Marked increase in leptospirosis infections in humans and dogs in the Netherlands, 2014

R Pijnacker [1], MG Goris [2], MJ te Wierik [1], EM Broens [3], JW van der Giessen [1,4], M de Rosa [1,5], JA Wagenaar [3,4], RA Hartskeerl [2], DW Notermans [1], K Maassen [1], B Schimmer [1]

1. Centre for Infectious Disease Control (CIb), National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
2. Leptospirosis Reference Centre, Royal Tropical Institute (KIT), KIT Biomedical Research, Amsterdam, The Netherlands
3. Department of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands
4. Central Veterinary Institute of Wageningen University and Research centre (WUR), Wageningen, the Netherlands
5. Veterinarian Incident and Crisiscentre, Food and Consumer Product Safety Authority (NVWA), Utrecht, the Netherlands

Correspondence: Roan Pijnacker (roan.pijnacker@rivm.nl)

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In the Netherlands, 97 human leptospirosis cases were notified in 2014. This represents a 4.6-fold increase in autochthonous cases (n = 60) compared with the annual average between 2010 and 2013. Most cases had symptom onset between June and November. This marked increase in humans coincided with an increase of leptospirosis in dogs. In 2014, 13 dogs with leptospirosis were reported, compared with two to six dogs annually from 2010 to 2013. The majority of the autochthonous cases (n = 20) were linked to recreational exposure, e.g. swimming or fishing, followed by occupational exposure (n = 15). About sixty per cent (n = 37) of the autochthonous cases were most likely attributable to surface water contact, and 13 cases to direct contact with animals, mainly rats. A possible explanation for this increase is the preceding mild winter of 2013–2014 followed by the warmest year in three centuries, possibly enabling rodents and *Leptospira* spp. to survive better. A slight increase in imported leptospirosis was also observed in Dutch tourists (n = 33) most of whom acquired their infection in Thailand (n = 18). More awareness and early recognition of this mainly rodent-borne zoonosis by medical and veterinary specialists is warranted.

