This is the peer reviewed version of the following article:

Taylor-Brown, F. E., Meeson, R. L., Brodbelt, D. C., Church, D. B., McGreevy, P. D., Thomson, P. C. and O'Neill, D. G. (2015), Epidemiology of Cranial Cruciate Ligament Disease Diagnosis in Dogs Attending Primary-Care Veterinary Practices in England. Veterinary Surgery, 44: 777–783. doi: 10.1111/vsu.12349

which has been published in final form at http://dx.doi.org/10.1111/vsu.12349.

This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving."

The full details of the published version of the article are as follows:

TITLE: Epidemiology of cranial cruciate ligament disease diagnosis in dogs attending primary-care veterinary practices in England

AUTHORS: Taylor-Brown, F. E., Meeson, R. L., Brodbelt, D. C., Church, D. B., McGreevy, P. D., Thomson, P. C. and O'Neill, D. G.

JOURNAL TITLE: Veterinary Surgery

VOLUME/EDITION: 44

PUBLISHER: Wiley

PUBLICATION DATE: 29 June 2015 (online)

DOI: 10.1111/vsu.12349



1	Epidemiology of cranial cruciate ligament disease diagnosis in dogs attending primary-care
2	veterinary practices in England
3	
4	Frances E. Taylor-Brown ¹ BSc (Hons) BVetMed (Hons), London, UK
5	Richard L. Meeson ¹ MA VetMB MVetMed DipECVS, London, UK
6	Dave C. Brodbelt ¹ MA VetMB PhD DVA DipECVAA FHEA, London, UK
7	David B. Church ¹ BVSc PhD, London, UK
8	Paul D. McGreevy ² BVSc PhD, Sydney, Australia
9	Peter .C. Thomson ² BSc MSc (Hons) MAppStat PhD, Sydney, Australia
10	Dan G. O'Neill ¹ MVB BSc (Hons) MSc (VetEpi) PhD, London, UK
11	¹ The Royal Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Herts AL9 7TA
12	² Faculty of Veterinary Science, The University of Sydney, Sydney, NSW 2006
13	
14	Corresponding Author: Frances Taylor-Brown, Clinical Services and Sciences, The Royal
15	Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Hertfordshire, AL9 7TA
16	Email: <u>ftaylor@rvc.ac.uk</u>

18 Abstract

Objective: Estimate prevalence and risk factors for cranial cruciate ligament (CCL) disease
 diagnosis in dogs and describe management of cases attending primary-care veterinary practices.

21 Study design: Historical cohort with a nested case-control study.

Sample population: 953 dogs diagnosed with CCL disease from 171,522 dogs attending 97
 primary-care practices in England.

Methods: Medical records of dogs attending practices participating in the VetCompass project that met selection criteria were assessed. Univariable and multivariable logistic regression methods evaluated association of risk factors with CCL disease diagnosis.

27 Results: CCL disease prevalence was estimated at 0.56% (95% CI: 0.52 - 0.59). Compared with 28 crossbred dogs, rottweilers, west highland white terriers, golden retrievers, Yorkshire terriers, and 29 Staffordshire bull terriers showed increased odds of CCL disease diagnosis whilst cocker spaniels 30 showed reduced odds. Increasing bodyweight within breeds was associated with increased odds of 31 diagnosis. Dogs aged over 3 years had increased odds of diagnosis compared with dogs aged less 32 than 3 years. Neutered females had 2.1 times the odds of diagnosis compared with entire females. 33 Insured dogs had 4 times the odds of diagnosis compared with uninsured dogs. Two thirds of cases 34 were managed surgically; insured and heavier dogs more frequently had surgery. Overall, 21% of 35 cases were referred, with referral more frequent in heavier and insured dogs. Referred dogs more 36 frequently had surgery and an osteotomy procedure.

Conclusion: Breed predispositions and demographic factors associated with diagnosis and case
 management of CCL disease in dogs identified in this study can be used to help direct future
 research and management strategies.

40 Introduction

Disease of the cranial cruciate ligament (CCL) is one of the most common causes of pelvic limb 41 lameness in the dog.¹ CCL insufficiency renders the stifle joint unstable and predisposes to 42 43 degenerative joint disease. In rare circumstances there can be acute traumatic rupture of the CCL, 44 however the majority of CCL ruptures are characterised by a gradual degeneration of the extracellular matrix (ECM), leading to ligament rupture.² The underlying aetiopathegenesis of this 45 46 degenerative disease process remains unclear and is considered to be complex and multifactorial.³ 47 Previous studies have reported prevalence estimates for CCL disease in dogs from 1.2-2.6% and identified risk factors including breed, sex, neutering, age and bodyweight.⁴⁻⁸ A study of 1.25 48 49 million dogs in the USA from a predominantly referral population over a 40-year period identified 50 the 5 breeds most commonly affected as the Newfoundland, rottweiler, Labrador retriever, bulldog and boxer.⁴ Subsequent studies have confirmed increased prevalence in the Labrador retriever, 51 52 Newfoundland, boxer and rottweiler as well as reporting predispositions in other breeds including 53 the west highland white terrier, Yorkshire terrier, golden retriever, Staffordshire bull terrier, 54 Neapolitan mastiff, akita, saint bernard, mastiff, Chesapeake bay retriever and American Staffordshire terrier.⁵⁻⁸ 55

