Outbreak of Severe Vomiting in Dogs Associated with a Canine Enteric Coronavirus, United Kingdom

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The lack of population health surveillance for companion animal populations leaves them vulnerable to the effects of novel diseases without means of early detection. We present evidence on the effectiveness of a system that enabled early detection and rapid response to a canine gastroenteritis outbreak in the United Kingdom. In January 2020, prolific vomiting among dogs was sporadically reported in the United Kingdom. Electronic health records from a nationwide sentinel network of veterinary practices confirmed a significant increase in dogs with signs of gastroenteric disease. Male dogs and dogs living with other vomiting dogs were more likely to be affected. Diet and vaccination status were not associated with the disease; however, a canine enteric coronavirus was significantly associated with illness. The system we describe potentially fills a gap in surveillance in neglected populations and could provide a blueprint for other countries.

Population health data is lacking for companion animals such as dogs, cats, and rabbits, leaving a surveillance gap for endemic diseases and delayed detection of incursions of disease, such as equine influenza virus (H3N8) (*1*), avian influenza (H3N2) (*2*,*3*), and parvoviruses (*3*). In the absence of legislated programs of population surveillance, several attempts have been made to fill this gap using secondary data, particularly from pet insurance providers (*4*). More recently, researchers have exploited the rapid digitization of electronic health records (EHRs) for passive surveillance. Data can be collected at great scale and analyzed in near–real time. EHR data are now routinely used in human heath efforts (*5*–*8*), in which their timeliness, simplicity, and breadth of coverage complements surveillance based on diagnostic data (*9*,*10*). Such approaches are beginning to find healthcare value in veterinary species, especially among companion animals (*4*,*11*–*13*), a high proportion of which visit veterinarians (*14*).

In January 2020, one of the authors of this article (D.G.), a primary care veterinarian in northwest England, contacted the other authors about seeing an unusually high number of cases (≈40) of severe vomiting in dogs; responses to a social media post suggested other veterinarians might have been experiencing similar events. Vomiting is a common complaint among dogs whose owners seek treatment for them (*15*,*16*). However, documented outbreaks are rare because established vaccines are available for most common known pathogens (*17*). In the absence of robust populationwide data, such sporadic reports frequently do not raise awareness of outbreaks.

For the response we describe, we obtained data from syndromic surveillance and text mining of EHRs collected from sentinel veterinary practices and diagnostic laboratories, which we then linked with data from field epidemiology and enhanced genomic testing. In 8 weeks, using this approach, we described the temporal and spatial epidemiology, identified a possible causative agent, and provided targeted advice to control the outbreak. Ethics approval was given by Liverpool University Research Ethics Committees (Liverpool, UK; VREC922/RETH000964).

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Methods

Data Sources

Veterinary Practices

During March 17, 2014–February 29, 2020, we collected data from 7,094,397 consultation records (4,685,732 from dogs and 1,846,493 from cats) from EHRs from the Small Animal Veterinary Surveillance Network (SAVSNET), a volunteer network of 301 veterinary practices (663 sites) in the United Kingdom, recruited based on convenience (*11*). In brief, EHRs included data collected during individual consultations on species, breed, sex, neuter status, age, owners' postcodes, and vaccination status. Each EHR is also compulsorily annotated by the veterinary clinician with a main presenting complaint (MPC) at time of visit, using a questionnaire window embedded in the practice management system. Options for reasons for visit included gastroenteric, respiratory, pruritus, tumor, kidney disease, other unwell, post-op check, vaccination, or other healthy.

Given that severe vomiting was a key outbreak feature, we undertook 2 complementary analyses. First, we used regular expressions to identify clinical narratives describing frequent vomiting, but excluded common false positive search results (Appendix Table 1, https://wwwnc.cdc.gov/EID/article/27/2/20-2452-App1.pdf). Second, we used data on prescriptions to describe the frequency of all veterinary-authorized products containing the antiemetic maropitant (*18*). We calculated trend lines using Bayesian binomial generalized linear modeling trained on weekly prevalence during 2014–2019 (*19*), which allowed us to identify extreme (>99% credible interval [CrI]) or moderate (>95% CrI) observations.

Laboratories

SAVSNET also collects EHRs from participating diagnostic laboratories on samples submitted from more than half of UK veterinary practices. Canine diagnostic test results from January 2017 through February 2020 were queried from 6 laboratories for 6 gastroenteric pathogens. Test numbers, percentage of positive results, and associated 95% CIs were summarized (Table 1). The number of sites was surmised from the submitting practices' postcodes.

Questionnaires

Online questionnaires to enable case reporting were made available to both veterinarians and owners beginning January 29, 2020. The required case definition of ≥5 vomiting episodes in a 12-hour period was based on clinical observations of early cases. Veterinarians were also asked to complete control questionnaires. Initially, we requested only controls matched to veterinary practices contributing case data; however, to increase recruitment, a nonmatched control questionnaire open to any veterinarian was deployed on February 5. The questionnaires (Appendix) requested a range of information including owner postcode, animal signalment, vaccination status, clinical signs, treatment and diagnostic testing, animal contacts, diet, and recovery status.

We performed all statistical analyses using R version 3.6.1 (https://cran.r-project.org). Case details were described for both veterinarian- and owner-reported data. We calculated proportions and 95% CIs for categorical variables and median and range for continuous variables. We constructed univariable and multivariable mixed-effects logistic regression models using data submitted by veterinarians using R package lme4. Explanatory variables from univariable logistic regression were considered in

Table 1. Results of laboratory diagnostic tests for pathogens associated with gastroenteric disease in dogs for samples collected during January 2017–February 2020, United Kingdom*

Pathogen	Method	No. tests	No. laboratories†	Unique sites‡	% Positive (95% CI)	Peak month, % positive (95% CI)
CeCoV	PCR	5,167	4	839	20.69 (19.58–21.79)	2020 Feb, 34.8 (27.81–41.85)
Canineparvovirus	PCR	5,499	6	965	6.62 (5.96–7.28)	2017 Nov, 13.28 (7.38–19.18)
Giardia	PCR	5,636	6	894	23.78 (22.66–24.89)	2018 Jan, 33.96 (26.58–41.35)
Salmonella spp.	Culture	114,722	6	2,951	0.87 (0.81–0.92)	2018 Nov, 1.28 (0.87–1.70)
Campylobacter spp.	Selective culture	111,983	6	2,947	16.10 (15.88–16.31)	2017 Dec, 23.02 (21.44–24.60)
Clostridium perfringens	Enterotoxin PCR	5,138	3	2,947	16.10 (15.88–16.31)	2017 Dec, 23.02 (21.44–24.60)

*CeCoV, canine enteric coronavirus.
†Number of diagnostic laboratories contributing test results.
‡Number of unique veterinary practices sites submitting samples to the laboratories.

multivariable models for likelihood ratios of p≤0.20, which underwent manual stepwise backward elimination to reduce Akaike's and Bayesian information criteria. Practice was included as a random effect. We assessed confounding by the effect on model fit with sequential removal of variables and assessed 2-way interaction terms for improved model fit. We defined final statistical significance as p <0.05.

Spatiotemporal Analysis of Cases

We obtained records of consults weekly during November 4, 2019–March 21, 2020; cases were geolocated by pet owners' postcodes. We considered records of gastroenteric MPC as a binary outcome (i.e., 1 for gastroenteric consult, 0 for nongastroenteric consult). We used a logistic geostatistical model to investigate spatial clustering of cases for each week. We defined a spatial hotspot as a location having 95% posterior probability of prevalence exceeding the national mean prevalence over any 1-week period. With no discernible epidemic wave apparent over successive weeks, we aggregated weekly measures across the study period to show the number of weeks each location was a hotspot (Appendix).

Sample Collection, PCR, and Phylogenetic Analyses

Veterinarians submitting questionnaires were also asked to submit samples for microbiological testing including mouth swabs, fecal samples, and for gastrointestinal cases, vomit. In brief, we extracted nucleic acids using a QIAGEN QIAamp viral RNA kit (https://www.qiagen.com), reverse transcribed samples using ThermoFisher Superscript III (https://www.thermofisher.com), and tested for canine enteric coronavirus (CeCoV) by M-gene PCR (*20*). To expedite results and reduce contamination risks, the PCR was run as a single-stage PCR rather than as the published nested reaction. We purified positive samples using QIAquick (QIAGEN) and sequenced them bidirectionally (Sanger sequencing; Source Biosciences, https://www.sourcebioscience.com) to produce consensus sequences (ChromasPro 2.1.8, http://technelysium.com.au).

To rapidly explore the potential involvement of other viruses, we extracted nucleic acid from 19 random cases and 5 controls for deep sequencing. RNA was amplified by sequence-independent, single-primer-amplification (*21*), multiplexed libraries were prepared using 30 ng of cDNA with an Oxford Nanopore SQK-LSK109 ligation sequencing kit (Oxford Nanopore, https://nanoporetech.com) and sequenced using an Oxford Nanopore MinION Mk1B device for 48 hours. To perform real-time fast basecalling, we used the Oxford Nanopore MinKNOW Guppy toolkit and FASTQ files uploaded to an Oxford Nanopore EPI2ME data analysis platform for identification.

For deeper sequencing coverage, we also processed 10 samples (6 CeCoV-positive cases, 3 negative cases, 1 control) for Illumina sequencing at the University of Liverpool Centre for Genomic Research (https://www.liverpool.ac.uk/genomic-research). We treated nucleic acids with RNase and prepared fragment libraries using a NEBNext Ultra II kit (https://www.neb.com) before performing paired-end, 2 × 150–bp sequencing on an Illumina HiSeq 4000 system (https://www.illumina.com). Adaptor sequences were trimmed using cutadapt (https://cutadapt.readthedocs.io) and sickle (https://github.com), with a minimum quality score of 20. Reads >19 bp matching the dog genome (CanFam3.1, http://genome.ucsc.edu) using Bowtie2 sequence alignment tool (http://bowtie-bio.sourceforge.net) were removed. Remaining reads were assembled using the SPAdes toolkit (https://github.com) and contigs >700 nt blasted against the NCBI RefSeq nonredundant proteins database (https://www.ncbi.nlm.nih.gov/refseq). Sequences matching CeCoV were aligned using the ClustalW multiple sequence alignment program (https://www.genome.jp) and phylogenies reconstructed using bootstrap analyses and neighbor-joining in MEGA6 software (https://www.megasoftware.net). Each sequence was assigned a local laboratory number based on the order in which the sequences were analyzed.

Results

Syndromic Surveillance

On the basis of MPCs identified in the EHRs, we found a specific and significant increase in the number of dogs recorded as exhibiting gastroenteric signs; the final 10 weeks, during December 2019–March 2020, were outside the 99% CrI (extreme outliers; Figure 1, panel A). A similar trend was observed in maropitant therapy for dogs (Figure 1, panel B). Both measures, peaked in the week ending February 2, 2020, at approximately double the preceding baseline. We observed no similar trends for respiratory disease in dogs, for gastroenteric MPCs, for maropitant treatment in cats (Figure 1, panels C–E), or for antibiotic use in dogs (data not shown), together suggesting the signal was specific to canine gastroenteric disease, a finding supported by similar increases in the regular expression identifying vomiting dogs (Figure 1, panel F).

Spatiotemporal mapping of weekly cases of gastroenteric MPC showed prevalence was spatially clustered (Figure 2). In particular, locations in northwest and southwest England and in Edinburgh, Scotland, had strong evidence of many weeks of prevalence higher than the national mean.

Diagnostic Tests

The patterns of test results for different PCR tests, generally carried out concurrently, were broadly similar (Figure 3, panels A–C). The same was true for results based on cultured samples (Figure 3, panels D, E). Of particular interest, CeCoV showed strong seasonality, positive tests peaking during the winter months (Figure 3, panel A). However, similar peaks seen in previous years suggested the observed peak in February 2020 could not itself explain this outbreak.

Questionnaire

By March 1, 2020, a total of 1,258 case questionnaires had been received. After excluding 59 questionnaires missing key data, we used data from 165 veterinary-reported cases, 1,034 owner-reported cases (Table 2), and 60 veterinary-reported controls (Appendix Table 2) for analyses.

