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A national outbreak of severe vomiting in dogs associated with a canine enteric coronavirus.

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Complete List of Authors:	Radford, Alan; University of Liverpool Faculty of Health and Life Sciences, Singleton, David; University of Liverpool Faculty of Health and Life Sciences Noble, PJ; University of Liverpool, Veterinary Clinical Sciences Jewell, Chris; Lancaster University Appleton, Charlotte; Lancaster University Rowlingson, Barry; Lancaster University, Lancaster, UK, Department of Mathematics and Statistics Hale, Alison; Lancaster University Tamayo, Carmen; University of Bristol Newton, Richard; Animal Health Trust Sánchez-Vizcaíno, Fernando; University of Bristol, Bristol Veterinary School Greenberg, Danielle; Liverpool Vets Brant, Beth; University of Liverpool Bentley, Eleanor; University of Liverpool Stewart, James; University of Liverpool Smith, Shirley; University of Liverpool Haldenby, Sam; University of Liverpool Pinchbeck, Gina; University of Liverpool, Epidemiology and Population Health
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University of Liverpool
Institute of Infection and Global Health
Leahurst Campus
Chester High Road
Neston
Wirral, CH64 7TE, UK

Regarding manuscript submission titled "A national outbreak of severe vomiting in dogs associated with a canine enteric coronavirus".

Dear Sir / madam.

Please find attached our research paper for consideration for publication in EID. We have chosen your journal specifically as this is extremely timely both in relation to the outbreak itself, but also because it involves another coronavirus, this time in dogs… we are all acutely aware of the potential of coronaviruses to cause new disease.

The paper describes a rapid multidisciplinary response to an extremely unusual national-scale outbreak of severe vomiting in dogs. We argue the outbreak response we describe has implications not just for animal health, but also for human health, most notably because of zoonotic infections.

I can confirm all the authors have seen and approved the manuscript.

Many thanks for considering this paper for your journal.

Best regards

Alan Radford BSc, BVSc, PhD, MRCVS

Professor of Health Informatics

A national outbreak of severe vomiting in dogs associated with a canine enteric coronavirus.

Alan D. Radford [1*], David A. Singleton [1], Chris Jewell [2], Charlotte Appleton [2], Barry Rowlingson [2], Alison C. Hale [2], Carmen Tamayo Cuartero [3], Richard Newton [4], Fernando Sánchez-Vizcaíno [3], Danielle Greenberg [5], Beth Brant [1], Eleanor G. Bentley [1], James P. Stewart [1], Shirley Smith [1], Sam Haldenby [6], P-J M. Noble [1], and Gina L. Pinchbeck [1]

[1] University of Liverpool, Leahurst Campus, Chester High Road, Neston, Wirral, CH64 7TE, UK.

[2] Centre for Health Informatics, Computing, and Statistics (CHICAS), Lancaster Medical School, Lancaster University, Lancaster, LA1 4YW, UK

[3] University of Bristol, Churchill Building, Langford Campus, Bristol, BS40 5DU, UK.

[4] Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk, CB8 7UU, UK.

[5] The Liverpool Vets, 11 Cleveland Square, Liverpool, L1 5BE, UK.

[6] Centre for Genomic Research, Institute of Integrative Biology, University of Liverpool, Crown Street, Liverpool, L69 7ZB, UK.

* Corresponding author; Alan Radford, University of Liverpool, Leahurst Campus, Chester High Road, Neston, S. Wirral, CH64 7TE, UK. Phone; 00 44 151 7946121; Email; alanrad@liverpool.ac.uk

Article summary: This study describes an integrated surveillance system for companion animals and its efficient response to a national outbreak of gastrointestinal disease in UK dogs.

Running title: vomiting outbreak in dogs

Keywords: canine enteric coronavirus, outbreak, gastrointestinal disease, vomiting, dogs, surveillance, syndromic surveillance

Abstract

Companion animal populations are largely devoid of population surveillance, leaving them vulnerable to novel disease incursions. We have developed an efficient system that fills this gap, and here demonstrate its ability to rapidly respond to an outbreak of canine gastroenteritis. In January 2020, sporadic reports of prolific vomiting were being reported in UK dogs. Electronic health records from a sentinel network of 301 veterinary practices confirmed a significant increase in dogs presenting with gastroenteric disease across the UK. Male dogs and those living with other vomiting dogs were more likely to be affected. Diet and vaccination status were not associated with disease. A canine enteric coronavirus identified by PCR and whole genome sequencing was significantly associated with being a case. The surveillance system described efficiently and flexibly fills a gap in population surveillance in hitherto neglected populations and can act as a blueprint for such surveillance in other countries.

INTRODUCTION

Companion animals largely lack population health data. This leaves a surveillance gap for endemic disease and exposes them to disease incursions such as equine influenza virus H3N8 (1), avian H3N2 (2,3), parvoviruses (3) and cat and dog susceptibility to SARS-CoV-2 (4). In the absence of legislated programmes of population surveillance, there have been several attempts to fill this gap using secondary data particularly from pet insurance schemes (5). More recently, researchers have exploited the rapid digitisation of health records (electronic health records; EHRs) for passive surveillance. These can be collected at great scale and analysed in near-real time, (6), and are now being routinely used in human heath (7-10), where their timeliness, simplicity and coverage complements other forms of surveillance based on actual diagnoses (11-12). Such approaches are beginning to find value in veterinary species, especially companion animals (6,13-14), where a high proportion of owned animals attend a veterinary surgeon (15).

In January 2020, we were notified of localised reports of severe vomiting in dogs in England. Vomiting is a common presenting complaint in dogs (16); outbreaks are rare, being largely controlled by vaccination (17). In the absence of robust population data, such sporadic reports frequently remain unsubstantiated.

Here we link syndromic surveillance and text mining of EHRs collected from sentinel veterinary practices and diagnostic laboratories, with field epidemiology and enhanced genomic testing. In eight weeks, this approach described the temporal and spatial epidemiology of the outbreak, identified a likely causative agent and provided targeted advice on control.

73 METHODS

74 **Ethics.**

75 Ethical approval was given by Liverpool University Research Ethics Committees (VREC922
76 and RETH000964).

77 **Practice data.**

78 EHRs were collected between 17th March 2014 and 29th February 2020 from SAVSNET, a
79 network of 301 volunteer UK veterinary practices (663 sites) recruited based on convenience
80 (6) and included 7,094,397 consultation records (including 4,685,732 from dogs and
81 1,846,493 from cats). Briefly, EHRs are collected for individual consultations including data
82 on species, breed, sex, neuter status, age, owner's postcode and vaccination. Each EHR is
83 also compulsorily annotated by the veterinary clinician with a main presenting complaint
84 (MPC; gastroenteric, respiratory, pruritus, tumour, kidney disease, other unwell, post-op
85 check, vaccination, or other healthy) using a unique questionnaire window embedded in the
86 practice management system.

87 Given severe vomiting was a key outbreak feature, we undertook two further complementary
88 analyses. Firstly, we used regular expressions to identify clinical narratives describing
89 frequent vomiting, whilst excluding common negations (Supplementary table1). Secondly,
90 data on product sales were used to describe the prescription frequency of a common anti-
91 emetic (maropitant) (18). Trend lines were calculated using a Bayesian binomial generalised
92 linear model trained on weekly prevalence between 2014 and 2019 (19), allowing us to
93 identify observations that were extreme (>99% credible intervals) or moderate (>95%
94 credible intervals).

95

Laboratory data.

SAVSNET also collects in near real-time EHRs from participating diagnostic laboratories on samples submitted from over half of UK veterinary practices. Available canine diagnostic test results reported January 2017 - February 2020 inclusively, were queried from six laboratories for six gastroenteric pathogens (table 1 and figure 3). Total numbers of tests, proportions testing positive and associated 95% confidence intervals (CIs) were summarised. Number of sites were surmised from the submitting practice's postcode.

