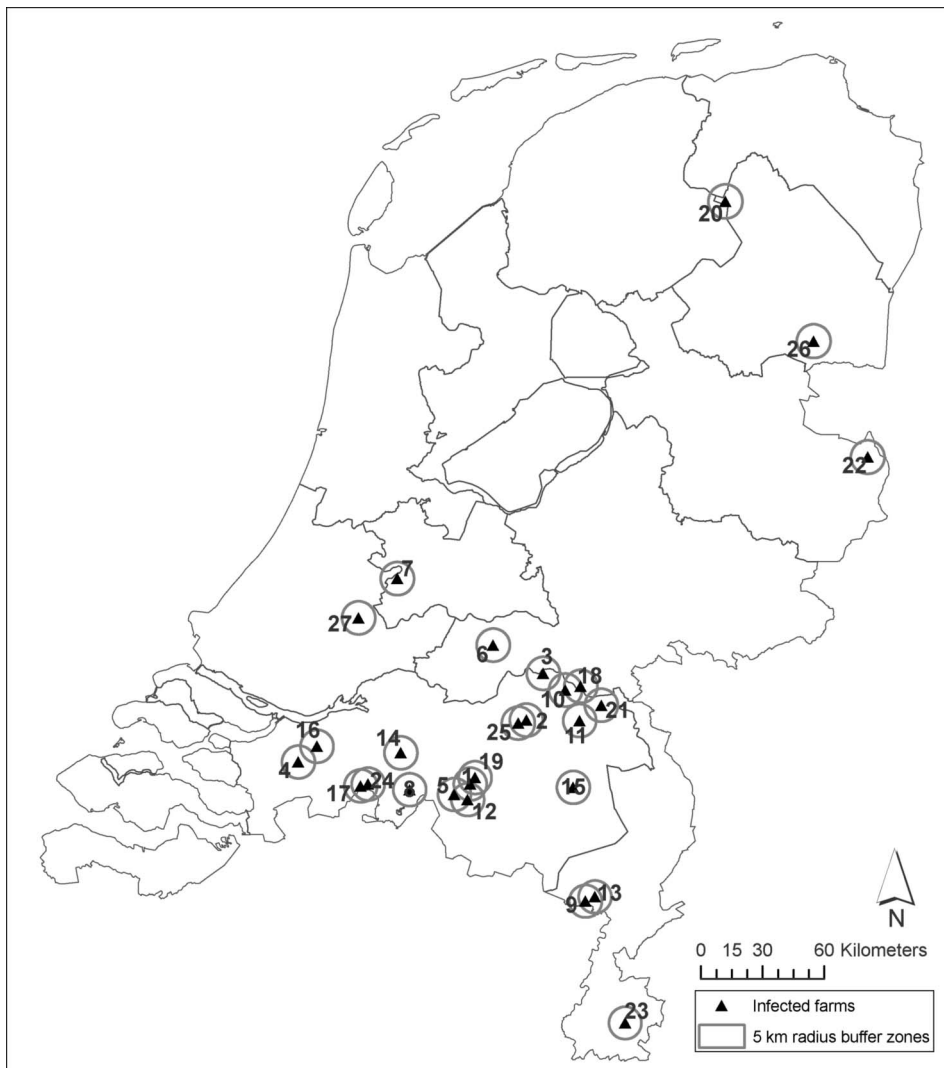

Figure 2. Location and 5 km exposure radius of the farms where Q fever abortion waves took place.

infected farms and residential addresses of notified human cases were plotted with the geographical information system software ArcView version 9 (ESRI, Redland, CA, USA). Environmental datasets were gathered for the 5 km area around each infected farm. A detailed description of the different environmental datasets is given elsewhere (Hunink et al. 2010).

Vegetation

Vegetation density was measured with the Normalized Difference Vegetation Index (NDVI). The NDVI was obtained as a gridded product with a spatial resolution of 250 m from the MODIS (Moderate Resolution Imaging Spectroradiometer) sensor on board of the NASA Terra and Aqua satellites. 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 fell entirely within the corresponding month. For April 2009 and June 2009 the quality of the images was affected probably due to hazy atmospheric conditions so the adjacent image in time was used.

Land use

Land cover was obtained from the Dutch land use database of 2004, which is a raster database with 25 m resolution covering the entire Dutch territory and presenting the land use in 39 classes. It is based on a combination of satellite imagery and ancillary data. The classes were converted into four main land cover classes found relevant for this study, being: (i) Arable and cultivated land; (ii) pastures; (iii) open spaces with little or no vegetation (including heath land); and (iv) forest. In addition, the surface of residential area was extracted.