Female dogs have been reported to be more frequently diagnosed with CCL disease compared to male dogs, while neutered dogs are at a greater risk than entire dogs.^{4, 9-10} When considering age as a risk factor for CCL disease diagnosis, Witsberger⁴ and others reported that dogs older than 4 years of age were significantly more likely to be affected. Other studies have further shown that large breeds are diagnosed with CCL disease at a younger age than small breeds.^{7,8,11,12} Bodyweight has also been identified as a risk factor with heavier dogs, as well as those dogs considered to be overweight, being more likely to be diagnosed with CCL disease.^{7,8,13}

63 Many CCL disease studies have been based on referral populations or relatively small populations of dogs and may therefore be less representative of the overall caseload seen in primary-care 64 practice.¹⁴ Referral caseloads may also show selection bias towards more complicated disorders.¹⁷ 65 66 Systematic collection and analysis of the VetCompass merged database of primary-care practice 67 data offer an opportunity to characterise the CCL disease caseload recorded in primary-care practice in England.^{15,16} Compared with questionnaire-based studies, access to clinical data 68 69 recorded at the time of the health event and that covers all animals attending the participating 70 veterinary practices should reduce selection and recall biases for studies using electronic patient records.¹⁵ 71

This study aimed to estimate the prevalence of CCL disease diagnosed in dogs attending primarycare veterinary practices in England. The study objectives included evaluation of purebred status, breed, sex, bodyweight, age and insurance status, as risk factors for the diagnosis of CCL disease and to describe the management of affected dogs. It was hypothesised that increased bodyweight in dogs is associated with increased risk of diagnosis with CCL disease.

77 Materials and methods

78 Ethics statement: Ethics approval was granted by the RVC Ethics and Welfare Committee79 (reference number 2010 1076F).

80 The VetCompass animal surveillance project collates de-identified electronic patient record data from primary-care veterinary practices in the UK for epidemiological research.²⁰ The sampling 81 82 frame for the current study included electronic patient record data relating to all dogs provided 83 with health care during the study period at every clinic within the Medivet Veterinary Group, a large network of integrated veterinary practices covering central and south-eastern England.²¹ 84 85 These clinics care predominantly for companion animal species and were located within both 86 urban and rural locations. Clinical data shared with VetCompass are de-identified and participation within VetCompass operates under an opt-out approach for owner consent.²² Participating 87 88 practices used a single bespoke practice management system that allowed practitioners to record summary diagnosis terms from an embedded standard nomenclature, the VeNom codes,²³ at 89 90 episodes of clinical care. Electronic patient record data were extracted from the practice management system using integrated clinical queries²⁴ and uploaded to a secure structured query 91 92 language database. Information collected included patient demographic (animal identification number, species, breed, date of birth, sex, neuter status, insurance status, microchip number and 93 94 bodyweight) and clinical information (free-form text clinical notes, VeNom summary diagnosis 95 terms and treatment, with relevant dates).

The study used a historical cohort design for prevalence estimation with a nested case-control design for risk factor analysis. The study sampling frame included all dogs with at least one electronic patient record (clinical note, bodyweight recording or treatment dispensed) recorded within the VetCompass Animal Surveillance database from September 1st, 2009 to July 7th, 2013. Sample size calculations²⁵ estimated an unmatched case-control study with 974 cases and 1,948 controls would have an 80% power to detect a risk factor with an odds ratio of 1.4 or greater (twosided $\alpha = .05$) and a 10% prevalence in the control animals.

103 Potential CCL disease cases were identified by searching the clinical free text and VeNom Code 104 fields using multiple search terms: cruciat, ccl, cranial draw, acl, tta, tplo, lateral sut, 105 extracapsular sut and de ang. Dogs identified from each search term were aggregated and 106 duplicates removed. The full clinical notes recorded during the study period for each identified 107 dog were reviewed in detail. The case definition for a case diagnosed with CCL disease required 108 that the dog presented with a pelvic limb lameness plus one of a) ipsilateral cranial drawer or tibial 109 thrust; b) CCL disease confirmed at surgery; or c) MRI/CT/ultrasound findings compatible with 110 CCL disease, leading to a final diagnosis by the attending veterinarian of the existence of CCL 111 disease.

For dogs that met the case definition, further data extraction described the case as incident or preexisting, date of diagnosis (for incident cases), type and date of any surgery performed (osteotomy, extra-capsular, intra-capsular) and whether the case was referred for secondary-care treatment. Control dogs for the case-control analysis were randomly selected from the overall study population using a web-based random number generator²⁶ with exclusion of dogs with a clinical history suggestive of possible CCL disease.