Most cases were from households in England (Table 2). Median case age at examination was 4.0 years (range 0.3–15.0 years) based on veterinary reports and 4.8 years (range 0.2–15.5 years) based on owner reports. Most animals had been vaccinated against core pathogens (*17*) and leptospirosis within the preceding 3 years and dewormed within the previous 3 months. A range of breeds (data not presented) were observed, broadly corresponding to previous studies (*6*). Most cases were fed dog food, but

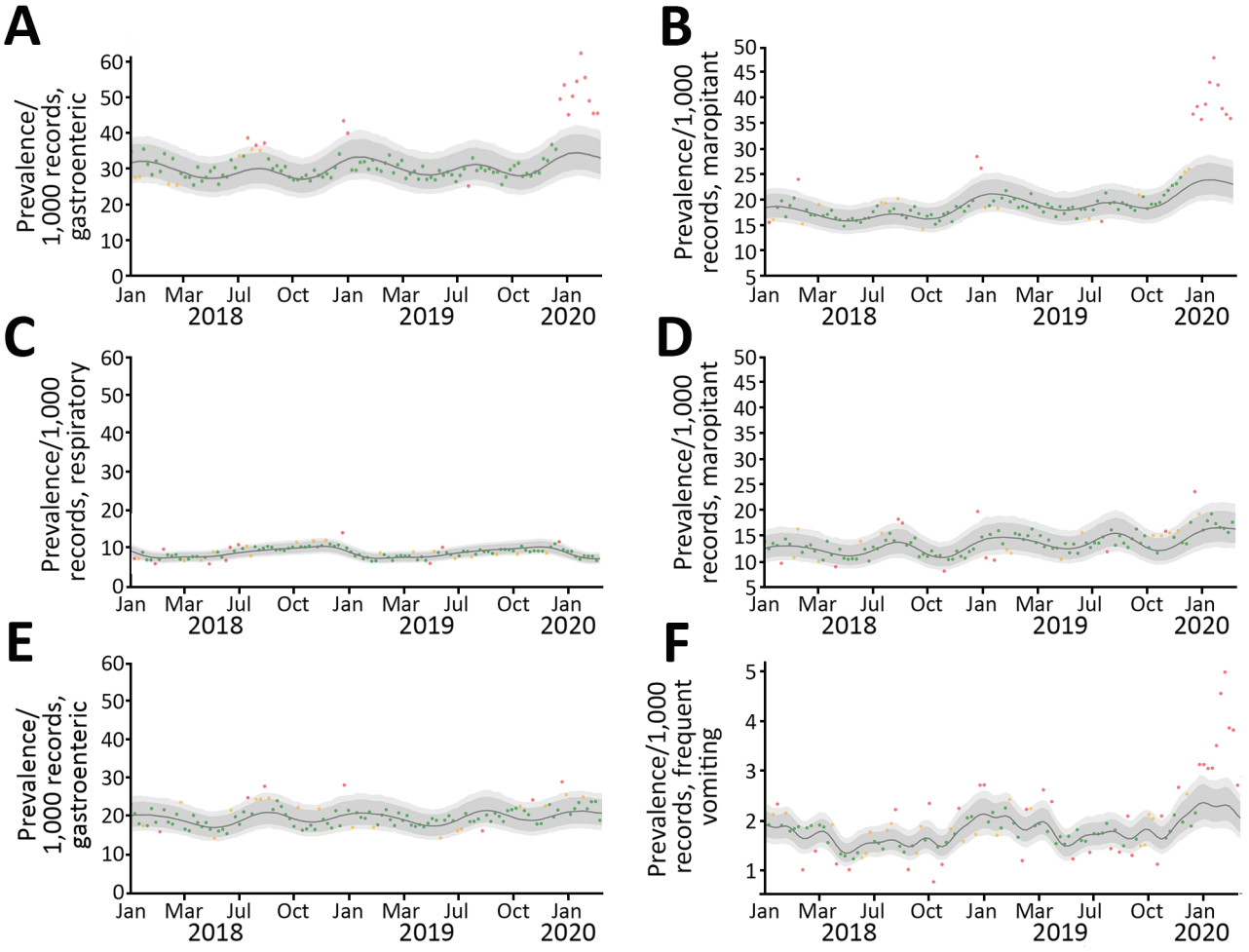

Figure 1. Observed prevalence of main presenting complaint (MPC) and maropitant use in cats and dogs, per 1,000 consultations, in investigation of dogs with vomiting, United Kingdom, January 2017–February 2020. A) Canine records labeled as gastroenteric MPC; B) canine records in which maropitant was prescribed; C) canine records labeled as respiratory MPC; D) feline records in which maropitant was prescribed; E) feline records labeled as gastroenteric MPC; and F) frequent vomiting in dogs based on regular expression searches of the clinical narratives. Red points represent the extreme outliers (outside the 99% credible interval [CrI]), orange points the moderate outliers (outside the 95% CrI, but within the 99% CrI), and green points the average trend (within the 95% CrI).

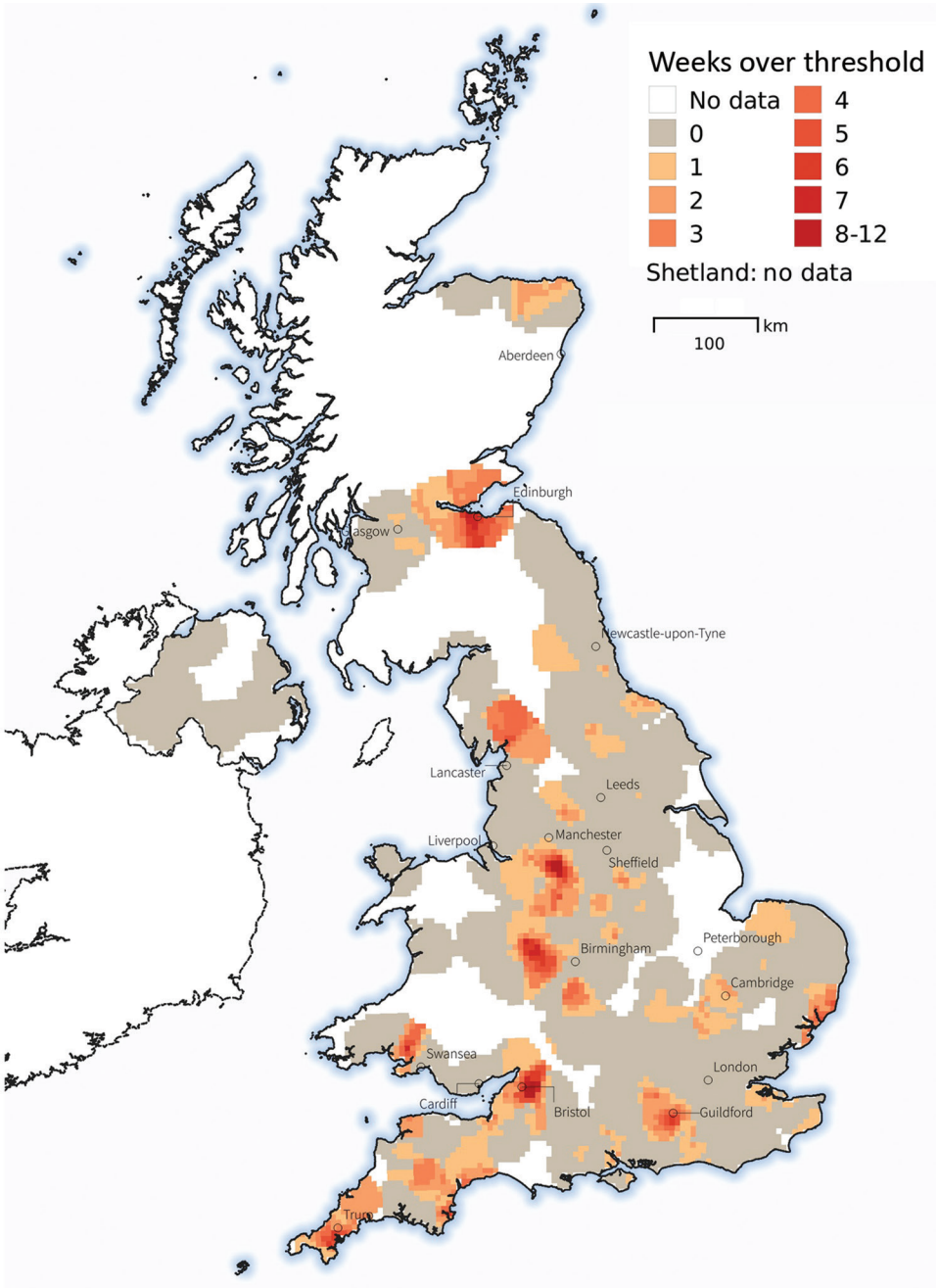

Figure 2. Rates of gastroenteric veterinary consults for dogs during November 4, 2019–March 21, 2020, in investigation of dogs with vomiting, United Kingdom. Consults were geolocated to owners' postcodes, with gastroenteric main presenting complaint as a binary outcome (1 for gastroenteric consult, 0 for a nongastroenteric consult). Colored areas represent the number of weeks a given location had a 95% posterior probability of prevalence exceeding the national mean prevalence in any week. The geostatistical modeling approach used is further detailed in the Appendix (https://wwwnc.cdc.gov/EID/article/27/2/20-2452-App1.pdf).

≈20%–37% of dogs scavenged food when walked. Of those from multidog households, just over half reported the presence of another dog recently vomiting within the same household. Around 30% of dogs had recently traveled, most commonly visiting a daycare facility.

Date of onset of clinical signs ranged from November 16, 2019, through February 28, 2020, for veterinary-reported cases, and September 4, 2019, through March 1, 2020, for owner-reported cases. Most cases involved inappetence (75.6%–86.1%) and vomiting without blood (88.7%–91.5%) (Table 3). Approximately half of cases reported diarrhea, most without blood. Diagnostic testing was performed in 32.1% of veterinary-reported cases, most (78.9%) using hematology or biochemistry assays, or both.

Dogs in >90% of veterinary-reported cases were treated, compared with in 61.7% of owner-reported cases. In both, antiemetics were most often prescribed: in 89.1% (CrI 84.3%–93.9%) of veterinary-reported cases and in 48.1% (CrI 45.0%–51.1%) of owner-reported cases. The most common recovery time was

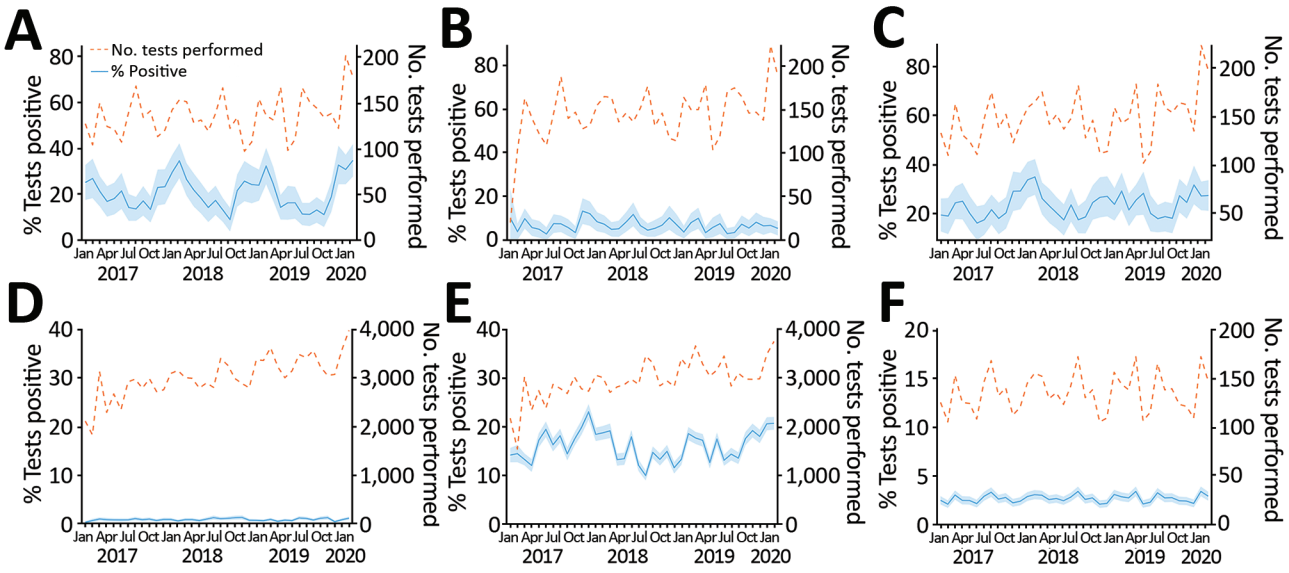

Figure 3. Diagnostic test findings during January 2017–February 2020 in investigation of dogs with vomiting, United Kingdom. A) Canine enteric coronavirus PCR; B) canine parvovirus PCR; C) *Giardia* PCR; D) *Salmonella* spp. selective culture; E) *Campylobacter* spp. selective culture; F) *Clostridium perfringens* enterotoxin PCR results. Blue shading represents 95% CI.

3–7 days; the dogs died in 0.6% of veterinary-reported and 1.0% of owner-reported cases.

Descriptive data about the control population, submitted by veterinarians, and univariable findings from analyses of the veterinary case controls are presented in Appendix Tables 2 and 3; multivariable findings are shown in Table 4. Both neutered and non-neutered male dogs were at significantly increased odds of contracting the illness, compared with neutered females, as were dogs living in the same household as another dog that had also been vomiting compared to those in households where other dogs were healthy. However, dogs living in a single-dog household were at increased odds of contracting the illness compared with dogs living in the same household as another dog that had not recently vomited. Dogs that had been in recent contact with another animal species (including humans) that had recently vomited were at reduced odds of vomiting, compared with those who had not. Other potential causes considered early in the outbreak, including foodborne etiologies, vaccine preventable diseases, or the possibility of interspecies transmission, were not significantly associated (Appendix Table 3).

