Seizure occurrence in dogs under primary veterinary care in the UK: prevalence and risk factors

Alexander Erlen1 | Heidrun Potschka2 | Holger A. Volk3 | Carola Sauter-Louis4 | Dan G. O’Neill5

1Inst. of Pharmacology, Toxicology, and Pharmacy, Ludwig-Maximilians-University, Munich, Germany
2Inst. of Pharmacology, Toxicology, and Pharmacy, Ludwig-Maximilians-University, Munich, Germany
3Clinical Science and Services, The Royal Veterinary College, Hatfield, UK
4Institute of Epidemiology, Friedrich-Loeffler-Institut, Greifswald, Germany
5Pathobiology and Population Health, The Royal Veterinary College, Hatfield, UK

Correspondence
Alexander Erlen, Address: Inst. of Pharmacology, Toxicology, and Pharmacy, Ludwig-Maximilians-University, Königstr. 16, 80539 Munich, Germany, Email: alexander.erlen@pharmtox.vetmed.uni-muenchen.de

Funding information
Bayer Animal Health GmbH, 51373 Leverkusen

1 | INTRODUCTION

Seizures in dogs are sudden, short lasting and transient events that are characterized by motor, autonomic or behavioral features.1 They are considered common events in dogs.2 Causes including genetic and insult-triggered brain diseases, peripheral diseases, electrolyte imbalances, intoxications and idiopathic.3 Seizure activity can have substantial impact on quality of life3–5 as well as causing emotional distress for owners.6,7 To date, most studies have focused on the subset of cases that are classified as epileptic.8,9

Seizures are either epileptic or reactive according to the classification of the IVETF. Epileptic seizures are manifestations of excessive synchronous neuronal activity in the brain that is usually self-limiting and that are promoted by a predisposition of the brain for ictogenesis.1,10 Epilepsy is usually defined as requiring at least two unprovoked epileptic seizures more than 24 hours apart11 and reactive seizures (also called provoked seizures) are considered as natural...
responses from the normal brain to some transient disturbance in function (e.g. metabolic or toxic) which is reversible when the cause or disturbance is rectified. Analysis of a large pet insurance database reported an epilepsy incidence of 18 per 10,000 dog years at risk (DYAR) in Sweden for either idiopathic epilepsy or epileptic convulsions. A study using primary-care veterinary clinical data reported a prevalence of 0.62% for epilepsy in dogs in the UK. A cross-sectional study compared period prevalence of epileptic seizures in a 2.5-year observation period between first opinion practices (0.43%) and a referral clinic in southern Germany (1.78%). Among the referral subset of dogs seen at a veterinary teaching hospital in Germany, 2.6% had a history of seizures reported. Epidemiological studies using first opinion databases that explore seizures in general rather than relying on semi-arbitrary classification into various subsets might offer novel and more clinically pertinent insights into this disease in dogs. There are breed predispositions to various forms of epilepsy, but predisposition studies often fail to describe the prevalence of seizures either in dogs overall and in individual breeds.

This study aimed to identify and explore seizure occurrence in the general dog population under primary veterinary care in the UK. The specific objectives were to estimate the 1-year period prevalence for dogs that showed seizures and to also identify demographic risk factors associated with dogs that showed seizures, with breed as a risk factor of special interest. These results could be especially valuable for practitioners, insurance companies, pharmaceutical and nutrition manufacturers and pharmacovigilance agencies by providing a representative evidence-base that can be generalized to the wider dog population and fill the evidential data gap on seizure occurrence.

2 | MATERIALS AND METHODS

This study was based on data collected within the VetCompass™ Animal Surveillance System at the Royal Veterinary College (RVC). VetCompass™ collates electronic patient record (EPR) data from hundreds of UK primary-care practices for epidemiological research. Demographic information collected included species, breed, date of birth, sex and neuter status, while clinical information includes free text notes, treatment data as well as summarized diagnosis terms from the VeNom Codes standardized lists. Clinical data from participating practices are extracted from practice management systems (PMSs) using automated queries, uploaded securely to the RVC server and reformatted for entry into the VetCompass™ online database system.

A cross-sectional analysis using cohort clinical data of dogs attending VetCompass™ practices was used to estimate the 1-year period prevalence and risk factors for dogs with at least one seizure during 2013. The denominator population for the current study comprised all dogs that had at least one EPR (clinical note, bodyweight or treatment) recorded in VetCompass™ during 2013 or dogs that had ‘at least one EPR before and one EPR after 2013’. These dogs were defined as being under veterinary care during 2013.

Sample size calculations estimated that a study with 149,698 dogs would be required to represent a disorder with 1% expected prevalence to a precision of 0.05% at a 95% confidence level from an estimated UK national population of 9.4 million dogs. Ethical approval was granted by the RVC Ethics and Welfare Committee (reference number 2015 1369).

A two-step letter-string search process was used to identify seizure cases in the VetCompass™ dog population. In step one, all EPRs were initially screened for candidate seizure cases using a range of letter-string search terms including seiz*, siez*, convul*, tonic*, clonic*, myoclo*, had fit*, had a fit*, epil*, diaz*, clonaz*, midazol*, phenobarb*, gabapen*, levetirata*, bromide, pregaba*, zonis*, imepit*, pexi*, keppra*, hypnov*, eph*, phenolep*, librom*, lyric*, alpraz* and zonge*. In step two, the EPRs of all candidate cases which had been identified as possible seizure cases were manually read and evaluated for inclusion as a seizure case according to the study case definition. A seizure case was defined as any dog with at least one seizure event occurring during 2013 recorded in the EPR. All dogs with reported seizure activity in 2013 were grouped as seizure cases and all remaining dogs were grouped as non-cases.