Questionnaire.

Online questionnaires for veterinary professionals and owners were made available on 29th January, enabling both case reporting and case control statistical analysis, and covering a range of features including owner postcode, animal signalment, vaccination status, clinical signs, treatment and diagnostic testing, contacts, diet and recovery status (full questionnaire: Supplementary material).

The required case definition of "five or more vomiting episodes in a 12-hour period", was based on clinical observations of early cases (DG). Initially, controls were only requested from veterinary professionals matched by veterinary practice. However, to increase recruitment a non-matched second control questionnaire open to both veterinary professionals and owners was deployed on 5th February.

All statistical analyses were undertaken using R language (version 3.6.1). Case details were described for both veterinary professional and owner reported data. Proportions and associated 95% CIs were calculated for categorical variables, and median and range for continuous variables. Univariable and multivariable mixed effects logistic regression models

were constructed using data submitted by veterinary professionals using R package 'lme4'. Explanatory variables from univariable logistic regression were considered in multivariable models for likelihood ratios of $P \leq 0.20$. Multivariable models underwent manual step-wise backward elimination to reduce Akaike's and Bayesian information criteria. Practice was included as a random effect. Confounding was assessed by the effect upon model fit with sequential removal of variables and two-way interaction terms were assessed for improved model fit. Final statistical significance was defined as $P<0.05$.

Spatio-temporal analysis of case data

Weekly consults between 4th November 2019 and 21st March 2020 were geolocated to owners' postcodes, with gastroenteric MPC as a binary outcome (i.e. 1 for gastroenteric consult, 0 for non-gastroenteric consult). For each week, a logistic geostatistical model was used to investigate special clustering of cases. We defined a spatial "hotspot" as a location having 95% posterior probability of a prevalence exceeding the national mean prevalence in any one week. With no discernible epidemic "wave" apparent over successive weeks, weekly measures were aggregated across the study period to show the number of weeks each location was a hotspot. Further details on the modelling approach are in Supplementary Information.

Sample collection, PCR and phylogenetic analysis.

Those submitting questionnaires were also asked to submit samples for microbiological testing including mouth swabs, faecal samples, and for cases, vomit. Briefly, nucleic acids were extracted (QIAamp viral RNA; Qiagen), reverse transcribed (Superscript III) and tested for canine enteric coronavirus (CeCoV) by M gene PCR (20); in order to expedite results and

reduce contamination risks, this was run as a single-stage PCR rather than the published nested reaction. Positive samples were purified (QIAquick; Qiagen) and sequenced bi-directionally (Source Biosciences) to produce consensus sequences (ChromasPro; Technelysium).

To rapidly explore the potential involvement of other viruses, nucleic acid was extracted from 19 random cases and five controls for deep sequencing (Oxford Nanopore). Briefly, RNA was amplified by SISPA (21), multiplexed libraries prepared using 30ng of cDNA (SQK-LSK109 kit) and sequenced (MinION Mk1B) for 48hours. Real-time 'fast' base calling was performed using Guppy (MinKNOW) and Fastq files uploaded to EPI2ME (METRICHOR) for species identification.

For deeper sequencing coverage, 10 samples (five CeCoV positive cases, four negative cases and one control) were also processed for Illumina sequencing (CGR, University of Liverpool). Nucleic acids were treated with RNase and fragment libraries prepared (NEBNext UltraII Kit; ~350bp inserts) prior to sequencing on a HiSeq4000 (paired-end, 2x150bp sequencing). Adapter sequences were trimmed (Cutadapt) and Sickle, with a minimum window quality score of 20. Reads >19bp were aligned against the dog genome (CanFam3.1) (Bowtie2) and matching reads removed. Remaining reads were assembled (Spades) and contigs greater than 700nt blasted against the NCBInr database. Sequences matching CeCoV were aligned (ClustalW) and phylogenies reconstructed using bootstrap analyses and Neighbour-Joining (MEGA6).

RESULTS

Syndromic surveillance.

Based on MPC, a specific and significant increase in the number of dogs recorded as presenting with gastroenteric signs was identified, with the last 10 weeks outside the 99% credible interval (extreme outliers; figure 1a); a similar trend was observed in antiemetic therapy (maropitant) in dogs (figure 1b). Both measures first became significant in week ending 29th December 2019, peaking in week ending 2nd February 2020, approximately double the preceding baseline. No similar trends were observed for respiratory disease in dogs or for the gastroenteric MPC or maropitant in cats (figure 1c-e), suggesting the signal was specific to canine gastroenteric disease, and fact that was supported by similar increases in the regular expression identifying vomiting dogs (figure 1f).

Spatiotemporal mapping of weekly cases of gastroenteric MPC showed no evidence for a discernable epidemic "wave" spreading across the country through time. However, prevalence was spatially clustered (figure 2), with locations particularly North West, and South West England, and Edinburgh having strong evidence of a high number of weeks where prevalence of gastroenteric MPC was higher than the national mean.

Diagnostic test results.

The patterns of testing for different PCR tests were broadly similar as these are generally carried out concurrently (figure 3a-c). The same was true for those based on culture (figure 3d-e). Of particular interest, CeCoV, showed a strong seasonality, positive tests peaking during the outbreak (figure 3a); however, similar peaks seen in previous years suggested the observed peak in February 2020 could not itself explain this outbreak.

Questionnaire analyses.

Between 29th January and 1st March 2020, a total of 1,258 case questionnaires were received. After excluding a small proportion with key missing data, a total of 165 veterinary-reported cases; 1,034 owner-reported cases, and 60 veterinary-reported controls were available for analyses.

Most cases originated from England (Table 2). From veterinary-reported cases, median case age at presentation was 4.0 years [range 0.3-15.0], and from owners, 4.8 years [0.2-15.5].

The majority of animals were vaccinated against 'core' pathogens and leptospirosis within the preceding three years, and de-wormed within the previous three months. A range of breeds (data not presented) were observed, broadly corresponding to previous studies (6). Most cases were fed proprietary dog food, with approximately 20-37% of dogs scavenging food when walked. Of those from multi-dog households, just over half reported presence of another dog recently vomiting within the same household. Around 30% of dogs had recently travelled, the majority visiting a day care facility.

Date of onset of clinical signs ranged between 16th November 2019 and 28th February 2020 for veterinary-reported cases, and 4th September 2019 and 1st March 2020 for owner-reported cases. Most cases presented with vomiting without blood and inappetence, with a small proportion of cases pyrexic (Table 3). Approximately half of cases reported diarrhoea, mostly without blood. Diagnostic testing was performed in approximately one third of veterinary-reported cases, the majority (78.9%) using haematology and/or biochemistry assays.

Over 90% of veterinary-reported cases were treated, compared to 60% of owner-reported cases. In both, anti-emetics were most commonly prescribed (89.1% of veterinary-reported cases, CI 84.3-93.9; 48.1% of owner-reported cases, CI 45.0-51.1). The most common recovery time was between three and seven days; 0.6% of veterinary-reported and 1.0% of owner-reported cases died.

Descriptive data of the control population submitted by veterinary professionals and univariable findings are presented in Supplementary material Tables 2-3, and multivariable findings in Table 4. Both entire and neutered male dogs were at significantly increased odds of being a case, compared to neutered females, as were dogs living in the same household as another dog that had also been vomiting. However, dogs living in a single dog household were also at increased odds of being a case, compared to 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 that had recently vomited (including humans) were at reduced odds of being a case, compared to those who had not.

Samples, molecular testing and sequence analyses.