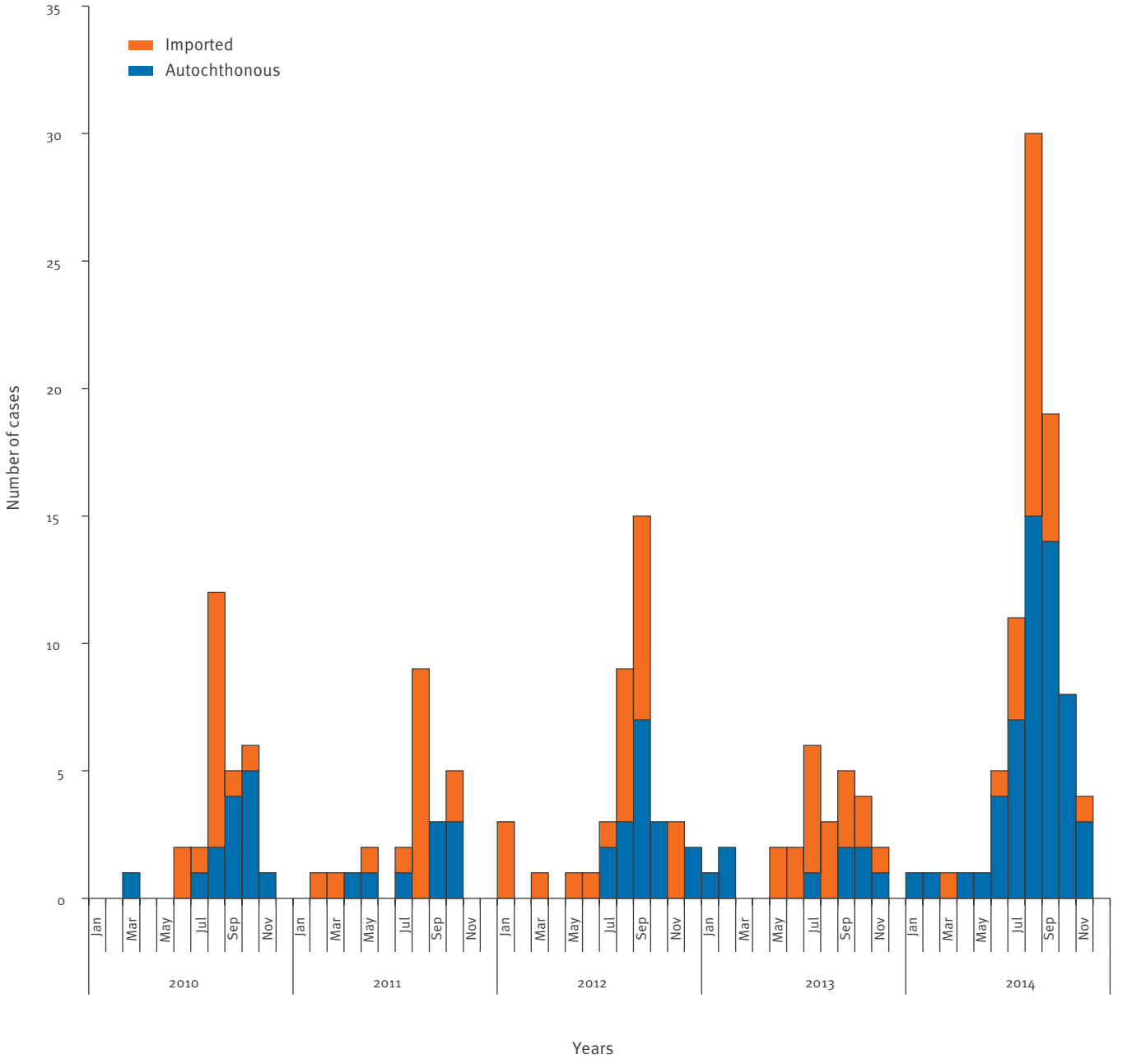
Background

Leptospirosis is a zoonosis caused by pathogenic *Leptospira* species (spp.) and may result in a broad clinical spectrum of disease, ranging from asymptomatic infections to severe disease manifestations known as Weil's syndrome, characterised by the triad of jaundice, acute renal failure and bleeding manifestations, and severe pulmonary haemorrhage syndrome (SPHS) with a high case–fatality rate [1-3]. Transmission to humans usually occurs via direct or indirect contact with urine of infected animals. A wide variety of animal species, primarily mammals such as rodents, cattle and dogs, may serve as a reservoir of leptospires [1]. The usual port of entry is the skin via abrasions or cuts but infection may also occur via the conjunctiva [2]. In dogs, leptospirosis can cause severe, life-threatening infections with vascular damage, liver and renal failure. Pulmonary symptoms have recently been reported as well [4]. There are nearly 300 pathogenic *Leptospira* serovars, often specific to particular host reservoirs, belonging to 29 serogroups, and therefore an indication for the most likely source of human infections [2].

In the Netherlands, leptospirosis has been a mandatory notifiable disease in humans since 1928 [5]. It mainly occurs as a sporadic disease and is primarily caused by two serogroups of *Leptospira* spp.: Icterohaemorrhagiae (serovars Icterohaemorrhagiae and Copenhageni) with rats as reservoir and Grippotyphosa (serovar Grippotyphosa type Duyster) with mice as reservoir. In animals, only leptospirosis caused by *Leptospira borgpetersenii* serovar Hardjo is a notifiable disease. In the late 1980s and early 1990s, dairy cattle were a major source of serovar Hardjo [6]. Due to an effective control and monitoring programme in the 1990s, serovar Hardjo became rare in Dutch cattle [7], resulting in a marked decrease in autochthonous human dairy farm fever (Hardjo) cases [8]. Since 2000, approximately 30 human leptospirosis cases have been diagnosed annually in the Netherlands, mostly associated with recreational exposures [6,9]. Leptospirosis has an annual peak incidence occurring in late summer and autumn in temperate regions like the Netherlands [2]. Due to increasing globalisation, the proportion of imported human cases has gradually increased over time. Most cases acquired leptospirosis outside Europe, mainly in countries in south-east Asia [6].