Recognisable single breeds²⁷ were grouped as 'purebred' and all other dogs were grouped as 'crossbred'. Individual breeds with 50 or more dogs in the nested case-control study were listed as 'frequent breeds' and included separately in the analyses. Neuter status was defined by the final electronic patient record neuter value and combined with sex to create 4 categories: female entire, female neutered, male entire and male neutered. Insurance and microchip status characterised the existence of a positive status at any time during the study period. The maximum bodyweight (kg) recorded for dogs aged over 1 year was extracted and categorised across all dogs (< 10.0, 10.0-19.9, 20.0-29.9, 30.0-39.9, \geq 40.0, 'no recorded bodyweight') and also as tertiles within the frequent breeds (high, mid, low, 'no recorded bodyweight') to allow the effect of variation of body weight *within* these breeds to be assessed. Age (years) at a randomly selected episode of care during the study period was calculated for the case and control animals and was categorised into 5 groups (< 3.0, 3.0-5.99, 6.0-8.99, 9.0-11.99, \geq 12.0).

130 Study data were exported from the VetCompass database to a spreadsheet (Microsoft Office Excel 131 2007, Microsoft Corp.) for checking and cleaning before further export to Stata Version 11.2 (Stata 132 Corporation) for statistical analyses. The prevalence of CCL disease was estimated, with 95% confidence interval (CI) based on approximation to the normal distribution.²⁸ Demographic results 133 134 were reported for the case and control dogs. Exploratory evaluation of statistical associations 135 between a range of categorical variables (purebred, breed, sex/neuter, insurance, age group, 136 bodyweight tertile, surgery performed, surgery type) used the chi-squared (or Fisher's exact test if the expected counts were fewer than 10 in any cell).²⁸ Risk factor analysis firstly screened all 137 138 demographic risk factors using univariable logistic regression; factors with a liberal P < .20 were 139 further evaluated using multivariable logistic regression. Model-building used manual backwards 140 elimination, beginning with the maximum model and iteratively testing and eliminating variables 141 using a cut-off of P<.05. All eliminated factors were re-evaluated for confounding effects within 142 the provisional-final model using the change-in-estimate approach: a change in the odds ratio for 143 a primary exposure variable of more than 10% was considered to represent important confounding.^{29,30} Biologically important pairwise interactions between final model variables were 144 assessed using the likelihood ratio test with a cut-off of P < .05.²⁹ Clustering in the final model was 145

evaluated using the clinic attended as a random effect to compare the results from mixed-effects logistic regression modelling with standard logistic regression modelling.²⁹ Model-fit was evaluated using the Hosmer Lemeshow goodness-of-fit test statistic and the area under the ROC curve.^{29,31} Statistical significance was set at P=.05. The results from the logistic regression modelling are reported as odds ratio which express the relative strength of association between the risk factor and the outcome of diagnosis with CCL disease.³²

152 **Results**

153 The study population comprised 171,522 dogs attending 97 clinics across central and south-eastern

154 England. From these, 953 cases diagnosed with CCL disease were identified, yielding an apparent

- 155 prevalence of 0.56% (95% CI: 0.52 0.59). This period prevalence value was based on an open
- 156 cohort of dogs with a median study time per dog of 2.1 years (IQR: 1.0 2.7, range; 0.0 3.8).
- 157 Risk factor analysis included 953 cases and 1,875 control dogs attending 91 clinics. Overall data
- 158 completeness varied between the variables: breed 100%, sex 100%, neutered status 100%,
- insured status 100%, bodyweight 73% and age 94%. Of the dogs diagnosed with CCL disease
- 160 with information available, 765/953 (80%) were purebred, 492/953 (52%) were female, 686/953
- 161 (72%) were neutered, 502/953 (53%) were insured and 354/953 (37%) were microchipped.
- 162 Median bodyweight was 25 kg (IQR: 12.0 36.4, range: 2.6 77.0) and the median age was 7.4
- years (IQR: 4.7-10.0, range: 0.26 16.3). The most frequent 11 breeds accounted for 503 (53%)
 of the case dogs.
- 165 Of the control dogs with information available, 1,470/1875 (78%) were purebred, 887/1875 (48%) 166 were female, 657/1875 (35%) were neutered, 298/1875 (16%) were insured and 502/1875 (27%) 167 were microchipped. Median bodyweight was 17 kg (IQR: 8.8 - 28.5, range: 1.6 - 73.9) and the 168 median age was 4 years (IQR: 1.2 - 8.0, range: 0.0 - 20.0). The most frequent 11 breeds accounted 169 for 830/1875 (44%) of the control dogs.