Sampling and Molecular Testing

During January 30–March 12, 2020, we collected a total of 95 samples from 71 animals (50 cases, 21 controls): 22 from feces, 60 from oral swabs, and 13 from vomit. Dogs with prolific vomiting were significantly more likely to test positive for CeCoV in ≥1 sample (17/50, 34%) compared with controls (0/21) ($p = 0.002$ by Fisher exact test). Positive test results were most likely in samples from feces (10/16 [62.5%] cases, 0/6 controls; $p = 0.01$) and vomit (6/13 [46%] cases, 0 controls). Samples from oral swabs were least likely to test positive (7/43 [16%] cases, 0/17 controls; $p = 0.17$). Of 17 CeCoV-positive cases, 12 met the case definition, 2 did not (<5 episodes of vomiting in 12 hours), and 3 lacked questionnaire data.

We gathered useable M-gene sequences from 21 samples (16 dogs). When we sequenced 2 samples from the same animal, the sequences were identical and subsequently represented only once in analyses (Figure 4). All sequences clustered with previously reported type II CeCoVs (22) in 1 of 3 lineages. Sequences from 14 of 16 dogs were identical, suggesting a single outbreak strain geographically distributed across England. Sequences from dogs 15 and 16 were phylogenetically distinct.

Results of MinION sequencing rapidly confirmed an alphacoronavirus as the predominant virus (24,190 out of 33,826,933 reads) and failed to identify any other prevalent candidates (next highest, betabaculovirus: 4,541 reads). Although bacterial reads were present in high numbers, none showed consistently high results across most samples.

Complete CeCoV genomes were assembled from 6 PCR-positive cases by Illumina sequencing. We identified no coronavirus sequences in 3 cases and 1 control that tested negative for CeCoV by PCR. The only other mammalian virus sequence detected

matched a canine rotavirus (1 case, 1 control; data not presented). Consistent with M-gene sequencing, 5 of the CeCoV genomes clustered together (>99% similarity), distinct from the genome from dog 15 (Figure 4). The outbreak strain was most similar to a virus from Taiwan isolated in 2008 from a young dog with diarrhea (94.5% similarity; L. Chueh, pers. comm. [email] Apr. 27, 2020) and did not show any obvious sequence differences to published strains that might explain the unusual pattern of disease observed in the outbreak. Based on spike gene analyses, the outbreak strain clustered with IIb, having a TGEV-like N-terminal spike domain (*23*). Sequences were submitted to GenBank (accession nos. MT877072, MT906864, and MT906865).

Discussion

Using EHRs annotated with syndromic information by veterinarians, we rapidly identified an outbreak of canine gastroenteric disease that had started in November 2019. This finding was corroborated by parallel increases in relevant prescriptions and records

Table 2. Veterinary- and owner-reported case questionnaire responses pertaining to signalment, health history, contacts, and feeding habits among dogs with vomiting, United Kingdom, January 2017–February 2020*

	Veterinarian-reported cases, n = 165		Owner-reported cases, n = 1,034	
Question	% Responses (95% CI)	No. unknown	% Responses (95% CI)	No. unknown
Veterinary practice location				
England	80.6 (74.6–86.7)	NA	89.8 (87.9–91.6)	NA
Wales	12.1 (7.1–17.1)	NA	4.5 (3.2–5.7)	NA
Scotland	4.9 (1.6–8.1)	NA	4.5 (3.2–5.7)	NA
North Ireland	1.2 (0.0–2.9)	NA	1.1 (0.4–1.7)	NA
Republic of Ireland	1.2 (0.0–2.9)	NA	0.1 (0.0–0.3)	NA
Isle of Man	0	NA	0.2 (0.0–0.5)	NA
Sex				
F	42.4 (34.9-50.0)	NA	43.7 (40.7-46.7)	NA
M	57.6 (50.0–65.1)	NA	56.3 (53.3–59.3)	NA
Neutered‡	69.1 (62.0–76.2)	NA	70.1 (67.3–72.9)	NA
Intact‡	30.9 (23.8-37.9)	NA	29.9 (27.1-32.7)	NA
Vaccinated within past 3 y†	94.6 (91.1–98.0)	NA	88.4 (86.5–90.4	13
Distemper	92.7 (88.8–96.7)	NA	49.7 (46.7–52.8)	NA
Infectious hepatitis	92.1 (88.0–96.2)	NA	40.4 (37.4–43.4)	NA
Parvo	92.1 (88.0–96.2)	NA	55.4 (52.4–58.5)	NA
Parainfluenza	53.9 (46.3–61.6)	NA	37.4 (34.5–40.4)	NA
Leptospirosis	92.7 (88.8–96.7)	NA	49.2 (46.2–52.3)	NA
Kennel cough	46.7 (39.0–54.3)	NA	40.4 (37.4–43.4)	NA
Rabies	2.4 (0.1–4.8)	NA	1.3 (0.6–1.9)	NA
Herpes	0.6 (0.0–1.8)	NA	NA	NA
Dewormed within past 3 mo	86.2 (80.5–92.0)	27	69.8 (67.0–72.7)	50
Lives in multidog household	34.6 (27.3–41.8)	NA	47.4 (44.3–50.4)	NA
≥1 dogs in household vomited	54.4 (41.3–67.4)	NA	55.9 (51.5–60.3)	NA
Regular contact with other species†	54.9 (46.1–63.8)	43	44.1 (41.1–47.1)	NA
Cats	64.2 (52.6–75.8)	NA	62.3 (57.8–66.7)	NA
Horses	20.9 (11.1–30.7)	NA	28.3 (24.2–32.4)	NA
Cattle or sheep or both	25.4 (14.9–35.9)	NA	22.2 (18.3–26.0)	NA
Pigs	3.0 (0.0–7.1)	NA	1.5 (0.4–2.7)	NA
Poultry	13.4 (5.2–21.7)	NA	14.0 (10.8–17.2)	NA
Rabbits	7.5 (1.1–13.8)	NA	5.7 (3.6–7.8)	NA
Other species	11.9 (4.1–19.8)	NA	20.6 (16.9–24.3)	NA
Contact with other vomiting species	13.5 (7.1–19.9)	54	17.4 (14.6–20.2)	320
Recent travel history†	31.4 (23.0–39.8)	47	26.7 (24.0–29.4)	NA
Boarding kennel	8.1 (0.0–17.0)	NA	9.1 (5.7–12.5)	NA
Group training/behavior classes	24.3 (10.3–38.3)	NA	35.5 (29.9–41.2)	NA
Doggie day care facility	48.7 (32.3–65.0)	NA	39.5 (33.7–45.3)	NA
Overseas	2.7 (0.0–8.0)	NA	0.7 (0.0–1.7)	NA
Rescue kennel	0.0 (0.0–0.0)	NA	0.4 (0.0–1.1)	NA
Other	18.9 (6.1–31.7)	NA	20.3 (15.5–25.0)	NA
Provided known food type†	95.2 (91.9–98.4)	8	100.0 (100.0–100.0)	NA
Proprietary dog food	95.5 (92.3–98.8)	NA	85.9 (83.8–88.0)	NA
Home-cooked diet	6.4 (2.5–10.2)	NA	10.4 (8.6–12.3)	NA
Raw meat	5.1 (1.6–8.6)	NA	15.9 (13.6–18.1)	NA
Table scraps	14.7 (9.1–20.2)	NA	16.1 (13.8–18.3)	NA
Scavenged food	36.6 (28.7–44.4)	20	19.9 (17.4–22.4)	24

*NA, not available.
‡Includes both female and male animals.
†Multiple responses for the same dog are possible.

Table 3. Veterinarian reported and owner-reported case questionnaire responses pertaining to clinical signs, diagnostic and management strategies, and case recovery likelihood and time among dogs with vomiting, United Kingdom, January 2017–February 2020*

	Veterinarian-reported cases, n = 165		Owner-reported cases, n = 1,034	
Question	% Responses (95% CI)	No. unknown	% Responses (95% CI)	No. unknown
Clinical signs				
Vomiting without blood	91.5 (87.3–95.8)	NA	88.7 (86.8–90.6)	NA
Vomiting with blood	8.5 (4.2–12.8)	NA	11.3 (9.4–13.3)	NA
Diarrhea without blood	37.0 (29.6–44.4)	NA	46.2 (43.2–49.3)	NA
Diarrhea with blood	10.9 (6.1–15.7)	NA	12.3 (10.3–14.3)	NA
Melaena	1.8 (0.0–3.9)	NA	NA	NA
Pyrexia	12.7 (7.6–17.8)	NA	15.4 (13.2–17.6)	NA
Inappetence	86.1 (80.8–91.4)	NA	75.6 (73.0–78.3)	NA
Weight loss	18.2 (12.3–24.1)	NA	34.9 (32.0–37.8)	NA
Lethargy	9.1 (4.7–13.5)	NA	6.3 (4.8–7.8)	NA
Diagnostic testing performed	32.1 (25.0–39.3)	NA	18.3 (15.9–20.7)	NA
Treatment provided to dog	92.1 (88.0–96.2)	NA	61.7 (58.7–64.7	13
Recovery status known	88.5 (83.6–93.4)	19	98.4 (97.6–99.1)	17
Recovery <24 h	5.5 (2.0–8.9)	NA	2.9 (1.8–3.9)	NA
Recovery in 24–48 h	17.6 (11.8–23.4)	NA	21.1 (18.6–23.7)	NA
Recovery in 3–7 d	30.9 (23.8–38.0)	NA	36.2 (33.2–39.1)	NA
Recovery in 7–14 d	2.4 (0.1–4.8)	NA	5.9 (4.5–7.4)	NA
Recovery in over 14 d	2.4 (0.1–4.8)	NA	2.1 (1.2–2.9)	NA
Dog currently vomiting	7.9 (3.8–12.0)	NA	9.4 (7.6–11.2)	NA
Dog not vomiting but still unwell	21.2 (15.0–27.5)	NA	21.4 (18.9–24.0)	NA
Dog died	0.6 (0.0–1.8)	NA	1.0 (0.4–1.6)	NA

*NA, not available.

of frequent vomiting. Those data were augmented by data from responses to a questionnaire, diagnostic laboratories, and enhanced microbiological analyses. This system enabled us to determine case definitions and outcomes and to identify risk factors as well as a potential viral cause, within a 3-month period; findings were rapidly disseminated to veterinarians (*24*,*25*) and owners. This combined approach represents an efficient system that can fill a previously neglected national population health surveillance need for companion animals.

The first indication of an outbreak came from time-series analyses of syndromic data. Such syndromic surveillance is increasingly being used to monitor the impact of national events like natural disasters and bioterrorism on human population health, as well as changes in gastroenteric and influenza-like illness (*6*–*9*). Such data can be simple to collect, provide real-time wide geographic coverage, and be flexibly applied to different conditions (*10*,*11*). Although in some cases these data can identify outbreaks earlier than more active surveillance, their predictive value can sometimes be low, particularly where there is a low signal to noise complaint ratio. In our case, the outbreak was large compared with background levels, associated with near doubling of the gastroenteric syndrome, and had many weeks in which the syndrome statistically exceeded the baseline.

The richness of data within EHRs enabled us to validate this outbreak using numbers of antiemetic prescriptions and text mining. Prescription data have been used to understand, for example, human health inequalities (*26*), and the use of critical antimicrobials in both humans (*27*) and animals (*28*,*29*). We used

Table 4. Mixed effects multivariable logistic regression model investigating odds of being a veterinarian-reported prolific vomiting case among 165 cases and 60 controls in investigation of dogs with vomiting, United Kingdom, January 2017–February 2020*

Variable	β	SE	OR (95% CI)	p value†
Intercept	–0.36	0.42	NA	NA
F, neutered	NA	NA	Referent	NA
F, intact	0.77	0.55	2.15 (0.74–6.26)	0.16
M, neutered	0.81	0.40	2.25 (1.03–4.91)	0.04
M, intact	1.34	0.59	3.82 (1.20–12.15)	0.02
Multidog household, no other dogs vomiting in the same household	NA	NA	Referent	NA
Multidog household, other dogs vomiting in the same household	1.15	0.53	3.16 (1.11–8.97)	0.03
Single-dog household	1.17	0.40	3.23 (1.47–7.11)	<0.01
No contact with other species vomiting	NA	NA	Referent	NA
Confirmed contact with other species vomiting	–1.23	0.48	0.29 (0.12–0.74)	0.01
Unknown contact with vomiting other species	0.63	0.42	1.88 (0.83–4.26)	0.13

*β, β-value (coefficient).
†p value <0.05 indicates significant findings.