Figure 1

Autochthonous (n = 60) and imported cases (n = 33) of leptospirosis by month of illness onset, the Netherlands, 2010–2014



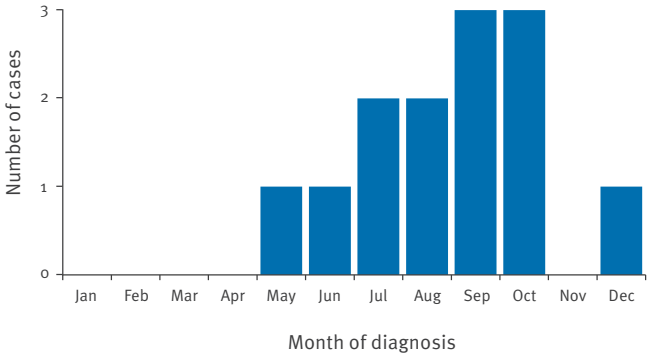
In September 2014, an increase in notified leptospirosis cases was observed by the National Leptospirosis Reference Centre (NRL), which alerted the National Institute of Public Health and the Environment (RIVM) as part of their national reference tasks. The NRL, which is also World Health Organization (WHO)/Food and Agriculture Organization of the United Nations (FAO)/World Organisation for Animal Health (OIE) Collaborating Centre for Reference and Research on Leptospirosis, shared this alert with the WHO Collaborating Centre on Leptospirosis in France, which, in turn, confirmed a coinciding increase in leptospirosis in mainland France. They posted their joint findings in an urgent inquiry in the Epidemic Intelligence Information System (EPIS) for Food and Waterborne Diseases of the European Centre for Prevention and Control (UI-272, EPIS) on 31 October 2014. An increase in confirmed leptospirosis in dogs and inquiries by veterinarians about suspected cases was noted by the Dutch Veterinary Microbiological Diagnostic Center in October 2014. In this report, we have combined all available data to describe this marked increase in leptospirosis infections in humans and dogs, and provide case characteristics such as symptoms, travel history, possible sources of exposure and serogroup information.

Figure 2

Geographical distribution of autochthonous (n = 60) and imported cases (n = 33) based on postal code of residence, the Netherlands, 2014

Figure 3

The number of dogs diagnosed with leptospirosis by the Veterinary Microbiological Diagnostic Center, by month of diagnosis, the Netherlands, 2014



Methods

We used surveillance reports stored in the national surveillance database at the National Institute for Public Health and the Environment (RIVM). Clinicians and general practitioners send clinical specimens of patients suspected for leptospirosis to the National Leptospirosis Reference Centre (NRL) for laboratory evaluation using microscopic agglutination test (MAT) and an in-house-developed IgM-ELISA for diagnostic confirmation based on detection of antibodies. When patient serum is collected before the 11th day after date of symptom onset, tests to detect leptospiral antigen (culture and PCR) are performed as well; PCR is always performed on urine because leptospiral DNA can be detected in urine at all stages of the disease. The presumptive serogroup was deduced from the highest MAT titre with a pathogenic serovar in a follow-up sample. A case of leptospirosis is considered confirmed positive for *Leptospira* when positive by culture and/or PCR and/or serology (MAT or IgM ELISA) and has fever or at least two of the following symptoms: rigors, headache, myalgia, running eyes, bleeding in skin and mucosa, rash, jaundice, myocarditis, meningitis, renal failure or pulmonary haemorrhagic symptoms.

Patients with confirmed leptospirosis are reported by the NRL to the Municipal Health Service (MHS) that collects case characteristics, performs source tracing and, if needed, instigates control measures [3]. Detailed travel history in the month before date of symptom onset and the most likely source of infection to determine whether a case is classified as autochthonous or imported. The MHS notifies each laboratory-confirmed case that adheres to the clinical case definition to the national surveillance database at the RIVM [3].

The MHS also notifies autochthonous cases to the Dutch Food and Consumer Product Safety Authority (NVWA) if site investigation is necessary, for instance if a petting farm is suspected as source of human infection [10]. GD Animal Health, which implemented a nationwide system for animal health surveillance 2003, notifies the NVWA when GD Animal Health test bulk milk from dairy herds or (slaughterhouse) blood samples from non-dairy herds positive for *Leptospira* spp. using ELISA. The NVWA then performs source investigation.

For this study, we compared all notified leptospirosis cases in 2014 with diagnosed patients in the NRL patient database based on birth year, sex and four-digit postal code, for completeness and confirmation of serogroup details and laboratory method. Case characteristics such as date of symptom onset, symptoms, travel history, relevant exposures and serogroup information were analysed. Diagnostic delay is defined as the median time period between day of symptom onset and laboratory confirmation by NRL.