A Purebred “variable classified all dogs of a recognizable breed as purebred”, all dogs recorded with a designer breed name as “designer” and all remaining dogs as “crossbred”. A “Breeds” variable included the breed name of any individual purebred or designer breed types with 15 or more seizure cases during 2013 while all remaining purebred and designer types were grouped as “Other purebreds and designers breed types” and a general category of crossbred dogs was also included. A “Kennel Club Breed Group” variable defined all KC recognized breeds according to their relevant UK KC breed groups (Gundog, Terrier, Utility, Hound, Working, Toy and Pastoral) and included all remaining dogs as “Breed not-Kennel Club recognized”. The age for all dogs described the age at 31st December 2013. An age variable “Age” contained 7 age categories in years (0.00 - 0.50, 0.50 - 3.00, 3.00 - 6.00, 6.00 - 9.00, 9.00 - 12.00, > 12.00, unrecorded) according to the IVETF guidelines. The Neuter status variable recorded the neutering status recorded at the final EPR. Sex and neuter status were also combined into a single variable (Sex-neuter) that reported the results across seven permutational categories. The variable “Adult (> 18 months) bodyweight” described the maximum bodyweight recorded during the study period for dogs older than 18 months and categorized adult bodyweight into 6 groups (< 10.00 kg, 10.00 - 20.00 kg, 20.00 - 30.00 kg, 30.00 - 40.00 kg, > 40.00 kg, unrecorded). A "Bodyweight relative to breed and sex mean" variable characterized the adult bodyweight of individual dogs as either below or equal/above the mean adult bodyweight for their breed and sex within the overall study population. This variable allowed the effect of adult bodyweight to be assessed within each breed/sex combination.

After data checking and cleaning in Excel (Microsoft Office Excel 2013, Microsoft Corp.), statistical analyses were conducted with IBM SPSS Statistics 24. The 1-year period prevalence with 95% confidence intervals (CI) described the probability for each dog of having at least one seizure at any time during the 1-year 2013 study period. The CI estimates were derived from standard errors, based on approximation to the normal distribution. Descriptive statistics characterized the count and proportions of cases and non-case dogs for each of the study variables. Binary logistic regression modelling was used to evaluate univariable associations between risk factors and being a
The study population comprised 455,553 dogs attending primary care under veterinary care. It benefitted from a large sample size of over 450,000 dogs. The study reports an overall 1-year period prevalence of 0.82% and identified the Pug, Boxer, Basset Hound, Border Terrier and Border Collie as the breeds with the highest seizure prevalence of 0.82% (95% CI 0.79 - 0.84) for dogs having at least one seizure. Individual breeds with the highest seizure prevalence included Pug (1.88% of the breed affected, 95% CI 1.52 - 2.24), Boxer (1.77%, 95% CI 1.44 - 2.09), Basset Hound (1.74%, 95% CI 1.02 - 2.46), Border Terrier (1.67%, 95% CI 1.33 - 2.01) and Border Collie (1.45%, 95% CI 1.24 - 1.66) (Table 1).

The most common breeds among the non-case dogs were the Labrador Retriever 32,998 (7.3%), Staffordshire Bull Terrier 32,407 (7.2%), Jack Russell Terrier 27,473 (6.1%), Cocker Spaniel 15,765 (3.5%), Yorkshire Terrier 15,248 (3.4%) as well as 100,249 (22.2%) crossbreds and 13,768 (3.0%) designers (Table 2). Of the non-case dogs, 337,805 (74.8%) were purebred and 232,080 (51.4%) were crossbreds and 13,768 (3.0%) designers (Table 2). Of the non-case dogs, 337,805 (74.8%) were purebred and 232,080 (51.4%) were crossbreds and 13,768 (3.0%) designers (Table 2).

Data completeness varied between the variables assessed: breed (95% CI 1.18 - 1.39, P < 0.001) compared with crossbred dogs. Compared with "Breeds not Kennel Club recognized", the "Toy" Kennel Club Breed group showed 1.68 times the odds (95% CI 1.52 - 1.86 P < 0.001), the "Working" group had 1.49 the odds (95% CI 1.40 - 2.59, P < 0.001) and the "Pastoral" group had 1.42 the odds (95% CI 1.26 - 1.61, P < 0.001). Dogs with an adult (≥ 18 months) bodyweight ≥ 40.00 kg had 1.24 times the odds (95% CI 1.08 - 1.41, P = 0.002) compared with dogs < 10.00 kg (Table 4).