The 953 case dogs comprised 621 (65%) incident cases that were diagnosed for the first time during the study period and 332 (35%) cases that had been diagnosed with CCL disease prior to the study period. The median age at first diagnosis of incident cases was 7 years (IQR: 4.2 - 9.6, range: 0.3 - 15.5) (Fig 1). Of the incident cases with information available, 423 (68%) were surgically managed, of which 209 (49.4%) underwent extra-capsular techniques and 214 (51%) 175 underwent osteotomy procedures. Of the incident cases, 129 (21%) were referred for specialist 176 management, with insured (Fisher's exact test P=.003) and higher bodyweight (chi-squared 177 P < .001) dogs more frequently referred. Referred dogs more frequently had surgery (Fisher's exact 178 test P < .001) and an osteotomy procedure (chi-squared P < .001) than dogs managed in primary-179 care practice (Table 1). The probability of surgery was higher in insured (80%) than uninsured 180 (55%) dogs (chi-squared P<.001) and increased with bodyweight (surgery - < 10.0 kg: 56%, 10.0-181 19.9: 63%, 20.0-29.9: 70%, 30.0-39.9: 75% and \geq 40.0: 86%) (chi-squared P<.001). Compared 182 with extra-capsular repair, osteotomy surgery was more frequent in insured (56%) than uninsured 183 (41%) dogs (chi-squared P<.001) and increased as bodyweight increased (osteotomy - < 10.0 kg: 184 14%, 10.0-19.9: 34%, 20.0-29.9: 47%, 30.0-39.9: 65% and \geq 40.0: 83%) (chi-squared P<.001). 185 Younger dogs more frequently had surgery (surgery < 3.0 years: 78%, 3.0-5.99 years: 73%, 6.0-186 8.99 years: 70%, 9.0-11.99 years: 69%, \geq 12.0 years: 20%) (chi-squared P<.001). Within age-187 bands of operated dogs, osteotomy was less frequent than extra-capsular repair as dogs aged: 188 (extra-capsular versus osteotomy < 3.0 years: 26% vs 74%, 3.0-5.99 years: 42% vs 58%, 6.0-8.99 189 years: 51% vs 49%, 9.0-11.99 years: 72% vs 28%, \geq 12.0 years: 80% vs 20%) (chi-squared 190 *P*<.001).

Univariable logistic regression modelling identified 8 statistically significant variables (P<.20):</p>
purebred status, frequent breeds, bodyweight overall, bodyweight categories within frequent
breeds, age, sex/neuter status, insurance status and microchip. Following evaluation using
multivariable regression, the final model comprised 5 statistical significant risk factors: frequent
breeds, bodyweight categories within frequent breeds, age, sex/neuter status and insurance status.
Bodyweight overall was removed from the final model because bodyweight and breed are
intrinsically related. No biologically-significant interactions were identified. The final non-

198 clustered model showed acceptable model-fit (Hosmer-Lemeshow test result: P=.391) and 199 discrimination (area under the ROC curve: .8235). The final model was improved by inclusion of 200 the clinic attended as a random effect (P=.004, rho =0.03 indicating that 3% of variation was 201 accounted for by the clinic attended). After accounting for the effects of the other variables 202 (bodyweight categories within frequent breeds, age, sex/neuter status and insurance status) 203 evaluated, 5 of the frequent breeds showed increased odds of a diagnosis of CCL disease compared 204 with crossbreds: rottweiler (OR: 5.4, CI:2.6-11), west highland white terrier (OR: 2.5, CI: 1.5-4.2), 205 golden retriever (OR: 1.9, CI:1.1-3.3), Yorkshire terrier (OR: 1.8, CI:1.0-3.0) and Staffordshire 206 bull terrier (OR: 1.6, CI:1.0-2.5); and one of the frequent breeds showed decreased odds of 207 diagnosis: cocker spaniel (OR: 0.4, CI:0.2-0.8). Increasing bodyweight within breeds was 208 associated with increased odds of diagnosis with CCL disease; dogs categorised as high 209 bodyweight within their breed had a 3.4 (P<.01) times odds of diagnosis compared to dogs 210 categorised as low bodyweight. Dogs aged 9.0-11.9 years showed 4.4 (P<.001) times the odds of 211 CCL diagnosis compared with dogs aged under 3 years. Neutered females had 2.1 (P<.001) times 212 the odds of diagnosis compared with entire females. Insured dogs had 4.0 (P<.001) times the odds 213 of diagnosis compared with uninsured dogs (Table 2).

215 Discussion

This study of dogs attending primary-care practices in England identified several breeds with increased odds of diagnosis with CCL disease compared with the remaining population of healthy and unwell dogs attending veterinary practices for any reason that did not have a diagnosis of CCL disease. The cocker spaniel had a significantly decreased odds of diagnosis. Neutered female dogs and dogs aged over 3 years had increased odds of diagnosis compared with dogs aged less than 3 years. Insured dogs were more likely to be diagnosed with CCL disease, and within breeds, heavier individuals were more likely to be diagnosed with CCL disease than lighter dogs.

The prevalence of CCL disease diagnosis reported in this study is lower than the previously reported range of 1.2%-2.6%.^{4,6} This difference may be the result of previous studies estimating prevalence of CCL disease based on referral caseloads whilst the current study looked at CCL disease diagnosed in primary-care practice.