A total of 95 samples were collected between 30th January and 12th March 2020 from 71 animals (50 cases and 21 controls) including 22 faeces, 60 oral swabs and 13 samples of vomitus. Cases of prolific vomiting were significantly more likely to test positive for CeCoV in at least one submitted sample (17/50; 34%) compared with controls (0/21) (p=0.002; Fishers Exact Test). Samples most likely to test positive were faeces (10/16 samples from cases; 62.5%, 0 of 6 samples from controls; p=0.01) and vomit (6/13 samples from cases; 46%, 0 samples from controls). Oral swabs were least likely to test positive (7/43 positive from cases and 0/17 controls, p=0.17). Of 17 CeCoV-positive cases, 12 met the case definition, two did not (less than five episodes of vomiting in 12 hours) and three were missing questionnaire data.

Twenty-one samples from 16 animals gave useable M-gene sequence. Where two samples from the same animal were sequenced, these always gave identical sequence and were subsequently only represented by single sequences (figure 4). All sequences clustered with

previously reported type II CeCoVs (22) in one of three lineages. Sequences from 14 animals were identical suggestive of a single "outbreak" strain geographically distributed across England. Sequences from dogs15 and 16 were phylogenetically distinct.

Results of MinION sequencing rapidly confirmed an alphacoronavirus to be the predominant virus in cases (24,190 out of 33,826,933 classified reads), failing to identify other prevalent candidates (next highest mapped to betabaculovirus; 4,541 reads). Although bacterial reads were present in high numbers, none showed consistently high results across a majority of samples.

Complete CeCoV genomes were assembled from six PCR positive cases by Illumina sequencing. No coronavirus sequences were identified in three CeCoV cases and one control that were CeCoV PCR negative. The only other mammalian virus detected matched a canine rotavirus in one case and one control (data not presented). Consistent with the M-gene sequencing, five of the CeCoV genomes clustered together (>99% similarity), distinct from dog15 (Figure 4). The outbreak strain was most similar to a Taiwanese virus isolated in 2008 from a young dog with diarrhoea (94.5% similarity; personal communication L. Chueh) and did not show any obvious sequence differences to published strains that might explain the unusual clinical signs observed in the outbreak. Based on spike gene analyses, the outbreak strain clustered with IIb, having a TGEV-like N-terminal spike domain (23) (data not shown).

DISCUSSION

Using EHRs that were syndromically annotated by veterinary surgeons, we were able to rapidly identify an outbreak of canine gastroenteric disease starting in November 2019. This was corroborated by parallel rises in both relevant prescriptions and mentions of frequent

vomiting in clinical narratives. These data were augmented by case and control questionnaire data, data from diagnostic laboratories and samples for microbiological analyses including whole genome sequencing. Together this system allowed for case definitions and outcomes, identification of both risk factors as well as a potential viral cause, all within a three-month period; findings were rapidly disseminated to veterinary practitioners (24-25) and owners. This combined approach represents an efficient system for national surveillance, one that can fill a population health need for previously neglected companion animal species.

The first confirmation 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 (7-10). To our knowledge, this is the first time they have been used in companion animals in this way. Such data can be simple to collect, providing real-time and wide geographic coverage, and be flexibly applied to different conditions (11-12). Although in some cases they 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 to background levels, associated with near doubling of the gastroenteric syndrome, and many weeks where the syndrome statistically exceeded the baseline.

The richness of data within EHRs allowed us to validate this outbreak using anti-emetic prescriptions and text mining. Prescription data have been used to understand, for example, human health inequalities (26) and the use of critical antibiotics in both humans (27) and animals (28-29). To our knowledge, this is the first example of using such data to identify and track an outbreak, benefitting from a clear link between the syndrome (vomiting) and its

therapy (anti-emetics). It will be useful to identify other therapies could also be used for such syndromic surveillance.

Text-mining was used to identify recorded 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 a case-definition is determined. Similar approaches have been described in human health for conditions like fever (30-32) but can suffer from low sensitivity (31). Indeed, the outbreak peak based on text mining was approximately 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 the regular expression developed here. Although text mining is unlikely to give an accurate estimate of the true prevalence of a given condition, it can still be used to track outbreaks.

To compliment syndromic surveillance, we implemented a rapid case control study, collecting over 1200 questionnaire responses from veterinary professionals and owners in 4.5 weeks. There was no evidence for similar disease in people or other species. The timing of the outbreak based on case data was in broad agreement with our syndromic surveillance. Questionnaires from owners and veterinary surgeons were in broad agreement on date of onset, geographical density, clinical signs and recovery. These data informed targeted health messages posted online and on social media on 28th February 2020, four weeks after we first became aware of the outbreak based on MPC.

Clearly, evidence of transmission driving the outbreak was vital to providing disease control advice. Dogs in multi-dog 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. Interestingly, dogs in single dog households were also at increased odds of being a case. Some authors have shown that such dogs are walked more, and therefore could be at greater risk of infection (33). Factors affecting dog walking are clearly likely to be important for control of infectious disease transmission and should be explored further.

As well as epidemiological data, we were also able to collect samples from cases and controls for microbiological testing. Based on its known (34) and observed seasonality (figure 3a), we tested all samples for CeCoV. Cases were significantly more likely to test positive both when all samples (oral swabs, faeces and vomit), as well as when just faecal samples, were considered, suggesting a possible role for CeCoV in the outbreak. However, many case samples tested negative, ranging from 33/50 overall, to 6 of 16 cases from which faeces were submitted and 7 of 13 cases for vomit. 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, 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, such that we might expect only one half of our cases to be truly associated with the outbreak.

Sequencing results identified a predominant strain of CeCoV in outbreak cases across the UK, in contrast to earlier studies showing strains clustering locally in households, veterinary practices or local areas (35). This lends further support to the role of this strain in the observed outbreak. In Sweden, a single strain was also implicated in several small canine winter vomiting outbreaks (36); genetically, however, the virus strain identified here was

distinct from the Swedish strains (data not presented). 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 was proven to be the cause, several features would mark out the pattern of disease as being unusual including the scale of the outbreak, its geographical distribution, the severity of the signs in some animals, a lack of other significant viral co-infections, as well as the effect on adult animals. CeCoV is generally associated with mild gastroenteritis (37). Although sporadic outbreaks of more severe haemorrhagic disease with high mortality (38-40) as well as systemic disease (41-42), have been reported, these typically affect individual households, and are often associated with mixed infections (43). These observations do suggest that genetic variability of CeCoV's may impact on 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).

Conclusions

In conclusion, this multidisciplinary approach allowed a rapid response to a newly described UK outbreak of canine gastroenteritis, identifying 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 targeted population health messaging. Several challenges remain for companion animals that lack national population health structures: i) to systematically capture discussions of disease in social- and main-stream media, ii) to sustainably fund these activities which to date have been largely

353 resourced by research grants and iii), to link surveillance to those empowered to act (12); this
354 is the subject of ongoing research by the authors.

355

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367

368 Biographical Sketch

369 Alan Radford is Professor of Veterinary Health Informatics at the University of Liverpool.
370 His primary research interests are in the molecular epidemiology of viral pathogens,
371 particularly those of veterinary importance, and combining this with electronic health data to
372 study at a population level, animal diseases and their impact on humans.

373

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504 Table legends.

505

506 Table 1. Results of laboratory diagnostic tests for pathogens associated with gastroenteric disease in
507 dogs collected between Jan 2017 and Feb 2020.

508

509 Table 2. Veterinary professional-reported (*n*=165) and owner-reported (*n*=1,034)
510 questionnaire responses pertaining to case signalment, health history, contacts and feeding
511 habits. 95% CI = 95% confidence interval.

