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Leptospirosis in Ireland: annual incidence and exposures associated with infection

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SUMMARY

Human leptospirosis is found throughout the world, albeit with a higher incidence in tropical regions. In temperate regions it is associated with certain occupational and recreational activities. This paper reports both on the incidence of human leptospirosis in Ireland and on possible associated exposures, using leptospirosis case notification, enhanced surveillance, hospital discharge data and death registrations. Based on official notification data, there was a threefold increase in the reported incidence of leptospirosis in Ireland between 1995–1999 and 2004–2009, which appears partially to be due to improved reporting. The exposures most associated with infection were those involving contact with livestock or water-based recreational sports, in particular kayaking. Advice on prevention should continue to be targeted in the first instance at these groups. The variety of potential transmission routes reported should inform clinicians to consider leptospirosis in individuals with a compatible clinical profile who were not from occupational groups historically considered at risk.

Key words: Epidemiology, leptospirosis.

INTRODUCTION

Human leptospirosis is uncommon in Ireland, occurring more commonly in tropical climates. Nevertheless, between 20 and 30 cases are notified annually, and key to devising and monitoring preventive strategies for Ireland is identification of persons at risk and behaviours associated with increased risk of infection. Maintenance hosts for leptospires include cattle, rats, pigs and dogs, and activities that have been associated elsewhere with human leptospirosis include farming, occupations that involve contact with wet rodent-infested environments, recreational activities such as water sports, and flooding [1–6]. Many countries have reported a change in leptospirosis epidemiology in recent years, with an increasing proportion of cases related to recreational rather than occupational exposures [7–10].

While a few studies have reviewed the epidemiology of leptospirosis in Ireland, none has reported exposure categories associated with leptospirosis infection [11, 12]. The aim of this paper is to report on the current epidemiology of human leptospirosis in Ireland, focusing in particular on possible exposures associated with acquiring leptospirosis, and drawing on data from a variety of data sources, including disease notifications, enhanced surveillance data, hospital discharge data and death registrations.

MATERIALS AND METHODS

Leptospirosis is a notifiable disease in Ireland and as for all notifiable diseases, basic demographic data

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is reported routinely on all cases. The case definition in use between 2004 and 2009 [13] was based on the European Union (EU) case definition [14].

Irish case definition for leptospirosis (*Leptospira* sp.)

Clinical description

Clinical picture compatible with leptospirosis, characterized by fever, headache, chills, myalgia, conjunctival suffusion, and less frequently by meningitis, rash, jaundice or renal insufficiency.

Laboratory criteria for diagnosis

- Isolation of *Leptospira* sp. from a clinical specimen.
- Demonstration of a specific increase in *Leptospira* agglutination titre ($\geqslant$ fourfold rise).
- Demonstration of *Leptospira* in a clinical specimen by immunofluorescence.
- Detection of *Leptospira* IgM antibody in serum.

Case classification

Possible: not applicable.
Probable: not applicable
Confirmed: a clinically compatible case that is laboratory confirmed.

Prior to 2004, there was no case definition in place in Ireland. Under the 2004 case definition, only laboratory-confirmed cases of leptospirosis were notifiable. Since 2000, enhanced data including details on possible source of infections and information on risk awareness were specifically sought by public health physicians. Basic notification data and enhanced data were maintained in the Computerized Infectious Disease Reporting (CIDR) database, a central national repository for all infectious disease notifications data in Ireland. The notification data used in this report were retrieved from CIDR (as of 20 January 2011) on notifications of leptospirosis between 1995 and 2009 inclusive, and enhanced data were retrieved at the same time for those notifications reported between 2000 and 2009.

Where information on the possible source of infection was reported, cases were categorized into one of the following classes: (i) occupational, e.g. farming, veterinary, waste/waste water management, fishing, abattoir worker, or any other occupation which involves potential exposure to cattle or rats or water which could have been contaminated by rats; (ii) recreational, e.g. caving, kayaking, swimming in a river, rowing, or travel to a tropical destination; (iii) residential, e.g. dog or other pet ownership, homelessness, working in yard/garden, exposure to flooding in or around the home, rodent sightings near home, living (but not working) on a farm; or (iv) accidental, e.g. accidental falls into water [7, 15].

