Received: 8 December 2020 | Revised: 15 March 2021 | Accepted: 4 May 2021

DOI: 10.1002/vetr.512

Vet Record

ORIGINAL RESEARCH

Incidence and demographic risk factors for leptospirosis in dogs in the UK

Collette Taylor | **Dan G. O'Neill** | **Brian Catchpole** | **Dave C. Brodbelt**

Department of Pathobiology and Population Sciences, The Royal Veterinary College, Hatfield, Herts, UK

Correspondence
Collette Taylor, BVSc(Hons), MSc(Veterinary Parasitology), MRCVS, Department of Pathobiology and Population Sciences, The Royal Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Herts AL9 7TA, UK.
Email: ctaylor18@rvc.ac.uk

Abstract

Objectives: To estimate the annual incidence risk of leptospirosis diagnosis in practice-attending dogs in the UK during 2016 and identify risk factors for diagnosis.

Methods: Incidence of leptospirosis diagnosis in dogs during 2016 was estimated from dogs in primary-care practices from the VetCompass Programme (n = 905,543). A case-control study of laboratory cases (n = 362) versus VetCompass controls explored factors (age, sex, neutering, breed, Kennel Club group, urban-rural location, indices of deprivation) associated with leptospirosis diagnosis through multivariable logistic regression.

Results: Annual incidence risk of leptospirosis in the VetCompass population was 0.8 cases per 100,000 dogs (0.0008%, 95% CI 9.1×10^{-8}–5.2×10^{-5}). Adult dogs, especially 1- < 5 years olds (odds ratio [OR] = 0.38, 95% CI 0.27–0.54), and dogs attending urban clinics (OR = 0.26, 95% CI 0.19–0.35) had reduced odds of leptospirosis versus dogs < 1 year old and rural dogs, respectively. Dogs attending clinics in less deprived areas had increased odds of diagnosis (OR = 3.63, 95% CI 2.28–5.78) compared to crossbreds, Cocker Spaniels (OR = 4.25, 95% CI 2.65–6.84), Collies (OR = 3.53, 95% CI 2.22–5.62) and Lurchers (OR = 3.49, 95% CI 1.50–8.11) had increased odds of diagnosis.

Discussion: Leptospirosis is rarely diagnosed in clinical practice, suggesting that many true cases may be missed. Demographic risk factors identified here may inform the index of suspicion and encourage increased use of confirmatory diagnostic testing.

INTRODUCTION

Leptospirosis is an important infectious disease reported in most mammalian species and is globally distributed.[1] Clinical manifestations of leptospirosis range from severe multisystemic disease such as renal failure, hepatic dysfunction, coagulopathies, gastroenteritis, respiratory distress to asymptomatic carriage.[2,3] Clinical signs are often variable and nonspecific and include anorexia, vomiting, lethargy, abdominal pain and dehydration. Jaundice, oliguria/anuria, weight loss and pyrexia are also reported.[2,4,5] Lack of pathognomonic clinical signs may result in under-diagnosis of leptospirosis.

Abbreviations: APHA, Animal and Plant Health Agency; CI, confidence interval; DOI, duration of immunity; ECVIM, European College of Veterinary Internal Medicine; EPR, electronic patient record; IQR, interquartile range; KC, The Kennel Club; MAT, Microscopic Agglutination Test; MLV, modified live virus; OR, odds ratio; PCR, polymerase chain reaction

Diagnosis is confirmed through serology, using the microscopic agglutination test (MAT), or through molecular tests on blood or urine, such as polymerase chain reaction (PCR).[1] MAT is the current gold-standard test.[1] Antibodies associated with leptospiral infections are produced typically 5–15 days after infection.[6,7] Interpretation of tests can be complicated by prior vaccination, concurrent antibiotic therapy and stage of infection.[2,8–11]

Incidence rates of clinical leptospirosis in dogs are infrequently reported, with apparently no studies reported in the UK. Previously reported incidence rates range from 5.8 to 37 per 100,000 dogs, although it must be noted these studies included referral hospitals and may be poorly generalisable to primary care practice or the wider general population of dogs in the UK.[5,12] Reported canine seroprevalence varies widely between countries, due in part to varied threshold values for assigning positive titres, populations

sampled and regional geography, which can affect maintenance host populations and environment survival of leptospires.[5,13–17] Within European dog populations, seroprevalence ranged from 3% to 25%.[2,14,18] The only published UK study identified a seroprevalence of 24% in clinically well dogs in Scotland; however this was based on antibody titres of >1:10 as the positive threshold, rather than the more widely accepted clinically relevant titre > 1:800.[13] In European studies involving dogs with suspected leptospirosis, 69%–73% of dogs were positive.[5,19] A lower proportion, of 8%–12%, has been reported in US studies.[20,21]

Previous studies identified increased age, small dog breeds, and being male as risk factors for disease.[5,12,22,23] Additionally, environmental and lifestyle risk factors such as flooding and access to water sources, urban or rural location and seasonality have been associated.[17,22,23] There are limited reports evaluating risk factors in the UK.

Using veterinary clinical data from the VetCompass Programme (VetCompass, 2019) and test results from Animal and Plant Health Agency (APHA) and IDEXX laboratories, this study aimed to explore the epidemiology of leptospirosis in UK dogs. Study objectives were: (1) describe presenting signs, diagnostic methods and outcomes of confirmed leptospirosis cases within the VetCompass primary-care population, (2) estimate annual incidence risk during 2016 of diagnosis in practice attending animals and (3) explore animal signalment and geographically linked risk factors for dogs under primary veterinary care.