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. For this study only the soil texture at the surface is a variable of interest as it controls the wind erosion threshold velocity. Therefore, the large number of classes was reduced in order to extract the dominant surface texture (clay, sand and peat) around the surrounding farm areas.

Soil moisture

Groundwater tables in The Netherlands are relatively shallow (between around 1 and 3 m depth) due to the low elevations of the ground surfaces. The entire country has been mapped using groundwater depth classes, which is the conventional way to express groundwater depths. Generally speaking, soils with shallow groundwater tables are wetter, while soils with average deep groundwater conditions are drier. Groundwater depth can therefore be used as an indicator of average soil moisture conditions. Historical data on soil moisture on a national scale are not available. The relative differences in time are mainly controlled by the water balance, i.e., daily precipitation and evapotranspiration. A simple model was set up to quantify temporal variation of the relative soil humidity using the information on precipitation and evapotranspiration from the Royal Netherlands Meteorological

Institute (KNMI) weather stations. The obtained daily time series were aggregated to 10 days and spatially interpolated using kriging. The resulting decadal maps gave insight in the relative temporal differences in humidity, assuming a uniform soil profile. It has to be noted that the model did not include any information on soil characteristics and was purely based on the water balance terms. However, soil characteristics were taken into account separately in the statistical analysis.

Weather conditions

The meteorological conditions that are likely to promote the production and dispersion of dust are dry and windy weather. Wind velocity triggers the dust production, depending on the wind erosion threshold. Temperature and global radiation may influence the persistence of *C. burnetii* in the environment, so they were taken into account as well for the statistical analysis. Daily time series on these variables were obtained from 18 KNMI weather stations. To obtain information on these variables at the surroundings of the infected farms, the daily time series were first aggregated to 10-day averages. These averages were spatially interpolated.

Data analysis

Analysis was done using 5 km buffers around the 27 infected farms as the radius of exposure. When these 5 km buffer zones overlapped, it was assumed that the human notifications located in the overlapping area could be attributed to the closest farm. In the analysis a distinction was made between areas with transmission to humans (defined as an incidence of >1 notification per 10,000 population per month with a minimum of two notifications) and areas without transmission. Areas with and without transmission were compared for the high incidence months of April–June in 2008 and 2009. Four farms were notified with Q fever for the first time in 2009 and for these farms only the three months in 2009 were included in the analysis. The entire dataset therefore had 150 cases: 23 infected farms observed for three months in 2008 and 27 infected farms observed for three months in 2009. The number of infected cases around the infected farms in 2007 was so low that no useful statistical analysis could be performed for that year.

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.

Normally distributed continuous variables were compared with Student's *t*-test. For risk factor analysis, logistic regression was used in which explanatory variables were dichotomized with the mean or median value as cut-off point, depending on the distribution of the variable.

Results

Of the 150 observation months for the 27 infected farms, 95 months were classified as non-transmitting and 55 as transmitting (Table 1). The monthly incidence rate in the 5 km area around the 27 infected farms ranged from 0–160 notifications per 10,000 inhabitants (Figure 2).

Table 1. Means and *p*-value (Student's *t*-test) for environmental variables for the complete dataset ($n = 150$ farm-months of observation).

	Transmission		
	No ($n = 95$)	Yes ($n = 55$)	*P*
NDVI*			
Median	0.70	0.67	<0.001
Minimum	0.27	0.24	0.14
Maximum	0.89	0.89	0.26
Land use (km^2)			
Arable lands	22.5	27.4	<0.001
Pasture lands	33.2	29.2	0.01
Forest cover	7.8	8.0	0.77
Bare cover and heath	0.3	0.2	0.10
Residential area	7.1	8.6	0.02
Soil texture (%)			
Peat covered	7.3	0.8	<0.001
Clay covered	24.2	26.4	0.67
Sand covered	59.5	62.6	0.58
Soil moisture			
Min groundwater table class	2.11	2.36	<0.001
Relative soil humidity (%)	0.62	0.66	0.19
Climate			
Mean wind velocity (0.1 m/s)	34.8	32.9	<0.001
Temperature (°C)	13.7	13.7	0.99
Global radiation (J/cm^2)	1,797	1,765	0.39

*NDVI, Normalized Difference Vegetation Index.

Considerable temporal and spatial variation was found for the NDVI distribution within and between the buffer zones during the six analyzed months in 2008 and 2009 (Figure 3). The temporal differences can be attributed to crop growth cycles and seasonal variations of the natural vegetation. The distribution of NDVI values within the buffer zones tends to have a lower median value at the farms where Q fever was transmitted to humans (Table 1). In general, it can be stated that the areas where no transmission to humans took place from the infected farms were more densely vegetated than areas with transmission.