4 | DISCUSSION

This study explored the occurrence of seizures in a UK dog population under primary veterinary care. It benefitted from a large sample size of over 450,000 dogs. The study reports an overall 1-year period prevalence of 0.82% and identified the Pug, Boxer, Basset Hound, Border Terrier and Border Collie as the breeds with the highest seizure prevalence. Increasing age, being male, being purebred and weighing over 40kg were highlighted as significant risk factors. These results can assist veterinary clinicians, researchers, breeders and pharmacovigilance agencies by providing a reliable evidence resource. This study also highlights the value of developing similar large-scale systems for collection and analysis of veterinary clinical data outside of the UK in order to generate evidence that will be more generalizable to their national animal populations.
The VetCompass™ database was selected as a useful data source for the current study that aimed to provide a prevalence estimate for dogs with seizures with high levels of validity, generalizability and precision for the general population of dogs in the UK. Primary-care veterinary clinical data might lack diagnostic precision for complicated disorders due to financial constraints on clinical work-up, but are much less affected by the selection biases and therefore the results are thought to have greater validity than referral studies that preferentially select for dogs that are by definition sick and generally affected with more complicated disease and more severe presentations and owned by more motivated owners. Primary-care data collected and merged from many hundreds of clinics now offers study sample sizes of sufficiently large size to allow much greater numerical precision in results than has previously been possible. It is estimated that 70% of UK dogs are registered with a veterinary practice and therefore results of studies using primary-care data offer good prospects of generalization to the wider dog population and clinical relevance of the emergent results to veterinarians.

| Breed                  | No. Cases | No. Dogs in study | Median age in years of cases (IQR) | Prevalence % | 95% CI* |
|------------------------|-----------|-------------------|-----------------------------------|--------------|--------|
| Pug                    | 101       | 5376              | 4.95 (2.76-6.99)                  | 1.88         | 1.52-2.24 |
| Boxer                  | 111       | 6288              | 9.52 (6.95-11.04)                 | 1.77         | 1.44-2.09 |
| Basset Hound           | 22        | 1263              | 6.22 (3.19-9.36)                  | 1.74         | 1.02-2.46 |
| Border Terrier         | 91        | 5449              | 7.06 (4.85-11.35)                 | 1.67         | 1.33-2.01 |
| Border Collie          | 178       | 12268             | 6.43 (4.18-12.18)                 | 1.45         | 1.24-1.66 |
| Beagle                 | 48        | 3508              | 5.71 (5.46-7.35)                  | 1.37         | 0.98-1.75 |
| King Charles Spaniel   | 21        | 1666              | 5.18 (3.03-11.33)                 | 1.26         | 0.72-1.80 |
| Dogue de Bordeaux      | 23        | 1858              | 3.76 (2.05-5.91)                  | 1.24         | 0.73-1.74 |
| British Bulldog        | 39        | 3374              | 2.54 (1.58-4.46)                  | 1.16         | 0.80-1.52 |
| Weimaraner             | 18        | 1568              | 8.30 (6.90-10.73)                 | 1.15         | 0.62-1.68 |
| Yorkshire Terrier      | 178       | 15426             | 8.23 (5.33-12.44)                 | 1.15         | 0.99-1.32 |
| Cavalier King Charles Spaniel | 112 | 10143            | 6.95 (4.91-9.20)                  | 1.10         | 0.90-1.31 |
| Patterdale Terrier     | 26        | 2433              | 5.58 (3.35-8.31)                  | 1.07         | 0.66-1.48 |
| Pomeranian             | 22        | 2147              | 4.91 (1.81-6.97)                  | 1.02         | 0.60-1.45 |
| Labrador Retriever     | 323       | 33321             | 7.21 (4.48-9.91)                  | 0.97         | 0.87-1.06 |
| Toy Poodle             | 18        | 1881              | 7.60 (4.06-12.83)                 | 0.69         | 0.52-1.40 |
| Golden Retriever       | 54        | 5670              | 8.33 (5.02-12.40)                 | 0.95         | 0.70-1.21 |
| German Shepherd Dog    | 116       | 12520             | 8.59 (5.35-10.98)                 | 0.93         | 0.76-1.09 |
| Chihuahua              | 101       | 11782             | 4.04 (1.85-6.67)                  | 0.86         | 0.69-1.02 |
| Akita                  | 17        | 2105              | 7.36 (3.45-13.32)                 | 0.81         | 0.42-1.19 |
| Miniature Schnauzer    | 31        | 3857              | 6.30 (3.04-10.66)                 | 0.80         | 0.52-1.09 |
| French Bulldog         | 19        | 2397              | 2.18 (1.56-6.00)                  | 0.79         | 0.44-1.15 |
| Jack Russell Terrier   | 218       | 27691             | 8.59 (5.39-12.83)                 | 0.79         | 0.68-0.89 |
| Labradoodle            | 23        | 3132              | 4.47 (3.73-6.80)                  | 0.73         | 0.44-1.03 |
| Miniature Dachshund    | 20        | 2792              | 5.64 (4.07-8.14)                  | 0.72         | 0.40-1.03 |
| Staffordshire Bull Terrier | 228    | 32635             | 7.97 (4.40-10.97)                 | 0.70         | 0.61-0.79 |
| Crossbred              | 681       | 98931             | 8.23 (4.57-12.71)                 | 0.96         | 0.64-0.74 |
| Lurcher                | 22        | 3222              | 5.78 (3.17-11.32)                 | 0.68         | 0.40-0.97 |
| Husky                  | 28        | 4162              | 4.55 (1.66-5.91)                  | 0.67         | 0.42-0.92 |
| West Highland White Terrier | 73  | 12017            | 10.94 (5.78-13.83)                | 0.61         | 0.47-0.75 |
| Springer Spaniel       | 35        | 5800              | 10.04 (5.71-12.78)                | 0.60         | 0.40-0.80 |
| Lhasa Apso             | 38        | 6840              | 8.80 (4.75-12.91)                 | 0.56         | 0.38-0.73 |
| Bichon                 | 36        | 6607              | 8.67 (3.84-12.63)                 | 0.54         | 0.37-0.72 |
| English Springer Spaniel | 29   | 5384              | 7.86 (3.92-11.71)                 | 0.54         | 0.34-0.73 |
| Unrecorded             | 10        | 2009              | 9.18 (4.58-14.76)                 | 0.50         | 0.19-0.81 |
| Rottweiler             | 24        | 5321              | 6.34 (4.91-10.69)                 | 0.45         | 0.27-0.63 |
| Designer               | 33        | 7492              | 3.11 (1.89-4.98)                  | 0.44         | 0.29-0.59 |
| Cocker Spaniel         | 62        | 15827             | 8.08 (4.72-11.15)                 | 0.39         | 0.29-0.49 |
| Shih-tzu               | 57        | 15038             | 8.24 (4.75-13.56)                 | 0.38         | 0.28-0.48 |
| Other purebreds and designers breed types | 445 | 54353            | 7.32 (4.19-10.90)                 | 0.82         | 0.74-0.89 |
| Overall total          | 3731      | 455553            | 7.27 (4.23-11.07)                 | 0.82         | 0.79-0.84 |