Hospital in-patient data collated by the Hospital In-Patient Enquiry (HIPE) and National Perinatal Reporting System (NPRS) unit of the Economic and Social Research Institute (ESRI) was obtained through the Health Intelligence Ireland portal, and used solely as an independent source of information on the trend in leptospirosis incidence in Ireland. An update was published in the International Classification of Diseases (ICD) coding during the study period, and thus data presented includes discharges based on different codes depending on the period in question: discharges of ICD-9 code 100* for the period 1995–2004 and discharges of ICD-10 code A27* for the period 2005–2009 but there was no material difference between codes. Any discharge which included a diagnosis of leptospirosis was included regardless of whether it was reported as the patient's primary diagnosis or an additional diagnosis. A caveat about these data is that there is no formal definition for ICD codes and therefore it has been suggested that a discharge recorded as leptospirosis would not require laboratory diagnosis, and could be recorded as such based on clinical diagnosis and decision to treat.

Leptospirosis death registration data were obtained from the Irish Central Statistics Office (CSO).

While in theory any of four methods of laboratory confirmation included in the notification case definition were acceptable for laboratory diagnosis, in practice, where known, the only form of initial diagnosis reported was antibody detection. Serum samples reactive in leptospirosis IgM tests at the National Virus Reference Laboratory (NVRL) University College Dublin, Ireland and other diagnostic laboratories in Ireland are referred for a microscopic agglutination test (MAT) to the United Kingdom Leptospirosis Reference Unit in Hereford (LRU). Serogroup/serovar data reported here were obtained from the LRU for the period 2000–2009 in aggregate form.

Average annual incidence rates were expressed as notifications/discharges/deaths per million population using the average annual number of notifications/discharges/deaths and the total Irish population recorded in the census closest to the mid-point of the 5-year

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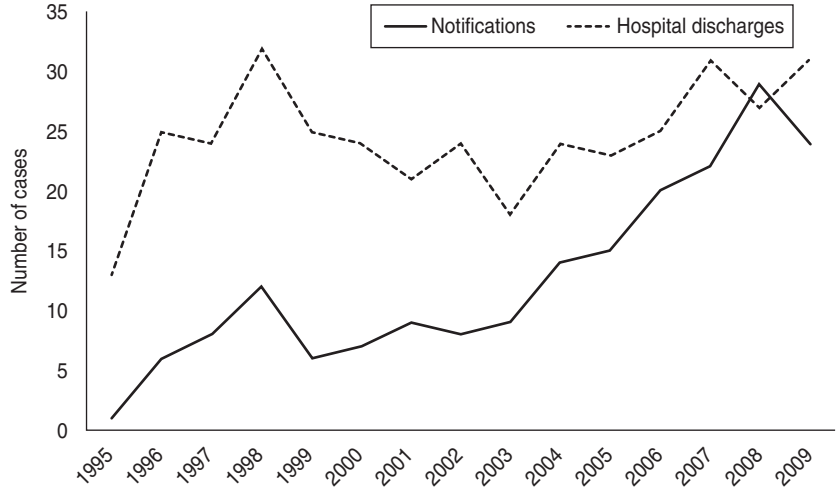

Fig. 1. Annual number of leptospirosis notifications and hospital discharges, Ireland 1995–2009. [Data source: Computerized Infectious Disease Reporting (CIDR), Hospital In-Patient Enquiry (HIPE) via Health Intelligence Ireland].

period, e.g. the population from the 2006 Irish census was used as the denominator in calculating the rates in the period 2005–2009.

The statistical significance of the difference in proportions was tested using the χ^2 test or Fisher's exact test, as appropriate, using Stata v. 11.1 (StataCorp., USA).

RESULTS

Incidence

Based on the notification data, there was a statistically significant difference ($P < 0{\cdot}0001$) in the reported incidence of leptospirosis in Ireland between 1995 and 2009, rising from a mean incidence of 1·8 notifications/million per annum in the period 1995–1999 to a mean incidence of 5·2/million per annum in the period 2005–2009 (Fig. 1, Table 1). In contrast, the estimated crude incidence rate of leptospirosis based on hospitalizations remained largely unchanged ($P = 0{\cdot}472$) in the same time period, ranging from 5·7/million in the period 2000–2004 to 6·6/million in the period 1995–1999 (Fig. 1, Table 1).