512

513 Table 3. Veterinary professional reported (*n*=165) and owner-reported (*n*=1,034)
514 questionnaire responses pertaining to clinical signs, diagnostic and management strategies
515 and case recovery likelihood and time. 95% CI = 95% confidence interval.

516

517 Table 4. Mixed effects multivariable logistic regression model investigating odds of being a
518 veterinary professional-reported prolific modelling case (165 cases and 60 controls). SE =
519 standard error, OR = odds ratio, CI = 95% confidence interval.

520

521 Figure legends.

522

523 Figure 1. Observed prevalence per 1,000 consultations A). the canine records labelled as
524 gastroenteric MPC, B. canine records where maropitant was prescribed, C). canine records
525 labelled as records labelled as respiratory MPC, D). Feline records where maropitant was
526 prescribed, E) feline records labelled as gastroenteric MPC, and F) frequent vomiting in dogs
527 based on regular expression searches of the clinical narratives. Red points represent the
528 extreme outliers (outside the 99 per cent credible interval [CI]), orange points represent the
529 moderate outliers (outside the 95 per cent CI but within the 99 per cent CI), and green points
530 represent the average trend (within the 95 per cent CI).

531

532 Figure 2. Weekly consults between 4th November 2019 and 21st March 2020 were geolocated
533 to owners' postcodes, with gastroenteric MPC as a binary outcome (i.e. 1 for gastroenteric
534 consult, 0 for a non-gastroenteric consult). Coloured areas represent the number of weeks a
535 given location had a 95% posterior probability of a prevalence exceeding the national mean
536 prevalence in any one week. Further details on the modelling approach used are in
537 Supplementary Information.

538

539 Figure 3. Diagnostic test findings between Jan 2017 and Feb 2020 for a) Canine enteric
540 coronavirus PCR, b) canine parvovirus PCR, c) giardia PCR, d) Salmonella spp. selective
541 culture, e) Campylobacter spp. selective culture and f) Clostridium perfringens enterotoxin
542 PCR results. Number of tests performed (orange dotted line) and percentage testing positive
543 (blue line) by month. Blue shading represents 95% confidence intervals.

544

545 Figure 4. Phylogenetic analysis of canine enteric coronavirus strains based on nucleotide
546 sequences for A) M gene (final alignment 299 positions) and C) whole genome (final
547 alignment 26564 positions). Evolutionary analysis was performed using the Neighbour-
548 Joining method. A bootstrap test using 1000 replicates was applied; only values greater than
549 70 are indicated. Sequences identified in this study are indicated in blue (strain 1), red (strain
550 2) or green (strain 3). * indicates samples from animals meeting the case definition. Each
551 phylogeny included closest matches in GenBank, as well as representative published
552 CeCoVs, feline coronavirus (FeCoV) and transmissible gastroenteritis virus (TGEV) isolates.
553 B) Approximate geographic location of sequences obtained in this study.

554

555

Supplemental Materials:

Supplementary 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.

Supplementary 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). CI = 95% Confidence interval.

Supplementary 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. SE = standard error, OR = odds ratio, CI = 95% confidence interval.

571

572 Table 1.

573

574

Pathogen	Method	Number of tests	Number of labs *	Unique sites †	Positive % (95% CI)	Peak date % positive / 95% CI
CeCoV	PCR	5,167	4	839	20.69% (19.58-21.79)	Feb 2020 34.8% 27.81-41.85
Canine parvovirus	PCR	5,499	6	965	6.62% (5.96-7.28)	Nov 2017 13.28% 7.38-19.18
Giardia	PCR	5,636	6	894	23.78% (22.66-24.89)	Jan 2018 33.96% 26.58-41.35
Salmonella spp.	culture	114,722	6	2,951	0.87% (0.81-0.92)	Nov 2018 1.28% 0.87-1.70
Campylo-bacter spp.	selective culture	111,983	6	2,947	16.10% (15.88-16.31)	Dec 2017 23.02% 21.44-24.60
Clostridium perfringens	enterotoxin PCR	5,138	3	2,947	16.10% (15.88-16.31)	Dec 2017 23.02% 21.44-24.60

575

576 * Number of diagnostic laboratories contributing test results. † number of unique veterinary

577 practice sites submitting samples to the laboratories.

578 Table 2.
579

Question	Veterinary professional-reported cases (*n*=165) % of responses (95% CI)	*n* unknown	Owner-reported cases (*n*=1,034) % of responses (95% CI)	*n* unknown
Veterinary practice location:				
England	80.6 (74.6-86.7)	-	89.8 (87.9-91.6)	-
Wales	12.1 (7.1-17.1)	-	4.5 (3.2-5.7)	-
Scotland	4.9 (1.6-8.1)	-	4.5 (3.2-5.7)	-
North Ireland	1.2 (0.0-2.9)	-	1.1 (0.4-1.7)	-
Republic of Ireland	1.2 (0.0-2.9)	-	0.1 (0.0-0.3)	-
Isle of Man	0	-	0.2 (0.0-0.5)	-
Sex: Male	57.6 (50.0-65.1)	-	56.3 (53.3-59.3)	-
Neutered	69.1 (62.0-76.2)	-	70.1 (67.3-72.9)	-
Vaccinated within last three years: *	94.6 (91.1-98.0)	-	88.4 (86.5-90.4	13
Distemper	92.7 (88.8-96.7)	-	49.7 (46.7-52.8)	-
Infectious hepatitis	92.1 (88.0-96.2)	-	40.4 (37.4-43.4)	-
Parvo	92.1 (88.0-96.2)	-	55.4 (52.4-58.5)	-
Parainfluenza	53.9 (46.3-61.6)	-	37.4 (34.5-40.4)	-
Leptospirosis	92.7 (88.8-96.7)	-	49.2 (46.2-52.3)	-
Kennel cough	46.7 (39.0-54.3)	-	40.4 (37.4-43.4)	-
Rabies	2.4 (0.1-4.8)	-	1.3 (0.6-1.9)	-
Herpes	0.6 (0.0-1.8)	-	-	-
De-wormed within last 3 months	86.2 (80.5-92.0)	27	69.8 (67.0-72.7)	50
Lives in multi-dog household	34.6 (27.3-41.8)	-	47.4 (44.3-50.4)	-
1+ dog in household vomited	54.4 (41.3-67.4)	-	55.9 (51.5-60.3)	-
Other species regular contact: *	54.9 (46.1-63.8)	43	44.1 (41.1-47.1)	-
Cats	64.2 (52.6-75.8)	-	62.3 (57.8-66.7)	-
Horses	20.9 (11.1-30.7)	-	28.3 (24.2-32.4)	-
Cattle and/or sheep	25.4 (14.9-35.9)	-	22.2 (18.3-26.0)	-
Pigs	3.0 (0.0-7.1)	-	1.5 (0.4-2.7)	-
Poultry	13.4 (5.2-21.7)	-	14.0 (10.8-17.2)	-
Rabbits	7.5 (1.1-13.8)	-	5.7 (3.6-7.8)	-
Other species	11.9 (4.1-19.8)	-	20.6 (16.9-24.3)	-
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)	-
Boarding kennel	8.1 (0.0-17.0)	-	9.1 (5.7-12.5)	-
Group training / behaviour classes	24.3 (10.3-38.3)	-	35.5 (29.9-41.2)	-
Dog day care facility	48.7 (32.3-65.0)	-	39.5 (33.7-45.3)	-
Overseas	2.7 (0.0-8.0)	-	0.7 (0.0-1.7)	-
Rescue kennel	0.0 (0.0-0.0)	-	0.4 (0.0-1.1)	-
Other	18.9 (6.1-31.7)	-	20.3 (15.5-25.0)	-
Provided food type known: *	95.2 (91.9-98.4)	8	100.0 (100.0-100.0)	-
Proprietary dog food	95.5 (92.3-98.8)	-	85.9 (83.8-88.0)	-
Home-cooked diet	6.4 (2.5-10.2)	-	10.4 (8.6-12.3)	-
Raw meat	5.1 (1.6-8.6)	-	15.9 (13.6-18.1)	-
Table scraps	14.7 (9.1-20.2)	-	16.1 (13.8-18.3)	-
Dog scavenges food	36.6 (28.7-44.4)	20	19.9 (17.4-22.4)	24