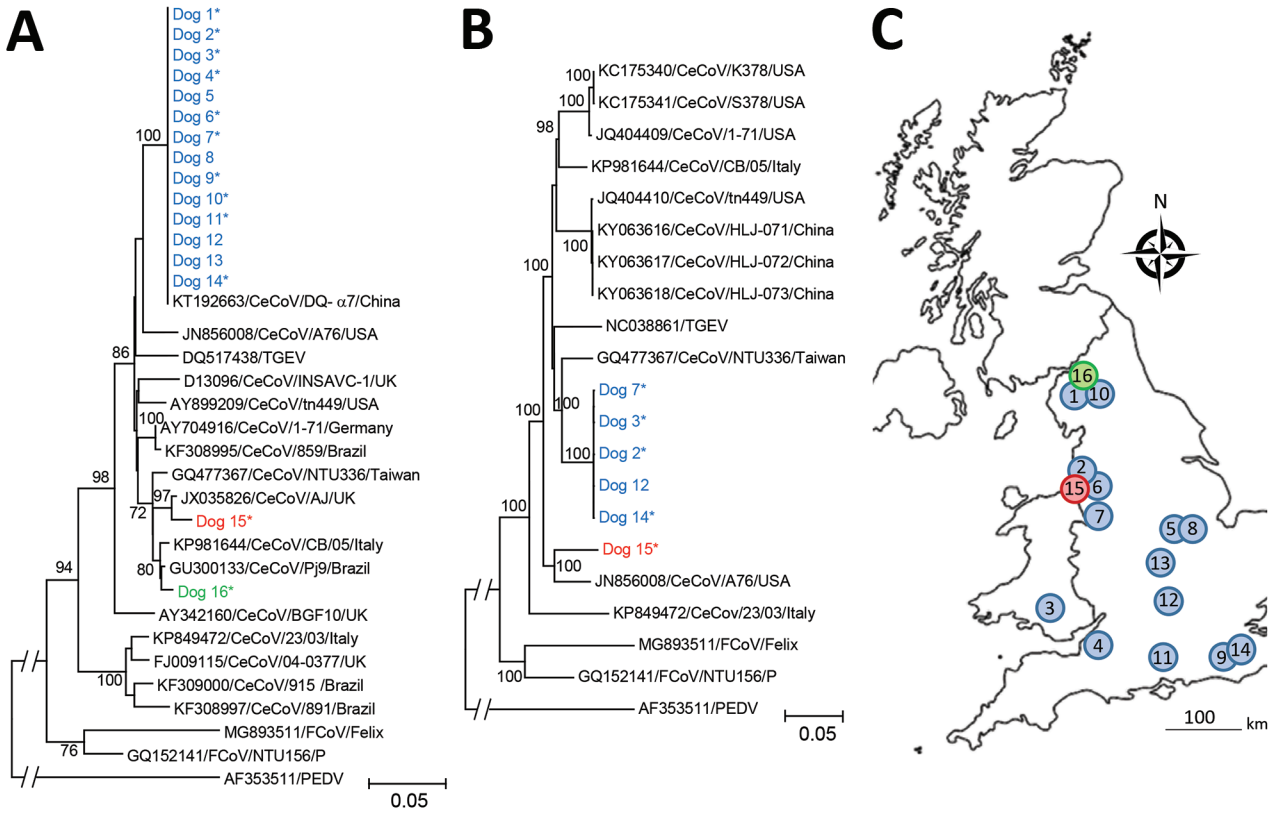

Figure 4. Phylogenetic analysis of canine enteric coronavirus strains, including locations were sequences were obtained, in investigation of dogs with vomiting, United Kingdom. Trees are based on nucleotide sequences for M-gene (final alignment 299 positions) (A) and whole genome (final alignment 26,564 positions) (B). Evolutionary analysis was performed using the neighbor-joining method. Bootstrap testing using 1,000 replicates was applied; only values >70 are indicated. Sequences identified in this study are indicated in blue (strain 1), red (strain 2), and green (strain 3). Asterisks (*) indicate samples from animals meeting the case definition. Each phylogeny included closest matches in GenBank, as well as representative published canine coronavirus, feline coronavirus, and transmissible gastroenteritis virus isolates. Scale bars indicate substitutions per site. C) Approximate geographic location of sequences obtained in this study, number- and color-matched to sequences shown in panels A and B.

these data to identify and track an outbreak, benefitting from a clear link between the syndrome (vomiting) and its therapy (antiemetic). It will be useful to identify other disease-therapy associations that could be used for similar surveillance.

We used text mining to identify records of frequent vomiting in clinical narratives. Such approaches can circumvent the need for practitioner-derived annotation and be flexibly and rapidly adapted to emerging syndromes as soon as case-definitions are determined. Similar approaches have been described in human health for conditions such as fever (*30*–*32*) but can suffer low sensitivity (*31*). Indeed, the outbreak peak based on text mining was ≈20% of that based on MPC analysis. However, it is also likely the outbreak as defined by the MPC included a considerable number of animals with milder signs that would not be detected by data mining using the regular expression developed here. Although data from text mining are unlikely to give an accurate estimate of the true prevalence of a given condition, they can still be used to track outbreaks.

To compliment syndromic surveillance, we implemented a rapid case-control study, collecting >1,200 responses from veterinarians and owners in 4.5 weeks. There was no evidence for similar disease in people or other species. The timing of the outbreak as shown by case data was in broad agreement with our syndromic surveillance. Questionnaires from owners and veterinarians were in broad agreement on date of onset, geographic density, clinical signs, and recovery. These data informed targeted health messages posted online and on social media on February 28, 2020, 4 weeks after we first became aware of the outbreak.

Clearly, evidence of transmission driving the outbreak was vital to providing disease control advice. Dogs in multidog households were more likely to

vomit if other dogs in the household were also affected, suggesting either transmission between dogs or a common environmental source; these observations informed advice to the public around isolating affected dogs. Of note, dogs in single-dog households were also at increased odds of being affected compared to multidog households where only a single dog was vomiting. Some authors have shown that dogs from single-dog households are walked more and therefore could be at greater risk for infection (*33*). Factors affecting dog walking are clearly likely to be important for control of infectious disease transmission and should be explored further.

In addition to collecting epidemiologic data, we collected microbiological samples from cases and controls. Based on its known (*34*) and observed seasonality (Figure 3, panel A), we tested all samples for CeCoV. Cases were significantly more likely to show positive results both when all samples (oral swabs, feces and vomit) were considered or when just fecal samples were considered, suggesting a possible role for CeCoV in the outbreak. However, many case samples tested negative: 33 of 50 overall, 6 of 16 dogs for which feces samples were submitted, and 7 of 13 dogs for which vomit samples were submitted. There are several potential reasons for these negative findings, including the sensitivity of the PCR, the high numbers of oral swabs (although simpler to collect, oral swabs were more likely to test negative), the timing of samples in relation to viral shedding, and the storage and transport of samples. In addition, it is important to note that our case definition, based as it was on a syndrome and lacking more specific confirmatory testing, is likely to include some animals that were not part of the outbreak. Indeed, at its peak, the outbreak only doubled the background level of gastroenteric disease seen at other times of the year; therefore, we might expect only half of our cases to be truly associated with the outbreak.

Sequencing results identified a predominant CeCoV strain in outbreak cases across the United Kingdom, in contrast with earlier studies showing that CeCoV strains tend to cluster in households, veterinary practices, or local areas (*35*). This finding lends further support to the role of this strain in the observed outbreak. In Sweden, a single strain was also implicated in several small wintertime canine vomiting outbreaks (*36*); genetically, however, the virus strain we identified was distinct from the strain from Sweden (data not shown). Ultimately, it will be necessary to perform a challenge study to confirm or refute the role of this CeCoV strain as the cause of this outbreak, as well as to explore the range of clinical signs associated with infection.

If this strain is proven to be the cause of the outbreak, several features mark the observed pattern of disease as unusual, including the outbreak scale, its geographic distribution, the severity of signs in some animals, a lack of notable viral co-infections, and the involvement of adult dogs. CeCoV is generally associated with mild gastroenteritis (*37*). Although sporadic outbreaks of more severe hemorrhagic diseases with high mortality (*38*–*40*), as well as systemic diseases (*41*,*42*), have been reported, these typically affect individual households, and are often associated with mixed infections (*43*). Such observations suggest that the genetic variability of CeCoVs may affect virulence and are supported by experimental infections recreating more severe disease (*38*). The genetic mechanism underlying such shifts in virulence in CeCoV have not been defined. However, mutations impacting virulence are described in closely related alphacoronaviruses (*44*–*47*).

In conclusion, this multidisciplinary approach enabled a rapid response to a newly described outbreak of canine gastroenteritis and identified a CeCoV as a potential cause. Previous CeCoV seasonality suggests further outbreaks may occur. Having such an efficient surveillance system provides the ideal platform to inform and target population health messaging. Several challenges remain for addressing the lack of national population health structures for companion animals: to systematically capture discussions of disease in social and mainstream media; to sustainably fund these activities, which currently are largely resourced by research grants; to understand and broaden the representativeness of such sentinel networks; and to link surveillance information with agencies empowered to act (*12*).

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References

1. Crawford PC, Dubovi EJ, Castleman WL, Stephenson I, Gibbs EP, Chen L, et al. Transmission of equine influenza virus to dogs. Science. 2005;310:482–5. https://doi.org/10.1126/science.1117950
2. Li G, Wang R, Zhang C, Wang S, He W, Zhang J, et al. Genetic and evolutionary analysis of emerging H3N2 canine influenza virus. Emerg Microbes Infect. 2018;7:1–15. https://doi.org/10.1038/s41426-018-0079-0
3. Allison AB, Kohler DJ, Fox KA, Brown JD, Gerhold RW, Shearn-Bochsler VI, et al. Frequent cross-species transmission of parvoviruses among diverse carnivore hosts. J Virol. 2013;87:2342–7. https://doi.org/10.1128/JVI.02428-12
4. O'Neill DG, Church DB, McGreevy PD, Thomson PC, Brodbelt DC. Approaches to canine health surveillance. Canine Genet Epidemiol. 2014;1:2. https://doi.org/10.1186/2052-6687-1-2
5. Smith S, Elliot AJ, Mallaghan C, Modha D, Hippisley-Cox J, Large S, et al. Value of syndromic surveillance in monitoring a focal waterborne outbreak due to an unusual *Cryptosporidium* genotype in Northamptonshire, United Kingdom, June–July 2008. Euro Surveill. 2010;15:19643. https://doi.org/10.2807/ese.15.33.19643-en
6. Fleming DM, Elliot AJ. Lessons from 40 years' surveillance of influenza in England and Wales. Epidemiol Infect. 2008; 136:866–75. https://doi.org/10.1017/S0950268807009910
7. Hiller KM, Stoneking L, Min A, Rhodes SM. Syndromic surveillance for influenza in the emergency department—a systematic review. PLoS One. 2013;8:e73832. https://doi.org/10.1371/journal.pone.0073832
8. Elliot AJ, Singh N, Loveridge P, Harcourt S, Smith S, Pnaiser R, et al. Syndromic surveillance to assess the potential public health impact of the Icelandic volcanic ash plume across the United Kingdom, April 2010. Euro Surveill. 2010;15:19583.
9. Thomas MJ, Yoon PW, Collins JM, Davidson AJ, Mac Kenzie WR. Evaluation of syndromic surveillance systems in 6 US state and local health departments. J Public Health Manag Pract. 2018;24:235–40. https://doi.org/10.1097/PHH.0000000000000679
10. Smith GE, Elliot AJ, Lake I, Edeghere O, Morbey R, Catchpole M, et al.; Public Health England Real-time Syndromic Surveillance Team. Syndromic surveillance: two decades experience of sustainable systems—its people not just data! Epidemiol Infect. 2019;147:e101. https://doi.org/10.1017/S0950268819000074
11. Sánchez-Vizcaíno F, Noble PM, 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;13:218. https://doi.org/10.1186/s12917-017-1138-9
12. McGreevy P, Thomson P, Dhand NK, Raubenheimer D, Masters S, Mansfield CS, et al. VetCompass Australia: a national big data collection system for veterinary science. Animals (Basel). 2017;7:74. https://doi.org/10.3390/ani7100074
13. O'Neill DG, Church DB, McGreevy PD, Thomson PC, Brodbelt DC. Prevalence of disorders recorded in cats attending primary-care veterinary practices in England. Vet J. 2014;202:286–91. https://doi.org/10.1016/j.tvjl.2014.08.004
14. Asher L, Buckland EL, Phylactopoulos CI, Whiting MC, Abeyesinghe SM, Wathes CM. Estimation of the number and demographics of companion dogs in the UK. BMC Vet Res. 2011;7:74. https://doi.org/10.1186/1746-6148-7-74
15. Elwood C, Devauchelle P, Elliott J, Freiche V, German AJ, Gualtieri M, et al. Emesis in dogs: a review. J Small Anim Pract. 2010;51:4–22. https://doi.org/10.1111/j.1748-5827.2009.00820.x
16. O Neill DG, Church DB, McGreevy PD, Thomson PC, Brodbelt DC. Prevalence of disorders recorded in dogs attending primary-care veterinary practices in England. PLoS One. 2014;9:e90501. https://doi.org/10.1371/journal.pone.0090501
17. Day MJ, Horzinek MC, Schultz RD, Squires RA; Vaccination Guidelines Group (VGG) of the World Small Animal Veterinary Association (WSAVA). WSAVA guidelines for the vaccination of dogs and cats. J Small Anim Pract. 2016; 57:E1–45. https://doi.org/10.1111/jsap.2_12431
18. Singleton DA, Sánchez-Vizcaíno F, Arsevska E, Dawson S, Jones PH, Noble PJM, et al. New approaches to pharmacosurveillance for monitoring prescription frequency, diversity, and co-prescription in a large sentinel network of companion animal veterinary practices in the United Kingdom, 2014–2016. Prev Vet Med. 2018;159:153–61. https://doi.org/10.1016/j.prevetmed.2018.09.004
19. Arsevska E, Singleton DA, Jewell C, Paterson S, Jones PH, Smyth S, et al. Small animal disease surveillance: pruritus and *Pseudomonas* skin infections. Vet Rec. 2018;183:182–7. https://doi.org/10.1136/vr.k3462
20. Pratelli A, Tempesta M, Greco G, Martella V, Buonavoglia C. Development of a nested PCR assay for the detection of canine coronavirus. J Virol Methods. 1999;80:11–5. https://doi.org/10.1016/S0166-0934(99)00017-8
21. Chrzastek K, Lee DH, Smith D, Sharma P, Suarez DL, Pantin-Jackwood M, et al. Use of sequence-independent, single-primer-amplification (SISPA) for rapid detection, identification, and characterization of avian RNA viruses. Virology. 2017;509:159–66. https://doi.org/10.1016/j.virol.2017.06.019
22. Pratelli A, Martella V, Decaro N, Tinelli A, Camero M, Cirone F, et al. Genetic diversity of a canine coronavirus detected in pups with diarrhoea in Italy. J Virol Methods. 2003;110:9–17. https://doi.org/10.1016/S0166-0934(03)00081-8
23. Decaro N, Mari V, Elia G, Addie DD, Camero M, Lucente MS, et al. Recombinant canine coronaviruses in dogs, Europe. Emerg Infect Dis. 2010;16:41–7. https://doi.org/10.3201/eid1601.090726
24. Smith SL, Singleton DA, Noble PJ, Radford AD, Brant B, Pinchbeck GL, et al. Possible cause of outbreak of prolific vomiting in dogs. Vet Rec. 2020;186:324. https://doi.org/10.1136/vr.m972
25. Singleton DA, Noble PJ, Radford AD, Brant B, Pinchbeck GL, Greenberg D, et al. Prolific vomiting in dogs. Vet Rec. 2020;186:191. https://doi.org/10.1136/vr.m553
26. Rowlingson B, Lawson E, Taylor B, Diggle PJ. Mapping English GP prescribing data: a tool for monitoring health-service inequalities. BMJ Open. 2013;3:e001363. https://doi.org/10.1136/bmjopen-2012-001363
27. Zanichelli V, Monnier AA, Gyssens IC, Adriaenssens N, Versporten A, Pulcini C, et al. Variation in antibiotic use among