MATERIALS AND METHODS

The study included two datasets: dogs under veterinary care in VetCompass during 2016 and leptospirosis PCR/MAT submissions to IDEXX/APHA laboratories between 2013 and 2019. Ethical approval for the study was granted by the RVC Social Science Research Ethical Review Board (SR2018-1652 and SR2019-0445).

Incidence and clinical management of leptospirosis in VetCompass primary-care practices

The cohort of dogs under veterinary care within VetCompass during 2016 was interrogated to identify all new cases of leptospirosis, estimate the incidence and describe clinical features of cases. The VetCompass Programme collates de-identified electronic patient record (EPR) data from participating primary-care veterinary practices in the UK for epidemiological research.[24] Dogs under veterinary care were defined as those with either (a) ≥1 EPR (free-text clinical note, VeNom diagnosis term, treatment or bodyweight) recorded during 2016 and/or (b) ≥1 EPR recorded during both 2015 and 2017. Patient records include a unique dog ID number alongside breed, sex, neutering status, age, bodyweight and clinic postcode. Clinical information and treatments administered are recorded as free-text and as semi-standardised invoiced items.

Diagnosis of leptospirosis required evidence of a positive PCR or SNAP result recorded in the EPR or at least one MAT titre of ≥1:800 or (if paired serology available) a four-fold increase in titres, as described in the European College of Veterinary Internal Medicine (ECVIM) leptospirosis consensus statement.[2] Identification of leptospirosis cases within the VetCompass 2016 cohort began with a keyword search in the free-text clinical records to identify dogs that may have undergone diagnostic testing for leptospirosis using the search terms: *lepto* + MAT, lepto* + PCR, lepto* + SNAP, lepto* + blood* and *lepto* + urine*. Full clinical records of these dogs were examined in the VetCompass online portal (vetcompass.org) to identify confirmed leptospirosis cases, and to extract further information on clinical management. Dogs were classified as azotaemic if their creatinine or blood urea nitrogen were elevated beyond reference levels. Dogs were recorded as unvaccinated if there was no recorded leptospirosis vaccination in the 12 months prior to leptospirosis testing; in accordance with manufacturer administration guidelines.[25] Data were extracted and cleaned in Excel (Microsoft Office Excel 2016, Microsoft Corporation). Incidence risk of leptospirosis was estimated from the number of newly diagnosed cases during 2016 divided by the overall number of dogs under veterinary care in 2016. Ninety five percent confidence intervals (95% CI) were estimated using exact methods.[26] Patient characteristics, diagnostic and management approaches were statistically summarised.

Risk factor analyses

A case-control study compared APHA / IDEXX laboratory cases to dogs under veterinary care in VetCompass during 2016 (i.e., the controls), following similar methodology utilised by Stevens et al.[27] This study was performed to explore risk factors for leptospirosis diagnosis in a population considered likely to be representative of primary-care practice attending dogs in the UK. Confirmed leptospirosis cases in the VetCompass 2016 population were removed from the risk factor analyses aspect of the study.

Sample size estimates indicated that approximately 150–200 cases and 1500–2000 controls (case:control ratio 1:10) would be required to detect a risk factor with an odds ratio (OR) of 2.0 with an exposure level in the controls of between 40% (neutering) and 10% (>8 years old age) (confidence level 95%, power 80%).[28]

Breed information recorded in VetCompass and laboratory submissions was cleaned and mapped to VeNom breed terms.[29] All dogs that were not a VeNom recognised breed were categorised in a separate 'crossbreeds' group. Purebreds were categorised by UK Kennel Club (KC) breed group (Gundog, Hound, Pastoral,

Terrier, Toy, Utility, Working or not recognised).[30] Individual breed associations were additionally explored in a further breed variable. In order to have sufficient power for analysis, only breed-types and crossbred with ≥5 leptospirosis cases were retained as individual breed-type terms, and all remaining animals were categorised as 'purebred-other'. Age (years) was defined for the laboratory submissions as the recorded age at the date when the sample was tested. VetCompass control dogs recorded the age (years) at December 31, 2016 which was the final date at which all dogs had confirmation that they were non-cases. Age was evaluated as a continuous variable and was categorised: 0- < 1, ≥ 1-5, ≥ 5-8 and ≥ 8 years. Neutering status ('Entire', 'Neutered' or 'Not Recorded') was as reported in laboratory submissions or status in the final VetCompass EPR at December 31st 2016 for controls. Sex was encoded as 'Female', 'Male' or 'Not Recorded'.

Clinic postcodes were used to assign an Indices of Multiple Deprivation (IMD) rank and urban/rural classification to all cases and controls to Lower Super Output Area (LSOA) level.[31,32] IMD rank was then divided into quintiles for each country (England, Wales and Scotland). Urban / rural classification was divided into simply 'urban' or 'rural' location.

Multivariable binary logistic regression was performed in R Studio v3.5.1 (R Core Team, Vienna, Austria). Initial univariable analysis using binary logistic regression assessed for potentially significant independent variables (neutering status, sex, breed, KC breed group, age, and clinic postcode derived factors). Variables with liberal associations ($p < 0.2$) were retained for consideration in multivariable logistic regression. Collinearity of variables was assessed through evaluation of the correlation matrices, the variance inflation factor (VIF) and tolerance.[33] Where two variables were highly related (correlation > 0.7 and VIF > 10), the variable considered most biologically important was retained for consideration. Due to KC breed group and breed variables being highly collinear, separate models were generated in the multivariable analyses to assess these variables separately. For the final multivariable models, a manual stepwise backwards elimination regression approach was adopted. Variables were retained if $p < 0.05$ from the Likelihood Ratio Test. Missing data were coded as 'record unavailable' for each variable and models were evaluated with and without these missing values, although only the model with missing data retained is reported here (model excluding missing data is reported in Supplementary Materials). Confounding was assessed for all variables retained in the final models through addition of each independent variable in a stepwise manner to the model and assessing for substantial (>20%) change in OR when each new variable was added to the model.[34] Interactions between all independent variables in the final models were assessed for significance. Model fit to the data was assessed by Hosmer-Lemeshow test. Statistical significance was $p < 0.05$.

