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Human Q fever incidence is associated to spatiotemporal environmental conditions

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ABSTRACT

Airborne pathogenic transmission from sources to humans is characterised by atmospheric dispersion and influence of environmental conditions on deposition and reaerosolisation. We applied a One Health approach using human, veterinary and environmental data regarding the 2009 epidemic in The Netherlands, and investigated whether observed human Q fever incidence rates were correlated to environmental risk factors.

We identified 158 putative sources (dairy goat and sheep farms) and included 2339 human cases. We performed a high-resolution (1 × 1 km) zero-inflated regression analysis to predict incidence rates by *Coxiella burnetii* concentration (using an atmospheric dispersion model and meteorological data), and environmental factors – including vegetation density, soil moisture, soil erosion sensitivity, and land use data – at a yearly and monthly time-resolution.

With respect to the annual data, airborne concentration was the most important predictor variable (positively correlated to incidence rate), followed by vegetation density (negatively). The other variables were also important, but to a less extent. High erosion sensitive soils and the land-use fractions "city" and "forest" were positively correlated. Soil moisture and land-use "open nature" were negatively associated. The geographical prediction map identified the largest Q fever outbreak areas. The hazard map identified highest hazards in a livestock dense area.

We conclude that environmental conditions are correlated to human Q fever incidence rate. Similar research with data from other outbreaks would be needed to more firmly establish our findings. This could lead to better estimations of the public health risk of a *C. burnetii* outbreak, and to more detailed and accurate hazard maps that could be used for spatial planning of livestock operations.

1. Introduction

1.1. Background

Q fever is a worldwide livestock-associated disease caused by the gram-negative bacterium *Coxiella burnetii*. The largest Q fever outbreak ever described occurred in The Netherlands from 2007 to 2010 with over 4,000 notified human cases [1]. In this epidemic, human Q fever was mainly associated with dairy goats, and to a lesser degree with dairy sheep [2]. The main reservoirs of *C. burnetii* are the goats' and sheep's placentas and birth products; the main clinical symptom is late abortion of lambs [3–5]. The birth products may contain up to about one billion *C. burnetii* bacteria per gram [4–6]. Other, but less important, excretion routes are milk [7–9] and feces and urine [9]. Excretion of the bacterium can last up to months after infection by *C. burnetii* [6].

Since goat stables are only partially enclosed, excreted bacteria can be transmitted from the indoor to the outdoor environment. *C. burnetii* has been detected in outdoor air samples in several particle size fractions in the surroundings of positive farms [10,11]. The bacterium and its spore-like forms may survive for weeks to months in the outdoor environment [12–14].

1.2. Human infection

Human infection generally occurs by inhaling the *C. burnetii* bacterium. The dose for 50% human illness (ID50) is about 1.18 bacteria

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[15]. There is no evidence for human illness being transmitted by the foodborne pathway [14].

Human Q fever is a notifiable disease in The Netherlands since 1978. Prior to the large epidemic in 2007–2010, the number of notified cases varied between 5 and 20 per year, with a maximum estimated seroprevalence of antibodies against *C. burnetii* in the general population of 2.3% in 2006 [16]. The total number of (a)symptomatic human infections during the epidemic was estimated to be about 12.6 times larger than the total number of notified cases [17]. The seroprevalence in the centre of the epidemic was estimated at 12.2% in 2009 [18] and 10.7% in 2010–2011 [19]. The Q fever prevalence on large dairy goat farms (>50 animals) was estimated to be 43.1% in 2009 [20].

1.3. Problem description

The number of humans infected by an airborne pathogen depends on:

(1) emission strength;
(2) airborne transmission from source to receptor as a function of meteorological and environmental conditions [21–28]; and
(3) human exposure: the exposure level is dependent on, among others, duration [29], location [30] and physical activity [31].