It was postulated previously by Hogan *et al.* [11] that the discrepancy between notification and HIPE data on leptospirosis in Ireland indicated that the disease was under-notified by as much as three-quarters in the period 1985–1996. That estimate was based on using the number of hospital discharges of leptospirosis reported under the HIPE reporting system as an indicator of the true number of cases.

Using a similar approach to Hogan *et al.* described above, it was estimated that completeness of notification had improved to 80% in the period 2005–2009 (Table 1) compared to only 26% notified in the period studied by Hogan *et al.* [11]. It is possible therefore that the reported increase in notifications may at least in part be due to improved reporting.

Mortality

Between 1995 and 2009, there were seven deaths due to leptospirosis in Ireland (CSO), which represents an annual mortality rate of between 0·05 and 0·22/million and a case fatality rate (CFR) of between 0·9% and 3·4% (when hospital discharge data are used as denominator) (Table 1). These were significantly lower than the average annual mortality of 0·47/million ($P < 0{\cdot}0001$) and CFR of 10% ($P = 0{\cdot}004$) as calculated previously by Hogan *et al.* (using HIPE data as denominator) for the period 1985–1996 [11].

Serovar distribution

Between 2000 and 2009, 150 leptospirosis cases from throughout Ireland were confirmed at the LRU. The predominant serogroups/serovars detected in cases during that time period were serogroup Icterohaemorrhagiae ($n = 49$, 33%) and serogroup Hardjo ($n = 37$, 25%) (Table 1). Other serogroups/serovars accounted for a further 5% of cases ($n = 8$), including serogroup Autumnalis ($n = 3$), and one each of serogroups Ballum, Pomona, Saxkoebing, Tarassovi and Mini. Serogroup/serovar was not determined for 56 (37%) cases.

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Table 1. *Comparison of leptospirosis notification data (CIDR), hospital discharge data (HIPE), death registration (CSO) and confirmations at UK LRU, 1995–2009*

	1995–1999	2000–2004	2005–2009
Incidence and completeness of notification			
Number notifications[a]	33	47	110
Annual crude notification rate/million* (95% CI)	1·8 (0·4–3·2)	2·4 (0·9–3·9)	5·2 (3·0–7·4)
Number hospital discharges[b]	119	111	137
Annual crude hospitalisation rate/million* (95% CI)	6·6 (3·9–9·2)	5·7 (3·3–8·0)	6·5 (4·0–8·9)
Estimated % notification	27·7%	42·3%	80·3%
Mortality and CFR			
Number of deaths[c]	4	1	2
Annual mortality/million population	0·22	0·05	0·09
CFR (denominator = hospital discharges)	3·4%	0·9%	1·5%
CFR (denominator = notifications)	12·1%	2·1%	1·8%
Serogroup/serovar (LRU Hereford data)[d]		(*n* = 62)	(*n* = 88)
Hardjo	–	18	19
Icterohaemorrhagiae	–	27	22
Other	–	5	3
Not determined	–	12	44

CIDR, Computerized Infectious Disease Reporting; HIPE, Hospital In-Patient Enquiry system; CSO, Irish Central Statistics Office; LRU, Leptospirosis Reference Unit; CI, confidence interval; CFR, case-fatality rate.
Data sources: [a] CIDR; [b] HIPE; [c] CSO; [d] LRU, Hereford.
* Census 1996 used for period 1995–1999, Census 2002 for 2000–2004 and Census 2006 for 2005–2009.

Interestingly, between the period studied by Hogan *et al.* [11] and 2000–2004, there was an increase in the proportion of cases for which a serovar was determined (80% in 2000–2004 *vs.* 56% during the Hogan *et al.* study period, $P = 0{\cdot}001$) but there was a subsequent decrease again in the period 2005–2009 (50%, $P < 0{\cdot}0001$).

Of the cases for which a serovar was determined, there was no significant difference in the proportion of cases caused by the main two serovars ($P = 0{\cdot}392$ and 0·736) for the three periods (Table 1); however, there was a significant increase ($P = 0{\cdot}003$) in the proportion of cases caused by 'other serovars' (8·5%) in the period 2000–2009 relative to the period studied by Hogan *et al.* (0%) [11].