A clear relation was found between land use and the risk for human transmission of Q fever (Table 1). Infected farms surrounded by relatively more arable fields co-occur with higher Q fever human incidence rates. On the other hand, lower incidence rates were observed within buffer zones with relatively more pasture fields. The other three land use classes did not show significant difference between the two groups. The share of bare and open surfaces within the buffer zones was probably too small for meaningful analysis. Forest cover was not found to be indicative for human transmission risk of Q fever.

A weak relationship was found between the texture of the soil surface and the transmission to humans of Q fever around infected farms. One variable showed a significant difference being the percentage area of peat covered soils within the 5 km buffer zones. Sand and clayey soils did not show any relationship based on the analyzed datasets.
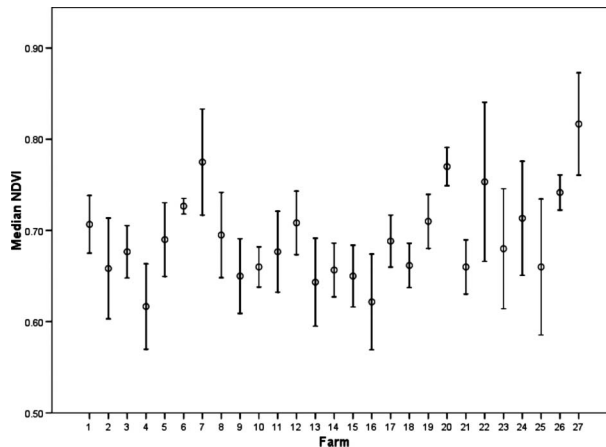
Figure 3. Temporal variation of the median Normalized Difference Vegetation Index (NDVI) values in the 5 km buffer zones around the infected farms for the six analyzed months in 2008 and 2009.

Groundwater tables were deeper around the farms where transmission to humans took place, compared to the non-transmitting farms (Table 1). The differences in average relative soil humidity based on precipitation and evapotranspiration data did not show a consistent tendency: During some months average values were higher while during other months they were lower for the human transmitting compared to the non-transmitting farms. The weather-based indicator of soil humidity did not seem to have any relation with the transmission of Q fever.

In contrast to what one expects, the average wind velocity was generally slightly lower around farms where transmission to humans took place compared to the non-transmitting farms (Table 1). The average temperature and global radiation around the farms did not show a tendency from which any conclusions could be drawn.

In Table 2 the relevant explanatory variables are dichotomized with the mean or median value as cut-off point and with transmission to humans (yes/no) as the outcome variable. Large farm size and high goat and cattle density in the 5 km areas around the farms were risk factors for Q fever. Median NDVI and minimum groundwater table class remained significant variables when adjusting for differences in animal densities and farm size. Cattle density, but not goat density, remained an independent explanatory variable in the multivariate logistic regression models (data not shown). It was verified that the proximity of the populated areas to the infected source was 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.

Discussion

Around Q fever-infected farms we found clear differences between areas with and without transmission to humans in vegetation density and in average groundwater conditions. Areas without transmission had higher vegetation densities, based on remotely sensed satellite imagery, and relatively shallow groundwater conditions.

Table 2. Univariate analysis of environmental risk factors for human Q fever in 5 km areas around farms with Q fever abortion problems ($n = 150$ farm-months of observations)

Variable	Categories	Odds ratio	95% CI
No. animals on infected farm	>920	2.41	1.21–4.77
	≤920	1*	
Goats (5 km area)	>2,400	2.13	1.08–4.20
	≤2,400	1	
Sheep (5 km area)	>1,300	1.19	0.61–2.31
	≤1,300	1	
Cattle (5 km area)	>12,200	2.39	1.20–4.76
	≤12,200	1	
Median NDVI	>0.68	0.32	0.16–0.65
	≤0.68	1	
Minimum groundwater table class[†]	<3	0.35	0.16–0.76
	3	1	

CI, Confidence interval; NDVI, Normalized Difference Vegetation Index; *Reference category; [†]Higher groundwater class numbers indicate potentially dry soils, while low numbers correspond to average wetter soil conditions.