and within different settings: a systematic review. J Antimicrob Chemother. 2018;73(suppl_6):vi17–29. https://doi.org/10.1093/jac/dky115
28. Singleton DA, Sánchez-Vizcaíno F, Dawson S, Jones PH, Noble PJM, Pinchbeck GL, et al. Patterns of antimicrobial agent prescription in a sentinel population of canine and feline veterinary practices in the United Kingdom. Vet J. 2017;224:18–24. https://doi.org/10.1016/j.tvjl.2017.03.010
29. Hur BA, Hardefeldt LY, Verspoor KM, Baldwin T, Gilkerson JR. Describing the antimicrobial usage patterns of companion animal veterinary practices; free text analysis of more than 4.4 million consultation records. PLoS One. 2020;15:e0230049. https://doi.org/10.1371/journal.pone.0230049
30. South BR, Chapman WW, Delisle S, Shen S, Kalp E, Perl T, et al. Optimizing a syndromic surveillance text classifier for influenza-like illness: does document source matter? AMIA Annu Symp Proc. 2008;2008:692–6.
31. Haas SW, Travers D, Waller A, Mahalingam D, Crouch J, Schwartz TA, et al. Emergency Medical Text Classifier: new system improves processing and classification of triage notes. Online J Public Health Inform. 2014;6:e178. https://doi.org/10.5210/ojphi.v6i2.5469
32. Chapman WW, Dowling JN, Wagner MM. Classification of emergency department chief complaints into 7 syndromes: a retrospective analysis of 527,228 patients. Ann Emerg Med. 2005;46:445–55. https://doi.org/10.1016/j.annemergmed.2005.04.012
33. Westgarth C, Christian HE, Christley RM. Factors associated with daily walking of dogs. BMC Vet Res. 2015;11:116. https://doi.org/10.1186/s12917-015-0434-5
34. Duijvestijn M, Mughini-Gras L, Schuurman N, Schijf W, Wagenaar JA, Egberink H. Enteropathogen infections in canine puppies: (co-)occurrence, clinical relevance and risk factors. Vet Microbiol. 2016;195:115–22. https://doi.org/10.1016/j.vetmic.2016.09.006
35. Stavisky J, Pinchbeck GL, German AJ, Dawson S, Gaskell RM, Ryvar R, et al. Prevalence of canine enteric coronavirus in a cross-sectional survey of dogs presenting at veterinary practices. Vet Microbiol. 2010;140:18–24. https://doi.org/10.1016/j.vetmic.2009.07.012
36. Escutenaire S, Isaksson M, Renström LH, Klingeborn B, Buonavoglia C, Berg M, et al. Characterization of divergent and atypical canine coronaviruses from Sweden. Arch Virol. 2007;152:1507–14. https://doi.org/10.1007/s00705-007-0986-1
37. Decaro N, Buonavoglia C. An update on canine coronaviruses: viral evolution and pathobiology. Vet Microbiol. 2008;132:221–34. https://doi.org/10.1016/j.vetmic.2008.06.007
38. Buonavoglia C, Decaro N, Martella V, Elia G, Campolo M, Desario C, et al. Canine coronavirus highly pathogenic for dogs. Emerg Infect Dis. 2006;12:492–4. https://doi.org/10.3201/eid1203.050839
39. Tennant BJ, Gaskell RM, Jones RC, Gaskell CJ. Studies on the epizootiology of canine coronavirus. Vet Rec. 1993;132:7–11. https://doi.org/10.1136/vr.132.1.7
40. Evermann JF, Abbott JR, Han S. Canine coronavirus-associated puppy mortality without evidence of concurrent canine parvovirus infection. J Vet Diagn Invest. 2005;17:610–4. https://doi.org/10.1177/104063870501700618
41. Decaro N, Campolo M, Lorusso A, Desario C, Mari V, Colaianni ML, et al. Experimental infection of dogs with a novel strain of canine coronavirus causing systemic disease and lymphopenia. Vet Microbiol. 2008;128:253–60. https://doi.org/10.1016/j.vetmic.2007.10.008
42. Zicola A, Jolly S, Mathijs E, Ziant D, Decaro N, Mari V, et al. Fatal outbreaks in dogs associated with pantropic canine coronavirus in France and Belgium. J Small Anim Pract. 2012;53:297–300. https://doi.org/10.1111/j.1748-5827.2011.01178.x
43. Dowgier G, Lorusso E, Decaro N, Desario C, Mari V, Lucente MS, et al. A molecular survey for selected viral enteropathogens revealed a limited role of canine circovirus in the development of canine acute gastroenteritis. Vet Microbiol. 2017;204:54–8. https://doi.org/10.1016/j.vetmic.2017.04.007
44. Porter E, Tasker S, Day MJ, Harley R, Kipar A, Siddell SG, et al. Amino acid changes in the spike protein of feline coronavirus correlate with systemic spread of virus from the intestine and not with feline infectious peritonitis. Vet Res. 2014;45:49. https://doi.org/10.1186/1297-9716-45-49
45. Chang HW, Egberink HF, Halpin R, Spiro DJ, Rottier PJ. Spike protein fusion peptide and feline coronavirus virulence. Emerg Infect Dis. 2012;18:1089–95. https://doi.org/10.3201/eid1807.120143
46. Licitra BN, Millet JK, Regan AD, Hamilton BS, Rinaldi VD, Duhamel GE, et al. Mutation in spike protein cleavage site and pathogenesis of feline coronavirus. Emerg Infect Dis. 2013;19:1066–73. https://doi.org/10.3201/eid1907.121094
47. Zhang X, Hasoksuz M, Spiro D, Halpin R, Wang S, Stollar S, et al. Complete genomic sequences, a key residue in the spike protein and deletions in nonstructural protein 3b of US strains of the virulent and attenuated coronaviruses, transmissible gastroenteritis virus and porcine respiratory coronavirus. Virology. 2007;358:424–35. https://doi.org/10.1016/j.virol.2006.08.051

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Nationwide Outbreak of Severe Vomiting in Dogs Associated with a Canine Enteric Coronavirus, United Kingdom

Appendix

Supplementary Information on Geostatistical Modelling

The geostatistical model used to investigate spatial clustering for severe vomiting in dogs makes use of owner-geolocated prevalence data based on total consults recorded in SAVSNet. Below, we first describe the geostatistical model setup, before describing how the results were presented using geographical information systems methods.

Geostatistical Model for Prevalence

For each week between 4th November 2019 and 21st March 2020, our data comprise an indicator $y_i \in \{0,1\}$ for $i = 1, \dots, n_t$ consults recorded. For each consult, we additionally have the centroid of the owner's postcode area x_i in Cartesian coordinates (OSGB 1936 coordinate system).

We model y_i as a Bernoulli random variable such that

$$y_i \approx \text{Bernoulli}(p_i)$$

with

$$\text{logit}(p_i t) = \alpha + S(x_i).$$

$S(x)$ is a spatial Gaussian process such that

$$S(x) \approx \text{MultivariateNormal}(0, \Sigma^2)$$

Σ^2 is a covariance matrix defined by a Matérn correlation function:

$$\Sigma_{ii}^2 = \sigma^2 \Sigma_{ij}^2 = \sigma^2 \left(1 + \frac{\sqrt{3\left\|x_i - x_j\right\|^2}}{\phi}\right) exp\left[-\frac{\sqrt{3\left\|x_i - x_j\right\|^2}}{\phi}\right]$$

where $\left\|x_i - x_j\right\|$ is the Euclidean distance between locations x_i and x_j, σ^2 is the sill variance of the spatial Gaussian process, and ϕ is the length scale (*1*).

The computation of the log posterior probability density for this model involves the inversion of Σ^2 which becomes computationally prohibitive beyond a few hundred points. Since in a typical week $n \approx 24000$, we use the inducing point approximation of Banerjee et al. (*2*). Here, we choose a set of m knot points $x_i^\star, i = 1, \ldots, m$ and let

$$S(x) \approx \Sigma_{xx^\star}^2 \left(\Sigma_{x^\star x^\star}^2\right)^{-1} s^\star \quad (1)$$

where $s^\star$ is a realisation of the Gaussian process at knots $x^\star$. In practice, we find that 300 knot points positioned using K-means clustering on x gives satisfactory computational performance with negligible information loss compared to 600 and 900 knot points positioned similarly.

Finally, we investigated the requirement for a "nugget", or uncorrelated, random effect by adding a variance component to the diagonal of Σ^2, i.e. $\Sigma_{ii}^2 = \sigma^2 + \tau^2$. However, this did not improve the model fit and was removed for the sake of parsimony.

This model was fitted to the consulting data in a Bayesian framework. The following prior distributions were chosen to reflect relative *a priori* ignorance about parameters:

$$\begin{aligned} \alpha &\sim \text{Normal}(0,100) \\ \phi &\sim \text{Gamma}(2,0.1) \\ \sigma_s &\sim \text{Gamma}(1,1) \end{aligned}$$

The No-U-Turn Sampling (NUTS) Markov-chain Monte Carlo method was used to draw samples from the joint posterior distribution $\pi(\alpha, \phi, \sigma^2, s(x)|x, y)$, and implemented in Python v3.6 using the PyMC3 v3.8 embedded probabilistic programming language. Source code is available at https://github.com/SAVSNET.

GIS Presentation of Results

Using Equation (1), the posterior samples of $S(x^\star)$ were projected onto a 5km resolution grid of points z within the outline of the UK (*3*). This gave a numerical approximation of the

predictive distribution $\pi(S(z)|y,x)$ of the posterior log odds ratio for a consult being for severe vomiting, relative to the national-level odds (i.e. $\hat{\alpha}$). These results were summarised by calculating the probability that $z_i > 0$ (or equivalently $e^z > 1$) for all grid locations.