RESULTS

Incidence and clinical management of leptospirosis in VetCompass primary-care practices

The VetCompass population included 905,543 dogs under veterinary care at 886 veterinary clinics during 2016. Median age was 4.44 years (IQR: 1.87−8.08). There were 469,606 (51.9%) males and 407,965 (45.1%) entire dogs. Most common breed types were crossbreeds (n = 193,930, 21.4%), Labrador Retrievers (n = 59,963, 6.6%), Staffordshire Bull Terriers (n = 53,055, 5.9%), and Jack Russell Terriers (n = 48,435, 5.4%). From this population, 37 dogs (0.00004%) were identified as having undergone diagnostic testing (either MAT, PCR or SNAP Lepto) for leptospirosis and had recorded test results. A further nine (0.00001%) dogs had tests recorded as performed but no result recorded. PCR was the most commonly performed test (n = 25/37, 67.6%,) followed by MAT (14/37, 37%). Of the dogs with an MAT performed, only two had paired samples recorded (2/14, 14.2%). Of the tested dogs, seven animals (7/37,18.9%) were positive on ≥1 test. The estimated incidence risk of leptospirosis during 2016 was therefore 0.8 cases per 100,000 dogs (0.0008%, 95% CI 9.1×10^{-8} – 5.2×10^{-5} %, 7/905,543).

All seven of the confirmed incident leptospirosis cases were unvaccinated. Age ranged from <1-year-old to 9-year-old, with a median of 3 years. Three (42.8 %) of the seven diagnosed dogs presented with vomiting and inappetence, and a further three presented with lethargy (3/7, 42.8% for both). The most commonly performed diagnostic test for confirmed cases was PCR (4/7 cases, 57%), followed by MAT (3/7, 42%), and SNAP Lepto test (3/7, 42%), with two animals (2/7, 28.5%) having ≥2 tests performed. Of the four (57%) cases that had serum biochemistry performed, all were azotaemic and two (50%) additionally had elevated hepatic enzymes. Cases received intravenous fluid therapy (6/7, 85.7%), antimicrobial therapy (5/7, 71.4%), anti-emetics (4/7, 57.1%) and diuretics (2/7, 28%). Of these seven cases, four died (57.1%,) or were euthanised, with the remaining three surviving to discharge. Only one case record reported infecting serovars, identifying *L. interrogans* serovars *Copenhageni* and *Bratislava* with equal titres of >1:1600.

Risk factors for canine leptospirosis in primary-care practice

There were 362 APHA / IDEXX laboratory-confirmed cases from 4750 tests submitted across the UK between 2013 and 2019. These cases were compared to the control group of non-case dogs (n = 905,536) under veterinary care at VetCompass practices during 2016 as described above, after excluding the seven confirmed leptospirosis cases. Univariable logistic

regression analysis identified eight variables with liberal significance (Table 1).

Missing data were retained as 'record unavailable' here but models were also explored with missing data excluded (Supplementary Material). The final multivariable logistic regression models included age, clinic IMD rank, clinic urban or rural location and either breed types or KC breed group (Tables 2 and 3).

Dogs ≥ 1-year-old had reduced odds when compared to dogs <1-year-old. Dogs had reduced odds of leptospirosis if they attended an urban clinic versus a rural clinic (OR = 0.26, 95% CI = 0.19–0.35). Odds were increased if dogs attended less deprived clinics (IMD ranking 3–5), with highest odds of diagnosis in least deprived (five) areas (OR = 3.63, 95% CI 2.28–5.78). Cocker Spaniels (OR = 4.25, 95% CI = 2.65–6.83), Border Collies (OR = 3.53, 95% CI = 2.22–5.62), Lurchers (OR = 3.49, 95% CI = 1.50–8.11), Greyhounds (OR = 2.94, 95% CI = 2.02–4.26), Labrador Retrievers (OR = 2.60, 95% CI = 1.04–6.55) and Jack Russell Terriers (OR = 2.04, 95% CI = 1.28–3.25) had increased odds of leptospirosis when compared to crossbreeds. Three KC groups exhibited significantly increased odds of leptospirosis compared to non-KC recognised dogs in the KC group model: Gundog (OR = 3.00, 95% CI 2.22–4.05), Pastoral (OR = 2.86, 95% CI = 1.93–4.24) and Hound (OR = 1.81, 95% CI = 1.09–3.01). Odds of leptospirosis were reduced for Toy (OR = 0.30, 95% CI = 0.16–0.56) and Utility (OR = 0.33, 95% CI = 0.17–0.64) KC groups compared with non-KC recognised dogs. In the final multivariable models built with missing data excluded, the associations between a leptospirosis diagnosis and age, clinic IMD rank and clinic urban/rural location were the same as the models built with missing data retained (Tables S2 and S3). The majority of breeds in the breed model built without missing data (Table S2) had similar associations with diagnosis as the model including missing data except for Cocker Spaniels odds of diagnosis reducing (OR = 2.15, 95% CI 1.10–4.22) and the odds of a diagnosis for Lurchers increasing (OR = 6.34, 95% CI = 2.67–15.04).

Sex and neuter status were not statistically significantly associated with leptospirosis. Interactions between all independent variables in the final models were assessed and were not statistically significant in the final model and therefore were not retained. There were no confounding variables identified in either final model. The final models with breed types evaluated and with the KC breed group replacing breed types in the model both exhibited a poor fit to the dataset (Hosmer-Lemeshow test, $p = < 0.001$ in both models).