227 When considering specific breeds diagnosed with CCL disease, this study detected significantly 228 increased odds of diagnosis with CCL disease in the rottweiler, west highland white terrier, golden 229 retriever, Yorkshire terrier and Staffordshire bull terrier compared with crossbred dogs presenting to primary-care practices, and these findings are consistent with findings of other studies.⁵⁻⁸ 230 231 Identification of the cocker spaniel as a breed with reduced odds of diagnosis is a previously 232 unreported finding and highlights a potential resource for further investigation. These findings may 233 justify a morphometric analysis of breeds at increased and reduced risk, as has been reported for hip dysplasia.³³ 234

In support of the study hypothesis that increased bodyweight in dogs is associated with increased risk of diagnosis with CCL disease, the results showed a strong association between higher bodyweight within breeds and increased odds of CCL disease diagnosis. Because body size in an 238 intrinsic descriptor for each breed, the study avoided conflating breed and body size effects by 239 specifically comparing between bodyweight tertiles within breeds for associations with a diagnosis 240 of CCL. Multivariable analysis demonstrated that bodyweight within breeds was significantly 241 associated with CCL disease diagnosis. Within the frequent breeds in this study, dogs in the 242 heaviest third of bodyweights had 3.4 times the odds of being diagnosed with CCL disease 243 compared with those in the lightest third of bodyweights. Although the underlying reason for this 244 is unclear, it is suggested that with increasing bodyweight, the load placed through the limbs and 245 subsequent strain placed on the ligaments increases, which accelerates the process of degeneration of the CCL.^{2,34} Without morphometric data, it is difficult to know whether those dogs in the 246 247 heaviest bodyweight category had an increased stature compared to those in the lowest category 248 or whether the dogs were overweight, however these data suggest that bodyweight plays a 249 significant role in the development of CCL disease. Further investigation is required to understand 250 the relative significance of bodyweight and obesity in the development of CCL disease.

The median age at first diagnosis of CCL disease was 7 years of age which parallels previous reports.^{6,8} The finding that dogs aged 9.0-11.9 years had 4.4 times the odds of having a diagnosis compared with dogs aged under 3 years may result from increased ligament degeneration in older dogs compared to younger counterparts.³⁵

255 Consistent with current published literature, female dogs and neutered dogs were at increased risk 256 of being diagnosed with CCL disease.^{4,7,8} Neutered female dogs had 2.1 times the odds of diagnosis 257 compared with entire females. The underlying reason for this finding remains unclear but may be 258 associated with increased obesity among neutered females^{7,8} but a recent study of CCL disease in 259 a UK population of dogs found no significant difference in body condition scores of neutered dogs 260 compared with their entire counterparts in either the case or control groups.⁶ It has also been suggested that hypoestrogenaemia associated with ovariohysterectomy may account for the increased incidence of CCL disease and oestrogen may confer a protective effect which is in contrast to findings in women.²

264 Insured dogs had 4 times the odds of diagnosis of CCL disease compared with uninsured dogs. 265 This finding may reflect that owners of insured dogs are more willing to seek prompt evaluation 266 and may reflect more thorough clinical investigation in insured dogs because financial constraints are less limiting and the owner's expectations are higher.¹⁹ There may also be some degree of bias 267 268 on the part of the veterinary surgeon - knowing the owners will want to pursue further 269 investigation. Insured dogs were also more likely to undergo potentially more expensive options 270 including surgery, referral for secondary-care management and osteotomy surgery rather than 271 extra-capsular procedures. Full diagnosis of CCL disease in uninsured dogs may have been more 272 difficult because primary-care practitioners were unable to establish the presence of cranial drawer 273 or tibial thrust in the conscious dog and financial constraints prevented further investigation of the 274 lameness.

275 Over two thirds of the dogs (68%) were managed surgically, with dogs referred for secondary-care 276 treatment more frequently having a surgical intervention. Heavier dogs more frequently underwent 277 surgery, which may be promoted by literature suggesting that dogs weighing greater than 15 kg 278 show persistent lameness when not surgically managed.^{36,37,39} Previous reports have also suggested that dogs weighing under 15 kg can do well with conservative management.^{36,37} 279 280 However these studies relied upon visual assessment of outcomes alone, and there is evidence that 281 lameness detection in smaller dogs is more difficult due to more rapid stride frequency and shorter 282 stride length leading to false assumption of greater improvement in small dogs than in larger

dogs.³⁸ It appears that the notion that smaller dogs have less need of surgery for cruciate ligament
disease persists today.

The current study identified a 50:50 split between extra-capsular and osteotomy techniques. A recent systematic review suggested that some osteotomy procedures offered a better outcome than extra-capsular methods, and it is perceived by many that osteotomy typically offers a more rapid early recovery than extra-capsular methods.⁴⁰⁻⁴⁴ However, current best evidence, including force plate analysis, mostly indicate no significant long term difference in long-term limb function, or osteoarthritis progression between a well performed extra-capsular suture and an osteotomy procedure.⁴⁰⁻⁴⁴