The model was run for all weekly intervals $t = 1, \ldots, T$ between 4th November 2019 and 21st March 2020. In the absence of a strong wave-like progression of disease throughout the UK, the results were summarized as

$$\omega_k = \sum_{t=1}^{T} [Pr(z_i > 0|y,x)] \geq 0.95$$

for all grid points k. In other words, ω_k represents the number of weeks where a particular grid point k was predicted to have a positive case odds ratio above 1 with a posterior probability of at least 0.95 compared to the national average prevalence in each week. It therefore provides an estimate of locations that were at higher risk of positive cases compared to the national average over time during the outbreak.

All calculations were performed in Python v3.6, and cartography was performed in QGIS v3.12.

References

<bok>1. Diggle P, Ribeiro PJ. Model-based geostatistics. New York: Springer. 2007.</bok>

<jrn>2. Banerjee S, Gelfand AE, Finley AO, Sang H. Gaussian predictive process models for large spatial data sets. J R Stat Soc Series B Stat Methodol. 2008;70:825–48. 10.1111/j.1467-9868.2008.00663.x PubMed https://doi.org/10.1111/j.1467-9868.2008.00663.x</jrn>

<eref>3. GADM database of Global Administrative Areas, version 3.6 [cited 2020 Feb 14]. https://biogeo.ucdavis.edu/data/gadm3.6/gpkg/gadm36_GBR_gpkg.zip.</eref>

Appendix Table 1. Regular expression used to screen for cases of frequent vomiting in the clinical free text of EHRs, including examples of true positive and false positive patterns it matches. Bold text identifies the precise text string matched by the regular expression.

Category	Code/description
Regular expression	(?:(?:\W(?:[3-9]\W?x|severe|profuse|prolific|non[\- \s]stop|frequent))\W?(?<!no)(?<!no\ssign\sof)(?<!not)(?<!no\Wmore)(?<!stopped)\W?(?:v[oi]?m+i ?t?t?(?:ing|ed)?|v\+{1,10}|(?:has\Wbeen|was)\Wsick)\W(?!stopped)\W?)|(?:(?<!no)(?<!no\ssign\s of)(?<!not)(?<!no\Wmore)(?<!stopped)\W?(?:v[oi]?m+i?t?t?(?:ing|ed)?|v\+{1,10}|(?:has\Wbeen|w as)\Wsick)\W(?!stopped)\W?\W?(?:frequently|profusely|(?:(?:[3-9]|\d\d?|(\d\d?\W?\- \W?\d\d?)|many|lots\Wof)\W?(?:times|x)|x\W?(?:[3-9]|\d\d)(?:x|times)?)))
Examples of matching text (bold text) that appear to match profuse vomiting definition	OR **V+ 3 times** over last 24h OR **vomited 7 times** since this lunch time **vomited 5 times** today **profuse vomiting** o'night , no diarrhoea empty abdo <<identifier>> **has been sick 2-3 times** this afternoon Has been **vomiting frequently** today
Example of a false positive matches	Booster tricat/fel**v+ 6 x** endectrid

Appendix Table 2. Descriptive findings of veterinary professional-provided control questionnaire responses, seeking to gain location, signalment, feeding and contact information from dogs that have not recently been observed to prolifically vomit (*n*=60).

Variables	% of responses (95% CI)	n unknown
Practice location		
England	83.3 (73.8–92.8)	NA
Wales	6.7 (0.3–13.0)	NA
Scotland	6.7 (0.3–13.0)	NA
North Ireland	3.3 (0.0–7.9)	NA
SAVSNET-participating practice	14.7 (2.6–26.8)	26
Sex		
F	58.3 (45.7-70.9)	0
M	41.7 (29.1–54.3)	0
Neutered‡	78.3 (67.8–88.9)	0
Intact‡	21.7 (11.1-32.2)	0
Lives in multidog household	51.7 (38.9–64.4)	0
Additional dog in household vomited	32.3 (15.5–49.0)	29
Vaccinated within past 3 years†	95.0 (89.4–100.6)	0
Distemper	93.3 (87.0–99.7)	NA
Infectious hepatitis	93.3 (87.0–99.7)	NA
Parvo	91.7 (84.6–98.7)	NA
Parainfluenza	56.7 (44.0–69.3)	NA
Leptospirosis	93.3 (87.0–99.7)	NA
Kennel cough	48.3 (35.6–61.1)	NA
Rabies	10.0 (2.3–17.7)	NA
Dewormed within previous 3 months	84.2 (74.7–93.8)	3
Other species regular contact†	66.0 (53.2–78.9)	7
Cats	74.3 (59.6–89.0)	NA
Horses	25.7 (11.0–40.4)	NA
Cattle and/or sheep	22.9 (8.7–37.0)	NA
Pigs	2.9 (0.0–8.5)	NA
Poultry	22.9 (8.7–37.0)	NA
Other species	14.3 (2.5–26.1)	NA
Recent travel history†	32.1 (19.4–44.8)	7
Boarding kennel	5.9 (0.0–17.4)	NA
Group training/behavior classes	35.3 (11.9–58.7)	NA
Dog day care facility	17.7 (0.0–36.3)	NA
Overseas	5.9 (0.0–17.4)	NA
Rescue kennel	0.0 (0.0–0.0)	NA
Other	47.1 (22.6–71.5)	NA
Provided food type known†	95.0 (89.4–100.6)	0
Proprietary dog food	89.5 (81.4–97.5)	NA
Home-cooked diet	3.5 (0.0–8.3)	NA
Raw meat	10.5 (2.5–18.6)	NA
Table scraps	14.0 (4.9–23.1)	NA
Dog scavenges food	23.6 (12.3–35.0)	5
Contact with other vomiting species	30.6 (17.6–43.7)	11

*NA, information not available.
†Multiple responses for the same dog are possible.
‡Both female and male dogs.

Appendix Table 3: Univariable findings from logistic regression model exploring the odds of being a veterinary professional-reported prolific vomiting case against a set of veterinary professional-provided control dogs*

Variable	β	SE	OR (95% CI)	p value
Veterinary location, country				
England†	1.02	0.20	1.00	NA
Northern Ireland or ROI	–0.32	0.92	0.73 (0.12–4.41)	0.73
Scotland	–0.30	0.66	0.74 (0.20–2.68)	0.65
Wales	0.63	0.59	1.88 (0.59–5.93)	0.28
Sex				
F†	0.73	0.23	1.00	NA
M	0.71	0.33	2.02 (1.06–3.86)	0.03
Neutered status				
Not neutered†	1.42	0.33	1.00	NA
Neutered	–0.49	0.36	0.62 (0.30–1.26)	0.18
Sex and neutered status				
Neutered F†	0.60	0.26	1.00	NA
F, intact	0.48	0.50	1.61 (0.60–4.29)	0.34
M, intact	1.25	0.57	3.47 (1.14–10.55)	0.03
Neutered M	0.70	0.38	2.01 (0.95–4.23)	0.07
No. dogs in household				
Single dog household†	1.36	0.24	1.00	NA
Multidog household	–0.72	0.32	0.49 (0.26–0.90)	0.02
No. dogs vomiting in multidog household				
0†	0.24	0.31	1.00	NA
One or more	0.93	0.48	2.52 (0.99–6.43)	0.05
Single dog household	1.11	0.37	3.04 (1.48–6.27)	<0.01
Vaccination status				
Not recently vaccinated†	1.13	0.69	1.00	NA
Recently vaccinated	–0.07	0.70	0.93 (0.23–3.70)	0.92
Deworming status				
Not recently dewormed†	0.76	0.42	1.00	NA
Recently dewormed	0.21	0.46	1.23 (0.50–3.06)	0.65
Unknown	1.55	0.76	4.73 (1.06–21.16)	0.04
Contact with other species				
No†	1.17	0.30	1.00	NA
Yes	–0.48	0.36	0.62 (0.31–1.24)	0.17
Unknown	0.74	0.51	2.09 (0.77–5.66)	0.15
Contact with cats				
No contact†	1.14	0.26	1.00	NA
Contact	–0.61	0.35	0.55 (0.27–1.09)	0.09
Unknown	0.78	0.48	2.17 (0.84–5.61)	0.11
Contact with horses				
No contact†	0.95	0.21	1.00	NA
Contact	–0.48	0.48	0.62 (0.24–1.61)	0.33
Unknown	0.96	0.47	2.62 (1.05–6.52)	0.04
Contact with cattle and/or sheep				
No contact†	0.90	0.20	1.00	NA
Contact	–0.11	0.49	0.90 (0.35–2.33)	0.83
Unknown	1.01	0.47	2.76 (1.11–6.87)	0.03
Contact with pigs				
No contact†	0.88	0.19	1.00	NA
Contact	–0.14	1.30	0.87 (0.07–11.06)	0.91
Unknown	1.03	0.46	2.79 (1.13–6.89)	0.03
Contact with poultry				
No contact†	0.99	0.21	1.00	NA
Contact	–0.90	0.56	0.41 (0.14–1.22)	0.11
Unknown	0.95	0.47	2.58 (1.03–6.43)	0.04
Contact with other species				
No contact†	0.88	0.19	1.00	NA
Contact	0.02	0.60	1.02 (0.32–3.31)	0.97
Unknown	1.03	0.47	2.81 (1.13–6.99)	0.03
Dog travel status				
No recent travel†	0.84	0.22	1.00	NA
Recent travel	–0.03	0.36	0.97 (0.48–1.97)	0.93
Unknown	1.10	0.46	3.01 (1.22–7.40)	0.02
Travel to boarding kennel				
No travel†	0.82	0.19	1.00	NA
Travel	0.29	1.19	1.34 (0.13–13.70)	0.81
Unknown	1.12	0.45	3.06 (1.28–7.32)	0.01

Variable	β	SE	OR (95% CI)	p value
Travel to training class				
No travel†	0.87	0.20	1.00	NA
Travel	–0.45	0.57	0.64 (0.21–1.95)	0.43
Unknown	1.07	0.45	2.91 (1.21–7.01)	0.02
Travel to dog day care				
No travel†	0.73	0.19	1.00	NA
Travel	1.14	0.66	3.12 (0.85–11.44)	0.09
Unknown	1.23	0.45	3.41 (1.41–8.25)	0.01
Overseas travel				
No travel†	0.84	0.19	1.00	NA
Travel	–0.84	1.46	0.43 (0.03–7.55)	0.57
Unknown	1.10	0.45	3.01 (1.26–7.20)	0.01
Other types of travel				
No travel†	0.95	0.21	1.00	NA
Travel	–1.08	0.57	0.34 (0.11–1.04)	0.06
Unknown	1.01	0.45	2.74 (1.13–6.61)	0.03
Food types				
Food types not known†	0.99	0.70	1.00	NA
Food types known	0.07	0.72	1.08 (0.26–4.40)	0.92
Proprietary dog food provided				
Not provided†	0.18	0.58	1.00	NA
Provided	0.95	0.60	2.59 (0.79–8.43)	0.12
Unknown	0.80	0.90	2.23 (0.38–13.06)	0.37
Raw food provided				
Not provided†	1.13	0.20	1.00	NA
Provided	–0.81	0.59	0.45 (0.14–1.40)	0.17
Unknown	–0.14	0.72	0.87 (0.21–3.58)	0.85
Food scraps provided				
Not provided†	1.06	0.20	1.00	NA
Provided	0.06	0.46	1.06 (0.43–2.59)	0.90
Unknown	–0.07	0.72	0.94 (0.23–3.86)	0.93
Dog food scavenger status				
Not a scavenger†	0.81	0.21	1.00	NA
Scavenger	0.62	0.37	1.86 (0.91–3.81)	0.09
Unknown	0.59	0.54	1.80 (0.62–5.23)	0.28
Other species vomiting contact				
No contact†	1.09	0.23	1.00	NA
Contact	–1.08	0.44	0.34 (0.15–0.80)	0.01
Unknown	0.55	0.40	1.74 (0.80–3.78)	0.16
No. dogs in household				
1†	1.29	0.23	1.00	NA
2	–0.58	0.36	0.56 (0.27–1.14)	0.11
3	–0.45	0.59	0.64 (0.20–2.05)	0.45
4	–0.61	0.76	0.54 (0.12–2.43)	0.42
≥5	–0.77	0.79	0.46 (0.10–2.17)	0.33
Age, y				
At time of illness†	2.24	0.58	1.00	NA
Linear term	–0.48	0.28	0.62 (0.36–1.08)	0.09
Quadratic term	0.07	0.04	1.08 (1.00–1.16)	0.06
Cubic term	0.00	0.00	1.00 (0.99–1.00)	0.04

* β, β-value (coefficient); NA, information not available
†Intercept

CASE QUESTIONNAIRE INFORMATION SHEET AND CONSENT FORM

Potential Outbreak Investigation: Prolific Vomiting in Dogs

You are being invited to participate in an outbreak investigation study, following reports of an outbreak of prolific vomiting in dogs. Before you decide whether to participate, it is important for you to understand why the survey is being conducted and what it will involve if you do choose to take part. Please consider the following information. Epidemiologist contact details are listed below should you have any further questions.