DISCUSSION

This study identified low levels of testing and a low incidence risk in 2016 of leptospirosis in dogs under the care of a large cohort of primary-care veterinary practices in the UK. The risk factors for leptospirosis included younger dogs, dogs attending clinics in rural areas, several individual breeds (Cocker Spaniels, Border Collies, Lurchers, Greyhounds, Labrador retrievers and Jack Russell Terriers) and the KC groups Gundog, Pastoral and Hound. Toy and Utility KC breed groups were associated with reduced odds compared to non-KC dogs.

The low frequency of diagnostic testing for leptospirosis and the subsequent low reported incidence of the disease in the VetCompass population suggested that there may be limited consideration of leptospirosis as a differential diagnosis by veterinary practitioners and/or that the presence of infection within the UK dog population is truly low. Assuming the latter, whether the low results were due to leptospira being a truly uncommon infectious agent in the UK or uncommon due to 'herd' immunity gained from widespread usage of leptospirosis vaccines is unclear.[35] The global burden of human leptospirosis cases was reportedly substantially underestimated, due to complexities with existing diagnostic tests and wide-ranging and vague presenting signs.[36] These issues likely also contributed to under-diagnosis in dog populations.[2] Of the 14 dogs that had MAT results reported, only two recorded paired serology titres. Given that Tangeman and Littman reported that 45% of leptospirosis cases in their study required paired serology to reach a diagnosis, it is likely that a significant proportion of the 'negative' cases identified in the VetCompass population could be false negatives.[10]

The incidence risk identified in this study (0.8 per 100,000) was lower than reported in Switzerland (5.88 per 100,000) and the US (37 per 100,000).[5,12] However, the Swiss and US studies utilised referral hospital populations and therefore report incidence within a generally sicker subset of the populations which was unlikely to represent the overall dog population of that country seen in first-opinion practices.[37] When compared to other studies, leptospirosis cases identified in the VetCompass study had slightly increased fatality rate (57% vs 25%–52%),[38–41] suggesting that leptospirosis was clinically considered in more severely affected dogs in the UK. This difference may also reflect that these UK dogs were managed in primary-care practice rather than at referral centres, as with other studies. No cases in the current study had evidence of prior vaccination, which might also explain why leptospirosis was suspected, whereas in vaccinated dogs, this diagnosis might not be considered. Cases in the current study presented with vomiting and/or lethargy, symptoms consistent with other studies.[38–41] The finding of azotaemia in all infected dogs was recognised in studies by Rentko et al and Major.[5,38] The median age of the VetCompass cases was 3 years old, but other studies reported higher median ages (4.8–7.4 years).[5,39,40] However, the current description of leptospirosis relates only to seven confirmed cases and comparisons with prior work should be interpreted with caution.

TABLE 1 Descriptive statistics of IDEXX / APHA Laboratory leptospirosis cases and VetCompass controls and variables examined in univariable analysis. Leptospirosis cases ($n = 362$) were from positive results from MAT and PCR test submissions at IDEXX Laboratories and the APHA. The control group ($n = 905{,}536$) were dogs under veterinary care in VetCompass in 2016. Records missing data were coded as a 'record unavailable'. Percentages shown in Leptospirosis cases and VetCompass controls are column percentages

Variable	Category	Leptospirosis cases (%)	VetCompass controls (%)	OR(95% CI)	Wald *p* value	LRT *p*-value
Sex	Female	147 (40.6)	431708 (47.7)	Base		<0.001
	Male	148 (40.9)	469606 (51.9)	0.93 (0.74-1.16)	0.51	
	Record unavailable	67 (18.5)	4229 (0.45)	46.53 (34.8-62.21)	<0.001	
Neutering status	Entire	119 (32.9)	493351 (54.5)	Base		<0.001
	Neutered	73 (20.2)	407965 (45.1)	0.74 (0.55-0.99)	0.05	
	Record unavailable	170 (47.0)	4227 (0.5)	166.73 (131.66-211.16)	<0.001	
KC recognised	Not KC recognised	74 (20.4)	263694 (29.3)	Base	<0.001	<0.001
	KC recognised	246 (68.0)	637793 (70.7)	1.37 (1.06-1.78)	0.02	
	Record unavailable	42 (11.6)	4056 (0.44)	36.9 (25.24-53.95)	<0.001	
KC groups	Not KC recognised	54 (22.8)	263694 (29.3)	Base		<0.001
	Gundog	74 (31.2)	135672 (15)	2.86 (2.13-3.85)	<0.001	
	Hound	13 (5.5)	31406(3.5)	2.27 (1.38-3.72)	<0.001	
	Pastoral	25 (10.5)	51693 (5.7)	2.76 (1.88-4.05)	<0.001	
	Terrier	25 (10.5)	145843 (16.2)	1.08 (0.74-1.56)	0.70	
	Toy	3 (1.3)	131901 (14.6)	0.30 (0.16-0.56)	<0.001	
	Utility	9 (3.8)	102635 (11.4)	0.35 (0.18-0.67)	0.02	
	Working	6 (2.5)	38643 (4.3)	1.11 (0.60-2.04)	0.75	
	Record unavailable	28 (11.8)	4056 (0.44)	36.90 (25.24-53.95)	<0.001	
Breed types (>5 cases per individual breed)	Crossbreed	67 (18.5)	239937 (26.5)	Base		<0.001
	Border collie	25 (6.9)	24388 (2.7)	3.67 (2.32-5.81)	<0.001	
	Cocker Spaniel	14 (3.9)	32145 (3.5)	1.56 (0.88-2.77)	0.13	
	English Springer Spaniel	24 (6.6)	20208 (2.2)	4.25 (2.67-6.78)	<0.001	
	German Shepherd Dog	10 (2.8)	22735 (2.5)	2.05 (1.13-3.71)	0.02	
	Golden Retriever	5 (1.4)	9793 (1.1)	1.83 (0.74-4.54)	0.19	
	Greyhound	5 (1.4)	5456 (0.6)	3.28 (1.32-8.15)	0.01	
	Jack Russell Terrier	26 (7.2)	48435 (7.6)	1.92 (1.22-3.02)	0.01	
	Labrador Retriever	49 (13.5)	59963 (9.5)	2.93 (2.02-4.23)	<0.001	
	Lurcher	6 (1.7)	6022 (0.9)	3.57 (2.02-4.23)	<0.001	
	Purebred - other	89 (24.6)	432405 (47.8)	0.71 (0.52-0.98)	0.04	
	Record unavailable	42 (11.6)	4056 (0.4)	37.08 (25.18-54.61)	<0.001	
Age	0-1	55 (15.2)	103850 (11.6)	Base		<0.001
	>1-5	75 (20.8)	382158 (42.8)	0.36 (0.26-0.51)	<0.001	
	>5-8	49 (13.6)	180111 (20.2)	0.50 (0.34-0.74)	<0.001	
	>8	57 (15.8)	227000 (25.4)	0.46 (0.32-0.67)	<0.001	
	Record unavailable	125 (34.6)	12424 (1.37)	18.66 (13.58-25.64)	<0.001	
Urban or rural clinic location	Rural	57 (15.7)	63344 (7.0)	Base		<0.001
	Urban	174 (48.1)	800283 (88.4)	0.24 (0.18-0.33)	<0.001	
	Record unavailable	131 (36.2)	41916 (4.6)	3.47 (2.54-4.74)	<0.001	
IMD ranking	1	26 (7.2)	174524 (19.3)	Base		<0.001
	2	45 (12.4)	293326 (32.4)	1.03 (0.64-1.67)	0.91	
	3	54 (14.9)	147231 (16.3)	2.46 (1.54-3.93)	<0.001	
	4	48 (13.3)	131276 (14.5)	2.45 (1.52-3.96)	<0.001	
	5	58 (16.0)	117270 (13.0)	3.32 (2.09-5.27)	<0.001	
	Record unavailable	131 (36.2)	41916 (4.6)	20.98 (13.77-31.96	<0.001	

