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Emerging canine leptospirosis in Sydney and the role of population demographics

James Gong | Christine Griebsch | Nicolle Kirkwood | Jacqueline M. Norris | Michael P. Ward 💿

Sydney School of Veterinary Science, The University of Sydney, Camperdown, New South Wales, Australia

Correspondence

Michael P. Ward, Sydney School of Veterinary Science, The University of Sydney, Camperdown, NSW 2006, Australia. Email: michael.ward@sydney.edu.au

Funding information Sydney School of Veterinary Science

Abstract

An outbreak of canine leptospirosis commenced in Sydney, Australia in 2017. The aim of this retrospective study was to determine if clusters of leptospirosis occurred during this outbreak, and if these were associated with host factors, to assist investigation of the drivers of emerging leptospirosis at this location. Within the City of Sydney local government area, 13 cases were reported during the outbreak. Administrative data on the canine population were collected and mapped. Clusters of leptospirosis cases were detected using a retrospective space-time analysis and a discrete Poisson probability statistical model. Sydney dog population registration [55.6%, 95% confidence interval (CI) 51.8-58.1%] was lower than the Australian national average (80%). The distribution of dog types, based on the United Kennel Club standards, was significantly (p < .0001) different to that of the national profile: there was a distinct preference in Sydney for companion dogs. The age distribution of dogs in Sydney did not reflect a typical right-skewed curve; instead, a relatively uniform distribution was observed between the age group of 1 to 8 years. A primary disease cluster (radius 1.1 km) in the eastern area of the Sydney City Council was identified (4 cases observed between 24 May and 9 August 2019 vs. 0.10 cases expected), p = .0450. When adjusted for the age, breed type and sex distribution of the population, similar clusters were identified; in the case of age-adjustment, the spatiotemporal cluster identified was larger and of longer duration (seven cases observed between 28 June and 11 November 2019 versus 0.34 cases expected), p = .0025. The presence of clusters of canine leptospirosis in the City of Sydney during this outbreak, which persisted after adjustment for demographics (age, sex, breed type), suggest that environmental factors - rather than host or pathogen factors - might be responsible for the emergence of leptospirosis. Environmental factors that potentially might be linked to this outbreak of canine leptospirosis and the clusters observed require investigation.

KEYWORDS

dog, epidemiology, infectious disease, leptospirosis, spatial

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1 | INTRODUCTION

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Between 2017 and 2020, 17 cases of canine leptospirosis within the Greater Sydney Area (13 of which were located within the City of Sydney) were confirmed. A high case fatality rate (88%) was reported due to severe hepatorenal disease (Griebsch et al., 2022). Previously, there had been no published reports of canine leptospirosis in Sydney since 1976 (Effler, 2020; Watson et al., 1976), and although it has been speculated that construction and flooding might have led to the Sydney outbreak,¹ the reasons for the emergence of this relatively large outbreak remain unknown.

Leptospirosis is a systemic bacterial disease caused by different pathogenic species. The most clinically important species affecting canines are *Leptospira interrogans*, *L. kirschneri* and *L. borgpetersenii* (Geisen et al., 2007). The pathogenesis of leptospirosis involves leptospiraemia, followed by vasculitis and invasion of multiple organs; the kidneys and liver are most commonly affected. Clinical signs early in the pathogenesis of disease are often non-specific and include inappetence, lethargy, vomiting and diarrhoea. On physical examination, common findings in more advanced stages of the disease include icteric mucous membranes, abdominal pain and pyrexia. Clinicopathological findings include azotaemia, hyperbilirubinaemia, elevated liver enzyme activities and thrombocytopaenia (Klaasen & Adler, 2015).