One-year period prevalence of seizures in commonly affected dog breeds under primary veterinary care in the UK; aCI confidence interval.

The VetCompass™ database was selected as a useful data source for the current study that aimed to provide a prevalence estimate for dogs with seizures with high levels of validity, generalizability and precision for the general population of dogs in the UK. Primary-care veterinary clinical data might lack diagnostic precision for complicated disorders due to financial constraints on clinical work-up, but are much less affected by the selection biases and therefore the results are thought to have greater validity than referral studies that preferentially select for dogs that are by definition sick and generally affected with more complicated disease and more severe presentations and owned by more motivated owners. Primary-care data collected and merged from many hundreds of clinics now offers study sample sizes of sufficiently large size to allow much greater numerical precision in results than has previously been possible. It is estimated that 70% of UK dogs are registered with a veterinary practice and therefore results of studies using primary-care data offer good prospects of generalization to the wider dog population and clinical relevance of the emergent results to veterinarians.
| Variable | Category | Case No. (%) | Non-case No. (%) | Odds ratio 95% CI | Category P-value | Variable P-value |
|----------|----------|--------------|------------------|-------------------|-----------------|------------------|
| Purebred | Crossbred | 681 (18.3) | 9250 (21.7) | Base | < 0.001 |
| Designer | Base | 65482 (17.4) | 8200 (1.8) | 0.78 | 0.65-0.92 | < 0.001 |
| Purebred | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Unrecorded | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Breeds | Labrador Retriever | 98250 (21.7) | 1250 (0.3) | 0.78 | 0.65-0.92 | < 0.001 |
| Pug | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Boxer | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Basset Hound | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Border Terrier | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Border Collie | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Beagle | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| King Charles Spaniel | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Dogue de Bordeaux | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| British Bulldog | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Yorkshire Terrier | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Weimaraner | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Cavalier King Charles Spaniel | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Patterdale Terrier | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Pomeranian | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Toy Poodle | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Golden Retriever | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| German Shepherd Dog | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Chihuahua | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Akita | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Miniature Schnauzer | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| French Bulldog | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Jack Russell Terrier | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Labradoodle (Designer) | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Miniature Dachshund | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Staffordshire Bull Terrier | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Crossbreed | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Lurcher (Designer) | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Husky | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| West Highland White Terrier | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Springer Spaniel | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Lhasa Apso | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Bichon | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| English Springer Spaniel | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Rottweiler | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Designer | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Cocker Spaniel | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Shih-tzu | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Unrecorded | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Other purebreds and designers breed types | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
| Kennel Club Breed Groups | Breed not Kennel Club recognized | 100 (2.7) | 1250 (0.3) | 0.81 | 0.66-0.97 | 0.007 |
The current study reported a 1-year prevalence of 0.82% for dogs affected by at least one seizure. To our knowledge, no previous studies have reported on the prevalence of seizures in the general dog population that can be used for direct comparison to this result. An earlier VetCompass™ study using primary-care data reported a prevalence of 0.62% for epilepsy of unknown origin in the UK. This earlier study covered a longer period from January 2010 to April 2011 and focused specifically on the subset of dogs with "epilepsy of unknown origin", excluding any dogs which had a clinically identified underlying disease causing epilepsy, whereas the current study included all dogs with seizures from any etiology during a 1-year period. Thus, the previous reported prevalence is lower than the value reported in the current study as would be expected. Analysis of claim data from a large insurance database in Sweden reported a 0.75% prevalence of insured dogs with a recorded claim for epilepsy. However, this prevalence among insured dogs might be higher than in the wider dog population under veterinary care because certain breed types perceived to have higher health risks may be preferentially insured. Furthermore, the study dogs contributed an average of 4.2 years to the insurance study compared with the 1-year period included in the current study. Further studies have also reported on referral populations. One of these studies reported a total seizure prevalence of 2.6% in a hospital population in Germany comprising 394 seizure case dogs admitted between January 2002 and March 2008. This prevalence may exceed the 0.82% reported in the current UK primary-care study because primary-care caseloads include 24.2% of dogs that have no diseases recorded and many of the remaining have minor ailments. However, further factors that could partially account for the differences need to be considered and may include geographic and temporal differences between the studies as well as differing sample size and breed compositions.