TABLE 2 Results of multivariable logistic regression models examining significant variables associated with laboratory leptospirosis diagnosis compared to VetCompass controls. The Leptospirosis case group ($n = 362$) were positive results from MAT and PCR test submissions at IDEXX Laboratories and the APHA. The control group ($n = 905{,}536$) were dogs under veterinary care in VetCompass. Missing data were recorded as 'record unavailable'

Breed model				
Variable	**Category**	**OR(95% CI)**	**Wald *p* value**	**LRT *p* value**
Age	0- < 1y	Base		<0.001
	1- < 5y	0.38 (0.27-0.54)	<0.001	
	5- < 8y	0.44 (0.30-0.65)	<0.001	
	8- < 21y	0.42 (0.29-0.61)	<0.001	
	Record unavailable	15.84 (11.28-22.35)	<0.001	
Breed types with >5 cases	Crossbreed	Base		<0.001
	Border Collie	3.53 (2.22-5.62)	<0.001	
	German Shepherd Dog	1.69 (0.94-3.01)	0.08	
	Cocker Spaniel	4.25 (2.65-6.83)	<0.001	
	English Springer Spaniel	1.59 (0.81-3.10)	0.18	
	Golden Retriever	1.80 (0.72-4.1)	0.21	
	Labrador Retriever	2.60 (1.04-6.55)	0.04	
	Jack Russell Terrier	2.04 (1.28-3.25)	0.003	
	Greyhound	2.94 (2.02-4.26)	<0.001	
	Lurcher	3.49 (1.50-8.11)	0.004	
	Purebred-other	0.73 (0.53-1.00)	0.05	
	Record unavailable	6.19 (4.02-9.51)	<0.001	
IMD rank clinic	1(most deprived)	Base		<0.001
	2	1.10 (0.68-1.78)	0.26	
	3	2.46 (1.54-3.940	<0.001	
	4	2.50 (1.55-4.04)	<0.001	
	5(least deprived)	3.63 (2.28-5.78)	<0.001	
	Record unavailable	22.92 (15.00-35.02)	<0.001	
Clinic location	Rural	Base		<0.001
	Urban	0.26 (0.19-0.35)	<0.001	
	Record unavailable	7.00 (4.28-11.44)	<0.001	

TABLE 3 Results for KC breed group after replacing breed in the final breed focussed multivariable logistic regression model (along with age, IMD rank and urban-rural clinic classification) with missing data retained as 'record unavailable'

Variable	**Category**	**OR(95% CI)**	**Wald *p* value**	**LRT *p* value**
KC groups	Not KC Recognised	Base		<0.001
	Pastoral	2.86 (1.93-4.24)	<0.001	
	Gundog	3.00 (2.22-4.05)	<0.001	
	Terrier	1.25 (0.85-1.82)	0.25	
	Hound	1.81 (1.09-3.01)	0.02	
	Toy	0.26 (0.14-0.49)	<0.001	
	Utility	0.28 (0.14-0.54)	<0.001	
	Working	0.91 (0.49-1.69)	0.77	
	Record unavailable	1.37 (0.89-2.10)	0.15	

Results from the evaluation of risk factors for leptospirosis in the primary-care practice attending dogs provide insight into which animal types were more likely to be diagnosed in the wider dog population. The association between age and leptospirosis risk varies between studies. Some previous studies identified reduced odds of infection in younger dogs (< 1 year)[5,15,42,43,44] whereas others recognised reduced odds in adult dogs (dogs > 1 years).[23,44] Meta-analysis of North and South American studies by Azócar-Aedo and Monti found the potential protective factor of <1 year of age to be not statistically significant. When only PCR submissions were examined (data not shown here), thereby avoiding potential vaccine antibody

interference, this age pattern persisted. This suggests that for this study population at least, younger dogs do have increased odds of leptospirosis.