580
581 * Multiple options are possible
582

583 Table 3.
584
585

Question	Veterinary professional-reported cases (*n*=165) % of responses (95% CI)	*n* unknown	Owner-reported cases (*n*=1,034) % of responses (95% CI)	*n* unknown
Clinical signs:				
Vomiting without blood	91.5 (87.3-95.8)	-	88.7 (86.8-90.6)	
Vomiting with blood	8.5 (4.2-12.8)	-	11.3 (9.4-13.3)	
Diarrhoea without blood	37.0 (29.6-44.4)	-	46.2 (43.2-49.3)	
Diarrhoea with blood	10.9 (6.1-15.7)	-	12.3 (10.3-14.3)	
Melaena	1.8 (0.0-3.9)	-	-	
Pyrexia	12.7 (7.6-17.8)	-	15.4 (13.2-17.6)	
Inappetence	86.1 (80.8-91.4)	-	75.6 (73.0-78.3)	
Weight loss	18.2 (12.3-24.1)	-	34.9 (32.0-37.8)	
Lethargy	9.1 (4.7-13.5)	-	6.3 (4.8-7.8)	
Diagnostic testing performed	32.1 (25.0-39.3)		18.3 (15.9-20.7)	
Treatment provided to dog	92.1 (88.0-96.2)		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 within 24 hours	5.5 (2.0-8.9)	-	2.9 (1.8-3.9)	-
Recovery in 24-48 hours	17.6 (11.8-23.4)	-	21.1 (18.6-23.7)	-
Recovery in 3-7 days	30.9 (23.8-38.0)	-	36.2 (33.2-39.1)	-
Recovery in 7-14 days	2.4 (0.1-4.8)	-	5.9 (4.5-7.4)	-
Recovery in over 14 days	2.4 (0.1-4.8)	-	2.1 (1.2-2.9)	-
Dog still vomiting	7.9 (3.8-12.0)	-	9.4 (7.6-11.2)	-
Dog not vomiting but still unwell	21.2 (15.0-27.5)	-	21.4 (18.9-24.0)	-
Dog died	0.6 (0.0-1.8)	-	1.0 (0.4-1.6)	-

587 Table 4.

588

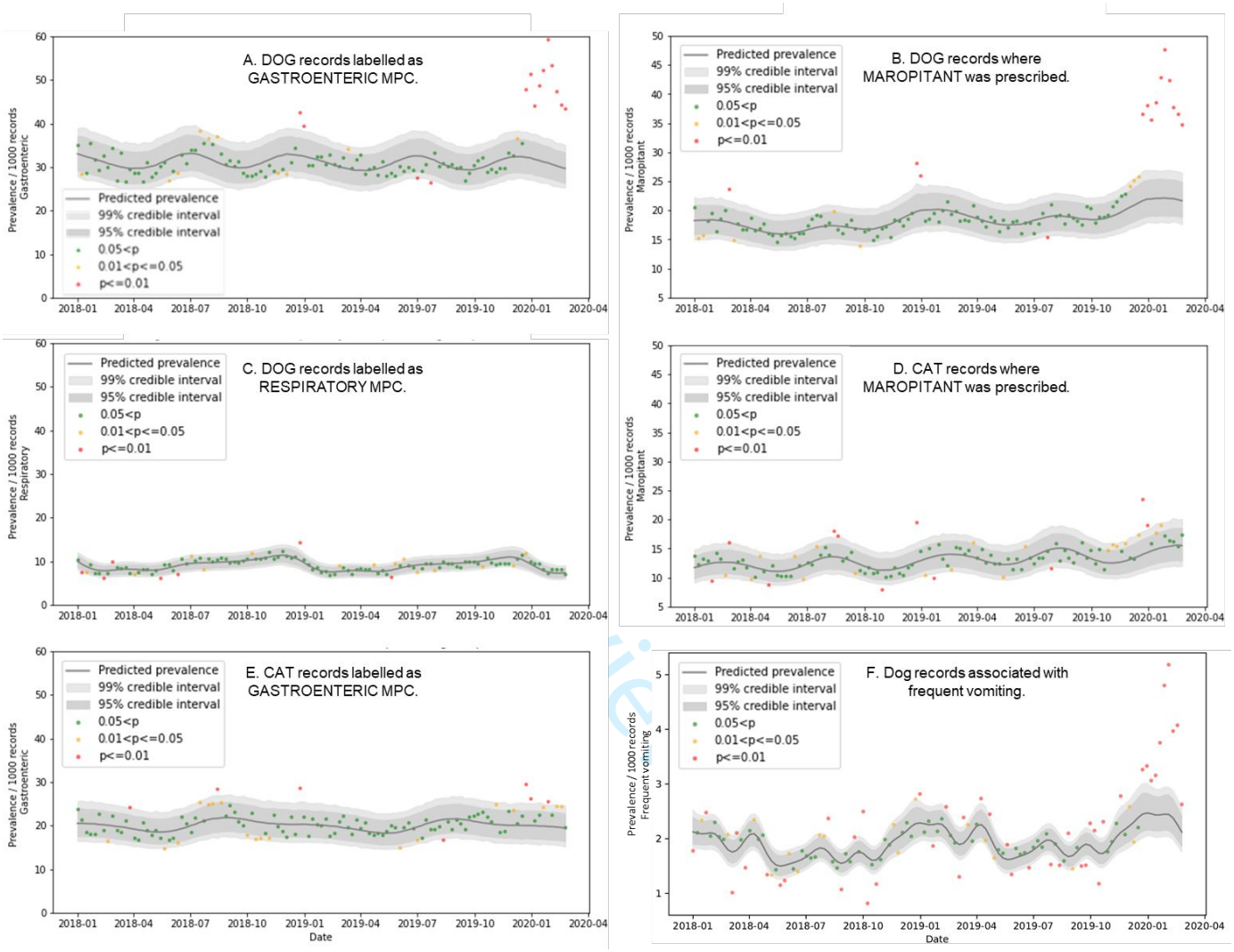
Variable	Category	β	SE	OR (95% CI)	*P-value*
	Intercept	-0.36	0.42	-	-
Sex & neutered status	Female neutered	-	-	1.00	-
	Female entire	0.77	0.55	2.15 (0.74-6.26)	0.16
	Male entire	**1.34**	**0.59**	**3.82 (1.20-12.15)**	**0.02**
	Male neutered	**0.81**	**0.40**	**2.25 (1.03-4.91)**	**0.04**
Household vomiting status	Mulitdog household – no other dogs vomiting in the same household	-	-	1.00	-
	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**
Other species vomiting contact	No contact with other vomiting species	-	-	1.00	-
	Confirmed contact with vomiting other species	**-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

589 Veterinary practice random effect variance was 0.15 (standard deviation = 0.39).

590

591 Figure 1.

592



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597 Figure 2.