### TABLE 2 (Continued)

| Variable Category                                      | Case No. (%) | Non-case No. (%) | Odds ratio | 95% CI | Category P-value | Variable P-value |
|--------------------------------------------------------|--------------|-----------------|------------|--------|-----------------|-----------------|
| Toy                                                    | 617 (16.5)   | 56704 (12.6)    | 1.54       | 1.39-1.70 | < 0.001         | < 0.001         |
| Utility                                                | 307 (8.2)    | 44855 (9.9)     | 0.97       | 0.85-1.10 | 0.62            |                 |
| Working                                                | 212 (5.7)    | 22118 (4.9)     | 1.36       | 1.17-1.57 | < 0.001         |                 |
| Adult (>18months) bodyweight (kg)                      |              |                 |            |        |                 |                 |
| < 10.00                                                | 878 (23.5)   | 98359 (21.8)    | Base       |        | < 0.001         | < 0.001         |
| 10.00 - ≤ 20.00                                       | 830 (22.3)   | 91219 (20.2)    | 1.02       | 0.93-1.12 | 0.69            |                 |
| 20.00 - ≤ 30.00                                       | 641 (17.2)   | 67845 (15.0)    | 1.06       | 0.95-1.17 | 0.29            |                 |
| 30.00 - ≤ 40.00                                       | 526 (14.1)   | 46004 (10.2)    | 1.28       | 1.15-1.43 | < 0.001         |                 |
| ≥ 40.00                                                | 313 (8.4)    | 24860 (5.5)     | 1.41       | 1.24-1.61 | < 0.001         |                 |
| Unrecorded                                             | 543 (14.6)   | 123353 (27.2)   | 0.49       | 0.44-0.55 | < 0.001         |                 |
| Bodyweight relative to breed and sex mean              |              |                 |            |        |                 |                 |
| Lower                                                  | 1636 (43.9)  | 182105 (40.3)   | Base       |        | < 0.001         |                 |
| Equal/Higher                                           | 1550 (41.5)  | 145848 (32.4)   | 1.18       | 1.10-1.27 | < 0.001         |                 |
| Unrecorded                                             | 545 (14.6)   | 123869 (27.3)   | 0.49       | 0.44-0.54 | < 0.001         |                 |
| Age (years)                                            |              |                 |            |        |                 |                 |
| 0.00 - ≤ 0.50                                         | 25 (0.7)     | 25508 (5.6)     | 0.28       | 0.19-0.42 | < 0.001         | < 0.001         |
| 0.50 - ≤ 3.00                                         | 522 (14.0)   | 148813 (32.9)   | Base       |        | < 0.001         | < 0.001         |
| 3.00 - ≤ 6.00                                         | 923 (24.7)   | 114584 (25.4)   | 2.30       | 2.06-2.56 | < 0.001         |                 |
| 6.00 - ≤ 9.00                                         | 832 (22.3)   | 76360 (16.9)    | 3.10       | 2.78-3.46 | < 0.001         |                 |
| 9.00 - ≤ 12.00                                        | 636 (17.1)   | 47228 (10.5)    | 3.84       | 3.42-4.31 | < 0.001         |                 |
| ≥ 12.00                                               | 767 (20.6)   | 33180 (7.3)     | 6.59       | 5.89-7.37 | < 0.001         |                 |
| Unrecorded                                             | 26 (0.7)     | 6149 (1.4)      | 1.21       | 0.81-1.79 | 0.35            |                 |
| Sex                                                    |              |                 |            |        |                 | < 0.001         |
| Female                                                | 1592 (42.7)  | 217440 (48.1)   | Base       |        | < 0.001         |                 |
| Male                                                  | 2131 (57.1)  | 232080 (51.4)   | 1.25       | 1.17-1.34 | < 0.001         |                 |
| Not recorded                                           | 8 (0.2)      | 2302 (0.5)      | 0.48       | 0.24-0.95 | 0.036           |                 |
| Neuter status                                          |              |                 |            |        |                 | < 0.001         |
| Entire                                                | 1150 (30.8)  | 177066 (39.1)   | Base       |        | < 0.001         |                 |
| Neutered                                              | 1767 (47.3)  | 203252 (45.0)   | 1.34       | 1.24-1.44 | < 0.001         |                 |
| Unrecorded                                             | 814 (21.8)   | 71504 (15.9)    | 1.75       | 1.60-1.92 | < 0.001         |                 |
| Sex-neuter                                            |              |                 |            |        |                 | < 0.001         |
| Female/Entire                                          | 412 (11.0)   | 83498 (18.5)    | Base       |        | < 0.001         |                 |
| Female/Neutered                                        | 832 (22.3)   | 100164 (22.2)   | 1.68       | 1.50-1.90 | < 0.001         |                 |
| Female/Unrecorded                                      | 348 (9.3)    | 33778 (7.5)     | 2.09       | 1.81-2.41 | < 0.001         |                 |
| Male/Entire                                            | 731 (19.6)   | 91692 (20.3)    | 1.62       | 1.43-1.82 | < 0.001         |                 |
| Male/Neutered                                          | 934 (25.0)   | 102968 (22.8)   | 1.84       | 1.64-2.06 | < 0.001         |                 |
| Male/Unrecorded                                        | 466 (12.5)   | 37420 (8.3)     | 2.52       | 2.21-2.88 | < 0.001         |                 |
| Unrecorded/Unrecorded                                  | 8 (0.2)      | 2302 (0.5)      | 0.70       | 0.35-1.42 | 0.33            |                 |

Descriptive and univariable regression results for risk factors associated with seizure events in dogs under veterinary primary-care in the UK. Percentages shown in brackets aCI confidence interval.
The 1-year period prevalence of 0.82% identifies seizures as a relatively frequent clinical presentation in the UK dog population under primary veterinary care. Seizures are a clinical manifestation that can result from a wide variety of causes, but are not limited to, genetic predisposition, primary brain disease, intoxication, cardiovascular disease, electrolyte disturbance and endocrine and metabolic disorders. The proportional contribution of reactive seizures to the total seizure case burden has been variously estimated at between 13.6% and 32% respectively. The differences between the study outcome might result from variation between study design (e.g. prospective versus retrospective analyses), countries, diagnostic procedures and animal population selection (e.g. primary-care versus referral caseloads). The results of the current study underline the relevance of undergraduate training and continuing education about the multiple causes of seizure events, the optimal diagnostic procedures, and the management options for seizure events in dogs. These period prevalence data should also be considered as a useful background presence of seizures when considering suspected adverse events reported to pharmacovigilance monitoring systems.