Breed was examined as a potential risk factor in the analyses to quantify individual and grouped breeds' relative magnitude of risk. Increased odds were observed in several breeds, Cocker Spaniels, Border Collies, Lurchers, Greyhounds and Labrador Retrievers. The increased odds associated with these breeds and their corresponding KC groups (Gundog, Hound and Pastoral) were comparable to findings in several previous studies and fit with the historical perception of larger breeds involved in contact with potential livestock reservoirs and hunting being positively associated with leptospirosis.[2,12,14,41] However, a reduced odds of diagnosis in toy breeds was identified in this study and contrasts with work by Lee et al, who found in a multi-decade study that increased risk of leptospirosis had changed more recently from being associated with larger breed types to urban and small breed dogs.[44] Cross-bred dogs have been found to have an elevated risk of contracting leptospirosis in previous research in clinically suspect populations.[22,44] This may be due to vaccine uptake being less common than for purebred dogs.[35] Some of the increased odds in breeds was likely attributable to socio-economic status. Dogs from less deprived areas (according to clinic postcode IMD rank) had increased odds, suggesting that testing and hence diagnosis may be more likely to be pursued in less deprived areas where purebred dogs are more common, fitting with previous work identifying these relationships in dogs in Great Britain.[45]

Urban/rural classification of clinics was included to attempt to crudely explore environmental risk. Dogs attending urban clinics had three-fold reduced odds of diagnosis. These findings are suggestive that dogs attending primary-care clinics in rural areas have an increased risk of leptospirosis, consistent with the recognised importance of the disease in farm animals and wildlife.[1,46] Additionally, it may reflect reduced deprivation in rural areas and therefore greater likelihood of submitting diagnostic tests, and as such the findings should not be over-interpreted.[47]

Sex and entire status have been recognised as risk factors for leptospirosis in previous studies, but no statistical associations between sex or neutering and leptospirosis diagnosis were found here.[12,38,41]

The study had several limitations. Sample size of cases limited analysis of individual breeds to just 10 breed types, none were small/toy breeds. Due to limited numbers of individual breed cases, a second model based on KC breed grouping was evaluated. Furthermore, the study had limited ability to evaluate breed types at reduced odds of leptospirosis, as most breed types at reduced odds would have had fewer than five cases, and hence would not have been considered for statistical reasons as individual breed types in the breed variable. In order to identify protective breeds we would need to include most common breeds, irrespective of their number of cases and/or undertake a larger study. When missing data were removed from the logistic regression models, the associations between leptospirosis and independent variables remained largely similar, with exception to a few categories (Cocker Spaniel and Lurcher in the breed model and Toy breed group in the KC model). The category of 'record unavailable' was often associated with very high odds of a leptospirosis diagnosis, for example in univariable analyses the odds of a diagnosis with leptospirosis was 37 times higher in dogs with breed information missing than crossbred dogs (OR = 37.08, 95% CI 25.18–54.61). These high ORs for missing data indicated that the laboratory submissions had a higher proportion of missing data than the VetCompass dataset.

The retrospective nature of the data from laboratory submissions meant that, some potentially important factors for leptospirosis diagnosis and positive testing could not be explored in the risk factor analysis. Laboratory records did not report vaccination status, which may have influenced test results. To minimise false positives in the MAT, due to vaccinal antibodies, a positive titre was defined as >1:800, according to consensus statement recommendations.[2] Other studies used a range of thresholds to identify positive cases, including titres > 1:100, potentially due to varying degrees of vaccination between countries. However, the UK dog population reportedly has an overall high rate of vaccine uptake therefore use of a lower antibody titre as a threshold would likely lead to an increase in false positives.[35] Similar to previous studies, it was not possible to identify whether samples were part of paired serology. Additionally, in the VetCompass case-control study the cases and controls were derived from separate populations, and hence controls were not the exact population from which the cases were derived.[34] However, it was considered this control group was sufficiently representative of the underlying veterinary attending population from which test positive cases were derived, to merit meaningful risk factor exploration.[28]

Finally, the geographical analysis should be considered as just preliminary and future work to explore spatial distribution could provide more detailed information to quantify exposure risk factors. Although clinic urban/rural classification was explored, the full postcode to identify precisely the owner's home location was not available. This precluded fuller evaluation for potential risk events such as flooding, contact with livestock or activities like swimming. These have been associated with leptospirosis outbreaks in humans and also dogs previously.[14,16,17]

The results of this work provide a valuable baseline and scope for further exploration of the epidemiology of canine leptospirosis in the UK. They provide evidence for the low frequency of testing and diagnosis of leptospirosis within the first opinion UK dog population. Challenges with diagnosis of leptospirosis in humans have led to underestimation of the global burden. Under-diagnosis is also likely in canine populations, this may be due to the disease not being

considered an important disease by veterinarians or due to hesitancy to utilise existing diagnostic tests. This research identifies risk factors for primary-care attending dogs, which will aid veterinarians develop a better index of suspicion for potential cases.