292 Whilst the current study addressed many of selection and recall biases of previous

293 epidemiological studies investigating canine CCL disease, it did still has limitations. The dogs 294 studied attended a single large veterinary partnership group that may have a more consistent 295 standard of care compared with the overall primary-care practices in England. Only dogs that 296 attended veterinary practices were included in the study and thus the results may not necessarily 297 generalise to the population of dogs that are not registered for veterinary care. It is worth noting, 298 however, that the VetCompass programme shares clinical data on all dogs that attend primarycare veterinary practices and these include 24% of dogs with no disorders diagnosed.⁴⁵ The study 299 300 relied on the attending veterinarians for diagnoses of CCL disease and it is possible that some 301 truly affected dogs were missed or that some recorded CCL cases were misdiagnosed. 302 In conclusion, certain breeds appear at increased risk of CCL diagnosis, whilst the cocker spaniel 303 had a reduced risk. Female neutered status, increased age and increasing bodyweight within breeds 304 was identified as a risk factor for CCL disease diagnosis. Dogs that were insured were also more likely to be diagnosed with CCL disease. Most dogs were managed surgically as per current 305

literature recommendations, and there was an even split extra-capsular and osteotomy techniques.
Breed predispositions and demographic factors associated with diagnosis and case management of
CCL disease in dogs identified in this study can be used to help direct future research and
management strategies.

Disclosure Statement

311 The authors declare no conflict of interest.

313 **References**

- 314 1 Johnson JA, Austin C, Breuer GJ: Incidence of canine appendicular musculoskeletal disorders
- in 16 veterinary teaching hospitals from 1980 through 1989. Vet Comp Orthop Traumatol
 1994;7:59-69
- 317 2 Comerford EJ, Smith K, Hayashi K: Update on the aetiopathogenesis of canine cranial cruciate
- 318 ligament disease. Vet Comp Orthop Traumatol 2011;24:91-98
- 319 3 Hayashi K, Manley PA, Muir P: Cranial cruciate ligament pathophysiology in dogs with cruciate
- 320 disease: a review. J Am Anim Hosp Assoc 2004;40:385-390
- 321 4 Witsberger TH, Villamil JA, Schultz LG, et al: Prevalence of and risk factors for hip dysplasia
- and cranial cruciate ligament deficiency in dogs. J Am Vet Med Assoc 2008;232:1818-1824
- 323 5 Guthrie JW, Keely BJ, Maddock E, et al: Effect of signalment on the presentation of canine
- 324 patients suffering from cranial cruciate ligament disease. J Small Anim Pract 2012;52:273-277
- 325 6 Adams P, Bolus R, Middleton S, et al: Influence of signalment on developing cranial cruciate
- rupture in dogs in the UK. J Small Anim Pract 2011;52:347-352
- 327 7 Duval JM, Budsberg SC, Flo GL, et al: Breed, sex, and body weight as risk factors for rupture
- 328 of the cranial cruciate ligament in young dogs. J Am Vet Med Assoc 1999;215:811-814
- 329 8 Whitehair JG, Vasseur P, Willits NH Epidemiology of cranial cruciate ligament rupture in dogs.
- 330 J Am Vet Med Assoc 1993;203:1016-1019
- 331 9 Buote N, Fusco J, Radash R: Age, tibial plateau angle, sex, and weight as risk factors for
- 332 contralateral rupture of the cranial cruciate ligament in Labradors. *Vet Surg* 2009;38: 481-489
- 333 10 Slauterbeck JR, Pankratz K, Xu KT, et al: (2004) Canine ovariohysterectomy and orchiectomy
- increases the prevalence of ACL injury. *Clin Orthop Relat Res* 2004;429:301–305.

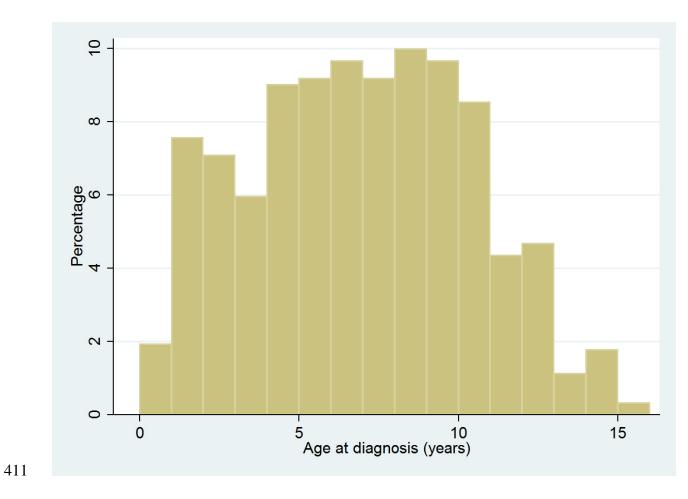
- 11 Bennett D, Tennant B, Lewis DG, et al: A reappraisal of anterior cruciate ligament disease in
 the dog. *J Small Anim Pract* 1988;29:275–297
- 12 Harasen G: Canine cranial cruciate ligament rupture in profile: 2002–2007. *Can Vet J*2008;49:193–194.
- 339 13 Barnes AJ: Rupture of the anterior cruciate ligament of the dog: a survey from practices in the
- 340 Kent region BSAVA. J Small Anim Pract 1977;18:55-59
- 341 14 Bartlett PC, Van Buren JW, Neterer M, et al: Disease surveillance and referral bias in the
- 342 veterinary medical database. *Prev Vet Med* 2010;94:264-271
- 343 15 Bateson P: Independent inquiry into dog breeding. University of Cambridge, Cambridge 2010
- 344 16 McGreevy PD: Breeding for quality of life. Anim Welfare 2010;16:125-128
- 345 17 Fleming JM, Creevy KE, Promislow DE: Mortality in North American dogs from 1984 to 2004:
- an investigation into age-, size-, and breed-related causes of death. J Vet Int Med 2011;25:187-198
- 347 18 Adams VJ, Evans KM, Sampson J, et al: Methods and mortality results of a health survey of
- 348 purebred dogs in the UK. J Small Anim Pract 2010;51:512-524
- 349 19 Egenvall A, Nødtvedt A, Penell J, et al: Insurance data for research in companion animals:
- benefits and limitations. Acta Vet Scand 2009;51:42
- 351 20 VetCompass, VetCompass: Health surveillance for UK companion animals. RVC Electronic
- 352 Media Unit, London 2013
- 353 21Medivet. Medivet: the veterinary partnership. 2014; <u>http://www.medivet.co.uk/</u>. Accessed
 354 January 14, 2014.
- 22 Watson N. Patients should have to opt out of national electronic care records: FOR. Br Med J
 (Clin Res Ed) 2006;333:39-40.