Replication of leptospires is limited to within the host, but leptospires are also known to possess high survivability in the natural environment, especially moist and wet environments. Previous research has shown there is a significant correlation between rainfall and disease incidence (Ward, 2002a), and annual mean temperature and disease presence (Taylor et al., 2021). Transmission between animals occurs via direct (urine, ingestion of tissue, blood-to-blood contact, venereal secretions) and indirect (contamination of infectious urine in water and soil) routes (Greene et al., 1998). Australian wildlife that might act as potential reservoirs include rodents and small marsupials, such as Northern brown bandicoots (Isoodon macrourus), brushtail possums (Trichosurus vulpecula) and flying foxes (Pteropus spp.) (Wildlife Health Australia, 2018). Species that have been reported to show clinical signs and pathology include wombats (Vombatus ursinus), platypus (Ornithorhynchus anatinus), water rats (Hydromys chrysogaster) and the Tasmanian devil (Sarcophilus harrisii) (Wildlife Health Australia, 2018). During the Sydney outbreak, most cases of canine leptospirosis occurred within or near to the City of Sydney Council, a highly urbanised area located far from the rural outskirts of greater Sydney. Thus a major role for wildlife species, other than rats (Rattus norvegicus, the brown rat and Rattus rattus, the black rat), appears unlikely. Urban and periurban areas have been previously reported to be at greater risk for leptospirosis in Japan, Malaysia and the United States (Koizumi et al., 2009; Pui et al., 2017; Ward et al., 2004a).

Other demographic risk factors (age, gender and breed) for canine leptospirosis have also been investigated. Male dogs were reported to be at greater risk than females, and dogs between 4 and 10 years old were more susceptible to infection than those under 12 months of age (Ward et al., 2002). However, in another study, positive associations between seropositive status and female dogs, as well as dogs that were in the age group of 1–3 years, were reported (Zwijnenberg et al., 2008).

There is one registered monovalent vaccine in Australia (Protech[®] C2i, Boehringer Ingelheim) available to protect against canine leptospirosis, containing serovar Copenhageni. In a survey of shelter dogs across Australia, this serovar was reported to be the most common, with the highest prevalence found in New South Wales. Other serovars reported in this survey included Canicola, Ballum, Medanensis, Panama, Zanoni, Robinsoni, Javanica and Arborea (Zwijnenberg et al., 2008). In the Sydney outbreak (2017=2020), the majority of cases tested (6/7) had antibody titres via Microscopic Agglutination Tests (MAT) to serovar Copenhageni and one had a negative titre likely due to insufficient time for seroconversion before death. During the same time period of the Sydney canine leptospirosis outbreak, the largest Australian leptospirosis outbreak in humans occurred in a berry farm located on the north coast of NSW (Katelaris et al., 2019). There were 84 cases identified in a population of 642 workers between 14 April and 31 August 2019. The majority of cases presented with mild symptoms, and no mortalities were reported. Leptospira serovar Arborea was identified as the disease agent in all confirmed cases, and it was also detected amongst rodents (Mus musculus) in the region (Katelaris et al., 2019). This serovar has been previously reported in Australian dogs (Zwijnenberg et al., 2008), but not in those dogs tested from the recent Sydney outbreak (Griebsch et al., 2022).

As the first step in understanding why the current outbreak of canine leptospirosis in Sydney has occurred, the aim of this study was to determine whether cases were clustered in time and space. The identification of clusters can support the generation of hypotheses about causation and common sources of exposure, aiding in the control and prevention of canine leptospirosis.

2 | MATERIAL AND METHODS

2.1 | Data management

The population at-risk of leptospirosis was created via dog ownership data held by the City of Sydney Council and accessed 1 April 2020. The data set contained 18,279 unique entries (live dogs), and included attributes such as street address, dog breed, gender, year of birth and microchip details. The microchip registration data was a subset of the dog ownership data set. The data were re-organised for geolocation processing. For example, apartment numbers were removed and street names and street numbers were placed in separate columns. Each address entry was manually inspected for validity. Addresses that were clearly erroneous (likely due to administrative input errors) were removed from the data set. Addresses of confirmed leptospirosis cases were obtained from medical records (Griebsch et al., 2022).

2.2 | Population analysis

Using date of birth information from the dog ownership data set, a frequency distribution was created. The international based United Kennel Club (UKC, 2021) standards were used to classify dog breeds into broad dog type categories, since it encompasses a wide range