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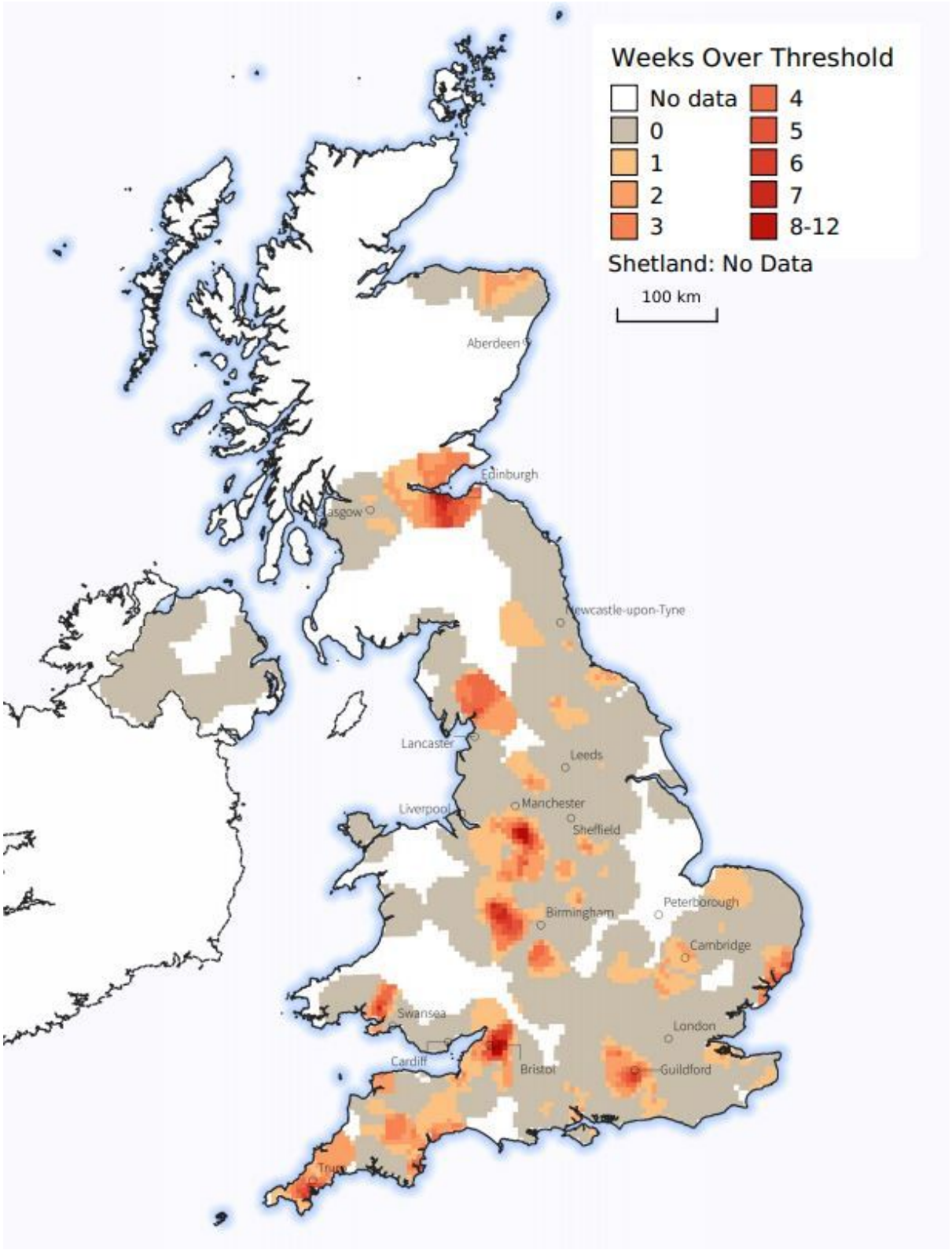
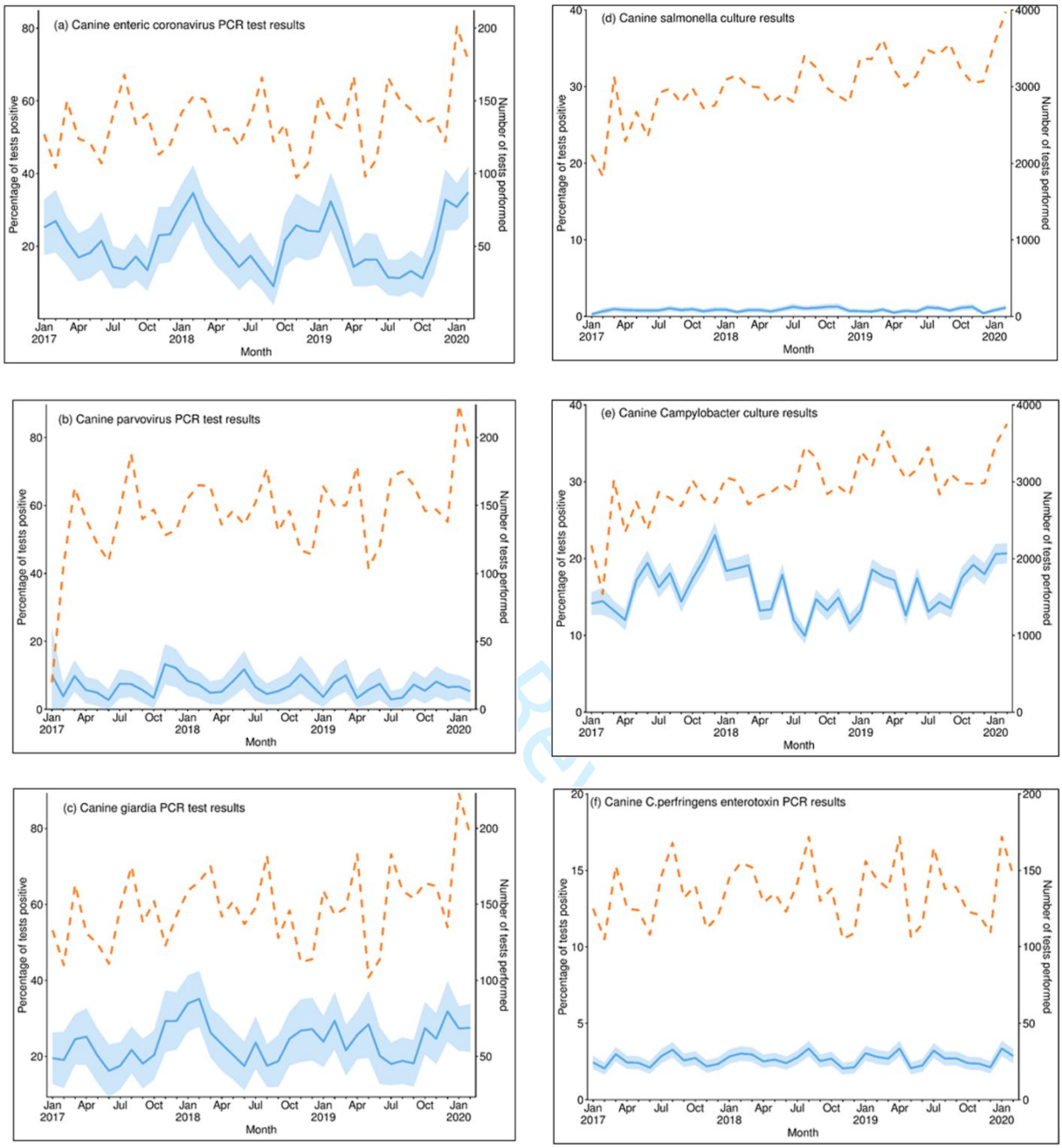