- 23 The VeNom Coding Group VeNom Veterinary Nomenclature. Ed T. V. C. Group. VeNom
 Coding Group 2013
- 359 24 Kearsley-Fleet L, O'Neill DG, Volk HA, et al: Prevalence and risk factors for canine epilepsy
- 360 of unknown origin in the UK. Vet Rec 2013;172:338
- 361 25 Epi Info 7 CDC Centers for Disease Control and Prevention (US): Introducing Epi Info 7. CDC,
- 362 Atlanta, Georgia 2012
- 363 26 Haahr M: RANDOM.ORG: True random number service. In: <u>http://www.random.org/</u>. TSDA
 364 2012
- 27 Irion DN, Schaffer AL, Famula TR, et al: Analysis of genetic variation in 28 dog breed
 populations with 100 microsatellite markers. *J Hered* 2003;94:81-87
- 367 28 Kirkwood BR, Sterne JA: Essential Medical Statistics, 2nd edn. Blackwell Science, Oxford
 368 2003
- 29 Dohoo I, Martin W, Stryhn H. Veterinary Epidemiologic Research, 2nd edn. VER Inc.,
 370 Charlottetown, Canada 2009
- 371 30 Rothman KJ, Greenland S. Measures of disease frequency. In: Rothman KJ, Greenland S, eds.
- 372 Modern Epidemiology. 2nd ed: Lippincott-Raven Publishers; 1998:29-46.
- 373 31 Hosmer DW, Lemeshow S: Applied Logistic Regression. 2nd edn. New York: Wiley 2000
- 374 32 Glas AS, Lijmer JG, Prins MH, Bonsel GJ, Bossuyt PMM. The diagnostic odds ratio: a single
- indicator of test performance. J. Clin Epidemiol 2003;56(11):1129-35.
- 376 33 Roberts T, McGreevy PD: 2010. Selection for breed-specific long-bodied phenotypes is
- associated with increased expression of canine hip dysplasia. Vet J 2010;183: 266–272
- 378 34 Griffon DJ: A Review of the Pathogenesis of Canine Cranial Cruciate Ligament Disease as a
- 379 Basis for Future Preventive Strategies. *Vet Surg* 2010;39:399–409

- 380 35 Vasseur PB, Pool RR, Arnoczky SP. et al: Correlative biomechanical and histologic study of
 381 the cranial cruciate ligament in dogs. *Am J Vet Res* 1985;46:1842–1854
- 382 36 Vasseur PB: Clinical Results Following Nonoperative Management for Rupture of the Cranial
- 383 Cruciate Ligament in Dogs. Vet Surg 1984;13:243-246
- 384 37 Strande A: Repair of the ruptured cruciate ligament in the dog. Williams & Wilkins, Baltimore
 385 1967
- 386 38 Off W, Matis U: Excision arthroplasty of the hip joint in dogs and cats. Clinical, radiographic,
- 387 and gait analysis findings from the Department of Surgery, Veterinary Faculty of the Ludwig-
- 388 Maximilians-University of Munich, Germany. 1997. Vet Comp Orthop Traumatol 2010;23:297–
- 389 305
- 390 39 Hohn RB, Miller JM: Surgical correction of rupture of the anterior cruciate ligament in the dog.
- 391 JAm Vet Med Assoc 1967;150:1133
- 40 Conzemius MG. Evans RB, Besancon MF, et al: Effect of surgical technique on limb function
 after surgery for rupture of the cranial cruciate ligament in dogs. *J Am Vet Med Assoc*2005;226:232–236
- 395 41 Nelson SA, Krotscheck U, Rawlinson J, et al: Long-term functional outcome of tibial plateau
- leveling osteotomy versus extracapsular repair in a heterogeneous population of dogs. *Vet Surg*2013;42:38-50
- 42 Aragon CL, Budsberg SC: Applications of evidence-based medicine: cranial cruciate ligament
 injury repair in the dog. *Vet Surg* 2005;34:93–98
- 400 43 Au KK, Gordon-Evans WJ, Dunning D, et al: Comparison of short- and long-term function and
- 401 radiographic osteoarthrosis in dogs after postoperative physical rehabilitation and tibial plateau
- 402 leveling osteotomy or lateral fabellar suture stabilisation. *Vet Surg* 2010;39:173–180