ACKNOWLEDGEMENTS

We would like to thank Noel Kennedy (RVC) for VetCompass software and programming development. We acknowledge the Medivet Veterinary Partnership, Vets4Pets/Companion Care, Goddard Veterinary Group, Independent Vet Care, CVS Group, Linnaeus Group, Vets Now and the other UK practices who collaborate in VetCompass. We are grateful to The Kennel Club and The Kennel Club Charitable Trust for supporting VetCompass. Also, thanks to MSD Animal Health for providing funding for the PhD project and expertise on leptospirosis. Thanks to the Biotechnology and Biological Sciences Research Council (BBSRC) for funding the LIDo PhD programme. Great thanks go to APHA Weybridge and IDEXX Laboratories for supplying laboratory submission datasets.

CONFLICT OF INTEREST

Collette Taylor reports grants from MSD Animal Health and the BBSRC, during the conduct of the study; and grants from MSD Animal Health and the BBSRC, outside the submitted work.

AUTHOR CONTRIBUTIONS

Laboratory datasets were acquired by Brian Catchpole and Collette Taylor. Laboratory datasets were tidied and explored by Collette Taylor. The VetCompass dataset was created and tidied by Dan G. O'Neill and Dave C. Brodbelt. Dan G. O'Neill and Dave C. Brodbelt provided assistance with study design, model building, analysis, and interpretation. The paper was initially prepared by Collette Taylor, with significant contributions from all coauthors.

DATA AVAILABILITY STATEMENT

The datasets generated and analysed during the current study are not publicly available due to their use in ongoing primary research, but subsections may be made available from the corresponding author on reasonable request.

FUNDING INFORMATION

This work was undertaken as part of a PhD jointly funded by the BBSRC (grant number BB/M009513/1) and MSD Animal Health.

REFERENCES

1. Adler B, de la Peña Moctezuma A. Leptospira and leptospirosis. Vet Microbiol. 2010;140(3–4):287–96.
2. Schuller S, Francey T, Hartmann K, Hugonnard M, Kohn B, Nally JE, et al. European consensus statement on leptospirosis in dogs and cats. J Small Anim Pract. 2015;56(3):159–79.
3. Sykes JE, Hartmann K, Lunn KF, Moore GE, Stoddard RA, Goldstein RE. 2010 ACVIM small animal consensus statement on leptospirosis: diagnosis, epidemiology, treatment, and prevention. J Vet Intern Med. 2011;25(1):1–13.
4. Goldstein RE, Lin RC, Langston CE, Scrivani P V., Erb HN, Barr SC. Influence of infecting serogroup on clinical features of leptospirosis in dogs. J Vet Intern Med. 2006;20(3):489–94.
5. Major A, Schweighauser A, Francey T. Increasing incidence of canine leptospirosis in Switzerland. Int J Environ Res Public Health. 2014;11(7):7242–60.
6. Andre-Fontaine G. Diagnosis algorithm for leptospirosis in dogs: Disease and vaccination effects on the serological results. Vet Rec. 2013;172(19):502.
7. World Health Organization. Human leptospirosis: guidance for diagnosis, surveillance and control. Geneva, Switzerland; 2003.
8. Goldstein RE. Canine leptospirosis. veterinary clinics of North America - small animal practice. 2010;40(6):1091–01.
9. Fraune CK, Schweighauser A, Francey T. Evaluation of the diagnostic value of serologic microagglutination testing and a polymerase chain reaction assay for diagnosis of acute leptospirosis in dogs in a referral center. J Am Vet Med Assoc. 2013;242(10):1373–80.
10. Tangeman LE, Littman MP. Clinicopathologic and atypical features of naturally occurring leptospirosis in dogs: 51 cases (2000-2010). J Am Vet Med Assoc. 2013;243(9):1316–22.
11. Adler B, de la Peña Moctezuma A. Leptospira and leptospirosis. Vet Microbiol. 2010;140:287–96.
12. Ward MP, Glickman LT, Guptill LF. Prevalence of and risk factors for leptospirosis small animals among dogs in the United States and Canada: 677 cases (1970–1998) [Internet]. J Am Vet Med Assoc. 2002;220(1):53–8.
13. van den Broek AH., Thrusfield MV, Dobbiet GR, Ellis WA. A serological and bacteriological survey of leptospiral infection in dogs in Edinburgh and Glasgow. Vet Rec. 1991;32(3):118–24.
14. Delaude A, Rodriguez-Campos S, Dreyfus A, Counotte MJ, Francey T, Schweighauser A, et al. Canine leptospirosis in Switzerland—A prospective cross-sectional study examining seroprevalence, risk factors and urinary shedding of pathogenic leptospires. Prev Vet Med. 2017;141:48–60.
15. Gautam R, Wu C, Potter A, Moore GE. Detection of antibodies against Leptospira serovars via microscopic agglutination tests in dogs in the United States, 2000–2007. J Am Vet Med Assoc. 2010;237(3);293–8.
16. Lau CL, Smythe LD, Craig SB, Weinstein P. Climate change, flooding, urbanisation and leptospirosis: Fuelling the fire? Trans R Soc Trop Med Hyg. 2010;104(10):631–8.
17. Raghavan RK, Brenner KM, Higgins JJ, Hutchinson JMS, Harkin KR. Evaluations of hydrologic risk factors for canine leptospirosis: 94 cases (2002-2009). Prev Vet Med. 2012;107(1–2):105–9.
18. Scanziani E, Origgi F, Giusti AM, Iacchia G, Vasino A, Pirovano G, et al. Serological survey of leptospiral infection in kennelled dogs in Italy. J Small Anim Pract. 2002;43(4):154–7.
19. André-Fontaine G. Leptospirosis in domestic animals in France: Serological results from 1988 to 2007. OIE Rev Sci Tech. 2016;35(3):913–23.
20. Glickman LT, Moore GE, Glickman NW, Caldanaro RJ, Aucoin D, Lewis HB. Purdue University-Banfield National Companion Animal Surveillance Program for emerging and zoonotic diseases. Vector-Borne Zoonotic Dis. 2006;6(1):14–23.
21. Moore GE, Guptill LF, Glickman NW, Caldanaro RJ, Aucoin D, Glickman LT. Canine leptospirosis, United States, 2002–2004. Emerg Infect Dis. 2006;12(3):501–3.
22. Azócar-Aedo L, Monti G. Meta-analyses of factors associated with leptospirosis in domestic dogs. Zoonoses Public Health. 2016;63(4):328–36.
23. Ward MP, Guptill LF, Prahl A, Ching Wu C. Serovar-specific prevalence and risk factors for leptospirosis among dogs: 90 cases (1997–2002). J Am Vet Med Assoc. 2004;224(12):1958–63.
24. VetCompass. VetCompass: health surveillance for UK companion animals. London: The Royal Veterinary College; 2019.
25. Veterinary Medicines Division. In: Committee for medicinal products for veterinary use (CVMP) CVMP assessment report for Vectra Felis (EMEA /V / C / 002746 / 0000); April 11 2014; London, UK.
26. Kirkwood BR, Sterne JAC. Essential medical statistics. 2nd ed. London: Blackwell; 2003.