599

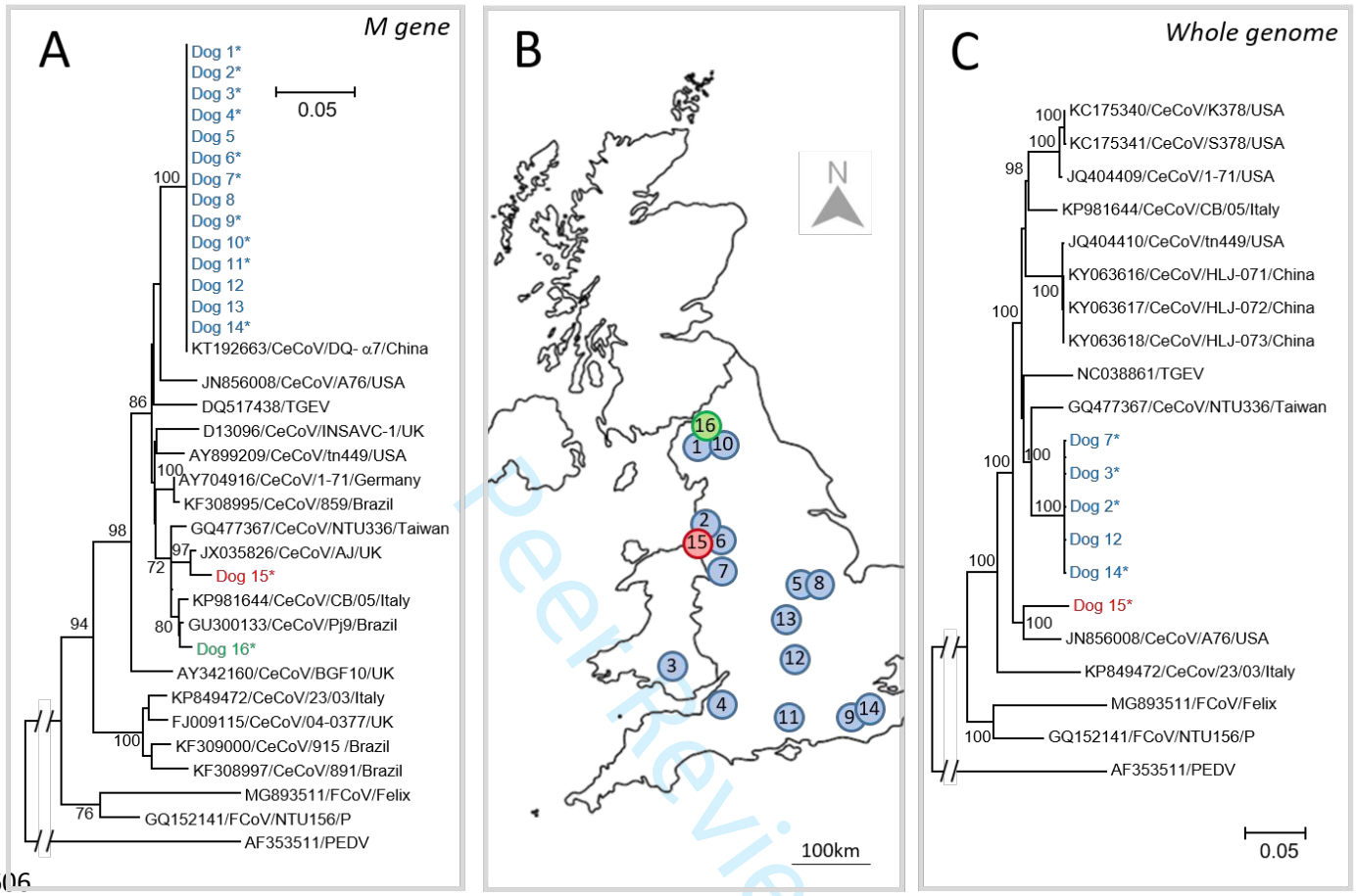
601 Figure 3.



602

604 Figure 4.

605



606

Supplementary 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 underlined text identifies the precise text string matched by the regular expression.

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\sof)(?<!not)(?<!no\Wmore)(?<!stopped)\W?(?:v[oi]?m+i?t?t?(?:ing|ed)?|v\+{1,10}|(?:has\Wbeen|was)\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 **<u>V+ 3 times</u>** over last 24h OR **<u>vomitted 7 times</u>** since this lunch time **<u>vomited 5 times</u>** today **<u>profuse vomiting</u>** o'night , no diarrhoea empty abdo <<identifier>> **<u>has been sick 2-3 times</u>** this afternoon Has been **<u>vomiting frequently</u>** today
Example of a false positive matches	Booster tricat/fel**<u>v+ 6 x</u>** endectrid

Supplementary table 2: Descriptive findings of veterinary professional-provided questionnaire responses, seeking to gain location, signalment, feeding and contact information from dogs that have not recently been observed to prolifically vomit (*n*=60). CI = 95% Confidence interval.

	% of responses (95% CI)	*n* unknown
Practice location: England	83.3 (73.8-92.8)	-
Practice location: Wales	6.7 (0.3-13.0)	-
Practice location: Scotland	6.7 (0.3-13.0)	-
Practice location: North Ireland	3.3 (0.0-7.9)	-
SAVSNET-participating practice	14.7 (2.6-26.8)	26
Sex: Male	41.7 (29.1-54.3)	0
Neutered	78.3 (67.8-88.9)	0
Lives in multi-dog household	51.7 (38.9-64.4)	0
1+ dog in household vomited	32.3 (15.5-49.0)	29
Vaccinated within last three years: *	95.0 (89.4-100.6)	0
Distemper	93.3 (87.0-99.7)	-
Infectious hepatitis	93.3 (87.0-99.7)	-
Parvo	91.7 (84.6-98.7)	-
Parainfluenza	56.7 (44.0-69.3)	-
Leptospirosis	93.3 (87.0-99.7)	-
Kennel cough	48.3 (35.6-61.1)	-
Rabies	10.0 (2.3-17.7)	-
De-wormed within last 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)	-
Horses	25.7 (11.0-40.4)	-
Cattle and/or sheep	22.9 (8.7-37.0)	-
Pigs	2.9 (0.0-8.5)	-
Poultry	22.9 (8.7-37.0)	-
Other species	14.3 (2.5-26.1)	-
Recent travel history: *	32.1 (19.4-44.8)	7
Boarding kennel	5.9 (0.0-17.4)	-
Group training / behaviour classes	35.3 (11.9-58.7)	-
Dog day care facility	17.7 (0.0-36.3)	-
Overseas	5.9 (0.0-17.4)	-
Rescue kennel	0.0 (0.0-0.0)	-
Other	47.1 (22.6-71.5)	-
Provided food type known: *	95.0 (89.4-100.6)	0
Proprietary dog food	89.5 (81.4-97.5)	-
Home-cooked diet	3.5 (0.0-8.3)	-
Raw meat	10.5 (2.5-18.6)	-
Table scraps	14.0 (4.9-23.1)	-
Dog scavenges food	23.6 (12.3-35.0)	5
Contact with other vomiting species	30.6 (17.6-43.7)	11

*Multiple selections possible

Supplementary 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. SE = standard error, OR = odds ratio, CI = 95% confidence interval.