Potential source of infection

Enhanced surveillance was introduced in 2000, and all subsequent analyses apply only to notification data from that time onward. Information on the possible source of infection was reported for over three-quarters of cases notified between 2000 and 2009. These were reviewed and categorized (Table 2). High-risk occupational and recreational activities accounted for the majority (85%) of leptospirosis cases with reported exposure during the study period.

Farm, fishery, forestry and veterinary workers accounted for almost three-quarters of all occupational cases. Of recreational cases, the largest subgroup were kayakers (57%), while exposure while engaged in open water swimming accounted for a further 16% of this group. Ten cases (20% of recreational cases) reported holidaying in a tropical destination. All ten cases occurred since 2005 suggesting that this is an emerging risk factor for leptospirosis in Ireland. This was the only exposure subcategory in which there was a statistically significant change in the proportion of cases between 2000–2004 and 2005–2009 ($P = 0{\cdot}033$). The majority (9/10) of these reported travelling to a destination within South East Asia.

Overall, the reported risk factor involved exposure to a body of fresh water in 42 cases [28 kayakers, eight swimmers (includes triathletes), one fisherman, three accidental cases and two occupational cases acquired following participation in river rescue courses]. Of these 42 cases, the river Liffey was reported in 23 instances as a location to which cases had been exposed, while the river Boyne was named in seven instances. No other location was named more than once, although for 12 cases, the name of the body of water was not reported. (It should be noted that cases may report exposure to more than

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Table 2. *Reported likely sources of infection for human leptospirosis cases in Ireland, 2000–2009*

Exposure category	2000–2004	2005–2009	*P* value
Occupational	17 (36%)	36 (33%)	0·714
Farming, forestry, fisheries, veterinary	10 (21%)	29 (26%)	0·551
Sewage worker/plumber/waste management	2 (4%)	2 (2%)	0·584
Construction worker	2 (4%)	1 (1%)	0·214
River rescue course	1 (2%)	1 (1%)	0·510
Other	2 (4%)	2 (2%)	0·584
Not specified	0 (0%)	1 (1%)	1·000
Recreational	13 (28%)	36 (33%)	0·577
Kayaking	11 (23%)	17 (16%)	0·259
Tropical holiday travel	0 (0%)	10 (9%)	**0·033**
Freshwater swimming	1 (2%)	7 (6%)	0·437
Freshwater fishing	1 (2%)	0 (0%)	0·299
Not specified	0 (0%)	2 (2%)	1·000
Residential	6 (13%)	9 (8%)	0·384
Accidental	0 (0%)	3 (3%)	0·555
No risk exposure identified/no information reported	11 (23%)	26 (24%)	1·000
Total	47 (100%)	110 (100%)	

Data source: Computerized Infectious Disease Reporting.

one body of water during their potential exposure period.) During the study time frame, two outbreaks were reported in the east of the country that were associated with kayaking on the river Liffey [3, 4]. These outbreaks accounted between them for ten of the kayaking-related cases notified.

Characteristics of notified cases

Of cases notified in the period 2000–2009, the majority (94%) were male with an age range of 13–85 (median 38) years (Table 3). For all exposure categories, male cases predominated; however, recreational cases appeared to be younger than occupational or residential cases. There are eight public health administrative regions in Ireland, the Health Service Executive (HSE) areas. While the majority of occupational cases were reported from more rural parts of the country, the majority of recreational cases were reported from HSE East (Table 3), a region which has a higher proportion of urban dwellers.

Overall, cases were more commonly notified in the latter half of the year (Table 3). This was particularly so for recreational and residential cases, with season having less influence on the distribution of occupational cases.

With regard to knowledge of risk (available for 53% of cases), recreational and occupational cases reported the highest level of awareness with 77% and 57% reporting awareness of risk prior to illness, respectively (Table 3).

Based on the serovar data linked to notification and enhanced data on CIDR (Table 3), serovar was reported for only 19 (12·1%) cases in the period 2000–2009, although there was a significant improvement ($P = 0·014$) in the proportion of cases for which linked serovar data was available in the 2005–2009 period (18/110, 16·4%) relative to the period 2000–2004 (1/47, 2·1%). Albeit based on limited data, serovar Hardjo was more commonly associated with occupational cases, while serovar Icterohaemorrhagiae was more commonly associated with recreational and residential cases (Table 3).