Reading this information sheet and completing the survey will be considered as consent to participate in this survey.

What is the purpose of the survey?

This survey has been created in order to collect more detailed case information, following veterinary surgeon and social media reports of a potential outbreak of prolific, acute vomiting in dogs during December 2019 and January 2020.

Why am I being invited to take part and what will happen if I take part?

You are being invited to take part because you are a veterinary surgeon or owner currently working in a companion animal-treating veterinary practice or an owner, in the United Kingdom, who has potentially identified a case fitting the case definition of "dog with acute onset of prolific vomiting, with 5 or more episodes of vomiting within a 12 hour period".

If you decide to take part you will need to complete the online survey, which will take around 10 minutes.

Participation is voluntary and you do not have to take part in this study. You are free to withdraw at any time until you have selected the ‘finish’ button on the final page of the questionnaire. You do not have to give a reason if you do not wish to take part.

If you are willing, we will also request your postcode, name and email address so that we can ask for further case details if this becomes necessary during the potential outbreak investigation. We will only use your name and email for the purpose of seeking further information, and will destroy data containing these personal identifiers on conclusion of the survey.

Are there any benefits or risks in taking part?

There are no direct benefits or risks to you or your practice associated with taking part in this survey, but we will use the data to further characterise this potential outbreak, and if necessary assist in controlling the potential outbreak.

What will happen if I want to stop taking part?

If you want to stop taking part in this survey you can withdraw at any time until completion and submission of the online survey.

How will my data be used?

The data you provide will be stored securely for up to 7 years in line with data protection requirements at the University of Liverpool and GDPR. All data is strictly confidential and only researchers involved in the study will have access to it. Fully anonymised data may be archived for use in other research projects in the future. Under UK data protection legislation, the University acts as the Data Controller for personal data collected as part of the University's research. The Principal Investigator acts as the Data Processor for this study.

What will happen to the results of the survey?

The data will be used to further characterise the potential outbreak of prolific vomiting in dogs, potentially assisting in identifying causative factors and informing attempts (if necessary) to control this potential outbreak. Anonymised results may also be published - you and your clients (if relevant) will never be identifiable.

What if I am unhappy or if there is a problem?

If you are unhappy, or if there is a problem, please feel free to contact the epidemiologists listed below and we will try to help. If you remain unhappy or have a complaint which you feel you cannot communicate directly to the researcher then you should contact the Research Ethics and Integrity Office on 0151 794 8290 (ethics@liv.ac.uk). When contacting the Research Governance Officer, please provide details of the name or description of the study (so that it can be identified), the researcher involved, and the details of the complaint you wish to make.

Dr David Singleton

Dr Gina Pinchbeck

University of Liverpool

Leahurst Campus

Chester High Road

CH64 7TE

Email: savsnet@liverpool.ac.uk

1. Please confirm that you have read and understood the above information and confirm your consent for data to be used for these purposes, as the owner or on behalf of the owner.

- I confirm that I have consent from the owner to collect and submit these data, and I understand that anonymised data may be used in publications

- I confirm that I am the dog's owner, give consent for collection and submission of these data, and I understand that anonymised data may be used in publications

Basic Case information

We are firstly going to ask some basic information pertaining to the case of canine prolific vomiting you would like to report.

2. Are you describing a current or retrospective vomiting case?

- Current (dog vomited 12 hours or less before completion of survey)
- Retrospective (dog last vomited over 12 hours ago)
- Don't know

2a. If describing a retrospective case, please state date of onset of vomiting:

- Free text response box

Current cases:

3. In the last 12 hours before completion of this survey, how many times has the dog vomited?

- Less than five times
- Five times or more*

Retrospective cases:

4. When the dog was vomiting most frequently, approximately how many times did the dog vomit over a 12 hour period?

- Less than five times
- Five times or more*

* Only participants who selected 'five times or more' in questions 3 or 4 (hence describing a case fitting the case definition) were able to proceed with answering the remaining questions in this survey.

5. Which of the following statements best describes yourself:

- I am a veterinary surgeon wishing to report a potential case of prolific vomiting in a dog under my care (1)
- I am an employee of a veterinary practice wishing to report a potential case of prolific vomiting in a dog (2)
- I am a dog owner / main keeper wishing to report a potential prolific vomiting case in my own dog (3)
- Other (4)*

5a. If you selected Other, please specify:

- Free text response box

* Only participants selecting 'Other' in Question 5 were able to answer Question 5a.

Participants selecting options (1) and (2) on question 5 were routed towards the ‘Veterinary Professional Questionnaire’, whereas those selecting (3) and (4) were routed towards the ‘Owner Questionnaire’. These two sub-questionnaires are outlined on the following pages.

Veterinary Professional Questionnaire

Practice: Case Details

This section will ask more details about the dog and veterinary practice under which (s)he is registered.

1. Please provide the name of the veterinary practice under which the dog is registered:

- Free text response box

2. Please provide the postcode of the veterinary practice under which the dog is registered:

- Free text response box

3. Please provide the phone number of the veterinary practice under which the dog is registered:

- Free text response box

4. Please provide the email address of the veterinary practice under which the dog is registered:

- Free text response box

5. Does the veterinary practice in which the dog is registered currently participate in the Small Animal Veterinary Surveillance Network (SAVSNET)?

- Yes
- No
- Don’t know

Dog

6. Please provide the name of the dog:

- Free text response box

7. Please provide the postcode of the dog's owner / main keeper:

- Free text response box

8. Please provide the dog's sex:

- Male
- Female
- Don’t know

9. Is the dog neutered?

- Yes
- No
- Don’t know

10. Please state the dog's age. If unknown, please state 'unknown':

- Free text response box

11. Please state the dog's breed. If unknown, state 'unknown'; if crossbreed, state 'crossbreed'.

- Free text response box

12. Are there any other dogs in the case's household?

- Yes*
- No
- Don’t know

*Only participants selecting ‘Yes’ on Question 12 were able to answer questions 12a and 12b.

12a. INCLUDING this dog, how many dogs are there in the household?

- Free text response box

12b. Since onset of vomiting, have any other dogs exhibited signs of vomiting?

- Yes
- No
- Don’t know

13. Has the dog been vaccinated within the last three years?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 13 were able to answer questions 13a, 13b (if relevant) and 13c.

13a. Please tick which of the following infectious diseases the dog has been inoculated against (please tick all that apply):

- Distemper
- Infectious hepatitis
- Parvo
- Parainfluenza
- Leptospirosis
- Kennel cough
- Don't know
- Other*

* Only participants selecting ‘Other’ in Question 13a were able to answer Question 13b.

13b. If you selected Other, please specify:

- Free text response box

13c. If known, please state which brand(s) of vaccine have been used at the LAST vaccination/booster of this dog:

- Free text response box

14. Has the dog been de-wormed within the last three months?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 14 were able to answer questions 14a.

14a. Which de-worming product was used?

- Free text response box

15. Are there any other animal species which the dog has regular contact (either directly, or with their faeces)? Please tick all that apply.

- None
- Cats
- Pigs
- Cattle / sheep
- Horses
- Poultry
- Don't know

- Other*

* Only participants selecting ‘Other’ on Question 15 were able to answer questions 15a.

15a. If you selected Other, please specify:

- Free text response box

16. In the last month, has the dog been to any of the following (please tick all that apply):

- None
- Boarding kennel
- Rescue kennel
- Overseas
- Dog day care facility
- Group training / behaviour classes
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 16 were able to answer questions 16a.

16a. If you selected Other, please specify:

- Free text response box

17. Which of the following food types does the dog regularly eat?

- Proprietary dog food
- Home-cooked diet
- Raw meat
- Table scraps
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 17 were able to answer questions 17a.

17a. If you selected Other, please specify:

- Free text response box

18. Does the dog scavenge food (e.g. from bins when out walking)?

- Yes
- No
- Don’t know

19. In the seven days prior to onset of vomiting, did the dog have any contact with other animals or humans that had been vomiting?

- Yes
- No
- Don’t know

20. Which clinical signs has this dog exhibited (please tick all that apply)?

- Vomiting without blood
- Vomiting with blood
- Diarrhoea without blood
- Diarrhoea with blood
- Melaena
- Weight loss
- Inappetence
- Pyrexia
- Other*

* Only participants selecting ‘Other’ on Question 20 were able to answer questions 20a.

20a. If you selected Other, please specify:

- Free text response box

21. At time of latest examination, if recorded please state the body temperature of the dog (in Celsius):

- Free text response box

22. Was any treatment prescribed for this dog?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 22 were able to answer questions 22a.

22a. If known, please state which treatments were provided:

- Free text response box

23. Were any samples taken, or diagnostic tests performed?

- Yes*
- No
- Don’t know

*** Only participants selecting ‘Yes’ on Question 23 were able to answer questions 23a.**

23a. Please state which samples were taken and which diagnostic tests were performed. If you know the result(s) of such diagnostic tests, please also state this here:

- Free text response box

24. How long did the dog take to recover?

- Less than 24 hours
- 24 - 48 hours
- 3 - 7 days
- 8 - 14 days
- More than 14 days
- Dog is still vomiting
- Dog has stopped vomiting, but is still unwell
- Dog died
- Don't know

25. Please provide ANY OTHER relevant information about this dog.

- Free text response box

Practice: Control Cases

When investigating a potential disease outbreak, it is important to collect information relating to a population of animals NOT exhibiting clinical signs associated with the outbreak under investigation (the 'control population'). If possible, please complete some further questions relating to **a randomly selected dog NOT exhibiting vomiting clinical signs** that presented at your veterinary practice **on the same day** the affected animal presented e.g. the next non-vomiting dog you see where the owner is happy to participate.

1. Please confirm that you are able, and willing, to provide information regarding a control dog that has not reported to the veterinary practice with vomiting clinical signs within the last month.

- I am willing and able to provide information on a non-vomiting control dog*
- I am NOT willing or able to provide information on a non-vomiting control dog

* Only participants who selected ‘I am willing and able to provide information on a non-vomiting control dog’ in Question 1 were able to proceed with answering the questions

pertaining to a control animal in this survey. Those who were not willing were directed to submit the case questionnaire details they had provided alone.

Practice: Control Details

1. Has the chosen control dog presented to the veterinary practice with vomiting clinical signs within the last month?

- Yes - please select another dog
- No*
- Don't know - please select another dog

* Only participants who selected ‘Yes’ in Question 1 were able to proceed with answering the questions pertaining to a control animal in this survey. Those who were not willing were directed to submit the case questionnaire details they had provided alone.

Veterinary Practice

1. Please provide the name of the veterinary practice under which the dog is registered:

- Free text response box

2. Please provide the postcode of the veterinary practice under which the dog is registered:

- Free text response box

3. Does the veterinary practice in which the dog is registered currently participate in the Small Animal Veterinary Surveillance Network (SAVSNET)?

- Yes
- No
- Don’t know

Dog

4. Please provide the name of the dog:

- Free text response box

5. Please provide the postcode of the dog's owner / main keeper:

- Free text response box

6. Please provide the dog's sex:

- Male
- Female
- Don’t know

7. Is the dog neutered?

- Yes
- No
- Don’t know

8. Please state the dog's age. If unknown, please state 'unknown':

- Free text response box

9. Please state the dog's breed. If unknown, state 'unknown'; if crossbreed, state 'crossbreed'.

- Free text response box

10. Are there any other dogs in the case's household?

- Yes*
- No
- Don’t know

*Only participants selecting ‘Yes’ on Question 10 were able to answer questions 10a and 10b.

10a. INCLUDING this dog, how many dogs are there in the household?

- Free text response box

10b. Have any other dogs exhibited signs of vomiting?

- Yes
- No
- Don’t know

11. Has the dog been vaccinated within the last three years?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 11 were able to answer questions 11a, 11b (if relevant) and 11c.

11a. Please tick which of the following infectious diseases the dog has been inoculated against (please tick all that apply):

- Distemper
- Infectious hepatitis
- Parvo
- Parainfluenza
- Leptospirosis
- Kennel cough
- Don't know
- Other*

* Only participants selecting ‘Other’ in Question 11a were able to answer Question 11b.

11b. If you selected Other, please specify:

- Free text response box

11c. If known, please state which brand(s) of vaccine have been used at the LAST vaccination/booster of this dog:

- Free text response box

12. Has the dog been de-wormed within the last three months?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 12 were able to answer questions 12a.

12a. Which de-worming product was used?

- Free text response box

13. Are there any other animal species which the dog has regular contact (either directly, or with their faeces)? Please tick all that apply.