of dog breeds comparable to other well-recognised standards such as the Australian National Kennel Council and the American Kennel Club. The dog breeds were sorted into the following 10 categories: companion, guardian, gun, herding, northern, scent hounds, terriers, sight hounds and pariahs and dogs of mixed or unknown breed origin. These categories were then compared with the national Australian distribution as well as that from another major urban city, New York City. The latter was obtained from a dog licensing system information (Department of Health & Mental Hygiene, 2021), in which duplicates caused by renewals were identified and removed prior to categorization based on the UKC standards. Breed information at the national level for Australia was extrapolated using information provided by the Australian National Kennel Council (Australian National Kennel Council, 2021). Unlike the Sydney and New York registration data sets that reflected the number of registrations at a specific point in time, the national statistic provides the number of new registrations for each dog breed in a specific year. To allow for an appropriate comparison, for every breed the annual registrations were summed considering the unique life expectancy estimate for each dog breed (World Life Expectancy, 2021). Registrations of a dog breed in a given year were only included in the total of that breed if the dog born in that year was expected to be alive in the year 2020. For example, if the average life expectancy of a Golden Retriever is 12 years and the current year is 2022, then we only used the new registrations data beginning in 2010 (12 years preceding 2022). Following summation of annual registrations, categorisation was based on the UKC standards. Dog types in Sydney, the Australian profile and New York were compared with chi-squared statistical tests. Dog population per Sydney suburb was linked with human population data (Australia Bureau of Statistics, 2016) and dog population per capita for each suburb was calculated.

2.3 Geocoding, mapping and cluster analysis

The edited dog ownership data set (registered and non-registered dogs) was batch imported into CSV2GEO, an online geocoding software.² This software generates geographical coordinates, with a relevance score (ranging from 0 to 1) which provides a quantitative estimate of the accuracy of geocoding. A subset of records with lower relevance scores was cross-checked with Google Maps³ to determine an ad hoc relevance score cut-point above which records with a high confidence of accuracy were retained.

The geocoordinates of the addresses were imported into a GIS program⁴ for mapping. The addresses were mapped as points using a shapefile of the City of Sydney local government area [Geocentric Datum of Australia (GDA), 1994], with internal boundaries based on Statistical Area Level 1 (SA1) and 2 (SA2).⁵ These statistical areas are the geographical zones used in the Australian census data, with SA1s being the smallest area unit. Addresses located outside the geographical boundaries of the City of Sydney Council polygon were then removed, since these were likely due to administrative errors in the original population data set. Using the same methods, confirmed

leptospirosis cases were mapped. All population records and cases were assigned to one of 31 suburbs within the City of Sydney Council.

Cluster analysis was carried out using a scan statistic⁶ and a Poisson model. The population at-risk was the estimated population within each suburb, using each suburb's centroid as the location. Cases reported during the 4-year study period (01/01/2017 to 31/12/2020) were scanned for high rates of disease in time and space using a scanning window of up to 1 km radius and up to 90 days duration. Statistical significance (p < .05) was estimated using Monte Carlo simulation with 999 replications. In addition, for each suburb the distribution of ages (< 1 to \geq 15 years), breed type (companion, guardian, gun, herding, mix, northern, scenthound, sighthound and pariah, terrier, unknown) and sex (male, female, unknown) were calculated and the data were scanned for high rates of disease in time and space using the same scanning window adjusting for each of these three covariates.

3 | RESULTS

Dog registration within the City of Sydney Council was 55.6% (95% Cl, 51.8%–58.1%), based on microchip data as a proportion of ownership. By suburb, registration ranged from 25.8% (Haymarket) to 66.7% (Kings Cross) (Figure 1). Per capita, there were 8.6 dogs (95% Cl 8.2%–9.0%) per 100 people within the City of Sydney Council. By suburb, the number of dogs per 100 people ranged from 2.1 (Haymarket) to 18.3 (Beaconsfield) (Figure 2).

The distribution of breed types was significantly different between Sydney City and the national estimates (Figure 3; p < .0001). Compared to national estimates for Australia, in Sydney there was a greater proportion of companion dog breeds (45% vs. 24%), but a lower proportion of herding (7% vs. 17%), gun (11% vs. 19%) and guardian (4% vs. 9%) dog breeds. In contrast, the distribution of dog breeds in Sydney City was more comparable to that of New York City (Figure 3).

The age distribution of dogs (Figure 4) in the City of Sydney Council (1-15 years) reflected an approximately uniform distribution between the age groups of 1-8 years, with a peak in the distribution between the age groups of 9-12 years. The median age category was 8 years.