Risk factors results can provide valuable information to improve veterinary diagnosis of disease and hence to improve animal welfare monitoring. The current study placed special focus on exploring breed as a risk factor for seizure occurrence because of prior evidence of genetic associations with epilepsy in dogs. As might have been expected, seizures proved to be more frequent in purebreds compared to crossbred and designer dogs although the purebred predisposition could be heavily influenced by the subgroup of dogs with idiopathic epilepsy. In a recent longitudinal study at Copenhagen University Hospital, dogs with idiopathic epilepsy exhibited a breed distribution of 83.6% purebred and 16.4% crossbred. However, hereditary factors might also contribute to structural epilepsy as well as non-epileptic seizures cases as the genetic background might, for instance, predispose to epilepsy development after a brain injury or might predispose to a peripheral disease associated with non-epileptic seizures.

Hybrid vigor (also known as heterosis or crossbred vigor) describes a phenomenon whereby the average performance of first-generation crosses for specified traits outperforms the average performance of their parental breeds and has been proposed to enhance the health of crossbred compared with purebred animals for over 150 years. Substantial evidence exists for these effects in production species of plants and animals. However, pet dogs are generally not kept for production traits and the strength of evidence to support the true impact of hybrid vigor in dogs has recently been questioned. The findings in the current study that purebred dogs had 1.28 times higher odds of being seizure cases compared with crossbreds might add further weight to the existence of hybrid vigor in domestic dogs. Although the difference in effect shown might not appear to be substantial, it is likely that many of the crossbreds in our study were not first-generation crosses and therefore would have lost much of the additional health gains shown by first-generation crosses. It is possible that any true reduction in seizure prevalence in crossbreds may have been much higher specifically in the first-generation subset of crosses but it was not possible to identify these dogs in the current study. The heterogeneity in genetics and health among the many individual breeds that exist among the purebred group should act as a further caveat to facile acceptance of the hybrid vigor concept. Relative changes in the proportions of some common breeds that are either predisposed or protected to certain diseases could dramatically affect the overall probability of disease in purebred dogs overall. From this it is clear that resolving the hybrid vigor question in dogs has quite some way to go.

Exploration of associations, in both predisposition and protective directions, between individual breeds and the occurrence of seizures was of particular interest in this study. After accounting for other relevant factors, the final multivariable identified predisposition to seizures in 11 breeds with odds ratios ranging up to 3.41 times higher than that of Labrador Retrievers. Although the Labrador Retriever itself has previously been reported as a predisposed breed for epilepsy with a reported lifetime prevalence of 3.1%, the current study elected to use the Labrador Retriever instead of crossbreds as the comparator breed in contrast to other previous studies. Crossbred dogs, by definition, provide highly uncertain genetic structure, body

FIGURE 1 A: Seizure cases per year (n = 3,704) in the UK dog population under primary veterinary care B: Seizure non-cases per year (n = 445,674) in the UK dog population under primary veterinary care
### TABLE 3  Final breed multivariable logistic regression results