The Veterinary Microbiological Diagnostic Centre (VMDC) receives sera from dogs in the Netherlands showing clinical signs of leptospirosis, which are confirmed by a combination of IgM and IgG-ELISA [11]. No information is available about the infecting serogroups in dogs. The VMDC also acts as an information desk for Dutch veterinary practitioners treating dogs suspected to have leptospirosis, and all phone calls are registered. These data were used to analyse the occurrence of leptospirosis in dogs in the Netherlands.

Table 1A

Characteristics of autochthonous (n = 60) and imported (n = 33) leptospirosis cases, the Netherlands, 2014

Characteristics	Autochthonous	Imported
Male sex	49	26
Median age in years (range)	48 (10–75)	42 (13–64)
Region		
North	9	1
West	28	24
East	20	5
South	2	3
Other [a]	1	0
Most likely type of exposure		
Recreational	20	29
Swimming	10	12
Fishing	5	0
Water sports	2	8
Water contact [b]	3	9
Occupational	15	0
Farmer	6	0
Dredging	2	0
Rat catcher	1	0
Gardener	1	0
Handyman	1	0
Kite surf instructor	1	0
Water management	1	0
Sheet piling	1	0
Police trainee	1	0
Residential	12	-
Gardening	3	-
Rat/mice presence around home	3	-
Cleaning pond	2	-
Pet mice	1	-
Water/mud	1	-
Not specified	2	-
Accidental	7	NA
Fell in water	4	NA
Rodent bite	3	NA
Not specified	7	4
Most likely route of infection		
Surface water	37	29
Ditch	9	0
Lake	9	4
Canal/river	7	9
Pond	2	0
Indoors	2	0
Unknown	8	16
Animal	13	0

NA: not available; -: not applicable.

[a] Not a Dutch resident

[b] Multiple types of water contact, or type of water contact not further specified

Results

Humans

In 2014, a total of 97 human cases (incidence 0.57/100,000 inhabitants) were notified in the Netherlands (Figure 1, Table 1). Twenty-five cases tested positive based on serology and culture or PCR. Thirty-three cases tested positive for culture or PCR and 39 cases only had positive serology. The majority of these cases (60/97) were autochthonous as they most likely contracted the infection in the Netherlands, representing a 4.6-fold increase compared with 2010–2013. Most of them became symptomatic between June and November, with a peak in August. The rise was one month earlier compared with the years from 2010 to 2013. A 1.6-fold increase (33/97) in imported cases was also observed. Country of infection was unknown for four cases. The median age was 48 years (range: 10–75 years) and 42 years (range: 13–64 years) for autochthonous cases and imported cases, respectively. The majority of autochthonous (49/60) and imported cases (26/33) were male. Autochthonous cases occurred sporadically based on the four-digit postal code of their residential address and were mainly resident in the western (28/60) and eastern (20/60) regions of the Netherlands. A small proportion was resident in the northern (9/60) and southern (2/60) regions (Figure 2). Imported cases were mainly resident in the agglomerated western region (24/33) of the Netherlands.

Symptoms and hospitalisation

Among cases for whom symptoms were reported, fever was the most frequently reported symptom (79/86). Other symptoms reported were, in order of prevalence, myalgia, headache, rigors, renal failure, jaundice (Table 2). Autochthonous cases more often presented with renal failure, jaundice and haemorrhagic symptoms compared with imported cases. Meningitis was reported in one autochthonous case and myocarditis in one imported case. Fifty-four of 60 of the autochthonous and 23/33 of the imported cases were hospitalised. No deaths were reported. The diagnostic delay was 15 days (range: 3–50 days) for autochthonous cases and 12 days (range: 3–49 days) for imported cases. From 2010 to 2013, the diagnostic delay was 14 days (range: 5–64 days) for autochthonous cases and 21 days (range: 3–84 days) for imported cases.

Serogroups

Among the autochthonous cases, 26/60 cases allowed the presumptive deduction of the infecting serogroup based on MAT titres: Icterohaemorrhagiae (9/26), Grippotyphosa (8/26), Javanica (3/26), Sejroe/Hebdomadis/Mini complex (2/26), Sejroe (2/26), Mini (1/26) and Pomona (1/26). Among imported cases, the presumptive serogroup could be deduced for 8/33 cases: Australis (2/8), Celledoni (2/8), Sejroe (1/8), Mini (1/8), Icterohaemorrhagiae (1/8) and Cynopteri (1/8). For the remaining 59 cases, the serogroup could not be determined, mostly because no follow-up serum sample was received.