From the Sydney City dog ownership data, more than 99% of the address entries had a geocoding relevance score of 0.95 or higher, with less than 150 address entries below this rating. These 150 lower ranked entries were cross-checked with Google Map and it was determined that entries below 0.92 had inconsistencies in accuracy. Therefore, all addresses below this score were excluded to further improve overall data accuracy. The final data set containing only dogs within the City of Sydney Council included 17,881 entries (97.7% of the original dog ownership data set). Mapping of the dog population demonstrated several areas of high dog numbers (Figure 5).

There were 13 leptospirosis cases reported from seven suburbs: Surry Hills, Haymarket, Redfern, Glebe, Newtown, Darlinghurst and Paddington. A significant (p = .0450) primary cluster was identified in the suburbs of Surry Hills and Darlinghurst (radius 1.10 km) in which four cases were reported between 24 May and 9 August 2019 (Figure 5). Similar clusters were identified adjusting for age, breed type

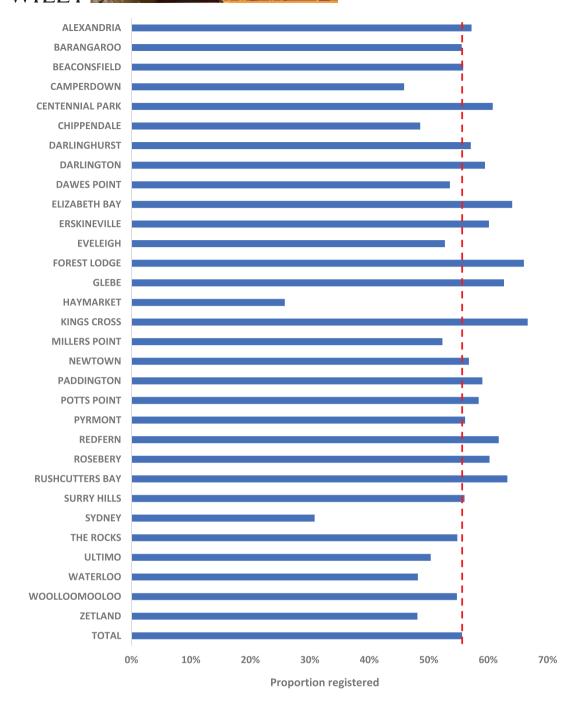


FIGURE 1 Proportions of dogs registered within suburbs of Sydney City Council local government area, 2020. The overall proportion registered (55.6%; 95% confidence interval 51.8–58.1%) is indicated.

and sex (Table 1). In the case of age, the cluster was larger (1.21 radius) and contained 7 cases reported between 28 June and 30 November 2019 in the suburbs of Surry Hills, Darlinghurst, Chippendale, Eveleigh and Redfern.

4 DISCUSSION

In this study, a persistent disease cluster of canine leptospirosis was identified within the City of Sydney Council local government area. The

existence of this cluster could not be explained by the Sydney dog distribution, its age, breed type or sex characteristics.

We found that the age distribution of dogs in the City of Sydney Council local government area does not follow the typical bell-shaped curve seen in human populations, or the right-skewed curve seen in some dog populations (e.g. Dobson et al., 2002). However, it should be noted that the dog ownership data included the early months of the COVID-19 pandemic when a dramatic increase in puppy adoptions across Australia at this time might have influenced the age distribution described (Animal Welfare League, 2021), and also other human



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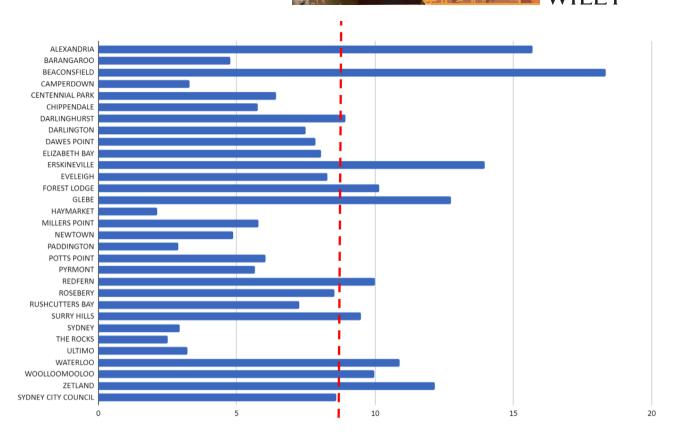


FIGURE 2 Number of dogs per 100 residents within suburbs of Sydney City Council local government area, 2020. The overall number of dogs per 100 residents (8.6; 95% confidence interval 8.2–9.0) is indicated.