- 403 44 Bergh MS, Sullivan C, Ferrell CL, Troy J, et al: Systematic review of surgical treatments for
- 404 cranial cruciate ligament disease in dogs. *J Am Anim Hosp Assoc*. 2014;50(5):315-21.
- 405 45 O'Neill DG, Church DB, McGreevy PD, Thomson PC, Brodbelt DC. Prevalence of disorders
- 406 recorded in dogs attending primary-care veterinary practices in England. PLoS ONE. 2014;9(3):1-
- 407 16.

- **Figure 1:** Age at diagnosis of cruciate disease in dogs (621 cases) attending primary-care
- 409 veterinary practices in England



412 **Tables**

413 Table 1: Comparison between non-referred and referred dogs that had an incident diagnosis of

414 cranial cruciate disease in a study of dogs attending primary-care veterinary practices in England.

Variable		Not referred No. (%)	Referred No. (%)	<i>P</i> -Value
Insurance	Non-insured	244 (84)	45 (16)	.003
	Insured	248 (75)	84 (25)	
Purebred status	Crossbred	112 (84)	22 (16)	.161
	Purebred	380 (78)	107 (22)	
Frequent breeds	Crossbreed	107 (85)	19 (15)	.254
	Rottweiler	17 (65)	9 (35)	
	West highland white terrier	44 (86)	8 (15)	
	Golden retriever	19 (76)	6 (24)	
	Yorkshire terrier	29 (88)	4 (12)	
	English springer spaniel	20 (83)	4 (17)	
	Staffordshire bull terrier	33 (83)	7 (18)	
	Jack Russell terrier	28 (85)	5 (15)	
	Labrador retriever	37 (69)	17 (32)	
	Other pure breeds	133 (76)	43 (24)	
	Border collie	6 (86)	1 (14)	
	German shepherd dog	9 (75)	3 (25)	
	Cocker spaniel	10 (77)	3 (23)	
Sex/neuter	Female entire	68 (86)	11 (14)	.181
	Female neutered	187 (75)	61 (25)	
	Male entire	66 (80)	17 (21)	
	Male neutered	171 (81)	40 (19)	
Bodyweight (kg)	< 10.0	100 (89)	13 (12)	<.001
	10.0-19.9	135 (84)	26 (16)	
	20.0-20.9	87 (82)	19 (18)	
	30.0-30.9	86 (72)	33 (28)	
	\geq 40.0	68 (65)	36 (35)	
	No recorded bodyweight	16 (89)	2 (11)	
Surgery	Surgery	294 (70)	129 (31)	< .001
	Not surgery	198 (100)	0 (0.0)	
Type of surgery	Extracapsular	177 (85)	32 (15)	< .001
	Osteotomy	117 (55)	97 (45)	

Variable	Category	Odds ratio	95% CI	P-Value
Frequent breeds	Crossbreed	Base		
	Rottweiler	5.4	2.6-11.0	< .001
	West highland white terrier	2.5	1.5-4.2	< .001
	Golden retriever	1.9	1.1-3.3	.017
	Yorkshire terrier	1.8	1.0-3.0	.039
	English springer spaniel	1.8	1.0-3.4	.051
	Staffordshire bull terrier	1.6	1.0-2.5	.042
	Jack Russell terrier	1.0	0.6-1.5	.909
	Labrador retriever	0.9	0.6-1.3	.478
	Other pure breeds	0.9	0.7-1.2	.377
	Border collie	0.5	0.3-1.1	.110
	German shepherd dog	0.6	0.3-1.2	.135
	Cocker spaniel	0.4	0.2-0.8	.012
Bodyweight categories within frequent breeds	Low	Base		
	Mid	1.7	1.3-2.2	< .001
	High	3.4	2.6-4.5	< .001
	No recorded bodyweight	0.4	0.3-0.6	< .001
Age (years)	< 3.0	Base		
	3.0 - 5.9	2.4	1.8-3.2	< .001
	6.0 - 8.9	3.7	2.7-5.0	< .001
	9.0 - 11.9	4.4	3.2-6.1	< .001
	≥ 12.0	3.3	2.3-4.7	< .001
Sex/neuter	Female entire	Base		
	Female neutered	2.1	1.6-2.9	<.001
	Male entire	0.9	0.6-1.2	.360
	Male neutered	1.3	1.0-1.8	.100
Insurance	Non-insured	Base		
	Insured	4.0	3.2-4.9	< .001

417 cruciate ligament disease in dogs attending primary-care veterinary practices in England.

Table 2: Final multivariable logistic regression model for risk factors associated with cranial