Table 1b

Characteristics of autochthonous (n = 60) and imported (n = 33) leptospirosis cases, the Netherlands, 2014

Characteristics	Autochthonous	Imported
Most likely route of infection		
Rat	8	0
Mouse	2	0
Cow	1	0
Not specified	2	0
Soil	4	4
Unknown	6	0
Rat presence reported		
Yes	21	NA
No	18	NA
Not reported	21	NA
Serogroup	n=26	n=8
Icterohaemorrhagiae	9	1
Grippotyphosa	8	0
Javanica	3	0
Sejroe/Hebdomadis/Mini	2	0
Sejroe	2	1
Mini	1	1
Pomona	1	0
Australis	0	2
Cynopteri	0	1
Celledoni	0	2

NA: not available; -: not applicable.

Country of infection

Imported cases mainly acquired leptospirosis in countries in south-east Asia, of which 18/33 in Thailand. Other countries were Cuba (three cases), Cambodia and Sri Lanka (two cases each), Indonesia, Laos, Malaysia, Nepal, Costa Rica, Guatemala, Suriname and France (one case each).

Transmission route and presence of rodents

Autochthonous cases mainly acquired leptospirosis during recreational activities (20/60) such as swimming (10/20) and fishing (5/20), followed by occupational activities (15/60), mostly observed among farmers (6/15). Cases also contracted leptospirosis during activities at their place of residence (12/60) such as gardening (3/11), and due to accidents (7/60), which included patients who fell in water (4/7) or were bitten by a mouse (3/7). About two-thirds (37/60) of the autochthonous cases were most likely attributable to surface-water contact, including contact with water in ditches (9/37), lakes (9/37), canals/rivers (7/37), ponds (2/37), indoor surface water (e.g. water in basement) (2/37). Direct animal contact (13/60), including rats (8/13), mice (2/13) and cows (1/13), and soil contact (4/60) were also reported. Around one-third (21/60) reported having seen rats or mice at the location where they most probably acquired the infection. Imported cases were almost all attributable to contact with surface water (29/33) and contracted the disease during recreational activities (29/33) such as swimming (12/29) or other water sports (8/29).

Source investigations based on notified human cases

The NVWA received 26 notifications of autochthonous cases in 2014, mostly from a MHS, accompanied by a request for animal source investigation. For nine notifications, site investigations were performed, and if necessary, animal or environmental samples were collected. In two site investigations, animal samples were found positive for *Leptospira* antibodies.

In August 2014, serovar Hardjo was identified in a Dutch farmer. He was most likely infected by his dairy cattle because his bulk milk had previously tested positive by GD Animal Health for the presence of *Leptospira* antibodies using ELISA. Investigation by the NVWA revealed that this cattle herd most likely acquired the infection via German cattle, since they accidently grazed on the same pasture at the same time.

The second source investigation included a carp farmer, positive for leptospirosis in November, who reported a rat infestation at his farm. A captured rat tested by the NRL was PCR-positive. Culture and further characterisation was not successful, but the PCR melting curve results of the farmer and rat samples were similar and matched with *L. interrogans*.

Dogs

The VMDC reported 13 dogs with leptospirosis in 2014, mostly diagnosed between June and October (Figure 3). From 2010 to 2013, two to six dogs were diagnosed annually according to VMDC. The number of inquiries on suspected leptospirosis in dogs doubled in 2014 (n = 54) compared with 2013 (n = 24).

Discussion

A marked increase in autochthonous cases of leptospirosis was observed in the Netherlands in 2014, particularly during the second half of the year, from June until November, resulting in one of the highest incidence rates in Europe [12].