DISCUSSION

Although substantially lower than the incidence in tropical regions, Ireland now has a considerably higher reported incidence of leptospirosis than many other temperate countries. In 2009 (the latest year for which comparative data are available across the EU), the incidence rate across the EU was 1·4/million inhabitants (range 0·0–7·3/million by country) [16], compared to 5·6/million in Ireland; only Romania and Malta reported higher incidence rates than Ireland that year [16]. Moreover, in the last 15 years, there have been seven deaths attributed to leptospirosis in Ireland, an estimated CFR of around 2%.

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Table 3. *Characteristics of leptospirosis cases by exposure category, Ireland 2000–2009*

Characteristics	Recreational ($n=49$)	Occupational ($n=53$)	Residential ($n=15$)	Accidental ($n=3$)	*P* value (Fisher's exact test)	Not identified/ not reported ($n=37$)	All cases ($n=157$)
Median age (years)	28	45	52	38		47	38
Male	44	52	14	3	0·327	34	147
Female	5	1	1	0		3	10
HSE East	36	6	3	1	**<0·001**	3	49
Other HSE areas	13	47	12	2		34	108
Awareness of risk before illness	27/35	20/35	0/11	0/2	**<0·001**	Not applicable	–
Quarter 1 of year	5	17	1	1	**0·001**	7	31
Quarter 2 of year	1	6	2	0		6	15
Quarter 3 of year	11	16	2	0		12	41
Quarter 4 of year	32	14	10	2		12	70
Hardjo	1	11	0	0	**0·002**	0	12
Icterohaemorrhagiae	3	1	3	0		0	7
Serovar not determined or not reported on CIDR	45	41	12	3		37	138

HSE, Health Service Executive; CIDR, Computerized Infectious Disease Reporting.
Data source: CIDR.

While from notification data it seems that the incidence has risen significantly in the last 15 years, comparison of the trend with an alternative data source suggested that the increase may at least in part in part due to improved reporting [possibly more latterly influenced by an amendment to the Irish Infectious Diseases Regulations 1981 (Infectious Diseases (Amendment) (No. 3) Regulations 2003, S.I. No. 707 of 2003)] which took effect on 1 January 2004 [17]. A key change effected by this legislation was the addition of laboratory directors to the list of notifiers; prior to this legislation, only clinicians had a legal obligation to notify cases of infectious disease.

The age and sex distribution of Irish notified cases was similar to that reported previously for Ireland and elsewhere [11, 12, 15, 16, 18]. This has been attributed to male predominance in the occupational and recreational groups most at risk of infection. The exposures most associated with infection were selected high-risk occupations, in particular, those who have contact with livestock, e.g. farmers/veterinary practitioners, and water-based recreational sports participants, in particular kayakers. An emerging risk factor in later years was holiday travel to a tropical destination.

In accordance with previous studies in Ireland [11, 19], the predominant serovars in the period 2000–2009 were Icterohaemorrhagiae and Hardjo. Serogroup Icterohaemorrhagiae has been associated with a rat reservoir, while serogroup Hardjo has been associated with cattle. These two reservoirs are consistent with the exposures reported by cases, with occupational (largely farming-related cases) being associated in this study with serogroup Hardjo, and recreational cases (largely water sports-related cases) being more commonly associated with serogroup Icterohaemorrhagiae.

The number of cases reporting exposure to the river Liffey during their incubation period is noteworthy. The river Liffey is a lowland river on which Ireland's capital city is built, and may have a higher number of recreational users than other rivers due its proximity to a large urban population. It also plays host to at least three major sporting events each autumn: an open water swim; a triathlon; and an international kayaking marathon, some of which are accompanied by artificial flooding from an upstream dam.

A number of countries have reported a change in the epidemiology of leptospirosis from being a mainly occupational disease to being increasingly a recreational one, and changes in the predominant serovars over time [7, 9, 10, 18, 20]. Exposures noted internationally include participation in water-based activities while travelling in tropical destinations [1, 15] and outbreaks have been reported associated with the Eco-challenge event in 2000 and other water-based adventure sports events [2, 21]. In tropical

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regions, flooding is a recognized factor preceding increases in cases, and was noted also in the Czech Republic after the flooding events of 1997 and 2002 when incidence rates of leptospirosis infection rose threefold, many of the cases reporting exposure to residual water or mud in cellars [6]. Urban exposures such as working in a large urban market were identified in cases in Israel [20], and in Germany, concerns have been expressed about companion animals as a source of infection for humans [15]. The only significant change in exposure category identified in Ireland over the last 10 years has been exposure during travel to a tropical destination.