Variable	Category	β	SE	OR (95% CI)	*P*
Veterinary location country	England (Intercept)	1.02	0.20	1.00	-
	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	Female (Intercept)	0.73	0.23	1.00	-
	Male	0.71	0.33	2.02 (1.06-3.86)	0.03
Neutered status	Not neutered (Intercept)	1.42	0.33	1.00	-
	Neutered	-0.49	0.36	0.62 (0.30-1.26)	0.18
Sex & neutered status	Female neutered (Intercept)	0.60	0.26	1.00	-
	Female entire	0.48	0.50	1.61 (0.60-4.29)	0.34
	Male entire	1.25	0.57	3.47 (1.14-10.55)	0.03
	Male neutered	0.70	0.38	2.01 (0.95-4.23)	0.07
Multi-dog household	Single dog household (Intercept)	1.36	0.24	1.00	-
	Multi-dog household	-0.72	0.32	0.49 (0.26-0.90)	0.02
Multi-dog household vomiting	No dogs vomiting (Intercept)	0.24	0.31	1.00	-
	1+ dogs vomiting	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 (Intercept)	1.13	0.69	1.00	-
	Recently vaccinated	-0.07	0.70	0.93 (0.23-3.70)	0.92
De-worming status	Not recently de-wormed (Intercept)	0.76	0.42	1.00	-
	Recently dewormed	0.21	0.46	1.23 (0.50-3.06)	0.65
	Unknown de-worming status	1.55	0.76	4.73 (1.06-21.16)	0.04
Contact with other species	No other species contact (Intercept)	1.17	0.30	1.00	-
	Other species contact	-0.48	0.36	0.62 (0.31-1.24)	0.17
	Unknown other species contact	0.74	0.51	2.09 (0.77-5.66)	0.15
Contact with cats	No contact (Intercept)	1.14	0.26	1.00	-
	Contact	-0.61	0.35	0.55 (0.27-1.09)	0.09
	Unknown contact	0.78	0.48	2.17 (0.84-5.61)	0.11
Contact with horses	No contact (Intercept)	0.95	0.21	1.00	-
	Contact	-0.48	0.48	0.62 (0.24-1.61)	0.33
	Unknown contact	0.96	0.47	2.62 (1.05-6.52)	0.04
Contact with cattle and/or sheep	No contact (Intercept)	0.90	0.20	1.00	-
	Contact	-0.11	0.49	0.90 (0.35-2.33)	0.83
	Unknown contact	1.01	0.47	2.76 (1.11-6.87)	0.03
Contact with pigs	No contact (Intercept)	0.88	0.19	1.00	-
	Contact	-0.14	1.30	0.87 (0.07-11.06)	0.91
	Unknown contact	1.03	0.46	2.79 (1.13-6.89)	0.03
Contact with poultry	No contact (Intercept)	0.99	0.21	1.00	-
	Contact	-0.90	0.56	0.41 (0.14-1.22)	0.11
	Unknown contact	0.95	0.47	2.58 (1.03-6.43)	0.04
Contact with other species	No contact (Intercept)	0.88	0.19	1.00	-
	Contact	0.02	0.60	1.02 (0.32-3.31)	0.97
	Unknown contact	1.03	0.47	2.81 (1.13-6.99)	0.03
Dog travel status	No recent travel (Intercept)	0.84	0.22	1.00	-
	Recent travel	-0.03	0.36	0.97 (0.48-1.97)	0.93
	Unknown travel status	1.10	0.46	3.01 (1.22-7.40)	0.02
Travel to boarding kennel	No travel (Intercept)	0.82	0.19	1.00	-
	Travel	0.29	1.19	1.34 (0.13-13.70)	0.81
	Unknown travel status	1.12	0.45	3.06 (1.28-7.32)	0.01
Travel to training class	No travel (Intercept)	0.87	0.20	1.00	-
	Travel	-0.45	0.57	0.64 (0.21-1.95)	0.43
	Unknown travel status	1.07	0.45	2.91 (1.21-7.01)	0.02

Travel to dog day care	No travel (Intercept)	0.73	0.19	1.00	-
	Travel	1.14	0.66	3.12 (0.85-11.44)	0.09
	Unknown travel status	1.23	0.45	3.41 (1.41-8.25)	0.01
Overseas travel	No travel (Intercept)	0.84	0.19	1.00	-
	Travel	-0.84	1.46	0.43 (0.03-7.55)	0.57
	Unknown travel status	1.10	0.45	3.01 (1.26-7.20)	0.01
Other types of travel	No travel (Intercept)	0.95	0.21	1.00	-
	Travel	-1.08	0.57	0.34 (0.11-1.04)	0.06
	Unknown travel status	1.01	0.45	2.74 (1.13-6.61)	0.03
Food type known	Food types not known (Intercept)	0.99	0.70	1.00	-
	Food types known	0.07	0.72	1.08 (0.26-4.40)	0.92
Proprietary dog food provided	None provided (Intercept)	0.18	0.58	1.00	-
	Provided	0.95	0.60	2.59 (0.79-8.43)	0.12
	Unknown provision status	0.80	0.90	2.23 (0.38-13.06)	0.37
Raw food provided	None provided (Intercept)	1.13	0.20	1.00	-
	Provided	-0.81	0.59	0.45 (0.14-1.40)	0.17
	Unknown provision status	-0.14	0.72	0.87 (0.21-3.58)	0.85
Food scraps provided	None provided (Intercept)	1.06	0.20	1.00	-
	Provided	0.06	0.46	1.06 (0.43-2.59)	0.90
	Unknown provision status	-0.07	0.72	0.94 (0.23-3.86)	0.93
Dog food scavenger status	Not a scavenger (Intercept)	0.81	0.21	1.00	-
	Is a scavenger	0.62	0.37	1.86 (0.91-3.81)	0.09
	Unknown scavenger status	0.59	0.54	1.80 (0.62-5.23)	0.28
Other species vomiting contact	No contact (Intercept)	1.09	0.23	1.00	-
	Contact	-1.08	0.44	0.34 (0.15-0.80)	0.01
	Unknown contact status	0.55	0.40	1.74 (0.80-3.78)	0.16
Number of dogs in household	1 dog in household (Intercept)	1.29	0.23	1.00	-
	2 dogs in household	-0.58	0.36	0.56 (0.27-1.14)	0.11
	3 dogs in household	-0.45	0.59	0.64 (0.20-2.05)	0.45
	4 dogs in household	-0.61	0.76	0.54 (0.12-2.43)	0.42
	5 or more dogs in household	-0.77	0.79	0.46 (0.10-2.17)	0.33
Age at presentation (years)	Intercept	2.24	0.58	1.00	-
	Age – linear term	-0.48	0.28	0.62 (0.36-1.08)	0.09
	Age – quadratic term	0.07	0.04	1.08 (1.00-1.16)	0.06
	Age – cubic term	0.00	0.00	1.00 (0.99-1.00)	0.04

A national outbreak of severe vomiting in dogs associated with a canine enteric coronavirus. Supplementary Information on geostatistical modelling

Alan D. Radford, David A. Singleton, Chris Jewell, Charlotte Appleton, Barry Rowlingson, Alison C. Hale, Carmen Tamayo Cuartero, Richard Newton, Fernando Snchez-Vizcano, Danielle Greenberg, Beth Brant, Eleanor Bentley, James Stewart, Shirley Smith, Sam Haldenby, P-J M. Noble, and Gina L. Pinchbeck

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.

1 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 $i = 1, \ldots, n_t$ 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

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

with

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

$S(\boldsymbol{x})$ is a spatial Gaussian process such that

$$S(\boldsymbol{x}) \sim \text{MultivariateNormal}(\mathbf{0}, \Sigma^2)$$

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

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

where $||x_i - x_j||$ 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 $x^\star_i, i = 1, ..., m$ and let

$$S(\boldsymbol{x}) \approx \Sigma^2_{xx^\star} (\Sigma^2_{x^\star x^\star})^{-1} s^\star \quad (1)$$

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 $\boldsymbol{x}$ 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. $\Sigma^2_{ii} = \sigma^2 + \tau^2$. 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:

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

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

2 GIS presentation of results

Using Equation 1, the posterior samples of $S(x^\star)$ were projected onto a 5km resolution grid of points $\boldsymbol{z}$ within the outline of the UK [3]. This gave a numerical approximation of the predictive distribution $\pi(S(\boldsymbol{z})|\boldsymbol{y}, \boldsymbol{x})$ 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 $\exp z > 1$) 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 summarised as

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

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

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