In the current study we mainly focused on the second point to investigate the possible effects of the transmission pathway (outdoor environment) between source (farms) and receptors (humans). The outdoor environment could play a threefold role: first, meteorological conditions (including wind speed/direction, precipitation and vertical motions in the atmosphere) influence the degree and pre-dominant direction of the airborne transmission of *C. burnetii* bacteria that were released from a farm's stable into the air [22,32]; secondly, landscape elements (including vegetation) are able to remove particles from the atmosphere by deposition (e.g., [33,34]). Thirdly, these landscape elements and specific environmental conditions possibly affect the *reaerosolisation* of bacteria [35,36].

The Dutch Q fever cases were spatially clustered with large regional differences in incidence rates. Highest rates were reported in the south-east of The Netherlands [1]; in several other regions positive farms were identified without hardly any reported human cases nearby (Fig. 1). Therefore, an explorative statistical analysis was performed in 2011 to investigate the correlation between Q fever incidence rate and specific environmental conditions (vegetation greenness, land use, soil texture, soil moisture content, wind velocity, temperature, and global radiation) [27]. The authors concluded that relatively low vegetation greenness and low soil moisture content levels were correlated to higher transmission levels of *C. burnetii*.

Since that study was explorative, several important assumptions were made:

- Cases were assumed to have been infected only by the nearest positive farm.
- Only farms with reported abortion waves (i.e. >5% of the parturitions [37]) ($n = 27$) were assumed to have emitted bacteria, while in practice many more had tested positive in one or multiple tests (see Methods section).
- Soil moisture content was based on static ground water level data with no temporal component.
- "Farm status" was dichotomised to months with "no transmission" (if the incidence rate was ≤1/10,000 within 5 km) or "transmission".

1.4. Aim

The aim of this research was to refine the study of [27] to test the hypothesis that transmission of *C. burnetii* from farms to humans was associated to environmental conditions and their spatial and temporal heterogeneity using a zero inflated regression analysis. In addition, we included additional variables: concentration and deposition of *C. burnetii* modeled by means of an hourly-based atmospheric dispersion model (which includes among others precipitation amount/duration, atmospheric stability, and wind speed/direction, and the relative geographical position of cases with respect to the position of putative sources), leaf area index, soil wind erosion sensitivity, and time-dependent soil

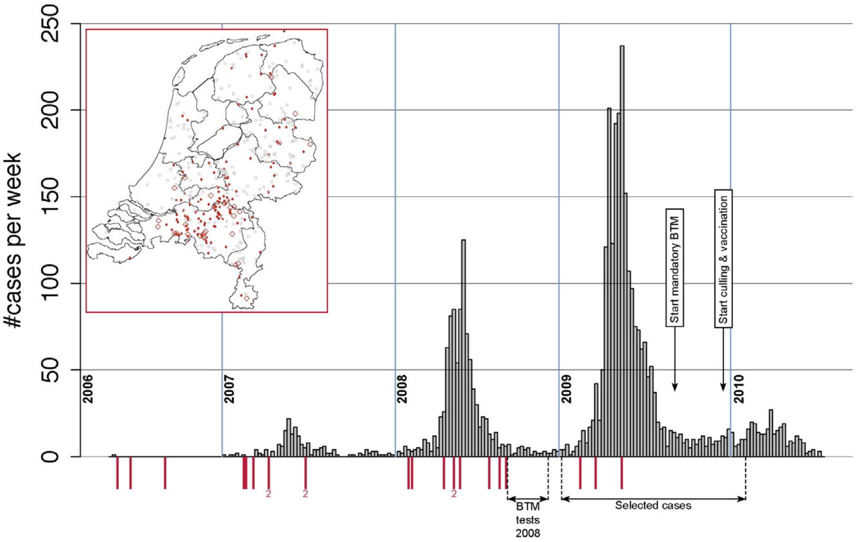

Fig. 1. Time course of the Q fever epidemics in The Netherlands with the number of notified cases per week (gray bars). Red bars indicate the week in which an abortion wave was registered at one (or two: '2') farms. The non-systematic bulk tank milk (BTM) tests were performed in the autumn of 2008; the mandatory and systematic BTM tests were performed from September 2009. Mandatory and systematic vaccination and culling started at the end of December 2009. The geographic map of The Netherlands shows the location of all large dairy goat farms with abortion waves ( ), all other positive (•) and negative (○) farms. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)