| Variable | Odds ratio | 95%CIa | p-value | Variable | Odds ratio | 95%CIa | p-value |
|----------|------------|--------|---------|----------|------------|--------|---------|
| Breeds   | Labrador Retriever Base | | < 0.001 | | | | |
| Pug      | 3.41 | 2.71-4.28 | < 0.001 | | | | |
| Basset Hound | 2.13 | 1.38-3.30 | 0.001 | | | | |
| Dogue de Bordeaux | 2.10 | 1.37-3.22 | 0.001 | | | | |
| Boxer    | 1.95 | 1.57-2.42 | < 0.001 | | | | |
| Beagle   | 1.91 | 1.40-2.59 | < 0.001 | | | | |
| French Bulldog | 1.87 | 1.17-2.98 | 0.009 | | | | |
| British Bulldog | 1.84 | 1.31-2.58 | < 0.001 | | | | |
| Border Terrier | 1.79 | 1.42-2.27 | < 0.001 | | | | |
| Pomeranian | 1.57 | 1.01-2.43 | 0.043 | | | | |
| Chihuahua | 1.50 | 1.20-1.89 | < 0.001 | | | | |
| Border Collie | 1.41 | 1.17-1.69 | < 0.001 | | | | |
| King Charles Spaniel | 1.39 | 0.89-2.17 | 0.15 | | | | |
| Patterdale Terrier | 1.26 | 0.84-1.88 | 0.27 | | | | |
| Cavalier King Charles Spaniel | 1.22 | 0.98-1.52 | 0.070 | | | | |
| Yorkshire Terrier | 1.14 | 0.95-1.37 | 0.16 | | | | |
| Labradoodle | 1.13 | 0.74-1.74 | 0.56 | | | | |
| Weimaraner | 1.13 | 0.70-1.82 | 0.62 | | | | |
| Akita | 1.11 | 0.68-1.81 | 0.68 | | | | |
| Toy Poodle | 1.06 | 0.66-1.72 | 0.80 | | | | |
| Husky | 1.05 | 0.71-1.55 | 0.81 | | | | |
| German Shepherd Dog | 1.02 | 0.82-1.26 | 0.88 | | | | |
| Designer | 1.00 | 0.70-1.44 | 0.99 | | | | |
| Miniature Schnauzer | 0.97 | 0.67-1.40 | 0.854 | | | | |
| Miniature Dachshund | 0.83 | 0.53-1.31 | 0.435 | | | | |
| Golden Retriever | 0.83 | 0.62-1.11 | 0.215 | | | | |
| Staffordshire Bull Terrier | 0.81 | 0.68-0.96 | 0.016 | | | | |
| Jack Russell Terrier | 0.79 | 0.66-0.94 | 0.007 | | | | |
| Crossbred | 0.75 | 0.66-0.86 | < 0.001 | | | | |
| Bichon | 0.69 | 0.49-0.97 | 0.034 | | | | |
| Lurcher | 0.68 | 0.44-1.05 | 0.083 | | | | |
| Springer Spaniel | 0.66 | 0.47-0.94 | 0.022 | | | | |
| Lhasa Apso | 0.65 | 0.46-0.91 | 0.011 | | | | |
| Rottweiler | 0.54 | 0.36-0.82 | 0.004 | | | | |
| Shih-tzu | 0.53 | 0.40-0.70 | < 0.001 | | | | |
| West Highland White Terrier | 0.52 | 0.40-0.67 | < 0.001 | | | | |
| English Springer Spaniel | 0.50 | 0.34-0.74 | < 0.001 | | | | |
| Cocker Spaniel | 0.44 | 0.34-0.58 | < 0.001 | | | | |
| Unrecorded | 0.72 | 0.38-1.37 | 0.31 | | | | |
| Other purebreds and designers breed types | 0.89 | 0.77-1.03 | 0.11 | | | | |
| Age (years) | | | | | | | |
| 0.00 - ≤ 0.50 | 0.30 | 0.20-0.45 | < 0.001 | | | | |
| 0.50 - ≤ 3.00 | Base | | < 0.001 | | | | |
| 3.00 - ≤ 6.00 | 2.13 | 1.90-2.39 | < 0.001 | | | | |
| 6.00 - ≤ 9.00 | 2.89 | 2.57-3.25 | < 0.001 | | | | |
| 9.00 - ≤ 12.00 | 3.63 | 3.21-4.11 | < 0.001 | | | | |
| ≥ 12.00 | 6.63 | 5.88-7.47 | < 0.001 | | | | |
| Unrecorded | 1.46 | 0.98-2.18 | 0.065 | | | | |
The high count of Labrador Retrievers in the study also enabled high statistical power to explore breed risks. However, interested readers who still wish to evaluate breed predisposition using crossbreds as the comparator category can still check for overlap of the 95% CI for each category; categories that do not overlap can be interpreted as showing statistically significant differences in their odds of diagnosis as seizure cases. The 11 breeds with significantly higher odds ratios compared to the Labrador Retriever were the Pug, Basset Hound, Dogue de Bordeaux, Boxer, Beagle, French Bulldog, British Bulldog, Border Terrier, Pomeranian, Chihuahua and Border Collie.

The majority of previous studies in this area have focused on epilepsy in dog breeds and often went even further by specifically targeting the epilepsy subset with a suspected inheritance of idiopathic epilepsy. Many of these earlier studies relied on relatively small groups of dogs or families that made it problematic to generalize the findings to the overall breed although recently some larger studies have reported breed-specific epilepsy prevalence estimates.

There are differing etiologies for epileptic seizures for Pugs (necrotizing encephalopathy) and the Basset Hounds (Lafora disease). Seizure activity in the Dogue de Bordeaux is associated with a genetic predisposition but based on a small sample size of 5 dogs.

Seizures and their etiology have also been investigated for 3 of the other predisposed breeds found in the current study: the Border Collie,  

TABLE 3  (Continued)

| Variable | Odds ratio | 95%CIa | p-value | Variable | P-value |
|----------|------------|--------|---------|----------|---------|
| Bodyweight relative to breed and sex mean | Lower | Base | < 0.001 | | < 0.001 |
| | Equal/Higher | 1.06 | 0.99-1.14 | 0.082 | |
| | Unrecorded | 0.76 | 0.69-0.84 | < 0.001 | |
| Sex-neuter | Female/Entire | Base | < 0.001 | | < 0.001 |
| | Female/Neutered | 1.14 | 1.01-1.28 | 0.039 | |
| | Female/Unrecorded | 1.43 | 1.24-1.65 | < 0.001 | |
| | Male/Entire | 1.47 | 1.30-1.66 | < 0.001 | |
| | Male/Neutered | 1.34 | 1.19-1.51 | < 0.001 | |
| | Male/Unrecorded | 1.73 | 1.51-1.99 | < 0.001 | |
| | Not recorded/Unrecorded | 1.00 | 0.49-2.05 | 0.99 | |

Multivariable logistic regression model for risk factors associated with seizures in dogs under primary care in the UK; aCI confidence interval.