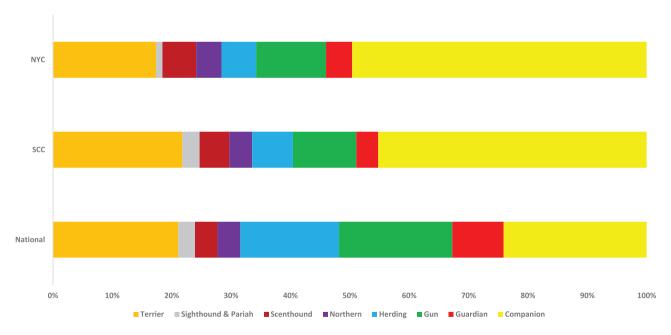


FIGURE 3 A comparison of dog breed type distribution in the Sydney City Council (SCC) local government area, New York City (NYC) and Australia (National), using the United Kennel Club standards to classify dog breeds. A significant (*p* < .0001) difference in dog breed type proportions was found between SCC and National distributions.

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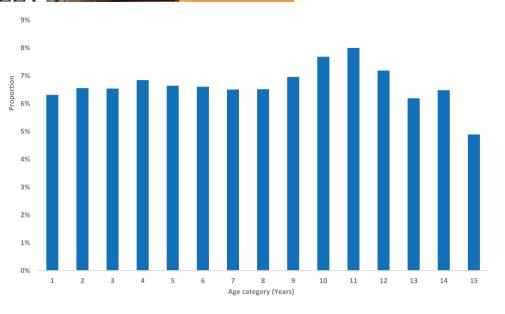


FIGURE 4 Age frequency distribution of dogs within the City of Sydney Council local government area, 2020. The median age category is 8 years.

TABLE 1 Spatiotemporal clusters of leptospirosis cases within the City of Sydney Council local government area, 2017–2020.

Adjustment	Observed cases	Expected cases	Observed- expected case ratio	Suburbs	Radius (km)	Time frame	Population	Cases per 100,000	Log likelihood ratio	P-value
-	4	0.099	40.25	Surry Hills Darlinghurst	1.10	24 May to 9 August 2019	2559	732	11.54	0.0450
Age	7	0.034	20.35	Surry Hills Darlinghurst Chippendale Eveleigh Redfern	1.21	28 June to 30 November 2019	4428	370	16.61	0.0025
Breed type	4	0.11	37.49	Surry Hills Darlinghurst	1.10	24 May to 9 August 2019	2595	672	11.26	0.0650
Sex	4	0.11	35.97	Surry Hills Darlinghurst	1.10	24 May to 9 August 2019	2827	661	11.10	0.0580

Note: A Poisson model and scanning windows of up to 90 days and 2 km were used. The centroid of all clusters was located at 33.8856°S, 151.2120°E.

demographic changes that occurred during this time. A high proportion of younger aged dogs could contribute to higher numbers of clinical leptospirosis, since it has been reported that leptospirosis has increased likelihood to cause more severe outcomes for younger aged dogs (Zwijnenberg et al., 2008). Within the City of Sydney, we found a clear preference for companion dog type breeds, compared to the national distribution, with herding, gun and guardian breeds under-represented. The distribution of dog breed types in the City of Sydney was more typical of another large city, New York City, than the national profile. Besides being at the centre of large, developed metropolises, the cities of Sydney and New York also have some similar housing profiles (apartments and terrace/row housing) and infrastructure. The similarity of breed distributions therefore perhaps is not surprising. Previous studies have shown that herding and gun type dogs are at the highest risk of contracting leptospirosis (Sykes et al., 2011; Ward, 2002b). Therefore, the dog breed distribution in the City of Sydney is unlikely to make it more susceptible to leptospirosis per se. The relatively low dog registration of 55.6% observed, compared to the national average of 80% (Petplan, 2016), is likely a reflection of socioeconomic status in some areas (Australian Bureau of Statistics, 2016), and perhaps dwelling types within this local government area. Low registration (perhaps due to socioeconomic status), if a reflection of overall pet care, might have implications for uptake of prevention programs, such as leptospirosis vaccination.