Cases mainly acquired leptospirosis during recreational activities such as swimming and fishing, in contrast with other western European countries, where autochthonous leptospirosis infections are predominantly associated with occupational activities [13-15]. A possible explanation for the increase of autochthonous cases is the preceding mild winter of 2013 to 2014 followed by the warmest year in three centuries in Europe [16,17], possibly enabling rodents and also excreted *Leptospira* to better survive [2,18,19]. Warm weather might also be related to increased outdoor recreational activities due to the early high temperatures in spring 2014, leading

Table 2

Main symptoms, hospitalisation and median diagnostic delays of autochthonous (n = 60) and imported (n = 33) leptospirosis cases, the Netherlands, 2014

	Autochthonous (n = 56)	Imported (n = 30)
Symptoms[a]		
Fever	51	28
Myalgia	35	21
Rigors	31	17
Headache	26	25
Renal failure	21	6
Jaundice	17	4
Skin rash	8	5
Hospitalisation		
Yes	54	23
No	4	7
Unknown	2	3
Median diagnostic delay in days (range)	15 (3–50)	12 (1–49)

[a] Multiple answers were possible

to more exposure, and an earlier seasonal rise in cases than the normal seasonal trend [20]. The increase in autochthonous cases supports a recent French study [13] hypothesising an increase in leptospirosis burden in European countries due to global warming, increasing populations of urban rodents or other animal reservoirs [21], human population growth, urbanisation and increasing international travels. Germany also noted a similar increase in autochthonous cases in 2014, which they likewise attributed to a warm and humid climate [22]. In the Netherlands, the number of imported cases was also elevated, but to a lesser extent. This might be due to increased awareness of leptospirosis in Dutch travellers among medical specialists, indicated by the decreased diagnostic delay compared with 2010 to 2013.

In 2014, serogroup Sejroe/Hebdo/Mini complex was identified in two autochthonous cases in the Netherlands, which is remarkable because this serogroup had only been identified in one previous autochthonous case in 1998 [6]. One of the cases acquired leptospirosis after being bitten by a mouse that was intended for feeding to a snake, and the other case had multiple possible sources of infection. For the first time in 16 years, serovar Hardjo was identified in a dairy cattle farmer in the Netherlands. This was surprising, because 99% of the dairy and beef cattle farms in the Netherlands had a Hardjo-free status in 2014 [7]. However, source investigations revealed that the case most likely acquired the infection via German cattle, in which serovar Hardjo is common [14].

Also remarkable, although based on small numbers, is the concomitant increase in canine cases in the second half of 2014, strengthening the hypothesis of increased environmental exposure. A monitoring programme in rodents begun in 2014 revealed that *Leptospira* are present and widespread in the rat population in the Netherlands (data not shown, personal communication, Joke van der Giessen, December 2014).

A major limitation of this study was the use of passive human surveillance data likely reflecting the more severe hospitalised cases, which leaves milder cases often unrecognised [1,23,24]. This should be taken into account when interpreting the clinical presentation of cases described in this article. Also the number of canine leptospirosis cases is likely to have been underestimated, as it depends on the veterinary clinicians' ability to identify leptospirosis in dogs. Unfortunately, the infecting serogroup based on MAT titres could only be presumed in less than half of the cases, because follow-up samples were often not received.

The results suggests that prevention efforts should be aimed at advising the general public and high risk occupational groups that have direct or indirect contact with rat or mouse urine about possible precautions to reduce exposure to *Leptospira*. In the future, monitoring programmes in rodents should focus on predicting risk of zoonotic transmission and developing preventive strategies [9]. Furthermore, vaccination of dogs should be promoted in the Netherlands, where currently only around 55% of dogs are vaccinated [9]. Preventive measures are generally advisable when a dog is suspected for leptospirosis. More awareness and early recognition of this mainly rodent-borne zoonosis by medical specialists is warranted.

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Conflict of interest

There are no competing interests for any of the authors.

Authors' contributions

Roan Pijnacker conceptualised, drafted and revised the manuscript as submitted; Marga G.A. Goris provided laboratory data on human leptospirosis cases, and critically reviewed and revised the manuscript as submitted; Margreet J.M. te Wierik conceptualised, reviewed and revised the manuscript as submitted; Els M. Broens provided data on leptospirosis in dogs, and critically reviewed and revised the manuscript as submitted; Joke W.B. van der Giessen provided data on rodent monitoring, and critically reviewed and revised the manuscript as submitted; Mauro de Rosa provided data on site investigations, and critically reviewed and revised the manuscript as submitted; Jaap A. Wagenaar critically reviewed and revised the manuscript as submitted; Rudy A. Hartskeerl: citically reviewed and revised the manuscript as submitted; Daan W. Notermans critically reviewed and revised the manuscript as submitted; Kitty Maassen critically reviewed and revised the manuscript as submitted and Barbara Schimmer conceptualised, reviewed and revised the manuscript as submitted.

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