TABLE 4  Multivariable logistic regression results for variables that replaced breed

| Variable | Category | Odds ratio | 95%CIa | p-value | Variable | P-value |
|----------|----------|------------|--------|---------|----------|---------|
| Purebred | Crossbred | Base | < 0.001 | | |
| | Purebred | 1.28 | 1.18-1.39 | < 0.001 | | |
| | Designer | 1.18 | 0.93-1.50 | 0.16 | | |
| | Unrecorded | 0.94 | 0.50-1.78 | 0.86 | | |
| Kennel Club Breed Groups | Breed not Kennel Club recognized | Base | < 0.001 | | |
| | Gundog | 1.05 | 0.95-1.16 | 0.34 | | |
| | Hound | 1.20 | 1.01-1.44 | 0.042 | | |
| | Pastoral | 1.42 | 1.25-1.60 | < 0.001 | | |
| | Terrier | 1.03 | 0.92-1.15 | 0.59 | | |
| | Toy | 1.68 | 1.52-1.86 | < 0.001 | | |
| | Utility | 1.09 | 0.96-1.24 | 0.16 | | |
| | Working | 1.49 | 1.28-1.72 | < 0.001 | | |
| Adult (>18months) bodyweight (kg) | < 10.00 | Base | < 0.001 | | |
| | 10.00 ≤ 20.00 | 0.92 | 0.84-1.01 | 0.092 | | |
| | 20.00 ≤ 30.00 | 0.92 | 0.83-1.02 | 0.110 | | |
| | 30.00 ≤ 40.00 | 1.11 | 1.00-1.24 | 0.061 | | |
| | ≥ 40.00 | 1.24 | 1.08-1.41 | 0.002 | | |
| | Unrecorded | 0.74 | 0.66-0.83 | < 0.001 | | |

Results for variables that replaced the breed variable in the final breed multivariable logistic regression model (with age category, bodyweight relative to breed mean sex and neuter status) to evaluate risk factors associated with seizures in dogs under primary veterinary care in the UK. Bodyweight relative to breed mean was also removed for adult bodyweight. aCI confidence interval.
Border Terrier, Labrador Retriever, and the Chihuahua. However, there are no reliable reports on seizure activity in the French Bulldog, British Bulldog and Pomeranian. The findings of the current study go further than many of these previous studies and additionally include dogs with seizures that are both reactive as well as epileptic in order to give a more holistic view of the seizure predispositions that includes both genetic and environmental proclivities.

A protective effect for seizures was identified in Shih-tzu, West Highland White Terrier, English Springer Spaniel and Cocker Spaniel. A previous primary-care veterinary study similarly showed reduced risk to epilepsy of unknown origin in English Springer Spaniels and West Highland White Terrier in the UK. Breed health studies to date have heavily focused on predisposition to disease. However, evidence to support protective disease effects, both between and within breeds, is increasing needed to support planned breed health reforms such as outcrossing to other breeds or to breed strains from other countries.

Increased risk for epileptic seizures in male dogs is recognized across all dogs types as well as within specific breeds. Our analysis of UK primary-care veterinary data that included both epileptic and reactive seizures also revealed a higher risk for male dogs. An interaction effect was noted between neutering and sex whereby the effect the neutering was not equal between the sexes. For this reason, the final multivariable model reported the values for each combination of sex and neuter status separately. Although neutering is a time dependent event whereby animals have an increased opportunity to become neutered as they age, the final multivariable model did take age into account and still showed an increased odds of seizures in neutered compared with entire bitches. This effect appears to be quite sex-specific however and no significant effect of neutering on seizure risk in males was noted. However, a word of caution in relation to the potential benefits of neutering in bitches: studies such as the current cross-sectional analysis can only show statistical associations with bodyweight might result from seizure disease management therefore constitute an important role in clinical practice, these factors should assist veterinarian practitioners to identify and alert owners to dogs at higher risk. Enhanced owner awareness could promote earlier, faster and more reliable diagnosis and treatment to support improved animal welfare. These results can also assist pharmacovigilance efforts by providing baseline data from the overall population to optimize interpretability of seizures when reported as suspected adverse reaction to medication use.

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CONFLICT OF INTEREST DECLARATION

Heidrun Potschka received consulting fees from Bayer Animal Health and MSD Animal Health, speaker fees from Desitin and Zogenix, and funding for collaborative projects from Bayer Animal Health and Roche.

Holger Volk served as paid consultant for Boehringer Ingelheim and CEVA animal health. Served as contract researcher for: Nestle 2012–2014 and 2017–ongoing, dietary modification of epilepsy in dogs; Desitin Pharma, 2012, the role of levetiracetam in a referral hospital; industrial Funding, 2014–2015, investigating the effects of imepitoin behavioural, physiologic and owner-reported indicators of anxiety in dogs treated for idiopathic epilepsy. Received competitive research grants for: RCVS pump primer grant, 2010–2013, pharma-metabonomic profiling of epileptic dogs; Waltham Foundation, 2011–2014, determination of plasma omega-3 fatty acid status in dogs with primary epilepsy and relationship to antiepileptic drug metabolism; CASE BBSRC PhD studentship, 2012–2016 metabolic profiling of epilepsy in dogs; American Kennel Club, American Health Foundation, 2016–2018, Investigating the Effect of a Ketogenic Medium Chain Triglycerides Supplement on the treatment of Canine Idiopathic Epilepsy and its behavioural comorbidities; BBSRC, 2017-2020, Investigating the relationship between epilepsy, drug-resistance and affective disorders in the domestic dog.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

ORCID

Alexander Erlen ORCID: http://orcid.org/0000-0002-2193-4684

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