- None
- Cats
- Pigs
- Cattle / sheep
- Horses
- Poultry
- Don't know

- Other*

* Only participants selecting ‘Other’ on Question 13 were able to answer questions 13a.

13a. If you selected Other, please specify:

- Free text response box

14. In the last month, has the dog been to any of the following (please tick all that apply):

- None
- Boarding kennel
- Rescue kennel
- Overseas
- Dog day care facility
- Group training / behaviour classes
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 14 were able to answer questions 14a.

14a. If you selected Other, please specify:

- Free text response box

15. Which of the following food types does the dog regularly eat?

- Proprietary dog food
- Home-cooked diet
- Raw meat
- Table scraps
- Don't know
- Other* * Only participants selecting ‘Other’ on Question 15 were able to answer questions 15a.

15a. If you selected Other, please specify:

- Free text response box

16. Does the dog scavenge food (e.g. from bins when out walking)?

- Yes
- No
- Don’t know

17. Has the dog had any contact with other animals or humans that had been vomiting?

- Yes
- No
- Don’t know

OWNER QUESTIONNAIRE

Owner: Case Details

This section will ask more details about the dog and veterinary practice under which (s)he is registered.

1. Please provide the name of the veterinary practice under which the dog is registered:

- Free text response box

2. Please provide the postcode of the veterinary practice under which the dog is registered:

- Free text response box

3. Does the veterinary practice in which the dog is registered currently participate in the Small Animal Veterinary Surveillance Network (SAVSNET)?

- Yes
- No
- Don’t know

Dog

4. Please provide the name of the dog:

- Free text response box

5. Please provide the postcode of the dog's owner / main keeper:

- Free text response box

6. Please provide the dog's sex:

- Male
- Female
- Don’t know

7. Is the dog neutered?

- Yes
- No
- Don’t know

8. Please state the dog's age. If unknown, please state 'unknown':

- Free text response box

9. Please state the dog's breed. If unknown, state 'unknown'; if crossbreed, state 'crossbreed'.

- Free text response box

10. Are there any other dogs in the case's household?

- Yes*
- No
- Don’t know

*Only participants selecting ‘Yes’ on Question 12 were able to answer questions 12a and 12b.

10a. INCLUDING this dog, how many dogs are there in the household?

- Free text response box

10b. Since onset of vomiting, have any other dogs exhibited signs of vomiting?

- Yes
- No
- Don’t know

11. Has the dog been vaccinated within the last three years?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 11 were able to answer questions 11a, 11b (if relevant) and 13c.

11a. Please tick which of the following infectious diseases the dog has been inoculated against (please tick all that apply):

- Distemper
- Infectious hepatitis
- Parvo

- Parainfluenza
- Leptospirosis
- Kennel cough
- Don't know
- Other*

* Only participants selecting ‘Other’ in Question 11a were able to answer Question 11b.

11b. If you selected Other, please specify:

- Free text response box

11c. If known, please state which brand(s) of vaccine have been used at the LAST vaccination/booster of this dog:

- Free text response box

12. Has the dog been de-wormed within the last three months?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 12 were able to answer questions 12a.

12a. Which de-worming product was used?

- Free text response box

13. Are there any other animal species which the dog has regular contact (either directly, or with their faeces)? Please tick all that apply.

- None
- Cats
- Pigs
- Cattle / sheep
- Horses
- Poultry
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 13 were able to answer questions 13a.

13a. If you selected Other, please specify:

- Free text response box

14. In the last month, has the dog been to any of the following (please tick all that apply):

- None
- Boarding kennel
- Rescue kennel
- Overseas
- Dog day care facility
- Group training / behaviour classes
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 14 were able to answer questions 14a.

14a. If you selected Other, please specify:

- Free text response box

15. Which of the following food types does the dog regularly eat?

- Proprietary dog food
- Home-cooked diet
- Raw meat
- Table scraps
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 15 were able to answer questions 15a.

15a. If you selected Other, please specify:

- Free text response box

16. Does the dog scavenge food (e.g. from bins when out walking)?

- Yes
- No
- Don’t know

17. In the seven days prior to onset of vomiting, did the dog have any contact with other animals or humans that had been vomiting?

- Yes
- No
- Don’t know

18. Which clinical signs has this dog exhibited (please tick all that apply)?

- Vomiting without blood
- Vomiting with blood
- Diarrhoea without blood
- Diarrhoea with blood
- Weight loss
- Inappetence
- Fever
- Other*

* Only participants selecting ‘Other’ on Question 18 were able to answer questions 18a.

18a. If you selected Other, please specify:

- Free text response box

19. Was any treatment prescribed for this dog?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 19 were able to answer questions 19a.

19a. If known, please state which treatments were provided:

- Free text response box

20. Were any samples taken, or diagnostic tests performed?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 20 were able to answer questions 20a.

20a. Please state which samples were taken and which diagnostic tests were performed. If you know the result(s) of such diagnostic tests, please also state this here:

- Free text response box

21. How long did the dog take to recover?

- Less than 24 hours
- 24 - 48 hours
- 3 - 7 days

- 8 - 14 days
- More than 14 days
- Dog is still vomiting
- Dog has stopped vomiting, but is still unwell
- Dog died
- Don't know

22. Please provide ANY OTHER relevant information about this dog.

- Free text response box

CONTROL QUESTIONNAIRE INFORMATION SHEET AND CONSENT FORM

Potential outbreak investigation: Prolific vomiting in dogs

CONTROL QUESTIONNAIRE

You are being invited to participate in an outbreak investigation study, following reports of an outbreak of prolific vomiting in dogs. Before you decide whether to participate, it is important for you to understand why the survey is being conducted and what it will involve if you do choose to take part. Please consider the following information. Epidemiologist contact details are listed below should you have any further questions.

Reading this information sheet and completing the survey will be considered as consent to participate in this survey.

What is the purpose of the survey?

This survey has been created in order to collect more detailed CONTROL information, following veterinary surgeon and social media reports of a potential outbreak of prolific, acute vomiting in dogs during December 2019 and January 2020.

Why am I being invited to take part and what will happen if I take part?

You are being invited to take part because you are a veterinary surgeon or owner currently working in a companion animal-treating veterinary practice or an owner, in the United Kingdom, who is willing to provide information on CONTROL dogs, as part of an ongoing investigation concerning dogs with acute onset of prolific vomiting, with 5 or more episodes of vomiting within a 12 hour period". If you would like to submit information about a CASE, please click here.

If you decide to take part you will need to complete the online survey, which will take around 10 minutes.

Participation is voluntary and you do not have to take part in this study. You are free to withdraw at any time until you have selected the 'finish' button on the final page of the questionnaire. You do not have to give a reason if you do not wish to take part.

If you are willing, we will also request your postcode, name and email address so that we can ask for further CONTROL details if this becomes necessary during the potential outbreak investigation. We will only use your name and email for the purpose of seeking further information, and will destroy data containing these personal identifiers on conclusion of the survey.

Are there any benefits or risks in taking part?

There are no direct benefits or risks to you or your practice associated with taking part in this survey, but we will use the data to further characterise this potential outbreak, and if necessary assist in controlling the potential outbreak.

What will happen if I want to stop taking part?

If you want to stop taking part in this survey you can withdraw at any time until completion and submission of the online survey.

How will my data be used?

The data you provide will be stored securely for up to 7 years in line with data protection requirements at the University of Liverpool and GDPR. All data is strictly confidential and only researchers involved in the study will have access to it. Fully anonymised data may be archived for use in other research projects in the future. Under UK data protection legislation, the University acts as the Data Controller for personal data collected as part of the University's research. The Principal Investigator acts as the Data Processor for this study.

What will happen to the results of the survey?

The data will be used to further characterise the potential outbreak of prolific vomiting in dogs, potentially assisting in identifying causative factors and informing attempts (if necessary) to control this potential outbreak. Anonymised results may also be published - you and your clients (if relevant) will never be identifiable.

What if I am unhappy or if there is a problem?

If you are unhappy, or if there is a problem, please feel free to contact the epidemiologists listed below and we will try to help. If you remain unhappy or have a complaint which you feel you cannot communicate directly to the researcher then you should contact the Research Ethics and Integrity Office on 0151 794 8290 (ethics@liv.ac.uk). When contacting the Research Governance Officer, please provide details of the name or description of the study (so that it can be identified), the researcher involved, and the details of the complaint you wish to make.

Dr David Singleton

Dr Gina Pinchbeck
University of Liverpool
Leahurst Campus
Chester High Road
CH64 7TE
Email: savsnet@liverpool.ac.uk

Please confirm that you have read and understood the above information and confirm your consent for data to be used for these purposes, as the owner or on behalf of the owner.

- I confirm that I have consent from the owner to collect and submit these data, and I understand that anonymised data may be used in publications

- I confirm that I am the dog's owner, give consent for collection and submission of these data, and I understand that anonymised data may be used in publications

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Basic CONTROL information

1. Which of the following statements best describes yourself:

- I am a veterinary surgeon wishing to provide information about a control dog
- I am an employee of a veterinary practice wishing to provide information about a control dog
- I am a dog owner / main keeper wishing to provide information about a control dog
- Other

* Only participants selecting ‘Other’ on Question 1 were able to answer questions 1a.

1a. If you selected Other, please specify:

- Free text response box

Control Cases

When investigating a potential disease outbreak, it is important to collect information relating to a population of animals **NOT** exhibiting clinical signs associated with the outbreak under investigation (the 'control population'). If possible, please complete some further questions relating to **a randomly selected dog NOT exhibiting vomiting clinical signs.**

2. Please confirm that you are able, and willing, to provide information regarding a CONTROL dog that has NOT exhibited vomiting clinical signs within the last month.

- I am willing and able to provide information on a non-vomiting control dog*

- I am NOT willing or able to provide information on a non-vomiting control dog

* Only participants who selected ‘I am willing and able to provide information on a non-vomiting control dog’ in Question 2 were able to proceed with answering the questions pertaining to a control animal in this survey.

Control details

Veterinary Practice

3. Please provide the name of the veterinary practice under which the dog is registered:

- Free text response box

4. Please provide the postcode of the veterinary practice under which the dog is registered:

- Free text response box

5. Does the veterinary practice in which the dog is registered currently participate in the Small Animal Veterinary Surveillance Network (SAVSNET)?

- Yes
- No
- Don’t know

Dog

6. Please provide the name of the dog:

- Free text response box

7. Please provide the postcode of the dog's owner / main keeper:

- Free text response box

8. Please provide the dog's sex:

- Male
- Female
- Don’t know

9. Is the dog neutered?

- Yes
- No
- Don’t know

10. Please state the dog's age. If unknown, please state 'unknown':

- Free text response box

11. Please state the dog's breed. If unknown, state 'unknown'; if crossbreed, state 'crossbreed'.

- Free text response box

12. Are there any other dogs in the case's household?

- Yes*
- No
- Don’t know

*Only participants selecting ‘Yes’ on Question 12 were able to answer questions 12a and 12b.

12a. INCLUDING this dog, how many dogs are there in the household?

- Free text response box

12b. Have any other dogs exhibited signs of vomiting?

- Yes
- No
- Don’t know

13. Has the dog been vaccinated within the last three years?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 13 were able to answer questions 13a, 13b (if relevant) and 13c.

13a. Please tick which of the following infectious diseases the dog has been inoculated against (please tick all that apply):

- Distemper
- Infectious hepatitis
- Parvo
- Parainfluenza
- Leptospirosis
- Kennel cough
- Don't know
- Other*

* Only participants selecting ‘Other’ in Question 13a were able to answer Question 13b.

13b. If you selected Other, please specify:

- Free text response box

13c. If known, please state which brand(s) of vaccine have been used at the LAST vaccination/booster of this dog:

- Free text response box

14. Has the dog been de-wormed within the last three months?

- Yes*
- No
- Don’t know

* Only participants selecting ‘Yes’ on Question 14 were able to answer questions 14a.

14a. Which de-worming product was used?

- Free text response box

15. Are there any other animal species which the dog has regular contact (either directly, or with their faeces)? Please tick all that apply.

- None
- Cats
- Pigs
- Cattle / sheep
- Horses
- Poultry
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 15 were able to answer questions 15a.

15a. If you selected Other, please specify:

- Free text response box

16. In the last month, has the dog been to any of the following (please tick all that apply):

- None
- Boarding kennel
- Rescue kennel

- Overseas
- Dog day care facility
- Group training / behaviour classes
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 16 were able to answer questions 16a.

16a. If you selected Other, please specify:

- Free text response box

17. Which of the following food types does the dog regularly eat?

- Proprietary dog food
- Home-cooked diet
- Raw meat
- Table scraps
- Don't know
- Other*

* Only participants selecting ‘Other’ on Question 17 were able to answer questions 17a.

17a. If you selected Other, please specify:

- Free text response box

18. Does the dog scavenge food (e.g. from bins when out walking)?

- Yes
- No
- Don’t know

19. Has the dog had any contact with other animals or humans that had been vomiting?

- Yes
- No
- Don’t know