Mapping of the City of Sydney dog population revealed several areas with high numbers of dogs. Although the City of Sydney Council is ranked the highest of all local government areas in New South Wales for human population density (Australian Bureau of Statistics, 2016),

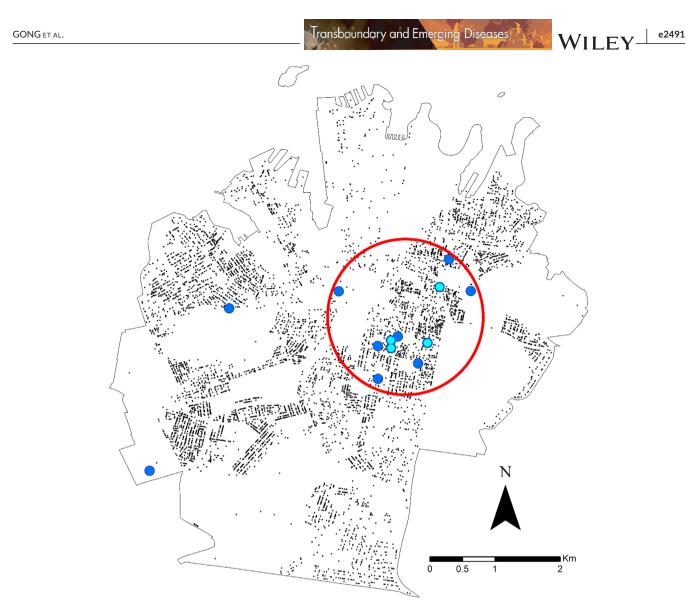


FIGURE 5 The distribution of 17,881 dogs, 13 reported cases of canine leptospirosis and a cluster of leptospirosis within the City of Sydney Council local government area, 2017-2020. A significant (p = .0450) primary cluster of canine leptospirosis was identified in the suburbs of Surry Hills and Darlinghurst (radius 1.10 km) in which 4 cases were reported between 24 May and 9 August 2019.

overall dog ownership per capita (8.6 per 100 residents) is not high. Considering that in this local government area the average household is 2.2 persons, there is about one dog for every 5.3 households, equivalent to a 19% household dog ownership rate, much lower than a national average of 40% reported in a recent online national survey (Animal Medicines Australia, 2019). Based on the Australian 2016 census, only 2% of dwelling structures are fully detached houses, versus 77% and 19.7% being apartments and terrace houses, respectively. Therefore, the high human population density together with the lack of fully detached houses is likely why there are local areas of high dog population density in the City of Sydney local government area.

It was within one of these higher density areas (the suburbs of Surry Hills and Darlinghurst) that we identified a cluster of canine leptospirosis. Because we used a Poisson statistical model, in which analysis is adjusted for the population at-risk, dog population density can be excluded as a likely cause of the cluster detected. Furthermore, adjustment for the underlying distribution of the dog population by

age, dog breed type and sex did not substantially alter the cluster detected. In combination, these results suggest that demographic factors do not explain the leptospirosis cluster that appeared in the latter part of 2019. In addition, historically in Sydney vaccination against leptospirosis was not commonly performed by small animal practitioners because it was a rare disease and leptospirosis vaccination is considered non-core by World Small Animal Veterinary Association (WSAVA) vaccination guidelines (Day et al., 2016). Therefore, it is possible that environmental factors, including wildlife reservoirs, might have contributed to this outbreak of leptospirosis and the subsequent cluster observed. This cluster occurred during the winter and spring months, a risk period previously observed for canine leptospirosis (Ward et al., 2004b). Suitable rainfall and temperatures might have contributed to this cluster. Overall, rainfall in Sydney in 2019 (852 mm) was substantially reduced compared to the long-term average (1213 mm). However, there was above average rainfall in March (292 mm vs. 132 mm), June (171 mm vs. 133 mm) and September (113 mm vs. 68 mm).⁷ This rainfall pattern – specifically in March and June 2019 – might have contributed to the exposure of dogs to Leptospira organisms in the environment (Ward, 2002a). Within the area of this cluster, there are multiple dog friendly parks, many of which are off-leash parks. In a local government area in which fully detached houses are in short supply, these public areas become popular for owners wanting to exercise their dogs. Thus, they might also become *Leptospira* exposure sites for unvaccinated dogs, if environmental conditions are suitable.