27. Stevens KB, O'Neill D, Jepson R, Holm LP, Walker DJ, Cardwell JM. Signalment risk factors for cutaneous and renal glomerular vasculopathy (Alabama rot) in dogs in the UK. Vet Rec. 2018;183(14):448.
28. Dean AG, Sullivan KM. OpenEpi. 2008. https://www.openepi.com. Accessed 30 March 2019.
29. VeNom Coding Group. VeNom veterinary nomeclature. http://venomcoding.org. Accessed 30 March 2019.
30. Kennel Club. The Kennel club breed standards. 2019. https://www.thekennelclub.org.uk/activities/dog-showing/breed-standards/. Accessed 30 March 2019.
31. DEFRA. Office of National Statistics. Guide to applying the rural urban classification to data. 2016. www.gov.uk/defra. Accessed 3 September 2020.
32. Department for Communities and Local Government. The english index of multiple deprivation (IMD) 2015 – guidance. 2015. https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015. Accessed 3 September 2020.
33. Pallant J. SPSS survival manual. 4th ed. Open University Press; 2010.
34. Dohoo I, Martin W, Stryhn H. Veterinary epidemiological research. Phoenix, Arizona, US: VER Inc.; 2009.
35. Sánchez-Vizcaíno F, Muniesa A, Singleton DA, Jones PH, Noble PJ, Gaskell RM, et al. Use of vaccines and factors associated with their uptake variability in dogs, cats and rabbits attending a large sentinel network of veterinary practices across Great Britain. Epidemiol Infect. 2018;146(7):895–903.
36. Abela-Ridder B, Sikkema R, Hartskeerl RA. Estimating the burden of human leptospirosis. Int J Antimicrob Agents. 2010;36(SUPPL. 1):S5–7.
37. O'Neill DG, Church DB, McGreevy PD, Thomson PC, Brodbelt DC. Approaches to canine health surveillance. Canine Genet Epidemiol. 2014;1(1):2.
38. Rentko VT, Clark N, Ross LA, Schelling SH. Canine leptospirosis: a retrospective study of 17 Cases. J Vet Intern Med. 1992;6(4):235–44.
39. Birnbaum N, Barr SC, Center SA, Schermerhorn T, Randolph JF, Simpson KW. Naturally acquired leptospirosis in 36 dogs: Serological and clinicopathological features. J Small Anim Pract. 1998;39(5):231–6.
40. Geisen V, Stengel C, Brem S, Müller W, Greene C, Hartmann K. Canine leptospirosis infections - clinical signs and outcome with different suspected Leptospira serogroups (42 cases). J Small Anim Pract. 2007;48(6):324–8.
41. Adin CA, Cowgill LD. Treatment and outcome of dogs with leptospirosis: 38 cases (1990-1998). J Am Vet Med Assoc. 2000;216(3):371–5.
42. Smith AM, Arruda AG, Evason MD, Weese JS, Wittum TE, Szlosek D, et al. A cross-sectional study of environmental, dog, and human-related risk factors for positive canine leptospirosis PCR test results in the United States, 2009 to 2016. BMC Vet Res. 2019;15(1):412.
43. Ghneim GS, Viers JH, Chomel BB, Kass PH, Descollonges DA, Johnson ML. Use of a case-control study and geographic information systems to determine environmental and demographic risk factors for canine leptospirosis. Vet Res. 2007;38(1):37–50.
44. Lee HS, Guptill L, Johnson AJ, Moore GE. Signalment changes in canine leptospirosis between 1970 and 2009. J Vet Intern Med. 2014;28(2):294–9.
45. Sánchez-Vizcaíno F, Noble PJM, Jones PH, Menacere T, Buchan I, Reynolds S, et al. Demographics of dogs, cats, and rabbits attending veterinary practices in Great Britain as recorded in their electronic health records. BMC Vet Res. 2017;13(1):1–13.
46. Fávero JF, de Araújo HL, Lilenbaum W, Machado G, Tonin AA, Baldissera MD, et al. Bovine leptospirosis: prevalence, associated risk factors for infection and their cause-effect relation. Microb Pathog. 2017;107:149–54.
47. Ministry of Housing & Communities & Local Government. English indices of deprivation. London, England: Ministry of Housing & Communities & Local Government; 2019.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Taylor C, O'Neill DG, Catchpole B, Brodbelt DC. Incidence and demographic risk factors for leptospirosis in dogs in the UK. Vet Rec. 2021;e512. https://doi.org/10.1002/vetr.512