The role of vegetation and soil moisture is supported by knowledge from the environmental sciences. 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 (Evstigneeva et al. 2007). Vegetation is known to reduce the production of dust from erodible surfaces and to remove dust from the air flow (Stockton and Gillette 1990; Lancaster and Baas 1998). To which degree dust concentrations are reduced inside and above a vegetation patch depends on its internal structure, density and height. The results confirmed that the risk for transmission to humans was reduced when higher vegetation densities occur in the direct surrounding of the infected farms. 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 association between human Q fever and low groundwater tables is likely caused by the influence of soil moisture on dust production and deposition. As groundwater tables are very shallow in The Netherlands, they are generally a good indicator of average soil moisture conditions *in situ*. Drier soils are more prone to wind erosion and are also correlated with lower vegetation densities. In contrast to groundwater level, relative soil humidity was not a significant variable in the analysis. However, this parameter was simply based on precipitation and evapotranspiration data from weather stations without taking spatial differences in soil water storage, soil characteristics, irrigation practices, and plant transpiration into account. To obtain better insight in the influence of temporal and spatial patterns of soil moisture it is recommended to simulate and analyze soil conditions in the area around the farms through detailed spatial modelling of drainage and soil hydrology.

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. In general, it can be said that many of the selected environmental variables are highly correlated with each other and this is certainly the case for land use and vegetation index. The vegetation index distribution is negatively correlated with the total area of arable lands within the buffer zones and there is a positive correlation with total area of pasture lands. The lack of a relation between transmission and forest area is somewhat surprising 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 was based on information from a few years before the outbreaks so some agricultural lands might have altered since then. Also, temporal differences related to the crop season during the year were not taken into account in this study.

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) with low dust production rates. 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.

Most likely the monthly time scale used for the analysis is too long to find reasonable relations for the weather-related variables. Moreover, wind direction was not considered in this study, but is known to be an important factor (Hawker et al. 1998; Schimmer et al. 2010). 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.

It has been known for a long time that abortion or parturition of infected small ruminants is responsible for the generation of primary aerosols of *C. burnetii* and that secondary infected aerosols can originate from the soil surface around infected farms (Welsh et al. 1958). However, the importance of environmental contamination in causing human disease over a long period of time remains unknown. In the United States, 25% of 1,600 environmental samples tested positive for *C. burnetii* indicating widespread environmental contamination (Kersh et al. 2010). However, the average number of notified human Q fever cases in the US is just over 50 per year (McQuiston et al. 2006).

Somewhat surprising, high cattle density but not goat density was a significant independent risk factor for human Q fever. Antibodies against *C. burnetii* are prevalent in all domestic ruminants, including cattle, in all European countries with often more than half of the herds testing positive (European Food Safety Authority [EFSA] 2010). However, cattle are generally considered not to play an important role in the transmission to humans. The possible role of cattle in the outbreaks in The Netherlands is investigated in more detail in a separate ongoing project.

Little is known about the pathogen characteristics that could play a role in transmission of Q fever from an infected source to humans. Large differences in

bacterial strains between farms are not expected as shown by preliminary findings of the Central Veterinary Institute of The Netherlands. One multiple-locus variable number tandem repeat analysis (MLVA) type is clearly dominant in all infected goat farms, suggesting a clonal origin (Roest 2010). This type has been related to the type that was found in human samples (Klaassen et al. 2009). MLVA types of two strains on cattle farms could clearly be distinguished from goat MLVA types.

Differences in awareness of Q fever among doctors and the public will impact on health seeking behaviour and the use of laboratory tests for *C. burnetii* infection in case of a febrile illness or pneumonia (van der Hoek et al. 2010b). Control measures in The Netherlands included mass vaccination of goats and sheep and large-scale culling of pregnant animals on farms that are found positive in bulk tank milk monitoring (Roest et al. 2010). The bulk tank milk monitoring started only in October 2009 and culling in December 2009 and has therefore not influenced the results of the study. However, local media attention might have influenced the health-seeking behaviour around some farms.

There is an ongoing public debate about the possible health risks of intensive livestock farming. Dairy goat farms in The Netherlands can have several thousand animals in one enclosure. Because of the Q fever epidemic, a temporary ban has been put on expansion of existing dairy goat farms and construction of new farms. Keeping a safe distance of several kilometres between farms and human habitation is not feasible because of the high population densities in agricultural areas. There is an urgent need to further quantify the role of environmental factors, such as vegetation patterns and soil conditions, so that these factors may be taken into account in decision making and future spatial planning.

Conclusion

Vegetation and soil moisture are relevant factors in the transmission of *C. burnetii* from infected small ruminant farms to humans. The findings could play a role in the discussion on mitigation of health risks of (large-scale) farming, for example by avoiding intensive goat and sheep husbandry in areas that are characterized by a combination of arable land with deep groundwater and little vegetation.

Acknowledgments

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