Within seroprevalence surveys of dogs in New South Wales and Victoria, serovar Copenhageni has been found to be the most prevalent (Dickeson & Love, 1993; Watson et al., 1976; Zwijnenberg et al., 2008). In the current Sydney outbreak, the highest microscopic agglutination titres in dogs tested were found for serovar Copenhageni (6/7 dogs) (Griebsch et al., 2022). The main reservoir host for serovar Copenhageni is the rat.⁸ Brown (Rattus norvegicus) and black (Rattus rattus) rats are common in Sydney (Bedoya-Perez et al., 2021a). In preliminary research conducted within the City of Sydney in 2020, an overall *Leptospira* prevalence of 29% was estimated in brown (31%) and black (17%) rats using PCR on kidney samples (Bedoya-Perez et al., 2021b). Together with identification of serovar Copenhageni as the likely cause of this outbreak (Griebsch et al., 2022), it appears that the local Sydney rat population is capable of acting as a reservoir for canine leptospirosis. In addition, the cluster of canine leptospirosis identified in the current study is adjacent to Centennial Parklands, a large urban precinct in eastern Sydney. Besides rat species, there are several other potential reservoir hosts of Leptospira which inhabit this precinct, including the common brushtail possum (Trichosurus vulpecula) and flying foxes (*Pteropus* spp.),⁹ with potential contact possible with adjacent urban areas. Further investigations are required to confirm the reservoir of Leptospirg in Sydney to be rat species (Bedova-Perez et al., 2021b), and environmental factors that have driven the emergence of leptospirosis in the Sydney dog population.

A limitation of this study was that cases were assumed to have been exposed to Leptospira at or near their place of residence. Information on the dogs' activity during 1-2 weeks prior to clinical disease was unavailable. If exposure occurred at parks and recreational areas more distant to their place of residence, some bias might have been introduced to the spatial analysis conducted. The dog registration data was assumed to capture the entire population at-risk. It is likely that dogs not captured within this system (e.g. non-compliant owners) are a negligible part of the population and that this bias would not substantially affect the clustering analysis conducted. However, this is non-verifiable since the true population at any given point in time is unobservable. The population data was acquired in 2020 and was assumed to be broadly representative of the population at-risk and its characteristics during the period 2017-2020. Within the City of Sydney, it is unlikely that dramatic shifts in the population at-risk have occurred over this relatively short timeframe; therefore, it is unlikely that the population data might have impacted on the spatial analysis. In this study, we defined a case of leptospirosis based on consistent clinical and clinicopathological findings, including positive PCR on blood, urine or kidney tissue, the presence of *Leptospira*-shaped organisms in kidney tissue identified with silver stain or seroconversion (4-fold

increase in MAT titre) or a MAT titre >1/800 in non-vaccinated dogs (Griebsch et al., 2022). A limitation of this study is that analysis was conducted irrespective of Leptospira serovar. Since only seven of the confirmed cases had MAT titres performed (and six were positive for serovar Copenhageni), restricting the inclusion criteria to only those cases with a serovar identified would have precluded statistical analysis. Serovar-specific analysis would generate more information and help to identify the reservoir of this outbreak, and might also assist with identification of the environmental drivers based on known eco-epidemiological cycles of serovar-specific transmission. For such investigations, wherever possible attempts to identify the infecting serovar in clinical cases of canine leptospirosis should be attempted. In addition, the small number (13) of cases likely reduced our statistical power to detect clusters. Case ascertainment involved both retrospective review of medical records and prospective enrolment following referral or direct contact from referring veterinarians. Therefore, it is likely that most cases were captured in this study, and study power maximised as much as possible given passive surveillance for canine leptospirosis. Active surveillance for this disease and other diseases of dogs within such an urban environment would generate benefits for animal health and welfare, and public health (Ward & Kelman, 2011).

5 CONCLUSION

Although leptospirosis is a nationally notifiable zoonotic disease in humans and reporting to the Australian National Notifiable Diseases Surveillance System is mandatory, canine leptospirosis is not a reportable disease in New South Wales. Continued monitoring for this disease via veterinary practices is needed, together with investigation of environmental factors that might drive the emergence of new disease outbreaks.

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ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as the data was collected as part of a regulatory local government program.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Michael P. Ward () https://orcid.org/0000-0002-9921-4986

ENDNOTES

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