The CFR of leptospirosis infection has been reported to vary with age and serovar [11, 22]. Both mortality and CFR decreased considerably in comparison to the period studied by Hogan *et al.* [11]. The reasons for this are unclear. It does not appear to be associated with serovar. Alternative explanations could include improved or more timely identification and treatment of cases, improved notification of less severe cases or a change in the age distribution of cases.

One of the limitations of routine surveillance highlighted in Ireland is the paucity of serovar information integrated with the notification dataset. This has improved considerably between the period 2000–2004 and 2005–2009, and with the continued implementation of CIDR in Ireland, we anticipate that reporting of linked serovar information will further improve, permitting more accurate evaluation of the association of serovar with exposure and outcome data within a single dataset.

Second, while there appears to have been an increase (80·6%) in the proportion of cases for which a serogroup/serovar was determined in 2000–2004, it was notable that there was a subsequent decrease (50%) in the proportion of cases for which a serogroup/serovar was determined in 2005–2009 (LRU data). A contributory factor appears to be a reduction in the number of cases for which follow-up samples were received by the LRU for serogroup/serovar determination (W. J. Zochowski, personal communication). Ideally, follow-up specimens should be submitted for all leptospirosis cases. If those cases for which a serovar was determined had the serovar details included in the national dataset, this would add considerable value.

As only 63% of the cases in this study had MAT confirmation and serogroup determination, there exists the possibility that some had other clinically compatible diseases. Hantavirus is a rodent-borne disease which has a worldwide distribution. Although a small number of indigenous cases infected with Seoul hantavirus have been described in the neighbouring UK, associated with exposure to pet rats, wild rats and laboratory rats [23–25], and there have been reports of hantavirus seropositivity in humans and rodents in Northern Ireland [26, 27], to date only one imported case of hantavirus infection in humans has been diagnosed in Ireland [28]. A study in 2009 in which 176 patients with evidence of either rural or rodent exposures, were investigated for hantavirus IgM and hantavirus IgG using EIA and immunofluoresence (Hantavirus IgM DxSelect and Hantavirus IgG DxSelect, Focus Diagnostics, USA) showed no serological evidence for acute or previous hantavirus infection (J. Connell, personal communication), providing evidence against a major role for hantavirus in Ireland. Nevertheless, as hantavirus disease is transmitted from rodents, the public health advice that minimizes contact with rodent excreta, should be effective in preventing the risk of both leptospirosis and hantavirus infection in humans.

A further potential limitation of the dataset is that details on potential exposure were not available for 37 (24%) cases. Cases not assigned to exposure categories had a higher median age and were more likely to be from non-HSE East (and possibly more rural) areas than categorized cases, suggesting that they are more likely to comprise occupational or residential cases than recreational cases. As several of the recreational cases were part of the two outbreaks [3, 4], it is also possible that some were identified through active case-finding and are even more unrepresentative of all cases that occurred in the time period.

Regardless of the completeness of reporting or the limitations of the available data, it is evident that leptospirosis incidence in Ireland is highest in those who work in high-risk occupations and those who engage in freshwater-based recreational activities. Prevention advice should continue to be targeted in the first instance at these groups. While no denominator data is available to evaluate if the river Liffey poses a higher risk than other freshwater bodies, the high number of cases associated with this river suggests that its users should be particularly vigilant against infection, and that organizers of events on this river should continue to advise participants about the risks of leptospirosis associated with water-based recreational activities.

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If the low level of awareness in those cases classified as residential is a reflection of the level of awareness in the general population about the risk of acquiring leptospirosis and other environmentally transmitted diseases, there may also be a need for general educational material regarding incidental environmental exposure.

Historically considered an occupational disease, the variety of possible transmission routes reported here and elsewhere serves as a reminder to clinicians of leptospirosis as a possible diagnosis when compatible symptoms are observed, not just for patients in the occupational groups historically considered at risk.

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DECLARATION OF INTEREST

None.

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